# ETHNOPHARMACOLOGIC SEARCH for PSYCHOACTIVE DRUGS • 1967

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# Ethnopharmacologic Search for PSYCHOACTIVE DRUGS

Within the symbolic chemical representation on the cover are shown a view of a mushroom stone from the Namuth collection and a morning glory blossom. The mushroom stone—early pre-classic, circa B.C. 1000–500—contains a figure believed to be that of a young woman before a *metate* or grinding stone.

Workshop Series of Pharmacology Section, N.I.M.H. No. 2

# Ethnopharmacologic Search for PSYCHOACTIVE DRUGS

**Proceedings of a Symposium held in San Francisco, California**
**January 28–30, 1967**


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**Sponsored by:**

**Pharmacology Section, Psychopharmacology Research Branch**
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**U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE**

The opinions expressed and any conclusions drawn are those of the participants of the Symposium and are not to be understood as necessarily having the endorsement of, or representing the viewpoints of, the Public Health Service of the U.S. Department of Health, Education, and Welfare.

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# PREFACE

The use of plants or their extracts for medicinal or religious ceremonial purposes is very old—practically as old as the human race. The information about the use of plants as psychotropic agents by man is probably found in the Bible. The apple that Adam ate (whatever the variety) could be considered as a psycho-energizer. Was it a stimulator, did it enhance memory or learning abilities, or did it activiate the desire for acquiring more information? As with our new psychotropic drugs, I don't know if it brought happiness and comfort, or new problems, aggravations, and unhappiness. Another example of early use and knowledge of medicinal plants we find in the fact that the most ancient medical god of Mesopotamia—Sin—was also the god of medicinal herbs.

The development of drug chemistry brought: first, isolation from plants of a number of pharmacologically active substances (e.g. curare, atropine ouabain, etc.), later, synthesis of these entities and their derivatives; and finally, creation of completely new molecules, formerly not known, in the plant or animal kingdom.

We know, also, that in the process of development and worship of chemistry we somehow forgot about our prime source, the plants. We forgot that we have used only some of the known substances of plant origin. At the same time, the intrusions of civilization have been progressively destroying the sources of our knowledge, as well as the source itself of many plants—plants which are used either in medicine or in ceremonial and sacred context. Today, time is running out if we want to save this information, and perhaps use for medicinal purposes some of the unknown compounds contained in plants.

The idea of acquiring knowledge about these plants and compounds we have neglected or forgotten was the reason for organizing this symposium. It was self-evident that this meeting had to be multidisciplinary. We invited pharmacologists, pharmacists, chemists, biochemists, psychiatrists, anthropologists, etc., etc. We wanted to exchange existing information, confront different points of view, and outline and stimulate research objectives for the future.

As one of the organizers of this symposium, I am certainly biased, but I feel that this meeting was very successful. I would like to include here the opinion of one of the participants.

"This," he remarked, "is the first meeting I have attended that at the end of the sessions we had as many or even more participants than in the beginning—this is a measure of the interest the meeting has created."

We discovered after the meetings how many scattered researchers in wide and varied fields could contribute to the knowledge which we seek. This finding alone was one of the very important immediate gains from the symposium. And we hope that in the future we will be able to organize a second

meeting on the same topics, and cover a much broader spectrum of problems in the ethnopharmacologic search for psychoactive drugs.

The meeting was divided into six sessions, all but the first ending in panel discussions. All authors who delivered papers at the session served also as panelists. They discussed different problems among themselves and answered questions from the floor. The discussion after Session IV covered a special topic: "Psychoactive Action of Various Tryptamine Derivatives," and experts in this field were invited. The discussions after Sessions V and VI were merged, and covered, besides specific topics of these sessions, all problems dealt with in the symposium. Speakers from other sessions also participated in this dicussion.

The discussions held after the sessions were recorded *in extenso*, and are printed here following the papers of each session. Because of the multidisciplinary character of the symposium, problems of terminology and the extent of discussion, no restrictions were imposed on participants with regard to nomenclature used, order of material or uniformity of presentation and reference listing. The diversity of form and style of the various presentations was not altered for publication; they remain in their original form.

We extend our deep appreciation and thanks to the local group from the Continuing Education in Medicine and Health Sciences, University of California, San Francisco Medical Center, for their excellent work in organizing this meeting in San Francisco. This group, under the chairmanship of Dean Seymour M. Farber, with the participation of Dr. Roger H. Wilson, and Mesdames Virginia Barrelier, Patricia K. Black, Florence Webster and Matilda Wilson, deserves a great deal of credit for the success of our meeting.

It would be remiss for me not to remark here (and I am doing so with delight) on the contributions of Drs. Bo Holmstedt and Nathan Kline, coeditors of this volume. Without their vision, interest, know-how, persistence and scientific knowledge, this meeting could not have taken place. I would like also to express my thanks to Dr. Albert A. Manian and Mrs. Shirley Maltz from the Pharmacology Section, N.I.M.H., for their help in the preparation of this manuscript.

Finally, many thanks to all speakers, discussants and participants. In final analysis, it was their contributions which made the meeting a success, and helped so much in the stimulation and delineation of new directions in research—directions which may bring us a new arsenal of useful drugs, especially in the field of psychiatry and neurological diseases.

D.H.E.

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# GREETINGS

WILLARD C. FLEMING, D.D.S. *Chancellor*
*University of California, San Francisco Medical Center,*
*San Francisco, California*

My name is Fleming. I am Chancellor of the San Francisco Medical Center. If you do not know me, I prefer to introduce myself always, because if my friends introduce me I am a little fearful of people I do not know—I do a much better job myself.

I was born some sixty-seven years ago in Sausalito of poor but honest parents. The poverty angle must have been a dominant genetic factor because my daughter has the same problem.

I came here as a student of dentistry in 1918. I became a member of the Dental Faculty in 1923. I became Dean of the Dental School in 1939. After three years of attempting to retire, I took three years to find my successor. I thought this was fine, until one of my "friends" said: "Bill, did it ever occur to you they don't want to make the same mistake twice?"

From there to Dean of Students; and I have since last July been Chancellor of this campus. I have no illusions about why a Chancellor, Mayor or Governor gives introductory speeches. This is for the audience to calm down, chat with one's neighbor, get the identification, and so on.

I will follow the same pattern. After residence here of almost fifty years, you should understand that the local history of this center is of interest to me. History can be a very static chronicle of what has happened; or on the other hand, it can be a very dynamic encounter, and establish a sort of a curve of progress that can be extended as a curve of probability into the future.

I welcome the participants of the symposium entitled, "Ethnopharmacological Search for Psychoactive Drugs." I have a great deal of difficulty with that word. This is really the first time I have gone through it quite smoothly.

If you agree with what I said about history being used as our prediction of events to come, you may agree this campus is historically the logical place to sponsor this idea.

The history of California and in particular the Bay Area, is replete with the part medicine has played in its development. Bear Flag Republic; vigilante movement in San Francisco; the role of California in the years of Civil War; the bubonic plague epidemic; the Golden Gate Park and the health crisis that grew out of the fire and earthquake of 1906; an interesting course of development.

At the start of the very facilities that were in here, now, to give you some idea of how this started: like some medical schools in the early days, this school started with the history of a proprietary school, in other words, a school for profit. Then in the Gold Rush days of '49 and '50, a great many physicians came to California. They were adventurers, charlatans, and also

some very highly qualified and respected professional people. They were inclined to be a quarrelsome lot. This is an attribute that has not quite died out yet; and it is hard to think of another group that was so individualistic.

Among them was Dr. Hugh Toland, a well trained and well qualified surgeon. He tried his luck in the gold fields, but like so many others shortly returned to private practice in San Francisco. He was eminently successful both professionally and economically. During the '60's his annual income was reported to be over forty thousand dollars—more than they pay the Chancellor today.

This phenomenal income for those days was accomplished by taking advantage of two situations: The pioneers of those days were subject to many medical conditions and diseases, and of all of these, scurvy and syphilis were high on the morbidity list. Like many physicians of those years, Dr. Toland compounded and dispensed his own drugs, so it is no surprise to learn that in the backroom of Dr. Toland's offices were two barrels. One was labeled "Anti-Syph" and the other, "Anti-Scrof". There were no mail order houses, but there was the Wells Fargo Express throughout the entire west.

Through the dispensing of drugs for treatment of syphilis and scurvy by mail order, Hugh Toland became wealthy. Like so many people of these days, he attempted to memorialize himself by founding a medical school in his name. It is an interesting and intriguing story how, with the aid of Dr. Richard Beverly Cole, his first Dean of the medical school, this pair persuaded Regents of the newly started University of California to take on the Toland Medical School as the medical school of the University of California.

The Regents refused to name it Toland School of the University of California, but they did agree that there should be a physical part or plant with the name of Toland. Thus, today we have in our University of California Hospital a small auditorium known as the Toland Auditorium.

Our Department of Pharmacology has always been strong, as has our School of Pharmacy. Possibly it is our heritage, the fact that our medical center has a strong pharmacological school here, resting on one barrel of Anti-Syph and one barrel of Anti-Scrof.

At any rate, one can see that this symposium and its participants are in a hospitable environment. You are a welcome addition to a long line of predecessors, a fair example of the past and a prologue to the future.

Again I officially welcome you to the opening of this symposium.

# INTRODUCTION

## The Psychology, Philosophy, Morality and Legislative Control of Drug Usage

NATHAN S. KLINE
*Research Center, Rockland State Hospital*
*Orangeburg, New York*

### Man's Need for Action

Man is an animal impelled by internal forces to act. Just what form that action will take depends on the sensations experienced, the learned modifications of innate response patterns, and the possible alternatives existing in the immediate environmental situation. Behavior based on purely rational decision, if it exists at all, is certainly rare. Action is usually evoked by the sensual and emotional, or at times by reflex or even motor needs.

### Provocations to Action

Each of us is continuously being teased, hoodwinked, wheedled, invaded, bluffed, seduced and assaulted. When such blandishments to action are at the cognitive or even the emotional level the attempts are often obvious enough. More basic and often underriding them are appeals and approaches to primitive patterns of sensation involving incense, drums, drugs, ritualistic postures, idols, pageantry; rhythmic sounds and motions interspersed with abrupt syncopes; vast or close repetitive visual designs, color shock and most of all, movement. There are elusive, lingering, attractive, unidentifiable odors or revolting stenches that stir some troubled layer that lies below consciousness; and the body itself, the skin with its ceaseless prickling, itching, stretching, hotness, coldness never really leaves us alone. Nor do the muscles that protest by making us fidget if they are not moved frequently and then ache if they are exercised too long or too hard; the vague internal stirrings, appetites, "all the nameless feelings that go coursing through our breast." Finally, there is the mind's own place, eternally restless, seeking, peeking, poking, squirming, probing. Quiet and silence is a kind of death, from which we fear we may never be able to rouse ourselves.

### The Role of Drugs in Altering Perception: and the Partial Dependence of Such Responses on Environment and Expectation

Evocation and certainly control of these response patterns is still largely "unscientific." Experience and a particular habit of mind are necessary, however, before experience can be decocted into an effective guide through these mazes. Fatigue, hyperexcitement and drugs, by producing dissociation, tend



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both to heighten such experiences but at the same time to break down sophisticated self-awareness.

The loss of ego integrity with its capacity for reality testing leaves the self wide and uncritically open to prior expectations and environmental influences. How the drug-induced perceptual, kinesthetic or other distortions will be interpreted will therefore vary from culture to culture and even from individual to individual. Occasionally the same drug may induce profound depression, Dionysian ecstasy, terror or bland indifference. Yet if we induce similar expectations and control environment, the response is usually predictable. Duration is yet all too short and side effects still all too great, but we are well along toward recognizing both the circumstances and the agents which will do what we ask of them, by way of temporarily altering the perceived universe.

## Society's Moral Attitude

Whether such para-universes lead to improved philosophic or psychologic insights is far from clear. The use of drugs for any thing other than medical therapeutic purposes has always been construed as a threat—even when the purpose was ostensibly religious—few except the in-group would sanction such use. Even at the most simple level there is confusion; "taking drugs" has an immoral connotation despite the fact that the particular drug may be life saving; there is only disapproval of escape from intolerable thoughts, feelings or situations. At times drugs serve to induce actions which would otherwise not be possible; the hope of ex-static (i.e., out of the status quo) movement leads man to seize upon whatever is at hand to try to bring about such alterations. "The desire to take pills" wrote Olser, "is the greatest feature which distinguishes man from the animals."

## Why the Increased Interest and Use of Drugs at This Time and Place in History?

Here I repeat what I have written elsewhere:

To varying degrees each of us mortgages the present for the future; we tolerate present discomfort in expectation of eventual relief or even reward. Those parts of the remembered past which make us queasy are usually justified as contributing to some useful purpose yet to be realized. In the process we create a cultural as well as a personal history involving the whence and hence of existence.

On rare and glorious occasions some individual or group floods through time with an epic tide and in sheer admiration we are all swept along. More frequently the individual narrative thread is thin and frayed. In place of the grand patterned fabric we see only the thrums of existence. The whole business becomes a drag. Bugged by what we trail along and hung up on what is yet to come, we seek temporary or semipermanent escapes.

Today we lack any viable universally accepted dramatic plot. The success (not the failure) of nineteenth century rationalism has left us at least momentarily without a denouement. Not that those dated objectives of adequate food, housing and racial equality for everyone have been attained but, as in the stock market, their achievement has been "discounted" since it is obvious that within another few hundred years they will be substantially achieved. The sense of great purpose and broad adventure which

these goals engendered has vanished. Instead of singing down the high road we are looking at our sore feet. It requires solid stupidity, bland carelessness or extraordinary courage to disregard signposts which say "To Nowhere." The road is studded with squatters who block those who would pass. The gatherings at the campfires are not for counsels or imaginative planning but to titillate with pointless ghost stories.

Curiosity and action are thus directed inward. Drugs that help sever the tenuous ties with the outside world become highly prized since they both assist and justify the disregard for external realities. . . .

In the search for new values to give rise to a new narrative the towering, probing mystics of the past have sought to recapture the UR-experience upon which every Establishment originally drew strength until it became formalized. This invariably demanded the shattering of the idols or the escape from the Concept. Visions, iconoclasm, transcendence took place as the inevitable realization of a whole life's agon. Smashing a few clay figures or experiencing visual hallucinations does not produce an Abraham or a St. Theresa. Every great mystic has had experiences dissociated from the time and culture in which he lived—but the dissociation arose out of inner necessity. Conversion in turn is facilitated by the ecstasy of dance, ritual death, drugs. Dissociation per se has no value and can become meaningful only as it is integrated into a conceptual framework.

This incorporation can be strongly directed from outside. . . .

The dissociation can also produce panic if the attempt is made to retain dissolving ego controls. Once these are surrendered a para-infantile acceptance of the universe is experienced in which there are no clear ego boundaries so that the One-ness with the All comes about. Whether this feeling (or any other) has important value depends entirely on how it alters the organization and action of the organism.

## Can We Legislate Control?

Pharmaceuticals, like firearms, in themselves can be described only by such terms as potent or precise. Not their effectiveness but their application determines whether they are "good" or "bad". We probably should not, and in any case *can* not effectively, legislate against exploration of these other worlds. But we must protect ourselves by knowledge of what to expect and by attempting to control who may use these agents and for what purposes. There will obviously be wide differences of opinion on this score. Past epidemics of opiate or of cocaine usage finally required legal restrictions which did serve some useful purpose. Attending, or reading the records of, the present sessions is an act of affirmation in that they lead to increased understanding. We push back the darkness a bit; the darkness of the mysterious world of drugs and the equally dark and mysterious realms of self-knowledge and self-control.

In addition to moralizing, proselytizing, speculating; new legislation has and will continue to emerge in an attempt to influence the natural history of this uniquely human venture in which man deliberately alters his experiences of the world. As to how effective or desirable such legislation has been or will be, I can best end with a comment of Ambrose Bierce about Satan:

Satan made himself multifariously objectionable and was finally expelled from Heaven. Half way in his descent he paused, bent his head in thought a moment and at last went back. "There is one favor that I should like to ask," he said.

"Name it."

"Man, I understand, is about to be created. He will need laws."

"What, wretch! You his appointed adversary, charged from the dawn of eternity with hatred of his soul—you ask the right to make his laws?"

"Pardon; what I have to ask is that he be permitted to make them himself."

# LETTER

FROM ALBERT HOFMANN, PH. D., PHARM. D., H.C.
*Deputy Director Sandoz A. G.,*
*Basel, Switzerland**

January 19, 1967

Mr. Chairman, dear Colleagues,

While it is undoubtedly possible, with the aid of psychoactive drugs, to span both time and space, this method of overcoming these factors is unfortunately possible only psychically and not physically. Would the latter be possible, you may rest assured that I would now have taken the appropriate dosage of LSD or psilocybin so as to be transported on the flying carpet to San Francisco, for the purpose of participating in the symposium on psychoactive drugs.

I very much regret the fact that, for reasons of company policy, it was impossible for me to actively participate in this Congress. It is nonetheless my desire to convey from here in Basel, to the numerous prominent research workers in the field of psychoactive drugs attending this conference, my best wishes and the expression of the hope that the exchange of ideas will be fruitful.

The investigations of the lysergic acid derivatives, from which LSD resulted, have continued uninterruptedly in a variety of directions in the Sandoz research laboratories.

Thus, for example, it was possible, in pursuing the serotonin antagonistic activity first observed in LSD, to develop new lysergic acid derivatives in which a specific serotonin antagonistic activity is of prime importance. One of these highly active compounds has been introduced into therapy for the interim treatment of migraine.

In a particular field of research closely related to the theme of this congress and initiated by the discovery of LSD, our investigations on psychotomimetic drugs have been pursued. In using the experiences gained with LSD as the foundation, the problem of the so-called Mexican magic mushrooms, which has been studied ethnomycologically by Gordon Wasson and botanically by Roger Heim, was solved from a chemical point of view. The active ingredients, psilocybine and psilocine have been synthesised and made available for psychiatric research. The magic mushrooms in turn led us to a further important Mexican magic drug, namely Ololiuqui. In the Ololiuqui seeds, provided us by Wasson, we found the active ingredients to be lysergic acid derivatives, the main components of which are lysergic acid amide and lysergic acid hydroxyethylamide.

It would have given me great pleasure had I been able, at this symposium, to discuss in detail this most unusual, one can almost say magic circle of research which, starting from lysergic acid amides, namely lysergic acid

*Dr. Hofmann was unable to attend this meeting and his letter was read to the audience by Dr. N. Kline.

diethylamide (LSD), proceeded via two Mexican magic drugs—the sacred mushroom "Teonanacatl" and the Morning Glory seeds "Ololiuqui" and led back to the lysergic acid amides. I sincerely hope that I shall be able to satisfy this desire at the next symposium on psychoactive drugs in the not too distant future.

In conclusion I should like to express a few general points of view on psychoactive drugs.

These drugs are of especial importance in the following three fields:

1. In neuro- and brain-chemistry they are useful tools for the investigation of biochemical processes which form the basis of the nervous and psychic functions.
2. In psychiatry they have proved themselves to be compounds which, upon sensible administration, are becoming ever more important medical aids in psychoanalysis and psychotherapy.
3. From a epistemological point of view we must face the consequences resulting from the fact that it is possible, with the aid of mere traces of a compound, to radically affect the psychic processes and mental functions. This finding may throw new light on the age-old problem of the relationship and interrelationship of body and soul, or more generally, of mind and matter.

To a large extent the non-medical, partially legitimate, partially illegitimate, interest in and use of hallucinogenics or psychedelics is as a result of the possibilities mentioned under 3 above, namely of attaining a profound transformation of the conscious with the aid of these drugs.

It is in fact this very general interest in psychedelics, which has unfortunately, in some cases, led to dangerous misuse, that behooves scientists to continue research in the field of psychoactive compounds in all directions as quickly as possible, so as to elucidate the possibilities of these potent drugs in order that they may be used for the benefit of mankind.

It is my fervent wish that, in this respect also, this congress will be successful.

Yours

Albert Hofmann

# SESSION I

## AN OVERVIEW OF ETHNOPHARMACOLOGY

Chauncey D. Leake, *Chairman*

# Chairman's Introduction

CHAUNCEY D. LEAKE
*Department of Pharmacology, University of California*
*San Francisco Medical Center, San Francisco, California*

Following the example set by Chancellor Fleming, I suppose I should introduce myself. I am Chauncey Leake, and I have little idea exactly why I should be honored by being asked to be the Chairman of this first session. I have had some contact with psychoactive drugs, largely through the association with the late Gordon Alles, who died unfortunately in 1963 at the age of sixty-two. He did a great deal of the work on the amphetamines and the extraordinary hallucinogenic agents that had been developed in the amphetamines in the old pharmacological laboratory that we had over here.

I did some work on the bufotenine, which, when it is injected, is a tough drug to handle. It is difficult to get into solution. I have reported on mushrooms, but they were not hallucinogenic, although it was stated they did cause peculiar feeling, but this was due to the agaric acid in them, which has a local irritant.

I am thrilled to see you here, even in the face of the rain. I understand pharmacologists are tough and I think psychopharmacologists are especially tough, they seem to like this type of weather. It has been this way all across the country last week where the pharmacologists have been meeting.

Our session this afternoon is going to be a good one, and we start appropriately with a consideration of the historical survey of the field of ethnopharmacology by Dr. Bo Holmstedt.

# Historical Survey*

Bo Holmstedt
*Department of Toxicology, Swedish Medical Research Council*
*Karolinska Institutet, Stockholm, Sweden*

The most fascinating part of ethnopharmacology is perhaps that dealing with man's use of intoxicating compounds. A few—not too many—books have been written encompassing this subject, the most prominent being Louis Lewin's "Fantastica" (Lewin 1924).[1] The story of the use of these drugs is as old as man himself. Many people have for example speculated over what drugs and arrow poisons are mentioned in the Iliad and the Odyssey. There is not much need for speculation on this matter since the possible alternatives have been thoroughly discussed in the light of the 19th century achievement in pharmacology by two such authorities as Oswald Schmiedeberg and Louis Lewin. (Schmiedeberg 1918, Lewin 1920). Likewise, the toxic substances used during the middle ages and particularly during the witch trials have been much discussed. There is no need to go into this here.

This review is supposed to cover ethnopharmacology, and there was no ethnopharmacology before there was pharmacology. With some exaggeration it can be said that pharmacology started during the nineteenth century independently in three places.[2] One was Paris where the work of Magendie and his successors paved the way, the second was Edinburgh, where Sir Robert Christison among other things investigated ordeal poisons and coca, and advocated the rapid withdrawal in opium addiction. The third place was Dorpat, later called Jurjew and Tartu, in Estonia, where pharmacology as an academic science started around the middle of the 19th century. Of particular interest to the ethnopharmacology of psycho-active agents are Paris and Dorpat. This review will deal with some of the men who worked at these places.

Taking for granted that no ethnopharmacology can exist without true pharmacology it is appropriate to start this review at the beginning of the 19th century. At that time, the knowledge of foreign people, their habits, food and drugs in Europe and USA was generally speaking negligible. A spearhead thrust into this ignorance was Napoleon's ill-fated adventure in Egypt.

Napoleon was a remarkable general in many respects, in this specific case because he took with him to Egypt a library and 175 learned men who observed, wrote down, sketched and collected information about languages,

*This investigation was supported by Grant MH–12007 from the National Institute of Mental Health, U.S. Public Health Service, Chevy Chase, Md.

[1] A new print of the original English edition has recently appeared: Phantastica, Narcotic and Stimulating Drugs; Their Use and Abuse, by Louis Lewin, Routledge & Kegan Paul Ltd., London, 1964.

[2] Those interested in the history of pharmacology are referred to Readings in Pharmacology by Holmstedt and Liljestrand, Pergamon Press 1963.

archeology and folk lore. This ultimately resulted in the publication of 24 volumes (Description de l'Egypte) printed between 1809–1813. These books stimulated enormously the interest in the Orient and led to a series of travels to Egypt, Asia Minor and Africa. Many people published travel accounts, such as the French poet and statesman A. de Lamartine (1790–1851), and the interpreter of the hieroglyphs, J. F. Champollion (1790–1832). Champollion made his expedition to Egypt 1828–1829.

Of particular importance to psychopharmacology is, however, the travel in this part of the world of J. J. Moreau (de Tours), a French psychiatrist whose work unfortunately is much forgotten. Moreau and Champollion apparently had the same guide or dragoman as it was called at the time (Moreau 1841).

Moreau was the first medical man to work systematically with centrally acting compounds. It is therefore appropriate to go into some detail about his life and works.

*Jacques-Joseph Moreau (de Tours)* was born at Montrésor (Indre-et Loire) June 3, 1804. (Baruk 1962. Collet 1962, Ritti 1887).

His father, a soldier in the armies of the Republic and the Emperor, traversed the whole of Europe, taking part in most of the battles and was finally awarded the cross of the Legion of Honour. He resigned only after the battle of Waterloo, and spent the rest of his life in Belgium, where he devoted all his time to mathematics, for which science he had a great passion.

While the father carried on this turbulent life, the son began his studies of the Classics at the college of Chinon, later terminating them at the college of Tours. Thanks to profound and brilliant studies he passed with success his matriculation examination.

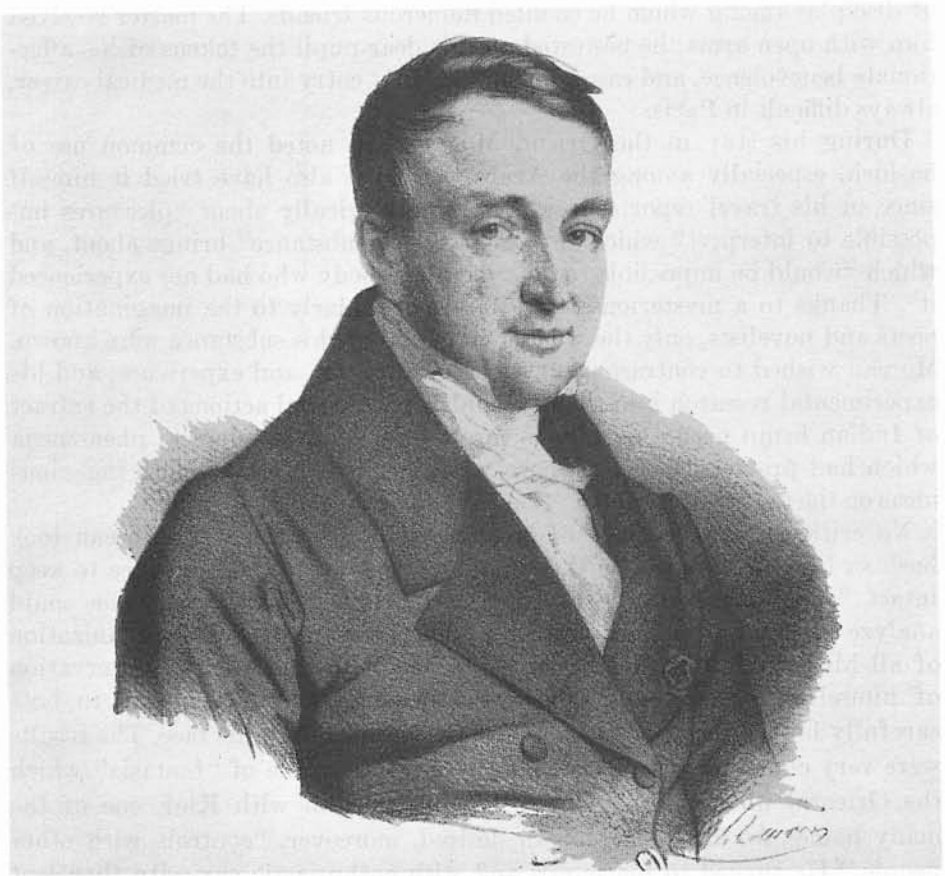
Moreau then continued his studies at the Medical School, where he was characterised as: A zealous and industrious student with a tremendous appetite for learning. The Medical School of the public hospital of Tours at that time was run by one of the most famous medical men of the period, Bretonneau. Moreau was fortunate in hearing the lectures of this teacher.

After a stay of two years with this master, Moreau went to Paris to complete his studies and to take his degree. We are not aware of the circumstances around his application for the position as assistant physician at the Charenton mental hospital, but there is no doubt that on July 6, 1826, the date of his nomination, he found the mission of his life to which he would devote himself as profit for science.

At that time the psychiatrist Esquirol had recently become head of the mental hospital, and thanks to him a number of useful reformations had been introduced for the benefit of the patient. Besides his great intelligence Esquirol was no less great as far as his character was concerned. The following maxim is ascribed to him "One must love the mentally ill in order to be worthy and capable of being of service to him."

Among the various methods of treatment for the mentally sick—travels—had been prescribed even as far back as ancient Greece. Esquirol had a great number of clients—people came from all parts of France and even from abroad to consult him. Among them were rich persons to whom he could prescribe long travels; he entrusted them to the intelligent care of his young assistants. Also Moreau was commissioned with such a task, and visited Switzerland and Italy with a patient.

Travel then became a necessity for Moreau. He had nothing to keep him in France; he was young and had no desire to settle down. He longed to see foreign countries. Esquirol entrusted him with the care of a new patient, this time for a very long absence: An absence of three years and a journey to the Orient. To visit the Orient! What a dream for a young man! And this at a time when eyes were turned towards these sunny countries from where came since ten years the most extraordinary news. Each stage of the journey would lead him to places where classic events faded in comparison with



J. J. Moreau (de Tours) 1804–1884

the more recent ones. One hardly thought of the Pharaohs when setting foot on the soil of Egypt, governed by the famous Mohammed Ali. When passing through Asia Minor interest was less lively for the rapid campaign of Alexander the Great than for the exploits of Ibraham-Pasha and his 30,000 Egyptians, the victories of whom had disturbed the Sultan's power.

The young and enthusiastic Moreau wished to learn and profit as much as possible from what he saw and heard, and for this reason he adopted the dress and the customs of the countries he passed through. He wrote down what he experienced, and it is much to be regretted that he never published his observations. Some of them are, however, contained in his medical books.

It is striking that in the Orient the mentally ill appear to be fewer than in Europe. Is this marked difference to be explained by climate, race, or by the political and religious institutions? Moreau adhered to the opinion of Montesquieu, who admitted the joint responsibility of these various causes:

> The heat of the climate can be so excessive that all strength leaves the body. The lack of strength passes on to the spirit—no curiosity, no noble sentiments, no generous feelings . . . . laziness is happiness . . . . resignation. . . .

Immediately upon his return to Paris, Moreau hastened to renew his old acquaintances and acquire new ones. He met Esquirol again and his circle

of disciples among whom he counted numerous friends. The master received him with open arms; he bestowed on this dear pupil the tokens of his affectionate benevolence, and eased for him his first entry into the medical career, always difficult in Paris.

During his stay in the Orient, Moreau had noted the common use of hashish, especially among the Arabs. He must also have tried it himself since in his travel reports he writes rather lyrically about "pleasures impossible to interpret" which this "marvellous substance" brings about, and which "would be impossible to describe to anybody who had not experienced it". Thanks to a mysterious legend and particularly to the imagination of poets and novelists, only the wonderful effects of this substance were known. Moreau wished to contrast poetry with observation and experience, and his experimental research into the psychopharmacological actions of the extract of Indian hemp permitted him to throw light on psychological phenomena which had previously been obscure. They inspired him also with ingenious ideas on the nature of insanity.

No criticism can be made of his investigative procedures. Moreau took hashish himself. Thanks to the singular property of the substance to keep intact "consciousness and the innermost feeling" of the user, he could analyze all his impressions and in a way be aware of the disorganization of all his mental faculties. In order to complete this internal observation of himself, he also commissioned the persons surrounding him to note carefully his words, acts, gestures and the expression of his face. The results were very characteristic. They fully justified the name of "fantasia" which the Oriental imagination gives to the intoxication with Kief, one of the many names for hashish. Moreau desired, moreover, "controls with other people." He turned to his pupils and with enthusiastic curiosity they lent themselves to experiments with hashish in the most varying doses, giving exact accounts of what they experienced. Moreau observed with scrupulous care every (external) symptom during the course of intoxication. The two series were compared and full conformity was proved.

The effect of the hashish reveals itself by a series of intellectual disturbances, Moreau described all the sensations with meticulous care.

In 1845 Moreau published his extensive book of more than 400 pages entitled Du Hachich et de l'aliénation mentale (Hashish and mental illness). Its detailed accounts of the hashish intoxication aroused the interest of numerous physicians and the curiosity of many writers, and was followed by a great deal of personal experimentation. Moreau's book gave rise to the modern researches regarding the effects of hashish, and can also be held responsible for its use in certain Paris circles in the middle of the 19th century. However, it never became a true epidemic in all parts of Europe, confining itself mainly to the Near and Middle East.

Such factors as origin, education and environment as well as the atmosphere in which hashish is consumed, affects individuals in different ways. Due to the great number and varying nature of the *psychic effects* of the hashish intoxication, these cannot be outlined in the same way as the

physical effects. However, Moreau enumerated eight main groups of symptoms. They are:

(1) General feeling of pleasure.
(2) Increased excitement combined with a heightening of all senses.
(3) Distortion of the dimension of space and time (generally a magnification of the actual dimensions: Minutes are changed into days or years, inches into feet, etc.).
(4) A keener hearing combined with a great susceptibility to music and the phenomenon that ordinary noise is enjoyed as though it sounded sweet.
(5) There often arise persistent ideas on the verge of persecution mania.
(6) Disturbances of the emotions, mostly in the form of an increase of already existing feeling.
(7) Irresistible impulses.
(8) Illusions and hallucinations of which evidently only the first named are related to objects of the exterior world.

Moreau pointed out that psychiatry could profit from these experiments by comparing the symptoms to those in mentally ill people. The illusions produced by the hashish—are they not attacks of insanity? These attacks will take on all the characteristics of violent insanity if only the dose of the toxic agent is increased. Moreau had the occasion of sadly experiencing this. His assistant in pharmacy wished to see the effects of the Indian hemp when taken in a larger quantity, and swallowed 16 grams of the extract.

A very intense delirium broke out, followed by agitation, incoherence and hallucinations of all kinds. Three days passed before the young man regained his ordinary calmness and the entire use of his power of reasoning. During the course of the attack he maintained, however, some idea of what was happening to him.

Moreau postulated that there exists in insanity a primary factor which is the source of all symptoms; *i.e.*, excitation, which is the primitive generative power. He attached special importance to this hypothesis, and considered it as equal to other great scientific laws. Moreau also compared insanity with dreams. The hypothesis is not new; it already preoccupied Aristotle. The learned philosopher from Stagira writes in his books on "Dreams" that "the reason why we, even awake, deceive ourselves in certain illnesses is the same which produces in us, in our sleep, an impression of a dream." The favorite formula of Moreau was: "Insanity is the dream of the man who is awake."

Even though Moreau cannot be said to be dependent on his countryman the French materialist and medical man La Mettrie (1709–1751) who said: "Man is what he eats", he still considered a range of causes for insanity. With regard to the conception of an organic origin he writes: "I am not against the conceptions of organic damage but I require to see the lesion: I only believe in damages which are proven, not in those that are supposed

# DU HACHISCH

ET DE

# L'ALIÉNATION MENTALE

## ÉTUDES PSYCHOLOGIQUES

PAR


**J. MOREAU** ✝

(DE TOURS),

Médecin de l'hospice de Bicêtre, Membre de la Société orientale de Paris.

**PARIS.**

LIBRAIRIE DE FORTIN, MASSON ET Cie.

PLACE DE L'ÉCOLE-DE-MÉDECINE, 1.

Même maison, chez Léopold Michelsen, à Leipzig.

**1845.**

to exist." This certainly was a very wise position to take. Even in our days, organic or biochemical lesions in mental illness have been difficult to prove.

Moreau loved art in all its forms. He gladly sought the company of writers and artists. His works on hashish had put him in contact with numerous poets and novelists and he was well acquainted with Balzac, Gérard de Nerval and Théophile Gautier. The author of "la comédie humaine" wrote him the day after a "fantasia" about an idea that he had had for twenty years: "To make a new brain in an idiot (with the aid of hashish)

in order to see if the mind could be expanded by development of the rudiments." It has a familiar ring.

Moreau passed away June 26, 1884, at the age of 80 after a short illness. He was undoubtedly the first psychiatrist with interest in psychopharmacology. It seems that during his life time he was never recognized as he should have been. Among those who did not understand his qualities was regretfully François Magendie (Collet 1962). On the other hand, Claude Bernard once called hashish a psychopharmacological counterpart of curare. Up to recent years, however, with regard to hashish people have been mostly interested in the literary feats of Théophile Gautier and Charles Baudelaire, and "Le Club des Haschischins" with its strange meeting in the old hotel on Ile St. Louis in Paris. It is perhaps typical that a very recent collection of papers around the subject hashish only mentions Moreau in passing. (Solomon Ed. 1966.)

Unlike Moreau *Ernst von Bibra* (1806–1878), was the prototype of a wealthy, private scientist. Although he acquired academic degrees he performed a good deal of his research in his own house.

Bibra was born in Unterfranken, studied in Würzburg, where he became M.D. and Ph. D. and later partly in Nürnberg living on his estate Schwebheim. He was mostly interested in chemistry, but also was a geographer and a numismatologist (Günther 1901). Of special importance to this account is his trip to South America 1849–1850. He was more or less forced to leave for political reasons, because of his liberal attitude during the revolution in 1848.

The most important result of this journey—except for his travel account ("Reise in Süd-Amerika, B. Mannheim, 1854") which is well worth reading—is the book "Die narkotischen Genussmittel und der Mensch" (Nürnberg 1855). The book was undoubtedly prompted by his South American trip, and is the first of its kind to summarize the effect of centrally acting compounds, in all seventeen. He devotes chapters both to compounds such as coffee and tea, and also to *Amanita Muscaria*, opium, hashish and coca, the chewing of which he had rich opportunities to observe during his trip to South America. Due to the fact that comparatively little was known about these drugs at the time, Bibra's book created quite a sensation. He did not pursue this line of research, but devoted the rest of his life to his private hobbies, such as numismatics and writing of novels.

There were other people who were to make such compilations during the nineteenth century. One of them was *Georg Noël Dragendorff* (1836–1898).

Dragendorff was born in Rostock, Germany, as the son of a medical man, studied chemistry in Heidelberg and learned the trade of pharmacy in his home town (Hartwich 1897–1898). His main interest was chemistry. The famous Witte pharmacy in his home town soon expanded into a house of medicinal chemistry and Dragendorff became employed there. He heard lectures by Bunsen, Kirchhoff, Helmholtz and Erlenmeyer, but it is said that he never had an opportunity to hear a lecture in pharmacognosy either in Rostock or Heidelberg. The first one he ever heard was the one he had to give himself when he had become professor in Dorpat.

In 1862 Dragendorff was called to St. Petersburg to help organize the editing of a journal of pharmacy. He learned to speak Russian and also helped organize the pharmacies in Russia. From St. Petersburg he was called to become professor of pharmacy



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and director of the Pharmaceutical Institute of Dorpat, 1864. Dorpat came to be his home for 30 years, and when he finally resigned his chair in 1894 he returned to his home town of Rostock, where he organized a private laboratory and carried on research until his death.

Dragendorff's work dealt with two things: one, relevant to the present account, was the chemical investigation of plants; the other was toxicological analysis. He was particularly interested in the medicinal plants used by foreign people, and had acquired collections from far off countries in his institute at Dorpat. His most famous work and a summary of his activities in the field, was published shortly after his death and is now a rare book: "Die Heilpflanzen der verschiedenen Völker und Zeiten", 1898.[3] With regard to his chemical activities we only have to point out that he had numerous pupils from many countries, and that no reputable phytochemist is unfamiliar with Dragendorff's reagent for alkaloids.

Another German pharmacist who perhaps accumulated even greater knowledge in one field of ethno-pharmacology was *Carl Hartwich* (1851–1917). (Schröter 1917.)

Hartwich was born in Tangermünde where his father had a pharmacy, the management of which the son took over in 1879. He was, however, so interested in scientific activities that he sold the pharmacy and moved to Braunschweig. From there he went to Bern in order to take his doctor's degree and then again to Braunschweig to become university lecturer in pharmacy and pharmacognosy. A few weeks afterwards (also in Hartwich's case before he had given one single lecture) he accepted a call to the Swiss Polytechnical Institute in Zürich. He began his service in the autumn of 1892 and stayed for 24 years, as professor and head of the Pharmacology Department.

Hartwich published a multitude of papers dealing with numerous drugs and stimulants. In these studies the historical and ethnographical questions are strongly emphasized. Of a particularly historical interest is "Die Bedeutung der Entdeckung von Amerika für die Drogenkunde" (1892).

Hartwich's most important publication, however, is "Die menschlichen Genussmittel", 877 pages with 24 tables and 168 pictures in the text (1911). He worked on this monumental volume during a decade, with considerable joy and even with the passion of a fanatic collector. The gigantic quantity of material is astounding and includes drawings, photographs, observations of his own, and literary notes from the most remote sources. The physical, historical, ethnographical and commercial and ethical aspects of the compounds are treated with the same love. The richly decorated book is a true gold mine of information that was previously widely dispersed.

In addition to these voluminous collections of ethno-pharmacological and ethno-botanical material there arose during the second part of the 19th century the science of psychology. The pioneers in this field were *Hermann v. Helmholtz* (1821–1894), *Gustav Theodor Fechner* (1801–1887) and *Wilhelm M. W. Wundt* (1832–1920).

The foremost service of W. Wundt to psychology was the introduction of laboratory investigation. Before his time experimental research in psychology had been mainly individual. He gathered around him enthusiastic

[3] At the time of writing a reprint of the original has been issued.
Georg Dragendorff, Die Heilpflanzen der verschiedenen Völker and Zeiten, Neudruck der Ausgabe Stuttgart 1898. Antiquariat Fritsch, Postach 1043, 79/Ulm/ Do. Germany.

students and assistants whom he trained in the methods of exact experimentation. The first real institute for psychological studies was erected by Wundt in Leipzig 1879 (Kraepelin 1920). It consisted of two rooms and some tables with equipment, some of which was Wundt's personal property. No grant for equipment was available and Kraepelin tells how it had to be made by hand from wood, tin, strings and cardboard. They had, however, accumulators and chronoscopes. In spite of the obvious poverty the new institute was filled with a pioneering spirit and enthusiasm.

Wundt had never had near contact with psychiatry or drug research even though he had to do with it now and then. One of his first pupils was *Emil Kraepelin* (1856–1926).

Kraepelin was born in Neu-Strelitz (Mecklenburg-Strelitz), studied in Leipzig and Würzburg with the intention at the very start to become a psychiatrist. He graduated in 1878 and came to the Munich Mental Hospital. In 1882 he became assistant of Flechsig in Leipzig, but soon left in order to work in the Institute of Wundt. At the start working with experimental psychology, he later turned wholly to clinical psychiatry which he endeavored to put on a new basis that brought world-wide fame to his Munich Clinic.

Kraepelin published the first account on the use of the new psychological methods in clinical pharmacology which he undertook during his tenure of a professorship in Dorpat (1886–1890). In that remarkable university at this time worked also not only Dragendorff but Rudolf Kobert, who held the chair in pharmacology. Obviously, Kobert was the one who interested Kraepelin in applying his psychological tools to the study of drug effects in man (Jelliffe 1931). Among the drugs he studied were morphine and alcohol, and after he had left Dorpat this resulted in the first real monograph of psycho-pharmacology where the new methods were applied: "Ueber die Beeinflüssung einfacher psychischer Vorgänge durch einige Arzneimittel—Jena, 1892."

Kraepelin maintained a lifelong interest in the pharmacology of alcohol. In his hospital he introduced variously colored lemonades immediately christened "Kraepelin liquors" (Kolle 1956).

Kobert's association with the clinic of psychiatry in the meantime had resulted in the publication of another epoch-making paper, written together with one of Kraepelin's co-workers (Kobert R. and A. Sohrt: "Ueber die Wirkung des salzauren Hyoscin," 1887.).

*Rudolf Kobert* (1854–1918) started his medical career in Halle under Theodor Weber and spent many years as assistant to Schmiedeberg before he was called upon to become H. H. Meyer's successor at the famous department of pharmacology in Dorpat (Sieburg 1919). He remained in Dorpat until 1897. The title of his chair was Pharmacology and Physiological Chemistry; he was also a teacher in History of Medicine and Pharmacy. In 1899 Kobert became professor at the university of Rostock where he remained until his death.

From Kobert's hand originate a great many publications concerning pharmacodynamics and toxicology. He wrote a textbook in toxicology which has had a considerable influence on many fields including forensic medicine. He was one of the two great toxicologists of the nineteenth century, the other being Louis Lewin. The great learning and wide scope of his interest is witnessed among other things by the issue during his time in Dorpat of "Historische Studien aus dem Pharmakologischen Institut". This work in five volumes is an invaluable source, among other things for information to early research of drugs, also to research of drugs affecting the central nervous system.

The above mentioned paper by Kobert and Sohrt is of considerable psychopharmacological interest. For the first time here, dissimilarities and sim-

Emil Kraepelin 1856–1926

ilarities between atropine and scopolamine are pointed out, the latter compound at this time called hyoscine. Kobert and Sohrt in their carefully conducted investigation demonstrated the sedative action of the latter compound. The experiments were made both on animals and man, and included a series of self-experiments. Kobert writes the following:

. . . During the past autumn vacation I had the opportunity to arrange at the Department of Psychiatry in Dorpat and supervise directly an investigation of the actions of a pharmacological agent. This investigation, which lasted several months, was undertaken because work on animals is of value if it is extended to man. The pharmacological agent involved was hyoscine.

. . . Mr. Sohrt, the assistant in the Department of Psychiatry, wrote up these experiments at my instigation for his inaugural thesis. In view of its limited circulation I wish to present here the following account taken from the thesis:

. . . Sohrt gave himself at 10.04 p.m. an injection of 0.5 mg hyoscine hydrochloride. The pulse rate before injection was 64 per minute. After a latent period of 10 minutes Sohrt observed as the first symptom a ptosis which made it difficult for him to keep his eyes open. Gradually a feeling of heaviness without headache occurred. His head tended to drop to his shoulders and it became difficult to keep the head upright. His limbs felt as if they were lumps of lead attached to the body. There was a marked tiredness.

Throughout this period S. was fully conscious and able to give an account of everything and to answer questions speedily. He was able to read his own writing without much difficulty and did not feel sick. At 11.25 p.m. he stood up, but his walk was unsteady. He went to bed, therefore, and at once fell asleep. He had a quiet sleep without dreams. On the following morning S. woke up at 9 a.m., instead of at 5 or 6 a.m., which was his usual time. His head felt slightly numb, but this symptom disappeared after breakfast.

These experiments show that hyoscine, 0.5 to 1 mg, given subcutaneously, produces in healthy man dryness of the mouth, dilation of the pupils, marked sleepiness and tiredness, but is devoid of other special actions.

. . . In nearly all those cases of illness which are associated with a state of excitation hyoscine produced sleep promptly or at the very least induced sedation, even when all other drugs used for this purpose failed to produce an effect.

By far the most interesting personality of all psychopharmacologists of this time was *Louis Lewin* (1850–1929).

Lewin was born in the small town of Tuchel in Western Prussia. In 1854 he came to Berlin where he remained more or less until the end of his life. He graduated from the University of Berlin. In 1875 as an M.D., he studied for a while with Pettenkofer and Voit in Munich, and became "Privatdozent" in pharmacology in Berlin in 1881. In 1894 he became titular professor at the University of Berlin but held no full academic position. Only as late as 1919 did he become permanent honorary professor at the Technical Academy. There has been much speculation about the reasons why Lewin did not advance academically in pharmacology and toxicology, and it has been said that he could have become head of the greatest pharmacology department in Germany had he renounced his Jewish faith and consented to become baptized. Whatever truth there may be in this, he established his own private laboratory and lecture hall in No. 3 Ziegelstrasse in an old tenement house in the centre of the medical district of Berlin. He preferred to teach and to do his research with his own means in these surroundings. Financially, he was partly enabled to do so through the fact that although he had no official position, the courts preferred him to all other experts in Germany in toxicology and industrial hygiene.

Lewin's way of lecturing was extraordinary and held the audiences spellbound. It has been said that he expounded facts with a contagious enthusiasm and performed his

# Ueber die Beeinflussung einfacher psychischer Vorgänge durch einige Arzneimittel.

Experimentelle Untersuchungen

von

**Dr. Emil Kraepelin,**
Professor der Psychiatrie in Heidelberg.

Mit einer Curventafel.

**Jena,**
Verlag von Gustav Fischer.
1892.

experiments with loving care. Any narrow specialization was foreign to him. He could quote flawlessly in foreign languages, and marshal facts from all four corners of the world and all periods of history. Classical and contemporary authors were all familiar to him. Many famous men who visited his lectures were deeply influenced by him. Among them was J. J. Abel who has been called the father of American pharmacology. Lewin's outstanding wide general knowledge meant that he had many friends among scholars in other faculties.

Among Lewin's personal acquaintances were the explorer Georg Schweinfurth, and Albert Einstein. In history, geography and anthropology his knowledge was enormous; he showed special interest in travel and topography. It is said that scarcely a travel book of importance was unknown to him. His own travelling included visits, among other places, to the United States, Switzerland and Italy.

When surveying Lewin's works one is greatly helped by a list he compiled himself before his death. The list includes 248 major publications in the years 1874–1929. From the list are excluded book reviews, printed discussions and other minor communications of his which were also numerous. Among the publications there are about a dozen books and monographs. Lewin himself claimed that by 1880 he had already decided to devote most of his time to the side effects of drugs.

Lewin's first major work, in 1881, "Nebenwirkungen der Arzneimittel", Pharmakologisch-klin. Handbuch (Berlin, A. Hirschwald), dealt with this topic and became a classic and the first of its kind. This book had two more editions and was translated into three languages, including English. Notable among the other books are his outstanding textbook in toxicology, a summary of all available knowledge of arrow poisons, two volumes on the effects of drugs on the eye, and another work in which he gives the world's history as seen by a toxicologist, "Die Gifte in der Weltgeschichte" (J. Springer, Berlin 1920).

It is not possible here to summarize all the fields of interest to which Lewin made original contributions, but it is appropriate to dwell on his activities in psychopharmacology, a topic in which he published some 20 articles. His own contributions to the field occurred mostly in the 1880's. Then he more or less left this field, but in 1924 summarized admirably his own work and those of others in the first edition of his book "Phantastica". The long delay certainly did not mean that he remained unfamiliar with the progress in the field; on the contrary, the books show that he kept up to date with all achievements made.

Lewin's first publication, in 1874, was a study of chronic morphinism, which he was one of the first to investigate scientifically. In 1886 there appeared his monograph on *Piper methysticum* (Kawa Kawa) : "Ueber Piper methysticum (Kawa)." (Monographie. Berlin. A. Hirschwald). This is a very comprehensive review of all aspects of the use of *Piper methysticum* and current research on its constituents and their chemistry, pharmacology and clinical effects. This admirable monograph is now understandably much out of date in its chemistry and pharmacology, but it was a pioneering work, and the period following its appearance saw the first real progress being made in the chemistry of kaava. In 1889 appeared another similar monograph: "Ueber Areca Catechu, Chavica Betle und das Betelkauen." (Monographie. Stuttgart. F. Enke) an equally comprehensive review.

Before that, however, Lewin had had occasion to get into polemics with Sigmund Freud about coca and cocaine. This strange episode in the history of science runs as follows:

A century ago the height of nationalistic pride was to have a man-of-war circumnavigate the globe. Austria, a sea power in those days, planned to send the Novara on such a trip. Prof. Wöhler of Göttingen just before departure requested the naturalists on the expedition to bring him back a sufficient quantity of coca leaves to carry out a thorough investigation. Dr. Scherzer, one of the scientists, did manage to get some 30 lbs. of leaves to

Louis Lewin (1850–1929). Picture taken about the time of his trip to the United States.

Prof. Wöhler. His assistant, Niemann, succeeded in isolating an unusual crystalline organic base.

The first description of cocaine occurs in Tagesber. allgem. med. Zentral-Zeitung, 25 April 1860, p. 262–263. It is noted that, "It would seem that Coca will be of great use to the medicine of the future. . . . It has the remarkable action on the nerves of the tongue that after a few moments the place of contact becomes anaesthetized and almost insensitive". In 1859 Paolo Mantegazza's description of the therapeutic versatility of coca aroused much interest but little confidence, although subsequently his reports have been largely verified. However, early investigations in Austria, Germany and England were largely negative in their findings, and by the 1870s there was general disillusionment.

A military surgeon, Aschenbrandt, in 1883 claimed a remarkable effect of cocaine upon Bavarian soldiers enabling them to better endure hunger, strain, fatigue and heavy burdens. He anticipated a demand of today's purists in experimental design by adding the cocaine to the drinking water and not telling the soldiers. Unfortunately the use of control subjects was overlooked and Aschenbrandt was anything but unbiased. Palmer (1880) in the Louisville Medical News, and Bentley in the Detroit Therapeutic Gazette (1880), had described the use of coca in the treatment of morphinism. The Louisville Medical News said in its editorial comment "one feels like trying coca with or without the opium habit. A harmless remedy for the blues is imperial."

In 1884 Sigmund Freud wrote to his fiancée that he had been experimenting with "a magical drug". After dazzling success in treatment of a case of gastric catarrh he continues "If it goes well I will write an essay on it and I expect it will win its place in therapeutics by the side of morphium, and superior to it. . . . I take very small does of it regularly against depression and against indigestion, and with the most brilliant success." He urged his fiancée, his sisters, his colleagues, and his friends to try it (Jones 1956). That same year he published an article "Über Coca" which among other virtues extolled the drug as a safe exhilarant which he himself used and recommended as a treatment for morphine addiction. For emphasis he stated, in italics, that "Inebriate asylums can be entirely dispensed with" and a cure effected in 10 days. That same fateful year he used it for this purpose in treating his close friend, Ernst Fleischl. For a while the treatment succeeded but increasingly larger doses were needed. Freud spent one frightful night nursing Fleischl through an episode of cocaine psychosis and thereafter was bitterly against drugs, rarely permitting them even for himself during operations for the painful carcinoma of the jaw which finally killed him.

Freud's paper on Coca was subjected to a severe criticism by Louis Lewin (1885). Among other things, he said:

> I want to state explicitly that according to all available evidence coca is no substitute for morphine and that a morphine addiction cannot be cured by the use of coca. . . .
>
> I am convinced that coca cannot be a substitute for morphine for any length of time since the real morphine addict wants the specific morphine effect and since he can very well distinguish the euphoria of other substances. Such an exchange does not suit his

Ueber

# PIPER METHYSTICUM (KAWA).

## Untersuchungen

von

Dr. L. Lewin,
Docent der Pharmakologie an der Universität Berlin.

Mit 1 lithographirten Tafel.

Berlin 1886.
Verlag von August Hirschwald.
NW. Unter den Linden 68.

special needs. The morphinist wants more than the euphoria which can be brought about in normal man and which Freud experienced himself when taking 0.05–0.1 gr. cocaine hydrochloride.

However, even if it were possible to treat a morphine addict for a time exclusively with cocaine and even if he were given very large doses producing hallucinations and a pleasant sopor, there would very likely occur a case of what I would like to call double addiction. The man in question would use cocaine in addition to morphine in the same way as many morphine addicts use chloroform, chloralhydrate, ether, etc.

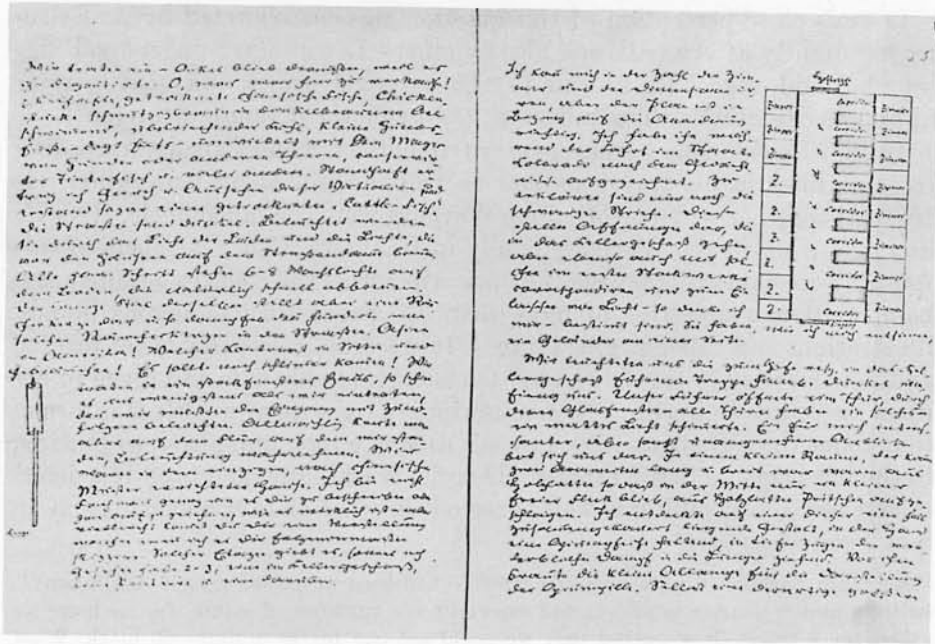
Lewin's clear perception of this question was corroborated by A. Erlenmeyer slightly afterwards, and also by others. Lewin never understood Sigmund Freud, especially not his psychoanalytical works, and used to refer to him as "Joseph der Traumdeuter" ("Joseph, the dream interpreter").

In 1887 Lewin made a cross country trip in the US and Canada. According to some lines in his travel account he had thought about emigration. He traveled together with one Mr. John Warburg whom he called uncle. His wife had grown up in the Warburg family in Hamburg. Other members of this family were famous botanists. Lewin's trip across the country resulted in a hand-written manuscript of more than 300 pages with numerous photos, illustrations and cuttings glued into it. It is a family property never printed and not intended to be.[4] It was written as a gift to his wife and given to her upon his return to Berlin. The manuscript is a treasure of wealth of information about the US about 1880. Lewin's itinerary took him also into Canada, to the big lakes, to San Francisco, Detroit, Washington and back His determined way of travelling is well borne out in what he says about his stay in San Francisco:

My main purpose in visiting San Francisco had been to see for myself "Chinatown", as the Chinese quarter is called, and especially the smoking of opium. In our hotel we asked for a guide. It appeared that we could get one for 10 dollars—40 mark. What an insolent overcharge! We asked in a ticket-office—the same charge, but with a reduction to half the price for a guided tour in the daytime. But during the day there is nothing to see there and everybody can then walk through the quarter and the shops. I decided to show those swindling yankees that we were able to find the right way by ourselves. We asked a policeman what to do to get a policeman as guide. He directed us to the main police-station. There I explained my request after having shown my card. When the captain began long deliberations with someone else I showed him the legitimation I had received from Washington. This proved effective. We were to meet our police-guide at 9 o'clock in the evening at the station. We told this to Mr. H. who wanted to see Chinatown too. Strange to say—the better society of San Francisco does not know it. On the way we passed the stock-exchange and went in. After a few paces we meet the strapping policeman, our companion for the excursion. After a short time we arrived. How many different impressions do I bring home from this visit! From the moment we entered this quarter in which approximately 30,000 Chinese live till we left it, an unpleasant odour did not leave us. It is impossible to describe it, it is so repugnant that even uncle was, at the beginning, somewhat repelled and disgusted. The streets were repulsively dirty and filthy. People throw everything in the streets to let it rot there. It is impossible to use the so-called sidewalks, partly because they are full of baskets and boxes, partly because there yawn everywhere cellar-holes one might easily fall into. I had to roll up my trousers. What a contrast to this filth, when we entered the first shop, a barber-shop! There two Chinese were sitting, under the hands of the barbers. They had just finished shaving the hair from the forehead to the top, and were occupied in tidying the ears and the noses of their clients with very small knives—not wider than a straw—and very fine sponges with handles. The barbers removed all hair and other substances. On the other side of the street there was a food-shop.

The streets are dark, lighted only by the shops and by candles burning in the street in front of the houses. Every few paces 6–8 wax-candles are stuck into the ground. These candles burn down very quickly, but their long stem consists of incense, so that there are hundreds of incense-candles fuming in the streets. Asia in America! What a contrast of customs and habits! But that was not yet the worst by far. We entered a

[4] The author wishes to express his gratitude to Mrs. Irene Sachs, N.Y., for permission to publish part of the travel account and to Mrs. Hertha Jaffé and Mr. Mordechai Yaffé, Israel, for help with the translation.



Pages from Louis Lewin's travel account related to visit to Chinatown in San Francisco.

pitch-dark house—or so it appeared to us as we went in, for we had to light up the entrance with matches. By and by we could see some light in the passage we were standing in. We were in the only house built in Chinese fashion. I am not expert enough to describe it to you as it really is or to make a drawing of it. Perhaps you will get some idea? I sketch it as follows. As far as I could see there are 2–3 such stories, a cellar-story, the groundfloor and one above. I might be mistaken as to dimensions and numbers of rooms but the arrangement in the plan is correct. I sketched it from memory while travelling through the State of Colorado. I must explain the broad dark areas. These are apertures leading to the cellar. There are corresponding apertures in the first story, I think for illumination. If I remember right, there is a banister on one side.

We lighted our way down the stairs leading to the courtyard and to the cellar-story. Darkness enveloped us. Our guide opened a door with a glass-window—all the doors have a window like this—through which a faint light was glimmering. What we could see was interesting to me, but in general an unpleasant view. In a small room, less than two arm-lengths long and wide, we saw plank-beds all around leaving only very little free space in the center of the room. On one of these I discovered a crouching figure holding an opium pipe and inhaling deeply the pernicious fume. Before him burned the small oil-lamp for the preparation of the opium-pill. Such a pill, even a bigger one, is, as I saw, enough for 2–3 draughts, seldom four. The extract of opium has an almost honeylike consistence. With a very fine metal-spatula—I have a similar one—he takes a small amount of the extract and puts it somewhere at the clay-top of his pipe. He then again takes the opium up, this time with the needle-like other end of the spatula, passes it lightly through the flame to condense it and make it more malleable and tries by turning the needle round and round to give the opium pill a cylindrical form. After passing the material another two or three times through the flame the desired form is achieved. He sticks the needle into the aperture of the pipebowl and, while drawing it back, he presses the small cylinder of opium into the aperture of the bowl with his index-finger.

Now he puts his mouth to the pipe-stem and sucks deeply, deeply, while letting the opium-cylinder evaporate near the lamp—it looks for all the world like a thirsty man putting his pint-glass to his lips and emptying it in deep endless draughts. After approximately half a minute he exhales the fumes which in the meantime have been partly absorbed through the mucous membranes of the lungs. This same procedure occurs 6, 8, 10 times and even more until the gratification of the opium-visions provide the compensation for the troublesome preparations. He feels himself transplanted from his wretched surroundings. He sees palaces, riches, opulent repasts, splendid garments, beautiful amorous women and perhaps officies, titles and decorations descending upon him. In the morning he awakes—on a straw-mat or a heap of rags in a lightless hole filled with pestilential air. Again he trudges by daylight to the hole where he lives. Who can blame this human being—with his low grade of education, deprived of moral support—if he returns again and again to the pleasurable world of the opium-vision at night?

Again we enter a house, going along what seem still narrower passages. You feel your heart beating at the thought of a sudden conflagration. Not the most precipitous point of the Canadian Pacific Railway gave me so much fright: The feeling of being shut-in in these passages nearly choked me!

Lewin also managed during the same trip to visit the stockmarket, Chinese restaurants and theatres, the house of the Salvation army, and another house from which he fled in Victorian dismay.

However interested Lewin may have been in San Francisco's China Town and the smoking of opium, the city he really longed to visit was Detroit. He arrived there on September 16, 1887:

My first errand was, of course, a visit to Parke Davis. We drove along a splendid wide avenue bordered by residences with beautiful gardens. Soon we were marvelling at a grand extensive building adorned with sand-stone. This building which belongs to the company, is not yet fully finished. We enter the office where there work well over fifty book-keepers, male and female, cashiers, clerks, stenographers etc. Mr. Wetzell showed us round the factory and the printing-shop—I had not expected such a magnitude and such a skilled exactitude of workmanship. It is impossible to enumerate all particulars to you. Summing up, I can only tell you that the different departments are exemplary, from the preparation of juices and extract, the extraction of drugs, bottling, labeling, the homogenization of plants to the manufacture of pilular mass, sugaring and coating of pills etc., etc. . . . In short, the manufacture of pharmaceutical preparations is worthy of the American genius for machinery and for exactitude and cleanliness of use. Whatever I received—preparations drugs etc.—you will see for yourself when everything arrives in Berlin.

Among these things he carried back with him to Berlin from Parke Davis Co. was Peyotl, the "Mescal buttons". We know this exactly because he has stated himself that he got it from the Parke Davis and Co. during his American trip. He was not long in investigating its properties and there appeared in Schmiedeberg's archives and the Detroit Therapeutic Gazette the first accounts of the pharmacologic properties of Peyotl (Lewin 1888). He says in his summary:

It has been proven for the first time that a cactus can possess an extraordinarily high toxicity. It will now be appropriate to elucidate the chemistry of this Anhalonium and then go further with the investigation of other species of Anhalonium. One must, however, also investigate to what purpose and to what extent these Múscal buttons (*Sic*!) are used as stimulants. In a not too distant future I hope to be able to give evidence about this.

For some reason he never did, although he wrote in 1894 a second long article on what was then called "Anhalonium Lewinii and other cactea" (Lewin 1894). By then, however, Arthur Heffter had already started his work on the active principles in the mescaline cactus.

*Arthur Heffter* (1860–1925) was born in Leipzig and representative of the old German school of pharmacologists with a thorough chemical background and a medical training. (Straub 1924, Heubner 1925, Joachimoglu 1960). He worked for some years in agricultural chemistry and then switched to study medicine in Leipzig, at the same time working in the laboratory of R. Böhm. His habilitation took place in 1892, after which he for some time worked under Schmiedeberg in Strassburg. Later he held positions in various universities, Leipzig, Bern, Marburg, and finally in 1908 became Liebreich's successor at the department of pharmacology, University of Berlin, where he held the chair until his death.

Heffter's research activities covered a wide scope of topics. As lecturer he was, however, to say the least, mediocre.

Lewin did not like Heffter and Heffter did not like him. They had very different opinions on many things—this concerned particularly Anhalonium Lewinii (Peyotl) on which Heffter also had done work. It was a priority competition between the two. I don't remember it exactly, but I have the feeling that it was something of the sort. Lewin was more the artist and interested in the social implications of these substances. Heffter was not very verbal, awkward, frankly in the presentation of his material. On the other hand, here was this tremendously stimulating, flamboyant orator Lewin who carried away his audience with his enthusiasm. The atmosphere fused into the most extraordinary experience every time we went to that place to listen to his lecture, and you did that in spite of the fact that you didn't have to—it was enough had you followed only Heffter's lectures. I went to Heffter's lectures, of course, and I was bored. Lewin lectured the first time and I was captured—I went there every time. (Krayer 1963).

Heffter proceeded systematically to find the psychoactive principle in Peyotl by working it up into chemical fractions and testing these on himself in heroic self experiments, much the same way as Albert Hofmann later did with psilocybine. It is psycho-pharmacologically interesting to see what kind of wonderful visions an obviously dry man like Heffter got out of mescaline. Here is his account of the first experiment carried out with pure mescaline in man, in 1897:

*Violet and green spots appear on the paper during reading. When the eyes are kept shut the following visions occur.* At first there are violet and green spots which are not well defined, then come visions of carpet patterns, ribbed vaulting, etc. From time to time single dots with the most brilliant colours float across the field of vision. The phenomena are generally not as clear as those in the two preceding experiments. Later on landscapes, halls, achitectural scenes (*e.g.* pillars decorated with flowers) also appear. The visions can be observed until about 5:30 p.m. Nausea and dizziness are at times very distressing. The appreciation of time is reduced during the first hours of the afternoon. In the evening well-being and appetite are undisturbed and there is no sign of sleeplessness.

*The results described above show that mescaline is exclusively responsible for the major symptoms of peyote (mescal) poisoning.* This applies especially to the unique visions. The experiment performed on 23rd November shows that mescaline hydrochloride, 0.15 g, produces a pattern of symptoms which differs in only a few respects from the one obtained with the drug. Both mescaline and the crude drug produced

bradycardia, pupillary dilatation, headache, dizziness, clumsiness of limb movements, loss of appreciation of time, and, what is most important, characteristic visions.

An attempt to discuss the action of mescaline in detail would not accomplish anything in view of the limited number of experimental data, but physiologists and experimental psychologists should find work in this field rewarding. It is very likely that we are dealing with an action on the central nervous system, although excitation of the peripheral visual apparatus can not be excluded. In this connection I would like to mention that Privatdocent Dr. Krückmann, the first assistant to the Ophthalmological Department in Leipzig, kindly examined me when I carried out the experiment on November 23. He was unable to find any reduction of the visual field either in general or in relation to colours.

At the present moment I would like to leave open the question of whether or not any of the peyote (mescal) alkaloids has a therapeutic value. As far as mescaline is concerned the answer is probably no. Weir-Mitchell and Ellis believe that peyote (mescal) will also become popular amongst cultured people as an intoxicating drug. I think that this is unlikely because the results which I obtained on myself show that the side-effects are so pronounced that they considerably spoil the appreciation of the beautiful visions.

The discoveries of Lewin and Heffter excited a lively interest in the application of the drug in man. Lewin's pupil, Beringer, carried out numerous experiments in man with mescaline.

*Kurt Beringer* (1893–1949) was born in Uehlingen (Schwarzwald) as the son in a peasant family (Jung 1949, Ruffin 1950). In 1911–1914 he studied medicine in Heidelberg, and in 1918 he took part in the war as assistant doctor. In 1921 he became attached to the Heidelberg Psychiatric and Neurological Clinic of Wilmanns, where he stayed for 12 years. In 1928 he took part in an expedition to Mongolia. In 1934 he came to Freiburg, where he stayed for the rest of his life.

Among many papers, Beringer published one regarding hashish intoxication: "Zur Klinik des Haschischrausches" (1932), and two papers on superstition: "Hexen- und Aberglauben im Schwarzwald" (1938), and "Formen des Aberglaubens in Schwarzwald" (1938). These papers bear witness to his interest in ethno-pharmacology. His *magnum opus*, however, is "Der Meskalinrausch" (1927), translated into Spanish but never into English. This book is to mescaline what Moreau's book is to hashish. It gives a clear cut description of the psychic and somatic symptoms, and should be consulted by whoever is interested in the actions of mescaline.

A renewed interest in psychopharmacology was awakened in Germany around 1928. It was at this time that Lewin and others became interested in the properties of the South American vine *Banisteria Caapi*.

On the 13th of February, 1929, Louis Lewin and Paul Schuster gave a paper at the Berlin Medical Association. They described the action of Banisterin prepared from Banisteria and later proved to be identical to harmine in experiments both in animals and man (Lewin and Schuster 1929). At this time they had only 1.2 g of the drug, of which they had given 0.02–0.04 g to 18 cases of Parkinsonism. The side-effects were reported to be a slight nausea, paleness, tremor and bradycardia. A quarter of an hour after the injection the patients had a feeling of being able to move more easily, even in difficult cases with contractures. An improvement was reported of, among other things, swallowing, chewing, speech, eating, movements of the arms and

Beiträge zur Giftkunde
Herausgegeben von
Professor Dr. Louis Lewin

Heft 3

# Banisteria Caapi ein neues Rauschgift und Heilmittel

von

Prof. Dr. Louis Lewin

Mit 2 Karten

1929
Verlag von Georg Stilke / Berlin

walking. They observed a lessening of muscular rigidity. The improvement lasted 2–6 hours, occasionally seven days.

It is remarkable that at this time a film of the action of the drug in three patients was shown. This undoubtedly constitutes the first documentation of the action of monoamineoxidase inhibitors. Lewin pointed out that the drug always affected the ability to move, and seemed inactive psychically. Their demonstration raised a tremendous interest, and the popular press took up the question of this so called "magic drug". Louis Lewin, sick and old at the time, managed to complete a monograph on the subject before he passed away: "Banisteria Caapi, ein neues Rauschgift und Heilmittel" (1929).

In the same year Beringer gave a review of the clinical papers where harmine had been used up till then. He also had occasion to comment upon its pharmacodynamics, and deplored the inaccurate knowledge of how the drug worked. The following sentences are perhaps prophetic:

> First of all it is necessary to find out how it affects the central nervous system; whether this is due to a direct action upon certain centers of the brain or indirectly through the autonomic nervous system through a change of metabolism. Many things speak in favour of the latter explanation.

Kurt Beringer (1893–1949)



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Beringer also commented that new experiments in his clinic showed that the action was not limited to the extrapyramidal system. In his review he pointed out that no differences could be found between banisterine and harmine. It seems at this time that all research workers considered harmine as a new drug for the symptomatic treatment of certain extrapyramidal diseases, and that in many cases it did more than previously known drugs. It proved useful, especially, in the cases of postencephalitic Parkinsonim that were prevalent at the time. Some patients had been on the medication continually for more than a year without decrease in drug effect. The treatment was in no way incompatible with previously used drugs, such as scopolamine.

The most remarkable account from this time is perhaps the description of the self experiments by *L. Halpern* (1930 a and b). Dr. Halpern gave herself doses of up to 0.04 g per os and 0.03 g subcutaneously. The action was sudden, and she had an immediate impression of excitement, with difficulty remaining in one place to continue her intellectual labor. Unrest was the dominant symptom at smaller doses. All actions were felt as if they were more easily done. No euphoria and no clouding of the senses was observed. These symptoms Dr. Halpern explained as stimulation of the cortex:

> In all probability, harmine acts upon the motor system as a central cortico-motor regulation as a stimulating agent acts upon the motor neurons, physiologically to increase excitation. By higher doses, this excitation was increased even in a belligerent way: The author, who normally is not belligerent, has herself experienced this discharge of the motor functions. The subject started a fight with a man in the street, where she was the one who attacked, even though according to the circumstances the prospect for the attacker was very unfavorable.
>
> The consciousness was in no way influenced and in no way abnormal, but the impression was felt as if the consciousness was packed in ether. An increased concentration of observance was felt. When lying on a sofa, the lightness increased to a feeling of a fleeting sensation, and the weight of the body was subjectively less. These clinical observations should be compared to the state of levitation frequently reported to occur with the crude drug *ayahuasca* or *caapi*.

Dr. Halpern continued her studies in Parkinson patients, and pointed out the differences in action between scopolamine and harmine and the duality of Parkinson's disease. As is now well known, the monoamineoxidase inhibiting property of the harmala alkaloid was found as late as 1958 by Udenfriend.

The enthusiasm for the harmala alkaloids vanished temporarily during the thirties, as did much of the interest in ethnopharmacology. A few people, however, worked remotely and undisturbed by the rising tide of synthetic chemicals and the general lack of interest in exotic poisons. Among them was Blasius Paul Reko, more commonly known as Blas Pablo Reko.

*Blas Pablo Reko* (1876–1953) was born in Prerau, Austria (Cook de Leonard 1955–1956). His mother came from Czechoslovakia. Under the influence of his grandfather he decided to study medicine at the University of Vienna, where he graduated in 1901. From the year 1903 he dwelled in America, first in Chicago, in 1907 in Guayaquil Ecuador, and finally in Mexico City. It would seem that he came to Mexico in 1911. He lived no less than 15 years in Oaxaca where he worked professionally for some mining companies. It was during this time that he became interested in the local

flora, especially medicinal plants. His interest in this field was combined with ethnographical and etymological studies. He published many articles in "El México Antiguo" about the flora of Oaxaca. He became interested in astromythology through his interest in ethno-botanics.

Reko said himself that he published his papers only to satisfy his personal taste. This concerns perhaps mostly his numerological work. To the present reader, his ethno-botanical papers seem to be of special importance. He was a good botanical observer and had a large collection of indigenous plants, among them the magic mushroom used by the Mazatecs. His studies were summarized in "Mitobotánica Zapoteca", México, 1945.

In Jan. 1937 Reko wrote the following letter to Henry Wassén, anthropologist and curator of the ethnographical museum, Gothenburg, Sweden:

Jan. 31, 1937.
Gelati 15, Tacubaya, D.F., Mexico

Mr. Henry Wassén
Göteborgs Museum
Göteborg, Sweden
My dear Mr. Wassén:

. . . Apparently you confound me with my cousin Victor A. Reko, the author of "Magische Gifte", a journalistic piece of work, by the way, which you need not to take very seriously, since its author is neither a botanist nor has he any personal experience with the drugs described, most of which he has not even seen and would not recognize if he saw them. It is a cleverly made up *mixtum compositum* of compiled facts and wild inventions of his own fancy, intended for popular consumation.

I have deep interest in the work of Prof. Santesson and would like to come in touch with him, as I can furnish him some very important botanical materials, awaiting the solution of their mystery by a competent chemist. I am forwarding to your direction a sample of the "Piule" seed, together with an article of mine on this topic (published in 1920 and reprinted in El. Mex. Ant. 1934) in the hope that Prof. Santesson might get interested in the problem and conduct some experiments in that line.

Very likely I get this year also specimen of the Teonanacatl, still used for religious rites in some secluded places, but so far never identified . . .

With best regards
Yours truly

Dr. B. P. Reko.

Both the Piule-Ololiuqui and the Teonanacatl did arrive.

*Carl Gustaf Santesson* (1862–1939) definitely has a place in ethno-pharmacology. He was professor of pharmocology in Stockholm from 1895 to 1927, and had studied both with Böhm in Leipzig and with Schmiedeberg in Strassburg. (Liljestrand 1939). These teachers influenced his interest in, among other things, the study of compounds such as strychnine, strophanthine and curare. He published about 20 papers on arrow poisons, collected from all parts of the world. Especially important, however, is the work he carried out after retirement. The Mexican drugs he obtained were investigated and the results published in journals that are not easily found nowadays (Santesson 1937, 1938). Among them were Ololiuqui and Teonanacatl, the magic mushroom of Mexico, subsequently investigated by Wasson, Heim and Hofmann. Santesson did not have much of the latter, but succeeded in carrying out animal experiments with Ololiuqui. It is to the credit of

Santesson that he was able to notice the central action of this drug in animals, and that in his paper he writes:

> In some way the animals had lost their initiative. It seems to me that there is a a partial paralysis of the brain, a kind of narcosis . . . in these animals there is a certain central depression without any other obvious symptoms.

He concludes his paper by saying:

> The drug deserves a thorough investigation which can only be done with a larger supply of material.

With Santesson's papers expire the old pre-World War II activities in the ethno-pharmacologic search for psychoactive drugs. The revival was to come about ten years later.

*Acknowledgment*

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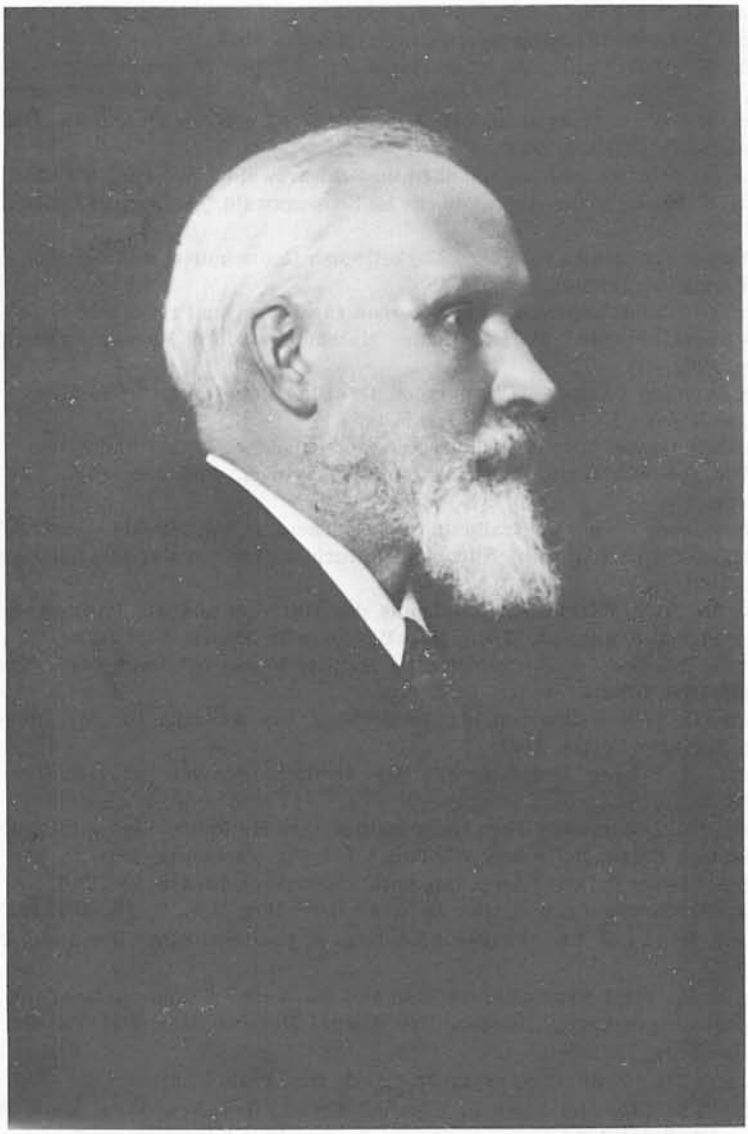
Plasius Paul (Blas Pablo) Reko 1876–1953.



Carl Gustaf Santesson (1862–1939)

## REFERENCES


ASCHENBRANDT, T. "Die physiologische Wirkung und die Bedeutung des Cocain muriat. auf den menschlichen Organismus." Deutsche Medizinische Wochenschrift, pp. 730–732, Dez. 12, 1883.

BARUK, *H.* "La vie et l'oeuvre de Moreau de Tours." Paris, Annales Moreau de Tours. Presses Universitaires de France. 1962.

BENTLEY, W. H. "Erythoxylon Coca in the Opium and Alcohol Habits." Detroit Therapeutic Gazette, pp. 253–254, 1880.

BERINGER, K. "Der Meskalinrausch, seine Geschichte and Erscheinungsweise." Monographien aus dem Gesamtegebiete der Neurologie und Psychiatrie, 49: 35–89, 119–315, 1927.

BERINGER, K. "Uber ein neues, auf das extrapyramidal-motorische System wirkendes Alkaloid (Banisterin)." Der Nervenarzt, 1: 265–275, 1928.

BERINGER, K. "Zur Banisterin- und Harminfrage." Der Nervenarzt, 2: 548–549, 1929 (Sept.)

BERINGER, K., W. v. BAEYER und H. MARX. "Zur Klinik des Haschischrausches." Der Nervenarzt, 5: 337–350, 1932.

BERINGER, K. "Hexen- und Aberglauben im Schwarzwald." Z. Neur., 161: 535, 1938.

BERINGER, K. "Formen des Aberglaubens im Schwarzwald." Arch. f. Psychiatr., 108: 228, 1938.

BIBRA, ERNST FREIHERRN VON. "Die Narkotischen Genussmittel und der Mensch." Nürnberg, Verlag von Wilhelm Schmid, 1855.

COLLET, C.-G. "Candidature de Joseph Moreau (de Tours) au Prix Montyon de l'Académie des Sciences en 1846." Paris, Annales Moreau de Tours. Presses Universitaires de France, 1962.

COOK DE LEONARD CARMEN. "Obituary on Dr. Blas Pablo Reko." "El México Antiguo" Vol. 8, 1955, págs. IX–XIV, México, D.F. 1956.

DRAGENDORFF, GEORG. "Die Heilpflanzen der verschiedenen Völker und Zeiten." Neudruck der Ausgabe Stuttgart, 1898. Antiquariat Fritsch, Postfach 1043, 79/Ulm/ Do. Germany.

FREUD, S. "Ueber Coca." Centralblatt f.d. ges. Therapie, pp. 289–314, 1884 (Juli).

GÜNTHER, S. "Ernst v. Bibra." Nürnberg, Naturhist. Ges. Säcular-Feier 1801–1901. Festschrift 1901.

HALPERN, L. "Der Wirkungsmechanismus des Harmins und die Pathophysiologie der Parkinsonchen Krankheit." Deut. Med. Wochenschr. 56: 651–655, 1930a.

HALPERN, L. "Ueber die Harminwirkung im Selbstversuch." Deut. Med. Wochenschr., 56: 1252–1254, 1930b.

HARTWICH, C. "Die Bedeutung der Entdeckung von Amerika für die Drogenkunde." Berlin, Springer Verlag, 1892.

HARTWICH, C. "Georg Dragendorff." Ber. Deutsch. Pharmaceut. Ges. 7–8: 297–320, 1897–98.

HARTWICH, C. "Die menschlichen Genussmittel, ihre Herkunft, Verbreitung, Geschichte, Anwendung, Bestandteile und Wirkung." Leipzig, Tauchnitz, 1911.

HEFFTER, A. "Ueber Pellote." Arch. exp. Path. Pharmakol. 40: 418–425, 1897.

HEUBNER, W. "Nachruf auf Arthur Heffter." Gew. Hyg. N.F., 2: 101–103, 1925.

HOLMSTEDT, B. and G. LILJESTRAND. "Readings in pharmacology." Pergamon Press Ltd., 1963.

JELLIFFE, S. E. "Emil Kraepelin, the Man and his Work." Transactions of the American Neurological Association. Boston, 57th Annual Meeting, May 1931. Ed. Dr. Theodore H. Weisenburg, Philadelphia.

JOACHIMOGLU, G. "Eröffnungsansprache." Arch. exp. Path. Pharmak. 238: 6–7, 1960.

JONES, E. "The Life and Work of Sigmund Freud." 1–3. New York, Basic Books Inc. Chapter VI, Vol. 1, 1956.

JUNG, R. "Kurt Beringer." Archiv f. Psych. und Zeitschr. Neurol. 183: 293–301, 1949.

KOBERT, R. and A. SOHRT. "Ueber die Wirkung des salzauren Hyoscin." Arch. exp. Path. Pharmak. 22: 396–429, 1887.

KOLLE, K. "Emil Kraepelin (1856–1926)." Stuttgart, Grosse Nervenärzte, Georg Thieme Verlag, 1956. pp. 175–186.

KRAEPELIN, E. "Ueber die Beeinflussung einfacher psychischer Vorgänge durch einige Arzneimittel." Jena, Verlag von Gustav Fischer, 1892.

KRAEPELIN, E. "Wilhelm Wundt." Zeitschrift f. Neurologic und Psychiatrie. pp. 35–362, Vol. 61, 1920.

KRAYER, O. Personal communication, 1963.

LEWIN, L. "Nebenwirkungen der Arzneimittel." Berlin, Pharmakologisch-klin. Handbuch, A. Hirschwald. 1881.

LEWIN, L. "Referat: Pharmakologie und Toxikologie." Berliner Klinischer Wochenschrift, *XXII:* 321–322, 1885.

LEWIN, L. "Ueber Piper Methysticum (KAWA)." Berlin, Verlag von August Hirschwald, 1886.

LEWIN, L. "Ueber Anhalonium Lewinii." Arch. exper. Path. u. Pharmakol. 24: 401–411, 1888.

LEWIN, L.: "Anhalonium Lewinii." The Therapeutic Gazette. *IV*, No. 4, April 16, 1888.

LEWIN, L. "Ueber Areca Catechu, Chavica Betle und das Betelkauen." Monographie. Stuttgart, F. Enke, 1889.

LEWIN, L. "Uber Anhalonium Lewinii und andere Cacteen." Arch. f. exp. Path. u. Pharm. 34: 374–391, 1. u. 2. Heft, 1894.

LEWIN, L. "Die Gifte in der Weltgeschichte." Berlin, J. Springer, 1929.

LEWIN, L. "Heilmittel und Gifte bei Homer." Münch. med. Wschr. 67: 966, 1920.

LEWIN, L. "Phantastica." Die Betäubenden und Erregenden Genussmittel, Für Ärzte und Nichtärzte. Berlin, Georg Stilke, 1924.

LEWIN, L. "Untersuchungen über Banisteria Caapi Spr." Arch. exper. Path. u. Pharmakol. 129: 133–149, 1928.

LEWIN, L. "Banisteria Caapi, ein neues Rauschgift und Heilmittel." Beiträge zur Giftkunde, herausgegeben von Professor Dr. Louis Lewin. Berlin, Verlag von Georg Stilke, 1929.

LEWIN, L. UND P. SCHUSTER. "Ergebnisse von Banisterinversuchen an Kranken." Deut. Med. Wochenschr. 55: 419, 1929. Literatur- und Verhandlungsberichte, 8 März 1929. S. 419, Berlin, Medizinische Gesellschaft, 13.II. 1929.

LEWIN, L. "Phantastica, Narcotic and Stimulating Drugs, Foreword by Bo Holmstedt." London, Routledge & Kegan, 1964.

LILJESTRAND, G., C. G. SANTESSON. "Skandinavisches Archiv für Physiologie." 83. Band. 1 bis 3 Heft. Berlin, Walter de Gruyter & Co., 1939.

MOREAU, J. J. (DE TOURS). "Mémoire sur le traitement des Hallucinations par la Datura Stramonium." Gazette Médicale de Paris IX, 1841, No. 41, 9.10. 1841.

MOREAU, J. J. (DE TOURS). "Mémoire sur le Traitement des Hallucinations par le Datura Stramonium—Suite—Voir" 1° No. 41. Gazette Médicale de Paris IX, 1841. No. 43, 23.10. 1841.

MOREAU, J. "Mémoire sur le traitement des hallucinations par le Datura Stramonium." La Librairie des Sciences Médicales du Just Bouvier, Paris 1841.

MOREAU, J. "Du hachisch et de l'aliénation mentale." Etudes psychologiques. Paris, Librairie de Fortin, Masson et C$^{ie}$, 1845.

PALMER, E. R. "Erythroxylon Coca as an Antidote to the Opium Habit." The Therapeutic Gazette, 1, new series, p. 172, 1880. Vol. IV—whole series.

REKO, B. P. "Mitobotanica Zapoteca." Tacubaya, D. F., 1945.

REKO,, V. A. "Magische Gifte." Rausche- und Betäubungsmittel der Neuen Welt. Stuttgart, Ferdinand Enke Verlag, 1949.

RITTI, M. "Eloge de J. Moreau (de Tours)." Annales Médico-Psychologiques, Paris 1887. 7$^{ème}$ Serie, Tome Sixième, 45th year. Paris, G. Masson.

RUFFIN, H. "Kurt Beringer." Deutsche Zeitschrift für Nervenheilkunde, 164: 199–208. 1950.

SANTESSON, C. G. "Notiz über Piule, eine mexikanische Rauschdroge." Ethnological Studies, 4, 1937.

SANTESSON, C. G. "Piule, eine mexikanische Rauschdroge." Archiv der Pharmazie und Berichte der deutschen Pharmazeutischen Gesellschaft. Berlin W 35, Verlag Chemie GMBH, 1937.

SANTESSON, C. G. "Noch eine Mexikanische 'Piule'-Droge Semina Rynchosiae Phaseoloidis DC." Ethnological Studies, 6, 1938.

SANTESSON, C. G. "Einige mexikanische Rauschdrogen." Archiv für Botanik—K. Sv. Vetenskapsakad. 29 A, No. 12, 1939.

SCHMIEDEBERG, O. "Uber die Pharmaka in der Ilias und Odyssee." Schriften d. wiss. Gesellsch. Strassburg. Strassburg, 1918, Heft 36.

Schröter, C. "Prof. Dr. C. Hartwich." Schweizerische Apotheker-Zeitung No. 10, Jahrg. 55, Zürich, March 8, 1917.
Sieburg, E. "Rudolf Kobert." Ber. Dtsch. Pharm. Ges. 29: 285–299, 1919.
Solomon, D., *Ed.* The Marihuana Papers, New York. The Bobbs-Merrill Company, Inc., 1966.
Straub, W. "Arthur Heffter." Arch. exp. Path. Pharmakol. 105: 1–4, 1924.

# The Place of Ethnobotany in the Ethnopharmacologic Search for Psychotomimetic Drugs

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## Introduction

The very descriptive word *ethnobotany* has been defined in sundry ways in the 70 years since it was created and first used by Harshberger (*23*). Although Harshberger indicated how ethnobotanical investigation could be integrated into overall research, he failed to offer a definition of his new term.

Years earlier, in 1874, Powers (*38*) had used the term *aboriginal botany* to refer to a study of "all the forms of the vegetable world which the aborigines used for medicine, food, textile, fabrics, ornaments, etc."

It was, apparently, not until 1916 that a truly broad concept emerged that went beyond mere identification and cataloguing of plants used by primitive peoples. This broad definition of the term *ethnobotany*, now rather widely held, was promulgated by Robbins, Harrington and Freire-Marreco (*42*), and, in effect, attributes to this discipline a study and evaluation of the knowledge of all phases of plant life amongst primitive societies, and of the effects of the vegetal environment upon the life, customs, beliefs and history of the peoples of such societies.

Jones (*27*) has offered the following precise definition: "the study of the interrelations of primitive man and plants." It is interesting to note that Jones and others (*9*) prefer to restrict *ethnobotany* to man in primitive states of culture. While this premise may and probably does almost always obtain, there is really no reason to circumscribe the term in this way. Vestal and Schultes (*62*) looked upon ethnobotany as a part of *economic botany*. Since I do not hold that ethnobotany need be limited exclusively to man in primitive society, my own definition (*46*) circumscribes *ethnobotany* as "a study of the relationships between man and his ambient vegetation."

# Ethnobotany and the Search for New Drugs

It is natural that an interdisciplinary field such as ethnobotany be replete with problems for investigation. These are and have been not only numerous but varied as well, and the burgeoning nomenclature bears witness to this variation. In recent years, such terms as *archaeoethnobotany*, *ethnomycology*, *ethnoecology* and *ethnopharmacology* have been proposed and have come into use.

Nowhere perhaps have the potentialities of ethnobotanical investigation been more scintillating than in the search for new psychotomimetic drugs (*57*). These potentialities have been realized in the case of a number of new and previously known hallucinogens that are now relatively well understood: the narcotic mushrooms and morning glories of Mexico; the ayahuasca-caapi-yajé complex of South America; the intoxicating snuffs of the Orinoco and Amazon basins. They remain to tantalise us, however, in the case of several narcotics known vaguely from common names or from sketchy reports of travellers and missionaries: several South American snuffs; the marari of lowland Bolivia; an intoxicating "tree-fungus" of the Yurimagua Indians of eastern Peru; the yurema root infusion of the Pankararú of Brazil; the magic woi of the Yekwana of southern Venezuela. Furthermore, they challenge us to find, through ethnobotanical avenues, new psychotropic plants that most certainly are still in use, but which have never been seen nor reported by the prying inquisitiveness of man outside of the culture that employs the narcotics.

I cannot help thinking that Linneaus himself must have had ethnobotany in mind, at least in part, when he in 1754 wrote in a museum catalogue the following philosophy: "Man, ever desirous of knowledge, has already explored many things; but more and greater still remain concealed; perhaps reserved for distant generations, who shall . . . make many discoveries for the pleasure and convenience of life. Prosperity shall see its increasing Musuems, and the knowledge of the Divine Wisdom, flourish together; and at the same time all the practical sciences . . . shall be enriched; for we cannot avoid thinking, that what we know of the Divine works are much fewer than those of which we are ignorant."

In the search for new hallucinogens, we have much to do and little time in which to do it. Peoples in primitive societies, because they live most intimately with their immediate vegetational environment, *do* possess a valuable understanding of the properties of plants, even though their knowledge of plants has sometimes been optimistically exaggerated by both lay enthusiasts and ethnopharmacological zealots. The aborigines' knowledge and understanding, furthermore, is probably everywhere far from complete. It, therefore, behooves all of us interested in a search for new psychotomimetic drugs to carry out our investigations along several avenues of approach, not following the ethnobotanical avenue to the exclusion of others (*52*). It is, however, the place of ethnobotany in this search that I shall here discuss, and I want merely, at the very start, to put it thus into proper perspective.

Civilization is closing in on many, if not on most, parts of the world still sacred to the less advanced cultures. It has long been pressing in, but its pace is now accelerated as the result of geographically extensive wars, extended commercial interests, increased missionary activity, widening tourism. Modern methods of travel and penetration have given civilisation the tools for this accomplishment. Road-building programmes in Latin America provide us with but one example of how fast this penetration of the hinterlands is proceeding.

Our great concern lies in the progressive divorcement of man in primitive societies from dependence upon his immediate environment. I have often stated that perhaps the greatest enemy or, at least, competitor, of ethnopharmachological research is the arrival and cheap availability of the aspirin pill. More than once this has initiated an astonishingly rapid disintegration of native medical lore. I doubt that social scientists are fully aware of the rapidity of this disintegration, but the ethnobotanist cannot fail to see it. That the aspirin (meaning, of course, modern medicines in general) may be more beneficial than herbs and magic is not ours to consider here. What does interest us academically and practically is how to salvage some of the medicobotanical lore of primitive cultures before it shall have been forever entombed with the culture that gave it birth (*51*).

In considering the ethnobotanical approach in our search for new drugs we must constantly bear in mind the widespread exaggeration of the usefulness of ethnobotanical data. Although we cannot afford to pre-judge reports of aboriginal uses of plants simply because they seem to fall beyond the limits of credence, we must nevertheless ever keep in mind that there is no reason to presume that, because man in primitive living does have knowledge as yet unknown to us, he may possess anything more than a limited intuition into the properties of plants.

Although now at long last there is more agreement concerning the larger aims of ethnopharmacological investigations, the field has suffered—as has ethnobotany in general—from lack of orientation and integration. Ethnobotanical research has often, of necessity, been done as a sideline by botanists untrained in ethnology; by anthropologists lacking any knowledge of biology; or even by laymen, dedicated enough, but devoid of preparation in both biology and anthropology. And in more recent years, the training commensurate with thorough ethnobotanical investigations has enlarged its scope to include some familiarity with topics such as chemotaxonomy, which once would never have been considered germane. As a result of this checkered history, ethnobotanical research, its purposes and its potentialities has too often suffered from smug depreciation at the hands of specialists in disciplines that have been academically more clearly delimited.

The potentialities of ethnobotanical research into folk medicine are far too extensive for proper treatment in a short lecture, but certain salient points may and should be made, and these points may be supported by specific examples. In delving into the medicine of primitive societies, we must never lose sight of the vast difference between "medicine" in our sense and that in primitive societies. In almost all, if not all, primitive cultures, the concept

of sickness and even of death from natural causes is unknown or incomprehensible. Instead—and we must here over-simplify the problem for our purposes—supernatural spirits or forces of evil work in sundry ways to bring about the impairment of health or cessation of life. We should realize that hexing and witchcraft were widely accepted as recently as three centuries ago in what was, in many respects, the advanced culture of Europe. Amongst the members of primitive cultures to-day, treatment usually comprises various kinds of exorcism; and diagnosis, and often treatment itself, must be carried out through communication with the spirit or supernatural world. Many ways of communicating have been developed, but the employment of vision-producing narcotics or hallucinogens of plant origin seems to have been widespread in both time and space, and to have occurred in many wholly unrelated cultures.

We do not know exactly how many species of plants there are. There may be as many as 800,000. Estimates for the Angiosperms alone vary from the usually cited 200,000 to about half a million (*55*).

It is interesting to compare the number of species of plants that man has found valuable for nutrition with those that he has employed to induce hallucinations. Of this vast assemblage of Angiosperms, only about 3000 are known to have been used directly as human food. The number of species that actually feed mankind is, however, very small. Only about 150 Angiosperms are important enough as foods to enter the world's commerce. Of these, only 12 or 13 stand, in effect, between the world's population and starvation, and these dozen or so plants are all cultivated species (*55*).

We find, likewise, that the number of species providing man with narcotic agents is very small. Between four and five thousand species are now known to be alkaloidal,[1] and we must realise that constituents other than alkaloids—glycosides, resins, essential oils and others—may also be responsible for narcotic activity. Probably no more than 60 species, including Cryptogams and Phanerogams, are employed in primitive and advanced cultures for their intoxicating effects. Of these, only about 20 may be considered of major importance. What is even more significant is that so few—coca, opium poppy, hemp, tobacco—are numbered amongst the world's commercially important cultivated plants. Four of these five, if not all five, species are cultigens, unknown in the wild state. This bespeaks long association with man and his agricultural practices (*55*).

It may likewise be of significance that, whether because of cultural differences or floristic peculiarities or for some other as yet unappreciated reason, the New World is much richer in narcotic plants than the Old. These statistics, naturally, relate merely to those plants the narcotic properties of which man has discovered in his trial and error experimentation during the course of human history. The longer I consider this question, the more I am convinced that there may exist in the world's flora an appreciable number of such plants not yet uncovered by the experimenting natives and still to be found by the enquiring phytochemist. This is an aspect of the problem in which ethnobotanical approaches cannot help, but even though our ethno-

[1] R. F. Raffauf, personal communication.

botanical research into narcotic plants is still embryonic, we know enough to realise that both the Old and the New Worlds offer rich fields for potential discoveries.

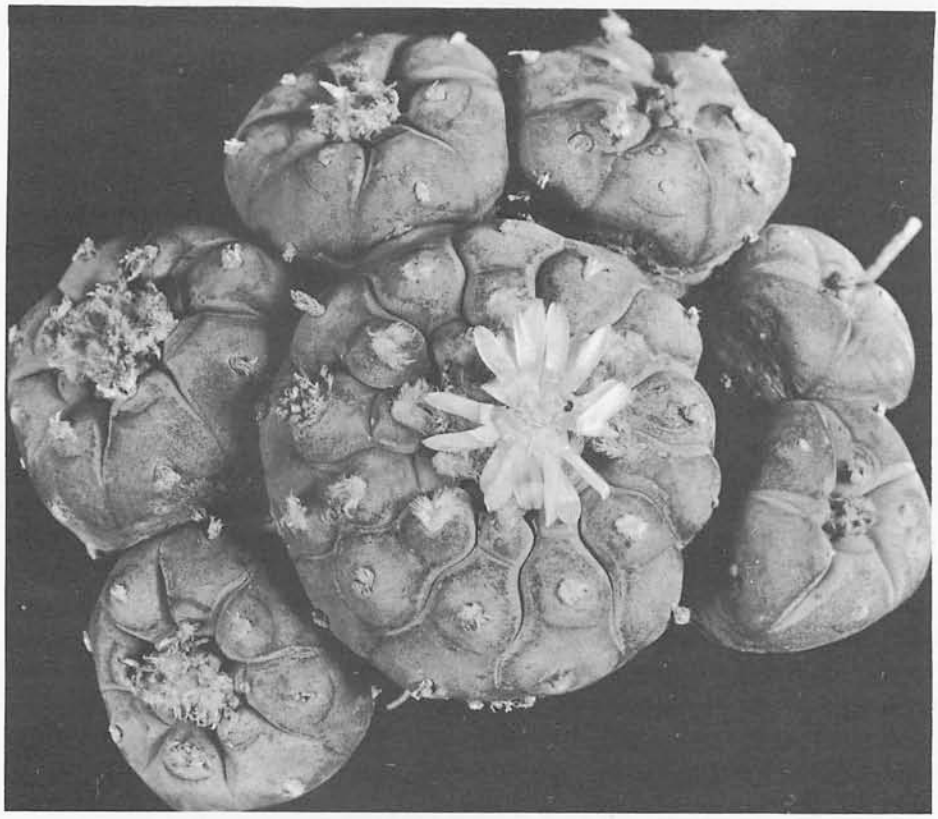
Where do some of the ethnopharmacological problems in connexion with our search for new and interesting psychotomimetic agents lie? Let us contemplate some of the hints that might guide such research in the future.

Geographically, the problems may be found almost throughout the globe, concentrated, to be sure, in areas where primitive societies still hold sway unmolested by the inroads of modern civilisation.

## Consideration of Pressing Problems

Some of the most interesting enigmas lurk in the desert stretches of northern Mexico, where what we might term the "prototype" of the New World hallucinogens—peyote or *Lophophora Williamsii*—has long been the centre of religious and curative rites in the Tarahumare and Huichol country. Peyote, of course, is well known from many aspects, and 13 alkaloids have thus far been isolated from it (*33*). The explorer Carl Lumholtz (*32*) mentioned, however, other narcotic cactus plants, some of which are as yet not even botanically identified. "High mental qualities," he wrote, "are ascribed especially to all species of *Mammilaria* and *Echinocactus*, small cacti, for which a regular cult is instituted. The Tarahumares designate several as *hikuli*, though the name belongs properly only to the kind most commonly used by them . . . The principal kinds are . . . *Lophophora Williamsii*. The Tarahumares speak of them as the superior *hikuli* (hikuli wanamé) . . . Besides hikuli wanamé . . . , the Tarahumares know and worship the following varieties: 1. *Mulato* (*Mammilari micromeris*). This is believed to make the eyes large and clear to see sorcerers, to prolong life and to give speed to the runners. 2. *Rosapara*. This is only a more advanced vegetative stage of the preceding species—though it looks quite different, being white and spiny. 3. *Sunami*. (*Mammilari fissurata*). It is rare, but it is believed to be even more powerful than wanamé and is used in the same way as the latter; the drink produced from it is also strongly intoxicating. . . . 4. *Hikuli walula saeliami*. This is the greatest of all, and the name means 'hikuli great authority.' It is extremely rare among the Tahahumares, and I have not seen any specimen of it, but it was described to me as growing in clusters of from eight to twelve inches in diameter, resembling wanamé with many young ones around it. . . . All these various species are considered good, as coming from Tata Dios, and well disposed toward the people. But there are some kinds of hikuli believed to come from the Devil. One of these, with long white spines, is called *ocoyome*. It is very rarely used, and only for evil purposes."

Several of these narcotic hukuli plants are still unidentified. They are obviously all cactuses. Several species of *Mammilaria* have yielded alkaloids of undetermined identity, but the genus, which is not far removed from *Lophophora*, might be expected to contain active principles. The same may



Flowering head of the peyote cactus, *Lophophora Williamsii*, the "prototype" of the New World hallucinogens. Photograph by R. E. Schultes.

be said of *Echinocactus*. In this connexion, it is well known that in Mexico a number of species in seven other genera of the *Cactaceae*—*Ariocarpus*, *Astrophytum*, *Aztekium*, *Dolichothele*, *Obregonia*, *Pelecyphora* and *Solisia*—are popularly classed as peyote, perhaps because they bear some resemblance to the true peyote, *Lophophora*, or perhaps because they have similar toxic effects and may be employed with *Lophophora* or as a substitute for it (*45*). There is much, indeed, that needs ethnobotanical clarification in this whole picture; and it would seem to be a promising problem (*16*). All that we know is that, of these last seven genera mentioned, three—*Ariocarpus*, *Astrophytum* and *Dolichothele*—have yielded alkaloids (*65*).

Witch doctors in northern Peru (in Piura, Lambayeque and La Libertad) prepare an hallucinogenic drink called *cimora* from at least six plants (*13*). Several of the ingredients are said to be members of the *Cactaceae*. There is indirect evidence of great age for the use of this narcotic drink which is concerned with moon rites of the region. It is taken for therapeutic effects, for diagnosis and divination, and to make oneself owner of another's identity. This intoxicating brew must be potent if the plant ingredients, identified apparently without voucher specimens, are correctly indicated. The principal ingredient is said to be *San Pedro*, a cactus, *Trichocereus Pachanoi*, from

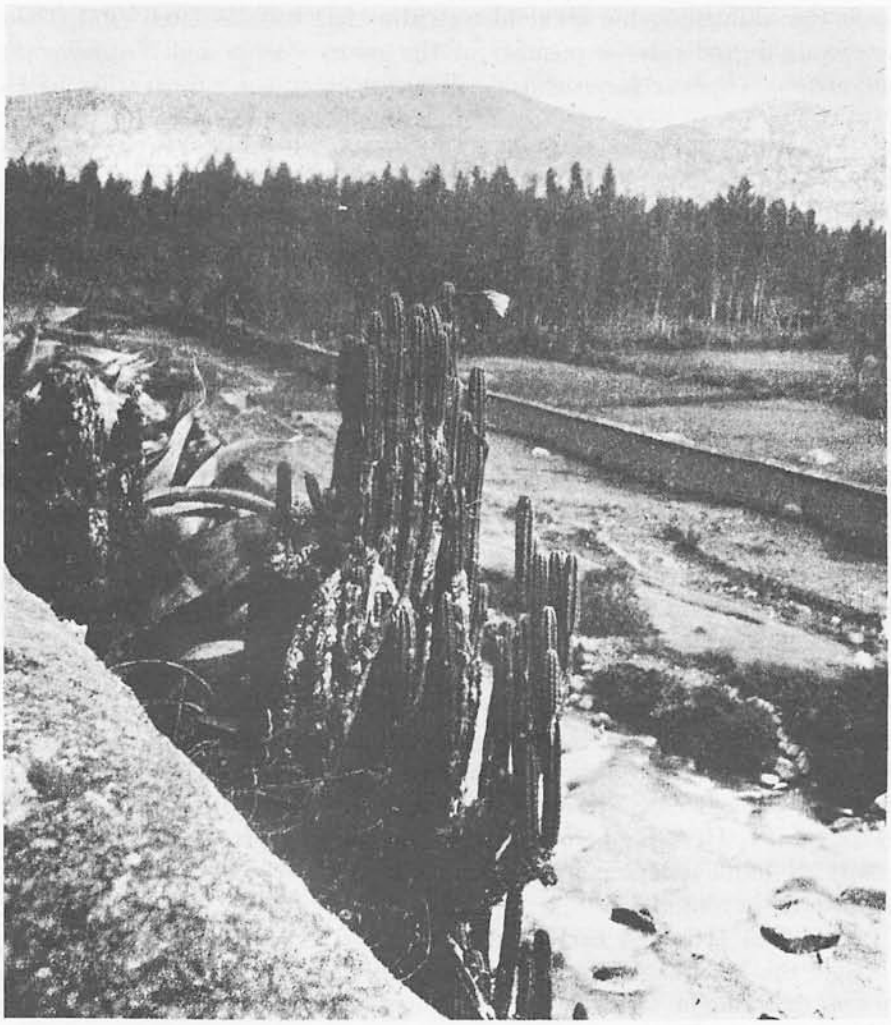
which the hallucinogenic alkaloid mescaline has been isolated (*21*). Other cactaceous ingredients—a member of the genus *Cactus* and *Neoraimondia macrostibas* (*Cereus macrostibas*)—likewise enter the preparation of the brew. A further addition is the campanulaceous *Isotoma longiflora*, known to contain the alkaloid lobeline. *Pedilanthus titimaloides* of the Euphorbiaceae is said also to be added. *Datura Stramonium* is furthermore cited as one of the plants in the formula, and this alone, of course, would provide a potent vision-producing base for the drink. With the apparent lack of voucher specimens, however, there is no way at present to verify the determination of these ingredients. An indication that there may be discrepancies in the determinations is that the chief ingredient was at first erroneously determined as *Opuntica cylindrica* (*12*). It has recently, however, been shown, on the basis of botanical collections, to represent *Trichocereus Pachanoi*, and has been ethnobotanically indicated as being a "magic and dangerous" plant (*18*). Whether or not the common name *San Pedro* applies to both *Opuntia cylindrica* and to *Trichocereus Pachanoi*, very dissimilar plants, has not been verified.

This problem is further complicated by a recent citation of the "magic and dangerous" *timora* of Huancabamba, Peru, as a species of *Iresine* of the *Amaranthaceae* (*18*). Is this *timora* perhaps the same word as *cimora*? We cannot tell at the present time. While several amaranthaceous genera contain alkaloids, no such constituents have been reported from *Iresine*. It is of interest to point out, however, that some of the Indians of southern Colombia are said to employ *Iresine* as an admixture in preparing their strongly hallucinogenic yajé drink (*Banisteriopsis* spp.) to increase its psychotomimetic potency (*49*). Here is one of the most challenging problems in the ethnobotany of hallucinogenic plants, and one which would not be difficult to investigate thoroughly.

In the late 17th and early 18th Centuries, Jesuit missionaries working amongst the Yurimagua Indians in the uppermost Amazon basin found the natives drinking a strongly intoxicating beverage prepared from a "tree fungus" ". . . the Yurimaguas mix mushrooms that grow on fallen trees with a kind of reddish film that is found usually attached to rotting trunks. This film is very hot to the taste. No person who drinks this brew fails to fall under its effects after three draughts of it, since it is so strong or, more correctly, so toxic" (*10*). Field work in the area has, up to the present time, not yet disclosed any practice of this kind, but it is a culture trait little likely to disappear spontaneously, at least without leaving traces, and the region is still inhabited by tribes in relatively primitive conditions of culture. It has been tentatively suggested that the tree fungus might be the known hallucinogenic *Psilocybe yungensis*,[2] but what might be the reddish film? Here certainly is a most challenging problem in ethnopharmacology.

The Mojo Indians, an Arawakan tribe living in eastern Bolivia, employ an unknown narcotic called *marari* (*34*). It has been reported that "whenever . . . the medicine-men had to interview the spirits, they drank a decoction prepared from a plant called marari, similar to our verbena, which caused

[2] R. G. Wasson, personal communication.



*Trichocereus Pachanoi* growing on the side of a cliff on the outskirts of Cuenca, Ecuador. Photograph by G. Rose. From Britton & Rose: *The Cactaceae* 2 (1920) fig. 196.

for 24 hours a general condition of excitement characterized by insomnia and pain" (*34*). According to reports, the medicine men try to avoid drinking marari whenever they "could operate without the narcotic." This may be interpreted as an indication of great potency or toxicity of the drug. By likening marari to "our verbena," the French ethnologist Métraux undoubtedly meant *Verbena officinalis*, a well known folk medicine of Europe. The marari might well represent one of the many South American verbenaceous species, but only direct field observation can clear up this enigma.

Oftentimes, no clear distinction has been made between stimulants and narcotics in the writings of early missionaries and other travellers. *Guayusa* is a case in point. Reports of a strongly stimulating plant of the westernmost Amazon, widely known as guayusa, place its use in the westernmost Amazon

of Colombia, Ecuador and Peru. The earliest report of guayusa dates from 1682 and comprises a missionary reference that pointed to a use surrounded by superstition in the region of the upper Marañon in Peru.[3] Amongst the several references to guayusa, perhaps the most important is that of Richard Spruce, who reported it to be a species of *Ilex* allied to *I. paraguariensis* "but with much larger leaves" and to be a tonic which, in strong infusions such as those prepared by the Jibaros, may be "positively emetic" (*59*).

The recent writings of Karsten (*28*) seem to indicate that guayusa may have narcotic properties as well, for he states that "just as the Jibaros take certain narcotic drinks when they are preparing for war, to see whether they will be lucky or not in the undertaking, so they also understand a kind of divination in regard to hunting. The drink then used is prepared of the guayusa (*Ilex* sp.), the leaves of which are boiled in water for the purpose. The guayusa is not a real narcotic but a tonic, to which the Indians ascribe magical purifying effects. The Jibaros, however, seem to believe that the drink produces dreams of divinatory significance or, more strictly speaking, what they call 'small dreams,' especially such as have reference to hunting." Other "supernatural virtues" or magical powers are ascribed to guayusa by the Jibaros.

Even though guayusa may not belong strictly to the category of psychotomimetic plants, it would be advantageous to know more concerning its curious effects—these "little dreams"—that the Jibaros ascribe to the infusion. Are these effects wholly imaginary, or may perhaps some other plant be occasionally boiled with the guayusa when the "little dreams" are experienced?

And then, what precisely is guayusa? Spruce noted that it was an *Ilex* and reported seeing a group of guayusa trees . . . over 300 years old . . . "that were not unlike old holly trees in England, except that the shining leaves were much larger, thinner and unarmed." A collection of *Ilex* from eastern Peru was described as *Ilex Guayusa* by Loessener, but it is sterile. Sterile material of a guayusa was gathered recently by one of my students in eastern Peru and represents undoubtedly an *Ilex*. It is not wholly improbable that this widely disseminated vernacular name may refer to a number of different plants with marked physiological action. The guayusa problem is certainly one that might occupy the attention of ethnobotanists interested in native narcotics and stimulants. It is rather disquieting that even the identity of such a plant should, after some three centuries, still be uncertain.

Another interesting reference concerning a plant with marked physiological activity which may or may not be narcotic in character reports the use by the Kakusi Indians of British Guiana of "peppers as a stimulant and excitant" (*43*). Even though the "peppers" were definitely identified as belonging to *Capsicum*, this report should be carefully checked by further field observations.

There is an interesting and very potent narcotic drink used in eastern Brazil that merits much more investigation. The Kariri (*30*) and Pankararú (*31*) Indians along the São Francisco River in Pernambuco have an ancient

[3] V. Patiño, personal communication.



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cult, still practiced, connected with a root known as *yurema*. Groups of warriors or strong young men are given a gourdful of the yurema root infusion by an elderly chieftain. With bowed heads, the celebrants see "glorious visions of the spirit land, with flowers and birds. They might catch a glimpse of the clashing rocks that destroy the souls of the dead journeying to their goal, or see the Thunderbird shooting lightning from a huge tuft on his head and producing claps of thunder by running about." The yurema rite was formerly much more widespread than at present, for it is known to have been practiced by at least three other tribes (the Guegue, Acroa and Pimenteira) of the general region. The ceremony exists also amongst the Tusha Indians, neighbours of the Pancararús.

There is reason to believe that the yurema-drink is the same narcotic as the intoxicating beverage of the Pankararús which has been reported under the Portuguese name *vinho de Jurema*. This drink is reportedly prepared from the roots of the leguminous tree *Mimosa hostilis* (*20*). Chemically, this plant is extremely interesting because of its close relationship to *Anadenanthera peregrina*, from the seeds of which the hallucinogenic yopo snuff of the Orinoco River basin is prepared. In 1946, an alkaloid was isolated from the bark of the roots of *Mimosa hostilis* (*20*) and was called nigerine, but recent chemical investigation has established the identity of nigerine and N, N-dimethyltryptamine, the same constituent found in yopo seeds from *Anadenanthera peregrina* (*36*).

In a remote tributary of the Apaporis River in Amazonian Colombia, the Peritomé-Tanimukas make use of an as yet unidentified plant to prepare a vision-producing drink employed in the adolescent initiation rites of boys (*57*). It is taken much as is the well known yajé or caapi of the same region prepared from *Banisteriopsis Caapi*, but the Tanimukas, who employ also this malpighiaceous vine, are quick to distinguish the two. The bark of the root of an extensive lacticiferous forest liana, without the admixture of any other plant material, is subjected to long boiling in order to prepare the drink. I was not able to see the vine nor to take the drug during my short stay amongst the Tanimukas, but all information pursuant to my questioning was constant. This liana, reported to be rich in latex, might represent an apocynaceous species, but the problem cannot be solved until extended field work is carried out with these isolated Indians.

There is evidence that natives of the New World have found psychotropic activity in plants introduced from the Old World. It has, for example, recently been reported that Yaquí medicine men from northern Mexico employ *Genista canariensis*, the genista of florists, for the purpose of inducing hallucinations (*17*), a property that has been experimentally substantiated. The genus *Genista* and the closely related *Cytisus*, in which *Genista canariensis* is sometimes included, are extremely rich in alkaloids. Cytisine, an alkaloid that formed the basis for the former hallucinogenic use amongst some North American Plains Indians of seeds of the leguminous *Sophora secundiflora* (*53*), has been isolated from leaves and beans of *Genista canariensis*.

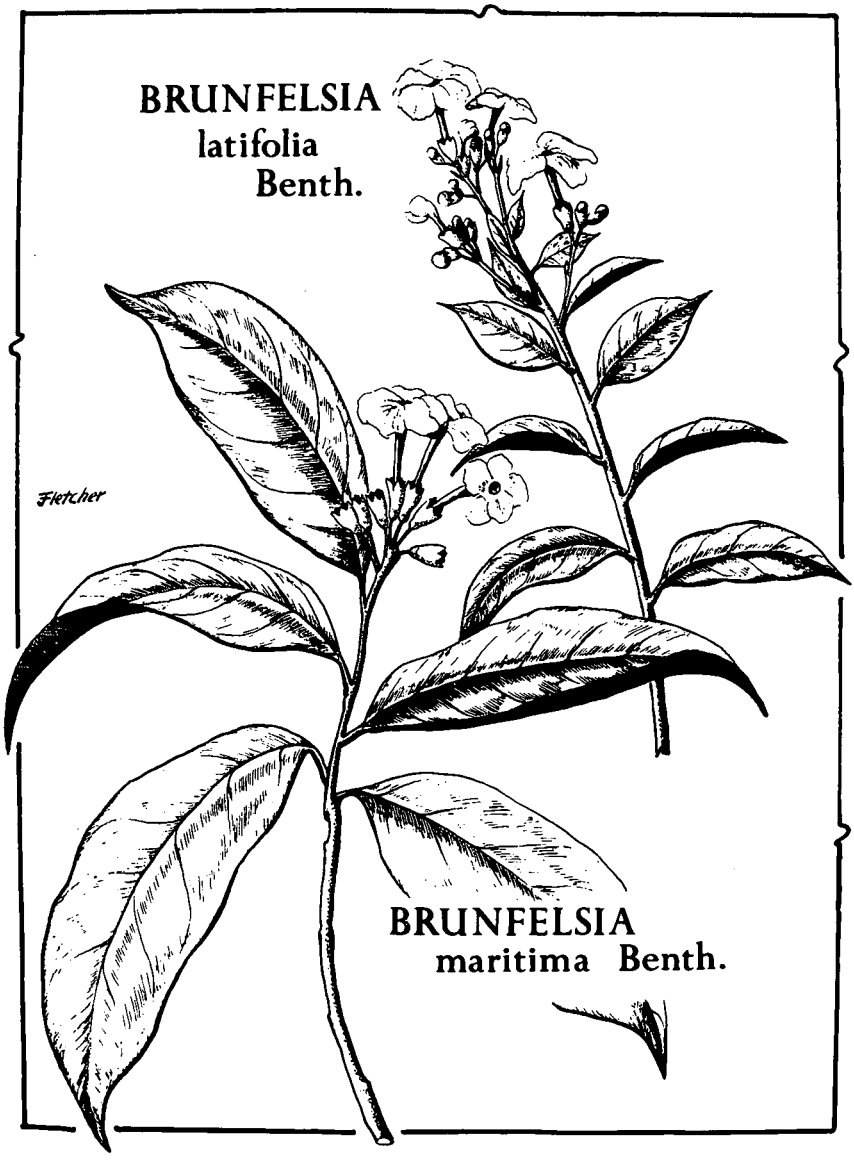
Other Old World plants that may have hallucinogenic uses amongst New World natives are several species of the labiate genus *Coleus*. Concurrent to the recent discovery by Wasson in the Mazatec Indian country of Oaxaca, Mexico, of the utilization of the leaves of *Salvia divinorum* as a narcotic (*63*), a similar employment of *Coleus pumila* and *C. Blumei*, both introductions from the Old World, was reported. The hallucinogenic effects of the *Salvia* have been experimentally substantiated, and it has been postulated that perhaps this plant, native to Mexico, might represent the ancient *pipiltzintzintli* of the Aztecs. Chemical examination of *Salvia divinorum* has not as yet disclosed a psychotropic constituent, and analysis of these two species of

*Coleus*, at least on the basis of the reputedly hallucinogenic material growing in southern Mexico, has apparently not been carried out. Other species of *Coleus* that are employed in the Old World as folk medicines have, however, been studied chemically, but no hallucinogenic substances have been reported from them. There is in Turkestan, nevertheless, another reputedly intoxicating mint—*Lagochilus inebrians* (*7*). The leaves are crushed and mixed with honey or sugar for ingestion. A physiologically active crystalline principle, lagochiline—a polyhydric alcohol—has been reported from this species (*1*, *61*).

Without any doubt, one of the most fascinating and promising possibilities of adding to our list of hallucinogens has recently been brought to my attention by one of my former students, Prof. Melvin L. Bristol of the University of Hawaii, who spent more than a year in ethnobotanical field work in southern Colombia. It concerns the solanaceous genus *Brunfelsia* in South America (*57*). A tropical New World genus of about 25 species, *Brunfelsia* plays an important role in aboriginal folk medicine in equatorial America. The fluid extract of one species—*Brunfelsia Hopeana*—is employed pharmaceutically in Brazil as an antidiuretic and antirheumatic. Although atropine-type alkaloids—brunfelsine, manacine and mandragorine—have been reported for *Brunfelsia Hopeana*, little if anything is known of the chemistry of other species (*65*). The aglycone scopoletine, a coumarine derivative found in a number of plant families, has also been isolated from *Brunfelsia*. Consequently, we know that this genus does possess active constituents of very definite physiological activity.

Evidence for the narcotic use of *Brunfelsia* is quite real, but it is not yet corroborated by a good body of field observation. Herbarium records are very helpful in this instance. There are two collections that indicate the use of *Brunfelsia* as a narcotic. One—*Tessmann 3243* from eastern Peru—reports simply that the plant is "a narcotic." The other—*Bristol 1364* from the Colombia Putumayo—states that the plant is a narcotic and medicinal cultivated in Kofán Indian houseyards. Other collections of this genus from Bolivia, Brazil, Colombia, Eucador and Peru indicate a broad spectrum of therapeutic uses ranging from treatment of "yellow fever" to snake bite. Its commonest use in folk medicine seems to be to relieve "rheumatism." Several collections indicate that *Brunfelsia* is toxic. In fact, in the vicinity of Leticia, a Colombian town on the Amazon River, *Brunfelsia maritima* (*Schultes, Raffauf & Soejarto 24108*), escaped from cultivation at an abandoned Indian site on the upper Amazon in Colombia, has been responsible for serious cattle poisoning. The plant is here referred to as *sanango*, which seems to be a somewhat general term applied in the upper Amazon to several plants with medicinal or toxic properties.

The Kofán Indians of the westernmost part of the Amazon of Colombia and Ecuador grow *Brunfelsia* extensively as an ornamental. They know the plant as *borrachera*, a vernacular term in Spanish applied to almost any kind of intoxicating plant, especially to the species of tree-Daturas, in Colombia. The Kofán indicate that they become very cold after taking an infusion of the scraped bark of *Brunfelsia*. This characteristic of the in-




toxication has been reported on herbarium labels of collections from Peru, and may well explain the wide use of the plant as a supposed febrifuge. One of my graduate students, Mr. Homer V. Pinkley, who has spent a year living with the Kofán, reports these medicinal applications of *Brunfelsia*, but found no direct evidence that could be interpreted as indicative of its use as an hallucinogen.

Intensive field work may still uncover a former use of *Brunfelsia* as an hallucinogenic agent in the western Amazon or on the eastern slopes of the Andes of Colombia, Eucador or Peru. But *Brunfelsia* is a genus that needs botanical revision and phytochemical investigation. A thorough study could

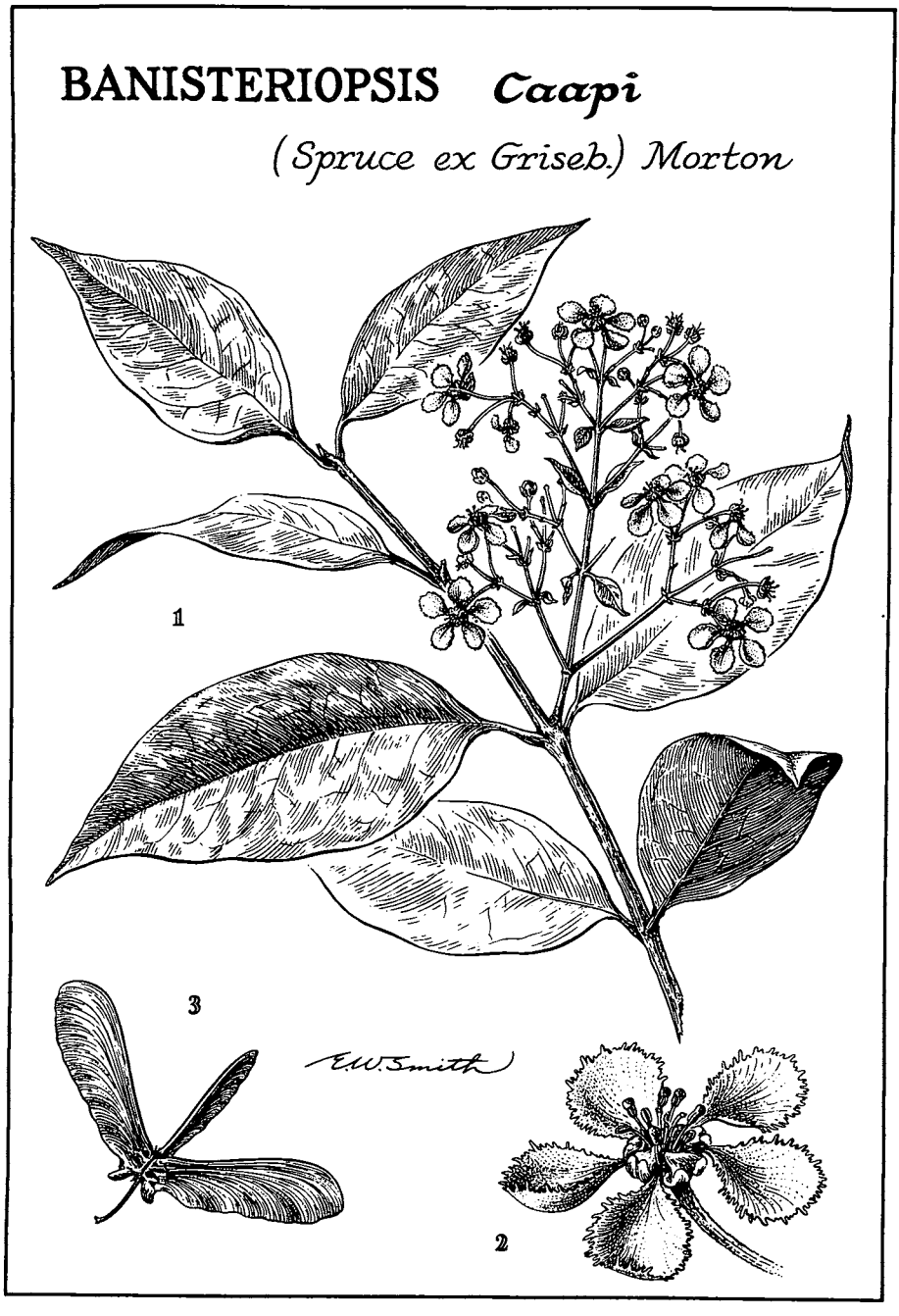
Flowering branch of *Brunfelsia maritima*, a medicinal and ornamental plant common in the western Amazon of Colombia and Ecuador. Río Aguarico, Ecuador. Photograph by H. V. Pinkley.

reward us with a clearer picture of this possible aboriginal American hallucinogen. Might its use as an hallucinogen have disappeared? We should realise that the disappearance of the use of a plant in a given area is not unknown. A century ago, for example, the sapindaceous caffeine-stimulant guaraná, *Paullinia Cupana*, was reported by Spruce as cultivated all the way up the Rio Negro of Amazonian Brazil and into southern Venezuela (*59*). I found that it has now almost completely vanished from cultivation in this region, and the use of the vine as the source of a stimulant is unknown along the Rio Negro at the present time. Might not the same fate have happened to the solanaceous genus *Brunfelsia?*

One of the most interesting enigmas in South America concerns the question of whether or not the apocynaceous genus *Prestonia* is or has ever been used narcotically. The literature is rich in reports, most of them uncritical and unfounded in field work, that *Prestonia amazonica* (*Haemadictyon amazonicum*) is the source of the hallucinogen known as *yajé*. All manner of confusion has attended this information. Although we believe that we

are warranted in asserting that *Prestonia* is not employed as a narcotic, there remains enough doubt to justify further field investigation (*58*). What, precisely, is the problem?

It is well established that a strongly hallucinogenic drink known variously, according to geographic area, as *ayahuasca, caapi and yajé* is prepared from one or more species of the malpighiaceous genus *Banisteriopsis*. Spruce in



1851 first identified the botanical source of this narcotic beverage. He discovered the natives along the upper Rio Negro in Brazil preparing it from a liana which he called *Banisteria Caapi.* It is now more appropriately accommodated in a related genus and bears the name *Banisteriopsis Caapi.* Several years later, he quite correctly identified a similar drink of the western Amazon of Ecuador, where it was called *ayahuasca,* as coming from the same species as caapi.

When he discovered caapi in northwestern Brazil and identified it correctly as a malpighiaceous narcotic, he also meticulously observed that another kind of caapi, known locally as *caapi-pinima* or "painted caapi," might be made from "an apocynaceous twiner of the genus *Haemadictyon,*" but he saw "only young shoots without flowers." "The leaves," he writes, "are of a shining green, painted with the strong blood-red veins. It is possibly the same species . . . distributed by Mr. Bentham under the name *Haemadictyon amazonicum.* It may be the caapi-pinima which gives the nauseous taste to the caapi . . . and it is probably poisonous, but it is not essential to the narcotic effect of *Banisteria* . . ." (*59*). I have consulted Spruce's unpublished handwritten field notes at the Royal Botanic Gardens at Kew and find his statement that the caapi drink is made from the lower parts of the stems of *Banisteriopsis Caapi* "beaten in a mortar with the addition of water and a small quantity of the slender roots of the Apocynac (apparently a *Haemadictyon*) called *caapi-pinima* . . . ." "May not be the peculiar effects of the caapi," he queried, "be owing rather to the roots of the *Haemadictyon* than to the stems of the *Banisteria?* The Indians, however, consider the latter the prime agent, at the same time admitting that the former is an essential ingredient."

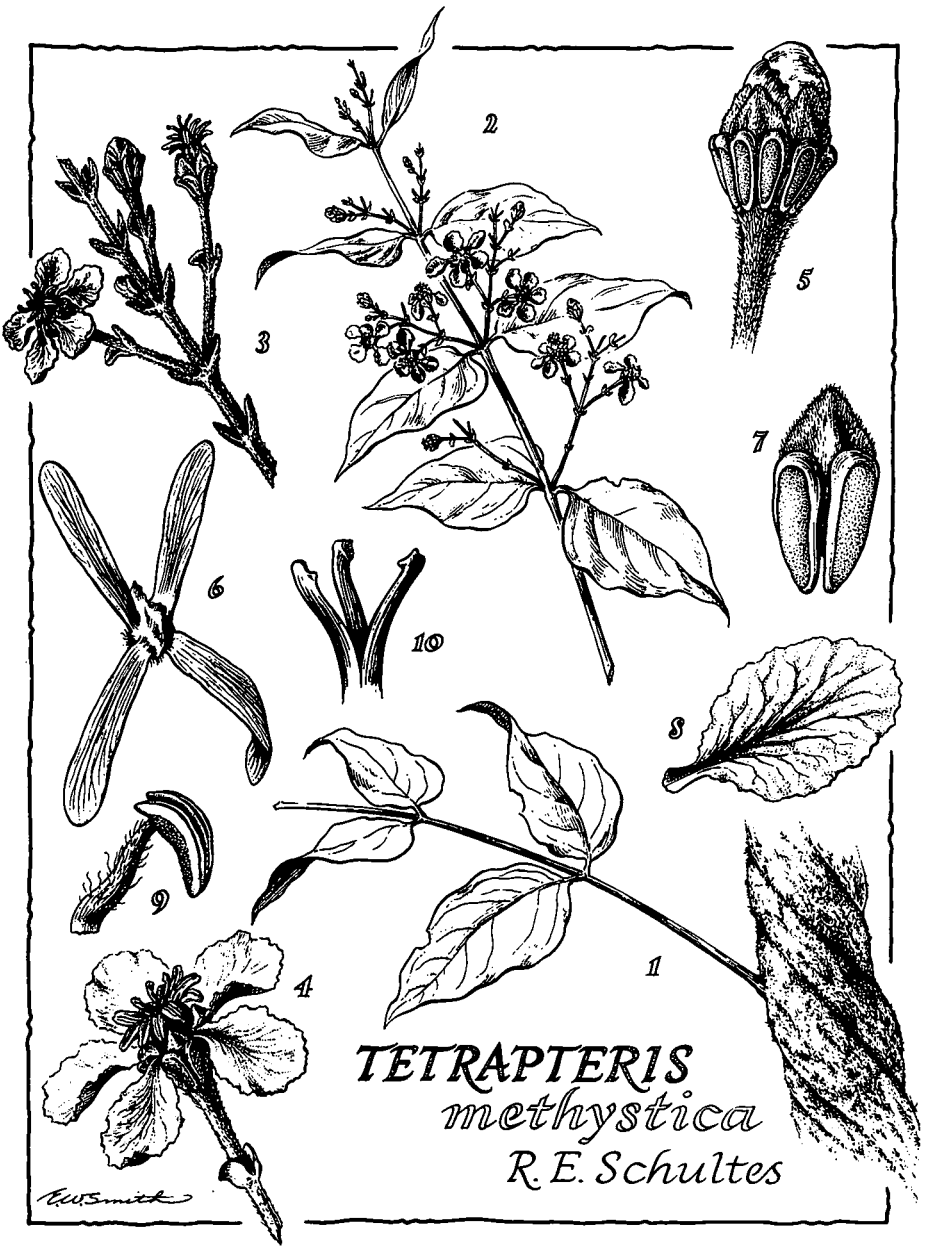
Spruce presumed that this apocynaceous admixture might play a role in caapi intoxication, but he was not certain. Nor did he make any definite assertions, pointing out cautiously that the malpighiaceous vine alone produces hallucinogenic effects. It was the French anthropologist Reinberg who, in 1921, without the benefit of voucher botanical specimens, tentatively suggested the possibility that yajé might be prepared from *Prestonia* or a related genus (*41*). Unfortunately, this suggestion has been taken up, its tentative nature forgotten or ignored, and is being propagated in technical papers.

While we know that ayahuasca, caapi and yajé are different local names for the same narcotic drink prepared from the same malpighiaceous plants, we cannot too lightly dismiss from further ethnobotanical and phytochemical study this interesting apocynaceous genus *Prestonia,* a tropical American group of some 30 species. It is curious that so little is known about the chemistry of *Prestonia,* a member of one of the phytochemically most assiduously studied families of plants (*39*). No alkaloids have as yet apparently been isolated from *Prestonia.* N, N-dimethyl tryptamine has been reported from "*Prestonia amazonica*" (*25*), but there is every probability that this analysis, for which no voucher specimen is available, was made on leaves of a species of *Banisteriopsis* mistakenly identified through the vernacular name yajé as *Prestonia amazonica* (*58*). The possibility that this alleg-

Makuna Indian witch doctor under the influence of caapi (*Banisteriopsis Caapi*). Río Popeyaká, Amazonas, Colombia. Photograph by J. Cabo O.

edly poisonous genus may be the source of an hallucinogenic drug makes the solution of the problem one of both academic and practical urgency.

That there remains much to learn concerning the ayahuasca-capi-yajé complex was recently emphasised by the discovery of the narcotic use of a new species of a genus allied to *Banisteriopsis: Tetrapterys methystica* (*47*).




It was my good fortune in 1948 to witness the preparation of and take a narcotic drink amongst nomadic Makú Indians along the Rio Tikié in the Brazilian Amazon. The extremely bitter beverage prepared from this plant had strong hallucinogenic effects, was yellowish, unlike the coffee-brown *Banisteriopsis* preparations. It may represent one of the other "kinds" of caapi that Spruce reported.

The identification of various admixtures utilized with *Banisteriopsis* in preparing the narcotic drink represents an interesting and still poorly under-

stood ethnobotanical problem (*19*). In addition to *Prestonia*, which may possibly be added to caapi during preparation of the drink, other plants are known to be employed in this way in sundry areas, and some of these species belong to families and genera that have physiologically active constitutents. It is to be supposed, therefore, that they may alter, sometimes significantly, the flavour and effects of the narcotic preparation. The Siona of the Colombian Putumayo, for example, add what is probably *Datura suaveolens* to *Banisteriopsis* in making yajé (*15*). The Ingano Indians of the same area are said to value *Alternanthera Lehmannii* as an admixture (*49*). I found that Makuna medicine men of the Río Popeyaká in eastern Colombia occasionally use a few crushed leaves of the apocynaceous *Malouetia Tamaquarina* (*49*). One of my graduate students has recently identified a species of *Psychotria* similarly employed by the Kofán Indians of Amazonian Ecuador. A most interesting anthropological report has recently appeared that enumerates five lianas, the barks of which are added to caapi by the Tukano Indians of the Brazilian part of the Rio Vaupés; unfortunately, these plants are as yet identified only by native names (*3*). How many other plants may be used as admixtures throughout the range of use of the South American malpighiaceous narcotics?

Now, what about the possibility of new hallucinogens in the Old World flora? Up to this point, we have concentrated our attention on plants employed in primitive cultures of the New World. As I have already mentioned, the New World seems to be far richer in known hallucinogenic plants than the Old. The argument that the New World flora might be richer in plants possessing psychotomimetic principles would be acceptable probably to few chemotaxonomists, including me. There may be several reasons for this real discrepancy, but most certainly one might be that Old World cultures as a whole seem, at least upon superficial examination, to be much less narcotic-conscious, to feel much less the "need" for these agents in magico-religious rites and in the practice of medicine—and this notwithstanding the great antiquity and probably original basic significance of narcotics to many Old World religious systems.

There must be an appreciable number of problems in the ethnopharmacological search for new hallucinogens in sundry parts of Africa and Asia, but I must content myself with a brief discussion of only a few potentialities.

What is the famous *kanna* or *channa* reported, more than 225 years ago, as a vision-inducing narcotic of the Hottentots who chewed it and held it in the mouth, much as the natives of South America employ coca? The intoxication is interesting, for "their animal spirits were awakened, their eyes sparkled and their faces manifested laughter and gaiety. Thousands of delightsome ideas appeared, and a pleasant jollity which enabled them to be amused by the simplest jests. By taking the substance to excess, they lost consciousness and fell into a delirium" (*29*). The name *kanna* designates, at the present time, in South Africa, various species of the aizoaceous genus *Mesembryanthemum*. While several species of *Mesembryanthemum* are known to be alkaloidal and to induce a state of torpor when ingested, at least one investigator (*29*) doubts that they could produce such startling effects.

The ceremonial clay pot in which caapi is prepared and from which it is served. The pot must hang always under the eaves at the left front corner of the house. Barasana Indians, Río Piraparana, Vaupés, Colombia. Photograph by R. E. Schultes.

He has suggested that the plant in question might have been *Cannabis sativa*, pointing out, the while, that other plants, like the anacardiaceous *Sclerocarya Caffra*, are employed in South Africa for their intoxicating effects. Here is an area where, because the inroads of civilisation have not been unduly drastic, ethnobotanical field investigation might be extremely productive.

Another Old World genus employed for its narcotic properties is the rubiaceous *Mitragyna*. *Mitragyna speciosa* seems to be the species most commonly used in southeastern Asia, especially in Siam, where the leaves are chewed alone or mixed with the betel quid or else prepared for smoking like opium (*26*). It was first reported as a substitute for opium apparently in 1836, and has cropped up constantly in the literature since that time (*8*). The use of *Mitragyna* is said now to be legally proscribed in Siam.

So much chemical attention has been given to *Mitragyna* in recent years (*5*, *40*) that the problems and potentialities offered by this genus are well

known. It might, however, be extremely helpful if we knew as much about its use amongst the natives.

Passing mention should further be made of two Old World plants known to possess hallucinogenic principles, but the narcotic use of which by native peoples for intoxication is not well documented. One of these is *Peganum Harmala* (*14*), a rather enigmatic plant that has been placed in the Rutaceae, although now it seems more properly located in the Zygophyllaceae. This species, native in North Africa, the Balkans and from Asia Minor west to China and India, is known to be toxic (*6*), to contain the alkaloids harmaline and harmine (the same constituents found in *Banisteriopsis*), and may have, in addition, a "narcotic hasheesh-like alkaloid" (*6*). Although the seeds of *Peganum Harmala* have proven narcotic properties and figure extensively in folk medicine, going back to the time of Dioscorides, I find no direct references to its religious or hedonistic use as an hallucinogen (*37*). That it may be so employed in Asia or Africa should not be ruled out of our thinking.

Another similarly interesting narcotic is *iboga* of the wet tropical forests of West Africa, especially of the Congo—the apocynaceous *Tabernanthe Iboga* (*61*). Its chemistry is relatively well known, with at least 12 active alkaloids reported, the principal one of which—ibogaine—has effects similar to that of cocaine (*60*). In high doses, it causes nervous excitement, mental confusion, a general state of drunkenness and is a true hallucinogenic agent (*44*). While it has been valued as a medicine and possibly also as an hallucinogen in primitive societies of West Africa, it is not clear that its use as a vision-inducing narcotic was extensive. Ethnobotanical field work is once again indicated.

There have been vague references to the zingiberaceous *Kaempferia Galanga*, to which the natives of several parts of New Guinea attribute hallucinogenic properties (*4*). We know, in fact, nothing about the psychotomimetic use of this genus, nor of its chemical constituents.

The role of mushrooms in the so-called "mushroom madness" of the Kuma people of the Wagti Valley in New Guinea has been, and still is, puzzling. A species of *Russula* has been suggested as the psychotropic agent that suddenly causes individuals or groups to go berserk. Even though the "natives attributed their extraordinary behaviors to mushrooms, several species of *Boletus*, *Russula and Heimiella*—or at least most of them—do not seem to cause physiological effects leading to madness." (*24*). I am convinced that much more field work must be done in this fascinating part of the world.

Undoubtedly the greatest enigma in the field of the hallucinogens has been the identity of *soma* (*61*). Some 3,500 years ago, a people who called themselves Aryans, who were the first so to style themselves and who had a right to the name, swept down from the north into the Indus Valley of India. They brought with them the cult of a sacred plant, called soma. They deified the plant and worshipped it, extracting its juice and drinking it. They composed more than one thousand hymns about it, and these have come down to us intact.

What was *soma?* No one knows at the present time. For more than two thousand years, its identity has been clouded in a mystery. For some unexplained reason, the Aryans abandoned the original plant soon after they arrived in their new home, and its identity was forgotten. Other plants took its place as substitutes—plants chosen for reasons other than the psychic effects which, in the case of the substitutes, seem to have been non-existent.

Western civilization discovered the enigma of soma about a century and a half ago when it began to learn about the cultural wealth that India had to offer to the world. Since then, more than a hundred species have been suggested as the source of the original soma, but none of the suggestions has won acceptance. Amongst these, the principal contenders were numerous species of *Ephedra*, *Periploca* and *Sarcostemma*: the first genus a gymnosperm; the last two asclepiadaceous genera; but all similar in being vine-like, fleshy, leafless or almost leafless desert plants.

For some years now, Wasson has devoted full time to a deep study of the historical, literary and ethnobotanical records concerning soma. He has spent several years in the Far East and much time in European university centers and libraries. We are justified in stating, I believe, that never has greater thoroughness and meticulous scholarship gone into the enigma of soma, for Wasson's avenues of ethnobotanical research have been ingeniously devious and complex. "When I first approached the problem in 1963," he (*63*) wrote, "I could hardly believe what I found . . . a clear-cut botanical question—a psychotropic plant that calls for identification. The clews should be in the Vedic hymns . . . True, the poems contain no botanical description . . . for those remote singers were not modern botanists . . . they were writing for contemporaries . . . and their imagery and terms often elude our understanding . . . But the hymns are all shot through with soma, and about 120 of them are entirely devoted to the plant-god. Was it possible that so much could have been written about a plant, over centuries . . . and its identity not revealed? It was no secret for the poet-priests. How extraordinary it would have been if all of them . . . had withheld from their verses the revealing descriptive terms, the tell-tale metaphors, that the trained reader today needs to spot the plant! But this did not happen. All that has happened is that no ethnobotanist with an interest in psychotropic plants has applied himself to an examination of the texts."

To this age-old enigma, Wasson has suggested a solution: that the true soma was a mushroom, the fly agaric, *Amanita muscaria*, the same mushroom used narcotically today by certain natives in Siberia. All of the many intricately interlocking pieces of indirect evidence gleaned from the Vedic hymns seems to fit in with this clever suggestion so well that Wasson has asked: "Could any key unlock this combination save the fly agaric?" He is now engaged in writing his conclusions and, in view of his contributions to our knowledge of the sacred Mexican mushrooms, of the narcotic morning glories and of the new hallucinogenic *Salvia* of Mexico, we await the completion of his fascinating study with great anticipation.

## Guidelines for the Future

The ethnobotanist, especially in his ethnopharmacologic search for hallucinogenic plants, is confronted with these and many more problems throughout the world. Faced with the ever more rapid disintegration of primitive societies and an extraordinary dearth of trained ethnobotanists, science would seem to be doomed to lose. The outlook, however, may not be so dour. Specialists in those fields upon which ethnobotany impinges are experiencing a growing realization of the potentialities of the interdisciplinary approach that ethnobotany affords. There is growing interest in ethnobotanical research amongst younger men going into botanical, anthropological and pharmacological fields. Some of the most startling scientific advances of the past twenty years have been made in various branches of ethnobotany. The future should, therefore, solidly be ours, and our trust must be to prevent its slipping from us.

It might here be appropriate to end with the words of Harshberger, author of the term *ethnobotany*, who wrote: "It is of importance . . . to seek out these primitive races and ascertain the plants which they have found available in their economic life, in order that perchance the valuable properties they have utilized in their wild life may fill some vacant niche in our own."

### BIBLIOGRAPHY


(*1*) Abramov, M. M. "The isolation of lagochilin" [English transl.] Journ. Appl. Chem. USSR, 30 (1957) 691.

(*2*) Ackerknecht, Erwin H. "Medical practices" in *Handbook of South American Indians*, Bur. Am. Ethnol. Bull. 143, Vol. 5 (1949) 621.

(*3*) Alves da Silva, Alcionilio Brüzzi. "A civilizacão indigena do Uaupés" (1962) 228.

(*4*) Barrau, Jacques. "Observations et travaux récents sur les végétaux hallucinogènes de la Nouvelle-Guinée" Journ. Agr. Trop. Bot. Appl. 9 (1962) 245.

(*5*) Beckett, A. H., E. J. Shellard, J. D. Phillipson and C. M. Lee. "Alkaloids from *Mitragyna speciosa* (Korth.)" Journ. Pharm. Pharmacol. 17 (1965) 753.

(*6*) Black, W. L. and K. W. Parker. "Toxicity tests on African rue (*Peganum harmala* L.)" N. Mex. Arg. Expt. Sta. Bull. 240 (1936).

(*7*) Bunge, A. "Beitrag zur Kenntniss der Flor Russlands und der Steppen Central-Asiens" Mem. Sav. Etr. Petersb. 7 (1847) 438.

(*8*) Burkhill, I. H. "A dictionary of the economic products of the Malay Peninsula" 2 (1935) 1480.

(*9*) Castetter, Edward F. "The domain of ethnobiology" Am. Nat. 78 (1944) 158.

(*10*) Chantre y Herrera, José. "Historia de las misiones de la Compañía de Jesus en el Marañon español . . . 1637–1737" (1901) 85.

(*11*) Cooper, John M. "Stimulants and narcotics" in *Handbook of South American Indians*, Bur. Am. Ethnol. Bull. 143, Vol. 5 (1949) 525.

(*12*) Cruz Sánchez, G. "Farmacología de *Opuntia cylindrica*" Rev. Farm. Med Exper. 1 (1948) 143.

(*13*) Cruz Sánchez, G. "Aplicaciones populares de la cimora en el norte del Perú" Rev. Farm. Med Exper. 1 (1948) 253.

(*14*) Dayton, Willam A. "Notes on harmel or 'Syrian rue'" Journ. Wash. Acad. Sci. 27 (1937) 349.

(15) DE CALELLA, PLÁCIDO. "Apuntes sobre los indios Sionas del Putumayo" Anthropos 35–35 (1944) 749.
(16) DER MARDEROSIAN, ARA. "Current status of hallucinogens in the Cactaceae" Am. Journ. Pharm. 138 (1966) 1.
(17) FADIMAN, J. "*Genista canariensis*—a minor psychedelic" Econ. Bot. 19 (1965) 383.
(18) FRIEDBERG, CLAUDINE. "Rapport sommaire sur une mission au Péru" Journ. Agric. Trop. Bot. Appl. 6 (1959) 439.
(19) FRIEDBERG, CLAUDINE. "Des Banisteriopsis utilisés comme drogue en Amérique du Sud." Journ. Agr: Trop. Bot. Appl. 12 (1965) 403–437, 550–594, 729–780.
(20) GONÇALVES DE LIMA, OSWALDO. "Observações sôbre o 'vinho de Jurema' utilizado pelos índios Pancarú de Tacaratú (Pernambuco)" Arqu. Instit. Pesqu. Agron. 4 (1946) 45.
(21) GUTIÉRREZ-NORIEGA, CARLOS. "Area de mescalinismo en el Perú" America Ind. 10 (1950) 215.
(22) GUTIÉRREZ-NORIEGA and G. CRUZ SÁNCHEZ. "Alteraciones mentales producidas por la *Opuntia cylindrica*" Rev. Neuro-Psiqu. 10 (1947) 422.
(23) HARSHBERGER, J. W. "The purposes of ethno-botany" Bot. Gaz. 21 (1896) 146.
(24) HEIM, ROGER and R. GORDON WASSON. "The 'mushroom madness' of the Kuma" Bot. Mus. Leafl., Harvard Univ. 21 (1965) 1.
(25) HOCHSTEIN, F. A. and A. M. PARADIES. "Alkaloids of *Banisteria caapi* and *Prestonia amazonica*" Journ. Am. Chem. Soc. 79 (1957) 5735.
(26) HOOPER, D. "The anti-opium leaf" Pharm. Journ. 78 (1907) 453.
(27) JONES, VOLNEY H. "The nature and status of ethnobotany" Chron. Bot. 6 (1941) 219.
(28) KARSTEN, R. "Headhunters of eastern Ecuador" (1935) 174, 380.
(29) LEWIN, LOUIS. "Phantastica—die betäubenden und erregenden Genussmittel" (1924).
(30) LOWIE, ROBERT H. "The Cariri" in *Handbook of South American Indians*, Bur. Am. Ethnol. Bull. 143, Vol. 1 (1946) 558.
(31) LOWIE, ROBERT H. "The Pancararú" in *Handbook of South American Indians*, Bur. Am. Ethnol. Bull. 143, Vol. 1 (1946) 561.
(32) LUMHOLTZ, CARL. "Unknown Mexico" (1902) 356.
(33) MCLAUGHLIN, J. J. and A. G. PAUL. "The cactus alkaloids I. Identification of N-methylated tyramine derivatives in *Lophophora Williamsii*" Lloydia 29 (1966) 315.
(34) MÉTRAUX, ALFRED. "The social organization and religion of the Mojo and Manasi" Prim. Man 16 (1943) 1.
(35) MÉTRAUX, ALFRED. "Tribes of eastern Bolivia and the Madeira headwaters" in *Handbook of South American Indians*, Bur. Am. Ethnol, Bull. 143, Vol. 3 (1948) 423.
(36) PACHTER, I. J., D. E. ZACHARIAS and O. RIBEIRO, "Indole alkaloids of *Acer saccharinum* . . ., *Dictyoloma incanescens*, *Piptadenia colubrina* and *Mimosa hostilis*" Journ. Org. Chem. 24 (1959) 1285.
(37) PORTER, DUNCAN M. "The taxonomic and economic uses of *Peganum* (Zygophyllaceae)" Unpubl. ms. (1962).
(38) POWERS, STEPHEN. Cal. Acad. Sci. Proc. 5 (1873–74) 373.
(39) RAFFAUF, ROBERT F. and M. B. FLAGLER. "Alkaloids of the Apocynaceae" Econ. Bot. 14 (1960) 37.
(40) RAYMOND-HAMET and L. MILLAT. "Les 'Mitragyna' et leurs alcoloides" Bull. Sci. Pharmacol. 40 (1933) 593.
(41) REINBURG, P. "Contribution à l'étude des boissons toxiques des indiens du Nord-ouest de l'Amazone, l'ayahuasca, le yajé, le huanto" Journ. Soc. Amer. Paris, n.s., 13 (1921) 25–54, 197–216.
(42) ROBBINS, W. W., J. P. HARRINGTON and B. FREIRE-MARRECO. Bur. Am. Ethnol. Bull. No. 55 (1916) 1.

(43) ROTH, E. E. "An introductory study of the arts, crafts and customs of the Guiana Indians" 38th Ann. Rept. Bur. Am. Ethnol. 1916–17 (1924) 25.
(44) SCHNEIDER, J. A. and E. B. SIGG. "Neuropharmacological studies on ibogaine, an indole alkaloid with central stimulant properties" Ann. N.Y. Acad. Sci. 66 (1957) 765.
(45) SCHULTES, RICHARD EVANS. "Peyote (*Lophophora Williamsii*) and plants confused with it" Bot. Mus. Leafl., Harvard Univ. 5 (1937) 61.
(46) SCHULTES, RICHARD EVANS. "La etnobotánica: su alcance y sus objetos" Caldasia No. 3 (1941) 7.
(47) SCHULTES, RICHARD EVANS. "Plantae Austro-Americanae IX. Plantarum novarum vel notabilium notae diversae" Bot. Mus. Leafl., Harvard Univ. 16 (1954) 202.
(48) SCHULTES, RICHARD EVANS. "A new narcotic snuff from the northwest Amazon" Bot. Mus. Leafl., Harvard Univ. 16 (1954) 241.
(49) SCHULTES, RICHARD EVANS. "The identity of the malpighiaceous narcotics of South America" Bot. Mus. Leafl., Harvard Univ. 18 (1957) 1.
(50) SCHULTES, RICHARD EVANS. "Native narcotics of the New World" Texas Journ. Pharm. 2 (1961) 141.
(51) SCHULTES, RICHARD EVANS. "Tapping our heritage of ethnobotanical lore" Chem. Dig. 20 (1961) 10; Econ. Bot. 14 (1961) 257.
(52) SCHULTES, RICHARD EVANS. "The role of the ethnobotanist in the search for new medicinal plants" Lloydia 25 (1962) 257.
(53) SCHULTES, RICHARD EVANS. "Botanical sources of the New World narcotics" Psyched. Rev. 1 (1963) 145.
(54) SCHULTES, RICHARD EVANS. "Hallucinogenic plants of the New World" Harvard Rev. 1 (1963) 18.
(55) SCHULTES, RICHARD EVANS. "The widening panorama in medical botany" Rhodora 65 (1963) 97.
(56) SCHULTES, RICHARD EVANS. "Ein halbes Jahrhundert Ethnobotanik amerikanescher Halluzinogene" Planta Medica 13 (1965) 125.
(57) SCHULTES, RICHARD EVANS. "The search for new natural hallucinogens" Lloydia 29 (1966) 293.
(58) SCHULTES, RICHARD EVANS and ROBERT F. RAFFAUF. "Prestonia—an Amazon narcotic or not?" Bot. Mus. Leafl., Harvard Univ. 19 (1960) 109–122.
(59) SPRUCE, RICHARD. "Notes of a botanist on the Amazon and Andes" Ed. A. R. Wallace 2 (1908) 413 ff. The MacMillon Company, London.
(60) STEINMETZ, E. F. "Tabernanthe Iboga radix" Quart. Journ. Crude Drug Res. 1 (1961) 30.
(61) TYLER, VARRO E., Jr. "The physiological properties and chemical constituents of some habit-forming plants" Lloydia 29 (1966) 275.
(62) VESTAL, PAUL A. and RICHARD EVANS SCHULTES. "The economic botany of the Kiowa Indians as it relates to the history of the tribe" (1939).
(63) WASSON, R. GORDON. "A new Mexican psychotropic drug from the Mint Family" Bot. Mus. Leafl., Harvard Univ. 20 (1962) 77.
(64) WASSON, R. GORDON. "Soma: divine mushroom of immortality" Unpubl. ms. (1966). Address presented at Peabody Museum Centennial Symposium, Yale Univ., July 14, 1966.
(65) WILLAMAN, J. J. and BERNICE G. SCHUBERT. "Alkaloid-bearing plants and their contained alkaloids" Tecn. Bull. No. 1234, U.S.D.A. (1961).



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# Empiricism and Magic in Aztec Pharmacology

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Indigenous pharmacology is always based on empiricism; however, magic procedures and religious ceremonies are often mixed in medical use. When a plant has been found to produce marked physiological effects it is likely than an explanation for those properties is to be looked for according to the substratum culture of the particular ethnic group.

That has been the case for *coca*, "the divine plant of the Incas"; for *peyotl*, "divine messenger"; *teonanacatl*, "God's flesh." These examples show that the magic or religious associations could not be taken as evidence of lack of empirical knowledge. Many times a plant used by medicine-men or priests has been found to be an active pharmaco.

However, the astronomical number of plants, minerals and animals used in popular medicine prescribed by all sorts of medicine men, herb-vendors, magicians, shamen, or used directly by the people, prevents an indiscriminate study of all this materia medica.

An ethnoiatric study (*1*) from the standpoints of social, historical, religious and philosophical contexts, is required for the evaluation of the medical uses of a community. Moreover, even for pharmacology, an extensive knowledge of the socio-cultural background and environment of a tribe is needed for understanding the orientation and purposes in the use of a drug.

The case of Azetc pharmacology is a very peculiar one. A brief history of Aztec civilization will help to evaluate the problem:

The Aztecs were a nomadic and primitive group that arrived in the Mexican Valley only two hundred years before the Spanish Conquest. They had been conducted and governed by a witch called *Malinalxochitl*, and later on by a warrior, *Huitzilopochtli*. They encountered in the Valley of Mexico human groups, the *Nahuas*, of much higher cultural development and with a religion based on spiritual values inspired by the great *Quetzalcoatl*, a god or perhaps a man full of wisdom, who gave to the *Toltecs* codes of ethics and love for art and science. All the *Nahua* groups settled in the Valley of Mexico, inheritors of the old *Toltec* civilization already disappeared, had a great veneration for *Quetzalcoatl*, god and man, father of knowledge and morals. Human sacrifices, the horror of Aztec Society, were not practiced among the *Nahuas* before the Aztec arrival (*2*).

The incongruity of a well-advanced culture with high moral principles as taught by the *Calmecac* or Aztec College, and brutal ritual butcheries, are to be explained by the merger of two different thoughts. One, the Toltec, spiritual and learned; the other, the original Aztec, magical, bellicose and


One of the multiple representations of *Quetzalcoatl* (Codex Borbonicus).

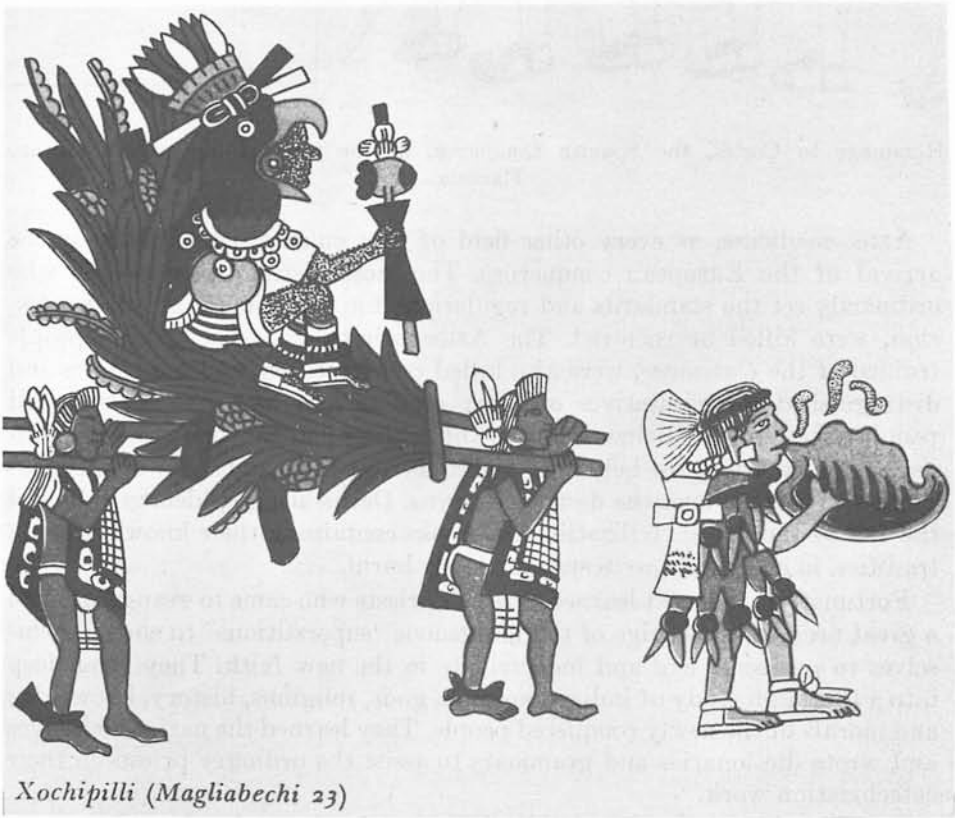
imperialistic. The Aztecs brought under their command all the *Nahuatl* groups through wars, treachery and terror, but took advantage of all the knowledge and cultural development of the conquered nations. They adopted the *Quetzalcoatl* title for their highest priest, paid devotion to *Quetzalcoatl* teachings and myths, and kept great respect for Toltec traditions (*3*).

Sahagún, the most eminent Spanish priest who studied the Mexican culture in the XVI Century, said with regard to the Toltecs: "They had great experience and knowledge: They knew the quality and virtues of the herbs, and they left marked and known those that nowadays are used for healing, because they were also physicians and essentially the first in this art. . . . They were the first inventors of medicine . . . So able were they in natural astrology . . . that they were the first to count the number of days in a year . . . They invented the art of interpretation of dreams, and were so learned and wise that they knew the stars of the sky, had named them and knew their influences and qualities. They also knew the movements of the skies through knowledge of the stars . . . The said Toltecs were good men and lovers of virtue . . . " (*4*).

When in 1519 the Spanish Conquerors arrived in Mexico they found a large number of nations or tribes under the tyrannical rule of *Tenochtitlan* Emperor. They were forced to pay heavy and growing tributes, and very often to provide human beings for the continuous sacrificial ceremonies at the Aztec capital. These sacrifices sometimes reached the incredible number of several tens of thousands of human beings, according to several Spanish chroniclers. No wonder that Cortes and their men easily found allies among those subjugated people, who candidly thought they would obtain their freedom.

The fall of the Aztec empire to a handful of Spanish adventurers was also helped by the magic-minded Moctezuma, who had a series of dreams and other warnings about the imminent return of *Quetzalcoatl.*

The complexity of Mexican culture was greatly increased by the arrival of the Spaniards who brought about movements of tribes, displacement of towns, mixtures of people, and emigrations. Terrible wars, destructions of cultural centers, persecution of all people representative of old beliefs and religious and magical practices, were systematically carried out in order to annihilate the influence of the devils. The new religion and the European concept of the world were enforced.



*Xochipilli (Magliabechi 23)*

Representation of Xochipilli, god of flowers, joy and love (Codex Magliabechi).


Hommage to Cortés, the Spanish Conqueror, at the time of his arrival. (Lienzo Tlaxcala).

Aztec medicine, as every other field of that culture, was shaken by the arrival of the European conquerors. The most distinguished people who ordinarily set the standards and regulations for the practice of any profession, were killed or removed. The Aztec priests, the most learned people trained at the *Calmacac*, were also killed or prosecuted, and the officers and distinguished representatives of every civilian activity were deposed. All people practicing medicine or any art of healing had to work at their maximal capacity trying to help the thousands and thousands of wounded, injured and sick all over the destroyed towns. Devastating epidemics followed the fall of the Aztec civilization. All books containing their knowledge and tradition in every field were systematically burnt.

Fortunately, the most learned Spanish priests who came to evangelize, had a great need of knowledge of the indigenous "superstitions" to enable themselves to prosecute evil and indoctrinate in the new faith. They went deep into a thorough study of indigenous rites, gods, religions, history, knowledge and morals of the newly conquered people. They learned the native languages and wrote dictionaries and grammars to assist the ordinary priests in their catechization work.

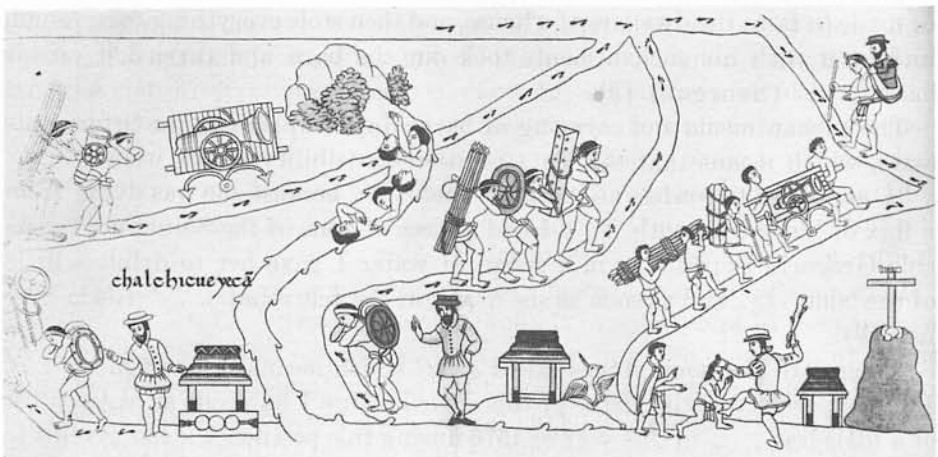
Some of them became seriously interested in the real value of mexican civilization, and developed extensive studies to obtain data and information

about every aspect of those cultures. The most distinguished of them, Fray Bernardino de Sahagun, was a true pioneer in the use of scientific methods for ethnological research. He obtained reports from groups of well-selected informers, specialists in every field, and kept protocols in Nahuatl of their statements. He wrote his well-known "General History of Things of New Spain" (*4*) based on that data. However, only recently have his protocols received attention, and are being translated from Nahuatl into Spanish (*5*) and English (*6*).

Another important fact to be mentioned in order to evaluate the information that has reached us is the establishment in 1536 of the Colegio of Santa Cruz de *Tlatelolco*, which was founded with the purpose of indoctrination in European culture of the potentially dangerous youngsters descending from the previously ruling class. These students became very valuable assistants to Father Sahagun and other priests, and even reached positions as lecturers in their own College. We certainly know that one of them, Juan Badiano, was a teacher of Latin and translated the only book of medicine we have that was written directly by an Aztec physician, Martin de la Cruz.

It is evident that Aztec pharmacology at the beginning of the XVI Century had reached an important degree of development: The multiple and well-kept botanical gardens mainly devoted to growing medicinal plants were known and admired not only by Cortes and his soldiers, but by botanists and physicians. Francisco Hernandez, physician to Philip II, collected, described and assayed, numerous plants from those gardens, particularly from the one at Oaxtepec (*7*).

The discovery of the medicinal properties of those plants was undoubtedly empirical. Contemporaneous chroniclers report that at those botanical gardens the plants were given free to the patients, under the condition that they would inform about the results. In addition to this example of institutional research, we have evidence that the professions of physician and




The conquerors receive assistance from local indians for the transportation of all sort of materials, At right lower angle is shown an example of the means used to obtain cooperation (Lienzo de Tlaxcala).

herb-vendor were practiced by individuals other than those devoted to sorcery, magic, witchcraft and religion. We are aware that active plants, mainly those with hallucinatory properties, were used by sorcerers and priests together with their own paraphernalia.

It is a difficult matter to say what part is played by the pharmacodynamic action of a drug, and what is due to suggestion, when psychological procedures are added. The test of healing has always been poor evidence of efficacy. However, in a long run, a conclusion based on repeated experience may be reached.

The plants used in Aztec medicine are mentioned in several chronicles, but ordinarily only the names are given and these in the Nahuatl language. In the case of the Cruz-Badiano manuscript, wonderful color illustrations were added in order to help the European people identify the plants, but even with this data, botanical identification has been difficult. After four and a half Centuries many of the plants contained in the materia medica of the Aztecs remain unknown.

Some authors (*8*) have thought that Sahagun and other chroniclers gave a too rationalistic idea of Aztec medicine because they tried with the European rationalistic mind to adjust what they saw to what they knew. However, remember that we have the almost *verbatim* protocols recorded in Nahuatl by Sahagun and his mexican assistants, which in this matter coincide with his writings. We believe that these protocols contain an almost literal transcription of the answers given by the informants because, written in Nahuatl, they maintain the peculiar repetitive structure of that language. Series of adjectives, verbs or phrases, one after another, make clear or emphasize the concepts. That style appears in the protocols but not in Sahagun History.

In order to have examples of XVI century European "rationality" in this matter, a few quotations may be useful:

"Thieves knew very well of enchantement, with which they used to deaden or made to faint the dwellers of a house, and then stole everything to be found, and even with his enchantments took out the barn and carried it on his back . . . " (Sahagun) (*4*).

The enchantments and carrying of barns do not appear in the informants texts, which means that this data is the responsibility of the writer.

"I was called to confess an indian woman . . . because she was dying from a flux of blood by mouth. . . . I had a piece of bone of the Saint and Venerable Gregorio López . . . in a spoon of water I gave her to drink a little of the bone . . . and as soon as she drank it, she felt relief. . . ." (de la Serna) (*9*).

"There are also some stones called *eztetl* which means stone of blood . . . I had experience of the virtue of this stone because I have one as big as a fist or a little less . . . in this year of 1576 during this pestilence it has given life to many whose blood and life were going out from his nose. Taking it (the stone) in their hand and having it for some time the bleeding stopped and they recovered from this disease from which many have died and are dying in

all this New Spain. There are many witnesses in this town of Tlatilulco of St. James" (Sahagun) (*4*).

Undoubtedly in order to judge the Aztec medicine in its entirety it is required to try to understand the cultural and religious atmosphere of that people living under exceptional conditions of anguish. Their own blood was required to keep the sun shining, everything was under the influence of exacting gods and thousands of major and minor priests were interpreters of the holy designs. Diseases, particularly when chronic, grave or epidemic, were considered as divine punishments for the group or the individual because of deviations from the strict rules of behaviour.

But religious, magical and other psychological methods were also used in order to solve ailments that had not responded to ordinary treatments. Under the circumstances described by Sahagun, one is inclined to believe in the effectiveness of his large stone *eztetl*, to stop epistaxis when that exceptional mineral was held into the tightly closed hand of the patient. The emotional liberation of epinephrine could explain that effect.

Sorcerers and priests used to give to patients and drink themselves *ololiuhqui* and mushrooms to produce hallucinations which would give them leads about the origin of a disease and the way to cure it.

All these facts could give the impression of an impenetrable mixture of magic, religion and empiricism in Aztec therapeutics, but that would be the case if we put together all the resources that present day people many times put in action when they suffer a grave or incurable disease.

Sometimes it is very difficult to decide if a practice is rational or magic, because there is interaction of procedures and influences. The use of amulets, stones, relics, conjures, is not magic any more when they are heavily charged of psychological meaning or had established conditioned reflexes.

Even the classical magician technics based on the use of music (melotherapy), odors (osmotherapy), colors (chromotherapy), dances, cabalistic words and phrases (versotherapy), are not to be disregarded as baseless. Those methods represent sensorial stimulations that could provoke favourable neuro-endocrine reactions.

If we fix our attention to pharmacology the problem has to be envisioned in a different way. It does not matter if a pharmaco has been used by a physician, a sorcerer, a witch or a medicine-man, if we have some evidence of a definite effect.

We know that Aztec pharmacology was based mainly in the use of plants selected by a long empirical testing. Present day laboratory assay has confirmed the activity of many of them. We are now interested in psycoactive drugs. The Aztecs gave us *teonanacatl*, *peyotl*, *ololiuhqui*, *piecetl*, *toloatzin*, already attested in their activity. There are others that have to be studied. We need no proofs that the action of those plants was discovered by empiricism. We would be magic minded if we would suggest that they had reached the hands of the sorcerers by supranatural inspiration. We have no reason for any doubt on what the XVI Century chroniclers tell us about the well trained Aztec physicians with an extensive knowledge of medicinal plants and long experience in diagnosis and treatments. Sahagun said very clearly that they

would not use sorcery and gives names of every one of the members of the group that he selected as informants for the chapters on medicine and related subjects of his History: "This relation given above of the medicinal herbs and the other medicinal things above contained was given by the physicians of *Tlatilulco*, James, old and very experienced in those things of Medicine; all of them are in general practice. The names of them and of the amanuensis that wrote it are the following, who, because they did not know how to write, begged the amanuensis to put their names: Gaspar Matías, neighbour of Concepción, Pedro de Santiago, neighbour of Santa Inés, Francisco Simón and Miguel Damián, neighbours of Saint Toribio, Felipe Hernández neighbour of Santa Ana; Pedro de Requena, neighbour of Concepción, Miguel García, neighbour of Saint Toribio, and Miguel Motolina, neighbour of Santa Inés".

It is surprising that Martín de la Cruz was not among them. He was the physician at Santa Cruz de Tlatelolco, Sahagun's beloved College; he wrote the book on the medicinal herbs of the Indians that was translated into latin by Juan Badiano. He could have been absent or dead, but we can not explain the fact that Sahagun does not mention the exceptional and wonderful book written on a subject he was studying at that time and when he refers *in extenso* to that School.

In a study of mine included in our recent edition of the Martín de la Cruz and Juan Badiano book, I discussed this strange fact and arrived at the conclusion that Sahagun might have considered Martín de la Cruz already under the influence of European medicine. In fact, many signs could be found of that contamination, mainly the names of diseases, the pharmaceutical mixtures and even the presence of a reference to Pliny (*10*).

It is a pity that the only book on medicinal plants written by an Aztec physician has to be read with a critical eye, because of European influences. It is interesting to note that *ololiuhqui*, *peyotl* and *teonanacatl* do not appear in the book, either because the use of them was exclusive for sorcerers or because of church censorship. On the other hand, many prescriptions that seem magical because they contain strange substances, now known inert, only means pharmacological mistakes. Lack of activity does not show absence of rationality in the use. Magic implies the performance of acts, pronunciation of words in presence of particular objects, from which only the magician or wizard is capable of managing to produce the effect (*1*). Nothing of that sort appears in the book: medicines could be used by anybody without devices or spells for supernatural powers (*11*).

Magical practices in Aztec society had their own fields and practitioners: sorcerers, necromancers, witches and magicians. However, there are no records of true shamans as defined by Mircea Eliade (*12*), that is with techniques for ecstasy and initiation ceremonies as practiced in Siberia.

Sahagun had left us the description of several of those professions: "The *naoalli* is properly called sorcerer; he frightens men and sucks blood from children during the night" (*4*). "The necromantic (*tlacatecululti*) has a pact with devil; he transforms himself into different animals, and because

MARTÍN DE LA CRUZ

# LIBELLUS DE MEDICINALIBUS INDORUM HERBIS

MANUSCRITO AZTECA DE 1552

*Según traducción latina de*
JUAN BADIANO

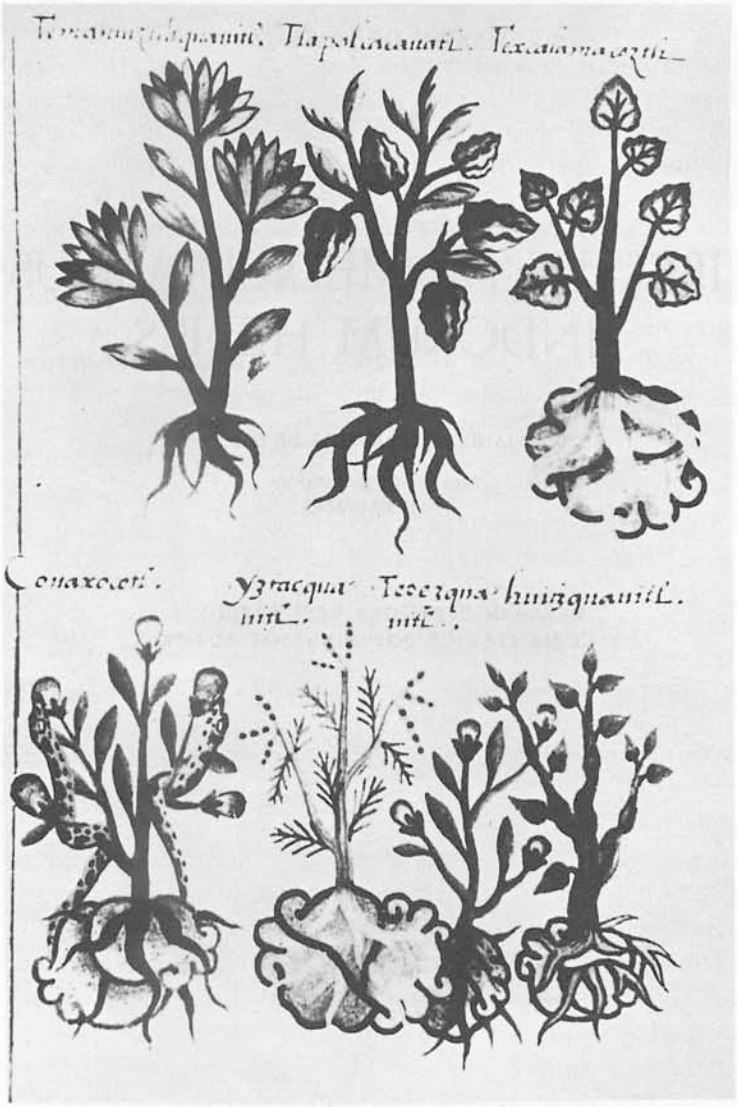
VERSIÓN ESPAÑOLA CON ESTUDIOS
Y COMENTARIOS POR DIVERSOS AUTORES

INSTITUTO MEXICANO DEL SEGURO SOCIAL
MÉXICO
1964

Title page of the recent edition of Martín de la Cruz' book (Instituto Mexicano del Seguro Social, México, 1964).

of hatred wishes death for others, using sorcery and many charms against them." (*4*).

The same Sahagun refers to the *ticitl* or physicain in a very different way: "The physician (*ticitl*) used to cure diseases and restore health; the good physician is a knower of herbs, stones, trees and roots, experienced in



Folio 38 v. of Martín de la Cruz manuscript. Notice the Aztec representation of stone *"tetl"* in the roots of five of these plants.

cures. He also has the profession of knowing how to set bones of people, to purge them, bleed them, to make incisions in them, to sew the wounds and to free people from the doors of death. The bad physician because he is not able, in place of curing the patients, worsens them with his potions. At times he uses sorceries and superstitions to make believe that he makes good cures" (*4*).

All precolumbian codices were intentionally destroyed, but we should remember that because of the lack of a true written language those documents were only guides for learned people, usually trained at the *Calmecac* who memorized the traditions, history and knowledge of that people. The destruc-

tion of that material, temples, sculptures, and every testimony of that culture, was thoroughly carried out for many years with all the zeal of the most fanatical epoch in the history of Spain. The Holy Inquisition soon was prosecuting any man denounced because of keeping in his house objects corresponding to superstition, witchcraft, rites, gods, idolatries and other uses of gentilism (*13*).

After the Conquest everything related to Aztec culture went underground and declined. When the leading representatives of pre-hispanic medicine were dead or had disappeared, it is natural to suppose that the standards of general practice would deteriorate. XVII Century descriptions of medical practices do not correspond to what had been said a Century before.

This shows the fundamental mistake of people who pretend to draw conclusions about Aztec pharmacology by studying the practices of present day indian communities. Today, Nahuatl groups live in extreme poverty in "refuge localities" far away from civilization; they live in ignorance and poor health. These degenerated vestiges of the Aztecs retain no inheritance from their glorious ancestors. Four centuries of isolation and neglect have left the people without most of the values of their culture; even their physical condition has been affected.

Nobody could expect to obtain from them astronomical or mathematical data, nor to find the marvelous sculptors and architects that left us impressive evidence of their inspiration. However there are investigators who pretend to judge Aztec medicine or pharmacology from the present practices in these deteriorated groups.

Ethnopharmacologic research in Mexico has a great work ahead for exploration of the Nahuatl knowledge and experience with plants. Many writings have not been studied thoroughly. There are documents that have not been translated or interpreted. A great number of plants described under Nahuatl names have not been botanically identified. Some of them, painted with colors in the Cruz-Badiano manuscript, have escaped classification.

Botanical knowledge was advanced among the Aztecs. They had made groups of plants according to morphology, size, structure, fruits and their uses (*14*). Medicinal plants was one of those groups, but the system allowed having many different plants with the same name. Hernandez used to add to the Nahuatl name of the plant the name of the nearest town where that specimen had been collected (*7*). The color paintings obtained by Hernandez would have helped for identification, but they were lost in the fire of the Escorial library in 1671. The drawings published in black in the Lincei edition of the New Spain Thesaurus (*15*) were redrawn from the originals (*16*). These figures were used again for our recent first complete edition of Hernandez Natural History (*7*).

A great many of the plants described by Hernandez have not been identified, and now collecting expeditions are planned in order to follow Hernandez' routes in Mexico. It is expected that fresh specimens will allow identification of some of the species described by the Spanish physician in the XVI Century.

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# OBRAS COMPLETAS
# TOMO II

*

## HISTORIA NATURAL DE NUEVA ESPAÑA

## VOLUMEN I


UNIVERSIDAD NACIONAL DE MÉXICO

1959

Title page of Volume 1 of the recent edition of Hernandez "Natural History of New Spain" (Universidad Nacional de México, México 1959).

Looking for an orientation to pick out active plants used in Aztec medicine we compared different reliable reports. We thought correlation would indicate reputation or general use of the plant. However the results did not justify our premises:

Sahagun mentions in his History 123 medicinal plants and only 86 of them appear in the texts of his informants. This means that he made a rigorous selection and that he used other sources of information that we do not know. The comparison of his protocols kept in Madrid and Florence libraries, showed only 78 plants in common. Of a total of 225 different plants in those texts, 163 appear in the first and 140 in the second. This is new proof of the differences between both manuscripts (*10*).

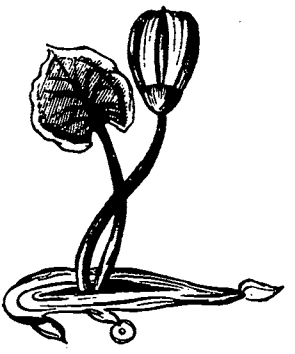
When we compared the botanical content of the materia medica in the Cruz-Badiano book, we discovered the surprising fact that among 251 plants mentioned there are only 15 of those included by Sahagun in his History. However, 14 more appear in the Informants' texts. We could speculate about the already mentioned possibility of basic discrepancies between the professional training and methods of Martin de la Cruz, physician at the Spanish College of Tlatelolco, and the Indian physicians put together by Sahagun, who were general practitioners among his folk.

Furthermore the plants that are mentioned in both documents sometimes appear with different therapeutic indications or they are not granted similar interest: *tlatlancuaye* (plants of the genus IRESINE) appear 17 times in Martin de la Cruz, only once in the texts of Sahagun informants, and none in his History.

With regard to Francisco Hernandez Natural History, we should remember that he was an European physician, representative of the medical and philosophical ideas of "humors" and qualities of diseases, and for the "contraries" or medicines. In that way Hernandez described 3076 plants and gives the "dryness" or "humidity", "warmness" or "coldness" degrees of every one of them. According to those European doctrines any plant could be useful in medicine if its qualities were contrary to the nature of disease. Once he says how bewildered he was at the use by the Indians of warm plants against fever.

We know that Hernandez was sent to New Spain to study the medicinal plants in the newly conquered land but he, as a naturalist, devoted himself to a wider field. During seven years, disregarding the royal and urgent requests, he kept collecting and assaying plants and writing his Natural History, instead of obeying the orders for sending his manuscripts. The large extension of his final report and his wider scope perhaps were the origin for the king's decision to entrust somebody else to make an abstract of his writings. That commission given to Recchi was greatly resented by Hernandez.

The difference between the approaches of the writings I have mentioned are evident: Martin de la Cruz wrote about the plants used by him and his kindred Indian physicians; Sahagun strived to obtain uncontaminated information about the pre-hispanic uses of plants by the best known physicians, uses that he described independently of the practices by sorcerers, wizards and soothsayers; Hernandez worked as a naturalist collecting specimens by himself and obtaining information on the spot about the popular uses of the



ATATAPÁLCATL
(Libro II, cap. IV)

CAPOLIN
(Libro VI, cap. LXXVIII)

TENOCHTLI
(Libro VI, cap. CX)

Nieremberg figures taken from Hernandez' originals that were kept at the Escorial library. Note the Aztec hieroglyphs for water (*atl*) under *Atatapalcatl* and for stone (*tetl*) under *tenochtli*.

plants. No wonder the reports differ. But they complement themselves if one analyzes the meaning of the data by keeping in mind the wide distance between the standpoints of view.

We have talked about only three of the most reliable sources, but there are many other important chronicles and writings, contemporaneous and posterior. Sometimes late reports relative to cultural and living conditions of

# TRATADO

DE LAS

# SUPERSTICIONES Y COSTUMBRES GENTILICAS

QUE OY VIUEN

## ENTRE LOS INDIOS NATURALES

DESTA NUEUA ESPAÑA.

ESCRITO EN MEXICO

POR EL BR. HERNANDO RUIZ DE ALARCON.

AÑO 1629.

PRIMERA EDICIÓN.

MÉXICO.
IMPRENTA DEL MUSEO NACIONAL.
1892

Title page of the 1892 edition of Ruiz de Alarcon book written in 1629.



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# MANUAL

DE

# MINISTROS DE INDIOS

PARA EL CONOCIMIENTO

## DE SUS IDOLATRIAS, Y EXTIRPACION DE ELLAS.

DEDICADO

**AL ILLMO. SR. DR. D. MATHEO DE ZAGA DE BUGUEIRO,**

Colegial del de Fonseca en Santiago de Galicia,
y del Mayor de Santa Cruz de Valladolid, su Rector, Cathedratico de letras humanas en la Vniversidad de Compostela,
en la de Valladolid de las Cathedras de Philosophia de Durando y de Prima de Sagrada Escritura,
Canonigo de la Santa Iglesia de Astorga,
Magistral de la Imperial de Toledo,
Arzobispo de la Santa Iglesia Metropolitana de Mexico, del Consejo de S. M.

COMPUESTO

## POR EL DR. JACINTO DE LA SERNA,

natural de Mexico,
Rector dos veces del Colegio Viejo de Todos Santos,
Dr. Theologo de esta Imperial Vniversidad, Rector tres veces de ella,
Cura mas antiguo del Sagrario de esta Santa Iglesia,
Visitador General
de los Señores Arzobispos D. Francisco Manso, y D. Juan de Mañosca, y Examinador Sinodal
de los mismos Govierños.

PRIMERA EDICIÓN.

MÉXICO.
IMPRENTA DEL MUSEO NACIONAL.
1892

Title page of the la Serna book.

the Indian population at the time of the observation, try to refer to the prehispanic society. That error is evident in XVII and XVIII Centuries writings when the old ruling class had disappeared and the Indians, deprived of their land, had been distributed as slave workers to the new owners. New religion and magic, new medicine and superstitions had been imported, and African rites and witchcraft had arrived with the African slaves brought by the Spaniards.

Ruíz de Alarcón, who in 1629 wrote one of the best known treatises on native idolatries (*13*) recognizes those facts and mentions that the Indians were dying at a fast rate because of bad health and drunkenness a vice not allowed in Aztec society.

Present research requires most careful analysis of data. No doubt we could still find valuable information, but great patience and comprehension have to be used in order to overcome the natural distrust of people that have been subjected to exploitation during Centuries.

Documents on magic are difficult to study. Translations and interpretations are full of problems because of the esoteric language (*Nahuatlatolli*). Literal translations refer to "the nine times beaten" for tobacco, the "red chichimec" for copper, the "red woman" for blood, "one water" for wood, "seven caves" for mouth, "snake" for pain (*9*). Most of these imaginative expressions have not been explained and many others have not been interpreted. As we say before, magic and its language represent very old myths and such study is full of obstacles.

The scientific study of Aztec pharmacology is very recent and has already given important discoveries. Many more will come if capable people from different fields work together. The personal work of Gordon Wasson and the valuable contributions from people inspired by him, is a good example of what has to be done (*17*). This symposium on an even wider scope, internationally oriented, is a promising step for closer collaboration.

## REFERENCES


(*1*) Scarpa, A., "Nozioni di Etnoiatrica," Stamperia Valdonega, Verona, 1962.

(*2*) Séjourneé, L., "Burning Water. Thought and Religion in Ancient Mexico," Thames and Hudson, London, 1956.

(*3*) Caso, A., "El Pueblo del Sol," Fondo de Cultura Económica, México, 1962.

(*4*) Sahagún, B. de, "Historia General de las Cosas de Nueva España," Porrúa, México, 1956.

(*5*) Garibay, A. M. and León Portilla, M., "Fuentes Indígenas de la Cultura Náhuatl. Informantes de Sahagún," Universidad Nacional de México, I, 1958; II, 1958; III, 1961.

(*6*) Anderson, A. J. O. and Dibble, C. E., "Florentine Codex." School of American Research and University of Utah, Sante Fe, New Mexico, II, 1950; III, 1951; IV, 1952; V–VI, 1957; VIII, 1953; IX, 1954; X, 1959; XI, 1961; XII, 1963; XIII, 1955.

(*7*) Hernández, F., "Historia Natural de Nueva España," Obras Completas. Universidad Nacional de México, 1959.

(*8*) Aguirre Beltrán, G., "Medicina y Magia." Instituto Nacional Indigenista, México, 1963.

(*9*) DE LA SERNA, J., "Manual de Ministros de Indios, escrito en 1656." Imprenta del Museo Nacional, México, 1892.

(*10*) DEL POZO, E. C., "Valor médico y documental del manuscrito." In de la Cruz, M., Libellus de Medicinalibus Indorum Herbis, Ms., 1552, Instituto Mexicano del Seguro Social, México, 1964.

(*11*) DE LA CRUZ, M., "Libellus de Medicinalibus Indorum Herbis," Ms., 1552, Instituto Mexicano del Seguro Social, México, 1964.

(*12*) ELIADE, M., "El Chamanismo," Fondo de Cultura Económica, México, 1960.

(*13*) RUIZ DE ALARCÓN, H., "Tratado de las supersticiones y costumbres gentilicas que oy viven entre los indios naturales desta Nueva España," Imprenta del Museo Nacional, México, 1892.

(*14*) DEL POZO, E. C., "La Botánica Medicinal Indígena de México." Estudios de Cultura Náhuatl, Vol. 5, México, 1965.

(*15*) RECCHO, N. A., "Rerum medicarum Novae Hispanie Thesaurus seu plantarum, animalium, mineralium mexicanorum historia ex Francisi Hernandez . . .," Tipografia Vitalis Mascardi, Roma, 1651.

(*16*) DEL PASO Y TRONCOSO, F., "Estudios sobre la historia de la medicina en México. I. La botánica entre los aztecas." Anales del Museo Nacional de México, 3: 137–235, 1886.

(*17*) WASSON, G., "Notes on the present status of *ololiuhqui* and the other hallucinogens of Mexico," Botanical Museum Leaflets, 20: 161–212, 1963.

# Perspectives on the Use and Abuse of Psychedelic Drugs

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## Introduction

It has been remarked that tradition-bound scientists will predictably conclude that the proper use of hallucinogens is for research and medical application; the illicit abuse is for kicks and cults (*69*). Our puritanical ethics are said to prohibit us from even exploring whether the use of hallucinogens could improve the healthy, or possibly transform Western society into a Zen elysium.

Whatever scientists may think, history does indeed record our unceasing urge to transcend limits and escape dreary reality or anxiety with the aid of magic, drugs, drama, festival rites, and (with biological regularity) through dreams. Even though we could doubt that drugs produce pleasure without the risk of harm, and wonder if man is built to sustain and to manage more than a brief chemically-induced glimpse of paradise, we must still examine the data of ethnology, pop culture, and clinical use for real evidence. Do such data indicate that there are drugs which specifically enhance these varied transcendent purposes? If so, how do they, why and how exclusively or to what extent do they work and at what cost? These questions will require

more explicit answers and more extensive research than we can presently report.

To discriminate and analyze drug effects, quite imperfect tools will have to be borrowed from a variety of disciplines and contexts: from the social psychology of religion, of deviant behavior generally, of recreation, of social change and self-help movements, as well as the social psychology of aesthetics, pleasure and euphoria, and that of groups and of altered mental states.

We should recognize that analysis of these problems occurs in the context of prevailing prejudices and publicity untempered by rational scrutiny. It already seems clear that whatever the motive for their use, the consequences of these drugs range from isolated awe or benign or even bored surprise, to reported shifts of values to transient or occasionally long-term psychoses, to varieties of religious or aesthetic experience, and to clique formation and ritual. There are now conflicting reports of therapeutic efficacy in alcoholism, depression, character disorders and severe neurosis (*2*, *12*, *19*, *57*, *62*, *66*, *73*, *79*, *80*, *82*, *87*). There is also a mushrooming psychedelic culture. This underlies the tribal motions (or brownian movements) of groups of long haired, barefooted dropouts, and the paraphernalia of fringe fashions, music and art—the trappings and trippings commercialized as psychedelic " go-go." Some serious theologians as well as our peripatetic prophets now seek the drugs as a promoter of love, of religious or self-enhancement (*8*, *21*, *44*, *83*, *91*). Some are sincere and private in these pursuits, some provocative and evangelistic.

We are in any event presented with a barrage of elaborately literate (though not thereby the more accurate) claims. Of course, prophets, seers, gentle and ferocious reformers, acting for good or evil, have often held that special visions were not only their inspiration but their guide. They promise salvation. They also threaten misery to those who do not accurately assess (i.e., agree with) the efficacy of such claims. Truly dispassionate assessment—the exercise of judgment—may, as the elect warn, deprive one of access to the mysteries revealed in special states; thus if one is "in," there may be no way out! The only answer to such dilemmas posed by any cult is exposure to experience, to knowledge and assessment over time—i.e., perspective.

Thus these drugs are often used for a variety of purposes more complex than the simple pursuit of pleasure. In any event, hedonistic kicks can be achieved far more reliably with other chemicals or activities. If we take LSD as a prototype, I believe that in their extreme and most potent form we are examining drugs which influence that complex psychological machinery with which we establish meaning and communion with others. There are few drugs which can so unhinge us from the constancies which regulate daily life, or so clearly present us with data from the "inside world" and from the many normally "inutile" perceptions potentially available to us. Surely, it is tempting to snatch some good from this. It also can do us little harm to place such experiences in the continuum of other states in

which a range of sensory impressions and insights revealed to the self are regarded with awe or claimed as therapeutic, or as personality if not world-transforming events (*1*, *3*, *5*, *10*, *56*, *57*, *67*, *80*, *86*, *88*). Given an ample smorgasbord of effects, claims and usages, we can eventually best gain perspective by concentrating on what—if anything—is common to all of these varied drug effects.

## The Drug Mystique

The young—who are being importuned by "friendly" advocates (and the young always have such friends) or lured by dire warnings—are entitled to what facts we now know about these problems. We in turn might learn from their interest, from not uncommon tragedies (of which we are seeing an increase) and ponder the adequacy of our responses to their probings and needs. My own patchwork impression of the growing use of marijuana and, to a lesser extent LSD, in intellectual groups is that these are *by and large* more socially interesting (or irritating) than socially important phenomena. Rather, a drug mystique has been welded to the underlyingly serious shifts and strains inherently experienced by the most potentially unstable group of any society—the adolescent and young adult. That our society and our youth have problems is not at issue. Nor can we determine here whether indeed this generation is a "now" group, tending to confrontations, valuing honesty, love, direct and uncomplicated action, and avoiding ideologies in favor of simple justice; these values—however germane to the LSD experience—were not born from the drugged mind. What *is* clear is that an ideology couched in the language of drugs or pseudo-zen philosophy has been insinuated into youth culture, and by a band of quite articulate writers and vagrant psychologists. These have replaced the old medicine show of yesteryear with an updated campus version complete with readings and alluring arguments, if not pills to sell: "drop out, tune in, turn on." Thus, this mystique has been generated by frenetic advertisements for themselves by the fad and fashion makers and idea mongers, and the press has been ready to exploit each sensation.

The philosophical arguments of the advocates are carefully dissociated from the social consequences of their publications. They insist they have the civil right to take any agent which "does not harm others." Such claims gained their real momentum when a few psychologists who peddled the drug resented the notion that scientific and medical—or at least nurse's—training were required for responsible drug administration; the requirement for such institutionalized "know-how" was viewed as a plot of a smug establishment. This argument, if carried to its extreme, would counsel a case requiring cardiac surgery to refuse care from a trained expert who votes Republican—and to do so, if necessary, on trumped up religious grounds. It seems ridiculous to have to state that while each of us in our infant development has attempted to assert the right to do what we want

when and where we want it, every society has shaped some constraints—ranging from some form of toilet training to traffic control—constraints impinging on our private views of our capacities, rights and bodily urges. Such is the uncivil level to which "debates" about the drugs lead! It is, of course, hardly a private matter (and it *is* a civil matter) when such proselytizing leads to a number of drug-related cases requiring medical and psychiatric care for brief or longer periods of time.

The irresponsibility of the psychedelic gurus is demonstrated in the fact that while they advertise the drug as only a part of *their* version of a way of life, they are not in a position to manage the consequences of their ideological schemes. Can they really be innocently surprised if the drug per se is more alluring and interesting to the immature than their philosophical preachings? They may reach certain segments of our youth far more readily than most conventional authorities, but nothing in their performance to date shows they know how to manage or anticipate what they so blithely initiate. Psychiatrists who have worked intensively in private institutions with young borderline or schizophrenic patients are quite familiar with some of the tribal behaviors, excesses, philosophizing, and "freak outs" similar to those which occur in psychedelic cults. "Wild analysis" and "psyching"—probing into one another's supposedly unconscious motives—characterized youth of previous generations, as did self-experiments with hypnosis even in the 19th century.

## Scope of Contemporary Problems

The increasing problem of drug abuse in most countries is alcohol, followed by barbiturates, amphetamines, opiates and mild tranquilizers. As I see it, the consequences to national health and social welfare of these drugs are not as yet startling—either in terms of the utility of LSD *or* its harm. Debates about whether to use or not to use LSD are hardly as consequential as the use of "The Pill" in our society. The agent most frequently used by youth for illicit purposes and with lethal effect is the automobile; and the most faithful monitor of the scope of such social problems is the prevailing high insurance rates for young males. I know of no rate changes for medical, psychiatric or mortician's coverage which have been instituted by this actuarial superego of our society in response to these chemicals. This is an interesting generation but they have not yet gone completely to pot! On the campus scene, *interest* in these drugs clearly flies high, but not in the majority of students. "Acid" commentaries are, if not more abundant, more influential than trips. While in the large picture, the scope and pattern of hallucinogenic drug use in our society must be said to be more sensational than consequential, the development of cults and a sharp increase in drug-taking behavior in relatively small, often elite or fringe segments of our society warrants investigation.

## Inherent Problems in the Study of Abuse

For opiate use and abuse and for the abusive potential in marijuana (*4*, *6*, *13*, *15*, *16*, *40*, *60*, *61*, *63*, *68*), excellent studies have been done. Designs for the study of LSD abuse could profit from these. It is clear that the motives for experimenting with a drug, for trying a drug, for interpreting the subjective effects of a drug (*81*), and for continuing drug usage and for seriously maintaining it can be quite different. The ability of the habituated to control their intake also varies; e.g., many people have the alcohol habit but control their intake in accord with their social obligations. It is also clear that the population of users shifts; e.g., cannabis users have shifted throughout history even in countries such as India, and before 1910, middle class women were frequently represented among our opiate addicted population. The response of society to drugs differs, often mecurially and rarely in response to sober judgments. For example, over 30 years ago, the Federal Narcotics Bureau saw no harm in marijuana and within 2 years—and with no more objective data—decided there was a menace. The complexities of the drug-taking, drug selling and drug policing groups (who form subsocieties "needing" each other), should be noted. When underworld vendors specialize in one class of illicit imports, they may also market others. Thus heroin and marijuana are occasionally though not usually sold by the same peddlers. This association is a social consequence of prohibition and policing—not an actual or pharmacological link of the drugs. Marijuana users, psychedelic drug or opiate users, "goofball" or amphetamine abusers, are not commonly the same population (although there is overlap), nor has the illicit supply of psychedelics yet been merged with that of heroin.

For the nonaddicting but so-called hallucinogenic drugs, we have much yet to learn about current practices. Only a minute fraction of persons who have taken these drugs could be said to constitute a reliable base for study of long-term users; groups of persons who drift in and out of the category of users are not easy to identify, and are hardly reliable reporters since some are always first discovering the drug while others are experiencing disillusion or worse. Indeed, over the past ten years we have been greeted with fresh pronouncements of new discovery of the effects of a synthetic compound (LSD) which has recurrently startled its takers since it was first known—well over 20 years ago. Scrutiny of the response to the mescaline-containing peyote—known since the last century—similarly reveals cycles of startled amazement as several new groups or persons came to learn of it and adapt to it; e.g., Havelock Ellis and William James (who did not, incidentally, form cults in 1902) (*28*, *30*).

Complications for research arise from the current publicity. Selling and propaganda create a bandwagon effect and complicate a sober assessment of the extent and nature of drug use. The hucksters gain attention, audiences and monetary support as they threaten the establishment with love and—long before the fact of truly increased drug usage—announce that hordes of young people are, if not their followers, then independently dedicated drug users. The establishment, on the other hand, must react with irritation

or even fright at the announced threat. The head of the Food and Drug Administration has a political hide which can be at stake since he must answer to readily alarmed legislators—not to research scientists. Accordingly, those scientists studying the effects of drugs on brain chemistry and behavior in animals have clear-cut procedures for obtaining and accounting for supplies of narcotics but not of psychotomimetics (in spite of the promise by the FDA in May of 1966 to set up machinery and explicit guidelines). Finally, as the advertising escalates and the empirical problem grows, the young and their parents must enter the debate and assess the claims of value. Physicians hysterically crying alarm rather than pointing rationally to danger join the melee. The use of these drugs in experimental psychiatry to study altered states or the genesis of symptoms or new learning or the nature of brain mechanisms related to altered perception (*10*, *29*, *48*, *52*, *58*, *72*, *93*) proceeds with National Institute of Mental Health support, but not without severe problems of sanction contingent upon sensationalism and fear in the bureaucracy.

Physicians who make headlines with reports of dire results both lure the susceptible and generate their clientele who are latently worried about what they are doing. Sober medical assessment would be *more* effective—and honest—as a deterrent. It is also most important to sort out the various factors which might complicate the picture the physician sees when patients are brought by drugged friends or in other disorganized circumstances to hospitals for one or another indication. The possibility of complicated drug-taking patterns in such patients, of prior instability if not mental disorder, is to be investigated. In brief, the fact that the drug is a precipitant or concommitant of an ongoing disorder must very clearly be distinguished before we determine anything really definitive about long-term effects (*22*, *23*, *24*, *31*, *32*, *42*, *45*, *64*, *77*, *92*). If we recall the reaction of the medical community to the psychotogenic effect of steroids, and if we take cognizance now of the fact that these disorders still occur, the difference is that we now know what the steroid psychoses portend; we can predict with more confidence what the results will be and accordingly (even though attending physicians are often uncomfortable) there is little scare literature presenting unevaluated snapshots of steroid psychoses in cross-section, so to speak. As a general public we are gullible, vulnerable to sensationalism and to over-reactions on any side of the issues involving behavior active drugs. This is true also not only of the press, of poets genuine and manqué, but of legislators, bureaucrats, and physicians.

## Inherent Problems in Ethnopsychopharmacology

We react with similar responses to a variety of drug-induced experiences, but there are characteristic behavioral patterns and social uses which cluster around one or another drug; e.g., opiates probably do differ not only pharmacologically and psychologically but in terms of patterns of social use from LSD or peyote. Research is required both at the psychopharmacological and

ethnological levels to be certain. A major problem exists anytime we study the varieties of so-called irrational behavior. This is that there is nothing intrinsic to the training and practice of a wide number of professionals which equips them knowledgeably to handle and interpret either the irrational itself or themselves when dealing with it. What little knowledge resides within the experienec of psychiatry has not been made sufficiently explicit to be extensively applied by others. If a historian documented the distractions inherent in trying to understand or deal with schizophrenia, with hypnosis, with dreams, or with such questions as religious conversion— and certainly with cannabis and LSD—we would see that it has not been easy for men to comport themselves with the best of rational, let alone scientific skill in these areas. Judgments and assertions, then, have to be continuously assessed.

The sorting of the intrinsic patterns of drug effects from their varied elaborations presents difficulties. For example, the social use of a drug cannot tell us infallibly about the basic pattern of its effects. What Barron, Jarvick and Bunnell (*5*) called "drug-induced ego disruptions" refers to a wide range of substances which can provide a change of scene, a moment of being out of it, a holiday from the constrictions of reality. A wide variety of agents can shift our normal engagement with the world, producing an altered state. This state *in intself* may promote the release of effects and be welcomed for its novelty value as a remarkable trip from reality. Etched upon it may be a specific pattern of the drug. I believe that LSD extends and accents this primary ego state in a salient and sustained way.

A second complication is that sufficiently strong motives can capture any opportune occasion in order to generate uninhibited or cultist behavior. Thirdly, in case a cultural pattern of drug effects seems at first glance invariant, the powerful role of set and setting should be assessed; for example, the exclusive "Mexican-ness" of Hoffman's visions when he first ingested psilocybin (derived from a Mexican mushroom) is hardly ascribable to a specific chemical action.

Pharmacological factors such as dose, route and dosage schedule, and the form and preparation of the active agent are also critical. For brevity, cannabis can be taken as an example: by and large, the more potent the preparation—the more concentrated the form of the resin—the more psychedelic or psychotomimetic the effects. Panic states, temporary psychosis and paranoid episodes similar to those observed currently with LSD, occur more freqeuntly with the more potent preparations illicitly available in India (*16*, *17*) and the Near East (*7*). Many abusers in Morocco and India are found in settings not unlike our alcoholic skid rows. The weaker marijuana used here has drastically fewer such effects. Inhalation or ingestion alters the intensity of effects (*69*).

The pattern of use of LSD is determined in part by the dose-dependent tolerance induced (*39*, *47*, *95*). Three or four days are required for its full development or its full loss: daily dosage leads to dramatically diminished effects unless the dose is considerably increased. "Cyclicity" in tolerance (*53*) is seen with higher daily dosages; e.g., tolerance is lost and regained with

every eighth or ninth consecutive daily dose. After a single dose there is "psychological satiation," as McGlothlin calls it, which is characteristic for any single LSD experience: one dose is emotionally sufficient, if not exhausting, for most people for quite a period—days, or weeks, or years.

If we wish to discern some universally basic pattern of effects (*37*), we also have to consider at what level drug effects on behavior can intrinsically be analysed. Dubos (*27*), expressed the fundamental notion that even a highly selective drug would react with some structure other than the one for which it was designed; absolute selectivity for effects is a chemical impossibility. This does not mean that there are not intrinsically discrete chemical controls or that chemical reactions within cells are not under exquisite feedback regulations, but the control of integrated sequences of behavior remains a complex problem. Yet, in view of the surprising associations and dissociations of which the nervous system is capable (for example, phenothiazine-induced sedation in the presence of motor excitation) it is not inconceivable that chemicals exist which can produce desirable modifications in components of the pattern of effects of a drug such as LSD. The fact that the indole and catechol derivatives which are psychotomimetic induce a response in brain (altering brain serotonin metabolism and probably increasing the utilization of norepinephrine (*33*, *34*, *35*, *36*, *38*, *43*), that most of these show cross tolerance, and that agents—such as atropine or Ditran—producing a deleriod type of response (*33*, *58*, *93*, *94*), affect brain acetylcholine indicates that we are dealing with agents for which some exquisite biological specificity exists; indeed this is the basic reason for scientific interest in the mode of action of the drug, a search that could lead to critical neurochemical mechanisms. Each of the brain monaamines appears to be lawfully related to specific, largely polysynaptic neural systems and it is not unlikely that with autoradiography (*90*), and fluorescence and electron microscopy that our knowledge of the involved neural systems and chemical changes induced by these drugs can be more finely specified (*33*, *38*).

Finally it will be noted that most of the drugs mentioned in this conference have had multiple therapeutic usages, from carbuncles to mania. The Navaho clearly seek the cure of all manner of both physical and psychic ailments with peyote. This fact means that the ethnologist must be wary of the extent to which reported effects are specifically drug related. The distinction between symptoms of organic dysfunction and those of bodily discomfort in various psychic states is never easy. We see this confusion in small children; there are quite probably differences in social classes, personalities, and cultures in the extent to which the body becomes a "sentient referent" for the consequences of social and personal anguish. This surely could lead to confounding reports of drug effects.

Apparently where drugs can disrupt normal ego functions they can comprise a polytherapeutics for the so-called functional factor in illness. How this is accomplished is not clear; perhaps through an ultimate shift of attention as in hypnosis; or through the effects of powerful wishes for cure—which observably dampen anxiety. Something as nebulous and as potent as faith and confidence is involved. When we ingest a drug because of anxiety

or weakness, there is a monotonous regularity in the "non-empirical" interpretations which may be evoked; psychologically, the drug is seen as a power, either one evoking terror (poison or devils) or one producing sexual, physical or spiritual strength leading to salvation or healing. Accordingly, in reviewing the folk usages of drugs for therapeutic clues and in obtaining discriminative information on the effects of drugs on patterns of behavior, we have to distinguish the general range of effects of ego disruption *and* what is commonly called the power of suggestion. Doing so, we can more confidently focus on what is *specific* about the so-called hallucinogenic drugs, including the ways in which they do and do not enhance suggestion.

## The Definition of a "Psychedelic" Dimension

Comparative psychopharmacological studies of the various potent drugs would lead to a better appreciation of the fundamental dimensions of behavior, of the ground out of which complex but related behaviors emerge. That element contributed by *specific drug* effects to the entire picture of drug usage will require more focus. Given such reservations, it seems that the recurrent theme in historical records is that certain drugs are compellingly related to learning, to self-revelation, and that they are involved in some mystical, often ritual, use. McGlothlin notes that the American Indian often states that "peyote teaches." He does not find this major theme running through accounts of marijuana usage (*69*). Again the potent preparations of cannabis are an exception and the milder preparations have been used to enhance contemplative states as well as for a "high". Apparently, there is a continuum of effects along the dimension of self-revealing and ritual usages.

To the extent that there are classes of agents which starkly reveal something about the depths or the dimensions of the mind—exposing these dimensions to our attention—we can say that both use and abuse stem from our amazed response to the subjective experience revealed by these drug states. If this is what Humphrey Osmond meant by the term "psychedelic" or "mind manifesting" for drugs such as LSD, it is an apt though not novel description. There is a wide range of contexts—including clinical disorder in which states of heightened awareness with varying degrees of mental clarity occur, and a variety of initiating causes. The mode of functioning and experiencing called psychedelic reflects an innate capacity (like the dream) of which the human mind, in a general sense, is capable (*10*). The fact that a certain class of drugs so sharply compels this level of function is what so intrigues the behavioral scientist.

A rather famous and wordy Harvard professor noted that drug-induced intoxication "expands, unites and says yes . . . it makes . . . (man) for the moment . . . one with truth." William James (*49*) went on to write that parted from normal consciousness " . . . by the flimsiest of screens, there lie potential forms of consciousness entirely different . . . apply the requisite stimulus and at a touch they are there in all their completeness . . . somewhere (they) have their field of application and adaptation. . . . How to regard them is

the question . . . *they may determine attitudes through they cannot furnish formulas and open a region though they fail to give a map.*" (Italic mine.)

Many authors have stressed that the human mind is apparently built with mechanisms for constancy with which to structure and use these fluid and irrational components. Indeed in the most systematic series of neuropsychological drug studies extant—those of Heinrich Klüver (*52*) with mescaline—the author concludes with speculations about the drug's differential action on those subcortical areas of brain which are characterized by emotionality and variability and those anchoring sensory-motor systems which aid in constancy. The question perhaps is not so much expanding the mind—it is expanded enough—but to see if there are drugs which can enhance a better and more creative coordination among these so-called regions.

## The Drug State and its Consequences

So whether we set out on a personal or on a scientific research effort to discover and explicate this order of the mind, whether we examine it by introspection or examine its effects on natives, patients and others, we embark on a search which is intrinsically difficult and fraught with misunderstanding. One can expect nothing else if we attempt to deal with the irrational. In any event, we shall try to describe a multipotential state which, in its most general sense, can underwrite a variety of outcomes: religious feeling and conversions, states of hyper-perception leading to inspirational insights, to psychosis, to exalted states or to behavior or value change.

The more we can grasp some of the intrinsic features of this state, the more we will be able to understand some of its variable outcomes. So if we had little experience with drugs, we might still be able to predict their consequences and understand, for example, why these drugs might be properly called, among other ascriptions, "cultogenic agents." Some of the modes of experience—the styles—which characterize the drug experience seem frequently to be linked to the outcome or to the style of life commonly centered around drug taking: whether this "hang-over" of drug effects is learning or reinformement of the ongoing trend of goals and adaptions, or based on more complex variables and mechanisms is not known.

### *Some Features of the Drug State*

The sequence of effects following the usual doses has been described elsewhere (*48*, *78*). During the first four and half hours there is generally a clear cut self recognition of effects—an internal "T.V. show" which is followed by another four or five hour period in which a subjective sense of change is not marked but during which heightened self centeredness, ideas of reference and a certain "apartness" are observed. At 12–48 hours after drug ingestion there may or may not be some let-down and slight fatigue. There is no craving for a drug to relieve this if it occurs and no

true physiological withdrawal, as is the case with opiates, alcohol, sedatives, and certain tranquilizers.

It is the intense experience without clouded consciousness—the heightened "spectator ego" witnessing the excitement, which is characteristic for these drugs in usual dosages. Thus there is a split of the self—a portion of which is a relatively passive monitor rather than an active, focusing and initiating force—and a portion of which receives vivid experiences. Some people seem to repeat this long after the drug state; standing apart from life or relying on the group to direct events, they turn away from the prosaic world—or else are turned away by society, as well as turned on by the drug. They may find a clique or a group which tolerates this disposition.

During the drug state, awareness becomes intensely vivid while self-control over input is remarkably diminished; thus there is the lurking threat of loss of inner control—loss of control of integral stability—of the "dying of the ego" so often reported in bad trips or in phases of mystical experiences with the drug. In the drug state, customary boundaries become fluid and the familiar becomes novel and portentous. Events take on a trajectory of their own; qualities become intense and gain a life of their own; redness is more interesting than the object which is red; meaningfulness more important than what is specifically meant; connotations balloon into cosmic allusiveness; the limits of sobriety are lost. The very definition of the importance of the external world shifts when most mental activity is absorbed either in monitoring the novelty of experience or in maintaining the integrity of the self. And, after the drug state, we may find more tolerance for ambiguity and a diminished readiness for the quick answer; we also can find an associated inability to decide, to discriminate, to make commitments. Spindler reported the latter as a Rorschach pattern in certain Indian peyote users (*89*). Such a tendency to avoid distinctions could lead to alienation and retreatism, even if these were not pre-existing traits (as they often are). A certain isolation, or sense of it, tends to occur as a trait in many drug experimenters; the after-effects may emphasize the pre-existing traits. For many the drug experience may represent a beginning which without luck or expertise, cannot easily come to a useful conclusion; neurotic acts also have been viewed as misguided attempts at self cure. Thus many reported immediate after effects of LSD—both good and bad—could depend largely on the motive for taking the drug and in fact could be transient rather than transforming.

In any event, when portentous implications and hidden meanings perpetually contaminate the response to the explicit signs and conventions of everyday life, "focus" and goal directed efficiency are usually impaired. Since judgment is not enhanced *during* the drug state and since isolation or apartness (even when sanctioned by a minority group) bring their own problems, it is clear that persons who continually overvalue the modes of experience of the drug state could develop patterns of poor practical judgment. The consequences of long-term and frequent use of the drug—involving probably 5–15 percent of those experimenting with LSD—would probably have to be evaluated in this context.

*Immediacy, Novelty and Creativity*

In the drug state, the experience of compelling immediacy diminishes the normal importance of past and future. One's organized anticipation of time dissolves (which may incidentally be why, when properly given, the drug can replace narcotics in dying cancer patients). It also is related to the overvaluation of "nowness," the fickle pursuit of the novel apparent in certain youth subcultures (*76*, *84*). The ability to see old and familiar events in a new light is a facet of the shift in organized anticipations and equally a facet in the poorly understood processes related to creativity. The impairment of goal directed efficiency also carries with it the impairment of integrative and synthetic functions and abilities. Thus the mere mergings of sensory objects (the synesthesias, the plastic rearrangements or the clear focusing upon fine details or usually disregarded elements) is hardly the same as an organized building and arrangement in which "boundaries" are, at some juncture, essential. Creativity requires some use of the drug-induced facility for seeing new meanings; but there is nothing about the drug effect which specifically enhances this synthetic and organizing facility. Indeed as we shall stress, the need for synthesis—not the ability to synthesize—is what is enhanced in the drug state.

*"Cultogenic" Actions*

An important feature of the state is an enhanced dependence upon the environment for structure and support as well as enhanced vulnerability to the surrounding milieu. With the loss of boundaries, persons or a group are used for such elemental functions as control—for helping one to know what is inside and what is outside, for comfort and for binding and balancing the fragmenting world (*10*). When one is absorbed either in monitoring the novelty of experience or in maintaining self integrity the major changes in the external world will be overlooked or slight changes will assume a critical role. Persons or objects in the environment have positive or negative value in terms of quite elemental functions: e.g. as threats or as anchors in maintaining control (quite as in the so-called psychotic transference). Persons are self-centeredly seen as objects—not to be related with nor evaluated in their own right—but either to be clung to or to be contemplated in terms of what essentially is a self centered, esthetic or ideologic frame of reference. At best this narcissistic reworking of one's relationship to others and to one's own ambitions can lead to outcomes which are socially valued—wisdom, humor, perspective—but such internal syntheses never guarantee socially pleasant behavior (e.g., non-competitive behavior or conduct which takes an ideal regard for others into account (*54*). In other words, the claims for a different perspective have to be evaluated both in terms of how this is integrated in the life and in the internal rearrangements of values of the user; one need not argue with the asserted shift in values (although even this can be monitored (*72*)), but the consequences of this can be assessed.

Thus with the dissolving boundaries of self and outside, with the fusion of self and surroundings some of the strain between harsh authority and personal strivings can for the moment be transcended or dissolved. At the same time there is a leaning on others for structure and control and hence, when the drugs are taken in a group setting, the breach with reality represented by the drugs can be filled by the directive mystique and support of the group. This is, in part, why I have termed these drugs "cultogenic."

*"Model Psychosis" in the Drug Experience*

The elements of a model psychosis are present. By model we do not mean identity; rather we mean an approach to certain processes which are present to some extent both in the drug state and psychoses; the conditions for either state have similarities and obvious differences (just as do dreams and psychosis (*41*)). For example, what is impinging on an ongoing perception is a vivid memory of what has *just* been perceived; these co-existing images can compete for attention and thus give rise to illusions. These can be immaginatively elaborated into hallucinations. Similarly, past memories can emerge vividly, competing for the status of current reality. The failure to suppress the prior perception or memory or thought characterizes what Bleuler called "double registration" in schizophrenia or what, in Rorschach parlance, is called contamination. Similarly the failure of identities and categories to be maintained underlies most of the descriptions of paralogic in schizophrenia. The capacity to direct one's focus is impaired; allocation of the source of a feeling, a sound, a sight, or a thought becomes difficult since inside and outside become fused. Accordingly there are frequent "projections" or misconceptions of motives. This tendency is reinforced when one must exercise energy to account for slight changes in the environment. It of course bears upon our thinking about any psychosis to recognize that primary or secondary shifts in the elemental ego functions of discrimination underlie a range of symptoms.

Similarly effects can be enhanced under the drug state but are difficult to specify since several contrary feelings co-exist or fluctuate—reminiscent of ambivalence. Thus euphoria mixed with tension may be seen. Laughing and/or crying in the first three hours are not uncommon. Subjects later refer to the total state as a pleasant-unpleasant experience. However these experiences are represented, they are evolved from a ground work entailing a co-existence, heightening, and fragmenting of component urges and feelings. With care, one observes that preceeding this there is a primary need for elemental tension-discharge—a welling up which requires laughing or crying for relief. Subjects have to laugh or cry and they then seem to find the appropriate setting to rationalize this; the cognitive and structural aspects of affect seem to follow the need for discharge.

Thus the enhanced value and intense attention placed on the self, the "double registrations" the ambivalence, heightened tension and diminished control all can represent the primary symptoms of a psychosis. The appearance of peak experiences (or acute psychedelic experiences) in psychosis has



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long been documented (*10*, *49*, *67*). Thus we have with these drugs at least a tool with which to study the genesis and sequence of a number of familiar phenomena in psychiatry. Whether this can lead us to a better sorting and description of the varied elements which are present in the range of clinical disorders is yet an unanswered question; it is for example, obvious that differences in outcome of LSD states depend upon specific prior strengths as well as varying circumstances. These various elements may also be relevant in the phenomena and outcomes we encounter in clinical psychiatry.

*Adaptations in the Drug Experience*

Some persons endure all this without evident harm. The spectator ego can simply be interested in the reversal of figure and ground, the visual tricks, or—with higher doses—the spectator is entranced or totally absorbed. The experiencing ego can—especially with increasing dosage—be overwhelmed. At any level, defensiveness can appear; the spectator shuts his eyes and a blind struggle for control may dominate. There are different modes of coping with the drug state which could be called protective. One protection is *not* to fight the experiences during the drug state. An upsurge of the traditional defensive operations may lead to temporary panic even in relatively stable people. This has been reported both in the LSD and peyote cults, and has been observed by medical therapists.

Most people working with the drug (either licitly or illicitly) note that unstable surroundings or confused motives may lead to "bad trips." The attitudes under which the drug is taken are important. The Indians of the Native American Church emphasize sincerity, and the desire to learn, and they link bad peyote experiences with the presence of aggression and competition rather than the setting of sincerity and brotherly love and a willingness to learn. It is striking that when self examination or confrontation with internal problems is the motive for drug-taking, effects are sometimes bad. When problems are aptly externalized or shared there is less panic and subsequent upset. Thus a certain yielding and surrender of ambition and personal autonomy helps some individuals to have a good experience, but this requires if not group support a certain personal strength, or at least a facility. *It also requires stable groups.*

Some people achieve an overall stability by a disposition to react with an astounded pleasure to the whole flux of events. Others are encouraged or equipped to transcend the fragmented disparate elements, letting them flow into the sway of a mystique, or letting them be steered by latent guiding interests or memories. Thus all that occurs is given a tone—or a very diffuse direction. With higher dosages and the increasing loss of the capacity for detailed focusing, the importance of guiding "sets" (music, mystique, affective expectations such as the doctrine of boundless love) is enhanced.

The drug experience is compelling and hard to convey but incredibly vivid, and the extent to which the experience of a specific "trip" is related to outcome requires finer study. So too does the fact that one good trip does not predict a second. Nevertheless the primary changes are the background

state from which a number of outcomes and adaptations ensue—adaptations *both* during and after the drug experience. No doubt the rearrangements of reality which occur during this state produce a memorable experience, but one is reminded of Sidney Cohen's remark that most people get what they deserve or what they are equipped at the time to experience as modified by set, equipment and setting (*21*).

*The Need for Synthesis*

Anyone who has experienced this intense episode must come to deal with it. Our dreams also are an episode in a sequence of states which we usually can somehow integrate into the normal fabric of living; similarly something must now be done with the total drug experience—nightmare, illusion or ecstasy. Some borrow stability from ready-made explanations. Still others will decide that the sense of cosmic comprehension is equivalent to mastery. They will tend to deny the anxiety about the loss or potential loss of control. In any event, when such a profound breach with normal functioning occurs, there is some need to synthesize and integrate this experience, to represent and to cope with it in some way.

Some individuals will isolate it; some will set it aside in an attempt to master it and still others, lacking any other means of mastery, will be compelled repeatedly and unexpectedly, to confront what was experienced. We see this in students who come in for help weeks after a trip.

In others the breakdown of those constancies and habits which normally smooth over the disparate details of our perceptions and actions can persist in benign ways. One scientist experienced his peripheral vision to be enhanced during the drug state; it is not uncommon that there is an equivalence of value for what is at the periphery and what is normally perceived at the center of the virsual field. He commuted daily, reading during the trip. For months after the drug, he was bothered by the telephone poles which flashed by his train window. He could no longer suppress what normally is background rather than a compelling figure. Similarly, the unconscious "background" to thoughts and feelings can emerge. (There are numerous anticipatory sets or constancies which operate to keep the body oriented in space and ready to meet the environment as we expect to experience it; the mind provides constancy wherever the sense organs deal with variability. We anticipate or correct for the images on our retina to keep the world stable and ordered; the hand stretched 8 inches before one, may appear small though on the retina or camera it is large. Coming off a boat one may still waddle anticipating the roll of the ship.) LSD appears to affect such perceptual anticipations and more complex regulatory systems. It rearranges our ideas of order. It is striking that prior to psychedelic ideology and experiments with self-therapy, mescaline produced more "perceptual" than self-revealing experiences, but the *mode* of breakdown of constancies is similar whether the self or perceptions are a referent.

The intensity of the drug experience manifest in the change of constancies can lead to a number of repetitive behaviors. Gordon Allport noted

that, once the vividly religious state is experienced, one seeks throughout life to recapture its inspiration (*3*). The search for synthesis may take the form of attempts to re-experience the intensity of elements within the drug experience in order to master it. The classic example, of course, is the traumatic neurosis in which, following a traumatic episode in the trenches, the soldier recurrently dreams the nightmare—apparently in order to master it. This has been noted in every major theory of psychopathology since the 19th century. The hypnoid state described by Breuer was one of two causes which he and Freud offered for mental symptoms. Put simply, in a state of altered consciousness where control over awareness is diminished, there is no way to bind the intensities experienced and symptoms may ensue. Similarly, in growth and development, many bits and pieces of impressions, many intense experiences—experiences which for the child are intense—have to be organized in the ongoing stream of developing psychological control, and often this fails.

Repetitive symptoms—such as acting out—may be viewed as misguided attempts to give structure to these pre-verbal impressions and intensities—to restore or find constancies and boundaries. Some experience a "loss" manifest by depression and an urge to recapture the illusionary world of the drug. We know that people may produce vivid consequences or experiences in order to see them in a new light. These are experiences which are presented to consciousness, but what often is lacking is the element of guidance, correction, reflection and structure which leads to authentic self-mastery; this may be the chief source of danger of LSD—the lack of structure and autonomy and the traumatic and potent intensity!

Thus acting out behavior with or without a drug often compels control, correction and guidance, and appears as a provocative accusation against authority. The young do not merely "turn on" themselves but seem to display great anger at the guides whom they feel failed them (indeed the prophets counsel students to "turn on" their parents—one of their metaphors which is most likely *not* to be concretely interpreted). Displacing the total experience and the anxieties inherent in it by attacks upon the establishment, they thereby keep a link—and a very strong one—to the very strictures which had previously absorbed them (just as a misbehaving child is tied to his parents by evoking their involved irritation or punishment). Others show delayed panic, depression or anxiety, and seek out friends for help, and still others aggressively talk about their experience as if they were trying to put it together. Some kind of continuity with the gap in reality is sought for. The bridge may be a book as it was with Huxley, a silent synthesis or change of values and tastes, or the understanding of a group or person. In the Native American Church, the Indian utilizes all these elements—religious explanation and adherence, specific ceremonies and the group with its ideology—to integrate the experience which serves a purpose in the total fabric of his life. It has been speculated that during the ceremonies, by borrowing the strength of "father peyote" and experiencing an enhancement of self, he transcends personal anxiety and inadequacy. Some sects are tutored to ignore the visions and disparate elements of the drug state to achieve this higher

cosmic state. The Indian does not accordingly seek a simple "high" or thrill with the drug (*1, 55, 86*).

For some, denial of inadequacy and enhanced omnipotence—delusional autonomy—may lead to various outcomes: that of the benevolent and foolish prophet, or the defensive, alienated therapist, angry at those who prevent his curing the rest of the world. Indeed we must seriously wonder why those who find salvation are so generous and so ready to proselytize and advertise! Implied are unsolved problems with authority figures. In any event it appears that salvation often involves renunciation of previous ties and that those who are saved must repetitively convince others in order to diminish their own doubt, isolation and guilt. At best, they may do this in order to reachieve union with those with whom they have been separated by their unique vision and experience, and to synthesize these breaches with important others.

### *The Role of Groups in Synthesis*

We have referred to the strain between the exertion of personal strivings for autonomy (i.e., needs to order reality and influence the world) and internal authority (the voice of conscience). Certain groups seem built to absorb this strain. Many successful self-help groups appear to be peer groups. With such arrangements the distance between authority and the miscreant (reminiscent of that between parent and child) is diminished and so too is the inner tension. The cost is a surrender of certain order of autonomy to the group and dependence upon it. It may be less painful to drop pretense and to permit less masking of inadequacy in the presence of uncritical and nonthreatening peers. Of course there may also be a tendency to externalize the conflict with authority, a tendency reinforced by peer-grouping. Still this can permit authentic self involvement at a level which is realistically available to the persons involved.

Ideally, autonomy and involvement might mean not to be distracted by arguments with authority; such terms should connote putting oneself in the place of authority—not imitatively—but in terms of real commitments involving risk, initiative and responsibility. To some extent self-help groups can aid members to move in these directions. Yet, such adjustments mean relying heavily on the concrete presence and reinforcement of a sane group which shares the burdens of initiative. This is not always achieved. In some chronic users one sees a bland impulsiveness—an indifference to the habitual and customary which may border on a supercilious posture of superiority. The elect of many cults either assume the attitude or the outsider *feels* this to be the attitude of those who know something he does not. This posture has also been remarked upon in the American Indian peyote users, although they, too (as with the Navaho), are often subcultures not infrequently at odds with established groups and leaders (*1*).

Group sanctioning of the drug state can diminish the intensity and isolation; the group mystique tends to give integration through a credible rendition, if not sanction to events which by their very nature cannot easily be

translated into public language. The mystique may not be more descriptive of the drug state but simply apparently precise and sufficiently allusive to serve as a representation of and compensation for the breach with reality.

Mystical or religious representations also are remarkably apt for synthesizing the experience. Religion relates man to his limits while taking account of his boundlessness which occurs in all aspects of this realm of the mind. It may be that religious symbolism aptly represents the transformations characteristic of this latent part of the mind. Against fragmentation and directionlessness something coherent lends continuity to experience. Against dread, transcendent love can prevail; loving like redness can apparently be enhanced and is remembered. The "lovingness" and "strongness" of a parent can be parted from the particular persons and transcendentally represented in various forms of power ascribed to deities.

## Use and Abuse of Conversion

There are, then, a number of features of this multipotential state related to its intensity, its novelty, its boundlessness which account for some of the expectable occurrences within it and some of the expectable—and observed—dangers and outcomes. There are observations about the uses and abuses of religous conversion which are not dissimilar from what we can describe in the current drug scene.

In Clark's topology (*20*), the outcomes can be: a sudden change of role—he calls this abrupt conversion. Another outcome entails an allegiance to values rather than a behavior change; e.g., adolescents who are converted to their parents' religion. Similarly there are student LSD users who talk like psychedelicists but continue to be headed for a career of suburbia and the office. Gradual conversion entails what Clark calls role assimilation (and this is reminiscent of the more protracted therapies). There are clearly various levels of personality which can be involved either in the drug experience or in conversion experience. Classifications of pathological outcomes of conversion (including irresponsibility and omniscience) startlingly resemble patterns we see with LSD (*20*, *88*).

Even the conversion experience, if we follow Christiansen's description (*18*), is not dissimilar from that described by therapists who have worked with LSD. He notes a pre-conversion conflict which reaches a peak, a moment of "giving up" (an intention to cease the struggle) which can be followed by an opportunity to come up with a new solution. The conflict must become sufficiently accessible to that part of the mind which can organize and synthesize it in religious terms. If this did not happen there might be a confrontation of old intensities and strivings and continuing struggle rather than yielding and reworking (very much as we described in the instance of acting out behavior). Such struggles in which past experience must be disowned yield pathologically defensive behavior, and symptoms easily ensue; there would be a lack of coherence of the personality which the conversion experience might achieve.

There are a number of psychotherapists who have attempted to use the loosening of associations *and* the intense experiencing produced by the drug in order to influence behavior change. Yet the history of LSD therapy by physicians represents a picture of both use and abuse. In the late 1950's many physicians were not only struck by the drug-induced phenomena, but apparently addled by them. Perhaps they were simply jealous of the subject when they insisted upon taking the drug concurrently with him. They certainly discovered a reality of the mind, but it was a region of mental activity about which they were supposed to be expert prior to the advent of these drugs. When a therapist in our culture has little sense of intellectual control over the events he is monitoring, we are dealing with a healing cult; what is rational about therapy is our obligation to study and control that with which we work. Critical observation and empathy have led us as far as we are in our present dealing with schizophrenia; there is no evidence that any further progress has been made by those therapists who insisted on being drugged themselves.

There are a number of ongoing controlled projects in this country and a long history of experience with the use of LSD in therapy. Two major modes of treatment prevail. The treatment employed by many European workers (often called "psycholytic") represents a method by which certain defenses are breached. With a strong drug-enhanced tie to the therapist, feelings and memories are allowed to emerge vividly and unforgetably before the eye of consciousness and their strength discharged. The events are later worked over with care. Dosages are regulated in part by the capacity of the patient to steer a course between being utterly lost on the one hand or overly constrained by habitual defenses on the other. A kind of active participation in the presence of a general loosening is sought. The need for a certain autonomy and directiveness, a certain inner capacity to integrate and pull together at least a part of the experience is recognized. The integration which follows is a collaborative venture requiring the active participation and the output of the patient (*2*). Yet how to reinforce any shifts in attitude which occur with the drug without running the risk of often repeated drug sessions is a largely unstudied issue.

In the so-called psychedelic therapies as they are now being tested, there is an awareness of an immense amount of preparation, of salesmanship with an evangelical tone in which the patient is confronted with hope and positive displays of it, before he has his one great experience with very high doses of drug. The experience is structured by music and by confident good feelings. With the support of the positive therapist throughout this experience, the patient is encouraged to see his life in a new light, to think of his future accordingly. There now tends to be a rather long period of follow-up and support before the patient is discharged. An earlier mode of intervention attempted to avoid the tangled problems of relationship between therapist and patient with one single high dose drug session as the chief therapeutic contact; the current approach is more explicitly ritualized (in the model

of nativistic movements), and the person and attitude of the therapist tends not to be analyzed but incorporated. It is speculated that the egocentric problems of the alcoholic may be specifically tailored for this ego-dissolving, ego-building technique. Other approaches lie somewhere between these two. It is interesting that peyote cultures also report cures of alcoholics, but the effects may not persist without sustained group support and leadership. The efficacy and selectivity of current therapies is far from settled and research is still ongoing (*2*). Obviously careful follow-up is essential, since the immediate glow which occurs with drug-induced personality change can be deceptive.

## Abuse of LSD

I have noted my current opinion that the chief abuse of LSD is irresponsible, alluring and provocative advertising. We are surely at an advanced enough stage of our culture to identify folly and even to study it. Professor McClelland at Harvard (*44*) noted some of the effects upon the research of the psychedelic fanatics at the height of their proselytising in the early 1960's. He documented certain features of their research which appeared to be related to the drug state. Of course whether poor research is to be considered a drug abuse is a moot point, but some of the features noted were a high opinion of their own profundity; dissociation and detachment—a feeling of being above and beyond the normal world of social reality; interpersonal insensitivity; omniscience and philosophical naivete—a simplistic satisfaction in visions. Finally he noted impulsivity which might be seen as intolerance of any limits, questions or skepticism, let alone inability to predict the consequences of irresponsible, provocative actions. These consequences of drug taking observed in the very home of transcendentalism have been observed in other settings; perhaps we are delineating one intrinsic pattern of outcome of extensive, repeated LSD use. While such descriptions may give us a guide for future research, conclusive and analytical studies simply are not available.

In a few current illicit self-help groups the drugs surprisingly are used reportedly to achieve a conventional outcome. A group of ex-convicts—allegedly—require that members have an honest job before becoming part of the LSD-taking religious group. Similarly one group of homosexuals are reported to use illicit LSD to enhance heterosexual behavior. Several groups, recognizing that overly frequent use might have insidious and profound effects on judgment and that careless use can lead to dangerous panic, have set up agencies to be phoned when required. We seem to be living in an era when many practices (half-way houses, group therapies, "cathartic" therapy) built into the fabric of psychiatric work are imitated by self-help groups. If these lay LSD groups learn from experience, they will do so with even less guidance and self critical checks than the professionals have had in coping with adolescent confusion and turmoil and even the more serious dysfunctions. It is the patient who pays for such experimentation by the gurus. On the other hand, other organizations such as Alcoholics Anonymous have

continued to evolve patterns of response to the problems with which they are concerned without damage to their adherents; members are free to get whatever professional help they need. The discipline of abstention and the general reality orientation of this group is important.

From the evidence available, it appears that users who end up in hospitals with prolonged and serious psychoses are initially a quite unstable group. They are, in any event, a small group. More frequently one sees a transient panic occurring during the drug state, from which recovery is generally rapid. Others who have come to the attention of physicians do not require hospitalization but often seek treatment because they are nervous or concerned about having taken the drug, or about some of their thoughts and experiences during the drug state. And a few others as noted may have non-drug induced panics some weeks after the drug state very much as a bad dream recurs. It is somewhat easier within a college population to get some gauge on the prior adjustment of the students. Certainly there are a group of students, even some of the repeaters, who appear relatively stable (*9,51,65,71,74,75*).

## Motives for Use

The motives for LSD use are varied. Sociologists refer to problems of commitment and alienation and at least add thereby to the younger generation's verbal mythology. A "need to feel"—to gain access to themselves and others—a pervasive sense of being constricted, seems to characterize some of the college takers I have studied. In a recent report (*9*) of a group in which Rorschach and other studies were available, this theme dominated even though outcomes sharply differed: these ranged from psychosis, to instability, to a reaction of bemused enlightenment. Some college students clearly tried the drug as a part of clique activity; thanks in part to sustained advertising, drugs and drug talk are a part of a student's vocabulary. Taking the drug puts the student one-up—he has "been there". This is a challenge evoking interest among friends and can provide the basis for a loose group cohesion. Others sincerely feel they should confront an experience advertised to be so important. They see the drug as an emotional fitness test, somewhat analogous to physical fitness. The issue for many is "control". They experiment with the right to drink and test their ability to stop. At this age they are doing the same, often, with cigarette smoking or with masturbation. In general they are rehearsing their strength and autonomy at a time when their lives are largely unwritten. Many behaviors of this age constitute a probing for consequences—an attempt to come to grips with life and to seize the fruits and risks promised in the future, the threshold of which is now visible. This underlies many of the grimmer statistics of the 18–25 age group, including accidents and suicide. One wonders if these represent the inevitable costs of learning the lesson of consequences, of limits, of mortality.

## Summary View of the Value of Psychedelic Drugs

In psychiatry we know something about how to use drugs to cope with grossly inadequate functioning and to compensate for deficit states. With respect to the LSD experience, we know that many serious persons have reported some transient or even long-term value in it. They say their aesthetic appreciation is enhanced, and McGlothlin indeed has some evidence for a slight shift of this sort in some but not all of a group of normal subjects (*70*). If though, we search for major productions of art, letters, music or visionary insight, few clear cut monuments to the drug are available. Related to creativity, the effects of the drug do not seem to have compelled it. Huxley's greatest output preceded his mescaline states; he thereafter, as I read him, tended to write *about* drugs, not to create with them. If we ask whether there have been cultures which have eradicated mental disorders and disease with these drugs, or groups which have seen the dissolution of deviant behavior or even deviant drug-linked behaviors (for example, alcoholism), we find some slight association but no clear cut overall differences that I know of in the general titre of human misery. In fact the use of these drugs is often associated with some form of psychosocial deprivation—or (equally) with marked privilege (as in Brahmins and college students). That private satisfactions might have been achieved, that groups with the presence of these plants could have attained some spiritual equilibrium seems apparent, but whether the plants and their effects are both necessary and sufficient to get such results—whether no alternative means exist within a culture—is another question.

We should not forget to assess the cost of sustained euphoria or pleasure states; we have to wonder whether the mind of man is built to accommodate an excess either of pleasure or of over-rationality. We do not know whether or not there are individuals with sufficient strength to take these drugs for growth or pleasure within the social order without enhanced and credulous alienation from it. Is a stable person really under sufficient control of his motives and shifting circumstance, let alone the dosage, to take these drugs as a civil right for whatever personal reasons he wishes? If so, who has to care for the consequences of his misjudgments? Some side effects cannot be avoided if we are correct about the way the mind is built, and if we learn from the effects of drugs on much simpler biological systems. How can the stability of religious custom protect drug takers who have little authentic orientation to religion and unstable groups and barely reliable leaders upon whom to lean?

Thus etched upon the variabilities of culture and personality are drugs with a certain skew toward that mystical realm of the mind which knows both psychosis and religion, both heightened and useful self insight, and impaired and distorted judgment about the everyday world. Perhaps similarities and differences of these various plants and their effects could—if analyzed—reveal means for finer control of these experiences—at least in terms of their intensities. Some research should point towards elucidation of critical neurochemical mechanisms.

In general, it seems to me that we have been more awed than aided by our experience with these drugs. They still remain agents which reveal but do not

chart the mental regions; to do that we must employ our mental faculties available in the undrugged state. Accordingly we should do better than repeat the ontogeny of past encounters with mind revealing drugs. We should strive to make distinctions so that—at some future date—if we knew how the elements of mind really were related, we could specify for the chemist the designs he should seek in nature. But to begin with we have to learn to analyze how behavior is organized, and to see what nature can teach us about the ways in which the chemical organization of the brain is related to the dimensions of mind.

## REFERENCES


(*1*) ABERLE, DAVID F., "The Peyote Religion Among the Navaho," Chicago: Aldine Publishing Company, 1966.

(*2*) ABRAMSON, H. A. (ed.), "The Use of LSD in Psychotherapy and Alcoholism," Indianapolis: Bobbs Merrill, 1967.

(*3*) ALLPORT, GORDON, W., "The Individual and His Religion," New York: Macmillan, 1950.

(*4*) AMES, F., "A Clinical and Metabolic Study of Acute Intoxication with Cannabis Savita and Its Role in the Model Psychoses", J. Mental Sci 104: 972–999, 1958.

(*5*) BARRON, F., JARVIK, M. E. and BUNNELL, S., Jr., "Hallucinogenic Drugs", Scientific American 210: 29–37, 1964.

(*6*) BECKER, H. S., "Becoming a Marihuana User", Amer. J. of Sociol. 59: 235–242, 1953.

(*7*) BENABUD, A., "Psycho-pathological Aspects of the Cannabis Situation in Morocco: Statistical Data for 1956", Bulletin on Narcotics, 9: No. 4, 1–16, 1957.

(*8*) BLUM, R., (ed.), "Utopiates, the Use and Users of LSD–25, New York: Atherton Press, 1964.

(*9*) BOWERS, M., CHIPMAN, A., SCHWARTZ, A., and DANN, O. T. "Dynamics of Psychedelic Drug Abuse—A Clinical Study", Archives of General Psychiatry 1967 (in press).

(*10*) BOWERS, M. B. and FREEDMAN, D. X., " 'Psychedelic' Experiences in Acute Psychoses", American Medical Association Archives of General Psychiatry 15: No. 3, 240, 1966.

(*11*) BOWERS, M. B., HARTMANN, E. L. and FREEDMAN, D. X., "Sleep Deprivation and Brain Acetylocholine", Science 153: No. 3742, 1416, 1966.

(*12*) CHANDLER, A. L. and HARTMAN, M. A., "Lysergic Acid Diethylamide (LSD–25) as a Facilitating Agent in Psychotherapy", Archives of General Psychiatry 2: 286–299, 1960.

(*13*) CHAREN, S. and PERELMAN, L., "Personality Studies of Marihuana Addicts", American Journal of Psychiatry 102: 674–682, 1946.

(*14*) CHEEK, FRANCES E., "Exploratory Study of Drugs and Social Interaction", Archives of General Psychiatry 9: 566–574, 1963.

(*15*) CHEIN, I., GERARD, D. L., LEE, R. S. and ROSENFELD, E., "The Road to H", New York: Basic Books, 1964.

(*16*) CHOPRA, I. C. and CHOPRA, R. N., "The Use of Cannabis Drugs in India", Bulletin on Narcotics 9: No. 1, 4–29, 1957.

(*17*) CHOPRA, R. N. and CHOPRA, I. C., "Treatment of Drug Addiction: Experience in India", Bulletin on Narcotics 9: No. 4, 21–33, 1957.

(*18*) CHRISTIANSEN, C. W., "Religions Conversion", American Medical Association Archives of General Psychiatry 9: 207, 1963.

(*19*) CHWELOS, N., BLEWETT, D. B., SMITH, C. M. and HOFFER, A., "Use of D-Lysergic Acid Diethylamide in the Treatment of Alcoholism", Quart. J. Stud. Alcohol. 20: 577–590, 1959.

(*20*) CLARK, W. H., "The Psychology of Religion," New York: Macmillian, 1958.

(21) COHEN, S., "The Beyond Within," New York: Atheneum, 1964.
(22) COHEN, S. and DITMAN, K. S., "Complications Associated With Lysergic Acid Diethylamide (LSD–25)", Journal of American Medical Association 181: 161–162, 1962.
(23) COHEN, S. and DITMAN, K. S., "Prolonged Adverse Reactions to Lysergic Acid Diethylamide", Archives of General Psychiatry 8: 475–480, 1963.
(24) COLE, J. O. and KATZ, M. M., "The Psychotominetic Drugs, An Overview", Journal of American Medical Association 187: 758–761, 1964.
(25) DEIKMAN, A. J., "Experimental Meditation", Journal of Nervous and Mental Disease 136: 329–343, 1963.
(26) DOZIER, EDWARD P., "Problem Drinking Among American Indians", Quart. J. Stud. Alcohol. 27: No. 1, 72–87, 1966.
(27) DUBOS, R., "On the Present Limitations of Drug Research", Drugs in Our Society edited by Paul Talalay, Baltimore, Maryland: The Johns Hopkins Press, 1964.
(28) Editorial, "Paradise or Inferno?", British Med. J., 1898, p. 390.
(29) EGGERT, D. C. and SHAGASS, C., "Clinical Prediction of Insightful Response to a Single Large Dose of LSD", Psychopharmacologia (Berl.) 9: 340–346, 1966.
(30) ELLIS, H., "Mescal: A New Artificial Paradise", Contemporary Rev. 73: 130–141, 1898.
(31) FINK, M., SIMEON, J., HAQUE, W. and ITIL, T., "Prolonged Adverse Reactions to LSD in Psychotic Subjects", Archives of General Psychiatry 15: 450–454, 1966.
(32) FINK, P. J., GOLDMAN, M. J. and LYONS, I., "Morning Glory Seed Psychosis", Archives of General Psychiatry 15: 1966.
(33) FREEDMAN, D. X., "Aspects of the Biochemical Pharmacology of Psychotropic Drugs", Psychiatric Drugs, p. 32, P. Solomon (ed.), New York: Grune and Stratton, Inc., 1966.
(34) FREEDMAN, D. X., "Effects of LSD–25 on Brain Serotonin", J. Pharmacol. Exptl. Therap. 134: 160, 1961.
(35) FREEDMAN, D. X., "LSD–25 and Brain Serotonin in Reserpinized Rat", Fed. Proc. 19: 266, 1960.
(36) FREEDMAN, D. X., "Psychotomimetic Drugs and Brain Biogenic Amines", American Journal of Psychiatry 119: 843, 1963.
(37) FREEDMAN, D. X., "Toward A Systematic Psychopharmacology", Internat. J. Psychiat. 2: No. 6, 666–670, 1966.
(38) FREEDMAN, D. X., and AGHAJANIAN, G. K., "Approaches to the Pharmacology of LSD–25", Llyodia 29: No. 4, 309, 1966.
(39) FREEDMAN, D. X., AGHAJANIAN, G. K., ORNITZ, E. M. and ROSNER, B. S.,, "Patterns of Tolerance to Lysergic Acid Diethylamide", Science 127: 1173, 1958.
(40) FREEDMAN, H. L. and ROCKMORE, M. J., "Marihuana, Factor in Personality Evaluation and Army Maladjustment", J. Clin. Psychopathology 7 & 8: 765–782 & 221–236, 1946.
(41) FREUD, S., "An Outline of Psychoanalysis," New York: W. W. Norton & Co., Inc., 1949.
(42) FROSCH, W. A., ROBBINS, E. S. and STERN, M., "Untoward Reactions of Lysergic Acid Diethylamide (LSD) Resulting in Hospitalization", New. Eng. J. Med. 273: 1235–1239, 1965.
(43) GIARMAN, N. J. and FREEDMAN, D. X., "Biochemical Aspects of the Actions of Psychotomimetic Drugs", Pharmacol. Rev. 17: 1, 1965.
(44) GORDON, NOAH, "The Hallucinogenic Drug Cult", The Reporter, August 15, 1963.
(45) GRINKER, R. R., "Bootlegged Ecstasy", Journal of American Medical Association, 187: 768, 1964.
(46) HUXLEY, A., "The Doors of Perception," New York: Harper Brothers, 1954.
(47) ISBELL, H. et al., "Cross Tolerance Between LSD and Psilocybin", Psychopharmacologia 2: 147–159, 1961.
(48) ISBELL, H. et al., "Studies on Lysergic Acid Diethylamide (LSD–25)", Arch. Neurol. Psychiat. 76: 468–478, 1956.

(*49*) JAMES, W., "Varieties of Religious Experience", New York: Longmans, Green and Company, 1916.

(*50*) KENISTON, K., "The Uncommitted", New York: Harcourt, Brace & World, Inc., 1960.

(*51*) KLEBER, H. D., "Student Use of Hallucinogens", Journal of American College Health Association 14: 109–117, 1965.

(*52*) KLÜVER, HEINRICH, "Mescal and Mechanisms of Hallucinations", Chicago: The University of Chicago Press, 1966.

(*53*) KOELLA, W. P., BEAULIEU, R. F. and BERGEN, J. R., "Stereotyped Behavior Cyclic Changes in Response Produced by LSD in Goats", International Journal of Neuropharmacology 3: 397–403, 1964.

(*54*) KOHUT, HEINZ, "Forms and Transformations of Narcissism", Journal of the American Psychoanalytic Association 14: No. 2, 1966.

(*55*) LABARRE, W., "Twenty Years of Peyote Studies", Current Anthropology 1: 45–60, 1960.

(*56*) LAING, R. D., "Transcendental Experience in Relation to Religion and Psychosis", Psychedelic Review 6: 7–15, 1965.

(*57*) LEARY, T. and ALPERT, R., "The Politics of Consciousness Expansion", The Harvard Review 1: No. 4, 33–37, 1963.

(*58*) LEBOVITS, B., VISOTSKY, H. M. and OSTFED, A. M., "LSD and JB318: A Comparison of Two Hallucinogens. Part III", American Medical Association Archives of General Psychiatry 7: 39–45, 1962.

(*59*) LENNARD, H., "Lysergic Acid Diethylamide (LSD–25): XII. A Preliminary Statement of Its Effects Upon Interpersonal Communication", Journal of Psychology 41: 186–198, 1956.

(*60*) LINDESMITH, A. R., "The Addict and the Law," Bloomington: Bloomington Indiana University Press, 1965.

(*61*) LINDESMITH, A. R. and GAGNON, J. H., "Anomie and Drug Addiction", Anomie and Deviant Behavior, pp. 158–188, M. B. Clinard (ed.), New York: The Free Press, 1964.

(*62*) LING, T. M. and BUCKMAN, J., "Lysergic Acid and Ritalin in the Treatment of Neurosis," London: Lambarde Press, 1963.

(*63*) LIVINGSTON, R. B., "Symposium on the History of Narcotic Drug Addiction Problems", National Institute of Mental Health, Bethesda, Maryland, 1963.

(*64*) LOURIA, D. B. et al., "The Dangerous Drug Problem", New York Medicine 22: No. 9, May 5, 1966.

(*65*) LUDWIG, A. M. and LEVINE, J., "Patterns of Hallucinogenic Drug Abuse", Journal of American Medical Association 191: 104–108, January 11, 1965.

(*66*) MACLEAN, J. R. *et al*, "The Use of LSD–25 in the Treatment of Alcoholism and Other Psychiatric Problems", Quart. J. Stud. Alcohol 22: 34–45, 1961.

(*67*) MASLOW, A. H., *Toward a Psychology of Being*, New York: D. Van Nostrand Co., Inc., 1962.

(*68*) *Mayor's Committee on Marihuana*, New York City: Cattell Press, Lancaster, Pa., 1944.

(*69*) MCGLOTHLIN, W. H., "Hallucinogenic Drugs: A Perspective With Special Reference to Peyote and Cannabis", Psychedelic Review 6: 16–57, 1965.

(*70*) MCGLOTHLIN, W. H., COHEN, S. and MCGLOTHLIN, M. S., "Long Lasting Effects of LSD on Normals", Arch. Gen. Psy. 17: 1967 (in press).

(*71*) MCGLOTHLIN, W. H. and COHEN, S., "The Use of Hallucinogenic Drugs Among College Students", American Journal of Psychiatry 122: 572–574, 1965.

(*72*) MCGLOTHLIN, W. H., COHEN, S. and MCGLOTHLIN, M. S., "Short-Term Effects of LSD on Anxiety, Attitudes and Performance", J. Nerv. Ment. Dis. (in press, 1967).

(*73*) O'REILLY, P. O. and REICH, G., "Lysergic Acid and the Alcoholic", Dis. Nerv. Syst. 23: 331–334, 1962.

(74) PEARLMAN, S. J., "Drug Experiences and Attitudes Among Seniors in a Liberal Arts College", Unpublished Manuscript, Brooklyn College of the City University of New York, 1966.
(75) PHILIP, A. F., "Drugs on Campus", Presented at Twentieth Anniversary Meetings, Group for the Advancement of Psychiatry. Philadelphia, Pa., November 12, 1966.
(76) POLSKY, NED, "The Village Beat Scene; Summer 1960", Dissent 8: No. 1, 339–359, 1961.
(77) ROSENTHAL, S. N., "Persistent Hallucinosis Following Repeated Administration of Hallucinogenic Drugs", American Journal of Psychiatry 121: 238–243, 1964.
(78) SALVATORE, S. and HYDE, R. W., "Progression of Effects of LSD", Arch. Neurol. Psychiat. 76: 50–59, 1956.
(79) SANDISON, R. A., SPENCER, A. M. and WHITELAW, J. D. A., "The Therapeutic Value of Lysergic Acid Diethylamide in Mental Illness", J. Ment. Sci. 100: 491–507, 1954.
(80) SAVAGE, C., TERRILL, J. and JACKSON, D. D., "LSD, Transcedence and the New Beginning", J. Nerv. Ment. Dis. 135: 425–439, 1962.
(81) SCHACTER, S., "Interaction of Cognitive and Physiological Determinants of Emotional State", Psychobiological Approaches to Social Behavior, Liederman, H. and Shapiro, D. (eds.), Palo Alto, California: Stanford University Press, 1964.
(82) SHORVON, H. M., "Abreaction and Brain", Hallucinogenic Drugs and Their Psychotherapeutic Use: Proceedings of the Royal Medico-Psychological Association, pp. 74–78, Croket, R., et al. (eds.), London: H. K. Lewis & Co., Ltd., 1963.
(83) SIEGEL, J., "The New Sound: Tune In, Turn On, and Take Over", The Village Voice, November 7, 1966.
(84) SIMMONS, J. I. and WINOGRAD, B., "It's Happening", Santa Barbara: MarcLaird Publications, 1967.
(85) SLATER, P. E., Morimoto, K., and Hyde, R. W., "The Effects of LSD Upon Group Interaction", Archives of General Psychiatry 8: 564–571, 1963.
(86) SLOTKIN, J. S., "The Peyote Religion", Glencoe: The Free Press, 1956.
(87) SMITH, C. M., "A New Adjunct to the Treatment of Alcoholism: the Hallucinogenic Drugs", Quart. J. Stud. Alcohol 19: 406–417, 1958.
(88) SOUTHARD, S., "Conversion and Christian Character", Nashville, Broadman Press, 1965.
(89) SPINDLER, G., "Personality of Peyotism in Menomini Indian Acculturation", Psychiatry 15: 151–159, 1952.
(90) STUMPF, W. E. and ROTH, L. J., "Dry-Mounting High-Resolution Autoradiography", Isotopes in Experimental Pharmacalogy, pp. 133–143, Roth, L. J. (ed.), Chicago: The University of Chicago Press, 1965.
(91) UNGER, S. M., "Mescaline, LSD, Psilocybin, and Personality Change", Psychiatry 26: 111–125, 1963.
(92) UNGERLEIDER, J. T., FISHER, D. D. and FULLER, M., "The Dangers of LSD", Journal of American Medical Association 197: 389–392, 1966.
(93) WILSON, R. E., and SHAGASS, C., "Comparison of Two Drugs with Psychotomimetic Effects (LSD and Ditran)", J. Nerv. Ment. Dis. 138: No. 3, 1964.
(94) WOLBACH, A. B., MINER, E. J. and ISBELL, H., "Comparison of Psilocin With Psliocybin, Mescaline and LSD–25", Psychopharmacologia 3: 219–223, 1962.
(95) WOLBACH, A. B., Jr., ISBELL, H. and MINER, E. J., "Cross-Tolerance Between Mescaline and LSD–25", Psychopharmacologia 3: 1–14, 1962.

# SESSION II

## PIPER METHYSTICUM (KAVA)

**Georg E. Cronheim, *Chairman***

# Chairman's Introduction

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The first session of this conference dealing with a particular plant, is devoted to Kawa or Kava-Kava or Piper methysticum, which is indigenous to many islands of the South Pacific.

The use of Kawa in certain parts of Oceania is apparently very old. It has been described already by early travelers, for instance by James Cook in 1768. It is important to remember that the Kawa drink is mentioned not only quite early, but also repeatedly by a number of observers. The descriptions uniformly indicated that the Kawa experience is apparently pleasant, and free from hangover or other side- or after-effects. Many travelers, and also such scientific investigators as L. Lewin, have reported that Kawa can induce a form of euphoria, described as a happy state of complete comfort and peace, with ease of conversation and increased perceptivity, followed by restful sleep.

In many areas, the use of Kawa was connected with religious cults and ceremonies. Thus, it is not surprising that missionaries tried to suppress the drinking of Kawa. In some islands, this campaign was very successful, especially when it coincided with the introduction of alcoholic beverages. This replacement of Kawa by alcohol may have some significance, which I hope will be discussed by some of the speakers. Could it be that enough people preferred the effects induced by alcohol over those of Kawa? Otherwise the change-over would not have taken place as rapidly or as completely as was apparently the case in many islands. Also, the preference for alcoholic beverages is—if not an absolute proof—at least a good indication that the Kawa drink did not contain or simulate alcohol.

The first major scientific examination of Kawa was published by L. Lewin in 1886. Subsequently, other investigators in Europe and in this country studied the chemical constituents and the pharmacological properties of Kawa and of its components. However, the number of people interested in this plant was always relatively small. Kawa did not become the subject of more wide-spread use (or mis-use), or of numerous scientific investigations. Perhaps our colleagues in anthropology and sociology can tell us whether this is purely coincidental or whether there is some specific reason that in spite of the sudden interest and cult-like fadism related to substances with hallucinogenic or euphoria-producing properties, Kawa remained, outside of the South Pacific Islands, a relatively little known drug. Moreover, the fact that Kawa did not gain any popularity may have another explanation. In more recent references to the Kawa Ceremony and present-day Kawa use, none of the previously described effects on the central nervous system were mentioned. This represented always a great puzzle. How could one explain numerous detailed eye-witness accounts of unmistakable central

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effects of Kawa when taken by natives or by white people, travelers or settlers? Even addiction has been described for these groups. Also, Kawa was an article of commerce. Still more important, it was not just collected as a wild plant, but was regularly cultivated. In other words, Kawa represented something which native people in the South Pacific Islands wanted and for which they were willing to pay in the form of money or physical labor. Doesn't it seem reasonable to assume that they derived some pleasure from Kawa? And wouldn't this explain that drinking of Kawa—both for ceremonial and social purposes—is still practiced?

Pharmacological studies of Kawa and certain of its constituents have shown some rather remarkable properties, which will be discussed in the course of this program. Studies in our laboratories were in fact so promising that we carried out the necessary chronic toxicity studies in animals, in order to permit an evaluation in human volunteers and in patients. Unfortunately, the results were not very striking. Some anti-epileptic activity was seen in patients, but none of the "tranquilizing" effects that had been described. At the same time, signs of skin reactions became apparent, which precluded further chronic administration.

So here we have some obvious discrepancies, for which I am sure there must be some explanation. It is the purpose of the present conference to present such discrepancies and questions to groups composed of anthropologists, botanists, chemists, clinicians and pharmacologists, because the complementary approach evolving from an interdisciplinary discussion has the best chance of solving some of the existing problems.

We are fortunate that the group of speakers in this Kawa symposium includes three investigators who have had extensive first-hand knowledge of the use of Kawa in various island groups of the South Pacific. This information will be supplemented by some clinical observations in patients, as well as special investigations of central nervous system effects of Kawa and some of its constituents in human volunteers. The pharmacological properties of these substances and the chemistry of Kawa will also be presented in adequate detail. All in all, a fairly comprehensive picture of Kawa should emerge. It is my hope that the combined knowledge of the seven speakers, each a specialist in his field, may provide some of the missing answers to the Kawa problem.

# The Function of Kava in Modern Samoan Culture

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In the Manu'a island group of American Samoa no formal or informal meeting of chiefs would be complete without the distribution of the traditional Polynesian beverage kava. This drink known locally as *'ava*, is prepared by steeping the pulverized roots of the *Piper methysticum* plant in a prescribed amount of water until a cloudy, khaki-colored liquid is produced.

Kava is in no way alcoholic, but much has been made of its narcotic properties. Early missionaries maintained that the concoction partially paralyzed the lower extremities, making it difficult to walk. More recent partakers of kava, including the author, have experienced no debilitating effect which could be attributed to consumption of the drink. Instead they have found it a refreshing, astringent drink which produces nothing more than a tingling sensation in the mucous membrane of the mouth and a short-lived numbness of the tongue. The partial paralysis of the lower limbs is not caused by the kava but by sitting cross-legged for hours while the kava ceremony is in process. Samoans who find the sitting posture a more natural one do not complain of any impairment to walking. Missionary V. A. Barradale, writing in 1907 stated, "I have heard it said that if people drink too much [kava], it makes them drunk in their legs; it paralyzes their lower limbs, and they have to sit where they are till the effect wears off. But it would certainly need a very large quantity to affect a man in that way, and I never saw or heard of any one in that condition"(*2*).

Although Beaglehole (*3*) reports rare cases of kava addiction in Pangai, Tonga, such a phenomenon was not personally observed in Samoa. The author's informants did on one occasion refer to one recently deceased chief whom they believed drank kava in excess because he had it prepared every morning so that he could partake throughout the day. They also felt this excessive use of kava was the cause of his death. Actually he had died at the age of seventy-five from cancer of the stomach. Another claim made by native informants is that over-indulgence of the drink can result in skin diseases and eye ailments. The literature produced by early missionaries contains numerous references to a scaly skin condition being attributable to kava drinking. These claims were not corroborated by the author. One European observer believed that the consumption of kava had the effect of preventing the Samoans from developing a taste for alcoholic liquors. The author has not observed this phenomenon either.

Krämer reports that he observed the addition of *Capsicum* pepper pods to the kava concoction and believes this strengthened its stimulating effect thereby rendering kava the equivalent in its use to *Piper betle* in Indonesia.

He tells of having broken open a *Capsicum* pod and accidentally having touched his face with his soiled hands. He complains of having "endured severe pain for a long time; thus the pepper affects even the epidermis." (*6*).

The addition of this pepper to the kava mixture was not observed in contemporary Samoa, and the extent of its use in earlier days is not known. Kramer is the only 19th century observed to record its use.

Kava is often drunk by Europeans, who upon acquiring the taste, find it very refreshing. Many urban centers in the South Seas boast kava saloons where local businessmen—native and European—take a kava break during the mid-morning hours. Some government offices have kava prepared in the morning for the comfort and enjoyment of their employees.

The relative importance of kava varies from island group to island group. Kava drinking in Polynesia is primarily a phenomenon of the cultures in the west, such as Tonga, Fiji and Samoa. The plant does not grow on the atolls of the Tokelaus. Beaglehole (*3*) reports universal use of the beverage in Tonga, but maintains that accompanying ritual is almost totally absent in villages inhabited by commoners. Hawaii and Tahiti had the drink at one time but it has practically disappeared in recent years. The Cook Island cultures formerly used the plant for drinking purposes also, but many of the Bernice P. Bishop Museum monographs on the cultures of this region do not even mention kava. The Maori did not drink kava although a variety of the plant which could have been used for such purposes was indigenous to New Zealand. Aitken (*1*) reports that in the Australs the occasional and somewhat unimportant practice of kava drinking was abolished by missionaries in 1822. New Caledonian Polynesian populations are described by Leenhardt (*7*) as ignoring the plant altogether.

Other centers of kava drinking in Oceania are Ponape in the Carolines, the Marind District of West New Guinea, the New Hebrides and the Wallis and Futuna islands. In Melanesia the drink is described as being made from fresh roots, and the concoction is said to have the effect of rapidly inducing deep sleep. Chronic drinkers in this area are said to suffer from a state of depression accompanied by a permanent decrease in appetite. Malnutrition is also said to be observed among some addicts. The difference in effect between this area and western Polynesia is possibly attributable to the state of the kava root at the time of production of the beverage. The dried roots used in Polynesia apparently do not produce as strong a drink as that concocted from fresh ones.

In Samoa it appears that kava drinking and its attendant ceremonies has a long history, the practice being intimately related to indigenous religious practices and village social and political organization. Mythology relates how kava drinking was given to mortals by the first high chief, Tagaloa Ui, and prescribes the form for modern kava ceremonies. The myth which provides these sanctions was recorded in Manu'a as follows:

> Not far from the village of Fitiuta there is a place where the rising sun is first seen in Samoa. This place is called *Saua*. Long ago there was a custom that one day a year one of the families of Fitiuta must sacrifice the daughter to the sun. On the day of the "celebration of the sun" a daughter from the family of Matainaumati went to Samoa

to be sacrificed. The girl's name was Ui. When the sun came for the girl he saw that she was very beautiful and instead of eating her he decided to take her as his wife. He took the girl to live with him in the sky. After a time she became pregnant and wanted to go home so that her first child could be born in her family's village, and she wanted to show her parents that she had not been killed.

While journeying home, Ui had a miscarriage, and the fetus floated away upon the waters where it was found by the hermit crab, the plover and the shrike. By manipulating the fetus and breathing life into it the animals created the first Samoan chief, Tagaloa Ui.

After his creation Tagaloa Ui made a kilt for himself out of *ti* leaves and started to walk toward the village of Fitiuta. On his way he walked through a grove of kava plants and discovered the house of the mortal, Pava. Pava invited the chief to enter his house and there the first kava ceremony involving mortal men was held.

When Tagaloa Ui entered the house he took a place at the end of the house (today the seat of honor), and Pava sat in the front of the house (the traditional place for talking chiefs) and began to prepare the kava. Pava chewed and spit the kava into a taro leaf (*laupula'a*) which served as the kava bowl. Cups consisted of *tautava* leaves, and Pava used his fingers to wring the kava as no strainer was then known.

While Pava was wringing the kava, his son, Fa'alafi, laughed and played near the bowl. Tagaloa Ui instructed Pava to make the boy sit down and be quiet, but nothing was done about the irreverent boy. After several unheeded warnings, Tagaloa Ui picked up a coconut frond, formed it into a knife, and cut Pava's son into two pieces. Then Tagaloa Ui said to Pava, "This is the food for the kava. This is your part and this is mine." Pava mourned and could not drink the kava.

Then Tagaloa Ui said, "Let us have a new kava ceremony." The kava and the leaf bowl and cups were thrown away and Tagaloa Ui told two of Pava's sons to go to the highest mountain, the house of Tagaloa Lagi, and bring down a wooden kava bowl, coconut cups, a hibiscus strainer and a new kind of kava, *latasi*, a single branch kava tree. These things were brought, and a second kava ceremony was started. Again Pava served as the kava wringer, and when the kava was ready, Tagaloa Ui said, "Bring me my cup first." Tagaloa Ui did not drink the kava but poured it onto his piece of the dead son of Pava and then onto Pava's piece. Then he said, "*Soifua*" (life). The two parts came together and the boy lived. Pava was so happy he clapped his hands. Pava drank his cup of kava and Tagaloa Ui gave the following orders: "Pava, do not let children stand and talk while kava is being prepared for high chiefs, for the things belonging to the high chiefs are sacred."

A number of ritual details of the modern Samoan kava ceremony seem to relate directly to this myth. They are:

1. The seating arrangement of the chiefs and the talking chiefs.
2. Prohibitions against children, or indeed any unauthorized untitled persons, attending the ceremony.
3. The solemn atmosphere which must prevail.
4. The proper equipment for the production and distribution of kava—a carved wooden kava bowl, a hibiscus strainer, a coconut cup, and a certain type of kava.
5. The order of drinking—high chiefs first, talking chiefs second.
6. The pouring of a bit of kava from the cup onto the mat.
7. The concept of food for the kava.
8. The use of the term "*Soifua.*"
9. The clapping of hands when the kava is ready.
10. The duty of talking chiefs to direct the kava ceremony.

The importance of the above is indicated by the fact that although short-cuts are often taken in the modern kava ceremony the features listed are seldom if ever altered.

Kava in contemporary Samoan society has been likened by Keesing (*5*) to the European cocktail or highball, in that it produces a relaxed and friendly atmosphere conducive to social cooperation.

Every chief is expected to keep a stock of dried kava on hand for his own use and for the many demands made upon him by the protocol of hospitality. Whenever any elite visitor enters the village, the welcoming ceremony requires that each of the host chiefs present him with a dried kava root.

The kava ceremony is invariably the initial act of any meeting of the village council (*fono*), and is therefore a definite part of formal discussion and decision making. It is also an essential part of all ceremonies associated with births, marriages, deaths and title installations. No bonito canoe or house is ever constructed without the labor being prefaced by the kava ceremony wherein the carpenter is served first kava in the name of Sao (a name which people claim was given to the first carpenter by the god Tagaloa). The ceremony is said to insure successful work.

Kava drinking is without doubt the most important element of the *aiavā*, the ceremony of greeting for visiting parties (*malaga*), and therefore carries much of the burden of Samoan hospitality.

In earlier, less peaceful days kava was consumed by warriors prior to battle. On such occasions, the ceremony was referred to as *'ava mua au.* Fe'epulea'i Ripley (*7*) reported observing such a ceremony wherein the chiefs lined up along each side of the road and set up the kava bowl in the middle of it.

Aside from its ceremonial use, kava is reported to have certain medicinal uses. It is often consumed in an attempt to counteract the chills which accompany filariasis. Some Samoans believe that kava chewed in large quantities will cause abortion. It is also claimed to be a cure for gonorrhea, and it is a matter of record that German drug houses at one time imported small quantities of the plant for this purpose.

Although the kava ceremony is considered the exclusive property of titled men there are certain ceremonial occasions, such as the entertainment of a visiting party, when the society of untitled men (*aumaga*) or the wives of the village chiefs (Woman's Committee) conduct their own social kava ritual. On such occasions the order of drinking is determined by one's relationship to the title holders of the village. Having a father or husband who is the village paramount chief entitles one to be honored with first kava.

Some regional variations in kava ritual may be observed from village to village, and even in a given village the ceremony is not always performed in the same way. Certain parts may be abbreviated or eliminated altogether, and perhaps the ceremony to be described in this paper is closer to the ideal than to the real. However, all the steps described herein have been observed frequently on occasions of high ceremony. Regional variations include differences in who may wring kava, the number of attendants involved in serving the kava, and in some cases, the status and sex of those served. In some villages only men are permitted to wring kava, but in others the ceremonial village maiden (*taupou*) may do the honors. On the island of Tutuila it is not uncommon for women to hold *matai* titles and serve on the village council. They are, therefore, as titled individuals, qualified to participate in the kava cere-

mony. In Manu'a women neither hold *matai* titles nor partake in the drinking of kava at formal ceremonies where chiefs are present. The one exception to this was the female sovereign Tuimanu'a Makelita.

## The Modern Kava Ceremony

In preparing for the modern Manu'an kava ceremony the talking chief who will later direct the kava distribution selects a piece of kava root. This part of the kava plant is called the Brother Roots (*'ava uso*). The name drives from a myth which recounts how two brothers, the sons of Tagaloa, found a piece of floating wood while swimming west from the Manu'a Group. They divided the wood and used the two pieces as floats. One of the brothers returned to Fitiuta where many similar plants were observed to be growing already, while the other brother swam on to Western Samoa where kava was unknown. Here he planted his piece of wood and thereby introduced kava drinking in this area.

After the initial selection of a piece of kava root, the society of untitled men (*aumaga*) takes over and the root is cut into still smaller pieces by one of their members. In this form kava is known as *una o le i'a sā*, scales of the sacred or forbidden fish. This term alludes the fact that like many other sacred or taboo foods kava is reserved for the exclusive use of the chiefs.

While the pieces of kava were formerly chewed, final processing today involves pulverizing in a crude stone mortar (*ma'a tu'i'ava*). Other preparations for the ceremony include washing the kava bowl and bringing water in coconut shell containers (sometimes a galvanized bucket is substituted today).

A full inventory of the ceremonial paraphernalia includes a carved bowl, eighteen inches in diameter, which traditionally had four legs but now may have as many as twenty-four, a strainer made of shredded hibiscus bast, and a polished coconut cup.

Village kava ceremonies are usually held in the house which serves as the meeting place of the village council. As the chiefs enter the council house an attitude of reverence prevails. Nothing may be worn above the waist, and body ornaments of all types must be laid aside. The men speak in whispers and refrain from smoking as the kava ceremony begins.

At a place near the back of the house three untitled men, members of the village *aumaga*, station themselves at the kava bowl while a fourth remains outside to clean the hibiscus strainer of kava fibers when it is periodically thrown to him by the wringer. The man who is to wring the kava sits immediately behind the bowl with a water pourer to his right, and to his left, the man who will carry the cups of liquid to the assembled chiefs. Several taboos must be observed by the wringer. These include never wearing a flower necklace, a ring, a shirt or any other clothing except a wrap-around (*lavalava*). *Lavalavas* of all untitled men involved in the ceremony must be worn so they do not extend below the knees. The wringing of the kava must be done correctly and with precision. Untitled men take pride in their ability

in this art. There are a number of specific steps in the preparation of the liquid, and each has a traditional name. They are:

1. *Fa'apulou*—Covering the kava in the bottom of the bowl with the strainer.
2. *Vau*—Pressing down on the strainer with the heels of the hands and with the fingers.
3. *Aōga*—Collecting pieces of kava fiber in the strainer by drawing it toward the back of the bowl.
4. *Tatau*—Wringing the kava. The strainer is lifted from the bowl and wrung three times only. It is grasped in both hands like one would grip a baseball bat. At the end of each wringing stroke the clenched hands are bent forward so the liquid will not run down the arms.
5. *Mapā*—Cleaning the strainer. After the above steps have been carried out three times the strainer is passed under the right knee of the wringer and thrown back, with a side arm motion, to the untitled person outside the house who catches it in his right hand and removes the kava particles in it by snapping it three or four times. The hibiscus strainer is then thrown back underhand and caught by the wringer in his right hand.

The above process is continued until the bowl is free of pieces of kava root. When this has been accomplished and the kava is ready for drinking, the wringer wipes the rim of the bowl, cleans the strainer himself by snapping, forms it into a ball, and plunges it into the kava, and lifts it above the bowl with both hands, allowing the stream of liquid to fall into the bowl. This final gesture, known as *sila alofi*, permits the chiefs to see whether the kava requires more water. It is said that the correct mixture is judged by the sound of the kava splashing into the bowl as well as by its color.

If the talking chief serving as kava announcer does not call for more water the hibiscus strainer is wrung out and placed on the rim of the bowl. The kava wringer then places his hands on the sides of the bowl, his right covering the strainer. He remains in that position until the kava has been distributed.

It is the responsibility of the talking chief directing the ceremony to watch the progress of the wringing from his position behind and to the right of the bowl. When the kava is nearly clear of fiber particles, he must commence the verbal part of the ceremony with a poetic recitation (*solo*) which recounts the mythical origin of the kava or particular kava ceremonies of importance held by the ancient Samoan gods. A typical *solo* is as follows:

Si'i le faiva e to'alua
Papa ma Lotulotua
Aumai se i'a setasi
Le Manini mai le Sami
Telemu ma Telea'i
O mai lua te taufetuli ile lagi
Fati mai se la tasi
Se la o le la 'ava o tu felata'i

Gaugau ma sasa
Gaugau ma falava

Translation

Two people went fishing
Papa and Lotulotua (members of the Tagaloa family)
They brought one fish
The Manini, from the sea.
Telemu and Telea'i (two brothers of the Tagaloa family)
Were sent to run to the heaven
To bring a branch of kava
They broke and hit the kava
They broke and hit the fierce kava

Many *solos* are traditional, but clever talking chiefs may and do compose their own. It will be noted that the example given above is composed of rhyming couplets. There is, however, little concern for rhythm. The *solo* is timed to be finished the moment the kava is completely clear of fibers, whereupon the kava announcer states, "*Ua usi le alofi*" (The kava is already cleaned). The color and consistency of the mixture is then analyzed and if pronounced acceptable, the assembled chiefs respond by clapping their hands several times. Informants state that this act of clapping corresponds to the clapping of Pava when his sons was returned to life through the action of Tagaloa Ui at the first kava ceremony.

The distribution of kava begins by calling the cup title of the high chief who, because of his rank, is permitted to drink first. It must be understood that the cup title is not the family title of the chief. For example, in Si'ufaga village High Chief Lefiti (Lefiti is the family title) has the cup title *Lupe lele talitali lau ipu* (The pigeon who flies, receive your cup). Only high chiefs have cup titles. Talking chiefs receive their cup after the announcement of their family title and the words "*Lau 'ava*" (your kava). Chiefs of secondary rank receive the cup after their family title and the word "*Taumafa*" (drink) is pronounced.

The order of drinking is of the utmost importance as it signifies the relative rank of the drinker. The chief of highest rank in the village receives first kava; the highest talking chief, second; second highest chief, third; second highest talking chief, fourth; and so on down the ranks of chiefs and talking chiefs. In some villages this procedure is altered, and certain divisions of chiefs, or certain sections of the village, drink before others. To drink last kava is as prestigeful as to drink first.

Drinking etiquette, which varies according to rank, is as follows: When the high chief receives the cup he does so with both hands. Before drinking he pours a few drops onto the floor mat and says, "*Ia fa'atasi le Atua ma i tatou i lenei aso*" (May God be with us today) *or* "*Ia ta'ita'i le Atua i lenei aso*" (May God be our leader for today). Smith (*8*) records a typical prayer as, "Let the god drink kava that this gathering may be pleasant."

Following this prayer the high chief raises his cup, says "*Soifua*" or "*Manuia*," and drinks what is contained in the cup. If the high chief says "*Soifua*" the other chiefs respond with "*Manuia.*" If the latter word is pronounced by the drinker the chiefs reply with "*Soifua.*" Informants point out the connection between this aspect of the modern kava ceremony and the action of Tagaloa Ui in the first kava ceremony. The pouring of kava onto the mat represents the pouring of the liquid onto the two parts of the dead son of Pava, and the word "*Soifua*," which may be translated "Life" or "May you live," alludes to the command given by Tagaloa Ui when he performed the miracle of returning the boy to life. The word "*Manuia*" may be translated "Blessings" or "May the gods bless you," and perhaps relates to an expression of gratitude by Pava. It is also contended by informants that the right of the high chief to drink first kava and to sit in the end of the house is sanctioned by the Tagaloa Ui myth.

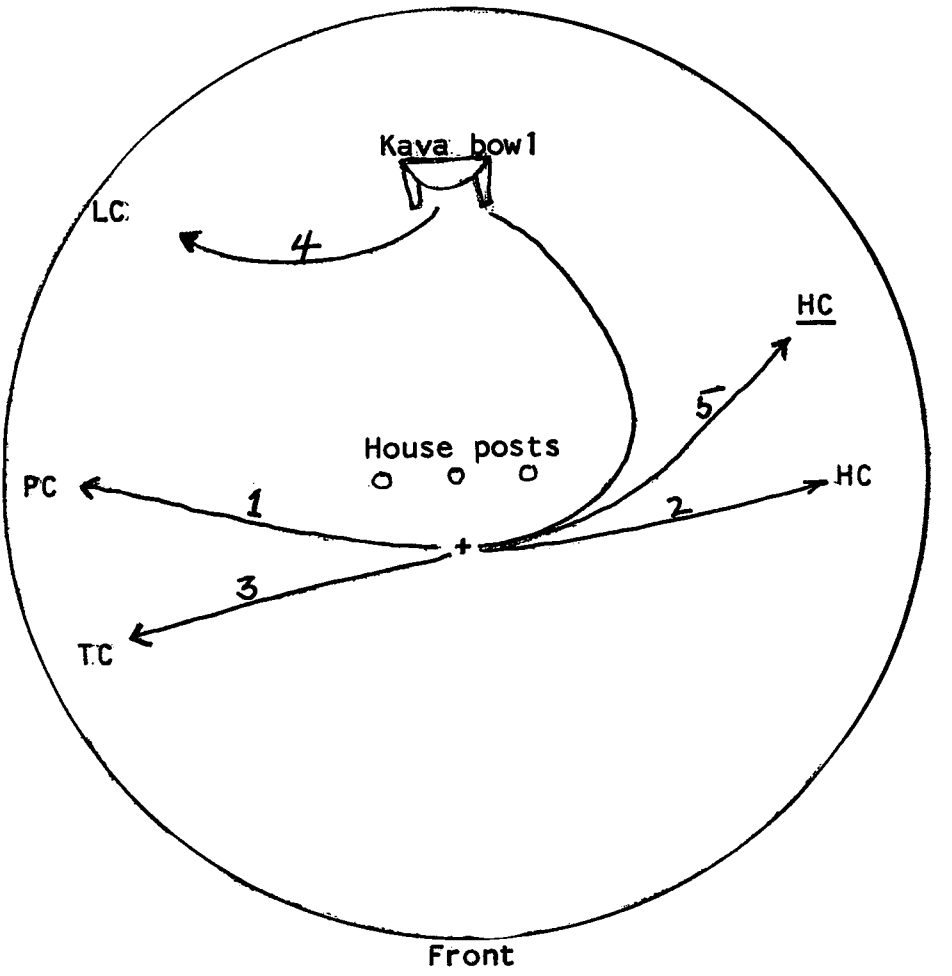
The drinking etiquette to be observed by a high talking chief varies somewhat in that he receives the kava cup with two hands if high chiefs are occupying both ends of the house, but if only one high chief is seated to the high talking chief's right, the cup must be received with the left hand to avoid showing the high chief the back of the hand. Of course the cup will be taken with the right hand if the high chief is seated to the talking chief's left. A high talking chief usually does not pour any kava onto the floor mat although he may say "Soifua" or "Manuia" before drinking.

Chiefs and talking chiefs of secondary rank do not pour kava onto the mat, nor do they say anything before drinking. Furthermore, they are not expected to respect the position of the high chief by receiving the cup with any particular hand.

Some Samoans do not care for kava and they "drink" symbolically by merely touching the bottom of the cup as it is passed to them. The cup may also be raised in a form of salutation and then returned to the cup bearer, with the kava untouched. On rare occasions a chief may take the liquid into his mouth, swish it about and then turn and spit it out onto the apron of the house outside. All these actions represent acceptable etiquette for the non-drinker.

When many chiefs are assembled there is often not enough kava to serve everyone. In such cases it is important for the kava announcer to judge when but a single cup of kava remains and then to announce rapidly the names of those who are entitled to drink. Following the recitation of this list of titles the announcer calls the cup title of the high chief who is then honored by drinking last kava, and the final cup is served to him. When talking chiefs of secondary rank are aware that there is not sufficient kava to go around they will often interrupt the announcer and call, "I will drink with my chief." When this occurs the lesser talking chief's title is not announced but the cup is taken to him immediately after the high chief of his family has been served.

Partially consumed kava must be cast away and the cup returned empty. It may be handed or thrown back to the server. If the cup is thrown to the server it is done to test his alertness.




1=Serving route to paramount high chief (PC); 2=Serving route to high chief (HC) 3=Serving route to talking chiefs (TC); 4=Serving route to lesser chiefs and talking chiefs (LC); 5=Serving route to high chief who will receive last kava (*HC*); + =Point at which the kava server stops before approaching chiefs of high rank.

All *aumaga* members who expect to take part in the kava ceremonies must master the etiquette of serving kava. Each rank of chief or talking chief must be served in a special and distinct manner. Respect is paid to the half of the house in which the paramount chief is seated, and the kava server must walk in this area as little as possible in making his rounds to the drinkers.

When serving a high chief the kava distributor dips the coconut cup into the kava and carries it with the thumbs and index fingers at the level of his waist to the center of the house where he stops, raises it to his forehead and walks in the direction of the high chief. About four feet from the chief, the server lowers his right hand and with his left, places the cup on his upturned right palm. The left hand is placed behind the back, and the cup is handed to the high chief chest high. The young man then walks to the

center of the house where he stands at attention until the chief has finished drinking.

Lower ranking chiefs are served kava with the right hand, but in the case of these lesser personages the cup is held by the edge with the thumb inside, thus showing the palm of the hand to the chiefs as it is presented to them.

In serving a high talking chief, the cup is held by the edge with the thumb, index and middle finger of the right hand. As it is carried from the bowl it is held just above the left shoulder. When in front of the high talking chief, the kava server swings the cup forward and down, presenting it with the back of his hand toward the talking chief. The kava cup for lower ranking talking chiefs is carried in the right hand, waist high, but is presented with the left. As in the case of high talking chiefs, the cup is held by the edge and the back of the hand is shown to the drinker.

After delivering the kava the server returns to the center post of the house and stands facing front while the kava is consumed. In rare cases he may return to a position in front of the kava bowl and face the front of the house.

When all of the assembled chiefs and talking chiefs have drunk or have been acknowledged as having the right to drink, the kava announcer concludes the ceremony with "*Ua moto le alofi*" (The kava is finished). "*Ale le fau ma le ipu e tautau*" (The bowl will hang with the *fau* (strainer) and the cup). Perhaps a more traditional closing is that recorded by Smith (*9*) as "*Le 'ava 'au motu*" (The kava is broken off). "*Ua matefa le fau*" (The strainer is poor). "*Ua pa'u le alofi*" (The company of chiefs has fallen down).

The assembled chiefs respond to these final words of the kava announcer with an expression of thanks, "*malo fa'asoasoa.*" At the conclusion of the kava drinking ceremony there is always the *fono o le 'ava* (food for the kava ceremony). According to the Tagaloa Ui myth the food for the first ceremony was the son of Pava and the food for the second was the sacred fish Manini and *talofa'afana* (recooked taro). Today the *Manini* and *talofa'afana* remain the traditional foods for the kava ceremony but there are frequent substitutions of rice, tinned beef, or other prestige foods.

The present day kava ceremony contains a number of elements which can be traced to older religious concepts of Samoan culture. The pouring of a bit of kava onto the mat not only relates to ancient mythology, but a number of scholars feel that it is a ritual reenactment of an ancient religious custom of pouring an evening offering to family or village gods. Steubel records in *Samoanische texte* (1895) that the typical prayer accompanying this act was "O the kava to drink of thy highness Sepo. Be lovingly disposed. Bless this village." (Sepo was primarily a war god, but in many villages served as a household god.)

Mead (*8*) suggested that the casting away of unconsumed kava may be related to ancient ceremonies wherein kava was entreated to depart and take all misfortune with it. On the other hand it may be related to precau-

tions about unconsumed food or drink which might be used for purposes of sorcery. Certainly the sanctity of the mixing bowl and gear, the air of solemnity and respect which accompany the entire ceremony, and the inclusion of poetic recitations which always allude to ancient Samoan gods, testify to the religious nature of the ancient ceremony.

Although the kava ceremony contains these unmistakable references to pre-Christian religion there seems to have been no great problem in fitting it into the Christian context. Bits of Christian prayer frequently accompany the pouring of kava onto the mat prior to drinking, and it is not uncommon to see local pastors included in the kava circle. On such occasions the village pastor (*faife'au*) drinks first kava, thus being accorded honors even greater than those shown to the village paramount chief. Since village pastors do not hold titles, their privileged position of drinking indicates their exalted status within the social structure of the village. Samoan medical practitioners and village school teachers are accorded similar honor by being served kava second only to the highest village chiefs.

Neither the church nor the American government has attempted to do away with the kava ceremony, and it is not unusual to see chiefs partake in a communion service in church, and then go home and conduct a kava ceremony while waiting for the midday meal. All visiting dignitaries in American Samoa, including President Lyndon B. Johnson in 1966, are honored with a kava ceremony by the paramount chiefs of the territory.

It has been said that while other Polynesian people worshipped gods, Samoans worshipped their village and social organization. The kava ceremony would seem to be a part of this veneration. The detailed etiquette of serving, the prescribed order of drinking, the use of special honorific cup names, and the insistence that the beverage be prepared and served only by specially qualified persons, have been tremendously important in dramatizing the whole system of Samoan rank and prestige. When the kava ceremony is completed there is little doubt of the status of those present and of the rights and privileges of their respective offices. Through continual ceremonial exercise, social relationships are reiterated and Samoan values are intensified. The result of this seems to be an unusual stability and resistance to change which is found among few other Polynesian peoples. In an attempt to explain this remarkable resistance to change, John Copp has commented, "Samoan custom now serves as a 'refuge' from the conflict of choice and judgment resulting from Western contacts." (*11*). Perhaps it has been the stabilizing influence of the kava ceremony and other rituals that has allowed the Samoans to make satisfactory adjustments to European influences. Traditional aspects of Samoan culture such as the kava ceremony are, in a manner of speaking, bits of solid ground on which to anchor in a changing world.

It is believed that the influence of the kava ceremony is one of the explanations for the amazing stability of a people who, as Douglas Oliver puts it, have survived "the strong impact of western civilization without losing their numbers, their strength, their dignity, or their zest for a good fight." (*9*).

## BIBLIOGRAPHY


(*1*) AITKEN, ROBERT T. "Ethnology of Tubuai." Honolulu, Bishop Museum Bulletin No. 70, 1930.

(*2*) BARRADALE, V. A. "Pearls of the Pacific." London, London Missionary Society, 1907.

(*3*) BEAGLEHOLE, ERNEST and PEARL. "Pangai: Village in Tonga." Wellington, Polynesian Society, Memoir Vol. 18, 1941.

(*4*) BUCK, SIR PETER. "Samoan Material Culture." Honolulu, Bishop Museum Bulletin No. 75, 1930.

(*5*) KEESING, FELIX. "Elite Communication in Samoa." Stanford, Stanford University Press, 1956.

(*6*) KRÄMER, AUGUSTIN. "Die Samoa-Inseln," Stuttgart, 1902.

(*7*) LEENHARDT, MAURICE. "Gens de la Grande Terre." Paris, 1937.

(*8*) MEAD, MARGARET. "Social Organization of Manua." Honolulu, Bishop Museum Bulletin No. 76, 1930.

(*9*) OLIVER, DOUGLAS. "The Pacific Islands." Cambridge, Harvard University Press, 1951.

(*10*) SMITH, S. PERCY. "Kava Drinking Ceremonies among the Samoans and a Boat Voyage round 'Opulu Island, Samoa." Journal of Polynesian Society Supplement, 1920.

(*11*) STANNER, W. E. H. "The South Seas in Transition." Sydney, Australasian Publishing Co., 1953.

# Recent Observations on the Use of Kava in the New Hebrides

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Of all the Pacific islands on which kava is still used today, Tongariki is the one on which its use has attained maximum frequency and intensity. I have had occasion to be resident, with Professors Jean Guiart and Robert Kirk, on this small island of the Sandwich group in the New Hebrides, for several weeks in two periods during the past three years, while working on an intensive study of human adaptability in isolated populations. Quite apart from our medical and genetic studies, we were soon aware that the entire social life, mood and spirit of the island villages changed nightly at dusk to a more subdued, whispering and cautious quiet than we had seen in native villages elsewhere in the Pacific. This restrained atmosphere we found to be caused by kava drinking: nightly, most of the men were drinking fresh kava.

Whereas on most Pacific islands kava prepared by the ancient technique of premastication (particularly of the fresh, undried root) has been abandoned in favor of a much less pharmacologically potent beverage made by grating or pounding the root, usually dried, here on Tongariki the current extensive nonceremonial drinking of kava makes use of the "green", freshly harvested, locally-grown root and of mastication and salivary digestion of the pulp by the adolescent and young men. Fresh cold water is used with hand mixing and wringing through a sieve of cocoanut fiber to extract the active ingredients from the chewed pulp. The many variations of this procedure have been described exhaustively since the earliest reports from Captain Cook's voyages, and similarities in minute details of the kava ceremony have been used to suggest affinities between peoples on different islands. On Tongariki the procedures are now relatively unformalized and thus subject to considerable variation. Kava drinking on this island is unusual, furthermore, in that its extent and pattern is a relatively recent phenomenon, and in that it has reached faddish proportions in terms of the number of kava drinkers and the frequency of their use of kava, which in both cases exceeds that of pre-European contact.

This resurgence of kava drinking suggests the extensive revival of kava usage on the southern New Hebridean island of Tanna in the early 1940's as a ritual of a flourishing cargo cult which repudiated much of the missionary teaching. Jean Guiart, in his study of this cargo cult, believed that the fierce battle the Presbyterian Church had waged against kava drinking had focused undue attention onto the traditional use of the beverage; this served to endow its new prohibition-defying use with such psychological import that the renewal of kava drinking became an important part of this anti-missionary

movement, which appeared on the island during World War II and has not yet subsided. Early in the cargo movement (called the John Frum movement after a neomythical man of that name) there was an anarchical use of the drink, without respect for the ancient ceremonial and age-group restrictions on its use; even adolescents drank it; the drinking took place in small informal groups at odd times of the day and in unappointed places, as was never permitted in pagan times.

Tongariki has a population of about 500 living in four small villages; it has not had a full-blown cargo cult or Messianic movement, but the resurgence of the use of kava has been associated with a reluctance to become involved in Protestant mission or government-instigated activities, an increased clannishness, and a withdrawal from outside contacts. No European missionary has ever been resident on Tongariki, but native missionaries from other islands have been sent there by the Presbyterian Church. In spite of attempts to suppress it, the use of kava here was never fully stopped; in recent years most adult male members of the population turn each night to kava. Moreover, only the fresh root and not the dry variety is usually employed. The users still attend Sunday church services on the island, and do not associate their use of kava with a revolt against the church such as occurred on Tanna.

Kava drinking on Tongariki is a relatively relaxed and unceremonious affair, without the strict adherence to prescribed etiquette characteristic of kava drinking in much of the Pacific. It is prepared entirely by chewing, never by the use of mortars, graters, or other mechanical aids. Boys from pre-adolescent age to young adulthood usually do the chewing for their kinsmen or guests, or out of courtesy for others. Older youths or young men mix, wash, and wring the kava from the chewed pulp. Girls and women may occasionally participate in the chewing, whereas this was not so in the past. Adolescents and, more rarely, women may drink kava without censure. It is drunk in various places within the village proper, usually in a quiet house, and strict exclusion of children and women from the proximity and view of the proceedings has lapsed. Thus, the current kava drinking on Tongariki is more like that of the early John Frum movement on Tanna in its lack of formality and restraints. On Tanna, however, by the 1950's kava usage had returned essentially to the old traditional ceremonially controlled forms.

Usually, half of a cocoanut shell or a bowl of the same capacity is used to prepare the kava and the full contents—about 100 ml.—drunk slowly in one draught. Sometimes twice this quantity is drunk. A kava drinker usually eats immediately after taking the kava; the kava is prepared while the evening meal is being cooked. The effects come on in a half hour or less, and the drinking is thus usually postponed until food is ready. Those who have drunk the kava find a comfortable place to sit, often beside a dying fire in the dark house, where they remain hunched over and avoiding light and sound disturbances of all sorts. Conversation ceases, and slowly they fall into a kava-induced stupor, which is not true sleep. This stage occurs about an hour after drinking. From it they can be aroused by being addressed or gently shaken, but this ruins the effect they are seeking from the kava. A

few hours after they have drunk kava they arise and walk to their own houses to fall asleep promptly again; others remain where they have first "fallen". In early morning they appear fresh and without any "hangover"-like sequelae. Those whom we have seen walking a few hours after the drinking are usually somewhat ataxic, photophobic, and slowed in their reactions. A few who have had a higher dose are extremely ataxic and could return to their homes only with assistance from the children or myself. There is no belligerency or irritability—only a quiet and friendly somnolence associated with the weakness of the lower limbs and the accompanying ataxia.

The drinkers reply rationally and are well oriented in time, place, and person; they respond intelligently, even sometimes quickly, to complex questions. Bright or moving lights, noise or other sound, touch, and even the subdued bustle of nearby activity annoy them, and the villagers of all ages have extreme respect for this. In discussions the kava users refer to a heaviness and weakness of their extremities, particularly of the feet and legs, and to an earlier paresthesia ascending from their feet to their trunk and described with such words as "numbness", "tingling", and "coldness". They demonstrate a tactful avoidance of the disturbance my questioning produces, a very subdued annoyance at my "breaking" their kava. I have taken pulse rates and blood pressure measurements on a number of kava drinkers at varying intervals from one to three hours after drinking and found no significant change in either from that observed on the same subjects during examinations in the daytime, when they had had no kava for the preceeding eighteen hours or more. Respiration is shallow and regular; deep tendon reflexes remain intact.

Of interest to us in our genetic studies has been the effects that kava might have on fertility, since it is quite evident that kava drinkers rarely engage in sexual activity on the nights when they drink. Interviews with the women substantiate this. There is no dearth of children on Tongariki, but the population is not increasing explosively as it is in some parts of the Pacific, and kava drinking may serve as an interesting means of birth control for the small island, which could be easily over-populated.

Dam-Bakker, DeGroot and Luyken have suspected the use of *wati*, as kava is called in southwest New Guinea, as a possible cause of the infertility in the Marind-Anim people. Their studies on chronic kava administration to rats, however, failed to demonstrate any impaired fertility, but they admit that they hardly reproduced essential features of kava use in the human community in their rat experiments.

Jean Guiart and I have occasionally taken kava with the natives, and have noticed subjectively little difference in the sequence of symptoms and reactions from those reported by many Pacific voyagers since Captain Cook's days. A few peculiar paresthesiae of the face, legs and arms—especially of the legs—a slight feeling of numbness, tingling, coldness and then weakness, accompanied early by shorter flashes of warmth or flush, occurred during the first half hour after ingestion. We have boorishly "broken" our kava at times, and walked off to engage in other activities without noticeable impairment of motor or sensory function. This has been after rather low



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doses. There is, with higher doses, a pleasant, relaxing, paresthesia-enjoying, refreshing state of somnolence without mental dulling which eventually leads to sleep. At times, members of our team have taken large doses—a large cocoanut shell full—and real weakness, even a paresis making walking impossible, has been present for several hours after ingestion. Such an overdose left one of us slightly ataxic with a persistent feeling of weakness in the lower limbs on into the next morning.

Several recent accounts report little or no pharmacological action from kava prepared from grated or pounded dried kava root and used socially or ceremonially on Fiji and Samoa. My own experience in drinking such kava in Fijian villages is the same lack of effect. It is this dried kava root that has entered commerce, particularly on Fiji, and I wonder whether it is not this product that has been used in the pharmacological and chemical laboratories. The freshly harvested root, prepared by chewing, appears to result in the more potent preparation, the effects of which I have described. The stronger physiological actions of the kava used on Tongariki and Tanna may well be from the use of freshly harvested root rather than dried root, but there is also the possibility that the chewing and salivary digestion that is used to break up the fibers and emulsify the ingredients may be responsible for the pharmacologically more potent product. It is also likely that a higher dose of active ingredients is taken on Tongariki, since a considerably more concentrated extract appears to be prepared; far more root is used per individual drinker than on Fiji or Samoa.

## APPENDIX

### *Historical and Ethnographic Accounts of Kava Usage*


AITKEN, R. T. "Ethnology of Tubuai." Bernice P. Bishop Museum, No. 70, (Bayard Dominick Expedition, publication no. 19), Honolulu, Hawaii, 42, 1930.

BEAGLEHOLE, E. and P. "Ethnology of Pukapuka." Bernice P. Bishop Museum, No. 150, Honolulu, Hawaii, 25, 1938.

BEARDMORE, E. "The natives of Mowat, Daudai, New Guinea." Journal of the Anthropological Institute of Great Britain and Ireland, 19: 460, 1889–90.

BEVAN, T. F. "Toil, travel, and discovery in British New Guinea." London, 258, 1890.

BIRO, S. L. "Neu-Guinea (Astrolabe Bai)." Ethnografische Sammlung des Ungarischer Museums, 3: (Budapest), 102, 1901.

BOURGAREL, A. "Des races de l'Océanie Française de celles de la Nouvelle-Calidonie. In particulier, seconde partie." Memoirs de la Societe d'Anthropologie de Paris, 2: 403, 1865.

BUCK, P. H. "Samoan material culture." Bernice P. Bishop Museum, Honolulu, Hawaii, No. 75, 92, 140, 147–164, 545, 548, 641, 679, 1930.

——— "Ethnology of Tongareva." Bernice P. Bishop Museum, No. 92, Honolulu, Hawaii, 81, 119–121, (April) 1932.

——— "Ethnology of Manihiki-Rakanga." By Te Rangi Hiroa. Bernice P. Bishop, Museum No. 99, Honolulu, Hawaii, 1932.

——— "Mangaian society." Bernice P. Bishop Museum, No. 122, Honolulu, Hawaii, 1934.

——— "Ethnology of Mangareva." Bernice P. Bishop Museum, No. 157, Honolulu, Hawaii, 1938.

——— "Arts and crafts of the Cook Islands." Bernice P. Bishop Museum No. 179, Honolulu, Hawaii, 18–20, 1944.

BÜHLER, A. "Versuch einer Bevölkerungs-und Kulturanalyse auf den Admiralitätsinseln." Zeitschrift für Ethnologie, 67: 1–32, 1935.

BURROWS, E. G. "Ethnology of Futuna." Bernice P. Bishop Museum, No. 138, Honolulu, Hawaii, 200–204, 1936.

——— "Ethnology of Uvea (Wallis Island)." Bernice P. Bishop Museum, No. 145, Honolulu, Hawaii, 75–76, 139–143, 1937.

CHRISTIAN, F. W. "The Caroline Islands." London, 86, 87, 100, 188–193, 211, 1899.

CHURCHILL, W. "Samoan kava custom." Holmes Anniversary Volume, Washington, 53–64, 1916.

CHURCHWARD, W. B. "My consulate in Samoa." London, 47–59, 313, 347, 348, 1887.

COLLOCOTT, E. E. V. "Kava ceremonial in Tonga." Journal of the Polynesian Society, 36: 21–47, 1927.

COOK, J. "A voyage to the Pacific Ocean." 3 Volumes, London, vol. 2; 145, 155–56, 1784–1785.

CORNEY, B. C. "The quest and occupation of Tahiti by emissaries of Spain in 1772–76"; 3 volumes, The Hakluyt Society, London. Second Series, Nos. 32, 36, 43. II: 85n, 130, 159, 168, 208, 218, 281, 472; III: 6, 51, 52, 59, 1913–19.

CUMMING, CONSTANCE F. G. "At home in Fiji." Edinburgh, 50–51, 1882.

D'ALBERTIS, L. M. "New Guinea, what I did and what I saw." 2 volumes, London; II: 197, 1880.

DAM-BAKKER, A. W. I. VAN, DEGROOT, A. P. and LUYKEN, R. "Influence of wati (Piper methysticum) on the fertility of the male rats." Tropical and Geographical Medicine, 10: 68–70, 1958.

DEIHL, J. R. "Kava and kava-drinking." Primitive Man, 5: 4, 61–68, 1932.

——— "Position of women in Samoan culture." Primitive Man, 5: 2 and 3, 25, 1932.

DILLION, P. "Narrative of the discovery of the fate of La Pérouse's expedition." 2 volumes, London, II: 42–52, 1829.

DURRAD, W. J. "Notes on Torres Islands." Oceania, 10: 389–403, 1940.

EILERS, ANNELIESE. "Inseln um Ponape." Ergebnisse der Sudsee Expedition 1908–10. G. Thilenius, ed., Hamburg, Friederichsen, de Gruyter and Co., II, B–8, 103, 1934.

ELLIS, W. "Polynesian researches." J. & J. Harper, New York, IV: 277–278, 1833.

EMERSON, O. P. "The Awa habit of the Hawaiians." The Hawaiian Annual, Honolulu, Hawaii, 130–140, 1903.

FINSCH, O. "Samoafahrten." Leipzig, 61, 1888.

——— "Südseearbeiten (Abhandlungen des Hambergischen Kolonialinstituts)," 14: 1–605, Hamburg, 1914.

FIRTH, R. W. "Primitive economics of the New Zealand Maori." New York, E. P. Dutton, 1929.

FORNANDER, A. "Hawaiian antiquities and folk-lore." Editor T. G. Thrum, Memoirs of the Bernice P. Bishop Museum, Honolulu, Hawaii, VI: 72, 110, 112, 258, 260, 405, 471, 505, 540, 1919–20.

FOSTER, G. A voyage round the world in his Britannic Majesty's sloop, Resolution. Two volumes, London, 1777.

FOX, C. E. "The Threshold of the Pacific." London and New York, 44, 67, 216, 1924.

GIFFORD, E. W. "Tongan society." Bernice P. Bishop Museum, No. 61, Honolulu, Hawaii, 156–170, 1929.

GUIART, J. "Un siècle et demi de Contacts Culturels à Tanna, Nouvelles-Hébrides." Publication de la Société des Océanistes, No. 5. Musée de l'Homme, Paris 15–16, 246–254, 1956.

HADDON, A. C. "Kava drinking in New Guinea." Man, 16: 145–152, (Oct.) 1916.

HAMBRUCH, P. "Die Kawa auf Ponape." Studien und Forschungen zur Menschen- und Völkerkunde, Stuttgart, 14: 107–115, 1917.

HAMBRUCH, P., and EILERS, ANNALIESE. "Ponape." Ergebnisse der Südsee Expedition 1908–10, 231–246, 1936.

HANDY, E. S. C. "The native culture in the Marquesas." Bernice P. Bishop Museum, No. 9 (Bayard Dominick Expedition, Publication No. 9), Honolulu, Hawaii, 202–203, 1923.

HANDY, E. S. C. "Polynesian religion." Bernice P. Bishop Museum, Honolulu, Hawaii, No. 34, 46, 136, 162–163, 173, 219, 322, 327–328, 1927.
——— "History and culture in the Society Islands." Bernice P. Bishop Museum, Honolulu, Hawaii, No. 79, 20–21, 1930.
——— "History and culture in the Society Islands." Bernice P. Bishop Museum, No. 79, Honolulu, Hawaii, 1931.
HAWKESWORTH, J., Editor. "An account of the voyages undertaken by the Order of His B. Majesty for discoveries," II: 200, 1773.
HENBY, T. "Ancient Tahiti." Bernice P. Bishop Museum, Honolulu, Hawaii, No. 48, 531, 538, 539, 562, 583, 587, 1928.
HOCART, A. M. "Lau Islands, Fiji." Bernice P. Bishop Museum, Honolulu, Hawaii, No. 62, 59–70, 108, 1929.
HOUGH, W. "Kava drinking as practiced by the Papuans and Polynesians." Smithsonian Miscellaneous Collection, 2: 85–92 (Aug. 6), 1904, Quarterly Issue, Washington, D.C., 1905.
HUMPHREYS, C. B. "The southern New Hebrides. An ethnological record." Cambridge, 1926.
KING, J. "A voyage to the Pacific Ocean." Second edition, 3 volumes, London, 3: 126–127, 1785.
KRÄMER, A. "Die Samoa-Insel." Stuttgart, 1902.
LEDYARD, J. "John Ledyard's journal of Captain Cook's last voyage." Munford, J. K., ed., with introduction by Hitchings, S. H. Oregon State University Press, Corvallis, Oregon, August 1777, Customs of Otaheite, 51, 1963.
LESTER, R. M. "Kava drinking in Vitilevu, Fiji." Oceania, 12:2, 97–121, 1941; 12:3, 226–254, 1942.
LEWIN, L. "Über Piper Methysticum (Kawa)." A. Hirschwald, Berlin, 60 pp., 1886.
——— "Phantastica: narcotic and stimulating drugs; their use and abuse." K. Paul, Trench, Trubner and Co., London, 215–225, 1931.
LING SHUN-SHENG. "A comparative study of kava drinking in the Pacific regions." Bulletin of the Institute of Ethnology, Academia Sinica, 5: 77–96, 1958.
LINTON, R. "The material culture of the Marquesas Islands." Memoirs of the Bernice P. Bishop Museum, Honolulu, Hawaii, VIII: 5, 366, 1923.
LLOYD, C. G. "The use of kava by the Samoan Islanders." Pharmaceutical Review, 18: (June), 261–266, 1900.
LOEB, E. M. "History and traditions of Niue." Bernice P. Bishop Museum, No. 32, Honolulu, Hawaii, 172, 1926.
MACGREGOR, G. "Ethnology of Tokelau." Bernice P. Bishop Museum, No. 146, Honolulu, Hawaii, 151, 1937.
MACGREGOR, W. "British New Guinea." Journal of the Anthropological Institute of Great Britain and Ireland, XXI: 76, 204, 1891–92.
——— "British New Guinea: country and people." London, 73, 75, 1897.
MARINER, W. "An account of the natives of the Tonga Islands." 2 Volumes, London, 1817.
MCFARLANE, S. "Among the cannibals of New Guinea." 126, 1888.
MELVILLE, H. "TYPEE: a peep at Polynesian life. During a four months' residence in a valley of the Marquesas." New York, 194–195, 1857.
MÉTRAUX, A. "Ethnology of Easter Island." Bernice P. Bishop Museum, No. 160, Honolulu, Hawaii, 159, 1940.
MIKLUKHO-MACLAY, N. VON. Bulletin of the Imperial Russian Geographical Society, X: ii, 1874.
——— "Ethnologische Bemerkungen ueber die Papuas der Maclay-Küste in Neu-Guinea." Natuurkundig Tijdschrift voor Nederlandsch Indie, 35: 71, 1875.
NEVERMANN, H. "Admiralitäts-Inseln." Ergebnisse der Südsee Expedition 1908–10, II–A3, Hamburg, 40, 1934.
——— "Kawa auf Neuguinea." Ethnos, 3: 179–192, 1938.
PARKINSON, R. "Dreissig Jahre in der Südsee." Stuttgart, 373, 1907.

PARKINSON, S. "A journal of a voyage to the South Seas, in His Majesty's ship, The Endeavour (1768)," London, 37, 1784.
PORTER, D. "A voyage to the South Seas." London, 95, 1823.
PRATT, M. A. R. "A kava ceremony in Tonga." Journal of the Polynesian Society, 31: 198–201, 1922.
PUKUI, MARY K. (WIGGIN). Translations in the Bernice P. Bishop Museum, Honolulu, Hawaii: 1) "Against Awa (Ka Elele)," 2) "The evils of Awa (Ke Au Okoa)," 3) "On Awa drinking (Ko Hawaii Ponoi)."
RIESENBERG, S. H. "The cultural position of Ponape in Oceania." Dissertation for Ph. D., University of California, Berkeley, 1949.
——— "The Ponapean aboriginal political structure." Smithsonian Institution, Washington, D.C., 1967.
RIVERS, W. H. R. "The history of Melanesian society." 2 Volumes, Cambridge, 1914.
SARASIN, F. "Ethnolgoie der Neu-Caledonier und Loyalty-Insulaner." 2 Volumes, München, 1929.
SARFERT, E. "Kusaie." Ergebnisse der Südsee Expedition 1908–10, Hamburg, II–B–XII, 410–412, 1919.
SMITH, S. P. "Uea; or Wallis Island and its people." Journal of the Polynesian Society, Wellington, 1: 112, 115, 116, 1892.
——— "Kava drinking ceremonies among the Samoans and a boat voyage round Opulu Island, Samoa." Journal of the Polynesian Society, supplement, 1920.
SPEISER, F. "Ethnographische Materialien aus den Neuen Hebriden und der Banks-Inseln." Berlin, 162–164, 1923.
STEINMETZ, E. F. "Piper methysticum: kava, kawa, yagona; famous drug plant of the South Sea islands. Amsterdam, 46 pp., 1960.
THOMPSON, LAURA M. "Southern Lau, Fiji: an ethnography." Bernice P. Bishop Museum, No. 162, Honolulu, Hawaii, 68–72, 97, 109, 168, 1940.
THOMSON, B. "Savage Island, an account of a sojourn in Niué and Tonga." London, 95, 97, 1902.
——— "The Fijians: A study of the decay of custom." London, 1908.
TITCOMB, MARGARET. "Kava in Hawaii." Journal of the Polynesian Society, 57: (June), 105–171, 1948.
TRUE, R. H. "Kava-kava." Pharmaceutical Review, Milwaukee, 14: 2, 28–32, 1896.
TYERMAN, D. and BENNET, G. "Journal of voyages and travels (compiled by James Montgomery)." 3 volumes, 2: 43, Boston, 1832 (from London edition 1831).
VANCOUVER, G. "A voyage of discovery to the North Pacific Ocean, and round the world." 3 volumes, London, 1: 116, 1798.
WILLIAMSON, R. W. and PIDDINGTON, R. "Essays in Polynesian ethnology." Cambridge, 1939.

# Chemistry of Kava

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Kava (*1*) is one of the popular names for the intoxicating drink prepared from the roots of the plant *Piper methysticum* Forst. by the inhabitants of the South Pacific Islands. The interesting tranquilizing properties ascribed to this romantic brew has prompted numerous chemical investigations over the last century, in the search for the physiologically active principles. These investigations have resulted in the isolation of a series of closely related substituted 5,6-dihydro-α-pyrones (Fig. 1), members of which have been shown to possess some of the actions on the central nervous system exhibited by the Kava extract, and a series of substituted α-pyrones (Figs. 2 and 3) which are relatively inactive in the test system employed.

The first of the compounds to be isolated in the 5,6-dihydro-α-pyrone series, methysticin, was reported by Cuzent in 1861, followed in turn by Winzheimers isolation of dihydromethysticin in 1908. The most extensive investigation of this plant, however, was carried out by Borsche and coworkers, who reported their findings in a series of fourteen papers published between 1914 and 1933. This work covered the isolation of Kawain and dihydrokawain, and their structural elucidation along with that of methysticin and dihydromethysticin. (Figure 1)

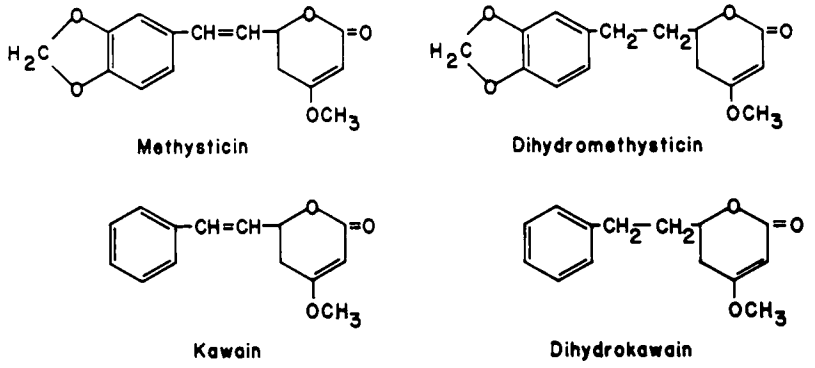
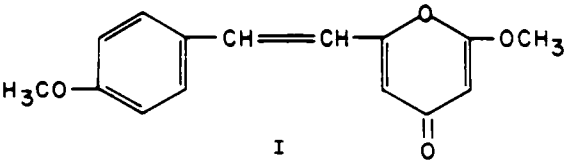
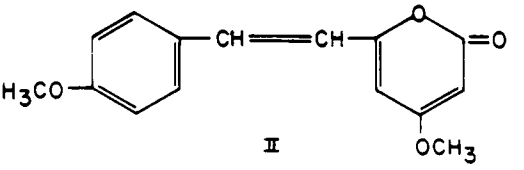



FIG. 1

Yangonin (Figure 2) was isolated by Reidel in 1904, and the γ-pyrone structure (I) was proposed by Borsche. This stood as the only naturally occurring 2-methoxy-γ-pyrone derivative until 1958 when Chmielewska, on the basis of spectral data, revised the structure to that of an α-pyrone (II). Secure support for these spectroscopic deductions has now been established by the unambiguous synthesis of yangonin by Bu'Lock and Smith.



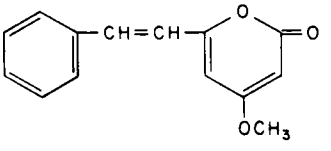

I



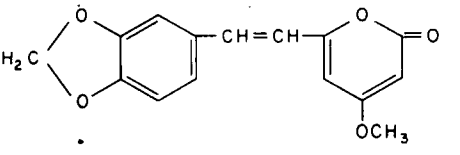

II

FIG. 2

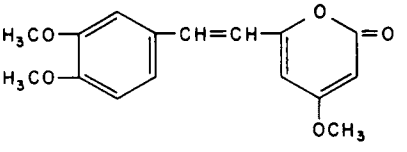
In more recent times subsequent investigators have added four new compounds to the α-pyrone series, with the isolation of 5,6-dehydromethysticin, desmethoxyyangonin, 11-methoxyyangonin and 11-methoxynoryangonin (*2*) (Figure 3). The Structures of these compounds have been confirmed by synthesis.



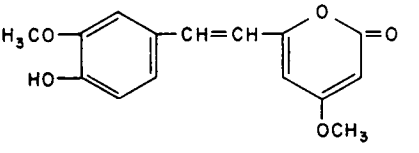

Desmethoxyyangonin




5,6-Dehydromethysticin




11-Methoxyyangonin




11-Methoxy-nor-yangonin

FIG. 3

With the structures of a physiologically active series of natural products established and the synthesis of analogues feasible, it is only natural for the medicinal chemist and pharmacologist to turn next to a molecular modification program to seek an optimum relationship between structure and activity. In studies with this objective in mind, which were carried out in our laboratory some twelve years ago, the physiological activities of the naturally occurring compounds (Table I) that had been isolated at that time were used as the base line for comparison with the activities of the synthetic ana-

logues. In these experiments the compounds were administered orally to mice in a 10% Tween suspension, and screened initially for their effect on the central nervous system as determined by their ability to antagonize strychnine induced convulsions and death, cause fall out in the roller cage experiments, and potentiate sodium pentobarbital induced sleeping time.

| Compound | Strychnine $ED_{50}$ + 95% C. L. mg/Kg | Roller cage dose mg/Kg | result | Sleeping time dose mg/Kg | in % controls |
|---|---|---|---|---|---|
| Dihydrokawain | 340 (270–430) | 300 | no effect | 160 | 150 |
| Yangonin | no protection at 1,000 | 300 | no effect | 160 | 150 |
| Kawain | 215 (160–290) | 300 | no effect | 160 | 235 |
| Desmethoxyyangonin | no protection at 200 | 300 | no effect | 160 | 130 |
| Methysticin | 160 (110–232) | 300 | no effect | 160 | 250 |
| Dihydromethysticin | 115 (97–152) | 300 | no effect | 60 | 413 |
| Chloroform extract | 140 (121–162) | 300 | 12/18 | 160 | 340 |
| Ground root | 1,700 (1,400–2,100) | 10,000 | 12/18 | 10,000 | 400 |

TABLE I

On the basis of these results it can be seen that the crude extract, methysticin and dihydromethysticin were particularly effective in affording protection against the lethal effects of strychnine. Using "fall-out" from revolving cages as an index, none of the crystalline compounds had significant activity which is in sharp contrast to the ground root and the crude extract. On the basis of this latter test it would seem reasonable to say that there are compounds present in the extract possessing this activity which have not as yet been isolated. Dihydromethysticin proved to be the most potent agent in increasing the pentobarbital-induced sleeping time, showing good activity at 60 mg/kg whereas the other compounds were only slightly or moderately active at 160 mg/kg.

The physiological activity observed with methysticin and dihydromethysticin as compared to yangonin and desmethoxyyangonin, indicated the importance of the 5,6-dihydro-α-pyrone ring to overall activity, and this was corroborated further by the complete loss of activity observed in the three test systems on opening the lactone ring of methysticin to yield methysticic acid (Figure 4).

With this knowledge on hand a number of $C_6$ substituted 5,6-dihydro-α-pyrone derivatives were prepared (*3*) by the Reformatsky condensation of the appropriate aldehyde and methyl-γ-bromo-β-methoxycrotonate, using the conditions as previously employed in our synthesis of dl-methysticin (Figure 5).

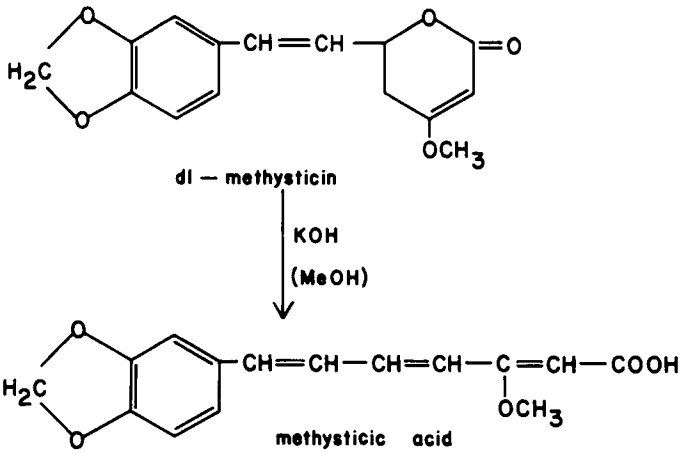



FIG. 4

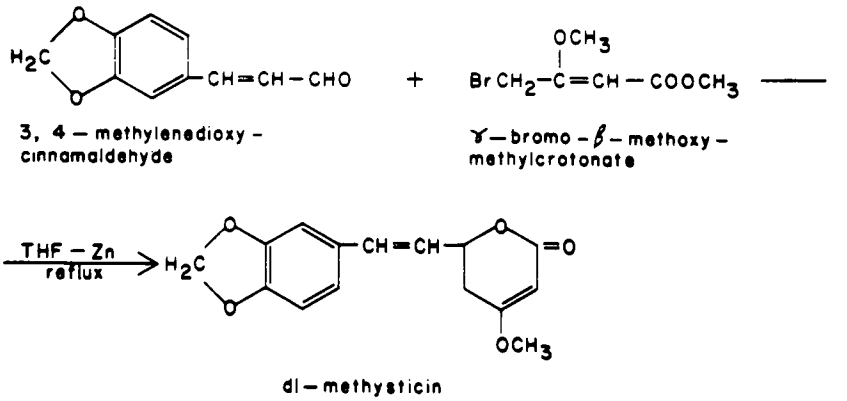



FIG. 5

In the first series of analogues (Table II), the ethylene bridge of dihydromethysticin was omitted as represented by compound 2, and methoxyl groups were substituted in place of the ethylenedioxy group as shown by compounds 3 and 4. These screening results would indicate that the methylenedioxy group is the preferred substituent and that the loss of the ethylene group causes a decrease in activity over dihydromethysticin as measured by its ability to inhibit strychnine convulsions and potentiate barbiturate sleep time. There is an indication, however, of activity in the roller cage where dihydromethysticin is inactive.

The effect of varying the ethylene bridge on activity is shown in Table III. The first and second compounds, where the bridge has been lengthened to butylene and butadienyl respectively, showed little activity with the exception of sleep time potentiation with the butylene analogue. The third com-

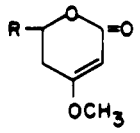
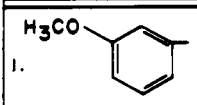
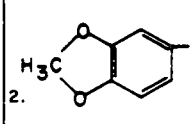
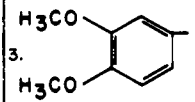
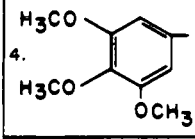
|  | Strychnine $ED_{50}$ ÷ 95% C.L. mg/Kg | Roller cage dose mg/Kg | result | Sleeping time dose mg/Kg | in % controls |
|---|---|---|---|---|---|
| 1.  | 470 (375-590) | 300 | 7/18 | 160 | 240 |
| 2.  | 260 (210-320) | 300 | 5/18 | 160 | 472 |
| 3.  | 950 (680-1480) | 300 | 5/18 | 160 | 152 |
| 4.  | no protection at 500 | 300 | 3/18 | 160 | 165 |

TABLE II

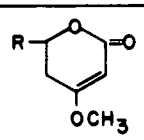
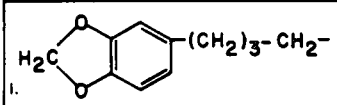
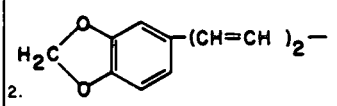
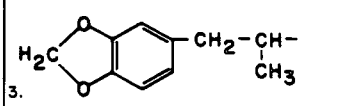
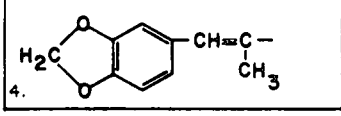
|  | Strychnine mg/Kg | Roller cage dose mg/Kg | result | Sleeping time dose mg/Kg | in % controls |
|---|---|---|---|---|---|
| 1.  | no protection at 500 | 300 | 1/18 | 160 | 536 |
| 2.  | 50% protection at 500 | 300 | 0/18 | 160 | 115 |
| 3.  | no protection | 300 | 3/18 | 20 | 283 |
| 4.  | 60% protection | 300 | 10/18 | 60 | 304 |

TABLE III

pound, in which a methyl group has been introduced on the carbon adjacent to the pyrone ring of dihydromethysticin, gave no protection at 500 mg/kg against strychnine, slight activity in the roller cage, and the highest activity of all the compounds in the potentiation of sleep time. The last compound, which is the corresponding analogue of methysticin, evidenced some activity in protecting against the effects of strychnine at 500 mg/kg, but good activity was observed in the roller cage and the potentiation of sleep time.

The last series of compounds (Table IV) represent a more radical departure from the structure of dihydromethysticin. In the first compound, where R is 3,4-methylenedioxyphenylethyl and $R^1$ is methyl, there was no protection obtained at 500 mg/kg against strychnine, moderate activity in the roller cage, and activity exceeding that of dihydromethysticin in the potentiation of sleep time. In the second compound where R is phenyl and $R^1$ is methyl, there was again no protection afforded against strychnine at 500 mg/kg, there was good activity in the roller cage and moderate activity in sleep time potentiation. In the last compound, where both R and $R^1$ are phenyl, no significant activity was observed in the first two tests and moderate activity was realized in the potentiation of sleep time.

All of the above synthetic compounds including dl-methysticin and dl-dihydromethysticin, with the exception of compounds 1 and 2 in Table III, were then screened against supramaximal electroshock at an oral dose of 770 mg/kg. At this dose range only compound 1 in Table II, compounds 3 and 4 in Table III, and dl-methysticin and dl-dihydromethysticin, showed significant activity, giving 50% protection or better.

On reviewing the structure activity relationship observed in this series of compounds it is apparent that the 5,6-dihydro-4-methoxy-α-pyrone ring plays

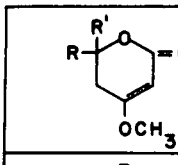
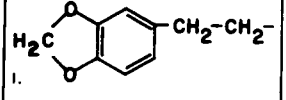
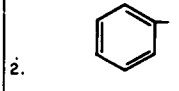
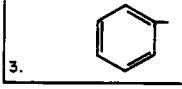
|  | | Strychnine mg/Kg | Roller cage 300 mg/Kg | Sleeping time dose mg/Kg | in % controls |
|---|---|---|---|---|---|
| R | R' | | | | |
|  1. | $-CH_3$ | no protection at 500 | 5/18 | 20 | 250 |
|  2. | $-CH_3$ | no protection at 500 | 10/18 | 160 | 266 |
|  3. |  | no protection at 500 | 3/18 | 160 | 331 |

TABLE IV

a key role in the physiological activities as evidenced by the loss of activity realized on opening of the lactone ring, or by the introduction of unsaturation in the $C_5$–$C_6$ position. Rigid overall specificity for drug receptor interaction in this series is discounted, however, by the variations of substituents which can be substituted at $C_6$ while retaining activity in one or more of the test systems employed.

## REFERENCES


(*1*) References to the work covered in this paper may be found, unless otherwise cited, in three recent reviews: (a) Keller, F., and M. W. Klohs, Lloydia, 26: 1–15 (1963); (b) Mors, W. B., M. T. Magalhaes and O. R. Gottlieb. In L. Zechmeister Progress in the Chemistry of Organic Natural Products, Vol. 20, Wien, Springer Verlag pp 131–164; (c) Hänsel, R., Deut. Apoteka ztg. 104 (15): 459–64 (1964) and 104 (16): 496–501 (1964).

(*2*) HÄNSEL, R., H. SAUER and H. RIMPLER, Arch. Pharm. 299: 507–511 (1966).

(*3*) TANABE, M., J. BOLGER, F. J. PETRACEK, F. KELLER, M. W. KLOHS and G. E. CRONHEIM, Unpublished work from these laboratories.

# Pharmacology of Kava

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Pursuant to a continuing study of the pharmacological properties of the Kava rhizome (Piper methysticum Forst), the six $C_6$-aryl-substituted alpha-pyrones kawain (K), dihydrokawain (DHK), methysticin (M), dihydromethysticin (DHM), yangonin (Y), and desmethoxyyangonin (DMY) isolated from the rootstock, were further investigated in attempts to bring the central nervous and peripheral effects observed in man after consumption of Kava preparations (Forbes 1875, Kesteven 1882, Thomson 1908, Deihl 1932, Leclerc 1937, Van Esveld 1937, Van Veen 1938, Titcomb 1948, Frater 1958) in relation to adequately characterized constituents of the plant. Major interest was attributed to the question, in how far these substances can be regarded as the active principles of the drug.

Because of low water solubility the pyrones were dissolved in peanut oil for the intraperitoneal and oral route of application. For intravenous injections and on isolated organs polyethylene glycol (Carbowax) 300 was employed.

As is shown in FIG. 1, the absorption of K and DHK from the gastrointestinal tract was remarkably rapid. The time of peak effect in mice

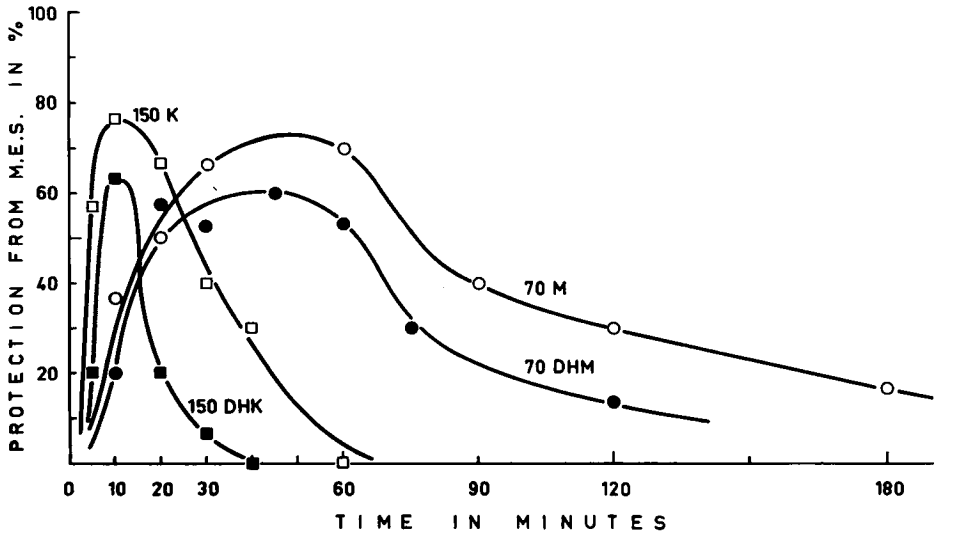


FIG. 1.—*Duration of action of genuine Kava pyrones after oral administration in mice.* Prevention of the tonic extensor component of maximal electroshock seizure (MES test). Corneal electrodes; square impulses of 50 mA, 60 Hz, 0.3 sec, 1 msec. Each point represents the mean of 15 animals. Doses employed: 150 mg/kg of kawain (K) and dihydrokawain (DHK), 70 mg/kg of methysticin (M) and dihydromethysticin (DHM). Notice the rapid onset of K and DHK action as compared to that of M and DHM, the latter being about twice as effective when given orally.

proved to be 10 min as judged by the MES test. M and DHM have a longer induction period (30–45 min) and an appreciably longer duration of action in equieffective doses.

The most characteristic central nervous action of all Kava pyrones, including Y and DMY, was shown to be their ability to produce a mephenesin-like muscular relaxation in all species of laboratory animals. According to Meyer and Kretzschmar (1966), who were the first to recognize this mechanism of action, Kava pyrones represent a new group of potent centrally acting skeletal muscle relaxants, the first of natural origin. Larger doses of the pyrones, with the exception of Y and DMY, produce ataxia and an ascending paralysis without loss of consciousness, followed by complete recovery. Pyrones were most effective when given intravenously (10–30 mg/kg); the oral median paralyzing dose is some 10 times higher. In doses causing muscular relaxation and paralysis Kava pyrones did not possess a curare-like action on the myoneural junction (Meyer 1966). Death after large oral or intraperitoneal doses is the result of respiratory failure.

Kava pyrones were found to depress polysynaptic responses such as the flexor, crossed extensor, skin twitch, pinna—prior to corneal—and linguomandibular reflexes in unanaesthetized animals. Effective doses ranged from 20–40 mg/kg iv., whereas in anaesthetized animals corresponding doses were found to be 5–10 times smaller. An example is presented in FIG. 2, showing the depressant effect of 5 and 10 mg/kg of Y and DHM on the crossed extensor reflex in the anaesthetized guinea-pig. The normal knee jerk was aside from a transient increase in reflex magnitude little or not affected. Most sensitive to the pyrones proved to be the tonic stretch reflex (Meyer and Kretzschmar 1966). Thus, in unanaesthetized rabbits and guinea-pigs the tonic responses of alpha montoneurons to muscle stretch were either

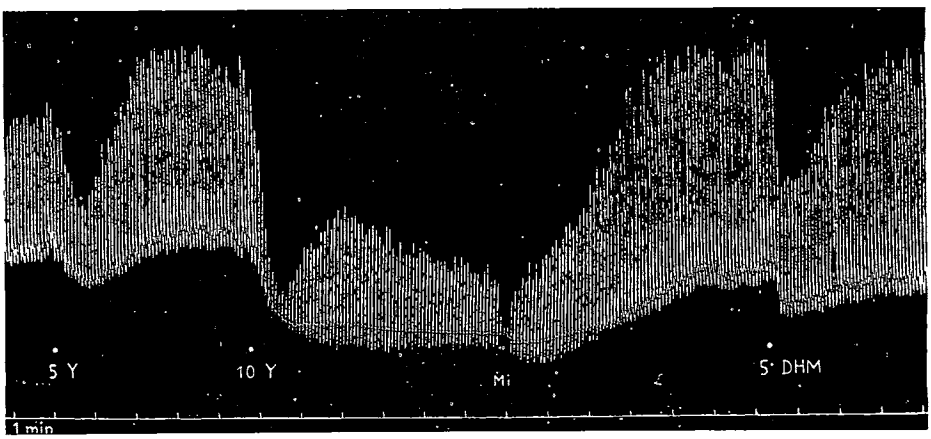


FIG. 2.—*Effect of yangonin (Y) 5 and 10 mg/kg and dihydromethysticin (DHM) 5 mg/kg on the crossed extensor reflex.* Guinea-pig, male, 740g. Urethane 1.0 g/kg intraperitoneally. Reflex elicited every 5 sec. Pyrones given intravenously in 30 sec. Stimulation of the afferent stump of sciatic nerve: 5.4 mA, 1 msec duration. Notice equipotency of Y and DHM relaxation of the quadriceps muscle indicated by the lowering of base line, and slower onset of Y action compared to that of DHM. Mi=miction.

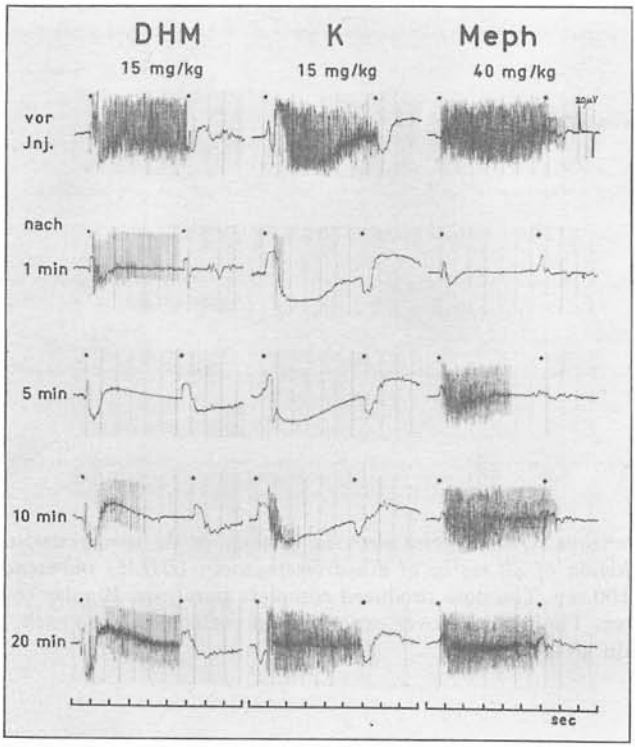


FIG. 3.—*Inhibition of the tonic stretch reflex by dihydromethysticin (DHM), kawain (K), and mephenesin (Meph).* Rabbit, male, 3.1 kg, unanaesthetized. Electromyograms of the quadriceps muscle, before and 1, 5, 10, and 20 min after injection. The injections were given intravenously with 2 hours interval. Time of stretch is indicated by points.

abolished or restricted to an initial phasic response by 15 mg/kg of K or DHM intravenously. The action of mephenesin was about 3 times weaker and much shorter in duration (FIG. 3). Doses which produce decrease or block of spinal reflexes had little effect on the electroencephalogram (FIG. 4), and left EEG arousal from stimulation of the midbrain reticular formation unimpaired.

In protecting mice from convulsions and death caused by toxic doses of strychnine Kava pyrones proved to be considerably more effective than mephenesin. Thus, complete protection from 4 mg/kg strychnine sulf. sc. was afforded by the intraperitoneal dose of 50 mg/kg of M, the most effective of the pyrones, whereas mephenesin was ineffective in antagonizing this degree of intoxication independent of the dose employed. With high doses of the pyrones (from 120 mg/kg intraperitoneally upwards) there was a seizure syndrome of long periods of generalized clonic convulsions (15–17/sec) similar to that observed after barbiturates or meprobamate (Loewe 1958; Simon 1959). In addition, all six Kava pyrones were effective in depressing or abolishing the maximal tonic seizure induced by electroshock in mice. At the time of peak effect the following $ED_{50}$ values (in mg/kg) were found after oral administration: 70 K, 98 DHK, 44.5 M,

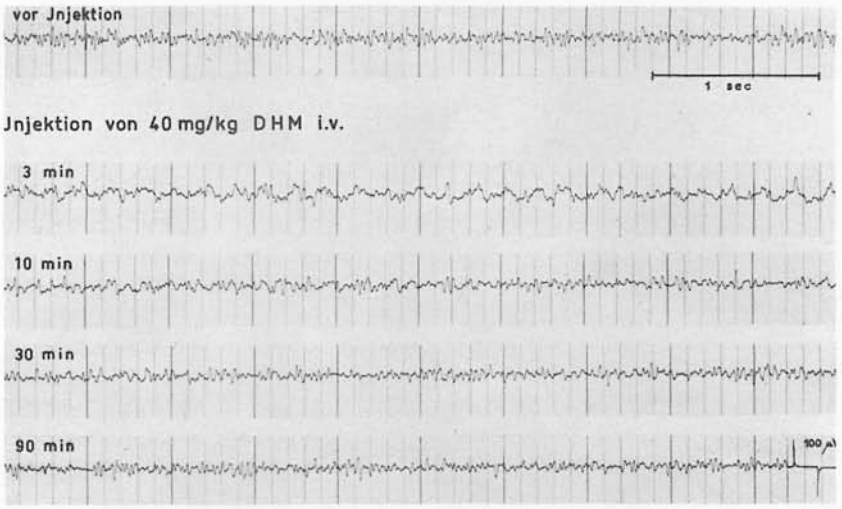


Fig. 4.—*Spontaneous cerebral cortex electrical activity in the unanaesthetized rabbit before and after injection of 40 mg/kg of dihydromethysticin (DHM) intravenously.* Duration of injection 100 sec. The dose produced complete paralysis. Bipolar electrodes on sensomotor cortex. The records cover experimental periods of 5 sec each, obtained 3, 10, 30, and 90 min after injection.

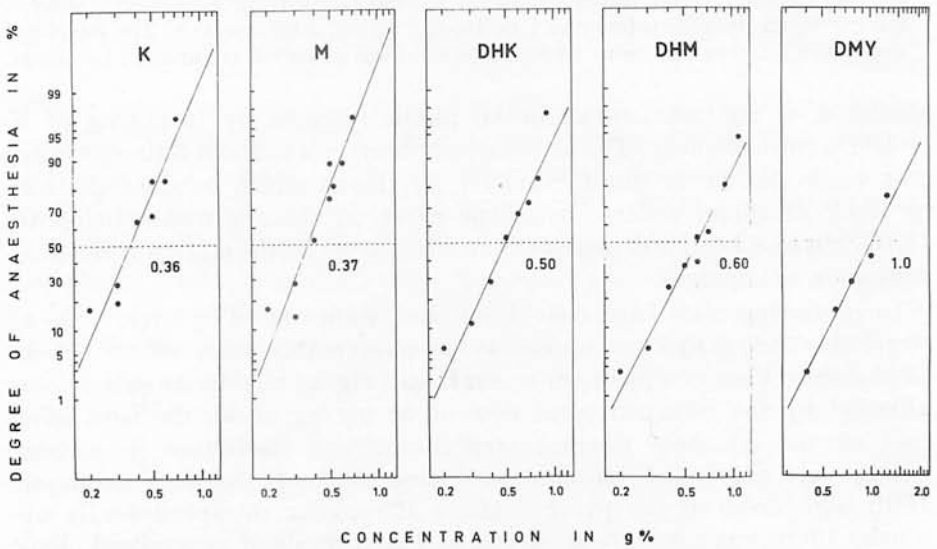


Fig. 5.—*Local anaesthetic activity of genuine Kava pyrones.* Mean effective concentrations as established by the intracutaneous wheal method in guinea-pigs. The graph shows the relation between the concentration of the various pyrones (abscissae, logarithmic scale) and the average response from 6 animals for each concentration (ordinates). The dose was always injected in 0.25 ml of peanut oil, which proved to be inert. The response was tested 6 times in succession 1 min after injection.

50.5 DHM, 420 DMY, and 740 Y; by intravenous injection these figures were: 6.0 K, 6.1 DHK, 6.2 M, 8.1 DHM, 6.25 DMY, 11.5 Y, respectively, showing the striking difference in Y and DMY potency with the route of administration. Pyrone anticonvulsant activity and time course of action after intravenous administration were intermediate between mephenesin and procaine HCl with maximum effects 1 min after injection, made in 15 sec. The effect produced by 10 mg/kg most commonly had worn off after 20 min.

In addition to inducing changes in motor function, reflex irritability and seizure threshold and pattern (Meyer 1964), Kava pyrones reduced the edema produced by formalin, serotonin, dextran, or carrageenin. Their antipyretic action is mild. Contractions of isolated ileum or uterus produced by histamine, barium, acetylcholine, bradykinin, 5-HT, or nicotine were inhibited by the pyrones in concentrations of 1:1.000.000 to 1:100.000. This applies to all pyrones, including DMY and Y. Kava pyrones posses local anaesthetic properties. Median anaesthetic concentrations as established by the intracutaneous wheal method in guinea-pigs (FIG. 5) increase in the following sequence: K 0.36%, M 0.37%, DHK 0.50%, DHM 0.60%, DMY 1.0%, and Y>1.0%. Comparable values of procaine HCl, benzocaine and mephenesin were found to be 0.10%, 0.34% and 0.36%, respectively. In surface anaesthesia K was shown to be equipotent to cocaine HCl, when concentrations of 0.5% were employed. Its duration of action was markedly longer than that of benzococaine (FIG. 6). Further details concerning the antiinflammatory, spasmolytic and local anaesthetic properties of the Kava pyrones were previously described (Meyer 1965a,b; Meyer and May 1964).

As can be seen in FIG. 7, rapid intravenous injection of 10–30 mg/kg DHM causes a transient drop in blood pressure which depends on speed of injection and which was stronger in anaesthetized than in unanaesthetized rabbits. The mechanism underlying this action appears to be primarily the result of peripheral vasodilatation. In intact cats, rabbits and mice the blood pressure fall after DHM was followed by a characteristic bradycardia lasting several hours with a maximum reduction of heart rate by 40%. This effect was not observed in anaesthetized animals and was almost completely prevented by previous injection of atropine or bilateral vagotomy. No intravascular hemolysis was obtained in cats with solutions containing 20 mg/ml DHM or pyrone mixture. Oral or intraperitoneal administration of Kava pyrones had little or no effect on cardiovascular functions.

It has been established that Y and DMY possess only weak central nervous activity when given orally or intraperitoneally. On intravenous injection and in experiments on isolated organs, however, the potency of both pyrones was shown to be of the same order of magnitude as observed with the other pyrones of the kavaroot, indicating poor absorption from the gut resp. peritoneum and/or rapid elimination of these materials. In further experiments it was found that the activity of orally or intraperitoneally administered Y or DMY is markedly increased when given in combination with other pyrones. Both Y and DMY proved to be synergistic with all other



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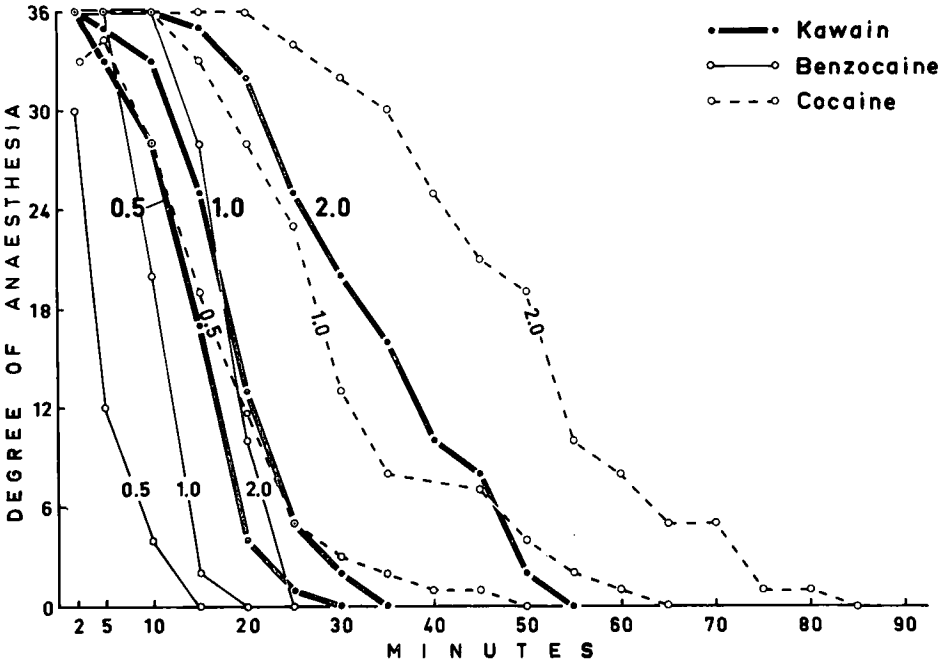


FIG. 6.—*Surface anaesthetic action produced by kawain, benzocaine and cocaine HCl in the cornea of the rabbit.* Concentrations tested were 0.5, 1.0, and 2.0%, respectively. Abscissa is time in minutes after instillation and ordinate is degree of anaesthesia in the range between zero and maximum possible effect (=36). Each point represents the mean of 6 animals. The corneal reflex was tested 6 times in succession at 5 min intervals until anaesthesia had worn off. Kawain and benzocaine were instilled in 0.25 ml of peanut oil, cocaine HCl in saline.

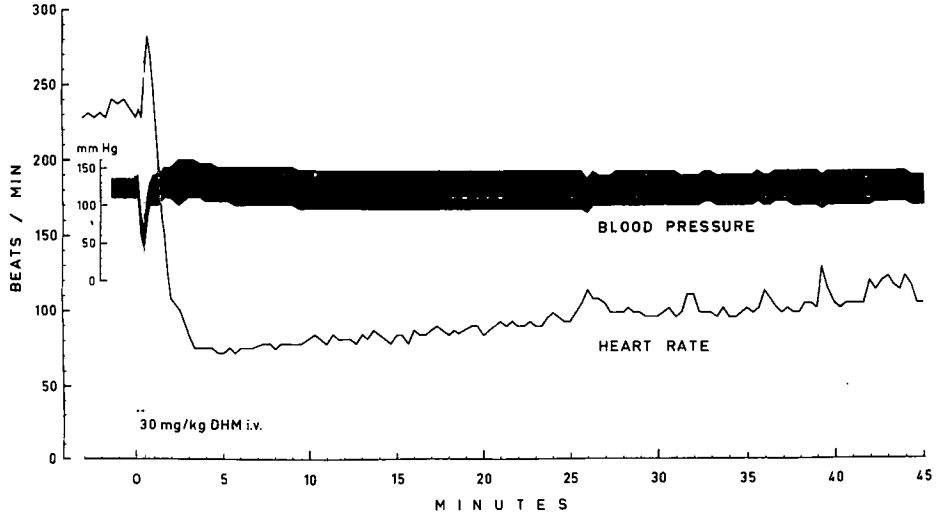


FIG. 7.—*Responses of heart rate and femoral arterial pressure to the intravenous injection of 30 mg/kg dihydromethysticin (DHM).* Rabbit, female, 2.7 kg, unanesthetized. The injection was given in 30 sec. Systolic and diastolic blood pressure obtained before injection are indicated throughout the whole experiment by the broken lines showing the increment in amplitude under DHM.

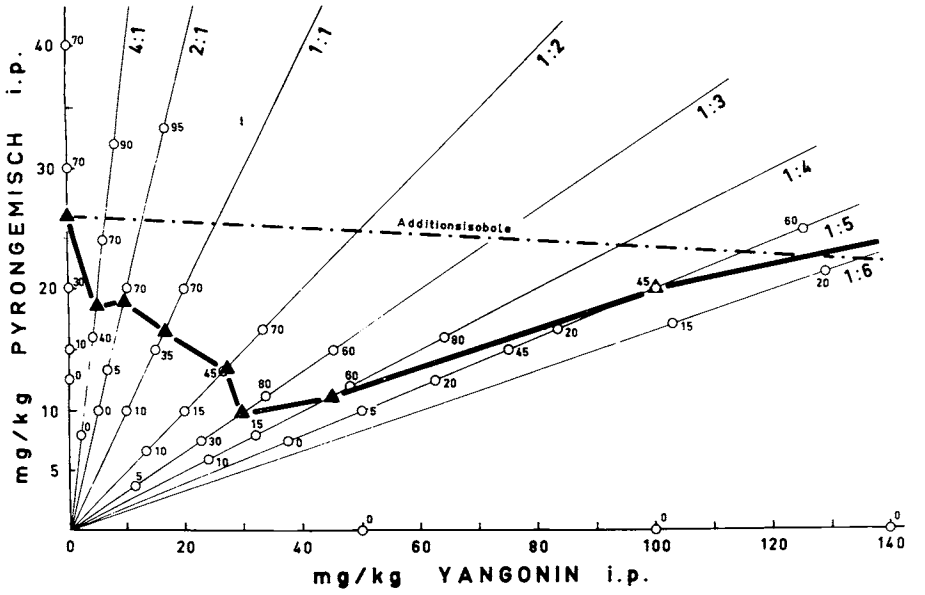


FIG. 8.—*Isobologram of combined yangonin-pyrone mixture effects in protecting mice from electrically induced convulsions (MES test).* Abscissae: dose scale of yangonin (Y), ordinates: dose scale of pyrone mixture (PM) consisting of methysticin, dihydromethysticin, kawain, and dihydrokawain in equal parts. All injections were given intraperitoneally, Y and PM at the same time. Ratios of PM : Y tested were 4 : 1 to 1 : 6. Open circles indicate percentage of protected animals, triangles the mean effective doses ($ED_{50}$). The isobole of combined doses having the same anticonvulsant effect ($ED_{50}$) is represented by the line connecting the triangles. Rectilinear connection between $ED_{50}$ of PM (26 mg/kg) and $ED_{50}$ of Y (1.000 mg/kg) = isobole of addition. Y was without any effect when given alone in doses up to 300 mg/kg ip.

pyrones studied in producing muscular relaxation, hypothermia or preventing mice from MES (Meyer et al.). This potentiation could be demonstrated in isobolometric experiments; an example is presented in FIG. 8. The greatly arcuate course of the isobole of median anticonvulsive doses running far below the rectilinear isobole of addition is characteristic of an effect more than additive. On the other hand, 5, 6-hydrogenated pyrones, behaved additive when given in combination.

The experiments have shown that all the six known pyrones of the Kava rootstock are pharmacologically effective, differences in action being largely quantitative in nature. The finding that Y as well as DMY, contrary to all previous reports on this matter since the beginning of Kava investigation, represent biologically active principles especially on combined administration with the other pyrones, is of particular interest in view of the relatively high amount of these two compounds in the kavaroot which is reported to be one quarter to one third of total pyrone content (Hänsel and Beiersdorff, 1959; Klohs et al., 1959). The synergism between Y and the other pyrones may provide an explanation for the high activity of a chloroform extract and of the crude root, reported by Klohs et al. (1959), which according to the authors was not evidenced by any of the pure isolated ma-

terials. The central nervous and peripheral activities of the pyrones as reported herein further substantiate the idea that the various ethnopharmacological phenomena ascribed to Piper methysticum are due to the pyrone content of the plant.

## REFERENCES


DIEHL, J. R.: Primitive Man, *5*, 61 (1932).

FORBES, L.: "Two Years in Fiji," London 1875, p. 190–195, 235–236.

FRATER, A. S.: Trans. Proc. Fiji Soc. Sci. Ind., *5*, 31 (1958).

HANSEL, R., and BEIERSDORFF, H. U.: Arzneimittelforsch., 9, 581 (1959).

KESTEVEN, L.: Practitioner (London), 199–201 (1882).

KLOHS, M. W., KELLER, F., WILLIAMS, R. E., TOEKES, M. I., and CRONHEIM, G E.: J. med. pharmaceut. chem., 1, 95 (1959).

LELEBC, H.: Presse médicale, No. 9, 164 (1937).

LOEWE, S.: Arch. int. Pharmacodyn., 114, 451 (1958).

MEYER, H. J.: Arch. int. Pharmacodyn., 150, 118 (1964).

MEYER, H. J., and MAY, H. U.: Klin. Wschr., 42, 407 (1964).

MEYER, H. J.: Arch. int. Pharmacodyn., 154, 449 (1965a).

MEYER, H. J.: Klin. Wschr., 43, 469 (1965b).

MEYER, H. J.: "Pharmakologie der Kawa-Droge- Zugleich ein Beitrag zum Problem des Kawa-Trinkens," Habilit, Schrift, Freiburg 1966.

MEYER, H. J., and KRETZSCHMAR, R.: Klin. Wschr., 44, 902 (1966).

MEYER, H. J., et al.: In press.

SIMON, I.: Proc. I. int. congr. neuropharmacol., Elsevier 1959, p. 414.

THOMSON, B.: "The Fijians. A Study of the Decay of Custom," London 1908, p. 213, 341–351.

TITCOMB, M.: J. Polynes, Soc., *57*, 105 (1948).

VAN ESVELD, L. W.: Ned. T. Geneesk., *81*, 3961 (1937).

VAN VEEN, A. G.: Geneesk. T. Nederl. Ind., *78*, 1941 (1938).

# Pharmacology of Kava[1]

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*Piper methysticum* Forst. (Piperaceae) is a perennial shrub indigenous to many islands of the South Pacific. Roots of this plant have been used by inhabitants of these islands to prepare a beverage known as Kava, Kawa, or Awa, which has been reported to allay anxiety and reduce fatigue (*1*, *2*). The pure crystalline alpha-pyrones, isolated from the roots of the plant which possess sedative-type activity, are soluble in the usual fat solvents but insoluble in water. Three of these, methysticin, dihydromethysticin, and dihydrokawain, possess sedative activity similar to that of the whole root (*3–6*). Since Professor Meyer and his colleagues have worked extensively on the pharmacology of these water-insoluble α-pyrones, this present report will be concerned primarily with the pharmacological activity of water-soluble fractions of Kava.

## Experimental

The plant material used was obtained from S. B. Penick Company, New York, New York, and consisted of finely pulverized root of *P. methysticum* (Piperaceae).

### *Steam Extraction*

One hundred grams of the finely pulverized root was mixed with approximately 100 ml of distilled water giving a slurry having a volume of approximately 200 ml. The slurry was steam distilled and the first 100 ml of distillate collected, filtered, and lyophilized. The yield for each extraction was approximately 50 mg of a yellow-white powder designated LE–1. When this fraction was reconstituted in a cencentration of 10 mg/ml in distilled water, some of the material was insoluble and formed a fine suspension. Since preliminary studies on the spontaneous activity of mice indicated that both the filtrate and suspension possessed depressant activity, the following procedure was used to prepare subfractions. LE–1 was suspended in distilled water in a concentration of 20 mg/ml, shaken for 3 minutes. The mixture was then filtered through Whatman #1 filter paper, the filtrate shaken with two equivalent volumes of chloroform, the remaining aqueous solution lyophilized, and the resulting amorphous solid labeled $F_1$. The residue from the initial filtration was washed from the filter paper and made up to 15 ml

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with distilled water, shaken for 3 minutes, and filtered. The filtrate was collected and the remaining minute residue discarded. This filtrate was also washed with two equivalent volumes of chloroform and the resulting aqueous solution lyophilized and the amorphous solids labeled $F_2$.

*Pharmacological Studies*

*Spontaneous and Forced Motor Activity Studies.*—The effects of LE–1, $F_1$, and $F_2$, on spontaneous motor activity of male albino Swiss-Webster mice were evaluated in photocell activity cages as described by Furgiuele et al. (*7*). Fifty to 60 minutes after receiving an intraperitoneal injection of one of the fractions or saline, 1 hour prior to testing. Maximum per- activity cages (Actophotometer, Metro Industries, New York) and a 15 minute count taken 10 minutes later. Each fraction was tested at 4 dose levels using 4 to 6 groups of 5 mice per group. The effects of the fractions on forced motor activity were investigated using the rotarod (*8*, *9*). Each group was trained to walk a 1.5 inch diameter hardwood rod rotating at 15 rpm or a 1 inch diameter rod rotating at 29 rpm (*10*, *11*). The mice were trained to walk the rotating rod and on test days received i.p. injections of either one of the fractions or saline, 1 hour prior to testing. Maximum per- formance time was set at 120 seconds for the 1 inch rod and 180 seconds for the 1½ inch rod.

*Septal Rats.*—LE–1 was investigated for possible antagonism of the exaggerated irritability and aggressiveness of rats having lesions in the septal area (*12*). Three to four days following production of the lesions behavioral abnormalities were scored as described by Schallek et al. (*13*). This involved scoring the responses obtained by (a) a puff of air on the back, (b) gently touching the whiskers with a probe, (c) gently prodding the animal's back with a probe, and (d) approaching the rat with a gloved hand. Each test was rated on a scale ranging from 0 for no response to 6 for the most violent response. Different groups of 5 rats were tested, 0.5, 1, and 2 hours following intraperitoneal injection of fraction LE–1. Since chlordiazepoxide has also been reported (*12*) to be particularly effective in this preparation, it was compared to the activity of LE–1. The $ED_{50}$ was determined graphically using the method of Miller and Tainter (*14*).

*Conditioned Avoidance Response.*—The rat pole climbing procedure of Cook and Weidley (*15*) was modified for these tests (*10*). Each cycle consisted of 15 seconds of tone followed by a maximum of 30 seconds of shock, at 2.75 minute intervals and the number of times the animal responded to either tone or shock was recorded. Each animal was subjected to 2 to 3 ten-cycle training sessions. Trained groups of 6 male albino Wistar rats received i.p. injections of either LE–1, 50, 100, and 200 mg/kg; chlordia- zepoxide, 10, 20, and 40 mg/kg; or saline, 0.1 ml, one hour prior to a 10 cycle session. The number of times that the rat failed to respond to tone but did respond to shock was a measure of the inhibition of the conditioned response.

*Electroencephalographic Studies.*—Cats with chronically implanted cortical and subcortical electrodes were prepared as described by Horovitz and Chow (*16*). Bipolar electrodes were implanted into the amygdala (AP=13, L=9, H=5), hippocampus (AP=5, L=12.5, H=1.5), and pontine reticular formation (AP=35 mm anterior to F=0, L=0, H=32 mm at an angle of 25 degrees) according to the atlas of Jasper and Ajmone-Marsan (*17*) and into the posterior hypothalamus (AP=9, L=0.5, H=2.5) according to the atlas of Bleier (*18*). Monopolar electrodes were placed over appropriate cortical areas, 5 to 10 mm apart. Simultaneous recordings were obtained from three different leads onto a Grass polygraph. A Grass square-wave stimulator was used to stimulate the posterior hypothalamus or brain stem reticular formation for a period of 15 seconds with pulses of 100 c.p.s. having a duration of 5 msec and at 0.5 to 8.5 volts. The animals were placed in a semi-soundproof constant environment chamber fitted with a one-way glass window and a small light. The animals were fed, placed into individual chambers, and allowed a period of one hour to acclimatize. Control recordings were obtained and the threshhold for EEG arousal determined following the electrical, visual (blinking lights) or auditory (clap) stimulation. A desynchronization of the resting EEG for a period of approximately twice the duration of the stimulus or longer was taken as the arousal response. The posterior hypothalamus of two cats and the brain stem reticular formation of two other cats were stimulated and cortical and subcortical activity recorded. After control recordings, the cats were removed from the chambers, and an aqueous solution of either LE-1 or chlordiazepoxide administered intraperitoneally. The effects on spontaneous EEG activity and upon arousal were observed 30, 60, 120, and 180 minutes following administration. An interval of at least 5 days was permitted between injections to insure recovery of the test animals. At the termination of the study, the animals were sacrificed, the brains perfused with 10% formalin and location of the electrodes verified.

*Antiserotonin Activity.*—A rat uterine horn obtained from virgin rats (Wistar) in the estrus stage, as determined by microscopic examination of vaginal smears, was suspended in a 10 ml tissue bath containing modified deJalon's solution (19), containing calcium chloride, 20 mg/1, and oxygenated with 95% $O_2$ and 5% $CO_2$ at a temperature of 37.5°. Uterine contractions were recorded on a smoked kymograph drum via a muscle lever so that the magnification was approximately 3×. All test substances were added in volumes not exceeding 0.15 ml and the α-pyrones investigated were administered in a suspension of 1% methylcellulose, 1500 cps. Maximal contraction of the uterine horn was induced by serotonin creatinine sulfate, 0.5 to 1.0 mcg/10 ml bathing solution. The dose producing maximal contraction was added to the bath every fourth minute; following the contraction the tissue was washed with fresh deJalon's solution. After two equivalent responses to serotonin were obtained, a given quantity of one of the α-pyrones or subfraction $F_1$ or $F_2$ was added to the bath, 30 seconds prior to the next dose of serotonin. Additional doses of the antagonists were not added until the serotonin response had returned to normal. Equivalent volumes of 1% methylcellulose did not affect the response of the uterine horn to serotonin.

*Effects on Brain Serotonin Content.*—Dihydromethysticin, 100 mg/kg, $F_1$, 100 mg/kg, $F_2$, 100 mg/kg, chlordiazepoxide, 5 mg/kg, and reserpine phosphate, 1.25 mg/kg were each administered to 5 mice. The animals were sacrificed one hour following i.p. administration by stunning and exsanguination. The brains were removed intact, weighed, and transferred to a glass homogenization tube containing sufficient 0.1 N HCl to make a total volume of 3.0 ml. The tissue was homogenized with a motor driven teflon homogenizer and the homogenate rinsed with 7.0 ml of glass distilled water and transferred to a 30 ml centrifuge tube containing 3.0 ml of borate buffer. Serotonin was extracted using the method of Bogdanski et al. (*20*) as modified by Aprison et al. (*21*) and serotonin concentration determined with a Turner fluorometer (*22*).

## Results

*Physical-Chemical Characteristics of Subfractions* $F_1$ *and* $F_2$.—Subfraction $F_1$ was found to be 16 times more soluble in water than $F_2$. The physical-chemical characteristics and average yield of $F_1$ and $F_2$ are summarized in Table 1. Nitrogen could not be detected in either fraction and aldehydes and/or ketones were detected in $F_2$ only.

TABLE 1.—*Some physical and chemical characteristics of subfractions* $F_1$ *and* $F_2$ *from the lyophilized steam distillate of Kava*

| Property | $F_1$ | $F_2$ |
|---|---|---|
| Physical state | Amorphous solid | Amorphous solid |
| Color | Amber | Yellowish white |
| Odor | Aromatic | Aromatic |
| Sodium Fusion | Nitrogen absent | Nitrogen absent |
| Ignition | Burned with a sooty flame, small residue | Burned with a sooty flame, no residue |
| Solubility | 8 mg/ml | 0.5 mg/ml |
| Av. yield | 60 mg/200 mg LE–1 | 18 mg/200 mg LE–1 |
| 2,4-Dinitrophenylhydrazine | No dinitrophenylhydrazone formed | Red needle shaped crystals of insoluble dinitrophenylhydrazone formed |

*Spontaneous and Forced Motor Activity.*—The effects of the aqueous fractions from Kava on spontaneous motor activity of mice are summarized in Table 2. LE–1, $F_1$, and $F_2$ depressed spontaneous motor activity in a dose-related manner. The estimated $ED_{50}$ for $F_1$ being 31.6 mg/kg and $F_2$ 5.4 mg/kg. Loss of righting reflex was not observed even at those doses which almost completely abolished spontaneous motor activity. Doses of the fractions showing marked inhibition of spontaneous motor activity did not alter the forced motor activity of mice placed on the rotarod.

*Septal Rats.*—The effects of LE–1 and chlordiazepoxide on the hyperirritability of septal rats are summarized in Table 3. LE–1 was approxi-

TABLE 2.—*Effects of lyophilized aqueous kava on spontaneous motor activity of mice*

| Fraction | I.P. Dose (mg/kg) | N[a] | Percentage Inhibition Photocell Activity |
|---|---|---|---|
| LE-1 | 42 | 6 | 67 |
| | 84 | 6 | 77 |
| | 120 | 6 | 89 |
| | 240 | 6 | 91 |
| $F_1$ | 5 | 4 | 14 |
| | 10 | 4 | 28 |
| | 25 | 4 | 35 |
| | 50 | 4 | 67 |
| $F_2$ | 5 | 4 | 47 |
| | 10 | 4 | 59 |
| | 25 | 4 | 84 |
| | 50 | 4 | 92 |

[a] Number of groups, 5 mice/group.

mately one-tenth as effective as chlordiazepoxide in reducing the hyperirritability of these animals; however, even the 50 mg/kg dose significantly affected the experimental animals and ataxia was not observed in those animals receiving doses as high as 200 mg/kg of LE-1 whereas moderate to marked ataxia occurred at the 20 and 40 mg/kg doses of chlordiazepoxide.

*Conditioned Avoidance Response.*—LE-1 in doses ranging from 50 to 400 mg/kg i.p. produced a significant inhibition of the CAR which was dose dependent. The $ED_{50}$ for LE-1 was 82 mg/kg and for chlordiazepoxide 21 mg/kg. (see table 4). LE-1 did not inhibit the shock response whereas chlordiazepoxide, 40 mg/kg, did produce a significant reduction in shock responses.

*Electroencephalographic Studies.*—The effects of LE-1 on the duration of the arousal response after threshold stimulus are summarized in Table 5.

TABLE 3.—*Effects of LE-1 and chlordiazepoxde on the rage score of septal rats*

| Drug | N[a] | Dose (mg/kg, i.p.) | Mean Score ± S.E. | $ED_{50}$ ± percent S.E. (mg/kg) |
|---|---|---|---|---|
| Control | 20 | | 62±3 | |
| LE-1 | 5 | 50 | 47±6[b] | |
| | 5 | 100 | 37±6[b] | 170±19 |
| | 5 | 200 | 26±6[b] | |
| Chlordiazepoxide | 5 | 10 | 48±3[b] | |
| | 5 | 20 | 26±12[b] | 17±20 |
| | 5 | 40 | 14±2[b] | |

[a] N, number of rats tested.
[b] Significantly different from controls ($p<0.05$).

TABLE 4.—*Effects of* LE–1 *and chlordiazepoxide on the rat conditioned avoidance response (CAR)*

| Drug | N[a] | i.p. (mg/kg) | Percent Inhibition of CAR | ICR$_{50}$ ± percent S.E. (mg/kg) |
|---|---|---|---|---|
| Control | 24 | ---------- | 8 | ---------- |
| LE–1 | 6 | 50 | [b] 48 | ---------- |
| | 6 | 100 | [b] 65 | 82±31 |
| | 6 | 200 | [b] 70 | ---------- |
| | 6 | 400 | [b] 92 | ---------- |
| Chlordiazepoxide | 6 | 10 | [b] 26 | ---------- |
| | 6 | 20 | [b] 37 | 21±14 |
| | 6 | 30 | [b] 64 | ---------- |
| | 6 | 40 | 100 | ---------- |

[a] N, number of rats tested.
[b] Significantly different from controls ($p<0.05$).

TABLE 5.—*Effects of* LE–1 *on duration of arousal following threshold stimulation in cats*

| Cat No. | i.p. (mg/kg) | Area Stimulated | Area Recorded | Duration of Arousal, Seconds | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | 0 hr [a] | 0.5 hr | 1 hr | 2 hr | 3 hr |
| 4 | 50 | Ret. Form. | P. Sigmoid | 32 | 20 | 15 | 30 | ------ |
| | | | A. Suprasyl. | 32 | 20 | 15 | 30 | ------ |
| | | | P. Hypothal. | 32 | 20 | 15 | 30 | ------ |
| 3 | 50 | P. Hypothal. | P. Sigmoid | 25 | 13 | 9 | 22 | ------ |
| | | | A. Suprasyl. | 25 | 13 | 9 | 22 | ------ |
| | | | Amygdala | 25 | 13 | 9 | 22 | ------ |
| 2 | 50 | P. Hypothal. | A. Sigmoid | 40 | 30 | 21 | 35 | ------ |
| | | | P. Sigmoid | 40 | 30 | 24 | 35 | ------ |
| | | | Amygdala | 40 | 30 | 21 | 35 | ------ |
| 1 | 100 | Ret. Form | P. Sigmoid | 29 | 0 | 0 | 16 | 22 |
| | | | A. Suprasyl. | 29 | 0 | 0 | 16 | 22 |
| | | | P. Hypothal. | 26 | 0 | 0 | 10 | 29 |
| 4 | 100 | Ret. Form. | P. Sigmoid | 42 | 10 | 0 | 0 | 36 |
| | | | A. Suprasyl. | 42 | 10 | 0 | 0 | 39 |
| | | | P. Hypothal. | 48 | 10 | 0 | 0 | 48 |
| 4 | 150 | Ret. Form. | P. Sigmoid | 60 | 0 | 0 | 0 | [b] 0 |
| | | | A. Suprasyl. | 50 | 10 | 0 | 0 | [b] 37 |
| | | | P. Hypothal. | 50 | 2 | 0 | 0 | [b] 0 |
| 2 | 150 | P. Hypothal. | A. Sigmoid | 37 | (c) | 10 | 0 | 12 |
| | | | P. Sigmoid | 37 | (c) | 10 | 0 | 11 |
| | | | Hippocampus | 37 | (c) | 10 | 0 | 12 |

[a] Predrug.
[b] Recovery in 4 hours.
[c] Unable to record.

The lowest dose of LE–1 shortened the duration of the arousal response for approximately one hour. Although this effect was observed in recordings from both cortical and subcortical sites, no significant changes in the EEG activity were evident. The larger doses of 100 and 150 mg/kg effectively blocked EEG arousal and caused a slowing of spontaneous cortical and subcortical activity. Mild to marked ataxia occurred following the 100 and 150 mg/kg doses, respectively. The duration of the arousal response after auditory stimulation was unaffected at the 50 mg/kg dose and shortened after 100 mg/kg and completely abolished following the 150 mg/kg dose of LE–1. The EEG arousal induced by visual stimulation was unaffected at the 50 mg/kg dose, shortened somewhat following 100 mg/kg, and blocked for more than 2 hours following the 150 mg/kg administration of LE–1. Moderate ataxia was observed in those cats receiving 150 mg/kg and was still evident 12 to 14 hours after drug administration.

Chlordiazepoxide effectively reduced cortical and subcortical arousal in doses ranging from 5 to 15 mg/ kg, i.p. In two cats, chlordiazepoxide induced a period of excitation of sufficient intensity that recording was prevented.

*Antiserotonin Activity.*—Desmethoxy-yangonin, dihydromethysticin, kawain, and $F_2$ antagonized the serotonin induced contractions of the isolated rat uterus whereas $F_1$ did not alter the serotonin activity in doses ranging from 100 to 400 mcg/10 ml bath (Fig. 1). The $ED_{50}$ (dose per 10 ml bathing

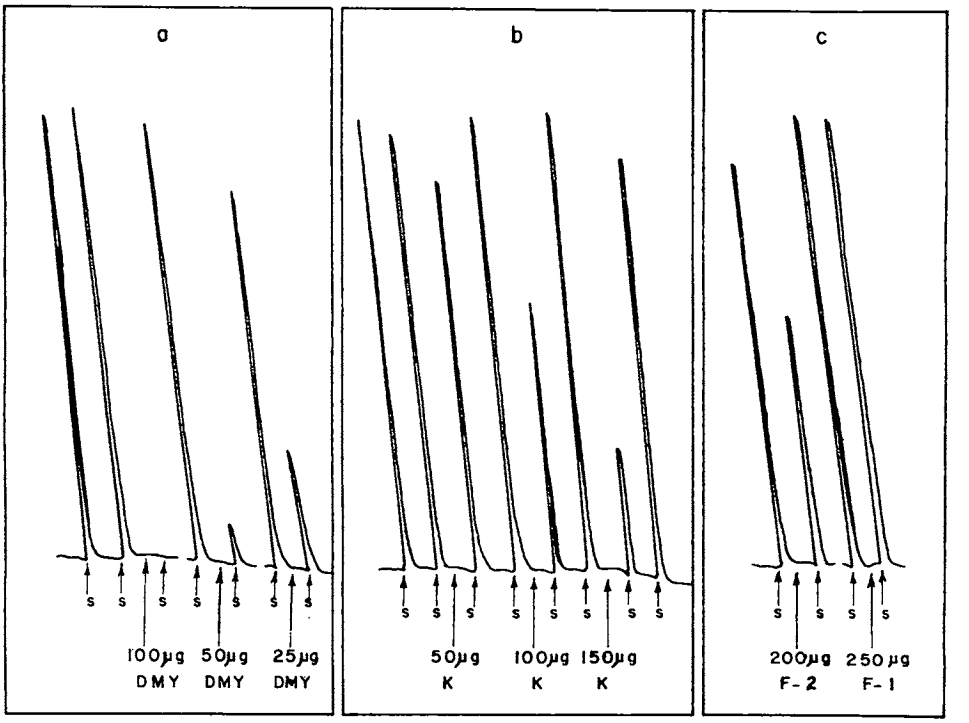


FIG. 1.—Kymograph tracings showing the effects of (a) desmethoxy-yangonin (DMY), (b) Kawain (K) and (c) $F_1$ and $F_2$ on serotonin induced contractions of the isolated rat uterus (from O'Hara, M. J., Kinnard, W. J., and Buckley, J. P., J. Pharm. Sci. *54*, 1021, (1965).

fluid inhibiting serotonin response by 50%) for desmethoxy-yangonin was 32 mcg, kawain 100 mcg, dihydromethysticin 75 mcg, and $F_2$ 225 mcg. This antagonism of the α-pyrones to the serotonin induced contraction of the isolated rat uterus appears to be specific since dihydromethysticin failed to alter the contraction induced by either bradykinin or acetylcholine (see Table 6 and Fig. 2).

TABLE 6.—*Responses of an isolated rat uterus to dihydromethysticin showing specificity of antagonism to serotonin*

| Serotonin (mcg/10 ml) | Acetylcholine (mcg/10 ml) | Bradykinin (ng[a]/10 ml) | DHM (mcg/10 ml) | Contraction (cm) |
|---|---|---|---|---|
| 1. 0 | 0. 0 | 0 | 0 | 4. 5 |
| 1. 0 | 0. 0 | 0 | 100 | 1. 4 |
| 0. 0 | 5. 0 | 0 | 0 | 7. 2 |
| 0. 0 | 5. 0 | 0 | 100 | 7. 2 |
| 0. 0 | 0. 0 | 400 | 0 | 7. 8 |
| 0. 0 | 0. 0 | 400 | 100 | 7. 8 |

[a] ng., nanogram.

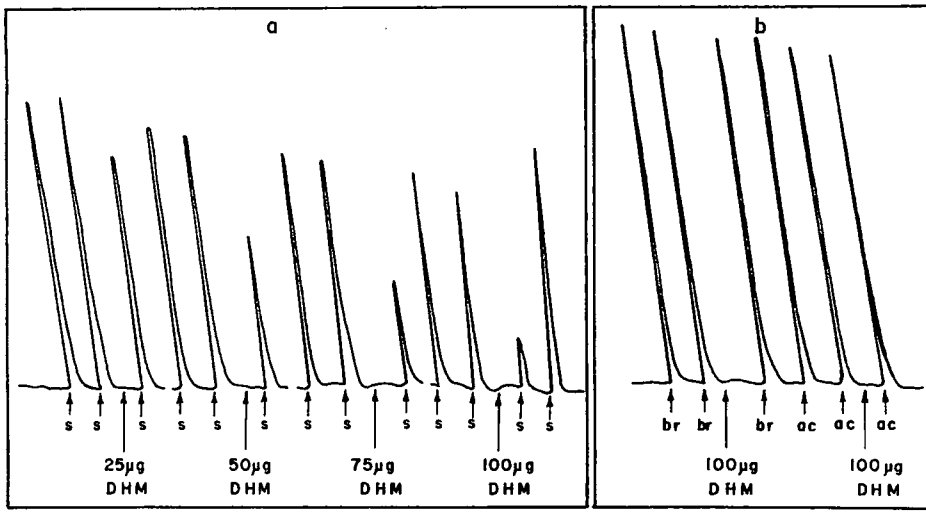


FIG. 2.—Kymograph tracings showing the effects of dihydromethysticin (DHM) on (a) serotonin, and (b) bradykinin (br) and acetylcholine (ac) induced contraction of the isolated rat uterus (from O'Hara, M. J., Kinnard, W. J., and Buckley, J. P., J. Pharm. Sci. *54*, 1021, (1965).

*Brain Serotonin.*—Brain levels of endogenous serotonin were not altered 1 hour after the i.p. administration of dihydromethysticin, $F_1$, $F_2$ and chlordiazepoxide. Reserpine reduced brain serotonium levels by 27%.

## Discussion

LE–1, a lyophilized steam distillate of *Piper methysticum* Forst., and the two water soluble apparently distinctive subfractions of the distillate produced marked depression of spontaneous motor activity of mice without altering the rotarod performance. Chromatographic data indicated that the pharmacological actions of this fraction were due to substances other than the known α-pyrones (*10*). LE–1 reduced the behavior abnormalities of septal rats in a manner similar to that of chlordiazepoxide in doses which exerted a specific blockade of the conditioned avoidance response. King and Meyer (*23*) have postulated that in the rat the septal area normally acts to dampen hypothalamic output, associated with an emotional state, whereas the amygdala may facilitate this hypothalamic activity. Destruction of the septal areas should remove its restraining influence and result in a hyperirritable animal. Schallek et al. (*13*) theorized that the reduced activity in the amygdala is related to the psychodepressant effects of chlordiazepoxide.

LE–1 caused moderate slowing of cortical, hypothalamic, and hippocampal activity with concomitant ataxia and motor deficiency. After cortical activity had returned to pretreatment levels, subcortical (hypothalamic and hippocampal) activity was still reduced, evidenced by the absence of EEG arousal. Although return of the arousal pattern generally marked the end of an experiment, ataxia and uncoordinated movements were still present, an indication that LE–1 was exerting a skeletal muscle relaxant effect. Ataxia was one of the most consistent responses obtained with LE–1 in mice and rats (with the exception of septal rats) also suggesting skeletal muscle relaxant activity. A single intravenous dose of 20 mg/kg of LE–1 completely blocked the flexor reflex for approximately 3 hours in two cats. It appears that at least part of the altered behavioral effects observed in mice and rats as well as cats could be due to blockade of the spinal interneurons, with progressive weaker depressant effects on the reticular formation, subcortex, and cortex respectively. Certain of the α-pyrones exhibited a dose-related antagonism of the serotonin-induced contraction of the rat uterus and exhibited potency comparable to N-(β-dimethylaminoethyl) cinnamamide (*24*). The α-pyrones isolated from Kava possessing this antiserotonin activity have a cinnamoyl moiety which may be responsible for this particular pharmacological action. Antiserotonin studies further substantiated the difference in activity between $F_1$ and $F_2$ in that $F_1$ did not affect the serotonin response whereas $F_2$ was antagonistic to it. Subfraction $F_1$ was a much weaker depressant on a weight-weight basis than subfraction $F_2$. Since thin-layer chromatograms demonstrated that $F_1$ is absolutely free of known α-pyrones (Fig. 3) and since the overall pharmacological profile may be quite different than that of $F_2$, studies are currently being undertaken to isolate the pharmacologically active constituents in this more water soluble subfraction.

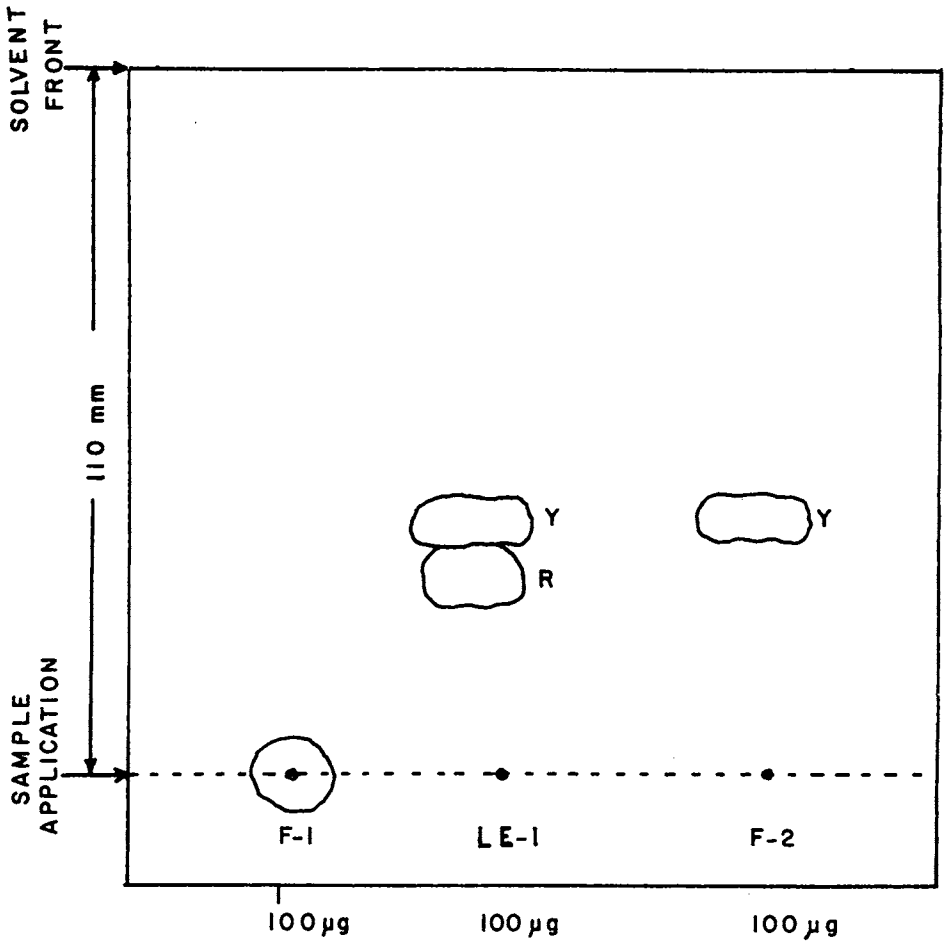


FIG. 3.—Thin layer chromatogram of certain aqueous fractions of Kava (from O'Hara, M. J., Kinnard, W. J., and Buckley, J. P. J. Pharm. Sci. *54*, 1021, (1965).

## REFERENCES


(*1*) SCHUBEL, K., J. Soc. Chem. Ind. 43, 766 (1924).

(*2*) VAN VEEN, A. G., Rec. Trav. Chim. 58, 521 (1939).

(*3*) VAN VEEN, A. G., Tijdschr. Nederland India 78, 1941 (1938).

(*4*) KLOHS, M. W., KELLER, F., WILLIAMS, R. E., TOKES, M. I., and CRONHEIM, G. E., J. Med. Pharm. Chem. 1, 95 (1959).

(*5*) MEYER, H. J., Arch. Int. Pharmacodyn, 116, 45 (1958).

(*6*) KELLER, F. and KLOHS, M. W., Lloydia 26, 1 (1963).

(*7*) FURGIUELE, A. R., KINNARD, W. J., and BUCKLEY, J. P., J. Pharmacol. Exp. Therap. 137, 356 (1962).

(*8*) KINNARD, W. J. and CARR, C. J., J. Pharmacol. Exp. Therap. 121, 354 (1957).

(*9*) WATZMAN, N., BARRY, H., BUCKLEY, J. P., and KINNARD, W. J., J. Pharm, Sci. 53, 1429 (1964).

(*10*) FURGIUELE, A. R., KINNARD, W. J., ACETO, M. D., and BUCKLEY, J. P., J. Pharm. Sci. 54, 247 (1965).

(*11*) O'Hara, M. J., Kinnard, W. J. and Buckley, J. P., J. Pharm. Sci. 54, 1021 (1965).
(*12*) Randall, L. O., Schallek, W., Heise, G. A., Keith, E. F., and Bagdon, R. E., J. Pharmacol. Exp. Therap. 129, 163 (1960).
(*13*) Schallek, W., Kuehn, D., and Jew, N., Ann. N.Y. Acad. Sci. 96, 303 (1962).
(*14*) Miller, C. L. and Tainter, M. L., Proc. Soc. Exp. Biol. Med. 57, 261 (1944).
(*15*) Cook, L. and Weidley, E., Ann. N.Y. Acad. Sci. 66, 740 (1957).
(*16*) Horovitz, Z. P. and Chow, M., J. Pharm. Sci. 52, 198 (1963).
(*17*) Jasper, H. H. and Ajmone-Marsan, C., "A Stereotaxic Atlas of the Diencephalon of the Cat", The National Research Council of Canada (1960).
(*18*) Bleier, R., "The Hypothalmus of the Cat", The Johns Hopkins Press, Baltimore (1961).
(*19*) Burn, J. A., "Practical Pharmacology", Blackwell Scientific Publications, Oxford, England, p. 13 (1952).
(*20*) Bogdanski, D. F., Pletscher, A., Brodie, B. B., and Udenfriend, S., J. Pharmacol. Exp. Therap. 117, 82 (1956).
(*21*) Aprison, M. H., Wolf, M. A., Poulos, G. L., and Folkerth, T. L., J. Neurochem. 9, 575 (1962).
(*22*) Udenfriend, S., Weissbach, H., and Brodie, B. B., "Methods of Biochemical Analyses", D. Glick (ed.), Academic Press, Inc., New York, N.Y. p. 105 (1958).
(*23*) King, F. A. and Meyer, P. M., Science 128, 655 (1958).
(*24*) Dombro, R. S. and Woolley, D. W., Biochem. Pharmacol. 13, 569 (1964).

# Electropharmacological and Behavioral Actions of Kava

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This compound in interesting for its consistencies, and I also want to make a point illustrating a concept of a potential mechanism of tranquilizer action. We first got interested in 1959, because of the descriptions and because of the confirmation of these descriptions by Dr. Franck of the American Medical Association Editorial Staff.

I simply wanted to show you two slides, and I need to show you two older slides for reference. (*Fig. 1*)

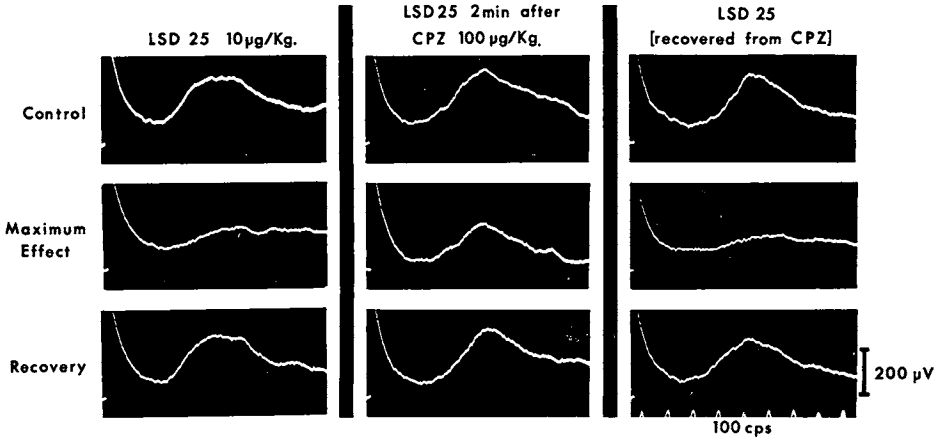


FIG. 1

In the first of these slides showing evoked cortical potentials in a cat, you see that a tranquilizer, in this case chlorpromazine (CPZ), prevents (2nd column) the cerebral synaptic inhibitory effect of LSD (1st column). It controls LSD. After the chlorpromazine has been dissipated, there is recovery (3rd column) and LSD again produces its cerebral action. This is one of the typical actions of a psychotogen, and we think that tranquilizers have a similar but weaker action. The data actually then lend themselves to the notion—and we have further data supporting it—that they have the same kind of action as the psychotogens, illustrated by LSD, but weaker, and therefore are able to compete for the same receptor.

It seemed interesting to see what Kava would do under similar circumstances. A preliminary water extract proved quite potent, and three-tenths of a cc given intracarotidly, elicited an affect very similar to that of LSD. (*Fig. 2*)

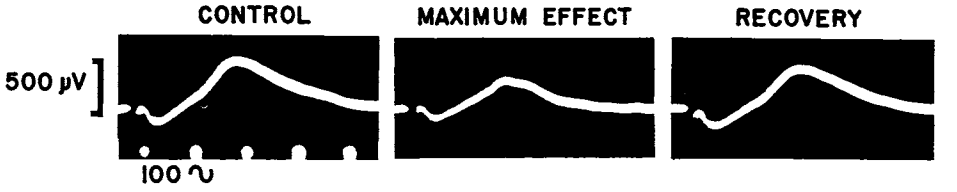


FIG. 2

Obviously we are interested in the relation of an electrical effect in anesthetized animals to the behavior that the nervous system controls. *Fig. 3* is interesting in this connection.

This happens to be a rat conditioned approach experiment, in which the response latency to the signal tone is indicated by the length of the upright lines. The effect of LSD is a prolongation of the response time. This would be expected from the synaptic inhibitory action. Inhibition of inhibition, i.e. disinhibition or a release phenomenon, occurs at smaller doses but is here masked by the over-riding over-all inhibition. I won't go into the chlorpromazine protection at the moment.

This (*Fig. 4*) is the same kind of an experiment with Kava. There is a great prolongation in the response time. The sharp cut-off at the top is simply because the equipment turns off after twenty seconds without a response.

It then seems interesting, in the first place, that this material is quite active, because that amount of synaptic inhibition is the equivalent of forty micrograms of serotonin.

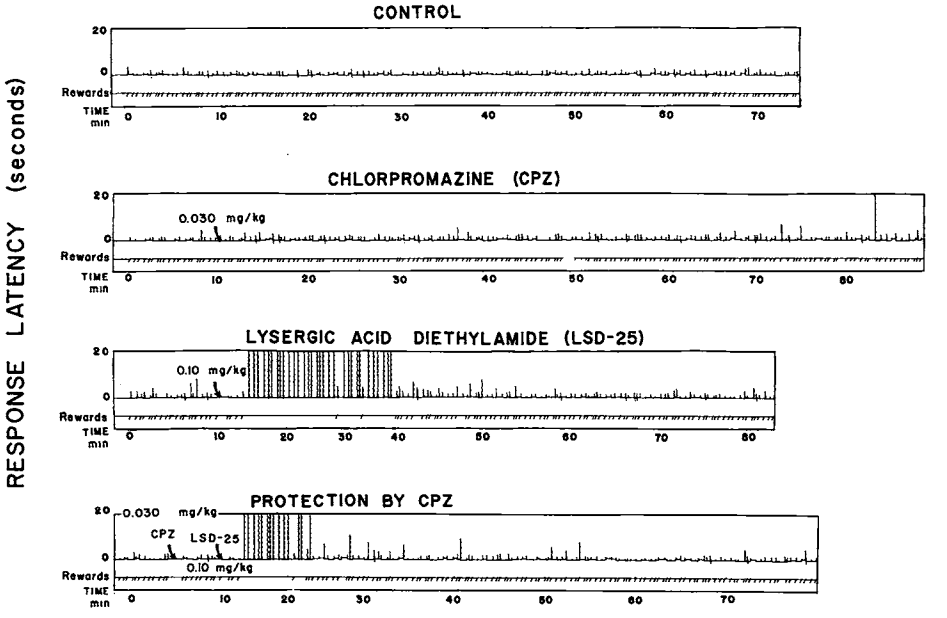


FIG. 3

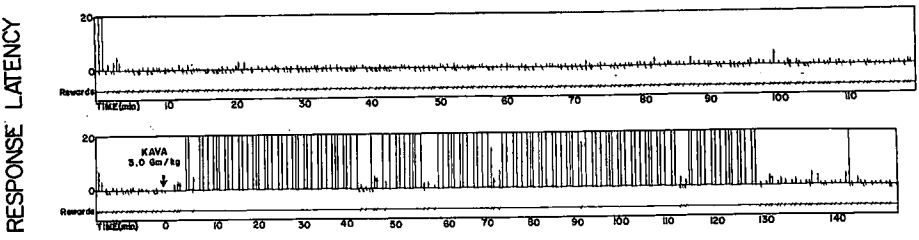


FIG. 4

In the second place, it acts like LSD on synaptic transmission and behaviorally, and you heard rather an extensive follow-up from Dr. Buckley and related data from Dr. Meyer.

The point that I was trying to bring out is the possibility that a tranquilizer is, in fact, a weak psychotogen, and this has very definite implications for the method of looking for new tranquilizers. Thank you.

# Effect of Kava in Normal Subjects and Patients

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Those of you who watched the television news last October saw that the Samoans offered cups of Kava to President and Mrs. Johnson. The New York Times (10–19–65) reported the incident as follows: (*1*)

> Mrs. Lyndon B. Johnson is the first woman ever offered the royal Kava drink, the highest honor Samoan chiefs can bestow on a visitor. She drank it, too.
>
> Samoans who turned out from every corner of the island to welcome the Johnsons yesterday applauded delightedly as the First Lady sipped the bitter juice from a coconut cup. The President only touched his lips to the cup.
>
> Later Mrs. Johnson said the drink tasted a little like the milk of coconuts—watered down—with a slightly medicinal taste.
>
> Drinking the brew, made from the pulverized root of the Kava tree, bound Mrs. Johnson in fellowship with the chiefs. Both she and her husband also made the traditional gesture of pouring a bit of the juice on the ground to get rid of evil spirits.

Subsequently President Johnson, the abstainer, needed two surgical operations while Mrs. Johnson's health has remained excellent! What is in this obviously marvelous brew made from the root of the Kava tree? This conference allows us to review data on Kava gathered in animals and man over the period 1954–1962. The data vary in their accuracy from global clinical impressions to objective double blind studies using quantitative amplitude analysis of the EEG.

In 1954 we made various extracts of the powdered Kava root and obtained brown gums which, while insoluble in water, could be easily suspended in gum tragacanth. The alcohol extracted gum appeared to be the most active in mice, particularly against strychnine convulsions.

One of the active ingredients, dihydrokawain, was compared to mephenesin and found to be effective but very fleeting in its anti-strychnine effect (*2*, *3*) Table 2. The testing in mice was perforce done in the first 30 minutes after oral dosing in order to see the characteristic anti-strychnine effect. The very short acting drug mephenesin had a comparable effect to that of dihydrokawain.

Our interest next turned to the two compounds which the Riker Laboratory Scientists found to be very active in their animal tests (*4*). These were dl-methysticin and dl-ethysticin. The methyl congener occurs in Kava while the ethyl congener was prepared synthetically. Both compounds are optically active so that synthesis provides the racemate while the natural compound is an optically active enantiomer.

We studied in two groups of six normal subjects at the Atlanta Federal Penitentiary both dl-ethysticin and dl-methysticin in single oral doses of

TABLE 1.—*Anticonvulsant effect of Kava Kava in mice*

[All tests at 1 hour after oral dose]

| Compound | Dose/kgm | Metrazol ratio | | Strychnine ratio | |
|---|---|---|---|---|---|
| | | FT | PC | PC | % Surv. |
| Crude Root | 2. 0 gm | *1. 6 | *1. 6 | 2. 1 | 50% |
| Hot Alc Extr. | 150 mg | 1. 4 | 1. 2 | 1. 7 | 28% |
| CH $Cl_3$ Ext. | 150 mg | 1. 2 | 1. 1 | 1. 8 | 35% |
| Alc. Extr. | 150 mg | 1. 5 | 1. 2 | 2. 2 | 32% |
| Control Mice | | 1. 0 | 1. 0 | 1. 0 | 0 |

FT=first twitch.
PC=persistent convulsion.
N=14 mice/group.
*Read 1.6 times the control group of mice.

800 mgm. This dose was chosen because therapeutic trials in epileptics showed some degree of seizure control. No significant changes in blood pressure, pulse rate, grip strength, hand steadiness, or pupil size occurred. The subjective responses were equally divided between stimulant, placebo and sedative reports. We conclude that these two congeners were not sufficiently active to be recognized by our crew of drug sophisticated tasters.

When the crude root was given to 9 selected, uncontrolled epileptics (*5*) in doses up to 6 grams per day a better degree of seizure control was obtained. The same degree of control was provided by an alcoholic extract of the root in a dose of 1.0 gm/day. However, continued therapy for several weeks produced a lemon tinted skin and sclera which was apparently owing to a chemical pigment and is seen characteristically in the Samoans who take Kava regularly. Because of this skin reaction the use of root and extract was discontinued in favor of the study of the pure, more active and uncolored principles of the root.

TABLE 2.—*Anticonvulsant effect of dihydrokawain*

| | Dose | Test time | Metrazol | | Strychnine, P.C. |
|---|---|---|---|---|---|
| | | | F.T. | P.C. | |
| DHDK | 200 | 10″ | | | *1.6 |
| | 400 | 10″ | 1.5 | 1.1 | 2.0 |
| | 400 | 30″ | 1.3 | 1.1 | |
| | 400 | 60″ | 1.1 | 0.9 | 1.1 |
| Meph. | 200 | 10″ | | | 1.2 |
| | 400 | 10″ | | | 2.0 |

Min. Atax. Does=250 mg/kg.
F.T.=first twitch.
P.C.=persistent convulsion.
*Read 1.6 times the control group of mice. 12 mice/group.

Of the available congeners dl-dihydromethysticin is the most active in animals. This compound became available for clinical trial in 1956 as Riker Laboratories #532, and was used in doses up to 1200 mgm/day to control epileptic seizures. The anti-epileptic effect was characterized by fewer grand mal seizures but no change in petit mal seizure activity. However, after one month of continuous therapy some patients showed conjunctival and circumorbital erythema, vomiting and diarrhea. These symptoms were considered to be drug induced so that dl-dihydromethysticin was discontinued.

Saunders and Kline (*6*) treated schizophrenics with this drug using doses of 800 mgm/day. After 3 months, 14 or 15 patients developed typical drug induced skin rashes of the groin and axillae. The reaction disappeared 10 to 20 days after the drug was stopped, but reappeared when the drug was again given to selected patients. The drug had no antipsychotic effect in the schizophrenic patients.

*EEG Studies in Normal Volunteers*

The quantitative EEG technique provides an accurate method to measure CNS stimulation, sedation or sleep. Quantitation of the EEG was performed with an electronic integrator. This device, the operation of which has been fully described elsewhere (*7*), transforms the complex EEG signals into pulses inscribed directly and concomitantly with the direct tracings. The number of pulses, for any given time period, is directly proportional to the cumulated electrical energy. Calibration is by the application of known energy constants. The values obtained therefore can be related to fixed standards. The basic time-unit chosen for data analysis was 20 seconds, that is, 2 pages of standard EEG recording. Thus any 10-minute recording run yielded 30 successive measurements.

All the corresponding values from each predrug and postdrug run, as obtained from all the subjects involved in each particular study, were averaged, and mean energy contents (MEC) for the group were thus determined. The statistical significance of the changes was ascertained with the t-test.

Besides these measurements of the level of electrical energy, a careful analysis of variability was performed for each time period. We find that this parameter of quantitated EEG data is highly informative, not only for the detection and characterization of drug effects, but also for baseline features. For example, we have found that male schizophrenic patients have much less EEG variability than nonpsychotics. In the Tables, the values of the standard deviation are computed from the "between subjects, within drug" covariance values. Statistical significance of the differences in variability was based on F-ratios. For convenience, the covariance levels are expressed as the coefficient of variation (CV). Table 3 summarizes our objective findings using this technique.

The subjective reaction of these normal subjects was that the Kava principles produced mild sedation or sleepiness. This would be in accord with the quantitative EEG findings of the most effective congener, namely

TABLE 3.—*Quantitative electroencephalographic studies in normal volunteers given Kava type chemicals*

| Drug | Oral dose, mgm | N | | C | Hours following admin. 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|---|---|
| Dihydrokawain | 200 | 5 | MEC | 100 | 105 | 101 | 99 | 112 | 117 | 114 |
| | | | CV | 20 | 20 | 22 | 20 | 19 | 19 | 16 |
| dl-dihydromethysticin | 160 | 10 | MEC | 100 | 99 | 103 | 110 | 104 | 101 | 105 |
| | | | CV | 20 | 27 | 31 | 30 | 17 | 23 | 25 |
| d-dihydromethysticin | 160 | 10 | MEC | 100 | 108 | 108 | 108 | 103 | 106 | 101 |
| | | | CV | 21 | 26 | 26 | 28 | *39 | *40 | *51 |
| Placebo | | 11 | MEC | 100 | 100 | 107 | 102 | 110 | 102 | 94 |
| | | | CV | 20 | 20 | 19 | 19 | 20 | 20 | 20 |
| Meprobamate | 800 | 10 | MEC | 100 | 96 | *71 | *77 | 88 | 89 | 107 |
| | | | CV | 19 | *29 | *32 | *38 | *46 | *56 | *39 |

*Significant at the 1 in 20 level of confidence.

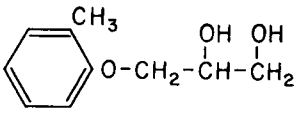
160 mgm of d-dihydromethysticin. This is evident in the increase in the coefficient of variation at the 4, 5 and 6th hours after the oral dose.

Computer analysis of the EEG after 160 mg of dl-dihydromethysticin revealed that there were significant increases in total electrical energy without significant increases in variability. These increases affected all frequencies and were maximal two to three hours after dosage. The increases were more evident in low-alpha records. When very prominent alpha was present, little or no change occurred in total energy or in energy in the alpha band, but significant increases occurred in the low frequency portion of the electroencephalographic spectrum, again without any significant change in variability.

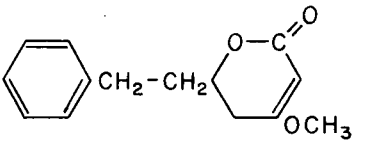
## Discussion

We have found that dihydrokawain is very similar to mephenesin in its effect on the strychnine thresholds of mice. Meyer (*8*) and Meyer and Kretzschmar (*9*) find a close similarity in the pharmacological action of the Kavapyrones and mephenesin when tested on the reflexes of guinea pigs. The chemical structures are similar in that both can be described as blocking compounds of simple oxygen functions.

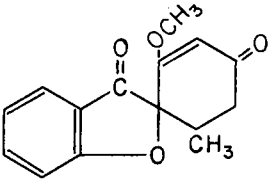
If more were known about the physiological deposition of the Kava-pyrones a second analogy might be made to the diketone *griseofulvin* which is also a mild CNS sedative, and is known to exert its antifungal effect by deposition in the skin, hair, and nails. This fungicide however is well tolerated by the human skin while the Kava-pyrones are not. If Samoan groups can be found who imbibe Kava only during a ceremonial week one would expect to find some degree of yellow banding of their finger and toe nails if the Kava-pyrones are deposited in keratin.



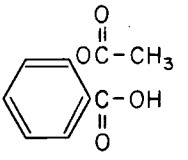
*Mephenesin*



*Dihydrokawain*



*Griseofulvin*



*Aspirin*

FIG. 1.—The Kava ketopyrones are blocking compounds of three oxygen and a methyl functional groups. Other molecules which have a similar sedative effect are griseofulvin and aspirin.

Perhaps the simplest chemical which is a blocking compound containing 3 oxygens and a methyl functional group is aspirin. This has not been studied in animals for its central relaxant action. Quite independently of the Kava study we have determined recently the effect of aspirin and other mild analgesics on the quantitative EEG of man. Aspirin is the only small analgesic which has a typical sedative or antianxiety effect on the human brain. One wonders then if aspirin is not a mild type of Kava which has been developed in modern society and used without ceremony by the tons (as long as the recommended dose on the label does not exceed two tablets).

TABLE 4.—*Comparison of meprobamate and buffered aspirin by the quantitative EEG technique*

| Drug | Mgm dose | N | | C | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|---|---|---|
| Meprobamate | 800 | 10 | MEC | 100 | 96 | *71 | *77 | 88 | 89 | 107 |
| | | | CV | 19 | *29 | *32 | *38 | *46 | *56 | *39 |
| Placebo | | 30 | MEC | 100 | 101 | 100 | 101 | 102 | 103 | 104 |
| | | | CV | 19 | 20 | 17 | 17 | 26 | 18 | 19 |
| Buffered asprin | 1000 | 20 | MEC | 100 | 90 | *83 | *75 | *85 | *85 | *83 |
| | | | CV | 26 | *37 | *40 | *42 | *39 | *40 | *34 |

*Significant at the 1 in 20 level of confidence.

Conversely one might ask if the Samoans use Kava as a "pain-killer". I have been told that the plains Indians have in times past used peyote as a pain killing drug.

We have heard the chemists describe the active Kava-pyrones which can be found in the Kava plant. We have studied one minor synthetic modification of a Kava principle, namely Ethysticin. We have not had reported today any serious attempt to synthesize more complex Kava pyrones with more adequate blocking groups. Thus in dihydrokawain the synthesis of a methylene bis compound would be of interest, as also would be a benzohydryl kawain. One should keep in mind that as the molecule becomes larger and more effective as a blocking moiety, the structure and perhaps the pharmacological effect will approach that of dihydrocannabinol another oxygen-containing molecule. Also the main physical characteristic of these Kava principles, that of poor water solubility and good lipid solubility, will always result in a preponderance of pharmacological action on the brain and skin i.e. ectodermal tissues. This selectivity should be put to good use in the transport of a properly tailored and more active molecule.

Finally the study of the Samoans and their Kava ceremony remains the best and possibly the last area of scientific interest insofar as the intoxicating effect of Kava is concerned.

## Summary

We have studied in animals and man various extracts, extracted chemicals and congeners of piper methysticum (Kava Kava). The main pharmacological action is like that of central relaxants of the mephenesin-type as shown by a specific antagonism to strychnine infusion. Compared to modern synthetic central relaxants all of the Kava congeners are relatively inactive. The most active congener appears to be dihydromethysticin, but this compound when given to man in the dosage range of 800 to 1200 mgm daily produces side effects and allergic skin reactions. The crude root and extract produces a yellowing of the skin similar to that reported in the Kava drinkers of Samoa. From the data now available, further study of Kava as a modern medicinal agent would not appear to be needed.

### REFERENCES

(*1*) New York Times October 19, 1966.

(*2*) Orloff, M. J., Williams, H. L. and Pfeiffer, C. C. Proc. Soc. Exp. Biol. 70: 25 257 (1949). Timed Intravenous Infusion of Metrazol and Strychnine for testing anticonvulsant drugs.

(*3*) Jenney, E. H. and C. C. Pfeiffer. Annals N.Y. Acad. Sci., 64: 679–89 (1956). The Predictable Value of Anticonvulsant Indices.

(*4*) Keller, F. and Klohs, M. W. Lloydia 26: 1–15 (1963). A Review of the Chemistry and Pharmacology of the Constituents of Piper Methysticum.

(*5*) Pfeiffer, C. C. Unpublished data this laboratory.

(*6*) Cronheim, G. Report of N. Kline to Riker Labs.

(*7*) Pfeiffer, C. C., Goldstein, L., Murphree, H. B. and Jenney, E. H. Arch. Gen. Psych. 10: 446–453 (1964). Electroencephalographic Assay of Anti-Anxiety Drugs.

(8) MEYER, H. J. Arch. int. Pharmacodyn. 150: 118–131 (1964). Untersochungen Uber Den Antikonvulsiven Wirkungstyp Der Kawa-Pyrone Dihydromethysticin Mit Hilfe Chemisch Induzierter Krampfe.

(9) MEYER, H. J. and KRETZSCHMAR. Klin. Woch. 44/15, 902–903, 1966. Kawa-Pyrone eine nenartige substansgruppe zentraler Muskelrelaxantien vom Typ des Mephenesins.

# Ethnographical Aspects of Kava

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The Polynesian term *kava* is generally used in English to specify the shrub *Piper methysticum* (Forster), its root, and a beverage made from it. With slight variation, this is the term used in western Polynesia, including Tonga. In Samoa the form is *'ava*, in Tahiti *ava*. In Hawaii it is *awa*. The Maori took with them to New Zealand tales concerning the use of kava but did not find the plant in their new home. They found another plant, *Piper excelsum*, which they did not make into a beverage, but which they named *kawakawa*. The term kava or its equivalent in Polynesia is also an adjective designating various properties of food and drink. In Hawaii it means bitter, sour, sharp, pungent. In the Marquesas it signifies bitter, sour, sharp. In Tahiti the range is broad, including bitter, sour, acid, acrid, salt, sharp, and pungent (Churchill p. 56).

The use of *Piper methysticum* is not confined to Polynesia. In Micronesia it is found in the Caroline Islands. It is found in many places in eastern Melanesia: in New Britain, New Ireland, the Admiralties, the Banks and Torres Islands, the New Hebrides, and in Fiji. In Melanesia its use is of spotty distribution. In some instances islands only a few miles apart differ from one another in regard to the use of kava. For example the people of Ambrym in the New Hebrides look down upon their neighbors on Pentecost Island, only seven miles away, because they drink the beverage. Sometimes, as in the case of Tikopia (a Polynesian outlyer in Melanesia), betel chewing and kava are found together. On Tikopia, interestingly enough, the beverage is not drunk but is poured on the ground as a libation to the gods.

Since our personal experience with kava and its uses is for the most part confined to Fiji and Tonga, the remainder of this discussion will relate to those islands. My wife and I have visited most of the major islands in Tonga, the islands of central and southern Lau, the Yasawas, Kandavu, Taveuni, Ovalau, and a number of villages on Viti Levu and on Vanua Levu. In practically all of these places we have participated in kava ceremonies of one sort or another, and I must admit that this has been an enjoyable experience.

The Fijian term for the plant, the root, and the beverage made from it is *Yaqona*. This term is apparently without parallel outside the archipelago, in either Melanesia or Polynesia. The word does not appear to be used in an adjectival form. Lester, however, reports that a word *Qona* is used on the northwest coast of Viti Levu to denote both "beverage" and "bitter." He suggests that this may indicate that it was to this part of Fiji that kava was first brought and that these were the people who supplied the name Yaqona, which is now universally used throughout the archipelago. More commonly in Fiji "bitter" is *gaga*, which also means "*poisonous*."

Our first introduction to kava was on the island of Naviti in the Yasawas off the northwest coast of Viti Levu. We had been taken there by a small copra vessel and dropped off on the reef in the early hours of the morning. We were met by a number of Fijians who carried us and our luggage ashore and who escorted us to the house of Roko, Ratu Filimone Kama, in the village of Kese.

It was, for us, an awkward situation. The Fijians on the island of Naviti had an English vocabulary of scarcely more than "quite," "rather," and "hello," and our Fijian was nil. We were in age approximately twenty-five and quite unaccustomed to the South Pacific. Of course we had read a good bit about the Fiji Islands and the indigenous customs, including kava drinking. We had, for example, been able to read about kava in the *Encyclopaedia Britannica*—you can still read it there—and I quote:

KAVA . . . an intoxicating, but non alcoholic beverage, produced principally in the islands of the south Pacific, from the roots of leaves of a variety of the pepper plant (*Piper latifolium* or *P. methysticum*). The preparation is peculiar. The roots or leaves are first chewed by young girls or boys, care being taken that only those possessing sound teeth and excellent general health shall take part in this operation. The chewed material is then placed in a bowl, and water or coco-nut milk is poured over it, the whole is well stirred, and subsequently the woody matter is removed by an ingenious but simple mechanical manipulation. The resulting liquid, which has a muddy or *café-au-lait* appearance or is of a greenish hue if made from leaves, is now ready for consumption. The taste of the liquid is at first sweet, and then pungent and acrid. The usual dose corresponds to about two mouthfuls of the root. Intoxication (but this apparently only applies to those not inured to the use of the liquor) follows in about 20 minutes. The drunkenness produced by kava is of a melancholy, silent and drowsy character. Excessive drinking is said to lead to skin and other diseases, but *per contra* many medicinal virtues are ascribed to the preparation. . . . [Anonymous].

We also had read various colorful reports about kava and its use written by earlier visitors to Fiji, as in the following examples:

In their devotion they have a kind of sacrament, using the root called on the Sandwich islands *ava*, but *angooner* in this country. In the first place they wash the root clean, and then chew it, and put it into a large plantain leaf, which is as big as a small tea table, which they lay in a hole in the ground, and then pour a small quantity of water to it, and rinse the substance out. This liquor the Rombetty serves out in small plantain leaves to his people, and as each one receives it, they all clap their hands and say *mannor angooner*, which is returning thanks to God in their way. After partaking of this they think they are happy, its effect being similar to that of laudanum [Patterson p. 90].

The great token of hospitality, when one enters a native house, and especially that of a chief, is the preparing and presenting to the guests the native drink, called kava, an article never lacking in tipling Fiji, as we were often convinced, to our sorrow. So we are not surprised that Patioli should call for kava the moment the conversation waned. In Samoa it is considered very rude to refuse to drink the beverage, but that is a punishment we can hardly inflict upon ourselves; so we will allow some pressing engagement to call us away. . . . Kava has medicinal qualities of not a little power. Drunk to excess, it acts like opium, and the habit once formed cannot easily be broken. There are white men, on some of the islands in the South Seas, who live almost entirely upon the baleful preparation. To them it is as much a necessity as is the morning dram to an inebriate in other lands. To the inexperienced, the very thought of drinking the stuff is repelling, but if he can summon courage to try it, he will find a cup of it refreshing and somewhat nutritive. The natives very justly attribute some of their ailments to an inordinate use of

it. The habitual kava drinker may be recognized by his fishy-looking eyes and the scaly appearance of his skin [Adams pp. 117–20].

I had tasted it on several occasions, this *kava* of the other islands, without enjoyment. But I recalled a warning from several old-timers I had met that one could not more grievously offend a Fijian than by refusing this beverage, whose serving is everywhere such a ceremonial, prescribed by such rigid custom. . . . "Will this go to my head?" I asked Sakobi, remembering the waiting boat.

"No. No go to head," he assured me. And *kava*, as a matter of fact, is not an alcoholic intoxicant. Rather it might be described as a mildly stimulating drug. A brownish murky fluid, slightly pungent and acrid, it is usually obnoxious to the novice, but Europeans in the islands often acquire a taste for it, and business men frequently keep it in the office for an occasional swig with their customers. Its constant and immoderate use over a long period of years is sometimes injurious to the eyes, so that old *kava*-topers often become nearly blind, but taken moderately or even in large quantity from time to time it is of acknowledged medicinal value, to such extent that the most zealous missionaries do not combat the native custom. And, not being an intoxicant, it does *not* go to one's head; one can drink any amount of it and remain clear minded. The funny thing about it, however, is that it *does* go to one's legs. Sakobi, answering my query literally, had neglected to tell me this. But I discovered it for myself when, bidding my hosts adieu at midnight, I felt my knees wobble and slid like a fireman down the slippery pole that led across the moat. At the moment, I attributed the mishap to the stiffness resultant from sitting cross-legged all evening in an unaccustomed posture. But when we started out across the maze of roads and tracks toward the wharf, where the skipper was conscientiously sounding the promised fog-horn as a summons to hasten, there was no question but that something was wrong with the legs themselves.

"Come here, Sakobi. Give me a hand."

He locked his arm through mine. But *his* legs were just as bad. For a quarter-mile we made progress, leaning against each other as our feet gravitated toward the center. Then, despite all efforts at control, his started for the left and mine for the right, and we both sat down heavily [Foster pp. 238–40].

These and many of the other early missionary and travel reports were equally disturbing, and it was with no little apprehension that we sat in the Roko's hut while the Yaqona was being prepared for our welcome reception. To our relief, the root had been pulverized with a mortar and pestle rather than chewed. But there were other sources of concern. We had been schooled to beware of water unless it had been boiled. And here was a stalwart Fijian plunging his brown hands and wrists into a wooden bowl to knead the mixture while another poured water over the powdered root. What risks were we taking: drunkenness, disease, polluted water, unclean hands? The boat had left, not to return for six months, and there was no other way off the island, not even by outrigger. And the only medical assistance on the island was said to be a Fijian "doctor" with one year's training in first aid. To drink or not to drink was the question.

We had been told by Europeans in Suva that it was imperative that we accept what we were offered, including kava, when we were in a Fijian village. Furthermore, we had been told that the brew was not as bad as it was made out to be and that the best thing to do was to drink it down rapidly—that if we sipped it we would be lost and never finish the cupful, which would be really bad mannered of us. So when the cupbearer, glistening with coconut oil, brought a cupful to me and then to my wife we downed it without hesitation. To me it tasted like the smell of a cedar lead pencil

when it is sharpened, and aside from a slight numbing sensation at the base of the tongue and in the throat, there was nothing out of the ordinary about the experience. In fact when we struck lights to our cigarettes after having had our first taste of kava, they seemed to be especially satisfying.

During the year that we spent in Fiji on that field trip in 1935–36 we drank a great deal of kava, probably as much if not more than many of the Fijians. We became quite fond of it and never experienced, insofar as we could detect, any of the ill effects attributed to the drink. Nor did we ever, during that trip or subsequent shorter trips to the islands of the South Pacific, see a native "drunk" from kava drinking. Exhausted, yes. Some of the all-night three- and four-day-long festivities that we attended could not fail to wear people out, but I am convinced that the kava did little to cause what could more accurately be described as a state of being "punch-drunk" with fatigue.

Apparently the early inhabitants of Fiji brought the kava plant with them from Indonesia. From Fiji it was probably introduced somewhat later to Tonga and to Samoa. In Fiji, as far as can be determined it appears that the root was originally grated on mushroom coral or pounded with stones before it was mixed with water to prepare the beverage. The practice of chewing (*mama*) the root seems to have been introduced to Fiji by Tongans or Samoans, although there is a possibility that it may have come to them from other parts of Melanesia. The custom of chewing kava was observed by early travelers and missionaries in the eastern islands of Lau and in the coastal settlements on Viti Levu. Young men chewed the root and deposited it in a bowl to form the basis of the kava mixture. But chewing the root was never practiced in much of the interior of Viti Levu or Vanua Levu. The church and the government discouraged the practice, and today the root is either brayed between two stones or pulverized in a wooden mortar with a pestle. An oft-repeated story justifying the discouragement of chewing kava as a method of preparation relates that in the 1870s a Dr. Macgregor weighed six ounces of the root, which was then chewed in the usual manner. When deposited in the bowl it weighed seventeen ounces (Gordon-Cumming p. 51).

There is some evidence to indicate that the beverage was at one time prepared in an earthen pit lined with leaves, constructed much like an earth oven. The development of pottery in Fiji took place quite early, however, and pottery bowls took precedence and were used in many parts of the islands for kava mixing. Very crude wooden bowls resembling the pottery ones were used elsewhere. At least four to five hundred years ago the modern wooden bowls came into general use and for the most part replaced the pottery bowls. As far as is known, these wooden bowls were made only on Kambara in Lau, and were thence disseminated to the rest of Fiji and to Tonga. Whether the design for the bowl originated in Kambara or was introduced there from Samoa and/or Tonga is not known, but since the term by which the bowl is known in Fiji, *tanoa*, is a Polynesian word, it seems likely that the bowls are of Polynesian origin. In any case, the tanoa has been in use throughout most of Fiji for the past few centuries.

The kava bowl varies in size and shape, but it is generally round, from one to three feet in diameter, and with four legs (occasionally more) all made from one piece of wood, vesi (*Afzelia bijuga*). The front of the bowl has a triangular suspension lug with two holes, to which sennit braid is attached to provide a means of hanging the bowl on the wall. Today all chiefly kava bowls have white cowrie shells attached to the end of the cord. The lug and its attached braid are important parts of the kava bowl and play a major role in the kava ceremonial, as will be described below. The tanoa is never used for any other purpose than that of mixing kava, and after a long period of use its interior surface collects a blue-green patina.

The most usual cups for serving kava are the pointed halves of coconut shells, scraped thin and highly polished. Most cups are about two inches in diameter, but some are much larger. We have one that was presented to me which measures six inches across and holds well over two cupfuls of liquid. It is very old and, like the older kava bowls, it has an interior patina.

When the time comes for the kava to be mixed, the pounded or grated root is placed in the bowl. To this is added water, which is kneaded together with the powdered root. More water is added and the mixing progresses. A strainer of *vau* (hibiscus fiber) is used at the end of the mixing to strain out the woody particles from the drink. As the strainer collects fibers, it is wrung out and taken out of the bowl so that the particles can be shaken out. This process is repeated several times until the liquid is relatively clear. If the mixture appears to be too concentrated, more water is added. Then the kava is ready for serving.

It is believed that the kava ceremony in Fiji was formerly a predominately religious rite, carried out by priests. The purpose was to establish communion with the supernatural. Through the kava ceremony the priests were believed to reach the gods and ensure their assistance in life here and hereafter. Rivalry existed between these religious leaders and the political leaders. As the latter grew in strength by virtue of consolidating more and more territory under their control, they ousted the priestly class from their position of power. Coincidentally, the missionaries came in to take over the all-important function of cementing the relationship between the people and the supernatural. The political leaders took over the kava ceremony, and from that time on it has been more socio-political than religious, though much of the ritual can be traced back to usages in the past that were strictly religious in character. This change in emphasis apparently occurred early in the eighteenth century, and the formal kava ceremony has remained much the same ever since.

In placing the current kava ceremony in perspective it is important to note that Fijian and Tongan society was and still is highly conscious of differences in rank or status. Persons are arranged according to inheritance in a hierarchy from kings to high chiefs, to lesser chiefs, and to commoners. One of the major functions of the kava ceremony is clearly to reaffirm (or establish) status. When visiting dignitaries arrive, this is the means by which strangers are accorded their position in the village or district to which they have come. Among a people whose inter-island and inter-district relationships

were more often than not of a warlike nature, this was a respected medium through which rapport could be established, at least a temporary truce declared, and a modicum of trade relations ensured.

Formal kava ceremonies, *yaqona vakaturaga*, are imbedded in a large complex of activities. Much has to be done in preparation, for many days in advance. When the participants have gathered and are properly seated, the ceremony begins with the formal presentation of offerings: kava roots, whales' teeth,[1] tobacco, food, and articles such as pandanus mats and tapa cloth. Then comes the kava mixing and drinking. After this solemnity there may be dances and songs. In any case there follows, perhaps an hour or two later, the distribution of the feast foods and all those assembled proceed to eat.

The seating of the participants during the presentation of offerings and the kava ceremony is most important. The kava bowl is located in the middle of the meeting place. Behind it is seated the kava mixer. At his side, both to the right and the left are what might be termed helpers. Behind the kava mixer and the bowl are seated a number of men who will form the chorus for the chanting which accompanies various parts of the ritual. The *wa ni tanoa*, the sennit braid with its white cowries, is stretched out directly away from the mixer pointing toward the most important personage present, the chief of the district or a visiting dignitary. The first cup of kava will be presented to him. To his left and slightly forward sits his talking chief. To his right sit a selected number of lesser chiefs, all slightly forward toward the bowl.

The significance in Tonga of the suspensary lug and its cord has been vividly described by Sir Peter Buck, himself part Polynesian (Maori):

> The following incident illustrates the method of indirection dearly loved by the Polynesians. After the death of the last Tui Tonga, two of the greatest supporting chiefs of the Tui Tonga dynasty came to George Tubou, who had been gathering the reins of temporal power into his hands, and informed him that they wished to make kava for him. They conducted him into the guest house and, seating themselves behind the kava bowl, proceeded to prepare the kava. George Tubou sat down opposite and waited. He looked casually across at his companions and saw what must have been a soul-stirring sight. The suspensory lug of the bowl was pointing at him. The chiefs had not spoken, but the speechless bowl was announcing a king [Buck p. 299].

The precise seating arrangement and the form of the ceremonial differs slightly from one island and district to another, and there is no need to describe these in detail here.

However, it may be useful to attempt a generalized description so that some picture of such an occasion is before us. Imagine then, the chiefs sitting

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[1] The *tabua*, or whale's tooth, is the ceremonial currency of Fiji. Holes are bored in each end of the tooth, to which is attached a cord of sennit braid or pandanus. A proper cord is made of four-ply braid, known as *sui ni gata* or "bones of the snake." Interestingly enough, the tabua is not just a whale's tooth; it must be old, oiled and polished, and it must have an acceptable cord. What was employed in its place before whales' teeth were available is not known. Stones shaped much like whales' teeth have been found dating back to early times. Wooden tabuas have been known to be used. A suggestion has been made that originally the human collar bone was used. Be this as it may, for many generations the tabua has been the most important possession of any Fijian, and generally speaking they are predominantly in the custody of high ranking chieftains. With the presentation of a tabua at a proper kava ceremony, one may obtain from a chief almost anything one is desirous of having.

facing the bowl and the proceedings about to begin. The occasion is that of a visiting chief from another village. All of the actual participants are in colorful costume: some with yellow pandanus kilts, some with green leaf *sulus*, some garbed with colorful tapa, the native bark cloth. All are glistening with coconut oil.

On both sides, at a short distance away from the circle of those participating, may be several hundred men, women, and children—observers only. Suddenly there is a hush of voices, and then complete silence. From this point on none of the participants, seated cross-legged in fixed position, will make any movement that is not a part of the prescribed ritual. There is no talking, no smoking, no uncrossing of the legs, no extraneous movements of the arms or head. All attention is focused on those who are performing their roles in accordance with traditional rules.

The visiting chief moves into the center of the circle, crawling on his knees. He carries with him in his hands the root of the kava plant, or perhaps a tabua. Now comes the presentation: *ai sevu sevu.* With cupped hands he claps three times and addresses the host chief. He says then in effect "here is a small offering . . . " The host's talking chief, or master of ceremonies and the chief himself interrupt to say "a great thing, a great thing," and an interchange of deprecatory remarks on the part of the visitor followed by complimentary comments by the host continues for a short time. Finally the master of ceremonies says "let it be presented." At this point the participants clap their hands in unison.

The master of ceremonies, with his hands lightly resting on the offering, announces in stylized form the acceptance. This concluded, the kava mixer tilts the bowl toward the host chief, to show him that the powdered root is ready. In response, the master of ceremonies says "*lomba*" which means "proceed to mix." An attendant pours water in the bowl and the kneading process takes place. After several minutes the kava mixer holds the strainer above the bowl, allowing some of the beverage to pour into it. If the master of ceremonies thinks the drink is too strong he calls out in effect "More water!" Water is added and the procedure repeated until the master of ceremonies, satisfied, says "Enough water, strain it." At this point the men behind the bowl begin to chant, and this will continue until the kava is served to the chief.

When the kava maker considers the beverage properly strained he strikes a pose with hands together and, looking into the bowl, murmurs that "the kava is ready to be served." Hearing this, the master of ceremonies says loudly "*Cobo*—i.e. Clap," whereupon the kava mixer and his attendants, one on either side of him, clap with cupped hands three times. The cupbearer, whose face is usually blackened and whose arms and legs bear circlets of leaves, appears at the bowl. The kava mixer lifts his strainer and allows the beverage to trickle into the cup which the cupbearer holds out for him. In time with the chanting the cupbearer, now partly upright with knees bent, sways and moves forward in graceful movements until he is quite near the chief. At this point the chanting stops. The cupbearer crouches down low, holding his cupful of kava in both hands with arms outstretched toward the

chief. The master of ceremonies says "Go ahead, rise up" and the cupbearer stands up and walks to the chief, to whom he gives the cup of kava. The chief now drinks the kava. As soon as the master of ceremonies sees that the chief has finished drinking (in some instances the chief may spin the empty bowl in the center of the mat) he signals again for the participants to clap three times.

The master of ceremonies receives a cup of kava from the cupbearer, and perhaps the visiting chief and his talking chief. This ends the formal part of the ceremony, and this is announced by the master of ceremonies who proclaims that the "chiefly kava is dry." The *wa ni tanoa* is pulled back out of sight. The kava mixer and his attendants clap three times. From then on the formalities are slackened. It is now permissible to talk and to smoke while the other chiefs are being served their kava. This may last from one half hour to more than two hours, until the bowl is emptied. Never is a kava bowl left containing unused beverage. Following this comes the division of feast foods and then the feast itself.

Good descriptive accounts much more elaborate than the sketch provided above are available in the literature (cf. Hocart, Lester, and Mariner). The important things to note here are, first, that throughout the entire proceeding the arrangement of participants and their behavior, including the chanting and the movements of the cupbearer who serves the kava, are rigidly prescribed by custom and, second, that the occasion is a very solemn affair. In the not-too-distant past, the entire village was compelled to be silent while kava was being prepared in formal fashion, and if anyone, even a child, made any noticeable noise, he was clubbed. We have a recording of a formal kava ceremony held at Naviti in the Yasawas in 1960 that was performed especially for the purpose of getting it on record. The tape recorded the ceremony clearly, and despite the fact that there was an audience of more than two hundred men, women, and children, no noise extraneous to the performance is to be heard except for the occasional cackling and crowing of the native fowl.

Apart from the Yaqona *vakaturaga*, the formal kava ceremony with which we have been concerned, kava drinking takes place in Fiji quite informally. It is frequently drunk in casual fashion by all inhabitants, including Europeans. Children do not drink kava, and at what age they begin to participate is difficult to determine. In native schools they are taught the ceremonial, using plain water as a substitute for kava and wooden tabuas. In Suva, kava is available in most stores and shops for the customer who wishes a cup. A large bowl of kava is always available at the Tourist Bureau, where, to please American tourists, there is usually a lump of ice floating in the drink to keep it cool—to my taste, definitely not an improvement. Among the Fijians, kava seems to be holding its own against the importation of alcoholic beverages and soft drinks. An interesting story concerning Ratu Sekuna relates that upon going to Oxford for his LL.D., he was concerned that he would not find kava there. So he had many bowls prepared, placed them in the sun, and took with him to Oxford the residue,

"instant kava," which he could then simply mix with water when he desired.

It is clear that after one gets used to its peculiar odor and flavor, kava does provide a pleasurable sensation. Added to this fact is the long tradition of kava drinking as a part of a large and important complex of activities, including gift exchange, chanting, dancing, and feasting. Drinking kava is considered appropriate to a wide variety of occasions, from birth through marriage and death. It is the only chiefly way to welcome an important visitor. Sharing a bowl of kava tends to foster socializing and friendship, and to the Fijian it is unthinkable that kava should not be a part of commemorating any important event. Kava is never, to my knowledge, drunk alone. The practice is solidly imbedded in social and political context.

The complex of the customs surrounding kava, which has been briefly described above, is unique to those islands in the South Pacific where it has been traditional for generations. It is impossible to find precise parallels in other parts of the world. On the other hand, if one concentrates upon one particular aspect of the complex at a time, it is possible to examine somewhat similar phenomena for comparative purposes. It is important to remember, however, that such parallels as may exist in other parts of the world rarely imply any direct historical connection.

If one singles out the practice of chewing the root as a method of preparing the beverage, which was widely practiced in western Polynesia, one can find many parallels elsewhere. Throughout southern Asia there are customs of premasticating rice or other grains to produce fermented drinks or wines. South American *chicha*, a fermented drink, is prepared in similar fashion from premasticated maize or sweet cassava. Despite the similarity between the preparation of these fermented drinks and the method of preparing kava in some parts of the South Pacific, there seems to be little justification for going further than to point out that premastication has its uses as a means of producing chemical changes in the substances chewed. And the premastication of food by mothers to feed their infants is such a universal custom that the probability of independent inventions using this method for the preparation of beverages is extremely high. There certainly does not appear to be any support for the notion, implied by Ling Shun-sheng (pp. 84–86), for example, that there is a specific historical connection between the practice of premasticating grains for fermented beverages in Asia and in South America and the chewing of kava in the South Pacific.

If one concentrates on kava itself, no direct equivalent is available. But a related plant, *Piper betel*, is used throughout a wide area to the west of the kava drinkers, including western Melanesia, Indonesia, Formosa, and much of Asia. In these areas, people chew a mixture of betel leaf or seed together with lime and the nut of the areca or other palm tree. The effects of chewing this mixture are said to be much like drinking kava, only more so. Betel chewing has its social connotations, and in many places, sharing the betel mixture, either before or after mastication, plays an important

role in establishing friendships, in courtship, and in marriage. But there the resemblance to the kava complex comes to an end.

As to other aspects of the kava ceremonial and its associated practices, there are many parallels elsewhere and many of these it might be interesting to examine, but it does not seem appropriate to do so here. For example, the attention paid to the precise seating arrangements has much in common with formalized gatherings in most societies that are conscious of status differences, including official dinners in Washingon, D.C. The sharing of food and drink as a means of declaring a temporary truce or ensuring protection through the establishment of a mutual bond has many parallels, extending from "breaking bread" to the establishment of "blood brotherhood." In its religious aspects, some of the rituals associated with kava drinking have parallels that come readily to mind, including certain aspects of Christian ritual.

Although certain aspects of the complex may be related functionally to practices in other parts of the world, it is clear that the kava ceremony and its associated practices as known in the South Pacific have become an institution which is unique in the part it plays in the life of the people.

There still remains the basic question: To what can the all-pervasive role of kava be attributed? Is it due to the physiological effects of the beverage itself? Are these so powerful that they in a sense demand recognition and that from this flows the development of the involved social, political, and ceremonial practices which surround its usage? Are the accounts of early travelers and missionaries to be trusted? If so, how is their evidence to be reconciled with our experiences?

It has been suggested that the accounts of the effects of drinking kava are simply erroneous fabrications by the early missionaries, which have been perpetuated throughout the decades (Churchill pp. 57–59). In this connection it is interesting to note that some of the early descriptive phrases continue to be repeated verbatim in later accounts, usually without any reference to an earlier source. At the same time, it is difficult to dismiss without consideration personal experiences reported by a trained observer, such as that related by Hocart (p. 59), who writes:

> The intoxication caused by kava is called *mateni*, meaning death from or illness from. The expression *mate ni yanggona* is also used. To recover is *mbula* (to live). This intoxication dulls the countenance. As I experienced it, it gives a pleasant, warm, and cheerful, but lazy feeling, sociable, though not hilarious or loquacious; the reason is not obscured. In time a certain dullness settles on the company, in which the kava and the late hour probably both have a part. Once after heavy drinking I felt miserable and found it difficult to walk straight; on turning into bed, I felt sick and could not get to sleep. Such intoxication is rare because in Lau the kava is so diluted and served in such small cups that many rounds can be drunk with impunity. Habitual drinkers are said to become intoxicated more quickly than occasional ones. Kava has no unpleasant reaction next morning, other than indolence and lack of appetite. Habitual drinkers can be noted by their watery and bleary eyes, their dull skins, which in bad cases become scaly.

On the other hand it will be noted that the latter part of his statement carries the usual description of the effects of drinking kava without any substantiation from personal experience. His illness might easily have

been from some other cause, since he does not indicate that on other occasions he was similarly affected.

One matter which has not been stressed but which might conceivably be important is that social kava drinking commonly takes place inside of a *bure*, or native house. The drinking may last for hours. During this time quantities of strong native tobacco are smoked. And if the doors are closed, as is the case in relatively cool weather, the atmosphere can become pretty thick with smoke. Several times this happened to us and the effects were not pleasant. The atmosphere, coupled with sitting cross-legged for such a long time, can easily produce some unsteadiness which, I suppose, could be attributed to the drinking of kava if one were predisposed to think so.

Of course it is possible that the experiences we have had are not comparable to those of earlier times. The drink may have been much stronger than that which we have been accustomed to. Kava prepared by premastication, which we have never had, may, through the action of saliva, have quite different properties. However, those who have drunk both remark merely that kava prepared by premastication is a smoother and more pleasant drink than that prepared by pounding and grating.

With the evidence available, it seems that early reports on the physiological effects of kava drinking were greatly exaggerated. That kava does have some rather noticeable reactions, including the slight numbing of the tongue and throat, is clear, and it is certain also that a desire for the odor, taste, and sensation provided by drinking kava can be acquired. But this seems hardly sufficient by itself to account for the part which kava plays in the socio-political and ceremonial life of the people.

It seems more likely that in considerable measure the importance of kava to the people of western Polynesia and Fiji is derived from the part it plays in their life rather than from whatever physiological effects it may have. Kava has become the focus of importance in so much of their lifetime activities that they have come to treasure it far more than seems warranted by its intrinsic properties. Kava drinking has become part of the traditional way of life. As the Fijian puts it kava is *vaka viti*—Fijian custom.

## REFERENCES


ADAMS, EMMA H. "Jottings from the Pacific. Life and incidents in the Fijian and Samoan islands." Oakland, Pacific Press Publishing Company, 1890.

ANONYMOUS. "KAVA (Cava or Ava)." Encyclopaedia Britannica 13: 299. Chicago, Encyclopaedia Britannica, Inc., 1944.

BUCK, PETER H. "Vikings of the sunrise." New York, Frederick A. Stokes Company, 1938.

CHURCHILL, WILLIAM. "Samoan kava custom." Holmes Anniversary Volume, pp. 56–66. Washington, 1916.

FOSTER, HARRY L. "A vagabond in Fiji." New York, Dodd, Mead and Company, 1927.

GORDON-CUMMING, CONSTANCE FREDERICA. "At home in Fiji." New York, A. C. Armstrong and Son, 1882.

HOCART, ARTHUR MAURICE. "Lau Islands, Fiji." Bernice P. Bishop Museum Bulletin 62. Honolulu, 1929.

LESTER, R. H. "Kava drinking in Vitilevu, Fiji." Oceania 12: 97–121, 226–254, 1941–1942.

LING SHUN-SHENG. "A comparative study of kava-drinking in the Pacific regions (summary)." Bulletin of the Institute of Ethnology, Academia Sinica 5: 77–96, 1958.

MARINER, WILLIAM. "An account of the natives of the Tonga Islands, in the South Pacific Ocean." Compiled and arranged from the extensive communications of Mr. William Mariner, several years resident in the islands. By John Martin. 2 vols. London, printed for the author, 1817.

PATTERSON, SAMUEL. Narrative of the adventures and sufferings of Samuel Patterson. Compiled by Ezekiel Terry. Palmer, Mass., from the press in Palmer, 1817.

# Discussion

*Chairman*—GEORG E. CRONHEIM
*Members of the Panel*—JOSEPH P. BUCKLEY
CLELLAN S. FORD
CARLETON GAJDUSEK
LOWELL D. HOLMES
MURLE W. KLOHS
HANS J. MEYER
CARL C. PFEIFFER

CHAIRMAN DR. CRONHEIM: Perhaps we can start with some of the written questions. I also want to make it plain that if any participant wants to ask a question of, please feel free to do so.

Here is a question that we may direct to either Dr. Holmes or Dr. Ford, or to both of them, and it reads as follows: "Several of the speakers have stated that, while Kava drinking produces ataxia and physical weakness, it leaves the intellect clear. Is there any corroboration for this other than introspective reports?"

DR. HOLMES: I might start with this. I would point out that much of the analysis of Kava drinking that I have done has been after the fact. In other words, this symposium came into view about two and a half years ago, and by that time I had already made a study of Kava drinking. It is one of the foremost institutions found in the area, and you can't help but notice it and write down all of the details, but I don't have any quantitative data.

I do have a few ideas that might relate to this: For example, the drinking of Kava by the young men very frequently is followed by very active dancing. It is a very energetic and physical sort of dancing, and if there were any problems with the legs I doubt if they could do it, because a lot of time it involves going down very slowly, that is to say, bending the knees very slowly until they almost touch the ground, and then raising up again. If there were any muscular problems, I doubt if they could do this sort of thing.

As far as keeping the intellect clear, I can recall one occasion when I was in the islands by myself—my wife was on another island teaching nurses. I found things kind of boring, having nobody to talk to for a portion of the day. I would have the boys prepare Kava, and I would sit there and work up my notes and drink Kava constantly.

I will admit I didn't get up very much. I was sitting there typing, but I was thinking and reasoning out certain things that I had observed, and as far as I am concerned, I did not experience any curtailment of intellectual abilities, nor did I experience any emotional problems.

DR. FORD: I might just add one observation. In Fiji they have meetings of the men who sit around and discuss what the day's activities are going to be, and what their long term, maybe two or three activities are going to be,

such as the building of a house, going on a fishing expedition, or whatever it might be. These meetings are invariably accompanied by a good deal of Kava drinking. It seemed to me that the Fijians were much sharper in their decisions and thoughts how to proceed while they were having Kava, than during other casual conversations.

I never noticed that drinking Kava made the men dull. If it were anything it would be the reverse; they would be more aware of what was going on after having had Kava than before.

CHAIRMAN DR. CRONHEIM: Maybe we can turn to a question on a completely different aspect. Here is a question directed to Dr. Pfeiffer: "Will you please describe the effect of alcohol on the mean energy content and coefficient of variance, and compare these effects with those of Kava Kava?"

DR. PFEIFFER: The effect of alcohol in a relatviely low dose, that of an ounce and a half of bourbon, or similarly diluted laboratory alcohol, is that of an anti-anxiety drug, meaning a depression in mean energy content and an increase in variability.

I would like to add that in the early days of mephenesin testing we had a ten percent suspension of mephenesin; this could be ingested at about the teaspoonful level and produce everything that has been described as happening with Kava. I wonder if there is any emulsifying agent in the natural Kava that would suspend some of the substances that we consider not water soluble but which have a definite effect?

CHAIRMAN DR. CRONHEIM: Does anybody want to comment on this last question from Dr. Pfeiffer?

MR. KLOHS: I would suspect in regard to the compounds we worked with, the d-pyrones, where water solubility is negligible, that mastication may result in a sort of an emulsion being formed where the particles are suspended in the water, and in that way you could get some of the physiological effects. That is the only thing that I could suggest.

DR. FORD: The Kava is stirred before each cup is provided.

MR. KLOHS: You would get suspended material here.

CHAIRMAN DR. CRONHEIM: I have a question here for Dr. Gajdusek: "What is the cargo cult," you spoke of?

DR. GAJDUSEK: Cargo cults form the subject of detailed studies by professional anthropologists for each area in New Guinea or the Islands. In the particular cult on Tanna, there was a gradual disenchantment of the people on the Island with the European planters, and the missionary people. There was a turning back to traditional ceremonies and the traditional way of life, with the addition of many of new features taken from the missionary teaching but re-interpreted in the way the people themselves wanted to interpret them.

This was definitely associated with a request that all Europeans leave the Island and that the Government not bother them. A great deal of mythology sprang up around it. There is a whole French book on it, published in Paris, devoted to the cults and myths associated with this movement, or "cargocult".

Kava came into the matter in that it became a part of the whole cult. Women and children occasionally drank, but all of the adult males were drinking a

great deal of Kava made from the fresh root. It is only on Tanna that a fully fledged cargo cult of that sort has developed in the New Hebrides.

Tongariki, where the observations I was reporting were made, is an isolated island with a very clannish community that has never really accepted any residents from Europe, British administrative people or missionaries on the island. We have good evidence that our own sojourn was the first that had been spent overnight.

CHAIRMAN DR. CRONHEIM: One question that I only want to mention because there is apparently some misunderstanding, says: "What is known of the chemistry or pharmacology of Kava Kava as distinct from Kava?" They are two terms for the same plant and the same material.

The next question is directed to Drs. Meyer, Pfeiffer and Buckley: "Dr. Pfeiffer dound dl-dihydromethysticin effective for only major sezures. Dr. Meyer, on the other hand, found it to behave like the diazopans, which are more effective in all but major seizures?"

DR. MEYER: I think there must be a mistake here, since I never quoted on the anticonvulsive effectiveness of the benzodiazepines which is indeed not very strong, at any rate much weaker than is found with the Kava pyrones. What I compared, however, was the muscular relaxant activity of both groups of drugs which is produced likewise by a central, most likely supraspinal mechanism of action.

DR. BUCKLEY: None of our work has been done on this problem, and the only finding we have to corroborate the work of Dr. Meyer is that the water soluble material that we are working with is a very potent muscle relaxant.

DR. PFEIFFER: If one compares in animals the effect of chlordiazepoxide against the Kava principles, the Kava has an anti-strychnine effect, and the chlordiazepoxide is barbiturate-like and has an anti-Metrazol effect. One can use both of them in epileptic seizures since the patients who are not responding to classical anti-epilepsy therapy have usually mixed epilepsy, and one can get a variety of beneficial effects. Our sample was at the most twelve patients. In these the predominant effect was a decrease of grand mal seizures and no change in their minor seizures. Had we had a larger sample, and had we done a careful comparison with chlordiazepoxide, we might have found different results.

CHAIRMAN DR. CRONHEIM: Here is another question: "Why is the characteristic Easter Island wooden statue of a man called Moa Kava Kava?" Maybe Dr. Holmstedt who sent in this question can provide also the answer.

DR. HOLMSTEDT: No.

CHAIRMAN DR. CRONHEIM: The next question, which perhaps can be answered by our anthropologist friends, who have seen the effects of Kava, is as follows: "Are cola drinks adequate substitutes for Kava insofar as claimed effects are concerned?"

DR. FORD: I suppose that by cola drink you mean soft drinks such as Coca Cola or Pepsi Cola. All I can say is that in my experience with the Fiji people, men particularly, would rather drink Kava than either a soft drink, such as the colas, or beer. That does not mean to say that they won't drink cola, but I am quite certain that there is a distinct preference for Kava, and

had if they had to choose one as opposed to the other, they would take their own native drink.

CHAIRMAN DR. CRONHEIM: The next question is to anyone on the panel: "Is there any specific therapeutic use of Kava by natives, or does any occur to you?" This can be answered by anyone on the panel. (No answer was forthcoming.)

DR. PFEIFFER: I have a question, and that is, since griseofulvin is fungicidal and deposits in the skin, I think it would be of interest to determine if there is any fungicidal effect of any of these Kava principles, because we know in this particular area of the world "jungle rot" or fungal infections are very common, so that the incidence of fungal infections might be less in the male than in the female.

I have already brought up the question of whether or not it is a pain killing drug and the consensus seems to be that it is not a pain killing drug in general.

DR. HOLMES: I did mention this morning that it is often taken to relieve the chills of filariasis, but other than that I know of no claims for Kava as a therapeutic drug.

DR. BUCKLEY: I can mention that the preliminary data that we have on the aqueous subfraction F-1 of Kava, indicated by the pharmacologic profiles, would suggest that if we are ever able to isolate the active constituent that it has potential tranquilizing activity, if it is effective orally.

CHAIRMAN DR. CRONHEIM: The next question is directed to Dr. Meyer and Dr. Buckley: "Since Kava ingestion causes a soporific effect, coupled with loss of muscle tone, have any studies been carried out relating the active principles of Kava to the physiological mechanisms of sleep in general, and to REM-sleep in particular?"

DR. BUCKLEY: I will introduce the subject. Data that we have obtained indicate that in the dosages used we get a very marked sedative effect, but not an effect as far as inducing sleep. These animals are very alert, and it appears that the reaction is at the subcortical level rather than the cortex. It is only when we get up to the higher doses that we get a true effect on the spinal cord and on the cerebral cortex.

DR. MEYER: One of the most striking manifestations during sleep revealed by electrophysiological recording is the reduction in the activity of skeletal muscles. In our experiments with Kava constituents of the pyrone group, we found a decrease of the tonic properties of the alpha motoneurones, followed by a loss of muscle tone which may resemble in some respect the reduced muscular activity observed in sleep.

On the other hand, there is no effect, no depressing effect, on the arousal response of the cerebral cortex elicited by electrical stimulation of the midbrain reticular formation, which is in contrast to the depressant action of the barbiturates on this system. We think that this is an appreciable difference between hypnotics and soporific agents like the Kava pyrones, the action of which are apparently more related to the physiological mechanisms of sleep. Moreover, animals put into sleep by Kava pyrones, easily can be aroused at any time of drug action.

Investigations with pyrones related to REM-sleep have not been carried out so far.

CHAIRMAN DR. CRONHEIM: I have a question here to Dr. Ford and the rest of the panel: "Would you please expand on the comment you made concerning possible enhancement of mental ability. Do any of the members have anything to add on this subject?"

DR. FORD: Well, all I can say is what I said before, and this is, of course, very tenuous judgment; but it did seem to me that the Fijians were just as alert, if not more alert, while they were drinking Kava, than when they were not.

It may be that other aspects of the situation account for part of this. For example, decision-making and considering future plans of the villagers might help to provide this alertness rather than the Kava itself.

From my own experience, and here again I think there might be individual differences, I never felt that Kava affected my thinking. Our youngest son, who was twenty-three years old at the time, came and spent two months with us in Naviti. The young men of the village sort of challenged him to Kava drinking bouts, much as beer drinking bouts might take place among such young people here. He claims that during the first half hour of such a drinking bout, during which he consumed maybe a quart or so of this diluted Kava, he became quite drowsy and sleepy, but that after this period passed he was well alert and wide awake enough to actually speak Fijian better than he felt he had normally been able to do.

DR. GAJDUSEK: I just never felt this drowsy feeling, and I don't know what the answers to this might be. The Tongarikans obviously are not drinking Kava socially. Often they are drinking alone. They are anxious to get the expected effect, and therefore having taken a large dose and eaten, and if they are not getting the effect, they often go back and have their boys chew more. They are subjectively evaluating what is happening; and if a sufficient reaction is not observed within the first half hour, they drink more; they raise the dose.

Those who are obviously casual drinkers, like myself, are likely to get a half portion, they are a little stingy about the Kava, they don't want to waste it on those who don't enjoy it, and with that half dose I could leave the area, go back to whatever work I was going to do that evening without any noticeable subjective impairment; and my colleagues do the same.

When one pushes the point and tries several doses one does get an effect. It is the effect I described: there is a market paresthesia of the lower extremities, numbness and cooling. It is not real anesthesia; you can still feel sensations with the extremities.

The men describe the same effect and they don't want to be disturbed as they subjectively observe it. They like the feeling and they refer particularly to numbness of their lower extremity up to the waist. They claim, and we find this to certainly be the case, that when one takes enough and tries to get up, one falls on one's face. They still have reflexes at this stage as I looked at them, but there are plenty of men who leave for home at too early a stage,

and need assistance to go home. They fall off the trail, but these are people who are concerned about their Kava and are drinking plenty of it.

Two other items which I think pharmacologically ought to be kept in mind. There is a great deal of concern whose Kava one is using, what garden plot it comes from, whether it is too dry, or if it is grown in the wrong soil or in the wrong place. I wonder whether one may not have a variety, depending on growth and hydration of the roots.

CHAIRMAN DR. CRONHEIM: I have a short question to Dr. Pfeiffer, and then one to the panel. The question to Dr. Pfeiffer is: "How would one reconcile the arousal or excessive cerebral activity of schizophrenics with the apparent decrease of synaptic transmission shown in the cat?"

DR. PFEIFFER: This represents two different test preparations, one the pentobarbitalized cat as a model on which to test hallucinogenic drugs. The other represents the natural state of psychosis in unanaesthetized patients. There is such a world of difference that I don't think one can compare the two, except in an average overall sample of brain wave activity. The brain wave of the schizophrenics are those of an over aroused or hyper-regulated type.

In regard to the previous question on performance under Kava, which asked if the mind was more clear, we know of many colleagues who are constantly over-stimulated and do their best when they have a sedative in them, whether it be meprobamate, chlordiazepoxide, or bourbon. I know one very fine author who can only write a book consuming a case of bourbon a week. It is a very fine book and this is the way the man works; he is productive on whiskey but not otherwise productive.

CHAIRMAN DR. CRONHEIM: I have two more questions, both pertaining to the same subject, and I am going to read them and will add to these questions one additional point, and then we will have to stop this discussion because of the time factor.

One question reads: "Will one of the speakers trace the introduction and migration of the beverage throughout the Pacific? Is it used throughout the range of the plant? What cultural modification of the natural range took place in the Pacific?"

The other question reads: "Dr. Ford mentioned parallel distribution and use of Betel and Kava, but cited as an example that in Tikopia, Betel was chewed, whereas Kava was poured on the ground. Parallel distribution of plants occurs in Micronesia, but usage is not parallel. Would Dr. Holmes care to comment on this?" I think in line with this, perhaps the most important, the most interesting question is a kind of summing-up question, namely:

We have heard from Dr. Gajdusek some very definite experiences of Kava effects that he has observed both on himself, on his associates, and also on the natives in the Islands where he worked. We have heard from Dr. Ford and Dr. Holmes that they did not see such effects or did not experience them on themselves; and so to relate it to the questions I just read to you, can the three of you in some way point out the differences, either in the time of the year or the type of the plant? Is it really botanically the same

plant, or are there other differences, conceivably other than the question of dosage that Dr. Ford already mentioned? Could you explain this very apparent dichotomy?

DR. HOLMES: I would like to answer that last question, because I would hate to try and trace the distribution in the short time we have. We did attempt to do a bit of this in our papers. But there are a couple of things I would like to say about this last question: I think we ought to resolve these problems, or at least attempt to do so. I would think that part of the answer might rest in the amounts, or concentration. The Kava ceremony that you observed in my film involved about as much Kava as would fill my hand level. I have no measurements of this. It is a very rough estimate. This would be placed in a fairly large bowl about sixteen inches across. I imagine there would be close to a gallon of water in there, because sometimes as many as thirty Chiefs will be served a cup of Kava, and the cup is pretty good sized. It might be that it is much more diluted in some places than in others.

There is the possibility of the saliva factor, and I might comment on this. The Kava that I have seen drunk and have drunk myself was not chewed and therefore did not involve saliva. I did not mention this in my talk this morning, but formerly Kava was prepared by chewing in Samoa also. However, all of my informants told me that the Kava chewers were trained not to get saliva on the Kava. I don't know how you do this, but the attempt was made not to get a big, messy cud and to keep the Kava as dry as possible. Apparently, at least according to my informants, the attempt was made not to get too much saliva in the mixture.

DR. FORD: A relatively amusing thing happened back in the early 1860's. The missionaries got disturbed about the fact that in parts of Fiji, particularly along the coast, they chewed the Kava root in preparation, and one fellow thought he had clinched things. What he did was to weigh pieces of Kava root before they were chewed and then swipe them from the chewer before he packed them back into the bowl; and from six ounces of Kava root, it increased to seventeen ounces after having been chewed. This was used as a stock example by everybody to justify stamping out this horrible, detestable habit of pre-masticating Kava. I have never tasted Kava that has been pre-masticated and this would seem to be one variable.

Another is the variable of the green versus the dry root.

Another is the variable of maybe different varieties in different soils, and the final one is obviously the tremendous difference in the amount of concentrate.

DR. GAJDUSEK: The dosage matter is very important. The quantity of Kava you are describing is less than is used in Tongariki for one man, let alone for thirty Chiefs. A large quantity sufficient for six young men is made, and I suspect this amount of root is more than you are using for your whole ceremony. This is one person's production.

FROM THE FLOOR: Did the chewers get a Kava effect?

DR. GAJDUSEK: The young men that are chewing the Kava have a thoroughly anaesthetized mouth. They claim that they cannot taste anything for

the rest of the evening. They also have a stiff mouth and claim they have difficulty in articulating.

Dr. Leake: We should always remember that the active principles in any plant vary enormously with respect to the soils in which they may grow. This is well known with nicotine and tobacco, or ephedrine. This may be a factor in the variation in Kava, since the soils in those areas do vary greatly.

Dr. Holder (from the floor): I am an anthropologist from the University of Nebraska. In 1943 on the Northern New Hebrides Islands, I drank Kava and helped prepare it, and in Dr. Gajdusek's comments and other comments this might be worthwhile. The Kava was dried and smoked in the roof timbers, and the preparation was made by taking a piece about twice as large as your thumb and chewing it for about three to four minutes. The natives themselves said it was necessary to get the saliva in to release the active principle.

I had been chosen as a chewer and did chew on many occasions, and I got anaesthetized tongue and the inner lining of my mouth was anaesthetized. This chewed mass was mixed with water in cocoanut cups and from four to five people drank; and it was chewed again. There was a marked diuretic effect; everybody had to leave about every twenty minutes, as in drinking beer. This was social, but the total effect was to loosen tongues and to talk far into the night, and no hangover the next day. There was absolutely none of this depression, and here again, these were small doses.

This was on the Island of Espiritu Santo on the southern slope of Mount Santo, at a village called Batuito at about five thousand feet, and they told me that in the past Kava had been used as part of the sexual ceremony, which was poured over a stone phallus prior to being mixed and drunk.

Dr. Gajdusek: Jean Guiart, our colleague who worked both in Santo and Malakoa, never himself experienced any reaction from the Kavas on Malakoa.

Chairman Dr. Cronheim: We have already exceeded by ten minutes the time allotted to us, so it is with great regret that I have to close the discussion.

I want to thank all the participants for a most enlightening and most stimulating panel.

# SESSION III

## MYRISTICA FRAGRANS (NUTMEG)

Edward B. Truitt, Jr., *Chairman*

# Chairman's Introduction

EDWARD B. TRUITT, JR.
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In this introduction, I would like to formulate several questions which I believe are crucial for this section of the program. The presentations to follow will likely answer very few of these questions. Rather, I think, the juxtaposition of these questions with the scanty information so far collected about the physical and physiological actions of nutmeg will emphasize the real need for further research into the dietary, ritualistic, and drug-seeking habits of man with this spice, and their possible significance.

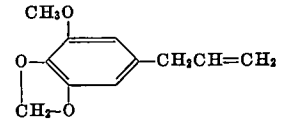
The uppermost question that plagues the conscious of an investigator in this field is whether, by discussing publicly a substance with a potential for abuse by the lay public, he is inadvertently opening another Pandora's box of human ills. One answer to this question, in the case of nutmeg, appears to be that this substance has enough unpleasant effects mixed with its centrally stimulating actions to discourage misuse by any but the most reckless psychodelic adventurers. This will certainly be borne out by the reports to follow about the toxic effects of human overdose by ground nutmeg in the crude drug form. Whether the same will be true of myristicin or other active components of the volatile fraction will need to be learned, because experience with the purified products is quite meager. A lesson from LSD should be applied here, so that the human risks of nutmeg derivatives, mental as well as organic, will be carefully evaluated by clinical pharmacologists in anticipation of the possibility of widespread misuse.

A second question might appraise the need for further investigation on a substance which appears to be another stimulant to a central adrenergic receptor already affected by mescaline, cocaine, the amphetamines, epinephrine, adrenochrome, and possibly by LSD and other tryptamine-like hallucinogens. An answer to this question certainly lies in the importance of the study of structure and activity variations. Pharmacologists and medicinal chemists are strong advocates of the advisibility of characterizing drug activity in terms of the effects of structural changes in the molecule. Thus, we should look in the session to follow for those clues to variation in the central activity produced by myristicin, which has a slightly different formula from mescaline, as shown in Figure 1.

Myristicin is unique among psychotropic agents in that it lacks a nitrogen atom. This unusual characteristic has led Dr. Shulgin to propose an interesting hypothetical mechanism for its action which I am sure he will find time to discuss.

Another question which can be asked is how the information to be presented here on nutmeg and myristicin can be helpful to a better understanding of the workings of the mind. Since a partial answer to the previous question appears to be that nutmeg intoxication is in some ways different from mescaline

Myristicin (5-allyl-2,3 methylenedioxyphenylmethyl ether or 3-methoxy-4,5-methylenedioxyallylbenzene)



Mescaline (3,4,5-trimethoxyphenylethylamine)

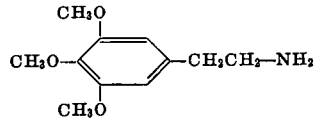


FIGURE 1.—*Structural formulas of myristicin and mescaline.*

and similar drugs, how does this difference contribute to better understanding? What is the relationship between the central feelings of anxiety, detachment, and excitation with somatic effects such as tachycardia, xerostomia, hypothermia, vasomotor lability, pupillary changes, and heaviness of the limbs? The marked degree and variety of peripheral effects prompts the question as to how much of the psychic action is attributable to the centripetal stimuli.

From a therapeutic viewpoint, one might ask whether some aspect of the syndrome induced by nutmeg might have a therapeutic application. This is, indeed, the most central question to the purposes of this conference. However, this goal has not yet been achieved for any of the drugs presently labeled as hallucinogens. Another useful advantage of this discussion could be the recognition of a means of treating nutmeg intoxication which occurs, although infrequently, and may be expected to increase.

The program to follow cannot begin to treat all aspects of nutmeg because extensive communication with other scientists and reviews of the scattered literature did not lead to the finding of experts on the anthropogical and other facets of the spice. It is perhaps appropriate that a pharmacologist, such as myself, inherited the chairmanship of this section. The reason for this is that three of the major early investigators, Arthur Cushny, Sir Henry Dale and George Wallace were all pharmacologists, and venerable ones also.

The first speaker, Mr. Andrew T. Weil, has produced perhaps the most detailed review of the nutmeg literature while essaying his honors thesis in botany. (*1*) Following this introductory review, Dr. Alexander T. Shulgin will describe research which already has put into practice one of the objectives of this conference. Dr. Shulgin and his associates have used the empirical observations of psychopharmacological activity in nutmeg and mescaline as a starting basis for the synthesis and testing of newer, more active and varied psycho-active drugs. Dr. Shulgin has also surpassed everyone for continued interest and publications on myristicin (*2–9*). My own interest in the action of nutmeg emerged from Dr. John C. Krantz's scientific curiosity in response to several cases of nutmeg poisoning referred to him by graduates of the University of Maryland Medical School. (*10*) It was

also continued by the then-growing importance of norepinephrine and 5-hydroxytamine in brain function. (*11*) The last speaker, Dr. Enoch Callaway, III, is an authority on nutmeg by reason of personal experience as well as having conducted clinical experimentation with a purified myristicin-containing fraction of oil of nutmeg. (*10*) I believe that his experience with the drug, if widely known, should certainly dissuade public abuse of nutmeg.

## BIBLIOGRAPHY


(*1*) WEIL, A. T. "Nutmeg as a Narcotic." Economic Botany, 19: 194, 1965.

(*2*) SHULGIN, A. T., S. BUNNELL, and T. SARGENT, III. "The Psychotomimetic Properties of 3, 4, 5-Trimethoxyamphetamines." Nature (Lond.), 189: 1011, 1961.

(*3*) SHULGIN, A. T. "Composition of the Myristicin Fraction from Oil of Nutmeg." Nature (Lond.), 197: 379, 1963.

(*4*) SHULGIN, A. T. "Psychotomimetic Agents Related to Mescaline." Experientia, 19: 127, 1963.

(*5*) SHULGIN, A. T. "Concerning the Pharmacology of Nutmeg." Mind, 1: 299, 1963.

(*6*) SHULGIN, A. T., and H. O. KERLINGER. "Isolation of Methoxyeugenol and Trans-Isoelemicin from Oil of Nutmeg." Naturwissenschaften, 15: 360, 1964.

(*7*) SHULGIN, A. T. "3-Methoxy-4,5-Methylenedioxyamphetamine, A New Psychotomimetic Agent." Nature, 201: 1120, 1964.

(*8*) SHULGIN, A. T. "Psychotomimetic Amphetamines: Methoxy-3,4-Dialkoxy Amphetamines." Experientia, 20: 366, 1964.

(*9*) SHULGIN, A. T. "Possible Implication of Myristicin as a Psychotropic Substance." Nature (Lond.), 210: 380, 1966.

(*10*) TRUITT, E. B., Jr., E. CALLAWAY, III, M. C. BRAUDE, and J. C. KRANTZ, Jr. "The Pharmacology of Myristicin. A Contribution to the Psychopharmacology of Nutmeg." Journal of Neuropsychiatry, 2: 205, 1961.

(*11*) TRUITT, E. B., Jr., G. DURITZ, and E. M. EBERSBERGER. "Evidence of Monoamine Oxidase Inhibition by Myristicin and Nutmeg." Proceedings of the Society for Experimental Biology and Medicine, 112: 647, 1963.

# Nutmeg as a Psychoactive Drug

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Clearly, nutmeg is unique among the less familiar psychoactive drugs. It is the only one widely known to millions of persons in all countries—albeit for other-than-pharmacological purposes. It is also the only one whose use as a drug may be on the verge of an enormous increase. The aim of this paper is to review the botany, history, and commerce of nutmeg as well as to describe the ways it is used for effects on consciousness.

Two spices—nutmeg and mace—come from the nutmeg tree, *Myristica fragrans* (family Myristicaceae), a handsome tropical tree native to the Banda Islands and other islands of the East Indian archipelago. The genus *Myristica* comprises about 100 species found throughout the torrid zone, especially in the Malayan region; but of these *M. fragrans* alone contains enough of an aromatic essential oil to make it worthy of cultivation. Usually 30 or 40 feet tall, the nutmeg tree has a dark gray bark, spreading branches, and alternate, oblong-ovate leaves that are four inches long, leathery, and glossy green. Normally, the species is dioecious. Flowers, male and female, look like those of the lily-of-the- valley; they are pale yellow, fleshy, and have a strong scent of nutmeg. The fruit is a pendulous, fleshy drupe resembling an apricot (*1*,*2*,*3*).

When ripe, the fleshy husk, or pericarp, of this fruit splits open into two halves, revealing a shiny brown seedcoat, or testa. Inside this shell is the seed, which is the nutmeg of commerce. Outside the shell, closely enwrapping it, is a bright crimson network, or arillus, which is the mace. In preparing the spices for export, fieldworkers first remove the pit with its mace from the husk. The aril is then carefully peeled away from the seedcoat. Fresh arils are brilliant red and leathery with a strong flavor of turpentine. The mace may be kept in one piece (called "double blade" in the trade) or separated into two halves ("single blade") before it is flattened by hand or between boards. It is then dried thoroughly in the sun or by artificial heat; during this process it gradually turns orange, then orange-yellow and acquires its characteristic aroma (*3*,*4*).

The nutmegs, still in their shells, are also dried, frequently over a smouldering fire. When completely dry, the seed rattles in the testa. Usually the shells are then cracked by machine or with wooden mallets and the seeds are removed for export. Sometimes, shelled nutmegs are treated with lime before shipping to protect them from insects. They are then sorted by size and packed. For the spice trade, nutmegs are valued according to size, smoothness, and freedom from adulteration with wild seeds (*2*,*4*).

The nutmeg tree requires a hot, humid climate. It is widely cultivated in the tropics, particularly on the Spice Islands (the Moluccas, an island group of eastern Indonesia), on Penang and other islands of Malaysia, and in the

Caribbean, notably on Grenada. The tree is slow-growing, taking 15 years to produce full yields. A good specimen produces 1,500–2,000 nuts annually—a weight of ten pounds of nutmeg to one-half pound of mace. The finest mace and the finest nutmegs come from Penang; because of their higher content of volatile oil, the East Indian spices are preferred to the West Indian (*4*).

## Products of M. Fragrans

*Nutmeg Husks:* The pericarp of the nutmeg fruit may be preserved in sugar, salted and dried as a condiment, or made into jellies. All of these preparations have the flavor of nutmeg and all are reported to be delicious. But they are unknown outside the regions in which the tree is grown (*2*,*3*).

*Nutmeg:* Whole nutmegs are oval and woody with a ridged or wrinkled, light brown surface. Most are about an inch long, three-quarters of an inch in diameter. On cross section they show a heavy network of dark brown "veins." Ground nutmeg, the familiar kitchen spice is a granular, orange-brown powder with characteristic aroma.

Depending on the variety, whole nutmeg contains from 5 to 15 per cent of a volatile oil that accounts entirely for the aroma and flavor of the spice. Ground nutmeg is subject to rather rapid losses of this component. In addition, dried nutmeg contains 25 to 40 per cent of fixed oil and 5 to 15 per cent ashes. The remainder is moisture, fiber, and starch (*5*). In the calendar year 1965, the United States imported nearly 5,300,000 pounds of nutmeg worth about $3,800,000. Of this total, nearly 72 per cent came from Indonesia, while 24 per cent came from the Caribbean, with the remainder from a number of smaller ports. Imports over the past ten years have been fairly constant (Table I), but there has been a change in the major source of this spice. Until 1955, the U.S. obtained about half of its annual supply of both nutmeg and mace from the West Indies. In that year, however, a hurricane devastated the island of Grenada, and the nutmeg groves there have still not recovered from the damage (*6*).

*Mace:* Mace, another popular spice, is a brownish-yellow or brownish-orange granular powder with a strong aroma closely resembling that of nutmeg. The flavor of mace is somewhat less sweet and less delicate than the flavor of nutmeg. Whole mace contains from 4 to 14 percent of a volatile oil very similar to that found in nutmeg, along with moisture, fat, starch, etc.

TABLE I.—U.S. imports of nutmeg and mace*

[pounds]

| | Average 1950–54 | Average 1955–59 | Average 1960–64 | 1963 | 1964 | 1965 |
|---|---|---|---|---|---|---|
| Nutmeg | 4, 852, 221 | 4, 141, 074 | 4, 151, 480 | 5, 124, 638 | 3, 505, 450 | 5, 271, 524 |
| Mace | 658, 193 | 549, 072 | 563, 874 | 558, 541 | 648, 900 | 619, 394 |

*Source: U.S. Department of Commerce, Bureau of the Census Compilation by American Spice Trade Association.

(*5; 7*, Vol V). In 1965, the United States imported 619,000 pounds of mace worth $750,000. Seventy-six percent came from Indonesia, the rest from Malaysia, Hong Kong, Japan, and the Caribbean. As with nutmeg, imports of mace have not varied much over the past ten years (Table I).

*Uses of Nutmeg and Mace:* Both spices are classified as "baking spices" since they are much used in foods like doughnuts and other sweet doughs. Both have a warm, aromatic, slightly bitter taste. Nutmeg is commonly added to custards, puddings, pies, and eggnog. Mace is used in soups, sauces, and pastries, particularly pound cake. In addition, both spices are important ingredients of frankfurters and other meat products, pickles, tomato ketchup, and similar condiments. The American Spice Trade Association estimates that 55 percent of nutmeg and mace imported into this country is sold through retail stores to home consumers. The rest goes to institutions (hotels, restaurants, bakeries, sausage manufacturers, and other bulk users). Formerly, housewives bought whole nutmegs and grated them at home; today, most of the nutmeg and all of the mace sold for home consumption is ground.

*Fixed Oil of Nutmeg:* Known also as "nutmeg butter," this vegetable fat is obtained by exposing the nuts to hydraulic pressure and heat. At room temperature, it is an orange, tallowy mass with a pronounced aroma of nutmeg and the consistency of butter. Formerly used in medicine as an external application for rheumatism and sprains, it has some commercial importance today as an ingredient of certain soaps, hair tonics, and perfumes (*2, 3, 5*).

*Essential Oils of Nutmeg and Mace:* The essential or volatile oils of nutmeg and mace are obtained by steam distillation. Commercial oil of nutmeg is a mobile, pale yellow liquid with an odor and flavor of nutmeg. It is not satisfactory as a substitute for the spice in cooking because it does not exactly reproduce the flavor of whole nutmeg. ("Essences" of nutmeg and mace sold by spice dealers are alcohol extracts not essential oils.) But oil of nutmeg has been widely used in industry as a flavoring agent for perfumes and dentifrices. Chemically, it is a complex mixture of alcohols, esters, and organic acids, including about four percent myristicin, the main pharmacologically active component (*7*, Vol V; *8*; *9*).

## History of Nutmeg

Nutmeg was unknown to the ancient Greeks and Romans, but probably, Arabian traders began importing it from the East Indies by the first centuries A.D. No definite evidence of Myristica's appearance in Europe is recorded until the 12th Century, and the source of nutmeg was not discovered by the West until the Portuguese reached Banda in 1512. Portugal controlled trade in nutmeg and mace from that year until the beginning of the 17th Century, when most of the Pacific spice-producing territories fell into the hands of the Dutch. In order to keep prices of the spices very high, the Dutch tried to limit cultivation of the nutmeg tree to two islands, but their monopoly

was eventually challenged successfully by the French and British. Gradually, commercial development of *M. fragrans* spread throughout the world, reaching Grenada, for example, in 1843 (*3*).

Like most aromatics, nutmeg was as important in early medicine as it was in cooking (*10*). Its therapeutic applications were first catalogued by Arab physicians as early as the 7th Century A.D. Originally, it seems to have been a remedy for disorders of the digestive system, but before long it was considered beneficial in such diverse conditions as kidney disease, pain, and lymphatic ailments; it was even described as an aphrodisiac. Many of these beliefs are preserved in contemporary Arab folk medicine; in fact, Yemenite men still consume it to increase virility.

Similarly, nutmeg was and is a significant item in the Hindu pharmacopeia, where it has been prescribed for fever, consumption, asthma, and heart disease. Traditional Malayan medicine designates nutmeg for madness as well. According to an adviser in the Indian Ministry of Health, nutmeg is still used as an analgesic and sedative by folk practitioners, and is given in small quantities to induce hypnotic effect in irritable children.

Medieval European physicians, who generally followed the precepts of their Arab colleagues, also prescribed nutmeg for a long list of ailments. By the 1700's the spice attained its greatest reputation; thereafter, with the development of modern pharmacy, its importance as a medicine gradually subsided.

Curiously, nutmeg's popularity as a folk remedy had a brief, spectacular resurgence less than one hundred years ago. Near the end of the 1800's, a rumor spread among women in England and America that nutmeg could bring on overdue menstruation and even induce abortion. The origin of this mistaken belief is unclear, but its influence is well documented in dozens of case reports of nutmeg poisoning published in British and American medical journals of the period (*10*). The idea has even persisted into our times: Green in 1959 wrote of a 28-year-old Virginia woman who ate "18.3 Gm. of finely ground nutmeg in an attempt to induce the menses, which had been delayed two days (*11*)."

Reports of nutmeg poisoning date back to the late Middle Ages when several early physicians first wrote down their observations on the stupor-inducing powers of the spice. Doubtless, most of these intoxications resulted from overdoses taken as remedies. A late example comes from *A Treatise on the Materia Medica* written in 1789 by an English physician, William Cullen. He wrote:

> I have myself had an accidental occasion of observing its [nutmeg's] soporific and stupefying power. A person by mistake took two drams or a little more of powdered nutmeg; he felt it warm in his stomach, without any uneasiness; but in about an hour after he had taken it, he was seized with a drowsiness, which gradually increased to a complete stupor and insensibility; and not long after, he was found fallen from his chair, lying on the floor of his chamber in the state mentioned. Being laid abed he fell asleep; but waking a little from time to time, he was quite delirious: and he thus continued alternately sleeping and delirious for several hours. By degrees, however, both these symptoms diminished, so that in about six hours from the time of taking the

nutmeg he was pretty well recovered from both. Although he still complained of headache and some drowsiness, he slept naturally and quietly through the following night, and next day was quite in his ordinary health.

There is no doubt that this was entirely the effect of the nutmeg. . . .

In 1829, the great physiologist J. E. Purkinje conducted self-experiments with nutmeg. Following a dose of three whole nutmegs, he experienced spatial and temporal disorientation similar to that of Cannabis intoxication. He wrote (*12*):

At half-past six, when it was almost dark, I woke up in order to go to the Royal Theatre at Brueder Street where I lived. The distance was long, but this time I thought it had no end. My movements appeared entirely adequate, but were lost momentarily in dream pictures, from which I had to extricate myself with considerable force in order to keep on walking. My feet did their duty and, since I had to stick to a straight road, there was no danger of going astray. I went forward in this dream, for, if I attempted to orient myself, I could not even recognize the cross streets. Time seemed long, but I got to the opposite side of the place where I was going. During this time dreams and physical activity battled one another. The return journey was good, and I slept well that night and next day.

There is a similar, more dramatic report of mace intoxication from 1848 (*13*). But as stated earlier, the greatest numbers of people poisoned by Myristica have been English and American women of the late 19th and early 20th Centuries. Summarizing many of these cases in 1962, McCord wrote (*14*):

. . . patients have consumed from 1 to 3 nutmegs and have experienced restlessness, dizziness, fear of death, coldness of extremities, occasional nausea and vomiting, abdominal pain, and precordial pain or oppression. These patients were found to be extremely agitated, delirious, and dyspneic and have had weak, rapid pulses and decreased body temperature. On several occasions patients were found unconscious. Occasionally there was flushing of the face while at other times pallor with cyanosis of the lips and nails predominated.

He attributed these intoxications to "a central nervous system depressive effect with periods of stimulation and associated respiratory and cardiovascular difficulties."

Only one fatality has ever been ascribed to nutmeg ingestion: near the beginning of this century, an eight year old boy ate two whole nutmegs, became comatose, and died less than 24 hours later (*15*).

## Use of Nutmeg as an Intoxicant

The apparent epidemic of nutmeg intoxications around the turn of the century subsided after the First World War. Cases since then have been rare. In 1963, Payne presented one of the only published reports of deliberate ingestion of Myristica for narcotic effects. He described two college students, 19 and 20 years old, who each consumed two tablespoonfuls (about 14 g. or the equivalent of two whole seeds) of powdered nutmeg suspended in milk (*16*). About five hours later

. . . each had the onset of a significant pharmacologic effect, heralded by a leaden feeling in the extremities and a nonchalant, detached mental state described as 'unreal' or 'dreamlike.' Rapid heart rates and palpitation were noted, and both complained

of dry mouth and thirst. Onlookers observed that one student became quite hyperactive and agitated and talked incoherently. It was noted that the faces of both were as 'red as beets.' Nausea, vomiting, and abdominal cramps were absent. . . . One described a sense of impending doom, as if he were 'breaking up inside.'

Extreme drowsiness occurred about seven hours after these symptoms began and continued for the next 24 hours. Recovery was complete, but "both patients stated emphatically that a sense of unreality persisted for 48 to 60 hours from the time of one oral dose of nutmeg."

A history of the use of nutmeg for the express purpose of inducing these bizarre physical and mental effects is hard to piece together simply because reliable data on Myristica narcosis are not available. The medical literature is of no help, for example, because nearly all the reported cases have resulted from accidental ingestions or overdoses taken as remedies. Most of the information on nutmeg as a psychoactive drug is anecdotal, and it has been most difficult to document the anecdotes.

Stories in circulation about nutmeg at the present time develop several recurrent themes. One is that Myristica is used as an intoxicant in certain parts of Asia. Another is that nutmeg is widely consumed by prison inmates in this country. A third is that students and 'beatniks' have adopted the the spice as a new hallucinogen.

For the first story little supporting evidence can be found. A suggestive clue is one of the synonyms for nutmeg used in Ayurveda, an ancient Hindu scripture. Here, nutmeg is called *Mada shaunda* meaning "narcotic fruit." There is reason to believe that nutmeg is, in fact, eaten as an intoxicant even today by some people in India who add it to betel chew. It may also be mixed with tobacco and snuffed in this part of the world. Equally vague is a report that nutmeg is taken as a stimulating snuff by natives in remote regions of Indonesia. Still another unsubstantiated assertion is that nutmeg is often substituted for hashish in Egypt when the hemp product is not available.

It is much easier to confirm rumors of nutmeg use by prison inmates, despite denials by prison officials. One interesting reference occurs in *The Autobiography of Malcolm X* (*17*), in which the late Black Muslim leader describes his incarceration in a Boston prison in 1946. He was then a user of marihuana and other drugs and found himself suddenly cut off from them. He wrote:

I first got high in Charlestown [prison] on nutmeg. My cellmate was among at least a hundred nutmeg men who, for money or cigarettes, bought from kitchen-worker inmates penny matchboxes full of stolen nutmeg. I grabbed a box as though it were a pound of heavy drugs. Stirred into a glass of cold water, a penny matchbox full of nutmeg had the kick of three or four reefers.

A more recent but less accessible reference was a short article on page 22 of the Chicago *Sun-Times* for March 3, 1961. It told of the dismissal of a Cook County Jail guard caught smuggling nutmeg and nose inhalers into the jail.

An officer of the Federal Bureau of Prisons has written (*18*):

We are aware of the narcotic reaction these spices may have when improperly used, and, therefore, it is standard practice in the Federal prisons to maintain careful control of both items [i.e., nutmeg and mace]. Due to this control and also to the

fact . . . that few people are aware of their stupor-inducing powers, we have no problems with these items. I have read articles in various publications which imply that the use of nutmeg and mace is widespread in prisons. However I do not know of a single instance in the Federal Prison system where either spice was used by inmates for its narcotic effect.

There is, however, ample confirmation of this rumored use of nutmeg in a study conducted by Weiss at the New Jersey State Prison at Trenton in 1960. Weiss wrote (*19*):

It is widely believed by inmates of correctional institutions that the drug action of nutmeg produces reactions similar to those of legally prohibited drugs which are considered habit-forming and addicting. Although its illicit application is most certainly not widely known in the extra-mural setting, personal communications by prisoners are to the effect that it is used, not only in the community [i.e., the outside], but was also used in the armed forces in Europe in World War II.

Weiss studied ten male inmates of the prison, most of whom had had previous experiences with marihuana and other drugs. Six of them had learned of the use of nutmeg during their imprisonment; the others had already known about it. The number of times these men had tried Myristica was impressive. One had taken nutmeg on 10 different occasions, one 30, one 52, and one 475. The minimum amount of ground nutmeg any man ingested was 2 to 3 tablespoonfuls, and one had once taken two cups of the spice as a single dose (apparently without untoward effects). The drug was always taken orally, usually stirred into hot liquids.

Weiss noted no uniformity of time of onset of action, which ranged from 10 minutes to four hours. Duration of action ranged from four to 24 hours. Most of the subjects compared nutmeg to marihuana, although some also likened it to heroin and alcohol. Most experienced a sense of being transported aloft, along with drowsiness in some cases and excitement in others. In all instances thirst was increased, but hunger was not stimulated. Reported side effects included nausea, abdominal spasm, vomiting, constipation, tachycardia, insomnia, and drowsiness.

Two cases of acute brain syndrome, with psychotic reaction due to nutmeg intoxication, were reported. Each of the two subjects had chronically ingested powdered nutmeg over a long period. . . . Aside from these cases of poisoning, the hallucinogenic effects reported were transitory and of brief duration.

Consumption of nutmeg was an important aspect of life in the prison. Weiss has added (*20*):

Inmates would carry little matchboxes in which they would store a supply of nutmeg (equivalent to one dose). They could then take the dose along with them to the shops in which they worked during the day. Users consider themselves to be more lively and cheerful. Thus, they feel they have dispelled their inner gloom. However, drug users seldom take nutmeg once they leave the prison since they consider its effects to be inferior to those of heroin or marihuana, whatever may be the similarity between them.

Shortly after Weiss's article appeared, nutmeg was banned from the New Jersey State Prison kitchen.

I have received information from several former prison inmates, suggesting the practice to be common. One correspondent writes: "During 16 months in a Massachusetts correctional institution, I knew three individ-

uals who on occasion did use nutmeg as a snuff for 'kicks.' It was done on weekends and widely dispersed as to time." Another, from California, writes: "I can tell you that nutmeg is a commonly used high within prison walls—so much so that it is frequently locked up apart from the other normally used spices. . . . Convicts, because of the nature of their environment, have rarely any alternative high."

A final reference is this line from William Burroughs's *Naked Lunch* (*21*): "Convicts and sailors sometimes have recourse to nutmeg. About a tablespoon is swallowed with water. Result vaguely similar to marihuana with side effects of headache and nausea."

Like prisoners, jazz musicians are said to have long used nutmeg as a substitute for other drugs, especially marihuana. Confirmation is hard to come by. The only clear reference I have been able to find is a 1962 biography of the late Charlie Parker, known as "Bird." The leader of the band in which Parker made his recording debut in 1942 is quoted as reminiscing (*22*):

> Bird introduced this nutmeg to the guys. It was a cheap and legal high. You can take it in milk or Coca Cola. The grocer across the street came over to the club owner and said, "I know you do all this baking because I sell from 8 to 10 nutmegs a day." And the owner came back and looked at the bandstand and there was a whole pile of nutmeg boxes.

To summarize thus far: The toxic properties of nutmeg have been recognized for hundreds of years, probably ever since the spice was first prescribed medicinally in large doses. Published reports of Myristica narcosis were most frequent around the turn of the last century when many women took nutmeg as an emmenagogue or abortifacient. Some evidence suggests that nutmeg may have long been used as an intoxicant in certain parts of Asia. In our century, for at least the past thirty years, prisoners, jazz musicians, sailors, and probably others have used nutmeg as a substitute for marihuana or other drugs. They either eat or snuff it in variable amounts and commonly experience symptoms much more like those of the familiar hallucinogens than those described in the old reports of nutmeg poisoning.

## Use by Students

In our own society the fastest-growing group of drug-takers is not the prison population or jazz world but rather students and "student-types." I do not care to add another guess to the many published estimates of what percentage of college youth experiments with hallucinogens. I will simply point out that most observers find that significant numbers of students now try marihuana and stronger drugs like LSD. It is especially noteworthy that many of these people would never have indulged in such activities even five years ago. I doubt, for example, that more than a handful of law students, medical students, or divinity students had experienced the effects of Cannabis before 1963, when hallucinogens first came to the full attention of the national press. But today many occasional marihuana

smokers come from these groups. Students have also been the initiators of drug fads in recent years. The flurry of excitement over morning-glory seeds in 1963 and 1964 was generated largely by college undergraduates and high school pupils. One would expect that nutmeg, because of its frequent use by other groups as an alternative hallucinogen, might also be included in the student's or beatnik's index of psychoactive substances.

I have been particularly interested in this possibility because I first learned of Myristica's psychopharmacological potential through an invitation to a "mace party" given by several undergraduates at Haverford College near Philadelphia in 1961. The students said they and many of their classmates had been introduced to the spice by a visiting beatnik from Baltimore, who had sponsored several mace parties on campus.

Only one case of this sort has appeared in the medical literature—Payne's report of 1963, mentioned earlier. His two students had gotten the idea of taking nutmeg from a "beatnik acquaintance," who told them it would provide "a mental state somewhat akin to ethanol intoxication without requiring the use of alcohol" (*16*). I have been able to find only one other published account—an article titled "Nutmeg Jag" in the summer, 1964 issue of a University of Mississippi student magazine. It described a nutmeg party attended by eight persons. One participant—a young man who consumed a whole standard-size can of the ground spice (nearly 40 g. or 1.5 oz.)—recalled afterward (*23*):

> I felt as if I were in an echo chamber . . . my voice sounded vague and distant . . . it was like being drunk without the ordinary alcoholic effects. . . . Two friends of mine had told me about the 30-cents, three-day drunk they had after taking nutmeg, so I tried it out of sheer disbelief.

Over the past six months I have been in touch with officials of student health services at representative universities throughout the country in an attempt to collect additional reports of Myristica intoxications. Significantly, most of the responding physicians were unaware of nutmeg's nonculinary uses. Only two university clinics had cases on record. Dr. Henry B. Bruyn of the University of California at Berkeley student health service notes two instances of intoxication. In October, 1963, two days after an issue of the *Ladies Home Journal* appeared with a reference to nutmeg in a story on hallucinogenic drugs, a 20-year-old female student was admitted to the hospital with a chief complaint of abdominal cramps. The night before she had taken 4 teaspoons of ground nutmeg because a friend had told her it would get her high. Her roommate joined her in this ingestion. The next morning she awoke drowsy and fainted in the bathroom. Physical examination was normal except for orthostatic hypotension, and she was recovered the day after admission. She told a physician she had taken the spice because she "felt she needed something to do."

In January, 1965, a second female Berkeley student was admitted, age 17, again with abdominal cramps. Four hours previously she had eaten 2½ teaspoons of nutmeg because she had heard it would give her hallucinations. She, too, recovered quickly.

Dr. B. W. Murphy of the University of Maryland contributes one other case. He writes that he knows of a male student who induces dreamy hallucinatory states by ingesting a whole can of ground nutmeg.

Does the scarcity of reported cases indicate a low frequency of nutmeg use by students? Probably not—just because students are reluctant to present themselves for medical treatment of drug intoxications, even when they suffer alarming symptoms. Relying solely on health services records, one would conclude that marihuana is also very little used by college students.

To get a more accurate idea of the extent of experimentation with nutmeg on college campuses, I placed advertisements requesting information on the spice in several student newspapers and also interviewed students from many areas of the country. By these methods, I easily collected a number of accounts of nutmeg narcosis. I have selected some of these to illustrate typical patterns of use.

Case #1 (college sophomore)—

I heard about the effects of mace from a beatnik who visited our campus and induced students to "turn on" with two teaspoons of this spice stirred into fruit juice. I didn't try it at the time, but a few months later five of us held a mace party in my apartment. To the disappointment of all, we felt just the same three hours after drinking down the mace. Convinced that the alleged hallucinogenic properties of mace were imaginary, we separated and I went to bed. I remember feeling somewhat lightheaded and having vague stomach pains before falling asleep, but I had no other sypmtoms until I woke up the next morning with a splitting headache, a burning thirst, and malaise. I later learned the other four had felt much the same on arising.

Case #2 (college juniors)—

Five of us tried to get high by eating two whole nutmegs each. They are terrible things to try to chew up and swallow. We all had warm feelings in our stomachs immediately afterward and began sweating more than usual. One of us eventually had a pronounced reaction, but the rest of us noticed nothing unusual and gave up after two hours. The next morning we all had headaches, extreme dryness of mouth and throat, creaking joints and dizziness.

One of us had a different experience. He went back to his room to read, and exactly four hours after taking the nutmeg he was suddenly overcome by a drowsiness so profound that he could hardly get up to turn off the light. As he fell into bed he had impressions of 'strange shapes floating' around him. He then sank into a heavy sleep. When he woke up seven hours later, he could barely move. He was very dizzy and staggered when he tried to walk; also, he could not see clearly for several minutes. His mouth and throat were parched, and water did not relieve the dryness. Two hours after he got up he again became drowsy and "sank into a sort of trance state." At this time he had a vivid impression that he was floating with his limbs separated from his body. Eight hours later he was fully recovered.

Case #3 (an ex-student in San Francisco)—

I have had completely negative results from nutmeg, perhaps partly precipitated by the environment and definitely partly by the nauseating effects of the drug. I ate three ounces, which may well have been too much. About two hours later I drank four beers. Then about three-quarters of an hour after the beer I began noticing unusual effects. I was in an unfamiliar night club and started to become disoriented. I talked continuously and repetitively, but it seemed as though another person were talking. I seem to have been wandering around in a daze, unaware of my surroundings. I was then ejected

from the club. Paranoid delusions set in. I believed the owners of the club had drugged me. I forced my way back in, which resulted in my being jailed for drunk and disorderly conduct. The day I spent in jail was one of total confusion. In fact, it was a full day before I realized I was in jail. I was very belligerent, a condition apparently precipitated by the belief that I was going to be executed. I became ill and vomited. I imagined the other prisoners were Nazis who were guarding me. One day in jail finally restored my reason, and I was released. No hallucinations occurred as far as I can recall.

Case #4 (college junior)—

I drank one ounce of nutmeg in water. Four hours later I began feeling feverish and delirious. These sensations continued for several hours and left me with a bad hangover. I would not repeat the experience.

Case #5 (21-year-old female secretary for a student newspaper)—

I took one teaspoon of nutmeg in water after reading about it in Malcolm X's autobiography. Nothing happened.

Case #6 (college junior)—

I took a whole can of nutmeg mixed with water. I had no effects at all from it.

Case #7 (medical student)—

When I was a junior in college at the University of Colorado, I got to know a group of nutmeg-takers because the leader of it had been a close high-school friend. In 1963, I went to his apartment for drinks, and he told me to take a matchboxful of ground nutmeg, packed into gelatin capsules. The method of these people was to take the nutmeg before they went to bed so that they would wake up high and avoid the nausea nutmeg often caused. Most said the effects were different from both morning-glory seeds and marihuana. Some experienced floating feelings. They took nutmeg occasionally for kicks, but did not attach too much importance to it. I do not know where they first learned of this habit, but my friend had worked as a volunteer in a prison before 1963 and may have been told about it there.

Case #8 (college sophomore)—

One evening my roommate and I each took a tablespoon of nutmeg in water after reading about it in Malcolm X's book. Nothing happened, so I went to bed. I woke up the next morning with incredible malaise and tachycardia. These symptoms eventually subsided but have recurred about once a week accompanied by severe anxiety for the past year. This reaction occurs spontaneously but also is brought on by eating anything containing more than a minute amount of nutmeg. One doctor has suggested that it may be an allergic reaction. My roommate had no effects except that he still cannot eat anything with nutmeg without experiencing an overpowering taste of the spice.

Case #9 (college junior)—

A friend told me about nutmeg and came over to show me how to do it. He mixed a drink of about half coffee and half nutmeg, which my roommate and I drank. Nothing happened to us in an hour, so we went to bed. Next morning I found myself on the floor with the worst hangover of my life. My roommate felt as bad. To this day neither of us can eat anything with nutmeg—we can't bear the taste.

Case #10 (a 42-year-old Berkeley woman who describes herself as "eccentric" with a "terrible fear of marihuana" and other drugs. After reading of nutmeg in a "manual of hallucinogenic drugs" she decided to try it since it was "cheap, legal, and available." She took nutmeg on several occasions and wrote extensively about her experiences. Here is one description.)—

I drank about five grams of nutmeg in a glass of fruit juice at about 9:30 a.m. An hour later I felt a surge of happiness when a freight train whistled. I closed my eyes

in search of hallucinations, but none came. A certain diuretic effect and pungent scent in my urine were evidence that the drug had already taken effect. I read the morning paper until 11:30 when there came a pleasant drowsiness. I closed my eyes and saw: silver spears of grass waving across an azure sky, silver waves of poplar trees swaying and dancing in the sun. I arose to walk and staggered. The light was flickering and dim as if I were partially blind, so I lay down on a couch in the kitchen. Closing my eyes again, I was overwhelmed by visions: golden spangles and rings of light on moving water, dancing moons and stars, everywhere a predominance of gold and silver images....

About 12:30 I opened my eyes and noticed that the stove was far, far away; the very walls had receded; the kitchen was cathedral-like in its dimensions. I stood up to look at myself, and I was unusually tall. My feet were small and far away; it was like looking through the wrong end of binoculars. I thought to myself, "This must be what marihuana is like."

The effect continued several hours until she fell asleep. There were no aftereffects.

## Conclusions

From these and other cases I draw the following conclusions:

1. Significant numbers of students and persons living in student communities attempt to induce hallucinations with Myristica.

2. Unlike prisoners or musicians, who resort to nutmeg when their supplies of standard drugs are cut off, students often take nutmeg as a first experience before they try Cannabis or other substances. Nutmeg and mace are cheap, legal, and available at the nearest grocery store.

3. Typically, the young nutmeg-eater first learns of the spice's psychoactivity from a friend or from a published reference.

4. Doses range from one teaspoon to a whole can of ground nutmeg. Almost always, the spice is drunk in a glass of juice or water.

5. Onset of action is commonly 2 to 5 or more hours after ingestion. Most neophytes are not aware of the delay. In a very common pattern of intoxication, a person takes an adequate dose of nutmeg in the evening, goes to bed after several hours of waiting in vain for effects, and wakes up the next morning with many of the physical symptoms of toxicity: malaise, headache, dry mouth, tachycardia, dizziness.

6. Some of the reported reactions to nutmeg must be purely psychological. A dose of one teaspoon is probably insufficient to cause true symptoms. Similarly, hallucinations or mental changes that come on within thirty minutes of ingestion are likely to be factitious.

7. Reactions to nutmeg vary from no mental changes at all to full-blown hallucinogenic experiences like those caused by hashish or LSD. There is no apparent correlation between dose and psychoactive effect. Might this extreme variability represent differences in pharmacological potency of different batches of nutmeg? Or do people vary greatly in their sensitivity to the active principle?

8. Visual hallucinations are rather less frequent with nutmeg than with drugs like LSD or mescaline, but distortions of time and space perception

with feelings of unreality are common, as with Cannabis. Sensations of floating, being transported aloft, or having one's limbs separated from the body are frequently reported.

9. Effects of a single dose of nutmeg usually subside within 12 to 48 hours An intriguing aftereffect occasionally mentioned is persistent sensitization to the taste of the spice.

10. Most young people who try nutmeg take it once or twice but do not use it habitually. Those who regularly smoke marihuana regard nutmeg as an inferior hallucinogen, largely because of the unpleasant side effects.

11. Ignorance of the psychoactive properties of nutmeg is unquestionably the most important factor limiting extent of its use as a drug.

I want to emphasize the last point. I began this general review by indicating the differences between nutmeg and other hallucinogens. From a public health viewpoint, the crucial difference is that most persons in the country have not yet heard that nutmeg is intoxicating. Not only is nutmeg cheap, legal, and available, it is also familiar, which makes it seem safe and inviting to those looking for a first hallucinogenic experience. These considerations lead to one inference: as publicity is accorded the psychopharmacological properties of Myristica, use of nutmeg and mace as intoxicants will certainly increase. Hopefully, we will soon have the knowledge to determine the dangers and potential values of this modern use of an ancient spice.

## BIBLIOGRAPHY


(*1*) FERGUSON, A. M. and J. FERGUSON. "All About Spices." Colombo, Ceylon, 1889.

(*2*) RIDLEY, HENRY N. "Spices." London, 1912.

(*3*) WARBURG O. "Die Muskatnuss." Leipzig, 1897.

(*4*) "What You Should Know About Nutmeg and Mace." New York, American Spice Trade Association, 1966.

(*5*) REDGROVE, H. STANLEY. "Spices and Condiments." London, 1933.

(*6*) U.S. Department of Commerce, Bureau of the Census figures complied by American Spice Trade Association, New York.

(*7*) GUENTHER, E. "The Essential Oils." New York, 1952.

(*8*) "The Pharmacopoeia of the United States of America." XV, Easton, Pa., 1955.

(*9*) POWER, F. B. and A. H. SALWAY. "The constituents of the essential oil of nutmeg." J. Chem. Soc., 91: 2037–2058, 1907.

(*10*) WEIL, ANDREW T. "Nutmeg as a Narcotic." Econ. Bot., 19: 194–217, 1965.

(*11*) GREEN, ROBERT C., Jr. "Nutmeg Poisoning." J. Amer. Med. Assoc., 171: 1342–1344, 1959.

(*12*) PURKINJE, J. E. "Einige Beitraege zur physiologischen Pharmakologie." Neue Breslauer Sammlungen aus dem Gebiete der Heilkunde. 1: 423–443, 1829; quoted in Hanzlik, "P. J. Purkinje's pioneer self-experiments in psychopharmacology." Calif. and Western Med., 49: July and Aug., 1938.

(*13*) WATSON, G. C. "Symptoms of poisoning after eating a quantity of mace." Prov. Med. Surg. J., Jan. 26, 1848.

(*14*) MCCORD, J. A. and L. P. JERVEY. "Nutmeg (myristicin) poisoning." J. S. Carolina Med. Assoc., 58: 436–438, 1962.

(*15*) CUSHNY, A. R. "Nutmeg poisoning." Proc. Royal Soc. Med., 1908–I: 39.

(*16*) PAYNE, ROBERT B. "Nutmeg intoxication." New Eng. J. Med., 269: 36–38, 1963. (Mention of this article was made a few weeks later in the "Medicine" section of TIME Magazine.)

(17) X, MALCOLM with ALEX HALEY. "The Autobiography of Malcolm X." New York, Grove Press, ~~1964.~~ 1965 PAPERBACK EDITION
(18) ALLDREDGE, NOAH L., Deputy Assistant Director, U.S. Bureau of Prisons. Personal communication, April 6, 1964.
(19) WEISS, GEORGE. "Hallucinogenic and narcotic-like effects of powdered myristica (nutmeg)." Psychiat. Quart., 34: 346–356, 1960.
(20) WEISS, GEORGE. Personal communication, April 18, 1964.
(21) BURROUGHS, WILLIAM. "Naked Lunch." New York, Grove Press, 1959.
(22) REISNER, ROBERT GEORGE. "Bird: The Legend of Charlie Parker." New York, Citadel Press, 1962.
(23) ANDRE, SIGRID. "Nutmeg jag." Mississippi Mag., 4: 18, 1964.

# The Chemistry and Psychopharmacology of Nutmeg and of Several Related Phenylisopropylamines

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Our report today has been divided into two separate portions. The discussion of nutmeg and its composition, and of the possible involvement of its chemical components. The psychotropic intoxication has a natural division into two areas of presentation. The first is a brief description of the plant; a presentation of the methods and procedures for the isolation and the identification of the many components in the oil from the plant, and a careful definition of those components that are most probably involved in the intoxicative syndrome.

The extension of these components in to the corresponding amphetamines, their effectiveness in humans, and the likelihood of their being an acceptable explanation of the effects of the total nutmeg, will constitute the latter part of this report. In the previous paper there was presented some of the history of nutmeg, and a description of the style and extent of its usage in various cultures. In the reports that will follow, specific descriptions of the human syndrome of intoxication, and some of the pharmacological ramifications of its study, will be presented.

At this point we would like to present a factual description of the various chemical materials that have been found to make up the volatile (and presumed active) fraction of nutmeg. On the hypothesis that one or more components may be appropriately assigned the responsible role for the nutmeg intoxication, there is a need for an exact chemical definition of nutmeg. But even before this, we must define in botanical terms just what is meant by the name nutmeg.

Properly the nutmeg tree is any plant found in the Genus *Myristica*. Two species are known to be native to India. *M. malabarica* produces a seed some four centimeters long and elliptically shaped, and *M. canarica* produces a small spherical seed about two centimeters across. Both contain primarily fats and myristic acid, and being virtually without odor or volatile oil have achieved no position of importance. In the East Indies the seeds of *M. succedanea*, known as "Pala Maba" in the Indonesian areas, are also small and quite elongate in shape, but they have proven valuable as rich sources of the nutmeg essential oils. Another species, *M. argentea*, has actually been used

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in the spice trade under the name of "New Guinea Nutmegs" or "Long Nutmegs". However the quantity and quality of the volatiles from its seeds are quite low. The plant that has achieved the widest study and commercial exploitation, and which is the subject of this portion of this symposium, is *M. fragrans*. This species originated in the Mollucas and has been propagated throughout the adjoining Indonesian islands, giving rise to the so-called East Indian nutmeg of commerce.

A little over a hundred years ago, the tree was introduced into the Carribean area and since the end of World War II has led to the establishment of a major industry. Grenada, of the windward islands, now supplies a major portion of the world's needs. The West Indian nutmeg is generally conceded as being of a somewhat lower quality than its East Indian forebears; the best grade of mace still comes from Asia.

The tree has also been translocated into Ceylon, and much of the early analytical work on the composition of the natural extracts was conducted on nutmegs from this source. It is no longer possible to obtain commercial samples with this designation however, and it must be assumed that any product from this area has been absorbed into the East Indian category.

The three areas of the plant *M. fragrans* that have received any analytical attention are the leaf, the arillode (which lies within the husk but outside of the shell of the seed, and which is known as mace), and the kernel of the seed itself, the nutmeg. The leaves have received only a cursory examination, which has indicated that although there is only a small amount of steam-distillable material present (about 1.5% of the dry weight) its composition is substantially the same as that of the plant parts associated with the seed (*1*). The studies that concern the volatile oils of mace are best presented later in direct comparison with the analysis of nutmeg itself. As it is only the nutmegs that are invested with the reputation of psychotropic efficacy, they have served as the primary focal point of our analysis.

The actual nutmeg, when removed from its hard brown shell or testa is a spherical kernel that weighs about five grams. The thorough work of Power and Salway (*2*) must serve as a definitive study of the composition of the entire nutmeg. There are two classical ways of extracting the potentially interesting materials from the whole fruit.

Figure 1 shows the approximate distribution to be expected with the employment of these methods. The process of expression, or the extraction with an organic solvent, provides about a third of the total original weight. This fraction is known as the fixed oils, and has also been called Nutmeg Butter or "Oleum Myristicae expressum". This fraction is substantially free of volatiles, and is composed primarily of triglycerides. Myristic acid is the principle compound here, although both oleic acid and linoleic acid are also found. This fraction has been used as a source of trimyristin (*3*). The small non-fat remainder is composed of unsaponifiable compounds, primarily oxygenated polyterpenes and phytosterols.

The subjection of the total crushed seed to distillation with live steam removes some 10 to 15% of the weight, known as the volatile oil fraction. The small overlap that is shown with the expression fraction is due to the

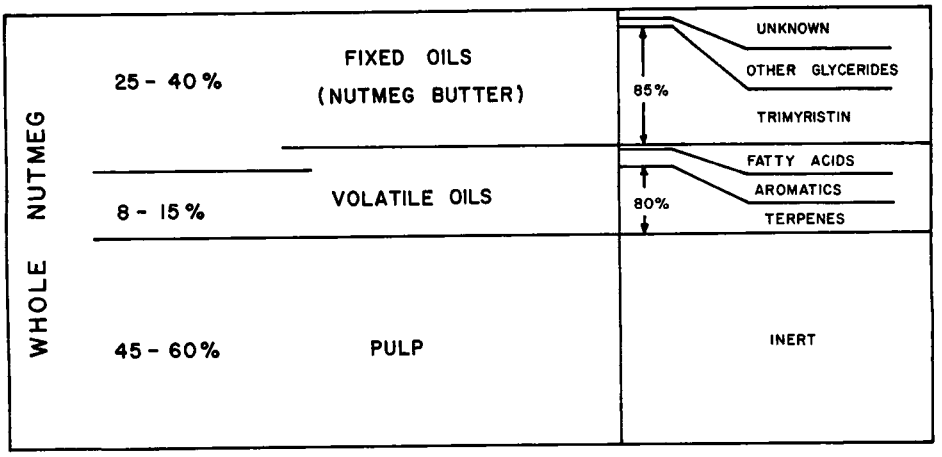



FIG. 1

fact that some of the volatile components are removed in the solvent extraction and are held tightly by the fixed components present. This volatile fraction is composed primarily of terpenes, which make up some 80% of its total weight. The remainder is the aromatic fraction, composed of ethers and phenolic bodies.

The residue that remains after the expression of the solubles and the distillation of the volatiles constitutes some 50% of the original mass of the nutmeg. It is presumably a cellulose-like pulp, and it remains totally unexplored as far as any chemical analysis is concerned.

It must be stated here, in anticipation of later discussions on the pharmacology of nutmeg, that no definitive evaluation of these fractions (fats and pulp) have been made. It has, however, been generally accepted that it is the volatile oil fraction to which one must look for the effective agents of nutmeg, and it is this "Oil of Nutmeg" that has been admitted to the U.S. Pharmacopeia as a medicinal. This oil comprises between an eighth and a twelfth of the entire fruit, and it serves as the object of the present study.

An exacting analysis of this volatile fraction has been performed. To this end a five pound sample of West Indian Oil of Nutmeg (from the George Lueders Company, New York) was subjected to fractional distillation employing a 70 tray Oldershaw column. Fractions were collected in a continuous sequence and each of these was in turn analysed and further fractionated employing a preparative gas liquid chromatographic procedure. Identity of each component was established by direct isolation, (employing a Varian A–700 Autoprep) and spectral comparison to reference samples (through infra-red and high resolution mass spectroscopy). Quantitative measurements were achieved employing a Varian Aerographer 1200 with a flame detector, and peak areas were established with an Aerograph 475 Integration System.

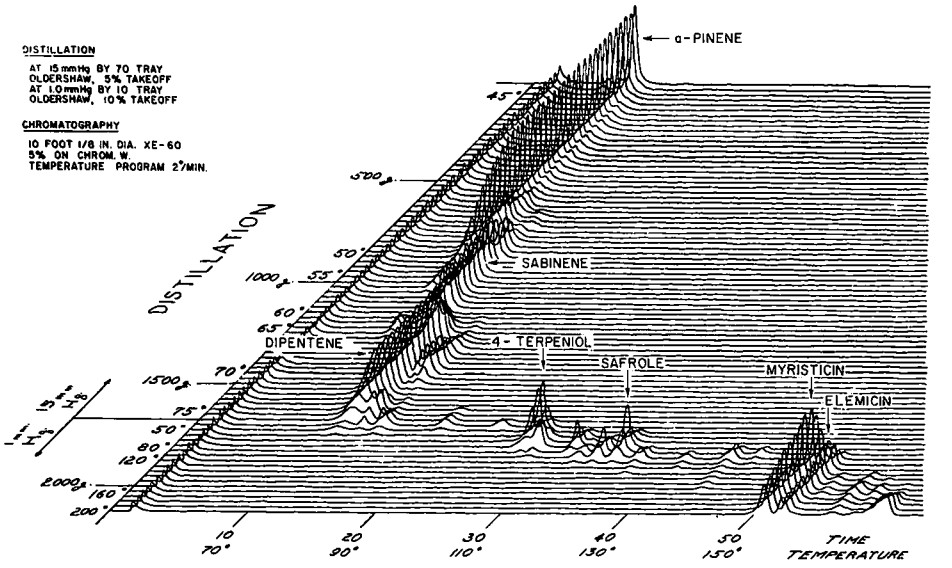



FIG. 2

Figure 2 shows what might well be called a fingerprint of the oil of nutmeg. On the z-axis is shown the results of the distillation. This was continued on the 70 tray column at 15 mm/Hg until the aromatic fraction was reached. Then the distillation was completed at 1 mm/Hg through a shorter column. Although the actual fractions collected were not exactly of 25 grams as is presented in the figure, the weights have been normalized to this amount, and each horizontal line thus represents an equal weight of distillate.

The x-axis represents the progress of gas liquid chromatographic separation. The time required for desorbtion of each of the peaks is shown, and as the system has been programmed for a rise of 2°/min., this also represents the temperature of desorbtion.

The y-axis is peak height and, as it is characteristic of temperature programmed GLC spectra to display a constant peak half-width, this height is proportional to peak area.

Several peaks (components) are obvious that would be superimposed by one of the techniques alone (GLC or distillation), but are readily separated by applying the other.

The long ridge down the left hand side of the presentation, parallel to the z-axis, represents the similar terpenes α-pinene, sabinine, and dipentene, and this is separated in a natural division from the second and smaller group, the aromatics.

The preponderance of α-pinene has been mentioned, but both sabinine and γ-terpinene (1, 4-menthadiene) warrant special note as neither has been observed in nutmeg before. The terpenyl alcohols have been included in this

group as are the two aromatic hydrocarbons cymene and the previously undetected toluene. On the other hand both cineole and camphor have been recently reported to be present to the extent of a percent or two, and citronellol and citronellal have been reported in trace amounts (*4*); none of these were present in the sample we investigated. d-Borneol, which had originally been assigned to nutmeg on indirect evidence (*5*) was not present in our sample.

The second and smaller group, the aromatic ether fraction, is the more interesting and as will be shown later is the more likely to be implicated in the psychopharmacology of nutmeg. In Table I are shown the nine aromatics that have definitely been established as being present in nutmeg, and it also shows the extent of their contribution to the sample analysed.

The three major components, myristicin, elemicin, and safrole constitute nearly 9/10 of the group. In the previously reported studies of nutmeg, myristicin has always been recognized as a major component, and has thus often been thought to be responsible for the psychopharmacological activity of the total extract. In the thorough study conducted on the Ceylonese Oil of Nutmeg (*5*) safrole was found only in very small quantities, but recently its identity as a significant component of East Indian oils has been reported, (*6*) although it appeared to be absent in the West Indian varieties.

COMPOSITION OF OIL OF NUTMEG
LUEDERS WEST INDIAN

| TERPENIC FRACTION | % | AROMATIC FRACTION | % |
|---|---|---|---|
| α-PINENE | 36.16 | SAFROLE | 1.29 |
| β-PINENE | 6.16 | METHYLEUGENOL | 0.62 |
| CAMPHENE | 2.97 | EUGENOL | 0.17 |
| SABINENE | 12.75 | METHYLISOEUGENOL | 0.36 |
| 1,4-p-MENTHADIENE | 3.47 | ISOEUGENOL | 0.19 |
| 1,4(8)-p-MENTHADIENE | 1.12 | MYRISTICIN | 7.04 |
| 1,8-p-MENTHADIENE | 12.78 | ELEMICIN | 2.36 |
| TOLUENE | 0.10 | ISOELEMICIN | 0.11 |
| p-CYMENE | 1.82 | METHOXYEUGENOL | 0.25 |
| l-MENTHENE-4-OL | 2.93 | | |
| l-MENTHENE-8-OL | 0.41 | OTHERS | |
| LINALOOL | 0.15 | MYRISTIC ACID | 2.87 |
| GERANYL ACETATE | 0.20 | UNIDENTIFIED | 3.72 |

TABLE I.

DISTRIBUTION OF THE PRINCIPLE AROMATICS IN VARIOUS MYRISTICA OILS

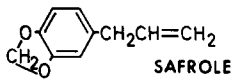
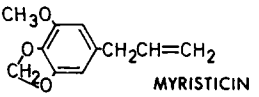
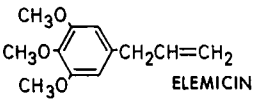
| | L. W.I. NUTMEG | F. W.I. NUTMEG | L. E.I. NUTMEG | F. E.I. NUTMEG | D. ? NUTMEG | L. ? MACE | F. E.I. MACE | D. ? MACE |
|---|---|---|---|---|---|---|---|---|
|  SAFROLE | 1.29 | 1.43 | 1.09 | 2.69 | 1.38 | 0.53 | 3.42 | 1.41 |
|  MYRISTICIN | 7.04 | 5.58 | 8.08 | 8.48 | 5.62 | 3.86 | 12.78 | 5.53 |
|  ELEMICIN | 2.36 | 0.02 | 0.48 | 0.02 | 0.99 | 2.07 | 0.05 | 0.69 |
| % OF TOTAL OIL THAT IS AROMATIC | 12.7 | 7.5 | 10.7 | 12.5 | 8.2 | 7.2 | 18.2 | 8.1 |
| % OF TOTAL AROMATIC THAT IS ACCOUNTED FOR ABOVE | 84 | 94 | 90 | 90 | 94 | 90 | 89 | 95 |

TABLE II.

We have made a comparative study of the aromatic fraction of several samples of Oil of Nutmeg from different geographical origins, and of Oil of Mace as well. These results are shown in Table II. Here the surprisingly wide variation that can occur between these principle components is apparent. The single consistent item is the presence of myristicin as a major component. In the figure the F found at the heads of the columns represents the source, Fritzsche Bros., New York. Similarly, L stands for Lueders Co. and D for Dreyers Co. The WI represents West Indian sources, and EI East Indian. The question marks refer to samples whose origin was undesignated. Safrole has been found in both East and West Indian oils and appears, in this analysis, to be present in an amount from 15–30% of the myristicin present. The amount of elemicin present is most erratic. It has been found to vary from over 2% in the Lueders West Indian Oil of Nutmeg, to only trace amounts in the Fritzsche samples. The various oils of mace show neither consistency nor correlation with the nutmeg samples, except that again, myristicin appears as the principle component.

The assignment of the chemical structures of these compounds is a direct and simple matter when compared to the task of assigning responsibility for the intoxicating and psychotropic properties of nutmeg. The kernel itself is the only component of the tree that is invested with the reputation for biological activity. Further, it may be asserted that the psychoactive compound or compounds probably reside in the volitale oil fraction of the nutmeg, for this fraction has been shown in animal toxicology studies to carry the effectiveness of the entire seed. Human experiments with ground nutmeg depleted of its volatiles have failed to show psychopharmacological responses (7).

With the satisfactory assignment of the identities of the various conspicuous components to be found in nutmeg, one must examine how each of these individually, or more likely in concert, may achieve a role in a reasonable explanation of the activity of the entire seed. Here there are two groups of compounds to consider, the terpenes and the aromatic eithers. It is tempting to dismiss the terpenes out of hand. Although they constitute by far the larger portion of the volatile fraction, the terpene hydrocarbons are generally held to be of biological effectiveness mainly as irritants. Turpentine has a composition quite similar in make-up to this terpene fraction; it has been widely used in many home remedies, but it has certainly not commanded reputation as an intoxicant. It may, however, have some function in assisting in the absorption of the various aromatic compounds through the gut.

The aromatic fraction, then, would seem to be the most likely source of the psychotropic activity of nutmeg. Table III shows the structure of each of the compounds we have found in the aromatic fraction. Also shown is the amount in milligrams of each of these components that would be present in 20 g. of the whole nutmeg, 20 g. being assumed to be that required to produce

AROMATIC FRACTION OF OIL OF NUTMEG

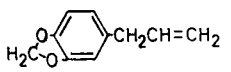
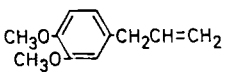
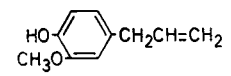
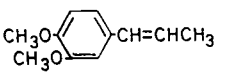
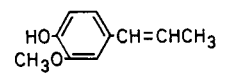
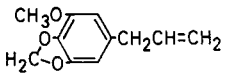
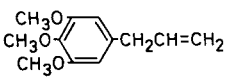
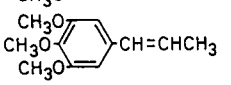
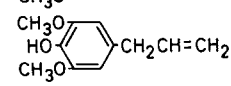
| STRUCTURE | NAME | AMOUNT TO BE FOUND IN 20 GRAMS TOTAL NUTMEG (IN MILLIGRAMS) |
|---|---|---|
|  | SAFROLE | 39 |
|  | METHYLEUGENOL | 18 |
|  | EUGENOL | 5 |
|  | METHYLISOEUGENOL | 11 |
|  | ISOEUGENOL | 6 |
|  | MYRISTICIN | 210 |
|  | ELEMICIN | 70 |
|  | ISOELEMICIN | 3 |
|  | METHOXYEUGENOL | 8 |

TABLE III.

psychotropic effects. As stated earlier, safrole, myristicin, and elemicin account for some 84% of the aromatic fraction, and thus are the primary materials that we will consider. The possibility must always be kept in mind that one of the minor components could have an unusually high potency and thus contribute to the activity.

Of the primary constitutents, myristicin is by far the most abundant, and for this reason was tested specifically for psychotropic activity by Truitt, *et al* (*7*). Doses of 400 mg. myristicin, almost twice the amount present in 20 g. of typical nutmeg, were given to human volunteers and the observed symptoms were at least suggestive of psychotropic effects in 6 out of 10 subjects. It will be seen later that those effects which might be expected from myristicin may be rather subtle, and so may require some synergistic activity of some of the other aromatic compounds to produce the full nutmeg syndrome.

Safrole is also a component of other natural oils and spices, the most notable being the Oil of Sassafras which contains some 80%. Both the oil and the derived sassafras tea have enjoyed wide use, modestly as a flavoring, and in larger amounts as an internal medicament; yet neither has a reputation for psychotropic activity as does nutmeg.

Elemicin is unusual in that among the flavoring oils and spices, it occurs in appreciable amounts only in nutmeg. Further, as mentioned earlier, even in nutmeg the amount of elemicin is highly variable and depends upon the source of the extract. It also occurs in several obscure essential oils, none of which have been reported to have been used pharmacologically. It is, further, not separable from myristicin by fractional distillation. The myristicin employed in all earlier pharmacology (including the human studies mentioned) was obtained by distillation from oil of nutmeg, and was taken to be the single substance myristicin. It thus may or may not have contained elemicin as well, depending on the origin of the oil. The variability of elemicin may account for the apparently highly variable degree of reported psychoactive effects of nutmeg, which in turn implies that elemicin may indeed be an active component. Of the aromatic components present in lesser amounts, only eugenol and isoeugenol have found use either as flavoring agents or as medicinals. They comprise about 80% of the Oil of Cloves for example, but again search of the literature on such natural products for some reputation for abuse as an intoxicant has been futile.

There are thus several possibilities by which one or more of the aromatic components might be implicated as psychotropic agents;

1. One of the compounds that is present only in very small amounts may have unusually high potency,
2. Elemicin may be a major contributor of activity, or
3. A combination of two or more of the aromatics present may be involved. The three most abundant ones, myristicin, elemicin and safrole may be sufficient to account for the total activity.

It is worth noting that nutmeg is the only plant source within which these three compounds have been reported as occuring together in any appreciable

quantity, and as will be seen later, each may contribute slightly different aspects to the total psychotropic effect.

With the exception of myristicin none of the individual components of the aromatic fraction have been evaluated specifically as to their psychological effects. The ring substitution patterns of these compounds are notable in that several of them, specifically myristicin, elemicin and safrole, are identical to the ring structures of materials of established psychotogenic activity. The allylic side chain is amenable to chemical modification, as shown is Fig. 3, which could convert the naturally occuring compounds into ones of known psychotropic activity. It has been suggested (*8*) that the *in vivo* addition of ammonia to the olefinic site in either the allyl or the propenyl isomer would yield amphetamines directly. To speak of amphetamines as a chemical class is not strictly correct, but we use it to refer to variously methoxylated phenylisopropylamines. The "RO" in the figure indicates the presence of any variety of ether groups on the ring, and thus would include all of the aromatic ethers in the oil of nutmeg and in many other natural oils as well. The possible mechanisms of such an *in vivo* transformation have been elaborated upon, and are plausible to the extent that each of the reactions has been achieved *in vitro*. Support for this transformation occurring *in vivo* has been obtained by Barfknecht (*9*), who found evidence for the production of amphetamine in rats after feeding them allylbenzene. This corresponds to ammonia addition in Fig. 3 without the "RO" ether groups.

## CONVERSION OF AROMATIC ESSENTIAL ETHERS TO ALKOXYAMPHETAMINES

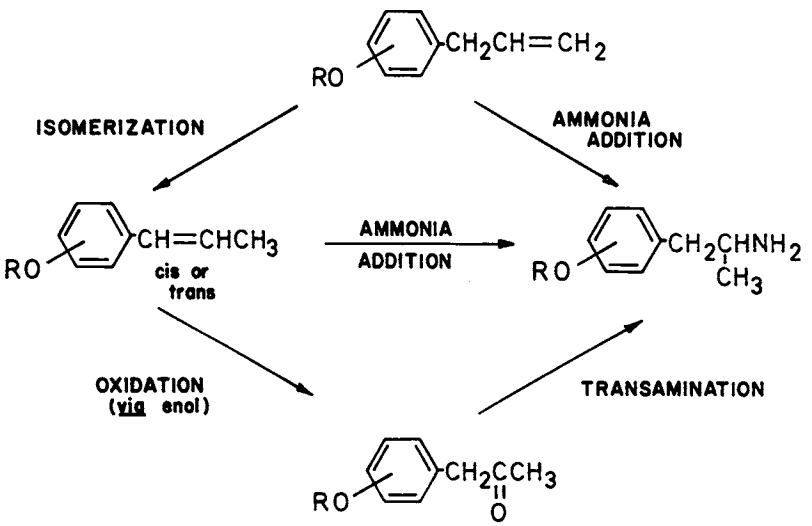


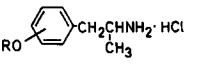

FIG. 3.

Throughout the general area of spices and of essential oils from plant sources there is about a score of substituted phenylpropenes, all of which are characterized by ring substitution of either methoxy groups or a methylenedioxy group (or both) and by the allyl or the propenyl side chain mentioned above. Of these a total of eleven different ring substitution patterns have been reported as occuring; the balance of the twenty known aromatics consists of isomeric variations of the side chain. The addition of an amine to this olefinic system might be extremely sensitive to substitutions near it, that is, whether the side chain be allyl, *cis*-propenyl or *trans*-propenyl. It may thus be in turn a determining factor in the psychotropic activity of any such substance under consideration.

In the preparation for the study of this possible *in vivo* amination of these ring-substituted natural oils, a series of amphetamines that would be the result of such an addition has been completed. These are tabulated in Table IV, showing the principle natural source of each of the natural oils, the common name as they occur in the allyl (A) or propenyl (P) form, the orientation of the ring substituents, the code letter abbreviation of the resulting base, the cogent physical and chemical data, and the potency of the compound in mescaline units. The latter measure is defined as the quotient of the effective dose of mescaline (assumed to be 3.75 mg/Kg as the base) divided by the effective dose of the substance in question, as determined by human titration. This ratio permits a direct comparison of relative potencies, based on mescaline equaling one. Mescaline has a ring substitution pattern identical with number 6, TMA, except that the side chain has only two carbons instead of three.

It will be noted that several of the possible amphetamine derivatives of the components of the aromatic fraction of nutmeg do not appear here;

**AMPHETAMINES RELATED TO THE NATURAL ESSENTIAL OILS**




| | COMMON NAME | PRINCIPLE SOURCE | RING ORIENTATION | CODE | SYNTHETIC ROUTE | M.P.°C. | YIELD | POTENCY MESCALINE=1 |
|---|---|---|---|---|---|---|---|---|
| 1. | ESTRAGOLE (A) | O. OF ANICE | 4-$OCH_3$ | MA | A | 211 | 60 | ? |
| 2. | NOTHOSMYRNOL (P) | O. OF N.JAPANICUM | 2,4-$(OCH_3)$ | 2,4 DMA | A | 147 | 90 | ? |
| 3. | METHYLEUGENOL (A) | O. OF CITRONELLA | 3,4-$(OCH_3)$ | DMA | A | 147 | 76 | ? |
| 4. | SAFROLE (A) | O. OF SASSAFRAS | 3,4-$(OCH_2O)$ | MDA | A | 186 | 29 | 2 |
| 5. | ASARONE (P) | O. OF CALAMUS | 2,4,5-$(OCH_3)$ | TMA-2 | B | 181 | 60 | 18 |
| 6. | ELEMICIN (A) | O. OF ELEMI | 3,4,5-$(OCH_3)$ | TMA | A | 209 | 63 | 2 |
| 7. | CROWEACIN (A) | O. OF E.CROWEI | 2-$OCH_3$-3,4-$(OCH_2O)$ | MMDA-3a | A | 154 | 59 | 18 |
| 8. | MYRISTICIN (A) | O. OF NUTMEG | 3-$OCH_3$-4,5-$(OCH_2O)$ | MMDA | B | 191 | 60 | 3 |
| 9. | — (A) | O. OF PARSLEY SEED | 2,3,4,5-$(OCH_3)_4$ | Tetra MA | C | 136 | 13 | ? |
| 10. | DILLAPIOLE (A) | O. OF DILL | 2,3-$(OCH_3)_2$-4,5-$(OCH_2O)$ | DMMDA-2 | C | 130 | 94 | ? |
| 11. | APIOLE (A) | O. OF PARSLEY SEED | 2,5-$(OCH_3)_2$-3,4-$(OCH_2O)$ | DMMDA | B | 175 | 64 | ? |

A: VIA BENZALDEHYDE, NITROETHANE, $LiAlH_4$.
B: VIA CLAISEN REARRANGEMENT, METHYLATION, ISOMERIZATION, $C(NO_2)_4$, $LiAlH_4$.
C: VIA NATURAL ALLYL COMPOUND, ISOMERIZATION, $C(NO_2)_4$, $LiAlH_4$.

TABLE IV.

namely those which contain an OH substituent in addition to the methoxyl groups. These comprise some 5% of the aromatic fraction, and still remain to be explored in the human subject, either as purified components themselves, or as their amphetamine extensions. Should the free hydroxyl group of any of these several materials confer an unusually high psychotropic potency on any of these compounds or on the corresponding amphetamines, this would contribute to the nutmeg intoxication beyond the explanations considered here. Eugenol itself has had some known medical uses however, and it would seem reasonable to expect that its psychotropic activity would have been noted had it existed.

Published detail has appeared on the psychotropic effects in normal human subjects for the four compounds that are trisubstituted, numbers 5, 6, 7 and 8 (*10*). In every case the compounds had a greater potency than that of the reference substance mescaline.

The base that corresponds to safrole, number 4, is 3,4-methylenedioxyamphetamine, or MDA. This was first described pharmacologically by Gordon Alles (*11*) who reported visual effects at some 120 mg. Subsequent experience (*12*) on a more extensive number of subjects has shown modest, if any, distortion or change of either visual or auditory perception, but rather a pronounced increase in emotional effect, which has proved to be of considerable value in psychotherapy.

The base that would be the result of the addition of ammonia to myristicin, number 8, is 3-methoxy-4,5-methylenedioxyamphetamine, or MMDA. A complete description of the animal and human pharmacology and psychopharmacology of this compound is forthcoming (*13*). With regard to the work mentioned earlier in which 400 mg. of myristicin was tested in human subjects, the experience with MMDA indicates that the effects although identifiable in a psychotherapeutic setting, or in subjects trained to identify psychotropic effects, are rather subtle and may not have been detected by the psychological tests used in the study. The psychotropic effects of MMDA are rather similar to those of MDA, but in addition some 30% of the subjects reported rather vivid and well structured visual images appearing when the eyes are closed, although there are virtually no changes in eyes-open perception. The possibility that myristicin in the amounts present in nutmeg may contribute to the total effects of nutmeg, cannot at this point be discarded.

The base that corresponds to number 6 is 3,4,5-trimethoxyamphetamine, TMA. This has been known as a psychotropic agent for some time (*14*, *10a*). It has variously been described as having potent hallucinatory effects and as leading to apparently hostile reactions. More extensive appraisal of this compound in psychotherapeutic settings has confirmed the eyes-opened distortions and occasional hallucinatory phenomena, and strongly suggests that its characteristic property is one of causing projection, in the psychological sense, by the subject. This can produce visual distortions, delusions (alterations in social perceptions), and sometimes apparently hostile projections which, however, have never led to any overt actions.

The analogous bases that correspond to the eugenols have not yet been evaluated, and as mentioned earlier represent another group of compounds that could contribute to the activity of nutmeg.

There are two ways in which further investigations might be pursued; namely human evaluation of the individual compounds of the aromatic fraction of the oil of nutmeg, preferably synthetically derived to avoid contamination, and secondly, the further evaluation of the effects of the amine derivitives. It is entirely possible that the combination of the amines derivable from the essential oil aromatics could produce the psychological effects of nutmeg, while the clearly toxic effects could be due to the terpene fraction. Human evaluation of a mixture of these amines, in the proportions found in nutmeg, would explore the possibility of any synergistic amplification of the activity of these compounds. A corollary study would involve the chemical investigation of the metabolic fate of both the essential oils and the derived amines, on administration to human subjects, and may clarify whether or not these oils are in fact converted to amines *in vivo*. From the results of these studies, it is hoped that the interrelationship between the complex composition, and the yet more complex psychopharmacological structure of nutmeg, can be resolved.

## REFERENCES


(*1*) "Essential Oil from the Leaves of Nutmeg (*Myristica fragrans* Houtt.)", Th. M. Meyer. Ing. Nederland.-Indie 8 No. 1 VII 7–8 (1941). (CA 35: 4549[4]).

(*2*) "The Constituents of the Expressed Oil of Nutmeg", F. B. Power and A. H. Salway, J. Chem. Soc., 93: 1653 (1908).

(*3*) "Trimyristin", O. D. Beal, Org. Syn., Coll. Vol. I., Second Edition p. 538 (1941).

(*4*) "Application of Gas Chromatography to a Study of Nutmeg Oil Flavor", G. D. Lee, F. L. Kauffman, J. W. Harlan and W. Niezabitowski, Intern. Gas Chrom. Symp., I.S.A. Proc. 301 (1961).

(*5*) "The Constituents of the Essential Oil of Nutmeg", F. B. Power and A. W. Salway, J. Chem. Soc., 91: 2037 (1907).

(*6*) "Gas Chromatographic Analysis of Oil of Nutmeg", E. A. Bejnarowicz and E. F. Kirch, J. Pharm. Sci., 53: 988 (1963).

(*7*) "The Pharmacology of Myristicin, A Contribution to the Psychopharmacology of Nutmeg", E. B. Truitt, Jr., E. Callaway III, M. C. Braude, and J. C. Krantz, Jr., J. Neuropsych. 2: 205 (1961).

(*8*) "Possible Implication of Myristicin as a Psychotropic Substance", A. T. Shulgin, Nature 210: 380 (1966).

(*9*) C. F. Barfknecht, University of Idaho (personal communication).

(*10*) *a*. "The Psychotomimetic Properties of 3,4,5-Trimethoxyamphetamine", A. T. Shulgin, S. Bunnell and T. Sargent, Nature, 189: 1011 (1961); *b*. "3-Methoxy-4, 5-Methylenedioxyamphetamine, a New Psychotomimetic Agent", A. T. Shulgin, Nature 201: 1120 (1964); *c*. "Psychotomimetic Amphetamines; Methoxy 3,4-dialkoxyamphetamines", Experientia 20: 366 (1964).

(*11*) "Some Relations between Chemical Structures and Physiological Action of Mescaline and Related Compounds." G. A. Alles, in Neuropharmacology, The Josiah Macy Jr. Foundation, Madison Printing Co., Inc., 1959.

(*12*) "The Psychological Effects of 3,4-Methylenedioxyamphetamine (MDA) Intoxication." C. Naranjo, T. Sargent and A. T. Shulgin (in preparation).

(*13*) "The Chemistry and Pharmacology of 3-Methoxy-4,5-methylenedioxyamphetamine (MMDA)." A Monograph. C. Naranjo, T. Sargent and A. T. Shulgin (in preparation).

(*14*) "A New Hallucinogen: 3,4,5-Trimethoxyphenyl-β-aminopropane, with notes on the stroboscopic phenomenon." D. I. Peretz, J. R. Smythies and W. C. Gibson, J. Mental Sci., 101: 316 (1955).

# The Pharmacology of Myristicin and Nutmeg

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The long history of observations concerning the pronounced psychotropic effect of Myristica fragrans (nutmeg) has not gone unnoticed by many distinguished investigators, including some famous pharmacologists. A central problem in the pharmacology of nutmeg has been identification of the active component of the crude drug. As early as 1676, van Leeuwenhoek, the original microscopist noted that a volatile component which evolved from pieces of nutmeg in a glass tube repelled or killed mites. (*1*) Although Warburg, as late as 1897, still expressed doubt (*2*) it was clear by then that the volatile fraction, the oil of nutmeg, was more toxic than the crude drug. The well-known English pharmacologist, Cushny, stated that the residue from which the volatile oil has been removed has no effect upon animals. (*3*) In our early studies at Maryland, we confirmed this observation by human testing of a steam-distilled residue and noted only gastrointestinal effects. (*4*)

Another pharmacologist, George Wallace, used the highest distillate fraction (149°C, 14 mm), which he found to be the most active and easily administered component, and observed that the cat was the most susceptible species among the mammalia to the toxic action of the drug. (*5*) Both Wallace and, a year later, Jurss (*6*) correctly attributed the high toxicity to hepatic fatty degeneration, but the cat is also most sensitive to the central excitation, tremor, salivation, and stupor produced by oil of nutmeg. Sir Henry Dale in 1907 most clearly differentiated the primary psychotropic effect from the secondary hepatic coma causing death in cats. (*7*) Although he noted, as others had, that the oil required a higher myristicin amount than the crude drug in order to produce symptoms, Dale attributed this to absorption difficulties with the purified product. Power and Salway, re-examining the question in 1908, concurred that myristicin was probably responsible for the central effect, but was unfavorable for absorption in the pure state. (*8*)

Pharmacologic interest in nutmeg then subsided for more than 50 years, until renewed by the curiosity of Dr. John C. Krantz at the University of Maryland who was consulted by several former students encountering cases of nutmeg intoxication. (*4*) This study was conducted with a myristicin-containing fraction distilled from oil of nutmeg at 145–155°C and 15 mm Hg pressure. Subsequent gas-chromatographic studies by Shulgin have shown this to be a mixture of myristicin with elemicin and perhaps a small amount of methylisoeugenol. (*9*)

Initial studies on the pharmacologic action of myristicin and nutmeg which were conducted at the University of Maryland sought to answer

a variety of questions. (*4*) Toxicity studies showed that the East Indian spice was more toxic than a West Indian product. Animal toxicity determinations before and after steam distillation also confirmed Cushny's original observation that the volatile fraction was more toxic than the residue (*3*) In planning for human administration of a dose of the myristicin-elemicin fraction amounting to 400 mg per subject, a chronic study in rats was conducted and showed no growth inhibition at a daily dose of 10 mg/kg.

A stimulant effect of myristicin was demonstrated by a shortening effect of the oil fraction on barbiburate sleeping time. These data are shown in Table 1.

TABLE 1.—*The effect of myristicin on the sleeping time induced by phenobarbital in the rat*

| Group | Mean sleeping time | Standard error | p value |
|---|---|---|---|
| Phenobarbital 120 mg/kg I. P | 162 min | ±5. 31 | |
| Phenobarbital 120 mg/kg I. P. plus 100 mg/kg myristicin I. P | 144 min | ±2. 27 | <0. 01 |

The intravenous injection of large doses in the order 50–76 mg/kg to dogs, monkeys, and cats confirmed the feline species toxicity and showed clearly that tranquilization of wildness is not produced in the jungle-bred monkey. It is of interest that the product was hypotensive in the dog as are other monamine oxidase inhibitors. These intravenous injections were suspensions of the oily substance in acacia solution. More recently a stable emulsion has been achieved having the following composition:

| | *Percent* |
|---|---|
| Myristicin | 1.0 |
| Pluronic F–68 | 0.3 |
| Dextrose | 4.2 |
| Ethyl alcohol | 1.0 |
| Distilled water qs | 100.0 |

Using this formula, mice were injected into the dorsal tail vein with doses of 100 mg/kg. Within 1 to 2 minutes, loss of righting reflex and apparent sedation appeared.

One contribution to the metabolism of myristicin has recently evolved from interest in its synergistic effect upon other insecticides. Casida and his associates have shown that the methlyenedioxy bridge is the initial point of metabolic attack by hepatic microsomes and requires $NADPH_2$ (*10*). This reaction is shown in Figure 1. This metabolic transformation increases the chemical similarity of myristicin to the catecholamines.

The structural resemblences of myristicin to mescaline and epinephrine prompted studies directed at measuring competitive inhibition of myristicin to other monoamine oxidase substrates. The method of Tedeschi et al, (*11*) was employed for estimation of monoamine oxidase (MAO) inhibition by potentiation of the central convulsant action of tryptamine HCl. A 0.5%

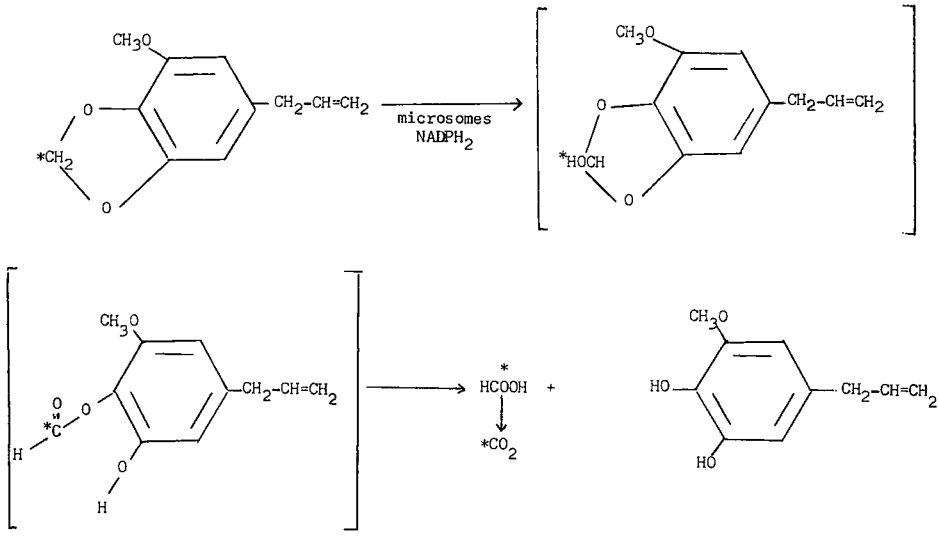


FIG. 1.—Major metabolic pathway for methylene $C^{14}$ dioxyphenyl labeled myristicin in liver microsomal systems of the mouse. (Modified from Casida, et al. (10).)

solution was injected intravenously into 10 mice per dose level. Three seconds or more of clonic jerking, tremors, and/or side-to-side head movements were the endpoint criteria used to calculate the $CD_{50}$ from dose-response lines by the method of Rubin et al. (*13*) in rats, scoring both eyes on a 5-point scale. Cerebral 5-hydroxytryptamine was measured by the Mead and Finger modification (*14*) of the method of Bogdanski et al. (*15*)

## Results

No apparent effect was evident from the drug vehicles on the $CD_{50}$ of tryptamine (Table 2). When given orally 18 hours in advance, East Indian ground nutmeg gave some evidence of tryptamine potentiation (Figure 2). The optimum dose was 500 mg/kg. However, a much larger dose, 1000 mg/kg showed reversal of the activity.

Several samples of synthetic myristicin [1] were tested by the tryptamine potentiation test 18 hours after their oral administration. These results are shown in Figure 3. Both of these preparations showed considerable activity when the sample was fresh and lemon yellow in color. Later tests (not shown) after the liquid had turned to a light amber color consistently showed a considerable decline in tryptamine potentiation. These deteriorated solutions when studied by gas chromatography showed the appearance of an unknown component in addition to the myristicin.

The distilled concentrate of oil of nutmeg was much less active than the synthetic myristicin and, like ground nutmeg, reversed its activity with a

[1] Synthetic myristicin was kindly made available by Dr. Carl D. Lunsford, A. H. Robins Company, Richmond, Virginia.

TABLE 2.—*Tryptamine convulsion test for monoamine oxidase inhibition* in vivo. *Summary of control tests*

| Species | No. | Vehicle-18 hr prior, cc/kg | $CD_{50}$, mg/kg | 95% confidence limits, mg/kg |
|---|---|---|---|---|
| Mouse | 40 | None | 25.0 | 15.4–40.5 |
| " | 21 | " | 17.3 | 12.1–24.7 |
| " | 28 | Liq. pet. | 24.5 | 19.9–30.1 |
| " | 38 | " " | 28.0 | 18.4–42.6 |
| " | 37 | Acacia-2% | 25.8 | 18.3–36.3 |
| Avg | 164 | | 25.0 | 21.6–29.0 |
| Rat | 54 | None | 18.6 | 13.6–25.5 |

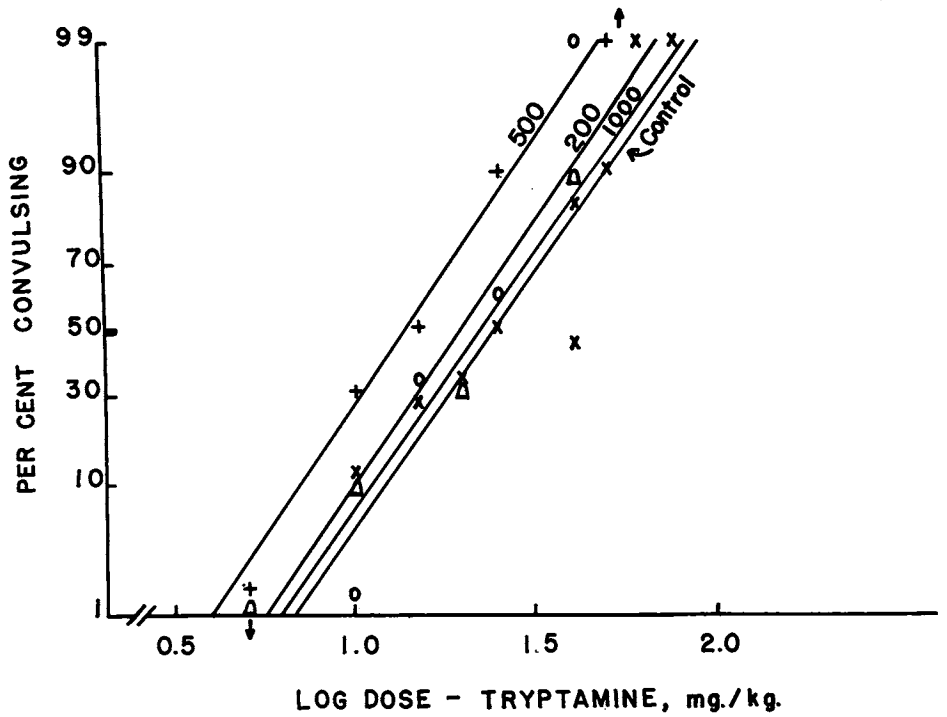


FIG. 2.—Effect of ground nutmeg on tryptamine convulsive threshold in mice when given orally in acacia suspension 18 hr before test: X——X Control, $CD_{50}$ mg/kg (±95% confidence limits) 25.0 (15.2-41.0); ○——200——○ 200 mg/kg nutmeg, 20.0 (14.2-28.2); +—500—+ 500 mg/kg nutmeg, 14.0 (10.1-19.5); △——1000——△ 1000 mg/kg nutmeg, 23.0 (16.1-32.9).

large dose (Figure 3). Gas-chromatographic analysis of this oil showed the presence of volatile components similar to ground nutmeg, but no increased concentration of the myristicin, as expected from the selected distillation temperature.[2]

[2] These analyses and supplies of ground nutmeg were kindly furnished by Dr. William K. Stahl, McCormick and Company, Baltimore, Maryland.

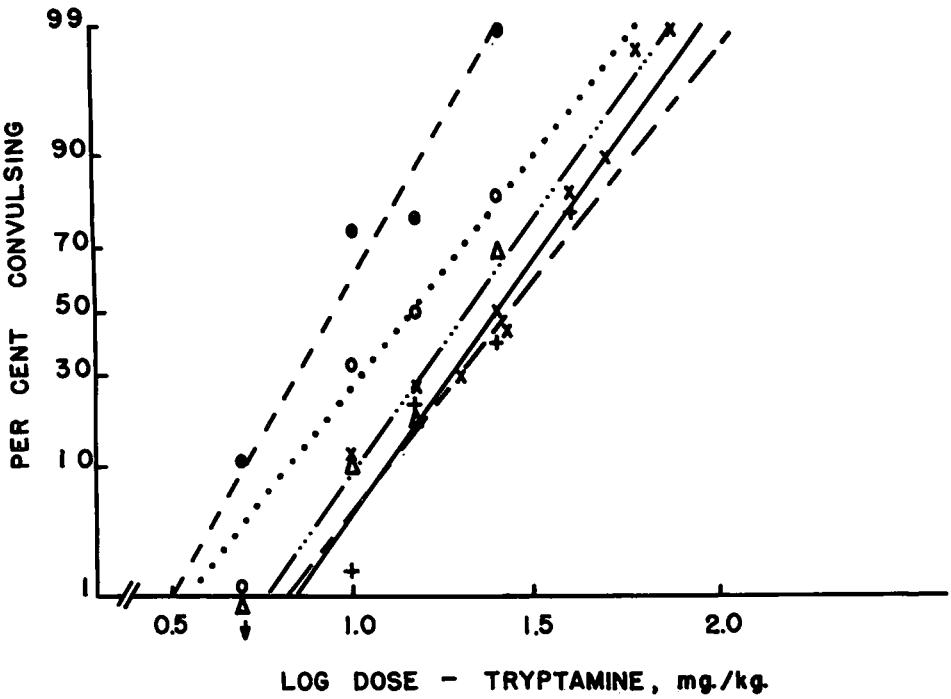


FIG. 3.—Effect of synthetic myristicin samples and oil of nutmeg concentrate on tryptamine convulsive threshold in mice when given orally in acacia suspension 18 hr before test: X— — —X Control, $CD_{50}$ mg/kg (±95% confidence limits) 25.0 (15.2-41.0); ○——○ Myristicin sample 1 at 500 mg/kg, 8.7 (5.7-13.4); ○— . . . ○ myristicin sample 2 at 500 mg/kg, 14.0 (9.3-21.0); . . . . . oil of nutmeg concentrate 500 mg/kg, 20.5 (14.5-28.9); +— — —+ oil of nutmeg concentrate — 1000 mg/kg, 27.0 (19.9-36.7).

In Figure 4 the slope and activity of the best tryptamine assay for myoisticin is compared to tranylcypromine and iproniazid. All three drugs were administered orally 18 hours before the test. It may be seen that myristicin is less potent but parallel to the comparative drugs. Safrole, isoborneol, and geraniol, which are other volatile components of nutmeg, did not cause potentiation of tryptamine in doses up to 1 g/kg despite obvious signs of hyperactivity and excitement in the mice.

In Figure 5 the antagonism of reserpine ptosis in rats was used to study variations in dose and time for myristicin activity. Myristicin appears to be less active in the rat. Comparable activity to other MAO inhibitors was obtained only with the largest dose 17 hours after oral administration.

Myristicin treatment of six rats increased brain 5-hydroxytrptamine from control values averaging 0.48 (± 0.05) μg/g to 0.82 (± 0.03) μg/g when given in an oral dose of 1 g/kg; the difference was statistically significant ($p<0.001$). Lower doses were not significantly active.

A further test of an hypothesis of monoamine oxidase inhibition was conducted using the kynuramine disappearance rate in brain homogenates as

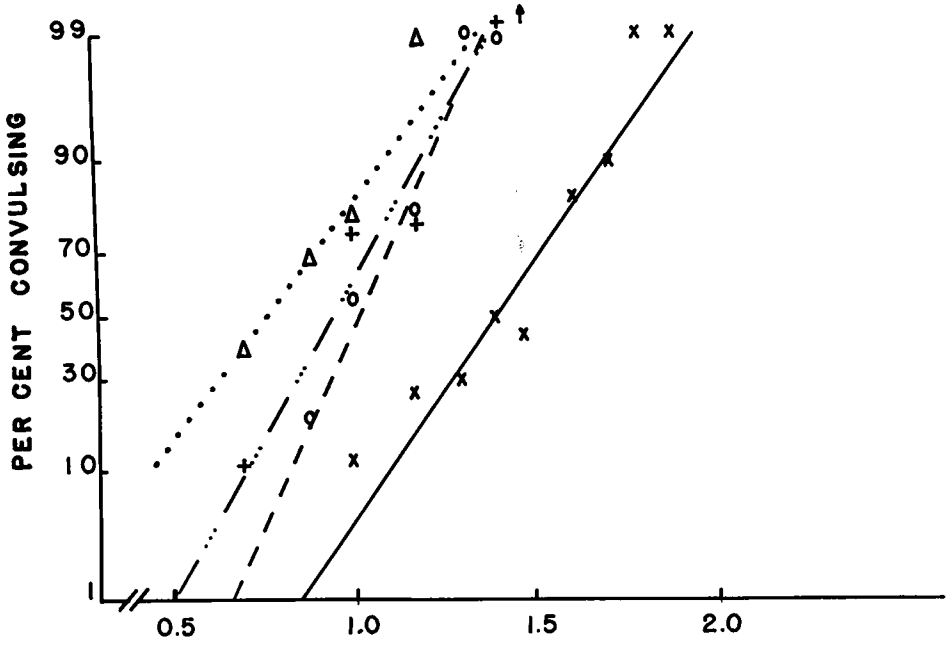


FIG. 4.—Effect of monoamine oxidase inhibitors and synthetic myristicin on tryptamine convulsive thresholds in mice when given orally in acacia suspension 18 hr before test: X———X Control, $CD_{50}$ mg/kg (±95% confidence limits) 25.0 (15.2-41.0); ○——○ 150 mg/kg iproniazid, 10.4 (8.8-12.2); △. . . .△ 4 mg/kg tranyleypromine, 5.8 (4.4-7.7); +— . . . + 500 mg/kg, 8.7 (5.7-13.4).

described by Weissbach et al. (*16*) The results of this test are shown in Table 3. Slight inhibition was found in the mouse but not in the rat-brain preparation. One year after these data were obtained, the same ground-nutmeg source was completely inactive in the mouse as well, and the declining activity was attributed to a loss of volatile components owing to a nearby heater.

## Discussion

Although the myristicin fraction from oil of nutmeg originally used in these experiments might not represent 100 percent myristicin, both this and elemicin most likely produce similar actions. The potency of myristicin is not adequate in most of these tests to account for the full action of nutmeg. The insufficiency is present with intravenous doses and therefore poor absorption is not a likely explanation. More rapid biodegradation of purified myristicin in contrast to its slow release from nutmeg might suggest a greater efficiency of the crude drug.

These data demonstrate a mild degree of monoamine oxidase inhibition by a variety of tests. The low potency of myristicin in comparison to tranylcypromine, a potent inhibitor, is in keeping with the large doses required for *in vivo* activity. The tryptamine potentiation test, although indirect, has been

shown to correlate with other *in vivo* assays. (*17*) It is quite likely that although myristicin displaces kynuramine from MAO with difficulty, it still may show inhibiting activity.

The main virtue of these data may be to reawaken interest in myristicin and its activity. Low activity of a prolonged nature, such as that shown by nutmeg, is sometimes a more useful drug attribute than high potency and rapid onset. An important question remains to determine if the myristicin stimulation is inevitably followed by depressed feelings, even upon continued intake. Work is indicated to improve absorption, and further pharmacologic studies are needed to define a proper course of treatment for nutmeg intoxication.

## Summary

A myristicin-elemicin fraction of oil of nutmeg produces many of the characteristics of crude ground nutmeg, but lacks adequate potency to explain the nutmeg intoxication syndrome on a quantitative basis. Nutmeg and

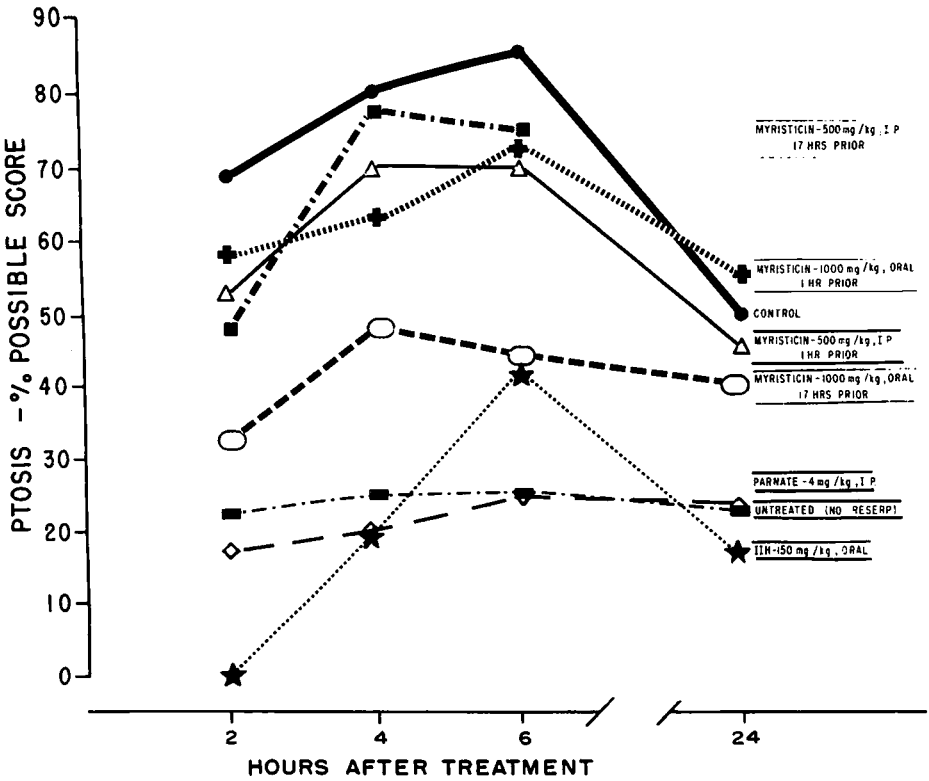


FIG. 5.—Effect of monoamine oxidase inhibitors and various schedules of myristicin on reserpine ptosis in rats. Ptosis score: 0=Eyelid fully open—5=Eyelid fully closed. Maximum score = 10/rat (both eyes). Group ptosis score (%)

$$= \frac{\text{No. rats/group X Max score/rat}}{\text{Sum of group eyelid scores}} \text{ X } 100.$$

TABLE 3.—*The effect of ground West Indian nutmeg on brain monoamine oxidase (MAO) activity in mice and rats measured by the kynuramine (Kyn) method of Weissbach, et al. (16)*

| Species | No. | μM-ynK/mg/hr x $10^{-3}$ [a] | No. | Nutmeg treated [b] percent of control |
|---|---|---|---|---|
| Mouse | 14 | 3.64±0.013 | 10 | 78.0±4.2% |
| Rat | 6 | 4.74±0.18 | 5 | 104.0±5.5% |

[a] Micromoles of kynuramine/mg of brain (wet weight)/hour x $10^{-3}$.
[b] 18 hours after 500 mg/kg—mice or 1000 mg/kg—rat, P.O.

the synthetically made myristicin demonstrate a mild degree of monoamine oxidase inhibiting activity by *in vitro* and *in vivo* tests. Activity of this synthetic product declines with aging accompanied by color change. Monoamine oxidase inhibition and other actions of crude extracts depend upon the volatile component.

## BIBLIOGRAPHY


(*1*) HANZLIK, P. J., "Purkinje's Pioneer Self-experiments in Psychopharmacology," California and Western Medicine, 44 : 1, July–August, 1938.
(*2*) WARBURG, O. "Die Muskatnuss" Leipzig, 1897.
(*3*) CUSHNY, A. R., "Nutmeg Poisoning." Proceedings of the Royal Society of Medicine 39 : I(3), 1908.
(*4*) TRUITT, E. B., Jr. E. CALLAWAY, III, M. C. BRAUDE, and J. C. KRANTZ Jr., Journal of Neuropsychiatry, 2 : 205, 1961.
(*5*) WALLACE, G. B., In Contributions to Medical Research, Vaughn, Ann Arbor, Michigan, 1903, pp. 351–364.
(*6*) JURSS, F., "On Myristicin and Some Closely Related Substances," Berichte, Schimmel & Company, Leipzig, 1904.
(*7*) DALE, H. H., Proceedings of the Royal Society of Medicine, 23 : 69, 1909.
(*8*) POWER, F. B. and A. H. SALWAY, American Journal of Pharmacology, 80, 563–580, 1908.
(*9*) SHULGIN, A. T., Nature (Lond.), 197 : 379, 1963.
(*10*) CASIDA, J. E., J. L. ENGEL, F. G. ESAAC, F. X. KAMIEUSKI, AND KUWATSUDA. Science, 153 : 1130–1133, 1966.
(*11*) TEDESCHI, D. H., R. E. TEDESCHI, E. J. FELLOWS, Journal Pharmacology and Experimental Therapeutics, 126 : 223, 1959.
(*12*) LITCHFIELD, J. T., AND F. WILCOXON. ibid., 96 : 99, 1949.
(*13*) RUBIN, R., M. H. MALONE, M. H. WAUGH, and J. C. BURKE. 120 : 125, 1957.
(*14*) MEAD, J. A. R., and K. F. FINGER, Biochemical Pharmacology, 6 : 52, 1961.
(*15*) BOGDANSKI, D. F., A. PLETSCHER, B. B. BRODIE, and S. UDENFRIEND. Journal of Pharmacology and Experimental Therapeutics, 117 : 82, 1956.
(*16*) WEISSBACH, H. V. T. E. SMITH, J. W. DALY, B. WITKOP, and S. UDENFRIEND. Journal of Biological Chemistry, 235 : 1160–1163, 1950.
(*17*) MAXWELL, D. R., W. R., GRAY, and E. M. TAYLOR. British Journal of Pharmacology, 17 : 310, 1961.

# Discussion

*Chairman*—EDWARD B. TRUITT, JR.
*Members of the Panel*—CLAUDIO NARANJO
THORNTON SARGENT
ALEXANDER T. SHULGIN
ANDRER T. WEIL

CHAIRMAN DR. TRUITT: We might begin with a comment. One of the guests found that there is a whole state in our fifty in the Union that has a reputation for nutmeg, and perhaps he would like to make his comment again, which was quite interesting: that of a psychotogenic substance identifying a state.

DR. PHILLIPS (from the floor): I am a psychiatrist. I understand that Connecticut is known as the Nutmeg State, and I remember when I was in college about twenty years ago there was some reference to the fact that people in Connecticut acted awfully crazy, because they ate so much nutmeg.

MR. WEIL: I am afraid the origin of Connecticut's nickname is somewhat less romatic. In colonial times, Connecticut traders often palmed off carved wooden nutmegs as the real thing. This practice was considered a fine example of Yankee shrewness in business; consequently, Connecticut acquired the name "Nutmeg State".

CHAIRMAN DR. TRUITT: I wonder if Dr. Naranjo would like to discuss the activity of the compound he is engaged in testing?

DR. NARANJO: This amphetamine substituted with the methylenedioxy group is the first that was tested. The subjective reactions had been described by Gordon Alles from experimentation on himself. It was first used in a group of subjects under the assumption that this would be a hallucinogen, as suggested by Dr. Alles. This did not appear to be quite the case, for the drug produced only enhancement in feelings. In the face of this, it was suggested that it could be used as facilitating agent in psychotherapy. It is not something to be used as an antidepressant, but only to increase communication during a therapeutic session.

When we used this compound on patients with psychoneurotic symptoms, we saw that the effects were sometimes very dramatic in an unexpected way. I have tried several drugs to facilitate psychotherapy, including the more widely known hallucinogens, and never as with this compound has there been such a frequency of reminiscence of childhood events, in a very dramatic and spontaneous way, completely unexpected by the subjects.

This has been described in therapy with LSD and mescaline, but in my own experience has occurred spontaneously only once in approximately fifty experiences with LSD (though I understand that if a therapist searches for this, it could be precipitated). On the other hand, about half of the persons who in a therapeutic setting took this compound, (MDA), had this kind of experience an experience with almost no symbolic content, without

the aesthetic or mystical overtones that is so characteristic of most hallucinogens.

This was quite rare and, in turn, there was the experience of reminiscence. It is notable that in many of the subjects there was amnesia after it, and this was very much like the similar events that take place sometimes in the hypnotic trance. In two instances out of thirty, at least, the effects were those of a delirium, and in one of these there was erratic behavior, none of which was remembered afterwards.

Now with the trimethoxy substituted compound, which has been previously described as evoking hostile reactions when we used this in a therapeutic setting, this did not occur overtly; but the compound was remarkable in that the delusional content was more frequent that with any of the others that I know. This delusional content was very often paranoid.

CHAIRMAN DR. TRUITT: Could I ask if there were any color effects, which are characteristic of mescaline, seen with it?

DR. NARANJO: This produces the greatest incidence of color effects, whereas the previously mentioned one, (MDA), is notable for the absence of distortions and color effects.

The 3-methoxy-4,5 methylenedioxyamphetamine, (MMDA), has a methylenedioxy bridge in common with MDA, but has the oxygen substitution pattern of TMA. MMDA produces the qualities of both, and what is typical of this substance is that the experience, which has mostly a personal quality, enhancement of feeling, warmth, but very little symbolic content, makes it different from mescaline.

CHAIRMAN DR. TRUITT: There is one point, I think, that many people have possibly underestimated, and that is the theoretical importance of this aspect, which is pointed out by one question from Dr. Waser: "What is the evidence for direct amination of the olefinic side chain of myristicin in the body?"

DR. SHULGIN: Dr. Sargent mentioned one experiment where the formation of amphetamine in rats was actually observed. Administration of allylbenzene led to chromatographically distinct spots, with the strong implication that these spots were amphetamine. Although allylbenzene may be converted to propenylbenzene first, the simple addition of ammonia to the allyl double bond would be the most direct route. I don't know if it has any validity.

CHAIRMAN DR. TRUITT: We have a related question: "Could the transformation of a non-saturated aromatic side chain to a carbonyl group be possible?"

DR. SHULGIN: I don't know of this specific transformation having occurred. Certainly the double bond can participate in oxidation reactions, and substitution isomers have been converted to their corresponding acids in the body. Therefore the double bond is capable of being oxidized, or at least partially oxidized.

CHAIRMAN DR. TRUITT: We have two questions apparently directed to Mr. Weil, and I wonder if he would like to read them and comment.

Mr. Weil: The first one is, "What are the comparative psychoactivating potencies of nutmeg and mace?"

They are the same, but mystiques about the uses of the two spices have sprung up. It is interesting, for example, that at Haverford College students believed they could only get "high" with mace, even though they knew nutmeg to be very similar in taste. Other groups use nutmeg only, and are unaware of mace as an intoxicant.

The second question is, "Do other kitchen spices have any psychoactive properties?"

Who knows? Perhaps in five years we will have a symposium just on spices. I have received scattered reports on the use of cinnamon for these effects: One bit of information is that cinnamon sticks are smoked by certain Indian tribes of Mexico. I have no documentation for this report.

People who are avid for experimenting with possibly active substances often try spices. In fact, a distant friend writes that anything in the spice cabinet except monosodium glutamate will get you "high". Ginger, paprika, cinnamon and pepper have all been said to have effects on the mind, but we have no reliable evidence on them.

Chairman Dr. Truitt: We really must resolve the action of somatic input on the gastrointestinal tract, and other sources on the psychic effects before we accept them, too.

I am a little chary of the next two questions. I have an antagonistic question from Dr. Efron, and a protagonistic question from Dr. Kline.

Dr. Efron (from the floor): Being a pharmacologist, I would like to comment on the pharmacology of the tested compounds. Dr. Truitt has really done an excellent pharmacological job but I have some small objections.

First, in my opinion the psychopharmacology testing is such a difficult one that we never can use one or two tests. One has to use a battery of tests, and even then, often we are not sure what they mean.

In this case, you have put all your chips on the monoamine oxidase inhibition. If this would be really the only action of these drugs, then we should forget about them, because we have much more potent reversible and irreversible monoamine oxidase inhibitors that we can use.

Further about the test that you used: the antagonism to reserpine, we all now agree that it is not valid as an antidepressant activity measurement. It was used for tricyclic types of drugs, and even then there was a question as to its validity. Is there a correlation between this test and the activity of nutmeg?

The other problem I would like to comment on is that I really don't know why everybody is working with myristicin, the compound represented mostly in this large mixture of compounds found in nutmeg extracts. There might be a possibility that one of the other compounds present in a very small amount may be much more potent.

The next thing that would be very interesting would be to elucidate for structural-activity relationship, and to see the activity of all the compounds in some battery of tests. Then we really could see how the location of one

methyl group, adding another methyl group or taking one off, affects the activity of the compounds.

CHAIRMAN DR. TRUITT: Thank you very much, Dr. Efron. I fully agree with your comments.

DR. KLINE: Dr. Efron's remarks are as a pharmacologist; mine are as a psychiatrist.

The anti-reserpine part of the story is the one I am protagonizing for you. A very curious cycle is involved, because every drug which has been useful in the treatment of schizophrenia or the major psychoses has produced Parkinsonism as one of its side effects. Another part of the curious business is that the monoamine oxidase inhibitors or other antidepressants, if given in large enough doses, will produce hallucinations, delusions and uncontrolled euphoria.

All this would seem to tie somewhere into the extrapyramidal system. We reviewed this problem a few years ago with Mettler, and although there is a lot of presumptive evidence, one cannot yet draw a comprehensive picture. At a meeting which Dr. Efron chaired last year, it was pointed out that tricyclic antidepressants reduce the frequency of extrapyramidal side effects from phenothiazines and reserpine. The rats and mice who developed reserpine depression were given much higher doses per kilogram than we use on humans. When asked how one judges if depression is present in rats and mice, the answer was that this is judged upon the basis of reduced activity and reduced "sociability"; i.e. they didn't go poking around at each other. Then I asked: "What about Parkinsonism in the rats and mice?"—and I discovered to my amazement that the animals were barely able to move because they were so Parkinsonized. What was called depression might simply be the fact that the animals couldn't get to sniff their neighbors. The monoamine inhibitors, and perhaps the tricycle antidepressants, act as anti-Parkinsonian agents. Professor Holmstedt mentioned yesterday that Lewin has found harmine, a monoamine oxidase inhibitor, useful in the treatment of Parkinsonism.

CHAIRMAN DR. TRUITT: I heartily agree with you, Dr. Kline, because you recognize our problems in the laboratory. We have a great deal of difficulty in defining these parameters, isolating them, and analyzing them. Certainly I would be the first to disclaim that we can extrapolate easily this way from a test to the whole animal. When we speak of the appearance of tremor and absence of tremor or antagonism of tremor, we are dealing with a fairly precise parameter. When we are speaking of emotional effects rising and falling, we are speaking of a complex set of behavior changes that we have a healthy respect for.

A couple of other related questions that might follow Dr. Kline's. This is from Dr. Buckley: "Does myristicin have anticholinergic activity?"

Only in the respect that generally anticholinergic activity in the CNS is in some ways similar to potentiation of adrenergic activity. We have not specifically tested this in any respect.

"Does myristicin inhibit adrenergic reuptake of norepinephrine by the nerve endings?"

This is postulated as the mechanism of action for the tricyclic antidepressants. This hypothesis is too new for our consideration. If it is, perhaps a combination of a weak monoamine oxidase inhibitor, such as nutmeg, and the trycyclic agents, might be of interest.

Going to the more physical aspects, we have a question from Dr. Beavers, concerning the effects of nutmeg on blood pressure in human subjects, and asking whether we have any evidence of monoamine oxidase inhibitors either increasing or decreasing effects of nutmeg in humans. We certainly need to know more about this. Dr. Naranjo, have you done blood pressure examinations with the compound?

DR. NARANJO: There is slight variation in blood pressure. There is occasionally an increase but this is not consistent, and it is hard to evaluate to what extent the observed changes are secondary to the emotional states, for sometimes anxiety is a prominent component of the induced reaction.

No lowering of blood pressure has been observed. This is in contradiction to the observations on some persons who experienced intoxication with nutmeg.

CHAIRMAN DR. TRUITT: Dr. Leake has a question.

DR. LEAKE: I want to amplify a point made by Dr. Efron. This concerns the systematic investigation of all of the phenyl amines. This actually was Dr. Gordon Alles' undertaking, as you know. One extremely important feature of it I would recommend to all workers in the field. It bears on some of the reports that were made today. Even though chemical compounds in a series are very close, insofar as their molecular weights are concerned, Gordon Alles insisted on using equal molecular concentrations so as to compare each drug with the other on a molecular basis. This is important, particular when there is any significant difference in molecular weight.

Alles had an enormous amount of material that has never been published, and I don't know whether it will be. He made a methylenedioxy derivative of an amphetamine, in which he found extraordinary enhancement of auditory sensation. This he did describe informally at one of the Macy Conferences. This compound produced another remarkable effect: if he were to strike his finger, he could see the strike, and feel it afterwards by a definitive period of time.

DR. SHULGIN: That was the methylenedioxyamphetamine compound that we called MDA earlier.

DR. LEAKE: He made similar observations of this sort on other compounds. Since he had them all on an equal molecular basis, and since he did most of the experimentation on himself as one subject, at least his findings had that comparative validity.

DR. MARRAZZI (from the floor): In line with what is being said, and the comparison with mescaline, I thought you might be interested in the comparison that we have been making of methoxyphenylethyl amines, using cortical synaptic inhibition. At the moment it looks like mescaline (a trimethoxy compound), would have a potency of 1, the dimethoxyphenylethylamine of 1.8, while the demethylated or dihydroxyphenylethylamine, dopamine, would have a potency of 10.

This is reminiscent of the old work of Gunn, which showed that the methoxylation has a muzzeling action, decreasing activity. Apparently in preliminary data it seems to decrease cortical inhibitory activity.

CHAIRMAN DR. TRUITT: How much do you think this variation in activity is due to rate of transfer across the blood-brain-barrier, and how much to the differences in actual potency?

DR. MARRAZZI: I am not able to answer that. These are closearterial injections, and the latency of beginning action is approximately the same. It should be measured more carefully than I have done so far, but there is no remarkable difference, which would suggest that it is not a difference in passing through the blood-brain-barrier.

CHAIRMAN DR. TRUITT: We have a question directed to Dr. Shulgin and Dr. Sargent: "Could you describe your human bioassay methods further?"

DR. SHULGIN: The human bioassay follows a preliminary pharmacological and pharmacodynamic analysis of the investigated material on animals. Generally, three species, the mouse, the rat and the dog, are used. Most of the cardiovascular work is done on the dog. The compounds were then assayed within our experimental group. The human threshhold level was established by successively increasing the dose in small increments until this level was reached. This testing and the subsequent psychopharmacologic comparisons of the several compounds were done essentially by the "double conscious" method of Alles. (see our reference *10*).

DR. SARGENT: I would like to comment on the remarks of Dr. Efron and Dr. Leake, as far as the structure-activity relationship studies go.

Actually this was originally Dr. Shulgin's and my interest in investigating these compounds, and we could perhaps elaborate a little bit on one of the slides in which two other substituted phenylisopropylamines are mentioned, the precursors of which are not present in nutmeg. They were tested specifically to measure the effect of the orientation of these methoxy groups.

Our scale in mescaline units is the same as Dr. Leake's. However, we assign some of the numbers a little differently from his. We grade LSD as 3000 in mescaline units, the effect dose being a tenth of a milligram.

DR. LEAKE: You understand that my grading was off the cuff.

DR. SARGENT: I might mention in regard to the previous discussion of Parkinson effects of harmine and harmaline, these compounds are also hallucinogenic. To get back to the structure-activity relationships of these methoxy-substituted amphetamines, which are summarized in our figure 7, note that when the structure of TMA with the 3,4,5-methoxy substitutions is changed to 2,4,5-, or TMA-2, the activity in humans of the compounds is increased tenfold. Again, when the structure of the 3-methoxy-4,5-methylenedioxy compound, MMDA, is changed to 2-methoxy-3,4-methylenedioxy or MMDA–3a, the activity is again increased, this time by a factor of 6. In both cases, the change of a methoxy group from a meta- to an ortho-position markedly increased the potency of the compound. The more active compounds are derived from croweacin and asarone, which occur in natural oils but not oil of nutmeg.

CHAIRMAN DR. TRUITT: We have one last question that I would like to direct to Mr. Weil: "What significance would you give to hypothermia observed after nutmeg intake?"

MR. WEIL: In the acute intoxications that have come to clinical attention—and there have been few—a number of symptoms suggestive of vasomotor instability has been noted. I suspect that many of the constituents of nutmeg might have effects on the autonomic nervous system and on general homeostasis that we have not spelled out very well: possibly, this fall in temperature is one of them.

CHAIRMAN DR. TRUITT: This is the end of our time for this afternoon. I thank you again for your indulgence.

# SESSION IV

## SOUTH AMERICAN SNUFFS

**Bo Holmstedt, *Chairman***

# Anthropological Survey of the Use of South American Snuffs

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## Early Reports and Archeological Evidence from the West Indies and the Contents

### *Introductory Remarks*

The first contacts between Amerindians and Columbus and his men were established in the West Indies. It is also from the Antilles and the surrounding mainland that we have our first information about the Indians' use of what we now understand to have been a psychotomimetic snuff. Although this early information is limited, and not until our days has it been really considered to its full worth, it is of outstanding importance. Thus, at least some evidence has been saved in the reports of the chroniclers from the Circum-Caribbean culture area, for, as stated about the tribes referred to as Circum-Caribbean, "whether insular or on the mainland, they were readily accessible from the coast, and were quickly overrun by the Spanish conquerors. The great majority of them have long been extinct culturally if not racially." [1]

The difficulty in defining what plant material an early description refers to must be considered in any serious study. In my opinion we cannot, as Jerome E. Brooks has done in his work on tobacco (1937),[2] take it for granted that observations by Amerigo Vespucci during his voyage with Alonso de Ojeda and Juan de la Cosa (May, 1499–June, 1500), bear on tobacco chewing—even though many kinds of American tobacco later have been observed. These observations related, supposedly, at least, to natives of Margarita Island, off the coast of Venezuela.

According to Brooks (1937: 189), Vespucci's notice in his letter of 1504 to his friend, Piero Soderini, "was the first published which relates to a

[1] Steward, Julian H. 1948 : 1.
[2] Brooks, Jerome E. 1937 : 189.



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habit we know to have been tobacco chewing." I quote the following from Vespucci's description in the rendering presented by Brooks:

> The customs and manners of this tribe are of this sort: In looks and behavior they were very repulsive, and each had his cheeks bulging with a certain green herb which they chewed like cattle, so that they could scarcely speak, and each carried hanging from his neck two dried gourds, one of which was full of the very herb he kept in his mouth; the other full of a certain white flour like powdered chalk. Frequently each put a certain small stick (which had been moistened and chewed in his mouth) into the gourd filled with flour. Each then drew it forth and put it in both sides of his cheeks, thus mixing the flour with the herb which their mouths contained. This they did very frequently a little at a time.

From the continuation of the description, we deduct that the European observers believed that the natives "carried the herb and flour in their mouths in order to relieve their thirst", and, also, "that the women did not themselves indulge in the habit" (Brooks 1937: 191).

If we now should give a description of how e.g. the actual Kogi (or Kágabba) Indians of Sierra Nevada de Santa Marta in Colombia use their *poporo* (bottle-shaped gourd for lime) and chew their coca (*hayo*), a process that I myself have observed many times, we could word for word repeat the description quoted from Vespucci. As a matter of fact his words can as well refer to the habit of coca chewing. Such an eminent Americanist as Erland Nordenskiöld of Gothenburg considered Vespucci's words as clearly referring to coca,[3] and Cooper (1949: 549) has included the Cumaná area of Venezuela among the regions from which "early historical sources report coca chewing and/or ritual use of coca leaves as prevalent." To this must be added also the observation by Vespucci that "the women did not themselves indulge in the habit." No rule is without an exception, but just as an addition, I wish to add that "more commonly, coca chewing is a masculine rather than a feminine habit" (Cooper 1949: 552).

*The Cohoba Snuff and Its Paraphernalia*

The *cohoba* snuff used by the Taino of the West Indies has, as we know, caused much discussion which I previously tried to summarize in two papers.[4] We must note that Columbus himself observed the use of a powder, though he does not mention it by name. During his second voyage, 1493–1496, Columbus not only commissioned the Friar Ramon Pane to undertake what we now call anthropological field work among the aboriginal population of Española ("to collect all their ceremonies and antiquities," Bourne 1906: 4), but he himself made valuable observations presented in his narrative of the second voyage.[5] As has been pointed out by Bourne, we possess this narrative "only in the abridgment of Las Casas and Ferdinand Columbus." The original is lost,[6] but both Las Casas and Ferdinand Columbus "in

[3] Nordenskiöld, Erland, 1919 : 14.

[4] Wassén, S. Henry and Bo Holmstedt. 1963 : 27–35 ; Wassén, S. Henry. 1964 : 97–120.

[5] Bourne, Edward Gaylord. 1906 : 3, quite correctly has credited Christopher Columbus as the person who "set on foot the first systematic study of American primitive custom, religion and folklore ever undertaken."

[6] Bourne. 1906 : 4, "The original Spanish text of these documents is no longer extant and, like the *Historie* which contains them, they are known in full only in the Italian translation of that work published in Venice in 1571 by Alfonso Ulloa."

condensing the original, incorporated passages in the exact words of the Admiral. It is from such a passage in Ferdinand's abridgment that we derive the Admiral's account of the religion in primitive Hayti" (Bourne 1906: 4). Ferdinand Columbus says that he recorded "the very words of the Admiral", and we can now, in Bourne's translation (p. 4–6), find the following information of a powder which evidently must be the same as that mentioned by Ramon Pane as *cohoba:*

I was able to discover neither idolatry nor any other sect among them, although all their kings, who are many, not only in Española but also in all the other islands and on the mainland,[7] each have a house apart from the village, in which there is nothing except some wooden images carved in relief which are called *cemis;*[8] nor is there anything done in such a house for any other object or service except for these *cemis*, by means of a kind of ceremony and prayer which they go to make in it as we go to churches. In this house they have a finely wrought table, round like a wooden dish in which is some powder which is placed by them on the heads of these *cemis* in performing a certain ceremony; then with a cane that has two branches which they place in their nostrils, they snuff up this dust. The words that they say none of our people understand. With this powder they lose consciousness and become like drunken men.

In addition to the secluded *cemi* houses for snuffing ceremonies, Columbus mentions two paraphernalia, namely a "finely wrought table" for the powder, and a "cane that has two branches" to snuff up this dust. Both are of immediate interest.

In a paper from 1964 dealing with the Neo-Indian epoch, Irving Rouse has referred to the statement that the Arawak in the West Indies placed the powder on top of *cemis*, adding that "many of the statues found in caves have a platform on top for this purpose."[9] In this connection Rouse has republished the 66 cm. high wooden British Museum *cemi*, in the shape of a bird standing on what seems to be a turtle. This figure, originally published by Joyce,[10] was republished also by Wassén 1965: fig. 4. A kneeling stone figure from Puerto Rico, published by Palmatary,[11] may also be taken into account as such a West Indian *cemi* with platform on top. I have in my work from 1965 (pp. 30–31, figs. 5 and 53), pointed out that we still find a South American ethnographic parallel to this in the ceremonially used tabletops for snuff, and snuffing paraphernalia used among the tribes of the rivers Branco and Colorado in western Brazil. These tabletops are carefully made and polished, but according to Franz Caspar's observations among the Tupari, the table has no special function beyond its mechanical use during the snuffing seances.[12] We can observe that the snuffing ceremony among the Tupari takes place inside the house. When used, the tabletop is supported by three wooden legs on which it is loosely placed. The tabletops are irregularly square-shaped and provided with a handle. They are

[7] According to Bourne, Cuba, which Columbus believed to be the mainland.

[8] Bourne. 1906: 5, footnote. "Ulloa in his Italian gives this word in various forms e.g. *cemi, cimi, cimini* and *cimiche*. The correct form is *cemi,* with the accent on the last syllable. Las Casas says, "Estas—llamaban *cemi,* la ultima silaba luenga y aguda."

[9] Rouse, Irving. 1964: 510–511.

[10] Joyce, Thomas A. 1916, pl. 21.

[11] Palmatary, Helen C. 1960, pl. 120 *d,* and text on p. 92.

[12] The photo published in Wassén, 1965, fig. 5, was taken by Dr. Franz Caspar among the Tupari, during his second expedition to this tribe in 1955.

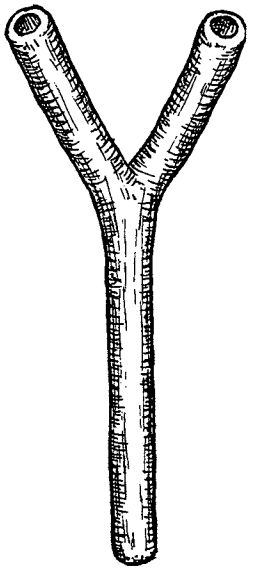

FIG. 1.—Y-shaped snuffing tube from Haiti. After Oviedo.

cut from the wood of flat supporting roots of a tree. Dr. Franz Caspar considers them as particular for the tribes of the Branco and Colorado Rivers.

If we now turn to the "cane that has two branches", Columbus evidently was observing the use of Y-shaped snuffing tubes, of which there were finely worked ones used by the chiefs and principal men, and others made of reeds for those who could not afford the finer ones. The "poor hermit" Ramon Pane apparently does not refer to a forked tube when he says that "the *Cogioba* is a certain powder which they take sometimes to purge themselves, and for other effects which you will hear of later. They take it with a cane about a foot long and put one end in the nose and the other in the powder, and in this manner they draw it into themselves through the nose and this purges them thoroughly" (Bourne 1906: 17; cf. Lovén 1935: 393).

In Wassén 1964 (pp. 102–103), there is a discussion of the West Indian snuffing instruments according to the sources, and I here again republish the tube from Haiti (Fig. 1) which we find in the work by Oviedo,[13] who also has stated that it was the Y-shaped snuffing instrument, and not the plant, which was called *tabaco* by the Indians (vol. I: 131). The famous Bishop and Historian, Bartolomé de las Casas, also described the West Indian snuffers, "made in the size of a small flute, all hollow as is a flute." To make his readers understand the Y-shaped form of the instrument, he uses the picture of the fingers in an out-stretched hand.[14]

Even if we accept the occurrence in the West Indies of Y-shaped snuffing tubes as an obvious parallel to tubes of the same type found in South America,

[13] The original is found in volume I, pl. I: 7, of Oviedo's *Historia general*, etc. (1851). The corresponding text on p. 130.

[14] Las Casas, Bartolomé de. 1909: 445. ". . .; la hechura de aquel instrumento era del tamaño de una pequeña flauta, de los tercios de la cual en adelante se abria por dos cañutos huecos, de la manera que abrimos los dos dedos del medio, sacado el pulgar, cuando extendemos la mano."

we must also note the observation made by Lovén (1935:393), that "the Tainos differ from the whole South America in that their forked snuff-tubes were not made from bones, and certainly not from those of birds, as in the Orinoco and Cayary-Uaupés regions. Suitable bones for tubes were not accessible on Española; other material had to be sought there." [15]

We find another parallel between Haiti and the northern South American mainland, in the round trays for snuff now found among the Indians of the Orinoco region (see Wassén 1965, fig. 1, p. 21), and the fine and polished round trays described by Las Casas from the island. He says that the snuffing instrument was made of the same kind of dark wood as the tray.[16]

That the snuffing tubes of wood used on Haiti in some cases were fine pieces of sculpture is clearly understood from the specimen found at La Gonâve (Fig. 2), first published in 1941 by Mangones and Maximilien, later also by Rouse and Wassén.[17] Dr. Grete Mostny of Santiago, Chile, has in a paper from 1958 [18] compared the elaborate tube from Haiti with specimens of finely sculptured straight snuffing tubes from the Atacaman region, where the Y-shaped tubes do not seem to exist. As the description of the tube from Haiti is very poor in the work by the two Haitian authors, it is fortunate that Mostny has been able to quote a letter from Louis Maximilien (Febr. 11, 1956). In this, some particulars are given regarding the motif on the specimen found in the Picmi cave on the island of Gonâve, namely a kneeling man crowned by a bird's head.

*Further Details about the Cohoba Powder*

At the end of his report from the second voyage, Christopher Columbus refers to an account he had ordered from "one Friar Roman (Ramon) who knew their language" (Bourne 1906: 6). As far as we know, through the Admiral's son and other chroniclers, who know Pane's text, "to this day our most authentic record of the religion and folk-lore of the long since extinct Tainos, the aboriginal inhabitants of Hayti" (Bourne 1906: 4), we meet in it not only the name of a certain powder they inhaled, but also most interesting field observations on the psychotomimetic effects of the drug.

Friar Ramon Pane whose text is best read in the careful edition of Bourne,[19] uses two words, *cohoba* and *cogioba*, for a snuff used for special

[15] For various types of South American snuffing tubes see Wassén, 1965.

[16] In the text of Las Casas, 1909: 445, a snuff tray is described as follows: ". . . plato redondo, no llano, sino un poco algo combado ó hondo, hecho de madera, tan hermoso, liso y lindo, que no fuera muy más hermoso de oro ó de plata; era cuasi negro y lucio como de azabache."

[17] Rouse. 1964, fig. 18; Wassén. 1964, fig. 2, and 1965, fig. 51. The original in Mangones and Maximilien, 1941, pl. 50.

[18] Mostny, G. 1958: 387–389. I quote from the text of the letter (p. 388): "Les deux branches supérieures du Calumet se terminaient par des bouts olivaires—afin de rendre aux marines un contact doux —; le point de jonction des trois branches porte le motif sculpté, représentant un homme agenouillé, les bras liés derrière le dos et la poitrine incliné dans une attitude de prière; le tout surmonté d'une tête d'oiseau d'un haute relief."

[19] Bourne. 1906: 8–9. "To facilitate a study of this material in its earliest record I have translated Ramon's treatise from the Italian, excerpted and collated with it the epitomes of Peter Martyr and Las Casas, and have prepared brief notes, the whole to form so far as may be a critical working text of this source for the folklorist and student of Comparative Religion in America. The proper names in each case are given as in the 1571 edition of the *Historie.*"—"At best the spelling of these names offers much perplexity. Ramon wrote down in Spanish the sounds he heard, Ferdinand, unfamiliar with the sounds, copied the names and then still later Ulloa, equally unfamiliar with the originals, copied them into his Italian. In such a process there was inevitably

purposes. We have already referred to the text where it is said that "the *cogioba* is a certain powder which they take sometimes to purge themselves," etc. (Bourne 1906: 17). Later, in this text, we meet the word *cohoba:*

When one is ill they bring the *Buhuitihu* (Bohuti) to him as a physician. The physician is obliged to abstain from food like the sick man himself, to play the part of sick man which is done in this way which you now will hear. He must needs purge himself like the sick man, and to purge himself he takes a certain powder called *cohoba* snuffing it up his nose, which intoxicates them so that they do not know what they do, and in this condition they speak many things incoherently, in which they say they are talking with the *cemis*, and that by them they are informed how the sickness came upon him.

Further on (Bourne 1906: 24), a description of great interest to the psychotomimetic studies follows, which I quote:

And when they want to know if they will be victorious over their enemies they go into a cabin into which no one else goes except the principal men; and their chief is the first who begins to make *cogioba*, and to make a noise; and while he is making *cogioba*, no one of them who is in the company says anything till the chief has finished; but when he has finished his prayer, he stands a while with his head turned (down) and his arms on his knees; then he lifts his head up and looks towards the sky and speaks. Then they all answer him with a loud voice, and when they have all spoken giving thanks, he tells the vision that he has seen, intoxicated with the *cogioba* which he has inhaled through his nose, which goes up to his head. And he says that he has talked with the *cemi* and that they are to have a victory; or that his enemies will fly; or that there shall be a great loss of life, or wars or famine, or some other such things which occur to him who is intoxicated to say. Consider what a state their brains are in, because they say the cabins seem to them to be turned upside down and that men are walking with their feet in the air.

I have had in my hands photographic copies of some pages of "*P.Martyris Angli-mediolanensis opera Legatio babylonica Occeani decas Poemata Epigrammata,*" the Gothic edition from Seville 1511, of Peter Martyr's *First Decade.* It is in this text (see Fig. 3, a–b), that the author, who never himself went to the New World, after having seen Pane's manuscript deals with the *cohoba* powder. For a translation I follow MacNutt,[20] however with some corrections and notes.[21]

*Translation of the Latin text of 1511 (fvi r. and v):*

It is the augurs, called bovites, who encourage these superstitions. These men, who are persistent liars, act as doctors for the ignorant people, which gives them a great prestige, for it is believed that the zemes converse with them and reveal the future to them.

If a sick man recovers the bovites persuade him that he owes his restoration to the intervention of the zemes.

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some confusion of u and n and u and v, (Spanish b). In the Italian text v is never used, it is always u. In not a few cases the Latin of Peter Martyr and the Spanish of Las Casas give us forms much nearer those used by Ramon than the Italian." It is now clear that both Las Casas and Peter Martyr underestimated the importance of Ramon Pane's work. For this see e.g. Bourne, p. 7.

[20] MacNutt, Francis Augustus. 1912. Vol. I: 172–174. As pointed out by Wassén, 1964: 105, Ramon Pane used *buhuitihu* and *bohuti.* This evidently Island-Arawak word has been latinized into *boitius* (pl. *boviti*) by Pedro Martyr and is written *buhuti* by Oviedo, and *bohique* and *behique* by Las Casas. If we try to connect it with other known words, we are probably safe to do so with the also Island-Arawak *buhío, bohío,* a common word in the Spanish reports for house but sometimes a designation for special houses, very probably also those for medicine-men's cures.

[21] The first printing of Decade One which was authorized by Martyr is that of 1516, in which the plural *boitii* for medicine-men occurs.

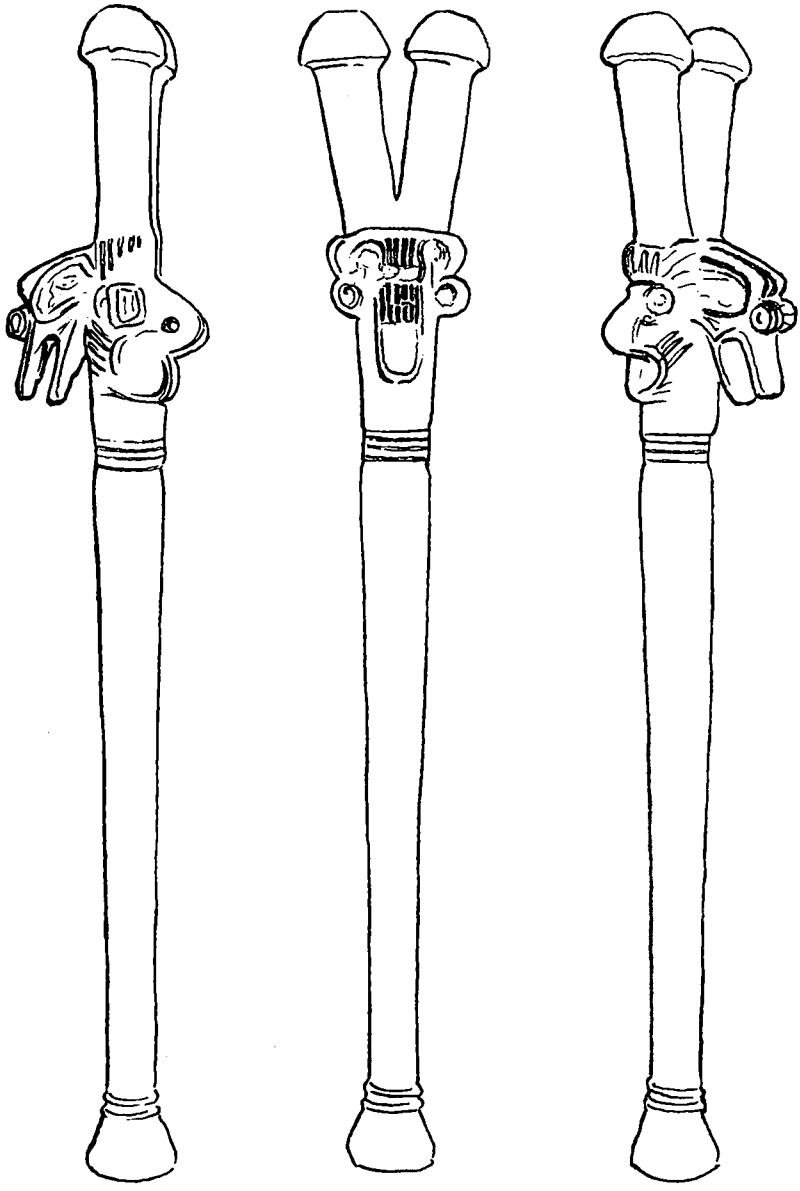

FIG. 2.—Sculptured snuffing tube of wood from La Gonâve, Haiti. L. 24 cm. Taino Culture. After photographs published by Mangones and Maximilien.

When they undertake to cure a chief, the bovites begin by fasting and taking a purge. There is an intoxicating herb which they pound up and drink,[22] after which they are seized with fury like the maenads, and declare that the zemes confide secrets to them. They visit the sick man, carrying in their mouth a bone, a little stone, a stick, or a piece of meat. After expelling every one save two or three persons designated by the sick person[23] the bovite begins by making wild gestures and passing his hands over

[22] MacNutt translates *drink*. The Latin text has *sorbeo*, absorb.
[23] The Latin says: "from a semicircle," etc.

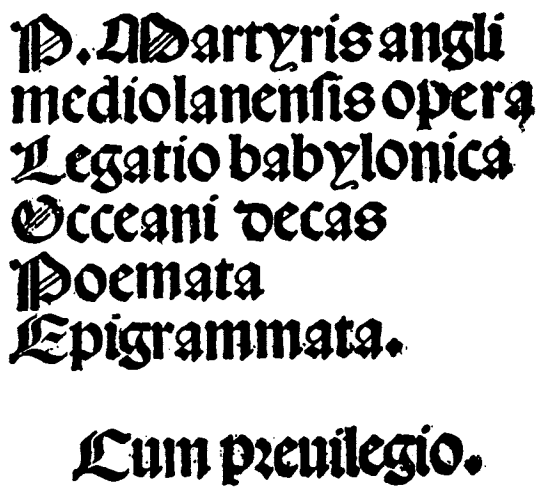


FIG. 3 a-b.—Title and text, fvi(r.), in Peter Martyr's work from Seville, 1511, in which Ramon Pane's notices of *cohoba* snuffing first appeared. After a copy in "Arents Tobacco Collection," The New York Public Library.

the face, lips, and nose, and breathing on the forehead, temples, and neck, and drawing in the sick man's breath. Thus he pretends to seek the fever in the veins of the sufferer. Afterwards he rubs the shoulders, the hips, and the legs, and opens the hands; if the hands are clenched he pulls them wide open, exposing the palm, shaking them vigorously, after which he affirms that he has driven off the sickness and that the patient is out of danger. Finally he removes the piece of meat he was carrying in his mouth like a juggler, and begins to cry, "This is what you have eaten in excess of your wants; now you will get well because I have relieved you of that which you ate."

If the doctor percieves that the patient gets worse, he ascribes this to the zemes, who, he declares, are angry because they have not had a house constructed for them, or have not been treated with proper respect, or have not received their share of the products of the field. Should the sick man die, his relatives indulge in magical incantations to make him declare whether he is the victim of fate or the carelessness of the doctor, who failed to fast properly or gave the wrong remedy. If the man died through the fault of the doctor, the relatives take vengeance on the latter. Whenever the women succeed in obtaining the piece of meat (*erroneous transl.*)[24] which the bovites hold in their mouths, they wrap it with great respect in cloths and carefully preserve it, esteeming it to be a talisman of great efficacy in time of childbirth, and honouring it as though it were a zeme.

The islanders pay homage to numerous zemes, each person having his own. Some are of wood, because it is amongst the trees and in the darkness of night they have received the message of the gods.[25] Others, who have heard the voice amongst the rocks, make their zemes of stone; while others, who heard the revelation while they were cultivating their ages—that kind of cereal I have already mentioned,—make theirs of root.[26]

Perhaps they think that these last watch over their breadmaking. It was thus that the ancients believed that the dryads, hamadryads, satyrs, pans, nereids, watched over the fountains, forests, and seas, attributing to each force in nature a presiding divinity.

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[24] This passage has evidently been wrongly translated by MacNutt. The women could hardly keep the pieces of meat. From the Latin, *"de lapillis aut ossibus quos ore gestasse bouijtus aliquis putatur: se femine,"* etc., it is clear that the women collected the stones and the pieces of bones for the said purpose.

[25] In the original *visionibus,* "visions", are mentioned.

[26] "That kind of cereal" for *genus panis* has in the Argentine edition of 1944 been translated as *"clase de alimento."* In the Latin text of 1516 it says *genus edulii.*

En illustrissime princeps omni preconio digna maris originem: nec ab eis parui cū fieri putes: qui hec illis recitare didicerit. Aiunt deinde fratres hos iaie metu tā diu per diuersa fuisse vagatos: vt fere iam fame perirent: quia nullubi sistere pedem audebant: hinc quoniā acrius vrgerentur: ad pinsoris domum pulsare ceperunt caza-bi. i. panem petentes pinsor autem in primo ingredientem cōspuisse ita acriter fertur: vt illi ex ictu sputi exortum sit turgidissimum intercus: quo fere interierit. Aist fratrus consilio accepto lapide acuto apertum est: ex cuius vlcere natam aiunt feminaz: qua mutuo post fratres illi omnes vsi sunt: atqz ab ea ferunt filios filiasqz genuisse. Jucundius aliud aduertito princeps illustrissime. Antruz extat aliud iouana boina nomine in cuiusdam reguli diocesi: qui Machinnech vocatur. Jd religiosius qz corinthium quondam aut cyrrham nisamqz greci colunt: ac venerantur: mille varijs ornatum picturis. In huius antri foribus duos habent sculptos zemes: quorum vnū bintaitellem. Marohum alterum vocant. Cur tanta specum colerent pietate: interrogati: quia sol inde lunaqz lumē orbi prebituri prodierunt: grauiter sensateqz respondent. Concursationibus antra veluti nos vrbem z baticanum nostre religiōis caput: aut Compostellam z Jherusalem domini sepulcrum frequentant. Subiacent z alteri superstitionum generi: mortuos putant noctu vagari: ac vesci guanuaba (fructu nobis incognito) cotono simili: lectisqz inter viuos versari aiunt ac decipere mulieres: sumpta namqz virili forma coire velle videntur: ast quom ad opus peruenitur euanescunt. Si quis autem apud se iacere mortuum aliquando suspicatur (quom quid nouī senserit in lecto) vteri attrectatione se dubio solui balbutit. Cuncta nāqz aiunt mortuos posse humana membra suscipere preter vmbilicuz: si vmbilico igitur mortuum esse dignoscit: tactus illico resoluitur. Noctu z sepissime (in itineribus precipue vijsqz publicis) mortuos occurrere viuis creduntur: contra quos si viator intrepidus sterterit: disoluit fantasma: si vero pertimescat: illum ita adorien do perterret: vt sepius ea formidine multi debilitentur ac stupeāt. Jnterrogati a nostris insulares vnde sibi cos ritus inanes tanqz contagionem comparauerint: a maioribus hereditarios respondent: rithmisqz aiūt vltra hominū memoriam: ista cōterta que neminem licet preter regulorum filios edoceri: memorie illa cōmendant neqz enim litteras vnqz habuere: diebusqz festis (alio pulsante populo) canentes veluti solemnia sacra preponunt: instrumentum habent vnicum ligneum: concauum: reboans tantum: q cōcutitur impanit more. His illos imbuunt superstitionibus eorum augures quos bouijtas vocant: sunt et ijdem medici qui plebeculē rerum insciē mille astruunt fraudes. Credere cogunt plebem hi augures (quia sunt apud eam auctoritatis erimie) q zemes ipsos alloquantur futuraqz predicēt: z si quis aduersa laborans valitudine conualuerit: se dono zemis id assecutum persuadent. Jeiunio z purgationi se obligant bouijte: q̄do curaz de primario sumūt aliquo. Herbamqz sumunt inebriātē quā quom pulueream sorpserit (veluti menades) in furorez versi multa se a zemibus audisse murmurant. Valitudinarium adeunt esse vel lapillo in os sumpto aut frustulo carnis. Ex hemicido ejciunt omnes preter vnum aut duos quos ipsemet elegerit. Circuit primarium bouijtes ter aut quater: faciem: labia nares qz ex ore quens fedis gestibus: in frontem: in tempora: in collum suflat egroti absorbens aerem: post hec se morbum ex laborantis venis exhaurire dicit. Per humeros deinde ac femora z crura egrotum fricans: cōtractas a pedibus manus deosculatqz sic manibus complexis: ad postium procurrit apertum: ac manus exeuntē

The islanders of Hispaniola even believe that the zemes respond to their wishes when they invoke them. When the cacique wish to consult the zemes, concerning the result of a war, about the harvest, or their health, they enter the houses sacred to them and there absorb the intoxicating herb called *kohobba*, which is the same as that used by the bovites to excite their frenzy.[27] Almost immediately, they believe they see the room turn upside down, and men walking with their heads downwards.

This kohobba powder is so strong that those who take it lose consciousness; when the stupefying actions of the powder begins to wane, the arms and hands become loose and the head droops.[28] After remaining for some time in this attitude, the cacique raises his head, as though he were awakening from sleep, and, lifting his eyes to the heavens, begins to stammer some incoherent words. His chief attendants gather round him (for none of the common people are admitted to these mysteries), raising their voices in thanksgiving that he has so quickly left the zemes and returned to them. They ask him what he has seen, and the cacique declares that he was in conversation with the zemes during the whole time, and as though he were still in a prophetic delirium, he prophesies victory or defeat, if a war is to be undertaken, or whether the crops will be abundant, or the coming disaster, or the enjoyment of health, in a word, whatever first occurs to him.

Bourne (1906: 20) accepted *cohoba* as a word for tobacco, and I have previously (see Wassén, 1964: 102) been inclined to accept the explanation by Friederici [29] that the Taino word *cohoba* probably stood for tobacco, while the word *cogioba* should stand for *Piptadenia*. Brooks (1937: 189), however, has made it perfectly clear that "none of the early commentators on the custom says that the substance inhaled was derived from the tobacco plant," and when taking into account all the forms of the word *cohoba*, such as *cohobba*, *cahoba*, *cojoba-cogioba*, *cojioba*, *cohiba*, *coiba*,[30] I am now of the opinion that it is one and the same word, and that *cohoba* as Brooks (1937: 196) expresses it "was employed by the medicine-men chiefly to induce a state of trance." We have every reason to believe that the *cohoba* identification by E. W. Safford and other writers as a snuff prepared from the seeds of *Piptadenia peregrina* is valid.[31] According to Brooks (1937: 197) "this plant, indigenous to certain parts of South America and to some places in the Antilles (including Haiti), still bears the name *cohoba*." Here it is interesting to add that Pittier (1926: 189) has found the word *cojoba* for the tree used in northern Venezuela (cf. Rosenblat, 1965: 272, 344).

In this connection I wish once again to underline the statement of Dr. Siri von Reis Altschul in her botanical thesis of 1964 (p. 42) that the Indians of the West Indies "may have found it easier to plant the trees than to maintain communication with the mainland for their source of supply" (of *cohoba*). It is interesting to add that Oviedo says that the snuff came from an herb (*hierva*), which the Indians valued much, and kept it cultivated.[32] Las Casas mentions that the Indians "had certain powders of certain herbs well dried and finely ground and of the color of cinnamon or powdered henna,

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[27] The Latin text has it, and this is important, that the *chohobba* was absorbed *per nares*.

[28] In the Latin edition of 1516 there is a small change in the text, ". . . *insania brachiis demisso capite genua complectitur* . . ."

[29] Friederici, Georg. 1925.

[30] Friederici, Georg. 1947: 198.

[31] Already in 1898, Max Uhle (p. 9) draws the conclusion that "the extreme strength of the powder as described by Petrus Martyr, exceeding that of tobacco, decides its different nature and its Piptadenia character."

[32] Oviedo, *Historia*, etc. 1851: 131.

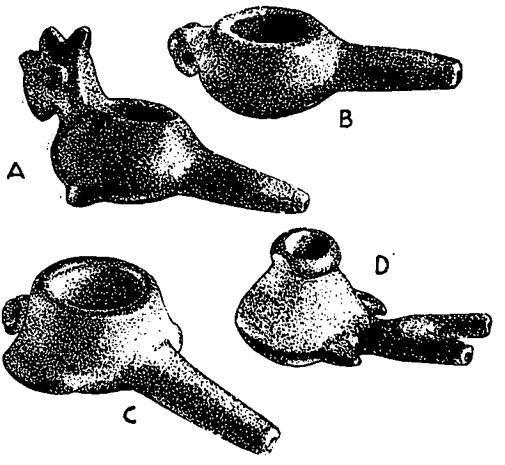


FIG. 4.—Archaeological bird-shaped pottery snuffers from Costa Rica. *A*, Guanacaste, *B–D*, Línea Vieja. Coll. Gothenburg Ethnographic Museum, *64.16*. Length of specimen *C*, 9 cm.

etc.[33]" With Brooks (p. 196) and others, we may assume that the "word *cohoba* may have meant snuff as well as the act of snuffing any powder. Pulverized tobacco seeds may have been mixed with the narcotic snuff inhaled by the medicine-men, and only the nicotian ingredient of this compound recognized by the Spanish observers." The Arawakan Jirara and Caquetio in N.W. Venezuela, tribes which according to Steward (1948: 21) had "certain specific resemblances to the Arawakan Taino of the Antilles," had medicine-men who "practiced divination with tobacco ash and communed with spirits while taking tobacco and a narcotic herb." The mixing of tobacco and *yopo* has been reported from many S. American tribes.

*Archaeological Evidence for the Use of Snuff*

If we consider the South American origin of the West Indian tribes, it is only natural that the close parallels referring to the snuffing complex in the West Indes should be sought in South America. I believe, however, that also the archaeologically found, often bird-shaped and bifurcated clay snuffers from Costa Rica, (Fig. 4), should be taken into account.[34] These small clay snuffers with one or two tubes were, according to Doris Stone, "probably used for *cojoba* (*Piptadenia* sp.) or tobacco."[35, 36]

As always, the South American influence as far north as in Costa Rica is worth studying. To a possible explanation of the bird motif in the clay snuffers I will return later. Here I, want to refer to Fig. 5, where I, after Dr. Otto Zerries, can show an old bifurcated and nicely carved bird-shaped snuffing tube from South America. This highly interesting old specimen is

[33] Las Casas. 1909 : 445.

[34] See Wassén and Holmstedt, 1963, fig. 6, and p. 24 ; also Wassén, 1965, fig. 2, and pp. 25–26.

[35] Stone, Doris. 1958 : 16. Her figures 19 *a*, *b*. Stone counts "snuffing and the playing of flutes by medicine men" as "southern traits" in Costa Rica's cultures (p. 25).

[36] See Wassén and Holmstedt. 1963 : 24.

FIG. 5.—Bifurcated snuffing implement of wood. Coll. *Mus. f. Völkerkunde,* Mannheim, "V. Am. No. 1894." According to Zerries, 1965, from Brazilian Guayana. Courtesy Dr. Otto Zerries.

now in the Ethnographical Museum of Mannheim, Germany, where it has been observed and studied by Dr. Zerries, who has attributed it to the region of Brazilian Guyana.[37] The old snuffer in the German museum undoubtedly points to a South American background also for the clay snuffers in Costa Rica.

In spite of many omissions and too hastily drawn conclusions, the study of Max Uhle of the bifurcated snuffing tube of bone that he found in 1895 at Tiahuanaco seems to be one of the first of a comparative interest for the use of snuffs among the South American Indians. A drawing after Uhle's illustration of the tube he found is shown in Fig. 6. According to Uhle (1898 : 1), "the tube consists of the wrist or leg bone (*metacarpus* or *metatharsis*) of a

[37] Zerries, Otto. 1965 : 185–193. In the same paper Zerries describes two more, richly decorated wooden objects from the Ethnographical Museum in Mannheim (numbers Am. 1987 and 1988), in the form of jaguars with bowls, which evidently have been receptacles for a powder. In the old museum entry it says *"Gerät zum Schnupfen,"* 'snuffing implement.' Zerries seeks the origin for all three in the lower R. Trombetas region.

young llama-like animal," . . . "and the bone has been cut off at each end, and while at the upper end a part of the shaft has disappeared, at the lower end, bifurcating naturally, only the distal articulations have been cut away and each part bored, so as to communicate with the main tube. The caliber of the former is ¼, and that of the latter 13/32 of an inch."

Uhle reported from Tiahuanaco. Following him it has only slowly and after a long series of attempts at all sorts of more or less fanciful explanations, become evident that the many finds in the region of the former Atacameño in Argentina and Chile of wooden trays and their corresponding tubes, must be classified as paraphernalia connected with the taking of some kind of a snuff. Several earlier references have been mentioned in Wassén 1965 (pp. 34–36 and p. 78) as well as in Wassén and Holmstedt (1963: 24–25); but I can perhaps best refer to the summary of the extensive literature presented in the archaeological thesis by A. M. Salas.[38] For the understand-

[38] Salas, Alberto Mario. 1945. Especially pp. 209–226, *"Area de dispersión de tubos y tabletas."*

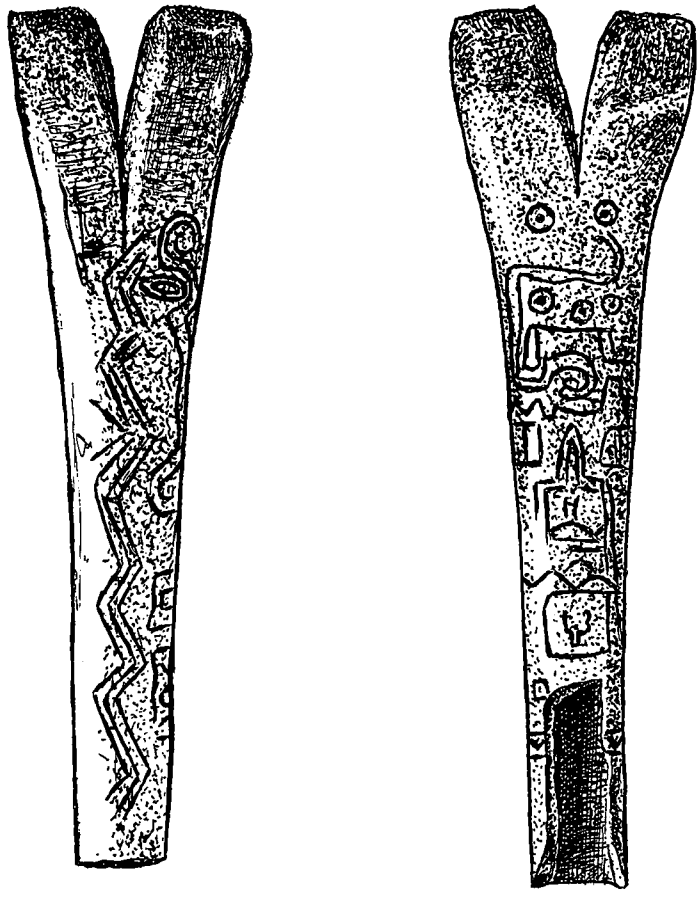

FIG. 6.—Naturally bifurcated snuffing tube of bone from Tiahuanaco. Drawing after Uhle's photographs in his publication from 1898.

ing of the snuffing complex in the Atacama region, important publications have recently been published. I want particularly to refer to the classificatory study by Lautaro Nuñez,[39] and the same author's references to the taking of *rapé* during successive cultural periods in northern Chile.[40] A small but interesting contribution is the paper by G. Mostny from 1958, in which she also refers to the tube from La Gonâve, Haiti. Her paper from 1952, in which she offers a recapitulation of the various opinions regarding the finds of *tabletas* and *tubos* in Chile and Argentina, is also of high interest for the description (p. 8) of a grave find of a *paricá* tray with one sculptured and one plain tube. The tray was protected by a surrounding leather wrapping, which when taken away showed the handle in the form of a nicely carved condor. The circumstances prove that the Indians had taken much care in protecting this specimen when the owner got it with him in the grave. The sculptured tube in the same find shows, according to Mostny's description (p. 11), a masked human being.

In a new work from 1965, Father Gustavo Le Paige is also writing about several highly interesting finds of snuffing paraphernalia used in the Atacama region.[41] The list could easily be made much longer, but it was neither here nor in my study from 1965 my intention to present a complete catalogue of all such finds from a given area. My intention has been to underline the importance of archaeologically found snuffing paraphernalia in relation to the ethnographically known details. Scientifically it must be of an overwhelming importance to learn what kind of powder the Indians in the Atacama regions used, and what we can deduct about the ceremonial importance of the habit from the finds.[42] In Fig. 7–10 three wooden tablets and a tube from Chiuchiu and Argentina are shown from material kept in the Museum of the American Indian, New York City. Fig. 11, taken from Fig. 57 in Casanova's paper of 1946, shows interesting Argentine specimens with features often discussed in this work.

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[39] Nuñez Atencio, Lautaro. 1963 : 148–168.

[40] Nuñez A., Lautaro. 1965. In this study the author has pointed out the use of snuffing tubes of bone among groups with a knowledge of both agriculture and pottery in the period he calls Early (0–700 A.D.), a period still without influence from the Tiahuanaco culture. During a Middle Period (700–1000 A.D.) the snuffing paraphernalia are continuously used, and a strong influence from Tiahuanaco is observed. The use of snuff trays and tubes continues during the Late Period (1000–1450 A.D.), when several local cultures developed after the influence from Tiahuanaco.

[41] Le Paige, Gustavo. 1965. His work from 1964 has been quoted at the end of this paper.

[42] I am most thankful to Dr. Lautaro Nuñez A., Director of the Department of Archaeology of the *Universidad de Chile, Zona Norte,* Antofagasta, for his kindness in sending to me with a letter of October 7, 1966, samples of snuff powder archaeologically found and associated with a snuff tray from a pre-Incaic grave at the coast of Chile, near Iquique (Bajo Molle). The material has been forwarded to Prof. Bo Holmstedt, Stockholm, for analysis. We certainly need qualified analyses of archaeological snuff. Dr. Alberto Mario Salas (1945 : 222) indignantly criticizes Max Uhle, who once found powder associated with a snuff tablet at Calama, and concluded he had found a narcotic powder only from the fact that he and his assistant started sneezing after having blown the powder into the nostrils. Ricardo E. Latcham (1938 : 133–135), started a discussion on which type of powder the Atacameño could have been using. He suggested *Piptadenia macrocarpa,* "common in the subtropical valleys of Tucumán and in the Chaco, and also used by the Calchaquíes," but immediately added that more probably it was some kind of tobacco. The *Piptadenia macrocarpa* should be the same as the Peruvian *vilca.* Latcham rejected the idea, suggested by Dr. A. Oyarzún, that *Piptadenia peregrina* had been used by the Atacameño.

FIG. 7.—Wooden snuff tray with human and condor motifs. Argentina. Photograph courtesy of Museum of the American Indian, Heye Foundation. Specimen No. 13/3658.

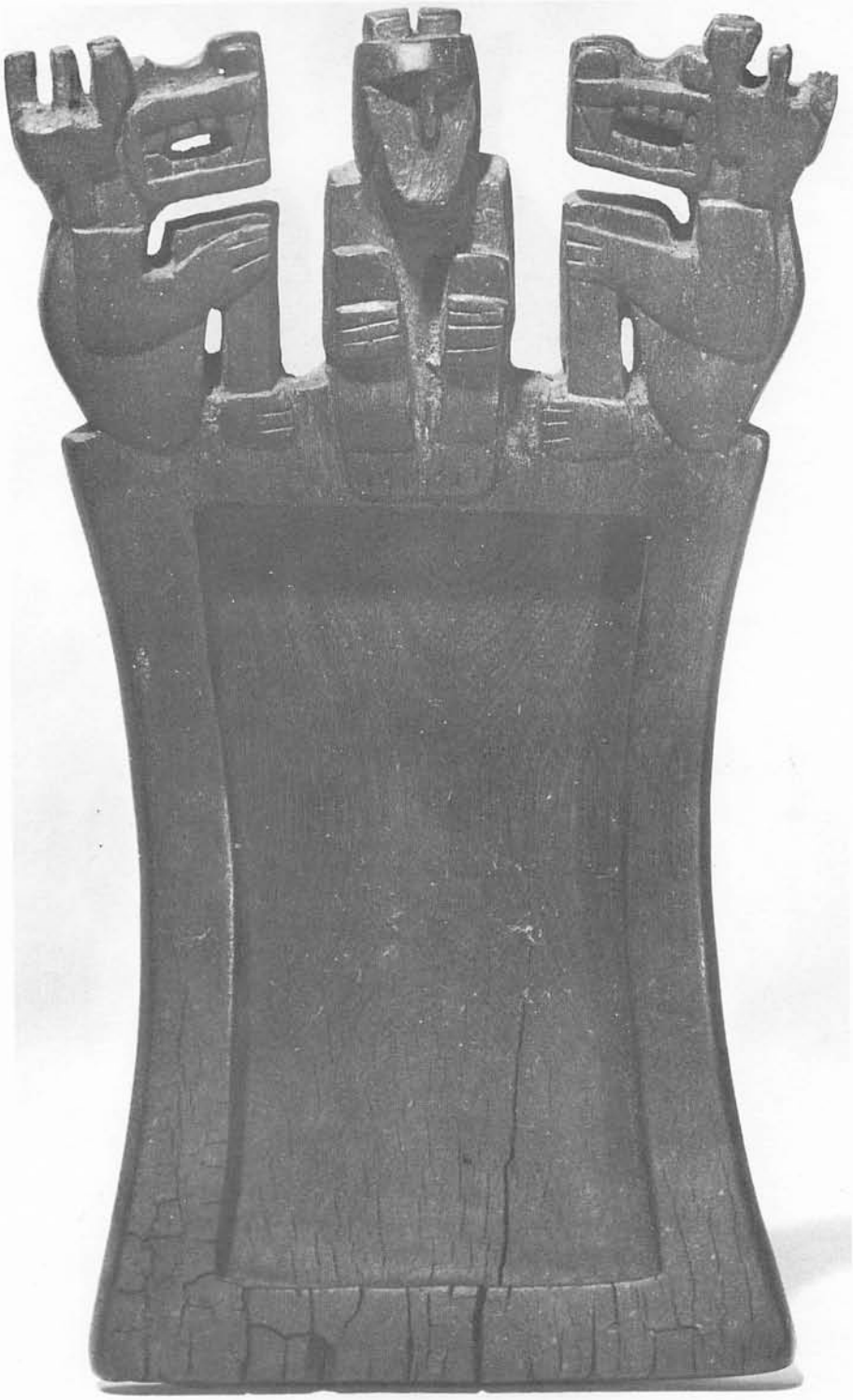

FIG. 8.—Wooden snuff tray with human and feline motifs. Argentina. 3¾″ x 7½″, specimen No. 15/1489. Photograph courtesy of Museum of American Indian, Heye Foundation.

FIG. 9.—Snuff tube from Argentina. Sculptured motif seems to show a man holding a tube. Photograph courtesy of Museum of the American Indian, Heye Foundation. Specimen No. 15/2407.



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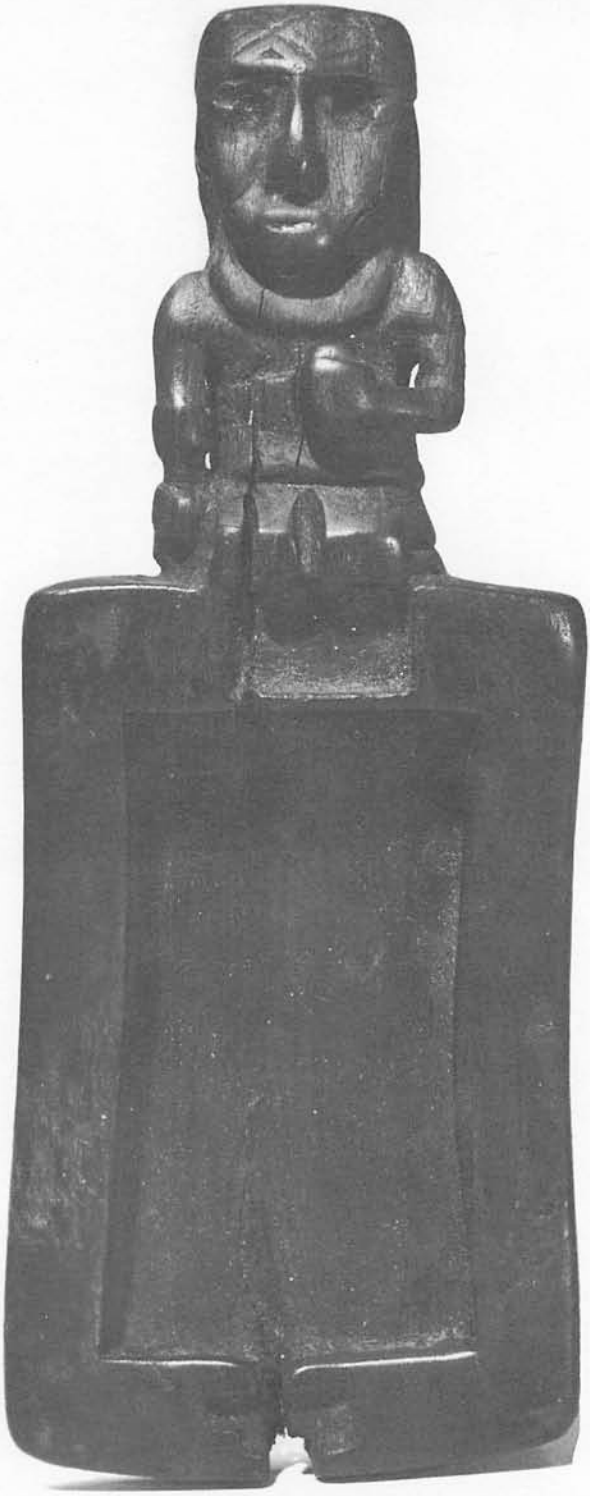

FIG. 10.—Wooden snuff tray, 2⅛″ x 5½″. Handle probably personification of deity. Chiuchiu, Chile. Photograph courtesy of Museum of the American Indian, Heye Foundation. Specimen No. 14/3741.

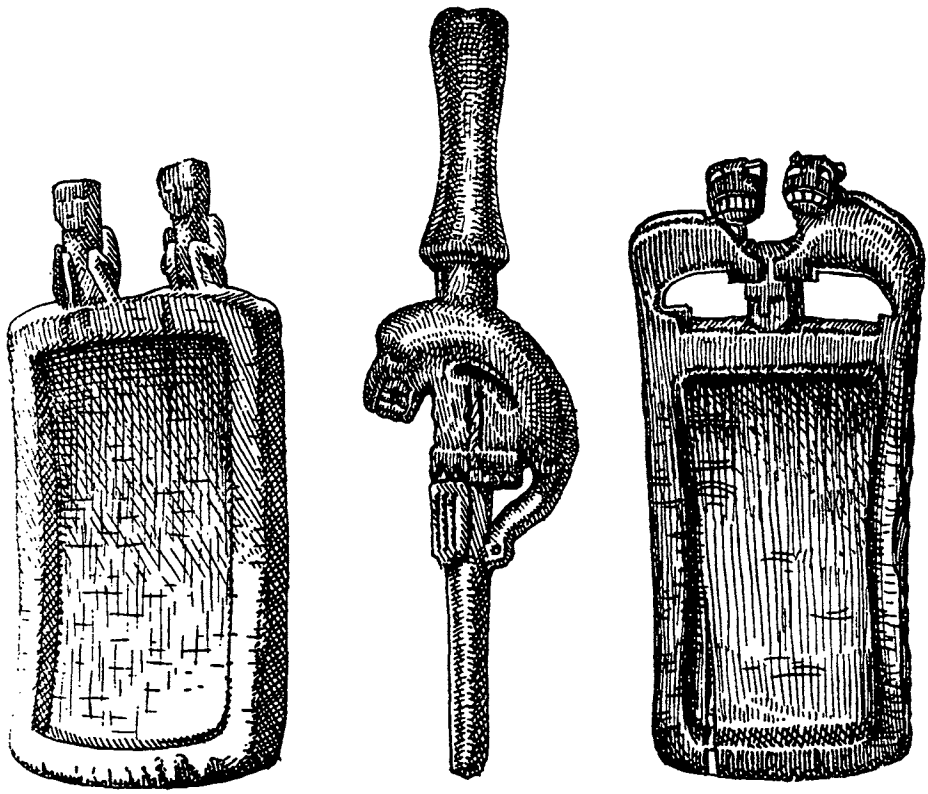

FIG. 11.—Snuffing paraphernalia, tablets and tube of wood decorated with zoomorphic and anthropomorphic figures. After fig. 57 in Casanova, 1946. Originals in Buenos Aires.

In 1885, the Brazilian archaeologist Ladislau Netto when commenting upon the zoomorphic stone figures (often bird-shaped) found in the *sambaquis* (shell middens) of Santa Catarina, Brazil, was long ahead of his time. With reference to the cavities observed in these figures (see Fig. 12), he took them to have served as a deposit for a vegetal powder, of exciting quality and ascribed with supernatural virtues.[43] This aspect is interesting and I must dedicate some time to it.

The so-called *antropolito de Mercedes*, a stone figure from Uruguay in the shape of a human being with a rectangular cavity on its front side (in the style of the Mexican *Chacmool* figures) has been labeled by Serrano (1939) as a *tableta*. This stone figure can be seen as Fig. 4 in the posthumous work by J. I. Muñoa about the prehistoric peoples of Uruguay. The author

[43] Netto, Ladislau. 1885: 516–517. "Uma advertencia cabe-me aqui interpor sobre a palavra vaso que tenho dado a estes ambuletos. Alguns, na verdade, pódem ter este nome, não outros, porém, que são, a bem dizer, fetiches zoomorphos com uma peqûena e mal distincta cavidade no dorso, no ventre ou no flanco, onde, ao que presumo, o pó vegetal excitante, a que attribuiam virtudes sobrenaturaes, era depositado e sorvido. Quanto aos vasos fetiches ou zoomorphos, muito é de crer que n'elles fossem depositadas substancias varias com attribuição de eguaes preconceitos, ou que servissem para pulverisar as folhas de alguma planta sagrada ou qualquer outra materia destinada a ceremonias religiosas."

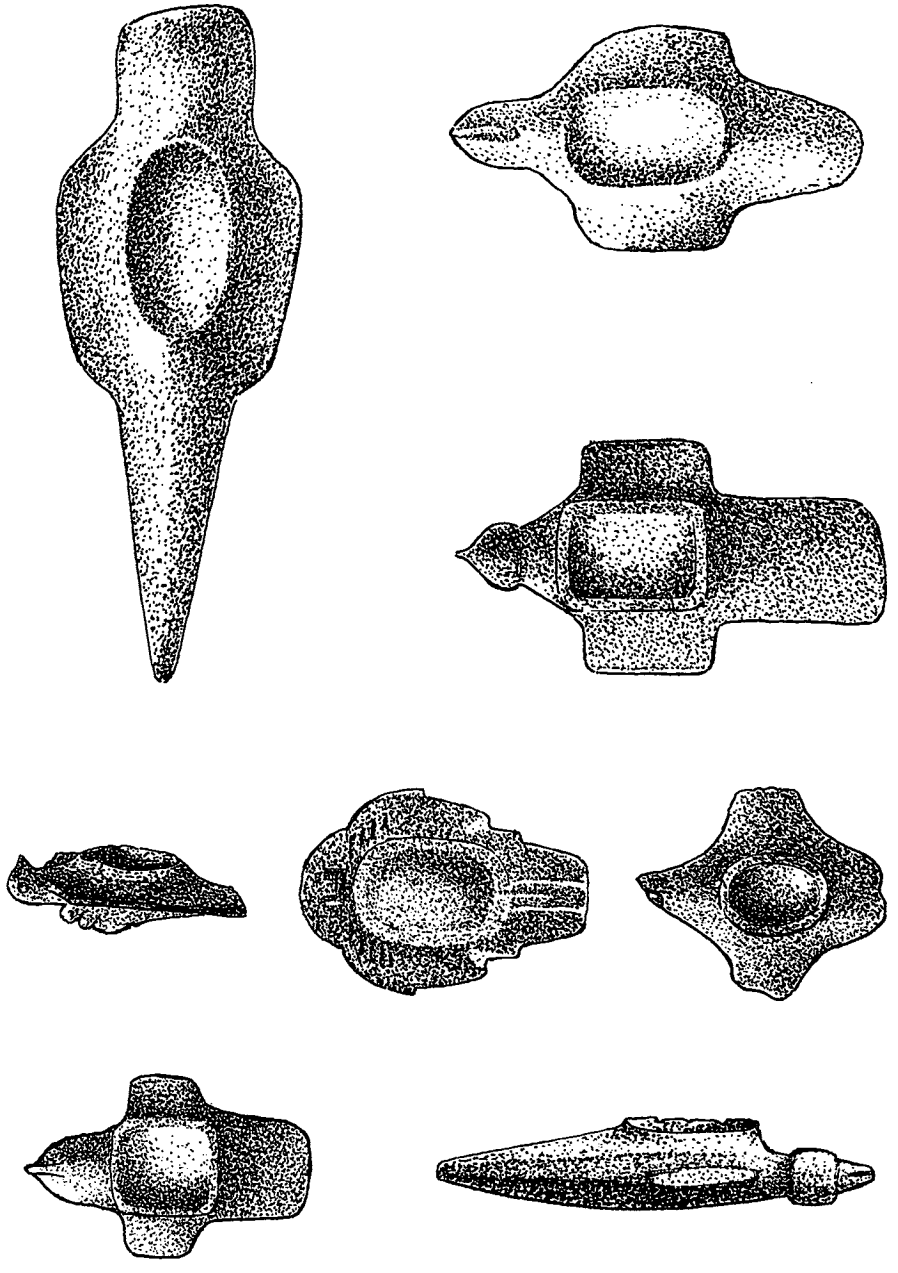

FIG. 12.—Bird-shaped so-called *zoolithos* from *sambaquis* in Santa Catarina, Brazil. Drawings after pl. VI in Netto's publication of 1885.

shows how the nicely sculptured stone specimens (*litos*) in animal form, and often birds ("*que figuran comunmente aves*") belong to a stone-working culture of the (later) Tupi-Guarani region of southern Brazil (Santa Catarina and Rio Grande do Sul) and the eastern parts of Uruguay.[44]

These special stone figures in human or animal form (birds, fishes, etc.) with cavities have been classified by Muñoa (p. 16) as "*tabletas shamánicas para aspirar paricá*", and included in what Serrano used to call the Guayaná Culture, which also goes under the name of the Rio Grande Culture. The Guayaná, according to Métraux (1946: 445), should be counted with the Caingang, a designation for several "non-Guaraní Indians of the States of São Paulo, Paraná, Santa Catarina, and Rio Grande do Sul, who previously were known as Guayaná, Coroado, Bugre, Shokleng, Tupí, Botocudo, etc., but who are all linguistically and culturally related to one another and form the southern branch of the *Ge* family." Nothing, however, seems to indicate that the Caingang were the masters of the stone objects mentioned here. On "Narcotics", Métraux (1946: 469) says only that "a great many stone pipes have been found in the Caingang area—a puzzling fact since smoking has not been observed among the Indians." This, however, was contradicted on the following page, where he says that "the Caingang shaman consults spirits at night, puffing his pipe until he is surrounded by a cloud of smoke."

But, as these *litos* evidently are of interest as possible ceremonial receptacles for snuff, to which culture do they really belong? The question seems open to discussion. Muñoa assigned them to a first wave of Indians in Uruguay, the *Sambaquianos*. Serrano placed the *litos* in a pre-Tiahuanaco period or *Middle Sambiqui* phase.[45] The culture is said to have come from the north. Vidart has on p. 61 of his edition of Muñoa's work dated the culture which left the shamanistic stone tablets ("*las tabletas shamánicas en piedra*") at 3.000 B.C., but no reasons for this very early dating have been given. For my own part I should prefer to consider the *litos* in southern Brazil and eastern Uruguay in some way related to the finds from the Amazon region (the *contas*, *muiraquitas*, etc. of the "Rio Trombetas," see Wassén, 1965: 34), perhaps so that a specialization in a craftsmanship connected with a ceremonial use of psychotomimetics has some center of origin until now unknown; however, within the Amazon region.

In Wassén, 1965: 34, the *Mercedes* figure from Uruguay has already been mentioned following a presentation of the "*idolo*" or "*conta*" from the Rio Trombetas region with its "Alter ego" motif, and its carefully hollowed out cavity on its back (Fig. 13) as having been used for holding some kind of a psychotomimetic snuff. When publishing this specimen from the Gothenburg Ethnographic Museum, I saw its "beautiful craftsmanship reflected in the snuff boards with animal motifs used by the Cashuena, and earlier also by

[44] Muñoa, Juan Ignacio. 1965: 14–19 (edition and notes by Daniel Vidart). I have not said that the Tupí used snuff of the kind discussed here. Alfred Métraux (1948 *a*: 127) has not mentioned the use of *paricá*, but that of tobacco smoking, "one of the favorite pastimes in daily life as well as on ceremonial occasions." He also points out that "stone pipes, found in several points of the Brazilian coast, perhaps belong to another culture anterior to that of the Tupí."

[45] Muñoa, ed. by Vidart. 1965. P. 16 and map on p. 12.

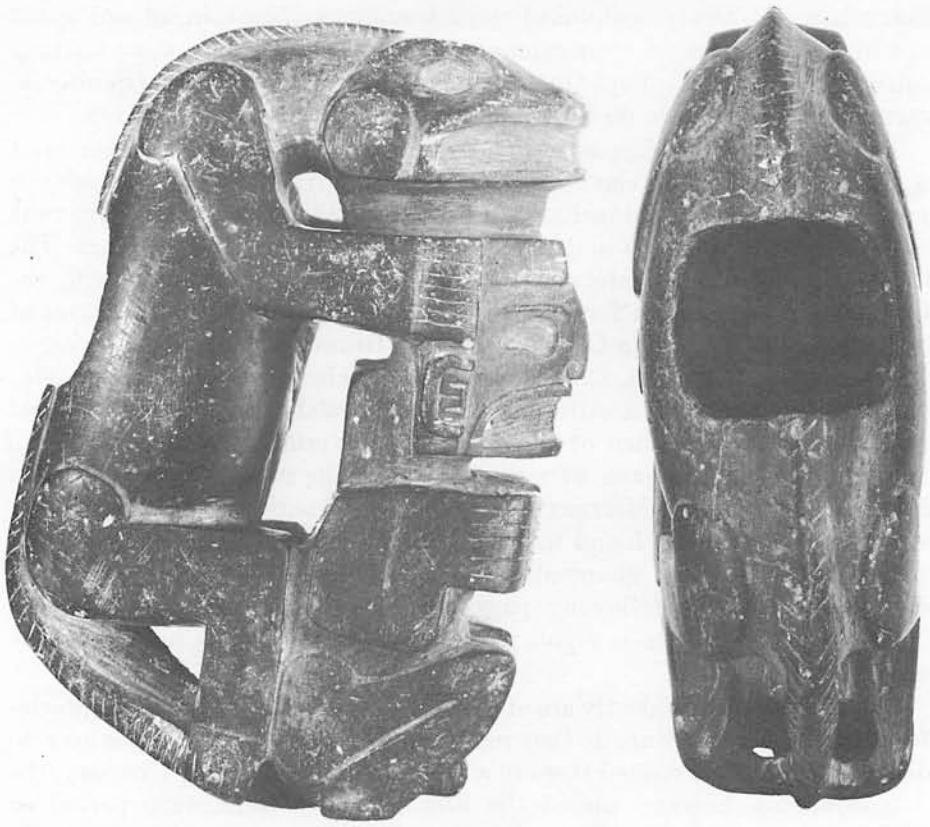

FIG. 13.—Stone figure with cavity. Sucurujú, R. Trombetas, Brazil. Gothenburg Ethnographic Museum, Coll. No. 25.12.1. Height 17.5 cm.

other Amazonian tribes." I could in 1965 also show a direct parallel to its artistic motif, a man being dominated by a jaguar on his back, when referring to a detail of a snuffing tube from Puna de Jujuy published by Ambrosetti in 1908 (see Wassén, 1965, Fig. 7, and this work Fig. 14). The figure shown in Fig. 14 is by no means a single example. In Fig. 15 we see the same motif, that is a jaguar dominating and above a human representation, on a fragment of a wooden snuffing tube found together with a tray with handles in the form of two human figures in an excavation in the Antigal de Ciénega Grande of the Puna de Jujuy, Argentina, and published by Salas (1945: 205–208, Figs. 86–89).

As mentioned in Wassén 1965: 36, Dr. A. A. Gerbrands in 1955 related the carved stone objects from lower R. Trombetas to the Maué Indian sculpture in wood. We can safely connect the *paricá* trays with two human figures found in Argentina and Chile, with the beautiful Tucano *paricá* tray in the Oslo University's Ethnographical Museum analyzed in 1965.[46]

The Jaguar, as a powerful and dangerous animal, has certainly always played a very important part in Indian beliefs as reflected in their ceremonial-

[46] Wassén. 1965: 68–80, and figs. 31–36 and 38–39.

ism. It is thus not without reason that we in the American Museum of Natural History, New York, find the Jaguar repeatedly represented in a series of snuff tablets and tubes originating from the "Gentilar de Caspana", north Chile.

In one special case, the comparison that can be made between ethnographically known snuff tablets in the Amazon region and a wooden snuff tray with feline head archaeologically found in Atacama, Chile, is absolutely surprising. For this I refer to Fig. 22 in this work, with kind permission published from a photo received from the *Museo de Arte Precolombino* in

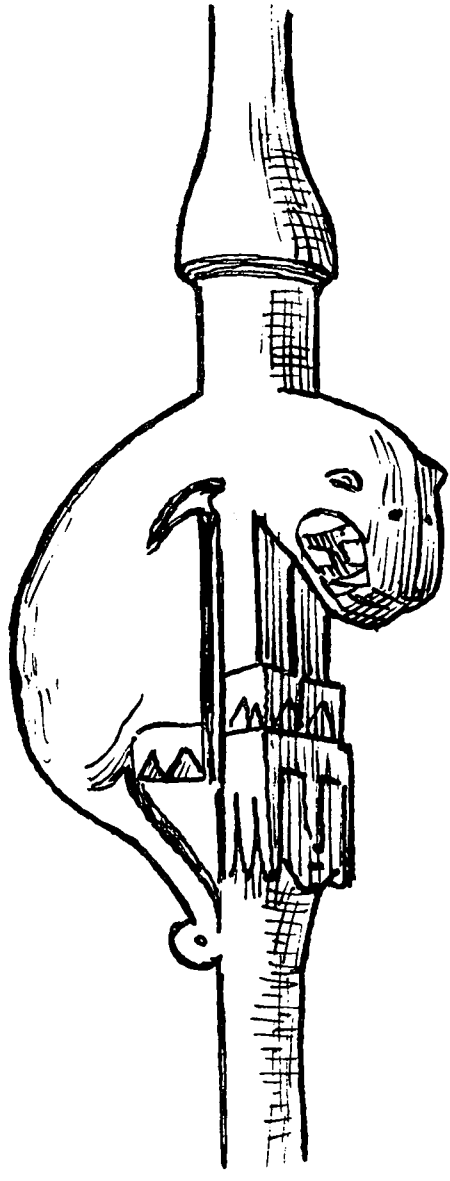

FIG. 14.—Detail of snuff tube from Puna de Jujuy. After Ambrosetti.

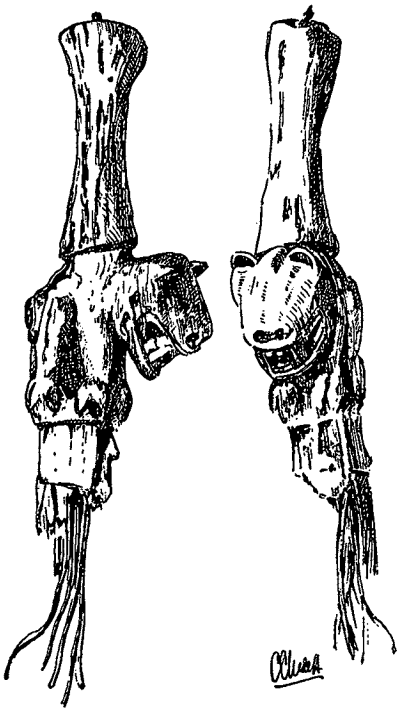

FIG. 15.—Section of snuff tube from Ciénega Grande, Puna de Jujuy, Argentina. After Salas.

Montevideo.[47] I am in this case nearly prepared to accept the Atacaman tray as a direct trade piece from the Amazon region. The late Dr. Stig Rydén, in his work on the archaeology of the Rio Loa region, was specifically interested in the trade relations between the Atacameño and the lowlands in the east.[48]

If we now look for other archaeological finds of snuffing paraphernalia in South America, the snuff tablet and its tube reported by Dr. J. B. Bird from near the Huaca Prieta, Chicama Valley, Peru, is the most interesting, as it appears in a very old culture sequence.[49] According to information received from Dr. Bird following my visit to New York in September, 1966, it is the question of a "snuff tablet of whalebone, Chicama Valley, Peru, near the Huaca Prieta. Test 4, House 3, associated with skeleton 99.1/880, the snuff tube 41.2/4722 a, b., and a broken jet mirror. The burial was made during the period when Guañape pottery was in use. (The oldest pottery known in this area). Estimated Age, c. 1200 B.C.; oldest known tablet (as of 1966)." (Letter of Nov. 2, 1966). See Fig. 23 for this specimen.

Dr. Bird has also had the kindness to inform me about a find of a snuff tray of wood collected by Mr. G. S. Vescelius in 1959, "from a Late Inter-

[47] See plate 38 in *"Arte Precolombino, Colección Matto,"* Museo de Arte Precolombino, Montevideo, 1948.

[48] Rydén, Stig. 1944. See his summary, pp. 206–212, also the discussion of the origin of the material of a leather cuirass made of the skins of alligator and monkey (pp. 115–116). According to Wendell C. Bennett (1946: 603) the "Atacameño were great traders."

[49] Bird, Junius B. 1948: 21–28. Also Wassén and Holmstedt, 1963: 25, and Wassén, 1965: 79–80.

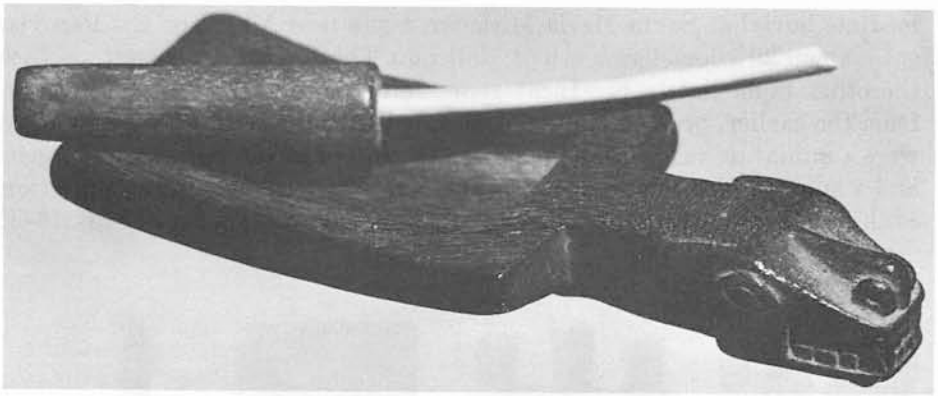

FIG. 16.—Snuff tray with feline motif and corresponding tube. Atacama. Specimen courtesy of the *Museo de Arte Precolombino*, Montevideo.


FIG. 17.—Both sides of whalebone snuff tablet and its corresponding tube. Specimens discovered by Dr. Junius B. Bird near the Huaca Prieta, Chicama Valley, Peru. Oldest known tablet (as of 1966). Coll. and courtesy of the American Museum of Natural History, New York. Specimen 41.2/4721 (tray), 41.2./4722 a, b, bird and fox bone snuff tube, found with the tray.

mediate burial at Santa María Miramar, a site near Mejía, on the Peruvian coast about 20 kilometers south of Mollendo. There are two phases (one Inca, the other immediately pre-Inca) represented at this site. The burial dates from the earlier, pre-Inca phase. Associated with the snuff tray in the grave were a miniature raft with its paddle, a bagfull of model harpoon foreshafts, and a spindle with rectangular whorl." Various specimens in the collections of the American Museum of Natural History, N.Y., are shown in Figs. 16–21.


FIG. 18.—Both sides of four snuff tablets of wood in the American Museum of Natural History, New York. Photographs courtesy of A.M.N.H. *A*, 41.0/8754, Cemetery at Chiuchiu, Chuquicamata, Chile; *B*, 41.0/8746, same data; *C*, 41.0/8911, Grave site near San Pedro, Chuquicamata region, North Chile; *D*, 41.0/8912, same data as *C*.

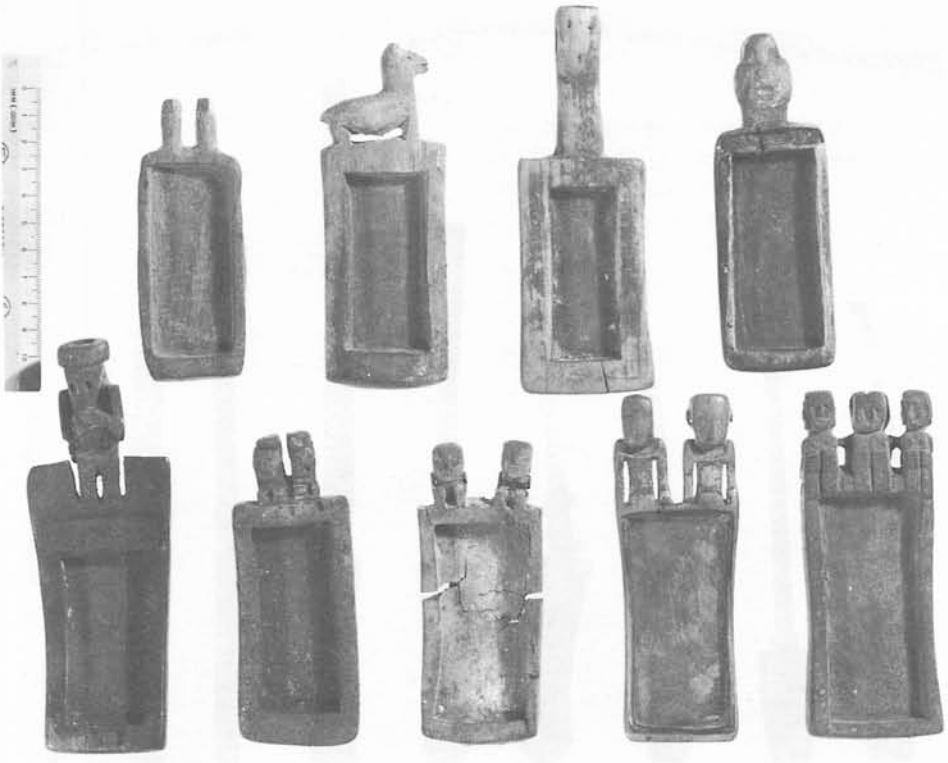

FIG. 19.—Nine snuff trays of wood from Chile. Coll. and courtesy of the American Museum of Natural History, New York. Eight specimens from Cemetery at Chiuchiu, one from Puntas Tetas near Antofagasta (bottom row, third from left).

FIG. 20.—Four snuff tablets of wood from Chile. Coll. and courtesy of the American Museum of Natural History, New York. From left: 41.0/8750, Cemetery at Chiuchiu; B/9568, "Taken from child's grave," Juan Lopez Bay, near Antofagasta; 41.0/8964, Cemetery about 3 km. from Chiuchiu, and 41.0/8751, Cemetery at Chiuchiu, Chuquicamata.

FIG. 21.—Snuff tubes of bird bone and bone and wood. Chile. Coll. and courtesy of the American Museum of Natural History, New York. These specimens come from Chiuchiu, Cobija and Lasana ruin, near Chuquicamata.

From the Huaca Prieta find, it is evident that snuffing paraphernalia were in early use in the Peruvian high culture area. I have in my book from 1965 (p. 80) referred to W. von Hagen's statement that "there is no doubt that the coastal yuncas, as their contemporaries, the Andean dwellers, had a wide knowledge of drug-yielding plants." Specific trade routes were mentioned: "Huancabamba had extensive trade alliances with the coast people. It was also a trade-axis for the jungle; a route less than sixty miles ran from the mountains about Huancabamba down to Jaen, near to the Rio Marañon, one of the tributaries of the Amazon rivers system." [50] It was, according to von Hagen, the milieu of the widely spread and trading Shuara (or Jívaro). Among various articles traded by these Indians, von Hagen (p. 150) especially mentions several narcotics, among them "*niopo* snuff (which was inhaled into the nose through the shank bone of the Oil-bird.") In this connection it is tempting to refer to a painting on a Mochica vessel from Period V (c. 600–700 A.D.) published by Alan R. Sawyer.[51] The vessel, which belongs to the Nathan Cummings Collection in the Metropolitan Museum of Art, New York, shows according to Sawyer an "ornately caparisoned war-

[50] Hagen, Victor W. von. 1965 : 149.
[51] Sawyer, Alan R. 1966 : 46.

rior-bird" which is "collecting the narcotic fruit of the *ullucho* tree, which grows in the highlands."

Following my publication of the claysnuffers from Costa Rica, Doctors Clifford Evans and Betty J. Meggers of the U.S. National Museum in a letter of March 24, 1966, raised the question if the so-called "pottery spoons from Marajoara Phase" published by them as plate 81 in Bulletin 167 of the Bureau of American Ethnology might be a snuff device. "These were ruled out as smoking pipes because of two factors; one, was position of the hole in all but one, and in that one, there was no indication whatsoever that it had been used for a pipe. Since they don't occur in the culture we use the term that has been used by others, namely pottery spoons. If they are actually used in snuff taking it would move the distribution down to the mouth of the Amazon and at a earlier time zone than the rest of your region." (Letter of March 24, 1966). The possibility that these objects served as some kind of snuffing paraphernalia should perhaps be taken into account. In the general form these clay specimens very much resemble the mortars of fruit shell used for preparing the *paricá* snuff in parts of the Amazon region.[52]

[52] Comp. for instance the object, pl. 81*b*, in the publication by Meggers and Evans (1957) with the mortar, fig. 25 (p. 60) in Wassén 1965.

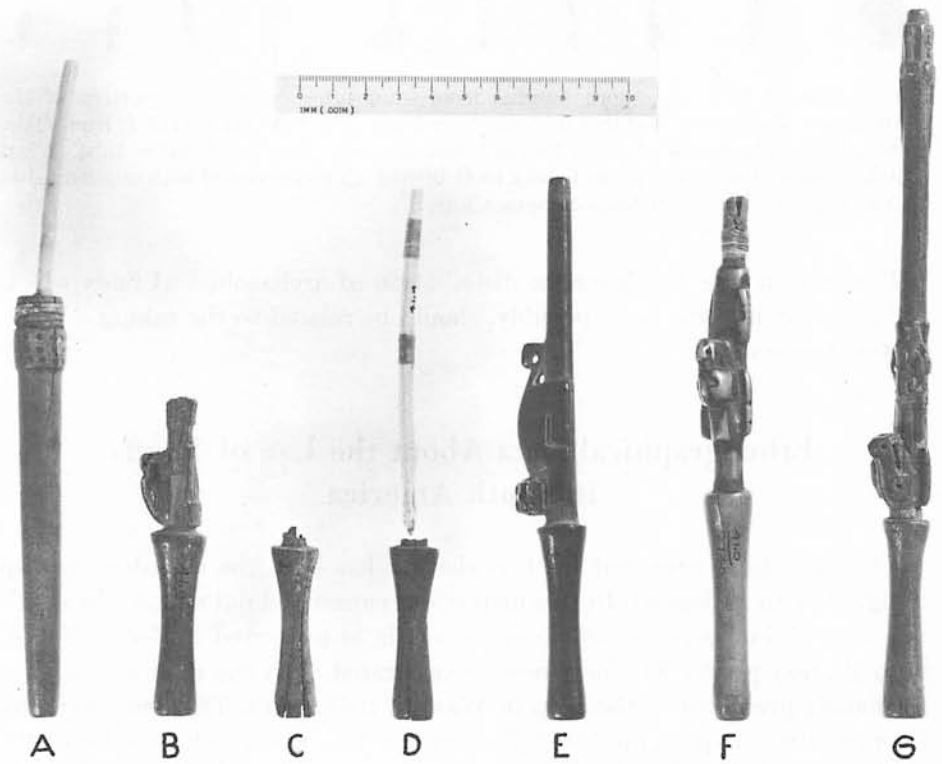


FIG. 22.—Snuff tubes from Chile. Coll. and courtesy of the Museum of Natural History, New York. *A*, B/4452, bone and wood, Arica; *B*, 41.0/8742, wood, Cemetery at Chiuchiu; *C*, 41.0./8994, wood, Chiuchiu; *D*, 41.0./3415, wood, Chiuchiu; *E*, 41.0.8739, wood, Cemetery at Chiuchiu; *F*, 41.0.8740, wood, metal at nd, Cemetery at Chiuchiu; *G*, 41.0.8741, wood, Cemetery at Chiuchiu.

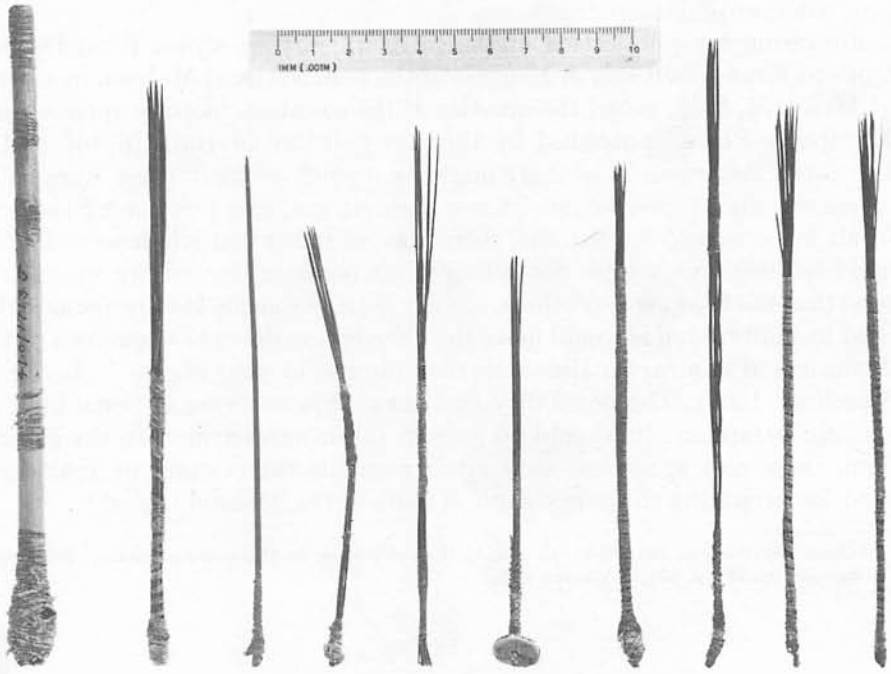

FIG. 23.—Snuff tube and thorn bundles from snuff tubes. Coll. and courtesy of the American Museum of Natural History, New York. The tube, 41.0/1713 J, from Chiuchiu, Chile. The bundle of seven thorns beside the tube was found in the tube. Wrapping is sinew. The other thorns belong to 41.0/8662, all unassociated with original tubes. Cemetery at Chiuchiu, Chuquicamata, Chile.

The map in Fig. 24 shows the distribution of archaeological finds which definitely, or in some cases possibly, should be related to the taking of psychotomimetic snuffs.

## Ethnographical Data About the Use of Snuffs in South America

The first thing prepared for this chapter has been the distribution map in fig. 25 with its legend. In this map tribal names and data about the snuffing of *paricá* or *yopo* as well as *epéna* snuffs as presented in Zerries (1964, map 10, text pp. 85–93) have been incorporated with the ethnographic information presented in the map in Wassén, 1965, p. 13. The data given by Cooper (1949, map 10, pp. 536–537) have also been used, as have some of the information from Colombia presented in the paper by Nestor Uscategui M. (1959). As far as I understand the final result must give a fairly complete picture of the distribution of psychotomimetic snuffing among the South American Indians according to published reports.

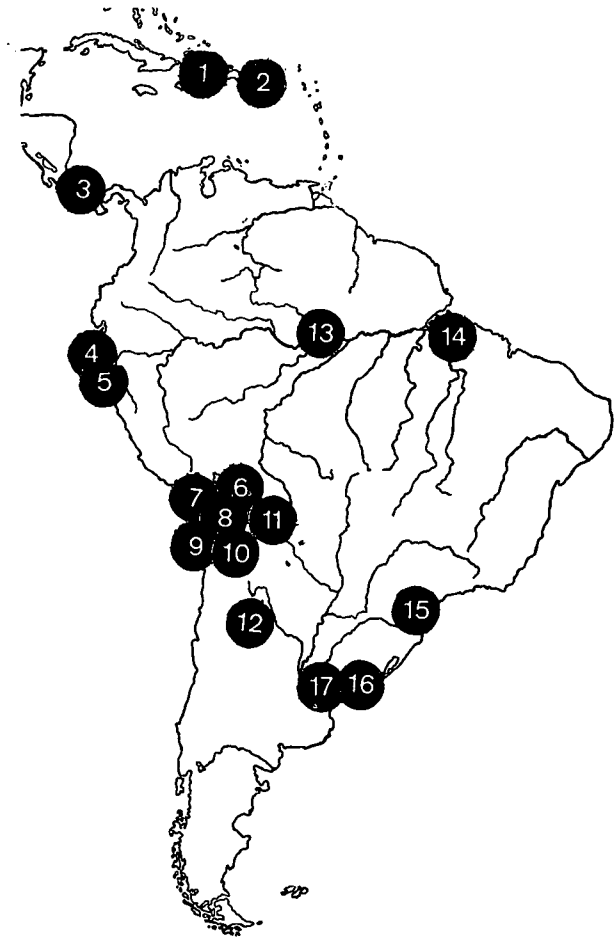


FIG. 24.—Distribution of Archaeological Finds. See Legend.

*Legend to Map in Figure 24.*

1. Haiti. Finds connected with the use of *cohoba*.
2. Puerto Rico. Stone *cemi* with platform on top.
3. Finds of clay snuffers in Costa Rica.
4. Mochica Culture, N. Peru. Painted motif on a pottery vessel supposed to show the collecting of the narcotic fruit of the *ullucho* tree (?).
5. Whalebone snuff tablet and bone tube. Huaca Prieta, Chicama Valley. Fig. 17.
6. Uhle's snuffing tube of bone from Tiahuanaco. Fig. 6.
7. Pre-Inca phase wooden snuff tray from Santa María Miramar, south of Mollendo.
8. Finds of snuffing paraphernalia at Chiuchiu, Chile.
9. Finds from the Changos, Coast of Antofagasta, Chile.
10. Finds from the Atacama region.
11. Finds from the Puna de Jujuy, Argentina.
12. Province of Córdoba, Argentina.
13. Stone figure (17.5 cm. high) with cavity on its back. Sucurujú, R. Trombetas, Brazil. Gothenburg Ethnographic Museum, Coll. 25.12.1.
14. So-called pottery spoons from the Marajoara Phase. (?)
15. Zoomorphic stone figures (*litos*) from S. Catarina and R. Grande do Sul, Brazil. Fig. 12.
16. Finds of *litos* in Eastern Uruguay.
17. The *antropolito de Mercedes*, Uruguay.

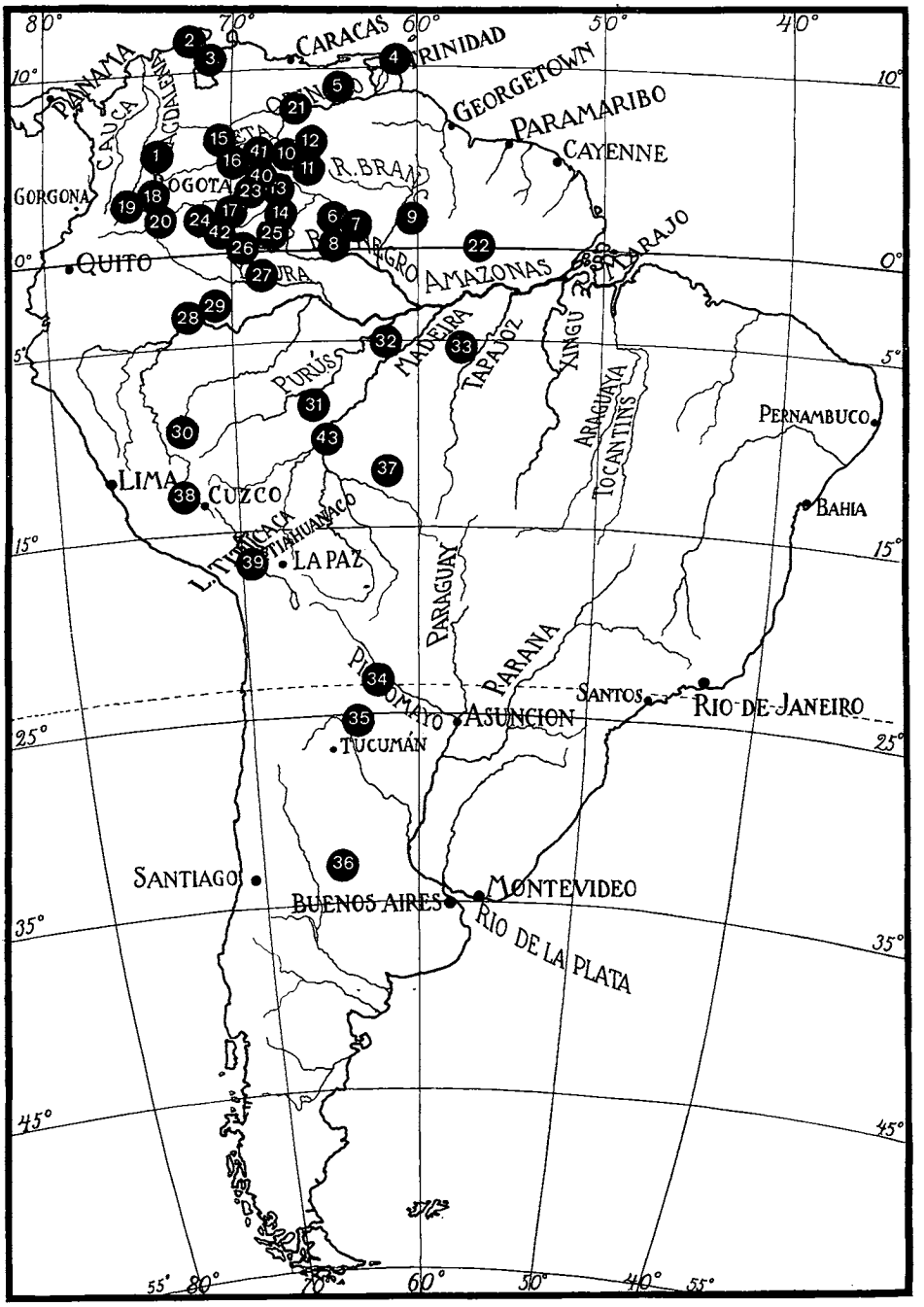


FIG. 25.—Ethnographical data, Distribution Map. See Legend.

*Legend to Map in Figure 25.*

1. Highland *Chibcha* and *Tunebo*, Chibcha neighbors on the east. *Piptadenia* snuff, see Cooper, 1949:536. According to Oviedo, *Historia* etc., vol. IV:607 (Madrid 1855), *yop* was a *"yerba de adivinacion, usada por los mojas ó sacerdotes del sol en los valles de Tunja y Bogotá. (Lengua de Nueva Granada)."* A reduced number of *Tunebo* are still found in "the humid jungle regions in the southwestern part of the Comisaria de Arauaca," Colombia (Uscategui, 1959:298–299). Same author, p. 299: "The custom of snuffing *yopo* was acquired probably from their Arawak neighbors in Venezuela and Colombia." A knowledge of nutmeg (at least for trade purposes) existed among the Tunebo of the early 18th century. According to Gumilla (1744:307) "el Padre Pompeo Carcacio, que fué Missionero de los *Tunevos* muchos años, nos asseguró, que en su tiempo traían aquellos Indios *Nuez moscada*, tan parecida en todo á la que traen del Oriente, que no se podian distinguir unas nueces de otras; pero yo no la he visto, ni sé que oy la saquen."
2–3. *Caquetío* and *Jirajara*, extinct tribes. The medicine-men took tobacco and a narcotic herb when they practised divination and communed with the spirits. Cf. Wassén, 1965:105. Probably *Piptadenia* snuffers.
4. *Inyeri*, Arawak Indians of Trinidad, *yopo* snuffers (Zerries, 1964:88, and Cooper, 1949:536, "early Contact Indians of Trinidad." Castellanos, 1950:93: (in "canto cuarto"),*"Uno toma tabaco y otro yopa para poder saber lo venidero."*
5. *Palenque* and *Piritú*. Two Carib tribes (Zerries, 1964:88). According to Hernández de Alba, 1948:411, "the *Palenque*, *Piritú* and *Sáliva* shamans also used "yopa" for divination."
6. *Waica*, *Samatari*, *Surára*, *Sanemá* and *Pakidái*, subgroups of the *Yanoama*, southern Venezuela. These Indians use snuff prepared from *Virola* sp., the snuff now internationally known as *epéna* (the Waica name). See information and references in Wassén *and* Holmstedt, 1963:8, and Wassén, 1965:98–99. Also, Holmstedt, 1965. According to Zerries, 1964:85, the *Waica* should also use *Piptadenia peregrina*.
7. *Karimé* (or *Shuári*), Indians culturally related to the Waica. According to G. Salathé, quoted in Wassén, 1965:99, and in Wassén *and* Holmstedt, 1963:14, these Indians prepare a snuff made of leaves from a small plant called *kokoime*. A 30 cm. long straight tube is used. Another person blows into the nostrils.
8. *Araraibo*, Indians at the upper Cauaburi River, an affluent of R. Negro, border region between Venezuela and Brazil. Visited by Georg J. Seitz, see his book from 1960. Information on the powder prepared of material from *Virola* sp. has been summarized in Zerries, 1964:85–86. Evidently closely related to the *Samatari* (Seitz, 1960:306, has published a short "Araraibo-Xamatari Word List"), or a Waica group.
9. *Paravilhana*, Carib Indians. Martius, 1867:631, has reported the use of *paricá* powder from *Mimosa acacioides*. Cf. Zerries, 1964:87.
10. *Yecuaná-Makiritare*, Carib Indians of southern Venezuela. See the translation of Th. Koch-Grünberg's description of the use of the *hakúdufha*, a "bark of tree"-powder from these Indians in Schultes, 1954:245, also quoted in Wassén, 1965:97. According to Schultes, an identification of the unusual narcotic *Virola*-snuff with the powder mentioned by Koch-Grünberg seems almost certain. Dr. Helmuth Fuchs (letter of March 9, 1962, quoted in Wassén, 1965:97), has described *a'ku:duwha* as a snuff powder with ingredients which botanically can be shown to have come from *Piptadenia peregrina*, or another *Piptadenia*. There are also other ingredients from a tree, probably *Virola* sp. See also discussion in Wassén *and* Holmstedt, 1963:10–12. Cf. Zerries, 1964:87–88. Cf. No. 24.
11. *Yabarana*. Carib Indians, related to the Makiritare. Johannes Wilbert, 1963:133, mentions the use of tobacco, *yopo*, and *cápi* among the Yabarana (Wassén, 1965:20). Zerries, 1964:88, quoting a paper by Wilbert from 1959, mentions that the Yabarana should obtain their *yopo* from a liana (?), and a tablet and Y-formed snuff tube are used.
12. *Piaroa*, Indians of the Salivan Family, Orinoco-Ventuari territory, see Wassén, 1965:103. According to Wilbert they use *yopo*, a strong *"tabaco-rapé,"* prepared from the seeds of *Piptadenia* sp. The powder is passed around in a round tray with



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handle in the form of a fin (of a fish) and Y-shaped tubes of bird bone are used. According to J. J. Wurdack, bark of *Lecythidaceae* is burned and the ash added to the *yopo* of *Piptadenia* seeds. Quotation in Wassén, 1965:103.

13. *Puinave.* Indians at the lower Inírida River, southeast Colombia and adjacent territory of Venezuela. Several quotations in Wassén, 1965:99–100. Dr. R. E. Schultes, 1954:248, has repeatedly observed the preparation of "a violently toxic snuff" among the Puinave. This snuff is prepared from an exudation of *Virola calophylla* and *Virola calophylloidea.*
14. *Kuripako,* Arawak Indians of the Guainía River. Schultes has described a narcotic snuff prepared of *Virola* sp. Quotations in Wassén, 1965:100.
15. *Achagua,* once widely distributed Arawak-speaking Indians in Venezuela and eastern Colombia. Hernández de Alba, 1948:409, says that "the Achagua used a snuff made of the narcotic powder of certain leaves called *"niopa"* or *"yopa."* Two Indians took this snuff simultaneously; with two crossed bird bones, each blew it into the other's nose." Cf. No. 19 in this list. Also Zerries, 1964 :89. Sven Lovén, 1935:387, says that *yopa* "is an Achaguan name." For a full quotation of the prognostication combined with the taking of *yopo* powder from the relation written by the Jesuit missionary Juan Rivero in 1736, I refer to Wassén, 1965 :19. "A nasal secretion from the right nostril signified success, from the left meant failure, and from both was an indeterminate sign."
16. *Guahibo, Chiricoa, Saliva.* Several references to these Colombian-Venezuelan Llanos tribes in Wassén, 1965:104. The Guahibo and Chiricoa men "invariably carried a shell or a jaguar bone containing parica. These tribes were said to carry the habit of parica snuffing to extremes not found among the neighboring tribes" (Kirchhoff, 1948:455). Cf. Zerries, 1964:89.
17. *Piapoco,* snuffers of *Piptadenia.* See Cooper, 1949:536.
18. *Guaupé* and *Sáe,* Arawak Indians. Zerries, 1964:89, has quoted Kirchhoff's article on these Indians in vol. 4 of the Handbook of South American Indians (Washington: 1948), p. 385–391, about the taking of "coca (yupa), and tobacco." The probably Arawak Indians once lived "in the southernmost section of the Venezuelan-Colombian llanos," the Guayupé "also in large parts also inhabited the dense rain forests of the Andean sloops" (Kirchhoff, p. 385.)
19. *"Ouitoto"* Indians of the upper Yapurá River. See Zerries, 1964:91, and the discussion of the crossed tubes for snuffing among the "Ouitotos" of Dr. Crevaux in Wassén, 1965:87–90. It is a possibility that hernández de Alba when formulating the statement about the *Achagua* (see No. 15 in this list) has been influenced by the drawing and text in the work of Crevaux. No source is given for the statement about the Achagua. Until such a reliable source has been presented, I prefer to consider the often published drawing in the publications of Dr. Crevaux of two Indians using crossed snuffing tubes, as dubious.
20. *Taiwano.* Indians of the R. Kananari, Comisaria del Uaupés, Colombia (Cerro Isibukurí). According to Schultes, 1954:242, they use a narcotic snuff of *Virola.*
21. *Otomac.* Tribe in the Venezuelan Llanos, between Orinoco, the Apure, and the Meta Rivers. According to Paul Kirchhoff's paper on these Indians in vol. 4 of the Handbook of South American Indians, pp. 439–444 (Washington, 1948), "Otomac shamans, under the influence of ñope, predicted the future." Humbolt was a witness of Otomac snuffing the powder of *Acacia niopo* seeds with lime as an ingredient. As he is one of the very few who really gives a description of the preparing of the snuff, I quote from the *"Personal Narrative"* (Humbolt and Bonpland, 1818–1929, vol. V:661–663): "The Otomacs are a restless turbulent people, with unbridled passions. They are not only fond to excess of the fermented liquors from cassava and maize, and of the palm wine, but they throw themselves into a peculiar state of intoxication, we might almost say of madness, by the use of the pwoder of *niopo.* They gather the long pods of mimosacea, which we have made known by the name of *acacia niopo,* cut them into pieces, moisten them, and cause them to ferment. When the softened seeds begin to grow black, they are kneaded like a paste, mixed with some flour of cassava and lime

procured from the shell of a helix, and the whole mass is exposed to a very brisk fire, on a grate of hard wood. The hardened paste takes the form of small cakes. When it is to be used, it is reduced to a fine powder, and placed on a disk five or six inches wide. The Otomac holds this disk, which has a handle, in his right hand, while he inhales the *niopo* by the nose, through a forked bone of a bird, the two extremities of which are applied to the nostrils. This bone, without which the Otomac believes that he could not take this kind of snuff, is seven inches long: it appeared to me to be the leg bone of a large sort of the plover (*échassier*). I sent the *niopo*, and all this singular apparatus, to Mr. de Foucroy at Paris." According to Rosenblat, (1965:272) nothing of all this is now remembered among the *Llanero* population said to be descendants of the Otomac. Also, their language has gone.

22. *Cashuena.* Indians of the Carib Family on the Casuro (Cashorro) River, a tributary of the middle Trombetas River, Brazil. From this tribe Protátasio Frikel has described a *mori* snuff, which can be made "simply of tobacco" or of other ingredients among which *paricá* is mentioned. A full quotation is found in Wassén, 1965:103, and also in Wassén *and* Holmstedt, 1963:21–23. The snuff mentioned by Mr. Gottfried Polykrates seems to originate from *Piptadenia* seeds. Details in Wassén, 1965:103.
23. *Tuyuca* and *Bará*, Tucanoan tribes on the upper Tiquié River. As quoted in Wassén, 1965:100, the use of *paricá* or *niopo* has been mentioned by Whiffen from the Tuyuca, and Zerries, 1964:90, refers to Koch-Grünberg's statement about the use of a snuff from *Mimosa acacioides* Benth. among both tribes.
24. *Cubeo*, one of the Eastern Tucanoan tribes at a section of the Uaupés River. Schultes, 1954:242, describes the Cubeo as users of *Virola* snuff. Cf. Wassén, 1965, about their use of *Banisteriopsis caapi*. According to Goldman, 1948:796, "the shamanistic novice spends a month learning the art from at least two professionals. He obtains tree resin, dupa (*Tucano*), and inhales it in a powdered form for 4 days." Bödiger, 1965:151, refers this to the Cubeo novices, and mentions also Koch-Grünberg's explanation of the word *dúpa* as meaning small white stones used for sorcery. In the meaning tree resin which is inhaled as a powder, the word is of direct interest through the term *hakúdufha*, offered us by Koch-Grünberg from a linguistically mixed region with contact zones between several language families.
25. *Tucano.* In this word an important group of Indians of the Uaupés and Papuri Rivers are included. Schultes has in 1954 reported the use of *Virola* snuff, and Uscategui has in 1959 mentioned a mixture of *Virola* and *Theobroma subincanum* powders. Mr. Georg J. Seitz has photographed a Tucano medicine man grinding the dry crust of evaporated *Virola calophylloidea* exudation to snuff powder with a stone. The photos were taken by him at Tapuruquara, upper R. Negro, Brazil, in 1965 (see Wassén, 1965:100–101, also p. 73). In Wassén, 1965:68–76, it has been demonstrated that the Tucano used very fine sculptured snuff trays in earlier days. Uscategui, 1959:294, remarks that the Tucano commonly use the Tupí-Guaraní loan-word *pa-ree-ká* (*paricá*) for the snuff prepared from "the blood-red resin of certain species of the myristicaceous tree, *Virola*, especially *V. calaphylla* and *V. calophylloidea.*"
26. *Barasana, Makuna, Yahuna, Yabahana, Menimehe.* Zerries, 1964:90–91, has mentioned that Koch-Grünberg found the same snuffing paraphernalia among the Tucanoan tribes (or groups) Makuna, Yabahana and Yahuna at the lower Apaporis River, as he had found among the Tuyuca and Bará (No.23) at the upper Tiquié River. Schultes found Barasana and Makuna Indians living together at the R. Piraparaná, both tribes snuffers of *Virola* (see Wassén, 1965:101). This drug seems also to be used among the Yakuna and Yabahana. Whiffen has listed the Arawak Menimehe at the Yapurá River as users of a narcotic snuff. See Zerries, 1964:91.
27. *Pasé, Juri* and *Uainuma*, once important Arawak tribes south of the Yapurá River, noted as *paricá* snuffers and also listed among such tribes by Zerries, 1964:91, as also by Wassén, 1965:66, according to Métraux. The Pasé have been mentioned in Wassén, 1965:68, as one of the Brazilian tribes called "black-faces," as they used a special tribal identification, the so-called *malhas*. They have been reported as excellent wood-carvers.

28. *Omagua.* In Wassén, 1965:83, there is a detailed description of this Tupí tribe through Father Samuel Fritz, who in 1701 had to calm an uprising in the Settlement of San Pablo. Pots with powdered *curupá* were found, "with which to deprive themselves of their senses, so as to carry out any evil deed without compunction." This material was all consumed with fire upon orders given by Father Fritz after his Mass. Métraux has stated that both the Omagua and Cocama, also a Tupí tribe further west, "inhaled powdered *curupá* leaves (*Mimosa acacioides*), to which they ascribed great therapeutic and magical powers." According to Métraux, the *curupá* "was blown into the nose through Y-shaped tubes or, with the help of small rubber syringes, administered as a clyster which provoked agreeable visions." Quotations in Wassén, 1965:83. Zerries, 1964:92, seems to doubt the use among the Cocama. According to La Condamine's *Relation*, etc. from 1778 (quoted in Wassén, 1965:84) the word *curupá* for *Piptadenia* should originate from the language of the Omagua. Monteiro de Noronha, writing in 1768 about the Omagua, which he calls *Umauá* or *Cambébas*, "Flat Heads," criticizes La Condamine for his statement that the *curupá* intoxication should last 24 hours, and corrects it to "apenas dura tres horas" (Monteiro de Noronha, 1862:58). The same author adds that the Cambébas used the juice from the bark of the *manacá*, which has been identified with *Brunfelsia hopeana* Benth. of the *Solanaceae* family.
29. *Tucuna.* As follows from the analysis in Wassén, 1965:82–83, these Indians who now only snuff tobacco, are known to have been using *paricá* snuff in earlier days for their ceremonial snuff called *ka'/vi*. The very important snuff tray found in the Oslo University's Ethnographical Museum and published in Wassén, 1965, fig. 41, has by an ethnographical analysis been shown to come from the Tucuna, and to represent the *prego* monkey demon. See Wassén, 1965:80–86.
30. *Piro.* One of the Arawakan-speaking tribes of the headwaters of the Ucayali and Madeira Rivers, by Julian H. Steward and Alfred Métraux counted as a primitive Montaña subgroup. The use of the seeds of *Acacia niopo* has been reported among the Piro by William Curtis Farabee in 1922. For the hunter and his dog, see Wassén 1965:94. Cf. No. 31 in this list.
31. *Catawishi*, Indians of the river Purús. Spruce has in 1874 reported from these Indians that they used to absorb *paricá* through a bent tube, and also that they administered an injection of *paricá* to dogs, thus a confirmation of that stated from the Piro. Full quotation in Wassén, 1965:96. See also Cooper, 1949:547.
32. *Mura.* For the once much feared Mura Indians of the Madeira River the use of *paricá* must have been of outstanding importance. This is clearly demonstrated in the descriptions quoted in Wassén, 1965:37. The roasted seeds of the *paricá* tree were taken either as a snuff or an enema. The snuff was blown into the nostrils by means of bone tubes. The effects of the drug consumption in this tribe have been drastically described. Schultes has warned that we cannot be absolutely sure that the snuff used by the Mura and Maué was prepared from *Piptadenia*, as a botanical consideration must be kept in mind. Cf. Wassén, 1965:23.
33. *Maué.* These Central Tupí Indians were formerly famous for their *paricá*, which they do not use any more (see Nunes Pereira, 1954:71). *Mimosa acacioides* is given as the source. They have also been carving very nice specimens of snuff trays, now kept in several museums. See the description in Wassén, 1965:39–63.
34. *Mataco.* Indians of the Gran Chaco, among whom the shamans have been reported to use snuff from the seeds of *cebil*, that is *Piptadenia macrocarpa*. Information collected by Métraux has been quoted in Wassén, 1965:29.
35. *Lule.* Extinct Indians in western Chaco, Argentina. Métraux has mentioned the Lule together with the Mataco. An old information from the Lule comes from Pedro Lozano (1733), who states that *cevil* was blown into the nostrils by a small tube in order to provoke rain when necessary for their cultivations. Full quotation in Wassén, 1965:11–12.
36. *Comechingones.* Cooper, 1949:536, has listed the extinct 16th-century Indians around Córdoba, Argentina, among those taking *Piptadenia* powder. See Zerries,

1964:93, for further references to the use of *cebil* and/or *wilca* in the southern region, where also the *Zanavirones* are reported to have used it. Max Uhle, 1898:9, has quoted vol. II of the "*Relaciones Geográficas de Indias, Perú*", p. 152, from a report dealing with "la Ciudad de Córdoba," where the Indians spoke *comechingona* and *zanavirona:* "*Toman por las narices el sebil, ques una fruta como vilca; hácenla polvos y bébenla por las narices.*" Uhle comments (p. 9): "The curious expression, they drink the powder with the nostrils, means without doubt that the Indians took the powder by means of an instrument like a tube. Concerning the word *sebil,* Napp (The Argentine Republic, 1876, p. 114) tells us that *sebil* is in Argentine the name of the Acacias. Now, the fact that Humboldt originally pointed out the *niopo* tree as a species of Acacia by mistake and von Martius called it *Mimosa acacioides* proves that Piptadenias and Acacias have sometimes been confounded. We know, further, that Piptadenia trees of the variety *niopo* are also common in eastern Bolivia and the Argentine (for instance *Piptadenia macrocarpa,* in the province of Tucuman). As the bark of the *curupau* tree, which from its name and general description may be a *niopo* tree, serves, according to Cardús, to tan hides in eastern Bolivia, so in like manner the bark of *sebil* is used to tan hides, as I noted, in the environs of Tucuman. All this leads to the conclusion that the tree, from whose seeds the powder was made, is related to *niopo,* and a scientific determination may perhaps show it identical with *niopo.* The custom of snuffing *sebil* in the environs of Córdoba was, therefore, derived from another part of the continent, where snuffing *niopo* was practiced." The conclusion by Uhle must be considered as very important also when we take the distribution of paraphernalia into account.

37. *Tupari, Guaratägaje, Amniapä,* and other tribes in western Brazil, in the R. Branco region and on the Mequéns River, affluents of the Guaporé River. Cooper, 1949:536, refers to "the upper Guaporé tribes." Zerries, 1964:91, has, according to a report of Dr. Etta Becker-Donner, Vienna, added the *Aikaná* or *Hauri,* as their medicine-men use a snuff of *Piptadenia peregrina* mixed with bark ashes. Dr. Becker-Donner has also reported the use of such powder among the *Salamay* in the same region, as quoted by Zerries, 1964:91. The most valuable information from the whole Guaporé region as regards snuffing has been given by Dr. Franz Caspar from the Tupari. I refer to his book from 1952, and his manuscript from 1953, both quoted in Wassén, 1965:102, and as regards the snuffing tubes, especially pp. 24–28.
38. *Quichua.* See Discussion in Zerries, 1964:92, for the use of *wilca* (or *vilca*) snuff among the Andean Quichua, according to data given by Safford in 1916 and by O. F. Cook in 1915. Cooper mentions the Highland *Quechua* of Peru among the consumers of *Piptadenia,* and this is also fully reflected in his Map 10 in his work for the *Handbook* (1949), where a solid black covers most of the central part of the western Highland.
39. *Aymara.* Zerries, 1964:95, has listed the Aymara, Tiahuanaco, as *yopo* snuffers and mentions the word *coro* as probably $=curupa=yopo$. His text seems to indicate that the yopo powder should have been known among the Aymara through the old tribes in northwest Argentina. La Barre, however, does not mention *yopo* among the narcotics in his work from 1948, but he has the information from Bertonio, "*Sincantatha:* Tomar tabaco por las narizes. *Thusa thusa* es el tabaco" (La Barre, 1948:66).

    Max Uhle (1898) was the first to take up a serious discussion about what kind of snuff really was used in the Highlands. Garcilasso de la Vega's information is clear and refers to tobacco: "The Indians made great use of the herb of plants which they call *Sayri,* and the Spaniards called tobacco. They applied the powder to their noses to clear the head" (Markham, 1869:188). According to Uhle, we learn from this source "that the practice of snuffing must have been nearly general in the Highlands of middle and southern Peru," . . . Uhle here refers only to the snuffing of tobacco.

    It is in one of the sources known to him, namely a report from La Paz found in the "*Relaciones Geográficas de Indias, Peru,*" vol. II, p. 76 (Madrid, 1885) that we

*Legend to Map in Figure 25*—Continued

find the word *coro*. "*Hay tambien entre los indios tabaco, que ellos le llaman sayre, de que los negros usan mucho, y los indios de la raiz que llaman coro, y se purgan con ello y lo toman en polvos.*" Uhle (1898 : 17) comments: "There is nothing published which points to the practice of snuffing the powder of *niopo* in Peru, if not in the report of the province of La Paz. In this province two powders were used as snuff—tobacco and *coro*. This *coro*, without any hesitancy, should be declared to be *curupa*, if it had not been reported as being a root. But the use of *niopo* being confirmed from the region of Córdoba, it seems more reasonable to suppose that the writer of the report was mistaken than that there existed a third powder, never elsewhere reported, with a name similar to that of *niopo*, which was taken as snuff in the environs of La Paz."

40. *Desano* and *Tariano*. Two Arawak tribes along the lower part of the Colombian course of the Uaupés River. According to Uscategui, 1959 : 295, they know "and employ *paricá* or *Virola*-snuff as do their Tukanoan neighbors." *Paricá* (*pa-ree-ká*) is a loan-word from the Tucano but of Tupí-Guaraní origin (cf. No. 25). The tribes are also called *Desana* and *Tariana*.
41. *Kuiva, Amorua, Sikuani*, and
42. *Guayaberos*. "Various tribes," according to Uscategui, 1959:299, "located between the Meta and Inirida Rivers, most of which belong to the Arawak and Guahibo linguistic families." He has for these tribes or tribal groups received personal communications from Meden and Schultes. Other tribes mentioned by Uscategui in this context are the Puinave, Piapoco, Saliva, and Kuripako, which already have been listed separately:

"All of these use or were formerly acquainted with *yopo*, especially for purposes of magic. *Yopo*, prepared from the toasted and pulverized seeds of *Piptadenia peregrina*, is normally taken only by men, for there exists a certain taboo which, however, seems no longer so strict as it once was. In the most acculturated of these people, both sexes take it. Snuffing of this violent intoxicant, which looks rather like ground coffee, is carried out with very different kinds of instruments, the most generally used of which is a double Y-shaped tube of bird bones (the arms of the Y being soldered into place with pitch) ending in two hollowed palm-nuts. These nuts are placed at the opening of the nostrils, and the powder is inhaled from the palm of the hand. Another kind is the long V-shaped snuffing tube, one leg of which is inserted into a nostril, the other into the mouth, thus making self-administration possible. There are additional types of snuffing-tubes as well, both of bone and of small bamboo-like grasses. One other primitive type is made of a palm-leaf: the apex of the leaf is cut off truncated, and this funnel-shaped end is placed over the snuff, while the snuffer draws in strongly through the petiole which is bound into a tube. Generally, some kind of wooden mortar and pestle is used to grind the *Piptadenia*-seeds which have previously been roasted in the fire. The powder is kept in a case made of the leg-bone of the jaguar, partly closed with wax and adorned with feathers. The addition of an alkaline admixture may or may not be the practice." This long quotation with its excellent description to which practically nothing could be added has been taken from Uscategui, 1959:299–300.

43. *Caripuna*. A Panoan-speaking tribe referred to by the Austrian naturalist Johann Natterer as having snuffing implements. Natterer himself encountered a Caripuna subgroup, probably the Sinabo, at the Madeira River (quotation from Métraux in Wassén, 1965:47). According to Métraux "the Caripuná provoke a state of trance by taking *paricá* (Piptadenia sp.) in the form of clysters they administer to each other with rubber syringes provided with a bone tube."

The distribution of tobacco snuffing (and other ways of taking tobacco as chewing, drinking, and licking) in many cases covers the same areas (see map 10 in Cooper, 1949, and maps 11–12 in Zerries, 1964). These data, however, have not been considered here, as I have had to limit myself to special

powders.[53] The legend to the map in fig. 25 gives the available information in a concentrated form.

What we learn from the map in Fig. 25 is the concentration of the use of psychotomimetic snuff drugs to certain regions of South America with a western and northwestern dominance, if we consider still remaining tribes or such extinct or no longer snuffing tribes from which data have been recorded. What we do not learn from the map, but perhaps may recognize by reading the legend, is how very few good observations there are. This fact is deplorable, as it is obvious that we now face in the Uaupés region a strongly disappearing usage (cf. Wassén, 1965: 16–17).

A scattered information on the use of *paricá* or *yopo*, by which words mostly a snuff prepared from *Piptadenia* seeds seems to be understood, has been saved. When we turn to other kinds of psychoactive drugs such as the snuff prepared of exudates of *Virola* species, the available data is sparse indeed. It is only through the intensive field work of such an eminent botanist as Richard Evans Schultes, the repeated collecting and observations among the Waica of Mr. George J. Seitz of Rio de Janeiro, and scientific research by Prof. Bo Holmstedt, that we now are able to fully grasp the outstanding importance of this drug.

It is in our days mostly impossible to find out merely from vague ethnographical descriptions, which kind of snuff many tribes have been using; if a pure powder or a mixture, and in the latter case which ingredients. It was only through a chain of lucky detective work in the documented museum material in Gothenburg, that I was able to trace back to the Tucuna Indians the perfect and unusual snuff tablet No. 1219 in an 100-year old Brazilian museum collection in Oslo (see Fig. 26, and Wassén, 1965: 80–86 with illustrations). It has also only been possible to consider another of the three snuff trays in Oslo (No. 1169) as probably Tucanoan (see Wassén, 1965: 68–80), through an ethnographical comparative ornamental study in several museum collections. It is this unique specimen with its double human figures as handles (Fig. 27) which especially leads us to look for an origin in the Amazon region also for the snuff trays among the Atacameño. There are many tablets in the Atacaman collections with two human figures as handles, but I use this opportunity to refer specially to a specimen from Calama, Antofagasta, Chile (fig. 27), now in the collection of the Field Museum of Natural History, Chicago. Dr. Carl Schuster of Woodstock, N.Y., who takes an extreme interest in all double-headed figures, writes to me (May 9, 1966) that "the fact that the two-headed snuff tray as a type occurs in N.W. Brazil, N.W. Argentina and Chile is very interesting. Double-headed human figures begin in South America archeologically very early—with the Valdivia Culture in Ecuador; and I know of some ethnological specimens (Caduveo, Mato Grosso), etc."

As already declared, this study is not dealing with the snuffing of tobacco. Such a study has, however, been undertaken by Zerries in his *Waika*-book (1964: 93–95, map 11). Naturally, this Americanist when trying to sum-

[53] For the *rapé dos indios* from the *Olmedioperebea sclerophylla* tree, see Schultes, R. E. 1963: 26.

marize the details of both distributions, had the same difficulties everyone must find in the sources, namely that many times we cannot differentiate the two kinds of snuff when reading the reports. For instance, the Guaporé tribes are mixing *yopo* and tobacco powders, and many tribes use both powders. Zerries (1964: 95) exemplifies the latter cases with Waica, Piro, Tupari, etc.

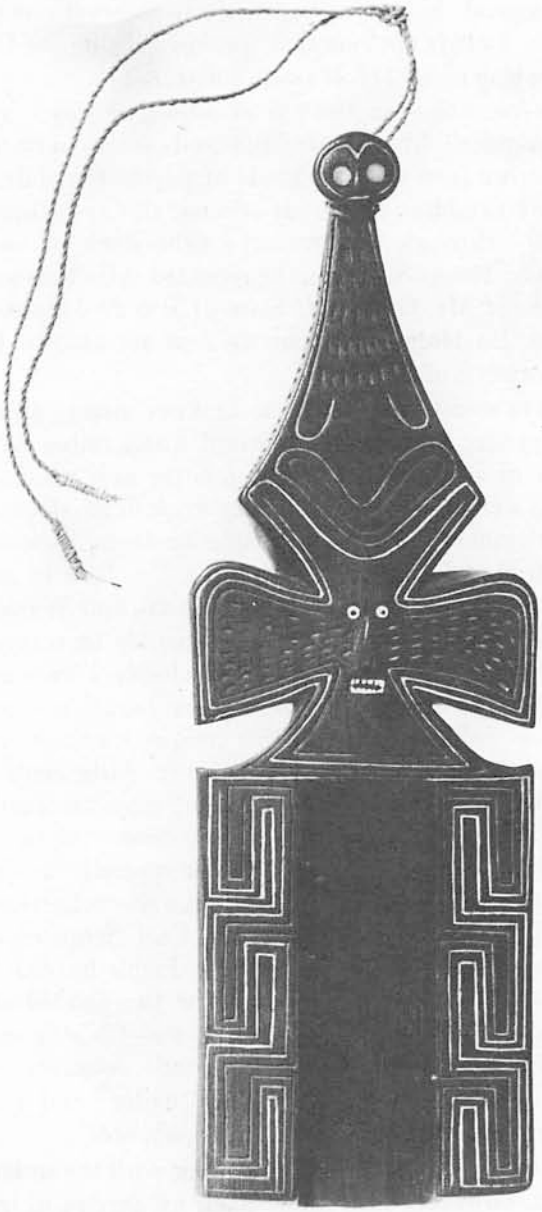

FIG. 26.—Wooden snuff tray representing the prego monkey demon of the Tucuna Indians. Length 25 cm. Coll. and courtesy of the Oslo Univ. Ethnogr. Museum. Specimen No. 1219.

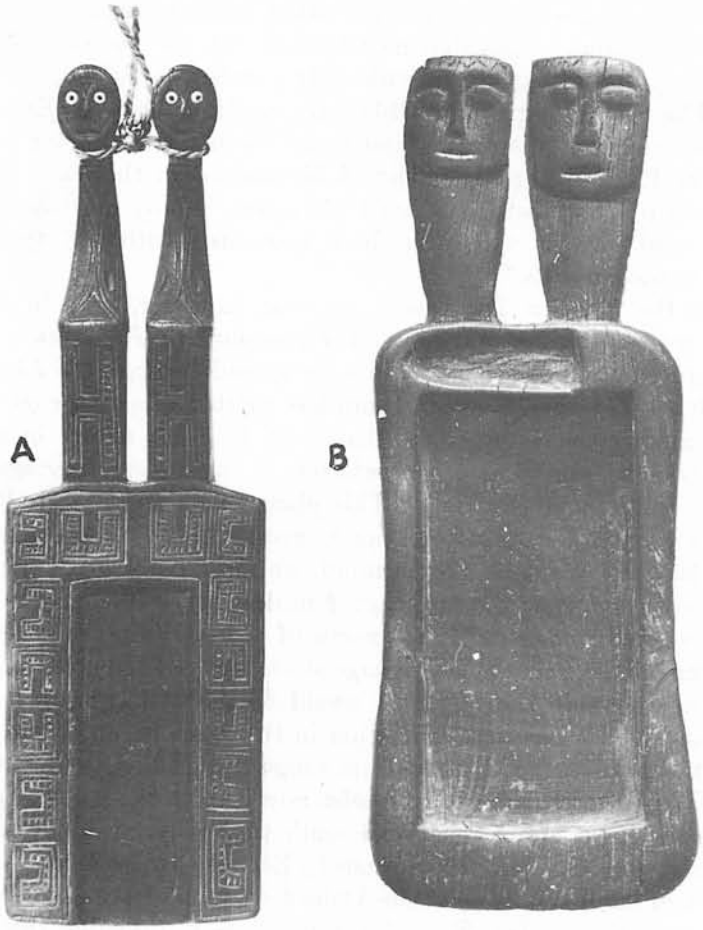


FIG. 27.—*A*, Wooden *paricá* tray, length 20 cm. Probably Tucano. Specimen No. 1169 in the Oslo Univ. Ethnogr. Museum. *B*, Snuff tray of wood, archaeological find from Calama, Antofagasta, Chile. Length 15 cm. Coll. Field Museum of Natural History, Chicago.

The distribution of the snuff taking indicates that we have to look upon northern and northwestern South America as the origin area for both powders. Zerries also stresses this fact and points out that we, with such an important exception as the Maué, generally do not find the habit of snuffing among the Central Tupí tribes. According to Zerries (p. 95) Eastern Brazil should not be taken into account at all, as the only statement is dubious. I translate the following from Zerries work (1964: 92): "When Uhle (1898, p. 163/4), following Martyr, wants to credit the Tupi of Eastern Brazil for snuffing *paricá*, this seems *unlikely*." He supports this statement with the information that such a specialist on the Tupí-Guaraní peoples as A. Métraux does not say anything about such a habit among them. This is perfectly correct, and as has been conclusively shown by Métraux in his work on the religion of the Tupinamba (1928: 88), these Indians were blowing smoke of the *petun* plant (tobacco) from a tube for

magic and healing purposes. On the other hand an examination of the text in Uhle's paper shows that he (dealing with the *paricá* snuffing) uses the phrase ". . . and has been occasionally ascribed to the Tupis of Eastern Brazil." The reference given by Uhle is the small paper by A. Ernst (1889), but Zerries had been misreading and found the name of Martyr on the line just above. The old chronicler should be omitted in this case, and Ernst on page 135 of his paper, to which Uhle refers, is only mentioning an Old Guarani word *petycui* which has been translated with "*pó* (powder) *de tabaco para ser aspirado.*"

Leaving the Eastern Tupí aside we must, however, keep in mind that the very words *curupá* and *paricá* for the snuff of *Piptadenia* originate in the Tupí-Guaraní languages, and were spread through the *Lingua geral* (Friederici, 1947: 229). Esteban Pinto has written in a paper on the medicine-men among the Tupinamba, that they, in order to get in a state of ecstacy, used "*ilusogénicos o estupefacientes, indicados genéricamente con el nombre de Kurupá* (Pardal)." This plant he identifies with *Piptadenia* species. As a source for the information he gives only "*algunos testimonios.*" [54]

With the Tupí word *curupá* in mind, we must realize that snuff taking does not always follow the language families. Zerries has found how, for instance, several Arawakan tribes north of the Amazon are *yopa* snuffers, while other tribes of the same language stock south of the river take tobacco snuff. Most probably the botanists would be the best equipped to find if such a varying use has its explanation in the distribution of the botanical species. In the following chapter, I am suggesting that the old word *cohoba* from the West Indies and a word *khoba*, now used in the Atacameño region, should be the same, and have spread south via the Arawak and the Andes. This finds a support in the observations by Zerries that we should ascribe the very habit of snuff taking to a sub-Andean stratum of tribes. Here the sub-Andean Arawakan tribes fit, and Zerries finds it probable that the clue to the snuffing should be found among the Arawak, and that the use of *yopo* should be considered as the oldest of the two main classes of snuff.

In my work from 1965 I have treated the same problems, pointing to "a common old tradition in the Amazonian and sub-Andean regions"; equally, I have stressed the fact of "an obvious northern Arawak influence far south into northwestern Argentina" (Wassén, 1965: 77–78).

## Comparative Outlooks and Symbolism

Certain living and extinct tribes and certain archaeological and ethnographical objects have been mentioned in this paper in regard to their importance for the whole study. We have first the ceremonially used *cemi*-figures of wood and stone in the West Indies, with platforms on top for the placing of *cohoba*. A mainland ethnographic equivalent to these Antillean *cohoba* "platforms" are the table tops used by the Tupari in Brazil when snuffing ceremonially.

[54] Pinto, Esteban. 1944 : 324.

We have through Oviedo's drawing, the descriptions in words and the find in the La Gonâve cave, a fairly good knowledge of the more simple and the more elaborated snuff tubes of wood on the Islands. These specimen have their counterparts in the Y-shaped tubes used among many mainland tribes. We recognize the round snuff trays, which Las Casas describes from the Antilles as perfectly made pieces, when we see the generally much simpler round trays used by the Llanos tribes of northern South America, and certainly also the more unusual round snuff trays found archaelogically in the marginal Atacameño region. For the latter I refer for instance to plate 34 in Le Paige's description of San Pedro de Atacama (1965), where the author refers to a grave for 25 adults, a child's offering and also the offering of snuff trays. Finally, we are certain to look for the origin of the *cohoba* drug itself in the now more and more studied species of plants which botanically belong to the South American mainland. But the very word *cohoba!* Would it be possible to trace it back to some actual situation and still find it used on the mainland? It looks as if it should be possible, and I will return to this problem later in this chapter. I have already mentioned that the word *cojoba* occurs in northern Venezuela.

In this paper I have repeated my opinion from 1965, that the elaborate stone figure from the R. Trombetas region shown in Fig. 13 has been especially sculptured and used to hold a psychotomimetic snuff. The whole character of this famous piece is ceremonial, and we meet in the sculpture a very important South American combination of man and jaguar. It is therefore a small but important piece of information that we have from Dr. Schultes, when he tells us that the Inga and Kamsá Indians in the Valley of Sibundoy, Colombia, called a narcotic prepared from the leaves of *Methysticodendron Amesianum, mits-kway borrachero*, or the "intoxicant of the jaguar." [55] Even if no further explanation has been given as to the nature of the relationship jaguar—intoxicant—we have at least an indication of a connection between the feline and an intoxicant with certain properties for the users. May we guess that the jaguar is thought of as the "owner" of the drug?

The alter-ego sculpture in Fig. 13 is of stone. When we try to get a picture of the archaelogical distribution of snuffing paraphernalia in the Amazon region, we must take into account that very little of perishable material, such as wood, has been saved to our days. As pointed out in Wassén, 1965: 77, an origin in the Highland Tiahuanaco has often been considered for the trays and other snuffing paraphernalia now found in northern Chile and northwestern Argentina. Apart from the fact that snuffing paraphernalia now have been dated in Chile to an earlier epoch than that with an influence from Tiahuanaco, I have for ethnographical reasons considered an origin of the marginal Atacameño snuffing material in the Amazonian and sub-Andean region. I have later found that René Naville, in an article published in Switzerland in 1959, more or less has been of the same opinion; that is, that we should look for the origin of the snuff ceremonialism in the Amazon region, possibly among the Arawak Indians; but that later a cult associated

[55] Schultes, R. C. 1955: 10.

with it in the Atacama region and manifested in human offering, had an Andean origin. Mr. Naville's contribution to the whole problem is valuable, and I prefer to quote him here in his language, French:

On peut conclure en disant que si l'absorption d'un narcotique au moyen de tubes et de tablettes semble être originaire d'Amazonie, peut-être arawak, son usage rituel et son association avec le culte rendu à une divinité accompagné de sacrifices humains est très probablement d'origine andine. Il est donc possible que ses deux pratiques se soient conjointes dans le Nord du Chili et le Nord-Ouest de l'Argentine, points d'intersections des grands courants culturels venus du Nord et de l'Est, pour donner naissance aux pièces décrites plus haut.[56]

From what already has been stated in this work, it is with full evidence clear that wooden tablets and tubes for the taking of some kind of a snuff must have been of outstanding importance in the now marginal region where once the Atacameño dominated. According to Bennett (1946: 599), "the term *Atacameño* (*Atacama*, *Kunza*) refers to a people, with a distinctive language and culture, who once occupied the northern Chilean provinces of Tacna, Arica, Tarapacá, Antofagasta, and Atacama, and much of the Northwest Argentine provinces of Los Andes, Salta, and Jujuy." "Today, the few remaining *Atacameño* are located in isolated sections of Chile and the Puna de Jujuy, but culturally and linguistically they have been absorbed by *Aymara* or Spanish."

One may ask if in such a region *anything is remembered about the ancient use of snuffing paraphernalia* among the modern mestizo population?

As the Atacameño were basically agriculturists and herders, my question came after I had read two special articles both dealing with the actual culture of typical parts of the old region.[57] Both authors, Horst Nachtigall (1965) and Ana María Mariscotti (1966) underline the importance of traditionally old offering ceremonies to Pachamama, so-called *señaladas*, during which the offers of llama animals (or part of them), alcohol, chicha, coca leaves, etc. are obligatory and important.

The cultural correspondence with the *samiri* concept among the Aymara and Chipaya Indians of the Highland as studied by the late Alfred Métraux during his expedition in 1930 seems important for a very special reason, namely that it has been suggested by Sven Lovén that we consider the Taino word *cemi* as related to Samiri, because of certain facts, among them that the Arawak had asserted themselves also in the western Highland.[58]

On my written question to authors Nachtigall and Mariscotti both declare that the former use of the *tabletas de rapé*, tubes, etc. now is absolutely unknown to anybody in the actual rural population.[59]

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[56] Naville, René. 1959: 3.

[57] Nachtigall, Horst. 1965. Mariscotti, Ana María. 1966.

[58] Wassén, H. 1934: 633. "Dr. Sven Lovén, at the museum of Gothenburg, has mentioned for me that he for certain reasons—among these the fact that the Arawaks have asserted themselves also in the western highland—considers the constituent *sami* of the word *samiri* to be the same as the Tainan *zemí*."

[59] Mrs. Mariscotti, after four different periods of investigation in the Quebrada de Huamahuaca and Puna de Jujuy can assure "that the use of the *tabletas de rapé* which with such frequency are embodied in the "Puna Complex" of Bennett, is absolutely unknown." (Letter, November 16, 1966).

If we now return to the *señaladas*, both Nachtigall (1965: 216) and Mariscotti (1966: 74) report *the burning of leaves of khoa or khoba*, an aromatic plant for which they botanically refer to *Mentha pulegium* (of the Family *Labiatae*). This is said by La Barre to be used also amongst the Highland Aymara.[60] With a letter of December 5th, 1966, Mrs. Ana M. Mariscotti has had the kindness to send me a botanical sample of *khoba* collected during her latest trip to Puna de Jujuy. This botanical sample has been examined by the botanist, Dr. Bo Peterson, chief of the Museum of the Gothenburg University's Botanical Institution. According to Dr. Peterson it is not at all the question of a genus of the *Labiatae* Family, but instead a genus of the Family *Compositae*, namely *Lepidophyllum quadrangulare*. Reference has been given to Angel Lulio Cabrera's "*Sinopsus del genero Lepidophyllum* (*Compositae*)" in the Boletín de la Sociedad Argentina de Botánica (vol. I: 48–58, La Plata, 1945), where the author also gives the popular names *chacha* and *coba* for this plant.

In accordance with what has been said above regarding a possible relation between the word *samiri* and the Island Arawak *cemi*, it is also interesting to suggest a relationship between the Island Arawak (Taino) word *cohoba* and the *khoba* for an aromatic herb in the former Aracameño region with its influence from the Highland and its trade relations. I would like to suggest that *cohoba* and *khoba* are the same words, even if they now refer to different plant material and are used in two widely separated geographic areas. The word we still meet so far south in the form *khoba* should in that case belong to an old stratum of Arawak influence. Professor Nils M. Holmer, specialist on Amerindian languages, write to me (November 17, 1966) that he is sure that an Andean *khowa* (*khoa*) with a strongly aspirated *kh*-, may have been heard as *cohoba*.

The *señaladas* among the present rural mestizo population in Puna de Atacama and Pune de Jujuy represent offshoots of an old Highland tradition with offering to a deity (Pachamama) principally ruling the agricultural cycle. To the Indians, gods, or spirits, were benevolent or ill-disposed, and the medicine-men or other important tribal functionaries had to face a situation which I described in 1965 as influencing the benevolent ones and to weaken or if possible destroy the ill-disposed ones. I have also said that "we are in our full right to believe that such important goals have been reflected also in the art of the Indians, even if we now mostly lack the mythological or other information explaining the connections" (Wassén, 1965: 38). As the psychotomimetic snuffs must be considered as a means of contact with the spirit world, it is consequently fully understandable that we find Indian representations of their supernatural beings expressed in the art concerning the snuffing paraphernalia. We can, as an example, mention the jaguar motif in the sculpture on ethnographically known snuff trays from the Cashuena Indians of the Trombetas and Cachorro Rivers, Brazil.[61]

[60] La Barre, Weston, 1948: 184. "The leaves and stems of *q̇oa* (*Mentha pulegium* Linnaeus) are burned in the fields "to make a good harvest," but it is uncertain if this is done for magical reasons, or for the same sound fertilizing reasons with which they place animal manueres on the field." Cf. same author, p. 56, about the use of *Mentha pulegium* as a condiment.

[61] See Frikel, 1961, describing the *morí* feast. Quoted in Wassén and Holmstedt, 1963: 21–23.

As the illustration on page 8 in Frikel's paper of 1961 on the *morí* feast among the Cachuena unfortunately is very unsharp, I am glad that, thanks to my friend Dr. Carl Schuster of Woodstock, N.Y., I can publish two photos here (Figs. 28 and 29) of the Cashuena specimens. Fig. 28 corresponds to the illustration on page 8 in Frikel's paper. Among the implement for snuffing *morí*, the "shovel" or tray at the right has two confronted jaguars on its handle. Frikel calls the snuff tray *yará-kukúru*, which in Cashuena means "figure of the mythological onça (jaguar) *yará*". The *yará* are "*bichos do fundo, da agua*," "water-jaguars", conceived as a pair, male and female,[62] a fact also of interest for the principle found in Amazonas that "magical substances are always in pairs, male and female" as discussed in Wassén 1965 (p. 76) in regard to the double-headed *paricá* tray of Tucanoan origin. The Cashuena used to have special songs, *iwarawá-yorêmuru*,

[62] Frikel. 1961 : 7–8.

FIG. 28.—Cashuena Indian snuffing paraphernalia for the *morí* feast. Mythological 'water-jaguars' form the handle of the tray. Photo courtesy Dr. Carl Schuster, Woodstock, N.Y. Collection in Brazil.

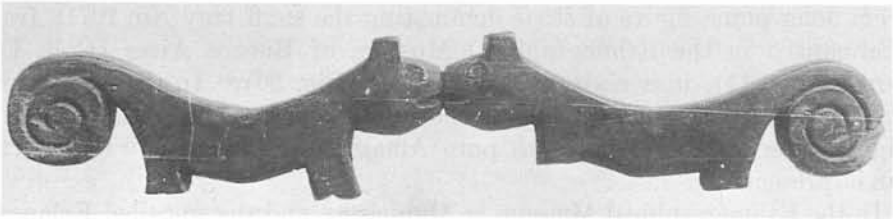

FIG. 29.—Pair of jaguars, one, as of 1954, "three or four generations old" handle of a Cashuena snuff tray. Coll. in Brazil. Photo courtesy Dr. Carl Schuster.

for their snuffing boards. It is deeply regretted that they now are lost (Frikel, 1961: 9) as they probably could have helped to explain the symbolism of the carved motives. As regards the Maué we have the statement by Pereira (1954: 68) that their medicine-men (*pagés*) used the *paricá* to get in trance and be able to contact their gods of the waters and the jungle. We are probably save to assume that the "water-jaguars" of the *Cashuena* stand for such deities or spirits.

Dr. Carl Schuster took his photo in Fig. 28 in the Convento dos Franciscanos in Santarem, and the objects were then said to be kept in a Franciscan museum at Ipauarana, Paraiba State. At the same time (November 1954) Schuster also copied a photo of an handle of an old snuff tray from the Cashuena, said to be 3 or 4 generations old, c. 80–100 years. This handle (Fig. 29) has been published in a drawing on page 7 in Frikel's paper from 1961. We see a pair of jaguars, originally with beads in their eyes. Father Frikel informed Dr. Schuster at the time, that a complete tray which he wanted was buried with a shaman. This information confirms my statement from 1965: "If also in former days the carved and ceremonially used snuff trays were placed with the dead this could very well explain their scarcity in collections.[63]

For the tribes of the Uaupés-Caquetá region, Goldman has informed us that "the shaman in the area is generally referred to as a jaguar, and combines the functions of medicine-man and sorcerer. Older shamans assume the guise of the jaguar and are particularly feared. Every jaguar who attacks human beings is assumed to be a shaman, and a shaman who is suppected of such an attack is not infrequently put to death. As the spirit of a murdered shaman enters another jaguar, however, little relief is expected from killing them" (Goldman, 1948: 796). Bödiger (1965: 150) has shown how the names for jaguar and shaman are similar or identical in many of the tribal languages, and how the shaman through this identity in name is considered to have the power of transforming himself into a jaguar—this in a detailed investigation of the Tucano religion.

Again and again we come back to the importance of the jaguar motif for paraphernalia related to snuffing. It is most likely that tribes using jaguar leg-bones as snuff containers do this out of some magical reasons related to the real and magical power of the animal. And, when we find a

[63] Wassén. 1965: 74.

4 cm. long puma figure of stone dominating the snuff tray No. 10718 from Tiahuanaco in the Ethnographical Museum of Buenos Aires (Coll. Debenedetti, 1911), it is really not surprising (Fig. 30).[64] In the *tabletas de rapé* of the Atacameño, the jaguar is seen as a mighty god. Also for this a highly interesting parallel with pure Amazonian ethnographical material can be presented.

In the Ethnographical Museum at Munich we find the so-called Erlangen ceremonial staff, an object which has been studied by Zerries[65] and by him found to be a medicine-man's staff, probably from the Carib *Waríkyana* or *Arikiêna* of the Kachúru (Cachorro) River. Frikel considers the Cashuena, often mentioned in this work, as descendants of the old Waríkyana (see Wassén, 1965: 33), and consequently every old piece of art from that tribe or region must to be of immediate interest also for a study of ceremonially used snuff trays. Zerries found on the Erlangen staff the supernatural vulture, the medicine-man's most important helper, and the figure of a jaguar, "the werwolf of the South American shamans." An anthropomorphic jaguar (or "werwolf" figures) is now seen in Fig. 31 from photos

[64] Photo kindly supplied by Dr. Carl Schuster.
[65] See complete description in Zerries, 1962, and his photo on p. 615.

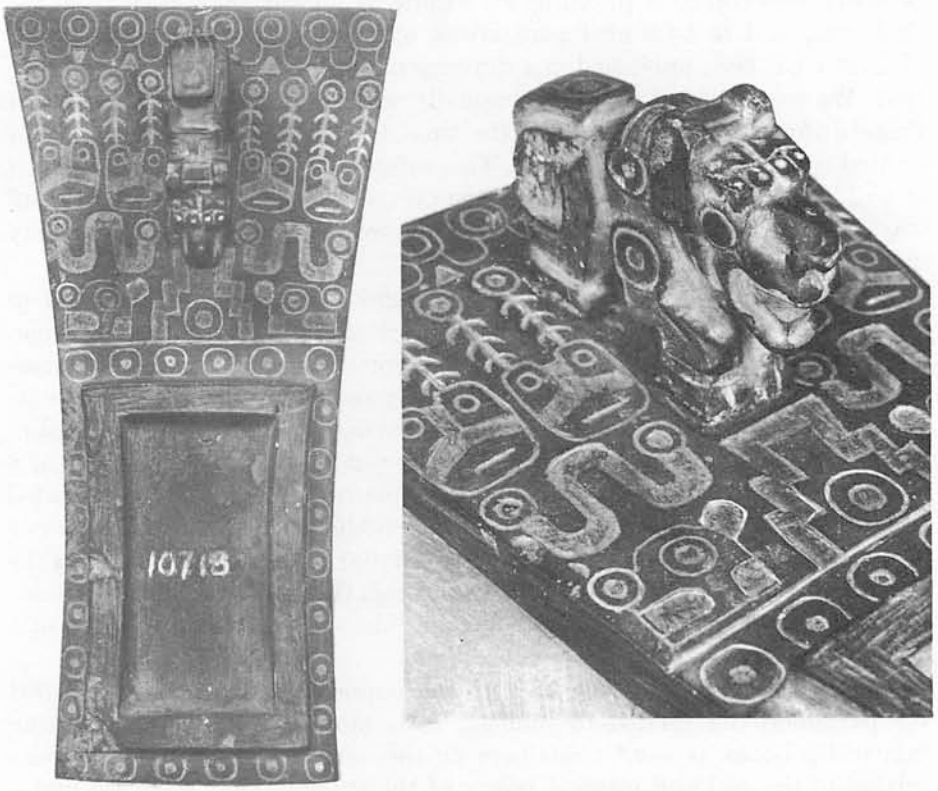


FIG. 30.—Snuff tray with 4 cm. long puma of stone. Tiahuanaco. Coll. No. 10718 (Debenedetti, 1911), *Museo Etnográfico*, Buenos Aires. Photo courtesy Dr. Carl Schuster.

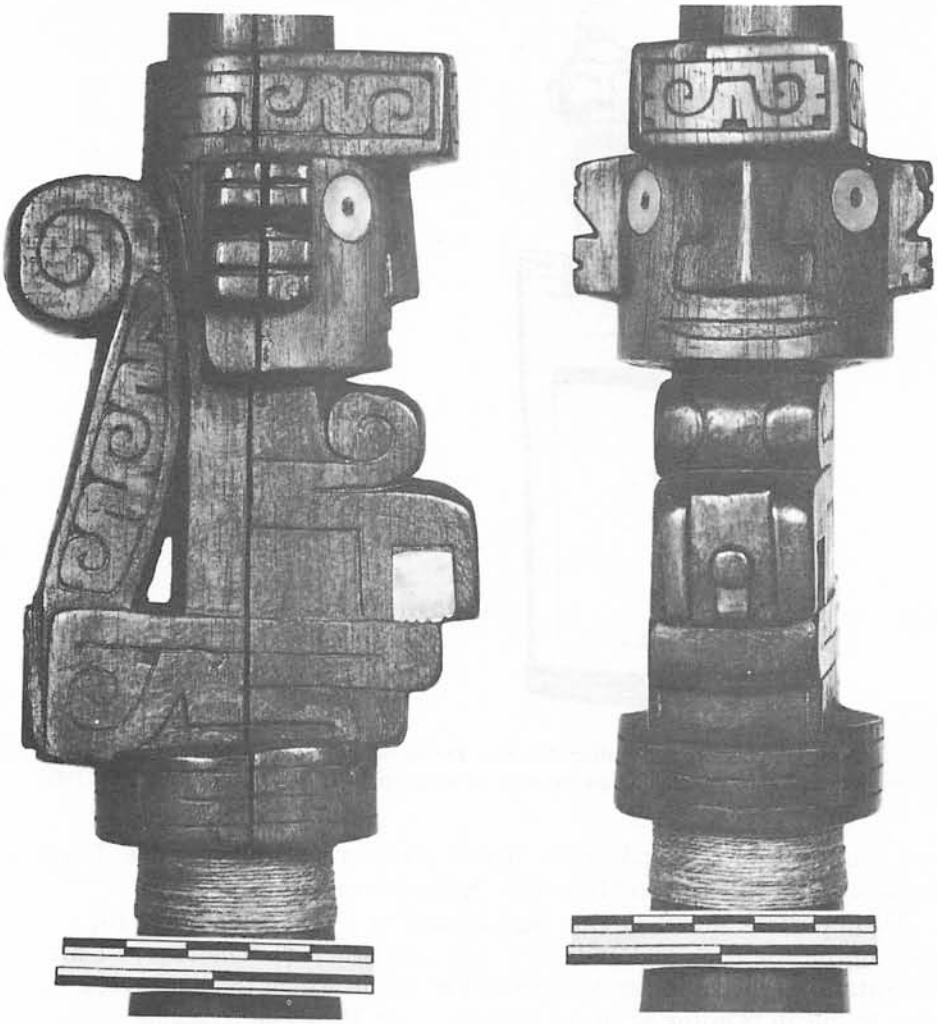

FIG. 31.—Ornamental detail, anthropomorphic jaguar on a trumpet of hard red wood. Old specimen in the Pitts Rivers Museum (No. 130, J. 44), without provenience but certainly from the Lower Amazon Region, probably the old Waríkyana. Photographs courtesy of Mr. Jeremy P. S. Montagu, London.

which have been kindly supplied by Mr. Jeremy P. S. Montagu, London. The figure shows a "side-blast trumpet made of two semicylindrical pieces of hard red wood." This specimen, now in the Pitt Rivers Museum (entry 130.J.44) came from "the Bodleian" to the University Museum in Oxford, presumably, then transferred to the Pitt Rivers Museum in 1886." It is an old piece of Indian art for which the provenience is lacking, but as far as I understand it should be referred to the same region as the Erlangen staff, that is, the Lower Amazon region and from the old Waríkyana in the art center of the *Rio das contas* (cf. Wassén, 1965 : 34). A similar 123 cm. long trumpet with jaguar motif (his tail curled down) from an old collection



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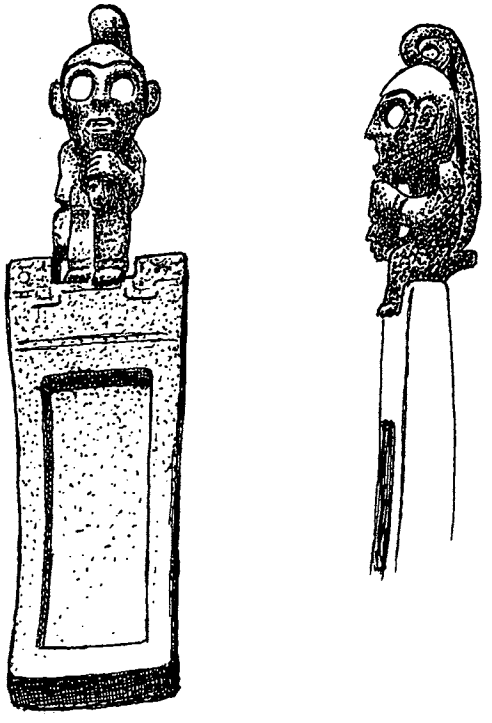

FIG. 32.—Snuff tray from "Quitor 5", San Pedro de Atacama, Chile. Dominating anthropomorphic feline god. Drawing after photographic illustration in Le Paige, 1964.

and the Amazon is found in the Rijksmuseum voor Volkenkunde, Leyden. It belonged originally to "Het Kon. Kabinet van Zeldzaamheden."

An important detail in this jaguar-man on a trumpet is the tail, which goes up on the back and ends in a characteristic curl. The reason I find it important might be understood from Fig. 32, in which the figure on a snuff tray found in "Quitor 5" in the region of San Pedro de Atacama, Chile, by Gustavo Le Paige, has been copied from plate 125 in Le Paige's work of 1964. The snuff tray from Chile is an expression of the same idea of a jaguar (or puma)-man-deity as found on the old trumpet, and the tail is a characteristic of both figures. To me these specimens form another link in a chain of evidence for an early Amazon cultural influence on the Atacaman region. Thanks to a numerous series of snuff tray finds in the dry region, Father Le Paige has been able to demonstrate specific manifestations of magico-religious art in which the taking of a man's head is involved. In snuffing paraphernalia which he found, he can follow a complete series of ceremonies, from the presentation of a condemned man with backbound hands and the executioner with his attribute, an axe, to the priest carrying the head of the victim—in that important moment imitating the sacred puma god by walking on all fours and carrying a puma mask and the wings of a condor.[66]

[66] Le Paige, Gustavo. 1964: 61. Mostny (1964) has been able to show such ceremonialism also in the petroglyphs of Angostura, Prov. of Antofagasta, Chile.

Gustavo Le Paige and other archaeologists working in the Atacaman region find this richness of evidence thanks to a dry climate. What the anthropologists have found, or may expect to find, in the eternally wet Amazon region, are just a few fragments of a formerly rich ceremonialism in which the taking of psychotomimetic drugs seems to have been integrated.

A group of snuff trays from the Amazon region with an obviously important zoomorphic motif are the Maué specimens said to depict caymans or snakes. Several of these old fine Maué wooden trays have fortunately been saved in museum collections.[67] The specimen in Oslo is shown also here (Fig. 33). Typical for most of the Maué trays, is the fact that they are rectangular in form and have a finely polished depository for the snuff, open on the edge of the board. The other edge of the tray ends in an animal's head, often with an accentuated tongue, a trait typical for representations of snakes but hardly for caymans in which the tongue is not easily observable. It is true that a Maué Indian has once stated that a *paricá* tray owned by him represented a *yacaré*, but as I have said, this label can not be stamped on all snuff trays from this tribe.[68] Anthropological colleagues such as Etta Becker-Donner in Vienna, and Antonio Serrano in Argentina, as well as Otto Zerries in Munich, seem to favor the idea of snakes.[69] The Atacama specimen published in Fig. 22 has, however, *a feline head.* As this archaeological specimen is much older than the 19th century ethnographical objects from the Maué, it is of interest also for the discussion of the Maué pieces. As a matter of fact, some of the Maué tray handles in the form of animal heads may be conceived as conventionalized feline heads, perhaps with some idea of "water-jaguars" behind as in the case with the Cashuena. The outstreatched tongue is accentuated in the feline powder cup published as Fig. 5 in Zerries: 1965. A most interesting snuff tray with two feline heads found in a grave at the Pucará de Lasana (Río Loa, Chile) has been published by Spahni (1964, Fig. 5). His Fig. 4, showing a snuff tray from another grave said to represent an armadillo, most probably also depicts a feline.

Another group of animals which in a particular symbolic and magic way seem to be connected with the use of drugs are birds with very good eyesight, such as eagles, vultures, very often condors, and also such good night-hunting birds as owls (the Cashuena snuff tray in Fig. 28). I have treated this in detail in my work from 1965 (pp. 24–29), and I can reiterate here, that we are entitled to consider birds as patrons for ecstatic intoxication in several Indian societies. I refer, for instance, to snuff trays with condors, bird-shaped snuffers, snuffing tubes which terminate in hollow nuts, often shaped like a bird's head (Fig. 34), and also, to direct explanations by medicine-men that they use feather crowns, etc. so that they may see better into the world of spirits. This connection between the shamans as users of drugs and the world of bird-spirits is a fact. The reason for it is probably to be found in

[67] See figs. 8, 10, 11, 12 and 15 in Wassén 1965.
[68] Wassén. 1965 : 43.
[69] Wassén. 1965 : 43 and 50.

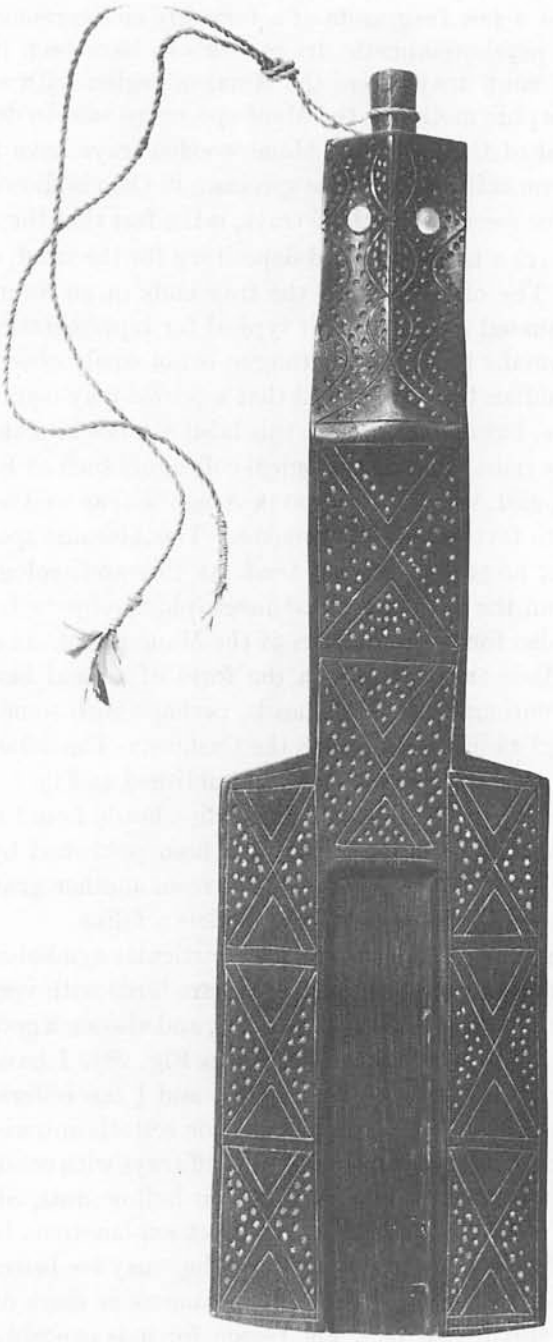

FIG. 33.—Maué Indian snuff tray of wood for *paricá*. Length 28 cm. Coll. and courtesy Oslo Univ. Ethnogr. Museum. Specimen No. 1170.

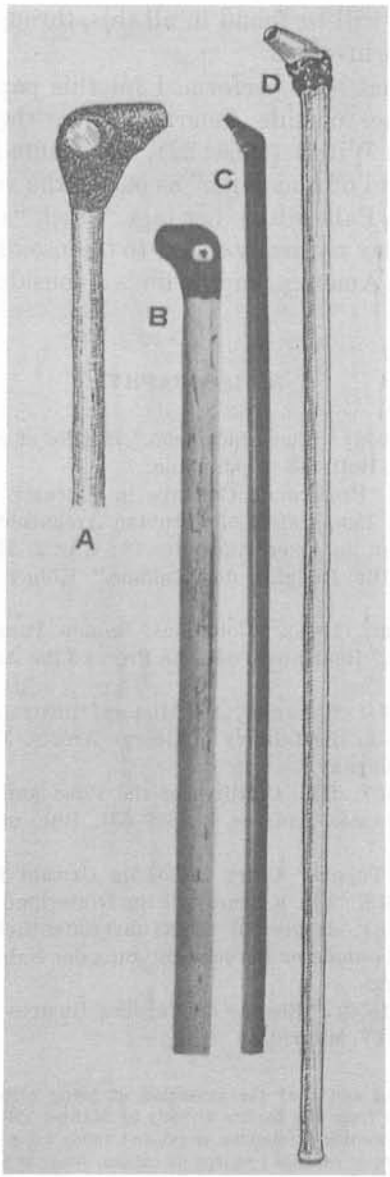


FIG. 34.—Snuff tubes from the Guaporé Territory. *A*, Mondé Indians, after photo by Caspar; *B*, Salamay Indians, coll. *Mus. f. Völkerkunde der Univ.*, Zürich, No. 11307; *C-D*, Tupari Indians, coll. Dr. Franz Caspar in the *Mus. f. Völkerkunde*, Basel, No. 1V C 9052, length 88 cm. (photo and drawing of the same tube).

the drugs,[70] and I point, in passing, to the complex of Siberian shamans being described as of bird-type, who visit the spirits up in the air. This, incidentally, is a contrast to the other type of Siberian shamans, who have their contacts in the world below.[71] The ideas among the Koryak about the Big-Raven and the fly-agaric give a good illustration of this.[72] I hope that later a common component will be found in all this, through the analytical work by experts on the drugs involved.

No specific search has been performed for this paper regarding the possible use of snuff tubes outside America, where they seem to be autochthonous.[73] Dr. Gordon Willey (1966: 22), has counted "the chewing of lime or ashes with some kind of a narcotic" as one of the very ancient traits, possibly the survival of a Palaeolithic heritage, which "are shared by Asia and the New World." Willey naturally refers to the use of betel-nut in Asia and the coca leaf in South America, and he finds a considerable age for the trait in the Americas.

## BIBLIOGRAPHY


Bennett, Wendell C. (1946). "The Atacameño." Handb. of S. Amer. Indians, 2: 599–618. Bur. of Amer. Ethn., Bull. 143. Washington.

Bird, Junius B. (1948). "Preceramic Cultures in Chicama and Virú." Pp. 21–28 in Wendell C. Bennett: A Reappraisal of Peruvian Archaeology. Mem. of the Soc. for Amer. Arch. No. 4, Suppl. to Amer. Antiquity 13: 4, pt 2. Menasha, Wisc.

Bödiger, Ute. (1965). "Die Religion der Tukano." Kölner Ethnol. Mitteilungen 3. Cologne.

Bourne, Edward Gaylord. (1906). "Columbus, Ramon Pane and the Beginnings of American Anthropology." Reprinted from the Proc. of the Amer. Ant. Soc., Worcester, Mass.

Brooks, Jerome E. (1937). "Tobacco." Its History illustrated by the Books, Manuscripts and Engravings in the Library of George Arents, Jr. Vol. I, 1507–1615. New York, The Rosenbach Company.

Casanova, Eduardo. (1946). "The Cultures of the Puna and the Quebrada of Humahuaca." Handb. of S. Amer. Indians, 2: 619–631. Bur. of Amer. Ethn., Bull. 143. Washington.

Caspar, Franz. (1952). "Tupari." Unter Indios im Urwald Brasiliens. Braunschweig.

Caspar, Franz. (1953). MS. "Ein Kulturareal im Hinterland der Flüsse Guaporé und Machado (Westbrasilien), dargestellt nach unveröffentlichten und anderen wenig bekannten Quellen, mit besonderer Berücksichtigung der Nahrungs- und Genussmittel." (Dissertation). Hamburg.

Castellanos, Juan de. (1850). "Elegías de Varones Ilustres de Indias." 2nd ed. Bibl. de Autores Españoles, t. IV. Madrid.


[70] Wassén. 1965: 29. I can add that the sensation of being airborne through the taking of *ayahuasca* has been described from the Zaparo already by Manuel Villavicencio in 1858 (p. 372) :" Su accion parece dirijirse á escitar el sistema nervioso; todos los sentidos se avivan i todas las facultades se despiertan; sienten vahídos i rodeos de cabeza, luego la sensación de elevarse al aire i comenzar un viaje aéreo; . . ."

[71] La Barre, Weston. 1964: 121. "En Sibérie, peuve être distingués deux types de chamans: le chaman-oiseau qui visite les esprits dans les airs et règne sur le temps qu'il fait, et le chaman-renne qui visite le monde souterrain et règne sur les esprits des vivants et de morts."

[72] Jochelsen, Waldemar. 1905: 120.

[73] Prof. B. Holmstedt has drawn my attention to a paper by Chinachoti and Tangchai (1957: 689), where the U-shaped metal tubes used in Thailand for the nasal absorbtion of a mixed tobacco powder has been treated. A pair of such tubes with the commercial packages of such ingredients as tobacco, quicklime and perfume, are found in the Gothenburg Ethnographic Museum (Coll. 64.25.97–102).

CHINACHOTI, NINART and PRASAN TANGCHAI. (1957). "Pulmonary Alveolar Microlithiasis Associated with the Inhalation of Snuff in Thailand." Diseases of the Chest, vol. 32, No. 1, pp. 687–689.

COOPER, JOHN M. (1949). "Stimulants and Narcotics." Handb. of S. Amer. Indians, 5: 525–558. Bur. of Amer. Ethn., Bull. 143. Washington.

ERNST, A. (1889). "On the etymology of the word tobacco." The Amer. Anthropologist, 2: 2, pp. 133–142. Washington.

FRIEDERICI, GEORG. (1925). (Review). "Sven Lovén, Ueber die Wurzeln der Tainischen Kultur." Göttingische Gelehrte Anzeigen, 187. Jahrg., pp. 32–43. Berlin.

FRIEDERICI, GEORG. (1947). Amerikanistisches Wörterbuch, Hamburg.

FRIKEL, PROTÁSIO. (1961). "Mori—A Festa de Rapé." Boletim do Museu Paraense Emilio Goeldi, Antropologia No. 12, Belém, Pará.

GOLDMAN, IRVING. (1948). "Tribes of the Uaupés-Caquetá Region." Handb. of S. Amer. Indians, 3: 763–798. Bur. of Amer. Ethn., Bull. 143. Washington.

GUMILLA, JOSEPH. (1744). "El Orinoco Ilustrado, y defendido." Historia Natural, Civil, y Geographica de este gran Río, etc., tomo I. Madrid.

HAGEN, VICTOR W. von. (1965). "The Desert Kingdoms of Peru." New York Graphic Soc. publ., Ltd. Greenwich, Conn.

HARRISON, D. F. N. (1964). "Snuff—Its Use and Abuse." British Medical Journal, 1964, 2, 1649–1651.

HERNÁNDEZ DE ALBA, GREGORIO. (1948). "The Achagua and their neighbors." Handb. of S. Amer. Indians, 4: 399–412. Bur. of Amer. Ethn., Bull. 143. Washington.

HOLMSTEDT, B. (1965). "Tryptamine derivatives in epená, an intoxicating snuff used by some South American Indian tribes." Arch. int. Pharmacodyn., 1965, 156, No. 2: 285–305. Brussells, Belgium.

HOLMSTEDT, B. (1966). "Gas Chromatographic Analysis of Some Psychoactive Indole Bases." Amines and Schizophrenia, Pergamon Press, Oxford & Now York, 1966, pp. 151–166.

HUMBOLDT, ALEXANDER VON and AIMÉ BONPLAND. (1818–1829). Personal Narrative of Travels to the Equinoctial Regions of the New Continent during the years 1799–1804, translated by Helen Maria Williams. 7 vols. London.

JOCHELSEN, WALDEMAR. (1905). "Religion and Myths of the Koryak." Mem. of the Amer. Mus. of Nat. Hist. X. New York.

JOYCE, THOMAS A. (1916). Central American and West Indian Archaeology, London.

KIRCHHOFF, PAUL. (1948). "Food-Gathering Tribes of the Venezuelan Llanos." Handb. of S. Amer. Indians, 4: 445–468. Bur. of Amer. Ethn., Bull. 143. Washington.

LA BARRE, WESTON. (1948). "The Aymara Indians of the Lake Titicaca Plateau, Bolivia." Mem. Series of the Amer. Anthrop. Ass., No. 68. Amer. Anthrop., Vol. 50: 1, pt. 2. Menasha, Wisc.

LA BARRE, WESTON. (1964). "Le complexe narcotique de l'Amérique Autochtone." Diogène 48: 120–134. Paris.

LAS CASAS, BARTOLOMÉ DE. (1909). "Apologética historia de las Indias." Historiadores de Indias, I, M. Serrano y Sanz, Ed., Madrid.

LATCHAM, RICARDO E. (1938). "Arqueología de la Región Atacameña." Prensas de la Univ. de Chile.

LE PAIGE, GUSTAVO. (1964). "El precerámico en la Cordillera Atacameña y los cementerios del período agro-alfarero de San Pedro de Atacama." Anales de la Univ. del Nort, Antofagasta: 3. Antofagasta.

LE PAIGE, GUSTAVO. (1965). "San Pedro de Atacama y su zona." Anales de la Univ. del Norte, Antofagasta: 4. Antofagasta.

LOVÉN, SVEN. (1935). Origins of the Tainan Culture, West Indies. Göteborg.

MACNUTT, FRANCIS AUGUSTUS. (1912). "De Orbe Novo. The Eight Decades of Peter Martyr d'Anghera." Transl. from Latin with Notes and Introduction. 1–2. New York and London.

MANGONES, EDMOND and LOUIS MAXIMILIEN. (1941). L'Art Précolombien d'Haïti. Port-au-Prince, Haïti.

MARKHAM, CLEMENTS R. (1869). First part of the Royal Commentaries of the Yncas by the Ynca Garcilasso de la Vega. Vol. I. Works issued by the Hakluyt Soc. London.
MARISCOTTI, ANA MARÍA. (1966). "Algunas supervivencias del culto a la Pachamama." El complejo ceremonial del 1°. de Agosto en Jujuy (NO. Argentino) y sus vinculaciones. Zeitschrift f. Ethnologie 91 : 1, pp. 68–99. Braunschweig.
MÁRTIR DE ANGLERÍA, PEDRO. (1944). "Décadas del Nuevo Mundo." Editorial Bajel. Buenos Aires.
MARTIUS, CARL FR. V. (1867). Beiträge zur Ethnographie und Sprachenkunde Amerika's zumal Brasiliens. I. Zur Ethnographie. Leipzig.
MATTO, FRANCISCO. (1964). "Arte Precolombino." Colección Matto. Museo de Arte Precolombino. Montevideo.
MEGGERS, BETTY J. and CLIFFORD EVANS. (1957). "Archaeological Investigations at the Mouth of the Amazon." Bur. of Amer. Ethn., Bull. 167. Washington.
MÉTRAUX, A. (1928). La Réligion des Tupinamba et ses rapports avec celle des autres tribus tupi-guarani. Paris.
MÉTRAUX, A. (1946). "The Caingang." Handb. of S. Amer. Indians, 1 : 445–476. Bur. of Amer. Ethn., Bull. 143. Washington.
MÉTRAUX, A. (1948). "The Guarani." Handb. of S. Amer. Indians, 3 : 69–94. Bur. of Amer. Ethn., Bull. 143. Washington.
MÉTRAUX, A. (1948 *a*). "The Tupinamba." Handb. of S. Amer. Indians, 3 : 95–134. Bur. of Amer. Ethn., Bull. 143. Washington.
MONTEIRO DE NORONHA, JOSÉ. (1862). Roteiro da viagem da Cidade do Pará, até as ultimas colonias do Sertao da Provincia. Pará.
MOSTNY, G. (1952). "Una tumba de Chiuchiu." Bol. del Museo Nacional de Hist. Nat. 26 : 1. Santiago de Chile.
MOSTNY, G. (1958). "Máscaras, tubos y tabletas para rapé y cabezas trofeos entre los atacameños." Miscellanea Paul Rivet Octogenario Dicata, Vol. II : 379–392. Mexico.
MOSTNY, G. (1964). "Petroglifos de Angostura." Zeitschrift f. Ethnologie, 89 : 1, pp. 51–70. Braunschweig.
MUÑOA, JUAN IGNACIO. (1965). "Los pueblos prehistóricos del Territorio Uruguayo." Ed. Daniel Vidart. Amerindia 3. Montevideo.
NACHTIGALL, HORST. (1965). "Beiträge zur Kultur der indianischen Lamazüchter der Puna de Atacama (Nordwest-Argentiniens)." Zeitschrift f. Ethnologie 90 : 2, pp. 184–218. Braunschweig.
NAVILLE, RENÉ. (1959). "Tablettes et tubes à aspirer du râpé." Bulletin No. 17, Soc. Suisse des Américanistes. Geneva.
NETTO, LADISLAU. (1885), "Investigaçoes sobre a Archeologia Brazileira." Arch. do Museu Nacional, VI : 257–554. Rio de Janeiro.
NORDENSKIÖLD, ERLAND. (1919). "Sydamerika." Kampen om guld och silver 1498–1600. Uppsala.
NUÑEZ A., LAUTARO. (1963). "Problemas en torno a la tableta rapé." Anales de la Univ. del Norte, Antofagasta : 2. Antofagasta.
NUÑEZ A., LAUTARO. (1965). "Desarrollo cultural prehispánico del Norte de Chile." Estudios Arqueológicos No. 1 : 37–115. Univ. de Chile, Antofagasta. Antofagasta.
OVIEDO, GONZALO, FERNANDEZ DE. (1851–1855). "Historia general y natural de las Indias, Islas y Tierra-Firma del Mar Oceáno." Vols. 1–4, Real Acad. de Hist., Madrid.
PALMATARY, HELEN C. (1960). "The Archaeology of the Lower Tapajós Valley, Brazil." Transactions of the Amer. Philosophical Soc., n.s. 50 : 3. Philadelphia, Pa.
PEREIRA, NUNES. (1954). "Os Indios Manés." Coleção "Rex". Rio de Janeiro.
PINTO, ESTEBAN. (1944). "La extraña figura del pagé tupinambá." Actas Ciba 11, La medicina de los tupí-guaraníes, pp. 319–328. Buenos Aires.
PITTIER, H. (1926). Manual de las plantas usuales de Venezuela. Caracas.
REIS ALTSCHUL, SIRI VON. (1964). "A Taxonomic Study of the Genus Anadenanthera." Contr. from the Gray Herbarium of Harv. Univ., No. 193. Cambridge, Mass.
ROSENBLAT, ANGEL. (1965). "Los Otomacos y Taparitas de los Llanos de Venezuela." Anuario I., 1964 : 227–377. Instituto de Antropología e Historia. Caracas.

ROUSE, IRVING. (1964). "Prehistory of the West Indies." Science, vol. 144: 499–513. Washington, D.C., May 1, 1964.

RYDÉN, STIG. (1944). Contributions to the Archaeology of the Río Loa Region, Göteborg.

SALAS, ALBERTO MARIO. (1945). "El antigal de Ciénega Grande (Quebrada de Purmamarca, Prov. de Jujuy)." (Publ. del Mus. Etnográfico de la Fac. de Fil. y Letras, Serie A V. Buenos Aires.

SAWYER, ALAN R. (1966). Ancient Peruvian Ceramics. The Nathan Cummings Collection. The Metropolitan Museum of Art. New York.

SCHULTES, RICHARD EVANS. (1954). A new narcotic snuff from the Northwest Amazon. Bot. Mus. Leaflets, Harv. Univ., vol. 16: 9, pp. 241–260. Cambridge, Mass.

SCHULTES, RICHARD EVANS. (1955). A new narcotic genus from the Amazon slope of the Colombian Andes. Bot. Mus. Leaflets, Harv. Univ., vol. 17: 1, pp. 1–11. Cambridge, Mass.

SCHULTES, RICHARD EVANS. (1963). "Hallucinogenic Plants of the New World." The Harvard Review, I: 4, pp. 18–32. Cambridge, Mass.

SEITZ, GEORG. (1960). "Hinter dem grünen Vorhang." Fahrt zu den nackten Indianern an der Grenze Brasiliens. F. A. Brockhaus, Wiesbaden.

SERRANO, ANTONIO. (1939). "Las tabletas para "paricá" del Museo Nacional de Rio de Janeiro." La Nación, June 4, 1939. Buenos Aires.

SPAHNI, JEAN-CHRISTIAN. (1964). "Le cimetière atacaménien du Pucará de Lasana, Vallée du Rio Loa (Chili)." Journ. de la Société des Américanistes, vol. 53: 147–179. Paris.

STEWARD, JULIAN H. (1948). "The Circum-Caribbean Tribes: An Introduction." Handb. of S. Amer. Indians, 4: 1–41. Bur. of Amer. Ethn., Bull. 143. Washington.

STONE, DORIS. (1958). Introduction to the Archaeology of Costa Rica. San José, C.R.

UHLE, MAX. (1898). "A Snuffing Tube from Tiahuanaco." Bull. of the Mus. of Science and Art, Univ. of Penna., Vol. I: 4. Phila., Pa.

USCATEGUI, M., NESTOR. (1959). "The present distribution of narcotics and stimulants amongst the Indian tribes of Colombia." Bot. Mus. Leaflets, Harv. Univ., vol. 18: 6, pp. 273–304. Cambridge, Mass.

WASSÉN, HENRY. (1934). "The Frog in Indian Mythology and Imaginative World." Anthropos 29: 613–658. St. Gabriel-Mödling at Vienna.

WASSÉN, S. HENRY. (1964). "Some General Viewpoints in the Study of Native Drugs Especially from the West Indies and South America." Ethnos 1964: 1–2, pp. 97–120. Stockholm.

WASSÉN, S. HENRY. (1965). "The Use of Some Specific Kinds of South American Indian Snuff and Related Paraphernalia." Etnologiska Studier 28: 1–116. Göteberg, Etnografiska Museet.

WASSÉN, S. HENRY and Bo HOLMSTEDT. (1963). "The Use of Paricá, an Ethnological and Pharmacological Review." Ethnos 1963: 1, pp. 5–45. Stockholm.

VILLAVICENCIO, MANUEL. (1858). Geografía de la República del Ecuador. New York.

WILBERT, JOHANNES. (1963). "Indios de la Región Orinoco-Ventuari." Monografía No. 8, Fundación La Salle de Ciencias Naturales. Caracas.

WILLEY, GORDON. (1966). An Introduction to American Archaeology. Vol. I, North and Middle America. Prentice-Hall, Inc., Englewood Cliffs, N.J.

ZERRIES, OTTO. (1962). "Der Zeremonialstab der Erlanger Sammlung aus Brasilien in Staatlichen Mus. f. Völkerkunde" in München. Akten der 34. Internat. Amer. Kongr., Vienna, 1960, pp. 613–620. Vienna.

ZERRIES, OTTO. (1964). "Waika." Die kulturgeschichtliche Stellung der Waikaindianer des oberen Orinoco im Rahmen der Völkerkunde Südamerikas. Klaus Renner Verlag, Munich.

ZERRIES, OTTO. (1965). "Drei unbekannte Holzschnitzarbeiten aus Brasilianisch-Guayana im Museum für Völkerkunde zu Mannheim." Tribus 14: 185–193. Stuttgart.

# The Botanical Origins of South American Snuffs

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## Introduction

Man in primitive societies the world around has found the most ingenious ways of administering narcotics. Intoxicating plants, or products from them, have been chewed in crude form or variously elaborated and consumed. They have been drunk as decoctions or infusions. A few have been prepared in the form of thick syrups or pastes that are licked or smeared on the tongue or gums. Some have been smoked directly, as in pipes, cigars or cigarettes, or the fumes of them have been inhaled in sundry ways. There are those that have been applied to the skin or membranes in the form of ointments or unguents. Several are known to have been taken as an enema. Snuffing has been the preferred method of using a number of these agents.

The verb *to snuff* (and the corresponding German *schupfen* and Skandinavian *snusa*), stems, of course, from the same Germanic root that has given us the English word *to sniff*. There is a significant difference between the two actions. Whereas one *sniffs* an odour or fragrance—that is, a substance such as an essential oil, smoke or ethereal component of the atmosphere—one *snuffs* actually solid substances variously inserted or drawn into the nostrils.

The snuffing of plant materials for narcotic, especially for hallucinogenic, effects seems to be peculiarly New World. To be sure, sternutation induced by various means is a recognized therapeutic practice in many cultures. In the Middle Ages, European medicine recommended sternutation to draw off bad humours. Hellebore, the German *Nieswurz* and English *sneezewort*, was one of the most favoured therapeutic sternutatory powders taken into the nostrils together with marjoram and other plants to cleanse the brain through sneezing. Sternutation was used even for prophesying and in superstition and magic. A person who sneezed on New Year's morning, for example, would not die during the year. *Snuffing* now refers usually to the use of tobacco. This is true in languages other than English. The German *schupfen*, for example, has been more or less restricted to the snuffing of tobacco and other stimulants since the 17th Century.

It does seem probable, however, that the use of narcotics as snuffs is of American origin and that it went to the Old World with tobacco. The custom of snuffing tobacco, widespread apparently in pre-Conquest America, became common and accepted as a recreational practice devoid of therapeutic intent in Spain during the first quarter of the 17th Century. There is evidence that it was imported directly from the New World and that tobacco snuffing, as well as chewing and smoking, represents one of the most significant culture traits passed on to the western civilisation from the American aborigines.

## Principal Sources of South American Snuffs

Undoubtedly the most important snuffing material in pre-Conquest America was tobacco. At least two species of tobacco, possibly several additional ones, are known to have been employed as a narcotic (*4*). These two are *Nicotiana Tabacum* and *N. rustica*. *Nicotiana Tabacum*, from which comes most of the tobacco that is smoked, snuffed and chewed at the present time, was likewise the source of most of the narcotic in pre-Conquest South America, Middle America and the West Indies. Originally a tropical species, it has been cultivated so long that it is not known in the truly wild state. *Nicotiana rustica*, native to North America, where it is still wild in some localities, is a hardier species thought to have originated in Mexico. It is this species that was smoked and probably snuffed by Indians of Mexico and North America before the arrival of the European. Europeans introduced *Nicotiana Tabacum* from the Old World to North America long after the Conquest, and until this introduction, it was apparently unknown in most of the territory now included in the United States and Canada (*9*).

Although there are indirect evidences that tobacco may have been taken as snuff in Mexico and other parts of North America, there can be no doubt that in much of South America this was the most widespread method of utilizing the narcotic, especially in the wet, tropical lowland areas, such as the Amazon Valley. So many observations attest to this fact that there would seem to be little if any need for a discussion of the custom, were it not that perhaps confusion as to the source of a number of snuff preparations may have led to the assumption that tobacco snuffing, though widespread, might have been even more widespread than it actually was. Yet botanists and anthropologists have consistently warned against such generalisations. Mason, for example, stated (*13*) that "the snuff taken throughout . . . most of the Amazon and West Indies . . . is more frequently made from other plants than tobacco." And Cooper owned (*4*) that "tobacco snuffing . . ." is "not always distinguishable in our sources from *Piptadenia* snuffing."

Garcilaso de la Vega (*8*) reported that the Inca did not cultivate tobacco or *sayri*, but they are thought to have utilised several varieties native to the Andes, the roots of which were pulverised and used medicinally and as a snuff (*15*).

Botanists are understandably wont to be somewhat more conservative in ethnobotanical generalisations than are anthropologists. Goodspeed, for

example, in his classic work (*9*) on the genus *Nicotiana*, wrote that "presumably *N. tabacum* was in pre-Columbian use, doubtless often in cultivation, in the West Indies, much of Mexico, Central America, Colombia, Venezuela, the Guianas and Brazil. Spinden . . . apparently would extend this range to Peru, Boliva, Chile and Argentina, since tubes 'for taking snuff, presumably of tobacco, occur far and wide' in those areas . . . . There is, however, considerable doubt that the material snuffed in the tubes so familiar in remains of certain ancient civilisations in the Americas was 'tobacco' obtained either from early races of *N. tabacum* or from progenitors of the species of *Nicotiana* which today are native in the regions concerned. In other words, there is little evidence that *N. Tabacum* was in pre-Columbian use in western North America or in lower South America."

Tobacco in snuffing—whether the source of the snuff be *Nicotiana Tabacum* or some other species of the genus—seems quite generally to have been used alone, although there are occasional reports that it is sometimes mixed with *Anadenanthera*. Amongst the tribes of the Guaporé River in Amazonian Brazil, tobacco snuff was mixed with "crushed angíco leaves [*angíco* refers to leguminous trees, especially to *Anadenanthera*] and ashes of a certain bark" (*12*). During my years of field work amongst the Indians of the northwestern Amazon, I witnessed the preparation of tobacco snuff on many occasions and actually employed the snuff myself instead of smoking. The species used was *Nicotiana Tabacum*, and with two exceptions, I never saw the admixture of any other plant to the snuff—that is, other than ashes. These two exceptions were with the Witotos of the Rìo Igaraparaná and the Yukunas of the Río Miritiparaná of Colombia, where powdered coca (*Erythroxylon Coca*) is added to the tobacco. It is my belief that the ashes (usually from bark of *Theobroma* or leaves of *Cecropia*) serve mainly or wholly a physical function to help keep the finely pulverised and sifted tobacco particle from absorbing humidity from the excessively wet atmosphere and lumping so that the material could not be used as a snuff.

South America boasts a wide variety of containers and implements for the administration and self-administration of snuffs. Since there is normally, I believe, no relationship between these paraphernalia and the botanical source of the snuffs, I need not here discuss this intricate topic which has already been thoroughly investigated by a more competent specialist (*27*).

A critical survey of tobacco snuffing in South America, incorporating all of the extensive literature interpreted against the background of intensive field observations, is overdue. I venture to predict that, as such a study unravels the enigmas, we shall see other narcotic snuffs assume greater roles and tobacco find a progresively less important role than it has been given in our ethnobotanical evaluation.

One of the most interesting and enigmatic snuffs of South America is yopo or niopo, prepared from the beans of the leguminous tree *Anadenanthera peregrina*. During its botanical history, this plant has been placed in the related genera *Acacia* and *Mimosa*. It is perhaps best known under the binomial *Piptadenia peregrina*, but recent studies have indicated that it is most appropriately accommodated within *Anadenanthera* (*1*).

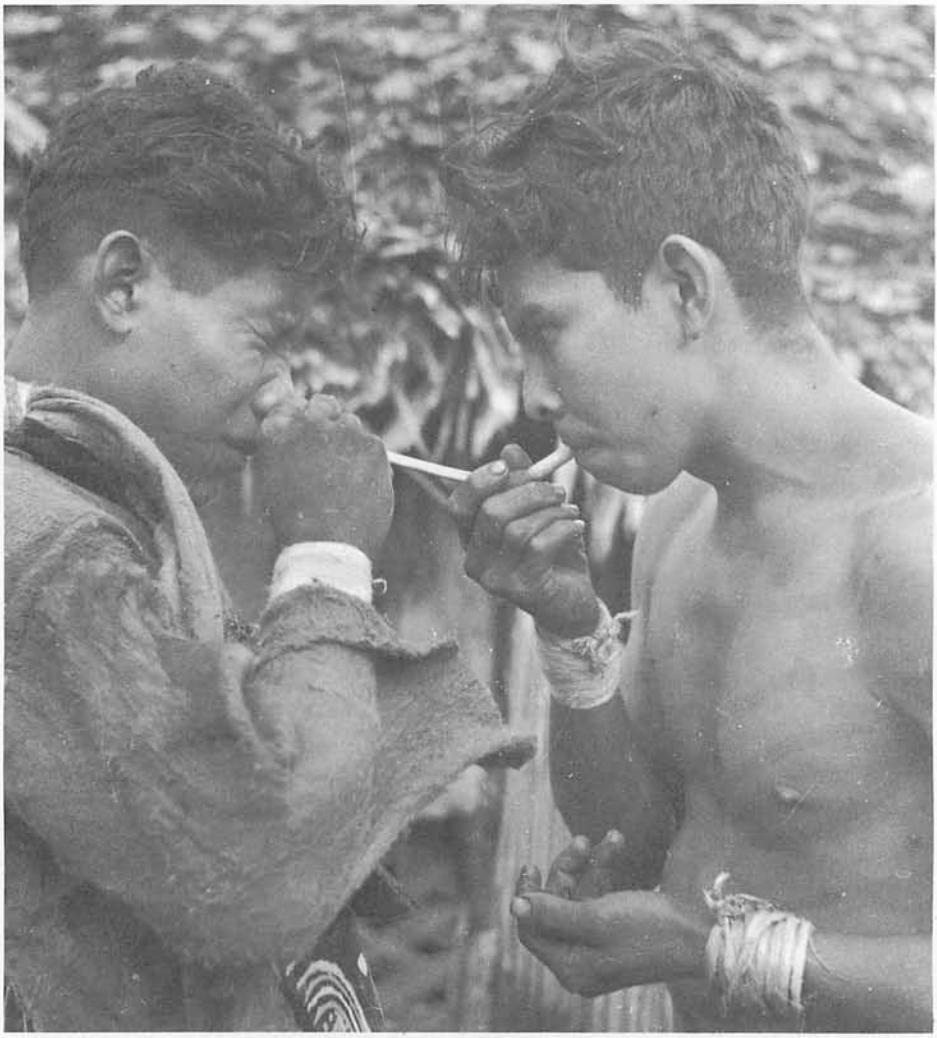

FIG. 1.—Use of the straight bird-bone snuffing-tube for administration of the tobbaco-coca snuff of the Yukuna Indians, Río Miritiparaná, Amazonas, Colombia. Photograph by R. E. Schultes.

Of possible significance is the curious fact that *Anadenanthera peregrina* is or has been employed not only in northern South America but probably in the Antilles as well. Tobacco snuffing was a well established custom in the West Indian islands long before the arrival of Europeans, and the snuffing in Hispaniola of a narcotic, vision-producing powder called *cohoba* was no cause for intellectual curiosity, since most early writers assumed that cohoba was merely another tobacco snuff. It was the American enthnobotanist Safford who first identified, quite correctly, I believe, the West Indian cohoba snuff with the yopo of the Orinoco basin of Venezuela and Colombia (*16*).

There were a number of reports in the literature ascribing the sources

of Amazonian snuffs to various leguminous trees, and its was Bentham who "came to the conclusion that all South American trees . . . referred to as the source of narcotic snuff were probably one species and were identical with Linnaeus' *Mimosa peregrina*, which was first described in 1737 from a seedling growing in the celebrated Clifford Garden in Holland" (*16*). It seems that one of the most extraordinarily mistaken generalisations in ethnobotany—that all of the narcotic snuffs of the Amazon that were not obviously tobacco must have been prepared from *Anadenanthera peregrina*—has stemmed from Benthem's conclusions. This generalisation, of course, has not been without influence, judging from the state of confusion and lack of clarity encountered in many of the earliest reports of "smoking" and "snuffing." We have no clear distinction, in many early instances, as to whether tobacco or cohoba represented the plant the use of which was being described, since tobacco was snuffed in the Caribbean area at the time of the arrival of the Spaniards.

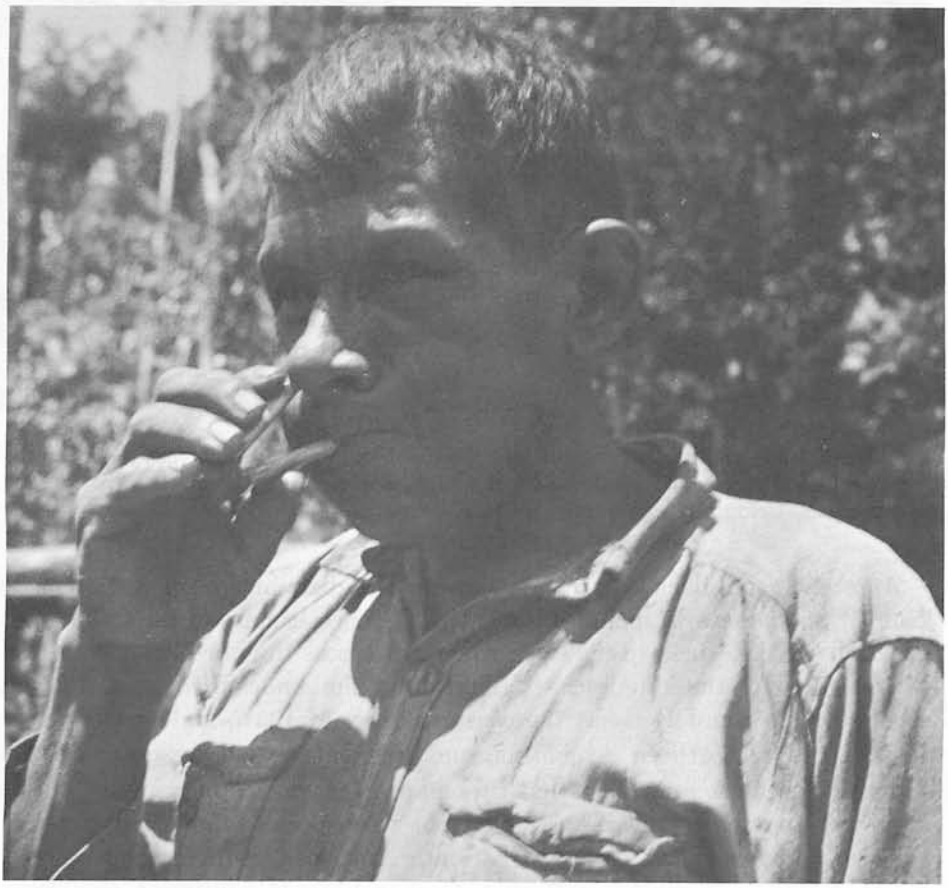

FIG. 2.—Tanimuka Indian administering tobacco-coca snuff with the V-shaped bird-bone snuffing tube employed for self-administration. Río Miritiparaná, Amazonas, Colombia. Photograph by R. E. Schultes.

FIG. 3.—Yukuna Indian pouring out into the hand from a snail-shell case a quantity of tobacco-coca snuff for insertion into the bird-bone snuffing tube. Río Miritiparaná, Amazonas, Colombia. Photograph by R. E. Schultes.

A recently published map (*4*), showng the distribution of snuffs made from *Anadenanthera*, includes the entire Orinoco basin and adjacent areas of southern Venezuela to the east; westward across the northern Colombian Andes, much of the Magdalena Valley; down the Andes through Columbia, Ecuador, Peru and Bolivia; the coastal region of Peru, and scattered isolated areas in northern Argentina, and the central and western Amazon Valley. One must remember that this map refers not to one species but to a genus—and there have been suggestions that species other than *Anadenanthera peregrina* have entered the South American snuff making picture. Furthermore, one must recall that Cooper himself cautioned that "our tribal records on which the . . . distribution map . . . is based are probably very incomplete. On the other hand, some of the attributions may not be correct, since in some cases the lack of exact botanical identification makes

it doubtful whether we have to do with *Piptadenia* snuff, tobacco snuff or snuff from some other plant . . . ."

When I first went to the northwesternmost Amazon in Colombia—a region the flora of which I investigated in the field from 1941 to 1953—I fully expected to meet with the use of yopo snuff. One of my reasons for choosing this geographcal area for my studies was our knowledge that here the aborigines were reported to be using more kinds of narcotic preparations than in any comparable region of the world. Consultation with the sparse literature for this part of the Amazon basin led me to believe that yopo snuff from *Anadenanthera peregrina* was known and employed throughout the area. True, amongst the Witotos, Kubeos, Yukunas, Tanimukas, Tukanos, Makunas and other native groups, I met with the use, oftentimes excessive use, of tobacco snuff. I never met with anything called yopo or niopo, and what was more confusing to me as a botanist was my failure to encounter, wild or cultivated, a single tree of *Anadenanthera peregrina.* This species grows cultivated in the Llanos of Colombia—the Orinoco drainage area of Colombia, northerly adjacent to its Amazon area. Furthermore, from the writings of Spruce (*24*) and other earlier travellers, as well as from reports of missionaries of the present day, we know that this hallucinating snuff was and is employed extensively and in large amounts by the naitves of the Llanos. My later explorations and researches in the Colombian Amazon convinced me that generalisation from reports in the available literature had led to gross error; that, in effect, yopo snuff not only is *not* used but is actually unknown, and that the tree does not occur, at least in the northwesternmost Amazon. Furthermore, since I was resident for three years in country of the Tikuna Indians of the uppermost Amazon River at the point where Brazil, Colombia and Peru join, I was especially interested in the assumption that these natives formerly made snuff from *Anadenanthera* (*3*). Inasmuch as I met no tree of this species in the area nor did I see the Tikunas (who do make tobacco snuff) prepare snuff from leguminous seeds, I must conclude that this specific instance is also one of the numerous erroneous generalisations.

How can we assume, or justify an assumption, that natives over such a vast area as the Amazon make a snuff from a plant that they do not know, that does not grow in their region, wild or cultivated, the seeds of which they would have to import for many, in some cases, for several thousand miles?

Let us contemplate what is known of the distribution of *Anadenanthera peregrina.* Safford, who apparently concurred with the ideas that such widely scattered Amazonian peoples as the Omaguas of Amazonian Peru and the Murus of the Rio Negro of Brazil prepared snuff from this leguminous tree, truthfully wrote that *Anadenanthera peregrina* "has a most appropriate specific name, for it has a wide geographical range." He further pointed out that its range had "undoubtedly been increased by human agency." But, when Safford cites for *Anadenanthera peregrina* a range comprising Hispaniola and Puerto Rico, Venezuela, northeastern Peru, southern Peru, Argentina, Guiana and "many parts" of Brazil, he was including with *Anadenanthera peregrina* two other species of the genus which he presumed to be employed as the source of making snuff. He cites no herbarium voucher specimens,



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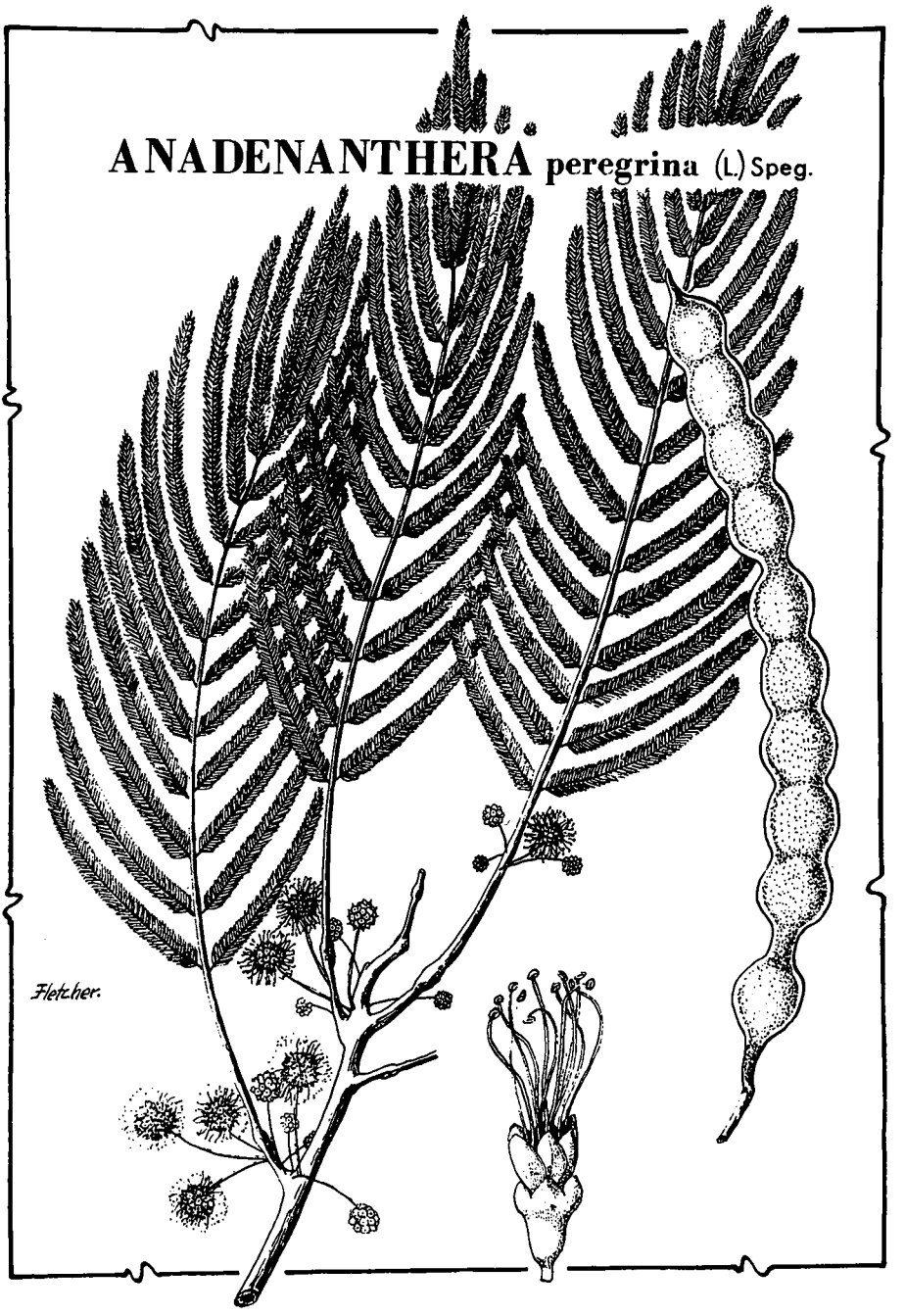


FIG. 4.—Anadenanthera peregrina (Piptadenia peregrina).

instead giving references to the use of snuffs in the literature and assuming that they did refer actually to snuffs from *Anadenanthera.*

Fortunately, we have several botanical studies of monographic nature that shed light on the distribution of *Anadenanthera peregrina.* It is these data, not "interpreted" literature reports, that must guide any definitive generalisations. Ducke, renowned Brazilian botanist who spent more than half a century studying the Amazon flora in field and laboratory, specialised in the Leguminosae. In his "Leguminosas da Amazonia", he (*5*) cites all known collections of *Anadenanthera peregrina* (under *Piptadenia peregrina*). If the species had been much commoner in the Amazon, Ducke would have made more collections than those that he cited. More recently, Altschul, in her studies of the genus of the yopo snuff (*1*, *25*), has treated *Anadenanthera* monographically, citing only collections, wild or cultivated, from South America. Thus, we know that, at least in the present century, *Anadenanthera peregrina* is far from common in the Amazon basin.

It is, therefore, somewhat exaggerated to expect us to conclude that many tribes are preparing an important hallucinogenic snuff, and a product often taken in excessive amounts, from a tree that is uncommon or even not found in their environment. Trees of this species are reported in Venezuela as "being forest dominants, belonging to secondary forests, inhibiting savannas, light forests and riversides," in British Guiana confined to "savannas and riverside forests," while in Brazil represented mostly in the *campos* or savannas (*1*, *6*). The distribution of *Anadenanthera peregrina* in the Amazonas of Brazil is, significantly, confined to savanna-like areas, usually in or near the lower Rio Madeira and the Rio Branco basins—significantly, I say, because the Maué and other tribes of the Madeira area have, probably correctly, been reported as using snuff from *Anadenanthera.* I have seen excellent specimens of *Anadenanthera peregrina* recently collected by Mr. Georg Seitz along the Rio Negro, in the vicinity of the mouth of the Rio Branco, in Amazonian Brazil; these were undoubtedly cultivated from material brought in from the savannas of the Rio Branco.

Now, let us contemplate the problems that arise. If *Anadenanthera peregrina* is not the source of a snuff employed over wide areas in the Amazon, what are the sources of the numerous snuff preparations that we know are or have been prepared in isolated localities from the mountains of Venezuela and the Guianas south to the Argentine and from the eastern slopes of the Andes to the Atlantic Ocean? We cannot fully answer this query at the present time, but we can offer several tentative approaches towards a solution.

To begin with, it is very probable that several, if not many, different plants formed the basis for the snuffs employed similarly and for similar purposes over such a vast area. We know very definitely that this is true. We do not, to be sure, know all of the plants involved in this complicated enigma, but we know enough to arrive at an overall picture to guide future research.

It was apparently Safford (*16*) who first suggested that species of *Anadenanthera* other than *peregrina* may be the source of narcotic snuffs in South America. He identified the *vilca* or *huilca* of southern Peru and Bolivia, and

the *cébil* of northern Argentina, with seeds of what he called *Piptadenia macrocarpa*, now correctly referred to as *Anadenanthera colubrina* var. *Cébil*. Although the evidence is, in my opinion, rather weak, several other species and varieties may have been employed in isolated localities in southern South America. Inasmuch, however, as a paper in the series is devoted precisely to the problem at hand, I shall refrain from considering it at greater length.

When I first went to the northwesternmost Amazon in Colombia, I heard numerous reports of a strongly hallucinogenic snuff made from the bark of forest trees. Known in the area as *yakee* or *paricá*, it was obviously not tobacco snuff nor was it prepared from seeds of *Anadenanthera*.

After eight years of search, I discovered that yakee was prepared from several species of *Virola*, *V. calophylla*, *V. calophylloidea* and, perhaps, *V. elongata* of the Myristicaceae (17, 18). The natives strip bark from the trunks before the sun has risen high enough to heat up the forest. A blood-red resin oozes from the inner surface of the bark. It is scraped off with a machete or knife and boiled in an earthen pot for hours, until a thick paste is left. This paste is allowed to dry and is then pulverized, sifted through a fine cloth, and finally added to an equal amount of ashes of the stems of a wild cacao species. The ashes give the snuff consistency to withstand the excessive dampness of the air which might otherwise quickly "melt" the powdered resin-paste to a solid lump.

FIG. 5.—Leaves and flowers of *Virola calophylloidea*, one of the species of *Virola* from which a strongly hallucinogenic snuff is prepared. Mitú, Vaupés, Colombia. Photograph by R. E. Schultes.

FIG. 6.—Puinave Indian preparing yakee-snuff from the red resinous exudate from the bark of *Virola*-trees. Río Apaporis, Vaupés, Colombia. Photograph by R. E. Schultes.

At the beginning of this century, the German ethnologist Koch-Grünberg mentioned (*11*) an intoxicating snuff prepared from the bark of an unidentified tree by the Yekwana Indians of the headwaters of the Orinoco in Venezuela. There seems to be every reason to believe that this snuff was made from a species of *Virola*. Seitz (*23*) has identified the *epená* snuff of the Waika Indians (who now live in the Rio Negro basin of Brazil, but who have migrated from the headwaters of the Orinoco) as representing *Virola calophylloidea*.

At one time, I presumed that the active principle in this myristicaceous snuff must be the same essential oil—myristicine—that is common throughout the family and that has been thought to make nutmeg a dangerous narcotic in appropriate amounts. Myristicine may have some effect, but Holmstedt has recently isolated tryptamine derivatives from *Virola*—snuff which itself could account for the hallucinogenic properties of the powder (*10*).

It may be interesting to append a few observations which I made personally after taking yakee (*17*). I took about one-third of a teaspoonful in two inhalations, using the characteristic V-shaped bird-bone snuffing tube. This represents about one-quarter the dose that a diagnosing medicine man will take to bring on an eventual state of unconsciousness.

The dose was snuffed at five o'clock one afternoon. Within fifteen minutes, a drawing sensation was felt over the eyes, followed very shortly by a strong tingling in fingers and toes. The drawing sensation in the forehead gave way to a strong and constant headache. Within a half hour, the feet and hands were numb and sensitivity of the fingertips had disappeared; walking was possible with difficulty, as with beri-beri. I felt nauseated until eight o'clock, and experienced lassitude and uneasiness. Shortly after eight, I lay down in my hammock, overcome with a drowsiness, which, however, seemed to be accompanied by a muscular excitation except in the hands and feet. At about nine-thirty, I fell into a fitful sleep which continued, with frequent awakenings, until morning. The strong headache lasted until noon. A profuse sweating and what was probably a slight fever persisted throughout the night. The pupils were strongly dilated during the first few hours of the intoxication.

Though performed under primitive conditions in the jungle by myself, this experiment does, I think, indicate the great strength of the snuff as a psychotropic agent. The witch doctors see visions in color, but I was able to experience neither visual hallucinations nor color sensations. The large dose used by the witch doctor is enough to put him into a deep but disturbed sleep, during which he sees visions and has dreams which, through the wild shouts emitted in his delirium, are interpreted by an assistant. That it is a dangerous practice is acknowledged by the witch doctors themselves. They report the death, about 15 years ago, of one of their number from the Puinave tribe during a yakee-intoxication.

## Sources of Snuffs of Lesser Importance

We are aware from the literature of references to narcotic snuffs in South America the botanical identities of which are still uncertain or unknown.

A most mysterious snuff of which we still know almost nothing is said to be prepared from the fruits of the gigantic moraceous jungle tree *Olmedioperebea sclerophylla* (*19*). It is reputedly employed in the central part of Brazil, especially along the upper Xingú, but is known only by the general Portuguese term *rapé dos indios* ("Indian snuff"). So far as I have been able to ascertain, chemical examination of the fruits of this tree has not yielded substance with psychotomimetic effects.

It would be satisfying to know the plant source of the clear amber-coloured and aromatic resin that is procured from a large forest tree, and that forms part of the sacred accoutrements of every medicine man of the Tukanoan tribes in the Apaporis and Vaupés Rivers of Amazonian Colombia (*17*, *22*).

In particularly difficult cases of diagnosis of disease, divination or other magic practice, minute amounts of this resin, powdered, are snuffed. Although it is said to induce dizziness, it is not reputed to have hallucinogenic properties. Nevertheless, botanical identification and chemical study of this resin-snuff should be made, if only because of the intriguing fact that it is quite generally referred to as *paricá*, the same name that is applied to the highly hallucinogenic snuff prepared from the blood-red resin of the inner bark of several species of the myristicaceous tree-genus *Virola*, by the same people in the same part of the Amazon.

A number of years ago, a missionary working in the headwaters of the Orinoco in Venezuela handed me a partially rotted, matted roll of plant material which he said was the source of one of the narcotic snuffs of the Waika Indians. The condition of the material was very poor, but it seemed to represent a species of *Justicia*. This identification was tentatively corroborated by Dr. E. C. Leonard, the American specialist on the Acanthaceae. I have never been able to visit this region to investigate the problem personally. With the unsatisfactory preservation of the material and the failure of other botanists who had visited the general region to report it (*31*), I more or less dismissed *Justicia* as a serious contender for inclusion in our list of hallucinogens. I am now, however, convinced that this problem must be investigated thoroughly in the field, for recently, the Brazilian botanist, Prof. João Murça Pires, informed me personally that the Waikas do indeed employ a species of *Justicia*, a species close apparently to *J. pectoralis*, in the preparation of a vision-producing snuff. We know that alkaloids have been reported from several species of *Justica*, and there has been some question of synonymy of *Justica* with *Adhatoda*, which is known to contain harman-type alkaloids. Several other genera of the Acanthaceae have been reported as alkaloidal, and this family might well bear an intensive phytochemical study. In this connexion, I might report here that one of the minor fish poisons that I found in use amongst the Taiwanos of the Río Kananarí of Colombian Vaupés is the root of an acanthaceous shrub, the genus of which is as yet phytochemically wholly unknown: *Mendoncia aspera* (*22*).

There is, apparently, a fertile field for the study of narcotic snuff preparations in the general area of the headwaters of the Orinoco. In fact, this part of South America would seem perhaps to represent the centre of complexity of this curious culture trait.

The Waikas of the upper Orinoco basin have been reported to prepare their yopo snuff from three plants (*27*). One source enumerates *hisioma*, *Anadenanthera peregrina*, as one ingredient; a second is called *masho-hara* or *yauardi-hena* and is said to be a piperaceous species; a third is a powder known as *bolek-hena*. It is a temptation to wonder whether or not this bolek-hena or "leaves of the spirit of death" might be a *Justicia*. Other sources (*2*, *23*, *27*, *32*) assert that the snuff of the Waikas and of a related tribe, the Samatari, was prepared from the bast of a tree called *epéna-késí* (referrible probably to *Virola*); the ashes of the outer bark of *ama-asita*, which has been identified in the literature as an *Acacia;* and the powder of *mashi-hiri*, a plant of about one foot in height which might conceivably also represent

*Justicia.* The Surára and Pakidái make their snuff (*30*) from seeds of *Anadenanthera peregrina*, ashes of *hekurahíhená*, the bark of a tree of uncertain identity but possibly representing also this same species, a piperaceous species, *maxarahá.* The Karimé, culturally related to and neighbours of the Waikas, eleborate a snuff powder (*30*) from leaves of "a small plant called *kokoime.*" Again, are we warranted in suspecting that kokoime might be the *Justica?*

The Kashuena of the Rio Trombetas in Amazonian Brazil, are reported by one source to have several kinds of snuff in addition to that made "simply of tobacco" (*7*). One is prepared by "blending the dried and powdered bark of a tree and a quantity of paricá with other substances taken from kernels or seeds of a variety of wild fruits." A third comprises a mixture of these two kinds of snuff. We are left in the dark about the species of tree from which the bark is taken, although it may possibly be referrible to an *Anadenanthera*, and the "wild fruits" remain unidentified. Could one be the fruits of *Olmedioperebea sclerophylla?*

## Final Query

The several attempts to synthesise and summarise our knowledge of the precise botanical identification of plants entering into the preparation of South American snuffs (*26*, *28*) have met with the same difficulties that I find in trying to discuss this topic here. Because of similarities in the tools and methods of snuffing, and especially as a result of the lack of voucher botanical specimens, we are too often reduced to conjecture as to the plants involved. In view of the importance of snuffing in many cultures—past and present—and of the possibility that a number of plants hitherto unknown as ingredients of narcotic snuffs might be uncovered, further field investigation of snuffs in South America is clearly indicated.

In connexion with the possibility of finding new plants as sources of narcotic snuffs, there is one point that has disturbed me for a long time. Why should only several of the narcotic plants be administered as snuff? Snuffing is a widespread New World culture trait. It is a relatively easy method of self-intoxication. It lends itself easily to ritual or ceremonial use. Snuffs usually tend to keep over longer periods, especially in the humid tropics, than infusions or decoctions. Why then are not more narcotics taken in this form? One limiting factor, to be sure, would be the requirements that the activite principle must be absorbable through the membranes to enter directly into the blood stream and be active. Nicotine, of course, answers these reqirements. Obviously, the active principles of the snuffs from *Anadenanthera peregrina* and *Virola* also satisfy these requirements. But would not the active constituents of other narcotics likewise follow this pattern? Why, for example, have we never found the sundry species of *Datura* powdered and employed as snuffs?

Would snuffs prepared from the bark of *Banisteriopsis* provide the desired psychotropic effects? And what about the narcotic properties of *Ery-*

*throxylon Coca*—would they be lost if the powdered leaves were introduced into the nostrils as a snuff? The rich variety of toxic plants in the flora of South America—would not many of these species have psychotomimetic effects which would be more controllable or perhaps less dangerous as snuffs then decoctions or infusions of the same plants? All of this leads to two questions that I would leave with you: Was not the snuffing of narcotic powders much more widely practiced in South America than it is at present? Was and is not the number and variety of plants snuffed for their peculiar physiological properties greater than we at present believe? The answer to both questions, I suspect, is "Yes." But only more intensive and extensive search and interpretation of the literature, and more immediate and insistent ethnobotanical field studies can provide us with answers.

## BIBLIOGRAPHY


(*1*) Altschul, Siri von Reis. "A taxonomic study of the genus Anadenanthera." Contrib. Gray Herb., Harvard Univ. 193 (1964), 1.

(*2*) Barker, James. "Memoria sobre la cultura de los guaika." Bol. Indig. Ven. 1 (1953), 433.

(*3*) Bates, Henry W. "The naturalist on the River Amazons," (1863). John Murray, London.

(*4*) Cooper, John M. "Stimulants and narcotics" in Handbook of South American Indians, Bull. No. 143, Vol. 5, Bur. Am. Ethnol. (1949), 525.

(*5*) Ducke, Adolpho. "As leguminosas da Amazônia brasileira." Bol. Tecn. Inst. Agron. Norte 18 (1949).

(*6*) Ducke, Adolpho and George A. Black. "Phytogeographical notes on the Brazilian Amazon." An. Acad. Bras. 25 (1953), 1.

(*7*) Friekel, Protásio. "Morí — a festa do rape (indios kachiryana, rio Trombetas)." Bol. Mus. Para. Emilio Goeldi, n.s., Anthrop. 12 (1961), 1.

(*8*) Garcilaso de la Vega, (El Inca) "Primera parte de los commentarios reales. . . ." Pt. 1, Book 2 (1723), Chapt. 25.

(*9*) Goodspeed, Thomas Harper. "The genus Nicotiana" (1954), Chronica Botanica Co., Waltham, Mass.

(*10*) Holmstedt, Bo. "Tryptamine derivatives in epená, an intoxicating snuff used by some South American Indian tribes." Arch. Int. Pharmacodyn. Therap. 156 (1965), 285.

(*11*) Koch-Grünberg, Theodor. "Zwei Jahre unter den Indianern." 1 (1909) 298. Ernst Wasmuth A.-G., Berlin.

(*12*) Levi-Strauss, Claude. "Tribes of the right bank of the Guaporé River" in Handbook of South American Indians, Bull. 143, Vol. 3, Bur. Am. Ethnol. (1948), 378.

(*13*) Mason, J. Alden. "Use of tobacco in Mexico and South America." Field Mus. Nat. Hist. Anthrop. Leafl. 16 (1924).

(*14*) Nimuendajú, Curt (Ed. R. H. Lowie). "The Tukuna" Univ. Cal. Publ. Am. Arch. Ethnol. 45 (1952).

(*15*) Rowe, John Howland. "Inca culture at the time of the Spanish Conquest" in Handbook of South American Indians, Bull. 143, Vol. 2, Bur. Am. Ethnol. (1946), 292.

(*16*) Safford, William Edwin. "Identity of cohoba, the narcotic snuff of ancient Haiti." Journ. Wash. Acad. Sci. 6 (1916), 548.

(*17*) Schultes, Richard Evans. "A new narcotic snuff from the northwest Amazon." Bot. Mus. Leafl., Harvard Univ. 16 (1954), 241.

(*18*) ———. "Un nouveau tabac à priser de l'Amazone du nord-ouest." Journ. Agric. Trop. Bot. Appl. 1 (1954), 298.

(*19*) SCHULTES, RICHARD EVANS. "Native narcotics of the New World." Texas Journ. Pharm. 2 (1961), 141.
(*20*) ———. "Hallucinogenic plants of the New World." Harvard Rev. 1 (1963), 18.
(*21*) ———. "Ein halbes Jahrhundert Ethnobotanik amerikanischer Halluzinogene." Planta Medica 13 (1965), 124.
(*22*) ———. "The search for new natural hullucinogens." Lloydia 29 (1966), 293.
(*23*) SEITZ, GEORG. "Einige Bemerkungen zur Anwendung and Wirkungsweise des Epená—Schnupfpulvers der Waika—Indianer." Ethnolog. Studier No. 28 (1965), 117.
(*24*) SPRUCE, RICHARD (Ed. A. R. Wallace). "Notes of a botanist on the Amazon and Andes." 2 (1908), 426. Macmillan & Co., Ltd., London.
(*25*) VON REIS, SIRI S. P. "The genus Anadenanthera: a taxomomic and ethnobotanical study." Ph. D. Thesis (ined.) (1961), Radcliffe College, Cambridge, Mass.
(*26*) WASSEN, S. HENRY. "Some general viewpoints in the study of native drugs, especially from the West Indies and South America." Ethnos 29 (1964), 97.
(*27*) ———. "The use of some specific kinds of South American Indian snuff and related paraphernalia." Ethnolog. Stud. 28 (1965).
(*28*) ———. "Sydamerikanska snusdroger." Nytt och Nyttigt, No. 1 (1966), 1.
(*29*) ——— and Bo Holmstedt. "The use of paricá, an ethnological and pharmacological review." Ethnos 28 (1963), 5.
(*30*) WILBERT, JOHANNES. "Indios de la región Orinoco—Ventuari." Monografía No. 8, Fundación La Salle de Ciencias Naturales, Caracas (1963).
(*31*) WURDACK, JOHN. "Indian narcotics in southern Venezuela." Gard. Journ. 8 (1958), 116.
(*32*) ZERRIES, OTTO. "Das Lasha—Fest der Waika—Indianer." Di Umshau 21 (1955), 662. Frankfurt-am-Main.

# Vilca and its Use

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It generally has been assumed that the Peruvian substance known as *Vilca* is, or was, a snuff made from a *Piptadenia* in the family *Leguminosae* (Safford, 1916; and later authors). However, there is evidence in the literature and in unpublished materials that *Vilca* may involve other plants as well, and that it may have been used in forms different from snuff. I would like to examine this evidence with a view to opening new areas in the search for psycho-active drugs.

The discussion which follows is based in part on research in the ethnobotany of the strictly New World genus *Anadenanthera*, which formerly was considered as section *Niopa* of the genus *Piptadenia* and is known commonly as the source of some hallucinogenic snuffs. The genus *Anadenanthera* contains two very similar species which have not been shown to differ significantly with respect to their psycho-activity, and which may have been used interchangeably. One species is *Anadenanthera colubrina*, found in southern Peru, Bolivia, northern Argentina, Paraguay and southern Brazil. The other species is *A. peregrina*, ranging from southeastern Brazil to the Greater Antilles. (von Reis, 1961; von Reis Altschul, 1964).

The discussion also will make use of information which recently has become available. This information has been selected from nearly 6,000 field notes from a search of almost 2,500,000 herbarium specimens at Harvard University (von Reis, 1962). Dr. Richard Evans Schultes and I have just completed this project and intend to publish our data as soon as it is feasible.[1]

Let us look first at the earliest references to *Vilca*, which are to be found not in the herbarium but in the post-conquest literature of Peru. Around 1571, Polo de Ondegardo reported that the witch doctors of the Incas [2] foretold the future by speaking with the devil in some dark place by means of various ceremonies, for which office they intoxicated themselves with an herb called *Villca*, pouring its juice into *chicha* or taking it another way. The reporter stated that, although only old women were reputed to practice this craft, in fact its use was widespread but concealed among men and boys, as well. In 1695, Santa Cruz Pachacuti spoke of a medicine called *villca* which was the seed of a tree. Two years later, González Holguín said that *Villca* referred to a tree with a purgative fruit. An early report by Falcón (1946 ed.; in Yacovleff & Herrera, 1935) indicated that the Indians took a purge called *Vilcas*

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[2] Murdock's *Outline of South American Cultures* (1951) has been used for classifying all the Indian cultures dealt with in this paper.

(or *elilcas*) which was beneficial to those who worked too hard. In 1629, Vásquez de Espinosa said that the pods of the *vilca* tree had small, round seeds which were the common purge of the Indians for all sorts of humors. Some years later, in 1653, Bernabé Cobo stated that the Indians used a decoction of the roots of a *Polypodium* fern with two or three *Vilca* seeds to remove phlegm and choler without pain or nausea. He gave a fair, but not diagnostically adequate, description of the tree called *Vilca*, and maintained that the Indians cured a variety of illnesses with the purgative seeds taken in *chicha*. These seeds were said to be both laxative and emetic and to dispel melancholy. Cooked and drunk in honey, they cleared the chest, stimulated urination and made women fruitful.

Modern writers usually identify the name *Vilca* with the species here called *Anadenanthera colubrina* (Herrera, 1934; Lastres, 1951). In 1916, Safford stated that seeds labelled *Huillca* and secured from an Indian drug vender in southern Peru had been identified as belonging to *Anadenanthera*. Herrera reported in 1940 that the seeds of *Huillca* (*Herrera 3210*) are a narcotic-cathartic element in the indigenous pharmacopoeia. Yacovleff & Herrera (1935) have said that the seeds are sold as purgatives in the local markets. Recently, Vargas confirmed in a letter (1966) from Cuzco that herb doctors in that vicinity continue to use the seeds for this purpose. Cárdenas has stated from Bolivia that the same species, known as *Willca*, is used as a stimulant and aphrodisiac by the *callahuayos* (1943), or itinerant medicine men who travel today between Chile and Mexico (H. C. Cutler in conversation, 1966). The seeds also have been used in our time as charms or fetishes by the Quechua Indians of northwest Bolivia. At the market in La Paz one may buy, among other goods for similar purposes, seeds of *A. colubrina* and of other leguminous species in the genus *Ormosia*. These seeds and other items are buried, for magical purposes, under houses in the process of construction (Nordenskiöld, 1907; Pardal, 1937).

In the course of the herbarium search mentioned above, we found two specimens labelled *Vilca*. Both belonged to *Anadenanthera colubrina*. One was from southern Peru (Departamento de Huancavelica, *Weberbauer 6505*). The other was from east of La Paz, Bolivia (Cañamina, *White 254*). These data indicate that *A. colubrina* indeed is identifiable with *Vilca*, but they do not insure that *Vilca* is referable exclusively to this plant.

For one thing, it is especially difficult to establish botanical identifications in the early literature. Apparent inconsistencies or omissions in plant descriptions, and the lack of voucher specimens require that we habitually entertain the possibility of altogether new interpretations, particularly among groups like the legumes, where many similar species may be mistaken one for another. In fact, the widespread representation of the *Leguminosae* in native medicine suggests that a pharmacological screening of its New World genera for psycho-active compounds might be a worthwhile undertaking.

In conjunction with our herbarium search at Harvard, we found three species with common names similar to *Vilca* but from families other than the legumes. These were a Peruvian specimen of *Banisteria leiocarpa* (*Malpighiaceae*, *Vargas 2044*) labelled *Vilca bejuco*, or climbing *Vilca;* a Vene-

zuelan specimen of *Virola sebifera* (*Myristicaceae, Steyermark 60758a*) labelled *wircaweijek*, whose inner bark is said to be dried and smoked by witch doctors to cure fevers; and a Peruvian specimen of *Baccharis floribunda* (*Compositae, West 3735*) labelled *Ullccochilca*, a species also reputedly curative (*Macbride & Featherstone 1631*).[3]

In addition to these interesting attributions, our herbarium search revealed information which does not relate directly to *Vilca* but which I will present here because it very much bears upon the search for psychoactive drugs. This information consists of common names of *Anadenanthera* species which have come to light in connection with new plants. The accompanying map (Fig. 1) shows the distribution of the common names of *Anadenanthera* species in South America, based upon labels of specimens examined. With these names and their locations in mind, I would suggest that the following species be examined chemically for possible pharmacological activity: in the *Asclepiadaceae*, *Asclepias curupi* (*Balansa 1361*) from Paraguay, labelled *Curupí*, the powdered leaves and a decoction of the plant said to be applied to snake bite; in the *Euphorbiaceae*, three species of *Sapium* from Uruguay, labelled *Curupí* (*S. gibertii, Lombardo 3048; S. haematospermum, Lombardo 3047; S. linearifolium, Lombardo 3344*); in the *Rubiaceae*, *Guettarda viburnoides* from Brazil, labelled *Angico* (*Mexia 5583*); and in the *Leguminosae* from Brazil an undetermined *Pithecellobium* (*Krukoff 1887*), *Piptadenia contorta* (*Mexia 4438*), both labelled *Angico Branco;* and *Mimosa malacocentra* (*Mexia 5624*) labelled *Angiquin*, whose leaves are used to make a tea for pain.

Further afield from *Anadenanthera* but pertinent to the objectives of the conference are a few surprising new combinations: in the *Convolvulaceae*: two species of *Ipomoea* (*I. denticulata, I. tiliacea, W. H. & B. T. Hodge 3323, 3318*, respectively) from the island of Dominica, West Indies, labelled *Caapi;* in the *Leguminosae*, *Calliandra calothyrsis* (*Standley 23846*) and *Leucaena guatemalensis* (*Standley 73562*), both from Guatemala and labelled *Yaje;* in the *Compositae*, *Trichocline incana* (*Meyer 3982*) from Argentina, labelled *Coro* and said to be smoked with tobacco. The word *Coro* has appeared now and then in the early chronicles and has been linked previously with *Anadenanthera* and (the root of) wild tobacco (Cobo, 1890–93 ed.; Uhle, 1898) but never, to my knowledge, with this plant: According to Cobo, *Coro* powder was drunk in water for detention of urine, or taken as snuff for headache and to clear the vision.

I would like to return now to *Vilca* and to review some of the botanical common names similar to it in the published literature. The species ascribed to these names perhaps should receive critical attention, too. *Vilcarán* has been associated with *Piptadenia rigida* (Burkart, 1949) in Argentina. *Vilcaparu* is a word for yellow maize (González Holguín, 1607) from Bolivia (A. Grobman in conversation, 1961). *Huillko* means species of *Ipomoea* and

[3] Any pharmacological research on these and other species cited in this paper should be preceded by a verification, by a competent botanist, of the correct identification of the specimens cited. The research should be based on the specimen cited, as designated by the collector's name and field number. All specimens are in the collections of the Arnold Arboretum and Gray Herbarium of Harvard University, Cambridge, Mass.

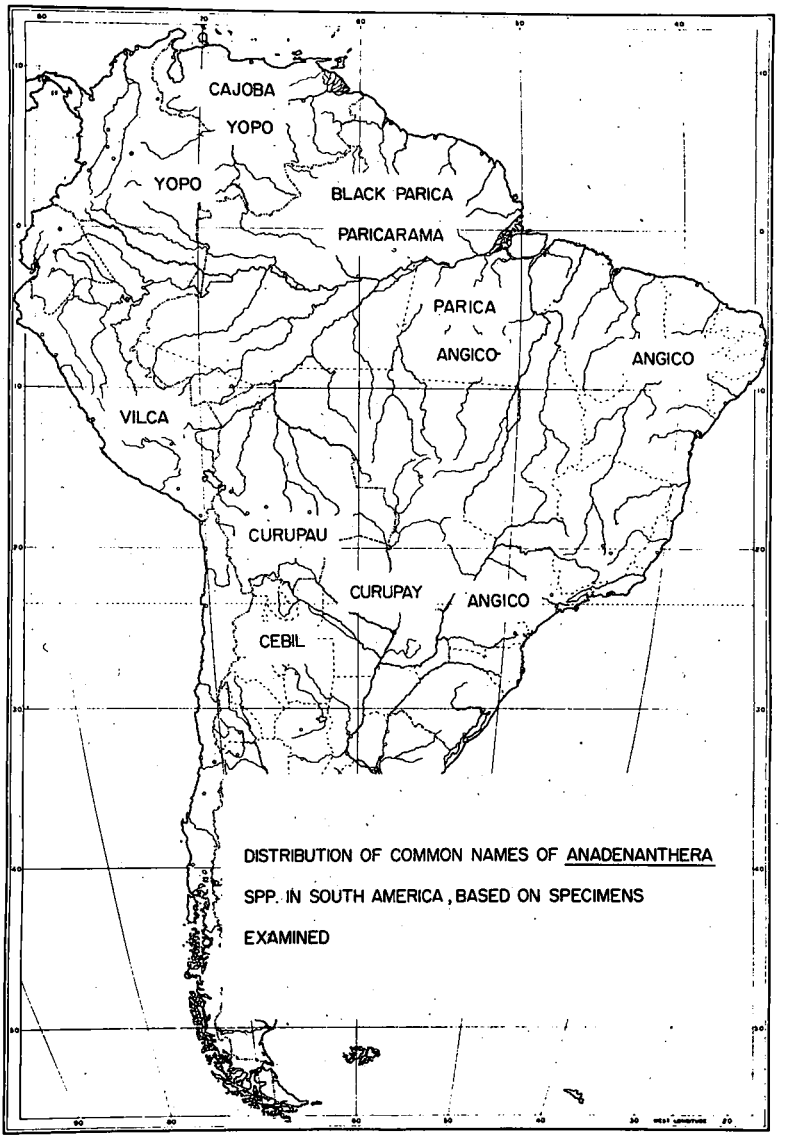


FIG. 1

the Nyctaginaceous genus *Mirabilis* (Herrera, 1934). *Tara Huillca* has been identified as *Anadenanthera colubrina* (Yacovleff & Herrera, 1935), but *Tara*, alone, refers to another legume, *Caesalpinia tinctoria* (Herrera, 1934). *Wilca Tarwi* has been assoicated with the leguminous genus *Lupinus* (Lastres, 1941). The chronicler Poma de Ayala (1936 ed.; Lastres, 1941) reported that the Indians purged themselves once a month with *bilca tauri*, made from some kind of seeds ground into a liquid, half of which was drunk and half of which was taken as an enema which was said to give the Incas strength, health and a 200 years life span. At the time of the conquest, the word *Vilcu* referred in Aymará to a plant with yellow, bird-like flowers (Cobo,

1890 ed., Vol. I). It also meant ivy (*Villcu*) González Holguín, 1607). Our herbarium search unearthed two specimens of the climbing *Compositae*, *Mikania cordifolia* (*Mexia 8042*) from Peru labelled *Huaco verde*, and *M. houstoniana* (*Caec. et Ed. Seler 5475* (*396*)) from the ruins of Palenque, Mexico. *Villca* or *Huacca* both meant idol (González Holguín, 1607) or something sacred to the Incas. Hence, the possibility that *Mikania* species might have been ritual plants deserves a thought.

One might sum up what generally has been known of the role of *Vilca* in Peru at the time of the conquest by saying that it seemed to be confined mostly to simple folk-medicine, its divinatory aspects divorced from formalized religion. Rowe has stated (in Steward, 1946) that narcotics were unimportant to the Inca culture and that none was taken expressly to obtain visions; the strongest substances reputedly used were *coca*, tobacco and *Vilca*. The main curatives were *Chicha*, *Vilca* and tobacco (Fornée, 1885 ed.), and Peruvian medicine consisted primarily in blood-letting, purging with *Vilca*, and in taking tobacco (*sayri*) snuff (Garcílaso de la Vega, 1688 ed.).

Besides its occurrence with reference to medical botany, the term *Vilca* appears so frequently and in such a variety of contexts in the historical narratives of Peru that one is led to suspect that it may have had a great antiquity and that plants passing under its name may have had greater ritual importance in earlier times than at the time of the conquest. Various forms of the word meant enema or clyster (*Vilca* or *Vilcas* in González Holguín, 1607; *Vilca Tarvi* or *Vilcatauri* in Lastres, 1941; *Vilcachima* in Lastres, 1951; *Vilcana* in González Holguín, 1607, Lavorería, 1902, Mossi, 1860); the giving of an enema (*Vilcani* in D'Harcourt, 1939, González Holguín, 1607, Mossi, 1860, Lavorería, 1902); a syringe (*Vilcana* in Mossi, 1860; *uilcachina* in Poma de Ayala, 1936 ed., Lastres, 1951); or a small stick commonly used to clean the rectum in the Cuzco area (*Vilcachina* in Lastres, 1951). The same root is found in the words for doctor or surgeon (*Vilca-Cama* in Velasco, 1840 ed.); priest or informant (*Villac* in Lastres, 1951); and ostrich-like chief (*Surivilca* in Lastres, 1941); and in designations of familial relationships (*Vilca* or *Vilcay* in González Holguín, 1607, in Mossi, 1857, 1860). In 1671, Ogilby stated that in the Chilean language *Vilca* meant mother-in-law; *Hilca* meant one-eyed person. Among the Araucanians, a *pivillca* was a flute (Medina, 1882). In the area of the Diaguita culture, *Vilka* is today a surname of Quechua or Calchaquí origin (Ambrosetti, 1917).

Essentially, however, *Vilca* was one of the two names mentioned earlier by which the Peruvian Indians called their idols or gods. It was used to describe whatever was first, original or important (Lastres, 1941), and to refer to any sacred place or thing (Cobo, 1890–93 ed.; Garcílaso de la Vega, 1688 ed., 1941–44 ed.; González Holguín, 1607; Mossi, 1860). These include words for an idol (*Huacavilca* in Lastres, 1941), a temple (*Huarivilca* in Cieza de León, 1864 ed.), a town or village (*Vilca* or *Vilcas* in Cobo, 1890–93 ed.), bodies of water (*Vilca* or *Vilcas*, a river in Garcílaso de la Vega, 1688 ed.; *Vilca-Mayo*, a river in St. Cricq, 1873–74 ed. *Vilca-cocha*, a lake which flows into the *Vilca-Mayo* in St. Cricq, 1873-74 ed.), a valley

called the Paradise of Peru (*Vilca-Mayo* in Cieza de León, 1864 ed.), a mountain peak (*Vilcanota* in Garcílaso de la Vega, 1688 ed., 1941–44 ed.; *Huanca Vilca* in Lastres, 1941; *Vilcaconga* in Cobo, 1890–93 ed.) or a sierra (*Vilca* or *Vilcas*, *Vilcanota* in Cobo 1890–93 ed.), a province (*Vilca Pampa* in Cobo, 1890–93 ed., Garcílaso de la Vega, 1688 ed., 1941–44 ed.; *Vilca* or *Vilcas* in Cobo, 1890–93 ed., Cieza de León, 1864 ed.) or a people (*Vilca* or *Vilcas* in Garcílaso de la Vega, 1688 ed., 1941–44 ed.; *Chumbivilcas* in Cobo, 1890–93 ed., Garcílaso de la Vega, 1688 ed., 1941–44 ed.; *Huancavilca* in Cieza de León, 1864 ed.).

Among the ritual paraphernalia which seem to relate to *Vilca* are the *vilca ronco* (González Holguín, 1607), small *coca*-filled baskets which were thrown into the fire at animal sacrifices in Cuzco. One might mention, also, the *vilques*, earthenware jugs with which the Indians toasted their dead, after which the *chicha* contained in them was poured over a round stone which they worshipped in the middle of a plaza (Cobo, 1890–93 ed.). The chronicler Acosta (1584, folio 104) relates that the Spanish conquerors ordered the Incas to stop worshipping the sun, moon and so on, ". . . ni tengays villcas, ni guacas, ni figura de hombre, . . ."

An Incaic version of the origin of the medicinal *Vilca* (Santa Cruz Pachacuti, 1927 ed.; Yacovleff & Herrera, 1935) states that an Inca captain named *Villcaquire*, being struck down in war by his nation's enemies, the Chanca, requested that he be buried in the trunk of a nearby tree which, he foretold, would produce *villca* seeds, to dispell all bad humors and choler from his people. The story takes place above a river on the Aporima road. Specimens of *Anadenanthera colubrina* (*West 3679, 3845*) have been identified from the Department of Apurimac. I would not be surprised to learn that the story was a relatively modern one which served the needs of the Incas to attribute to their own invention something which had its origins in much earlier times. It is tempting to wonder whether the medicinal *Vilca* had had an important role among the people named *Vilca*, who were numbered among the Chanca (Garcílaso de la Vega, 1688 ed.). Legend has associated the *Vilca* with edifices whose art and grandeur, built centuries before the Inca monarchy, was much admired and emulated by the Inca culture (Cobo, 1890–93 ed.).

Modern archaeology has cast doubt as to the veracity of some of the histories in the early narratives, and, geographically, it is not easy to locate many of the places referred to in the sixteenth and seventeenth century writings on Peru. However, a number of names incorporating the term *Vilca* can be found today on a map of southern Peru, correlating in general with the distribution of *Anadenanthera* in that country.

Archaeological data suggest that the use of enemas was more widespread in pre-conquest times than it was when the Spaniards arrived (Heizer, 1944; Nordenskiöld, 1930; Vélez-López, 1930). What was used in these enemas and in the tubes and tablets of the neighboring regions has not been determined, to my knowledge. *Anadenanthera* seeds have not been found at any Peruvian sites, as far as I know. The *Cebil* snuffs used at the time of contact among the Mataco and Vilela cultures of northern Argentina appear to

have been *Anadenanthera*-derived. But the use of this genus further south beyond its natural distribution is less likely. Yet there, further south, the Comechingon Indians took something called *Sebil* through the nose (Sótelo Narvaez, 1915 ed.), and the Huarpe Indians chewed a substance called *Cibil* for endurance (Ovalle, 1703). Perhaps one even should ask whether the monumental weeping god with the tear-streaked cheeks at Tiahuanaco in Bolivia might be depicted in a state of intoxication from a powerful snuff or emetic.

This paper has posed many more questions than it has attempted to answer, but it has been instrumental in pointing out some unusual approaches to a better knowledge of *Vilca*, which could serve as a model for studies on other little known so-called narcotics. The facts gathered here suggest that a number of hitherto unsuspected species should be analyzed for psychoactivity, and that the drug plants used by man in the New World may prove to constitute a richer and more elaborate complex than we yet have been led to believe. The early writings deserve to be read again, and herbarium information should be sought more assiduously.

## BIBLIOGRAPHY


ACOSTA, J. DE. Doctrina Christiana y Catecismo para instrucción de los Indios. Lima, 1584.

AMBROSETTI, J. B. Supersticiones y Leyendas. Buenos Aires, 1917.

BURKART, A. "Leguminosas Nuevas O Criticas, III." Darwiniana, 9: 63–96, 1949.

CÁRDENAS, M. Notas Preliminares sobre la materia medica Boliviana. Cochabamba, Imprenta Universitaria, 1943.

CIEZA DE LEÓN, P. DE. The Travels of Pedro de Cieza de León, A.D. 1532–1550. London, 1864 ed.

COBO, B. Historia del Nuevo Mundo. Sevilla, 1890–93 ed.

D'HARCOURT, R. La médicine dans l'ancien Pérou. Paris, 1939.

FALCÓN, F. "Daños que hacen a los indios." Pequeños Grandes Libros de Historia Americana Ser. I, 10: 141. Lima, 1946 ed.

FORNÉE, D. N. ED. "Descripción del Corregimiento de Abancay . . . In Jiménez de la Espada, M." Relaciones Geográficas de Indias, II: 218. Madrid, 1885 ed.

GARCÍLASO DE LA VEGA. The Royal Commentaries of Peru. London, 1688 ed.

GARCÍLASO DE LA VEGA. Los Comentarios Reales de los Incas. Lima, 1941–44 ed.

GONZÁLEZ HOLGUÍN, D. Vocabulario Qquichua, que es la lengua general de todo el Piru. Lima, 1607.

HEIZER, R. F. "The use of the enema among the aboriginal American Indians." Ciba Symposia 5: 1686–1693, 1944.

HERRERA, F. L. "Botánica Etnológica," Filológica Quechua III. Rev. Mus. Nac. Lima 3: 39–62, 1934.

HERRRERA, F. L. "Plantas que curan y plantas que matan de la flora del Cuzco." Rev. Mus. Nac. Lima 9: 73–127, 1940.

LASTRES, J. B. "La medicina en la obra de Guamán Poma de Ayala." Rev. Mus. Nac. Lima 10: 113–164, 1941.

LASTRES, J. B. Historia de la Medicina Peruana, I. Lima, 1951.

LAVORERÍA, D. E. "El arte de curar entre los antiguos peruanos." An. Univ. Mayor San Marcos de Lima 29: 159–263, 1902.

MEDINA, J. T. Los aborígines de Chile. Santiago, 1882.

MOSSI, F. H. Ensayo sobre las Escelencias y Perfección del Idioma Llamado comunmente Quichua. Sucre, 1857.


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Mossi, F. H. Diccionario Quichua-Castellano. Sucre, 1860.
Nordenskiöld, E. "Recettes magiques et médicales de Pérou et Bolivie." Jour. Soc. Am. Paris Nouv. Sér. 4: 153–174, 1907.
Nordenskiöld, E. "The use of enema tubes and enema syringes among Indians." Compar. Ethnogr. Stud. 8: 184–195, 1930.
Ogilby, J. America: Being the Latest and Most Accurate Description of the New World. London, 1671.
Ovalle, A. de. "An Historical Relation of the Kingdom of Chile." In Churchill, A. & J. Collection of Voyages and Travels. London, 1703.
Pardal, R. Medicina Aborigen Americana. Buenos Aires, 1937.
Polo de Ondegardo, J. Informaciones, acerca de la Religión y Gobierno de las Incas. In Urteaga, H. H. Colección de Libros y Documentos referentes a la Historia del Perú (Lima) 3: 29–30, 1916 ed.
Poma de Ayala, F. G. "Nueva Coronica y Buen Gobierno." Trav. et Mém. l'Inst. d'Ethnol. Paris 23: 71, 1936 ed.
Reis, S. von. The genus *Anadenanthera:* a taxonomic and ethnobotanical study, Part II. Unpublished Ph.D. thesis ms., Radcliffe College, 1961.
Reis, S. von. "Herbaria: sources of medicinal folklore." Economic Botany 16, 4: 283–287, 1962.
Reis Altschul, S. von. "A taxonomic study of the genus *Anadenanthera.*" Contr. Gray Herb., 193: 3–65, 1964.
Safford, W. E. "Ethnobotany—Identity of Cohoba." Jour. Wash. Acad. Sci. 6: 547–562, 1916.
Saint-Cricq, L. (Marcoy, P.) A Journey across South America. I–IV. London, 1873–34 ed.
Santa Cruz Pachacuti, J. de. "Historia de los Incas y Relación de su Gobierno." In Urteaga, H. H. Colección de Libros y Documentos referentes a la Historia del Perú (Lima) 2, 9: 180, 1927 ed.
Sótelo Narvaez, P. "Relación de las Provincias Tucumán. In Freyre, J. El Tucumán Colonial 1: 97–98. Buenos Aires, 1915 ed.
Steward, J. H., Editor. Handbook of South American Indians, I–II. U.S. Govt. Print. Off., 1946.
Uhle, M. "A snuffing-tube from Tiahuanaco." Bull. Free Mus. Sci. Art 1: 158–177, 1898.
Vargas, C. Personal communication, Nov. 10, 1966.
Vásquez de Espinosa, A. "Compendium and Description of the West Indies." Smith. Misc. Coll. 102: 1–862, 1942 ed.
Velasco, J. de. Histoire du Royaume de Quito I: 164. Paris, 1840 ed.
Vélez-López, L. "El clíster en el antiguo Perú." Proc. Intern. Congr. Am. 23: 296–297, 1930.
Yacovleff, E. & Herrera, F. L. "El mundo vegetal de los antiguos peruanos." Rev. Mus. Nac. 4: 31–102, 1935.

# Epéna, the Intoxicating Snuff Powder of the Waika Indians and the Tucano Medicine Man, Agostino [1]

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The WAIKA Indians belong to an isolated group of natives called YANOAMA or YANONAMI. They live in the triangle formed by the Rio Branco in the southeast, the Uraricuera and Upper Orinoco Rivers in the north and the Rio Negro in the southwest. This territory lies on both sides of the boundary between Brazil and Venezuela.

During the last ten years, my wife and I made six expeditions to several WAIKA tribes in the region of the Upper Rio Negro, that is the southwestern part of that habitat, situated in the Brazilian Territory near the Venezuelan boundary. We found these tribes

(1) near the TUCANO IGARAPÉ, one of the headwaters of the Cauaborí River,

(2) on the Maturacá Channel, in the south of the Fall of HUÁ,

(3) on the Marauiá River, near the Igarapé IRAPIRAPÍ and

(4) on the Upper Maiá River, a branch of the Cauaborí River.

These Indians are nomads. We had a lot of difficulties in finding them and their primitive villages, called "SHABONO". They are always rather distant from the rivers, and we had to march hours and hours through the thick jungle to reach them.

Without the assistance and the experience of a Catholic priest—the only white man who had made contact with the WAIKA Indians before—our expeditions scarcely would have been successful.

The name WAIKA means KILLER—a nice, gentle sort of name. Undoubtedly, the group is one of the most primitive in South America. They have never found out how to make a boat or a raft. As nomads, these Indians make pots; they do not know anything about alcoholic drinks, or mandioc, the most important vegetable of the southern Hemisphere besides corn.

In a region where the rivers provide the most important traffic routes, they have never found out how to make a boat or a raft, As nomads, these Indians wander about the jungle. They live in primitive, wall-less, palm-thatched huts only as long as the food lasts in the neighborhood. When they eat up all the food around, they go to another village with huts just as primitive. They are a restless people that live off the land. And they live in a period that for us is prehistoric.

[1] The presentation of this paper was given in conjunction with the showing of an excellent, informative film. The photographs in this paper come from this film. (Editor)

They have never learned anything from their more advanced neighbors, the ARUAK group, represented by the TUCANO and BANIVA tribes.

The existence of these WAIKA Indians has been known for more than a hundred years. However, explorers of the region—Humboldt, and at the beginning of our century, Koch-Grünberg and Hamilton Rice—gave only brief reports about the WAIKAS. They had only occasional meetings with a few Indians from this group. These quick meetings did not give any basis for more than superficial notes.

In general, the explorers knew about the WAIKAS from the stories of other Indians, who described the Indians as terrible enemies, who used their poisoned arrows to keep out trespassers.

In the Brazilian territory, the WAIKAS made their first mark in modern history in 1929, when they attacked the settlements of rubber-tappers in the area between the Imeri Range and the Upper Rio Negro—along the Demití, Cauaborí, Marauiá and Padauirí Rivers. The Indians attacked suddenly, killed the men and carried off the women and children. The survivors fled to the Rio Negro. For 25 years, until 1954, everybody kept away from the area for fear of the Indians. In 1954, a Catholic priest of the Salesian mission in Tapuruquara, Rev. Antonio Goes, entered the territory, went up the Cauaborí River by boat and made the first peaceable contact with a tribe of the WAIKAS.

We met the priest in 1955 when we went through Tapuruquara on an expedition to the Colombian frontier. One year later, in 1956, we went with him to the WAIKA village situated near the headwaters of the Cauaborí River, a few miles from the Venezuelan boundary.

It was the priest's third visit to the tribe, where we found about 200 Indians in their original, primitive state. They never had any previous contact with civilized people other than the priest and then, ourselves.

In two later visits, we were able to observe and to film their daily village life, but we saw nothing of the snuff. We saw them dancing under the influence of the EPÉNA, but we were not able to see the snuff prepared. When we asked, they told us that the ingredients did not grow nearby.

Our relations improved with the repeated visits. On our fourth trip in 1960, we were received like old friends. We were shown the ingredients. We saw that they were neither seeds of PIPTADENIA PEREGRINA nor of any other tree. They turned out to be two kinds of bark and the leaves of a small plant. For the first time, we were able to get some of the snuff by exchanging gifts. It was the same powder that I sent to Professor Holmstedt, who analysed it. He found tryptamine derivatives to be the active components. In 1965, finally, we had a chance to film the snuff-making process.

## The Preparation of the Epéna Snuff-Powder

We could observe and film the whole process of the EPÉNA preparation on the Upper Marauiá River in the village of the KARAUETARI tribe. First we looked, in the company of two Indians, for a tree of the species

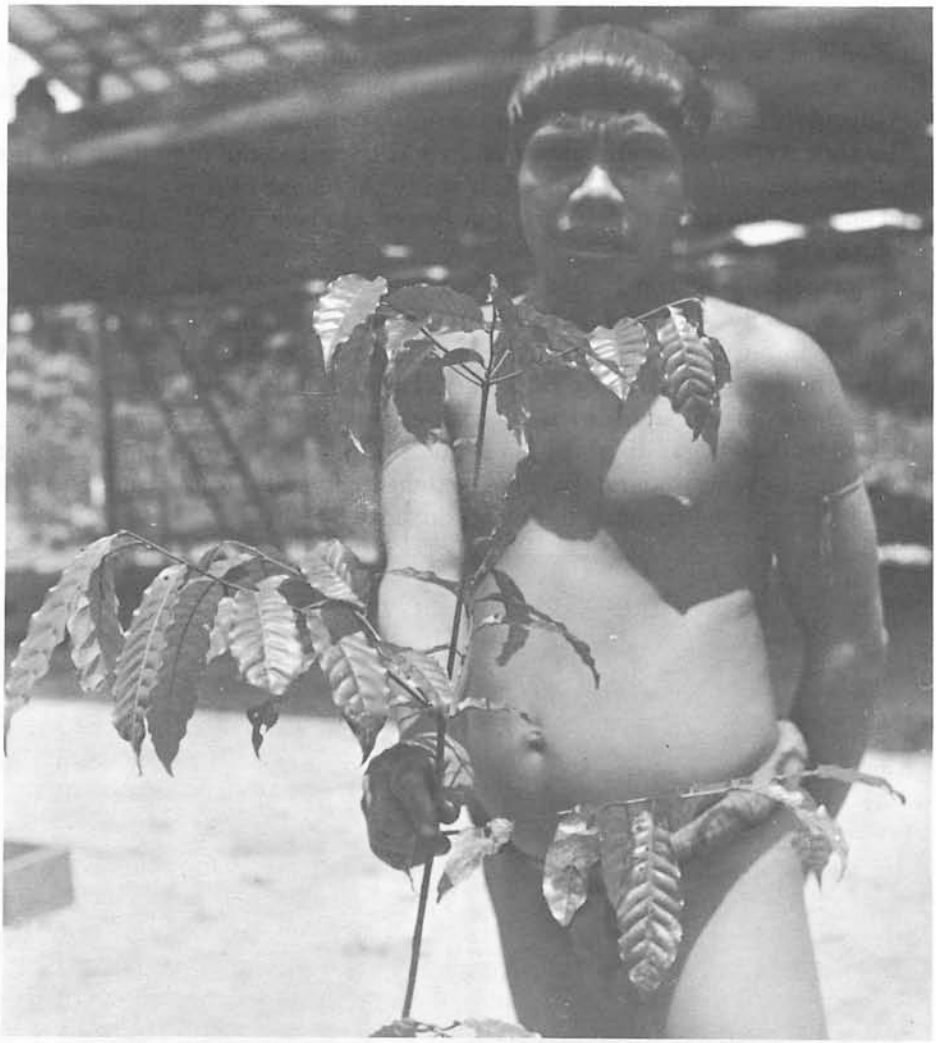

FIG. 1.—A sapling of "EPÉNA."

VIROLA CALLOPHYLLOIDEA, Markgraf, called by the Indians EPÉNA.

We had started in the early morning because the Indians said that the bark has to be stripped in the early hours of the day for the snuff powder to be good. The EPÉNA trees did not exist in any quantity. We marched three days through the jungle to find a group of them.

When the bark is stripped it appears white on its inner-side, but only a few seconds later a red brownish resin like liquid begins to exude in drops. The Indians told us that this "bleeding" is more intensive before the heat of the tropical sun begins to penetrate the forest.

The inner-side of the bark consists in a soft fibre-like layer that the Indians scrape off with a knife. These scrapings—moistened by the red brownish liquid—are collected on a palm-leaf and carried to the village for drying.

The drying process begins very slowly. The scrapings are fastened on a twisted disk which will be put approximately four feet above a slow fire, and there remain till the next morning. Then comes the second phase of the drying, more intensive, directly over the fire.

In this state the scrapings are stored till the second ingredient of the snuff-powder, called AMA ASITA, is ready. AMA ASITA is a tall tree that was not possible to classify as yet. But it seems to be a TRICHILIA species. Also, this tree seems to be scarce.

Before stripping the Indians looked for a specimen with smooth bark. They took only strips of bark whose outside was entirely perfect. This outside is important. It is the only part used. It was separated from the inner side of the bark immediately after the stripping and carried to the village. There these outside strips of the bark were cut in pieces and put in a fire. As soon as they began to glow, the Indians took them out of the fire and let them burn to ashes separately. They watched carefully, to see that no piece of any other wood or bark might be mixed with them.

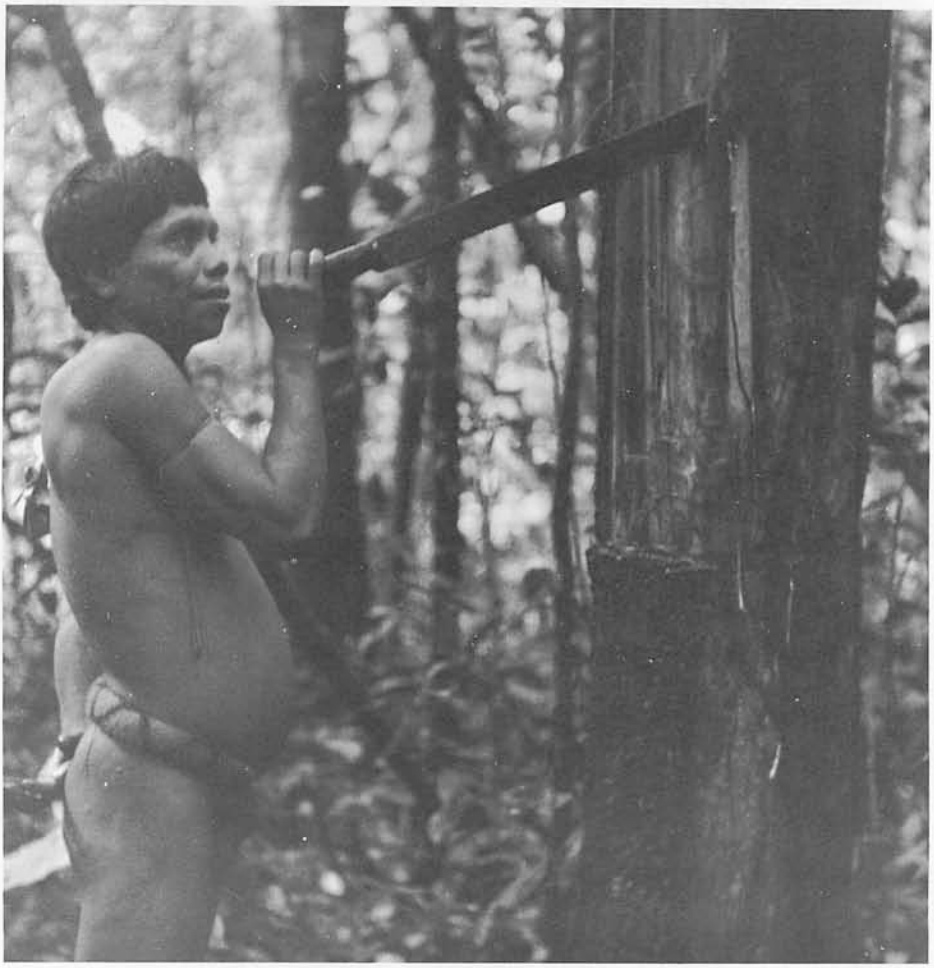

FIG. 2.—Stripping of the "EPÉNA" bark.

FIG. 3.—Only a few seconds after the stripping the red-brownish liquid begins to exude in drops and tinges the clearsighted wood of the trunk and the inner side of the bark.

These ashes of the AMA ASITA-bark are called by the WAIKA-Indians, "YUPU USHI".

While the bark was burning separately, our Indian began to rub down the dried EPÉNA scrapings with his hands. He did it sitting on the ground and pressing his knees against his hands.

After reducing the EPÉNA scrapings to a crumbled dust, the Indian roasted it for a short time over the fire. Then he mixed it with the ashes of AMA ASITA. The proportion of the mixture was 50 : 50. As it is measured by sight, the snuff-powders of the different manufacturers never have the same tone of colour.

The snuff was not yet sufficiently uniform and refined. It contained little spelts and crumbs that had to be eliminated. This was done in a little basket such as each WAIKA household owned. The Indian beat the basket gently, and the resulting dust was the final snuff-powder. It was kept in a bamboo-tube, the usual storage box of the WAIKAS. Four or five of these tubes are stuck between the palm-tree-leaves of each hut. The smaller tubes are usually used for snuff-powder, and the bigger ones for keeping feathers, arrow-heads and pigment for painting the body.

FIG. 4.—The inner side of the bark consists in a soft fibre-like layer that the Indians scrape off with a knife.

FIG. 5.—A branch of AMA ASITA.

FIG. 6.—The AMA ASITA bark is stripped. Note that the wood of the trunk remains clear-sighted.

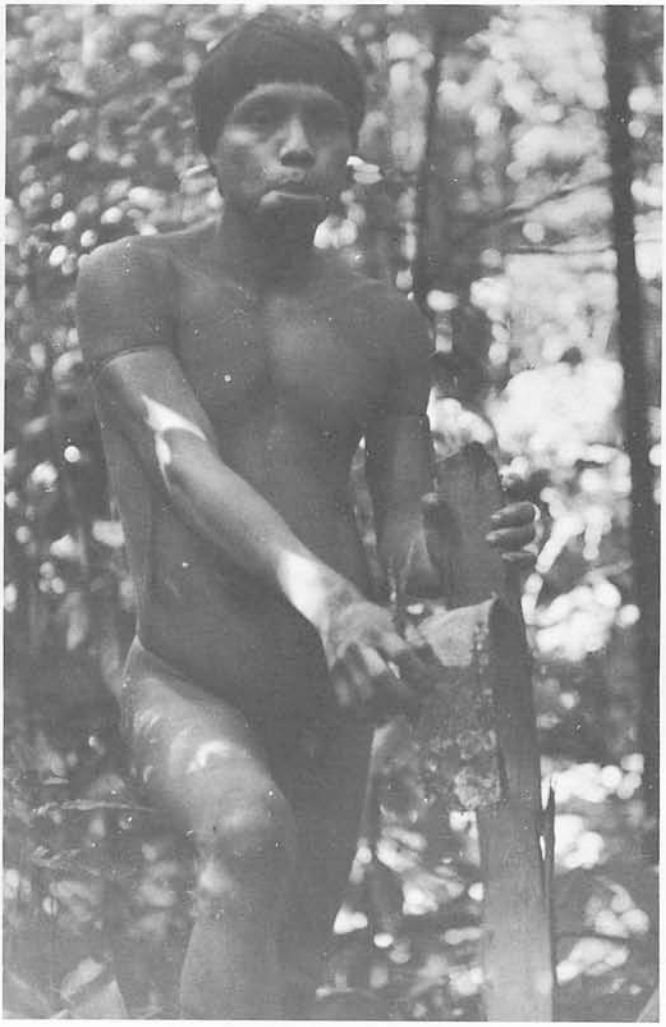

FIG. 7.—The outside of the bark is separated from its inner side.

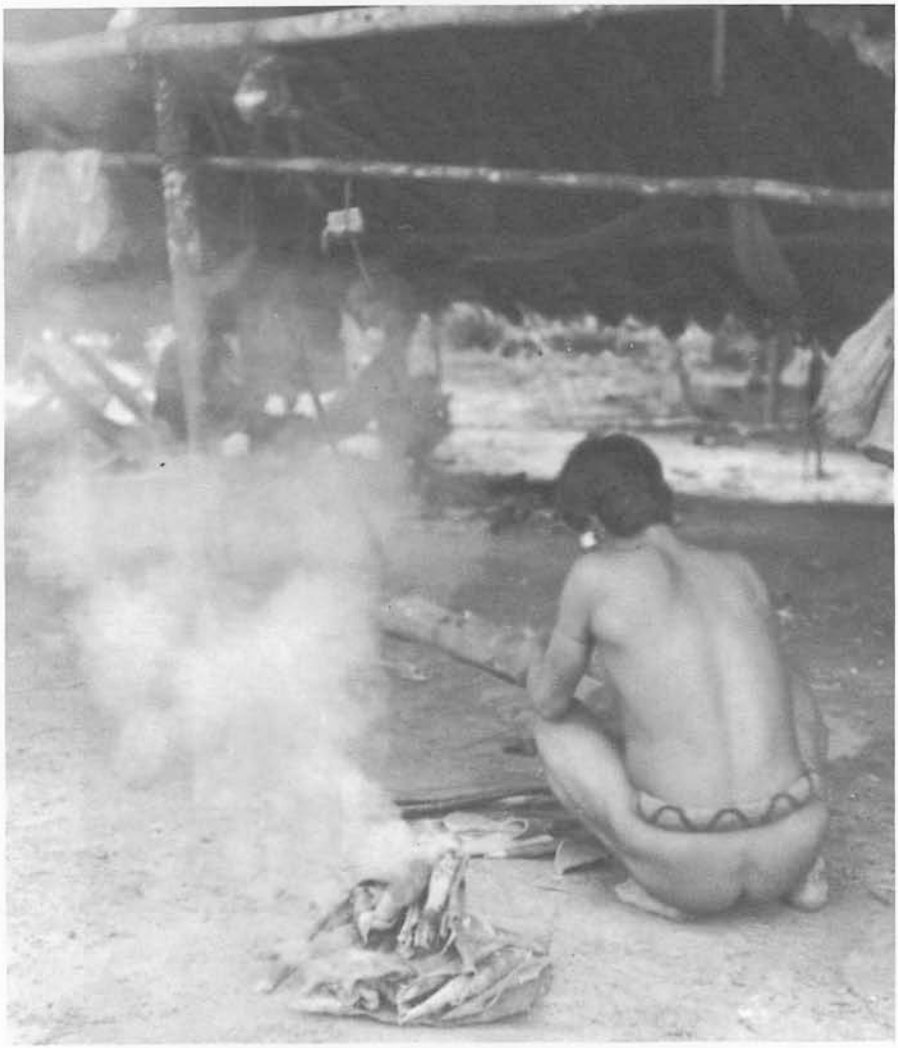

FIG. 8.—THE AMA ASITA bark burns to ashes separately.

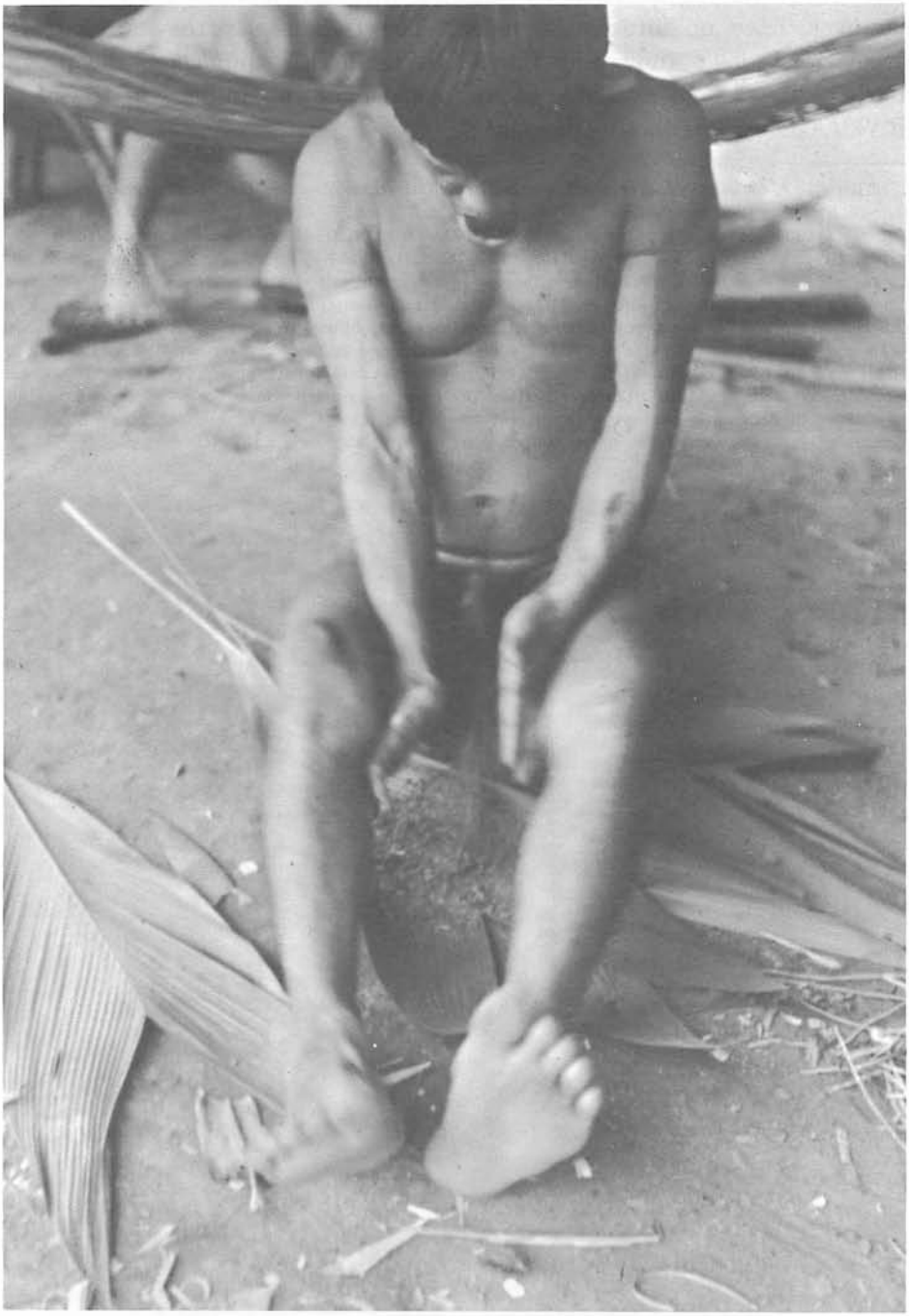

FIG. 9.—The dried "EPÉNA" scrapings are rubbed down with the hands.

In another WAIKA-village, near the Maturacá-channel, we saw that a third ingredient was added: the little leaves of a HERBACEUS-plant, called MASHI HIRI, like the EPÉNA-scrapings dried and powdered. These leaves, however, have no intoxicating effect. The Indians say they are merely aromatic. I don't know why the KARAUETARY didn't use the plant. Perhaps it was not available at the moment, or the Indians in the MARAUIÁ-River like another flavour.[1]

[1] There is also used another snuff powder which contains, besides the above mentioned three ingredients, the other vegetables:

(1) The leaves of a plant called POSCHI-HAVE-MOSCHI-Hena ("hena" means "leaf")

(2) The leaves of another vegetable called AI-AMO-Hena.

In the villages we visited, the Indians either could not or did not want to show us these two plants. They always said that they only grew in the higher region of the mountains, and not nearby. For this reason the powder compound of the five ingredients was not on hand.

In my opinion it is the same compound whose snuffing we saw in our first expedition, and whose effect was discribed as noxious for health. (People of the rain forest, page 167.) I cannot at the moment say more about this powder. Neither the missionary with whom I am corresponding and who lives in continued contact with several tribes, nor myself, saw in our other expeditions a similar effect again. And in no other visited tribe were we able to get this powder.

FIG. 10.—The Indian sifts the "EPÉNA" in order to eliminate spelts and crumbs.

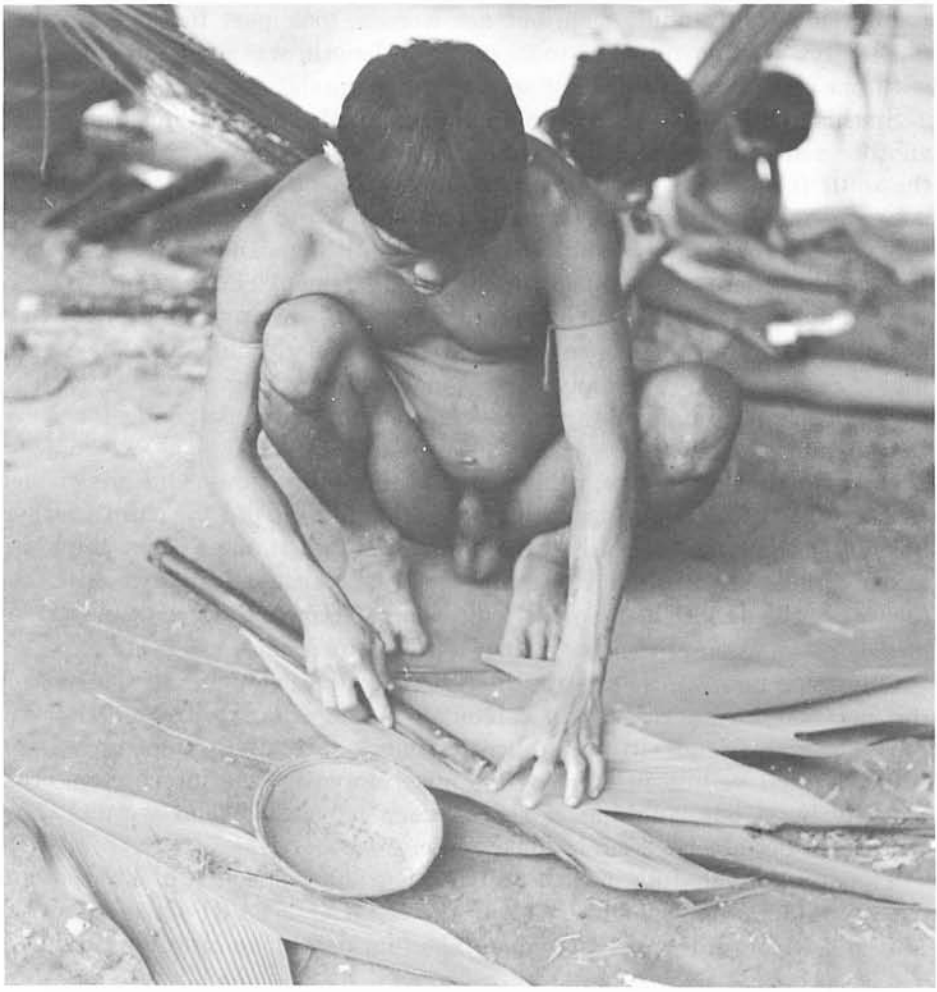

FIG. 11.—The final snuff powder is stored in a bamboo tube.

## Some Remarks on the Use of Epéna

We watched the use of EPÉNA in four WAIKA-villages: (1) near the Upper Cauaboŕi River; (2) near the Upper Maiá River; (3) near the Upper Marauiá River, and (4) near the Maturacá Channel.

Firstly: The snuff was never inhaled in the morning. At this time, we saw some of the corresponding preparations, such as painting the face and the upper part of the body. Another Indian helped to paint the back and legs. The feather ornament is tied on the upper arm. All in all a certain festive preparation is part of the ceremony.

Secondly, The snuff-Inhaling ceremony generally began in the early afternoon; rarely in the evening.

Thirdly: Once, we saw two Indians blow snuff into each other's noses. Generally, only one person inhaled the EPÉNA.

Fourthly: Only adult men, but not women, took part in the ceremony.

Fifthly: The blowpipe, 23 to 28 inches in length, was used for inhalation with one exception. We did not see any other inhalation instrument.

Sixthly: Only once did we see an Indian inhale snuff without the aid of another man, and without instrument. (See also footnote Nr. 4). He poured the snuff from the bamboo tube into his open hand, lifted his hand to his nose and inhaled the powder simply and neatly.

Seventhly: When we became able to distinguish one Indian from another, we saw that there is no system for the snuff ceremony. For example: There were Indians who took EPÉNA powder every day at any time in the afternoon; there were others who practiced the ceremony only once in a fortnight. Seldom did we see any formal motive for taking the snuff, such as curing a sick person, invoking success in the hunt or thanksgiving for a successful hunt.

Only for the first motive, we saw snuff taking a few times. One or two men took snuff to bring about the curing of a sick child. So did the child's father, but not at the same time. I had the impression that in most cases, snuff was taken without any profound meaning—such as treating the ill, exorcism, contact with the HÄKULA spirits, cult. There seemed to be only a sort of swagger—an attempt to show "What a great guy I am!"

Otherwise how can we explain the fact that a great number of the Indians did not take any notice of the ceremony in the village square. Or that a dancer's girl friend sitting in her hammock, proudly watched the man stamping and yelling in front of the hut? Moreover, the interpreters occasionally burst out laughing at the dancer's movements and words. These words did not always seem to make sense.

The dose for inhaling in each nostril was a coffee-spoon full. The Indians usually take two doses. Only once, in the KARAUETARI-village near the Marauiá River, did we see an Indian take four doses, one after another.

## Administration

The inhalation was practiced in general in the following manner: (with one exception observed in the KAUARETARI-village): At first the snuff power of one or two bamboo tubes was poured on a little board or plate, and the little crumbs—caused by the high humidity of the air—were carefully pinched between the fingers.

Then the two Indians, the carefully painted and adorned one as well as the "blower" cowered under the roof of a hut, one opposite the other. The "blower" filled a dose of powder with his fingers in the blowpipe, which the other Indian kept on his right nostril. With a forceful blow the powder entered the nose. The receiver immediately let fall the blow-pipe and held the back of his head with both hands.

Our interpreter, a portuguese speaking Indian, explained that he would feel in this moment a violent headache. Not seldom, the Indian curved himself, probably because of this headache. Saliva ran out his mouth and he vomited.

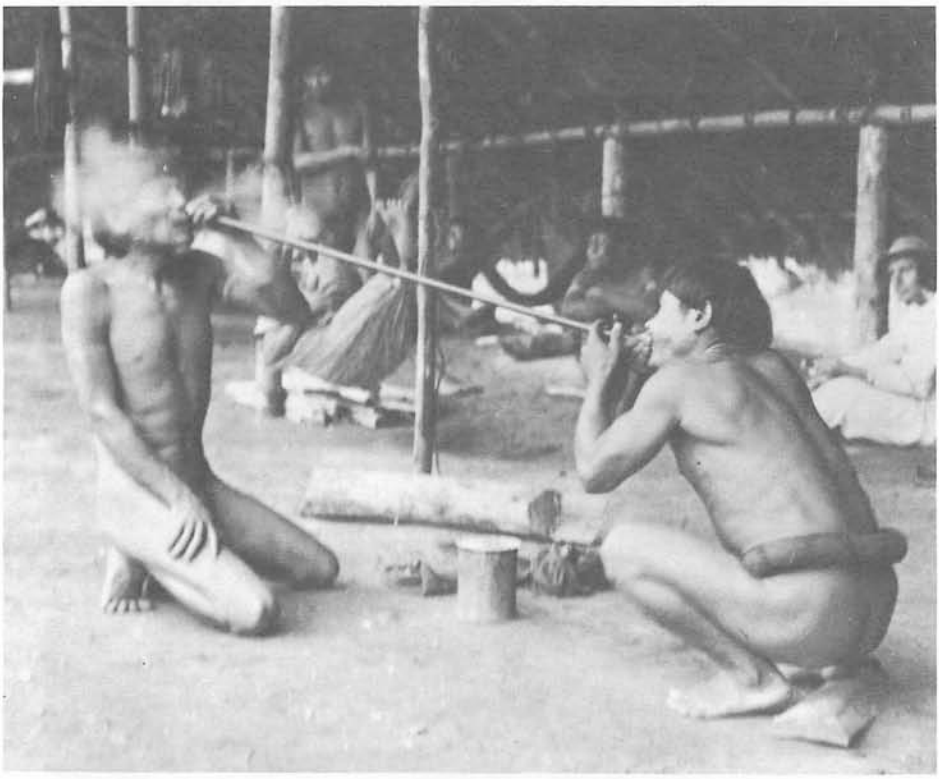

FIG. 12.—With a forceful blow the powder entered the nose.

After about 3 or 4 minutes it seemed that the first effect passed, and he took again the blow-pipe, which the other Indian, the "blower", had again filled up. The Indian now put the blow-pipe on the left nostril and got the second dose. The immediate consequences like headache, salivation and vomiting were repeated, however, not always so strongly.

## Effect

After inhaling the two doses of EPÉNA, the usual quantity of snuff powder at the beginning of the ceremony, the Indian continued for about two or three minutes in his cowered position. Then he stood up and walked swaying like a drunkard. On his way his walk became faster and steadier. His stare became fixed and he experienced a violent perspiration. In a few minutes his face and body were completely wet.

Then his steps changed into a stamping that generally was adapted to a certain rhythm: three or four steps forward, one step on the same place. This "dance" the man accompanied with a recitative, monotonous singing, which was relieved about every five to eight minutes by a terrible yell. During



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FIG. 13.—Saliva ran out of his mouth and he vomited.

this yelling the man generally stopped his "dance," and turned himself with high lifted or spread arms to the mountain-range that elevates itself, steep in the sky, a few miles to the north of the villages.[2, 3]

After about half an hour of stamping and singing and yelling an interval took place in most of the observed cases. The Indian stood some minutes with straddled legs, the upper part of his body bowed forward, nearly the position which we took as children for playing leap frog. After this interval, either the singing and stamping continued or the Indian—still singing and

[2] In some of the cases observed by us, this yelling toward the mountain range certainly was a threat against another tribe, living in hostility against our Indians. Some weeks ago they had killed two members of that tribe and expected now the requital attack.

I see in these yellings against the mountains where the other tribe was living, no invitation to the HÄKULA spirits for help, but translate them more in this way:

"Come on over when you get up the courage!—We will make hash of you!" Conclusion: Nothing but boasting, in consequence of the macropsia provoked by the EPÉNA. Certainly, this makes the dancer think he is physically superior.

[3] In the cases when they had inhaled EPÉNA to cure a sick child, the dance was stopped in front of the child's hammock, and the Indian accompanied his yells with the vehement movements of his arms, or the softly passing of his hands over the child's body. So, he tried to take out the illness of the patient's body.

stamping—fetched from his hut some arrows, and continued dancing with these.[4]

The snuff powder EPÉNA provokes a strong intoxication but by no means an entire state of trance. Otherwise the man would not be able during his "dance" to find with sure hand the arrows in the hut or—as it had happened with me when I had gone with the camera in spite of warning—would have

[4] The Indian of the KARAUETARI tribe who inhaled the powder without the assistance of another man, snuffing the EPENA by himself from his open hand, was the only one whose "dances" differed from the general manner:

(1) The phases of his "dance" lasted not more than 15 minutes, (2) In the intervals of his "dance" he inhaled some further doses of EPÉNA. He was the only one we saw snuffing *during* the intoxicating state and not only *before* it.

It is possible that in his case the initial doses, inhaled without the powerful blow of another man, had not provoked the common intoxicating effect. So he was forced to snuff again.

FIG. 14.—The "dance" under the effect of "EPÉNA."

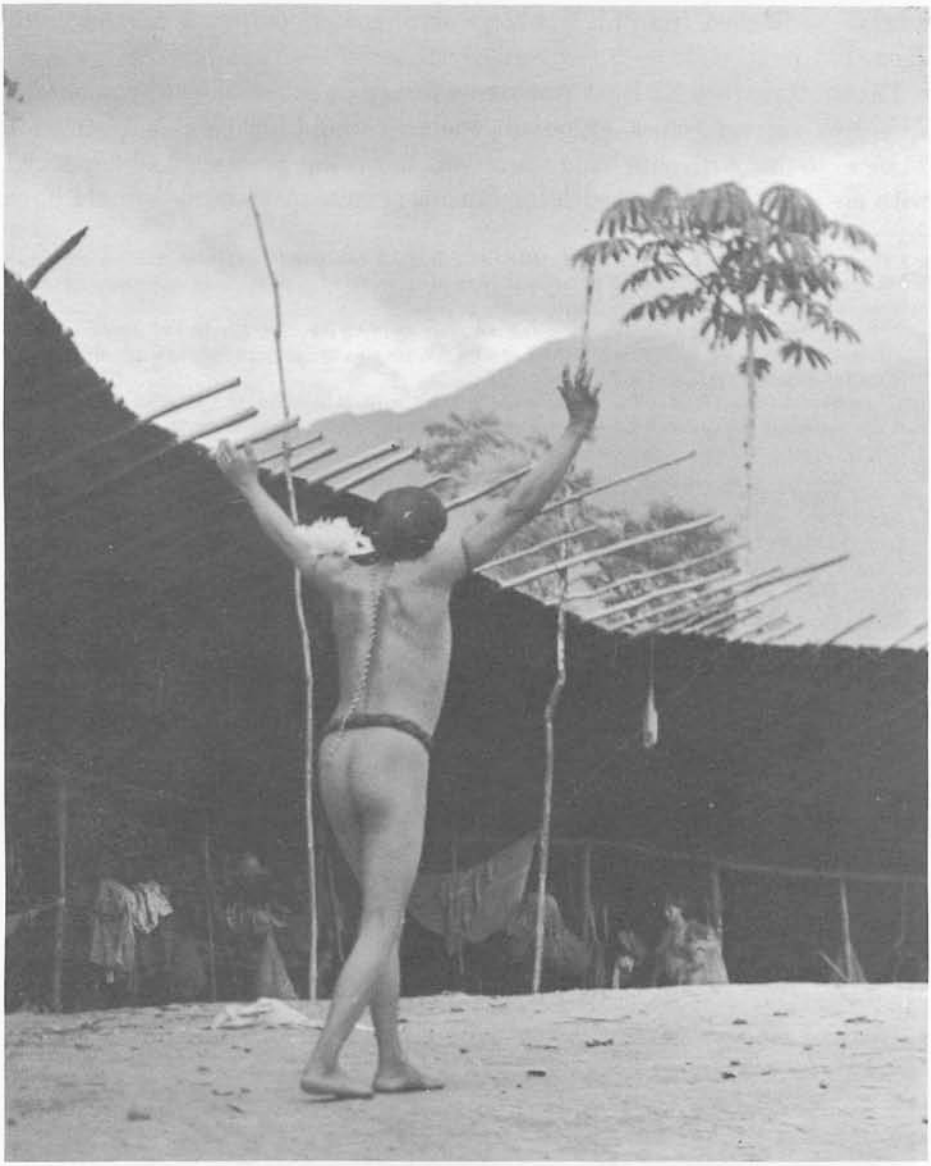

FIG. 15.— . . . turned himself with high lifted arms to the mountain-range.

been able to threaten to throw a poisoned arrow at me, if I had not disappeared. My interpreter, who had understood these words—in contrast to me—had hastened to fetch me back to the hut and translated the threat.

The "dances", the movements of the arms in the normal intoxication state—as such it could be said—were very different from those seen on our first expedition, in the few minutes when the two young men were dancing on the square under the effect of the other snuff powder, mentioned in footnote 1. These Indians doubtless had lost consciousness.

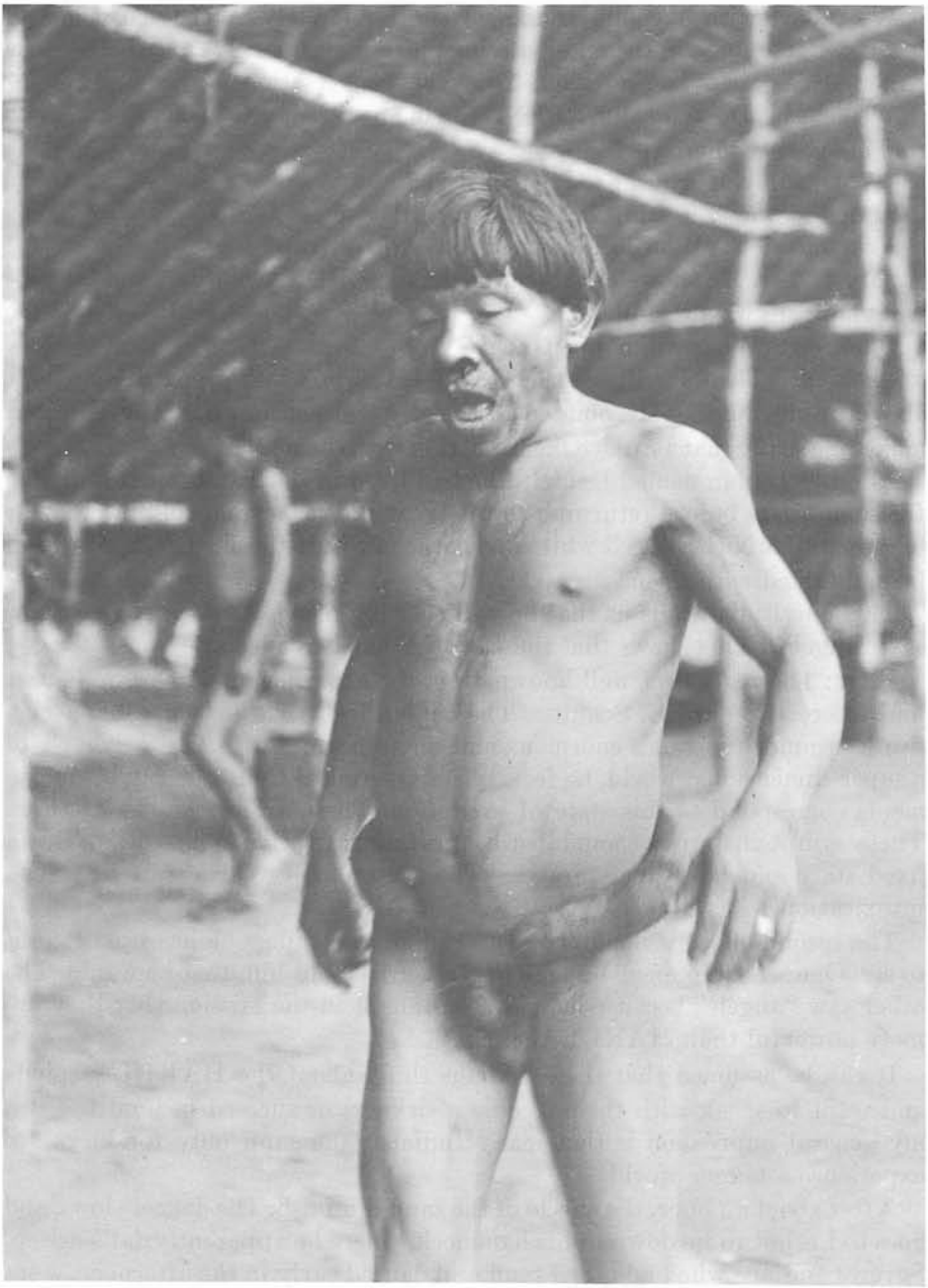

FIG. 16.—Typical face expression during the intoxication.

We talked with a young Indian of the KAUARETARI-tribe who had learned Portuguese in the mission-school in Tapuruquara. We gathered some explanations about the ceremony from this conversation:

We asked, "Do you snuff EPÉNA?" He answered, "No, I am not allowed to. I am not grown up yet!"

"When will you grow up?", we then asked.

"I don't know", he said, "but I think it will be soon."

Next question: "Who decides when you are grown up?"

"My father. He shows me how to make the EPÉNA powder, and tells me what happens when I sniff it."

Question: "What will happen then?"

Answer: "Then I will see the HÄKULA, who are big men living there above in big huts."—He pointed to the sky and continued: "The EPÉNA makes me so big that I can see them and talk with them!"

Another Indian named Daniel, who had lived in the Tapuruquara-mission for some years before returning to the tribe and marrying, told me that he had seen " A N G E L S " while under the effect of the EPÉNA. And that he had talked with them!

This one Indian tells us that he will see "big men". Another says that he saw "angels". This shows that the EPÉNA has two effects:

First: The real effect well-known from the experiments of Doctor Becher and Doctor Richard E. Schultes. The Indian feels that he is a giant; everything around him takes enormous and magnificant forms. In the midst of a super-dimensional world, he feels like a superman! Consequently his movements correspond to this state of excitation. These are braggart's gestures. These symptoms are accompanied by profuse salivation, a bad headache, a fixed stare and heavy perspiration. The symptoms reveal a state of strong intoxication.

The second effect is imagined. The Indian sees things he has been taught to see. One sees "big men" because his father has told him that he would. The other saw "angels" because he had been taught in the mission that they are more powerful than HÄKULA-spirits!

It can be assumed that these Indians think about the HÄKULA spirits and want to speak with them to cure a sickness or succeed in hunting. But my general impression is that many Indians take snuff only for kicks—to experience a bigger world.

After about an hour, the effects of the snuff diminish. The dancer slows, and goes to his hut to lie down in his hammock, where he apparently falls asleep. Several Indians who had taken snuff and danced early in the afternoon, were seen in the evening at about eight o'clock seated around the fire as if nothing had happened. The duration of the snuff effects is comparatively short. One of our interpreters said to me that they don't like to take snuff in the evening because they can't sleep afterward. We can conclude from this that perhaps the apparent sleep in the hammock after the dance is not really sleep but exhaustion, or the need to rest an aching head.

It is certain, however, that the violent headaches and nausea are caused by the way that the snuff is taken—blown into the nostrils—that the head-

ache is temporarily relieved by the drug. Otherwise, the Indian would not be able to behave so violently in the square. After about an hour, the exilarating, euphoric effect of the snuff backfires and turns into a hangover.

## The "Paricá" of the Tucano-Medicine Man Agostino

Most of the Indians who live in the village of Tapuruquara on the Upper Rio Negro are TUCANOS, who abandoned their old tribe territory on the PAPURÍ River. Agostino is the "Pagé", the medicine man, in this village, and he still uses "PARICÁ", a snuff that he prepared in our presence. He uses the same raw-material as the WAIKA Indians—the inner layer of the bark from VIROLA CALOPHYLLOIDEA, Markgraf, but he prepared the powder in a very different manner.

With his knife he scraped off the inner layer of the bark moistened by the red-brown liquid. Then he threw these scrapings into a pot partly filled with water. In this water they were thoroughly kneaded, and squeezed so that the water turned muddy and took a reddish-brown colour. Then this muddy liquid was set to evaporate over a slow fire.

FIG. 17.—The reddish-brown liquid was set to evaporate over a slow fire.

"It should not boil very rapidly", explained Agostino. And, indeed, three hours passed before the quart of liquid had become a hard, dark crust on the bottom of the bowl. From time to time a dirty foam rose to the surface, and the "Pagé" Agostino removed it with a little branch. Also, other impurities like fibres of the bark rose up with the bubbling and were eliminated in the same way. Finally nothing remained except a thick, dark brown syrup with a strong smell. Now, Agostino lowered the fire still more. The final drying was done very slowly, probably to prevent burning.

The residue was a hard crust that was scraped off with a knife. It was the concentrate of that red-brown liquid that had begun to exude from the inner side of the bark, as well as from the trunk of VIROLA CALOPHYLLOIDEA, Markgraf. The scraped residue was ground into a fine powder with a smooth stone.

With this process the "paricá" was ready as Agostino said. It was not mixed with ashes or other ingredients. He explained that he, the medicine man, is the only one allowed to inhale the snuff powder.

We didn't see the intoxicating effect, here, but it was confirmed by inhabitants of the village that it is very strong. Therefore Agostino can snuff his "PARICÁ" only twice a month at the most. He inhales the "PARICÁ", as he told us, before diagnosing the trouble with his patients. In the intoxicated state he stammers confused words which are interpreted by his brother. Later on he tries to cure the patient, using for the treatment the rattle "NASH SÃ" and the quartz crystal "MARIA PIRÍ".

FIG. 18.—Finally nothing remained except a thick, dark-brown syrup.

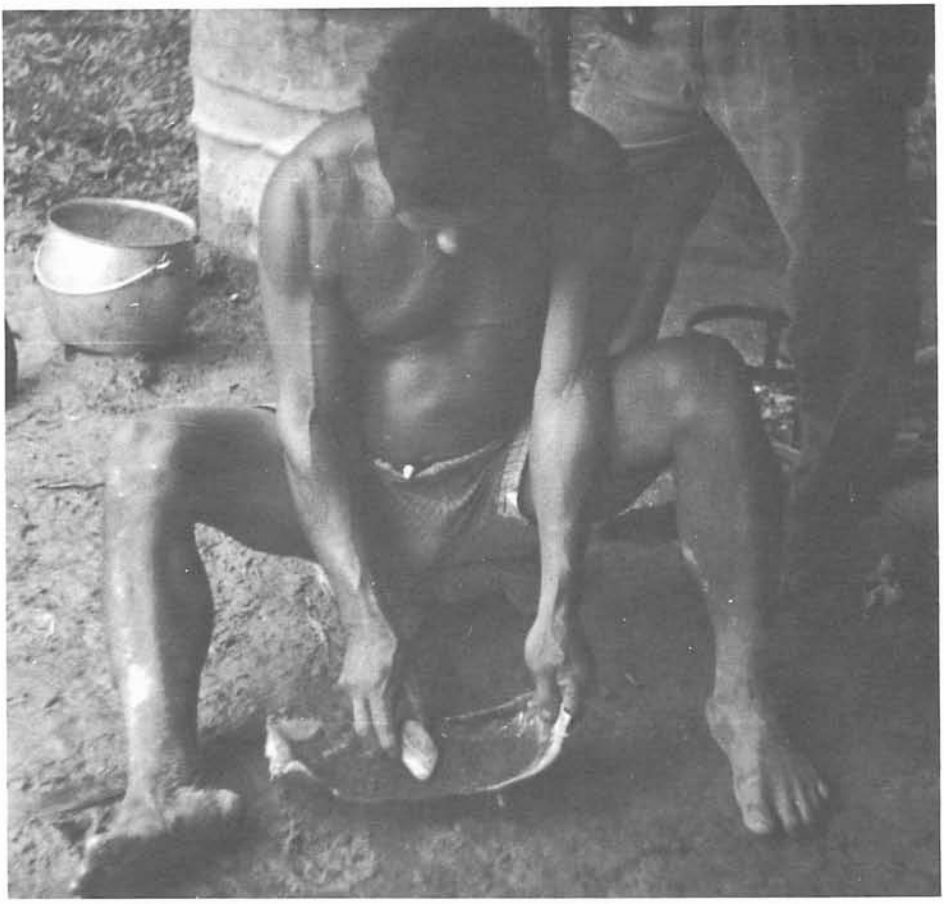

FIG. 19.—The residue was ground into a fine powder with a smooth stone.

## BIBLIOGRAPHY


BECHLER, H. "Die Surára and Pakidái, zwei Yanonámi-Stämme in Nordwestbrasilien." Hamburg, Cram, De Gruyter & Co. 1960, 133 pp.

HOLMSTEDT, B. "Tryptamine Derivatives in Epena, An Intoxicating Snuff used by some South American Indian Tribes." Arch. int. Pharmacodyn. 156: 2, p. 285–305. 1965

KOCH-GRÜNBERG, TH. *"Vom Roroima zum Orinoco, Erlebnisse einer Reise in Nord*-brasilien und Venezuela 1911–1913," Stgt. Band III (1923) 386 pp.

SCHULTES, R. E. "A new narcotic snuff from the Northwest Amazon." Bot. Museum Leaflets, Harvard Univ. 16 (1954), 297–316.

SCHULTES, R. E. "Ethnobotanik amerikanischer Halluzinogene," Planta Medica, 13. Jahrgang, Heft 2, Mai 1965, Hippokrates, Stgt.

SEITZ, G. J. People of the rain forest, Heinemann, London, 1962

WASSÉN, S. H. "The Use of Some Specific Kinds of South American Indian Snuff and Related Paraphernalia," Etnologiska Studier, vol. 28, Göteborg 1965

WASSÉN, S. H., and HOLMSTEDT, B. "The use of paricá, an ethnological and pharmacological review," Ethnos 28, 5–45, 1963

ZERRIES, O. "Medizinmannwesen und Geisterglauben der Waika-Indianer des Oberen Orinoco," Ethnologica 2, Köln, E. I. Bill (1960), 487–507.

ZERRIES, O. "Waika, Die kulturgeschichtliche Stellung der Waika-Indianer der Oberen Orinoco in Rahmen der Völkerkunde Südamerikas." 1964. Klaus Renner Verlag, München (Ergebnisse der Frobenius-Expedition 1954/55 nach Südost-Venezuela. Band I. Waika.)

# Chemical Constituents and Pharmacology of South American Snuffs*

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About ten years ago E. C. Horning and co-workers isolated from seeds of *Piptadenia peregrina*, a leguminous plant, indole alkaloids which were identified by means of paper chromatography, colour reactions, fluorescence and infrared spectra (Stromberg 1954, Fish, Johnson and Horning 1955). They found the seeds to contain dimethyltryptamine-*N*-oxide (DMT-*N*-oxide) and Bufotenine (5-OH-DMT) and its corresponding N-oxide. The seeds of *Piptadenia peregrina* is the most commonly known botanical source of snuffs made by South American Indian tribes, and is inhaled to produce visions and hallucinations. The interest of Horning and co-workers arose from the properties of the crude drug. As a result of these analyses synthetic dimethyltryptamine (DMT) has come to be used experimentally by psychiatrists, in order to produce shortlasting states of illusions and hallucinations (Szara et al. 1957, 1961, Böszörményi and Grunecker 1957).

Ethnological and botanical evidence in recent years demonstrates clearly that *Piptadenia peregrina* by no means is the main constituent of all snuffs used by South American Indians. In view of this it was felt necessary to make a general investigation of whatever material of this kind that could be collected. The first results of these studies are reported here. Modern techniques of analysis such as gas chromatography and the combination of gas chromatography and mass spectrometry (Ryhage 1964) offer possibilities for an accurate analysis even of very small amounts of material, such as can usually be obtained from museum specimens.

## Material and methods

*List of abbeviations used*

DMT =*N*,*N*-Dimethyltryptamine
MMT =*N*-Monomethyltryptamine
5-MeO-DMT=5-Methoxy-*N*,*N*-dimethyltryptamine
5-MeO-MMT=5-Methoxy-*N*-monomethyltryptamine
5-OH-DMT =5-Hydroxy-*N*,*N*-dimethyltryptamine (bufotenine)
GLC =Gas-liquid-chromatography
MS =Mass spectrometry

*Ethnological and botanical specimens*

Epéna snuff collected in 1965 at Rio Marauiá. Epéna snuff collected in 1965 at Rio Maturacá. Snuff prepared by Pagé Agostino collected in 1965 in Tapuruquara. All were obtained from Mr. Georg J. Seitz, Caixa Postal 2605, Rio de Janeiro.

Paricá obtained from Dr. Stig Rydén at the Ethnographical Museum in Stockholm.

*This investigation was supported by Grant MH–12007 from the National Institute of Mental Health, U.S. Public Health Service, Chevy Chase, Md.

The specimen was collected in 1955 by the late Gustav Bolinder among the Piaroa Indians (Orinoco region, Venezuela). Sample No. 56–7–282 Statens Etnografiska Museum, Stockholm.

Yopo snuff, obtained from Mr. Donald Overton, School of Tropical and Preventive Medicine, College of Medical Evangelists, Dept. of Biotoxicology, Loma Linda, Calif., collected in Colombia 1956. Sample No. P56–70–11.

Epéna snuff, obtained from Dr. H. Becher, Niedersächsisches Landesmuseum, Abteilung für Völkerkunde, Hannover, collected among the Surára Indians in 1956.

Seeds from *Piptadenia peregrina*, obtained from the Abbott Laboratories, collected in 1948 in San Juan, Puerto Rico, Sample No. (N–2003–C).

Seeds from *Piptadenia peregrina*, obtained from Dr. W. Haberland, Museum für Völkerkunde, Hamburg, collected by Dr. Franz Caspar among the Tupari Indians (Caspar 1953).

Bark from *Piptadenia peregrina*, obtained from Mr. Donald Overton, collected in Colombia 1956. Sample No. P56–70–7.

Bark from *Virola calophylla*, obtained from Mr. William A. Rodrigues, Manaus, Brazil, 1964.

*Material used in gas chromatography—mass spectrometry*

Gas Chrom P 100–120 mesh, Applied Science Lab., State College, Pa., U.S.A. F–60 (a methyl *p*-dichlorophenylsiloxane polymer, Dow Corning, Midland, Mich., U.S.A.). EGSS–Z ( = Z a copolymer from ethylene glycol, succinic acid and methyl phenyl siloxane monomers, Applied Science Lab.). SE–30 silicone, Applied Science Lab. PDEAS (phenyldiethanolamine succinate, Wilkins Instrument & Research, Walnut Creek, Cal., U.S.A.).

Dichlorodimethylsilane, Hopkins & Williams Ltd., Essex, England.

*Reference compounds and reagents*

5-Methoxy-N,N-dimethyltryptamine, 5-methoxy-N-monomethyltryptamine, N-monomethyltryptamine bioxalate were kindly placed at our disposal by Dr. A. Hofmann, Sandoz A.G., Basle. Harmine and tetrahydroharmine hydrochloride were kindly placed at our disposal by Dr. K. Bernauer, F. Hoffmann-La Roche & Co., A.G. Basle. *N,N*-Dimethyltryptamine (Aldrich Chemical Co., Inc., Milwaukee, Wis., U.S.A.). Harmine (Fluka A.G. Buchs SG, Switzerland). Bufotenine was prepared from *Piptadenia peregrina* by E. C. Horning, Baylor University, College of Medicine, Texas Medical Center, Houston, Texas, U.S.A. All other reagents used were of "reagent grade" and from different manufacturers.

*Isolation of organic bases*

5–20 g of the powdered material was treated according to a procedure known to be satisfactory for phenolic amines in the indole series (Fish, Johnson and Horning 1955). The isolation procedure was followed in detail but the amounts of solvents were reduced with respect to the initial weight of the sample.

The steps of isolation procedure were followed by tests using Ehrlich's reagent. After drying with magnesium sulphate the final product was obtained upon removal of the solvent. The total alkaloids obtained were then dissolved either in methanol or in tetrahydrofurane.

*Gas chromatography (GLC)*

Gas chromatographic analysis was performed with an F & M Model 400 apparatus equipped with a hydrogen flame ionization detection system.

The column support, 100–120 mesh Gas Chrom P, was acid washed and silanized according to the method described by Horning et al. (1963). The coating was applied by the filtration technique (Horning, et al. 1959, 1963). The stationary phases used were (1) 6% F–60 and 2% EGSS–Z (2.25 m x 3.2 mm glass tube), (2) 5% SE–30 (4 m x 3.2 mm glass tube). The F–60–Z column was operated at 190° and the SE–30 column at 210°. The flash heater and detector cell were kept 30–40° above the column temperature. The flow rate of the carrier gas, nitrogen, was 60 ml/min. Samples were injected in methanol or tetrahydrofuran solution with a Hamilton syringe.

*Gas chromatography-mass spectrometry (GLC-MS)*

The principles of the technique have been described in detail by Ryhage (1964). The mass spectrometry work was carried out with LKB 9000 gas chromatograph-mass spectrometer including a fast scan system and the Ryhage "molecule separator." The ion source was 270°, the electron energy was 70 eV and the electron ionization current 60μA, respectively. The separations were made on systems consisting of 3% PDEAS at 190° or 5% SE-30 at 200°. The column consisted of a 2 m x 3.2 mm glass tube. Helium was used as the carrier gas. At the outlet of the column, the separated compounds were concentrated and continuously fed into the mass spectrometer. The mass spectrometer simultaneously serves as a gas chromatographic detector and for recording of mass spectra of the compound as they emerge from the column. The reference compounds were run through the column, and the mass spectra of the compounds recorded. The alkaloid fractions prepared as described above, were then run under identical conditions, and mass spectra were recorded from the gas chromatographic peaks having the same retention times as those of the reference compounds.

## Results

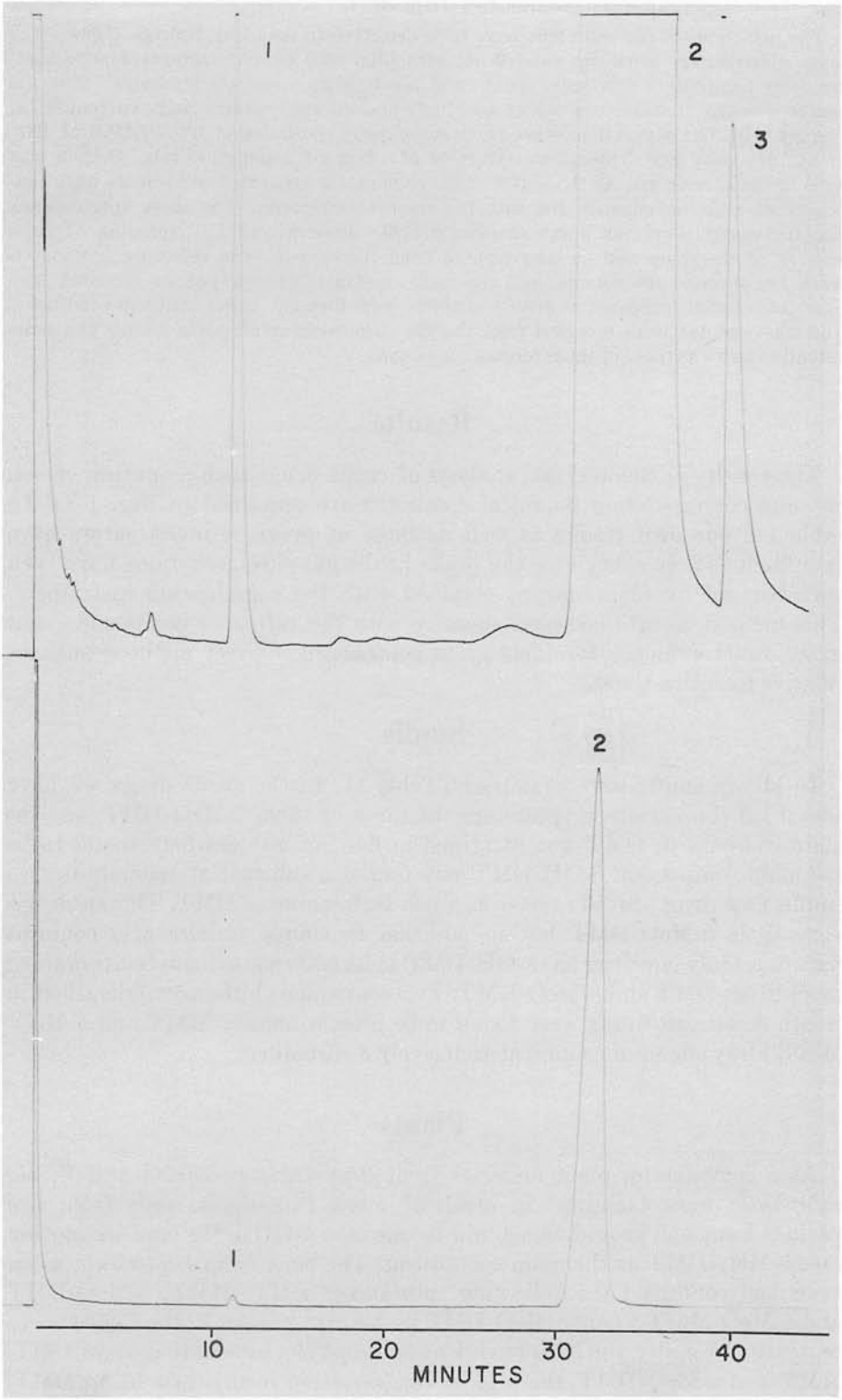
The results of the authors' analysis of crude drugs such as paricá, epéna, etc. and corresponding botanical specimens are contained in Fig. 1–14. In table 1–2 our own results as well as those of previous investigators have been included. In every case the peaks in the gas chromatograms have been corroborated by mass spectra obtained with the combination instrument. This method assures complete identity with the reference compounds, and gives direct evidence for identity in contrast to indirect methods such as relative retention times.

## Snuffs

In all six snuffs were examined (Table 1). In the crude drugs we have identified the various tryptamines. In three of them 5-MeO-DMT was the main component. DMT was identified in five but was nowhere found to be the main component. 5-OH-DMT was found in substantial amounts in two snuffs. One drug proved to have as much Bufotenine as DMT. This snuff has very little 5-MeO-DMT but in addition to simple indoles also contains harmine. Only one drug has 5-OH-DMT as its main constituent but contained in addition DMT and 5-MeO-DMT. Two compounds hitherto unidentified in South American snuffs were found to be present namely MMT and 5-MeO-MMT. Only one snuff contained exclusively β-carbolines.

## Plants

As a comparison, plant material from *Piptadenia peregrina* and *Virola calophylla* were examined in identical ways. Piptadenia seeds from two various locations proved to contain in one case 5-OH-DMT and in another case 5-MeO-DMT as the main constituent. The bark from *Piptadenia* when examined contained the following substances: DMT, MMT, 5-MeO-DMT and 5-MeO-MMT where 5-MeO-DMT by far was present in the highest concentration. Finally, the bark from *Virola calophylla* proved to contain DMT, MMT and 5-MeO-DMT, the highest concentration in this case being DMT.


1
2
3
2
1
10
20
30
40
MINUTES

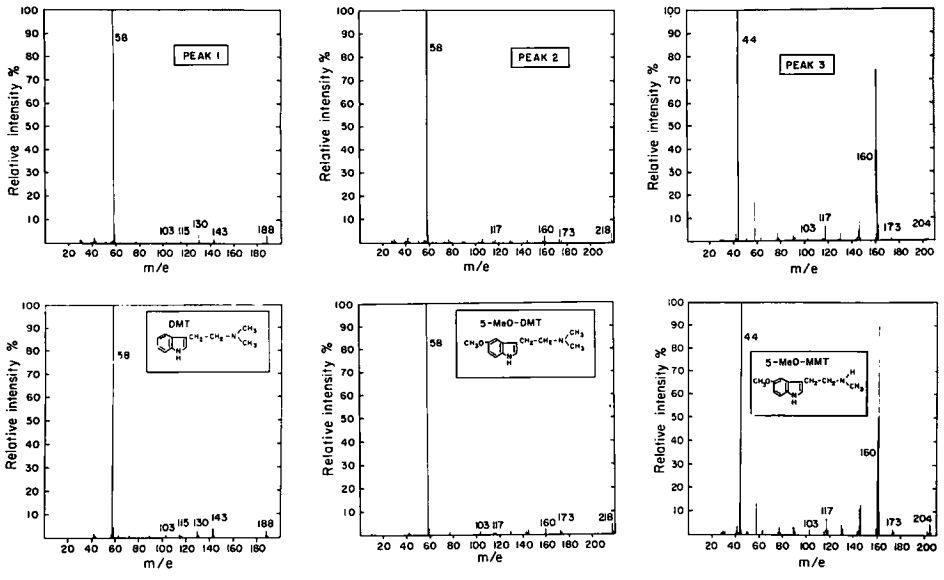



FIG. 2.—Mass spectrometric recording of compound in peak effluents from alkaloid fraction (Fig. 1) and reference compounds. Conditions: Column 2 m; i.d. 3.2 mm; 3% PDEAS; 100–120 mesh Gas Chrom P; temp. 190°.

FIG. 1.—Gas chromatogram of alkaloid fraction from South American snuff prepared by Pagé Agostino, obtained from Mr G. Seitz. Tucano Indians, Tapuruquara, 1965. GLC conditions: Column 2.25 mm; i.d. 3.2 mm; 6% F 60 and 2% EGSS—Z on 100–120 mesh Gas Chrom P; temp. 190°; flow 60 ml per min. Upper panel high magnification. Lower panel low magnification. Mass spectra recorded simultaneously from peak effluents of extract and model substances injected under similar conditions, see Fig. 2.

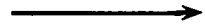


FIG. 3.—Gas chromatogram of alkaloid fraction of Epéna snuff obtained from Mr G. Seitz. Waica Indians, Rio Marauiá, 1965. GLC conditions: Same as for Fig. 1. Upper panel high magnification. Middle panel low magnification. Lower panel reference substance recorded simultaneously. Mass spectra from effluent from peak 2 and model substances injected under similar conditions, see Fig. 4. Mass spectrometric control of peak effluents: Peak 1 and DMT: Molecular ion at $m/_e$ 188; other peaks at $m/_e$ 58 (base peak), 103, 115, 130, 143. Peak 3 and 5-MeO-DMT: Molecular ion at $m/_e$ 218; other peaks at $m/_e$ 58 (base peak), 103, 117, 160, 173.

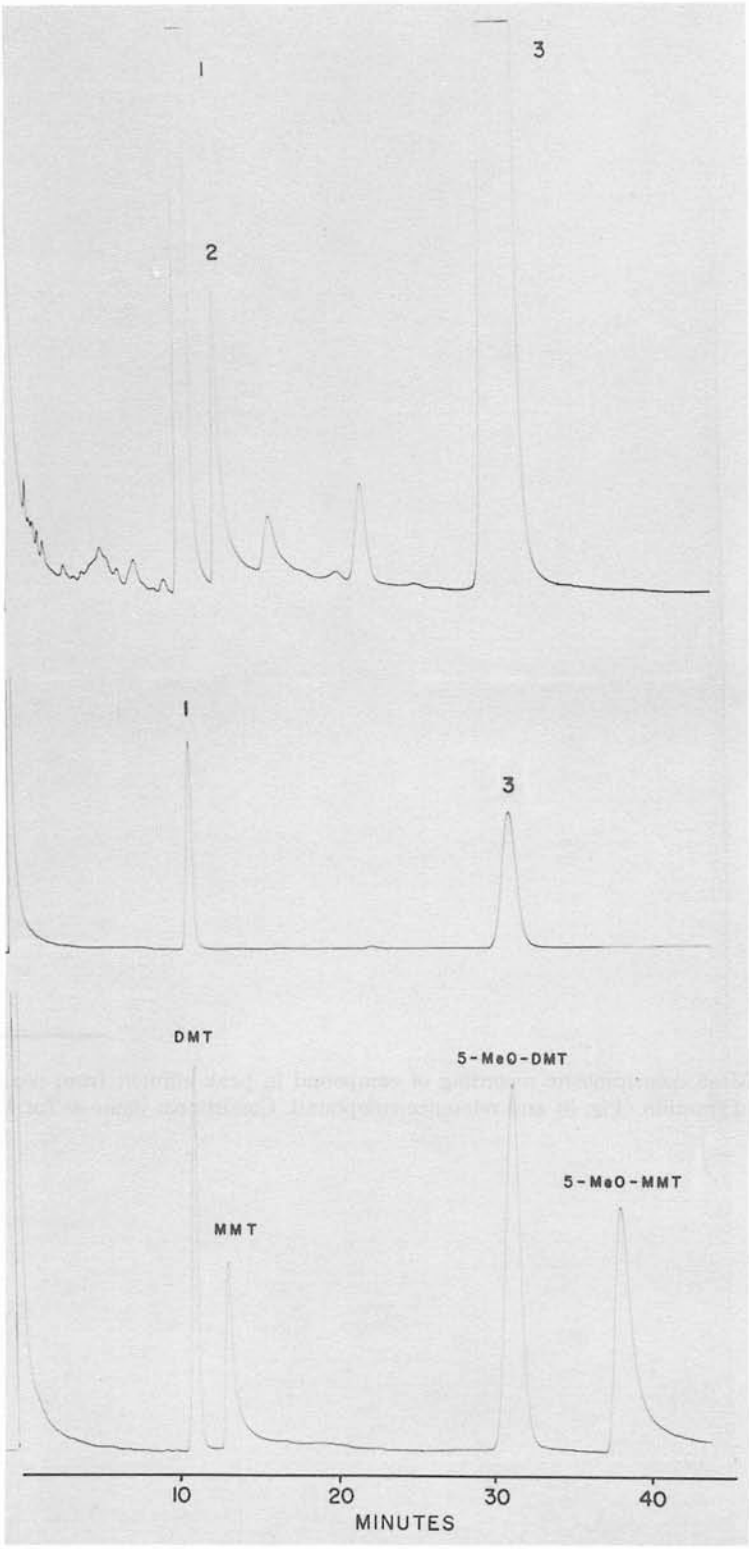





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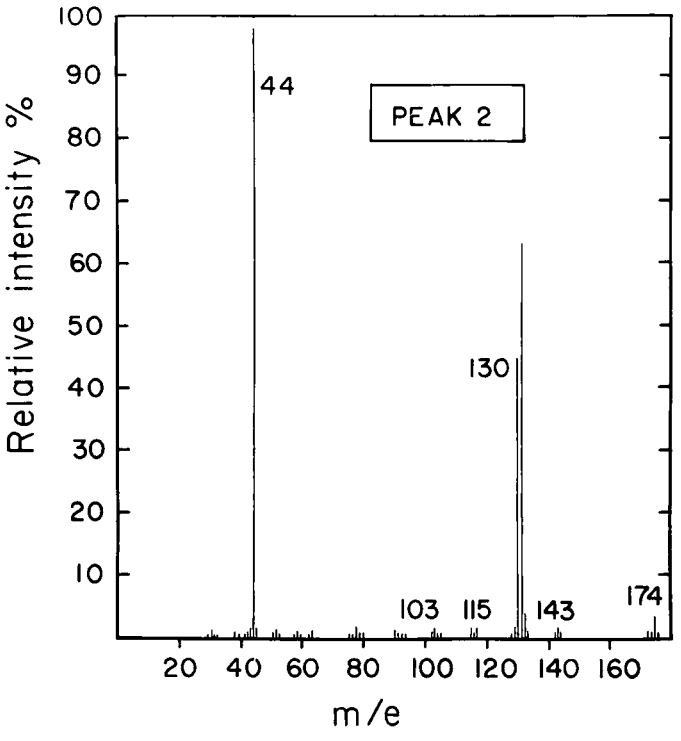
FIG. 4.—Mass spectrometric recording of compound in peak effluent from peak 2 from alkaloid fraction (Fig. 3) and reference compound. Conditions: Same as for Fig. 2.


Relative intensity %
100
90
80
70
60
50
40
30
20
10
44
PEAK 2
130
103
115
143
174
20
40
60
80
100
120
140
160
m/e

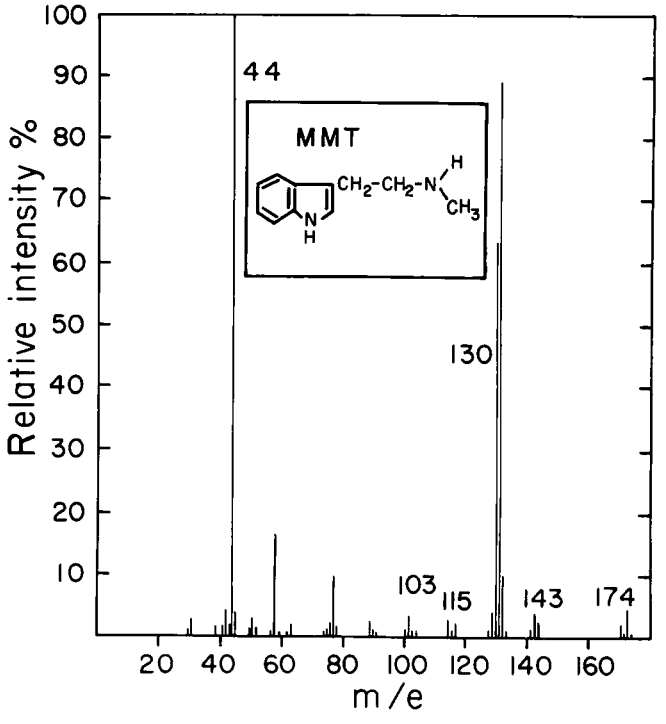
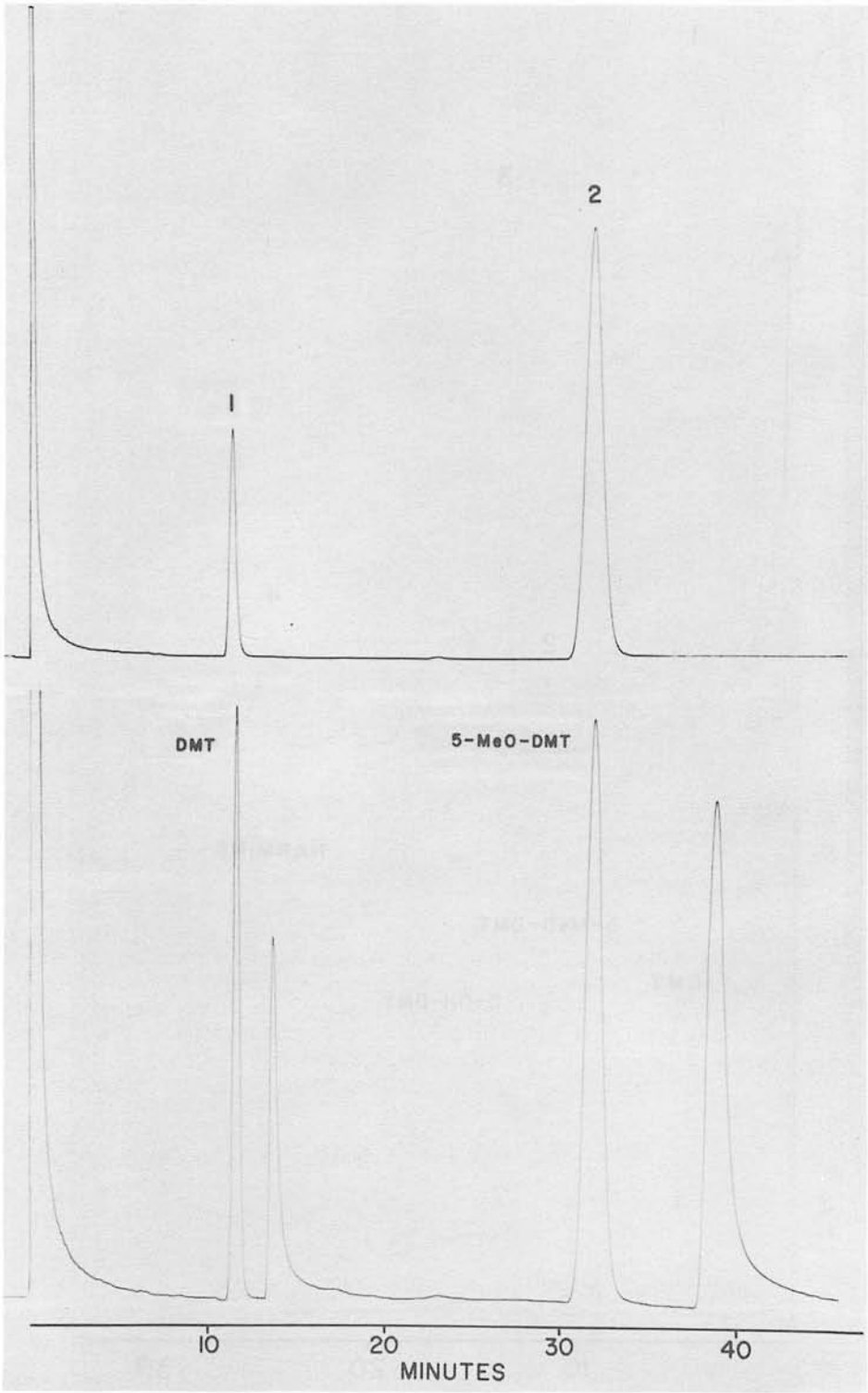
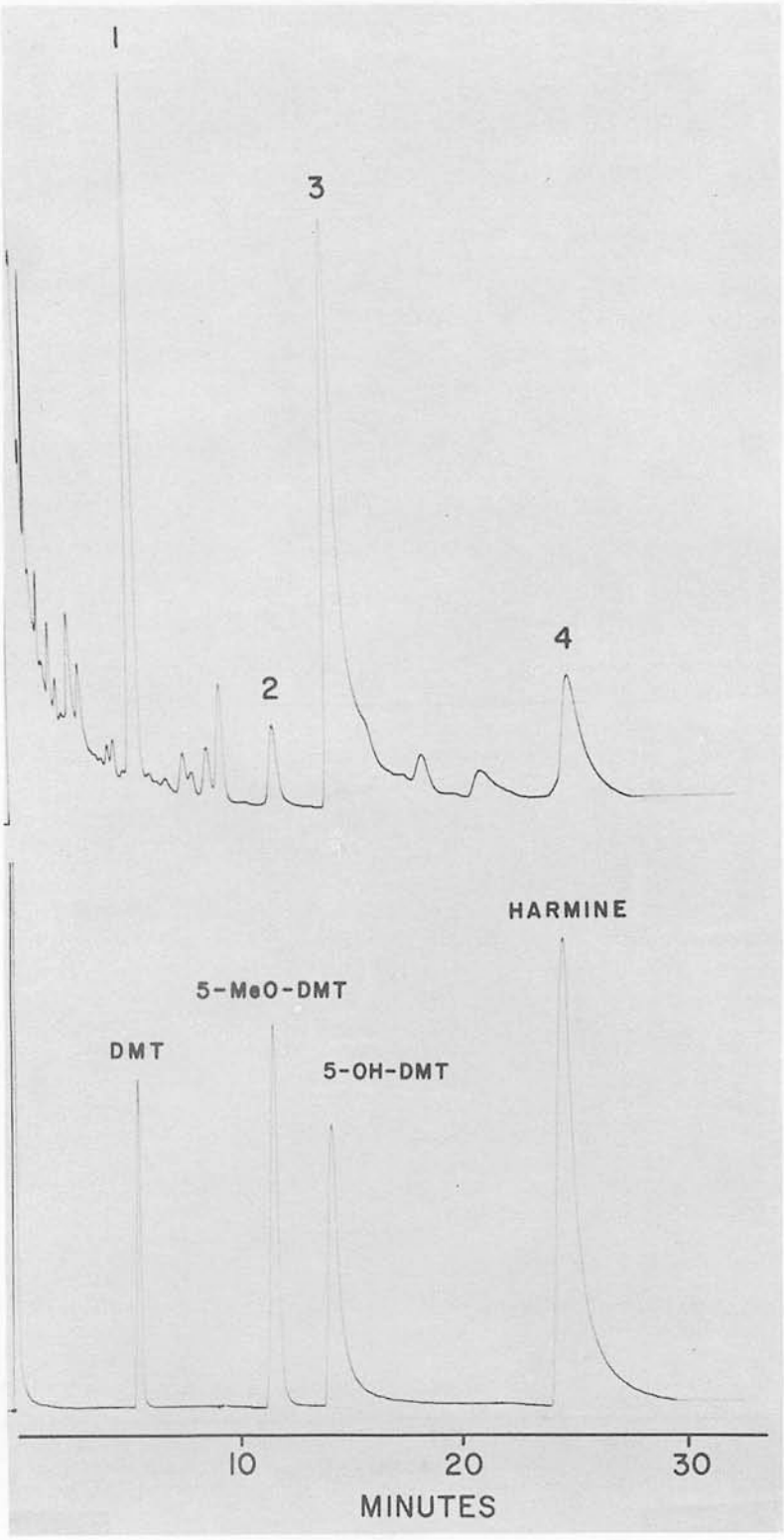

Relative intensity %
100
90
80
70
60
50
40
30
20
10
44
MMT
CH2-CH2-N
H
CH3
N
H
130
103
115
143
174
20
40
60
80
100
120
140
160
m/e

FIG. 5.—Gas chromatogram of alkaloid fraction of Epéna snuff obtained from Mr G. Seitz, Araraibo Indians, Rio Maturacá, 1965. GLC conditions: Same as for Fig. 1. Upper panel alkaloid fraction. Lower panel reference substances. Mass spectrometric control of peak effluents: Peak 1 and DMT: Molecular ion at $m/_e$ 188; other peaks at $m/_e$ 58 (base peak), 103, 115, 130, 143. Peak 2 and 5-MeO-DMT: Molecular ion at $m/_e$ 218; other peaks at $m/_e$ 58 (base peak), 103, 117, 160, 173.


2
1
DMT
5-MeO-DMT
10
20
30
40
MINUTES


1
3
2
4
HARMINE
5-MeO-DMT
DMT
5-OH-DMT
10
20
30
MINUTES

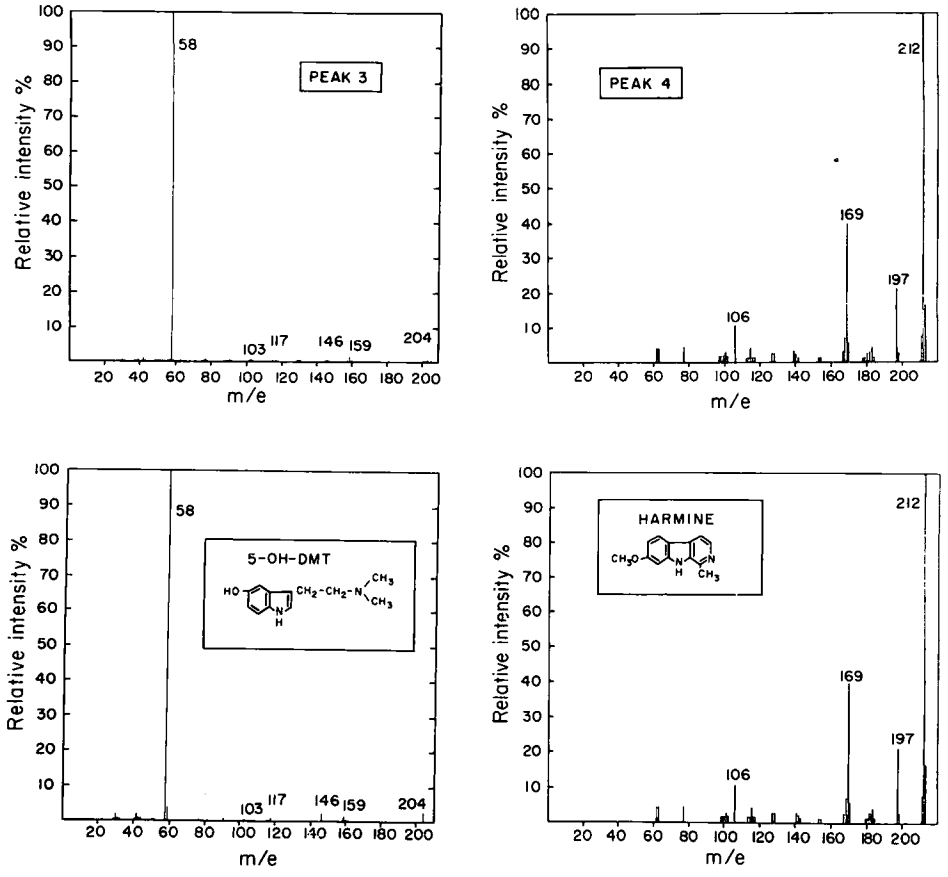



FIG. 7.—Mass spectrometric recording of compound in effluents from peak 3 and 4 from alkaloid fraction (Fig. 6) and reference compounds. Conditions: Column 2 m; i.d. 3.2 mm; 5% SE-30; 100–120 mesh Gas Chrom P; temp. 200°.

FIG. 6.—Gas chromatogram of alkaloid fraction from Paricá obtained from the Ethnographical Museum, Stockholm, collected by the late Prof. Bolinder. Piaroa Indians, Venezuela, 1955. Column 4m; i.d. 3.2 mm; 5% SE-30 on 100–120 mesh Gas Chrom P; temp. 210°; flow 60 ml per min. Upper panel alkaloid fraction. Lower panel reference substances. Mass spectrometric control of peak effluents: Peak 1 and DMT: Molecular ion at m/e 188; other peaks at m/e 58 (base peak), 103, 115, 130, 143. Peak 2 and 5-MeO-DMT: Molecular ion at m/e 218; other peaks at m/e 58 (base peak), 103, 117, 160, 173. Mass spectra from effluents from peak 3 and 4 and model substances, see Fig. 7.

FIG. 8.—Gas chromatogram of alkaloid fraction from Yopo, Colombia, 1956, obtained from Mr Donald Overton. Sample number P56–70–11. GLC conditions: Same as for Fig. 6. Upper panel alkaloid fraction. Lower panel reference substances. Mass spectrometric control of peak effluents: Peak 1 and DMT: Molecular ion at $m/_e$ 188; other peaks at $m/_e$ 58 (base peak), 103, 115, 130, 143. Peak 2 and 5-MeO-DMT: Molecular ion at $m/_e$ 58 (base peak), 103, 117, 160, 173. Peak 3 and 5-OH-DMT: Molecular ion at $m/_e$ 204; other peaks at $m/_e$ 58 (base peak), 103, 117, 146, 159.

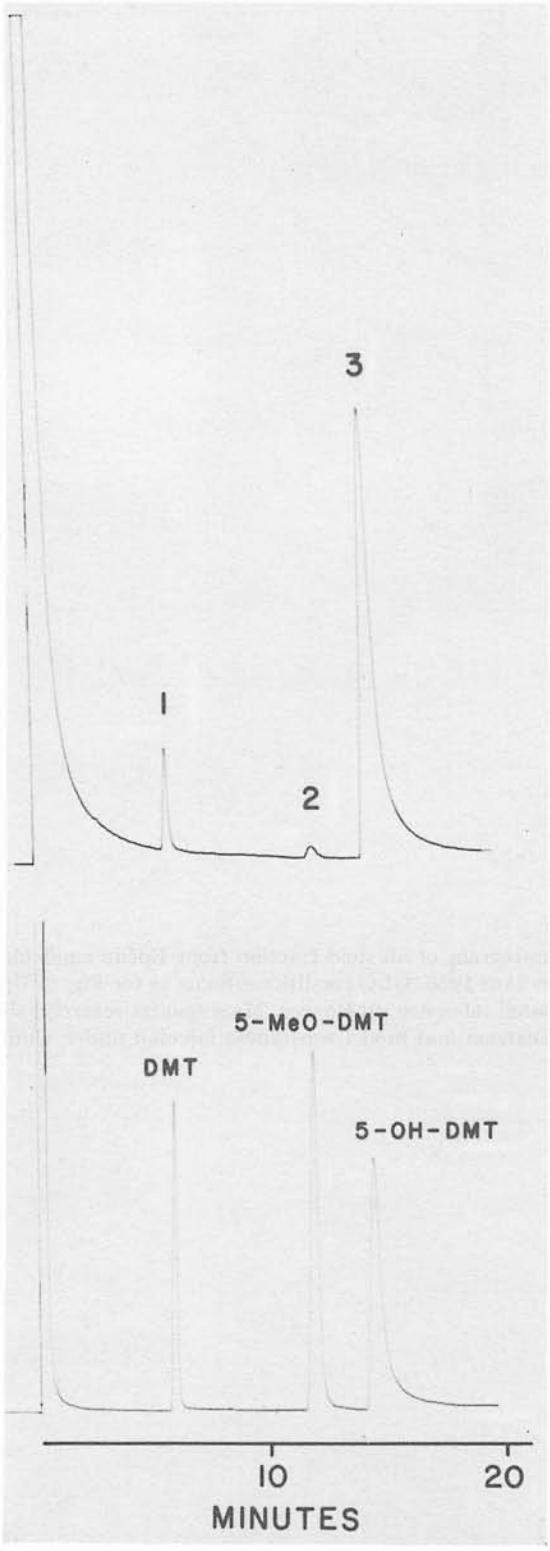
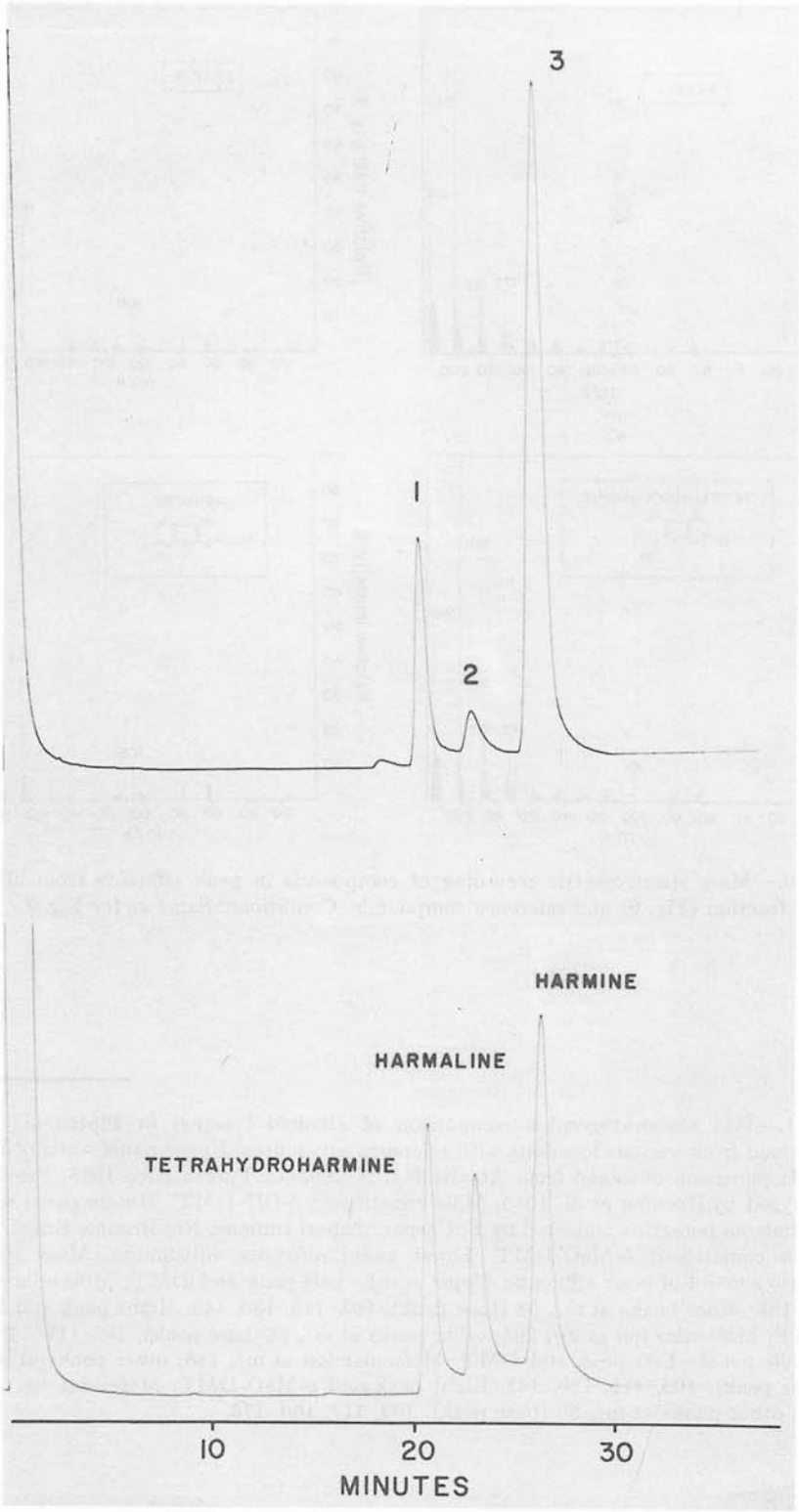

3
1
2
5-MeO-DMT
DMT
5-OH-DMT
10
20
MINUTES

FIG. 9.—Gas chromatogram of alkaloid fraction from Epéna snuff obtained from Dr H Becher. Surára Indians 1956. GLC conditions: Same as for Fig. 6. Upper panel alkaloid fraction. Lower panel reference substances. Mass spectra recorded simultaneously from peak effluents of extract and model substances injected under similar conditions, see Fig. 10.


3
1
2
HARMINE
HARMALINE
TETRAHYDROHARMINE
10
20
30
MINUTES

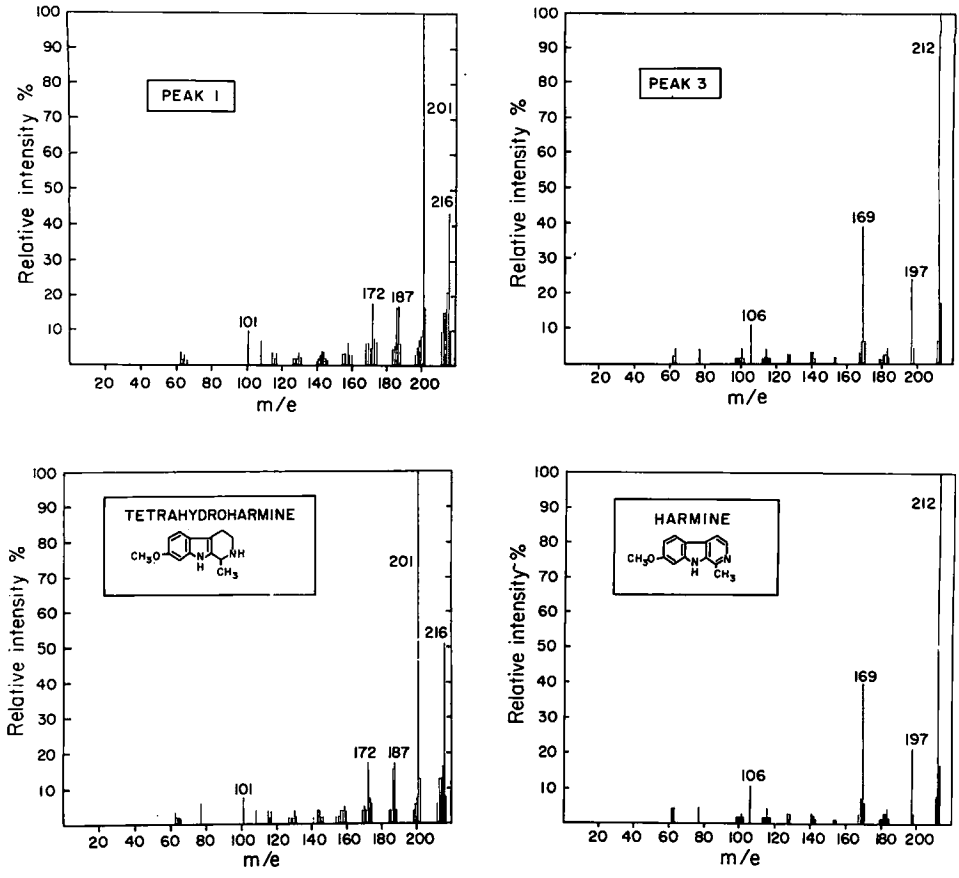
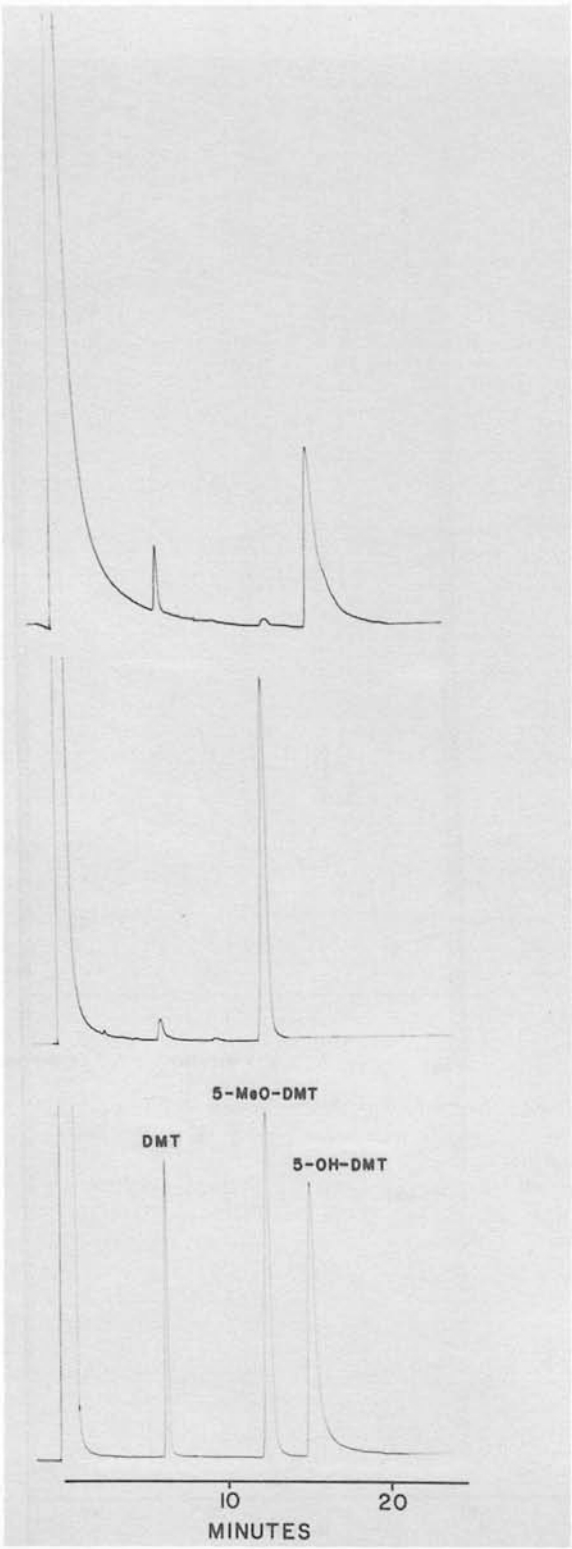
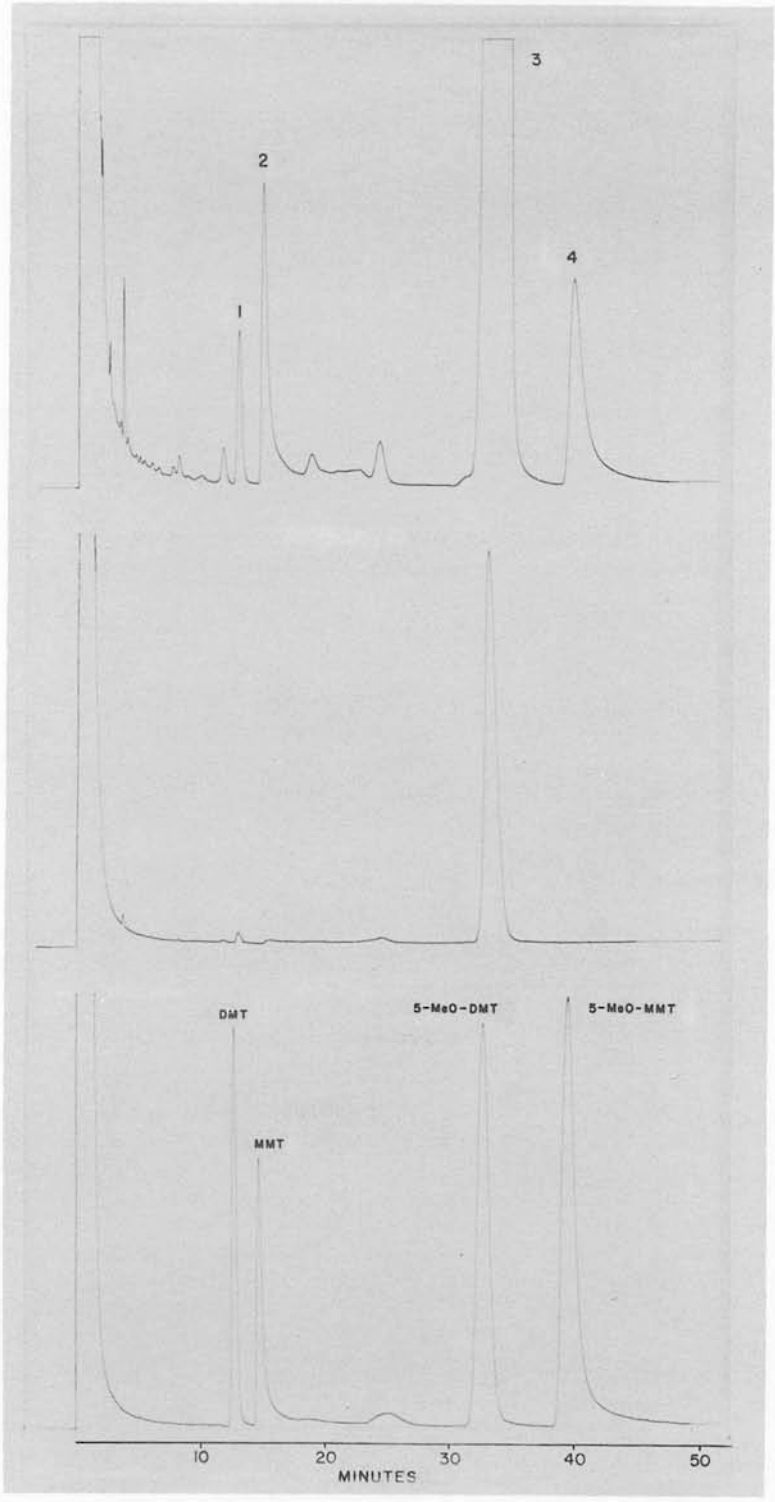



FIG. 10.—Mass spectrometric recording of compounds in peak effluents from alkaloid fraction (Fig. 9) and reference compounds. Conditions: Same as for Fig. 7.

FIG. 11.—Gas chromatographic comparison of alkaloid fraction in Piptadenia seeds obtained from various locations with reference substances. Upper panel seeds of Piptadenia peregrina obtained from Abbott No. N-2003-C, Puerto Rico 1948. Previously analysed by Horning et al. 1955. Main constituent 5-OH-DMT. Middle panel seed of Piptadenia peregrina collected by F. Caspar. Tupari Indians, Rio Branco, Brazil, 1953. Main constituent 5-MeO-DMT. Lower panel reference substances. Mass spectrometric control of peak effluents: *Upper panel*—Left peak and DMT: Molecular ion at $m/e$ 188; other peaks at $m/e$ 58 (base peak), 103, 115, 130, 143. Right peak and 5-OH-DMT: Molecular ion at $m/e$ 204; other peaks at $m/e$ 58 (base peak), 103, 117, 146, 159. *Middle panel*—Left peak and DMT: Molecular ion at $m/e$ 188; other peaks at $m/e$ 58 (base peak), 103, 115, 130, 143. Right peak and 5-MeO-DMT: Molecular ion at $m/e$ 218; other peaks at $m/e$ 58 (base peak), 103, 117, 160, 173.


5-MeO-DMT
DMT
5-OH-DMT
10
20
MINUTES


3
2
4
1
DMT
5-MeO-DMT
5-MeO-MMT
MMT
10
20
30
40
50
MINUTES

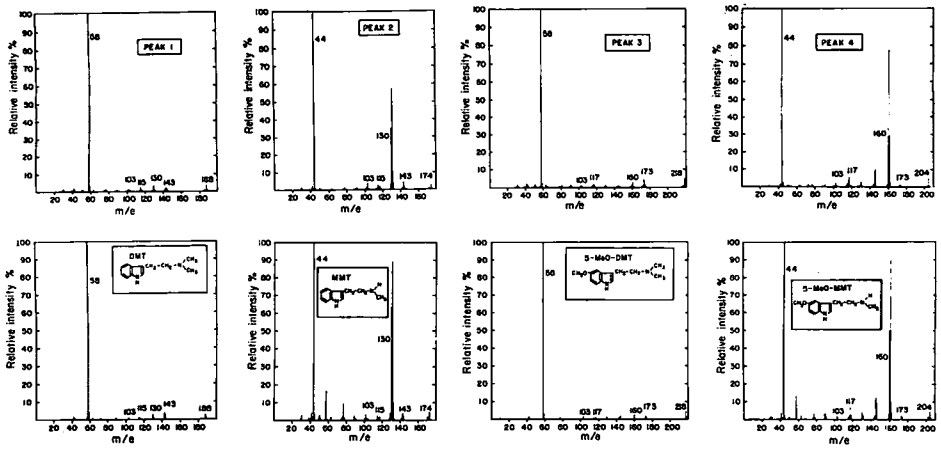



FIG. 13.—Mass spectrometric recording of compounds in peak effluents from alkaloid fraction in Fig. 12 and reference compounds. Conditions: Same as for Fig. 2.

FIG. 12.—Gas chromatogram of alkaloid fraction from bark of Piptadenia peregrina obtained from Mr. Donald Overton, collected in Colombia. 1956. Sample number P56–70–7. Column conditions: Same as for Fig. 1. Upper panel high magnification. Middle panel low magnification. Lower panel reference substances. Mass spectra recorded simultaneously from peak effluent of extract and model substances injected under similar conditions, see Fig. 13.

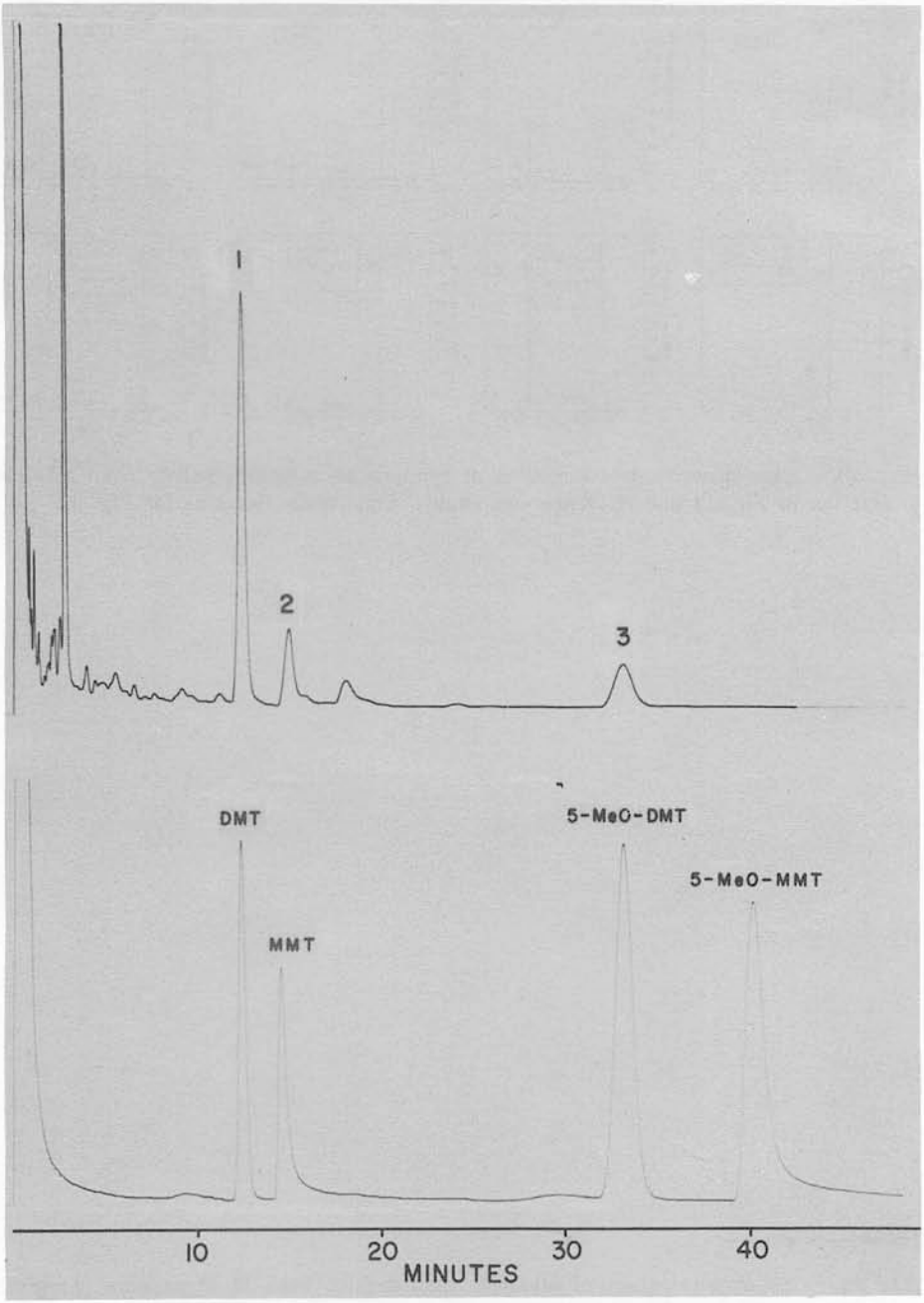



FIG. 14.—Gas chromatogram of alkaloid fraction from bark of Virola calophylla. Manaus 1964. GLC conditions: Same as for Fig. 1. Upper panel alkaloid fraction. Lower panel reference substances. Mass spectrometric control of peak effluents: Peak 1 and DMT: Molecular ion at $m/_e$ 188; other peaks at $m/_e$ 58 (base peak), 103, 115, 130, 143. Peak 2 and MMT: Molecular ion at $m/_e$ 174; other peaks at $m/_e$ 44 (base peak), 103, 115, 130, 131, 143. Peak 3 and 5-MeO-DMT: Molecular ion at $m/_e$ 218, other peaks at $m/_e$ 58 (base peak), 103, 117, 160, 173.

TABLE 1.—*Distribution of indole alkaloids in South American snuffs*

| Name | Origin | Alkaloid | Reference |
|---|---|---|---|
| Paricà | Venezuela | 5-OH-DMT | Fish and Horning 1956 |
| Paricà | Colombia | 5-OH-DMT | |
| Epéna | Waica Indians | DMT<br>5-OH-DMT<br>5-MeO-DMT | Holmstedt et al. 1964 |
| Epéna | Yanonámi Indians | DMT<br>DMT-N-oxide<br>5-OH-DMT<br>5-OH-DMT-N-oxide | Marini-Bettolo et al. 1964 |
| Epéna | Surára Indians | Harmine<br>Tetrahydroharmine | Bernauer 1964 |
| Paricà | Tucano Indians | Harmine<br>Harmaline<br>Tetrahydroharmine | Biocca et al. 1964 |
| Epéna | Tucano Indians | DMT<br>5-MeO-DMT<br>5-MeO-MMT | Present investigation |
| Epéna | Waica Indians | DMT<br>MMT<br>5-MeO-DMT | |
| Epéna | Araraibo Indians | DMT<br>5-MeO-DMT | |
| Yopo | Colombia | DMT<br>5-OH-DMT<br>5-MeO-DMT | |
| Paricà | Piaroa Indians | DMT<br>5-OH-DMT<br>5-MeO-DMT<br>Harmine | |
| Epéna | Surára Indians | Harmine<br>Tetrahydroharmine | |



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TABLE 2.—*Distribution of indole alkaloids in South American plants used for snuff preparation*

| Plant | Part | Origin | Alkaloid | Reference |
|---|---|---|---|---|
| Piptadenia peregrina Benth. | Seeds | Puerto Rico | 5-OH-DMT | Stromberg 1954 |
| Piptadenia peregrina Benth. | Pods | Puerto Rico and | DMT | Fish, Johnson, and Horning 1955 |
| | Seeds | Brazil | DMT-N-oxide<br>5-OH-DMT<br>5-OH-DMT-N-oxide | |
| Piptadenia peregrina Benth. | Seeds | Puerto Rico | DMT<br>5-OH-DMT | Present investigation |
| | Seeds | Rio Branco region, West Brazil | DMT<br>5-MeO-DMT | |
| Piptadenia peregrina Benth. | Bark | Brazil | MMT<br>5-MeO-DMT<br>5-MeO-MMT | Legler and Tschesche 1963 |
| Piptadenia peregrina Benth. | Bark | Colombia | DMT<br>MMT<br>5-MeO-DMT<br>5-MeO-MMT | Present investigation |
| Piptadenia macrocarpa Benth. | Pods<br>Seeds | Brazil | DMT<br>DMT-N-oxide<br>5-OH-DMT<br>5-OH-DMT-N-oxide | Fish, Johnson, and Horning 1955 |
| Piptadenia macrocarpa Benth. | Bark | Argentine | 5-MeO-MMT | Iacobucci and Rúveda 1964 |
| | Pods | | DMT<br>5-OH-DMT | |
| | Seeds | | DMT<br>5-OH-DMT<br>5-OH-DMT-N-oxide | |
| Piptadenia excelsa (Gris.) Lillo | Pods<br>Seeds | Argentine | DMT<br>5-OH-DMT<br>5-OH-DMT-N-oxide | |
| Piptadenia colubrina Benth. | Seeds | Brazil | 5-OH-DMT | Pachter, Zackarias, and Riberio 1959 |
| Mimosa hostilis Benth. | Root | Brazil | DMT | |
| Virola calophylla | Bark | Manaus Brazil | DMT<br>MMT<br>5-MeO-DMT | Present investigation |

## Discussion

*Mass spectrometric fragmentation of tryptamines*

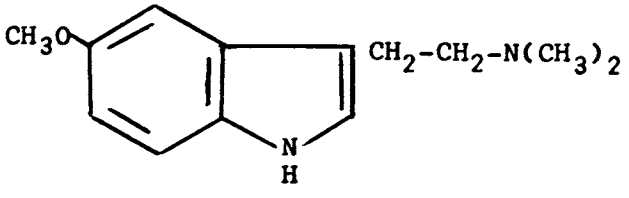
In the past years the mass spectrometer has taken its place beside other methods in studies of natural products. The unique function of this instrument is to delineate the molecular size and composition of a compound; in many cases it can also provide information on the arrangement of atoms in the molecule. The classical application of mass spectrometry, one in which its precision is superior to that of any other method, is in determining the molecular weight of an unknown compound. More extensive deductions regarding structures of complex molecules may often be derived from careful examination of the entire mass spectrum of a compound.

The combination of mass spectrometry and gas chromatography as invented by Ryhage (1964) is even more advantageous, because it combines the means of identification described above with the best method so far described for the separation of a series of compounds.

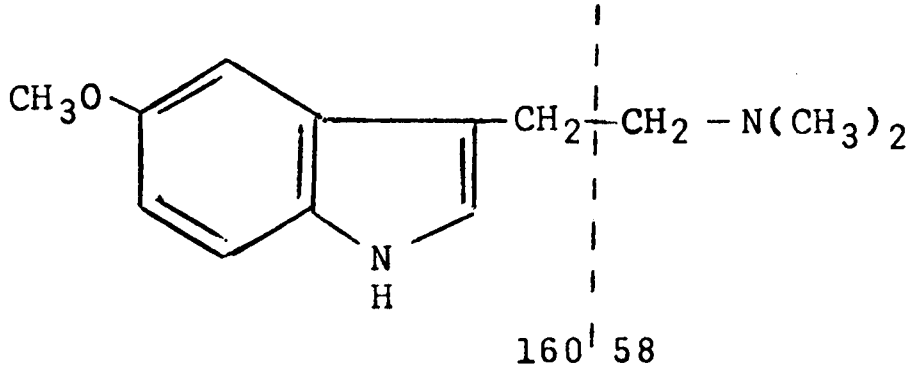
In the instrument available (LKB 9000), a mass spectrometer is coupled to a gas liquid chromatography (GLC) column. As the compounds emerge from the column they are ionized in the ion source of the mass spectrometer and about 10% of the total ion current is used for continuous registration of the effluent. Two molecule separators are coupled in series between the column and the gas inlet line of the mass spectrometer. With this technique the sample-to-helium ratio is increased at least a hundred times. Less than one $\mu$g of material introduced into the column suffices for a good mass spectrum. GLC-MS has the great advantage not only to resolve various substituted and non-substituted tryptamines, but also to give accurate identification. It is conceivable that the nonspecificity of the most commonly used method spectrophotofluorometry has prevented the elucidation of other normally occurring compounds than serotonin and tryptamine, and that with the progress in GLC-MS additional biogenic amines of physiological and pharmacological importance may be found. No doubt, the combination of GLC and mass spectrometry will be one of the powerful tools used in biological research for years to come.

According to Budzikiewics, Djerassi and Williams (1964) simple indoles have a characteristic fragmentation pattern. By analogy with this the psychotomimetic substance 5-MeO-DMT discovered by us in South American snuff would have the following fragmentation pattern.

5-MeO-DMT MW 218



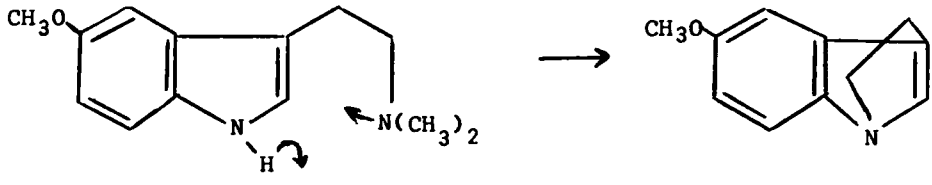
Here the main cleavage occurs as follows:



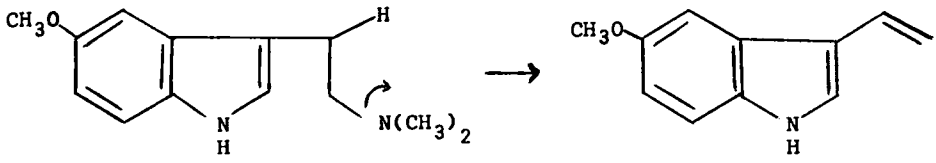

The ions m/e 160 and 58 are clearly seen in the mass spectrum. If one $CH_3$ on N is replaced by H such as occurs in 5-MeO-MMT the corresponding ions occur at m/e 160 and 44. The latter ion is found as the base peak of the spectrum. If one $CH_3$ on N are replaced by other groups such as acetyl in melatonine a corresponding ion is formed.

On the other hand m/e 160 will change according to different substitution in the indole nucleus such as occurs in bufotenine (m/e=146).

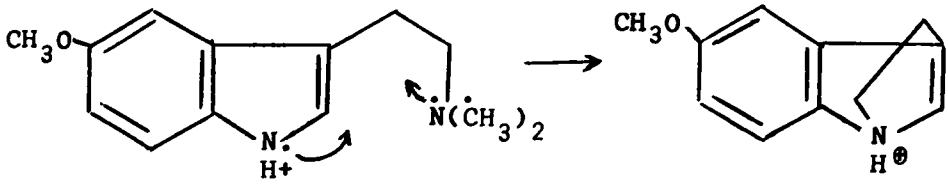
m/e 173 may represent




or




m/e 174 may represent




For m/e 115, 116, 117 in the spectrum the origin is not known, but the presence of these peaks seems to confirm previous belief that they are a good qualitative

indication of indoles. The mass spectra of 5-OH-DMT, 5-MeO-MMT and MMT when scrutinized confirm the fragmentation pattern proposed for 5-MeO-DMT.

*Plants containing indoles*

The first indoles in plants were isolated in the beginning of this century (Saxton 1965). Since then the number has been steadily increasing. Good accounts of their occurrence are available (Hochstein and Paradies 1957, Stowe 1958, Cerletti 1960, Downing 1962, Poisson 1965, Saxton 1965 and Morimoto et al., 1965, 1966). Unsubstituted and 5-substituted indoles command special interest with regard to pharmacological effects in two instances.

Firstly there are reports of cases of a disease called "staggers" in sheep pastured largely on a perennial grass, *Phalaris tuberosa L.* (Gallagher et al. 1964). Investigation of this and related species of Phalaris has led to the isolation of DMT, 5-MeO-DMT, 5-MeO-MMT and 5-OH-DMT (Wilkinson 1958, Culvenor et al. 1964).

Secondly, the same tryptamines as presented in table 1–2 of this review occur in the snuffs used in South America for intoxicating purposes. From the tables it is evident that tryptamines both unsubstituted and substituted in the ring (5-OH- and 5-MeO-) occur, and that both secondary and tertiary amines are present. In addition to this some snuffs contain β-carbolines, either in combination with the simple tryptamines or solely. In South American botany β-carbolines (harmine, harmaline and tetrahydroharmine) are usually associated with the species of *Banisteriopsis*, wherefore it is very likely that this is their origin in the snuffs. Very likely this is an admixture to the snuff, although definite botanical proof for it is lacking at the moment. To the knowledge of the authors, simple indoles and β-carbolines have not yet been isolated *from the same plant.*

The occurrence of both tryptamines and β-carbolines in the South American snuffs is pharmacologically interesting. The β-carbolines are monoamineoxidase inhibitors (Udenfriend et al. 1958), and could potentiate the action of the simple indoles. The combination of β-carbolines and tryptamines would thus be advantageous. However, pharmacological actions of the β-carbolines unrelated to monoamineoxidase inhibition has also been proven to exist (Schievelbein et al. 1966). Further botanical and chemical studies are obviously needed to see if the two groups of compounds in the snuff are derived from one plant or a mixture of plants.

*Deposition and absorption of snuffs*

The equipment used for the administration of the powder in some cases consists of a straight tube equipped at one end with a palmkernel through which a hole has been bored. This end is fitted into the nostril of one person while another blows the powder forcefully through the opposite end of the tube. Another variation is a V-shaped tube, used for self-administration, where one end is put into the mouth and the other end into the nostril and the snuff is blown into the nasal cavity. Other equipment for the administration

exist among other tribes, the usual apparatus being the frequently described bifurcated tube (Safford 1916). This is used for administration by means of direct inhalation.

The two means of administration, forceful blowing or inhalation can be expected to differ in the effect produced. It is necessary to consider here the broad features of normal nasal physiology. The stream of inspired air does not pursue a straight course from anterior nares to choana, but passes in a wide curve beginning at the nostril, extending through the olfactory fissure, and ending in the choana (Proetz 1953). The negative pressure produced in the nose on inspiration, reaches a maximum figure of 55 mm. of mercury. The air fluctuations are rarely of sufficient force or magnitude to carry foreign particles into the sinuses. During normal sniffing (inspiration) air is projected against the nasal mucosa and the anterior portion of the nose, producing eddies. Harrison (1964) let volunteers sniff pinches of barium sulphate powder up one nostril. Inspection revealed that in every case the powder collected primarily in the middle meatus. By forceful blowing as with the straight and the V-shaped tube a more widespread deposition on the nasal mucosa may be expected, and some particles even reach the lungs (Chinachoti et al. 1957). However, we must assume that the main part of the administered material affects the brain from the nose. From a theoretical point of view several possibilities exist.

(a) The tryptamines reach the brain, via absorption from the richly vascularized nasal mucosa into the blood stream. It is well known that many other drugs have a very rapid action when applied in this way.

(b) The compounds act directly on the brain without having been transported through the general circulation.

Anatomical reasons have been proposed for the direct action on the CNS of certain drugs, such as cocaine, through the nasal mucosa (Lewin 1927). The following veins communicate directly with the cranial cavity, the concomitant veins of the *arteriae ethmoidales*, and a vein which accompanies a ramification of the anterior ethmoidal artery. The last one is an important connection between the nose and the cranial cavity. This vein accompanies the artery through the ethmoidale plate and makes connection within the cranial cavity, either with the network of veins of *Tractus olfactorius* or directly with a bigger vein in the orbital lobe. All the vessels mentioned are accompanied by lymph vessels, and it is conceivable that drugs can act directly on the brain without having to be transported through the general circulation. Experimental proofs for this are, however, lacking.

Several observers have described the passage of simple solutions from the nose into the cranial cavity. (For references see Yoffey and Drinker 1938). Clark (1929), for example, stated that a solution of potassium ferrocyanide and iron ammonium citrate, dropped into the nasal cavities of rabbits, reaches the surface of the brain *within one hour* (Sic!). He believed that there was a pathway along "the perineural sheaths of the olfactory nerves". The existence of a current running centripetally in these perineural sheath spaces of the olfactory nerves under normal conditions was postulated. Faber (1937), came to similar conclusions as a result of experiments on rabbits.

In the series of experiments by Yoffey and Drinker (1938), this was definitely not the case. The results were of especial interest since by cannulation of the cervical lymph duct it was possible to show that dye was present in the lymph in high concentration over many hours, and yet could never be detected in the interior of the cranium.

It seems evident that for anything but solutions of simple crystalloids, the cribriform plate offers an effective barrier to the passage of substance (non-living) from the nose to the interior of the skull. The rapidity of action of the tryptamines (minutes) also speaks against a direct transport from the nasal to the subarachnoidal cavity via the lymph vessels.

*Symptomatology*

The first written account of the action of the American intoxicating snuffs is that by Friar Ramon Pane on cohoba, published first in 1511 and quoted in detail by Wassén (this volume). Ramon Pane's observation of symptoms is revealing:

> . . . he takes a certain powder called cohoba, snuffing it up his nose, which intoxicated them so that they do not know what they do and in this condition they speak many things incoherently in which they say they are talking with the *cemis* and that by them they are informed how the sickness came upon him. Having snuffed cohoba into their nostrils (so they call the intoxicating plant by which the bovites also are thrown into a frenzy), they say that the house is turned upside down the roofs and floors being interchanged and that men walk with their feet upward. Such is the strength of the powder of cohoba that it takes away the senses of using it. When the stupefaction begins to go away, he hangs down his head and clasps his knees with his arms. He remains in this state of suspended animation for a little while; then he raises his head as one awakening from sleep and casting his eyes up at the sky at first he mutters a few rambling words to himself. The words which they say, none of our people understand. With this powder they lose consciousness and become like drunken men.

This undoubtedly constitutes the first written account of the psychotomimetic effects of the tryptamines, and is astonishing in its correctness when compared to later descriptions only some of which will be quoted here. Ramon Pane's description also corresponds very well to what one can see in the film about the use of the epéna among the Waicas made by Mr. Georg Seitz. Later explorers have, however, pointed out additional effects. Nimuendajú (1948), (quoted from Wassén 1965) says:

> . . . the powder caused a general state of excitement and exaltation with auditory hallucinations, and a condition of feverish activity which ended with prostration or unconsciousness. According to Martius, individuals who were over-excited by the narcotic and suffocated, died on the spot. On the morning following "a narcotic spree" the bodies of persons were often found shot with arrows or stabbed with knives. These murders were not considered as crimes and were blamed on the paricà.

Cohoba, according to Columbus, Ramon Pane, Las Casas and others who observed and reported its use in Haiti, was employed by the medicine-men chiefly to induce a state of trance; more hedonistic uses have been described later (see Seitz this volume). The violent effect of this snuff indicated that

its chief ingredient was a powerful substance. None of the early commentators on the custom says that the substance inhaled was derived from the tobacco plant, but before the close of the sixteenth century the snuff used in the cohoba ceremonies reported was assumed to be tobacco, and the association was continued up to our own time (Lovén 1935). Only a person entirely inexperienced in pharmacology and toxicology would, however, confuse the illusions and hallucinations described under the influence of cohoba, with a nicotine intoxication. The confusion of cohoba and tobacco was also largely dispelled by the paper by Safford (1916).

All modern evidence confirms the psychotomimetic action of the snuffs. Zerries (1964) and Seitz (this volume) describe how in the Waica tribe individuals quickly become intoxicated by repeated inhalation of the snuff. The somatic symptoms are headache, salivation, vomiting, profuse perspiration, unsteady gait and a typical facial expression. During the intoxication the Indians are able to establish contact with the Hekula, the spirits of rocks and waterfalls in order to induce them to bring mishap and sickness to the enemies of the village. The medicine man becomes possessed by spirits, excited and sometimes loses consciousness. The best description of the use of epéna is the one given by Becher (1960) relating details about the religious use of the compound, and how during the ritual the Indians become so obsessed with the spirits that they have to be exorcised. Under the influence of the drug, the Indians identify themselves with the gigantic spirits of animals and plants Hekura (Hekula), and also have the impression that they personify themselves the Hekura (Surára tribe). Becher, who became a member of this tribe, gives a rare description of his own experience when taking the snuff. His symptoms were the following (translation by the authors):

> A few minutes (after taking the snuff) I felt terrible with a headache and nausea just as the boy who comes into contact with the drug for the first time. Shortly afterwards, I had a very strange experience, I felt myself to be a giant among giants. Everybody around me, people as well as dogs and parrots, seemed suddenly to have become giants.

Interestingly enough this is a description of macroptic illusions.

*Dysmegalopsia*, synonymous with *dysmetropsia*, is a disturbance of the visual appreciation of the size of objects which occurs with certain drugs. It can be subdivided into *macropsia* and *micropsia*. These conditions may result from disturbances in the peripheral motor perception, *i.e.*, eye muscles, but they also occur in toxic psychoses. Macropsia has been described, particularly in alcoholic delirium. Its most famous manifestation is the well known "pink elephants." It also occurs in intoxications with *Amanita muscaria* (Kracheninnikov 1764). The macroptic phenomenon has been treated in detail by di Gaspero (1908). It is interesting to know that these experiences are described by people who are fully oriented in time and space, and that during experience living persons and animals *but not dead objects*, change size (compare Becher). The latter may be perceived in a different colour as to the giants. Macropsia seems to be more common than micropsia, but the latter has been described as a result of intoxication with ether, alcohol, cocaine, chloral hydrate and cannabis (de Clerambault 1909). Apparently

it can occur also in intoxications with *Banisteriopsis* (Preuss 1921). Beringer (1934), who has devoted a study to optic illusions and hallucinations, describes a third phenomenon, a change in size in one direction or the other somewhat reminiscent of what can be achieved with a modern zoom lens of a camera.

Shortly after Horning et al. had isolated DMT and 5-OH-DMT from *Piptadenia peregrina*, Szara (1957), conducted experiments on himself with the injection of DMT. The symptoms he reported are in good agreement with what has been described by the explorers:

> In the third or fourth minute after the injection vegetative symptoms appeared, such as a tingling sensation, trembling, slight nausea, mydriasis, elevation of the blood pressure and increase of the pulse rate. At the same time eidetic phenomena, optical illusions, pseudohallucinations and later real hallucinations, appeared. The hallucinations consisted of moving, brilliantly coloured oriental motifs, and later I saw wonderful scenes, altering very rapidly. The faces of the people seemed to be masks. My emotional state was elevated sometimes up to euphoria. At the highest point, I had compulsive athetoid movement in my left hand. My consciousness was completely filled by hallucinations, and my attention was firmly bound to them; therefore I could not give an account of the events happening around me. After ¾–1 hour the symptoms disappeared, and I was able to describe what had happened.

Macropsia is also a frequent phenomenon in experimental DMT-intoxications (Isbell, personal communication).

The action of 5-OH-DMT (bufotenine) is more controversial. Fabing and Hawkins (1956), reported that intravenous injection, over a three minute period, of 8 to 16 mg of bufotenine in human volunteers resulted in primary visual disturbances, alteration of time and space perception, and paresthesias. It is difficult to judge by this account whether any illusions and hallucinations really occurred. It seems that the observed phenomena can as well be interpreted as general somatic symptoms of intoxication. Neither Isbell nor Turner and Merlis (1959) themselves in their carefully conducted studies, could substantiate the claim that bufotenine injections had any effect on the central nervous system, whereas DMT under the same experimental conditions had psychotomimetic effects.

Control experiments with various preparations of snuff have been carried out by two groups but have not proven the capability of the used preparations to produce the intoxication attributed to it by natives or explorers. In a letter, Dr. Harris Isbell describes his experiment with the same compounds in the following way:

> We studied several forms of the material: Untreated snuff, roasted snuff, limed and roasted snuff, fermented snuff, fermented and limed snuff, fermented, limed and roasted snuff. Our subjects inhaled the snuff through straws. We obtained no reports that there were any subjective effects after inhalation of this material in amounts ranging up to 1 gram, and we further were unable to obtain any evidence of objective effects on pupillary size, tendon reflexes, body temperature, respiration, blood pressure etc., after doses ranging up to 1 gram orally.
>
> Inhalation of pure bufotenine in aerosol suspension, or oral ingestion of bufotenine in doses running up to 100 mg (total dose) also were without effect.

The above quoted experiments were all performed with snuff made from the sample of *Piptadenia peregrina* in which Horning et al. had found

5-OH-DMT (bufotenine) to be the main component, and *this fully explains the negative results.*

One measure of the ability of compounds to penetrate the nervous system is the lipid solubility, as determined by the lipid solvent-water partition coefficients. Gessner and Page (1962), found a low value for the chloroform-water partition coefficient of 5-OH-DMT, indicating a low lipid solubility attributable to the hydrophilic phenolic hydroxy group. Hence, the low activity of 5-OH-DMT could be related to its relative inability to cross the blood-brain barrier. The 5-MeO-DMT shown by the present investigation to be the major component of most South American snuffs was, however, found to be a compound in which the right structure is present both for lipid solubility and central action.

The animal experiments by Gessner and Page (1962) have pointed to the strong action of synthetic 5-MeO-DMT on the central nervous system, and its important role in the elucidation of central nervous mechanisms. The effect of 5-MeO-DMT on the conditioned avoidance response of trained rats was compared quantitatively, using a shuttle-box, with that of several other substituted tryptamines and LSD-25. At a dose level of 19 $\mu$M/kg it had a pronounced effect on the conditioned avoidance response, much more pronounced than that due to DMT. A similar response was elicited by LSD-25 at a dose level of 6 $\mu$M/kg.

Benington et al. (1965), report that the effect of 5-MeO-DMT on cat behaviour is dramatic. An intense sham rage response was induced within a few minutes. Of all drugs examined that induce sham rage in the cat, 5-MeO-DMT is one of the most potent, and its potency was very close to that of LSD-25. From the rapid onset of the rage response induced by 5-MeO-DMT by any route of administration, it is evident that the drug reaches the sites of action rapidly. The nature of the response suggests a central effect of a relatively short duration.

It is outside the scope of the present investigation to go into the detailed effects of the various tryptamines with regard to their circulatory and other peripheral effects. (With regard to 5-MeO-MMT see Marczyński, 1959, 1960). It ought to be mentioned, however, that the effects of 5-MeO-DMT on the general circulation are negligible compared to those of 5-OH-DMT (bufotenine). Detailed pharmacological and metabolic studies of 5-MeO-DMT are still lacking. No doubt its resemblance to serotonine, its solubility properties, its relative lack of peripheral and marked central action of an obvious psychotomimetic nature will in the future make 5-MeO-DMT an important tool in psychopharmacological studies. Once again, one cannot but marvel at the ingenuity of the South American Indians who relentlessly seem to be able to find their way to the right herb containing the most active component.

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## REFERENCES


BECHER, H. "Un viaje de investigación por los rios Demini y Aracá (Brasil) Trabajos y Conferencias." Seminarion de Estudios Americanistas, vol. II, 3: 149–160, 1958.

"Die Surára und Pakidái, zwei Yanonámi-Stämme in Nordwest-Brasilien." Hamburg, Kommisionsverlag Cram, de Gruyter & Co., 1960.

"Dringende ethnologische Forschungsaufgaben in Nordwest-Brasilien." Sonderdruck aus Akten des 34. Intern. Amerikanistenkongresses Wien, 1960.

BENINGTON, F., R. D. MORIN and L. C. CLARK. "5-Methoxy-*N*, *N*-Dimethyltryptamine, A Possible Endogenous Psychotoxin." The Alabama Journal of Medical Sciences, 2: 397–403, 1965.

BERINGER, K. "Optische Wahrnehmungsveränderungen und Sinnestäuschungen bei Rauschgiften." Augenärztliche Tagesfragen (Böhlein-Wegner), 77: 2711, 1934.

BUDZIKIEWICS, H. C., C. DJERASSI and D. WILLIAMS. "Interpretation of Mass Spectra of Organic Compounds." San Francisco, Holden Day Inc., 1964.

"Structure Elucidation of Natural Products by Mass Spectrometry." San Francisco, Holden Day Inc., 1964.

BÖSZÖRMÉNYI, Z. and G. GRUNECKER. "Dimethyltryptamine (DMT) experiments with psychotics." Psychotropic drugs. Milano, ed. by S. Garattini and V. Ghetti, 580 pp., 1957.

CASPAR, F. "Ein Kulturareal im Hinterland der Flüsse Guaporé und Machado (Westbrasilien), dargestellt nach unveröffentlichten und anderen wenig bekannten Quellen, mit besonderer Berücksichtigung der Nahrungs- und Genussmittel." Hamburg. Dissertation, 1953.

CERLETTI, A. "Über Vorkommen und Bedeutung der Indolstruktur in der Medizin und Biologie." Progr. Drug, Res., 2: 227–249, 1960.

CHINACHOTI, N. and P. TANGCHAI. "Case Report Section. Pulmonary Alveolar Microlithiasis Associated with the Inhalation of Snuff in Thailand." Diseases of the Chest, 32: 687–689, 1957.

LE GROS CLARK, W. E. "Anatomical investigation into the routes by which infections may pass from the nasal cavities into the brain." Reports on Public Health and Medical Subjects No. 54. Ministry of Health. London. Published by his Majesty's Stationary Office 1929.

DE CLÉRAMBAULT, M. "Diskussionsbemerkung zu R. Leroy: Les Hallucinations liliputiennes." Ann. Med. Psychol., 286, 1909.

CULVENOR, C. C. J., R. DAL BON and L. W. SMITH. "The occurrence of indolealkylamine alkaloids in Pharalis Tuberosa L. and P. Arundinacea L." Australian J. Chem., 17: 1301–1304, 1964.

DOWNING, D. F. "The chemistry of the psychotomimetic substances." Quart. Rev. of the Chem. Soc. of London, 16: 133–162, 1962.

FABER, W. M. "The nasal mucosa and the subarachnoid space." Amer. J. Anat., 62: 121–148, 1937.

FABING, H. D. and J. R. HAWKINS. "Intravenous Bufotenine Injection in the Human Being." Science, 123: 886–887, 1956.

FISH, M. S., N. M. JOHNSON and E. C. HORNING. "Piptadenia Alkaloids Indole Bases of P. peregrina (L.) Benth. and Related Species." J. Am. Chem. Soc., 77: 5892–5895, 1955.

GALLAGHER, C. H., J. H. KOCH, R. M. MOORE and J. D. STEEL. "Toxicity of Phalaris tuberosa for Sheep." Nature, 204: 542–545, 1964.

DI GASPERO, H. "Über das Phänomen der Makropsie als Symptom bei akuter toxischer Halluzinose." J. Psychol. u. Neur., 11: 115, 1908.

GESSNER, P. K. and I. H. PAGE. "Behavioral effects of 5-methoxy-*N*:*N*-dimethyltryptamine, other tryptamines and LSD." Am. J. Physiol., 203: 167–172, 1962.

HARRISON, D. F. N. "Snuff—Its Use and Abuse." Brit. Med. J., 2: 1649–1651, 1964.

HOCHSTEIN, F. A. and A. M. PARADIES. "Alkaloids of Banisteria caapi and Prestonia amazonicum." J. Am. Chem. Soc., 79: 5735–5736, 1957.

HORNING, E. C., E. MOSCATELLI and C. C. SWEELEY. Chem. Indust., 751, 1959.

HORNING, E. C., W. J. A. VAN DEN HEUVEL and B. G. CREECH. "Methods of Biochemical Analysis." D. Glick, Ed., XI, Interscience, London 1963.

ISBELL, H. Letter to the author, October 25, 1957.

KRASHENINNIKOV, S. P. "Opisanie zemli Kamchatki (A Description of Kamchatka)." Akademia Nauk, 1755. New critical edition in 1949.

LEWIN, L. "Phantastica. Die betäubenden und erregenden Genussmittel." Für Ärtze und Nichtärtze. Zweite Auflage, Berlin, Verlag von Georg Stilke in Berlin, 1927.

LOVÉN, S. "Origins of the Tainan Culture, West Indies," Göteborg, 1935.

MARCZYNSKI, T. "Some pharmacological properties of a recently isolated alkaloid, 5-methoxy-*N*-methyltryptamine." Bull. Acad. Pol. Sci., 7: 151–154, 1959.

MARCZYNSKI, T. and J. VETULANI. "Further investigations on the pharmacological properties of 5-methoxy-*N*-methyltryptamine." Dissertationes Pharmaceuticae, 12: 67–84, 1960.

MORIMOTO, H. and H. OSHIO. "Über Lesbedamin, ein neues Alkaloid." Inhaltsstoffe von Lespedeza bicolor var. japonica, I. Liebigs Ann. Chem., 682, 212–218, 1965.

MORIMOTO, H. and N. MATSUMOTO. "Inhaltstoffe von Lespedeza bicolor var. japonica, II." Liebigs Ann. Chem., 692: 194–199, 1966.

NIMUENDAJÚ, C. "The Mura and Piraha." HSAM, 3: 245–254, 1948.

PANE, R. "Quoted from Pietro Martire d'Anghieras." Opera Babylonica Oceani decas Poemata Epigrammata Sevilla 1511.

POISSON, J. "Note sur 'Natem', boisson toxique péruvienne et ses alcaloides." Ann. Pharm. fr., 23: 241–244, 1965.

PREUSS, K. T. "Religion and Mythologie der Uitoto." Vol. I. Göttingen 1921.

PROETZ, A. W. "Essays on the applied physiology of the nose." St. Louis, Annals Publishing Co., 2nd ed., 1953.

RYHAGE, R. "Use of Mass Spectrometer as a Detector and Analyzer for Effluents Emerging from High Temperature Gas Liquid Chromatography Column." Anal. Chem., 36: 759–764, 1964

SAFFORD, W. E. "Identity of cohoba, the narcotic snuff of ancient Haiti." J. Wash. Acad. Sci., 6: 547–562, 1916.

SAXTON, J. E. "The Alkaloids." Vol. VIII. New York, London, Academic Press, R. H. F. Manske (editor), 1965.

SCHIEVELBEIN, H., H. PETER, I. TRAUTSCHOLD and E. WEELE. "Freisetzung von 5-Hydroxytryptamin aus Thrombocyten durch Harmalin." Biochem. Pharmacol., 15: 195–197, 1966.

STOWE, B. B. "Occurrence and metabolism of simple indoles in plants." Fortschritte der Chemie organischer Naturstoffe (Herausgegeben von L. Zechmeister), Springer Verlag, Wien, 16: 248–297, 1958.

STROMBERG, V. L. "The isolation of Bufotenine from Piptadenia peregrina." J. Am. Chem. Soc., 76: 1707, 1954.

SZARA, S. "The comparison of the psychotic effect of tryptamine derivatives with the effects of mescaline and LSD-25 in selfexperiments." Psychotropic drugs. Milano. Ed. by S. Garattini and V. Ghetti, 460–467, 1957.

"Hallucinogenic effects and metabolism of tryptamine derivatives in man." Fed. Proc., 20: 885–888, 1961.

SZARA, S. and L. H. ROCKLAND. "Psychological effects and metabolism of *N,N*-diethyltryptamine, an hallucinogenic drug." Proceeding of the Third World Congress of Psychiatry, 1: 670, 1961.

TURNER, W. J. and S. MERLIS. "Effect of some indolealkylamines on man." Arch. Neurol. Psychiatr., 81: 121–129, 1959.

UDENFRIEND, S., B. WITKOP, B. G. REDFIELD, and H. WEISSBACH, Biochem. Pharmacol., 1: 160, 1958.

WASSÉN, S. H. "The use of some specific kinds of South American Indian snuff and related paraphernalia." Etnologiska Studier 28, 1965.

WILKINSON, S. "5-Methoxy-*N*-methyltryptamine: A new indole alkaloid from Phalaris arundinacea L." J. Chem. Soc., 2079–2081, 1958.

YOFFEY, J. M. and C. K. DRINKER. "The lymphatic pathway from the nose and pharynx." J.. Exp. Med., 68 : 629–640, 1938.

ZERRIES, O. "Waika, Die kulturgeschichtliche Stellung der Waika-Indianer des oberen Orinoco in Rahmen der Völkerkunde Südamerikas." München, Klaus Renner Verlag, 1964. (Ergebnisse der Frobenius-Expedition 1954/55 nach Südost-Venezuela. Band 1. Waika).

# Discussion on the Psychoactive Action of Various Tryptamine Derivatives

*Chairman*—Bo Holmstedt
*Members of the Panel*—John W. Daly
Efrén Carlos del Pozo
Evan C. Horning
Harris Isbell
Stephen I. Szara

Chairman Dr. Holmstedt: We have some questions from the audience, and I know that some of the participants are also prepared to elaborate upon what they have done themselves.

Perhaps we should start with Dr. Szara, who had the courage to use dimethyltryptamine as an experimental tool for the first time, and we would be glad if he would give us a description of the symptoms he observed.

Dr. Szara: I think the picture was very clear. We saw in Mr. Seitz's movie what the drugs can do, and how quickly; so I would rather like to give a little summary of what we have done in the past twelve years with dimethyltryptamine, and how we came to start using it. Actually it was when I first read an article by Fish, Johnson and Horning in the Journal of American Chemical Society 77, 5892 (1955). These authors have found N,N-dimethyltryptamine, together with bufotenine, in snuff powder prepared by Haitian natives from *Piptadenia peregrina* seeds which the natives used in their religious ceremonies. The psychotropic effect was blamed on bufotenine, but it was unknown whether dimethyltryptamine was hallucinogenic or not. So I decided to synthesize it, and then tried it out on myself and other volunteers and friends who were courageous enough to volunteer. It was not active orally. I started taking this compound in very small quantities up to 250 mgs, but it was inactive. Then we started giving it intramuscularly, doses of one mg/kg, which give a very fast and very strong reaction. This resembled very closely symptoms which were described by Dr. Freedman the day before yesterday about LSD, so I would rather just summarize those symptoms which are similar to those of LSD, and point out some striking differences.

The perceptual distortions are primarily visual in nature, and with closed eyes you can see illusions and color patterns, primarily geometrical patterns, moving very fast, having sometimes very deep emotional content and connotation.

There is an inability to keep attention focused on any outside task. It seems to be very difficult to maintain contact with reality, and this often leads to a panicky action. There is an enhanced dependence on the environment for structure and for symbolic meanings, and increased association and search for synthesis, as Dr. Freedman mentioned.

There are some dissimilarities, however, when you compare the effects of dimethyltryptamine with those from LSD. The main difference is the rapidity of the onset and the shortness of the duration of action. After being given an injection intramuscularly, the symptoms begin in two or three minutes, and they last for only about thirty to forty-five minutes, or a maximum of an hour, and then it is just hangover and nothing else. The effects of LSD and mescaline last for four, six, eight and sometimes twelve hours, depending on the dose and on the individual variations.

Some other minor differences exist. In dimethyltryptamine there are more primary visual hallucinations, light flashes, colors, abstract forms and figures with oriental designs. There is a consistently larger but short-lasting autonomic effect, consisting of increased blood pressure and dilated pupils. The rapid onset of the strange experience and the overwhelming loss of control can cause panic reaction much faster than other known longer lasting hallucinogens.

We have worked very extensively since this on the metabolism of dimethyltryptamine, and I don't know if now is the time to go into it. We have synthesized several compounds which are also hallucinogenic. They differ slightly in duration. They are slightly longer acting than dimethyltryptamine, and the autonomic reaction is slightly less.

We were interested in the metabolism of this compound, and we have suggested that 6-hydroxylation may be a way of producing a psychoactive metabolite. This has been questioned by Dr. Isbell and by some others, based on the work of 6-hydroxy-5-methoxydimethyltryptamine, which was supposedly metabolized and has been found inactive in the behavioral tests.

I have repeatedly stressed in the last couple of years that our data strongly supports the notion that the 6-hydroxy pathway is somehow involved, although not necessarily through the first, and the main metabolite, which has been found to be the 6-hydroxydialkyltryptamine. The data on which we rely for this judgent are primarily clinical, obtained first on normal volunteers, later on alcoholic patients, in double blind tests. These studies have shown strong correlation between the rate of 6-hydroxylation and the hallucinogenic action as measured by rating scales and psychological reports.

The other support for the role of 6-hydroxylation is the fact that if you prevent this pathway by substituting the 6-position by a fluorine, thus having a 6-fluorodiethyltryptamine, this compound has not been found to have hallucinogenic properties in patients. It does produce autonomic effects, pupillary changes, blood pressure changes; but it does not produce the drifting away into a dream world and other phenomena characteristic for the hallucinatory activity.

We have used these compounds mainly as tools in learning about the mechanism of action of this particular type of drug, in which there seems to be a very deep interest in psychiatry.

Perhaps I could mention some experiments with tritium-labeled dimethyltryptamine, which illustrate very nicely how quickly this compound penetrates the brain and reaches the area involved in the central nervous effects.

In one of the experiments we gave 10 mg/kg of DMT intraperitoneally to mice, the brain was taken out at various time intervals, and the small areas were analyzed by chromatography and scintillation spectrometry. In ten minutes you can get a maximum amount of unchanged DMT in the cortical areas, and slightly less in other areas which gradually subside, but some of the basic metabolites which contain the hydroxylated metabolite have a slightly different course, and reach different areas of the brain later in time, but not in the first couple of minutes.

This is just some of the data which we have not published yet, but we have done a lot of work combining these drugs with a precursor of serotonin, 5-hydroxytryptophan. In these experiments there seems to be a very delicate regional change in the serotonin metabolism, primarily the hypothalamus area, when we give hallucinogenic diethyltryptamine, but not when we gave the nonhallucinogenic, 6-fluoro analog.

We have published some of these data in the proceedings of a symposium on "Amines and Schizophrenia," (H. Himwich et. al., Editors: Amines and Schizophrenia, Pergamon Press, Oxford, New York, 1966).

I would like to stop now.

CHAIRMAN DR. HOLMSTEDT: Thank you.

The thing which I personally would like to know from the two psychiatrists on the panel is, what are the visual phenomena of these experimental patients? Do they have microptic and macroptic phenomena? Dr. Isbell.

DR. ISBELL: Do they have micropsia and macropsia? Yes, they do, and the same individual may have both, in rapid or alternating fashion, and this may involve not only extraneous objects and people, but also his own body image. He may feel that he is nine feet tall, and then he may shrink to a point where he begins to get worried that he is going to get so small that he will completely disappear. The same alterations in size will occur in the environment. The room gets very small or very big, and simultaneously there are distortions of shape, color; practically every kind of thing that you think of that would happen in the visual sphere does happen.

DR. KLINE: Are these alterations in part emotional, or do you think they are totally physiological?

DR. ISBELL: I can't answer you, Dr. Kline. Things will happen in the same man at almost one time, and you can sometimes get from the patients themselves very interesting explanations why these things happened.

DR. KLINE: Rinkle did some work with adrenolutin or adrenochrome in which the size of the person and the apparent distance from the observer was quite dependent, according to this report, on whether he liked the person or not. Some subjects even managed to see "through" certain people if they didn't like them. I have never heard any confirmation of this, and I was wondering whether it might not be an interesting subject for investigation.

DR. ISBELL: I have personally never been able to correlate any particular subjective experiences that a given individual has with anything, except if one has observed him under drug on a previous occasion, it is very likely that the same type of phenomena will be seen on the second occasion.

I think that I might speak a little bit about some of the tryptamines other than dimethyltryptamine. One of these is bufotenine. It has been said that bufotenine is not a psychotomimetic drug. I don't think we should say that.

The difficulty is that bufotenine is a drug that has extremely powerful and dangerous cardiovascular effects, and for that reason it is not possible to push the dose in man. Also, it would be difficult to differentiate whether psychotic reactions were due to central effects or to cardiovascular actions. Cardiovascular actions include hypertension and development of an arrhythmia which actually amounts to a ventricular standstill. The auricle does not beat, the beat drops out, and the ventricle takes over, and it is very frightening. Simultaneously with the hypertension and ventricular escapes, one sees spectacular cynanosis in the upper part of the body, similar to that which has been described in the carcinoid flush, which is presumably due to serotonin. So bufotenine is a difficult drug to work in man for this reason, and it would not be too surprising if it did not have some kind of a central action if it were possible to extract it out.

6-Hydroxydimethyltryptamine had no effect in a dose of 1 mg/kg in our subjects, in fact. In contrast, my subjects had spectacular reactions to dimethyltryptamine. My men spoke of taking trips long before this term came into general use. They used to say that with dimethyltryptamine, "You can go to the moon and get back in time for breakfast"—so, they went to the moon long before the rockets landed. I hope they left a flag up there, but the 6-hydroxy derivatives were without effect. The 5-methoxy congener, as Dr. Holmstedt said, has not been tested, and we are still awaiting animal pharmacology on it.

I think we are, perhaps, forgetting that the psilocybin and psilocyn found in the mushroom are derivatives of tryptamine and serotonin with the hydroxyl group in the 4-position. These drugs give us the same kind of effect as does DMT. They are somewhat longer acting, and slower to start.

One interesting thing is that the resemblance of the clinical phenomena one sees with dimethyltryptamine and LSD is very striking. If you get LSD daily you soon develop such a high grade of tolerance that one might as well be issuing water. Then, if you take people who are tolerant to LSD and test them with psilocybin and mescaline, you will find that they are markedly cross-tolerant. We were unable to show a high degree of cross-tolerance between dimethyltryptamine and LSD, so despite the similarity of chemical structure it may be that dimethyltryptamine and LSD may act by somewhat different mechanisms within the brain, although we cannot be sure of this. The only thing we can be sure of, is that there is no great degree cross-tolerance.

CHAIRMAN DR. HOLMSTEDT: I can mention that as far as the animal experiments undertaken with the 5-methoxy compound are concerned, they have shown it to have a very weak effect on the circulation. My statement that bufotenine was not a psychotomimetic agent was based on two things: First your own work, Dr. Isbell; secondly, that its solubility properties are such that it is not very likely to penetrate the blood-brain-barrier.



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We have several questions. One is from Dr. Kline, and he wants to know whether all alkylated tryptamines are psychotomimetic. I don't think anybody can answer that fully. Dr. Szara did, however, try out a number of them.

DR. SZARA: N,N-dibutyl- and N-monohexyltryptamines, which are higher homologues, were inactive in a few patients. There is no systematic study.

CHAIRMAN DR. HOLMSTEDT: Another question: Can these states be terminated with phenothiazine derivatives, as is the case with LSD and mescaline?

DR. SZARA: We never had to terminate it, because it is so short acting, it is over before you realize it happens.

CHAIRMAN DR. HOLMSTEDT: Question: "What ingredients in the snuff do you think caused the untoward side effects, based on similar experiments with purified chemical constituents?"

The answer to that is that the tryptamines themselves may very well cause the side effects, as pointed out by Dr. Szara.

Somebody also wants to ask Dr. Schultes a question: Why does he use the words "narcotic snuffs" or "hallucinogenic snuffs", and what is the difference? Do you want to answer that question, Dr. Schultes?

DR. SCHULTES: There are any number of definitions of the word "narcotic". Having had a classical education, I use it as it was coined from the Greek, meaning any substance that benumbs the central nervous system, whether ever so slightly or producing a comatose state. There is no one good definition of the term.

In this country, a substance is not a narcotic unless the Senate has declared it so. It has to be so declared under the Harrison Narcotics Act. For this reason, marijuana is not legally a narcotic. Then you have the popular and newspaper definition, meaning only the addictive and dangerous ones. Faced with this plethora of "definitions", I have decided to stay with the Greeks.

CHAIRMAN DR. HOLMSTEDT: Thank you, Dr. Schultes.

May we return again to the phenomena of micropsia and macropsia. It has been said—this is mostly Mr. Gordon Wasson, who is of the opinion that these drugs have played a very great role in religion (not only the Christian religion but previous religions as well)—that such things as the ideas of giants and dwarfs may have come from these intoxications.

Can I ask Dr. Del Pozo, who is very familiar with the Mexican literature on this subject, if there are any indications of these distortions of perception in the Mexican literature. In other words, do the Gods have any definite size?

DR. DEL POZO: The Chroniclers describe the different hallucinatory visions that the Aztec priests used to have. They ate the mushrooms because they thought that those visions would provide them with some information about the future, or about the interpretation of different facts, but I don't know of any paritcular descriptions of macropsia. They usually mention devils, figures and colors.

I had an experience, I would say a collective experience: We were working with mushrooms, and a group of young collaborators who joined to celebrate the birthday of one of them suddenly decided to go to the laboratory in the evening and eat mushrooms.

They were so worried about the effects that they called me at about three o'clock in the morning. All of them were very amused because of the color visions, the forms and things that appeared to them. They were talking one to another and saying: "Look at this yellow color, look at this green color". I am sure they were simultaneous, but more or less the same type of visions. This makes me believe that it is a physiological action, in which there is little influence of the psychological background. There were no reports of macropsia or any other deformation in size.

DR. SZARA: I would like to emphasize something here which has not been overlooked, but it has not been emphasized enough, and that is the tremendous importance of the set and the setting in determining the kind of reaction which a person can get. If you suggest to the subject that you are a little mouse or you are an amoeba, you feel like it, or if you suggest that he is God, he is powerful, then he will have macropsia—so that setting is very, very important. I think here what Mr. Seitz has referred to, this initiation ceremony during the taking of the snuffs—the father tells the son what to expect, what to hallucinate and what to experience—is apparently very much imbedded into the ritual use of these drugs.

DR. SCHULTES: You asked me to define "hallucinogenic", and I forgot to do so. I believe that the man who coined this very useful and definitive word is Mr. Wassén. I am happy to note that in this meeting the etymologically impossible word "psychedelic" has not frequently been used.

One of the "psychedelic giants" asked my advice when he planned to use the term *psychedelic* in the title of a journal. I pointed out that one does not, in coining an English word from Greek roots, make a combination with "e"; it is made with "o". The word then would have to be "psychodelic". He pointed out that *psycho* had acquired a very special meaning in English, and that it could not be used without intimating that specialized meaning. Still, with the many good terms available, this etymological error would seem superfluous.

CHAIRMAN DR. HOLMSTEDT: May I at this point ask Dr. Daly or Dr. Horning what one would expect from a chemical point of view, when the OH group in tryptamines sits in the 4, 5, 6 and 7 position? Would there be chemically important differences in these compounds?

DR. HORNING: We made an observation some years ago, which was never published, for the hydroxy compounds. I think it is very clear that the properties would be different both chemically and, I am sure, physiologically, with different positions of subtitution.

In the crystalline form, bufotenine has an ionic structure. However, by certain chromatographic techniques, it is possible to get a second form of bufotenine. I think that probably the second form has a phenolic amine (non-ionized) structure (Fig. 1) because of infrared spectroscopic evidence. It was obtained in the absence of polar solvents (a non-polar system was used).

I think it is fairly clear that in the ionized form, in a polar medium, the compound would not penetrate the blood-brain-barrier. This is one of the problems in talking about the 6-hydroxy compound, as Dr. Holmstedt said.

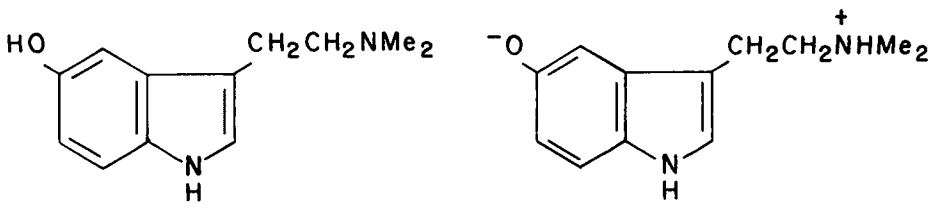


FIG. 1.

CHAIRMAN DR. HOLMSTEDT: Why would it necessarily be in the 6-position?

DR. HORNING: This recalls the argument over specific and non-specific hydroxylation. I think that the other isomers are formed, too, but they are hard to find.

At any rate, the 6-position hydroxylation is a well-defined reaction. This would be the expected compound. On the other hand, I would expect no action for this metabolite.

DR. SZARA: How about psilocybin?

DR. HORNING: The question of active transport and mechanism of penetration into a cell runs through many areas of chemistry and pharmacology. If one has a phosphate, there may be an active transport mechanism. Also, polar compounds including glucose enter the brain. "Active transport" exists, although we know very little about the mechanism.

DR. SZARA: Psilocin is a free hydroxy. It has no phosphate.

DR. HORNING: I would ask what your own view of this is, since you have studied it so extensively.

DR. SZARA: What my feeling is about the hydroxy derivatives is that they don't have to penetrate the brain all the way, entirely. It might be enough to penetrate only some trigger points, where the blood-brain-barrier is more leaky, like the hypothalamus or other areas which have been shown to be able to let larger molecules through. It might be enough for a hydroxy derivative to penetrate those areas and produce some very fine regional changes, and this is, I think, really what happens with the hydroxylated derivatives.

DR. HORNING: You may not need to postulate transport as such.

DR. SZARA: This is hypothesis, really. I might mention here that the 6-flurodiethyltryptamine is equally lipid soluble, and it penetrates the brain but is not hallucinogenic.

DR. HORNING: You feel that the 6-position is indeed critical?

DR. SZARA: It might be.

DR. HORNING: I have one other thing to say: Dr. Holmstedt has been a pionere in many ways, and one of the ways is in the chemical techniques he is using to deal with these compounds. It is possible to study all of the materials in small quantities by gas chromotography, and this is due largely to a whole series of developments, not the least of which was the development in Stockholm by R. Ryhage of the "molecule separator". This permits the use of gas chromatography and mass spectrometry in a combined fashion.

This is at present the most powerful chemical way we have of investigating substances. I think this work will point the way for both pharmacologists and chemists, and investigations may go faster in the future.

I will ask if Dr. Daly agrees with any of these comments?

DR. DALY: It may be that in 4-hydroxytryptamines such as psilocybin, the nitrogen and the phenolic hydroxy group may interact intramolecularly in such a way as to increase the lipid solubility over that of other hydroxytrytamines, and thus facilitate penetration into the brain. Again, while we assume that hydroxylation of tryptamines occurs only in the liver, we have no good proof that such hydroxylations do not take place in certain specific areas of the brain, in which case the hydroxytryptamine would be formed *in situ*, and would not have to penetrate the blood-brain-barrier.

In keeping with this idea, we thought to develop a sensitive assay for 6-hydroxylation based on the release of tritiated water from 6-tritiotryptamine on enzymatic hydroxylation. On studying this transformation with liver microsomes, we found that the tritium atom migrated to another position in the aromatic ring as a result of 6-hydroxylation. Similar migrations occur during the hydroxylation of other aromatic compounds, and cognizance of this unusual reaction should allow us to develop a sensitive and specific assay for the hydroxylation of tryptamines.

Regarding recent reports on hydroxylation of indoles in other than the 6-position, one finds that microsomal enzymes usually hydroxylate in positions of high electron density, so that for a 5-methoxyindole in which the electron density is higher in the 4- rather than the 6-position, one might expect preferential hydroxylation of the 4-position. We have done studies on microsomal hydroxylation of melatonin (5-methoxy-*N*-acetyltryptamine), and have isolated three products. The major product is 6-hydroxymelatonin, while one of the others has properties compatible with those expected of 4-hydroxymelatonin.

Our microsomal studies on hydroxylation of tryptamines support Dr. Szara's statement that the 6-fluorotryptamines do not undergo hydroxylation. Since 5-fluorotryptamines do undergo hydroxylation, to form what we believe is 5-fluoro-6-hydroxytryptamines, *in vivo* evaluation of the hallucinogenic properties of 5-fluoro-N,N-dimethyltryptamine would be of interest.

The 5-methoxy-N,N-dimethyltryptamine, found in plants and an active component of certain South American snuffs, also occurs in the skin of a certain toad. The presence of large amounts of this compound in these toads, and the occurrence in other toads of structurally related tricyclic indoles (dehydrobufotenine), led Dr. Witkop and myself to our present studies on O-methylnordehydrobufotenine, the cyclic analog of the 5-methoxy-N,N-dimethyltryptamine. This tricyclic indole prepared under the auspices of the Psychopharmacology Research Branch, NIMH, has CNS activity which is, however, markedly different from the open chain analog.

I would like to ask Dr. Holmstedt whether during his studies on the gas chromatographic and mass spectral analysis of snuffs, he also investigated the 4-methoxy, 6-methoxy and 7-methoxy-*N*,*N*-dimethyltryptamines, which would have virtually the same mass spectra as the 5-methoxy compound?

CHAIRMAN DR. HOLMSTEDT: That is right, but we have previously shown that the methoxy group was in the 5-position by using spectrofluorometric techniques and changing the pH of the solution; furthermore GLC resolves position isomers. This proves once more how advantageous the combination gas chromatrography-mass spectometry is.

DR. DALY: This might be worth looking at, whether other methoxy compounds occur which may not be separated in the snuffs and have hallucinogenic activity.

CHAIRMAN DR. HOLMSTEDT: Why has not anyone studied the 4-methoxy-N,N-dimethyltryptamine?

This session started out with anthropology, covered botany and pharmacology, and it now ends on a chemical note. I think it has been a good combination.

Thank you all.

# SESSION V

## AYAHUASCA, CAAPI, YAGÉ

**Daniel H. Efron,** ***Chairman***

# Psychotropic Properties of the Harmala Alkaloids

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*Department of Anthropological Medicine*
*University of Chile, Santiago, Chile*

The use of plant materials containing harmala alkaloids is probably very old. *Peganum harmala*, a zygophyllaceous plant, the seeds of which contain harmine (*1*), harmaline (*2*), and harmalol (*3*), is thought to be native to Russian Turkestan or Syria, and has been used throughout the Middle East both as a spice and as an intoxicant. Its medical and psychotropic properties are known in India, where it was probably taken by the Moslems, and where the seeds may now be purchased in bazaars (*4*). It is also believed that it was the Arabs who took the plant along the African Mediterranean and into Spain, where it may be found growing wild at present.

The species of *Banisteriopsis* that constitute a source of harmala alkaloids are used in an area lying between the rain forests of South America and the Andes. This is approximately the area designated as the "montaña" in the classification of South American cultures. It consists of a tropical elevated territory along the headwaters of the Amazon and Orinoco Rivers, where live some of the least known Indian groups.

Of much interest is the recent discovery of substances closely related to the harmala alkaloids in animals. One of these is adrenoglomerulotropine, a hormone of the pineal body, the chemical identity of which has been indicated as 2, 3, 4, 9-tetrahydro-6-methoxy-1-methyl-1H-pyrido(3, 4, 6)indole (*5*). This substance is identical to 6-methoxytetrahydroharman which has been shown to be formed *in vivo* from 5-methoxytryptamine and acetaldehyde (*6*). 6-Methoxytetrahydroharman is an isomer of tetrahydroharmine, one of the alkaloids in *Banisteriopsis* (*7*), and in the African *Leptactinia densiflora* (*8*). One more substance, 6-methoxyharmalan, has been shown to derive, at least *in vitro*, from melatonin (*9*), which in turn results from the methylation of acetylserotonin. The enzyme which makes this methylation possible, hydroxyindole-O-methyltransferase (HIOMT), has only been found in the pineal body. (See Fig. 1.)

6-Methoxyharmalan is an isomer of harmaline differing in the position of the methoxy group, which is attached to the same point of the ring as the phenolic group in serotonin or the methoxy group in ibogaine, a demonstrated hallucinogen (*10*). (See Fig. 2.)

As will be seen in the rest of the paper, I have found both synthetic 6-methoxyharmalan and 6-methoxytetrahydroharman to be hallucinogenic (*11*), a fact which invites speculation on the possible role of the metabolites on the psychoses. It is suggestive that the highest concentrations of serotonin have been found in the pineal glands of schizophrenics, and that 6-methoxyharmalan is a powerful serotonin antagonist.

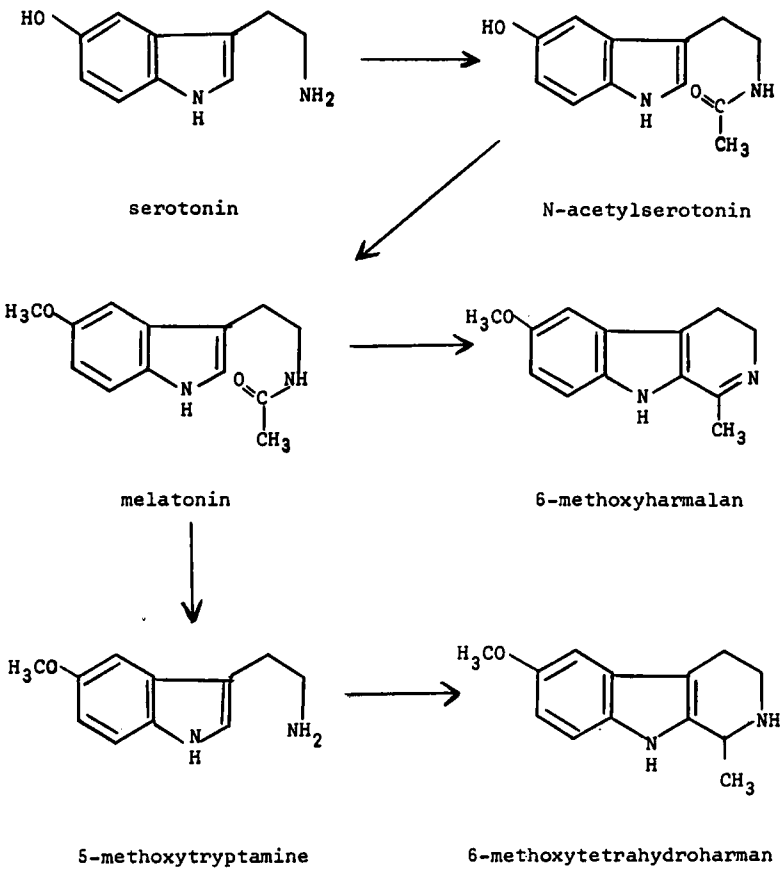
serotonin
N-acetylserotonin
melatonin
6-methoxyharmalan
5-methoxytryptamine
6-methoxytetrahydroharman

FIG. 1.

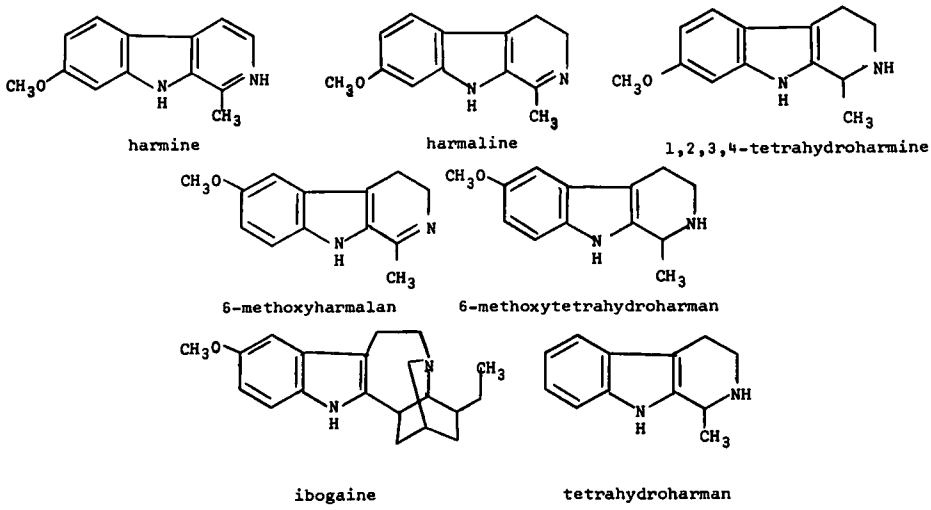
harmine
harmaline
1,2,3,4-tetrahydroharmine
6-methoxyharmalan
6-methoxytetrahydroharman
ibogaine
tetrahydroharman

FIG. 2.

It may be noted that the above reported finding constitutes the first demonstration of an endogenous hallucinogen, twenty years after the motion of a psychotoxic metabolite was proposed by Hoffer, Osmond and Smythies (*12*).

Lastly, one may wonder whether the pineal body—associated by Tibetan traditions with higher states of consciousness—may not actually play a part in the regulation of attention or the rhythm of sleep and wakefulness. An indirect indicated of this is the demonstration of increased pineal HIOMT activity in rats kept in constant darkness for six days (*13*).

Studies carried out some 30 years ago by Gunn et al., showed that some synthetic *beta*-carbolines had similar pharmacological properties, which in turn resembled those of quinine (*14*). Thus, both quinine and the harman derivatives were toxic to protozoa, inhibited the contraction of the excised muscle of the frog, caused relaxation of most smooth muscle, but contraction of uterine muscle, and caused convulsions followed by paralysis in mammals.

The only compound in this chemical group reported to have hallucinogenic properties, to my knowledge, is harmine (*15*), which may be regarded as identical to telepathine, yageine, and banisterine, and constitutes most of the alkaloid content in the *Banisteriopsis* extracts. Yet the question poses itself as to whether the qualitative similarity of harman derivatives, as evidenced by many pharmacological effects, would also apply to the psychological syndrome produced. For instance, Gunn finds that harmaline is twice as active as harmine, judging from the lethal doses of both compounds for the rabbit, and from their toxicity to protozoa. I have indeed found harmaline to be hallucinogenic at dosage levels above 1 mg./kg. i.v. or 4 mg./kg. by mouth, which is about one half the threshold level for harmine. It may be interesting to note at this point that the onset of effects of harmaline or other derivatives is about one hour after ingestion by mouth, but almost instantaneous after intravenous injection, if circulation time from elbow to brain is taken into account. In this, harmaline resembles the chemically related tryptamines and differs from the slow-acting phenylethylamines.

Tetrahydroharmine, the reduction product of harmaline, is another substance studied by Gunn and shown to be similar to its more saturated homologs, but three times less active than harmaline.

Racemic tetrahydroharmine, up to the amount of 300 mg. by mouth, was administered by us to one volunteer, who reported that at this dosage level there were subjective effects similar to those he experienced with 100 mg. of harmaline. More trials would be required to assess the mean effective dosage of tetrahydroharmine as a hallucinogen, but this single experiment suggests that racemic tetrahydroharmine is about one-third as active as harmaline, corresponding to Gunn's estimation on the basis of lethal dosage.

The effect of relocating the methoxy group of harmaline was not tested by Gunn but was of special interest here, in view of a possible function of the 6-methoxy homolog in the body. 6-Methoxyharmalan was indeed shown to be hallucinogenic, as was anticipated, subjective effects becoming apparent with approximate oral dosages of 1.5 mg./kg. The ratio between threshold doses of harmaline and its 6-methoxy analog is 3:2, 6-methoxyharmalan being the more active.

6-Methoxytetrahydroharman, probably identical with pineal adrenoglomerulotropine, was also shown to be psychoactive, eliciting mild effects at a dosage level of 1.5 mg./kg. The relative activities of the two 6-methoxyharmans are approximately 1:3, the harmalan being more active than its unsaturated homolog, which confirms once more Gunn's statement as to the relationship between double bonds and pharmacological effect.

It would seem premature to make any statement as to whether there is a qualitative difference in the subjective reaction to the different carbolines tested. Such appeared to be the case, in that experiences with the 6-methoxy compounds happened to be of a less hallucinogenic nature in the strict sense of the word, their effect being more akin to a state of inspiration and heightened introspection. Among the 7-methoxy compounds, harmaline seemed to cause more withdrawal and lethargy than harmine, but both substances showed a highly hallucinogenic quality in the visual domain. However, more systematic study would be needed to confirm differences such as these, in view of the variability which exists even between consecutive experiences of the same individual with the same chemical. This is well known for LSD–25, and was quite marked in four of the seven subjects to whom harmaline was administered more than once. Yet it seems clear that the various *beta*-carbolines are similar enough in their effect to be told apart from mescaline, as was shown by the comments of persons to whom mescaline, harmaline and some other harman derivative were administered on consecutive occasions. The third compound, the nature of which was not known to the experimental subjects, was invariably likened to harmaline rather than to mescaline. The same can be said of instances in which harmaline was administered on a second or third occasion without divulging the drug's identity. Regardless of the differences between consecutive harmaline experiences, these were classified together as distinct from that of mescaline.

It is quite possible that further research with a larger number of subjects may demonstrate qualitative differences of a subtle kind between the different carbolines, analogous to those shown for variously substituted phenylisopropylamines (*16*, *17*). Nevertheless, it may be adequate for the time being to regard the effects of harmaline as an approximately valid indication of a syndrome shared, with minor variations, by compounds of similar structure.

This information that I am presenting here on the effects of harmaline is based on the reactions of 30 volunteers to whom the drug was administered as a hydrochloride, either by mouth or intravenously, under standard conditions. One aspect of these was the absence of all information regarding effects other than those primarily psychological in nature.

As part of the interest lay in knowing the difference between the harmaline syndrome and that of mescaline, both drugs were administered to each volunteer on different occasions.

In the case of every one of the 30 subjects it was evident to the observer that both the subjective and behavioral reactions of the person were quite different for the two drugs, and this was corroborated without exception by the subjects themselves. Yet the quality of the difference was not clearly

the same in all instances, so that it is hard to find regularities to which no exception can be mentioned. Recurring differences between harmaline and mescaline can be observed however, and in what follows, the most salient of these are cited.

Physical sensations in general are more a part of the harmaline intoxication than of that produced by mescaline (or similar substances). Parasthesias of the hands, feet or face are almost always present with the onset of effects, and are usually followed by a sensation of numbness. These symptoms are most marked when the alkaloid is injected intravenously, in which case some subjects have likened them to those experienced under ether anesthesia. Distortions of the body image, which are quite frequent with mescaline or LSD–25, were very exceptional with harmaline. Instead, subjects indicated isolated physical symptoms such as pressure in the head, discomfort in the chest, or enhancement of certain sensations, as those of breathing or blinking.

Nausea was reported by 18 subjects and this sometimes led to intense vomiting. It was usually associated with dizziness or general malaise, which would in turn appear or disappear throughout a session in connection with certain thoughts or stimuli.

In the domain of perception, one of the most noticeable differences between the drugs is in the visual appearance of the environment. While distortions of forms, alterations in the sense of depth and changes in the expression of faces are of frequent occurrence under most hallucinogens, these phenomena were practically never seen with harmaline. The same was true in regard to color enhancement, or perception of apparent movement—flowers breathing, shapes dancing and so on—frequently seen with LSD–25. With harmaline, the environment is essentially unchanged, both in regard to its formal and its aesthetic qualities. Phenomena which most frequently occur with open eyes are the superposition of images on surfaces such as walls or ceilings, or the viewing of imaginary scenes simultaneously with an undistorted perception of surrounding objects. Such imagery is not usually taken for reality but there was an exception to this in the case of a man who saw a cat climbing a wall, then turning into a leopard, when in fact, not even the cat existed.

Other recurrent visual phenomena were a rapid lateral vibration in the field of vision and double or multiple contours in objects, especially when these were in motion or when the subject's eyes turned away from them. Some described lightning-like flashes.

With closed eyes, imagery was abundant and most often vivid and bright colored, with a predominance of red-green or blue-orange contrasts. Long dream-like sequences were much more frequent for harmaline than for mescaline. Certain themes, such as felines, negroes, eyes, and flying are frequent and have been reported elsewhere (*18*).

Perception of music was not altered or enhanced with harmaline as is the case with mescaline or LSD–25. Yet noises became very prominent and generally bothersome. Buzzing sounds in the head were reported by more than half of the subjects.

Synaesthesias were not reported, and the sense of time was unaltered.

Many of the differences between harmaline and mescaline may be related to the facts that the effect of the former on the emotions is much less than that of mescaline, and thinking is affected only in subtle ways, if at all. Concern with religious or philosophical problems is frequent, but there is not the aesthetic or emphathetic quality of the mescaline experience. Thus, the typical reaction to harmaline is a closed-eye contemplation of vivid imagery without much further effect than wonder and interest in its significance, which is in contrast to the ecstatic heavens or dreadful hells of other hallucinogens. Despite this lesser effect of harmaline on the intensity of feelings, qualitative changes do occur in the emotions, which may account for the pronounced amelioration of neurotic syptoms evidenced by 8 of our 30 subjects, as detailed in a separate report (*19*).

Desire to communicate is slight under the effect of harmaline, since other persons are felt to be a part of the external world, contact with which is usually avoided. Possibly related to this withdrawal is the extreme passivity which most subjects experienced in regard to physical movement. Most of them lay down for 4 to 8 hours and reported a state of relaxation in which they did not feel inclined to move a muscle, even to talk. In view of this observation, it is hard to understand how the Indians, according to some authors (*20*), engage in dancing or even whip one another under the effects of caapi.

Summing up, harmaline may be said to be more of a pure hallucinogen than other substances whose characteristic phenomena are an enhancement of feelings, aesthetic experiences, or psychotomimetic qualities such as paranoid delusions, depersonalization, or cognitive disturbances. Moreover, harmaline appears to be more hallucinogenic than mecaline (the most visually acting drug in its chemical group), both in terms of the number of images reported and their realistic quality. In fact some subjects felt that certain scenes which they saw has really happened, and that they had been as disembodied witnesses of them in a different time and place. This matches the experience of South American shamans who drink ayahuasca for purposes of divination.

The remarkable vividness of imagery viewed under the effect of harmaline, together with phenomena such as double contours and persistence of after images, had led us to suspect a peripheral, i.e. retinal, effect of the drug, and this was tested by the recording of electroretinograms in cats. The suspicion was confirmed, in that harmaline causes a definite increase in the alpha wave and a decrease in the beta wave of the electroretinogram, both of which become apparent before any change is observed in the brain cortex.

It would be beyond the scope of this paper to deal with electrophysiological studies, but I will briefly mention some recent results we have obtained in cat experiments at the University of Chile, which add to the general picture of the harmaline intoxication:

(1) Electrocorticograms recorded in chronically implanted cats showed either electrocortical desynchronization or synchronization in correspondence with the animal's behaviour, alternating between arousal and lethargy. In addition to this spindle bursts of high voltage and low frequency were observed in all instances and these did not seem to be related to the animal's behaviour.

(2) Experiments performed in cats with a chronically isolated forebrain showed even more clearly the above mentioned spindle bursts in the brain cortex, and regular wave bursts of high voltage in the pontine reticular formation, which we have not seen described under other pharmacological conditions. These cats were behaviourally overactive.

These facts may be interpreted as an indication that harmaline acts as a stimulant on the midbrain reticular formation. The direct action of harmaline on the brain cortex is hard to interpret and seems more that of a depressant, but this is counteracted in the intact animal by the arousing influence of the reticular formation. The neurophysiological picture matches well that of traditional yagé "dreaming", in that the state we have described involved lethargy, immobility, closed eyes and generalized withdrawal from the environment, but at the same time an alertness to mental processes, and an activation of fantasy.

## REFERENCES


(*1*) Goebel, Annalen, 38, 363, 1841.
(*2*) Fritsche, Annalen, 64, 365, 1847.
(*3*) Fischer, O., Chem. Soc. Abstr., 1901 (i), 405.
(*4*) Maxwell, M. M. "Caapi, its source, use and possibilities." Unpubl. MS., 1937.
(*5*) Farrel, G. and W. M. McIsaac, "Adrenoglomerulotropin." Arch. Biochem. Biophys., 94 : 443–544, 1961.
(*6*) McIsaac, W. M. "Formation of 1-methyl-6-methoxy-1,2,3-tetrahydro-2-carboline under physiological conditions." Biochem. Biophys. Acta 52 : 607–609, 1961.
(*7*) Hochstein, F. A. and A. M. Paradies. "Alkaloids of Banisteria Caapi and Prestonia Amazonicum." J. Am. Chem. Soc. 79, 5735, 1957
(*8*) Paris, R. R., F. Percheron, J. Manlil and Goutarel. Bull. Soc. Chim. France, 750, 1957.
(*9*) McIsaac, W. M., P. A. Khairallah and I. H. Page. "10-methoxyharmalan, a potent serotonin antagoinist which affects conditioned behaviour." Science 134, 674–675, 1961.
(*10*) Naranjo, C. Psychological effects of Ibogaine. In preparation.
(*11*) Naranjo, C. and A. Shulgin. Hallucinogenic properties of a pineal metabolite : 6-methoxytetrahydroharman. Science. In press.
(*12*) Hoffer, A., H. Osmond and J. Smythies. "Schizophrenia : a new approach II." J. Ment. Sci., 100 : 29–45, 1950.
(*13*) Axelrod, J., R. J. Wurtman, and S. Snyder. "Control of hydroxyindole-O-methyltransferase activity in the rat pineal gland by environmental lighting." J. Biol. Chem. 240 : 949–954, 1965.
(*14*) Gunn, Arc. Int. Pharmacodyn., 50, 793, 1935.
(*15*) Pennes, H. H., and P. H. Hoch, Am. J. Psychiat. 113, 885, 1957.
(*16*) Shulgin, A., T. Sargent and C. Naranjo. "Chemistry and psychopharmacology of nutmeg and related phenylisopropylamines." Paper presented at the Symposium "Ethnopharmacologic Search for Psychoactive Drugs." U. of Calif., S. F., 1967.
(*17*) Naranjo, C. MMDA in the facilitation of psychotherapy. Book in preparation.
(*18*) Naranjo, C. "Psychological aspects of the yagé experience in an experimental setting." Paper presented at the Annual Meeting of the American Anthropological Association, 1965.
(*19*) Naranjo, C., Ayahuasca, the Vine of the Dead. Book in preparation.
(*20*) Taylor, N., Flight from Reality. 1949.
(*21*) Villiblanca, J., C. Naranjo, and F. Riobó. Effects of harmaline in the intact cat and in chronic isolated forebrain and isolated hemisphere preparations. Psychopharmacologia. In press.

# The Making of the Hallucinogenic Drink from Banisteriopsis Cuapi in Northern Peru

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A moving-picture film showing the ceremonies and procedures for the preparation of the drink was presented.

# Chemical Compounds Isolated from Banisteriopsis and Related Species

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The Malpighiaceae, to which the genus *Banisteriopsis* belongs, is a family distributed in tropical and sub-tropical humid regions of Africa and America. The genus *Banisteriopsis* is represented by about 75 species, which grow in America from Mexico and Cuba to Argentina, most of them in South America (*1*).

Only a few species of *Banisteriopsis* have been investigated chemically, and the first stimulus for the chemical work was the finding in the middle of the last century by the British explorer Spruce that a woody vine, which he classified as *Banisteria caapi*, later known as *Banisteriopsis caapi*, was the main ingredient employed in the preparation of an intoxicating drink by certain tribes living in the Amazonian Brazil. It was later found that the preparation and use of a similar beverage extended to a larger region, to what is today known as the eastern parts of Colombia, Ecuador, Perú and Bolivia, where it was given different vernacular names: ayahuasca, caapi, yagé, yajé, natem, natema, etc., names which were also applied to the plants employed for their preparation. Other plants were added and mixed with the former.

The history of the botanical, chemical and pharmacological implications of the beverage has been told in several opportunities and from several angles (*2*, *3*). While at the beginning there were difficulties in the identification of the alkaloids isolated from the extracts of the plants, and which were made responsible for the activity of the intoxicating drink, it seems that today, with the improvement of the methods of identification and the use of new techniques, we know exactly which are the bases isolated. There seem to be more difficulties from the botanical side. The lack in many chemical studies of plant specimens, or of a rigorous identification of the botanical material worked by the chemists, makes it impossible to know exactly which were the species employed. It is with this qualification that some of the botanical names are quoted in this paper.

Early chemical investigation of the plant employed in Colombia by the natives indicated the presence of an alkaloid which was given the name of telepathine as early as 1905 by Zerda Barron (*4*). A base supposed to be responsible for the activity of the drink was isolated in 1923, no doubt in impure form, by Fischer Cardenas (*5*) who conserved the name of telepathine.

Another isolation was carried out two years later by Barriga Villalba (*6*), who seems to be the first who obtained a crystalline product, to which he gave the name of yajéine. From the assigned formula, $C_{14}H_8N_3O_3$ and from its m.p.206°, we have now to conclude that it was an impure substance, al-



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though the lack of rotation is in agreement with what can be expected for an aromatic β-carboline structure. Another base was present in the mother liquors and named yajénine, but no constants were mentioned in the paper. According to Barriga Villalba, he worked the stems of a vine which was known by the vernacular name of yajé, and which according to Reinburg was *Haemadictyon amazonicum* (*Prestonia amazonica Spruce*), which is an Apocynaceae. Rios, in his review on the ayahuasca, mentions that in a later paper, Barriga Villalba states (*7*) that the plant he worked was not *P. amazonica*, but *B. caapi*, which is in agreement with the investigations of Schultes and Raffauf (*8*) on the use of the former species as a narcotic.

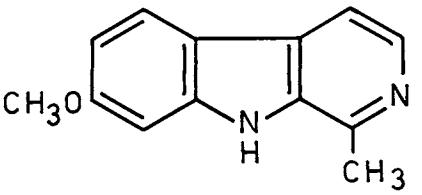
From what can be considered an authentic specimen of *B. caapi*, Perrot and Raymond-Hamet (*2*) isolated for the first time in pure condition one of the bases present in the plant (m.p.258°), for which they conserved the name of telepathine. A year later Lewin (*9*) described the isolation of an alkaloid from the same source, which he called banisterine. In his paper, Lewin says that the chemists from E. Merck (Darmstadt, Germany), considered banisterine identical to the base harmine (*I*), an alkaloid isolated more than a century ago from *Peganum harmala* L. (Zygophyllaceae). Two papers on the identification were published the same year almost simultaneously; one by Elger (*10*) and the other by Wolf and Rumpf (*11*), the latter workers being members of the Merck laboratories.

Elger employed plant material supplied by Raymond-Hamet and which was identified as *B. caapi*, according to A. W. Hill, then Director of the Kew Botanical Gardens. Sir Robert Robinson compared the alkaloid isolated by Elger (m.p.263–264°), with the harmine (*I*) from *P. harmala*, and with a synthetic sample, and concluded that they were identical. He comments on the difficulties of purifying harmine, which can explain the low melting point of the base obtained by Barriga Vallalba. Chen and Chen (*12*), who worked also with an authentic botanical specimen, confirmed the identification, and could isolate harmine from stems, leaves and roots.

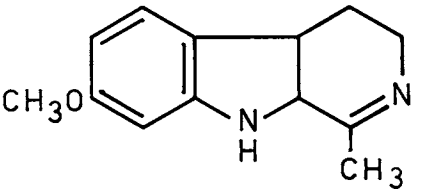
A plant identified as *B. caapi* Spruce was investigated many years later by Hochstein and Paradies (*13*). It was harvested near Iquitos, in Peru, where it was named ayahuasca. They confirmed the presence of harmine (I) and isolated also harmaline (II) and (+)-tetrahydroharmine (III). They state that the two latter alkaloids were found in a rather large amount. The same bases were also present in an aqueous extract of the plant "as used by the natives" but which appeared richer in harmaline and tetrahydroharmine than the extracts of the plant. They suggested that these two alkaloids may be the most active psychotomimetic components of the extracts.

All the bases isolated from *B. caapi* have a β-carboline skeleton, with different degrees of hydrogenation in the pyridine ring. Their structure was already known because of the interest of the chemists in similar alkaloids isolated from *P. harmala L.*, harmine (I) and harmaline (II), which culminated in the synthesis of harmaline (II) by Manske, Perkin and Robinson (*14*).

Although the racemic tetrahydroharmine had already been prepared in the laboratory, it was the first time that one of the enantiomers, (+)-tetra-




(I)

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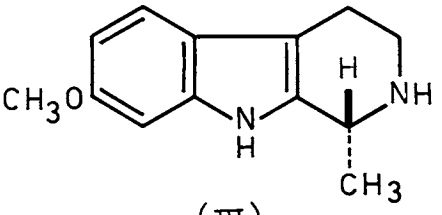


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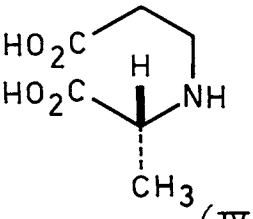


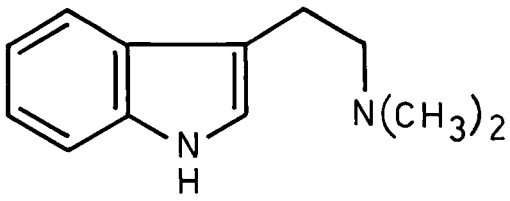

(IV)

hydroharmine (III), had been found in Nature. The dextro compound isolated by Hochstein and Paradies (*13*) was in fact a new natural base, and because of its pharmacological activity it was of interest to determine its absolute configuration. This was done recently by Koblicová and Trojánek (*15*), who found that its asymmetric carbon atom has the same chirality as the asymmetric carbon of D-alanine (IV), which is opposite to that of the protein aminoacid L-alanine.

Another species investigated has been *B. inebrians* Morton. O'Connell and Lynn (*16*) isolated harmine (I) from the stems of an authentic specimen collected by Schultes, and found that the leaves probably contains the same base. They could not detect harmaline nor harmalol. The same species was worked again by Poisson (*17*) in 1965, the plant being collected in a place named Nazareth, on the shores of the Marañon River, in Perú. He confirmed the presence of harmine in the stems and pointed out that another base, with the chromatographic properties of harmaline (II), was present in small amount.

Poisson investigated also the leaves of another species, *B. rusbyana* (Niedenzu) Morton, known to the natives as yajé, which were added to the stems of *B. inebrians* when ayahuasca was prepared. Surprisingly, this species did not contain alkaloids with a β-carboline structure, and the only base which he could identify was dimethyl-tryptamine (V). The amount was rather high (0.64%).

The species worked by Poisson were identified by Cuatrecasas. The finding of dimethyltryptamine (V) in *B. rusbyana*, a species used together with *B. inebrians* for the preparation of ayahuasca, is interesting for several reasons. One is that the same base was isolated by Hochstein and Paradies (*13*) from the extract of a plant which they considered to be *P. amazonica*, which received the local name of yagé, and which was used by the natives




(V)

to prepare ayahuasca as an additional component to *B. caapi*. Hochstein and Paradies received only an extract of the plant, whose identification is doubtful (*8*, *18*).

The second point of interest is that bases of the tryptamine type are typical components of other plants which have been used by the natives in many places of South America and in the Caribbean, for the preparation of intoxicating snuffs. They belong to the *Piptadenia* (Leguminosae) (*19*) and *Virola* (Myristicaceae) genus (*20*).

Other *Banisteriopsis* species have been mentioned as the main or additional ingredients employed in the preparation of ayahuasca. They are *B. quitensis* (Ndz) Morton (*21*), which according to Cuatrecasas (*1e*) is identical to *B. caapi* Spruce, *B. longialata* (*21*), and *B. metallicolor* Juss. (*B. lutea* Ruiz) (*3*).

I have not found in the literature any indication that authentic specimens of those plants have been submitted to chemical research, but because they are used in the preparation of intoxicating drinks, their investigation will be of much interest.

On the other hand, *B. crysophylla* Lam. a species which grows in Australia, is reported to contain alkaloids (*22*) and *B. nitrosiodora* Griseb, which is one of the species found in Argentina, is practically devoid of alkaloids (*23*). There remain a large number of species which have not even been submitted to a preliminary chemical investigation.

Harmine (I) has been isolated by Mors and Zaltzman (*24*) from the stems and leaves of another South American Malpighiaceae, *Cabi paraensis* Ducke, which is closely related to the *Banisteriopsis* genus. It grows in Brazil, in the upper Amazonian region and also in Perú (*3*). According to Duke (*25*), it is employed in popular medicine, although not for the preparation of intoxicating drinks.

It is worthwhile to note that only a few other species of Malpighiaceae have been investigated for alkaloids. One of them is *Lophantaera lactecens* (*L. longifolia*) which grows in the Amazonian, and is employed for the preparation of a kind of tea. Ribeiro and Machado (*26*) isolated from extracts of that plant a new base, lophanterine, which structure is unknown.

In his review on the Botanical Sources of the New World narcotics, Schultes (*21*) mentions in relation with the preparation of ayahuasca, two Malpighiaceae which, if botanical material became available, will deserve chemical attention. They are *Tetrapterys methystica*, from which an halluci-

nogenic drink is prepared in Colombia, on the limits of Brazil, and *Mascagnia psilophylla* var. *antifebrilis*, which was pointed out by Niedenzu as a source for the preparation of ayahuasca which in the opinion of Schultes is doubtful.

To my knowledge harmine (I), harmaline (II) and tetrahydroharmine (III), have never been isolated from other original American plants. They have been found to be present in intoxicating snuffs prepared by the natives from unknown botanical sources. We have two almost simultaneous reports. One is by Biocca, Galeffi, Montalvo and Marini-Bettolo (*27*), who from a snuff prepared by Tukano and Tariana Indians living in the valley of the Uaupes River, isolated harmine (I), harmaline (II) and tetrahydroharmine (III), exactly the same bases found in *B. caapi* by Hochstein and Paradies (*13*). According to the Italian authors, the snuff is named paricá and is prepared from a vine, which is also employed for the preparation of a drink. The species remained undetermined.

On the other hand, Bernhauer (*28*), has investigated a snuff employed by the Surara and Pakidai Indians, living near the River Demeni, a subsidiary of the Negro River, which he says is known as paricá, yopo, ebená or epená. He could isolate harmine (I) and (+)-tetrahydroharmine (III), while harmaline (II) was absent. The series of names given by Bernhauer to the drug that he investigated, shows how confused is its identification because samples of snuffs named epená, which were investigated not long ago by Holmstedt (*20*) and Marini Bettolo, Delle Monache and Biocca (*29*), contained only tryptamine bases. In my opinion this is a nice proof of the importance of the future interdisciplinary work, which is needed to clarify the botanical sources and the chemically active substances in the plants and in the drugs prepared by the natives.

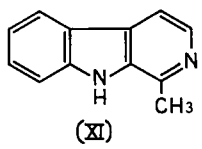
Both types of bases isolated from *Banisteriopsis* species are related to tryptamine. Tryptamine or a precursor, is one of the intermediates in the biogenesis of a large number of indole alkaloids, most of them with a more elaborate structure than the simpler β-carboline bases.

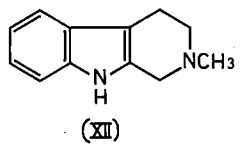
The type and distribution of the simple tryptamine bases found in plants have been recently reviewed (*30*). Work done in several laboratories in recent years have shown that bases with a typical β-carboline structure are also, like the tryptamines, not restricted in botanical or geographical distribution (see Table I).

The earlier representatives were isolated from *Peganum harmala* L. (Zygophyllaceae) more than a hundred years ago: harmaline (II) (1841), and harmalol (XVIII) (1841). The simplest base, harman (XI), was isolated from a Rubiaceae growing in Brazil in 1861 (*Arariba rubra* Mart., *Sickinga rubra* K. Schumm), and a few years later (1878) from *Symplocos racemosa* (Symplocaceae), indigenous to India.

Research in the last few years has lead to the isolation of other β-carbolines from plants growing in America. Bächli *et al.* (*31*), were isolated from *Strychnos melinoniana* Baill. (Loganiaceae), the quaternary base which is known as melinonine-F (XIV), and Antonaccio and Budzikiewicz (*32*)

TABLE I. OTHER β-CARBOLINE BASES FOUND IN PLANTS[a]


(XI)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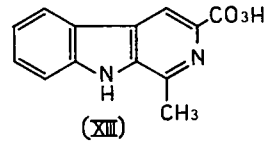
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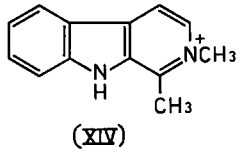
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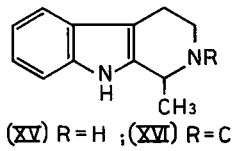
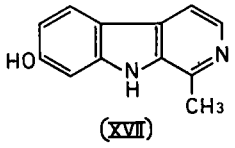
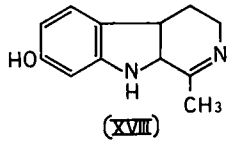
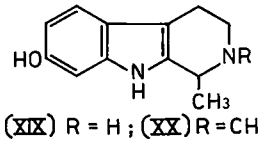

(XV) R=H ; (XVI) R=CH3


(XVII)


(XVIII)


(XIX) R = H ; (XX) R=CH3

(XI) Harman. *Peganum harmala* L. (Zygophyllaceae) ; *Passiflora* spp. (Passifloraceae) (*39*) ; *P. incarnata L.* (*40, 41*) ; *Calligonum minimum* Lipski (Polygonaceae) (*42*).

(XII) *N*-Methyl-tetrahydro-β-carboline. *Hammada leptoclada* M. Iljin (*Arthrophytum leptocladum* Popov) (Chenopodiaceae) (*43*).

(XIII) Harman-3-carboxylic acid. *Aspidosperma polyneuron* Müll. Arg. (Apocynaceae) (*32*).

(XIV) Melinonine F. *Strychnos melinoniana* Baillon (Loganiaceae) (*31*).

(XV) Tetrahydroharman, elaeagnine (R=H). *Petalostyles labicheoides* R. Br. (Leguminosae) (*44*) ; *Elaeagnus angustifolia* L. (Elaeagnaceae) (*45*) ; *Leptactina densiflora* Hook. f. (Rubiaceae) (*38*) ; *Hammada leptoclada* M. Iljin (*46*) ; *Calligonum minimum* Lipski (*42*).

(XVI) *N*-Methyl-tetrahydroharman, leptocladine (R=$CH_3$). *H. leptoclada* M. Iljin (*43*) ; *Acacia complanata* A. Cunn. (Leguminosae) (*47*).

(XVII) Harmol. *P. incarnata* L. (*40*) ; *Zygophyllum fabago* L. (Zygophyllaceae) (*48*).

(XVIII) Harmalol. *P. harmala L.*

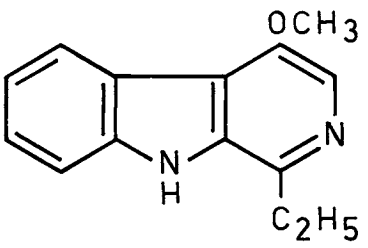
(XIX) Tetrahydroharmol (R=H). *Elaeagnus angustifolia* L. (*49*).

(XX) *N*-Methyl-tetrahydroharmol (R=$CH_3$). *E, angustifolia* L. (*49*).

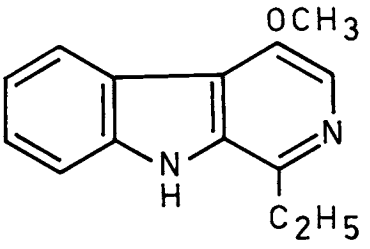
[a] This list of species is not exhaustive. They have been selected to show the distribution of bases in different families.

harman-3-carboxilic acid (XIII) from *Aspidosperma polyneuron* Müll. Arg. (Apocynaceae).

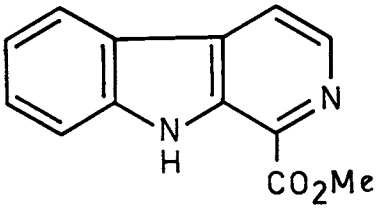
Recently, in our laboratory Sanchez and Comin (*33*), found β-carbolines in *Aeschrion crenata* Vell., a Simaroubaceae which grows is Southern Brazil, Paraguay and Argentina. Although it is used in popular medicine, there is no indication that its extracts have intoxicating properties. The bases crenatine (VI) and crenatidine (VII) were isolated, together with 1-carbomethoxy-β-carboline (VIII), which has been formerly found in *Pleiocarpa mutica* Benth. (Apocynaceae) (*34*).




(VI)




(VII)



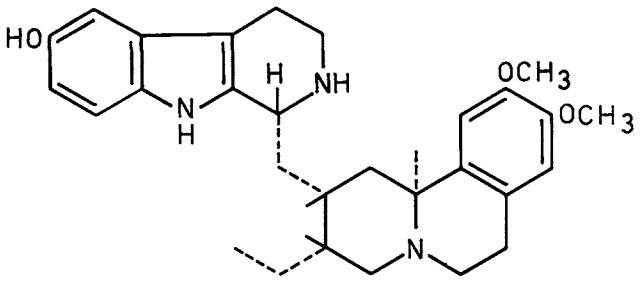

(VIII)

A β-carboline alkaloid with a more elaborated, novel type of structure, was isolated also in our laboratory by Brauchli *et al* (*35*), from *Pogonopus tubulosus* (DC) Schum. a Rubiaceae which grows in the Central and Northern part of Argentina, where in some places it is employed against fever. The base was named tubulosine (IX), and is structurally related to emetine (X) the tetrahydroisoquinoline moiety of the latter alkaloid being replaced by a β-carboline. Bases with this typical skeleton have been latter identified in *Alangium lamarckii* Thw. (Alangiaceae) (*36*) and in *Cassinopsis ilicifolia* Kuntze (Icacinaceae) (*37*).

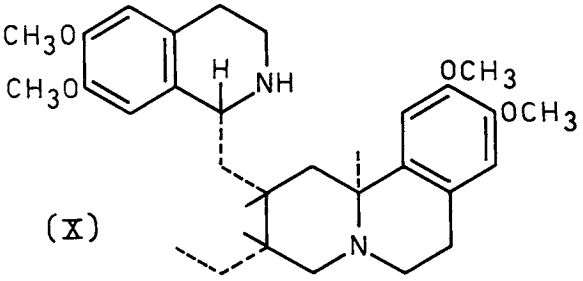
It is of interest to note that besides *P. harmala*, the typical β-carbolines present in the *Banisteriopsis* species, have been isolated from a few species indigenous to other continents. In an African Rubiaceae, *Leptactine densiflora* Hook (±)-tetrahydroharmine (leptaflorine) (III) have been found (*38*). *Passiflora incarnata* L. and possible other *Passiflora* species (Passifloraceae) (*39*), contain harmine (I), which has also been found in *Zygophyllum fabago*, (*48*).

Other simple β-carbolines closely related in structure to the *Banisteriopsis* alkaloids have been isolated from other plants. They are listed in Table I with an indication of the source of isolation.

Many of the species containing β-carboline alkaloids have been used in popular medicine and several of the bases isolated have been submitted to pharmacological studies, and a few of them even employed in therapeutics. But outside America, so far as I know, plants containing those alkaloids have not been employed for their hallucinogenic properties.




(IX)




(X)

## BIBLIOGRAPHY


(*1*) (*a*) NIEDENZU, F. in A. Engler and K. Prandl, *Die Naturlichen Pflanzenfamilien*, III, 4: 41–74. Leipzig, W. Engelmann, 1896. (*b*) NIEDENZU, F. in A. Engler, *Das Pflanzenreich*, IV, 141. Leipzig, W. Engelmann, 1928. (*c*) O'DONELL, C. A., and A. LOURTEIG. Malpighiaceae Argentinae. Lilloa, 9: 221–316, 1943. (*d*) PEREIRA, E., Contribuçao ao Conhecimento da familia Malpighiaceae. Arquiv. Servic. Forestal (Rio de Janeiro). 7: 11–70, 1953. (*e*) CUATRECASAS, J., Prima flora Colombiana. Webbia, 13: 343–664, 1957/1958.

(*2*) PERROT, E., and RAYMOND-HAMET. "Yagé, Ayahuasca, Caapi et leur alcaloïde: telepathine ou yagéine." Bull. Scienc. Pharmacol., 34: 337–347, 417–426, 500–514, 1927.

(*3*) RIOS, O. "Aspectos preliminares al estudio Farmaco-Psiquiátrico del Ayahuasca y su Principio Activo." Anales Fac. Med. Univ. Nacl. Mayor San Marcos, Lima. 45: 22–66 (1962). Chem. Abstr. 59: 3215, 1963.

(*4*) ZERDA BARRON, B. Quoted by E. Perrot and Raymond-Hamet in reference (*2*) and by O. Rios and reference (*3*).

(*5*) FISCHER CÁRDENAS G. "Estudio sobre el principio áctivo del Yagé." Thesis, Fac. Medic. Cienc. Natural. Bogotá, 1923. Quoted by E. Perrot and Raymond-Hamet in reference (*2*) and by O. Rios in reference (*3*).

(6) BARRIGA VILLALBA, A. M. "Yajéine. A new alkaloid." J. Soc. Chem. Ind. 44: 205–207, 1925.

(7) BARRIGA VILLALBA, A. M. El yagé. Bebida especial de los indios ribereños del Putumayo y el Amazonas." Bol. Lab. Semper-Martinez, N° espec. 9, 1927. Quoted by O. Rios in reference (*3*).

(*8*) SCHULTES, R. E., and R. F. RAFFAUF. "*Prestonia:* An Amazon narcotic or not." Bot. Museum Leafl. Harvard Univ., 19: 109–122, 1960.

(*9*) LEWIN, L. "Sur une substance enivrante, la banisterine, extraite de *Banisteria caapi.*" Compt. Rend., 186: 469–471, 1928.

(*10*) ELGER, F. "Ueber das Vorkommen von Harmin in einer südamerikanischen Liane (Yagé)." Helv. Chim. Acta, 11: 162–166, 1928.

(*11*) WOLFE, O., and K. RUMPF. "Ueber die gewinnung von Harmin aus einer südamerikanischen Liane." Arch. Pharm., 266 : 188–189, 1928.

(*12*) CHEN, A. L., and K. K. CHEN. "Harmine, The Alkaloid of *Caapi*." Quart. J. Pharm. Pharmacol., 12 : 30–38, 1939.

(*13*) HOCHSTEIN, F. A., and A. M. PARADIES. "Alkaloids from *Banisteria caapi* and *Prestonia amazonicum*." J. Am. Chem. Soc., 79 : 5735–5736, 1957.

(*14*) MANSKE, R. H. F., W. H. PERKIN, and R. ROBINSON. "A synthesis of harmaline." J. Chem. Soc., 1–14, 1927.

(*15*) KOBLICOVÁ, Z., and J. TROJÁNEK. "The Absolute Configuration of (+)-1,2,3,4-Tetrahydroharmine." Chem. Ind. (London) 1342, 1966.

(*16*) O'CONNELL, F. D., and E. V. LYNN. "The Alkaloid of *Banisteriopsis inebrians* Morton." J. Am. Pharm. Assoc., 42 : 753–754, 1953.

(*17*) POISSON, J. "Note sur le 'Natem' boisson toxique péruvienne et ses alcaloïdes." Ann. Pharm. Franc., 23 : 241–244, 1965.

(*18*) RAFFAUF, R. F., and M. B. FLAGLER. Alkaloids of the Apocynaceae. Econ. Botany, 14 : 37–55 (1960).

(*19*) DEULOFEU, V. "Chemical Aspects of American Medicinal Plants." Lecture, III Internat. Pharmacol. Congress. Sao Paulo, Brazil, July 24–30, 1966.

(*20*) WASSÉN, S. H., and B. HOLMSTEDT. "The use of paricá, an ethnological and Pharmacological review." Ethnos, 5–45, 1963. Holmstedt, B., Tryptamine derivatives in epená, an intoxicating snuff used by some South American indian tribes. Arch. Intern. Pharmacodyn., 156 : 285–305, 1965.

(*21*) (*a*) SCHULTES, R. E. "The identity of the Malpighiaceous narcotics of South America." Bot. Museum Leafl. Harvard Univ., 18 : 1–56, 1957. (*b*) SCHULTES, E. R. "Botanical Sources of the New World Narcotics." Psychedelic Rev., 1 : 145–166, 1963. (*c*) SCHULTES, R. E. "Ein halbes Jahrhundert Ethnobotanik amerikanischer Halluzinogene." Planta Medica, 13 : 125–157, 1965.

(*22*) WEBB, L. J. Australian Phytochemical Survey. Part I, Bulletin 241. Melbourne, CSIRO, 1949. pag. 34.

(*23*) Unpublished results from our Laboratory.

(*24*) MORS, W. B., and P. ZALTZMAN. "Sobre o alcaloide da *Banisteria caapi* Spruce e do *Cabi Paraensise* Ducke." Bol. inst. quim. agr. (Rio de Janeiro) N° 34 : 17–27, 1954. Chem. Abstr., 49, 14906, 1955.

(*25*) Quoted by Mors and Zaltzman in reference 24.

(*26*) RIBEIRO, O., and A. MACHADO. Lophanterine, a new alkaloid. Anais assoc. quím. Brasil, 5 : 39–42, 1946. Chem. Abstr., 41, 3109, 1947.

(*27*) BIOCCA, E. C. GALEFFI, E. G. MONTALVO, and G. B. MARINI-BETTOLO. "Sulle sostanze allucinogene impiegate in Amazonia. Nota I. Osservazioni sul Paricá dei Tukâno e Tariâna del bacino del Rio Uaupés." Ann. Chim. (Roma), 54 : 1175–1178, 1964.

(*28*) BERNHAUER, K. "Notiz ueber die Isolierung von Harmin und (+)-1,2,3,4-Tetrahydro-harmin aus einer indianischen Schupfdroge." Helv. Chim. Acta., 47 ; 1075–1077, 1964.

(*29*) MARINI-BETTOLO, G. B., F. DELLE MONACHE, and E. BIOCCA. "Sulle sostanze allucinogene impiegate in Amazonia. Nota II. Osservazioni sull'Epená degli Yanoáma del bacino del Rio Negro e dall'Alto Orinoco." Ann. Chim. (Roma), 54 : 1179–1186, 1964.

(*30*) STOWE, B. R. "Occurrence and Metabolism of Simple Indoles in Plants." Prog. Chem. Org. Nat. Prod., 17 : 248–297, 1959. Saxton, J. E. The Simple Bases. In R.H.F. Manske, The Alkaloids, Vol. 8 : 1–25. New York, Academic Press, 1965.

(*31*) BÄCHLI, E., C. VAMVACAS, H. SCHMID, and P. KARRER. "Uber die Alkaloide aus der Rinde von *Strychnos melinoniana* Baillon." Helv. Chim. Acta, 40 : 1167–1187, 1957.

(*32*) ANTONACCIO, L. D., and H. BUDZIKIEWICZ. "Harman-3-carbonsäure ein neues Alkaloid aus *Aspidosperma polyneuron*." Monatsh. Chem., 93 : 962–964, 1962.

(*33*) SANCHEZ E. and J. COMIN. Unpublished results.

(*34*) ACHENBACH, H., and K. BIEMANN. "Isotuboflavine and Norisotuboflavine. Two new Alkaloids Isolated from *Pleiocarpa mutica*." J. Am. Chem. Soc., 87: 4177–4181, 1965.

(*35*) BRAUCHLI, P., V. DEULOFEU, H. BUDZIKIEWICZ, and C. DJERASSI. "The Structure of Tubulosine, a Novel Alkaloid from *Pogonopus tubulosus* (DC.) Schumann." J. Am. Chem. Soc., 86: 1895–1896, 1964.

(*36*) PAKRASHI, S. C. "Indian Medicinal Plants XI. A new Alkaloid from the root bark of *Alangium lamarckii*." Indian J. Chem., 2: 468, 1964.

(*37*) MONTEIRO, H., H. BUDZIKIEWICZ, C. DJERASSI, R. R. ARDT, and W. H. BAARSCHERS. "Structure of Deoxytubulosine and interconversion with Tubulosine." Chem. Comm., 317–318, 1965.

(*38*) PARIS, R. R., F. PERCHERON, J. MAINIL, and R. GOUTAREL. "Alcaloïdes du *Leptactina densiflora* Hook." f. Bull. Soc. Chim. France, 780–782, 1957.

(*39*) NEU, R. "Inhaltssoffe der *Passiflora incarnata*. 3. Mitt." Arzneimittel-Forsch., 6: 94–99, 1956.

(*40*) LUTOMSKI, L. "Isolation of the major alkaloids from *Passiflora incarnata* L." Biul. Inst. Roślin Leczniczych. 6: 209–219, 1960. Chem. Abstr., 55: 21479, 1961.

(*41*) HULTIN, E. "Partition coefficients of ether extractable passionflower alkaloids." Acta Chem. Scand., 19: 1431–1434, 1965.

(*42*) ABDUSALAMOV, B., A. S. SADYKOV, and KH. A. ASLANOV. "Alkaloids and aminoacids of *Calligonum*." Nauchn. Tr. Tashkentsk. Gos. Univ., N° 263: 3–7, 1964. Chem. Abstr., 63: 3314, 1965.

(*43*) PLATONOVA, T. F., A. D. KUZOVKOV, and P. S. MASSAGETOV. "Alkaloids of Chenopodiaceae: *Anabasis jaxartica* and *Arthrophytum leptocladum*." Zhur. Obshchei Khim., 28: 3128–3131, 1958. Chem. Abstr., 53: 7506, 1959.

(*44*) BADGER, G. M., and A. F. BEECHAM. "Isolation of Tetrahydroharman from *Petalostyles labicheoides*." Nature (London), 168: 517, 1951.

(*45*) MENSHIKOV, G. P., E. L. GUREVICH, and G. A. SAMSONOVA. "Alkaloids of *Elaeagnus angustifolia*. Structure of eleagnine." Zhur. Obshchei Khim., 20: 1927–1928, 1950. Chem. Abstr., 45: 2490, 1951.

(*46*) ORAZKULIEV, I. K., O. S. OSTROSHENKO, and A. S. SADYKOV. "An adsorption method for the separation of alkaloids of *Hammada leptoclada*." Zhur. Prikl. Khim., 37: 1394–1395, 1964. Chem. Abstr., 61: 11014, 1964.

(*47*) JOHNS, S. R., J. A. LAMBERTON, and A. A. SIOUMIS. "Alkaloids of the Australian Leguminosae VII. $N_b$-Methyltetrahydroharman from *Acacia complanata*." Australian J. Chem., 19: 1539–1540, 1966.

(*48*) BORKOWSKI, B. "Chromatographic determination of alkaloids of *Zygophyllum fabago*." Biul. Inst. Roślin Leczniczych. 5: 158–168, 1959. Chem. Abstr., 54: 15844, 1960.

(*49*) PLATONOVA, T. F., A. D. KUZOVKOV, and P. S. MASSAGETOV. "Alkaloids of plants of the Elaeagnaceae family. Isolation of tetrahydroharmol and *N*-methyl-tetrahydroharmol." Zhur. Obshchei. Khim., 20: 3220–2323, 1956. Chem. Abstr., 51: 8765, 1957.

# SESSION VI

## AMANITA MUSCARIA (FLY AGARIC)

Daniel H. Efron, *Chairman*

# Fly Agaric and Man

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*Botanical Museum of Harvard University*
*Cambridge, Massachusetts*

For the past three or four years I have devoted some of my time to the quest for information about the fly agaric, as this mushroom is called in England, *Amanita muscaria* Fr. as it is known to mycologists, and especially concerning its historic role in the Eurasian cultures, where its use as an inebriant has survived down to recent times. The results of my inquiries have led me to write a book on the subject, which is almost ready for the printer. Today it is my privilege to lay before you some of my findings and conclusions.

My theme has surprising ramifications, as I think you will agree when I have done. Indologists will review my evidence, but if I am right, it will be necessary for us all to make room in our own remote past for the part played by this mushroom, and the fly agaric will take its place by the side of alcohol, hashish, and tobacco as an outstanding inebriant utilized by *Homo sapiens* living in Eurasia.

The documented history of this inebriant goes back only to the 17th century and is confined to the northern reaches of Siberia. That its unwritten history begins earlier is certain, but how much earlier and how widespread its use was, are questions that remain to be answered. So far as I can learn, my inquiries mark the first fumbling effort to arrive at those answers.

The intellectual element in Europe learned for the first time of the fly agaric as an inebriant in 1730, when Philip John von Strahlenberg, a Swedish army officer, published in Stockholm a book written in German on the twelve years he had spent as a prisoner of the Russians in Siberia. This work, translated into English, came out in London in two printings, in 1736 and 1738, under a lengthy title beginning *An Historico-Geographical Description of the North and Eastern Parts of Europe and Asia* (*1*). Somewhat earlier, in 1658, a Polish prisoner in Siberia had observed the fly agaric being consumed for its inebriating effect by the Ostyak (or Khanty) in the valley of the Irtysh, a tributary of the Ob in western Siberia; but his diary was not published until 1874 (*2*). The first Russian to record the practice seems to have been Stepan Petrovich Krasheninnikov in 1755 (*3*), who, like von Strahlenberg, was writing about the Koryak, in the extreme Orient. Since their time more than a score of observers have given us accounts of this curious custom. They have included Russian anthropologists, linguists (many of these Hungarian or Finnish), and a varied assortment of travelers and adventurers, some of whom are remarkably superficial and supercilious. In my forthcoming book I am planning to publish *in extenso*, in English, what these men have had to say about the consumption of the fly agaric in Siberia. In addition to these primary sources, whether good or bad, there are a number of serious writers who have concerned themselves with the problem: the phar-

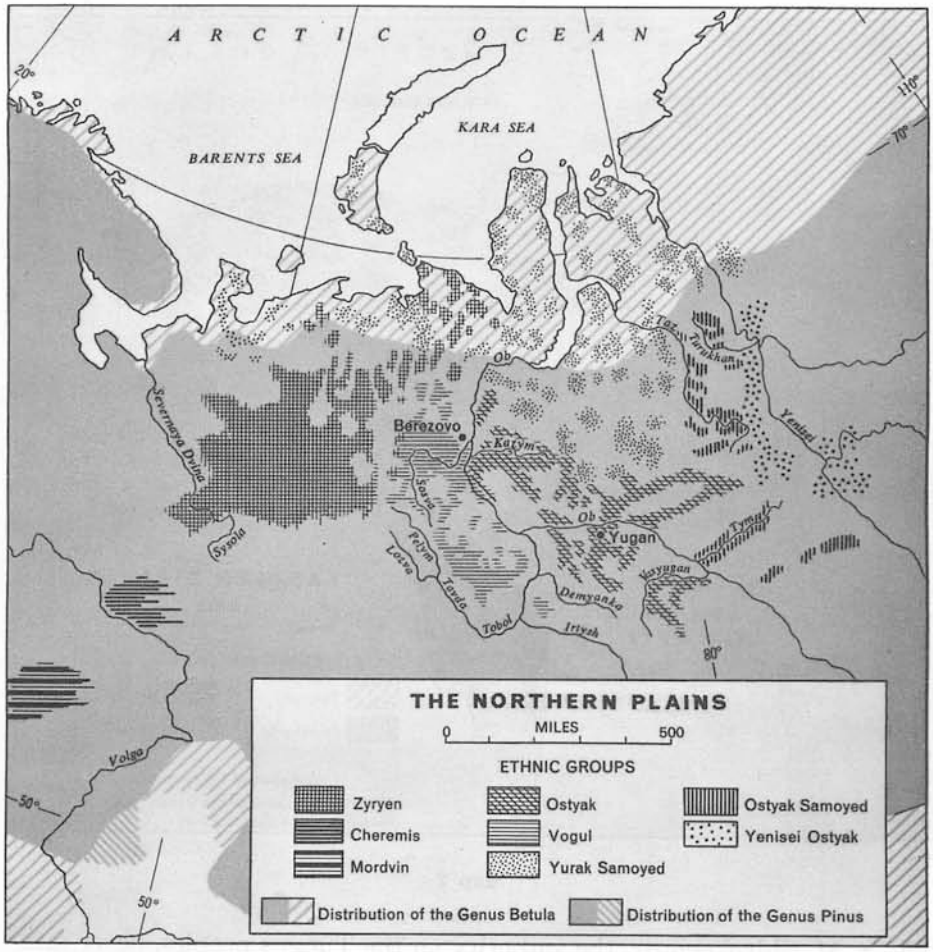
macologists Ernst von Bibra (*4*), C. Hartwich (*5*), and Louis Lewin (*6*)—all German—and the Frenchman Philipe de Félice (*7*), the Swede Åke Ohlmarks (*8*), and the Hungarian J. Balázs (*9*). In addition, there have been innumerable literary allusions traceable to the marvelous properties of the fly agaric. One need only mention as examples, in English, Oliver Goldsmith in his *Letters from a Citizen of the World* (No. 32), an immensely popular book in the 18th century, and the celebrated mushroom in *Alice in Wonderland.*

## The Distribution of the Practice

We possess reliable testimony permitting us to say that in recent centuries there have been two foci where the fly agaric has been used as an inebriant.

1. In the Ob Valley, in the extreme west of Siberia, and along the Ob's eastern tributaries until they interlock with the tributaries of the upper Yenisei, and along the upper Yenisei (Map 1). In this region tribes belonging to the Uralic family of languages have been historically dominant, and these are the ones that have been addicted to the fly agaric. Along the Ob and its tributaries dwell the Ostyak and the Vogul, called in the Soviet Union the Khanty and the Mansi, respectively. They are Ugrians, linguistically the nearest of kin to the Hungarians, who together with the Finnic peoples constitute the Finno-Ugrian linguistic group. The Ostyak and Vogul historically have been great consumers of the fly agaric. Their next of linguistic kin, the Hungarians, have no recollection of the practice, but *bolond gomba*, a familiar expression or cliché in the Hungarian language, means "mad mushroom," as when one says to a person behaving foolishly, "Have you eaten of the *bolond gomba?*", and this may well be a linguistic fossil dating from a time when the Magyar people still shared in the eating of the fly agaric. Among the Finnic peoples, as distinct from the Ugrian, none take the fly agaric today. However, it is of the highest interest that T. I. Itkonen, a reliable investigator, has reported that according to a tradition of the reindeer Lapps of Inari, their shamans formerly ate it, and that it had to have seven white spots. This places the practice well within Europe's borders, on the assumption that the Inari Lapps have not migrated to the West since they abandoned the practice. In the upper Yenisei the Selkup (a Samoyed people), called in the West the Ostyak-Samoyed, and in addition the southern-most of the Yurak-Samoyed, until recent times still used the fly agaric as an inebriant. (The peoples speaking Samoyed languages and those speaking Finno-Ugrian languages together constitute the Uralic family.) Their neighbors, the Ket, also have consumed it. The Ket, called in the West the Yenisei Ostyak, speak a language without known affiliation.

2. In the extreme northeast of Siberia there are three tribes—the Chukchi, the Koryak, and the Kamchadal—who have used the fly agaric (Map 2). They are neighbors and linguistically closely inter-related, but their language family, like the Ket, is unrelated to any outside linguistic family. The Yukagir, surviving in tiny communities in the extreme north and to the west of the Chukchi, recall that their forebears made use of the fly agaric. They

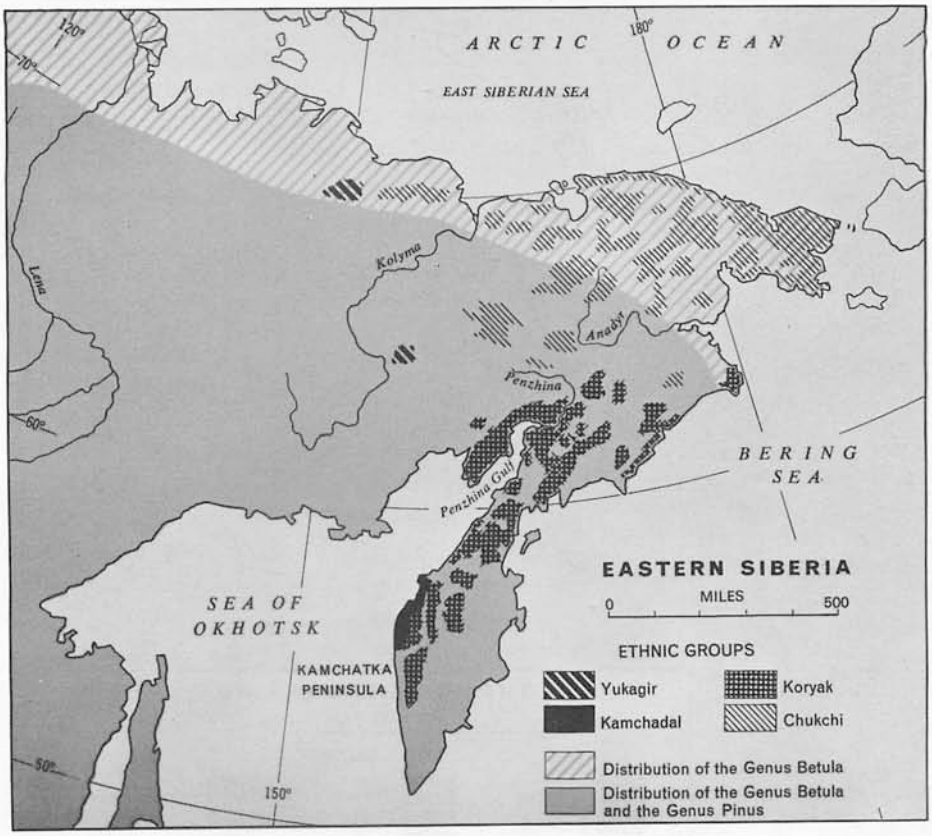



Map 1

also speak an isolated language. It is perhaps worth noting that the Gilyak, and the Ainu in Hokkaido, also peoples linguistically isolated, know nothing of the fly agaric as an inebriant.

The remoter communities of these peoples that I have been discussing did not know alcohol until the Russians or western whalers brought it to them. On a number of occasions the question has been put to individuals, when they have known both alcohol and the fly agaric, as to which they preferred. The answer, so far as it is recorded, was invariably the fly agaric.

What about the vast expanse of territory between the Uralic peoples on the West and the Chukchi group in the Far East (Map 3)? When the Russians arrived on the scene in the 17th century, this intermediate area was already occupied by the numerous Tungus tribes (including the Lamut), and by the Yakut, both of them belonging to the Altaic linguistic family identified with the Manchu, the Mongolian, and the Turkic-Tartar languages. Some western writers who have not visited these peoples have included them among the eaters of the fly agaric, but I can find no eye-witness authority for



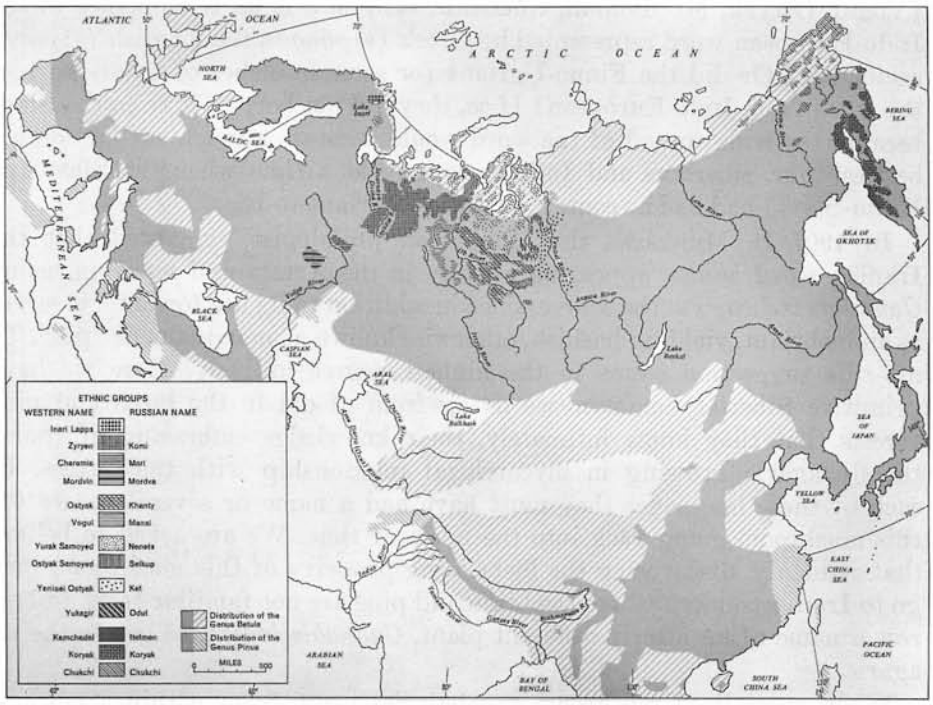

Map 2

this. S. M. Shirokogorov, the authority on the Tungus peoples, never mentions such usage, and Ivan A. Lopatin, also with extensive personal experience, has assured me in a personal communication that their shamans know nothing of the practice.

I think the answer to this question lies in history. The Tungus and Yakut erupted into northern Siberia in historic times. It was they who, forming a wedge, split apart the peoples using the fly agaric. Soviet historians say that the migration of the Tungus people took place at the end of the first millennium A.D., and the invaders came from the steppes far to the south, where the fly agaric does not grow. As they were the conquering people of somewhat superior culture, they were less likely to adopt the practices of those whom they conquered and dislodged.

## The Linguistic Evidence

A strange linguistic pattern marks the name used for fly agaric among the Siberian tribes. This word pattern undoubtedly holds the key to cultural secrets, but the key proves difficult to use.




Map 3

The Obugrian peoples—the Ostyak and Vogul—and the Ket share the same work for "fly agaric". In Vogul that word takes the shape of *panæ* or *peŋk*. In Ostyak the more northerly settlements say *poŋ;* the Irtysh folk, *pāŋ*. The Ket say *haŋgo*. The Selkup and the Yurak Samoyed use words of their own, except that from one village of the southern Yurak Samoyed *pōŋka* is reported.

Franz Boas (*10*) tells us that the Chukchi form for "mushroom" is *pómpo* (from a stem *poŋ*), to which *pósnposn* corresponds in Koryak. But in these tribes on the Pacific Coast the words in every case is generic for all mushrooms, and the fly agaric is specifically named *wapaq*.

It seems that words derived from a single root circulate in the western and the eastern area of fly agaric addiction, and this lends support to my supposition that in former times (before the intrusion of the Tungus) the Western and Eastern groups were contiguous. We do not know what the Yukagir and the Inari Lapp words for the fly agaric are.

The story of this word cluster does not end here. Two Finnic peoples living in Eastern Europe, the Mordvinians and the Cheremis, known in the Soviet Union as the Mordva and the Mari, make use of this same word as a general term for all mushrooms. The Mordvinians say *paŋga* or *paŋgo*, and the Cheremis say *poŋgo*. But these two peoples do not know the fly agaric as an inebriant.

This word cluster has stimulated some discussion among philologists, chiefly Hungarian and Finnish. Is the root *poŋ* originally Finno-Ugric



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(Vogul, Ostyak, Mordvinian, Cheremis, etc.) and is its resemblance to the Indo-European word represented by Greek (*s*)*póngos*, the English (*s*)*punk*, accidental? Or did the Finno-Ugrians (or some branches of them) borrow the word from Indo-European? If so, they did not borrow it from the Slavs because the wide spread of the word would indicate a much earlier contact between our Siberians and Indo-European, at a time when the Slavs (or Proto-Slavs) had had no contact with the Siberians-to-be.

In 1907 B. Munkácsi, the Hungarian philologist, suggested that the Iranian word *baŋha*, appearing already in the Avesta and meaning hemp, *Cannabis indica*, was the source, since in addition to its use for fibre, it serves as an inebriant, yielding hashish, otherwise known as marijuana or "pot". To me this suggestion seems in the highest degree unlikely. Here we have primitive Siberian communities living from of old in the birch and pine forests that they know intimately, their knowledge embracing of course the fly agaric growing in mycorrhizal relationship with these trees. In each of these languages they must have had a name or several names for this mushroom going back into the mists of time. We are asked to believe that suddenly, discovering the inebriating property of this mushroom, they go to Iran, a country where the birch and pine are not familiar trees, to borrow a name of an utterly different plant, *Cannabis indica*, to gve to the fly agaric.

When specialized mushroom vocabularies grow from within a cultural milieu, the rule is that the specific names precede the generic term. But this rule does not apply when words are borrowed from an outside source. In this case a general term may be borrowed and given a specific meaning, or a specific name may acquire a new application, and the same name may be clothed with different applications in different communities, and may change its application according to the evolving use of the various wild mushroom species in the given cultural milieu.

If the root *poŋ* was borrowed from an Indo-European people, the loan of the word must have marked a new and significant utilization of a species of mushroom, a use that must have swept across Siberia with the word, perhaps rather quickly. Let us suppose that an Indo-European people making use of the inebriating effect of the fly agaric in their religious life imparted this practice to the Siberian tribes; or perhaps in war-time to help their soldiers screw their courage to the sticking point. This application of a mushroom to a supernatural use or as a secret weapon would surely have been a sufficient reason for them to adopt the Indo-European name of that mushroom.

But in our preoccupation with the inebriating effect of the fly agaric we must not overlook an alternative possibility. The basic fungal sense of the word (*s*)*póngos*, identical with the Germanic *Schwamm* and the Slavic *gomba*, is "sponge". The generation of fire was of overwhelming importance in the lives of the northern tribes, indeed making life possible in the northern latitudes. Whether by percussion or by friction, the spark that was struck had to be received in inflammable tinder, and the best tinder for this purpose has long been considered *Fomes fomentarius*, a heavy shelf or bracket fungus

that grows on many species of trees, but that is generally identified with the birch. When it is dried it is light as a feather and quickly converts a spark into a flame. In archaeological diggings *Fomes fomentarius* has been found next to the stones of fire places in dwellings at Maglemose in Denmark and Star Carr in Yorkeshire, these diggings going back almost to the last ice age, some nine or ten thousand years ago. If an Indo-European people introduced to the Siberian tribes the use of this *punk*, or *spunk* (sic), or touchwood (all of these meaning primary tinder), the Indo-European name for it would probably accompany the product wherever it went. That name meant "sponge", and it is striking that the original "sponge" was probably fungal and not marine, the marine sponge being a substitute given us by the Greeks after they had arrived in the Aegean. The preparation of this fungus for its purpose must have been one of the earliest industries of mankind in the northern latitudes—the making of the *amadou* of the French, the *esca* or *yesca* of the Italians and Spaniards, the *Zunderschwamm* of the Germans, the *trut* of the Russians.

Either this or the inebriating property of the fly amanita or a combination of both would have been of sufficient meaning in the lives of the ancestors of the Siberian tribesmen to explain the adoption of the root (*s*)*pon*, meaning "sponge" or "fungus", into the languages of Siberia. By a startling coincidence, the birch is the primary host for both *Fomes fomentarius* and the fly agaric, and the special place occupied by the tall Siberian birch in the imaginations of the Siberian peoples is certainly due not only to the ethereal beauty of the tree itself, but also to the fact that the fly amanita grows in mycorrhizal relationship with the roots of the birch, and that *Fomes fomentarius* grows from its trunk. It is true that the pine also is host to the fly agaric, but less often than the birch, and it is true that the beech and other trees are hosts to the *Fomes fomentarius*, but it is most commonly found on the birch. The birch is the Tree of Life for the man of the forest or taiga, supplying him with fire for his body and fire for his soul.

Surely I do not need to emphasize the speculative nature of these thoughts. To be dogmatic in terrain such as this is to court disaster. The etymology of words, the sequence of events, where there is so little to go on, is little more than guesswork. But I would have been derelict had I failed to call your attention to the linguistic problem presented by the wide diffusion of the root *pon* among the scattered Siberian tribesmen.

As those of you who are familiar with the writings of Mircea Eliade will perceive, I am forced to part company with him both on the etymology of the peculiar fungal word of the Siberian tribes and on the antiquity of the role of the fly agaric as an inebriant in Siberian shamanism (*11*). What Munkácsi advanced as a bold surmise he has converted into a statement of fact, elaborating on the etymology of *pon* with frightening self-assurance. His view that the use of narcotics to attain ecstasy is recent and only a "vulgar substitute for 'pure' trance" seems to run counter to such evidence as we have. For as far back as our records go, the area where the fly agaric was used by shamans has been shrinking, until its use is now virtually extinct. Consider primitive man groping his way forward, leading a precarious

existence, and in his ever urgent quest for food experimenting with every plant and animal and insect and fish: his fund of knowledge and beliefs being derived exclusively from his own experience and from what he learned by word of mouth from his parents and neighbors. He must sooner or later have discovered the properties of the hallucinogenic plants, a discovery made almost certainly before he discovered how to control the processes of fermentation and to make beer or wine or mead. These hallucinogenic plants opened the doors for him to horizons beyond any he had known in his cruel daily existence. They translated him to utterly different planes of existence, where ecstasy reigned. The discovery of these plants must have had an explosive effect on his soul. He would resort to them in moments of soul-hunger. They would suggest to him possibilities sparking his imagination and inventive zeal. Surely this creature, limited in his range of knowledge and living by rules taught him by his own experience, his imagination peopling the world with invisible spirits benevolent and malevolent, would regard the hallucinogenic plants as miraculous gifts of the gods, and in moments of need he would resort to them without hesitation as a channel of communication with the Immortals. Only after having known them and in default of them would he devise ways through disciplined austerity and self-imposed mortification of the flesh to achieve the same result, and later, having attained sophistication in these matters, would he perceive what many regard as the moral superiority of this road to beatitude.

## The Hallucinogenic Properties of the Fly Amanita

We do not know nearly enough about the fly agaric as an hallucinogen. But the evidence indicates certain traits to be defined thus:

a. It begins to act in fifteen or twenty minutes and the effects last for hours.

b. First it is a soporific. One goes to sleep for about two hours, and the sleep is not normal. One cannot be roused from it, but is sometimes aware of the sounds round about. In this half-sleep sometimes one has coloured visions that respond, at least to some extent, to one's desires.

c. Some subjects enjoy a feeling of elation that lasts for three or four hours after waking from the sleep. In this stage it is interesting to note that the superiority of this drug over alcohol is particularly emphasized: the fly agaric is not merely better, it belongs to a different and superior order of inebriant, according to those who have enjoyed the experience. During this state the subject is often capable of extraordinary feats of physical effort, and enjoys performing them.

d. A peculiar feature of the fly agaric is that its hallucinogenic properties pass into the urine, and another may drink this urine to enjoy the same effect. Indeed it is said that the urine of three or four successive drinkers may be thus consumed without noticeable loss of

inebriating effect. This surprising trait of fly agaric inebriation is unique in the hallucinogenic world, so far as our present knowledge goes.

The soporific and kinetic effects of the fly amanita are utterly unlike anything produced by the mushrooms of the genus Psilocybe of Mexico.

## The Indo-Aryans and Soma

An Indo-European people who called themselves Aryans conquered the valley of the Indus in the middle of the second millennium B.C. Their priests deified a plant that they called Soma, which has never been identified: scholars have almost despaired of finding it. The hymns that these priests composed have come down to us intact in the RgVeda, and many of them concern themselves with Soma. Lately there have been a number of fresh translations of the RgVeda, better than any of their predecessors.

This plant, Soma, was an hallucinogen. The juice was extracted from it in the course of the liturgy and forthwith drunk by the priests, who regarded it as a divine inebriant. It could not have been alcoholic, for various reasons; for one thing, fermentation is a slow process which the Vedic priests could not hurry.

I have studied these recent translations and it is apparent, I think, that Soma was the fly agaric. There are many touches in the lyric poems that fit the fly agaric as a glove, and I believe there are none that contradict it. To detail them here today would take too long, and I must ask you to wait for my book for the full dress presentation of my thesis.

If I am right that Soma is the fly agaric, we must revise our judgment about the role of fungi in the cultural history of Eurasia. The RgVeda is the earliest literary monument in the Hindu religion, and behold! it is a paean to the fly agaric! The RgVeda is one of the earliest texts that we possess from the Indo-European world, and behold! it is a paean to the fly agaric! If the Indo-Iranians really used the fly agaric, it means at an early date, before they left their homeland somewhere north of the Caucasus-Caspian-Oxus line, these tribes were consumers of the fly agaric. They or their congeners, fellow Indo-Europeans, may have given the fly amanita cult to the ancestors of the Obugrians of today, and the root *(s)poγ* to their languages. If I am right, the adoration of the fly agaric was at a high level of sophistication 3,500 years ago (and who can say how much further back?) among the Indo-Europeans, and we are witnessing in our own generation the final disappearance of a practice that has held the peoples of northern Eurasia enthralled for thousands of years.

### REFERENCES

(*1*) PHILIP JOHN VON STRAHLENBERG: An Historico-Geographical Description of the North and Eastern Part of Europe and Asia, but More Particularly of Russia, Siberia and Great Tartary, Both in Their Ancient and Modern State, Together with an Entire New Polyglot-table of the Dialects of 32 Tartarian Nations, London, 1936. The citation is from p. 397 of the English edition.

(2) ADAM KAMIEŃSKI DLUZYK: "Dyarusz Wiezienia moskiewskego, miast i miejsc" (A diary of Muscovite Captivity, Towns and Settlement), published in *Warta*, a Collection of Articles, edited by the Rev. A. Maryański, Poznań, 1874, pp. 378–388.

(3) STEPAN PETROVICH KRASHENINNIKOV: "Opisanie zemli Kamchatki" (A Description of Kamchatka), Akademiïa Nauk, 1755. New critical edition in 1949.

(4) ERNST VON BIBRA: "Die narkotischen Genussmittel und der Mensch" (Narcotic Substances and Mankind), Nüremberg, 1855, pp. 135–139.

(5) C. HARTWICH: "Die menschlichen Genussmittel: ihre Herkunft, Verbreitung, Geschichte, Anwendung, Bestandteile, und Wirkung" (Human Stimulants: their Origin, Distribution, History, Use, Components, and Effects), Leipzig, 1911, pp. 255–260.

(6) LOUIS LEWIN: This work, written in German and published in 1924, was translated into English and French, and the English edition, Phantastica: Narcotic and Stimulating Drugs, their Use and Abuse, was reprinted in 1964 by Routledge & Kegan Paul, London. The passage about the fly agaric is on pages 123–129 of this edition.

(7) PHILIPPE DE FÉLICE: "Poisons Sacrés Ivresses Divines: Essai sur quelques Formes Inférieures de la Mystique" (Sacred Poisons Divine Inebriations: Essay on Some Inferior Forms of Mysticism), Paris, 1936, pp. 110–113.

(8) ÅKE OHLMARKS: "Studien zum Problem des Schamanismus" (Studies on the Problem of Shamanism), Lund, 1939, pp. 100–125.

(9) J. BALÁZS: "Über die Ekstase des ungarischen Schamanen" (On the Ecstasy of the Hungarian Shamans), in Glaubenswelt und Folklore der Sibirischen Völker, edited by V. Diószegi, Budapest, 1963, pp. 57–83.

(10) FRANZ BOAS: "Handbook of American Indian Languages," Smithsonian Institution, Bureau of American Ethnology, Bulletin 40, Washington, 1922, p. 693.

(11) VIDE, e.g., MIRCEA ELIADE: Shamanism, Archaic Techniques of Ecstasy, Pantheon Books, New York, 1964; originally published in Paris by Librairie Payot in 1951 as Le Chamanisme et les techniques archaïques de l'extase. In the English edition, pp. 400–410; in the French edition, p. 360.

# Ethnopharmacological Investigation of Some Psychoactive Drugs Used by Siberian and Far-Eastern Minor Nationalties of U.S.S.R.*

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The authors discuss the practice of eating the fly agaric in the extreme east of Siberia, among the Kamchadals, the Koryak, the Chukchi, and the Yukagir. They quote from the writings of Stepan Krasheninnikov, the Russian traveler who first reported in Russian the practice in the 18th century, from G. V. Steller, a junior colleague of Krasheninnikov's, and from the work on the Chukchi of V. G. Bogoras, a Russian anthropologist who wrote in English and whose work was later translated into Russian. According to Krekhman and Sam, the use of the fly agaric was unknown among the Tungus. The fly agaric was used in its natural state, gathered in the spring or summer or less often the fall, and swallowed whole in a slightly desiccated condition; or else by infusion, after soaking for five or six days in water. Sometimes the infusion was taken with *Epilobium angustiforlium* L., the latter being soaked in water and then boiled down into a sweet, thick liquor. Sometimes underproof vodka was added. The mushrooms are personified as little men, one dwarf to a mushroom, and when under its influence one used to speak of these dwarfs as all-powerful. Only men took the fly agaric; it was not used by women.

The Kamchadals made also a wine from a 'sweet herb'—*Heracleum dulce* Fisch., fam. Umbelliferae. It was eaten, like betel nut, in its fresh state, and the effects were similar to alcoholic intoxication. Various other plants were taken for their psychic effect by the Tungus tribes, among them *Ledum palustre* L. and *Ledum hypoleucum* Kam. The dried leaves were laid on a hearth or in a frying pan, and the fumes had a stupefying effect, this serving perhaps as an analgesic for the sick. All these drugs need further study.

*Paper submitted but not read at the meeting. We are presenting here only a summary of the paper.

# Isolation, Structure and Syntheses of Central-Active Compounds from Amanita Muscaria (L. ex Fr.) Hooker

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It has been desecribed that the carpophores of Amanita muscaria belong to the class of plant drugs affecting the central nervous system and possibly producing hallucinatory effects (*1*).

Since the classical work of Schmiedeberg and Koppe in 1869, the chemical investigation of these active substances has, until the present day, been almost exclusively concerned with muscarine, whose chemistry is now fully understood (*2*). The pharmacological investigations have shown in fact, that muscarine itself is not the prime cause of the previously mentioned central-activity of A. muscaria. The low plant content (2–3 mg per kg undried fungus), in conjunction with its relatively weak activity on oral consumption, leads to the conclusion that muscarine can only be considered as a minor active component of A. muscaria.

During the last few years it has been proposed that one or another of the bases *bufotenine*, *atropine*, *hyoscyamine* and *scopolamine* could be responsible for the main central-activity of A. muscaria (*3*). With regard to these suggestions the following comments can be made. The amounts of these compounds reported to have been isolated (0.1–0.2 mg atropine; 0.4–0.7 mg scopolamine per kg undried carpophores), although not rigorously confirmed, in relation to their known activity, exclude them as possible causes of A. muscaria poisoning. Moreover, other authors have demonstrated that Belladonna alkaloids (atropine, hyoscyamine, scopolamine) do not occur in A. muscaria (*4*). In addition in our hands, investigation of both Swiss and South German varieties of A. muscaria has led to the isolation of several indolic substances, the structures of which have not yet been elucidated. Bufotenine, however, was found not to be present.

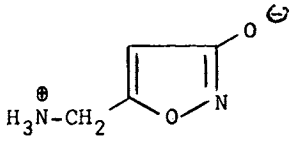
Recently the, in contrast to the above-mentioned products, highly active muscimole and ibotenic acid have been isolated from A. muscaria (*5*).

The pharmacological tests (narcosis-potentiation), which were used as an aid in the isolation of these substances, lead us to the conclusion that they are in fact active on the central nervous system. Their structures have been elucidated and several syntheses published (*6*).

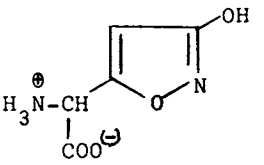
Muscimole, $C_4H_6N_2O_2$, mp. 155–156° (from water), 174–175° (from methanol-water), is a very polar and extremely water soluble substance. It is the enol-betaine of 5-aminomethyl-3-hydroxy-isoxazole (formula I), i.e., it is an unsaturated cyclic hydroxamic acid. Muscimol is easily formed by decarboxylation and loss of water from ibotenic acid, $C_5H_8N_2O_5$ mp. 145°

(dec.). The latter is the zwitterion of α-amino-α-[3-hydroxy-isoxazoylyl-(5)]-acetic acid monohydrate (formula II). It is to be considered a principal active constituent of A. muscaria, being present to the extent of 0.3–1 g per kg of undried carpophores.

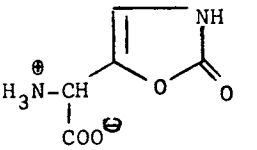
The pharmacologically less active muscazone (*7*), $C_5H_6N_2O_4$, mp. 190° (dec.), co-occurs in varying proportions with muscimole and ibotenic acid in A. muscaria. It is also an amino-acid, namely α-amino-α [2(3H)-oxazolonyl-(5)]-acetic acid (formula III), and can be produced in the laboratory by UV-irradiation of ibotenic acid. It is probable that, in the plant also, ibotenic acid acts as a precursor for muscazone. We therefore assume that the widely known variation in toxicity of A. muscaria results from fluctuations in the ibotenic acid-muscazone ratio.



I



II



III

Our latest investigations have shown that A. muscaria produces still further physiologically active substances, the structures of which are not yet known.

## REFERENCES


(*1*) GESSNER, O., Die Gift- und Arzneipflanzen von Mitteleuropa, Winter, Heidelberg 1953; RAMSBOTTOM, J., Mushrooms and Toadstools, Collins, London 1959; WASSON, V. P., and WASSON, R. G., Mushrooms, Russia and History, N.Y. 1957; HEIM, R., Les champignons toxiques et hallucinogènes, Paris, Boubée 1963.

(*2*) EUGSTER, C. H., "The chemistry of muscarine," in Advances in organic chemistry, Vol. II, Interscience, N.Y. 1960; WILKINSON, S., "The history and chemistry of muscarine," Quarterly reviews of the Chemical Society (London) 15: 153 (1961).

(*3*) FABING, H. D., and HAWKINS, J. R., Science 123: 886 (1956); TYLER, V. E., Amer. Jour. Pharmacy 130: 264 (1958); LEWIS, B., South African Medical Jour. 29: 262 (1955); MANIKOWSKI, W., and NIEZGODZKI, L., ref. Chem. Abstr. 58: 11703 (1963); TYLER, V. E., Lloydia 24: 71 (1961).

(*4*) SALEMINK, C. A., TENBROEKE, J. W., SCHULLER, P. L., and VEEN, E., Planta medica 11: 139 (1963); KWASNIEWSKI, V., Süddeutsche Apoth. Zeitung 94: 1177 (1954).

(*5*) (*a*) MÜLLER, G. F. R., and EUGSTER, C. H., Helv. Chim. Acta 48: 910 (1965); EUGSTER, C. H., MÜLLER, G. F. R., and GOOD, R., Tetrahedron Letters 1965: 1813; GOOD, R., MÜLLER, G. F. R., and EUGSTER, C. H., Helv. Chim. Acta 48: 927 (1965); MÜLLER, G. F. R., Beiträge zur Kenntnis der Inhaltsstoffe des Fliegenpilzes (Amanita muscaria), Dissertation, Universität Zürich 1961.

(*b*) TAKEMOTO, T., NAKAJIMA, T., and SAKUMA, R., Yakugaku Zasshi 84: 1233 (1964).

(*c*) BOWDEN, K., DRYSDALE, A. C., and MOGEY, G. A., Nature, *206*, 1359 (1965); Tetrahedron Letters *1965*, 727.

(*d*) EUGSTER, C. H., and TAKEMOTO, T. Zur Nomenklatur der neuen Verbindungen aus Amanita-Arten, Helv, Chim. Acta *50*, 726 (1967).

(6) Review: EUGSTER, C. H., Über den Fliegenpilz, Neujahrsblatt Nr. 169 der Naturforschenden Gesellschaft in Zürich, Verlag Leemann AG. Zürich, 1967;

Synthesis of muscimole: Patents to J. R. Geigy AG. Basle (Swiss Priority of Dec. 6th, 1963, Belg. Pat. No. 656.759 of Dec. 7th, 1964; see Chem. Abstr. 63: 16356 (1965)); Gagneux, A. R., Häfliger, F., Good, R., and Eugster, C. H., Tetrahedron Letters 1965: 2077.

Synthesis of ibotenic acid: Patents to J. R. Geigy AG. Basle (Swiss Priority of July 22nd, 1964, Belg. Pat. No. 665.249 of Dec. 10th (1965):, see Chem. Abstr. 65, 2266 (1966); Gagneux, A. R., Häfliger, F., Meier, R., and Eugster, C. H., Tetrahedron Letters 1965: 2081; Sirakawa, K., Aki, O, Tsushima, S., and Konishi, K., Chem. Pharm. Bull. (Japan) 14: 89 (1966); Kishida, Y., Hiraoka, T., Ide, J., Terada, A., and Nakamura, N., Chem. Pharm. Bull. (Japan) 14: 94 (1966).

(7) Isolation: see (*5*) (*a*); Structure: Fritz, H., Gagneux, A. R., Zbinden, R., and Eugster, C. H., Tetrahedron Letters 1965: 2075; Reiner, R., and Eugster, C. H., Helv. Chim. Acta 50: 728 (1967); Reiner, R., Dissertation, Universität Zürich 1966; Synthesis: Göth, H., Gagneux, A. R., Eugster, C. H., and Schmid, H., Helv. Chim. Acta 50: 137 (1967).

# The Pharmacology of Amanita Muscaria

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## Introduction

Rarely, to-day, are new natural products with an interesting pharmacological action found in Swiss plants. Most alkaloids have been discovered and extensively investigated in the past 50 years. For us remains the search for new active compounds (alkaloids, amines and aminoacids etc.), which are present only in small concentrations, or which show interesting biological properties not yet investigated.

The starting point most often is the centuries-old knowledge of remarkable and unusual actions of a plant or its crude drug form, on man after ingestion. Intoxication after an overdose is the overall response of the organism to the toxic principles in the plant. This reaction is a sum of very different pharmacological actions, and may be very complicated. As plants vary in metabolism and production of active principles corresponding to their environment, comparison of intoxication symptoms will show regional differences. Different varieties of the same species may produce quite different metabolites.

The pharmacologist first has the problem of carefully scrutinizing the symptoms of intoxication, or, if these are already known, the therapeutic use by primitive tribes. He then must try to classify these symptoms as pharmacological actions on different organ systems, following the large knowledge of typical drug-actions. Then he develops a method for screening the active principles to isolate and concentrate these from the extracts, with the help of specific tests. For this part, cooperation with an interested chemist is the most important mutual help. Both have to adjust their extrac-

tion and screening methods in order to isolate the active compounds. Very often the pharmacologist works with several independent tests, or a test battery which allows him to differentiate between several active principles. Finally, he has the rewarding task of investigating the actions of new and pure compounds of a plant, which so far were known only in primitive medicine.

The investigation of the pharmacology of amanita muscaria is a typical example of this procedure. It gave us the opportunity to investigate for the first time muscarine in its pure form. Now, the psychoactive principles are getting more of our interest. Already important facts are known and new active principles are discovered, but we feel that more must be found to explain the different astonishing effects of the fly agaric on man. My report therefore is not a final explanation and scientific description of active compounds, but more an account of our present knowledge and experiments under way. Finally, I want to describe our mode of detecting new hallucinogenic principles.

## Muscarine

### *General*

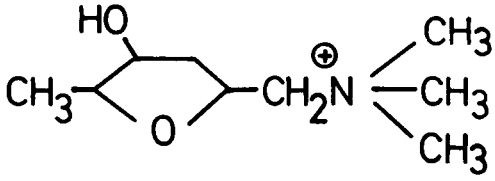
Because of its potent pharmacological actions muscarine, the best known alkaloid of amanita muscaria, has been studied by pharmacologists for over 100 years. It was the first drug with a selective action on organs innervated by the autonomic nervous system. The findings of these investigations, however, were uncertain and inaccurate until the isolation and crystallization of muscarine chloride from amanita muscaria (Eugster and Waser, 1954) (Table 1). The first preparations contained large amounts of choline, which is biologically less active, and unstable acetylcholine, which may be found in different mushrooms. These contaminations made standardization inaccurate.

All screening methods used for isolation of muscarine are based on its strong parasympathomimetic activity. Until to-day, muscarinic activity is the most used term for direct peripheral action on cholinergic receptors, situated in different smooth muscles, especially of the gastrointestinal tract and eye, exocrine glands and heart. Nicotinic action is reserved for cholinergic receptors in ganglionic synapses and endplates of skeletal muscle, where nicotine is stimulatant and depressant, and where muscarine has only small or no action. Lately, even in the central nervous system these types of muscarinic (cortical neurons, Betz cells), nicotinic (Renshaw cells) and intermediate synapses (thalamic neurons, caudate nucleus), have been demonstrated (McLennan, 1965). Without doubt acetylcholine plays a major role as a chemical neuro-transmittor in the brain.

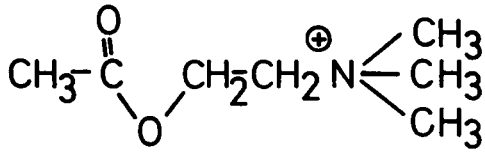
### *Screening methods for muscarine*

As other investigators (Kögl, Duisberg and Erxleben, 1931) before us, we used the isolated frog heart of Straub, which is very sensitive, (0.003–0.01$\mu$g muscarine-chloride) for small amounts of cholinergic drugs, their action be-

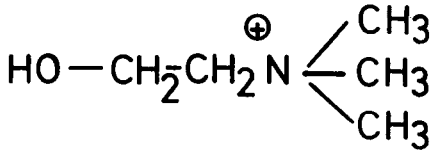
TABLE 1.—*Compounds isolated from Amanita muscaria (1966)*



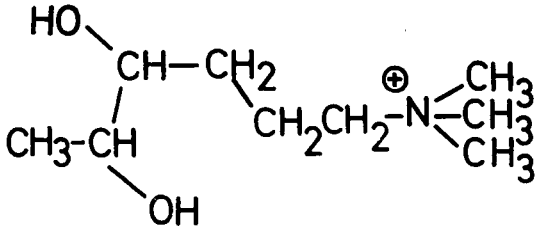
Muscarine
0,0002 %



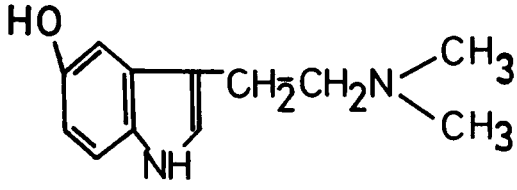
Acetylcholine



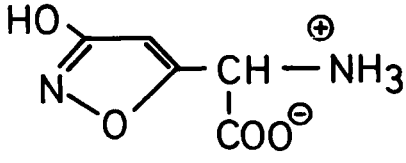
Choline



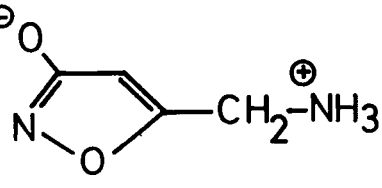
Muscaridine ?



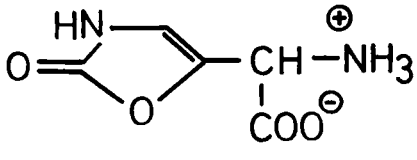
Bufotenine ?



Ibotenic acid
0,03 - 0,1 %



Muscimol



Muscazon

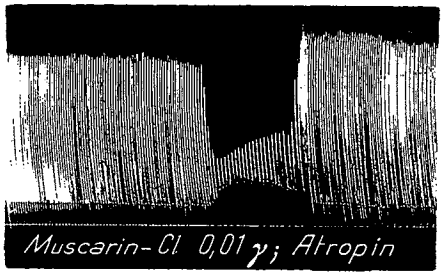



FIG. 1a.—Isolated frog heart (Straub). Muscarine diminishes amplitude of contraction and slows heart rate. Atropine ($10^{-6}$ m) is an immediate antagonist.

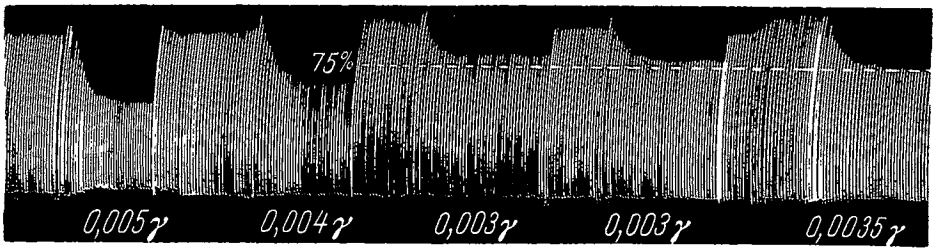



FIG. 1b.—Quantitative determination of muscarine with isolated frog heart. 25% paralysis is produced by 0.0035 μg muscarine-chloride.

ing immediately antagonised by atropine (Fig. 1). Concentration of muscarine from extracts by chromatography was followed until the final crystallization of pure muscarine-chloride. Biological methods are indispensable for the first isolation of the active principle, but later more specific coloration methods of the paper chromatograms were used.

Less suited for screening purposes are miosis and salivation of mice after intraperitoneal injection of 60–130 μg/kg, and chromodacryorrhoea produced in rats by subcutaneous or intraperitoneal injection of 20–35 μg/kg muscarine-chloride. The diameter of mouse-pupils is normally 0.3–0.4 mm wide, and must be measured with a magnifying device (low power microscope) (Pulewka, 1932). Mydriatic opening of the pupil is much easier to measure than miotic contraction. Furthermore, quantitative determination of salivation, lacrimation or chromodacryorrhoea is quite difficult. It may be accomplished by sucking these fluids from mouth or eye on filter paper and measuring the wet or coloured area (Malone and Robichaud et al., 1961).

*Effects on the animal*

In addition to the secretory and miotic action on larger animals (rabbit, cat, dog, monkey), a variety of other effects may be seen (Waser, 1961). The cardiovascular system is very sensitive to muscarine. Blood pressure is lowered rapidly by small intravenous doses, (cat: 0.002–1.0 μg/kg) and heart rate is slowed. Cardiac arrest may occur when the action of muscarine is not antagonized by atropine (Fig. 2). Vagotomy does not influence the only

peripheral action of muscarine. Respiratory effects are noted with small doses: increase in volume and rate of respiration (0.02–1.0 μg/kg i.v.), probably due to stimulation of the chemoreceptors of the carotid body, is followed by bronchoconstriction and obstruction of the respiratory pathways by profuse secretion of mucus. Again all these effects are antagonized by atropine.

Transmission through ganglionic synapses (superior cervical ganglion) is not changed with high intravenous doses (500 μg/kg) of muscarine, and no neuromuscular block develops in atropinized cats. But with isolated and perfused ganglion preparations, higher concentrations of muscarine evoke postganglionic response, especially when the ganglion has been chronically denervated (Konzett and Waser, 1956).

*Effects on isolated organs*

The intense action of muscarine on the isolated frog heart has already been mentioned. Most investigations were done on smooth muscle organs for the purpose of comparing its potency with that of acetylcholine. The preparation best suited is the ileum of the guinea pig. Acetylcholine makes an immediate contraction during 15–30 minutes and later spontaneous relaxation

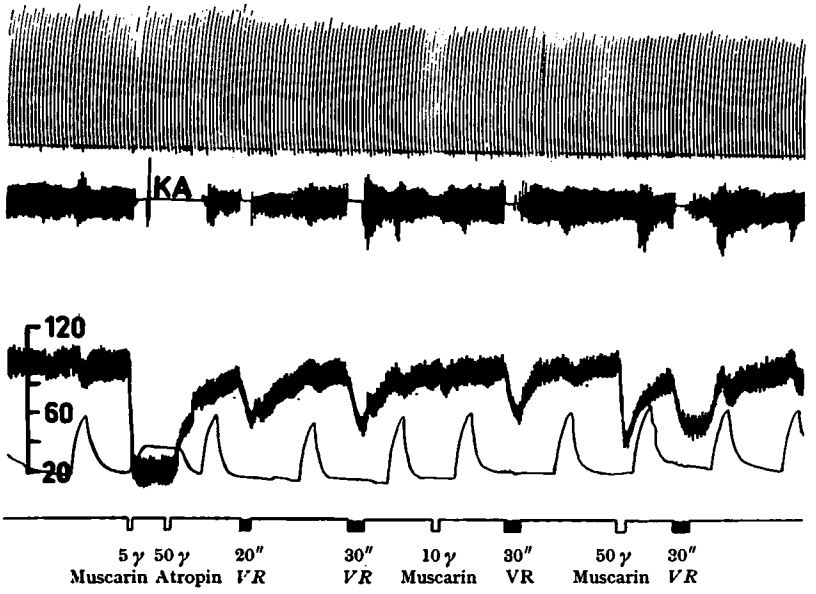



FIG. 2.—Cat in dial-nembutal narcosis. Registered are from top: twitches of m. gastrocnemius stimulated from n.ischiadicus tracheal respiration, blood-pressure in a.carotis, contractions of nictitating membrane stimulated from preganglionic sympathetic nerve. Signal: injected doses and denation of vagal stimulation (VR). Muscarine has no action on endplates in skeletal muscle, stops respiration by bronchoconstriction (KA=artificial respiration), lowers blood pressure and contracts nictitating membrane directly, atropine acts as antagonist.

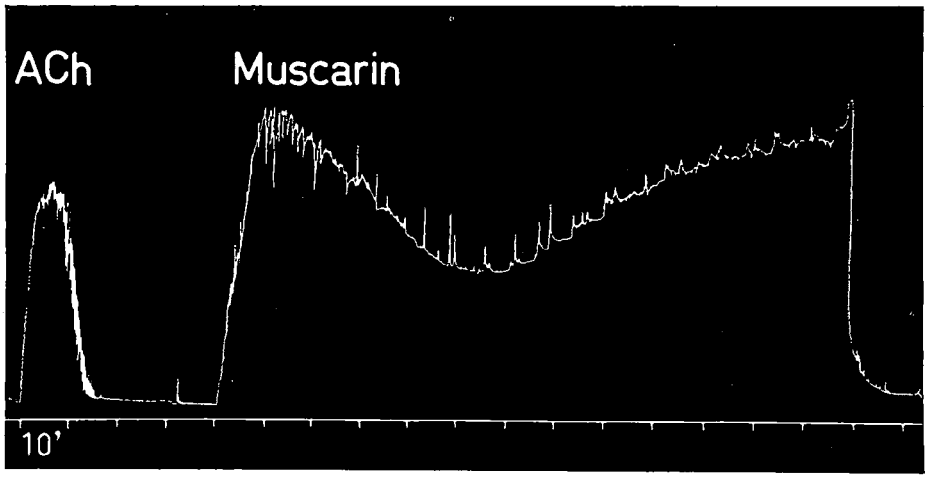



FIG. 3.—Guinea pig ileum. Contraction by acetylcholine ($5\times10^{-8}$ m Ach) and muscarine ($3\times10^{-8}$ m). Washing after 125 minutes. Slow and persistent contraction by muscarine with little twitches.

of the smooth muscle, by hydrolytic destruction of the molecule by tissue cholinesterases (Fig. 3). Muscarine shows a biphasic action. A rather quick but interrupted contraction is followed within 30 seconds by a slow phase of maximal contraction during 5–10 minutes. The relaxation after washing is at least two times slower than that after acetylcholine. Muscarine is not destroyed by cholinesterases; accordingly its action persists until the drug is removed by washing. Other contractions and twitches may follow.

Similar effects of muscarine on smooth muscle of other organs are found in many different species of animals. The average potency of contraction is much greater than with acetylcholine (Table 2). The isolated sphincter of the iris of pigs contracts with 10 times smaller concentrations of muscarine ($10^{-7}$m) than with acetylcholine ($3.5\times10^{-6}$m). This explains well the miotic action on the intact animal (Fig. 4). Even high concentrations of muscarine (500 $\mu$g/ml) are not able to induce contraction of rectus muscle of the frog, and on nerve-muscle preparations no neuro-muscular block develops, as with curare.

TABLE 2.—*Spasmogenic activity of muscarine in isolated muscles. Average values from different animal species, activity ratio of muscarine to acetylcholine (=1)*

| | | |
|---|---|---|
| Tracheal chain | (guinea pig, rabbit) | 150 |
| Bladder wall (longitudinal and circular) | (guinea pig, rabbit, dog, rat, frog, horse, monkey) | 46 |
| Ureter | (horse) | 29 |
| Intestine (longitudinal and circular of duodenum, ileum, colon) | (frog, mouse, guinea pig, rabbit, dog, cat, horse, monkey) | 8, 4 |
| Uterus (longitudinal and circular) | (mouse, guinea pig, rat, horse, dog, rabbit) | 4, 5 |

*Central nervous effects of muscarine*

Until to-day nobody has been able to show a direct psychotropic action of muscarine on animal or man. This is probably due to its difficulty as a quaternary amine in passing the blood-brain barrier. Passage may be possible in combination with an amino acid or lecithin. The low oral toxicity of *d*,l-muscarine on mice (200 mg/kg), compared to its intravenous action (0.8 mg/kg), shows that resorption through the intestinal wall probably by a transport system, as with other depolarizing agents, is slow (Lüthi and Waser, 1965 and 1967). An interesting experiment on the monkey showed muscarine to have little effect orally (Fraser, 1957). No effect followed oral administration of 2 mg, despite the fact that the amount given was many times that which causes poisoning by the ingestion of amanita muscaria in the human being.

Gyermek and Unna (1960) attempted to eliminate the peripheral actions of muscarine by blocking the cholinergic receptors with atropine-methylbromide 15–20 minutes before the administration of muscarine. By this procedure the intravenous minimal lethal dose of *d*,l-muscarine was elevated from 1 mg/kg to over 160 mg/kg, but no central effects were recorded.

The electrophoretical local administration of acetylcholine, *d*,l-muscarine and other cholinomimetics has shown quite different neurones of the central nervous system (pyramidal cells of the cortex, cerebellar and thalamic neurons and Renshaw cells) to possess excitable muscarinic and nicotinic receptors (Curtis et al., 1961, 1964, 1966) (Krnjevic and Phillis, 1963). Cortical cells are extremely sensitive to acetylcholine, muscarone, muscarine and acetyl-$\beta$-methylcholine. There may be many other neurons which behave in a similar way, and we have to conclude that muscarine entering the brain will have different central and psychotropic actions. Although *choline* is well absorbed through the intestinal wall, most of it is rapidly metabolised and esterified in the tissue. Generally the action of free choline is similar to

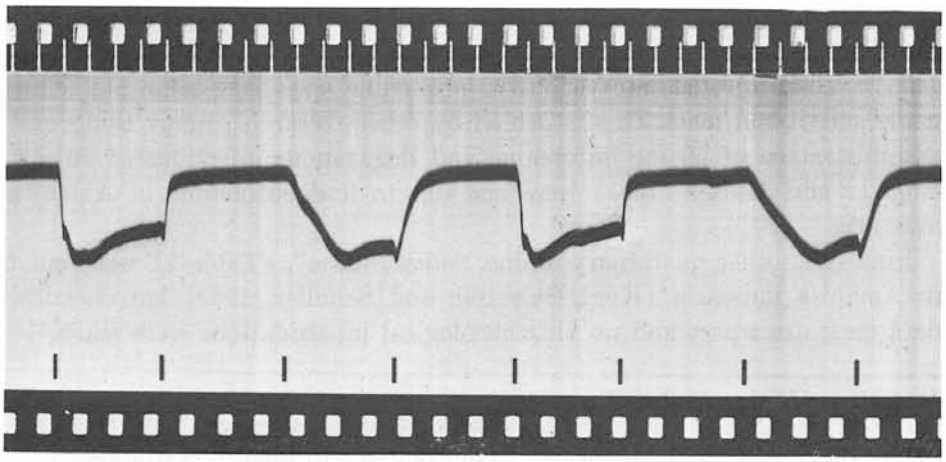


FIG. 4.—Contractions of m.sphincter iridis of pig by acetylcholine ($1:3{,}5\times10^{-6}$ m) and muscarine ($2:10^{-7}$ m). Time in minutes. Slow, gradual contraction by muscarine.



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acetylcholine, but the dose needed in different experiments is 200–100,000 times higher (Bovet, 1948). Direct electrophoretical application of choline to different neurons in the brain has no effect.

## Centrally Acting Compounds

*Atropine and tryptophane derivatives*

As we have seen, the oral ingestion of muscarine cannot be responsible for the colourful amanita-intoxication of asian people described by travellers touring Siberia. Different explanations were given and additional central active ingredients were proposed. The unknown active principle was unfortunately given the name *Pilzatropin* or *muscaridine* by Kobert in 1891. The search for an atropine-like alkaloid in amanita muscaria has continued since then. Lewis (1955), reported the isolation of hyoscyamine from amanita muscaria and amanita pantherina in South Africa. Later, Polish chemists made a similar statement concerning their local mushrooms. Regardless of the very small concentration found in the mushrooms (<0.0001%), the symptoms of the intoxication do not fit the central effect of 10–30 mg of orally ingested atropine or belladonna-alkaloids, as scopolamine. Profuse salivation and perspiration, nausea, vomiting, bradycardy, mydriasis, are found, together with central excitation and delirious intoxication. Even small doses of atropine with hallucinations would immediately block the peripheral actions of muscarine (salivation, perspiration etc.). It would be prejudicial to treat here the pharmacology of atropine and similar bases before the presence of these alkaloids in the mushroom is demonstrated with certainty by chemical methods. Until now this evidence has not been substantiated or repeated by other research groups.

Another dubious proposal as a psychotropic principle in amanita muscaria is *bufotenine* (Table 1). This amine was isolated in considerable quantities from Amanita mappa, and detected in small amounts by paper chromatography in Amanita muscaria and Amanita pantherina (Wieland et al., 1953). When injected intravenously, bufotenine may have some hallucinogenic activity in man. This is denied by other research groups using oral administration of 50 mg bufotenine and intravenous injections of 20 mg. Eugster and Müller (1961) were not able to find bufotenine in Amanita muscaria.

Finally another quaternary amine, "*muscaridine*", (Table 1) was found in Amanita muscaria (Kögl, Salemink and Schuller, 1960) but chemical data on it are scarce and no pharmacological investigations were made.

*Ibotenic acid, muscimol and muscazon*

Lately, Eugster and co-workers have isolated and identified different new active substances from amanita muscaria which may—at least partly—explain its psychotropic action. The pharmacological screening of the isola-

tion process was developed by W. Theobald.[1] It is based on the potentiating effect of these compounds on the narcosis produced by a short acting hypnotic (2-methoxy-4-allyl-phenoxyaceticacid-diethylamide), (Müller and Eugster, 1965; Good, Müller and Eugster, 1965). The narcosis potentiating principle of the mushroom consists of three different compounds (table 1). Sedative action of *muscazon* was much less than with *ibotenic acid* and *muscimol.* These two have a very pronounced hypnotic effect, and it is very probable that they also are psycho-active, although nothing definite has been described.

In order to demonstrate this sedative/hypnotic effect, we have injected mice with different doses intraperitoneally, and put them together with controls in activity cages (Fig. 5, 6). Sedative action is evident with 4–8 mg/kg ibotenic acid and 1–2 mg/kg muscimol. Oral administration is approximately half as effective as intraperitoneal injection.

These new compounds are rather toxic for mice. Muscimol is roughly 5–10 times more potent than ibotenic acid. Rats seem to be less sensitive (Table 3).

TABLE 3

| | | i.p. | p.o. |
|---|---|---|---|
| Toxicity in mice (LD 50) | Ibotenic acid | 25 mg/kg | 50 mg/kg |
| | Muscimol | 6 mg/kg | 12 mg/kg |

Typical signs of intoxication develop similarly from both substances: nervousness, excitation, wide open eyes and dilated pupils, convulsions, twitches, tonic cramps, typical signs of catalepsy, irregular often accelerated respiration, later sedation and sleep.

## Screening Methods for Hallucinogenic Drugs

In order to search for new active principles, we have to use other screening methods, which should be especially useful for finding compounds with psychotonic activity. The symptoms of intoxication most often show pharmacological effects resulting from the stimulation of central sympathetic structures. We find three methods to be of value for a general screening of numerous fractions of extracts with mice.

The most simple may be to measure the diameter of the mouse pupil during the toxicological assay. We use groups of ten mice per dose. Most hallucinogens, as LSD, Psilocybin, produce a marked dilatation. When the starting diameter with a standardized light source is small, this effect may be measured with ease. Of the new compounds, muscimol is especially effective (Fig. 7). The best way of application is intraperitoneal injection, but for comparision with the intoxication symptoms with the mushroom, oral ingestion may be preferred (Fig 8). Direct application of muscimol (0.5%) on the eye has no dilatory effect.

[1] Dr. W. Theobald, J. R. Geigy, A. G. Basel.

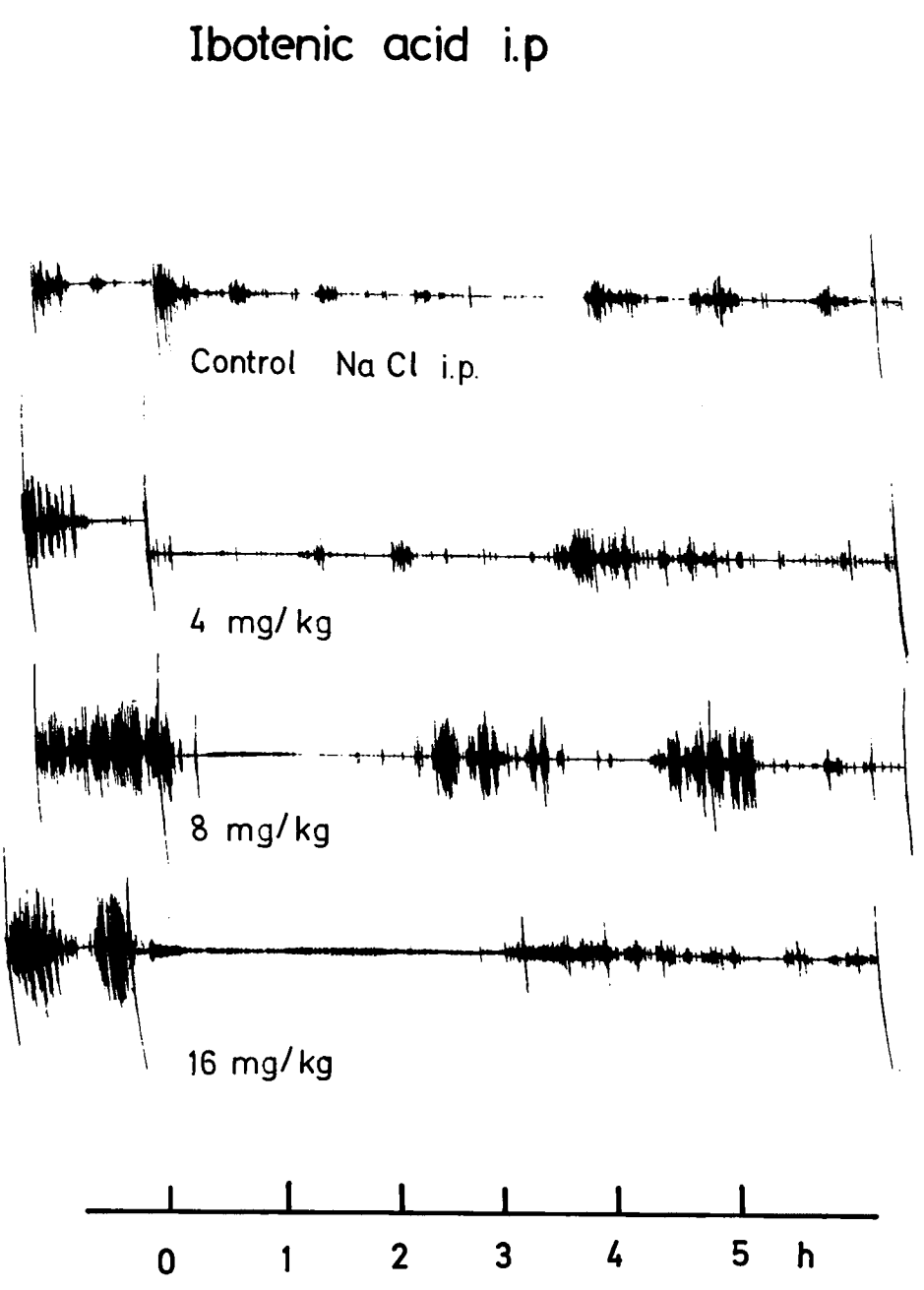


FIG. 5.—Mice in jiggle cage, intraperitoneal injection of ibotenic acid. 8 and 16 mg/kg produce sedation of 2 and 3 hours. In the first phase muscle twitching was recorded.

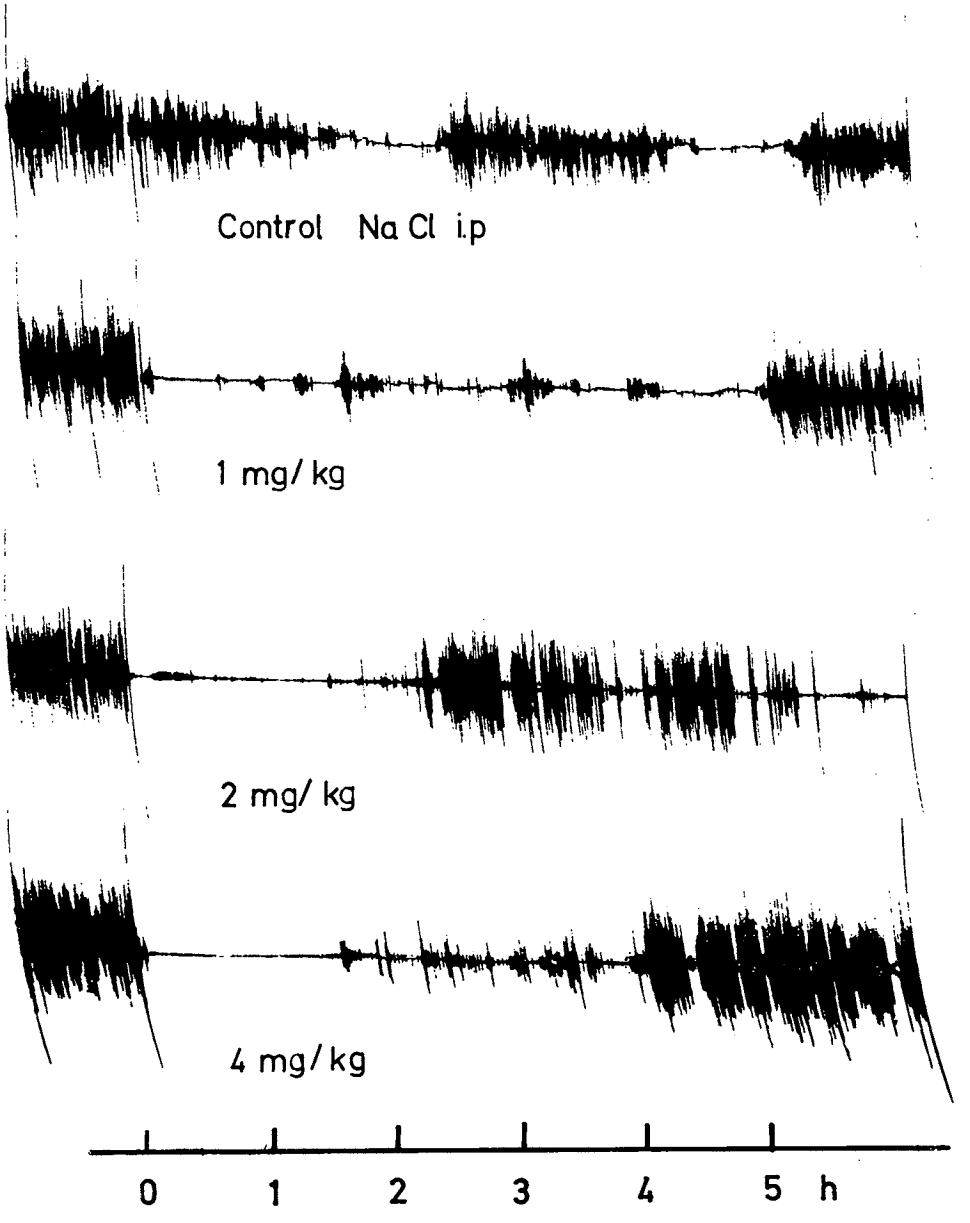


FIG. 6.—Muscimol sedates mice in jiggle cage with doses of 1, 2, and 4 mg/kg during 1–2 hours. Myoclonic cramps were recorded.

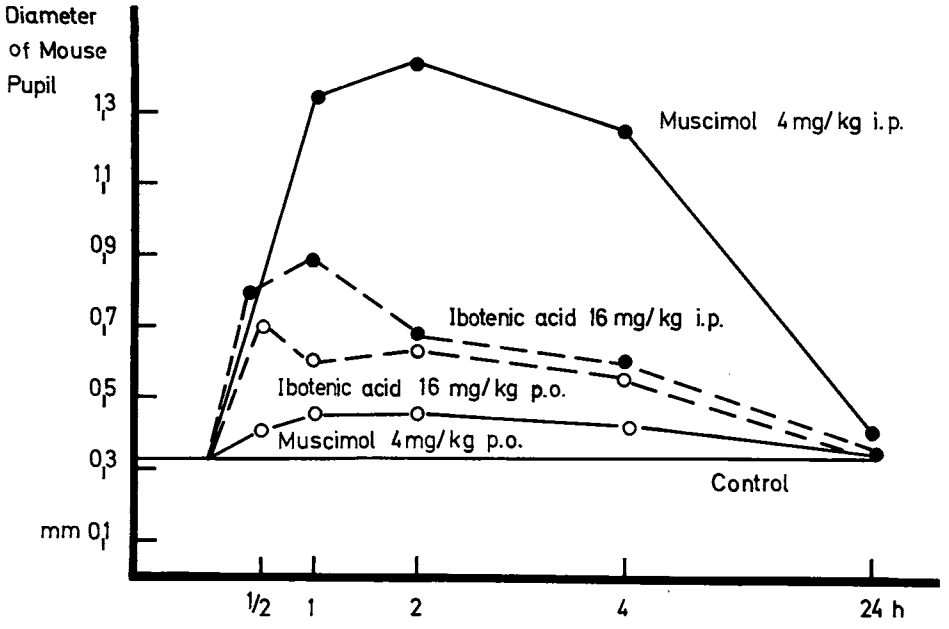


FIG. 7.—Dilatation of pupils by ibotenic acid and muscimol (groups of ten mice, statistical error not marked).

Another method we use is similar to the determination of antidepressant activity of neuro- and thymoleptics. It is based on the antagonism of reserpine-induced hypothermia. Liberation of catecholamines and serotonine in the brain makes mice sensitive to psychostimulating drugs (Askew, 1963). Mice are injected subcutaneously with 2 mg/kg reserpine and kept overnight at room temperature of 20° C. The rectal temperature is measured using a thermo-couple inserted to a depth of 2 cm. Groups of 8 mice are then injected intraperitoneally with the test drug or saline as control. CNS-stimulants (phenmetracine, amphetamine, methamphetamine, cocaine) and hallucinogenic drugs (LSD, Psilocybin), reverse the effect of reserpine and increase the rectal temperature within a few hours to normal values (Fig. 9, 10). The only exception is mescaline; it strongly depresses the temperature. Muscimol has an increasing effect on temperature like other hallucinogens, but only after 2–4 hours, whereas ibotenic acid keeps rectal temperature low (Fig. 11).

A third simple method to test psychotomimetic drugs is checking their effect on food intake. Hunger or appetite are the strongest drives in animal or man. They are easily influenced by central drug action. We have developed over the years different test methods to measure anorexogenic action (Spengler and Waser, 1957, 1959). Rats with a well controlled food intake are trained to a feeding period between 10 a.m. and 4 p.m. One hour before feeding time the test drug is injected intraperitoneally. At 12 a.m. and at the end of the feeding period (4 p.m.), the consumption of food is measured.

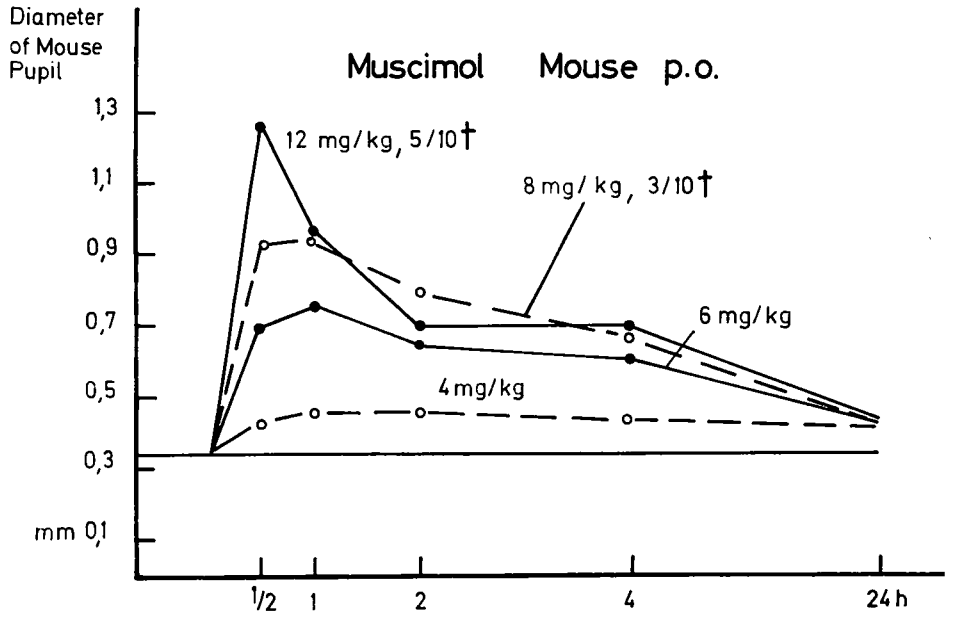


FIG. 8.—Action of muscimol per os on pupils of mice. Strong dilatations with toxic doses.

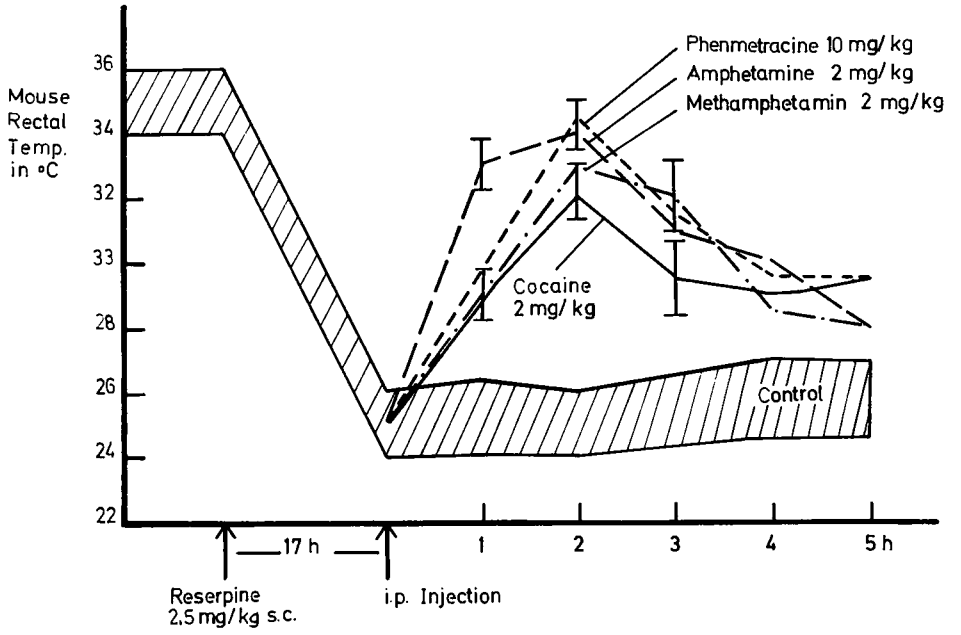


FIG. 9.—Rectal temperature of reserpinized mice (groups of 6 animals). Action of central stimulating drugs compared to control.

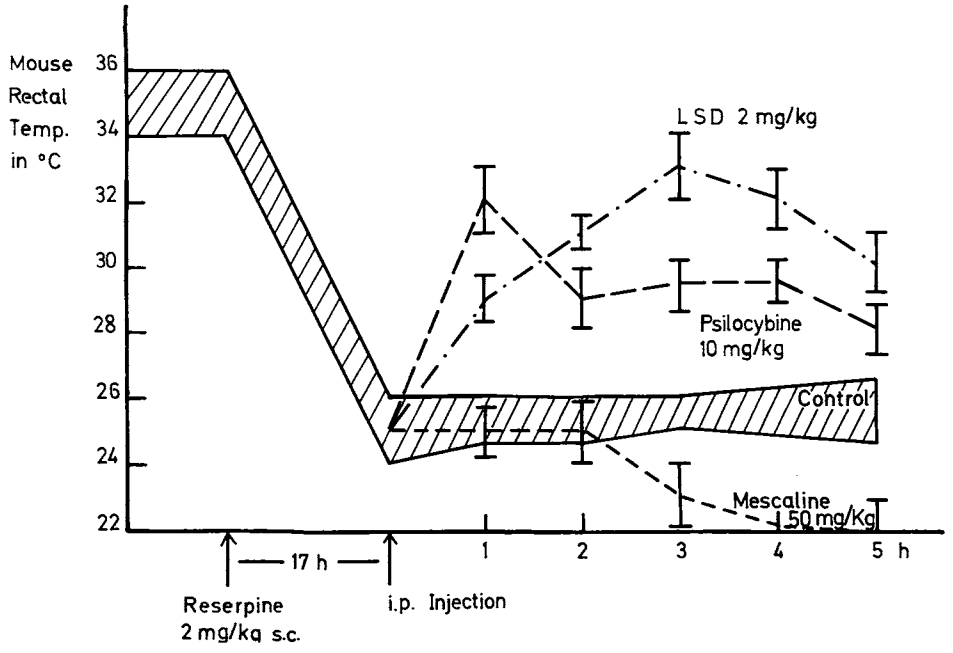


FIG. 10.—Rectal temperature of reserpinized mice under the influence of hallucinogenic drugs.

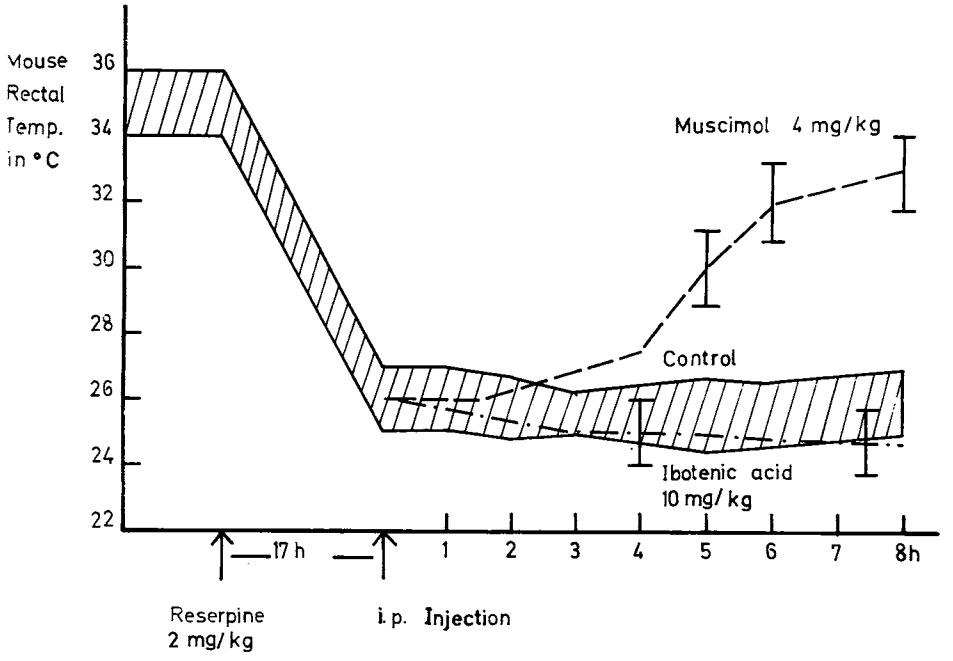


FIG. 11.—Rectal temperature of reserpinized mice under the influence of muscimol and ibotenic acid from Amanita muscaria.

Most sympathomimetics and hallucinogens have a pronounced anorexogenic effect during some hours, probably by stimulating the satiety center in the hypothalamus (Waser and Spengler, 1963) (table 4). Muscimol and ibotenic acid act in a similar way in doses which are not hypnotic. After the experiment the rats may recover during two days with standardized feeding period before the next injections.

TABLE 4.—*Anorexogenic activity of drugs in diminishing normal food intake of rats to one half (ED 50)*

| | mg/kg i.p. | Excitation |
|---|---|---|
| *d*-Amphetamine | 2, 5 | ++ |
| Ephedrine | 17 | + |
| Phenmetrazine | 15 | + |
| Methylphenidate | 17 | + |
| Scopolamine | 0, 8 | |
| Atropine | 2, 5 | + |
| Carbachol | 1, 0 | |
| Parpanit | 35 | |
| Mescaline | 90 | (+) |
| LSD | 1 | (+) |
| Psilocybin | 18 | + |
| Cocaine | 30 | + |
| Caffeine | 250 | + |
| Ibotenic acid | 5, 0 | |
| Muscimol | 4, 0 | |

We have adapted this method to mice for a screening of small amounts of Amanita extracts. Mice are not as clean and trainable as rats, and we have not finally decided on the best technique. Using a special food container from which the fine grain cereal cannot be scattered and which remains tolerably clean, we are able to determine small differences in food intake. On mice the effects of muscimol and ibontenic acid are even stronger than the actions of LSD and amphetamine (Fig. 12, 13). We therefore think this kind of approach to be very promising for the screening of psychotropic compounds.

## Central Nervous Effects In Man

Besides the well known descriptions of amanita-intoxication, not much is known about experiments with pure substances on man. Ibotenic acid and muscimol are now under careful investigation by a psychiatrist.[2] The work of the pharmacologist ends at this stage.

Curiosity is one of the main qualities of a scientist, and this may be the reason why a pharmacologist watching the behaviour of his animals under

[2] Prof. H. Heimann, Clinique psychiatrique universitaire Lausanne.

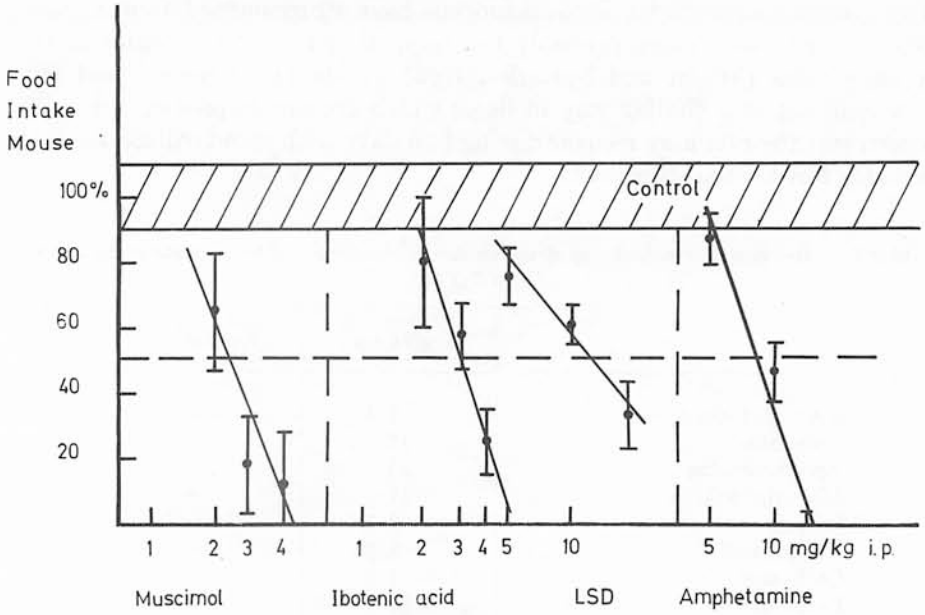


FIG. 12.—Diminished food intake of mice with different psychotropic drugs. Mice are much less sensitive to LSD and amphetamine than rats.

FIG. 13.—Mice two hours after i.p. injection of 5 mg/kg muscimol: different phases of sedation, catatonia, myoclonic cramps, with eyes open or closed.

certain drugs wants to know more about the emotions and changes in reaction they produce. Another reason is ethical. We have to foresee the accidents and dangerous actions new compounds of general interest may produce on man. My report on some experiments done on myself by ingesting ibotenic acid and muscimol under careful psychiatric control [3] may give you an unauthoritative view on this.

A 20 mg ibotenic acid dose ingested in water tastes like mushrooms, but produces little immediate action. Within half an hour a warm and slightly flushed face was noticed, without changes in blood pressure or heart rate with no psychic stimulation, but lassitude followed by sleep. One day later a migraine with classical one sided visual disturbance developed for the first time in my life. The occipitally localized headache continued in a milder form for two weeks.

Next I turned to muscimol. A dose of 5 mg in water orally ingested had little effect except a feeling of laziness. Ten mg produced a slight intoxication after 90 minutes with dizziness, ataxia and elevated mood, psychic stimulation (in psychological tests), no hallucinations but slight changes in taste and colour vision. Some myoclonic muscle twitching followed, then sleep with dreams. After two to three hours I felt normal, rested and able to undertake anything, even work. During the next night I slept well, deep and long. No other signs followed.

With 15 mg muscimol administered orally the intoxication started after 40 minutes and was more pronounced. Dizziness made walking with closed eyes impossible, but reflexes were not changed. Speech was sometimes inarticulate and dysarthric. Appetite and taste were diminished. After a phase of stimulation, concentration became more difficult. Vision was altered by endlessly repetitioned echo-pictures of situations a few minutes before. Hearing became noisy and sometimes was followed by echo. Most disturbing were repeated myoclonic cramps of different muscle groups. I felt sometimes as if I had lost my legs, but never had hallucinations as vivid and colourful as with LSD. The pupils remained always the same size. After 2 hours I fell asleep, but I cannot remember any dreams. Two hours later I awoke again and was glad that the muscle twitching was less frequent. I did not feel relaxed and fresh as after 10 mg. muscimol but rather dull and uncertain. Blood pressure was only a little elevated during the psychoactive phase. In preliminary experiments muscimol was detected in the urine by ion exchange separation and thin layer chromatography (C. H. Eugster).

Muscimol makes a toxic psychosis with confusions, dysarthria, disturbance of visual perception, illusions of colour vision, myoclonia, disorientation in situation and time, weariness, fatigue and sleep. Concentration tests show an improved performance with small doses (5 mg), but diminished performance and learning with an increased number of errors with higher doses (10–15 mg).

[3] PD Dr. J. Angst, Psychiatrische Universitätsklinik Zürich.

## Discussion

Different biologically active principles have been isolated from amanita muscaria. Some, as muscarine, acetylcholine, choline, ibotenic acid, muscimol and muscazon, were found by different scientists, but others were not confirmed by later research.

The action of muscarine is well known today, and it is generally accepted that muscarine is one of the most active parasympathomimetic drugs. This is partly due to its stability, as it is not hydrolized by cholinesterases. On the other hand, muscarine does not inhibit acetyl-cholinesterase in concentrations up to $10^{-4}$ m. It acts on the same receptors as acetylcholine, but its action is restricted predominantly to peripheral effector organs innervated by the autonomous nervous system. All cholinomimetic effects are antagonized by atropine.

Muscarine affects ganglionic synapses only by much higher doses than acetylcholine. With electrophoretic application on cortical Betz cells, muscarine shows an action 1–4 times as powerful as acetylcholine (Crawford and Curtis, 1966). But as we have seen, muscarine passes only with great difficulty through the intestinal wall, and the oral toxicity is remarkably low. The same must be said for the passage through the blood-brain barrier. Therefore, with the very low concentration of muscarine in the orally ingested mushroom, it is impossible that this alkaloid produces the psychotomimetic symptoms observed in amanita intoxication.

Acetylcholine and choline which are found in small, but varying amounts in the mushroom can as well not be held responsible for this action. Acetylcholine is immediately hydrolyzed by ubiquitous cholinesterases, and choline is practically inactive, especially when applied directly on central neurons.

The central action of amanita muscaria must be caused by the new aminoacids and amines detected in considerably high concentration in the mushroom. The described screening methods show especially for muscimol an intense central action, which is linked with the sympathetic system of the brain stem, as shown by the typical hyperthermic effects of reserpinized mice, central pupillary dilation and anorexia. Furthermore, the pyramidal and extrapyramidal motor systems are probably involved in some of the classical reactions as ataxia, catalepsy, convulsions and muscle twitches. But only with a further analysis may these symptoms be linked to specific sites of action as central ganglionic nuclei or spinal interneurons. The amines are considerably more active than the aminoacids, which are different with other centrally active catecholamines or tryptamines.

The most important finding surely is the psychotic action of muscimol as demonstrated in man. Although intense hallucinations as with LSD were missing with doses of 10–15 mg, there resulted considerable disturbance of psychic functions, such as orientation in situation and time, visual perception, process of thinking, speech, and some new psychic phenomena of illusions and perseveration of optical perception (echo pictures). Here again muscimol was more active than ibotenic acid, which showed only some unpleasant effects on the local circulation.

When we compare now my personal psychotropic experiences with some descriptions of intoxications by amanita muscaria, we see in some respects an interesting parallelism. In the old literature (Donalies and Völz, 1960, Buck, 1963) and during this symposium (Brekhman and Sam, Wasson), the following symptoms were mentioned after ingestion of 1–4 mushrooms: dizziness, nausea, vertigo, somnolence, euphoria, sense of lightness, and coloured visions. Slight acoustic and optic hallucinations were noticed within the next few hours. A higher dose (5–10 mushrooms) produces severe effects of intoxication such as muscular twitching, leading to twitches of limbs; raving drunkenness with agitation and vivid hallucinations. Later, partial paralysis with sleep and dreams follow for many hours. Ingestion of more than 10 mushrooms is usually fatal. The hallucinogenic principle is excreted in the urine. It evokes the same symptoms when the urine is drunk again.

With 15 mg muscimol symptoms of the first group and muscular twitching were noticed. Hallucinations were not as vivid and colourful as expected. The picture would fit best for a dose of 5 mushrooms. As ibotenic acid produces only slight central action, probably muscimol is mainly responsible for these central effects. Further studies will show if muscimol is excreted unchanged and quantitatively in the urine. Other compounds in the mushroom may be responsible for its complex psychotic effect.

## Summary

Because of its extraordinary pharmacological activity muscarine, the best known alkaloid of amanita muscaria, has been investigated for more than 100 years by chemists and pharmacologists. It was the first known drug with selective action on the autonomous nervous system. After its isolation in a pure and crystalline form (Eugster and Waser, 1954), its chemical structure and synthesis were established (Reviews by C. H. Eugster, S. Wilkinson). During the isolation process different screening methods were used. They are based on the strong parasympathomimetic activity of muscarine (Review by P. G. Waser, 1961). Until today nobody was able to show a direct psychotropic effect of muscarine on animal or man, probably due to its difficulty in passing the blood-brain barrier. In contrast, muscarine applied directly into the brain was shown to have an excitatory effect.

The active principles responsible for hallucinogenic or sedative symptoms described by different authors are only partly identified. Belladonna-like alkaloids, serotonin and bufotenin have not been extracted from the mushroom with certainty, but possibly there are other hydroxy-indoles present.

Lately Eugster, Theobald and colleagues (1965) discovered muscimol, ibotenic acid and muscazon in different varieties of amanita muscaria. These $\alpha$-aminoacids and amine have pronounced sedative and hypnotic actions in mice, but little is known on their hallucinogenic activity. Their pharmacology on small animals was investigated with different methods. The temperature of reserpinized mice (2 mg/kg i.p.) is increased with orally 4 mg/kg

muscimol as with LSD, psilocybin, amphetamine or cocaine, but not changed with 10 mg/kg ibotenic acid.

The diameter of mouse pupils is enlarged by intraperitoneal injection and oral ingestion of muscimol (4–8 mg/kg) and ibotenic acid (16 mg./kg). Both compounds showed a marked anorexogenic effect on mice (2–3 mg/kg oral) with sedation, hypnosis, muscle twitchings and catalepsy.

Most important is the psychotomimetic effect on man. Muscimol (10–15 mg oral dose) creates a toxic psychosis with confusions, dysarthria, disturbance of visional perception and hearing, illusions of colour vision, muscle twitching and myocloni, disorientation in situation and time, weariness, fatigue and sleep with dreams. Small doses (5 mg) improve performance in concentration tests, but large doses diminish psychic performances and learning. Ibotenic acid and muscazon have less central action. Muscimol is excreted in the urine.

Using different screening methods, we are now looking for other psychoactive principles in amanita muscaria.

## REFERENCES


ANDERSEN, P., CURTIS, D. R., "The pharmacology of the synaptic and acetylcholine induced excitation of ventrobasal thalamic neurons." A. physiol, scand., 61: 100–120 (1964).

ASKEW, B. M. "A simple screening procedure for imipramine-like antidepressant agents." Life sciences, 10: 725–730 (1963).

BOVET, D., BOVET-NITTI, F. Médicaments du system nerveux végétatif. S. Karger, Basel, 1948.

BREKHMAN, I. I., SAM, Y. A. "Ethnopharmacological investigation of some psychoactive drugs of siberian and far-eastern minor nationalities of U.S.S.R." Ethnopharmacological Search for Psychoactive Drugs. Proceedings of a Meeting. Ed. Daniel H. Efron. Public Health Service Publication, U.S. Printing Office, 1967.

BUCK, R. W. "Toxicity of Amanita muscaria." J. Amer. Medical Assoc., 185; 663–664 (1963).

CRAWFORD, J. M., CURTIS, D. R. "Pharmacological studies on feline Betz cells." J. Physiol., 186: 121–138 (1966).

CRAWFORD, J. M., CURTIS, D. R., VOORHVEVE, P. E., WILSON, V. J. "Acetylcholine sensitivity of cerebellar neurons in the cat." J. Physiol., 186: 139–165 (1966).

CURTIS, D. R., PHILLIS, J. W., WATKINS, J. C. "Cholinergic and non-cholinergic transmission in the mammalian spinal cord." J. Physiol., 158: 296–323 (1961).

CURTIS, D. R., RYALL, R. W. "The excitation of Renshaw cells by cholinomimetics." Exp. Brain Res., 2: 49–65 (1966).

DONALIES, G., VÖLZ, G. "Ein Selbstmordversuch mit Fliegenpilz" Der Nervenarzt, 31. Jahrgang, Heft 182–185, 1960.

EUGSTER, C. H., WASER, P. G. "Zur Kenntnis des Muscarins." Experientia, 10: 298–300 (1954).

FRASER, P. J. "Pharmacological actions of pure muscarine chloride." Brit. J. Pharmacol., 12: 47–52 (1957).

GOOD, R., MÜLLER, G. F. R., EUGSTER, C. H. Prämuscimol und Muscazon aus Amanita muscaria." Helv. Chim. Acta., 48: 927–930 (1965).

GYERMEK, L., UNNA, U. R. "Spectrum of action of muscarone and its derivatives." J. Pharmacol. exp. Therap., 128: 30–36 (1960).

KOBERT, R. "Ueber Pilzvergiftungen." St. Petersburg med. Wochenschrift, No. 51: 463–466, No. 52: 471–474 (1891).

Kögl, F., Duisberg, H., Erxleben, H. "Untersuchungen über Pilzgifte I: Ueber das Muscarin I." Liebigs Ann., 489: 156–192 (1931).
Kögl, F., Saleminк, C. A., Schuller, P. L. "Ueber Muscaridin." Rec. Trav. chim. Pays-Bas, 79: 278–281 (1960).
Konzett, H., Waser, P. G. "Zur ganglionären Wirkung von Muscarin." Helv. physiol. Acta, 14: 202–206 (1956).
Krnjevic, K., Phillis, J. W. "Acetylcholine sensitive cells in the cerebral cortex." J. Physiol., 166: 296–327 (1963).
Krnjevic, K., Phillis, J. W. "Pharmacological properties of acetylcholine sensitive cells in the cerebral cortex." J. Physiol., 166: 328–350 (1963).
Mc Lennan, H. "Synaptic transmission in the central nervous system." Page 399 in Physiological Pharmacology, volume II, Academic Press, New York, 1965.
Lewis, B. "Atropine in mushrooms—therapeutic implications." South African Medical Journal, 29: 262–263 (1955).
Lüthi, U., Waser, P. G. "Verteilung und Metabolismus von $^{14}$C-Decamethonium in Katzen." Arch. int. Pharm., 156: 319–347 (1965).
Lüthi, U., Waser, P. G. "Verteilung und Metabolismus von $^{14}$C-Carbachol bei atropinisierten Katzen." Arch. int. Pharm., 1967 (in press).
Malone, M. H., Robichaud, R. C. Tyler, V. E. Jr., Brady, L. R. "Bioassay for muscarine activity and its detection in certain inocybe." Lloydia, 24: 204–210 (1961).
Müller, G. F. R., Eugster, C. H. "Muscimol, ein pharmakodynamisch wirksamer Stoff." Helv. Chim. Acta, 48: 901–926 (1965).
Pulewka, P. "Das Auge der weissenMaus als pharmakologisches Testobjekt." Arch. exp. Path. Pharm., 186: 307–318 (1932).
Spengler, J., Waser, P. G. "Ein Apparat zur Messung des Futterverzehrs und zur Registrierung des Fressverhaltens von Ratten." Helv. Physiol. et Pharmacol. Acta, 15: 444–449 (1957).
Spengler, J., Waser, P. G. "Der Einfluss verschiedener Pharmaka auf den Futterkonsum von Albino-Ratten im akuten Versuch." Arch. exp. Path. Pharm., 237: 171–185 (1959).
Waser, P. G. "Chemistry and Pharmacology of muscarine, muscarone and some related compounds." Pharmacol. rev., 13: 465–515 (1961).
Waser, P. G., Spengler, J. "Die pharmakologische Beeinflussung von Hunger und Sättigung." Schweiz. med. W'schrift, 93: 90 (1963).
Wasson, R. G. "Fly agaric and man." Ethnopharmacological Search for Psychoactive Drugs. Proceedings of a Meeting. Ed. Daniel H. Efron. Public Health Service Publication, U.S. Printing Office, 1967.
Wieland, T., Motzel, W., Merz, H. "Ueber das Vorkommen von Bufotenin im gelben Kollenblätterpilz." Liebigs Ann., 581: 10–16 (1953).

# Discussion[4]

*Chairman*—DANIEL H. EFRON
*Members of the Panel*—VENANCIO DEULOFEU
CONRAD H. EUGSTER
CLAUDIO NARANJO
DERMOT TAYLOR
PETER G. WASER
R. GORDON WASSON

DR. KLINE: I would like to start with a philological question for Dr. Wasson: Why is *Amanita muscaria* called Fly Agaric?

MR. WASSON: The origin of the name Aminita Muscaria is a folk word; it goes back in the Germanic world many generations. Mukhamor is the Slavic word, the fly killer, and in Japan one of the names used for this mushroom is Haitori, the fly killer, and that is quite independent of Europe.

This mushroom has weak insecticidal powers. If fresh fly agarics are cut up properly and laid out, flies will suck the juice and succumb in a stupor. They do not die as a rule, and will revive in a matter of hours or a couple of days. This is the current explanation. I think the name can be explained in another way: the association throughout the middle ages and earlier, of madness with the fly. People who were possessed were believed to be infested with flies. This was true throughout northern Eurasia. In Russia, Denmark, Germany, England, the fly spelled insanity. When you were treated, they waited for a fly to emerge from your nostril and you were cured. The mad mushroom, the Bolond gomba of the Hungarians, the Narren Schwamm of the Germans—these were the fly agaric.

DR. EUGSTER: I would like some comments. I agree with Mr. Wasson's view; these flies in Fly Agaric are in my opinion, symbols for the demonic power of Fly Agaric.

The insecticide properties of these compounds (e.g. muscimole and ibotenic acid) are very, very weak, and you have to use starved flies for these tests, so your explanation is the best one, in my opinion, too.

CHAIRMAN DR. EFRON: This question is to Dr. Waser: "How might one treat an intoxication by Amanita Muscaria?"

DR. WASER: The intoxication is not caused only by the small amount of muscarine, and, generally, atropine is of no big value. (Atropine is of big value only if you have an intoxication with *inocybe lateraria* where you have muscarine intoxication). Amanita muscaria creates intoxication of the central nervous system with hallucinogenic principles, and you should probably use chlorpomazine.

[4] This discussion covers papers of Sessions V and VI, as well as a general discussion of the entire meeting. In addition to the members of the panel, other members of the Faculty participated in the discussion.



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CHAIRMAN DR. EFRON: The next question is the following—it is not addressed to anybody: "Is there a pharmacological explanation for the retained activity of Fly Agaric in the urine?" Who would like to answer this question?

DR. WASER: I can only say we do not know yet; we are investigating that Dr. Eugster found a compound in my urine which looks like muscimole, but this has to be confirmed.

CHAIRMAN DR. EFRON: I may speculate on this problem. There is a probability that the active principle of Fly Agaric—I don't want to say which one of the compounds it is—is not enzymatically metabolized. In the same way as we can find penicillin in urine after penicillin has done its job in the body, we may find also the active principle of Fly Agaric in the urine of the user. This is only pure speculation; I don't have any proof.

MR. WASSON: There is one factor: it is possible that some of the objectionable aspects of the raw mushroom, especially the emetic effect, is filtered out when you get it into the urine, and the urine seems to be popular as a beverage.

CHAIRMAN DR. EFRON: This question is for Mr. Wasson: "Would you speculate as to why the use of Fly Agaric has been decreasing during the last two hundred years?"

MR. WASSON: I don't think it is a matter of speculation. The superior and stronger culture of the Russians among Siberian tribes have brought lots of pressure to bear on these tribes to abandon their native ways. This is universial. I think we are just as guilty, if you wish to call it guilty, or we are just as noble, if you wish to call it noble, but the superior culture does not like native ways. In fact, we had a paper submitted to us for this session by Dr. Brekhman of Vladivostok, and he boasted at the end that this thing is being abolished by the beneficent influence of the great Soviet Union, and that is obvious; but before the Soviet Union, it was the Czars.

There is the commercial aspect that Vodka is sold to the natives, and if the natives prefer Fly Amanita, which they go out and gather in the field, they wouldn't drink vodka.

DR. HOLMSTEDT: Dr. Eugster and Dr. Waser, after this magnificent work that you presented, what is it that makes you think there are still other psychoactive principles in the Amanita?

DR. WASER: This is, I should say, only a feeling related to research work underway. Mr. Wasson has told, and we know of other statements, about the very vivid hallucinations; but I did not have this kind of hallucinations that we expected. Surely the dose and the psychoactive state of the volunteer are important—maybe I am a very sober Swiss man! But if you take at the same time maybe alcohol or other plant extracts, which we do not know, you might have a stronger reaction. Do you agree, Mr. Wasson?

MR. WASSON: Five of us took the mushrooms three days running in 1965. Three of us took the mushrooms three days running in 1966. We took it raw, we took it with the juice pressed out, and drank the pure juice. We mixed the juice with milk, we toasted the caps and then mixed the juice with *miso shiru*, the Japanese soup. Only one of us had the right reaction. We all threw up, we all slept then for two hours, but the feeling of elation was con-

spicuous in only one of us, and that man was a compulsive speaker for the next three or four hours. He was in a state of bliss beyond compare. He said, "This is nothing like alcohol, it is so superior, it belongs to a different class." He was one of the foremost mycologists of Japan.

DR. WASER: Maybe I should add about muscimole, that it gives me a very interesting feeling with small doses (5–10) mg). I felt just like walking on glass or on ice. The thinking was just like gliding on ice; if I started to think on something I would go like a curling stone without any friction. It was so easy to think about everything; but no distinct hallucinations were experienced.

CHAIRMAN DR. EFRON: Maybe Dr. Eugster would like to add something to this, because I saw his smile before.

DR. EUGSTER: There are some reports in the literature about Amanita Muscaria eating. You remember, Mr. Wasson, it also mentioned that the liquor made of *Epilobium angustifolium* L., an alcoholic drink, is taken simultaneously, and we don't know anything yet about the joint action of alcohol, for instance, and these compounds.

CHAIRMAN DR. EFRON: This question is to Mr. Wasson: "Have you ever seen a picture in Indian Art of a mushroom, or mention of mushroom itself in Indian literature to support your theory that Soma might be Fly Agaric?"

MR. WASSON: There is no mention in Indian literature and there is no picture in the hall of Indian art. Of course, that is perfectly easy to explain; it disappeared before there was any literature, except the RgVeda; it disappeared long before Christ; it disappeared about the time of Buddha, from which epoch we have no statuary, we have no art. Of course, there is mention of a mushroom in Indian history, a famous, famous mushroom. It is in connection with the death of Buddha; he is supposed to have died of mushrooms. The circumstances of Buddha's death are rather baffling, but I don't advance this theory of his death seriously. The oldest of the stupas in India, the ones that survive from the first to the third century before the Christian era, are topped with what the Indians call a 'parasol', a *chattra*. This *chattra* or parasol is the symbol of lay authority in Indian culture, of the rajput caste. Chattra means not only 'parasol' but mushroom, and I was much impressed by the triple-capped mushroom when I saw it surmounting the stupa at Ranchi.

DR. EUGSTER: Please explain ambrosia, your opinion about ambrosia.

MR. WASSON: Of course, it seems to me an insoluble problem. In Sanskrit the same word is *amrita*, and Sanskrit is just as old as Greek; you can say it is even older. Soma is called amrita, time and again in the RgVeda. My own view is that amrita is Soma, and that Soma is a mushroom.

CHAIRMAN DR. EFRON: This question says: "Have kinesthetic flying sensations been noted when taking Amanita Muscaria?"

MR. WASSON: Idon't remember any in the literature, any flying sensation. We had no flying sensations, certainly.

The one man who had what would be called a perfect reaction—he wished to exert himself—he shouted at the top of his lungs to a man who was standing three feet from him; and the literature is full of that kind of thing. Of

course, the thing behind this is, I suppose, witchcraft, the flying of the witches going to the Sabbat. But in the records of witchcraft, there is no mention of anything resembling mushrooms.

FROM THE FLOOR: Natives took mushrooms and they were flying off in the Yukagi, the Shaman. It is a well known thing in Asia, and you have the Shaman, they go up into the clouds.

MR. WASSON: With mushrooms?

FROM THE FLOOR: Yes.

MR. WASSON: Can you give me the citations?

FROM THE FLOOR: Shaman flying is not associated with mushrooms.

FROM THE FLOOR: They drink mushrooms, and they pass it on in the urine.

FROM THE FLOOR: The experience of your body leaving is very prominent in Muscaria intoxication; the body is separated or called the astro body.

DR. FREEDMAN: There is a recent article in the British Journal of Psychiatry on witchcraft.

DR. KLINE: Barnett has a recent article in which he tells us about the witches' sabbath, but I don't think he mentions mushrooms.

DR. NARANJO: I would like to comment that the experiences with harmaline have been similar, not only to tropical American Shamanism, but to Shamanism as described for Siberia. Siberian Shamans often describe an experience that involves flying and transformation into a vulture, or that of being taken by a big bird, or torn into pieces by a bird of prey, and the persons under the influence of the harmaline either felt transformed into birds of prey or had a very vivid imagery of the same type, which was blended with the motives of the big cats. Another way in which the idea of flying was expressed in harmaline visions is that many of them were scenes viewed from above, as if the person were soaring through space.

MR. WASSON: I find no difference between the flying episodes that have been pointed out and the flying episodes in people who have not taken any drugs, and I eliminated them for that reason.

It seems to be part of the cultural tradition that you fly, not as a part of the cultural tradition that after taking mushrooms you fly. The Tungus fly, too, or am I mistaken?

DR. WASER: I had a question: "You did not mention the use of Amanita Muscaria by the Norse Bersekers that you discussed in your article found in Psychopathology. Have there been any further findings on the use of the mushrooms by this prehistorical group?"

MR. WASSON: I don't remember having discussed it in any article for Psychopathology, but everybody in Scandinavia, almost everybody learned it in school, and it is in the encyclopedias, that Berseker-raging was provoked by Amanita Muscaria. A man named Odman in about 1760 propounded this thesis, after having read von Strahlenberg's book dealing with Siberia. That has led to a great debate pro and con, in Sweden, Norway and Denmark. There is no mention in the sagas of the mushrooms. I think there is no tradition in any remote valley in Norway or Sweden about mushrooms.

The symptoms of the Berseker-ragers do suggest exhilaration and the desire for physical activity that mushrooms would cause, but until we get

some positive evidence that the cause was mushrooms, it seems to be hazardous to assume that there were mushrooms.

CHAIRMAN DR. EFRON: Next question: "Is there any evidence of Fly Agaric among the Eskimo or northern Athabaskan peoples? Did it cross the Behring Strait from the Koriak, etc?"

MR. WASSON: I have looked through this literature with great care, and many of the people who are reading the literature have been asked to tip me off for any possible reference to it, and there is none.

CHAIRMAN DR. EFRON: Question: "Could Fly Agaric have been used in Tibetan magic—Bon Culture, 2000 B.C.?"

MR. WASSON: I don't think we have any report of Bon Culture that far back.

CHAIRMAN DR. EFRON: "Has anyone taken the urine and analyzed the chemicals present?"

MR. WASSON: I am ashamed that no one has analyzed the urine, no one has tasted it, except the natives of Siberia. Among the anthropologists there are some who feel they should participate in any native culture they are studying. I have never read of any anthropologist in Siberia who lived up to this idea!

CHAIRMAN DR. EFRON: Question: "Is the drinking of urine of people that used mushrooms considered a better source of the hallucinogen?"

MR. WASSON: There is no comment in the Siberian sources distinguishing the qualities of the urine from the mushroom. Naturally more take the urine, because there is more of it. I have a hunch that the urine would filter out some of the objectionable qualities of the mushroom, and that you might get a pure inebrient in the urine, but that is just a hunch.

CHAIRMAN DR. EFRON: Question: "Why a urine culture in association with "trips?" Does it happen in any other culture?"

MR. WASSON: I don't know, I have never heard of it with LSD.

CHAIRMAN DR. EFRON: I have the last two question for Dr. Naranjo: "Dr. Naranjo spoke of electrical changes in retina with harmaline. Are there similar changes with other hallucinogens, or does this characterize harmaline only?"

DR. NARANJO: There has been a report of retinal changes of LSD in a cat, and this paper has been debated, and others have tried to reproduce the results, with no success.

What we have studied in Chile thus far is only harmaline, but we are planning to compare these results with those brought about with other substances.

CHAIRMAN DR. EFRON: The other question is: "Could banisteriopis have been used in Tibetan brews of this and later eras? For example, Millerepa, the mystic hermit, spoke of a root brew that was made from vines. It is found in Turkestan?"

DR. NARANJO: I am practically sure that banisteriopsis did not grow in this region. The climate is the absolute opposite. Peganum Harmala does grow in Asia, and probably in the frontiers of Tibet, and I feel attacted to the idea that Soma could be Peganum Harmala because I am impressed

with the similarity of the effects of hamaline with presumable effects of Soma. What harmaline produces resembles states of Yogic trance, and involves withdrawal from the environment, instead of the LSD experience of communication and empathy.

MR. WASSON: "When has Peganon last been identified? Not the modern Peganon, but the Greek Peganon?"

That is what some people have talked about as being Soma, the Green Peganon. It is not the modern plant with the same name. There was a plant in antiquity, and if there is any connection with Soma it would have to be the plant called Peganon.

DR. NARANJO: My only information on this is what you told me yourself, which is that Angnetil Duperron, the translator of the Avesta, was the first to propose that Soma was Peganum.

CHAIRMAN DR. EFRON: The last question is for Dr. Wasson, and then we have to go to the general discussion. "Why did you say Fly Agaric mushrooms are better or stronger than *Psilocybe mexicana?*"

DR. WASSON: I did not say they are better, I did not say they are stronger; they are entirely different.

DR. KLINE: In the fifteen or twenty minutes remaining there are some general questions which may point to the direction in which we are going in the future.

One of the things which concerns me as a clinician is that there are certain entities which are untreatable at present. I have a half suspicion that either my colleagues in anthropology or my colleagues in the laboratory have on occasion looked at solutions to my problems but not recognized that they had them in hand, because they don't know what I'm looking for.

I suspect likewise that there are questions which the anthropologists and the laboratory scientists are asking, to which I have the answers. However, I, in turn, don't know that I have these answers.

For instance, in psychiatry, we have no fully satisfactory treatment of patients with obsessive, compulsive behavior. These are individuals who repeat things over and over either in terms of action, thinking or feeling. If those of you observing laboratory animals or peoples in other cultures happen to chance across anything that either produces or seems to rectify this condition, it would be a great boon to us in the clinical field.

I will add one or two other problems, and if anyone can provide a quick solution, we will ask Dr. Holmstedt to arrange for a Nobel Prize.

There are the problems of arteriosclerosis and the diseases of the senium, which constitute slightly more than twenty-five percent of admissions to mental hospitals in the United States. If there are either in laboratory animals or in other cultures some agent or technique which reverses the process or preferably retards or prevents it, we would very much like to know.

Further, in the treatment of certain kinds of mental deficiency, there is now at least some evidence that these may be due to such things as phenylpyruvic acid. This would suggest that there are specific proteins or other chemical substances, the presence or absence of which are necessary for the disease to occur. It may well be that there are other disorders of this kind.

CHAIRMAN DR. EFRON: During the three days of this meeting we have found—and we expected this—that there exist some substances for which there is evidence that they are active in the central nervous system, but that they are not used or checked for use in patients. During the meeting we described their activity; sometimes it was a very harsh description or a very broad description, without any particulars or details. We spoke very much about hallucinogens, or hallucinogenic activity. Why? Very simply, because the hallucinogenic activity is the easiest to observe, and even a man not trained in medicine or pharmacology can observe it. So, this was the easiest observation to make by different people going to remote parts of different countries to observe their native culture, customs and medicine. But in reality we are not specifically interested in hallucinogenic activity. This may be only an indication of central activity, and this is our main interest.

For the future we would like very much to gather more information about more compounds used in native medicine and culture, and to find out their mechanism of action. By doing the type of job Dr. Shulgin was doing—changing the molecules by replacing different chemical groups or adding or removing radicals—we could change the pharmacological activity of the compounds. Maybe by this type of chemical manipulation, we could lose also their undesired hallucinogen activity but keep their other central actions, and create new compounds that could be used in the clinic. They may enable us to treat some of the problems Dr. Kline has mentioned.

This would be the point where we would like now to start for the future. But we may think about these compounds not only as drugs, but also as pharmacological tools which will help us to elucidate information as to how the central nervous system is working. We may find also the locus of action of a compound. Some of this type of investigation has been done already by many researchers with other compounds. We now have new beautiful and powerful analytical chemical techniques. I will mention here only Drs. Holmstedt and Horning, who represent the most advanced techniques of the use of gas chromatography connected with mass spectrometry, which permits us to find very minute amounts of compounds either in plants or in brain or in other biological tissues, and chemically characterizes them. We have other pharmacological tracing techniques that can be used for the same purposes. This shows us that we are now equipped for doing the proper job with the compounds spoken about during the meeting.

The time is late. We are in the last moments where we can catch the information about the use of compounds and plants in native cultures. The intrusion of civilization and the changing ways of life destroy both the sources of information about them, as well as the uses of them.

DR. KLINE: Your reference brings up another acute clinical problem, namely that all the antidepressants, although they are a tremendous advance, still average two or three weeks before they act.

We would like to have an antidepressant that works effectively in twenty minutes—we would even wait forty minutes. Perhaps there may be some

modification of the drugs described which could do this. The absence of hallucinations would be an advantage, but perhaps their occurrence may be a lead.

Dr. Holmstedt has given a good deal of thought to the matter of why the conference was held, and what he hoped it might do in terms of future investigation; and I think he deserves the credit as the second Godfather in the field, and certainly the Godfather of the modern generation of ethnopharmacology, by reopening the whole area. Would you give us the advantage of your knowledge on this, Dr. Holmstedt?

DR. HOLMSTEDT: We have been working on this conference for four years, I guess, and filled many, many files with correspondence of various kinds. The idea was to bring together, as we have done, people in very many different fields in order to see what this would produce. I think it has been amply proven during this conference that there are problems that should be attacked.

Think of the discrepancies and the opinions of how Kava Kava acts. For example: Think of Dr. Deulofeu's brilliant report of harmaline alkaloids, of which there must be two dozens, of which only three or four have been worked on, and so the idea would be for the future to take advantage of what has been presented here in some way—just exactly how I don't know. That is up to Dr. Efron, I believe—to organize the future in such a way that people in these various fields know about the different advances or, for that matter, about the lack of knowledge that exists.

DR. KLINE: How would you educate anthropologists in terms of going out into the field? Would there be some way, perhaps, of even preparing a field guide for them? Perhaps it should be prepared by a botanist in terms of what should be looked for from the botanical point of view, and perhaps from a clinical point of view.

Professor Ford raised the question as to what to do with it after you get the specimen.

DR. HOLMSTEDT: That is a problem, and I can add to that the following: When we were working with the methoxytryptamines, we approached an eminent specialist in this country, Dr. Axelrod, who knows everything about the methylating enzymes, to find out if the collected plants had these enzymes. Dr. Schultes at this time was going down to one of the places he loves best in the world, a small town called Leticia in Southern Colombia, and Dr. Alexrod prepared a package for him with ampoules and instructions for everything that Dr. Schultes was supposed to do to collect the desired material for enzymological studies. That package, including the radioactive methionine, has disappeared into the interior of South America. It was disastrous, and I think something should be done to prevent such a recurrence in the future.

DR. KLINE: I would like to point out a problem that Dr. Efron raises; with current regulations of the Food and Drug Administration, even if Dr. Schultes had brought it back, he might not have been able to do anything with it in terms of human testing.

DR. HOLMSTEDT: That was not the point. Dr. Schultes was going to investigate whether there was a methylating enzyme, and he was going to incubate the radioactive ampoules on the spot.

DR. SCHULTES: These packages were apparently sent through the Embassy and I was not in contact with the Embassy at all.

DR. HOLMSTEDT: It completely disappeared.

CHAIRMAN DR. EFRON: I have already made three contacts about going farther in this field. I spoke with Dr. Ford, and he didn't have to be educated in the field; he knew about all procedures. He only didn't know how to avoid the bureaucracy, and we made arrangements for discussion on how to facilitate the sending of investigational material from abroad to this country.

I have invited Dr. Schultes and Dr. Altschul to Washington to give us more information, because their presentation was a real mine of new information on active compounds in plants.

MR. WEIL: May I suggest that an area of research which seems to have been largely neglected at this conference, and which may be helpful in attaining some of the larger goals, is anthropological research in this country.

For example, take a clue that can be gotten from tribes in San Francisco who use tryptamines. People here smoke DMT; they don't snuff it as we saw in the film. Significantly, they don't have many of the toxic effects we saw. This observation might suggest that the violent intoxication caused by the South American snuff is not primarily due to tryptamines.

If we paid attention to the ways in which many of these compounds are now being used close at hand, (and there is extensive self-experimentation by many persons looking for new effects) we might get important leads which we can follow up in the laboratory.

DR. HOLMSTEDT: You opened up this field. You gave an excellent account of this.

FROM THE FLOOR: There is an incredible amount of information among people who experimented with themselves. They could give their firsthand accounts to some of the scientists.

DR. KLINE: I am volunteering Mr. Weil, who has established his credentials as a reliable non-informer.

FROM THE FLOOR: I am not terribly worried about this question.

DR. KLINE: It would be very useful if those of you who had an interest, from both sides of the fence, were to set up an information bureau of this sort. If Mr. Weil would be agreeable, we will try to protect him so he might well become a center of information. He is interested in the problem and obviously sympatico in discussion of it. Could you have information of this sort directed to him? His address is in the program, or you can send it to any of us and we would forward it to him. Perhaps at the next congress of this sort, which we will start planning immediately—since they take four years on the average to create—he will be able to give much more detailed information than he presently has.

I think he in turn would know where to direct those inquiries which seem to him to have therapeutic or other relevancy. Are you agreeable to this?

MR. WEIL: Very much.

DR. KLINE: He is very much agreeable; we have it for the record.

FROM THE FLOOR: I want to volunteer to be on that thing.

DR. KLINE: He can appoint such assistants as he likes. He should be the responsible individual and be vested with privileged communication.

DR. TREANOR: I am a neurologist, and the neurologists seem to have been left out. I think that a great deal might be accomplished in brain physiology, as Dr. Efron has suggested, if a compilation of the important articles that have appeared be cataloged—those articles that have to do with brain localization and brain function after the use of these drugs—and be given some circulation among Neurologists who would be in a position to think about it and perhaps to give help.

DR. KLINE: I think that is an excellent suggestion. We did neglect the field, but I might point out, as my friend and colleague Dr. Henry Brill has pointed out, sometimes the site of highest concentration is not necessarily the site of action. He proved this once and for all by pointing out that the highest concentration of most ingested drugs is the bladder, and this is usually not the site of action. Thus there is a danger involved in work which assumes that concentration implies activity.

The same is true for digitalis, since the heart is not the site of greatest concentration.

DR. TREANOR: A neurologist would not be restricted to such a narrow concentration. Dr. Harvey Cushing, whose assistant I was at one time some fifty years ago, used to say that he was probably a neurologist and surgery became secondary, but brain function does not entirely depend on drug concentration. When you are concerned with a patient who has a physical-mental disturbance, it is important to know as much as you can about brain function, and we do not have the information that we could have, say, from Dr. Efron's department, which he could give us.

You might say a compilation of those articles that appeared among the two thousand that would lead the way to or indicate the localization within the nervous system.

DR. KLINE: In bureaucratic fashion, we will go back to the Institute of Neurological Diseases.

CHAIRMAN DR. EFRON: Everybody who is really interested in research can go through Index Medicus every month.

To do such a job as is requested would be very costly and time consuming, and we will end again with a big book.

DR. KLINE: The National Library of Medicine is excellent in compiling these articles from the Index Medicus.

DR. TREANOR: It is not only the comprehensive item but looking through this. . . .

DR. LEAKE: I suggest another important source of information. Historically, we have a huge amount of untapped information, especially in the herbals that became so prominent in the 16th century. There is a vast amount of manuscript material which needs the same kind of examination that you have given in the field.

CHAIRMAN DR. EFRON: Before closing this session, I think we should thank all the participants for their contribution, and especially the local organizers from the University of California; the Dean, Dr. Seymour Farber, Dr. Roger Wilson and their staff, Mrs. Florence Webster, Mrs. Pat Black and Miss Virginia Barrelier. Their help was invaluable, and contributed to a very large extent to the success of this meeting.

Thank you.

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