Indole Alkaloids In Plant Hallucinogens

RICHARD EVANS SCHULTES, PH.D.*

> . . .I learnt that caapi was cultivated. . .and I went. . .to get specimens of the plant, and. . .to purchase a sufficient quantity of the stems to be sent to England for analysis. . .I saw, not without surprise, that it belonged to the order Malpighiaceae and the genus Banisteria, of which I made it out to be an undescribed species. . .My surprise arose from the fact that there was no narcotic Malpighiad on record, nor indeed any species of that order with strong medicinal properties of any kind.
>
> Richard Spruce (1852)

I

Many psychoactive plants owe their activity to structures containing an indole nucleus. This nucleus is evident in the synthetic LSD and in such well known compounds as yohimbine, reserpine, physostigmine and the strychnos alkaloids. And it is to the presence of indole alkaloids that many of the most striking hallucinogenic plants owe their biodynamic activity: iboga in Africa (with ibogaine and related alkaloids); the sacred mushrooms (with psilocybine) and morning glories (with ergoline alkaloids) of Mexico; and, in South America, the drinks called ayahuasca (with β-carbolines) and in vinho de jurema (with N,N-dimethyltryptamine) and the snuffs known as yopo, huilca and epena (all with various tryptamines).

Indole alkaloids are not confined to plants: bufotenine (5-hydroxy-N,N-dimethyltryptamine) is found in the skin of certain toads and the biogenic amine serotonine (5-hydroxy-tryptamine) is present in minute amounts in the central nervous tissue of warm-blooded animals.

There are about 600 alkaloids with an indole nucleus or a nucleus very close to an indole group in their molecule (Hesse 1968; Manske 1965; Saxton 1960; Saxton 1965; Schultes 1970; Schultes & Hofmann 1973; Taylor 1965; Taylor 1966). It is an extremely difficult class of alkaloids to delimit and to classify because of chemical complexity. Of the more than twenty classes of indole alkaloids, those involved in hallucinogenic plants may be placed in four categories: 1) lysergic acid derivatives (the ergoline alkaloids); 2) tryptamines (N,N-dimethyltryptamine, psilocybine); 3) the carbolines (harmine); and 4) the iboga alkaloids (ibogaine).

It is believed that indole alkaloids arise from tryptophane and a monoterpenoid moiety (Gibbs 1974). Tryptamines are recognized as possible intermediates in the biogenetic pathways to the harman-type (β-carboline) alkaloids on the one hand (Malpighiaceae, Rutaceae) and many of the more complicated indole types (Apocynaceae) on the other (Hegnauer 1958). The simple indole derivatives are rather widely distributed amongst the dicotyledons; whereas the more complex indole alkaloids are frequent in the metachlamydeous families Apocynaceae, Asclepiadaceae, Loganiaceae and Rubiaceae, although they occur also in the fungi (Gibbs 1974; Taylor 1966). Indoles have been recognized since

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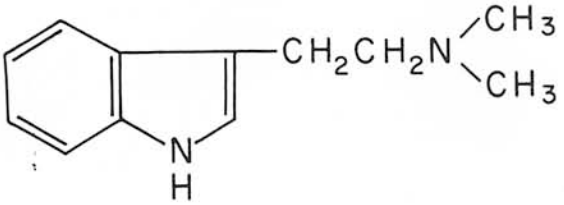
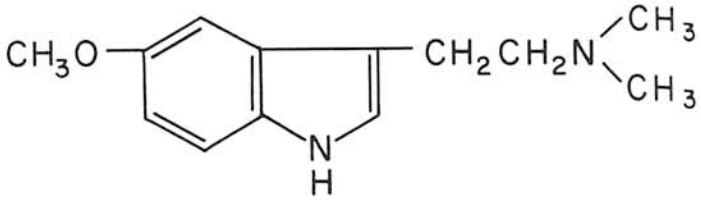
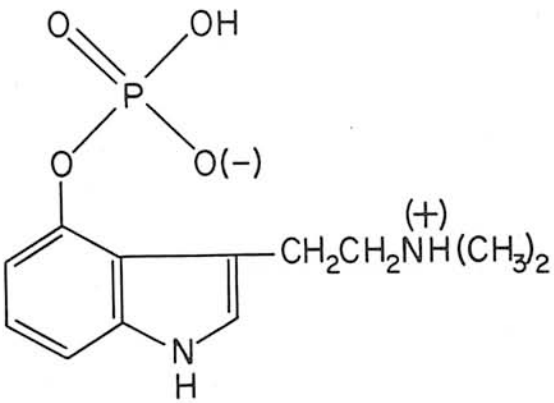
Principal indole alkaloids in hallucinogenic plants



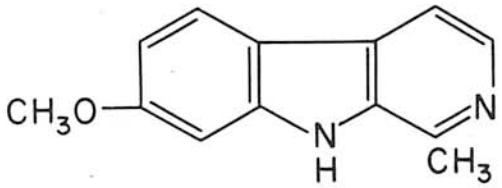
N,N-dimethyltryptamine
(Anadenanthera, Mimosa)



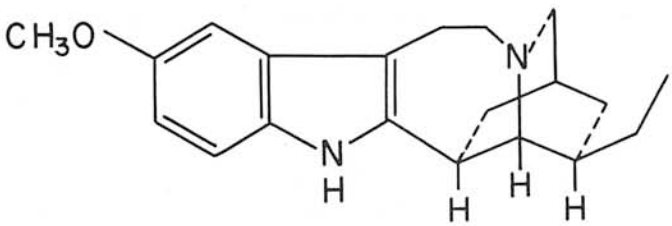
5-Methoxy-N,N-dimethyltryptamine
(Virola)



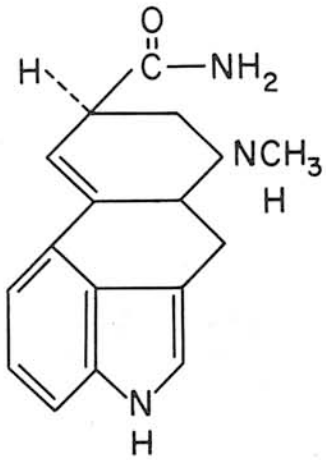
Psilocybine
(Panaeolus, Psilocybe, Stropharia)



Harmine
(Banisteriopsis)



Ibogaine
(Tabernanthe)



d-Lysergic acid amide
(Ergine)
(Ipomoea, Rivea)

Panaeolus sphinctrinus. Courtesy: G.-M. Ola'h.

arly years of the present century (Saxton 1965).

II

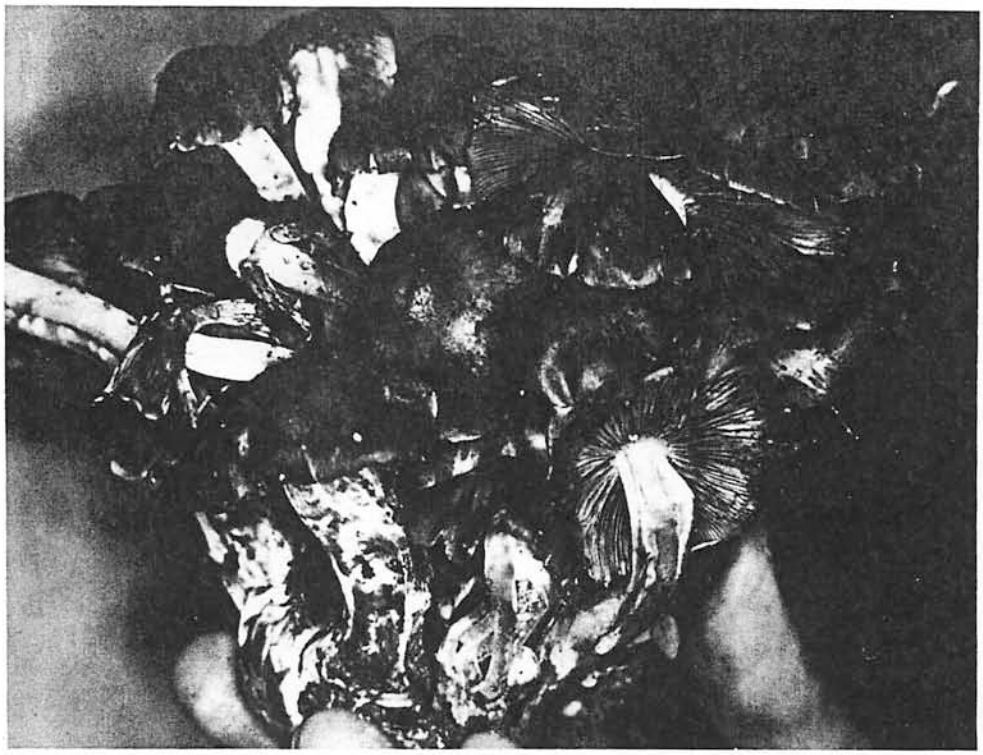
The ancient Aztecs used mushrooms in religious, ical and curative ceremonies, calling them *teonana-* ("flesh of the gods"). These fungi are still employed cred hallucinogens in southern Mexico, especially in aca. Evidence points to this use in adjacent temala as far back as 3500 years ago (Wasson & son 1957).

The many references to and descriptions of ritually administered intoxicating mushrooms in the early literature notwithstanding, there was, until 1939, doubt that teonanacatl did, in reality, refer to mushrooms; and the belief that it was another name for the peyote cactus was widely accepted (Safford 1922). It is now known that two dozen or more species of mushrooms in four genera (Conocybe, Panaeolus, Psilocybe, Stropharia) are variously employed (Heim 1963; Heim & Wasson 1958). Medicine-men may use different mushrooms at different times of the year, for different purposes or from personal preference. All are, however, psychoactive, and psilocybine or 4-phosphoryloxy-N,N-dimethyl tryptamine has been found in all four genera (Heim 1965; Heim & Wasson 1958; Hofmann *et al.* 1959; Schultes & Hofmann 1973).

Psilocybine is unique in several respects. It is the first indole with a phosphorylated hydroxy radical to have been isolated from plants. It occurs apparently nowhere else in the Plant Kingdom. It is the only tryptamine with a 4-substitution. Since psilocybine is rather unstable, the phosphoric acid part disintegrating rapidly upon ingestion of the mushrooms, most of the activity may be due to psilocine or 4-hydroxy-N,N-dimethyltryptamine which results from the breakdown of psilocybine (Hofmann *et al.* 1958; Schultes & Hofmann 1973).

In 1939, Schultes and Reko collected *Panaeolus sphinctrinus* (Fr.) Quélet in the Mazatec Indian country of Oaxaca, where it was one of the mushrooms in ritual use for hallucinogenic intoxication (Schultes 1939). Later work, principally by Wasson (1963) and Heim and Wasson (1958), indicated that species of Psilocybe and Stropharia were more important and that many species of Psilocybe were involved. The list of species has grown as a result of additional work by Singer (1958) and Guzman (1959). At the present time, well over twenty-four species are known to be employed by at least nine tribes of Mexican Indians.

The principal mushrooms involved are several species of Psilocybe (*P. aztecorum* Heim, *P. caerulescens* Murrill, *P. Hoogshagenii* Heim, *P. mexicana* Heim, *P. zapotecorum* Heim) and *Stropharia cubensis* Earle. *Panaeolus sphinctrinus,* it appears, represents one of the minor species used. Psilocybine has been found, however, to be the active principle in all of these genera, and this psychoactive indolealkylamine derivate has been isolated from other species of Psilocybe and Panaeolus in various parts of the world where, however, they are not used for their hallucinogenic properties (Schultes & Hofmann 1973). Further chemical research will probably show that psilocybine is more widespread among the mushrooms. It is curious that apparently only



Psilocybe caerulescens var. *aztecorum*. Oaxaca, Mexico. Photograph: R.G. Wasson.

in Mexico and adjacent Central America did the aboriginal cultures value the effects of this compound in magico-religious rites.

Psilocybine and psilocine were first isolated from *Psilocybe mexicana* in 1958 by Hofmann and others (Hofmann *et al.* 1958). The chemical work was made possible by the successful laboratory cultivation of the mushroom by Heim. Later, other species of Psilocybe were examined, and the active principles were found in many. Hofmann elucidated the structure of both compounds and confirmed the results by synthesis. The biogenetic precursor of psilocybine appears to be tryptophane.

The morning glories or Convolvulaceae comprise another group of Mexican hallucinogens that owe their activity to indoles.

The early chroniclers referred frequently to ololiuqui and tlitliltzin (Schultes 1941; Wasson 1963). Although descriptions and several illustrations of the period indicated that ololiuqui was convolvulaceous, no use of morning glory seeds as intoxicants had been seen in modern Mexico, and no toxic constituent was known from this plant family. Consequently, the suggestion was offered and widely accepted that, to protect this sacred hallucinogen from persecution by the Spanish authorities, the Indians were pointing out morning glories as ololiuqui, whereas the true identity of the narcotic was a species of Datura (Safford 1922).

Several Mexican botanists had long argued that ololiuqui did, in reality, represent a morning glory, but it was not until 1939 that Schultes and Reko collected a botanical specimen of a convolvulaceous plant employed in Oaxaca as a divinatory narcotic (Schultes 1941). It was *Rivea corymbosa* (L.) Hallier fil. and was identified as the ololiuqui of Aztec times. Later, MacDougall (1960) and Wasson (1973) established the narcotic use of the seed of another morning glory, *Ipomoea violacea* L., also in Oaxaca, and identified the tlitliltzin of the Aztecs as this species.

It was not until 1960 that the active principles – ergoline alkaloids or lysergic acid derivaties – were isolated (Hofmann 1961; Hofmann 1963; Hofmann & Tscherter 1960).

The main constituent of the seeds of *Rivea corymbosa* is ergine or d-lysergic acid amide. Minor alkaloids present are the related d-isolysergic acid amide (isoergine), chanoclavine, elymoclavine and lysergol. The seeds of *Ipomoea violacea* have a similar composition but, instead of lysergol, they have ergometrine (ergonovine). Later, very minor amounts of two alkaloids – ergometrinine and penniclavine – were found in *I. violacea* by chromatography (Schultes & Hofmann 1973).

The total alkaloid content of seeds of *Ipomoea*

violacea is approximately five times as great as that of the seeds of *Rivea corymbosa:* 0.06% in the former; 0.012% in the latter. This difference in alkaloid content explains why Indians employ smaller doses of seeds of the Ipomoea than of the Rivea (Hofmann 1963).

These ergoline alkaloids have subsequently been found in various other convolvulaceous species in the genera Argyreia, Convolvulus, Ipomoea and Stictocardia (Der Marderosian & Youngken 1966; Schultes & Hofmann 1973). They have also been reported to occur in the vegetative tissues of convolvulaceous plants (Taber, Heacock & Mahon 1963).

The discovery of ergoline alkaloids in the Convolvulaceae is of extreme chemotaxonomic significance: they are known from only one other place in the Plant Kingdom: in the lower fungi – Claviceps, Penicillium and Rhizopus – wholly unrelated to the highly evolved metachlamydeous family Convolvulaceae (Schultes & Hofmann 1973). The ascomycete, ergot or *Claviceps purpurea* (Fr.) Tulasne, was the cause of occasional mass poisonings of European towns in the Middle Ages when rye flour was contaminated with the sclerotium of the parasitic fungus which replaced the endosperm of the caryopsis. These mysterious attacks – causing delirium and hallucinations, loss of fingers, toes and ear lobes as a result of peripheral vasoconstriction

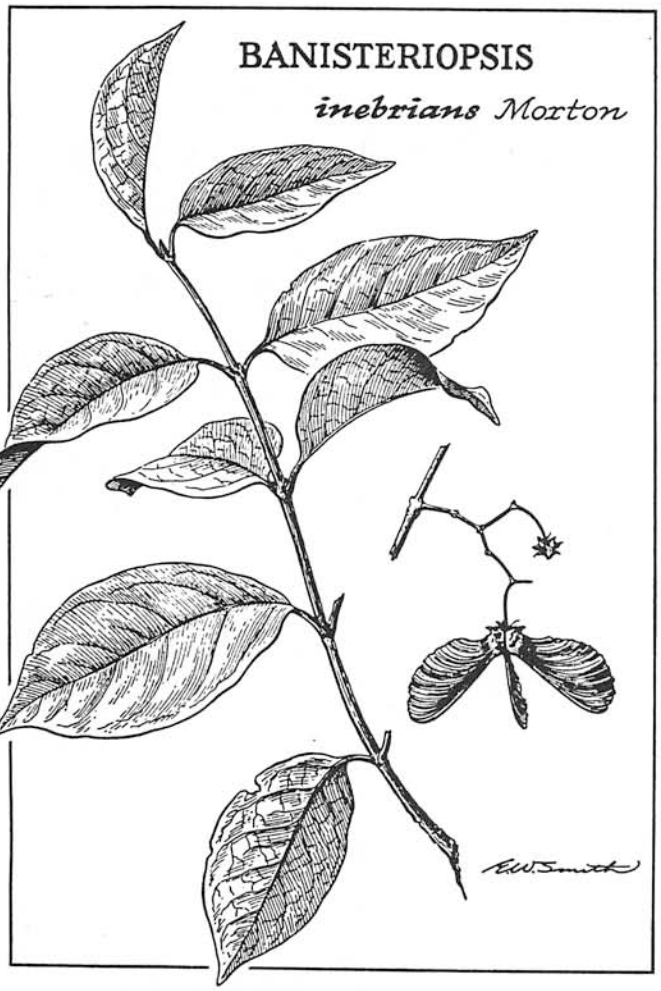
Ipomoea violacea. Oaxaca, Mexico. Photograph: R.G. Wasson.

and gangrene, often permanent insanity and sometimes death – were known as St. Anthony's Fire. Ergot was widely used by European midwives during the Middle Ages to aid in cases of difficult delivery, and several of the active principles are still employed for the same purposes in modern medicine (Fuller 1968).

III

South American indolic hallucinogens are of two kinds: those having β-carboline alkaloids as their active principles and those having various tryptamines.

The most famous South American hallucinogen is the drink variously known as ayahuasca, caapi, natema, pinde or yajé. Basically, it is prepared from the bark of either *Banisteriopsis Caapi* (Spruce ex Griseb.) Morton or *B. inebrians* Morton, extensive lianas of the Malpighiaceae (Friedberg 1965; García-Barriga 1958; Naranjo 1970; Schultes 1957). First identified botanically by the British explorer Spruce in 1852, it has fascinated investigators ever since. Ayahuasca is prepared in either a cold-water infusion or a decoction boiled for a long period. Now known to be employed in the western Amazon of Brazil, Colombia, Ecuador, Peru and Bolivia, in the headwaters of the Orinoco in Venezuela and in isolated localities on the Pacific coast of Colombia and Ecuador, this narcotic, despite years of investigation, still is poorly understood from many points of view.



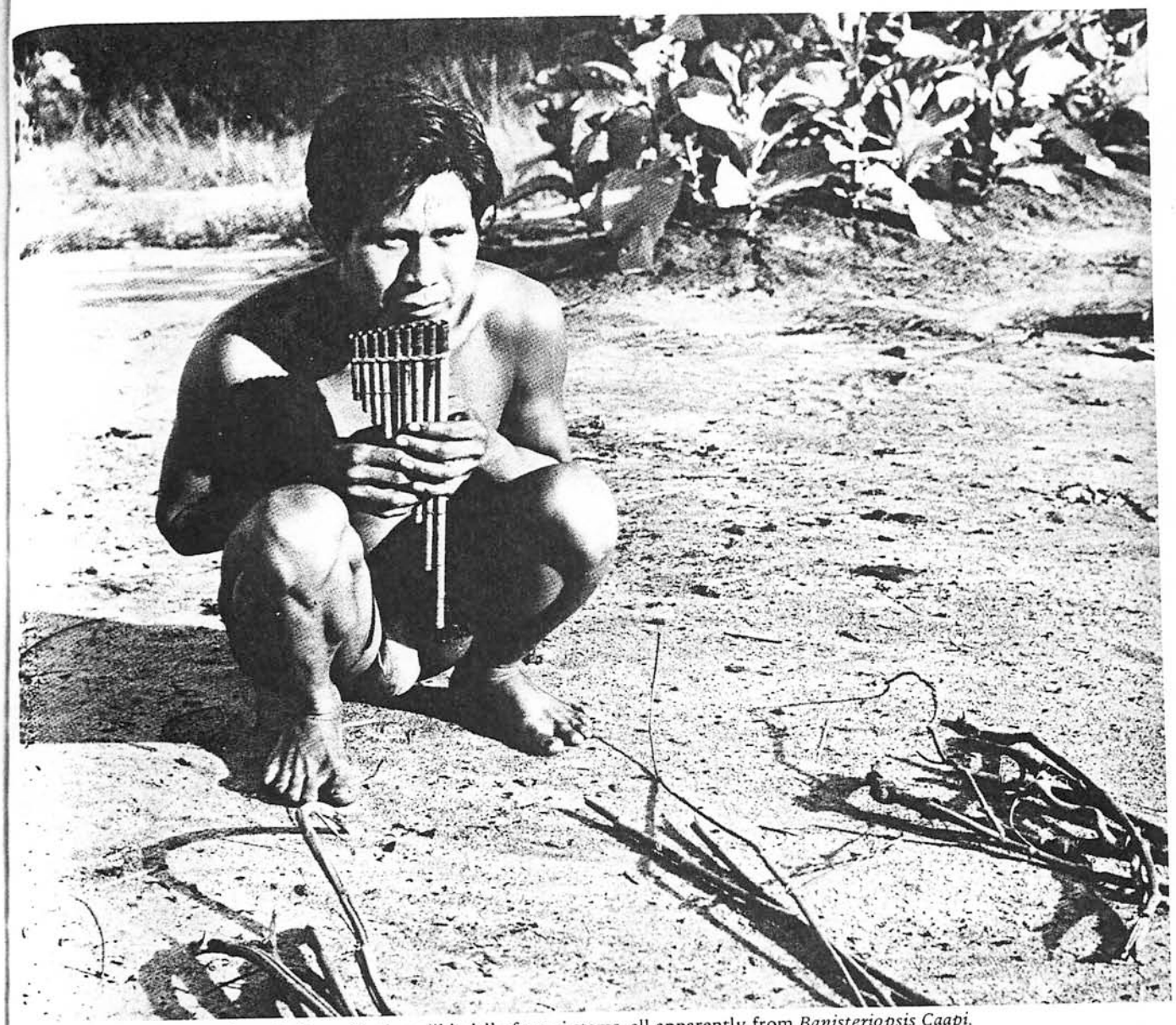
The active principles in the bark of *Banisteriopsis Caapi* and *B. inebrians* are β-carboline alkaloids: harmine, harmaline and tetrahydroharmine (Deulofeu 1967, Schultes & Hofmann 1973). These and several related simple indole derivatives, known as the "harmala bases," occur in a number of families, including (in addition to the Malpighiaceae) the Apocynaceae, Cyperaceae, Leguminosae, Passifloraceae, Rubiaceae and Zygophyllaceae (Gibbs 1974). It is believed that the carboline alkaloids are derived from tryptophane.

Harmine was first isolated from the Asiatic *Peganum Harmala* L. of the Zygophyllaceae – the so-called Syrian rue – more than a century ago (Gibbs 1974). This plant is known to possess hallucinogenic constituents, but, although extensively employed in folk medicine, there is no evidence that it was used purposefully as a hallucinogen in Asia.

The earliest chemical investigations of what is presumed to have been *Banisteriopsis Caapi* did not yield pure compounds (Deulofeu 1967). As early as 1905, a Colombian chemist, Zerda Bayon, isolated an alkaloid and called it telephathine (Deulofeu 1967). In 1923, Fischer Cardenas found an alkaloid which he identified with telepathine (Fischer Cardenas 1923). At about the same time, Barriga-Villalba crystallized an alkaloid from stems of a vine known as yajé and called it yajeine (Barriga-Villalba 1925; Barriga-Villalba 1927); the vine was erroneously identified as the apocynaceous *Prestonia amazonica* Bentham (*Haemadictyon amazonicum* [Benth.] Macbride).

The first chemical work on authentically identified botanical material was reported in 1927 by Perrot and Raymond-Hamet, who isolated a pure alkaloid with a melting point of 258°; they retained the name telepathine for it (Perrot & Raymond-Hamet 1927). In 1928, Lewin published a report of the isolation of an alkaloid which he named banisterine (Lewin 1928). In the same year, Elger (1928) and Wolf and Rumpf (1928) identified banisterine as harmine. Elger's plant material, supplied by Raymond-Hamet, was determined as *Banisteriopsis Caapi* at Kew. Chen and Chen, studying vouchered material of *B. Caapi*, isolated harmine from the leaves, stems and roots (Chen & Chen 1939).

In 1957, Hochstein and Paradies analyzed material of *Banisteriopsis Caapi* and found harmine, harmaline



Tukano Indian with three "kinds" of caapi stems, all apparently from *Banisteriopsis Caapi*. Río Vaupés, Colombia. Photograph: G. Reichel-Dolmatoff.

and tetrahydroharmine. The concentration of harmaline and tetrahydroharmine were rather high (Hochstein & Paradies 1957).

In 1969, Schultes, Holmstedt and Lindgren published a report of the phytochemical examination of Spruce's original material of *Banisteriopsis Caapi* collected in the Brazilian Amazon in 1852. By the combination of gas chromatography-mass spectrometry, it was shown that the stems contained only harmine, no harmaline or tetrahydroharmine. Whether the plant originally contained only harmine or whether the harmaline and tetrahydroharmine were transformed in the 117 years since collection into the chemically more stable aromatic β-carboline harmine, there is no way of telling at the present time. The latter would seem to be the more probable explanation (Schultes, Holmstedt & Lindgren 1969).

In the westernmost Amazon of Colombia and Ecuador, *Banisteriopsis inebrians*, closely related to *B. Caapi*, may be employed in preparing the hallucinogenic drink (Schultes 1957). Vouchered material of this species was analyzed by O'Connell and Lynn (1953) who reported that the stems contained harmine and the leaves "an alkaloid which was partly identified as harmine." They did not find other β-carbolines in this species. In 1965, Poisson examined *B. inebrians* and found harmine in the stems and, in very small amounts, another alkaloid which he presumed was harmaline

(Poisson 1965).

Although often prepared from a single ingredient, the drink occasionally has one or more additives. The list of these additives is already long, and there are still more to be identified (Pinkley 1969; Plowman 1973; Rivier & Lindgren 1972; Schultes 1957; Schultes 1972a; Schultes 1972b; Schultes & Raffauf 1960). Only a few of the additives have been subjected to chemical study, but those that have been analyzed are extremely significant. Among the plants added to the basic drink are such well known psychoactive species as *Datura suaveolens* Humboldt et Bonpland ex Willdenow (containing several tropane alkaloids) and *Nicotiana Tabacum* L. (with nicotine). Over the extensive area of use of this narcotic preparation many poorly known plants are reported as admixtures: several ferns – *Lomariopsis japurensis* (Mart.) J. Sm. and *Lygodium venustum* Sw.; several species of Cactaceae of the genera Epiphyllum and Opuntia; *Malouetia Tamaquarina* A. DeCandolle (Apocynaceae); a species of Cyperus (Cyperaceae); Capsicum sp., *Datura suaveolens* Humboldt et Bonpland ex Willdenow and *Brunfelsia Chiricaspi* Plowman and possibly *Juanulloa ochracea* Cuatrecasas (Solanaceae); *Alternanthera Lehmanii* Hieronymus and a species of Iresine (Amaranthaceae); *Calathea Veitchiana* Veitch ex Hooker filius (Maranthaceae); possibly *Pontederia cordata* L. (Pontederiaceae); *Phrygilanthus eugenioides* (HBK.) Eichler (Loranthaceae); *Teliostachya lanceolata* Nees var. *crispa* Nees ex Martius and another unidentified acanthaceous plant; a species of Clusia (Guttiferae); *Ocimum micranthum* Willdenow (Labiatae); and an unidentified bignoniaceous species.

Perhaps, however, the most important additives are the leaves of the rubiaceous *Psychotria viridis* Ruíz et Pavón (Schultes 1969a) and the leaves of the malpighiaceous *Banisteriopsis Rusbyana* (Ndz.) Morton (Schultes & Hofmann 1973). These plants apparently are never used together as additives. The natives assert that they employ these additives on occasion to lengthen and strengthen the hallucinatory effects of the drink, a

Makuna Indian standing by cultivated *Banisteriopsis Caapi*.
Río Piraparaná, Colombia. Photograph: R.E. Schultes.

PSYCHOTRIA viridis R. & P.

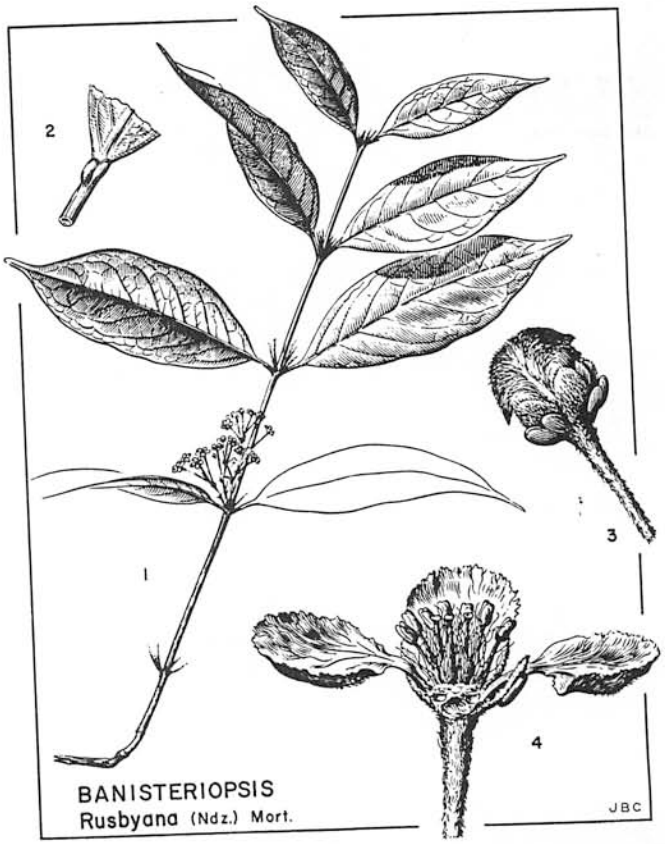
purpose which they successfully accomplish. Analyses have revealed the presence in the leaves of both plants relatively high concentrations of N,N-dimethyltryptamine – the first time that this tryptamine has been known from either family (Agurell, Holmstedt & Lindgren 1968; Der Marderosian, Pinkley & Dobbins 1968; Schultes 1970; Schultes & Hofmann 1973). There is some evidence that several other species of Psychotria may be similarly used (through an erroneous identification, *Psychotria psychotriaefolia* was reported as one of the admixtures [Schultes 1969a]), but corroboratory field studies are necessary before it can be positively stated.

Chemotaxonomically perhaps the most extraordinary discovery concerning additives of the ayahuasca-caapi drink is the finding of a tryptamine alkaloid in the leaves of *Banisteriopsis Rusbyana,* a species so closely related to *B. Caapi* and *B. inebrians.* In 1965, Poisson reported that *Banisteriopsis Rusbyana* contains N,N-dimethyltryptamine in relatively high concentration (0.64%) (Poisson 1965). This was confirmed by Der Marderosian (1968); and, again in 1968 Agurell, Holmstedt and Lindgren using gas chromatography-mass spectrometry methods, confirmed the presence of this tryptamine and noted minor constituents (Agurell, Holmstedt & Lindgren 1968): N-methytryptamine, 5-methoxy-N.N-dimethyltryptamine, N-methyltetrahydro-β-carboline and a non-indolic compound still to be identified.

Hochstein and Paradies (1957) reported an analysis of an aqueous extract of the leaves of what they called "yajé." Their "identification" of the source of this extract – the apocynaceous *Prestonia amazonica* – was made without voucher specimens through an erroneous identification of the common name yajé. The source of their aqueous solution, which came from the Iquitos region of Peru, was probably either *Psychotria viridis* or *Banisteriopsis Rusbyana,* since the active constituent of the solution was N,N-dimethyltryptamine (Schultes & Raffauf 1960).

It is generally believed that dimethyltryptamine is inactive when taken orally, unless in the presence of a monoamine oxidase inhibitor. In the case of this narcotic preparation, the monoamine oxidase inhibitor may be the β-carboline content of the basic species, *Banisteriopsis Caapi* and *B. inebrians* (Udenfriend *et al.* 1958).

In the dry parts of Pernambuco, Brazil, an infusion of the roots of the leguminous *Mimosa hostilis* (Mart.) Bentham is called vinho de jurema and is the



Leaves of *Banisteriopsis Rusbyana*, Putumayo, Colombia. Photograph: H. García-Barriga.

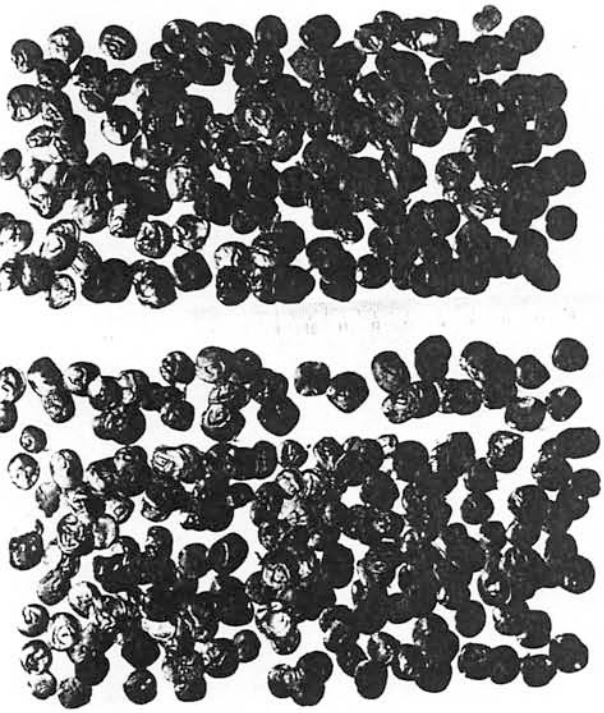
hallucinogenic basis of the ancient Jurema Cult. The drink induces glorious visions of the spirit world and was formerly taken before battles and other difficult feats. In 1946 Gonçalves de Lima reported a new alkaloid from this plant and called it nigerine (Gonçalves de Lima 1946). It was later shown to be identical with N,N-dimethyltryptamine (Schultes & Hofmann 1973). How this tryptamine can be effective without a monoamine oxidase inhibitor is still an enigma. Is there possibly an inhibitor still undetected in the roots, or do the natives perhaps add some other ingredient which contains the needed inhibitor?

Of the sundry snuffs employed in South America, three owe their psychoactivity to tryptamines.

Historically, the most important hallucinogenic snuff is yopo, used in the Orinoco basin in Colombia and Venezuela and possibly in isolated areas in the southern part of the Brazilian Amazon (von Altschul 1972). The flat, black beans of a tree known now as *Anadenanthera peregrina* (L.) Spegazzini, formerly as *Piptadenia peregrina* (L.) Bentham, are toasted, pulverized and mixed with an alkaline admixture — usually ashes of vegetal materials or calcined shells. The tree grows in open plains areas, not in tropical forests. It was early taken by invading Indians to the West Indies, where even today its distribution indicates its adventitious nature. Shortly after their arrival, the European conquerors discovered the use of the snuff under the name cohoba in Hispaniola, but its use completely disappeared with the extinction of indigenous populations in the West Indies.

Until recently, there was much uncertainty concerning the intoxicating principles of *Anadenanthera*

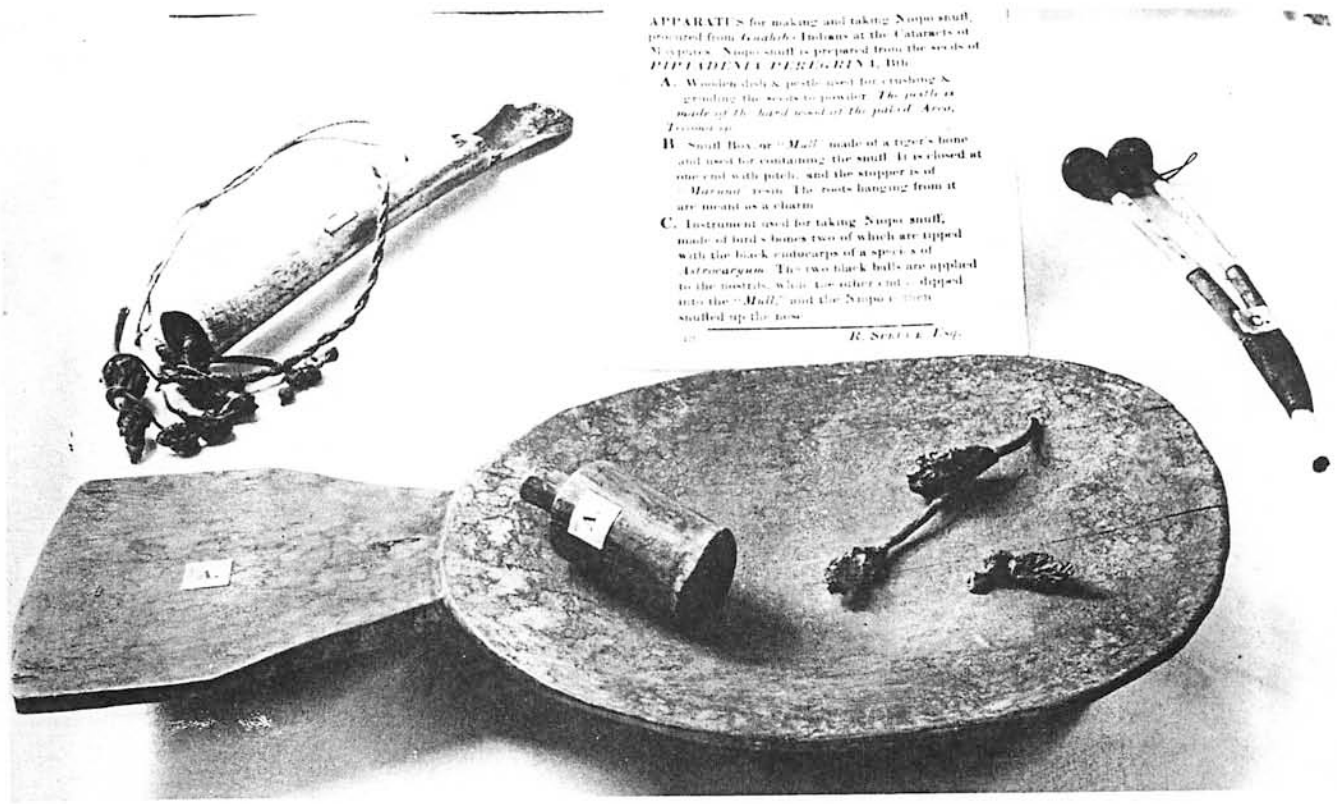
ANADENANTHERA PEREGRINA



Beans of *Anadenanthera peregrina*, collected in Puerto Rico.

peregrina and the snuff prepared from its seeds. Early explorers – Gumilla and von Humboldt – believed that the activity of the snuff was attributable to the alkaline admixture. During the 1950's, Horning and his co-workers (Fish, Johnson & Horning 1955; Horning, van der Heuvel & Creech 1963; Horning, Moscatelli & Sweeley 1959), interested in the properties of the crude snuff, discovered, by means of paper chromatography, colour reactions, fluorescence and infrared spectra, that indole alkaloids were the active constituents, and they reported the presence of N,N-dimethyltryptamine-N-oxide and bufotenine (5-hydroxy-N,N-dimethyltryptamine). Their work led eventually to the use by psychiatrists of synthetic dimethyltryptamine to induce temporary states of hallucinations. Later, the mass spectrometer and gas chromatography have enabled Holmstedt and Lindgren (1967) to show the presence in seeds of *Anadenanthera peregrina* the following indole derivatives: N,N-dimethyltryptamine, N-monomethyltryptamine, 5-methoxy-N-monomethyltryptamine, 5-methoxy-N,N-dimethyltryptamine, N,N-dimethyltryptamine-N-oxide, and 5-hydroxy-N,N-dimethyltryptamine-N-oxide.

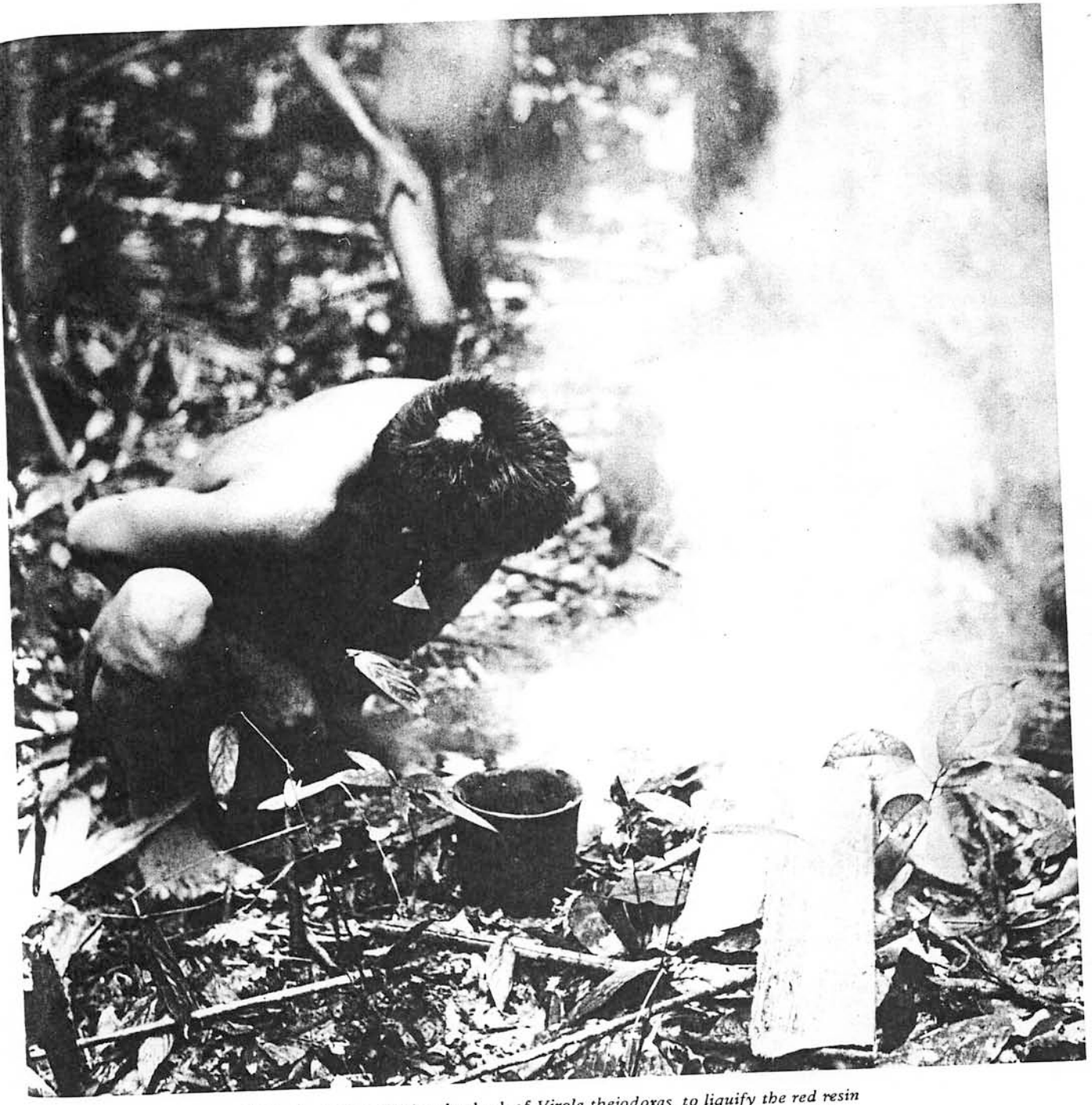
below – *Anadenanthera peregrina*. Boa Vista, Territorio de Roraima, Brazil. Photograph: R.E. Schultes.



Paraphernalia for preparing and snuffing yopo, collected by Richard Spruce on the upper Orinoco in 1855 and preserved in the Royal Botanic Gardens, Kew.

Another South American snuff, only recently identified botanically (Schultes 1954), is variously called epena, nyakwana and yakee. Prepared from any of several species of the myristicaceous genus Virola – *V. calophylla* Warburg, *V. calophylloidea* Markgraf, *V. elongata* (Spruce ex Benth.) Warburg and *V. theiodora* (Spruce ex. Bentham) Warburg – this snuff is used by tribes in the Rio Negro basin of Brazil, in the Colombian Vaupés and in the headwater regions of the Orinoco in Venezuela (Prance 1970; Schultes & Hofmann 1973). Methods of preparation vary from locality to locality, but the basis of the narcotic powder is always the blood-red resin of the inner bark. Among certain groups of Waiká Indians in Brazil, for example, the resin is scraped into a pot, boiled down to a thick syrup which is allowed to sun-dry, powdered with a stone and sifted. An alkaline ash of the bark of *Theobroma subincanum* Martius or *Elizabetha princeps* Schomburgk ex Bentham is added (Schultes & Holmstedt 1968).

When the source of the snuff was first identified, it was suggested that perhaps the active principle was myristicine, common in the Myristicaceae. Examination by Holmstedt and his co-workers of different parts of several species of Virola trees and of snuff prepared from *Virola theiodora,* however, established the presence of



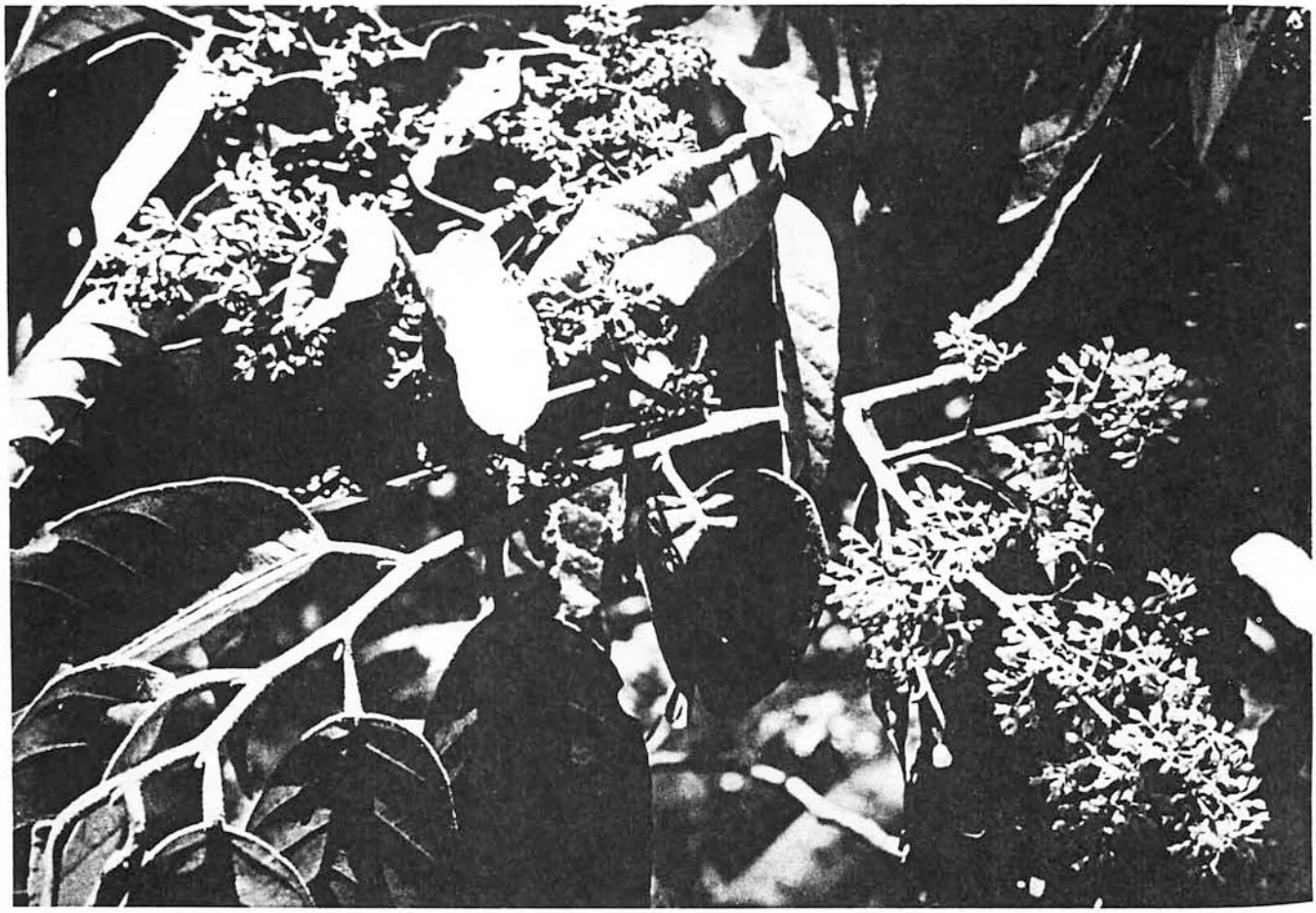
Waika Indians gently heating bark of *Virola theiodoras, to liquify the red resin from which the hallucinogenic nyakwana snuff is prepared.* Rio Tototobĭ, Territorio de Roraima, Brazil. Photograph: R.E. Schultes.

several tryptamines – the first evidence of indole alkaloids in the Nutmeg Family (Agurell 1969; Holmstedt & Lindgren 1967). Tryptamines are present in some species of Virola but absent in others. Snuff prepared by the Waiká Indians of Tototobĭ in Amazonian Brazil, for example, may contain up to 11% of several tryptamines, including 8% of 5-methoxy-N,N-dimethyltryptamine and lesser amounts of N,N-dimethyltryptamine (Schultes & Holmstedt 1968). Furthermore, the new β-carboline alkaloids 2-methyl-6-methoxy-1,2,3,4,-tetrahydro-β-carboline are known to occur in *Virola theiodora* and *V. rufula* (Agurell *et al.* 1968). These β-carboline alkaloids are monoamine oxidase inhibitors which are probably the reason for the psychoactivity of pellets of the resin of *Virola theiodora* when they are taken orally among the Witoto and Bora Indians of Colombia and when the resin is ingested directly from the bark by the very primitive Makú of the Colombian Vaupés (Schultes 1969b).

There are still unsolved problems in the preparation and use of Virola snuff. Many Indians who prepare ebena or nyakwana add to the powder the pulverized leaves of the highly aromatic acanthaceous *Justicia pectoralis* Jacq. var. *stenophylla* Leonard (Schultes & Holmstedt 1968). Their reason for using this admixture is reputedly to scent the snuff. While it is true that Virola-snuff is active without this added powder, there is ample evidence that some tribes elaborate a psychoactive snuff solely from the leaves of the Justicia, suggesting that Justicia itself may have hallucinogenic constituents (Chagnon, Le Quesne & Cook 1971). Indeed, it has been reported that tryptamines have been found in species of Justicia used in the preparation of snuff (Chagnon, Le Quesne & Cook 1971), but corroborative evidence is needed.

IV

It is extraordinary that the Apocynaceae, the family believed to be richest in alkaloids, has given apparently only one hallucinogenic species to primitive cultures: iboga. Iboga, an African narcotic of great and increasing social importance in Gabon and the Congo, is the root of



Leaves and inflorescences of *Virola theiodora*.
Manáos, Brazil. Photograph: R.E. Schultes.

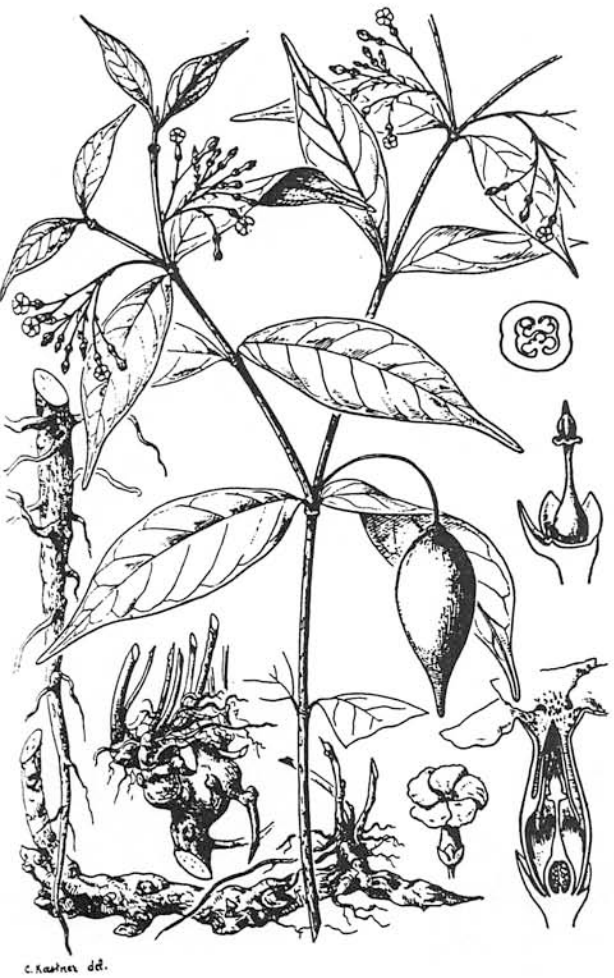
Waika Indians filling snuffing tubes with nyakwana powder preparatory to administering the drug. Rio Tototobĭ, Territorio de Roraima, Brazil. Photograph: R.E. Schultes

a bush, *Tabernanthe Iboga* Baillon (Pope 1969). It was discovered by Europeans in the middle of the last century, and, by the turn of the century, the principal alkaloid-5-methoxy-indole ibogaine – had been isolated. Later work has established the presence in *Tabernanthe Iboga* of twelve closely related alkaloids, and the total alkaloid content of the yellowish root may reach 5% or 6% in dried material (Schultes 1970; Schultes & Hofmann 1973).

Although possessing an indole nucleus, the iboga-alkaloids are often not classed with the indolic groups. It is believed that they arise from tryptophane and two mevalonate residues. They are closely related to the voacanga alkaloids, which include the Vinca alkaloids. Both groups are confined to the Apocynaceae.

Ibogaine, to which probably the greater part of the psychoactivity may be attributed, acts as a cholinesterase inhibitor, as a strong central stimulant and as a hallucinogen. Its structure, together with its stereochemistry, has only recently been clarified (Schultes & Hofmann 1973).

Other plants – as many as ten – may be taken together with iboga, but few have been botanically identified, and fewer have been chemically studied. One of the most interesting is the euphorbiaceous *Alchornea floribunda* Mueller-Argoviensis, which, it has been



Tabernathe Iboga. From A. Landrin *De l'iboga et de l'ibogaine* (1905).

stated, can be used in the same way as *Tabernanthe Iboga*. The intoxicating principle of *Alchornea floribunda* has been reported to be yohimbine, another indole alkaloid, but this report has not yet been confirmed (Paris & Goutarel 1958).

V

There is every probability that future research will show that other narcotic preparations from both the New and the Old World are effective because of indole alkaloids. At the present time, however, we do know that many of the most important of the hallucinogenic plants of tropical America owe their activity to these compounds. We know, also, that primitive cultures in the New World have exhibited an uncanny perspicacity in discovering in such an overwhelmingly rich flora a large number of psychoactive species. And, finally, we know that undoubtedly new hallucinogenically active chemical constituents still await discovery in the rich psychoactive flora of both the Old and the New Worlds..

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