Peter A.G.M. de Smet

Ritual enemas and snuffs in the Americas

The objectives of ethnopharmacology are to rescue and document a vast cultural knowledge before it is lost to the world, and to investigate and evaluate the agents employed without any prejudice or bias in order to find the rationale for their use.

Jan G. Bruhn and Bo Holmstedt

To my parents
Aan mijn ouders

CONTENTS

PREFACE

From prehistoric times till the present day, mankind has employed biologically active agents for various purposes. The scientific evaluation of these practices requires a multi-disciplinary approach that comprises the observation, identification, description and experimental investigation of the ingredients and the activity of the agents used. This complex field of research between anthropology, archaeology, philology, botany, zoology, chemistry, pharmacology and medicine has now become known as ethnopharmacology. Its principal objective is not to advocate a return to aboriginal practices, but to document the use of traditional preparations and to validate or invalidate their alleged activity (Bruhn and Holmstedt 1981). It is obvious that the results of a critical scientific evaluation will permit an advantageous feed-back to traditional medicine. The efficacy of useful indigenous drugs may be improved, once their therapeutic principles have been identified, whereas harmful or ineffective herbal therapies may be discouraged. For instance, over the last fifteen years, overwhelming evidence has been obtained that many plants containing pyrrolizidine alkaloids should no longer be used because of their hepatotoxicity (Buurma and Vulto 1984). Ethnopharmacological research may also give impulses to modern western medicine. In contrast to common belief, investigations of tradionally used plant material still lead to the discovery of new substances that may deserve a place in our modern therapeutic arsenal. The evaluation of Chinese medicinal plants would seem to be particularly fruitful in this respect (Xiao 1981), with the antimalarial compound qinghaosu from Artemisia annua as a spectacular example (Jiang et al. 1982; Li et al. 1984). When a biologically active principle of a natural product cannot be applied as such, it still may be useful as a lead in drug design by providing a novel molecular structure with potentially interesting effects (Krogsgaard-Larsen et al. 1984).

Not only studies of aboriginal medicinal plants, but also investigations of ritually used psychoactive drugs are within the scope of ethnopharmacology. In various parts of the world, aboriginal peoples and tribes have taken intoxicating vegetal preparations as facilitating agents in religious trance induction, divination, witchcraft and healing ceremonies (Efron et al. 1967; Furst 1976a; Emboden 1979a; Schultes and Hofmann 1980a,b; Völger et al. 1981; Dobkin de Rios 1984). The recovery of Sophora secundiflora from well dated archaeological sites in northeastern Mexico and Trans-Pecos Texas suggests that such

ritual plant uses may date back to millenia before our era (Adovasio and Fry 1976).

It is obvious that only the ethnological discipline can highlight the attitude of the aboriginals themselves towards their sacred drugs. The essence of the catholic mass for the church-goer is certainly missed by saying that mass wine is prepared from Vitis vinifera L. (Vitaceae) and that it contains about 13 per cent of the inebriating substance ethyl alcohol before it is diluted by the priest. There is an essential difference, however, between the catholic priest and the native shaman. The former has no intention whatsoever of becoming drunk, whereas the latter tries to reach an intoxicated state that will enable him to enter supernatural realms. Nobody has put this into words more eloquently than the peyotist Quanah Parker: 'the white man goes into his church and talks about Jesus; the Indian goes into his tipi and talks to Jesus' (Grinspoon and Bakalar 1981). Due to this fundamental difference, it is not merely allowed, but even necessary, to supplement field observations of native drug rituals with the results of laboratory experiments on the alleged activity of the drugs employed.

Such investigations have perhaps nowhere arrived at more scintillating results than in the domain of hallucinogenic plants. Today, only a few western clinicians consider hallucinogens to have any therapeutic value. According to a chapter in an authoritative pharmacological text book, the use of LSD (lysergic acid diethylamide) has been abandoned, either because controlled studies have failed to demonstrate its therapeutic value, or because the elaborate precautions required to minimize adverse psychological reactions dampened enthusiasm and rendered its therapeutic use impractical (Jaffe 1980). Yet ethnopharmacological studies on ritual psychoactive drugs may have an impact on medical care in western society. Firstly, they may lead to an improved clinical management of careless western youngsters who arrive in emergency wards after self-experiments with herbal 'highs' derived from native practices (Hall et al. 1978; Stienstra et al. 1981; Young et al. 1982). Secondly, they may provide new pharmacological tools for neurochemical research. For instance, the Banisteriopsis alkaloid harmaline has turned out to be a valuable selective inhibitor of MAO-A enzymes (Fuller et al. 1981). Thirdly, they may result in the discovery of synthetic substances with potentially therapeutic properties. A recent example is the development of specific agonists of the central GABA-ergic system from the fly agaric constituent muscimol (Flach et al. 1984). Fourthly, might there never come another time when the present categorical condemnation of

hallucinogenic drug therapy will be reevaluated (Grieco and Bloom 1981)?

Aside from any direct or indirect medical significance, ritual native intoxication is a fascinating area of research in its own right. It constitutes an important culture trait of primitive man which, just as other parts of our cultural heritage, deserves to be carefully documented and evaluated. I became interested around 1978 when I was shown an enema scene on a polychrome Maya vase. Such scenes were thought to represent intoxicating enema rituals, and their existence had only just been brought to light by Furst and Coe (1977). Here I saw an opportunity to combine my artistic preference for pre-Hispanic American cultures with my pharmaceutical education in botany, chemistry and pharmacology. I started to collect additional data on enema rituals in the New World, and soon found out that a comprehensive approach to the subject had never been published. I therefore intensified my literature search, which first resulted in brief articles on South American Anadenanthera enemas (de Smet 1981a) and on ritual enema scenes on ancient Maya pottery (de Smet 1981b), and then in a general overview of the subject (de Smet 1983b).

During my search for ritual enemas, I kept looking for information on other non-oral ways of ritual intoxication among Indians. I thus learnt that intoxicants have always been more widely used as snuffs than as clysters, especially on the South American continent. In contrast to ritual enemas, snuffs had already been given a comprehensive outlook in the sixties (pp.231-373 in Efron et al. 1967). So many new data had come to light, however, since this survey had been published, that the compilation of an up to date overview appeared to be warranted (de Smet 1985a).

My reviews on ritual enemas and on ritual snuffs in the western hemisphere form the basis of this thesis. Adapted and extended versions are presented in chapter one and in chapter two, respectively. The relevant data published before October 1, 1984 are summarized and a few important references appearing after this date are also included. The remaining gaps are filled as much as possible with unpublished information from experts and with the results of some self-experiments. Nasal self-experiments became possible by the clinical facilities and plasma level determinations of Jan Jonkman and Wim van der Boon (caffeine) and those of Laurent Rivier and Pierre Baumann (harmine). Their analytical procedures are described in Appendix D and Appendix E.

Chapters one and two have been given a similar structure. In part one of each chapter, I review the ethnobotany, phyto-chemistry and basic psychopharmacology of the intoxicating dosage form. A psychoactive plant may only elicit a pharmacologically induced subjective response, however, if at least one active constituent (or active biotransformation product) reaches an appropriate central site of action in an adequate amount. This amount is governed not only by the dosage of the constituent, but also by its manner of administration and by its subsequent fate in the body, i.e. by the absorption, distribution, metabolism and excretion of the constituent. In other words, the pharmacological validation of the reputed central effects of a native ritual dosage form must take into account that its active constituents, besides having intrinsic pharmacological effects, are molecules with a characteristic pharmacokinetic profile. This concept, which I propose to call the ethnopharmacokinetic aspect of native ritual intoxication (vide chapter three), still has to be fully recognized by many non-pharmacological scholars. To set an example, data on the pharmacokinetics and efficacy of possible enema and snuff constituents via their native route of administration are reviewed separately in part two of chapter one c.q. in part two of chapter two.

Cooperation with other researchers has allowed me to present original chemical and archaeological data in chapter one and chapter two.

Part three of both chapters is devoted to the gas chromato-graphical/mass spectrometric investigation of some Indian enema and snuff materials, located by me in European collections. The analyses were generously performed by Laurent Rivier, who outlines his procedures in Appendix A. Part three of chapter one describes the chemistry of 19th century paricá seeds, which reportedly were used as an enema and snuff ingredient by the Brazilian Maué Indians (de Smet and Rivier 1985b). Part three of chapter two reports the composition of two contemporary yopo snuffs of the Venezuelan Piaroa Indians (de Smet and Rivier 1985a).

Part four of chapter one discusses enema scenes on pottery of the classic Maya civilisation (300-900 A.D.). I could not have written this part without the help of Nicholas M. Hellmuth, who unselfishly guided me through the complex iconography of Maya enema scenes. This Maya specialist already reviewed the principal diagnostic accessories of Maya enema scenes in an unpublished paper in 1978. To give him credit, a revised version of this paper is included here as Appendix B. Hellmuth has based his

review primarily on photographical material from the large archive of his Foundation for Latin American Anthropological Research. By courtesy of the Foundation, this material is largely presented here (vide Appendix C). The publication of so many photographs is essential, since the ritual enema paraphernalia on classic Maya pottery can only be fully highlighted by showing vase painting after vase painting. Part four of chapter one firstly presents an iconographical and linguistic view, and then provides a multidisciplinary outlook on reputed Maya intoxicants (de Smet and Hellmuth 1985).

During the preparation of my reviews on enemas and snuffs, I discovered various scientific flaws in the consulted literature. When Richard Schultes invited me to contribute a chapter to a new book on ethnobotany, I therefore decided to review some botanical, chemical and pharmacological pitfalls in the multidisciplinary approach to native ritual intoxication (de Smet 1985c). This more general paper on certain methodological aspects underlies the third and final chapter of this thesis.

One of the most striking mistakes in some sources on ritual drugs is the inappropriate handling of pharmacological data. Actually, this does not come as a great surprise, because authors in this field often lack a pharmacological background. As a consequence, the concluding chapter is particularly meant to provide a non-pharmacological audience with an easily readable outline of a few important pharmacological principles. An inevitable drawback of this objective is, of course, that readers trained in pharmacology will find few, if any, startling points of view in the concluding chapter.

Some of the ideas in chapter three are not derived from my quest for Indian enemas and snuffs, but from the preliminary results of other research projects, viz. the taking of intoxicating drugs by New Guinea natives (de Smet 1983a), and the ritual use of fumigatories in Middle and South America (de Smet 1985b). The former communication stems from my eagerness to learn more about ritual drug practices in former Dutch colonies, the latter is a logical consequence of my continuing interest in non-oral intoxication among American Indians.

I felt that the inclusion of these papers in the thesis would not only enforce certain points in chapter three, but would also contribute to the general usefulness of the thesis as an ethnobotanical and ethnopharmacological work of reference. Since the preliminary character precluded the presentation as full-fledged chapters, I decided to add them as appendices, viz.

appendix F on New Guinea practices and appendix G on Latin American fumigatories. Appendix F may seem to compromise the coherency of the thesis by focusing on another part of the world, but this is only true in the geographical sense. From the methodological point of view, the ethnobotanical uniformity of the thesis remains unaffected.

The scope of the data presented in the thesis is determined by its particular purpose, i.e. the multidisciplinary search for scientific evidence of the alleged psychoactivity of Indian ritual preparations.

Ethnobotanical data

American Indians have used the enema and the snuff not only as a ritual intoxicant, but also as a medicinal cure (Densmore 1928; Nordenskiöld 1930; Hallowell 1935; Heizer 1944; Cobo 1964; Vogel 1970). The former type is included as much as possible so that sometimes even vague and unsubstantial data are discussed. In contrast, the latter type may only be mentioned when the reported ingredient is a plant with proven or reputed psychoactive properties.

Details are mostly restricted to certain secular aspects, such as the native group, the vegetal ingredient, the vernacular name, the botanical identity, the method of preparation, the specific use and the claimed activity. No systematic attempt is made to place the various practices into their cultural context, as this would go beyond the bounds of the subject. For instance, the iconographical and linguistic approach to enema rituals on ancient Maya pottery is limited to the enema paraphernalia portrayed in these scenes, and pays little attention to other aspects, such as the identification of the participants and their occurrence in other Maya rituals.

Since botanical information is crucial for any experimental approach, the availability of at least some tentative botanical identification has been applied as a decisive factor for the inclusion of field data. As a result, the snuff review bypasses the topasayri snuff of the early Peruvians (Cobo 1964), the saakona snuff of the Sanema Indians (Wilbert 1963), the kokoime snuff of the Karimé tribe (Salathé 1931), the baduhu-tsiña snuff of the Denís (Prance 1972) and the ayukuma snuff of the Mahekodotedi (Zerries and Schuster 1974).

In many cases, ethnological references designate plants with incomplete, misspelled or obsolete scientific names, and the indication of a herbarium voucher specimen is far from common. To avoid false impressions of botanical accuracy, the authors of Latin binomials have been excluded throughout the text. Complete

scientific names of the species and varieties mentioned in the ethnobotanical sections are found at the beginning of each section.

Chemical data

Chemical information is given about the qualitative and quantitative composition of the vegetal sources and, where possible, on the ultimate dosage forms themselves. With respect to the phytochemistry of the source-plants, data are mostly restricted to the parts used as an ingredient by Indians.

The consulted literature often indicates lengthy chemical names of plant constituents with an abbreviation. The abbreviations used in the thesis are listed at the end of this preface.

Pharmacological data

The pharmacological approach to intoxicating enemas and snuffs is specifically directed to the question of whether they may effectively produce a state of central intoxication. As this question may well be answered without in-depth attention to biochemical mechanisms, current ideas on the neurophysiology of hallucinogens (Jacobs 1984) and other ritual plant constituents have been left out of the discussion. Instead, the thesis focuses on the most eloquent evidence of psychoactivity, i.e. on the demonstration of central symptoms in human studies. Peripheral actions in man are not listed consistently and a glance at behavioural activity in laboratory animals is mostly reserved for those cases where no or few human data are available.

An hallucinogen is often defined as a non-addictive substance which consistently produces changes in perception, thought and mood, occurring alone or in concert, without causing serious disabilities like major disturbances of the autonomic nervous system; high doses may elicit disorientation, memory disturbances, hyperexcitation, stupour or narcosis, but these reactions are not characteristic. This definition is widely accepted, but some authors apply it more rigorously than others (Hoffer and Osmond 1967; Brimblecombe and Pinder 1975; Díaz 1979; Schultes and Hofmann 1980b; Grinspoon and Bakalar 1981), so that two types of hallucinogenic agents emerge from the literature:

- hallucinogens in a very strict sense, which are always classified as hallucinogens (e.g. indolalkylamines like psilocybin and phenethylamines like mescaline);
- hallucinogens in a broader sense, which are not always, but sometimes classified as hallucinogens (e.g. tropane derivatives like scopolamine and dibenzpyran derivatives like Δ^9-tetra-hydrocannabinol).

In the thesis, the term hallucinogen is used in its broader sense.

Index

The index does not contain broad terms like names of countries or plant families. It is restricted to the native plants and drugs, indigenous tribes and peoples, botanical genera and species, and chemical substances mentioned in the preface, chapters one, two and three, and appendices F and G.

The Hague, 1985

ABBREVIATIONS OF CHEMICAL COMPOUNDS

BBT	= 5-(3-buten-1-ynyl)-2,2′-bithienyl
DMT	= N,N-dimethyltryptamine
H	= harmine
5-HT	= 5-hydroxytryptamine
LSD	= lysergic acid diethylamide
5-MeO-DMT	= 5-methoxy-N,N-dimethyltryptamine
5-MeO-MMT	= 5-methoxy-N-monomethyltryptamine
6-MeO-MTHC	= 6-methoxy-2-methyl-1,2,3,4-tetrahydro-beta-carboline
6-MeO-DMTHC	= 6-methoxy-1,2-dimethyl-1,2,3,4-tetrahydro-beta-carboline
MMT	= N-monomethyltryptamine
MTHC	= 2-methyl-1,2,3,4-tetrahydro-beta-carboline
5-OH-DMT	= 5-hydroxy-N,N-dimethyltryptamine
T	= tryptamine
THC	= Δ^9-tetrahydrocannabinol
THH	= tetrahydroharmine

CHAPTER ONE

A MULTIDISCIPLINARY OVERVIEW OF INTOXICATING ENEMA RITUALS IN THE WESTERN HEMISPHERE

CHAPTER ONE PART ONE

THE ETHNOBOTANY, CHEMISTRY AND PSYCHOPHARMACOLOGY OF RITUAL ENEMAS IN THE WESTERN HEMISPHERE

1.1.1. Agave species
Amaryllidaceae

1.1.1.1. Ethnobotany

Before the conquest, distillation was unknown in the New World, but Mesoamerican Indians were familiar with a variety of alcoholic drinks prepared by fermenting maguey (Agave), maize, honey or pineapple (Tozzer 1913; Gonçalves de Lima 1956; Erosa Barbachano 1976; Furst and Coe 1977). The principal alcoholic beverage of the Aztecs was octli, referred to as pulque by the Spaniards; it was prepared from the sap of Agave species (Gonçalves de Lima 1956; Sahagún 1963; de Barrios 1971). Among the ancient Aztecs, getting drunk without incurring the wrath of society was a privilege of old age; drunkards could receive severe punishments, ranging from public disgrace to death by stoning or beating (Ross 1978).

Wilder drinking habits prevailed among the Huastecs of the Mexican northern Gulf Coast, who were considered barbarian by the Aztecs (Wasson 1980). According to the early chronicler Sahagún (1961), the Huastecs also knew octli, and 'always went about as if drunk'. Several early records speak of rectal administration in connection with their inebriating practices (Bourke 1892; Nordenskiöld 1930; Furst and Coe 1977; Robicsek 1978). The conquistador Diaz del Castillo (1916) gives the following account, clearly from his European point of view: 'About drunkards I do not know what to say, so many obscenities take place among them; I wish to note only one here which we found in the province of Panuco; they make an injection by the anus with some (hollow) canes and distend the intestines with wine, and this is done among them in the same way as among us an enema is applied'. An anonymous companion of Cortés (El Conquistador Anonymo 1941) states: '(they) worship figures showing different forms of pleasure between a man and a woman and figures of human beings with their legs lifted different ways ... the men are great sodomites, cowards, and – bored drinking wine with their mouths – lie down and, extending their legs, have the wine poured into their anus through a tube until the body is full'. A similar description is found in yet another anonymous early record

(Relación Anonima Segunda 1963). The 'wine' in these reports most likely refers to pulque (Von Winning 1972; Furst and Coe 1977). Some caution in accepting the term at face value may be in order, however, since the Spaniards lacked experience with and a vocabulary for hallucinogenic drinks (Wasson 1980).

There is circumstantial evidence that other Middle American peoples besides the Huastecs may have known of ritual alcoholic clysters. Firstly, the worshipped human figures with lifted legs, mentioned by El Conquistador Anonymo (1941), are reminiscent of certain rather poly-interpretable pre-Hispanic clay figurines from the central Veracruz region in Mexico. Evidence of a relationship between these so-called 'bed figures' and the alcoholic beverage pulque has been reviewed by Von Winning (1972). A definite explanation for their peculiar raised leg position cannot be offered, but perhaps it is concomitant with the Huastec way of taking intoxicating enemas (Von Winning 1972; Furst and Coe 1977). Secondly, there is evidence from scenes on classic Maya pottery that the ancient Maya may have taken alcoholic clysters (vide 1.4.2).

1.1.1.2. Chemistry and psychopharmacology

Early Mesoamerican alcoholic drinks were prepared from Agave sap or other sources by fermentation, and only contained about 3-6% of ethyl alcohol (Erosa Barbachano 1976). According to Hegnauer (1963, pers. commun. 1985), Agave species are rich in saponins, and such constituents may well have entered into the pulque drink, as this beverage was not prepared by destillation.

Ethyl alcohol is a reversible general central nervous system (CNS) depressant, and its acute ingestion can lead to an inebriation characterized by stupour (Ritchie 1980; Eckardt et al. 1981). Hallucinations may be expected only after chronic administration, in particular, as signs of a withdrawal syndrome (Thompson 1978). They occur usually after a prolonged drinking bout (Eckardt et al 1981) but are sometimes experienced while the alcoholic is severely intoxicated (Jaffe 1980). Isbell et al. (1955) studied withdrawal symptoms in well-nourished, healthy volunteers, who were given different amounts of 95% alcohol: sudden abstinence induced hallucinations in most of the subjects who had been drinking 383-489 ml for 48-87 days but in none of the subjects who had been taking 266-346 ml daily for 7-34 days.

Taken orally, alcohol can be readily absorbed from the gastrointestinal tract. Since most absorption occurs in the small intestine, the absorption rate depends on the rate of gastric emptying, which in its turn is determined by factors like the

properties of the beverage and the presence of food in the stomach (Wilkinson et al. 1977; Ritchie 1980; Eckardt et al. 1981).

Alcohol is known to affect the actions of many other drugs. Direct interactions occur at the pharmacodynamic level, e.g. when alcohol enhances the deleterious effects on performance and skills of another CNS depressant. Indirect interactions involve the pharmacokinetic level, e.g. when alcohol increases the absorption rate of a drug by enhancing its gastric solubility or the gastrointestinal blood flow (D'Arcy and Merkus 1981). As to classical New World hallucinogens, the medical literature contains some undetailed claims that the drinking of alcohol potentiates the action of tree Daturas (Anonymous 1976a) and of Psilocybe mushrooms (Benjamin 1979; Young et al. 1982). Well-documented clinical studies on this subject do not seem to be available. It has been shown only that atropine taken together with alcohol can impair attention more strongly than either substance alone (Linnoila 1973) and that pretreatment with atropine may cause a reduction in alcohol absorption, presumably because this anticholinergic inhibits the rate of gastric emptying (Gibbons and Lant 1975).

1.1.2. Anadenanthera species

Leguminosae

Anadenanthera colubrina (Vell.) Brenan
var. cebil (Griseb.) Altschul

Anadenanthera peregrina (L.) Speg.
var. falcata (Benth.) Altschul

1.1.2.1. Ethnobotany

Many South American Indians valued a snuff, known as paricá, as a ritual intoxicant (Wassén and Holmstedt 1963; Wassén 1965, 1967; von Reis Altschul 1972). Several tribes of the Amazon Basin made small rubber syringes which were used occasionally to blow paricá into the nostrils (Métraux 1949), but most often to administer clysters prepared with the same intoxicant (Horwitz 1921; Nordenskiöld 1930; von Reis Altschul 1972). Unfortunately the ethnological literature on these practices is often vague, generalizing and repetitious.

The Caripuna Indians of the Brazilian Madeira River are said to have provoked a state of trance by taking paricá in the form of an enema (Horwitz 1921; Métraux 1948a; von Reis Altschul 1972; Wassén 1972a). These statements can be traced back to the

Austrian zoologist Johann Natterer, who undertook several travels in the inlands of Brazil in the first half of the 19th century. He collected numerous ethnographical objects, which are now in the Museum for Ethnology in Vienna. His travelling diaries were destroyed by fire before they could be published, but fortunately there is still a museum inventory of his ethnographical collection, written under his supervision (Kann 1981, pers. commun. 1984).

Number 1050 of the inventory list refers to a small rubber syringe provided with a bird-bone tube: 'Kleine Spritze, besteht aus einem länglichen Ballen aus Gummi elasticum, in welchem ein kleiner Vogelknochen als Rohr steckt, womit die Caripuna berauschende Parica-Klystiere nehmen. Parica heissen die flachen Samenkörner des Angicobaumes, welche zerstossen und mit der Asche des Imbauvabaumes gemischt, dann mit Wasser angemacht werden. Die Murás, Mauhés, Porupurus und Catauixis nehmen auch solche Klystiere. Man heisst dies tomar paricá'.

Number 1369 of the list is even more interesting, as it describes a large sample of well preserved paricá seeds, collected from the Brazilian Maué tribe: 'Samenkörner des Paricábaumes (in Matogrosso Angico genannt). Diese Körner werden zerstossen (zerrieben) und mit der Asche des Imbauvabaumes gemischt und dann zum Schnupfen und zu berauschende Klystieren gebraucht. Wird namentlich bei den Mauhés, Muras, Caripunas und andere Nationen gebraucht'.

The rectal use of paricá seeds among the Mura Indians is mentioned not only by Natterer, but also by other early travellers. For this once much feared tribe of the Madeira River, the use of paricá, both as a snuff and as an enema, must have been of outstanding importance (Martius 1867; Nimuendajú 1948b; Wassén and Holmstedt 1963; von Reis Altschul 1972). The initiation ceremony of the Mura started with a general mutual flagellation which was followed by the nasal and rectal application of paricá (Marcoy 1867; Barbosa Rodrigues 1875). Barbosa Rodrigues (1875) states that 'All those who have been flagellated take parica either as snuff or dissolved in water as a clyster... Taken either way, the effect is terrible and so violent that many die of suffocation or fall unconscious, while still others, resisting, continue the dance... Usually, the clyster causes a violent intoxication'. Marcoy (1867) reports that on such occasions the rectal use of paricá was preceded by the snuffing of paricá and the drinking of palm wine in copious quantities. According to Spix and Martius (1831) the Mura clyster had a similar but not so strongly intoxicating effect as the snuff.

Likewise, the Catawishi or Catauxi Indians of the Purús River took a paricá decoction rectally (Horwitz 1921; Cooper 1949; Kennedy 1982). According to Spruce (1864, 1908), paricá was taken as a snuff to speedily induce a sort of intoxication, but 'taken in injection, it is a purge, more or less violent according to the dose'. This statement clearly opposes the general view that such enemas were intoxicating. Spruce adds that before the hunt the Catawishi administered the paricá clyster not only to themselves but also to their hunting dogs for a clearer vision and greater alertness.

The Casharari or Cacharary Indians, an Arawakan tribe of the western Amazon Basin, are reputed to have known paricá clysters (Métraux 1948b, 1949). Drawing from a Portuguese source on these Indians (Mâso 1919), Nordenskiöld (1930) describes the effects of the paricá enema as follows: 'After about five minutes it acts in about the same way as intoxication from opium, inducing lovely and blissful dreams. Twenty minutes later the dreamer is fully normal again, and does not appear to suffer from any after-discomfort as is the case after snuffing paricá'.

To the north of the Casharari lived the Omagua or Umaua Indians and further west the Cocama Indians. These Tupian tribes are said to have used powdered curupa leaves which were blown into the nose or administered as a clyster with the help of small rubber syringes (Métraux 1948c). Usually only the Omagua are implicated as curupa users (Veigl 1785; Marcoy 1867; Martius 1867) and there seems to be some doubt about the curupa use among the Cocama (Wassén 1967). According to De La Condamine (1778), the Omagua employed enema syringes especially at feasts, when an obliging host distributed them to all his guests.

Other South American tribes claimed to have taken paricá clysters, are the Maina Indians (Métraux 1949), known merely to have made rubber syringes (Chantre y Herrera 1901; Nordenskiöld 1930), the Poruporo Indians (Naterrer, vide supra; Horwitz 1921) and the Pasé, Juri and Uainuma Indians (Métraux 1948c).

The vagueness of the ethnological literature on paricá enemas is especially evident from the absence, or insufficient reliability, of botanical data. Sometimes the source is not identified at all (Horwitz 1921; Métraux 1948b,c; Natterer, vide supra) and sometimes the source is said to be Piptadenia (Métraux 1948a, 1949) or more specifically Piptadenia seeds (Nordenskiöld 1930). The paricá seeds which the Mura used for their clysters (Martius 1867; Barbosa Rodrigues 1875; Nimuendajú 1948b) as well as the curupa leaves from which the Omagua prepared their enemas (Marcoy 1867; Martius 1867; Lowie 1948; Métraux 1948c) have been attributed to a plant named Mimosa acacioides or Acacia niopo.

This leguminous tree has also been known under the binomial Piptadenia peregrina, and is now considered to belong to the genus Anadenanthera which comprises the two species A.peregrina and A.colubrina (von Reis Altschul 1964).

The botanical identifications of paricá clysters correspond well with the once common view that paricá snuffs were generally prepared from seeds of a Piptadenia species, especially P.peregrina (Roth 1924; Lowie 1948; Cooper 1949; Wassén and Holmstedt 1963; Schultes 1967b). Cooper (1949) has rightly cautioned, however, that some of these attributions may not be correct, as exact botanical evidence is lacking in some cases. It has now become clear that the vernacular term paricá is not used exclusively for the genus Anadenanthera, as it also refers to Virola preparations (Schultes 1954; Seitz 1967) and to snuffs containing harmine (Holmstedt and Lindgren 1967). Furthermore, it is uncertain that Anadenanthera peregrina is the species used throughout the Amazon. Schultes (1972a) who speaks of a widespread rectal administration of Anadenanthera in South America, points out in a personal communication (1981) that 'Other species may be used, such as A.colubrina. I believe that A.peregrina is a species primarily of the Orinoco and adjacent parts of the northern Amazonia of Brazil. Whether the species used in the Peruvian Amazon or the central Amazon of Brazil are A.peregrina is questionable. The reason is that snuffs, etc. have not been accompanied by voucher herbarium specimens'. In other words, the geographical distribution of Anadenanthera peregrina is now assumed to be far more limited than was previously believed (von Reis Altschul 1964, 1972; Schultes 1967b). It is quite likely that the Maué and other tribes of the Madeira area prepared enemas and snuffs from A.peregrina. The tree occurs in this region (Schultes 1967b; von Reis Altschul 1972), and the paricá seeds collected by Natterer from the Maué Indians are apparently Anadenanthera seeds (vide 1.3). On the other hand, the tree is unknown anywhere near the area of the Omagua and Cocama, so its use by these tribes of Amazonian Peru is open to serious question (von Reis Altschul 1972; Schultes and Hofmann 1980b). Similarly, there is no good botanical evidence that the Catawishi, Casharari, Pasé, Juri or Uainuma Indians knew A.peregrina (von Reis Altschul 1972).

It should be noted that there are two varieties of Anadenanthera peregrina: the variety peregrina occurs in northern parts of South America and in the West Indies; the variety falcata in southern Brazil and Paraguay (von Reis Altschul 1964).

It is sometimes claimed that the Incas, well-known inhabitants of ancient Peru, intoxicated themselves with rectal infusions of

wilka or huilca seeds (Furst 1976a; Furst and Coe 1977). The early chronicler Poma de Ayala (1969) indeed refers to such enemas and another early writer states that Inca witch doctors foretold the future by speaking with the devil, for which they intoxicated themselves with villca, pouring its juice into the alcoholic beverage chicha or taking it another way (von Reis Altschul 1967, 1972). Most early records, however, including the original report on the vilca clyster, emphasize the laxative properties of vilca seeds (von Reis Altschul 1967) and it is not sufficiently clear whether the seeds helped to produce visions or were taken only for their purgative qualities (Rowe 1946). Poma de Ayala (1969) says that the Incas purged themselves once a month with bilca tauri, half of which was drunk and half of which was taken 'por debajo' to give strength, health and a 200 years life span. Larrain Barros (undated) suggests that the phrase 'por debajo' implies nasal administration, but it is far more likely to indicate the rectal route, not in the least since various forms of the word vilca meant enema, syringe or the giving of an enema (von Reis Altschul 1967, 1972; Wassén 1972b). The botanical source of the vilca clyster is usually thought to be Anadenanthera (Larrain Barros, undated), in particular A.colubrina (Rowe 1946; Furst and Coe 1977). It should be noted that the evidence for this attribution is circumstantial rather than conclusive (von Reis Altschul 1967; Schultes and Hofmann 1980a,b) and that A.colubrina occurs in eastern Brazil, whereas the variety A.colubrina var. cebil is known in Peru (von Reis Altschul 1964).

1.1.2.2. Chemistry and psychopharmacology

Seeds of Anadenanthera peregrina (Piptadenia peregrina) were found to contain one or more of the following indole alkaloids: N,N-dimethyltryptamine (=DMT); its corresponding N-oxide (=DMT-N-oxide); 5-hydroxy-N-N-dimethyltryptamine or bufotenin (=5-OH-DMT); its corresponding N-oxide (=5-OH-DMT-N-oxide); 5-methoxy-N,N-dimethyltryptamine (=5-MeO-DMT) (Holmstedt and Lindgren 1967; Schultes et al. 1977). The question arises of whether the N-oxides might be artifacts, as Saxton (1965) points out that DMT may be oxidized on exposure to air. During storage, DMT and 5-MeO-DMT may transform into 5-OH-DMT (Schultes et al. 1977). A Venezuelan sample was reported as containing as much as 7.4% of 5-OH-DMT (Chagnon et al. 1971). According to Schultes (pers. commun. 1982), this report is not based on identified herbarium voucher specimens. In other samples 5-OH-DMT was present in amounts up to 3.5% (Schultes et al. 1977). DMT, 5-OH-DMT,

DMT-N-oxide and 5-OH-DMT-N-oxide were reported to be present in seeds of Piptadenia macrocarpa (Fish et al. 1955; Iacobucci and Rúveda 1964), now considered to be Anadenanthera colubrina var. cebil (von Reis Altschul 1964). From seeds of Anadenanthera colubrina (Piptadenia colubrina), 5-OH-DMT has been isolated (Holmstedt and Lindgren 1967).

The paricá seeds of the Brazilian Maué Indians, reportedly used as an enema source (vide 1.1.2.1), have recently been submitted to gaschromatographical/ mass-spectrometric analysis. Despite their considerable age, the seeds still yielded as much as 15 mg/g of bufotenin, which corroborates their botanical identification as Anadenanthera seeds (vide 1.3).

DMT is a well-established hallucinogen, which elicits a brief but profound LSD-like response when given in intramuscular doses ranging from 0.7 to 1.1 mg/kg, i.e. 49-77 mg/70 kg (Szára 1956; Rosenberg et al. 1963; Kaplan et al. 1974). Intramuscular administration of 0.25 mg/kg (17.5 mg/70 kg) has similar effects in certain tests measuring psychoticism as the Cannabis constituent Δ^9-tetrahydrocannabinol (Bickel et al. 1977). In schizophrenics, intramuscular doses of 25-50 mg can induce psychological changes (Turner and Merlis 1959), such as exacerbation of the psychosis (Gillin and Wyatt 1977).

Human experiments with 5-MeO-DMT seem to have been conducted only by Shulgin (1970), who reported briefly that a parenteral dose of 5-10 mg is active. In 1981, the following details were revealed in a letter to me: 'My clinical studies involved a total of 9 subjects, 4 males and 5 females, within the age range of 33 to 65 years. All were healthy volunteers, all with considerable experience with drugs that can alter one's state of consciousness. The parenteral route of administration was in all cases by inhalation of the fused free base suspended on Tanacetum vulgare in cigarette form. The onset of action occurs in less than 60 seconds, reaches a plateau in the 2nd to 3rd minute, and is largely dissipated at 20 minutes, although there may be some lingering awareness for the remainder of an hour. Centrally, there is the loss of some reality sense, some eyes-closed imagery and a general feeling of being enclosed and isolated in a sensory sense. Peripherally, there have been occasional tremors noted, and occasional mydriasis. These effects are from 6 to 10 mg of the free base. I have personally conducted no oral experiments and do not know its effects via this route'.

5-OH-DMT is mostly found to act briefly, altering the perception of colours and sometimes of space, when given in intramuscular doses of 10-15 mg (Isbell, quoted by Turner and Merlis 1959 and by Wassén and Holmstedt 1963) and in

intravenous doses of 4–16 mg (Fabing and Hawkins 1956) or 12–16 mg (Bonhour et al. 1967). In schizophrenics, intravenous quantities of up to 20 mg, given by bolus injection (e.g. 10 mg within 1 min) or by infusion (e.g. 20 mg in 77 min), produced neither visual disturbances nor the psychological changes seen after DMT administration (Turner and Merlis 1959). Many secondary sources doubt the hallucinogenic capacity of 5–OH–DMT following peripheral administration and then point to its poor lipid solubility at physiological pH and its consequent inability to enter the central nervous system readily (Holmstedt and Lindgren 1967; Luchins et al. 1978; Glennon et al. 1979). Experiments with laboratory animals have demonstrated that, in contrast with the lipid soluble DMT (Cohen and Vogel 1972) and 5–MeO–DMT (Sanders and Bush 1967), 5–OH–DMT does not cross the blood–brain barrier in appreciable amounts (Sanders and Bush 1967; Luchins et al. 1978; Glennon et al. 1979). This suggests that the reported effects of 5–OH–DMT may well be somatic symptoms of intoxication rather than signs of true hallucinogenic activity. According to Isbell (1967), it is difficult to say whether 5–OH–DMT is a hallucinogen or not because of its powerful and dangerous cardio–vascular effects. For this reason, it is not possible to push the dose in man and it would be difficult to differentiate whether psychotic reactions were due to central effects or to cardio–vascular actions.

Oral experiments with Anadenanthera alkaloids have failed to demonstrate hallucinogen–like effects, although the tested amounts were much higher than parenterally active doses. DMT was ineffective in a normal subject who took this compound in quantities of up to 150 mg (Szára 1957), as well as in schizophrenics who received single doses of up to 350 mg (Turner and Merlis 1959). 5–OH–DMT was without effect when ingested by a healthy individual in doses of up to 50 mg (Hofmann 1963) or in doses of up to 100 mg totally (Isbell, quoted by Wassén and Holmstedt 1963). This inefficacy of oral dosing is likely to be due principally to extensive first–pass metabolism. The physicochemical properties of Anadenanthera alkaloids, in particular those of DMT and 5–MeO–DMT (Glennon et al. 1979), exclude a defective absorption. Chemical evidence for inactivation by gastric juices has not been found. DMT and 5–OH–DMT are almost completely metabolized in man when given parenterally; the urinary recovery of unchanged drug was 1–6% of an injected dose of 5–OH–DMT (Sanders–Bush et al. 1976) and as low as about 0.07% in the case of DMT (Kaplan et al. 1974). The structurally related neurotransmitter 5–hydroxytryptamine (5–HT) is promptly degraded by intestinal and hepatic monoamine oxidase

(MAO) when taken orally (Douglas 1980). Although Anadenanthera alkaloids have a dimethylated amino-group, there is experimental evidence that they are inactivated in a similar way. MAO-inhibition prolongs the half-life of DMT in rats (Wang Lu and Domino 1976). Other animal experiments have shown that 5-MeO-DMT is deaminated by MAO and, just as with 5-HT, preferentially by MAO-A (Squires 1975). In a human subject, MAO-inhibition was found to double the urinary excretion of endogenous DMT (Oon et al. 1977). Not only MAO, however, but also hepatic microsomal enzymes may be capable of oxidating the dimethylated amino-group of Anadenanthera alkaloids (Fish et al. 1955). The deamination of 5-HT leads mainly to 5-hydroxyindole acetic acid, which is the principal urinary metabolite (Douglas 1980). Intravenously given 5-OH-DMT was found to be excreted for 68-74% in the form of 5-hydroxyindole acetic acid (Sanders-Bush et al. 1976); whereas in an early study on DMT the urinary excretion of indoleacetic acid, free and in alkali-labile form, accounted for only one-third of the intramuscular dose (Szára, 1956). This implies that deamination is a major metabolic pathway for these compounds, but not the only one, especially not in the case of DMT. This alkaloid was reported to be 6-hydroxylated to the extent of about 5-20% of the administered dose (Gillin and Wyatt 1977).

The N-oxides of DMT and 5-OH-DMT have not been studied extensively by pharmacologists. They are said to have much less cardiovascular activity in the dog and the cat than the bases themselves (Fish and Horning 1956).

1.1.3. Banisteriopsis species
Malpighiaceae

1.1.3.1. Ethnobotany

The genus Banisteriopsis which comprises many species of tropical vines, is a major ingredient of certain intoxicating drinks taken in South American rituals (Cooper 1949; Friedberg 1965; Rivier and Lindgren 1972; Schultes 1982). Some recent sources (Furst 1976a; Emboden 1979a) claim that Banisteriopsis may have been taken as a clyster, but fail to provide an original report on such practices. The comprehensive monograph by Friedberg (1965) on the ritual use of Banisteriopsis does not even hint at enemas prepared from this genus. Despite the apparent lack of substantial ethnobotanical data on such dosage forms, the chemistry and pharmacology of Banisteriopsis preparations are discussed here.

1.1.3.2. Chemistry and psychopharmacology

The principal alkaloids in Banisteriopsis species used by natives are beta-carbolines, in particular harmine, harmaline and (+)-1,2,3,4-tetrahydroharmine (Deulofeu 1967; Allen and Holmstedt 1980). The well-studied species B.caapi was found to contain 0.11-0.83% of alkaloids in the stem, 0.14-0.37% in the branches, 0.28-0.70% in the leaves and 0.64-1.95% in the root. These total alkaloid percentages consisted primarily of harmine (40-96%) and, to a lesser extent, of tetrahydroharmine (1-44%) and harmaline (0-17%). Small amounts of harmol, 6-methoxytryptamine and an unidentified compound were sometimes also present (Rivier and Lindgren 1972). More recent analytical work on the same species has revealed that other beta-carbolines may be present as minor components: harmine-N-oxide, harmic acid methyl ester, harmalinic acid, harmic amide, acetyl norharmine, ketotetrahydronorharmine and harmalol (Hashimoto and Kawanishi 1975, 1976; McKenna et al. 1984a). In addition, the pyrrolidine bases shihunine and S-(+)dihydroshihunine have been shown to occur in Banisteriopsis caapi (Kawanishi et al. 1982).

In a study by Pennes and Hoch (1957), harmine was hallucinogenic at an intravenous threshold dose of 150-200 mg in mental patients, which elicited visual hallucinations in 5 out of 11 patients. Some other effects of these intravenous doses were also produced by oral quantities higher than 300-400 mg, but it is doubtful that indisputable visual hallucinations occurred with oral quantities of up to 960 mg. Naranjo (1967) found harmaline (as the HCl salt) to be hallucinogenic in volunteers at dosage levels above 1 mg/kg intravenously (70 mg/70 kg), or 4 mg/kg orally (280 mg/70 kg). In the same study, racemic tetrahydro-harmine elicited subjective effects similar to those of 100 mg of harmaline, when given to a single volunteer by mouth in quantities of up to 300 mg. Vargas (1959) states that harmine, LSD and mescaline produce essentially similar reactions in both normal and psychotic patients, but the volunteers of Naranjo (1967) clearly distinguished the experience with harmaline from an intoxication with mescaline.

It has not been unequivocally established why the psychoactivity of major Banisteriopsis constituents is largely route-dependent. Extensive hepatic first-pass metabolism certainly cannot be discarded as an unlikely cause. In rodents, harmine and harmaline are extensively O-demethylated by hepatic microsomal enzymes (Ho et al. 1971; Burke and Tweedie 1979).

It is doubtful that indigenous Banisteriopsis drinks, known as

ayahuasca, may generally contain mind-altering concentrations of harmine and other major Banisteriopsis alkaloids. Chemical analysis of such drinks from the upper Purús region revealed that an average native dose of 200 ml contained only 6-38 mg of harmine, 1-46 mg of tetrahydroharmine, 0-5 mg of harmaline, 0-20 mg of an unidentified Banisteriopsis constituent and, due to an admixture of Psychotria leaves, 0-32 mg of DMT (Rivier and Lindgren 1972). More recently, McKenna et al. (1984a) found substantially higher alkaloid levels in Peruvian ayahuasca beverages prepared from Banisteriopsis caapi cultivars and Psychotria species. Based on an average of five samples, 100 ml of ayahuasca contained 467 mg of harmine, 160 mg of tetrahydroharmine, 41 mg of harmaline, and, due to the Psychotria admixture, 60 mg of DMT. The intramuscular threshold dose of DMT for producing subjective perception changes is only 30 mg (Szára 1957), so the implication of these analytical results is obvious: DMT can be present in ayahuasca beverages in parenterally active amounts.

This finding is quite interesting, since the beta-carbolines in Banisteriopsis are known as potent reversible MAO-inhibitors (Udenfriend et al. 1958; Pletscher et al. 1959; McIsaac and Estevez 1966; Buckholtz and Boggan 1977; McKenna et al. 1984a). In particular as selective inhibitors of MAO-A (Fowler et al. 1978; Fuller et al. 1981). Since there is evidence that oral tryptamines undergo first-pass inactivation by MAO, especially by MAO-A (vide 1.1.2.2), not surprisingly it is often suggested that the beta-carbolines enhance the effects of DMT (Holmstedt and Lindgren 1967; Furst 1976a; Emboden 1979a; Schultes and Hofmann 1980b; McKenna et al. 1984a). Decisive in vivo experiments have not yet been reported in the literature, but McKenna et al. (1984a) offer in vitro evidence to support this suggestion. It should be noted, however, that inhibition of degradation is not the only reported mechanism of interaction between MAO-inhibitors and DMT. In the sixties, the response to DMT (Sai-Halász 1963), as well as that to LSD (Resnick et al. 1967), was found to be diminished by pretreatment with a non-selective irreversible MAO-inhibitor, and this phenomenon was attributed to elevation of central 5-HT levels by the MAO-inhibitor.

The pharmacokinetics of an ayahuasca beverage with harmine and tetrahydroharmine as its main constituents have been assessed in two volunteers (Rivier and Holmstedt 1982). After a dose of 200 ml, plasma levels were determined to be in the range of 0.01 µg harmine and 0.04 µg tetrahydroharmine per ml by a gas chromatographical/mass spectrometric method. Unfortunately, quantitative data on the composition of the tested drink are no

longer available (Rivier, pers. commun. 1982, 1984).

1.1.4. Brugmansia species

Solanaceae
Brugmansia arborea (L.) Lagerh.
Brugmansia suaveolens (H. and B. ex Willd.) Bercht. and Presl.

1.1.4.1. Ethnobotany

Many South American tribes, especially in western South America, ingested preparations from tree Daturas in a ritual context (Safford 1922; Cooper 1949; Lockwood 1979; Plowman 1981a). Among the Jivaro, headhunters of eastern Ecuador and Peru, the rectal route of administration was employed as well (Wassén 1972b; Emboden 1979a). It is said that a decoction of a tree Datura was drunk or taken as an enema through a straw by Jivaro warriors desiring to gain power and foretell the future (Steward and Métraux 1948). Karsten (1935) tells that a Datura preparation called maikoa was given during the initiation ceremony in the form of a clyster, if the novice could not continue drinking this intoxicating liquid: 'The oldest men of the family or tribe arrange themselves in two parallel rows facing each other. Each man holds a pininga containing a small quantity of maikoa. The novice must now go from the one to the other in due order and take a sip from each pininga, starting with the oldest member of the family. Generally it is easy for him to do this with the first ones, but frequently it is impossible for him to drink from the clay vessels of the last men in the rows. Their contents are then given him in the form of a clyster... It is considered absolutely necessary, it should be understood, that the novice should receive something from the clay vessel of each man'.

Tree Daturas, all of which are native to South America, have usually been regarded as the Brugmansia section of the genus Datura, but on morphological and biological grounds this section is now treated as a separate genus (Lockwood 1979). There is usually no danger of confusing Brugmansia with any other hallucinogen, but when the older literature offers an indentification of the plant used, the statement is not usually supported by a voucher specimen (Schultes and Hofmann 1980b). According to Karsten (1935), the maikoa drink was simply prepared by squeezing the juice from the bark of Datura arborea. There has been a tendency in the past, however, to apply this binomial to any white-flowered tree Datura (Bristol et al. 1969), so it is

uncertain how frequently the plant actually did represent Brugmansia arborea. Other authors have attributed maikoa preparations to Datura candida (Emboden 1979a) and to Brugmansia suaveolens (Lockwood 1979).

1.1.4.2. Chemistry and psychopharmacology

As far as is known, all Brugmansia species and hybrids contain tropane alkaloids (Hegnauer 1973; Schultes and Hofmann 1980b), so there seems to be no serious uncertainty about the active principles, even though information on the species utilized is often inconclusive. In most cases, scopolamine, also called hyoscine, has been isolated as the predominant alkaloid (Evans et al. 1965; Shah and Saoji 1966; Bristol et al. 1969; Leary 1970). Aerial parts of white-flowered Brugmansia trees, referred to as Datura arborea from India (Shah and Saoji 1966) and as Datura candida and its Sibundoy cultivars from Colombia (Bristol et al. 1969), contained about 0.1–0.3% of scopolamine, whereas up to about 1% of this alkaloid could be found in the red-flowered Brugmansia sanguinea (Evans et al. 1965). The structurally related atropine and/or its laevo-isomer hyoscyamine may also be present (Evans et al. 1965; Shah and Saoji 1966; Bristol et al. 1969; Leary 1970). It should be noted that the distinction between these two compounds can be affected by racemisation upon extraction (List and Hörhammer 1972) and by inseparability on a paper chromatogram (Evans et al. 1965; Shah and Saoji 1966; Bristol et al. 1969). Various other minor Brugmansia alkaloids have been isolated, including aposcopolamine, norscopolamine, norhyoscyamine, noratropine, pseudotropine, tropine, oscine and meteloidine (Bristol et al. 1969; Leary 1970).

The central toxicity of the tree Daturas (Anonymous 1976a; Belton and Gibbons 1979) and their pure alkaloids (Longo 1966; Shader and Greenblatt 1971) is commonly known. As the following discussion focuses on scopolamine and atropine, it should be noted that hyoscyamine is the pharmacologically active laevo-isomer of the racemic atropine, of which the dextro-isomer is practically inactive (Shader and Greenblatt 1971; Reynolds 1982).

Ketchum et al. (1973) have demonstrated that parenteral scopolamine and atropine produce a virtually indentical syndrome of delirium, when allowances are made for differences in time of action and potency. The delirium lasts for 6–8 h with scopolamine and for 10–12 h with atropine. The intramuscular dose of atropine necessary to produce hallucinations in half the subjects was estimated to be about 0.15–0.17 mg/kg (about 11 mg/70 kg). Intramuscular scopolamine was found to be 7.5, 8 and 11 times as

potent in this respect, dependent on the test employed (mean 8.8 times; about 1.3 mg/70 kg). In a cross-over study by Mirakhur (1978) on peripheral activity of tropane alkaloids, the ratio of equivalent intramuscular to oral doses of atropine appeared to be 1:2 and that of scopolamine about 1:5-6. If these ratios also apply to central activity, the difference in central potency of both alkaloids would be reduced from 8.8 times parenterally to 3.2 times orally. Unfortunately, a cross-over study comparing central effects after ingestion and injection does not seem to be available. It is known only that oral doses of up to 10 mg of atropine sulphate or of up to 3 mg of scopolamine HBr do not induce delirium, whereas 4.5 mg of scopolamine HBr orally causes illusions and hallucinations in half the subjects (Ostfeld et al. 1959; Ostfeld et al. 1960). It may well be that scopolamine and atropine undergo substantial first-pass metabolism, which would explain why the activity of these alkaloids is route-dependent. Neither their physicochemical properties (Windholz 1983) nor the rapid appearance of peak plasma levels after oral administration (Beermann et al. 1971; Chandrasekaran et al. 1978) are suggestive of a faulty absorption. Furthermore, the observed activity ratios correspond rather well with reported urinary recoveries of non-metabolized drug, viz. 30-50% and 70-95%, respectively, for oral and intravenous atropine (Beermann et al. 1971), in contrast with only 4-5% and about 10% for oral and parenteral scopolamine, respectively (Chandrasekaran et al. 1978).

Naturally occurring tropane alkaloids have been found to produce delirium with various ways of administration (Shader and Greenblatt 1971), including tracheal inhalation (Bergman et al. 1980) and tropical application into the eye (Freund and Marin 1970) or on the skin behind the ear (Osterholm and Camoriano 1982). Furthermore, scopolamine (Tonndorf et al. 1953) and atropine (Hyde et al. 1953) have been shown to produce systemic effects when taken nasally.

1.1.5. *Capsicum* species
Solanaceae

1.1.5.1. Ethnobotany

Roth (1924) has included *Capsicum* in a review on narcotics and stimulants of the Guiana Indians, because the Makusi of the Rupununi used peppers as a stimulant and excitant. Although Spix and Martius (1828) once experienced a narcotic-like action of pepper (vide 3.4), it is not possible to draw any ethnobotanical

conclusion without further field observations (Schultes 1967a). Roth (1924) also points out that, 'in the Pomeroon district it is a very common practice for the Indian women to give capsicum enemata to themselves and children'. Unfortunately, he fails to indicate whether the intended effect of the Capsicum clyster was stimulation or purgation (Heizer 1944). The latter possibility is strongly supported, of course, by the irritating properties of Capsicum. According to an informant, who may or may not have been joking, the Makusi of the Roraima area use Capsicum to discipline children by anal insertion of the fruit as severe punishment (Gorinsky, pers. commun. 1982). The Jivaro of western South America employed Capsicum clysters for medicinal purposes. For instance, to try to cure patients from the consequences of a snake-bite (Karsten 1935). Among the Shuar-Jivaro, the whole Capsicum fruit is inserted rectally to distract from the pain of the snake-bite and also the broken fruit is rubbed on the wound itself (Van Asdall, pers. commun. 1982).

1.1.5.2. Chemistry and psychopharmacology

The fruits of most Capsicum forms, at least those used in official western medicine, contain the pungent principle capsaicin (Hegnauer 1973; Reynolds 1982), so native preparations are much more likely to have strongly irritating properties than any central effect. Since capsaicin selectively stimulates and then blocks the chemosensitive unmyelinated sensory afferents from the skin and mucous membranes, the initial irritation may be followed by local anaesthesia (Anonymous 1983a).

Perhaps it should be noted that solanine and solanidine have been reported as occurring in Capsicum annuum (Wojciechowska and Dombrowicz 1966) and that solanines are central intoxicants when taken in substantial quantities (Anonymous 1979). Hegnauer (pers. commun. 1983) questions, however, whether Solanum alkaloids are indeed present in the genus Capsicum.

1.1.6. Datura species
Solanaceae
Datura ceratocaula Ort.
Datura innoxia Mill.
Datura stramonium L.

1.1.6.1. Ethnobotany

Herbaceous Datura species have been widely employed by the

aboriginal inhabitants of North and Middle America (Safford 1922; Díaz 1979; Schultes and Hofmann 1980a,b). The ethnological record of their rectal administration is less impressive than the data on Brugmansia enemas (vide 1.1.4.1). In the initiatory ritual of the Algonquin Indians, a tribe of the eastern United States, the youths were kept intoxicated for 18 or 20 days by means of wysoccan liquid (Beverly 1705). The chief ingredient is believed to have been the root of Datura stramonium (Safford 1922; Schultes and Hofmann 1980b). Emboden (1979a) points out that such a prolonged state of intoxication would more easily be maintained through enemas than through oral fluids.

The ancient Aztecs of Mexico have been recorded as taking Datura rectally, but only for medicinal purposes. An authoritative early account on Aztec medicinal plants states that tlapatl leaves were applied in the form of suppositories to relieve fever (Hernández 1959). Tlapatl has been identified as D.stramonium (Safford 1922), but it referred more probably to D.innoxia (Schultes, pers. commun. 1982) or D.ceratocaula (Díaz 1979).

1.1.6.2. Chemistry and psychopharmacology

All herbaceous Datura species contain a mixture of tropane alkaloids, and the principal alkaloids in the leaves are mostly scopolamine and/or hyoscyamine (Hegnauer 1973; List and Hörhammer 1973; Schultes and Hofmann 1980b).

The deliriant activity and pharmacokinetic behaviour of tropane alkaloids are discussed in section 1.1.4.2.

1.1.7. Ilex guayusa
Aquifoliaceae
Ilex guayusa Loes.

1.1.7.1. Ethnobotany

Indians of the South American Montaña region, such as the Jivaro (Karsten 1935), are known to have valued Ilex guayusa as a ritual stimulant and emetic (Cooper 1949; Patiño 1968; Schultes 1972a). Bundles of I.guayusa leaves have been found together with small syringes in an archaeological Tiahuanacoid medicine-man's tomb in Highland Bolivia (Wassén 1972b). This has raised the question of whether guayusa might have been employed as a clyster (Schultes 1972a, 1981a; Furst 1976a). It should be added that the grave also contained Nicotiana fragments in a skin pouch

(Bondeson 1972; Bruhn et al. 1976) and that small syringes were sometimes also used for nasal application (Veigl 1785; Métraux 1949).

1.1.7.2. Chemistry and psychopharmacology

I.guayusa leaves from the grave in question were demonstrated to contain caffeine in amounts of 0.1–1%, whereas 1.8% of caffeine was present in a newly collected specimen (Holmstedt and Lindgren 1972). This well known alkaloid is a CNS stimulant (Stephenson 1977), which only rarely has been reported as eliciting a psychotic reaction, usually after prolonged use of excessive doses (Mc Manamy and Schube 1936; Shen and D´Souza 1979).

1.1.8. Lophophora williamsii
Cactaceae
Lophophora williamsii (Lem.) Coult.

1.1.8.1. Ethnobotany

The ritual use of peyote among North American and Mexican Indians has been documented extensively (Furst 1976a; La Barre 1975, 1981; Schultes and Hofmann 1980a,b). Peyote is mostly eaten in the form of so–called ´mescal–buttons´, the dried tops of the cactus, which are usually taken into the mouth, softened with saliva and swallowed without mastication. They can also be soaked in water to yield an intoxicating fluid (Schultes and Hofmann 1980b). The Huichols of the Sierra Madre in western Mexico, renowned for their peyote pilgrimages (Furst 1976a), use peyote in a different way. They only leave one–third of the cactus, and use either the fresh ground form or the dried ground form, thereby masticating a lot (Negrín, pers. commun. 1983). The use of a peyote enema among the Huichols has been reported by the ethnographer Knab who was shown an enema syringe by an elderly female shaman in the community of Santa Catarina (Furst and Coe 1977). In a personal communication (1982) to me, Knab detailed the following: ´Old men and women use a mixture of either fresh ground peyote with its juice or dried peyote mixed with water. Among the Huichols an enema is applied through a short piece of deer bone tied to a bladder. The mixture is applied by filling the bladder, tying the bone to it and sitting on the bladder´. As it is unclear whether the enema will be easily retained this way, it is unfortunate that actual use has not been witnessed. At one

time, Furst (1976a) suggested that the practice probably has a deeper symbolic meaning, as the sacred cactus is equated with and identified as the deer by the Huichols. On reconsideration, he suspects the reported event to have been idiosyncratic and not something to be generalized to Huichol culture, as the practice would be atypical of known Huichol behaviour (Furst, pers. commun. 1982). This view is shared by Negrín (pers. commun. 1983) who seriously questions the truthfulness of the enema story, since the Huichols are very puritanical and would not give such delicate information to a visitor known for only a few weeks. Negrín adds that the Huichols like to reverse things (viz. rectal instead of oral administration) and like to tell scabrous jokes.

There are no indications that peyote has ever been taken rectally north of Mexico (Aberle, pers. commun. 1982; Stewart, pers. commun. 1982).

Peyote is a vernacular term applied to a number of plants (Bruhn and Bruhn 1973). For the Huichols, the common source of peyote is unquestionably Lophophora williamsii (Furst 1976a, 1981; Knab, pers. commun. 1982; Negrín, pers. commun. 1983).

1.1.8.2. Chemistry and psychopharmacology

Mescaline, the main alkaloid in Lophophora williamsii, may occur in peyote to the extent of 6%, but rarely exceeds 1% in the dried whole plant (Crosby and McLaughlin 1973; Kapadia and Fayez 1970, 1973). A chemical study on fresh greenhouse-grown peyote revealed an average total alkaloid percentage of 0.4%, consisting mainly of mescaline (30%), pellotine (17%), anhalonidine (14%), hordenine (8%), anhalamine (8%), lophophorine (5%), anhalonine (3%), N-methylmescaline (3%), anhalidine (2%), 3-demethyl-mescaline (1-5%) and N,N-dimethyl-4-hydroxy-3-methoxyphenyl-ethylamine (0.5-2%) (Lundström 1971). In total, more than 50 alkaloids have been isolated from peyote (Kapadia and Fayez 1970, 1973), but Schultes (pers. commun. 1982) may be quite right in wondering how many of these constituents are artifacts.

Mescaline is not the only peyote constituent with pharmacological activity (List and Hörhammer 1976; Shulgin 1979). However, the peyote tetrahydroisoquinoline alkaloids pellotine, anhalonidine, lophophorine and anhalonine are not hallucinogenic in man, even at rather high oral doses (Shulgin 1973, 1979), and neither are the minor phenylethylamine components N-acetyl-mescaline (Charalampous et al. 1966), N-methylmescaline (Shulgin 1973) and 3,4-dimethoxyphenylethylamine (Shulgin et al. 1966). There does not seem to be clinical evidence for hallucinogenic activity of any minor peyote alkaloid in naturally occurring

quantities (Shulgin 1973, 1979). Studies on certain synthetic modifications of the structure of mescaline have been more rewarding in this respect (Shulgin et al. 1969; Nichols 1981). Consequently mescaline seems to be mainly responsible for the visual hallucinogenic properties of L.williamsii (Shulgin 1979; Schultes and Hofmann 1980b). This classical hallucinogen is usually ingested in quantities between 300 and 500 mg of the sulphate (Shulgin 1979). The average oral dose of mescaline needed for a medium response has been estimated at 3.75 mg/kg, i.e. about 260 mg/70 kg (Shulgin et al. 1969). Schultes and Hofmann (1980b) warn that there is an often overlooked difference between peyote intoxication and mescaline intoxication, but so far as I know, the influence of minor peyote alkaloids on the effects of mescaline still needs to be properly tested in a clinical setting.

Early experiments on the fate of mescaline in man have yielded divergent results (Patel 1968). In a later study, a maximum of radioactivity appeared in the plasma within 3 h of oral administration of ^{14}C-mescaline to humans; 87% of the dose could be recovered from the urine during the first 24 h, mainly as unchanged mescaline (55-60%) and its inactive metabolite 3,4,5-trimethoxyphenylacetic acid (27-30%) (Charalampous et al. 1966). According to these results, mescaline taken orally is readily absorbed from the gastrointestinal tract without undergoing extensive first-pass metabolism.

1.1.9. Nicotiana species
Solanaceae
Nicotiana rustica L.
Nicotiana tabacum L.

1.1.9.1. Ethnobotany

Neither botanists nor pharmacologists consider tobacco to be a true hallucinogen, but it may be conceptually and functionally indistinguishable from hallucinogens in American Indian ritual practices (Wilbert 1972). The references to its use in indigenous rituals are numerous and there are ethnological reports on its induction of trance-like states analogous to those induced by hallucinogens (Castiglioni 1943; Spinden 1950; Wilbert 1972; Janiger and Dobkin de Rios 1976; Siegel et al. 1977; Robicsek 1978). Several recent secondary sources state that tobacco was taken rectally in the western hemisphere (Schultes 1981a), in particular on the South American continent (Schultes 1972a, 1984;

Furst 1976a; Furst and Coe 1977), but neither the purpose nor other details are clearly mentioned. The main ways in which South American Indians have used tobacco are smoking, snuffing, chewing, drinking, eating and licking (Stahl 1925; Cooper 1949; Wilbert 1975; Hartmann 1981). As to the rectal route, a pre-Hispanic Bolivian grave was found to contain both tobacco fragments and small syringes (vide 1.1.7.1), and early accounts on Surinam (Fermin 1775) and Brazil (Spix and Martius 1831) touch lightly on tobacco enemas. These data, however, can hardly be considered as substantial evidence for the non-medical rectal use of tobacco by South American natives. Neither Schultes (pers. commun. 1981) nor Wilbert (pers. commun. 1982) are aware of any detailed primary reference on this subject.

Decisive data are equally hard to find for Middle America. Several early sources describe the rectal administration of tobacco, but only as a medicinal cure. The 16th century physician Monardes (1574) includes the use of clysters among the various methods of applying tobacco as a medicine, and the Relación de Texcoco says that the Spaniards used the herb to clear malaria, 'taking it as a suppository because it purged them' (Pomar 1941). The famous Aztec herbal known as the Badianus Codex recommends a 'clystere oriculario' prepared from tobacco and various other ingredients as a remedy for rumbling of the abdomen (Anonymous 1940). Since it would be very peculiar to treat such a complaint by instilling liquid into the ear, I am inclined to interpret this dosage form as a rectal fluid rather than as an auricular one. In another passage of the Badianus Codex, a tobacco clyster is recommended to relieve recurrent disease. Emboden (1979a) feels that this enema was designed to produce inebriation, but according to the original text purgation was intended (Anonymous 1940). Evidence suggesting that the ancient Maya may have used tobacco as an ingredient of their ritual enemas is discussed in section 1.4.2.

Drawing from an early French account (De Charlevoix 1744), several references indicate that the Indians of eastern Canada revived those nearly drowned by forcing tobacco smoke up the rectum. Then the victim was hung up by his feet to a tree so that he could cast up the water he had swallowed (Brooks 1937, 1941; Van Wart 1948; Gorter 1953). In past centuries, resuscitation of drowned people by a rectal tobacco fumigation was practised in Europe as well (Brooks 1937, 1938, 1941; Gorter 1953).

The two principal tobacco or Nicotiana species which have been employed ritually in the western hemisphere, are N.tabacum and N.rustica. At the time of the Spanish invasion, the first species was known in Central and South America and much of the West

Indies, and the second one in North America and Mexico (Schultes 1967b, pers. commun. 1982). Although the literature sometimes warns that there is no certain information to prove the existence of N.tabacum in pre-Hispanic Mexico (Spinden 1950), this species is frequently implied to have occurred there (Setchell 1921; Castiglioni 1943; Schultes 1981a). Long after the conquest, N.tabacum which comprises most varieties of commercially grown tobacco, was introduced from the Old World to the North American continent (Schultes 1967b).

1.1.9.2. Chemistry and psychopharmacology

The principal Nicotiana alkaloid is nicotine, as it may account for about 95% of the total alkaloid content of tobacco (Wenusch 1940; Rotenberg 1982). The amount in the leaf of N.tabacum varies widely from 0.6% to 9% (Hoppe 1975; Schultes 1981a), but in commercial cigarette tobacco it seldom exceeds 3% (Siegel et al. 1977; Robicsek 1978). N.rustica usually has a higher nicotine content, which was found to range from 4.5% to 8.6% in African samples and from 1.89 ± 0.02% to the surprising figure of 18.76 ± 2.6% in west Mexican samples (Siegel et al. 1977). Minor constituents include many other pyridine alkaloids such as anabasine, anatabine, 2.3'-dipyridyl, myosmine, nicotelline, nicotyrine and nornicotine (Wenusch 1940; Hegnauer 1973; List and Hörhammer 1977). In addition, very small amounts of the beta-carboline alkaloids harman and norharman have been isolated from commerical tobaccos and their smoke; the amounts in the smoke are about 0.01-0.02 mg per cigarette which is some 40-100 times greater than that in the tobacco leaf, indicating that pyrosynthesis occurs in the leaves during burning (Janiger and Dobkin de Rios 1976).

Although practised smokers are tolerant of some of its effects, nicotine is highly toxic and acute poisoning with a dose of 60 mg may cause death due to respiratory failure within a few minutes. It acts on a variety of neuro-effector and chemosensitive sites and has both stimulant and depressant phases of action. The ultimate response of an organ or system is the product of such different and opposing effects. The central nervous system, for instance, is markedly stimulated by nicotine, but depression may follow (Rasche González 1980; Taylor 1980; Reynolds 1982). Although smoking might contribute to mental changes (Janiger and Dobkin de Rios 1976), and extreme acute doses of nicotine could produce hallucinations and catatonia (Siegel et al. 1977), nicotine is not considered to be an hallucinogen from the pharmacological view (Siegel et al. 1977; Taylor 1980; Reynolds

1982). Other constituents in tobacco smoke, such as harman and norharman (Janiger and Dobkin de Rios, 1976), might be hallucinogenic per se, but all of these compounds appear to be present in such small quantities, at least in commercial tobaccos, that any suggestion of endogenous hallucinogens present in tobacco in behaviourally active quantities should be viewed with appropriate caution (Siegel et al. 1977; Baumann et al. 1984).

Recent pharmacological studies have demonstrated that the smoking (Benowitz et al. 1982, 1983), snuffing (Russell et al. 1980, 1981) and chewing (Gritz et al. 1981) of tobacco can all lead to substantial blood levels of nicotine.

Oral nicotine is said to be largely inactivated during its first passage through the liver (Russell et al. 1976; McNabb et al. 1982). It is also said that after oral ingestion of tobacco, the absorption of nicotine is apparently delayed because of slowed gastric emptying, so that vomiting caused by the central effect of the initially absorbed fraction removes much of the tobacco remaining in the stomach (Taylor 1980). Nevertheless, oral tobacco infusions are considered quite toxic and may even be lethal (Harrison 1964; Opitz 1982).

Tobacco is known to affect the pharmacokinetic behaviour of many drugs, but most of these alterations appear to involve stimulation of hepatic drug metabolism by smoking and are caused probably by the polycyclic hydrocarbons present in tobacco smoke (Jusko 1978; Dawson and Vestal 1982; Hansten 1982). I am not aware of clinical studies on the combined use of non-smoked tobacco and a classical New World hallucinogen.

1.1.10. Conclusion

From the ethnobotanical, chemical and psychopharmacological approach to intoxicating enema rituals in the western hemisphere, the following categories of ritual enema ingredients arise:

1) It is well established that the plant provides one or more psychoactive principles and the Indian use of the plant as a ritual enema ingredient is confirmed or is quite probable: Agave, Anadenanthera, Brugmansia.
2) It is well established that the plant provides one or more psychoactive principles, but the Indian use of the plant as a ritual enema ingredient is not well recorded or is even unlikely: Banisteriopsis, Datura, Ilex guayusa, Lophophora williamsii, Nicotiana.

3) The Indian use of the plant as a ritual enema ingredient is confirmed or is quite probable, but it is not well established that the plant provides one or more psychoactive principles: none.
4) The Indian use of the plant as a ritual enema ingredient is not well recorded, and it is not well established that the plant provides one or more psychoactive principles: Capsicum.

CHAPTER ONE PART TWO

RECTAL PHARMACOKINETICS AND EFFICACY OF POSSIBLE RITUAL ENEMA CONSTITUENTS

1.2.1. General introduction

Drug uptake from the rectum does not appear essentially different from that in other parts of the gastrointestinal tract. Passive diffusion through a lipid membrane is probably the main governing mechanism of absorption. In contrast to the small intestine, the rectum has no primary function as an absorbing organ. It is approximately 15–20 cm long, and there are no villi and microvilli on the rectal mucosa. Consequently, the absorption surface is far more limited than that of the duodenum. Under normal conditions, the rectum merely contains 2–3 ml of inert mucus, so the small intestine has much more fluid available than the rectum for drug dissolution from solid dosage forms. Despite these potential disadvantages, it has been demonstrated that numerous drugs reach effective plasma levels when given rectally, and in many countries rectal therapy is generally viewed as a convenient alternative to oral dosing (Senior 1974; Moolenaar 1979; Thoma 1980; de Boer et al. 1982).

Systemic therapy via the rectal route is considered particularly useful when the patient is unwilling or unable to take his medicine by mouth. For instance, because of nausea and vomiting. The preceding pages amply demonstrate that the American Indian has not failed to notice this obvious advantage.

The presence of food in the stomach delays the absorption of many drugs when they are taken orally (Welling 1977; Toothaker and Welling 1980), but this is impossible in the case of rectal application. In other words, when a patient has just enjoyed a meal, drug absorption may be more rapid following rectal administration than it would be after oral dosing.

Another advantage of rectal application may be that the breakdown of acid–labile drugs by the stomach is avoided. Sometimes the rectal route is also recommended as a means to prevent first–pass elimination by liver enzymes (Ansel 1976). There is considerable doubt, however, that an enema usually provides the advantage of adequately bypassing hepatic inactivation. It is true that, while the upper rectal vein drains into the hepatic circulation, the inferior and probably also the middle rectal veins pass directly into the systemic circulation. A complicating anatomical factor, however, is the presence of

anastomoses between the rectal veins (de Boer 1980). Also, rectal dosage forms do not remain in the lower parts of the rectum, but move upward into a higher region (Moolenaar and Schoonen 1980). Studies on the degree of enema penetration indicate that penetration as far as the ascending colon may be achieved and that, depending on the enema volume, penetration at least as far as the descending colon is likely (Lima and Jusko 1980). Therefore, a large enema cannot be expected to provide a substantial by-pass of the liver (Quevauviller and Jund 1951). A recent study on lidocaine has shown that in principle the use of a micro-enema can result in partial avoidance of a hepatic first-pass effect (de Boer et al. 1979). However, in various other experiments with codeine (Moolenaar et al. 1982), 5-methoxy-psoralen (Stolk 1982), paracetamol (Moolenaar et al. 1979), promethazine (Moolenaar et al. 1981), propranolol and salicylamide (de Boer 1980), the systemic availability of a micro-enema did not substantially surpass that of an oral dosage form. It certainly cannot be concluded from these experimental findings that a high-clearance drug will generally show higher systemic availability when it is taken as an enema. Unless the tested compounds were well absorbed after oral ingestion and poorly absorbed following rectal application, this implies that substantial first-pass metabolism may not be avoided even when a non-voluminous enema is used.

The principal drawback of rectal administration is the risk of interrupted drug absorption by the inability of the subject to retain the dosage form. For instance, retention time was a major determinant of bioavailability in studies on aminophylline suppositories (Zuidema et al. 1976; Anonymous 1980).

A second problem may be a lack of patient acceptability. Rectal therapy is generally recognized as useful in West European countries on the continent, but it is far from common in Britain and in the United States. In a large British study on phenylbutazone suppositories in general practice, 10% of the patients refused to participate, because they were not prepared to accept a suppository, and half of them did not complete the eight-week course (Anonymous 1983b). Opposite views on rectal administration are not only seen in western civilisation, but also in the native societies of South America. The Peruvian Omagua Indians even distributed enema syringes to their guests (De La Condamine 1778), but such instruments were less appreciated among the Abipones of Paraguay (Dobrizhoffer 1822): 'They will not even bear the mention of an enema. In the town of St. Jeronymo, a Spanish soldier who professed the art of medicine, being requested by Father Brigniel to attend upon a

sick Abipon, declared the necessity of an injection. No sooner did the sick man feel the syringe applied to him, than he started furiously out of bed, snatched up a lance, and would have slain the soldier physician, had he not saved himself by hasty flight'.

Another disadvantage of rectal administration arises from the relatively small absorption surface of the rectum. As a consequence, the usefulness of the rectal route may vary considerably with the physicochemical properties of the drug substance and with the biopharmaceutical properties of the dosage form. These aspects of rectal drug administration and their clinical implications are extensively discussed in recent reviews by de Blaey and Polderman (1980), Thoma (1980), and de Boer et al. (1982).

Data on the rectal pharmacokinetics and efficacy of ritual enema constituents are summarized below. It should be borne in mind that the dosage form tested in a western study will differ from the dosage form used in native rituals, and that this may somewhat limit the pertinence of the clinical data to Indian practices. Unfortunately, the ethnological literature rarely describes the properties of the native dosage form. Only in the case of the paricá clysters of the Brazilian Caripuna and Maué Indians, some interesting information is given, viz. the addition of plant ash to the clyster (vide 1.1.2.1). This admixture has an alkaline nature (Rivier 1981), and may thus enlarge the non-ionized proportion of an alkaloid, which in its turn might facilitate the rectal absorption of the alkaloid. An animal study on suppositories with methylhomatropine shows that the rectal mucosa is not generally an impenetrable barrier for ionized drugs (Cramer et al. 1978), but in principle non-ionized molecules diffuse much more easily through the rectal mucosa than ionized ones (Senior 1974; de Boer et al. 1982).

1.2.2. Specific constituents

1.2.2.1. Atropine

Vide section 1.2.2.9.

1.2.2.2. Bufotenin

Vide section 1.2.2.4.

1.2.2.3. Caffeine

The physicochemical properties of caffeine (Windholz 1983) and its rapid and complete absorption after oral administration (Blanchard and Sawers 1982, 1983) suggest that its absorption from rectal dosage forms may well be substantial. Indeed Maier-Lenz et al. (1981), who recently compared the absorption of caffeine and other drugs from a certain multiple drug tablet and suppository called Migräne-Kranit, did not find a large difference between the serum levels of caffeine following oral and rectal application. A recent case report describes two deaths related to unofficial therapy with voluminous coffee enemas, but these were assumed to be due to electrolyte disturbances; toxicological results in both cases indicated that not enough caffeine had been absorbed to cause a substantial toxic effect (Eisele and Reay 1980), possibly because of the difficulty to retain the large volumes used.

1.2.2.4. Dimethyltryptamine and related compounds

There is considerable evidence to suggest that the active constituents of Anadenanthera undergo extensive first-pass metabolism by intestinal and hepatic MAO and by hepatic microsomal enzymes (vide 1.1.2.2). This may well explain why this genus is most often taken nasally, for the nasal route certainly can provide the advantage of bypassing the gut wall and the liver (vide 2.2.1). It is less easy to presume that the rectal taking of Anadenanthera will be advantageous. Since it is likely that the availability of drug metabolizing enzymes in the gut wall decreases in the direction jejunum, caecum, colon, rectum (de Boer et al. 1982), it may be speculated that inactivation by intestinal MAO is avoided by rectal application. There is considerable doubt, however, that the use of an enema is a reliable way to escape hepatic first-pass elimination (vide 1.2.1), so the Anadenanthera tryptamines may still be inactivated following rectal administration. To obtain anecdotal experimental evidence, I took enemas containing up to 125 mg (1.6 mg/kg) of DMT in self-experiments. At the time of the experiment, I was a non-smoker and a regular user of coffee and beer. The highest rectal dose was 185 mg of DMT bioxalate (Schuchardt, Munich) in 15 ml of tap water, and it was taken with the aid of a syringe and a special adaptor, developed for the rectal application of Valium injection fluid (Anonymous 1981). Even though this dose of 125 mg was much larger than 30 mg, the reported threshold dose of intramuscular DMT (Szára 1957), I failed to notice any

discernible effect. The most likely explanation for the inactivity is that first-pass elimination was not completely avoided. Further experiments in more than one volunteer are needed, however, especially with still higher doses, to ascertain whether or not any partial avoidance is possible. So long as such testing has not been done, it can neither be safely excluded nor concluded that Anadenanthera alkaloids produce systemic effects, when orally inactive amounts are taken in the form of an enema.

1.2.2.5. Ethyl alcohol

In view of the good oral absorption characteristics and physicochemical properties of ethyl alcohol (Offerhaus 1979), a rapid and complete absorption should be possible, if it be rectally administered. To test this theoretical view, I twice took 0.5 l of 5% v/v alcohol, once as an oral drink and once in the form of clysters. Solutions were prepared by diluting 26 ml of 96% v/v alcohol (OPG, Utrecht) with tap water to 0.5 l. At the time of the experiment, I was a non-inhaling smoker and a regular user of coffee and beer. A percentage of only 5% was chosen, since a clyster with an alcoholic content of 20% is quite irritating to the rectal tissue (Moolenaar, pers. commun. 1982), and since the early Indian drinks also had low alcohol percentages (vide 1.1.1.2). Because of this choice, the oral drink and the enema had to be voluminous to provide a substantial dose of alcohol. According to the pharmaceutical literature, the volume of an enema should be less than 0.2 l, if it is to be retained in the intestine (Fishburn 1965; Pernarowski 1975). Therefore the total rectal volume was divided in four equal parts, which were administered within 25 min with the aid of a Flex-Klis flacon (Spruyt-Hillen, Vianen). The clysters had been warmed to body temperature before administration, and they were taken in a prostrate position. Due to these precautions, rectal retention of as much as 0.5 l turned out to be quite easy.

As the sole purpose of the experiment was to obtain an impression of alcohol absorption via the rectal route, alcohol blood levels were not monitored by blood analysis, but by simple breath testing with an Intoxilyzer Model 4011 A (CMI, Mintum). The manufacturer of this equipment guarantees an absolute error of less than 0.1 mg/ml. In a calibration test of the used apparatus, zero set values turned out to be more accurate than test mode values and did not deviate more than 0.02 mg/ml from actual blood levels (Zweipfennig, pers. commun. 1984). The results presented here are therefore not test mode values, but zero set values.

The oral dose was taken after an overnight fast, and resulted in maximal blood levels of 0.4 mg/ml at 30–45 min, followed by a practically linear decline to 0.2 mg/ml at 120 min. Similar data were reported by Wilkinson et al. (1977), who tested 30 ml of 95% of alcohol (diluted to 150 ml) in fasting subjects. In the next 25 min, the total rectal dose was administered, and it produced a rise from 0.2 mg/ml to 0.6 mg/ml at 165 min, whereafter at 240 min the level fell again to 0.4 mg/ml in a practically linear way. These results certainly support the theoretical suggestion that alcohol is absorbed well from an enema.

As pointed out in section 1.1.1.2, alcohol may affect the actions of many other drugs directly or indirectly. In the present context it is interesting to note that in an experiment by Moolenaar (pers. commun. 1982), the presence of alcohol enhanced the absorption rate of the drug sodium salicylate from an enema.

1.2.2.6. Harmine

There does not seem to be any study on the rectal taking of harmine. In view of the physicochemical properties of this alkaloid (Hultin 1965), rectal absorption should well be possible. However, harmine may undergo substantial hepatic first-pass metabolism (vide 1.1.3.2), and there is recent evidence that rectal application is not a reliable way of adequately avoiding this phenomenon (vide 1.2.1). Consequently, there is no obvious reason to assume that an enema will be effective if it contains harmine in an orally inactive amount.

1.2.2.7. Mescaline

The solubility profile of mescaline (Windholz 1983) and the reported good absorption of this hallucinogen after oral ingestion (Charalampous et al. 1966) suggests that substantial absorption can be possible after rectal application. This is a theoretical view which still awaits experimental confirmation, for in the only rectal experiment known to me, 200 mg of mescaline in a suppository caused nothing but a dubious mydriasis (Möller 1935).

1.2.2.8. Nicotine

When tobacco is injected into the rectum, it might sometimes operate as a cathartic (Osol and Farrer 1955), but in official Western medicine tobacco enemas certainly are considered obsolete

because of their toxicity (List and Hörhammer 1977). Rectal infusions prepared from 15 to 20 g of tobacco (Fabre et al. 1957) or even as low as 2 g (List and Hörhammer 1977) are said to have caused fatal intoxications, although recovery after 15 g rectally has also been observed (Lewin 1962). A recent case report describes nausea and confusion followed by hypotension and bradycardia due to unorthodox self-medication with an enema prepared apparently from 5-10 cigarettes (Garcia-Estrada and Fischman 1977). Furthermore, nicotine could be recovered from the urine of a male non-smoking subject, who had received this alkaloid via the rectal route (Jenner et al. 1973). In view of these data, there can be no doubt that a tobacco clyster can produce systemic effects.

1.2.2.9. Scopolamine and related compounds

The synthetic quaternary compounds butylscopolamine and methylatropine are very poorly absorbed after rectal administration (Soeterboek et al. 1980), but the natural tropane alkaloids scopolamine and atropine are tertiary compounds, which should allow a better rectal absorption. Suppositories containing belladonna liquid extract were included in the British Pharmacopeia of 1948 (Reynolds 1982). However, there are only vague and conflicting experimental data on the efficacy of rectal atropine and scopolamine. Well-designed studies on the rectal usefulness of natural tropane alkaloids are still awaited.

Tardos et al. (1959) studied the mydriatic activity of rod-shaped suppositories with atropine sulphate in the rat. They reported a very large difference between equivalent intravenous and rectal doses of atropine, viz. 0.02 mg/kg vs. 0.5 mg/kg, for rods prepared from cacao butter, and the difference was even larger when the rod base was carbowax.

Neuwald et al. (1962) examined the mydriatic effect of fatty suppositories with atropine base or atropine sulphate in rabbits. A dose of 20 mg atropine or atropine sulphate produced mydriasis in all animals tested, but a suppository with 10 mg of the sulphate did not have this effect in each rabbit. According to the authors, the large difference in mydriatic efficacy between a rectal dose of 20 mg (6-8 mg/kg) in the rabbit and a systemic dose in man should be attributed to the insensitivity of the rabbit for atropine.

More recently, Hendrickx and Govaerts (1980) compared enemas with 0.00, 0.01, and 0.02 mg/kg of atropine in small children. Apparently, they did not find statistically significant

differences in cardiac and anti-sialogogic activity, but their report is too confusing to permit firm conclusions.

In other investigations, rectal preparations containing one or more natural tropane alkaloids were found to be useful as premedication for children (Chayen and Sarnat 1973; Lindahl et al 1981) and for the facilitation of delivery (Weinstock 1934; Rittmeyer 1935; Lehmann 1952). All these studies were uncontrolled, however, and each tested drug preparation contained at least one other active substance besides the tropane alkaloid(s).

1.2.3. Conclusion

The literature yields convincing evidence that caffeine and nicotine are effective following rectal application. A good rectal efficacy could also be expected from mescaline and from tropane alkaloids, but this is a hypothetical view which stills awaits experimental confirmation.

In self-experiments, ethyl alcohol produced substantial blood levels via the rectal route, whereas dimethyltryptamine did not produce any effect when parenterally active quantities were taken as an enema. First-pass elimination is the most likely explanation for the observed inactivity of dimethyltryptamine via the rectal route.

CHAPTER ONE PART THREE

THE CHEMISTRY OF PARICÁ SEEDS OF THE BRAZILIAN MAUÉ INDIANS

1.3.1. Introduction

In 1817, the Austrian Emperor Franz I. gave his daughter Leopoldine in marriage to the later Brazilian Emperor Dom Pedro I. When the Archduchess made the crossing to the New World, she was accompanied by an Austrian expedition, which included the zoologist Johann Natterer (1787–1843). At the request of King Max Joseph von Bayern, the German explorers Spix and Martius also joined this party. Most of the expedition members returned to Europe in 1821, because the Brazilian civil war broke out, but Natterer stayed behind and continued his travels in Brazil until 1835. During this time, he collected not only numerous biological objects, but also almost 2000 ethnological items, which are now in the Museum for Ethnology in Vienna (Kann 1981). Since various Indian tribes from those days have become extinct or have lost their cultural identity, the importance of these early Brazilian ethnographical objects is obvious. There are only two other collections of this kind in the world, viz. the one from Spix and Martius (Zerries 1980), and an unpublished one from a Russian expedition led by the Earl Langsdorff (Kann 1981).

In contrast with Spix and Martius (1823–1831), Natterer never published his travelling diaries, and unfortunately they were destroyed by fire a few years after his death, when the roof of the Viennese court library caught fire. Still remaining, however, is his correspondence to Europe, and the museum inventory of his collection, written under his supervision. Both sources provide valuable information (Kann 1981, pers. commun. 1984).

The Natterer collection includes several objects of the Maué, Caripuna and Marauá Indians, which are related to ritual drug taking. Detailed descriptions of these paraphernalia are given by Wassén (1965, 1972a) and Kann (1971). It should be noted that volume three of the renowned Handbook of South American Indians does not discuss the Marauá, but only the Maraguá, who are thought to be a probable subdivision of the Maué (Nimuendajú 1948a).

From the ethnobotanical view, the most interesting item is a large sample of well preserved paricá seeds, collected from the Maué tribe (museum inventory 1369): 'Samenkörner des Paricábaumes (in Matogrosso Angico genannt). Diese Körner werden zerstossen (zerrieben) und mit der Asche des Imbauvabaumes gemischt und dann zum Schnupfen und zu berauschende Klystieren gebraucht. Wird namentlich bei den Mauhés, Muras, Caripunas und andere Nationen

gebraucht'.

The tracing of these seeds is important, as it has often been implied that the Maué and Mura Indians of the Brazilian Madeira River prepared paricá snuffs and enemas from Anadenanthera seeds. Up to now, however, these assertions have not been supported by an early collection of the seeds (Schultes 1967b; von Reis Altschul 1972). Furthermore, the seeds are unique in the sense that no other ethnobotanical material from the western hemisphere has ever been directly associated with ritual rectal intoxication.

The seeds have a black-brown colour, a flat and orbicular shape, and a diameter of 1-2 cm. These features are certainly reminiscent of Anadenanthera seeds (von Reis Altschul 1964), and this botanical view is shared by von Reis (pers. commun. 1984). Since there are no clear differences between the seeds of the two Anadenanthera species A.peregrina and A.colubrina (von Reis Altschul 1964), the species cannot be determined without the availability of additional plant parts.

In view of the ethnobotanical importance of the seeds, it was quite interesting to obtain data on their chemical composition. Schultes et al. (1977) isolated 0.6% of bufotenin from seeds of A.peregrina, which Richard Spruce had collected in 1854 from the Guahibo Indians of the upper Orinoco River. It was to be hoped that the even older Maué seeds would also give a positive result, corroborating their botanical identification as Anadenanthera seeds.

1.3.2. Analytical methods

By cooperation of Laurent Rivier (Institute of Legal Medicine, Lausanne), the seeds were submitted to a gas chromatographical/mass spectrometric analysis comparable to that described by Schultes et al. (1977). Details are provided in Appendix A.

1.3.3. Results and discussion

Despite their considerable age, the seeds still yielded as much as 15 mg of the Anadenanthera alkaloid bufotenin per g dry seed matter, as identified by retention time on capillary column and mass spectrum. This chemical finding certainly supports the botanical view that they are Anadenanthera seeds. Other tryptamine alkaloids could not be detected. This is not surprising, since Schultes et al. (1977) report that storage of freshly collected Anadenanthera seeds for two years results in the disappearance of all tryptamines except bufotenin. It can

therefore not be excluded that the Maué seeds originally may have contained more than one alkaloid.

CHAPTER ONE PART FOUR

ENEMA SCENES ON ANCIENT MAYA POTTERY

1.4.1. Introduction

Pottery of the classic Maya civilization, in particular the polychrome pottery of the late classic period (A.D. 600–900), provides much information on this Mesoamerican culture by portraying a variety of scenes like palace scenes, ball games, hunting parties, and special dances after human sacrifice by decapitation (Coe 1975, 1978, 1982; Hellmuth 1978; Robicsek 1978; Robicsek and Hales 1981). Some years ago, Furst and Coe (1977) added a new theme to this list after they had discovered a polychrome Maya jar showing the actual administration of an enema (vide plate 3 of Appendix C). According to early colonial references, the Maya employed clysters for diarrhoea and chills or for a swollen abdomen (Roys 1976), and present–day Maya have been reported as taking the purgative castor oil as an enema to treat constipation (Steggerda and Korsch 1943). Yet the discovered scene was revealing, since it appeared to Furst and Coe (1977) that some non–medicinal ritualistic use of clysters was represented: 'Seven male–female pairs, the women easily distinguished by their robes and long hair, are depicted in two horizontal rows. That one woman is fondling a child suggests a familial setting. The activity being portrayed would have brought blushes to the cheeks of the traditional Maya specialist, for while one man is inserting a syringe into his rectum, this delicate task is being carried out for another male by his consort. One male also has a bulbed enema syringe tucked into his belt. Nine vases, identical in shape to the actual vessel, are painted between the couples, and painted dots at the mouth of each represent a foaming, fermented liquid that is probably balche, the common alcoholic drink among the Maya at the time of the conquest. We must conclude that the people on the vase are taking intoxicating enemas, a practice previously unrecorded for this culture'. The discovery of this crucial vessel allowed the identification of other Maya vase paintings as enema scenes (Furst and Coe 1977), and soon others were also led to believe that the ancient Maya took intoxicating enemas for ritual purposes (Hellmuth 1978; Robicsek 1978; Nicholson and Cordy–Collins 1979; Anonymous 1984; Dobkin de Rios 1984; Torres 1984; Schele, pers. commun. 1985).

In my opinion, there can be little doubt indeed that the enema

scenes on Maya pottery, or at least part of them, represent some kind of ritual. The mere fact that deities or their devotees, and animals or humans dressed up like animals are common actors in these scenes (vide Appendix B) leaves little room for another interpretation. This does not automatically signify, however, that the Maya vases show the use of intoxicating retention enemas. Starting from the assumption that these enemas served a specific ritual purpose, an alternative possibility could be raised, viz. purifying evacuation enemas. The concept of ritual purification falls well within the range of established Indian culture traits. The South American Jivaros, for instance, use a solution prepared from Ilex guayusa as a ceremonial mouth rinse, which is spat out instead of being swallowed (Karsten 1935). With respect to the rectal way of administration, ritual purification may be less well documented, but the Peruvian Incas seem to have employed their vilca clysters for cleansing (Poma de Ayala 1969).

Apart from this argument, the idea that the ancient Maya took enemas to reach or intensify a state of intoxication, is a plausible and attractive suggestion. When the Spaniards arrived in Middle America, they found that the Indians living there were familiar with numerous botanical intoxicants like alcoholic beverages (Gonçalvez de Lima 1956), tobacco (Robicsek 1978) and hallucinogens (Guerra 1967), and that the rectal route was sometimes used to administer an intoxicant (vide 1.1.1.1). It is also beyond question that intoxicating practices had already occurred in Middle America far before the coming of the white man. The recovery of pre-Hispanic smoking pipes (Porter 1948), snuffing equipment (Furst 1974a), peyote buttons (Bruhn et al. 1978), etc. from Mexican archaeological sites all point in this direction. It is therefore worthwhile to trace which ritual intoxicants were known to the Maya, and what evidence for their rectal use can be found in the enema vase paintings themselves. Taking this as a starting point, the following pages first review which enema paraphernalia are shown in Maya vase paintings, and then provide a multidisciplinary outlook on the ethnobotany, chemistry and psychopharmacology of Maya intoxicants. In my iconographical approach, I follow in the track of other researchers. Furst and Coe (1977) were already able to interpret previously baffling objects as enema syringes and to identify a specially shaped jug as a common object in the enema scenes. Coe (1978) subsequently proposed that a certain spiral glyph, number 627 in the Maya glyph catalogue of Thompson (1962), may be the sign for the enema ritual and he added the speculative notion that this glyph represents an anal sphincter muscle. Additional accessories in the enema vase paintings were listed by Nicholas

M. Hellmuth in an unpublished paper from 1978, which still is the only detailed iconographical survey on the subject. A recently revised version of this paper is included in this thesis (Appendix B), and much of the underlying photographical material is also presented here (Appendix C). In the next paragraphs, I refer to the photographs by giving their plate numbers between brackets.

1.4.2. Maya enema paraphernalia

1.4.2.1. Iconographical approach

A principal diagnostic trait of the enema scenes on classic Maya vessels is the presence of an enema syringe. Actual insertion of this apparatus into subjects bending forward is depicted on some early classic pottery (1, 2) and on the late classic vase (3), which led to the discovery of Maya enema scenes (vide 1.4.1). The syringe often has a clearly visible tube (e.g. 7, 10, 16) and an oval bulb with a semi-circle at the middle of the top (e.g. 7, 19, 42), and can thus be distinguished from a round rattle (18, 34). A striking feature of many syringes is their large size (e.g. 16, 19). In modern western practices, enemas larger than 0.2 l are only applied to evacuate the bowels (Fishburn 1965; Pernarowski 1975), so if the size of the syringe is realistic, it would seem to suggest a purifying evacuation enema rather than an intoxicating retention enema. In a recent self-experiment, however, I could easily retain an alcoholic enema with a total volume of 0.5 l by taking certain precautions (vide 1.2.2.5), which takes the edge off this pharmaceutical argument.

Many scenes portray the enema syringe on top of a specially shaped jug (e.g. 7, 10, 19). This type of jug is seen so often in the enema ritual that it is assumed to contain the enema liquid (Furst and Coe 1977; Coe 1978; Hellmuth 1978). This assertion about the function of the jug is probably correct, when it occurs in enema rituals, but its appearance is not limited to such scenes. The jug is also seen, for instance, in scenes of ceremonial self-sacrifice (Stuart 1975) or in simple palace scenes (Coe 1978). Occasionally, the jug is of a small, portable size (e.g. 39, 40), but most scenes display large jugs, standing in front of a participant or near a throne.

In many scenes, something is shown as coming out or sticking out of the jug: this may be scrolls (5, 13, 21), dots (3, 6, 12), rod- and plume-like forms (15, 29, 33, 37, 41), occasionally

arranged in bundles (17), small circular forms (12, 38), larger, often black-eyed circular and oval forms (4, 29, 34, 35, 38), or a large flower (fig.5 in Boglár and Kovács 1983). Even on one bowl, some kind of mammal is shown jumping out of the jug (43). Since the enema may be present in the jug, a closer look at current ideas on the protruding items is certainly warranted.

In an elaborate enema scene, syringes are emitting scrolls (18) similar to those coming out of jugs in other scenes (5, 21). This seems to reinforce the idea that the syringes and jugs in enema scenes have the same content. Coe (1978) identifies the scrolls as stylized smoke. This is an acceptable suggestion, since the classic Maya were undoubtedly a smoking people, and their vase painters often depicted smoke in this way (Robicsek 1978). In another enema scene, cigars and objects that might be small jugs are shown as emitting similar scrolls (13). The smoke symbol would be an appropriate sign, if the jug contained the same plant that was smoked. Alternatively, the scrolls might symbolize odour (Deletaille, pers. commun. 1984) or pungency (Hellmuth, pers. commun. 1980). A pungent clyster would, of course, be more suitable for cleansing than for intoxication.

The display of dots at the mouth of a jug (3, 6, 12) has its counterpart in pre-Hispanic Mexican codices. In Aztec codices, like the Codex Mendoza, such dots indicate the alcoholic drink octli, prepared from the maguey plant (Gonçalvez de Lima 1956; de Barrios 1971; Ross 1978). In the Maya Codex Dresdensis from the post-classic period, dots are depicted above a large jug, considered to contain fermented honey wine, because it bears the cib sign (Seler 1902; Gonçalves de Lima 1956; Thompson 1972). In view of such data, Furst and Coe (1977) and Robicsek (1978) may be right to postulate that the dots in Maya enema scenes signify the presence of some fermented liquid, such as the alcoholic honey mead balché. For Hellmuth (pers. commun. 1984), the dots do not have a specific meaning.

A definite interpretation of the rod- and plume-like forms in Maya jugs is not yet available. Even if they are prominent (15, 29), it is difficult to come up with a botanical suggestion (Schultes, pers. commun. 1984). The forms should be distinguished from scrolls, for there is a bowl painting where both are coming out of the same jug (fig.120 in Boglár and Kovács 1983). In one scene (37), they merely seem to indicate that fluid is spilling out of a tumbling jug (Robicsek and Hales 1981). Justeson (pers. commun. 1985) feels that the form of the rod-like objects (41) is roughly consistent with maguey leaves, but admits that the execution is not distinctive enough to make a specific botanical identification (vide 1.4.2.2). Hellmuth (1978, pers. commun.

1984) wonders about some forms; they may possibly be plant segments or actual bird plumes, and about others; they might represent cigars or pointed blood-letting perforators. If the correctness of the last suggestion could be proven, this would raise the possibility that the effect of the enema was enhanced by self-torture. The ancient Maya are known to have practised ritual self-mutilation, especially by scarifying the penis or the tongue (Joralemon 1974; Furst 1976b; Robicsek 1978).

The circular and oval forms on top of the jug (12, 29, 34, 35, 38) or coming out of it (4) are as enigmatic as the oblong forms. Robicsek (1978) suggests that the small variety (12, 38) indicates the presence of a fermented liquid, whereas Hellmuth (pers. commun. 1984) feels that the small circles are real objects. The larger variety may also be stacked up in a plate or bowl elsewhere in the scene (8, 17, 18). Coe (1978) remarks about such round objects in a throne scene; they might be the maize preparation tamales, but they look suspiciously like disembodied death-eyes. If food was ingested during the ritual it could have a pharmacological bearing, as the presence of food in the stomach often delays drug absorption after oral ingestion (Welling 1977; Toothaker and Welling 1980), but this cannot happen after rectal application. Hellmuth (pers. commun. 1984) wonders, if the round forms might be some kind of food such as cookie balls or fruits. According to Schultes (pers. commun. 1984), the large round items (4, 8, 38) might possibly represent some kind of fruit, such as that of Annona, which could be eaten or used to prepare a fermented beverage.

Fig.5 of Boglár and Kovács (1983) shows a Maya vase painting with a jaguar next to a large jug, from which a huge flower emerges. The jaguar is wearing a netted bib and a netted headdress, both of which are garments worn in the enema ritual (vide infra). There is also an enema scene, in which an indeterminate creature is holding an enormous flower (13). These scenes open up the possibility that such flowers served as an ingredient of ritual Maya enemas, which raises the issue of their botanical identity. Rands (1953) associates comparable floral forms in Maya art with the American water lily Nymphaea ampla. In accordance with this view, Hellmuth (pers.commun. 1984) considers the flower in plate 13 to represent the water lily. This flower is so stylized, however, that its identification as N.ampla should not be accepted without reserve, and this is also the case with the flower in fig.5 of Boglár and Kovács (1983).

The syringe on top of the enema jug is sometimes replaced by a cup (20, 27), so ritual drinking must have occurred as well. Hellmuth (pers. commun. 1984) rightly draws attention to the

similarity between these drinking scenes and the Mural de los Bebedores in the pyramid of Cholula at Puebla in Mexico, which is partly shown on the cover of de Barrios (1971) and on the wrapper of Guerrero Guerrero (1980). As some vases show the drinking cup and the enema syringe together (9, 19), both objects could obviously be used in the same ritual. Robicsek and Hales (1981) have elegantly demonstrated that different Maya vases may show successive scenes of one event (Robicsek and Hales 1981), so the enema scenes and drinking scenes may well represent different stages of the same intoxication ceremony.

Occasionally U-shaped objects are displayed on top of the jug (7) or in the hand of actors (3, 18). In one of the scenes, God N is holding such an object in his left hand, while painting his face with his right hand (18). Coe (1978) suggests that it is a paint-pot in this scene, which suggestion corresponds with the painted faces in other scenes showing U-shaped objects (3,7).

The participants in the ritual often wear a special garment around the neck as a bib, analogous to an oyster bib (3, 7, 13). In one scene, a bib-wearing male has his right hand in the jug, apparently to fill up a syringe or cup (26). Hellmuth (1978; pers. commun. 1980) has suggested that the bib is worn in the ritual because of vomiting, as some scenes portray a vomiting creature (24, 25, 27). This remains uncertain, for the bib may also be worn as a head-dress (3), and not every vomiting personage is wearing the bib (24). Robicsek (1978) thinks that the bib is in some way related to the iconography of God N, who regularly wears a netted element in his headdress (e.g. 19). Whatever the bib may mean, the display of vomiting actors does provide a plausible reason why the Maya opted for rectal application. If a subject is vomiting or is going to vomit, the rectal route of administration offers an obvious advantage over the oral one.

Other objects, which may appear together with enema paraphernalia, include vegetation decorating the head of a jaguar (e.g. 13, 28), cigars or cigarettes (12, 13, 14, 32), musical instruments like drums and rattles (18, 34), and bouquet-like objects (35, 36).

A jaguar with a leaf or flower sprouting from the head is often displayed besides a jug and/or with a bib around the neck (e.g. 25, 27, 32). Just like the flower in plate 13 (vide supra), these plant parts are commonly associated with the water lily Nymphaea ampla, even to the point that the jaguar in question is indicated as the Water Lily Jaguar (Coe 1978, 1982; Robicsek 1978; Hellmuth, pers. commun. 1984). Once more, however, a botanical reserve should be kept in mind, since it is difficult, if not

impossible, to exclude all other plants. In this connection, it should be emphasized that the leaf of the so-called Water Lily Jaguar may be much more acuminate (e.g. 28) than the leaf of N.ampla, as judged from photographs of a herbarium specimen (Emboden 1981a) and of the living plant (Torres 1984).

The presence of smokers opens up the possibility that the effect of the enema may have been enhanced by smoking, whereas the presence of musicians could possibly signify non-pharmacological potentiation. There is ample ethnographical evidence that the American Indian valued rythmical music as a means of intensifying drug-induced experiences (Wasson 1980; Dobkin de Rios 1984). The bouquet-like objects are so stylized that it is not possible to interpret them as any known psychoactive plant (Schultes, pers. commun. 1984).

1.4.2.2. Linguistic approach

Mostly, the special jug appearing in Maya enema rituals and related scenes has a plain surface or a simple painted design, but some jugs are provided with an obvious glyph, although not always the same glyph is shown (10, 14, 15, 30, 34, 35, 40, 41). Since the jug is thought to contain the enema, the interpretation of such glyphs is of paramount importance. Most of the jug glyphs cannot readily be found in the Maya glyph catalogue of Thompson (1962). This is not surprising, since Thompson focused on glyphs from monuments and manuscripts and not on glyphs from pottery. Some glyphs can be identified, however, and in one case it is even possible to give an interesting interpretation:

1) In his book on tobacco among the Maya, Robicsek (1978) describes a Multiple Resist vase painting with smoking and dancing skeletons (vase A-14). He interprets the infix on a small portable jug in this scene as akbal, the sign of darkness (number 504 in Thompson's catalogue).
2) Justeson (pers. commun. 1985) has found the manik glyph, which represents the name of a day (number 671 in Thompson's catalogue), on a large jug (41).

In an unpublished manuscript from 1982 on 'Hieroglyphic evidence for the languages of the classic Maya', Fox and his co-author Justeson (pers. commun. 1985) remark on the occurrence of the manik glyph on the jug in plate 41: 'Logographically, this sign represents the day Manik. The day name in Yucatec is clearly ancient, since the name is preserved from Chol and/or Tzeltal as <manich> in calendrical names in the Comitan Libro de Bautismos (see Baroco 1970: 138, 146) and the Yajalon Libro de Bautismos y Matrimonios (Campbell in press). This day name corresponds to the

day Deer of other Mesoamerican calendars, and the sign is used as a logogram DEER in the codices. The sign is never read phonetically as ke, which Yucatecan ké:h 'deer' terms would suggest as phonetic generalization; however, there is ample evidence for its value či, which presupposes the Cholan-Tzeltalan *čihx 'deer'. This sign origin supports Cholan-Tzeltalan development of either the sign's phonetic value či or semantic value DEER, but indicates nothing concerning a Cholan-Tzeltalan involvement in any spellings which make use of it in either value. Some such spellings, however, do implicate the Cholan-Tzeltalan group. (The figure) illustrates a vase depicting two seated figures, leaning toward a central vessel with cups in their outstrectched hands. Long leaves appear to be rising from the (enema?) vase, which is marked with the sign či. We suspect that the sign and the leaves are intended to indicate that the figures are drinking, or are preparing to drink, an alcoholic extract of the maguey. The same sign marks depicted vases in a scene on a polychrome vase which Kerr suggests represents a drunken display. In Cholan and Tzeltalan languages, čih means 'maguey'; či?, whose basic meaning is 'sweet; delicious', means by extension 'alcoholic beverage' or, as an adjective, 'inebriated', while *a:x-či is 'drunkard'. These terms are cognate with Yucatecan kih 'maguey' and ki? 'sweet, delicious; alcoholic beverage; inebriated' and x-ki? 'drunkard'.'

In this comment on the manik glyph, two separate steps are taken, viz. the reading of the glyph as 'či' and the connection of this phonetic value with terms like maguey (Agave plant) and alcoholic beverage. Yucatecan parallels of the latter step are easily found in the literature. According to Roys (1976), the Yucatecan Maya had at least nine names all ending in 'ci' for various species of Agave. Bolles (1981) indicates that 'ci' in Yucatecan texts may be translated as wine. With respect to the former step, Justeson sent me a second letter (1985) detailing the following: 'The evidence for the či value is varied. First the contrast between it and the sign T534 la in the words for 'west' and 'east' (čik'in and lak'in) are generally acknowledged, and this is the context that initially suggested the reading. Other good examples in the codices are the spelling k'u-č(i) for k'uč, which verifies the consonant at least; the spelling is in position to be the name of the bird depicted, which is the k'uč 'buzzard'. The sign is in alteration with T669, which has the two values k'a and ča, in spelling what should be the same word in different pages of the Madrid Codex, namely pa-č(a) and pa-č(i). At Chichen Itza, a preposition is spelled i-či-l(a) that must have the function of marking a day as falling within or in a

given tun in the long count; only the prepositions ti?, ič, and ič-il could serve that function, so the spelling i-T671-l(a) makes a prima facie case for both the consonant and vowel of the či value. The sign is used for the day Deer, and *čihx (or chihj in Spanish-based orthography; i.e., my x is the velar fricative, not the š or sh sound) is the word for 'deer' in proto-Tzeltalan, proto-Cholan-Tzeltalan, and perhaps proto-Cholan (I think proto-Cholan is actually *čih, but I'm not positive; the choice depends on data I don't have concerning accent in Chontal, an accented form pointing to *čihx and an unaccented for pointing to *čih). Also, the form of the sign is a pan-Mayan gesture for eating; *či? is proto-Yucatecan for 'to bite; to eat meat' from proto-Mayan *ti? A telling case that the sign T765, used as a verb for enter, represents Yucatecan *ok, Cholan *oč 'to enter', being also the sign for the day name Oc (i.e., *ok or perhaps *o:k); at Tortuguero, which is demonstrably a Cholan site and thus would have read this verb as *oč, there is an infixed or suffixed T671, presumably for či as a phonetic complement to indicate the final č of oč and perhaps the i as a grammatical suffix. The sign is also used in the Madrid in varying spellings of the word for 'bathing, baptism', in texts accompanying baptism scenes; the spellings are somewhat defective, but can be interpreted as i-č(i)-ki or as i-či-VL for ič-k-il 'baptism'; the variation is in order of signs, the first i sometimes being last, but the words are clearly the same so reordering must be assumed.

I think all of this evidence is reasonably solid, with the possible exception of the gestural origin for the či value in pYu *či?. Other contexts that may be interpretable in terms of the či value do not have as much solid semantic control or linguistic control over the terms that are being represented. In all the above examples, it would take special pleading to see other terms or values being involved.

References: k'uč and čik'in contexts: generally known, first argued in 19th century.

'deer' = čihx: first argued, although I'm not sure in quite this form, by Kelley in his phoneticism paper (Fonetismo en la escritura maya, Estudios de Cultura Maya, 1962).

či/ča alternations: James A. Fox and John S. Justeson, "Polyvalence in Mayan hieroglyphic writing", in John S. Justeson and Lyle Campbell, eds., Phoneticism in Mayan Hieroglyphic Writing, pp. 17-76. Institute for Mesoamerican Studies: Albany ,1984

i-č(i)-ki or i-či-VL for ič-k-il 'baptism': also in the above, although the basic baptism reading and the recognition of the i-či elements goes back again to the 19th century.

i-či-l(a) for iČ-il and T765-či for oČ or oČ-i 'enter(ed)' in Fox and Justeson (1982), "Hieroglyphic evidence for the languages of the Classic Maya", unpublished manuscript (the same one from which you have the discussion of the maguey).

The i-či-l(a) case is also discussed in Peter Mathews and John S. Justeson, "Patterns of sign substitution in Mayan hieroglyphic writing: the Affix Cluster", pp. 185ff of Justeson and Campbell, cited above, but this discussion relies on Fox and Justeson (1982).

pYu *Či? 'bite, eat meat' as the basis for the form of the či sign is discussed in Fox and Justeson (1982) and equivalently in a forthcoming source The Foreign Impact on Lowland Mayan Language and Script, Middle American Research Institute Publication 53, Tulane University: New Orleans, by John S. Justeson, William M. Norman, Lyle Campbell, and Terrence Kaufman.'

Since the scene in plate 41 fails to show any specific enema related object, it could be argued that the jug with the manik glyph in this scene contains an oral drink rather than an enema liquid (vide 1.4.2.1). There is another scene, however, where a probable enema syringe is lying on top of a similar jug which is unquestionably ornamented with the same manik sign (14). There is a prefix on the left of this glyph, but it is rather problematic to identify this side-sign (Justeson, pers. commun. 1985): 'The best match in form I think is with T238, AH5, and this would make sense as Ah Chih, 'Maguey' or 'He of Maguey' (or 'Liquor' or 'He of Liquor'). ' According to Bolles (1981), the phrase 'ah ci' occurs in colonial Yucatecan Mayan texts and may be translated as drunk or drunkard.

As Justeson's linguistic interpretations have great ethnobotanical implications, it appeared essential to obtain an independent expert's comment on the manik glyph. When asked for this second opinion, Schele (pers. commun. 1985) first expressed some reservations:

'Justeson's suggestions seem very plausible to me. He reads the 'manik' hand as chi (he uses linguistic orthography so the diacritic in his comments indicates a phoneme we would record in our alphabetic system as chi). He apparently assumes the pot read in Cholan-Tzeltalan and comments that there is no substantiation for a ki value for the 'manik' hand, which I agree with. The 'deer' term is part of the k/ch correspondence set in Yucatec (keh 'deer')/ Cholan (chih 'deer'). Therefore, his suggested reading does not require a Yucatec chi value for the 'drunken' term is in the same correspondence set. His proposal is possible,

even probable. My only reservation is that there is evidence from the west glyph (Yucatec chik'in/ Cholan ti-k'in) and from other substitutions that the 'manik' hand participated in the correspondence set that requires ch in Yucatec and t in Cholan. The latter glyphs in which the 'manik' hand replaces signs with the value of ti do not have accepted readings as words, so they can only be taken as supporting evidence for the ch/t correspondence set. The 'deer' set is equally strong evidence for the other side. However, the chi reading for the pottery glyph does not have an equivalent in the codices and, therefore, does not require a ki reading in Yucatec. In other words, the 'manik' hand may be used on the pot solely as a phonetic glyph without a meaning assigned to it. I would rate Justeson's reading as a good possibility to be further tested by watching for new examples, but I would not consider it secure enough to be used to prove the 'manik' hand was used for the k/ch correspondence set in the inscriptions, as he seems to be doing. I think the question is still open.'

Just before this thesis went to press, however, Schele (pers. commun. 1985) informed me in a second letter that her former doubts have waned substantially:

'In the process of pursuing other research in the last months, I have found evidence sufficient to convince me that the manik hand T671 was indeed phonetic chi in the Classic period and not ti. I have also been able to see a great many photographs of pottery scenes that include pots, especially the round bodied ones, that have the manik hand on them. The weight of this evidence now makes me about 90% certain that John is correct in his reading of the chi glyphs as "sweet" and "intoxicating".'

1.4.3. Ritual Maya intoxicants

1.4.3.1. Ethnobotany

The principal ethnobotanical question is, of course, which intoxicating enemas the Maya may have taken. An alcoholic liquid, tobacco and hallucinogens have all been proposed as possible ingredients (Furst 1976a; Furst and Coe 1977; Hellmuth 1978; Robicsek 1978; Torres 1984).

As outlined above, the enema scenes themselves present a fair amount of evidence to support the first suggestion. It is well established that alcoholic beverages were known to the Maya in early-contact times (Tozzer 1913; Landa 1978). Rectal use of such preparations has not been recorded for the Maya, but it is

reported for other early native inhabitants of Middle America (vide 1.1.1.1). The balché drink of the Maya has been described as a mild intoxicant, concocted of fermented honey and water, to which was added the bark or root of the balché tree Lonchocarpus violaceus (= L.longistylus) (Roys 1943, 1976; Gonçalves de Lima 1956; Gonçalves de Lima et al. 1977; Landa 1978). This admixture has been reported to contain antibacterial longistylines (Delle Monache et al. 1977), but it is not known to contain any hallucinogenic principle. According to early sources, there were other alcoholic beverages as well: their base is said to have been pineapples and sugar-cane (Tozzer 1913), or honey, together with maize or the root of an Agave, and roots of unidentified plants (Roys 1943). It should be added, however, that sugar-cane cannot have entered into the composition of pre-Hispanic Maya drinks, as this plant was introduced by the Europeans (Schultes, pers. commun. 1984; Coe, pers. commun. 1985).

The use of tobacco among the Maya has been reviewed extensively by Robicsek (1978). In contrast with the sources on alcohol, early historical records on the Maya relating to tobacco appear to be questionable and confusing. There can be no doubt, however, that numerous Maya vase paintings from the classic period portray fumigatories, which are often provided with smoke scrolls (e.g. 13). As pointed out in section 1.4.2, enema paraphernalia are occasionally shown to emit similar scrolls. With respect to the botanical identity of the fumigatories on Maya pottery, Robicsek (1978) rightly remarks: 'Of course, the only way to state with absolute certainty that the ancient Maya indulged in tobacco smoking would be to discover tobacco cigars or cigarettes or pipes stuffed with tobacco (preferably still smoking) in Classic graves. Unfortunately, the only bona fide discovery of tobacco at a Maya site was the cache of cigars discovered by C. Rudy Larios in Group H at Tikal. This (review), however well supported, is, therefore, speculative. The only thing we know for certain is that the Mayas smoked something. This something was most likely tobacco, a conclusion based on archaeological material found at Classic and post-Classic sites, stone monuments, ceramic artifacts, and codices.'

The conjecture that the Maya employed hallucinogenic clysters necessitates a glance at the current ideas about Maya hallucinogens. The only hallucinogen which is suggested again and again as a possible ritual Maya intoxicant, is the psilocybian mushroom (Dobkin de Rios 1974; Robicsek 1978; Torres 1984). Apart from the chemical and pharmacological data (vide 1.4.3.2), the evidence includes linguistic findings (entries found in early Maya vocabularies relating to inebriating

mushrooms), botanical findings (psilocybian mushrooms found in the Maya region), and archaeological findings (mushroom-shaped stone objects found at pre-Hispanic Maya sites) (Greene Robertson 1972; Lowy 1977; Mayer 1977; Wasson 1980; Torres 1984). Not every scholar, however, considers the mushroom-shaped stone objects as substantial evidence of the Maya mushroom use in early times (Brown 1984). It should also be noted that the evidence of such use is not associated with the central Maya area, from which most enema vase paintings originate, but with other Maya regions, especially with the Highlands. Even though it cannot be excluded that mushrooms could have been brought into the central region by trade (Brown 1984; Mayer, pers. commun. 1984), it is certainly not safe to claim that the Maya prepared ritual enemas from mushrooms. The vase paintings fail to provide any evidence for this conjecture. The mushroom-shaped objects, which sometimes appear in front of a face on classic Maya pottery, unquestionably represent nose-beads.

The fly agaric Amanita muscaria also occurs in the Maya highlands and it has sometimes been suggested that it is represented in post-classic Maya codices (Lowy 1972; Torres 1984), but the objects interpreted as mushrooms might also be rattles, maces or fans (Thompson 1972; Robicsek 1978). At present, there would not seem to be paramount evidence that the ancient Maya may have preferred the fly agaric to psilocybian mushrooms (Mayer, pers. commun. 1984).

The literature on ritual plants mentions various other potential Maya intoxicants besides mushrooms, but all of these possibilities still require more evidence from chemical and pharmacological studies (vide 1.4.3.2) and/or from the ethnobotanical field, before they can be accepted without hesitation.

The divinatory tsité tree of the Popol Vuh, a famous epic of the Quiché Maya, is said to have been an Erythrina species (Girard 1960; Schultes 1972b). In 1970, Furst (1974b) presented a paper about this subject at the Annual Meeting of the Society for American Archaeology in Mexico. This paper is no longer available (Furst, pers. commun. 1985). Rumours that Guatemalan shamans ingest Erythrina beans for ritual purposes are still extremely tenuous and open to doubt (Schultes and Hofmann 1980b).

Dobkin de Rios (1974) has put forward that the Maya may have taken the water lily Nymphaea ampla in a ritual context, but other scholars did not generally approve of this idea. More recently, the available evidence for the suggestion that the water lily was a ritual Maya plant has been surveyed by Emboden (1981a, 1981b) and by Torres (1984). Enema paraphernalia and

plant parts associated with the water lily are known to occur together in Maya vase paintings. In one case, a possible water lily flower is even shown to emerge from the specially shaped jug, which features in enema scenes on other vases (vide 1.4.2). This raises the possibility that the flower could have entered into the composition of ritual Maya enemas. It is still insufficiently clear, however, whether or not Nympaea ampla can serve to induce a central intoxication (vide 1.4.3.2). Consequently, it would be unwise at this stage to discard alternative explanations, such as nutritional, sexual, or symbolic purposes, as being impossible. There is a vague claim, for instance, that the farinaceous rootstocks of N.ampla are edible (Sturtevant 1972). This corresponds with a herbarium annotation that the bulbs of an indeterminate Nymphaea species from Mexico are dug and eaten during the dry season (von Reis Altschul 1973). Furthermore, the rootstock of N.ampla is said to be considered an aphrodisiac in Yucatan (Morton 1981). It should be noted that these ethnobotanical data refer to the submerged parts and not to the flowers. A non-materialistic suggestion is offered by Furst (pers. commun. 1982) who feels that the Maya water lily 'is a perfect visual metaphor for the connection between the surface of the water, or the earth, and the watery lower regions.'

Dobkin de Rios (1974) has also suggested toad poison as a ritual Maya intoxicant, but this conjecture was not generally approved of either. There is a classic Maya vase which displays one or more jugs together with a toad-like creature, characterized by its 'ear' with three dots (30), but it is unclear whether it is a toad or a frog.

The Maya flora is known to include Datura candida (Hopkins 1974), but Schultes (pers. commun. 1982) doubts very much that this tree occurred in Central America in ancient times, as all the Brugmansia species are South American. Toh-ku, of which the Maya made many medicines for hemorrhoids, has been identified as Datura innoxia (Roys 1976), but there is no ethnobotanical record that the Maya intoxicated themselves with this plant. And, its characteristic spiny fruit does not occur in classic enema scenes. Litzinger (1981) has reported that ceramics resembling the spiny fruit of Datura have been found in the Maya area, but Hellmuth (pers. commun. 1981) feels that these may represent the stem of the Ceiba tree rather than the fruit of Datura. The latter view is supported by the cylindrical form of spiny ceramics from the Amátitlan Lake in southern Guatemala, which I have seen in the Museum for Ethnology in Vienna. What is more, Litzinger (pers. commun. 1982) himself informed me that the

present–day Lacandon Maya still make spiked ceramic vessels, and refer to the spikes as to those of the Ceiba tree, which is an important symbolic plant for them.

1.4.3.2. Chemistry and psychopharmacology

Data on alcohol, tobacco and Daturas can be found in sections 1.1 and 1.2.

The truly hallucinogenic nature of Psilocybe mexicana and related mushrooms is well documented; both psilocybin, which is usually the main active principle, and psilocin, which may be present as well, are LSD–like hallucinogens (Schultes and Hofmann 1980a,b; Beug and Bigwood 1982; Young et al. 1982). The medium oral dose of psilocybin, which elicits symptoms similar to those induced by about 2 g of dried Psilocybe mexicana, is said to be 4–8 mg; doses of 6–20 mg evoke more profound psychic changes than doses of up to 4 mg (Delay et al. 1958; Heim et al. 1958; Hofmann 1963; Berkenbaum 1969; Schultes and Hofmann 1980b). Experimental data on the rectal application of Psilocybe alkaloids do not seem to be available. The physicochemical properties of psilocybin (Windholz 1983) are not suggestive of a good and rapid absorption from rectal dosage forms.

The fly agaric Amanita muscaria is also frequently classified as an hallucinogen. Its major active principles are stated as being ibotenic acid and muscimol, which is probably not a genuine constituent but an artifact formed during drying or extraction (Eugster 1967; Wasson 1967; Gray 1978; Schultes and Hofmann 1980a,b). Recent analytical work suggests that the muscimol content may decrease with time: fresh material was found to contain 0.15–0.22%, calculated on dry matter, whereas a maximum of 0.02% could be detected in 3–5 year old samples (Stijve 1982). Clinical evidence for hallucinogenic activity is not so impressive as it is in the case of psilocybian mushrooms. Ott (1976) ingested about 30 g of dried caps, and this resulted in sedation and slight visual phenomena. McDonald (1978) drank an aqueous extract from 30 g of the dried mushroom, and did not experience hallucinations or obvious visual distortions. He also gave an oral dose of 12 g/72 kg body wt to healthy volunteers, who partly reported visual and auditory distortions, but not overt hallucinations. Plomp (1982) felt some heightened perception of colours and deeper awareness, but 'no sensational action' from oral doses up to five fresh caps. A truly visionary experience has no more been found in clinical experiments with isolated constituents. In healthy subjects, ingestion of 7.5–10 mg of muscimol elicited changes in mood, affective detachment and

loss of concentration, but hallucinations did not occur. In the same study, ibotenic acid in a dose of 75 mg produced a weaker and less characteristic effect (Theobald et al. 1968). In schizophrenics, oral administration of 7–10 mg of muscimol caused exacerbations of certain psychotic manifestations, but deterioration of hallucinations was not observed (Tamminga et al. 1978). Studies on the fate of tritiated muscimol in the mouse indicate substantial metabolism and poor penetration of the intact substance into the brain (Ott et al. 1975; Maggi and Enna 1979), so it is open to question that the behavioural effects of muscimol are due to the compound itself. Muscimol has extreme water-solubility, but also a low molecular weight (Eugster 1967). It is rather difficult to predict from these properties, whether or not muscimol will be absorbed well after rectal application.

The genus Erythrina appears to be rich in alkaloids, many of which have a peripheral curare-like action (Deulofeu 1959; Boekelheide 1960; Hill 1967; Dyke and Quessy 1981). Central depressant and convulsant activity has also been reported for some Erythrina alkaloids, but the intensity of action was considerably lower than that observed in the case of peripheral activity (Boekelheide 1960). Pharmacological evidence for hallucinogenic properties appears to be lacking (Schultes and Hofmann 1980b; Dyke and Quessy 1981).

Early phytochemical data on the genus Nymphaea have been reviewed by Hegnauer (1956). According to this survey, Nymphaea alba contains the non-alkaloidal compound nymphaline with digitalis-like activity, and a mixture of unstable alkaloids with hypno-sedative effects. The Old World species Nymphaea caerulea has been tested by Emboden (1979b; pers. commun. 1984) who twice drank a decoction of its flower buds. The effect of the decoction was very mild and more akin to a hypnotic, but there were alterations in visual and auditory perception. With respect to Nymphaea ampla, the water lily of the New World, Torres (pers. commun. 1985) has recently informed me of an experiment with negative results: 'About 2 months ago, a psychiatrist friend, tried to experience the hallucinogenic effect of Nymphaea ampla collected in Lake Petén Itzá (in the center of the Maya Classic area), in Petén, northern Guatemala, with absolutely no effects. The experiment was done according to instructions given me by Emboden'. Various sources indicate that N.ampla contains apomorphine-like alkaloids (Emboden 1979a, 1981a; Schultes and Hofmann 1980a; Dobkin de Rios 1984; Torres 1984). For instance, Emboden (1979a, 1981a) claims that apomorphine-like compounds as well as nupharine and nupharidine were found in the flowers of N.ampla and that aporphine could be extracted from its bulbs and

roots. All such statements are said to be based on the analytical work of Díaz on N.ampla (Emboden, pers. commun. 1984; Dobkin de Rios, pers. commun. 1985; Torres, pers. commun. 1985). So far as I have been able to ascertain, however, this investigator has merely reported the isolation of an unidentified alkaloid from the leaves (Díaz 1976, 1977) and several unspecified alkaloids from the submerged parts (Díaz 1979). As to the possible psychopharmacology of N.ampla, Díaz (1976) points at the presence of tetraisoquinoline, benzylisoquinoline and aporphine alkaloids in other Nymphaeaceae, and subsequently at the central dopaminergic activity of apomorphine, which has an aporphine structure. It should not be overlooked, however, that only aporphines like apomorphine and N-propylaporphine, which have (or obtain in vivo) an intact dopaminergic moiety in their structure, may be expected to have substantial dopaminergic activity (Pinder et al. 1971; Cotzias et al. 1976). In a later publication, Díaz (1979) reports on auto-experiences with the intact bulb and extracts. On one occasion, 7 g of the pulverized dried bulb were ingested and on another, an aqueous extract equivalent to 35 g of the bulb was taken. There were no detectable psychological modifications. It should be noted that Díaz (1976, 1977, 1979) does not provide experimental data on the flowers of N.ampla. This is rather unfortunate, for if the Maya used the water lily as a ritual intoxicant, this anatomical section is the most likely plant part to have served this purpose (vide 1.4.2).

It has been demonstrated that poison from the skin glands of various Bufo species contains bufotenin (Bonhour et al. 1967; Schultes and Hofmann 1980b). This tryptamine alkaloid is extensively discussed in section 1.1.2.2. Besides bufotenin, steroidal bufogenins and bufotoxins, with a similar chemical structure and cardiotoxic action as scilla glycosides, may be present (Stoll 1937; List and Hörhammer 1972; Flier et al. 1980). The cardiotoxicity of these compounds would obviously place severe restrictions on the use of toad poison in ritual practices (Alger 1974).

1.4.4. Conclusion

The enema scenes on classic Maya pottery undoubtedly represent rituals and may very well indicate that the ancient Maya took intoxicating enemas in a ritual context. This idea is quite contrary to the traditional view that the ancient Maya were a contemplative people, who did not indulge in ritual ecstasy. The occasional display of vomiting actors would seem to provide a

plausible reason why the Maya opted for rectal application. Some scenes present a fair amount of evidence that an alcoholic beverage may have been taking rectally. Other scenes open up the possibility that tobacco and the water lily may have served as an enema ingredient. It is sometimes speculated that the latter plant is hallucinogenic, but pharmacological confirmation of this view is still awaited.

CHAPTER TWO

A MULTIDISCIPLINARY OVERVIEW OF INTOXICATING SNUFF RITUALS IN THE WESTERN HEMISPHERE

CHAPTER TWO PART ONE

THE ETHNOBOTANY, CHEMISTRY AND PSYCHOPHARMACOLOGY OF RITUAL SNUFFS IN THE WESTERN HEMISPHERE

2.1.1. Acorus calamus

Araceae

Acorus calamus L.

2.1.1.1. Ethnobotany

Acorus calamus, commonly known as rat root or sweet flag, is often included in reviews on ritual botanical intoxicants (Farnsworth 1972; Emboden 1979a; Schultes and Hofmann 1980a,b). Therefore its nasal use by North American tribes should not go unrecorded here. The Chippewa Indians snuffed pulverized rat root to treat colds (Densmore 1928), and the Omaha gave the plant as a snuff to horses to make them spirited and run faster (Morgan 1980). These data confirm the general impression that North American Indians valued the rhizomes of sweet flag as a medicine and stimulant rather than as a true ceremonial intoxicant (Morgan 1980).

2.1.1.2. Chemistry and psychopharmacology

Most publications on the phytochemistry of Acorus calamus concern the rhizomes, which may contain 0.4 to 10.8 % of essential oil (Hegnauer 1963; Röst 1979; Stahl and Keller 1981). It is often stated that this oil has sedative effects, which are thought to be due to its constituents alpha-asarone and beta-asarone (Hoffer and Osmond 1967; Brown and Malone 1978; Schultes and Hofmann 1980a,b). Such statements are based on phytochemical and pharmacological studies with Old World samples, in particular with samples from India (Baxter et al. 1960; Dandiya and Menon 1965; Dhalla and Bhattacharya 1968). There is now considerable evidence, however, that a substantial asarone fraction can only be expected in triploid and tetraploid plants from the Old World, and not in diploid plants from the New World (Hegnauer 1963; Röst and Bos 1979; Stahl and Keller 1981, 1983).

Calamus oil from rhizomes of the North American diploid variety americanus contains acoragermacron, acorone, acorenone, preisocalamendiol, and hydrocarbons as its main constituents, when the oil is extracted with supercritical carbon dioxide

(Stahl and Keller 1983). When it is obtained by water destillation, the thermolabile compound acoragermacron is no longer present, and the major principles are shyobunone derivatives, acorone, acorenone, preisocalamendiol, and hydrocarbons (Röst and Bos 1979; Keller and Stahl 1983).

An unspecified type of Acorus calamus is said to have produced an LSD-like response in two sophisticated subjects who had both taken 10 inches of rat root 5 times (Hoffer and Osmond 1967). This report should not be viewed without caution, for the subjects had taken LSD several times under controlled conditions, so perhaps they were preconditioned to have a similar experience (Morgan 1980).

2.1.2. Anadenanthera species

Leguminosae
Anadenanthera colubrina (Vell.) Brenan
var. cebil (Griseb.) Altschul
Anadenanthera peregrina (L.) Speg.
var. falcata (Benth.) Altschul

2.1.2.1. Ethnobotany

The ethnological literature on South America includes numerous references on a most interesting, but somewhat enigmatic group of intoxicating snuffs, denoted as paricá, yopo, yupa, niopo, hisioma, and angico (Wassén and Holmstedt 1963; Wassén 1965, 1967, 1972a; von Reis Altschul 1972). At one time, such snuffs were generally attributed to the seeds of Piptadenia species, in particular Piptadenia peregrina (Roth 1924; Lowie 1948; Cooper 1949; Wassén and Holmstedt 1963; Schultes 1967b). This leguminous tree has a rather complex nomenclatural history, for it has also been known under the binomials Acacia niopo and Mimosa acacioides. It is now considered to be Anadenanthera peregrina, which occurs in northern parts of South America and in the West Indies. From southern Brazil and Paraguay the variety A.peregrina var. falcata is known (von Reis Altschul 1964). The once common attribution of all paricá snuffs and the like to the seeds of Anadenanthera species like A.peregrina reflects the general belief in those days that South American snuffs had either Nicotiana or Anadenanthera as their botanical origin. Since the fifties, however, it has become increasingly clear that this generalization is a misconception, kept alive by the uncritical acceptance of infirm or invalid botanical data. Schultes and co-workers have rightly emphasized this fact again and again,

thereby pointing at the abundance of Virola snuffs in the Amazon basin, and at the relatively restricted geographical range of A.peregrina. This tree can be expected to occur in open savannah country, but it is not likely to grow spontaneously in the deep forest areas of Amazonian Brazil (Schultes 1954, 1967b, 1984; Schultes and Holmstedt 1968; Schultes and Hofmann 1980b). However, the actual use of A.peregrina is not necessarily confined to its natural distribution range. A Waiká group of the Brazilian Marauiá river yearly undertakes a long canoe journey to open pastures, where they collect the seeds of A.peregrina with the purpose of preparing a snuff (Prance 1972). Interestingly, the tree has been observed in the Marauiá area itself, where it is probably cultivated from imported seeds (Wassén 1965; Schultes and Holmstedt 1968).

The domestication of A.peregrina and the trade in its seeds have also been reported in the Orinoco basin (Granier–Doyeux 1965; Chagnon et al. 1971). From the available botanical evidence it would appear that this territory is the major South American area of A.peregrina snuffs, principally known there as yopo, yupa, niopo, and hisioma (Wurdack 1958; Granier–Doyeux 1965; Wassén 1965, 1967; Chagnon et al. 1971; Coppens and Cato–David 1971; von Reis Altschul 1972; Reichel–Dolmatoff 1975; Schultes et al. 1977; Schultes and Hofmann 1980a,b). Detailed accounts by early travellers like von Humboldt (1958) and Spruce (1908) indicate that the use of such snuffs is not a recent culture trait of the Orinoco region. Most snuffs are prepared from the roasted and powdered seeds, and in many cases vegetable ash or lime obtained from shells is added (Granier–Doyeux 1965; Wassén 1965, 1967; Coppens and Cato–David 1971; von Reis Altschul 1972). There is some evidence to suggest that the Yecuaná–Makiritare Indians of southern Venezuela may employ the bark (Fuchs, quoted by Wassén and Holmstedt 1963).

According to the classical descriptions, the snuffs have a stimulating effect, producing great excitement and the onset of hallucinations. This is followed by sleepiness, which often passes to a hypnotic or unconscious state (Granier–Doyeux 1965). Among the Venezuelan Cuiva Indians, who prepare a yopo snuff from A.peregrina seeds and shell lime, a single dose does usually not exceed 5 grams, and this amount may be taken one to three times a day. One dose is said to cause an intoxication of 1/4 to 2 hours (Coppens and Cato–David 1971).

A detailed discussion of all the snuffs, which rightly or wrongly have been associated with A.peregrina is beyond the scope of this section. For good overviews of this subject, the reader is referred to the meticulous publications of Wassén (1965, 1967,

1972a) and von Reis Altschul (1972). Examples of snuffs, which have probably correctly been attributed to the seeds of A.peregrina, are the paricá snuffs of the Mura Indians and other tribes of the Brazilian Madeira region (Martius 1867; Barbosa Rodrigues 1875; Schultes 1967b; von Reis Altschul 1972). The recent isolation of 1.5% of the Anadenanthera alkaloid bufotenin from 19th century paricá seeds of the Maué Indians supports this botanical assertion (vide 1.3). The famous cohoba snuff of the early colonial natives of the West Indies is also said to have had A.peregrina as its probable source (Safford 1916; Schultes 1967b; von Reis Altschul 1972).

There is evidence to suggest that snuffing was not the only method of using A.peregrina. Various South American tribes have been reported as having taken paricá as an enema (vide 1.1.2.1). Schomburgk (1848) describes the occurrence of A.peregrina in British Guiana and gives paricá and paricarama as vernacular names. According to this 19th century traveller, the natives of this region burnt the pulverized beans and inhaled the smoke.

The genus Anadenanthera comprises a second species, A.colubrina. It occurs in eastern Brazil, and its variety cebil is known in Argentina, Bolivia, Paraguay, Peru, and several localities in southeastern Brazil (von Reis Altschul 1964). The variety cebil has been frequently associated with certain early snuffs called vilca or huilca in southern Peru and Bolivia, and cébil or sébil in northern Argentina. Although the evidence is circumstantial and sometimes weak, it is quite possible that the association is correct, not in the least because phytochemical studies have revealed the presence of tryptamine alkaloids in the seed of A.colubrina var. cebil (Safford 1916; Cooper 1949; Wassén 1965, 1967; Schultes 1967b; von Reis Altschul 1967, 1972; Schultes and Hofmann 1980b). There is a recent report that a mixture of tobacco and cebil (or jatáj) is smoked by Argentinian aboriginals (Califano 1975). According to the 18th century missionary Dobrizhoffer (1822), Indians of the Paraguay region inhaled the smoke of burnt cevil pods.

2.1.2.2. Chemistry and psychopharmacology

Chemical data on the seeds of Anadenanthera species and the psychopharmacology of Anadenanthera tryptamines with a dimethylated aminogroup are summarized in section 1.1.2.2.

The occurrence of the Anadenanthera alkaloids DMT, 5-MeO-DMT and/or 5-OH-DMT (=bufotenin) in Venezuelan and Colombian snuffing material has been repeatedly demonstrated (Fish and Horning 1956; Holmstedt and Lindgren 1967; De Budowski et al. 1974; Schultes et

al. 1977; vide also section 2.3).

The bark of A.peregrina has been shown to contain N-monomethyltryptamine (=MMT), 5-methoxy-N-monomethyltryptamine (=5-MeO-MMT), N,N-dimethyltryptamine (=DMT), and 5-methoxy-N,N-dimethyltryptamine (=5-MeO-DMT) (Legler and Tschesche 1963; Holmstedt and Lindgren 1967; Schultes et al. 1977). Besides these tryptamine alkaloids, small amounts of 6-methoxy-2-methyl-1,2,3,4-tetrahydro-beta-carboline (=6-MeO-MTHC) and 6-methoxy-1,2-dimethyl-1,2,3,4-tetrahydro-beta-carboline (=6-MeO-DMTHC) are occasionally found in the bark (Schultes et al. 1977). Such compounds might be expected from the point of view of biosynthesis and workup procedure (Holmstedt et al. 1980).

The pharmacological effects of the beta-carbolines and the monomethylated tryptamines found in the bark of A.peregrina are discussed in section 2.1.15.2.

2.1.3. Banisteriopsis species
Malpighiaceae

2.1.3.1. Ethnobotany

Banisteriopsis preparations are widely employed by the indigenous inhabitants of the South American continent (Cooper 1949; Friedberg 1965; Schultes 1982). Most reports concern the use of Banisteriopsis as an ingredient of intoxicating drinks, but it has also been reported that Indians of the upper Orinoco area chew the dried stem (Spruce 1908; Roth 1924). There does not appear to be any ethnobotanical evidence for the preparation of snuffs from Banisteriopsis (Friedberg 1965; Schultes 1982, 1984). In chemical studies, however, harmine was found in snuffs from the Venezuelan Piaroa Indians, while harmine, harmaline, and tetrahydroharmine could be isolated from a snuff of the Surára Indians, a Waiká group of northwestern Brazil (vide 2.1.3.2). Unfortunately, no botanical material was collected together with the snuffs, so their botanical origin remains uncertain. In South American ethnobotany, the beta-carbolines harmine, harmaline, and tetrahydroharmine are commonly associated with Banisteriopsis, so these chemical findings certainly open up the possibility that Banisteriopsis may have been used as a source of snuff (Holmstedt and Lindgren 1967; Schultes 1982). However, the most comprehensive review on the use of Banisteriopsis by South American Indians (Friedberg 1965) includes neither the Piaroa nor the Surára as tribes familiar with Banisteriopsis drinks.

2.1.3.2. Chemistry and psychopharmacology

The chemistry and psychopharmacology of Banisteriopsis and its native beverage ayahuasca are discussed in section 1.1.3.2.

The presence of Banisteriopsis constituents in South American snuffs has been reviewed by Holmstedt and Lindgren (1967). According to table I of their review, the presence of one or more Banisteriopsis alkaloids has been demonstrated on four different occasions, once by Biocca et al. (1964), once by Bernauer (1964), and twice by the authors themselves. On closer examination, only two actual snuffs seem to be involved.

Biocca et al. (1964) did not study a snuff, but the fragment of the stem of a liane, from which they isolated harmine, harmaline and tetrahydroharmine. The material was said to serve as a source of paricá snuff among the Tukano and Tariana Indians of the Upper Rio Negro area. Biocca (1983) has recently provided a photograph of such a liane. Unfortunately, the collectors have not been able to witness the preparation of the snuff, so it remains uncertain whether the liane actually served as a snuff source and not as an oral ingredient.

Bernauer (1964) has analyzed an epéna snuff of the Surára Indians of northwestern Brazil. He isolated harmine (H), (+)-1,2,3,4-tetrahydroharmine (THH) and an unidentified amorphe compound (X) with yields of 1.3 % H, 0.22 % THH and 0.36 % X before purification, and 0.38 % H and 0.08 % THH after purification.

Holmstedt and Lindgren (1967) have also demonstrated the presence of harmine and tetrahydroharmine in an epéna snuff of the Surára Indians, thus duplicating the findings of Bernauer (1964). The gaschromatogram pertinent to the second snuff shows a third unidentified peak (fig. 9 of the original publication), and the snuff was collected by Dr. H. Becher, who also supplied the epéna sample studied by Bernauer (1964). It seems likely that the same snuff was studied twice, and Holmstedt (pers. commun. 1983) is inclined to agree with this view. In addition, Holmstedt and Lindgren (1967) have found harmine together with DMT, 5-OH-DMT and 5-MeO-DMT in a paricá snuff of the Venezuelan Piaroa Indians.

Other original publications on Banisteriopsis alkaloids in South American snuffs do not seem to be available. Section 2.3 of this thesis, however, reports on the isolation of harmine and bufotenin from a yopo snuff of the Piaroa Indians, which result corroborates the unusual findings in the sixties.

2.1.4. Cannabis species
Cannabaceae

2.1.4.1. Ethnobotany

Although Cannabis is smoked among the Brazilian Tenetehara Indians (Wagley and Galvão 1949), and eaten among Mexican aboriginals like the Tepehua Indians (Heffern 1974; Williams-Garcia 1975), it is not a major intoxicant in native rituals of the western hemisphere. Plausible explanations might perhaps be that Cannabis was introduced after the conquest and had to compete with the numerous psychoactive plants already available (Partridge 1975), and that nowadays it is an illegal intoxicant in many countries.

Substantial data on the snuffing of Cannabis by American aboriginals appear to be lacking. A 19th century Portuguese catalogue of objects from Amazonian tribes states that 'parica tobacco' was much used as a snuff and that 'pango, an African tobacco', served as a substitute for parica (Teixeira de Aragão 1892). Since the word pango is a vernacular name for Cannabis, the question arises as to whether the catalogue may possibly indicate the snuffing of hashish (Wassén 1972a). However, there are no additional data whatsoever to support this suggestion.

2.1.4.2. Chemistry and psychopharmacology

Since hemp has become a major recreational drug in western society, more chemical and pharmacological research has been directed to this plant than to any other natural hallucinogen (van Praag 1972; Miller 1974; Braude and Szára 1976; Schultes and Hofmann 1980b; Turner et al. 1980). In view of its minor role in native American practices, the complex chemistry and pharmacology of Cannabis are not discussed in detail here.

The most important constituents of Cannabis are cannabinoids. Up to now, more than sixty cannabinoids have been detected in hemp or in crude drugs prepared from hemp. Most of these are trace components, and some are considered to be artificial (Schultes and Hofmann 1980b; Turner et al. 1980). Δ^9-tetrahydrocannabinol (THC) is by far the most psychoactive one. In seized samples from various countries, THC concentrations were in the range of 0.4-5.0% in unspecified Cannabis parts and 1.1-8.7% in Cannabis resin (Baker et al. 1981).

Acute intoxication with a Cannabis product appears to be a reasonably benign experience. To elicit LSD-like activity, high doses of THC are needed; modest doses merely induce

depersonalization and mild hallucinogenic effects (Meyer 1972). Although neither smoking nor oral ingestion of hemp results in a high bioavailability of THC, both methods of application can produce a subjective response (Ohlsson et al. 1980).

2.1.5. Capsicum species
Solanaceae

2.1.5.1. Ethnobotany

Some reviews on South American 'narcotics and stimulants' have included Capsicum, because the Makusi of the Rupununi used peppers as a stimulant and excitant (Roth 1924; Cooper 1949). The Makusi poured a liquid preparation from crushed peppers and water into the nostrils of patients with a headache (Roth 1924). More recently, Uscátegui Mendoza (1965) reported the nasal use of a Capsicum preparation among a Tukano group of the Colombian Vaupés region. After they have danced and drunk alcoholic beverages the night before, they pour a mixture of crushed pepper and water into the nose to drive away the effects of the festivities. The Tukano also practise this administration during their initiation period. Occasionally, the initiates cleanse themselves by taking drops prepared from fresh chili peppers through the nose, using for this a small funnel made of a leaf (Reichel-Dolmatoff 1975).

When the consulted literature speaks about pepper, it either identifies pepper as Capsicum or fails to offer a botanical name. In the last case, it should be borne in mind that pepper is a vernacular term which might also refer to a Piper species (Hegnauer, pers.commun. 1983).

2.1.5.2. Chemistry and psychopharmacology

The chemistry and psychopharmacology of Capsicum fruits are discussed in section 1.1.5.2.

2.1.6. Datura species
Solanaceae
Datura innoxia Mill.

2.1.6.1. Ethnobotany

From pre-Hispanic times until the present day, Mexican Indians have known the hallucinogenic properties of oral Datura

preparations (Safford 1922; Guerra 1967; Díaz 1979). According to a journalistic rather than scientific source, the dust of dry toloachi leaves was taken in the Mexican town of Guanajuato as a snuff (Reko 1949). Toloachi, more often denoted as toloache, is a vernacular name used for various Datura species, such as D.innoxia (Díaz 1979; Schultes and Hofmann 1980b).

Although tree Daturas, now treated as the genus Brugmansia, are common intoxicants in South American rituals (Cooper 1949; Plowman 1981a), there does not seem to be evidence that they have served as a source of snuffs (Schultes 1967b).

2.1.6.2. Chemistry and psychopharmacology

The chemistry and psychopharmacology of Datura species are discussed in sections 1.1.4.2 and 1.1.6.2.

2.1.7. Erythroxylum species
Erythroxylaceae
Erythroxylum coca Lam.
var. ipadu Plowman
Erythroxylum fimbriatum Peyr.
Erythroxylum macrophyllum Cav.
Erythroxylum novogranatense (Morris) Hieron.
var. truxillense (Rusby) Plowman

2.1.7.1. Ethnobotany

The widespread use of coca among the Indians of western South America is well established (Bühler 1948; Cooper 1949; Schultes 1957, 1981b; Antonil 1978; Plowman 1979, 1981b; Wiedemann 1979; Scheffer 1981). Its role as a true ceremonial drug seems to be of minor importance, at least in present times (Cooper 1949; Wiedemann 1979). The principal Indian way of taking coca is usually designated as chewing. A common method consists of placing coca leaves in the mouth and rolling them around or chewing them briefly until a wad has formed. The wad is held reasonably still between cheek and gums, and lime or ash is added periodically. The juice is swallowed and some of the leaf material may occasionally be ingested (Bühler 1948; Cooper 1949; Antonil 1978; Holmstedt et al. 1979). Another common method, sometimes denoted as eating, consists of taking coca powder prepared from pounded coca leaves and alkaline plant ash. Moistening of the powder with saliva results in a pasty quid which is held between the cheek and gums, and the juice is

swallowed. In contrast with a quid from whole leaves, which cannot be totally swallowed, most and occasionally all of the coca powder will pass to the stomach (Schultes 1957, 1981b; Holmstedt et al. 1979; Plowman 1981b; Scheffer 1981).

Exceptional ways to utilize coca include the drinking of an infusion from the leaves – among the Peruvian Pánobo Indians (Tessmann 1930; Schultes 1981b). And, the injection of coca powder into the mouth by means of a bag with a bone tube – by certain tribes in the Vaupés region (Plowman 1981b; Schultes 1981b). It is said that the Omaguas of northeastern Peru have smoked coca leaves (Bühler 1948), but this claim is not supported by a primary reference. In recent years, the urban youth of Peru has developed the practice of smoking cigarettes containg coca paste mixed with tobacco or marihuana; coca paste is a crude extract from coca leaves (Jeri et al. 1978).

There are various undetailed statements on the Indian use of coca snuffs (Hartmann 1890, Bühler 1948; Wilbert 1975; Plowman 1981b; Scheffer 1981), in particular by certain tribes of the northwest Amazon (Schultes and Hofmann 1980b). Schultes (1967b) mentions the addition of powdered coca to tobacco snuff among the Colombian Witoto and Yukuna Indians. In later publications he reports, on the basis of reliable hearsay, that the Yukunas as well as the Tanimukas may have utilized coca–ash powder as a snuff in certain annual ceremonies (Schultes 1981b, 1984). The use of coca powder as a snuff by the Witotos has also been reported by Wavrin (1948). Such use would seem a considerably rare practice, since the Witotos are a relatively well–known tribe, and most field workers fail to describe this method of administration (Plowman 1981b).

The genus Erythroxylum includes perhaps as many as 250 species, but only E.coca and E.novogranatense are cultivated in South America. Both species include two varieties. E.coca var. coca (Bolivian or Huánuco coca) occurs throughout the wet tropical valleys of the eastern Andes from Ecuador south to Bolivia, whereas E.coca var. ipadu is cultivated in many parts of the Amazon Basin. E.novogranatense var. novogranatense (Colombian coca) is grown in drier regions of Colombia and Venezuela, whereas its variety truxillense (Trujillo coca) is cultivated in the dry Marañon valley and on the desert coast of northern Peru (Holmstedt et al. 1977; Plowman 1979, 1981b; Plowman and Rivier 1983). The type of coca cultivated in the northwest Amazon, where coca snuffs are said to occur, is E.coca var. ipadu, but it should be added that the Witotos and other tribes in this area may also employ the wild species E.fimbriatum and E.macrophyllum (Schultes 1981b).

2.1.7.2. Chemistry and psychopharmacology

Dried leaves from the two main cultivated Erythroxylum species are stated as having a total alkaloid content of about 0.5–2 % (Hegnauer 1966; Grinspoon and Bakalar 1976). Their principal alkaloid is undoubtedly cocaine (=benzoylmethylecgonine). It is often claimed that the Trujillo leaf has a higher total alkaloid content than the Bolivian leaf, but that the latter has a greater proportion of cocaine to other alkaloids (Grinspoon and Bakalar 1976; Reynolds 1982; Novák et al. 1984). Recent studies on dried South American coca leaves have revealed cocaine percentages of 0.13–0.96% in E.coca var. coca, 0.11–0.41% in E.coca var. ipadu, 0.17–0.93% in E.novogranatense var. novogranatense, and 0.42–1.02% in E.novogranatense var. truxillense (Holmstedt et al. 1977; Plowman 1981b; Plowman and Rivier 1983). In other words, the highest percentage of cocaine was found in the last variety, which contradicts the belief that Trujillo coca is lower in cocaine content than other varieties (Plowman and Rivier 1983). There is some evidence to suggest a distinct phytochemical difference between E.coca var. coca (Andean coca) and the variety ipadu (Amazonian coca). After Amazonian and Andean coca plants had been grown in the greenhouse under the same uniform conditions, the dried leaves of the former yielded only 0.34–0.41% of cocaine, whereas the latter showed consistently higher percentages of 0.51–0.81%. If this finding can be confirmed, it might explain why Indians of the Amazon Basin pulverize the coca leaf before use (Plowman 1981b; Plowman and Rivier 1983).

Apparently no or very little cocaine is present in most wild Erythroxylum species like E.fimbriatum and E.macrophyllum (Hegnauer 1966; Holmstedt et al. 1977; Plowman 1981b; Plowman and Rivier 1983). In a recent study of 29 different species, a cocaine percentage of 0.1% or more could only be demonstrated in E.recurrens and E.steyermarkii (Plowman and Rivier 1983).

Reviews of the minor alkaloids, claimed as occurring in the two main cultivated Erythroxylum species (Hegnauer 1966, 1981; Evans 1981; Novák et al. 1984), show the following picture:

- 11 ecgonine alkaloids (cis–cinnamoylcocaine, trans–cinnamoyl–cocaine, ecgonine, norecgonine, norformylecgonine, methyl–ecgonine, benzoylecgonine, cinnamoylecgonine, methylecgonidine, alpha–truxilline, beta–truxilline);
- 5 tropine alkaloids (tropine, pseudotropine, dihydroxytropane, tropacocaine, benzoyltropine);
- 4 pyrrolidine alkaloids (hygroline, hygrine, cuscohygrine, dihydrocuscohygrine);
- 2 other alkaloids (choline, nicotine).

The question arises as to how many of these reported minor constituents are artifacts instead of naturally occurring substances in living material. Rivier (1981) examined crude ethanolic extracts of E.coca leaves without any further purification by a GC–MS method, and could only demonstrate cocaine, cis–cinnamoylcocaine and trans–cinnamoylcocaine as endogenous alkaloids.

Depending on leaf age, species and variety, the cinnamoyl–cocaines may represent 2–60% of the total alkaloid content (Rivier 1981; Turner et al. 1981).

The acute and chronic toxicity of cocaine is discussed at length by Grinspoon and Bakalar (1976). The most striking acute systemic effect is stimulation of the central nervous system, which can result not only from intravenous injection, but also from oral ingestion (Van Dyke et al. 1978; Wilkinson et al. 1980), nasal application (vide 2.2.2.4), and smoking (Perez–Reyes et al. 1982; Siegel 1982). The central stimulation manifests itself as a feeling of well–being and euphoria, although sometimes dysphoria occurs. These effects may be accompanied by garrulousness, restlessness, excitement, confusion, apprehension, and anxiety (Ritchie and Greene 1980; Oderda and Klein–Schwartz 1982). When used for a long time or in high doses, cocaine may provoke a psychosis; an iatrogenous case has been recently observed in a patient with oral stomatitis, who had been given 3 ml of a 10 % solution every 4 hours for more than two weeks (Lesko et al. 1982).

Over the last few years, growing attention has been paid to the metabolism of cocaine in man (Lindgren 1981; Oderda and Klein–Schwartz 1982), and to the plasma levels of this alkaloid (Barnett et al. 1981; Javaid et al. 1983).

Only a small portion of cocaine is excreted unchanged in the urine. Major metabolites in human urine are the hydrolysis products benzoylecgonine (Fish and Wilson 1969; Jindal and Vestergaard 1978) and ecgonine methylester (Inaba et al. 1978; Ambre et al. 1983). There is evidence to suggest that the latter compound is formed largely by esterases, and that the former one results from spontaneous, nonenzymatic hydrolysis in the body (Stewart et al. 1979). A minor metabolic pathway in man is N–demethylation of cocaine to norcocaine (Inaba et al. 1978), which in its turn might undergo hydrolysis (Stewart et al. 1979; Lindgren 1981). Other minor metabolites, such as ecgonine, have been demonstrated in multiple intoxication and overdose cases (Lindgren 1981).

The pharmacological effects of cocaine and its metabolites, after intravenous dosing, have been studied in the rat. No

observable effects were noted with benzoylecgonine after doses of 250 mg/kg and with ecgonine methylester or ecgonine after doses of 200 mg/kg. Cocaine and norcocaine caused excessively rapid heart beat, convulsions and death after injection of 20 mg/kg, and lower doses of 5–10 mg/kg produced similar results without mortality (Misra et al. 1975). In monkeys, norcocaine is effective in maintaining intravenous self-administration, although it is less potent than cocaine itself (Bedford et al. 1980; Spealman and Kelleher 1981). In contrast to cocaine, however, norcocaine does not stimulate locomotor activity or fixed-interval feeding behaviour of rats, which suggests that the two compounds do not have the same behavioural profile (Bedford et al. 1980).

These data indicate that only norcocaine is a pharmacologically active metabolite of cocaine. Norcocaine seems to be a minor metabolite in man, however, accounting only for 2.4% and 6.2% of an oral dose in two subjects (Inaba et al. 1978). Consequently it would appear that the activity of cocaine in man is not principally due to metabolites, but to the alkaloid itself.

Studies on nasal application do not show a close correlation between the time course of effects and the curve of the plasma level. Maximal central effects tend to occur prior to peak plasma levels, and a certain level during the increasing phase of the curve is associated with a more intense 'high' than the same level during the decreasing phase (Van Dyke et al. 1978, 1982). This phenomenon, which is known as acute tolerance, has also been observed with central depressants like alcohol (Jaffe 1980).

In a study on the chewing of coca powder and coca leaves, material containing 16.8–48 mg of cocaine produced maximal cocaine plasma levels of 11–149 ng/ml after about 1–2 hours. Only one of the studied subjects was an Indian, and the highest level of 149 ng/ml after 1 hour was obtained when this subject chewed leaves containing 21 mg of cocaine. Just as is the case with pure cocaine, the subjects felt stimulated during the rising phase of the plasma curve, and they reported no more stimulation during the falling phase, when the quid was still in the mouth. These results suggest that central stimulation by coca leaves or powder is primarily due to cocaine (Holmstedt et al. 1979).

This view is supported by a recent survey on the pharmacology of minor Erythroxylum alkaloids. With respect to cinnamoyl-cocaines, apparently the most important alkaloids besides cocaine, the survey claims a lack of pharmacological activity. Unfortunately, no discrimination is made between the cis- and trans-form (Novák et al. 1984). Furthermore, there is a recent report that water-soluble alkaloid-free fractions of coca leaves

are not centrally active in the mouse (Harland et al. 1982).

Significant plasma levels of cocaine from coca chewing have also been demonstrated by Paly et al. (1980). One of their test groups included pure Indians and subjects of mixed ancestry who were experienced in the use of coca. They received 50 g of coca leaves containing 0.65% of cocaine. Single blood samples drawn during the chewing yielded plasma levels ranging from 130 to 859 ng/ml with a mean value of 249 ng/ml.

Until recently, it was commonly felt that cocaine is ineffective after oral administration because of poor bioavailability. However, in recent human studies on the oral and nasal application of 2 mg/kg cocaine HCl, oral administration did not result in less euphoria or in lower bioavailability than nasal dosing. In the oral experiments, cocaine was given in a gelatine capsule, and plasma levels could not be detected until half an hour after administration. This finding suggests that orally ingested cocaine is not well absorbed until it reaches the small intestine (Van Dyke et al. 1978; Wilkinson et al. 1980). Such a time lag is not observed in coca chewers, who show measurable plasma levels of cocaine after only 5 minutes of chewing (Holmstedt et al. 1979). This implies that there is a significant buccal absorption in coca chewers. Intestinal absorption will occur as well, since coca chewers swallow the juice and may also swallow plant material (vide 2.1.7.1). Since coca chewing involves significant buccal absorption, it is somewhat a misnomer from the pharmaceutical point of view to denote this practice as oral administration.

The literature is not unanimous about the reason why coca chewers add alkaline material like lime or plant ash to their coca quid (Rivier 1981). Some authors express the view that these admixtures produce an alkaline environment, in which cocaine is hydrolyzed into benzoylecgonine and ecgonine before it is absorbed. According to this supposition, not cocaine itself, but metabolites like ecgonine have a central place in the pharmacology of coca chewing (Nieschulz 1971; Burchard 1975). This hypothesis does not appear to be acceptable. Firstly, recent in vitro experiments simulating natural conditions do not show an immediate extensive hydrolysis of cocaine in an alkaline environment (Rivier 1981). Secondly, experienced coca chewers report local anaesthesia in the mouth, and this effect is considered as an indication of the yield of alkaloid extracted from the coca quid (Antonil 1978). Cocaine is known to be a potent local anaesthetic (Ritchie and Green 1980), whereas neither benzoylecgonine nor ecgonine have appreciable local anaesthetic properties (Novák et al. 1984). Thirdly, the

metabolite hypothesis fails to explain why coca chewers show substantial plasma levels of cocaine and why they report central stimulation (Antonil 1978; Holmstedt et al. 1979; Paly et al. 1980). Another, much more acceptable explanation is, of course, that the alkaline material facilitates the cocaine absorption through the buccal mucosa (Antonil 1978; Holmstedt et al. 1979; Rivier 1981; Siegel 1982). Furthermore, the addition of lime is reported to transform the bitter and unpleasant flavour of coca leaves into a more sweet and agreeable taste (Antonil 1978; Siegel 1982).

Principal effects of coca chewing by South American Indians are said to be a reduction of hunger, cold and fatigue (Hanna and Hornick 1977). Considerable controversy still exists as to whether the practice is detrimental or not (Holmstedt et al. 1979). Cases of acute overdosage or obvious chronic toxicity seem to be uncommon among South American coca chewers (Grinspoon and Bakalar 1976; Hanna and Hornick 1977; Antonil 1978). In contrast, the heavy use of coca paste is strongly associated with a variety of psychopathological states, including full-blown psychoses (Jeri et al. 1978; Siegel 1982). Coca paste is a concentrated extract from coca leaves, reported to contain 40–85% of cocaine sulphate (Siegel 1982). Recently, coca paste cigarettes, each containing 75 mg of cocaine, have been tested in regular users. The smoking of one cigarette in 3 minutes produced cocaine plasma levels of 91–462 ng/ml, and ad libitum smoking of five cigarettes resulted in levels of 266–882 ng/ml after only 25–47 minutes (Paly et al. 1982).

2.1.8. Ilex guayusa

Aquifoliaceae

Ilex guayusa Loes.

2.1.8.1. Ethnobotany

The use of Ilex guayusa as a ritual stimulant and emetic by natives of the South American Montaña area is well established (Cooper 1949; Patiño 1968; Schultes 1972a). Bundled leaves of I.guayusa have been found, together with several snuff trays, in a pre-Hispanic medicine-man's tomb of Highland Bolivia. This joint occurrence in an archaeological context raises the possibility that guayusa leaves may have once served as a source of snuff, but there is no direct evidence for this supposition (Schultes 1972a, 1984; Wassén 1972b).

2.1.8.2. Chemistry and psychopharmacology

The chemistry of I.guayusa and the psychopharmacology of its principal alkaloid caffeine are discussed in section 1.1.7.2.

2.1.9. Justicia pectoralis
Acanthaceae
Justicia pectoralis Jacq.

2.1.9.1. Ethnobotany

Several groups of Waiká Indians prepare a snuff from Virola exudate, the dried leaves of mashihiri, and vegetable ashes. Technically, these Indians are known as the Yanomamö or Yanonami Indians (Schultes and Holmstedt 1968; Prance 1972). The mashihiri plant, which is cultivated for this purpose, has been identified as Justicia pectoralis var. stenophylla (Seitz 1965, 1967; Schultes and Holmstedt 1968; Brewer-Carias and Steyermark 1976; Schultes 1978). Chagnon et al. (1971) report that different types of Justicia are cultivated, all of which they tentatively classify as different varieties of Justicia pectoralis or as different forms of Justicia pectoralis var. stenophylla. Schultes (pers. commun. to MacRae and Towers 1984b) feels that the variety stenophylla is a growth form of J.pectoralis rather than a genetic variant. In keeping with this suggestion, the varietal epiphet is left out of the following discussion.

In some Waiká villages of the Brazilian Roraima territory, the dried leaves of Justicia pectoralis are commonly added to Virola snuffs, apparently without adding vegetable ashes (Prance 1972). A Waiká name for this plant is paxararok (Schultes 1978). The Waikás of the Brazilian Totobobí River likewise prepare Virola snuffs without ashes, and J.pectoralis (known as masha-hára-hanak or boo-hanák) is added very occasionally (Schultes and Holmstedt 1968).

According to various field reports, Indians themselves consider Justicia leaves an aromatic admixture, which has no intoxicating effect, but merely improves the aroma of the Virola snuff (Seitz 1965, 1967; Schultes and Holmstedt 1968; Prance 1972). Yet here is evidence that the Waikás may use Justicia as the sole source of a snuff (Schultes 1967b; Chagnon et al. 1971; Schultes and Hofmann 1980b; McKenna et al. 1984b). The Caburiwe-Teri group, living in the border region of Venezuela and Brazil, uses mashihiri powder mostly to strengthen their more powerful Virola snuff, but mashihiri can also be used alone. Since the powder is

too fine by itself, it is generally mixed with plant ashes before use (Brewer-Carias and Steyermark 1976). Prance (pers. commun. 1984) has observed Waiká Indians at the Tototobí River 'taking pre-Justicia snuff without Virola; after the shaman took this he was apparently in a trance'.

2.1.9.2. Chemistry and psychopharmacology

Many reviews on botanical hallucinogens have included J.pectoralis, stating that tryptamines (in particular dimethyltryptamine) might be present, but that the preliminary indications for this suspicion should be verified (Furst 1976a; Emboden 1979a; Schultes and Farnsworth 1980; Schultes and Hofmann 1980a,b). These statements go back to the end of the sixties, when preliminary chemical indications for the presence of alkaloidal principles were reported (Schultes and Holmstedt 1968). At that time, a small amount of an indole alkaloid had been isolated from J.pectoralis, but the material had been harvested by Indians with Virola exudate on their hands, so it may well have been contaminated (Holmstedt, pers. commun. 1984). Additional studies by Holmstedt failed to detect an hallucinogenic alkaloid in the dried leaves of J.pectoralis, used as an admixture in the Roraima territory (Prance 1972). This negative chemical result corresponds with ethnological reports that natives do not attribute hallucinogenic properties to the aromatic herb.

Recently, coumarin and its 7-hydroxyderivative umbelliferone have been found in Peruvian J.pectoralis (MacRae and Towers 1984b). These non-alkaloidal benzopyran compounds could also be isolated from two Venezuelan Yanomamö snuffs, labeled as mashahari and as buhenak + mashahara (McKenna et al. 1984b).

Coumarin is a fragrant principle, which has been used in cosmetics and detergents (Opdyke 1974). According to toxicological text books, it may produce nausea, vomiting, headache, dizziness, and loss of consciousness (Lewin 1962; Braun and Dönhardt 1975). Its pharmacokinetics in man have been studied by Ritschel et al. (1977, 1979). After oral ingestion, the compound is absorbed completely, but only 2-6% reaches the systemic circulation in intact form because of extensive first-pass metabolism. The major metabolite is 7-hydroxycoumarin, which in its turn undergoes glucuronidation. In a recent study in gerbils, intraperitoneally administered coumarin distributed rapidly into the cerebral tissue, whereas its metabolites 7-hydroxycoumarin and 7-hydroxycoumarin glucuronide entered the brain only to a small extent, if at all. The tested dose of 40

mg/kg produced transient sedation, and this effect corresponded rather well with the time of maximal coumarin brain concentration and with the subsequent rapid removal of coumarin from the brain (Ritschel and Hardt 1983). The same intraperitoneal dose of 40 mg/kg of coumarin was found to cause a longer and deeper level of sedation in the rat, but this species is a poor 7-hydroxylator of coumarin (Hardt and Ritschel 1983).

All in all, 7-hydroxycoumarin (=umbelliferone) is unlikely to have any central effect, and coumarin will thus not readily show psychoactive symptoms when taken orally. Whether coumarin might be centrally active in man via other routes of administration, is still far from clear.

As Justicia pectoralis is mostly used as an admixture to Virola, the question arises if this plant could modulate the activity of Virola. To test this possibility, MacRae and Towers (1984b) examined the influence of J.pectoralis extracts on the effects of the Virola alkaloid 5-methoxy-dimethyltryptamine (5-MeO-DMT) in the mouse. None of the aqueous, ethyl acetate and ethyl ether extracts tested had any significant effect upon the changes in behaviour and in locomotor activity induced by 5-MeO-DMT.

Hegnauer (1964, pers. commun. 1985) points out that many acanthaceous plants have cells enclosing calcium carbonate (cystoliths). If such cells would occur in J.pectoralis, this admixture to Virola snuffs might give an alkaline reaction, which might facilitate the absorption of the Virola alkaloids (vide 2.2.1). This could be of importance when the snuff is prepared from Virola and Justicia without the addition of alkaline plant ash.

2.1.10. Maquira sclerophylla

Moraceae

Maquira sclerophylla (Ducke) C.C. Berg

2.1.10.1. Ethnobotany

An enigmatic snuff, known only by the general Portuguese term rapé dos indios, is said to have been formerly employed in the central part of the Brazilian Amazon, especially in the Pariana region. Direct observation of its preparation and use has never been possible. The source of the snuff is reputed to be the fruit of Maquira sclerophylla, which was first known as Olmedioperebea sclerophylla (Schultes 1967b, 1984; Schultes and Farnsworth 1980; Schultes and Hofmann 1980b). According to von Reis Altschul

(1972), the seeds of this gigantic forest tree are said to be a traditional snuff source of the Mundurucú Indians.

2.1.10.2. Chemistry and psychopharmacology

Chemical and pharmacological data on Maquira sclerophylla have apparently not been reported in the literature (Schultes and Hofmann 1980b). According to Carlini and Gagliardi (1970), water and ethanol extracts from wood of the related Maquira calophylla are devoid of Cannabis-like activity in animal experiments, even at doses ten times those required for Cannabis sativa to demonstrate such effects. These investigators announced that their studies would be continued with extracts from leaves and flowers of M.calophylla and M.sclerophylla, but results have not as yet been published (Schultes and Farnsworth 1980). Recently, another research group has reported the isolation of the coumarin derivatives marmesin, oxypeucedanin hydrate and pranferol from the stem bark of Maquira calophylla (Rovinski and Sneden 1984).

2.1.11. Nicotiana species
Solanaceae
Nicotiana rustica L.
Nicotiana tabacum L.
Nicotiana thyrsiflora Bitter ex Goodsp.

2.1.11.1. Ethnobotany

South American Indians are known to have used tobacco since their earliest contacts with Europeans, and these practices undoubtedly go back to pre-colonial times (Stahl 1925; Castiglioni 1943; Cooper 1949; Bondeson 1972; Elferink 1983). Most South American tribes of the twentieth century take tobacco in one form or another for magico-religious, medicinal and/or recreational purposes. The major South American method of using tobacco is smoking, but chewing, drinking, eating, licking and snuffing are also well documented (Stahl 1925; Cooper 1949; Zerries 1964; Wilbert 1972, 1975). Snuffing is said to be the most widespread method of tobacco use in certain parts of South America, especially in the wet, tropical lowland areas like the Amazon valley (Schultes 1967b; Schultes and Hofmann 1980b). According to Cooper (1949), the three main regions for which tobacco snuffs have been recorded, are the Orinoco territory, the Montaña region, with an extension down the Purús river, and early colonial Peru. This author rightly cautions that, in the

literature, tobacco snuffs are not always clearly distinguishable from truly hallucinogenic snuffs. Consequently, the actual use of tobacco snuffs may have been somewhat less widespread than generalizing statements would suggest (Schultes 1967b).

The Peruvians of the early colonial days have been reported as taking a snuff prepared from tobacco root for medicinal reasons (Cobo 1964), but most tobacco snuffs were and still are prepared from the dried leaves (Cooper 1949; Schultes 1967b).

The mixing of tobacco powder with plant ashes has been recorded for Arawak groups of the Purús river (Cooper 1949), such as the Dení, Jarawara, and Jamamadí Indians (Prance 1972, 1978). Tribes of the Brazilian Guaporé River are said to have mixed tobacco powder with vegetable ash and crushed angico seeds (Snethlage 1937). Angico may well refer to Anadenanthera (Schultes 1967b), but also to other genera (von Reis Altschul 1972). Other reported admixtures include Tanaecium (Prance et al. 1977) and Erythroxylum (Schultes 1967b).

Not only tobacco snuff, but also tobacco juice has been used nasally. This practice has been documented for several tribes of northeast Peru (Tessmann 1930), the famous Jivaro Indians (Karsten 1935), and the Bush negroes of the Guiana region (Roth 1929). Recently, it has been reported that the Creoles of French Guiana and the Bush negroes of Surinam inhale a liquid through the nostrils, which is prepared from tobacco leaves and plant ash, for recreational purposes (Plotkin et al. 1980).

Of the 36 Nicotiana species occurring in South America (Goodspeed 1954), Nicotiana tabacum is undoubtedly the principal source of South American tobacco preparations (Schultes 1967b). In his elaborate monograph on the genus, Goodspeed (1954) even goes so far as to state that no other species can be shown to have been, or, with the possible exception of N.rustica, to be today a source of tobacco in South America. This statement would not seem entirely correct, however, as a herbarium annotation on Peruvian N.thyrsiflora explicitly mentions the use of its leaves for smoking (von Reis and Lipp Jr. 1982).

Harrington (1932) reports that the Karuk Indians of California use the expression imcakare.he.raha to designate the snuffing of tobacco, and the Nootka Indians of the northwest coast are said to have snuffed tobacco (von Welck 1981). The snuffing of tobacco powder in ancient Mexico has been recorded by the early authors Hernández (1959) and Clavijero (1970). There appear to be few references of this kind, so the practice is not believed to have been widespread in North and Middle America (Wilbert 1975; Elferink 1983).

2.1.11.2. Chemistry and psychopharmacology

The chemistry and psychopharmacology of tobacco are discussed in section 1.1.9.2.

2.1.12. Pagamea macrophylla
Rubiaceae
Pagamea macrophylla Spr. ex Benth.

2.1.12.1. Ethnobotany

Among the Colombian Barasana Indians, the pulverized leaves of Pagamea macrophylla are aspirated by medicine men, in the form of a snuff, during ceremonies of divination. The Barasana name for the plant is ma-nu-su-ka-ta (Schultes 1980a).

2.1.12.2. Chemistry and psychopharmacology

The chemistry and psychopharmacology of Pagamea macrophylla appear to be unknown (Schultes 1980a, 1984).

2.1.13. Piper interitum
Piperaceae
Piper interitum Treal. ex Macbr.

2.1.13.1. Ethnobotany

Among the Kulina Indians of eastern Peru, Piper interitum is known as tetsi. These Indians are said to prepare a snuff from the dried leaves and roots, which is used as a substitute for tobacco (Schultes 1980b).

2.1.13.2. Chemistry and psychopharmacology

I am not aware of phytochemical or pharmacological research on Piper interitum.

2.1.14. Tanaecium nocturnum

Bignoniaceae

Tanaecium nocturnum (Barb.-Rodr.) Bur. et K. Schum.

2.1.14.1. Ethnobotany

The Paumarí Indians of the Brazilian Rio Purús region prepare a ritual snuff by mixing tobacco powder with the roasted, grounded leaves of a vine called koribó. This vine has been botanically identified as Tanaecium nocturnum. According to the Indians, the snuff has the same effect as another snuff, which they prepare from the bark of Virola elongata. Paumarí women do not usually take the snuff, but they drink an aqueous brew from the root bark of koribó. This brew is said to produce drowsiness, inability to concentrate, and reduced awareness (Prance et al. 1977).

2.1.14.2. Chemistry and psychopharmacology

The fresh leaves of Tanaecium nocturnum have been reported as containing a very high concentration of hydrogen cyanide (Grajales Diaz 1967). Field investigators found the fumes from freshly collected material poisonous, causing dizziness and headache in one of them. When the snuff is prepared, however, the leaves are toasted and this probably removes the cyanide (Prance et al. 1977). Which compounds are formed or left intact during the preparation of the snuff is still unclear. In 1978, chemical and pharmacological studies were announced (Prance 1978), but to my knowledge, the results of these investigations have not yet been published.

The stem of Tanaecium nocturnum contains an essential oil consisting almost exclusively of benzaldehyde (Gottlieb et al. 1981). Animal experiments have shown that this compound has antispasmodic, local anaesthetic and antibacterial properties (Macht 1923). According to toxicological textbooks, it is also capable of producing central nervous depression (Gleason et al. 1969; Braun and Dönhardt 1975; Dreisbach 1977).

2.1.15. Virola species
Myristicaceae
Virola calophylla Warb.
Virola calophylloidea Markgr.
Virola cuspidata (Spr. ex Benth.) Warb.
Virola elongata (Spr. ex Benth.) Warb.
Virola rufula Warb.
Virola sebifera Aubl.
Virola theiodora (Spr. ex Benth.) Warb.

2.1.15.1. Ethnobotany

Many South American Indian tribes prepare potent psychoactive snuffs from Virola species for ceremonial and recreational uses (Schultes 1954, 1967b, 1984; Uscátegui Mendoza 1959; Seitz 1965, 1967; Wassén 1965, 1967; Schultes and Holmstedt 1968; Prance 1970, 1972; Chagnon et al. 1971; Reichel-Dolmatoff 1975; Brewer-Carias and Steyermark 1976; Prance et al. 1977; Schultes and Hofmann 1980a,b). All important ethnobotanical references to these snuffs appear to be comparatively recent. Older reviews on the botanical sources of South American snuffs tend to focus on Nicotiana and Anadenanthera, and fail to pay any attention to Virola (Cooper 1949). This raises the question as to whether this merely reflects the insufficiency of certain early ethnobotanical investigations, or whether it may also indicate a difference between past centuries and the present. Whatever the answer may be, it has become more and more clear that Virola is one of the major sources of psychoactive South American snuffs, and that the use of Anadenanthera snuffs is less widespread than was once believed (Schultes 1954, 1967b; Schultes and Holmstedt 1968).

The principal native users of Virola snuffs are tribes in the Colombian Vaupés region, and the Waiká Indians inhabiting the upper Orinoco area in Venezuela and the Brazilian territory north of the Rio Negro (Schultes and Holmstedt 1968; Schultes and Hofmann 1980b). Depending on tribe and locality, the snuffs are known under different native names, such as yá-kee, yá-to and paricá in Colombia, and epéna, ebene, paricá and nyakwána in Brazil (Seitz 1967; Schultes and Holmstedt 1968; Schultes and Hofmann 1980b). It should not be forgotten that these indigenous names have no distinctive botanical value. Paricá may also refer to Anadenanthera (vide 1.1.2.1) and epéna or ebene tends to be a general term designating snuffs, regardless of their exact botanical origin (Chagnon et al. 1971; Brewer-Carias and Steyermark 1976).

The preparation of Virola snuffs is described in detail by

field workers like Schultes (1954), Seitz (1967), Schultes and Holmstedt (1968), Prance (1970, 1972), Brewer-Carias and Steyermark (1976), and Prance et al. (1977). Most snuffs appear to be based on the powdered blood-red exudate from the inner bark of Virola species (Schultes and Holmstedt 1968; Schultes and Hofmann 1980b), but the Paumarí Indians of central Amazonia use the entire bark and not merely its exudate (Prance et al. 1977). Seitz (1967) did not observe an admixture to Virola among the Tukano Indians, but several Colombian tribes are reported as mixing the Virola dust with plant ashes (Schultes 1954). Some Waiká groups use the dusted exudate without an admixture, whereas other groups add aromatic Justicia leaves and/or vegetable ashes (Schultes and Holmstedt 1968; Prance 1970, 1972; Brewer-Carias and Steyermark 1976). Other admixtures have been reported as well, but unfortunately botanical identifications are not available (Seitz 1967; Chagnon et al. 1971). The addition of ashes is thought to serve as a means of drying, to free the alkaloids more easily from the exudate, to keep the snuff from rapid deterioration during storage, or merely for mechanical purposes (Schultes and Holmstedt 1968). The addition of Justicia is discussed in the section on this genus.

The effects of Virola snuffs seem to vary, but in Indians they often include initial excitability, beginning within several minutes of the first snuffing. This is followed by numbness of the limbs, twitching of the facial muscles, inability to coordinate muscular activity, nausea, visual hallucinations with frequent macropsia, and afterwards, a deep, disturbed sleep (Schultes and Hofmann 1980b). The Indians themselves acknowledge that it can be a dangerous practice to use large doses of a Virola snuff. An informant illustrated this with the death of a medicine-man, from the Colombian Puinave tribe, during a yá-kee intoxication (Schultes 1954, 1967b). The Waiká Indians visited by Seitz (1965, 1967) usually inhale two coffee-spoons full, one in each nostril, which results in a short intoxication of approximately one hour.

While snuffing is the most common way to administer Virola, it is certainly not the only method employed by South American natives. Venezuelan witch doctors are said to smoke the dried bark of V.sebifera to cure fevers (von Reis Altschul 1967; Schultes and Hofmann 1980b), and Brazilian witch doctors reportedly smoke the bark of an indeterminate Virola species as an additive to tobacco (McKenna et al. 1984b). In the past decade, the oral ingestion of Virola preparations by the Witoto and Bora Indians of Amazonian Colombia and adjacent Peru has become well documented (Schultes 1969; Schultes and Swain 1976;

Schultes et al. 1978). A recent publication describes the effect of such oral preparations in a field investigator, who tested four different samples in amounts exceeding those recommended by native informants. Two of the samples exhibited oral activity, but no strictly hallucinogenic response could be observed. The most potent sample had the effect of a pressor amine or general anaesthetic rather than the effect of an hallucinogen (McKenna et al. 1984b).

Principal Virola species utilized to prepare snuffs are V.calophylla and V.calophylloidea in the Colombian region, and V.theiodora in the Waiká area (Schultes 1954; Schultes and Holmstedt 1968; Prance 1970, 1972; Holmstedt et al. 1980). Another important Virola species appears to be V.elongata. This plant is used as a snuff source by certain Waikás (Brewer-Carias and Steyermark 1976), by the Paumarí Indians in central Amazonia (Prance et al. 1977), and possibly by the Taiwanos in Amazonian Colombia (Schultes 1954). In a recent taxonomic monograph on Virola, Rodrigues (1980) treats V.theiodora as equivalent to V.elongata, but Schultes (1982) prefers to consider the two as separate species, since they look very different in the field and are widely recognized as distinct by Indians who use them.

Other species of which the nasal use has been suggested in the literature, include V.cuspidata and V.rufula (Biocca 1968). Unfortunately, these suggestions are not supported by herbarium voucher specimens (Schultes, 1982). Rodrigues (1980) considers both binomials as synonyms of V.elongata, but the different phytochemistry of V.cuspidata casts doubt on its disposition under V.elongata (Schultes 1982).

2.1.15.2. Chemistry and psychopharmacology

The chemistry of Virola species has been studied by Agurell et al. (1969), Holmstedt et al. (1980), and McKenna et al. (1984b). These studies have shown that the following tryptamine alkaloids can be present in the Virola genus: tryptamine (=T), N-monomethyltryptamine (=MMT), 5-methoxy-N-monomethyltryptamine (=5-MeO-MMT), N,N-dimethyltryptamine (=DMT), and 5-methoxy-N,N-dimethyltryptamine (=5-MeO-DMT). Although the Indians usually employ only the bark and especially its exudate, tryptamines have not only been demonstrated in bark samples, but also in samples of leaves, flowering shoots, and roots. In addition to tryptamine derivatives, beta-carbolines could be isolated as minor components: 2-methyl-1,2,3,4-tetrahydro-beta-carboline (=MTHC), 6-methoxy-2-methyl-1,2,3,4-tetrahydro-beta-carboline (=6-MeO-MTHC), and 6-methoxy-1,2-dimethyl-1,2,3,4-tetrahydro-beta-carboline

(=6-MeO-DMTHC). Such compounds might be expected from the point of view of biosynthesis and workup procedure (Holmstedt et al. 1980).

Bark samples of V.calophylla, V.calophylloidea, V.rufula and V.theiodora were found to have DMT and 5-MeO-DMT as their main alkaloids (Agurell et al. 1969; Holmstedt et al. 1980). An exudate sample of V.elongata contained T, MMT, DMT and MTHC; a bark sample of this species yielded MMT and DMT as principal alkaloids (Holmstedt et al. 1980). The bark of V.sebifera may contain DMT, 5-MeO-DMT and MMT (Corothie and Nakano 1969; McKenna et al. 1984b), whereas 6-methoxy-harman, 6-methoxy-harmalan, and 6-methoxy-tetrahydroharman are present in V.cuspidata (Cassady et al. 1971).

When these chemical data on Virola species are considered, the possibility must be kept in mind that a natural alkaloid composition might alter during the preparation and the storage of a snuff (Holmstedt et al. 1980). For instance, one step in the preparation of Virola snuffs involves concentration of the exudate to a thick syrup. The effect of such a treatment on 6-methoxy-tetrahydroharman, the major component in V.cuspidata, was determined in the laboratory. Refluxing in water for eight hours resulted in partial aromatization to 6-methoxy-harmalan and 6-methoxy-harman (Cassady et al. 1971). However, snuffs from tribes familiar with Virola contain the same simple tryptamine alkaloids which are also found in Virola plant material (Holmstedt and Lindgren 1967; Agurell et al. 1969; McKenna et al. 1984b). A nyakwána snuff, which had been prepared solely from the exudate of V.theiodora by the Waiká Indians of the Brazilian Rio Tototobí, yielded an unusually high total alkaloid content of 11%, consisting mainly of 5-MeO-DMT and DMT (Agurell et al. 1969). The Anadenanthera alkaloid bufotenin, which apparently does not occur in Virola plants, is also absent in Virola snuffs (Holmstedt et al. 1980).

Pharmacological data on DMT and 5-MeO-DMT, the major alkaloids in utilized Virola species, are summarized in section 1.1.2.2. The pronounced hallucinogenic activity of these N,N-dimethylated tryptamine derivatives is probably not seen with T, MMT and 5-MeO-MMT (Brimblecombe and Pinder 1975). T was reported as producing changes in perception and sensation in patients by intravenous infusion of 0.025-0.364 mg/kg/min for a total dose of 23-277 mg during an experimental day (Martin and Sloan 1970). There is little doubt, however, that the observed effects were largely autonomic in nature (Brimblecombe and Pinder 1975; Kantor et al. 1979). In an earlier study, intravenous infusion of 1 mg/min for a total dose of 10-40 mg, did not change the

subjective state or the blood pressure and pulse of depressed patients pretreated with a MAO-inhibitor (Coppen et al. 1965). Human studies on the activity of MMT and 5-MeO-MMT seem to be lacking (Kantor et al. 1979). Behavioural studies in animals suggest that these compounds are probably not hallucinogenic (Brimblecombe and Pinder 1975; Gillin and Wyatt 1977). In the rat, 5-MeO-MMT was found to cross the blood-brain barrier only to an extremely small extent, whereas a rapid crossing of 5-MeO-DMT could be shown (Vogel 1969). Consequently 5-MeO-MMT is not likely to exert profound central effects.

Animal experiments show that T, MMT and 5-MeO-MMT are rapidly and extensively metabolized into their corresponding indoleacetic acids. Since T and its N-monomethylated congeners are good substrates for monoamine oxidases, these enzymes are held responsible for the conversion (Vogel 1969; Brimblecombe and Pinder 1975).

Besides the tryptamines, the commonly utilized Virola species may contain small amounts of the beta-carbolines MTHC, 6-MeO-MTHC and 6-MeO-DMTHC (Holmstedt et al. 1980). One of the best studied pharmacological properties of such simple beta-carbolines is their MAO-inhibiting activity. Over the years it has been demonstrated that series of beta-carbolines have this effect in vitro (Udenfriend et al. 1958; Pletscher et al. 1959; McIsaac and Estevez 1966; Buckholtz and Boggan 1977; McKenna et al. 1984a). Experimental data on MTHC and 6-MeO-DMTHC are still awaited, but a recent study has compared 6-MeO-MTHC with various common beta-carbolines. On a molar base, the Banisteriopsis constituents harmine and harmaline were the most potent MAO-inhibitors, and the Virola alkaloid 6-MeO-MTHC was found to be in the same intermediate range of potency as harman and harmol (McKenna et al. 1984a). It should be noted, however, that studies on the relative potency of beta-carbolines have used different methods of assessing MAO-inhibition, and that their results are partly conflicting (McIsaac and Estevez 1966; Buckholtz and Boggan 1977; McKenna et al. 1984a). Since the tryptamine alkaloids in Virola species serve as substrates for MAO (vide 1.1.2.2), it is sometimes speculated that 6-MeO-MTHC and its congeners may modify the activity of the Virola tryptamines by acting as MAO-inhibitors (Furst 1976a; Schultes and Hofmann 1980b). However, these beta-carbolines usually occur in Virola in trace amounts, unlikely to be of pharmacological importance (Holmstedt et al. 1980; McKenna et al. 1984b). In other words, unlike the DMT in ayahuasca beverages (vide 1.1.3.2), the tryptamines in oral Virola preparations stand little or no chance of being protected from first-pass metabolism by beta-carbolines.

Recently, various lignans have been isolated from the bark of Virola elongata, and some of these non-alkaloidal constituents, when given intraperitoneally to mice, could be shown as reducing isolation induced aggression and spontaneous locomotor activity (MacRae and Towers 1984a). It is not yet clear, however, whether the reported oral activity of native Virola drugs should be attributed to these lignan derivatives (McKenna et al. 1984b).

The MAO-inhibiting activity of 6-methoxy-harman, 6-methoxy-harmalan and 6-methoxy-tetrahydroharman, the alkaloids in V.cuspidata, is well documented (McIsaac and Estevez 1966; Buckholtz and Boggan 1977; McKenna et al. 1984a). Interestingly, 6-methoxy-harmalan and 6-methoxy-tetrahydroharman have been found to be psychoactive in man. They appear to produce a state of inspiration and heightened introspection rather than an hallucinogenic experience in the strict sense. In the case of 6-methoxy-harmalan, subjective effects become apparent with approximate oral dosages of 1.5 mg/kg (Naranjo 1967).

2.1.16. Conclusion

From the ethnobotanical, chemical and psychopharmacological approach to intoxicating snuff rituals in the western hemisphere, the following categories of ritual snuff ingredients arise:

1) It is well established that the plant contains one or more psychoactive principles and the Indian use of the plant as a ritual snuff ingredient is confirmed or is quite probable: Anadenanthera, Erythroxylum, Nicotiana, Virola.
2) It is well established that the plant contains one or more psychoactive principles, but the Indian use of the plant as a ritual snuff ingredient is not well recorded or is even unlikely: Banisteriopsis, Cannabis, Datura, Ilex guayusa.
3) The Indian use of the plant as a ritual snuff ingredient is confirmed or is quite probable, but it is not well established that the plant contains one or more psychoactive principles: Justicia pectoralis, Pagamea macrophylla, Tanaecium nocturnum.
4) The Indian use of the plant as a ritual snuff ingredient is not well recorded, and it is not well established that the plant contains one or more psychoactive principles: Acorus calamus, Capsicum, Maquira sclerophylla, Piper interitum.

CHAPTER TWO PART TWO

NASAL PHARMACOKINETICS AND EFFICACY OF POSSIBLE RITUAL SNUFF CONSTITUENTS

2.2.1. General introduction

Since the 1920s, medical practitioners have treated diabetes insipidus with the nasal insufflation of posterior pituitary powder (Choay and Choay 1946; Carter and Shorr 1947). In the last two decades, this treatment has been superseded by the application of synthetic substances like lypressin and desmopressin. Just like the pituitary snuff, these pure compounds show substantial antidiuretic activity when applied to the nasal mucosa (Dashe et al. 1964; Kosman 1978). Despite this long-standing evidence, nasal administration has never been adopted in the medical profession as a generally useful method of systemic delivery of drugs. Until recently, the nasal route has been employed almost exclusively for local treatment. Common examples are the topical use of corticosteroids, sympathicomimetics and antihistamines for perennial rhinitis and the like (Empey and Medder 1981). Such topical drugs are not intended, of course, to be absorbed into the general circulation from the nose, but the occasional systemic side-effects of nasal sympathicomimetics and antihistamines indicate that systemic availability is not always negligible (Parr 1983). Recent case reports associate nasal sympathicomimetic preparations with the development of a psychotic syndrome after long-term abuse (Snow et al. 1980; Escobar and Karno 1982), and with central excitation or depression in small children after apparently normal dosing (Söderman et al. 1984).

Before the seventies, human studies on the systemic efficacy of nasal preparations were limited to a handful of therapeutic drugs besides pituitary snuff and synthetic antidiuretic compounds (Riegelman and Sorby 1971; Gorman and Hall 1973; Ritschel 1973). In the last few years, the interest in nasal administration as a convenient way to introduce drugs into the body has revived. Recent research has especially confirmed the potential usefulness of nasal application for drugs, which show a very poor effect in man after oral administration, such as: insulin (Hirai 1982; Pontiroli et al. 1982), buserilin (Bergquist et al. 1979; Koch 1981), testosterone (Danner and Frick 1980), nitroglycerin (Hill et al. 1981), glucagon (Pontiroli et al. 1983), and protireline (Borkenstein 1983). The advantage which the nasal route appears

to have for certain drugs over the oral route, can be easily explained. Drugs which are absorbed through the nasal mucosa, immediately enter the general circulation, and thus evade any form of presystemic degradation by the acid gastric juice and first-pass elimination by intestinal and hepatic enzymes. Among the various drugs of which the oral efficacy is greatly reduced by first-pass metabolism, are the sex hormones progesterone and testosterone. In recent studies on the kinetics of these hormones in the rat, nasal and intravenous administration resulted in practically similar systemic availability, whereas the availability following duodenal administration was approximately 1% that of intravenous dosing (Hussain et al. 1981, 1984). With respect to humans, the most striking data have been obtained for the beta-receptorblocking agent propranolol HCl, which is known to suffer from an extensive first-pass effect when taken orally. Intravenous and nasal doses of 10 mg produced practically identical serum levels; an oral amount of 80 mg produced relatively low serum levels and, after adjustment for the dose difference, the oral availability was only 25% of the intravenous availability (Hussain et al. 1980).

Nasal application does not only prevent presystemic elimination, it is also a rapid way of drug delivery. Most of the recent human studies mentioned above show peak levels and/or maximal activity within half an hour after nasal dosing. It is not difficult to understand such findings, when the anatomy and physiology of the nose are taken into consideration. The nasal cavity comprises an olfactory region in its extreme upper area and a respiratory region in its lower and greatest part. In the different regions, the nasal mucous membrane varies in its thickness and its vascularity. It is thick and most vascular in the upper area and over the septum, but on the floor of the nasal cavity and in the sinuses the membrane is very thin. The surface area is enlarged by the subdivision into sinuses, and it is further increased by the presence of microvilli comparable to those in the small intestine. In addition, the vascular bed of the respiratory mucosa within the nose appears to be designed for the rapid passage of fluid and dissolved materials from the blood vessels to the tissues and vice versa. All in all, the nose is a suitable site for drug absorption, and this seems to be particularly true for the respiratory region (Parr 1983).

The use of nasal dosage forms for systemic therapy may have its drawbacks. A large variability in systemic effects, resulting in an erratic response, has been strongly emphasized by some early investigators (Talledo et al. 1964; Hankiss 1982). In the case of cocaine, the rate of absorption from the nasal mucosa appears to

be highly variable, and as this alkaloid is a potent vaso-constrictor, this might be due to a fluctuating degree of local vasoconstriction (Wilkinson et al. 1980). A recent major concern is the ciliotoxicity of active constituents and additives (van de Donk and Merkus 1981).

Clinical studies on the nasal application of psychoactive alkaloids are summarized below. Wherever possible, the relationship between dose and activity is indicated. Field investigators report that an Indian snuff dose usually does not exceed 5 g (Coppens and Cato-David 1971) or about one to two teaspoons full, which would be equal to some 5-10 g (Schultes 1954; Turner and Merlis 1959). It seems difficult, if not impossible, to retain such large doses completely. In other words, when a snuff contains 1 % of a psychoactive alkaloid, the nasal threshold level of this alkaloid should be less than 50-100 mg to get an effect from one dose, and when only 0.1 % is present, a threshold level lower than 5-10 mg will be required. It must be emphasized, however, that the pertinence of clinical results to snuffing rituals may be somewhat limited. Nasal absorption does not only depend on the physicochemical properties of the active compound (pKa, partition coefficient, molecular size), but it is also governed by other factors. Potentially influential differences between experimental and native practices include:

- characteristics of the drug product

In situ recirculation tests with the nasal cavity of the rat have shown that the absorption rate of weak electrolytes is pH-dependent. In the case of aminopyrine (=aminophenazone), the absorption behaviour even closely followed the rules of the pH-partition theory, which assumes that only unionized drug molecules are capable of passive diffusion across a mucous membrane (Hirai et al. 1981). It would thus appear that the common addition of alkaline plant ashes or lime to South American snuffs may be significant. Up to half of a snuff can consist of plant ash (Seitz 1967; Schultes and Holmstedt 1968; Prance 1972). Just as is the case in coca chewing practices, the addition of such alkaline material may facilitate the diffusion of the alkaloids through the mucous membrane. Vegetable ash might further promote absorption by helping to prevent agglomeration of the snuff powder (Schultes 1967b).

Clinical studies on insulin (Hirai 1982), gentamicin (Rubinstein 1983), and scopolamine (Tonndorf et al. 1953) have demonstrated that surfactants have a great potential for enhancing nasal drug absorption. Consequently it would be interesting to ascertain, whether South American snuffs contain

surface-active compounds like saponins (Hegnauer, pers. commun. 1984), and if so, whether these compounds improve the absorption of the alkaloidal constituents.

- characteristics of the user

A potential difference between western individuals and South American Indians is that the western subjects may be less able to retain a nasal powder. In clinical studies on Piptadenia snuffs, most of the dose was discharged by sneezing and coughing, because of the inexperience of the test subjects (Turner and Merlis 1959).

Another potential difference may be the condition of the nasal mucosa. British tobacco snuffers who had used commercial snuff for at least twenty years turned out to have a generalized atrophy of the nasal mucosa. Biopsy in four snuffers confirmed metaplasia of the ciliated columnar epithelium to squamous epithelium over the middle turbinal and adjoining nasal septum (Harrison 1964). Similarly, chronic abuse of cocaine via the nose may lead to inflammatory changes and perforation of the nasal septum (Sawicka and Trosser 1983). Natanson (1975) feels that the nasal perforation seen in immoderate cocaine sniffers should be attributed to the intense vasoconstrictor effect of cocaine.

In view of such data, it may well be that the regular use of snuff by South American Indians results in degeneration of their nasal mucosa. This factor should be taken into account, since nasal drug absorption may be decreased (Ritschel 1973) or increased (Parr 1983) by local inflammation. In recent rat experiments, the nasal absorption of the quaternary ammonium compound clofilium was substantially better when the administered concentration became so high that it damaged the nasal mucosa (Su et al. 1984).

- method of administration

Among some tribes, one Indian blows the snuffing powder forcefully through a tube into the nostril of another Indian, whereas other tribes know self-administration, either by direct inhalation through a bifurcated or straight tube, or by placing one end of a V-shaped tube into the mouth and the other end into the nostril (Cooper 1949; Wassén 1965; Schultes 1967b; Seitz 1967; Coppens and Cato-David 1971; Prance 1972; Reichel-Dolmatoff 1975). The forceful blowing through a V-shaped or straight tube is likely to give a more widespread deposition than direct inhalation (Holmstedt and Lindgren 1967). When tobacco snuff is inhaled cautiously, the snuff will probably reach no further than the anterior part of the nasal tract, whereby a small quantity will go down into the pharynx (Fraser Roberts 1962). In a study with chronic tobacco snuffers, inhaled pinches of barium sulphate

powder with an average size of 20 µm could be primarily collected in the middle meatus of every snuffer (Harrison 1964). The forceful blowing in Indian practices will project the snuff against the well perfused semicavernous tissue of the nasal conchae (Holmstedt, pers. commun. 1983), and small particles may even reach the lungs (Chinachoti and Tangchai 1957; Fraser Roberts 1962; Huggins et al. 1962). According to text books, the particle size of a nasal powder should not be below 10–20 micrometer to prevent passage into the tracheal and pulmonary area (Gorman and Hall 1973; Dolder 1978). Holmstedt and Lindgren (1967) assume that, even in the case of forceful blowing, the main part of the administered material will affect the brain from the nose. There does not appear to be solid evidence that snuff constituents may pass directly into the brain without being transported through the general circulation. Consequently it should be accepted that snuff constituents are absorbed through the richly vascularized nasal mucosa, and reach the brain via the general blood–stream (Holmstedt and Lindgren 1967).

2.2.2. Specific constituents

2.2.2.1. Atropine

Vide section 2.2.2.8.

2.2.2.2. Bufotenin

Vide section 2.2.2.5.

2.2.2.3. Caffeine

Recent studies have demonstrated that an oral dose of 5 mg/kg of caffeine results in maximal plasma levels of 9–10 µg/ml after half an hour, and in complete bioavailability (Blanchard and Sawers 1982, 1983). These good oral absorption characteristics and the physicochemical properties of caffeine (Windholz 1983) suggest that this alkaloid may be rapidly absorbed from nasal dosage forms.

To obtain anecdotal experimental evidence for this supposition, I have taken pure anhydrous caffeine (OPG, Utrecht) as a nasal powder. The powder had a particle size of 10–30 µm, but many agglomerates of 100–300 µm were present. At the time of the experiment, I was a non–inhaling tobacco smoker and a regular user of coffee and beer. After abstention from xanthine–

containing products for two days and after an overnight fast, a total dose of 6.4 mg/kg was self-administered into both nostrils with a glass tube. A small fraction of the dose was lost because of some nasal mucous discharge. Venous blood samples were drawn at 0, 10, 20, 35, 50, 100, 120, 240, and 360 min after administration. Each sample was centrifuged and the resulting plasma was kept frozen until submission to analysis.

Plasma levels were assayed by Jan H.G. Jonkman and Wim J.V. van der Boon (Pharma Bio-Research International, Assen). They used a sensitive high pressure liquid chromatographical method comparable to that developed by Jonkman et al. (1980) for theophylline. Details are provided in Appendix D.

After administration, some mild transient stimulation was felt, not unlike the effect of a first tobacco cigarette in the morning. The plasma level was already 7.9 µg/ml at 10 min and 10.9 µg/ml at 20 min. The level was still 9.8 µg/ml at 120 min, whereafter it declined in a semilogarithmic way to 6.3 µg/ml at 360 min. Some unabsorbed caffeine powder could be recovered from the nasal cavity one hour after the end of the experiment.

All in all, the nasal absorption of pure caffeine powder was rapid in onset, but still incomplete after seven hours.

2.2.2.4. Cocaine

In official western medicine, cocaine is no longer used systemically, but because of its good local anaesthetic effects and potent vasoconstrictive properties, cocaine is still applied as a surface anaesthetic, especially in nasal surgery (Johns et al. 1977; Ritchie and Greene 1980). Cocaine is also a major drug of abuse, and a common method of recreational administration is snorting into the nostrils (Jaffe 1980). Consequently the medical profession needs clinical data on the kinetic behaviour and systemic toxicity of this alkaloid after nasal administration. Such data were not available some years ago, but this picture has been changed completely by the recent development of specific and sensitive methods for the determination of cocaine in biological fluids (Lindgren 1981; Barnett et al. 1981). Since 1976, there has been a continuous flow of publications on the plasma levels and/or systemic effects of nasal cocaine in an experimental setting (Van Dyke et al. 1976, 1978, 1982; Byck et al. 1977; Resnick et al. 1977a,b; Javaid et al. 1978, 1983; Wilkinson et al. 1980). It should be emphasized that most of the crucial results have been obtained in small series of three or four subjects. This is not surprising, as cocaine has a notorious reputation as a dangerous drug, and it is classified under

narcotic laws, so that legal problems are involved with its experimental use. Investigators in the United States spent approximately one year clearing the permissions and various consent forms through the requisite committees (Byck et al. 1977). From the methodological view, a small number of subjects is unfortunate, since the kinetic studies on nasal cocaine show large interindividual differences (Wilkinson et al. 1980; Javaid et al. 1983).

Van Dyke and associates have reported extensively on nasal cocaine kinetics (Van Dyke et al. 1976, 1978, 1982; Byck et al. 1977; Wilkinson et al. 1980). Their first study was carried out before they had solved the problem of the in vitro hydrolysis of cocaine (Barnett et al. 1981), and the subjects were surgical patients, who received other drugs concomitantly. However, the study shows some interesting results. Cocaine plasma levels could already be detected within 3 min after giving a nasal solution with 1.5 mg/kg of cocaine HCl, so the onset of nasal cocaine absorption was extremely rapid. The presence of unabsorbed cocaine on the nasal mucosa could be demonstrated for as long as 3 hours after administration, so the absorption was also prolonged. The latter phenomenon was attributed to the potent vasoconstrictive effects of the alkaloid (Van Dyke et al. 1976).

Van Dyke and associates have subsequently used healthy volunteers with a previous history of recreational cocaine use (Byck et al. 1977; Van Dyke et al. 1978, 1982; Wilkinson et al. 1980). In 1980, they reported on the influence of dose and dosage form on nasal cocaine kinetics. An increase in dose resulted in a higher peak plasma level of cocaine: nasal solutions with 0.19 mg/kg to 2.0 mg/kg of cocaine HCl produced mean peak concentrations of 13 ng/ml (after 41 min) to 170 ng/ml (after 91 min). The relative bioavailability was found to be independent of the dose. Unfortunately, these results were obtained in only a partially cross-over fashion. A cross-over comparison was made between the levels from a nasal solution and levels after snorting the same dose of crystalline cocaine HCl. The crystals tended to produce an earlier and higher peak as well as a larger area under the plasma concentration/time curve, but major differences in kinetics were not observed (Wilkinson et al. 1980).

Javaid et al. (1978, 1983) have tested nasal powders of 100 mg (consisting of 16, 64 or 96 mg of cocaine HCl mixed with lactose) in healthy volunteers with a history of cocaine use. In their first study, plasma levels were analyzed without the use of an internal standard, and Barnett et al. (1981) estimate the lower limit of reliability of their analytical assay to be in the range

of 50–100 ng/ml. The highest dose in the study (96 mg) produced a mean peak level of 206 ng/ml after 30 min (Javaid et al. 1978). An internal standard was included in the analytical procedure of the second study, which lowered the limit of sensitivity to 5 ng/ml. In contrast with the findings of Wilkinson et al. (1980), not only the mean peak concentration was found to be dose-dependent, but also the relative bioavailability. A nasal powder with 64 mg of cocaine HCl gave an average peak level of 67 ng/ml after 37 min, whereas a mean peak of 133 ng/ml was observed 41 min after the administration of 96 mg. The mean bioavailability (relative to an intravenous dose of 32 mg of cocaine HCl in the same subjects) was 28% for the dose of 64 mg, and 57% for the dose of 96 mg (Javaid et al. 1983).

From the preceding data, it can be concluded that cocaine absorption from nasal dosage forms is rapid in onset, but that unabsorbed cocaine remains present in the nose for a considerable time. This may explain, at least partly, why the bioavailability of nasal cocaine powders was found to be incomplete.

Several studies have compared the plasma levels and subjective effects of nasal cocaine in volunteers who had previously used cocaine recreationally. In general, maximal central effects tend to occur before the plasma level has reached a peak value (Van Dyke et al. 1978, 1982; Javaid et al. 1978). Van Dyke et al. (1982) found that 0.75 mg/kg and 1.5 mg/kg of cocaine HCl as a nasal solution produced maximal 'highs' within 30 min, whereas mean peak plasma levels of 43 ng/ml and 108 ng/ml, respectively, did not occur before 60 min. They also demonstrated that central stimulation is more intense during the rising phase of the plasma concentration/time curve than during the falling phase. The same phenomenon has been observed in coca chewers (Holmstedt et al. 1979).

The subjective effects of nasal cocaine are, not unexpectedly, dependent on dose, personality and setting. In the cross-over study by Van Dyke et al. (1982), 1.5 mg/kg of cocaine HCl produced a greater subjective response than 0.75 mg/kg. Their report shows, however, that the 'highs' produced by 0.75 mg/kg were less intense than those observed after an initial familarization dose of 0.4 mg/kg. Apparently, the subjects responded differently during the first experiment than during the actual study. A dose of 0.2 mg/kg was also tested, but this dose did not elicit a greater reponse than 0.2 mg/kg of lidocaine HCl, a local anaesthetic without euphorizing properties. It would therefore appear that 0.2 mg/kg (14 mg/70 kg) is below the minimum threshold dose of cocaine HCl needed for central activity by the nasal route, whereas 0.4 mg/kg (28 mg/70 kg) is probably

above this threshold level. Similar data have been obtained by Resnick et al. (1977a,b), who compared subjective and somatic effects of nasal cocaine with those of lidocaine and tetracaine without analyzing cocaine plasma levels. Subjective effects after placebo and after 10 mg of cocaine (as a solution) were the same, whereas 25 mg of cocaine produced some significant subjective changes. More experienced cocaine users rated subjective effects lower than others who showed an equally large somatic repsonse.

2.2.2.5. Dimethyltryptamine and related compounds

There is substantial evidence to suggest that the active tryptamines in Anadenanthera and Virola species undergo extensive first-pass elimination by intestinal and hepatic enzymes (vide 1.1.2.2). Since the nasal route certainly can provide the advantage of bypassing such presystemic inactivation, this may explain why both genera are most often taken nasally in South America. So far as I know, conclusive clinical support for this assumption has not been published. Human studies on the nasal application of tryptamine alkaloids were conducted in the fifties, but they failed to demonstrate hallucinogen-like activity via the nasal route. This is probably due, at least in the case of DMT, to the testing of low and therefore subactive doses.

Turner and Merlis (1959) have assessed the effects of nasal DMT in one healthy volunteer and four schizophrenic individuals. DMT powder in quantities of 5 to 20 mg merely caused a burning sensation in the back of the nose and throat. On one occasion, 10 mg elicited a feeling of being 'hit on the head' in a patient, and this sensation was concomitant with unilateral flushing of the face and mydriasis. Since DMT is well lipid soluble at pH 7.4 (Glennon et al. 1979), poor nasal absorption is not the most likely explanation for the observed lack of psychoactive symptoms. A more obvious reason is inadequate dosing, as the tested nasal amounts were below the threshold dose of 30 mg, needed to elicit subjective perception changes in man by intramuscular injection (Szára 1957).

Turner and Merlis (1959) have also given bufotenin nasally to schizophrenic subjects, and just as in their nasal experiments with DMT, the tested dose range was low. When bufotenin (as pure base or as creatinine sulphate) was blown into the nares, quantities of up to 10 mg merely produced a feeling of fear, associated with flushing of the face, lacrimation, tachycardia, and tachypnea.

The inhalation of bufotenin by humans has also been studied by Isbell. In a letter to Turner and Merlis (1959), Isbell stated

that 'no subjective or objective effects were observed after spraying with as much as 40 mg of bufotenine creatinine sulphate'. This compound consists of 1 part bufotenin base and 1.8 parts creatinine sulphate (Fabing and Hawkins 1956), so 40 mg provides 14.3 mg of bufotenin base. In a letter to Wassén and Holmstedt (1963), Isbell declared that 'inhalation of pure bufotenine in aerosol suspension, or oral ingestion of bufotenine in doses running up to 100 mg (total dose) were without effect'. Isbell's statements provide insufficient details on the manner of inhalation (nasal or tracheal), the test subjects (psychotic patients or not), and the studied doses (100 mg by inhalation or not). Fortunately, Isbell (pers. commun. 1984) has recently informed me that bufotenin was inhaled nasally, and that the subjects were physically healthy male volunteers, aged between 25 and 50, who were imprisoned for narcotic law violations. His communication leaves open, however, whether as much as 100 mg of bufotenin was inactive by oral ingestion only, or also by inhalation.

The subjects of Isbell experienced visual disturbances from 10–15 mg of intramuscular bufotenin (Isbell, quoted by Turner and Merlis 1959, and by Wassén and Holmstedt 1963), and other investigators have reported visual disturbances from 4–16 mg of intravenous bufotenin (Fabing and Hawkins 1956; Bonhour et al. 1967). This would seem to suggest that bufotenin may induce perception changes more readily by injection than by nasal application, which would be consistent with the chemical finding that bufotenin is poorly lipid soluble at pH 7.4 (Glennon et al. 1979) and might thus not readily diffuse through the lipid nasal membrane. Confirmation of this suggestion is still needed, however, especially in view of recent reports that hydrophilic drugs are absorbed from the nose in the rat (Hirai et al. 1981; Su et al. 1984; Fisher et al. 1985).

2.2.2.6. Harmine

Experimental information on the nasal efficacy of harmine appears to be lacking. The physicochemical properties of this alkaloid (Hultin 1965) should permit a good diffusion through the nasal membrane. Harmine may possibly undergo substantial first-pass metabolism after oral ingestion, so that the nasal route might be superior to the oral one (vide 1.1.3.2).

To test this hypothesis, I have taken the same dose of 0.5 mg/kg of harmine base (Fluka, Buchs) nasally and orally on two different occasions. The dose was derived from a report by Slotkin et al. (1970) that 0.5 mg/kg of harmine HCl intravenously

results in substantial plasma levels and in transient somatic effects, but not in distinct central stimulation. At the time of the experiment, I was a non-inhaling tobacco smoker and a regular user of coffee and beer. First, harmine was self-administered into one nostril with a plastic tube as a pure nasal powder, consisting of needles with a length of 10-40 µm. Five days later, harmine was ingested as an oral drink, prepared by dissolving the pure base in 100 ml of tap water, to which some citric acid (Merck, Darmstadt) was added. On both occasions, the harmine was taken after an overnight fast, and venous blood samples were drawn at 0, 15, 30, 60, 120 and 240 min after administration (in the case of the oral drink also at 90 min). Each sample was centrifuged and the resulting plasma was kept frozen until submission to analysis.

Plasma levels were assayed by Laurent Rivier (Institute of Legal Medicine, Lausanne) and Pierre Baumann (Psychiatric University Clinic, Lausanne). They used a gas chromatographical/mass spectrometric (GC-MS) method comparable to that described by Baumann et al. (1984) for harman and norharman. The assay is sensitive down to 2 ng/ml. Details are provided in Appendix E.

On neither occasion was a notable psychoactive or somatic effect felt, and harmine could not be detected in any of the plasma samples. Since Slotkin et al. (1970) reported levels in the range of 300-400 ng/ml at 10-60 min and 80 ng/ml at 240 min after a similar dose intravenously, the last result is unexpected, especially in the case of the nasal powder. Without additional experiments, it is difficult to ascertain, why there is such a large discrepancy between the nasal and intravenous data. The good nasal absorption of caffeine in another self-experiment (vide 2.2.2.3) would seem to argue against faulty absorption as the major cause. A more plausible explanation might perhaps be that the GC-MS method used in the nasal experiment is more reliable than the fluorometric assay used in the intravenous study.

2.2.2.7. Nicotine

In the last few years, smokeless tobacco products have received increasing attention as potentially less harmful alternatives to cigarettes, since they provide nicotine to the craving user without introducing tar and carbon monoxide into the lungs and without contaminating the atmosphere for non-users (Rasche González 1980; Russell et al. 1980). This possibility has prompted studies on the pharmacokinetics of tobacco administration via the buccal route (Gritz et al. 1981), and via

the nasal route (Russell et al. 1980, 1981).

In the seventies, pharmacokinetic evidence that nicotine is absorbed from nasal tobacco snuffs was provided by Temple (1976) who demonstrated nicotine and its major metabolites in the urine of tobacco snuffers.

Russell et al. (1980, 1981) subsequently reported experimental data on the plasma concentrations of nicotine in tobacco snuffers, as measured by gas chromatography. Their first publication describes extremely rapid absorption in an experienced user of tobacco snuff: a single pinch of snuff raised his nicotine plasma level in 5 min from a baseline level of about 20 ng/ml (due to previous snuffing) to more than 40 ng/ml (Russell et al. 1980). The second report confirms this preliminary result, but substantial absorption could only be demonstrated in experienced users. In twelve occasional snuffers, the average increase in nicotine plasma concentration, measured within 8–17 min after a single pinch of snuff, was only 2 ng/ml. Four volunteers who had never used snuff before, did not show any increase at all. This lack of nicotine absorption in the novices may have been related to their initiation with small doses of a very mild snuff. In contrast, a single pinch of snuff raised the mean plasma level of nicotine in seven daily snuffers from 21.9 ng/ml to 34.5 ng/ml after 7.5–11 min. This mean value almost matched the average peak level of 36.7 ng/ml found in a large group of heavy cigarette smokers. As with cigarette smoking, the interindividual differences in nicotine plasma concentrations were large, and the observed increases varied considerably from 2.6 to 34.8 ng/ml. This divergence is probably partly due to the fact that the strength of the snuff, the size of the pinch, and the exact way of snuffing were uncontrolled variables (Russell et al. 1981).

Nicotine is said to undergo substantial first-pass elimination after oral ingestion (vide 1.1.9.2), and snuffing may provide the advantage of avoiding such an effect (vide 2.2.1). However, the principal Indian manner of tobacco use is not oral ingestion but smoking (vide 2.1.11.1). The latter method is rather complex, as it may lead to a bypass of the liver on the one hand and to partial pyrolytic conversion of nicotine (Larson 1960) on the other. Russell et al. (1983) have compared nicotine plasma levels produced by a nasal viscose solution containing 2 mg of pure nicotine with the levels from a commercial cigarette expected to deliver the same dose of nicotine. Both preparations already produced peak plasma levels at 7.5 min, and these levels averaged about 14 ng/ml and 26 ng/ml for the nasal solution and the cigarette respectively. The area under the plasma concentration/

time curve found after nasal administration amounted to 75 % of that produced by smoking. This result cannot be viewed without caution, however, since only three subjects were studied.

More recently, Russell and co-workers have studied the kinetics of repeated nasal doses of pure nicotine in viscose solution. The initial doses of 2 mg produced increases of 0.9–25.7 ng/ml after 7.5 min, and resulted in noticeable light-headedness in four of the five subjects (West et al. 1984).

2.2.2.8. Scopolamine and related compounds

In the fifties, Tonndorf and co-workers conducted various experiments on the nasal administration of scopolamine and atropine in healthy human subjects. Comparisons were made with other routes of administration. The influence of certain parameters on the nasal absorption of these tropane alkaloids was also studied (Tonndorf et al. 1953; Hyde et al. 1953). Data were not obtained in a proper cross-over fashion, but in most experiments at least ten subjects were used for each different treatment. Gas chromatographical/mass spectrometric methods (Bayne et al. 1975) or radioimmunoassays (Wurzburger et al. 1977) with sufficient sensitivity to measure the very low therapeutic plasma concentrations of tropane alkaloids were not yet available. Instead, the research group assessed the anti-sialogogic activity during the first two hours after administration as an indication for the rapidity and degree of drug absorption. This test period of two hours is rather short, especially for the oral experiments, since the anti-sialogogic activity of oral scopolamine and atropine reaches a peak value after 1–2 hours (Mirakhur 1978). In other words, the results say more about the onset and degree of activity than about the duration of effects.

Scopolamine was studied because of its protective action against motion sickness. If its nasal absorption would be rapid, nasal dosing might be a practical way of self-administration with an obvious advantage over oral dosing in already nauseated patients. To test this premise, subjects received 0.65 mg as a subcutaneous injection, as an oral capsule or an oral liquid, and as nose drops. In all cases, the salivary flow dropped below control values. The decline was most marked and rapid after subcutaneous administration. The effect of nasal instillation occupied an intermediate position, and oral ingestion produced the slowest and least marked decrease. Testing of other doses revealed that nasal quantities of 0.1–0.4 mg gave a perceptible drop in salivary production, whereas an oral quantity of 0.35 mg

was without effect. An apparent superiority of the nasal route over the oral one was also found when a dose of 1.0 mg was given via both routes (Tonndorf et al. 1953).

There is substantial evidence to suggest that scopolamine undergoes extensive first-pass metabolism after oral administration (vide 1.1.4.2), so the observed superiority of nasal dosing may well be due to a bypass of presystemic elimination.

The efficacy of nasal atropine was tested, because this tropane alkaloid is an antidote against organic phosphoryl compounds. A comparison was made between 1.0 mg as subcutaneous injection, 1.5 mg as a nasal spray with detergent and as nose drops, and 1.6 mg in the form of sublingual tablets. The preparations did not yield the same reponse at each measure point, but there were no major differences which persisted throughout the test period. It is rather difficult to draw firm conclusions from these results, since nasal instillation of different doses did not clearly show that 1.5 mg was more effective than 1.0 mg or less effective than 2.0 mg (Hyde et al. 1953).

A comparison between nasal application and oral ingestion was not included in the studies. It may well be that oral atropine undergoes first-pass elimination (vide 1.1.4.2), so an advantageous bypass via the nasal route may be suggested not only for scopolamine, but also for atropine. In a recent cross-over study on the peripheral activity of these alkaloids, the ratio of equivalent intramuscular to oral doses appeared to be about 1 : 5-6 for scopolamine and 1 : 2 for atropine (Mirakhur 1978). Consequently scopolamine may profit more markedly than atropine, if nasal administration indeed povides the advantage of avoiding first-pass metabolism of tropane alkaloids.

As to the systemic toxicity of nasal atropine, it is noteworthy that instillation of 2.0 mg produced mild symptoms in some cases. One subject, who accidently received more than 3.0 mg as a nasal spray with detergent, suffered from a moderately severe reaction, consisting of mydriasis, mild nausea, dizziness, and disorientation (Hyde et al. 1953).

2.2.3. Conclusion

The literature yields convincing clinical evidence that atropine, cocaine, nicotine and scopolamine are effective following nasal application, but experimental confirmation of the efficacy of nasal tryptamine alkaloids is still awaited. This seems to be due, at least in the case of DMT, to the testing of

low and therefore inadequate doses.

In self-experiments, caffeine produced substantial plasma levels via the nasal route, but harmine, when 40 mg was taken as a nasal powder, did not produce measurable plasma levels. Without additional experiments, it is difficult to give a definite explanation for this negative result.

CHAPTER TWO PART THREE

THE CHEMISTRY OF YOPO SNUFFS OF THE VENEZUELAN PIAROA INDIANS

2.3.1. Introduction

The Piaroa Indians are a tropical forest people of the Salivan family. They are settled along tributaries of the Orinoco in the Guiana Highlands of the Federal Territory of Amazonas, Venezuela (Wilbert 1958; Kaplan 1975). Several sources indicate that the men of this tribe use an intoxicating snuff called yopo, niopo or niopa (Wavrin 1948; Gheerbrant 1952; Wilbert 1958; Wurdack 1958; Kaplan 1975). Gheerbrant (1952) states that this snuff is the crushed black-brown mixture of unidentified ingredients and the fine white ash of certain herbs. The evidence available from other authors suggests that Anadenanthera seeds are a common ingredient of Piaroa snuffs. The genus Anadenanthera, formerly considered as the section Niopa of the genus Piptadenia, is the probable source of various South American yopo snuffs (von Reis Altschul 1972). According to Wilbert (1958), the Piaroa obtain their yopo snuff from the seeds of Piptadenia trees. The pulverized seed is passed around in a round tray with a handle in the form of a fish-fin and the men snuffing use Y-shaped tubes of bird bone. Wurdack (1958) reports that the Piaroa are avid yopo snuffers, who annually visit the savannas of the upper Ventuari River and those of the middle Parguaza River to collect mature Piptadenia seeds. To prepare the snuff, the bark of Coco de mono (a species of the Lecythidaceae) is burned and the ashes are added to the pulverized seeds. Von Reis Altschul (1972) has identified a yopo specimen, the seeds of which were said to be the source of an intoxicating Piaroa snuff, as Anadenanthera peregrina (formerly known as Piptadenia peregrina). The seeds of this species contain the indole alkaloids N,N-dimethyltryptamine (=DMT), bufotenin (=5-OH-DMT), and 5-methoxy-N,N-dimethyl-tryptamine (=5-MeO-DMT) (Schultes et al. 1977).

Although the Piaroa appear to be familiar with tobacco (Chaffanjon 1889; Gheerbrant 1952; Wurdack 1958; Kaplan 1975), the consulted literature has not yielded evidence that they ever use tobacco as a snuff source. Yet it would appear that ingredients other than Anadenanthera seeds may enter the composition of Piaroa snuffs. There is a vague field report that the Ventuari Piaroa also employ the vegetative parts of an unidentified bush for preparing a snuff (Wurdack 1958). Much more significantly, Holmstedt and Lindgren (1967) have provided

chemical evidence that Anadenanthera is not the only snuff source of the Piaroa. They isolated not only Anadenanthera tryptamines (DMT, 5-OH-DMT, 5-MeO-DMT), but also harmine from a paricá snuff sample of this tribe, collected by Bolinder. The beta-carboline harmine is not an Anadenanthera constituent, but a major Banisteriopsis alkaloid. Unfortunately the snuff was collected without botanical voucher specimens, so it remains unknown, whether the harmine originated from Banisteriopsis or from some other vegetal ingredient. The most comprehensive review on the use of Banisteriopsis by South American natives does not include the Piaroa as a tribe familiar with Banisteriopsis drinks (Friedberg 1965).

Since harmine only rarely occurs in South American Indian snuffs (Bernauer 1964; Holmstedt and Lindgren 1967), the opportunity to study two different yopo samples of the Piaroa Indians was welcomed.

Sample A was obtained from an European art dealer, who had purchased the snuff and some snuff-taking paraphernalia of the Piaroa tribe from the missionary museum in Puerto Ayacucho in Venezuela. The equipment is now in a private collection.

Sample B was collected by a German named Baumgartner, probably during the fifties or sixties. It is presently deposited in the Royal Museum of Central Africa at Tervuren, Belgium. Other than its name would suggest, this museum has a large collection of objects from Venezuelan Indians, including various snuff-taking paraphernalia. Among these items is a Piaroa snuff, which is still in its original 'kherime' container (museum number 74.76.594).

Sample A consisted of dry snuff lumps, while sample B was a dry granular powder.

2.3.2. Analytical methods

In cooperation with Laurent Rivier (Institute of Legal Medicine, Lausanne), both samples were submitted to gas chromatographical/ mass spectrometric procedures comparable to those described by Schultes et al. (1977). Details are reported in Appendix A.

To determine the presence of alkaline substances, 20 mg of ground snuff material was dissolved in 2 ml of freshly distilled water by ultrasounds for 5 min. The pH was determined by a combined electrode (Radiometer PHM 83 Autocal pH meter, Copenhagen).

2.3.3. Results and discussion

Sample A turned out to contain 10 mg/g of 5-OH-DMT, whereas sample B yielded a trace of 5-OH-DMT (<1 mg/g), as identified by retention time on capillary column and mass spectrum. The pH measurements gave values of 9.4 for sample A, and 9.2 for sample B. Neither the presence of the Anadenanthera alkaloid 5-OH-DMT nor the alkaline reaction of the snuffs is surprising, since the Piaroa Indians are reported as using Anadenanthera seeds and plant ashes as snuff ingredients. The substantial difference in quantitative 5-OH-DMT yield might perhaps be related to the condition of the two snuff samples, viz. solid lumps (sample A) versus granular powder (sample B).

Sample B also contained a trace of a second substance with the same retention time on capillary column and mass spectrum as those of harmine. This finding is quite significant and corroborates the report of Holmstedt and Lindgren (1967), who also found harmine in a Piaroa snuff. Harmine is substituted at C-7, so it could not be produced by ring closure of an Anadenanthera tryptamine. In other words, there is at last additional evidence that the Piaroa must have prepared snuffs not only from plants rich in tryptamines, but also from an vegetal source yielding harmine. This conclusion indicates that the tracing of Indian drug materials in European museums and private collections for chemical analysis may lead to interesting results.

CHAPTER THREE

SOME FACTORS TO BE TAKEN INTO CONSIDERATION IN THE MULTIDISCIPLINARY APPROACH TO RITUAL INTOXICATING PLANTS

3.1. Some botanical considerations

In the multidisciplinary approach to native ritual plants, botany forms the crucial hinge between field observations and laboratory results. By providing the scientific identity of the ritual plant, botany opens the way to chemical and pharmacological studies. It goes without saying that careful botanical recording requires the collection of a herbarium voucher specimen. Any field report which does not indicate voucher specimen numbers, does not live up to modern scientific standards and may therefore be open to question. Especially in the early days, many explorers failed to do this, which usually makes it impossible to check the validity of their botanical information. However, a voucher specimen in itself is not the ultimate proof of reliability. Indigenous informants may deliberately supply wrong material, because they do not want to disclose the botanical source of their sacred drug, or because they like to pull the investigator's leg. It is, of course, not the responsibility of the natives, but that of the botanist to collect accurate data.

Original data may be obtained not only by going out into the field but also by studying already collected material. The Amerindian collections of many ethnographical museums comprise paraphernalia for ritual drug-taking, and sometimes the drug itself or its vegetal source is also present. Such materials have often been gathered by travellers who merely recorded ethnological data because they lacked specific botanical interest or training. In such cases, botanical examination may still reveal the identity of the drug source, especially if it can be backed up by the results of chemical analysis. For instance, the Museum for Ethnology in Vienna possesses well preserved paricá seeds of the Brazilian Maué Indians, who are said to have used these seeds as an enema and snuff ingredient. The seeds certainly look like Anadenanthera seeds, and this botanical impression is corroborated by the recent isolation of the Anadenanthera alkaloid bufotenin (vide 1.3). This example clearly illustrates the importance of museum material as a tool to extend our ethnobotanical knowledge on native ritual practices.

Botanical reviews on hallucinogens tend to offer relatively much information about the western hemisphere. This is hardly surprising in the case of proven hallucinogens, for nowhere in the world has the aboriginal use of truly hallucinogenic plants been more varied and extensive than in Middle and South America.

The same tendency, however, is also seen with alleged hallucinogenic plants which have not been properly evaluated by additional field studies, phytochemical analysis, and pharmacological experiments. This appears to be due not only to cultural and botanical differences between the western and the eastern hemisphere, but also to a scientific predilection for the New World. Appendix F clearly illustrates this point by providing an ethnobotanical view of ritual plants and reputed botanical intoxicants of New Guinea natives. It must be emphasized that the table has been compiled without regard to pharmacological validity and that New Guinea sorcerers commonly try to obtain a magical 'heat' or power which is unfolded or augmented by the chewing of spicy plants like ginger (Sterly 1970; Glick 1972; Wolff-Eggert 1977). In other words, certain plants in the table, such as cinnamon, curry and stinging nettles are most probably valued for their 'heating' properties rather than for specific effects on the central nervous system. Other plants, however, may ultimately be proven to have profound psychoactive effects. An interesting candidate would seem to be the Elaeagnus species, which is ritually smoked by the Gimi of the Highlands (Glick 1967). The genus Elaeagnus is rich in beta-carbolines like tetrahydroharman (Hegnauer 1966; Allen and Holmstedt 1980), and such alkaloids are not likely to be pyrolyzed during smoking (Holmstedt, pers. commun. 1983). Nothing appears to be known at present about the effects of tetrahydroharman in man, but central neurochemical changes have been observed after intraperitoneal administration to mice (Buckholtz 1979). While these data are far from sufficient to draw any conclusion, they are interesting enough to warrant closer examination.

A last specific point which should be outlined here, is a tendency in the ethnological and botanical literature to disregard pharmacological definitions of certain terms. For instance, the pharmacological literature associates systemic oral therapy with gastrointestinal absorption. Consequently it is somewhat a misnomer from the pharmacological point of view to denote coca chewing as oral administration, as this practice involves significant buccal absorption (vide 2.1.7.2). A more notable example is the custom to designate hallucinogenic plants as narcotic plants. In pharmacological parlance, the term 'narcotic' does not refer to hallucinogens, but to stupifying agents in general and to morphine-like analgesics in particular (Jaffe and Martin 1980).

3.2. Some chemical considerations

In multidisciplinary studies on ritual plants, chemistry is an important link between the botanical and pharmacological disciplines. It is difficult to speak in scientific terms of the pharmacology of psychoactive plant material until the relevant constituents have been identified and made available for pharmacological studies.

Chemical reports on ritual plants must give careful attention to the investigated material. Voucher specimens are as essential for chemical laboratory data as they are for botanical field data. The material should preferably come from the area where the plant is ritually utilized. For example, suggestions that North American Indians may have taken Acorus calamus in a ritual context, are frequently accompanied by statements that this plant has sedative properties due to its asarone fraction. Unfortunately, such statements are based on studies with samples from India. There is considerable evidence that a substantial asarone fraction cannot be expected in diploid plants of North America, but only in triploid and tetraploid specimens of the Old World (vide 2.1.1.2).

It is well known that the composition of a plant may vary with its parts. In other words, chemical research on ritual plants should include the plant parts used by the natives. Less obvious factors, which may also be relevant, include the method of harvesting and the freshness of the studied sample. For instance, the scopolamine content of a peach flowered Datura candida form varies with leaf age (Griffin 1976), and storage may alter the tryptamine spectrum of Anadenanthera peregrina seeds (Schultes et al. 1977).

Chemists should not limit their research to the botanical sources of ritual dosage forms, but they must also include the ultimate dosage forms, as the original composition may alter during preparation. For example, one step in the preparation of Virola snuffs involves concentration of the exudate to a more viscose liquid. The effect of such a treatment has been assessed in the laboratory for 6-methoxy-tetrahydroharman. This is the major alkaloid in V.cuspidata, which species could possibly serve as a snuff source. Refluxing in water for eight hours results in partial aromatization to 6-methoxy-harmalan and 6-methoxy-harman (vide 2.1.15.2).

The usefulness of chemical results clearly depends on the specificity and sensitivity of the analytical method by which they have been obtained. Illustrative are the paper chromatographical studies on tree Daturas in the sixties. Their failure

to distinguish between l-hyoscyamine and atropine is pharmacologically relevant, since atropine is the racemic mixture of active l-hyoscyamine and practically inactive d-hyoscyamine (vide 1.1.4.2). Chemical data may not only be devalued by inaccuracy of the final assay, but also by the reactivity of the workup procedure. For instance, ecgonine methyl ester is not a genuine Erythroxylum alkaloid, but an artifact arising from prolonged extraction with sulfuric acid or chloroform (Rivier 1981). Similarly, the cannabicyclol-type and cannabielsoin-type cannabinoids reported for Cannabis sativa are artificial (Turner et al. 1980).

3.3. Some pharmacological considerations

In the scientific approach to native ritual drugs, there is a clear-cut distinction between ethnological field observations and pharmacological test results (Alger 1976). All ethnological data on the psychoactivity of indigenous vegetal drugs require careful pharmacological evaluation, whereby due attention must be paid to differences between native and experimental drug administration.

From the pharmacological point of view, the best aid to enter supernatural worlds is an hallucinogenic agent. At present, there appears to be no generally applicable method for detecting hallucinogenic activity except by administering an agent to man and observing its effects. The use of a universal animal model can already be rejected on the ground that there are several classes of hallucinogens which have different effects and different mechanisms of action. Only within a specific class of closely related agents, animal testing may be useful to obtain an impression of the hallucinogenic potency in man. A plausible example is the observed correlation between the human central potency of classical anticholinergic hallucinogens like the Datura alkaloid atropine and the ability to block oxotremorine-induced tremors in laboratory animals. In the majority of cases, however, it is still too early to assess the predictive value of an animal model, or the method has already been found to have insufficient specificity (Brimblecombe and Pinder 1975). In other words, animal testing is not very useful, when a compound does not belong to a group of well established hallucinogens, and even when this is the case, the results may well be inconclusive. If a relationship with an established hallucinogenic class is lacking, animal studies can merely assess the somatic toxicity of the test compound prior to human experiments.

The type and degree of hallucinogenic symptoms depend on individual personality, mental condition, and experimental setting, and they may vary with the dose level (Szára 1961; Faillace and Szára 1968; Stark-Adamec et al. 1981). Perceptual changes are not a reliable criterium, as their origin may be peripheral rather than central, and they may be less prominent than alterations in thought and mood. Nor can these latter symptoms be used indiscriminately as a diagnostic feature, since many non-hallucinogenic drugs are known to affect mood (Schultes and Hofmann 1980b; Grinspoon and Bakalar 1981). A simple and objective criterium for hallucinogenic activity would be cross-tolerance with LSD, but this phenomenon is not observed with hallucinogens in the broader sense (Fanchamps 1978; Jaffe 1980). All in all, the classification of a new compound as a hallucinogen will depend primarily on the integrity and experienced judgement of the clinical investigator and the test subjects. Obviously, observed effects must be carefully recorded to allow comparison with future results on the same compound and with clinical data on other substances which are already recognized as hallucinogens.

Ethnological reports on the trance-inducing effects of tobacco (Wilbert 1972) attest to the fact that a ritual plant may have effects in the native which are more based on cultural preconditioning than on pharmacological activity. Methodologically, the only conclusive way to distinguish between pharmacological and psychological actions is the cross-over double-blind design. Hereby the subject receives the test drug and a dummy drug (placebo) on two different occasions, and neither the subject nor the investigator knows at the time of administration, which drug is being taken. In an experiment by Manno et al. (1974), subjects who had been given placebo cigarettes, but thought that they had received marihuana cigarettes, indicated that they were high and some became actually stimulated. Only after marihuana cigarettes had been smoked in the next testing session, did several subjects question whether they had received marihuana the first time. Hochman and Brill (1971) tested cigarettes with marihuana extracts, varying in strength from 0 mg to 7.5 mg of Δ^9-tetrahydrocannabinol (THC), in regular marihuana users. These volunteers reported the greatest intoxication from the most potent material, but they experienced a higher degree of subjective intoxication from the THC-free extract than from low-potency cigarettes. This might indicate that the THC-free extract contained some other psychoactive constituent, but it may also signify that only the

most potent extract exceeded the threshold level needed for a pharmacological intoxication. A similar pattern has been observed in a recent study on the activity of nasal cocaine in healthy recreational users of this alkaloid. Central stimulation from 0.2 mg/kg, 0.75 mg/kg and 1.5 mg/kg of cocaine HCl was compared with that from 0.2 mg/kg of lidocaine HCl as a placebo. This local anaesthetic induced a more intense 'high' than did the same dose of cocaine HCl, and it was only slightly less psychoactive than 0.75 mg/kg of cocaine HCl (Van Dyke et al. 1982). Such data show that any vegetal drug or constituent which is only mildly psychoactive in uncontrolled studies must be properly compared with a placebo. For potent principles, the placebo-controlled approach is needed to determine the pharmacological threshold level of the drug.

The validity of clinical data is not only enlarged by the inclusion of a placebo in the experimental design, but also by testing a compound in more than one subject. It should be clear that individual experimentation is one thing and that a scientific dose-response study is something else. An experiment in a single individual will seldom, if ever, provide sufficient information. This may be particularly true, when the subject is an experienced user of hallucinogenic drugs. It is well documented that non-hallucinogenic stimuli may precipitate a flashback phenomenon in individuals with a history of LSD-use (Abraham 1983).

Other relevant factors include the influence of concomitant drug use and the mental state of the test subjects. For example, the response to LSD is attenuated by pretreatment with the Rauwolfia alkaloid reserpine and accentuated by pretreatment with the monoamine oxidase inhibitor isocarboxazide (Resnick et al. 1967). It is also known that schizophrenics are less sensitive to the hallucinogenic effects of LSD than normal or neurotic individuals (Fanchamps 1978).

Another point of interest is the duration of the experimental administration. When pharmacological data do not relate to acute effects, but to symptoms of prolonged use, they should not be applied to native practices, unless there is substantial ethnological evidence that the frequency and duration of the native use are equal. For instance, alcohol can induce a psychotic syndrome in alcoholics (Jaffe 1980), but it would be absurd to extrapolate this chronic effect to non-alcoholic natives, who indulge in drinking alcoholic beverages during occasional ritual festivities.

Pharmacological data are mostly not obtained by testing the

whole indigenous dosage form via the indigenous route of administration. Most experiments are performed with isolated constituents, which may be taken in another dose and by another route of administration. Such differences between experimental and native drug uses must be given careful consideration.

It must be verified that the amount of active constituent, which is present in the usual native dose, exceeds the threshold level observed in the pharmacological experiment. Obviously, a native dose will be limited by the somatic toxicity of the active constituents, and the dose problem will be especially relevant for trace components, which occur next to a potent major principle. For instance, among the numerous identified constituents of tobacco smoke, there are various compounds with suspected hallucinogenic properties, such as carbon dioxide, myristicin, nitrous oxide, and beta-carbolines, and there are also hydrocarbons and ketones with deliriant effects. However, all of these compounds appear to be present in such small amounts, at least in commercial tobaccos, that any suggestion of endogenous hallucinogens present in Nicotiana in behaviourally active amounts must be viewed with appropriate caution (Siegel et al. 1977). Another example is the presence of beta-carbolines in Virola species. Since such compounds have monoamine oxidase inhibiting properties, it is sometimes suggested that they prevent the degradation of hallucinogenic tryptamines, which are the main alkaloids in indigenously utilized Virola species. However, the trace amounts in which the Virola beta-carbolines occur, are unlikely to be of pharmacological importance (vide 2.1.15.2).

It must be checked whether there are pharmacological data on the activity via the native route of administration. The difference between oral ingestion in the aboriginal ritual and parenteral injection in the clinical setting could be of particular importance. Some drugs, such as quaternary ammonium compounds, show a poor absorption from the gastrointestinal tract because of their low lipid solubility. Other drugs are inactivated by the acid gastric juices or undergo elimination by intestinal or hepatic enzymes before they reach the general circulation. This last phenomenon, which is commonly known as first-pass metabolism, is observed with many drugs, including the opium alkaloid morphine (Routledge and Shand 1979). A parenterally active amount will only be effective via the oral route, when the drug is absorbed, and is not degraded prematurely. In general, centrally active compounds can be expected to be absorbed well, since passage into the brain and absorption from the gastrointestinal tract are both processes

which require sufficient lipid solubility. Consequently poor absorption of hallucinogenic principles would not appear to be a general problem, although exceptions might occur. There is substantial evidence to suggest, however, that first-pass inactivation is not uncommon for naturally occurring hallucinogens. Extensive metabolism and route-dependent activity have been reported for the tryptamine derivative dimethyl-tryptamine, for the beta-carbolines harmine and harmaline, and for the tropane alkaloid scopolamine (vide 1.1).

Among the native inhabitants of the western hemisphere, oral ingestion is certainly not the only way to elicit ritual intoxication. Major non-oral ways are rectal application (vide chapter one), snuffing (vide chapter two), and smoking (vide Appendix G). Rectal administration is not generally an adequate method to avoid first-pass metabolism, but nasal administration can undoubtedly provide a bypass, and this may also apply to smoking. As to the last way of administration, the picture is complicated by the possibility that the developing heat may destroy existing components (pyrolysis) and may form new ones (pyrosynthesis). For instance, the beta-carbolines harman and norharman in tobacco smoke are largely formed during smoking (Janiger and Dobkin de Rios 1976), whereas the Δ^9-tetrahydro-cannabinol present in a marihuana cigarette only partially survives the burning process (Ohlsson et al. 1980; Turner 1980). Another Indian practice which may lead to a direct passage into the sytemic circulation is the holding of a chewing quid between the gum and the cheek or lip (Wilbert 1975; Plowman 1981b). This is not a pure method to avoid first-pass metabolism, however, when the juice or the plant material is swallowed (vide 2.1.7).

The substantial influence of drug absorption, distribution and elimination on drug action has long been recognized by pharmacologists, who have even devoted a special part of their discipline, viz. pharmacokinetics, to the investigation of such processes. On analogy, ethnopharmacology deserves a branch called ethnopharmacokinetics, which must be aimed at the fate of indigenous drug constituents in the body. This branch must assess whether adequate concentrations of native drug principles are reached and sustained at their appropriate sites of action. In practice, it is quite laborious or even impossible to perform direct measurements at a specific site of action in the human body. Instead, most pharmacokinetic studies perform measurements in a readily accessible body fluid, such as blood, urine or saliva. Although monitoring at these convenient sites has its limitations, it has proved to be very useful in many

cases (Rowland and Tozer 1980). A good ethnopharmacokinetic example is the recent demonstration of substantial cocaine plasma levels in coca chewers (Holmstedt et al. 1979; Paly et al. 1980), which puts an end to speculations that cocaine might be hydrolyzed in the mouth before it is absorbed (vide 2.1.7.2).

The pharmacological activity of a naturally occurring mixture may be different from that of the most active isolated constituent or fraction. Classical in this respect are the rabbit studies by Hijmans (1961) on the expectorant effects of thyme herb, ipecacuanha root, and Allium cepa. This investigator was able to demonstrate that different fractions derived from the same plant were more secretolytic in combination than alone. An interesting experiment on the difference between a crude hallucinogenic preparation and a pure active constituent has been performed by List et al. (1969), who measured the permeation of l-hyoscyamine through the isolated small intestine of the rat. When an aqueous solution with pure l-hyoscyamine was compared with a fresh extract of Atropa belladonna leaves, the permeation rate was found to be 70-80% higher in the case of the extract. As it is difficult to assess the clinical significance of this in vitro result, it is unfortunate that the experiment was not followed by an in vivo investigation.

The most striking example of superiority of a whole native dosage form over its isolated principles may well be the South American beverage ayahuasca, containing mostly Banisteriopsis beta-carbolines like harmine, together with dimethyltryptamine from Psychotria. Although conclusive clinical evidence has not been published, there is growing evidence to suggest that the beta-carbolines may protect the dimethyltryptamine from first-pass inactivation by monoamine oxidase A enzymes, thus rendering the tryptamine derivative less inactive orally (vide 1.1.3.2).

The activity of a constituent may also be modified by other components of the native dosage form, which do not have a systemic action by themselves. Many South American tribes prepare their intoxicating snuffs by mixing psychoactive vegetal ingredients with lime or plant ash. Such alkaline admixtures may facilitate the absorption of the psychoactive alkaloids through the nasal mucosa (vide 2.2.1).

It is clear from these data that the influence of accompanying substances should not be neglected, but it should not be exaggerated either. Hofmann (1982) gave some pills with pure psilocybin to the famous Mexican curandera Maria Sabina who attested that there was no difference in efficacy between the pills and her own psilocybian mushrooms. In contrast with this

report, some ethnological and botanical publications tend to overemphasize the difference between isolated constituents and whole native dosage forms. This may even reach the point where vegetal constituents are assumed out of hand to act in a synergistical manner. It should always be borne in mind, however, that antagonism may also occur, and in many cases the effects will be additive rather than synergistic. For example, Heimann (1965) showed that a mixture of the ololiuhqui constituents d-lysergic acid amide, d-isolysergic acid amide and lysergol in healthy volunteers merely elicits the combined symptoms of each separate alkaloid.

The pharmacological view on hallucinogenic drug rituals must not only consider the influence of accompanying ingredients in the aboriginal dosage form, but also the concomitant use of other separate drugs. This is well illustrated by the clinical finding that alcohol adds significantly to the subjective effects of marihuana smoking (Manno et al. 1974). As is the case with single drugs, folkloristic data on combinations should not be accepted without experimental confirmation. In India, the tamarind fruit is reputed to antagonize the effects of bhang (Cannabis), but Hollister (1976) found the fruit to be ineffective in doses up to 180 g, when it was given an hour before, simultaneously, or an hour after administration of Δ^9-tetrahydrocannabinol orally to man.

3.4. Concluding remarks

Many factors which have been discussed here, are so obvious that it may seem superfluous to review them. Nothing is less true, however, for various publications fail to afford them proper attention. Perhaps the most poignant example why they should never be overlooked is the famous case of the reports by Castaneda (1970, 1972). This author described the use and hallucinogenic effects of a smoking mixture consisting of dried mushrooms with the addition of other dried plants as sweeteners. The mushrooms were vaguely suggested to be a Psilocybe species, possibly P.mexicana. There are substantial scientific reasons to believe that these reports are not authentic, but fictional. For instance, there are no voucher specimens, and the suggestion that these mushrooms could have been P.mexicana must be refuted on the basis of their habitat (de Mille 1980). What is more, the smoking mixture is unlikely to have contained sufficient psilocybin to elicit the profound effects described by Castaneda. In addition, psilocybin is said to be largely degraded during smoking in a

pipe, whereby its availability is further reduced by condensation and deposition on the inner surface of the bowl and stem of the pipe (Siegel 1981). In other words, if proper attention had been given immediately to dose and to way of administration, scientific doubts about the authenticity of Castaneda's accounts would have arisen sooner.

On the other hand, it may also be hazardous to dismiss field data too rapidly as being invalid. This might be illustrated by an early claim that the South American Makusi Indians used Capsicum as a stimulant and excitant (Roth 1924). Since the fruits of most Capsicum forms contain the very pungent principle capsaicin (Hegnauer 1973), I was inclined to conclude that a native Capsicum preparation will not produce any psychoactive effect, but merely extreme local irritation. This idea was somewhat unsettled, however, by the following passage in a 19th century account of travels in Brazil by the German scientists Spix and Martius (1828): 'Auf der Tafel des gastfreien Pfarrers von Chapada fanden wir eine kleine Art von spanischem Pfeffer (Malaqueta), welche hier zu Lande, wie in ganz Brasilien, nebst der kleinen grünen sauren Citrone (Limâo acedo) das gemeinste Gewürz ist, und sich in reinlichen Porcellanschaalen schon durch die schönrote Farbe empfiehlt. Ihr Genuss brachte aber, obgleich die Früchte nicht auffallend scharf waren, uns Beiden die übelste Wirkung: plötzliche Kopfschmerzen, Schwindel, Flimmern vor den Augen und alle Zeichen einer narkotisch-scharfen Vergiftung; doch verschwanden diese Symptome alsbald nach dem Einziehen von Essigdampf in die Nase und einigen Löffeln Essigs innerlich genommen. Weder früher, noch später im Verlaufe der Reise, wo wir diess Gewürz mit Vorliebe gebrauchten, erfuhren wir ähnliche Wirkung desselben. Es ist deshalb wahrscheinlich, dass sich bisweilen das sogenannte Capsicin, welches der Frucht die brennende Schärfe ertheilt vorherrschend in derselben entwickeln könne, während in andern Fällen, wie in den unsrigen, das narkotische Alkaloid entschiedener hervortritt, das den säurefähigen Basen in andern Solaneen, dem Atropin, Daturin, Hyoscyamin u.s.w., entspricht. Welche äussere Verhältnisse zu dieser Verschiedenheit disponieren, verdiente eine genaue Untersuchung'. This report does certainly not provide proof that South American Indians could have valued Capsicum for psychoactive properties, as the uncommon reaction to the malaqueta might have been due to infestation with a toxin producing fungus (Hegnauer, pers. commun. 1984). Yet it shows the risk of dismissing such a possibility off-hand.

APPENDICES

APPENDIX A
PROCEDURES FOR THE CHEMICAL ANALYSES OF THE MAUÉ SEEDS AND THE PIAROA SNUFFS

by
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I. MAUÉ SEEDS (vide 1.3)

Isolation of alkaloids

Ground dry seed material (200 mg) was extracted with ethanol and a small amount of sodium hydrogen carbonate overnight at room temperature. After filtration and evaporation to dryness under nitrogen, the residue was dissolved in a suitable amount of ethanol and submitted to gas chromatographical/mass spectrometric procedures comparable to those described by Schultes et al. (1977).

Gas chromatography/mass spectrometry (GC–MS)

Analyses were carried out on a combined GC–MS instrument (Model 5985A, Hewlett–Packard, Palo Alto). Typical GC conditions used throughout were: SE–54 WCOT fused silica capillary column (25 m x 0.3 mm i.d.), temperature of the oven isothermal at 100°C for 1 min and programmed at 10°C/min to 260°C. Split mode injections of 1.5 µl were used at a helium carrier gaz–flow of 1,2–1,5 ml/min through the column and a split ratio of 50:1. The capillary column was connected directly to the MS source which was kept at 250°C. The ion source parameters were set by the Autotune program providing a 70 eV ionization energy and a 300 µA emission current. Repetitive scanning from m/z 40 to m/z 340 was performed at one scan per sec. The tryptamines that may occur in Anadenanthera seeds were used as reference compounds. Mass spectrometric data for these substances are given by Schultes et al. (1977). Both retention time and mass spectrum of authentic reference compounds served as criteria for the identification of the unknown compounds.

Quantitative analyses were performed by using the same analytical conditions. Solutions of known concentrations of reference compounds were injected after each extract sample. Calculation was made by external standardization of the detector response for each detected compound.

In order to check the occurence of minor alkaloids, a more sensitive setting of the GC–MS was used. By using the selective ion monitoring mode (SIM) the detection could be increased 20 to

50 fold. Appropriate MS peaks of each compound to be detected were chosen and extracts injected. If the selected peaks emerged at the expected retention time for the reference compound, it was concluded that the substance was present in the extract.

II. PIAROA SNUFFS (vide 2.3)

Isolation of alkaloids

Ground dry snuff material (100–200 mg) was extracted with ethanol overnight at room temperature. After filtration and evaporation to dryness under nitrogen, the residue was dissolved in a suitable amount of ethanol and submitted to gas chromatographical/mass spectrometric procedures comparable to those described by Schultes et al. (1977).

Gas chromatography/mass spectrometry (GC–MS)

Analyses were carried out on a combined GC–MS instrument (Model 5985A, Hewlett–Packard, Palo Alto). Typical GC conditions used throughout were: SE–54 WCOT fused silica capillary column (25 m x 0.3 mm i.d.), temperature of the oven isothermal at 100°C for 1 min and programmed at 10°C/min to 240°C. Split mode injections of 1.5 µl were used at a helium pressure of 0.5 kg/cm^2 giving a carrier gaz–flow of 1 ml/min through the column and a split ratio of 50:1. The capillary column was connected directly to the MS source which was kept at 200°C. The ion source parameters were set by the Autotune program providing a 70 eV ionization energy and a 300 µA emission current. Repetitive scanning from m/z 40 to m/z 340 was performed at one scan per sec. The tryptamines and beta–carbolines that may occur in South American snuff materials and their source–plants were used as reference compounds. Mass spectrometric data for these substances are given by Holmstedt and Lindgren (1967), by Agurell et al. (1969), and by Rivier and Lindgren (1972). Both retention time and mass spectrum of authentic reference compounds served as criteria for the identification of the unknown compounds.

Quantitative analyses were performed by using the same analytical conditions. Solutions of known concentrations of reference compounds were injected after each extract sample. Calculation was made by external standardization of the detector response for each detected compound.

In order to check the occurence of minor alkaloids, a more sensitive setting of the GC–MS was used. By using the selective ion monitoring mode (SIM) the detection could be increased 20 to 50 fold. Appropriate MS peaks of each compound to be detected were chosen and extracts injected. If the selected peaks emerged

at the expected retention time for the reference compound, it was concluded that the substance was present in the extract.

APPENDIX B

PRINCIPAL DIAGNOSTIC ACCESSORIES OF MAYA ENEMA SCENES

by
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1978, revised November 1984

[Figure numbers refer to plate numbers in Appendix C of the thesis]

1. ENEMA JUG: Furst and Coe were the first to recognize a certain shaped pottery jug as a central feature in the enema ritual (1977). The direct association between jug type and specific ritual comes from the Coe scene and from a second Tepeu 1 jug in a private collection (Hellmuth Photo Archive A-313). None of the three Tzakol 3 cylindrical tripods which show enema administration include a jug (or any other ceremonial paraphernalia in the simple scenes (Figs. 1a-b; 2). The two paintings showing the actual enema administration are both on vases of the "enema jug" shape. Five additional vases show jugs of the same shape with enema clysters on top or nearby (e.g. Fig. 18b). These paintings of the definite enema clyster in direct association with a pottery container of a specific shape suggest this type of pot was characteristic of the enema ceremony. More than 100 Classic period pictures of such jugs are now known for Petén and Campeche-Yucatan style paintings. Some throne scenes have two to five jugs, often of varying size.

The shape, not the size, is the distinguishing characteristic. Enema jugs have a neck much narrower than the rim. The neck may either be tall or squat. The top rim is wide and sometimes quite thick. The ratio between the rim, neck, and body dimensions varies widely. The jugs can vary in height from .25 m to over one meter, holding an estimated 4 to 20 liters (1 to 5 gallons) of liquid if filled. Some enema jugs have handles on the body. Two jugs - possibly of the enema sort - on a Chipoc style painting (R. Smith 1952: Fig. 15h, C.I.W. Contrib. 56) have handles on the neck. Occasional enema jugs are bound with ropes. One Petén vase and a Petén plate each show a Dance after Decapitation Sacrifice dancer carrying an enema jug with a tumpline (native carrying strap around the forehead holding the jug on the back). One of these scenes includes a clyster. In a complex jug presentation scene (Hellmuth 1976; not a sacrifice related portrait) two

monkeys and a deer-like animal each carry enema jugs on netted tumplines. Enema jugs may be plain, painted with a variety of designs or with a single hieroglyph. Since some enema jugs have round bottoms and thus would have tended to tip over, certain jugs are pictured resting securely in pot stands. One painting pictures an enema jug with a lid (Middle American Research Institute, Tulane University, labeled as being from Honduras).

Once the basic shape of an enema jug is recognized, two can readily be identified from Tikal polychrome vases, one from Temple I's Burial 116; another which I excavated in Burial 196 from Structure 5D-73, the burial of a ruler closely related to Ruler A in Burial 116. Many of the sherds of large jugs found in excavations on the palace floors of Tikal and of Uaxactun, labeled traditionally in technical pottery monographs as "water jugs" or "storage jugs" could in fact have been used in enema rituals. Chemical analysis needs to be done on the residue on the bottoms of excavated jugs.

Several enema scenes picture celebrants drinking next to the same jugs from which the clysters are evidently filled. This fact has led me to recognize that the overall ritual was dedicated to deliberate consumption of large amounts of a certain liquid. Taking an enema was only part of a much longer ceremony. The enema manner of ingestion was used after the celebrant could take no more orally. Thus the jugs which conservative colleagues prefer to term "water jugs" does not rule out their simultaneous utilization in the enema ritual. And, in all those cases where any special use can be determined for these jars, that use is associable with enema clysters. Enema clysters are easy to identify on vases, even when they are not inserted into anuses (see Trait 3).

Although jugs often seen in the Dresden Codex have the same general shape as 8th century enema jugs, no enema symbolism is yet identified in any codex. In the Classic period, smaller, portable jugs, have handles on them and are carried by dancers in the Dance after Decapitation. Such jugs sometimes are decorated with Akbal hieroglyphs. Whether these are portable versions - containing the same essentially alchoholic beverage - as the large enema jugs is not yet ascertained. I do not believe they are "copal bags."

2. "ROW IN JUG TOP" of unidentified objects sticks out of the top of some enema jugs (Fig. 17). These objects are usually in a parallel row, standing out 2 to 6 inches. They are each about the size of a large, wide, bird plume. These objects are not always rigid; otherwise their constitution is unknown. They may be of cloth or perhaps even actual plumes. In one instance a pair of

stylized "smoke" curls issue from the jug through the row of bars. I postulate that these may be essence bars – leaves or segments of a plant steeping in the watery concoction to add flavor or other chemical essence deemed a necessary ingredient for this apparently potent liquid. There is though, no proof whatsoever for this hypothesis. Further study of additional examples from private collections is needed.

Several Yucatecan/Campeche region polychrome paintings on low bowls have fat, rounder, nipple–ended objects sticking out from enema jugs. These are either a regional variation or a different substance. It is also possible that these are food solids meant to soak into themselves essence already in the enema jug liquid, so the bar can later be sucked, eaten, or smoked. We need to find a painting where these bars are being handled outside of the jug to see their full size, and perhaps thereby learn something of their content and function.

3. ENEMA CLYSTER. The clyster is most likely formed of a bone tube (which is insterted into the anus) and a squeezable bulb (of native rubber or animal intestine). The whole apparatus is the same size and shape of modern "ear syringes" used for blowing water into the ear to cleanse them. A beautiful specimen is pictured in color on the polychrome graffiti at Tikal in the palace buried intact by the Maya under Structure 5E–55 (Orrego and Larios 1983: front cover and Lam. 11,A). More than 25 other examples are clearly rendered in Petén paintings (Figs. 3; 7a; 8; 10; 11; 12a; 14b; 16a; 17; 24; 32b; 33; 42). The long bone tube is clearly pictured in a polychrome painting in the Museo Popol Vuh (Fig. 42). Another naturalistic rendering is in Fig. 16a. The specimens of Fig. 18b were repainted in Miami and are not accurate in minute detail (the Miami painter misunderstood the bone tube), though the overall scene is correct in a general sense. Sometimes a little "gasket" can be seen holding the bone tube in place on the bulb. The bulbous end of the clyster often has a nipple–like end. A frequent, diagnostic trait of the clyster is the oval or semi–circular black design on the top middle of the bulb. Feline personage 22 on the Grolier Vase of the 31 Gods holds an exellent example (M.Coe 1973: Grolier 37). The seashells held by personages 1 and 24 on the same vase includes the same symbol.

In use, the enema clyster was dipped into the water jug to suck the liquid into the bulb. Then the enema was either self–administered (especially during the Early Classic; Hellmuth 1985) or insterted or assisted by a young female attendant (Late Classic). Several scenes picture an enema clyster and a drinking cup or U–thing resting directly on top of the enema jug.

To get a rigid bone tube into the anus could have been painful without a preliminary lubricant, and indeed on one bowl a celebrant has his hand near his anus seemingly applying something (Fig. 13e), while a spider-monkey-man behind him holds the syringe ready to inject.

I suspect that many of the deer bone tubes found in excavations of Maya temples, palaces, middens, and burials are actually the tubes of enema clysters. Willey comments on the frequency of such bone tubes: "The bone tube, usually a short polished section of an animal long bone, is a very typical Maya Lowland artifact" (1978:168), which to him (before the Furst and Coe article) were of then unknown function.

Musical rattles may at first be confused with enema syringes, since they both consist of a bulb on a stick. But, enema clysters never have pendants or attached decorations as do musical rattles. No enema celebrant ever has two clysters, one in each hand (or one rattle and one drum (tucked under the arm)) – the standard arrangements for rattle musicians. The clyster has its characteristic side decoration, and the person holding a rattle will not usually wear the clothing of an enema participant or attendant. Associations and costumes – in addition to differences in the object itself – permit ready differentation for the iconographic specialist.

4. BIB of overlapping segments of material is the single most diagnostic trait after the enema jug and clyster (Figs. 7a–b; 13a–c; 17). The direct association of these bibs to scenes with enema jugs or syringes is so fixed that I originally termed these "enema bibs," but of course they are worn on the wrong end for that. The identification as vomit bib came from a Tepeu 1 bowl in the Museo Popol Vuh (Fig. 25). Regurgitation was a natural result of the excessive drinking which was a prelude to the enema (Figs. 24; 25; 27). Bleeding after mouth torture or tooth pulling is a possibility for Fig. 24 but is not yet suspected in the other scenes. Artistic portrayal of bleeding after tongue sacrifice is not documented even in scenes of known relationship to tongue piercing, such as at Yaxchilan. Anthropologists have recorded that when the Lacandon Maya consume fermented balche beer that the natives normally regurgitate the first sips they take due to the unpleasant and harsh taste of this intoxicating beverage. Late Classic paintings demonstrate that most of the "enema" ceremony involved ritualized preliminary drinking and toasting.

After I had identified the bibs, during a presentation of the enema ritual diagnostics at a lecture, Dept. of History of Art, Yale University, ca. 1978–79, Michael Coe accepted the bib identification and pointed out to me that the bib was the same

size, shape, and of the same material as the turbans worn in the same enema scenes. From this observation I suggest the term bib–turban (when worn on the head) or turban–bib (when worn as a bib). The Whipple Vase and a vessel in a West Berlin museum each show the turban–bib held by a female attendant near the man who will be dressed.

These special items of dress are made of hundreds of overlapping segments of unidentified material. On some paintings the segments look like feather ends, in other paintings like flower petals. They could also be bits of painted cloth. The suspicion that perhaps the little oval units of the bib construction might possibly be flower petals (or painted copies on cloth) comes from the overlapping pattern of suspected flowers on stems in bouquets being sniffed in certain throne room enema scenes. One of the pots I excavated from Tikal Burial 196 shows a suspected bouquet of flowers or leaves in a wicker basket next to a small enema jug. In the only scene yet found where the contents of the enema jug itself are pictured (when the jug is turned upside down and emptied) comparable little overlapping units are coming out of the jug (Fig. 4).

When the accessory is worn as a bib, then an enema ceremony is thereby identified. When worn as a turban (especially in Chama style paintings) an enema ceremony is not necessarily being enacted.

5. U–THING: a Red Band style, Tepeu 1 bowl in the Museo Popol Vuh shows three enema enactments, each with two net–headdressed God N devotees on either side of a large 5 gal. enema jug (Fig. 7a–b). Two of the jugs have clearly identifiable enema syringes on top. All three jugs include an enigmatic U–shaped thing on top also. Since other enema jugs picture drinking cups on top (with or without an adjacent enema clyster) perhaps the U–things are just a special shape of drinking cup. Three of the celebrants hold identical U–shaped things as though they were going to eat them – or drink out of them. A woman on the Whipple Vase holds a U–thing while she applies make–up (?) to an enema participant. Whatever its use, it appears restricted to enema scenes.

6. OFFERING BALLS: On the right of the throne in the Princeton 7 scene is a ceramic container with five little balls which Coe correctly identifies as "offerings." With the advantage of a photographic archive of other Maya paintings from private collections and museums it is now possible to relate this bowl to others, and then to use this identification to recognize the same balls on vases of the traditional corpus, such as on a Tikal Burial 116 vase under a lord's throne. In the adjacent panel is another throne with an enema jug underneath it. This ceramic

container in the palace scene has tripod supports and contains the same little oval offerings as on a lively presentation of enema celebrants, a syringe, enema jug with stick bundle (Fig. 17) (see item 7, next). I suspect the offering balls were edible. They may have a little semi-circle painted at their tops, sometimes just like the design on the enema clyster.

A bowl possibly from Campeche shows a man seated in front of a large enema jug holding a large bowl (different than the plates with the offering balls) full of what seems to be comparable offering balls, except here they seem almost to be some kind of fruit. Four of the identical round objects are sticking out of the top of an enema jug in the same position that essence bars are normally found. Still another Campeche or Yucatan bowl has two more clearly defined balls right on top of the jug with the diagnostic little split or semi-circle (really a thin "U"). These little balls may well be to steep in the enema liquid to impart essence, or to soak up essence already in the jug's liquid.

7. STICK BUNDLES are pictured just below the bowl of offering balls on the scene with a Holmul Dancer backrack. These sticks are in two bundles projecting out of a medium sized enema jug. A man holds a clyster nearby and several other attendants wear vomit bibs. On a vase in a West Berlin museum a woman (wearing clothing with a painted, tabbed "turtle carapace" symbol associated with enema attendants, see diagnostic trait 12) offers a bundle of sticks to a man. On a Dance after Decapitation vase (Fig. 33) the sticks are again projecting out of an enema jug, here carried by a feline actor with turban-bib and with a syringe strapped onto his belt front. He looks like a drug peddler coming into town with his wares. Any such sticks as these would traditionally be identified as perforators, especially for bloodletting by penis perforation. But so far no personal bloodletting is associated with the enema ceremony. The only blood is from occasional decapitation. Since in two cases the stick bundles are inside the enema jug, possibly again they are steeping or soaking up some flavor or stimulant. They seem too thin to be cigars, but tobacco should not be ruled out. Their identity and function is unclear. Are the little bundles held in Grolier 43 (non-enema scene) and contained in a serving dish in Grolier 48 (a definite enema jug scene) the same? We can only hope to find in a private collection a painting where these sticks are being handled in some manner where their full size and shape is clearer. So far they are partially obscured by the container in which they are held.

8. DRINKING CUPS in a variety of sizes and shapes are held by enema attendants and celebrants in many scenes. The normal

pattern is two men on either side of an enema jug drinking and toasting one another for some time before actually receiving an enema. Often atractive young ladies serve the cups. Obviously drinking cups are so common in other non-enema contexts that the mere presence of a drinking cup is not enough to identify a scene as related to an enema unless the celebrants are wearing a bib. Paintings often show a drinking cup resting on top of the enema jug. It is possible that U-things (Trait 5) are a special form of drinking cup.

The Cholula murals of the drunkards is certainly similar to many of the drinking scenes around enema jugs on Maya polychromes (Artes de Mexico, Ano XVIII, No. 144, 1971).

9. PELLETS: is a general name for small unidentified objects. In two or three scenes with enema jugs the celebrants are popping little pellets or cookie sized edibles into their mouth. The way they hold these items so reverently as they eat them, the general posture of the celebrant in his setting, suggests that these little snacks are either mighty tasty or else pack quite a stimulating effect upon ingestion into the body system. My original notes nicknamed these "ecstasy cookies" but that term of course could not be objectively substantiated. The pellets are so small that it was hard for the Maya artist to add any symbols to aid in the identification of their content or meaning.

10. CIGARS are smoked in several enema rituals (figs. 12c; 13b-c), but are so widely used elsewhere that they are not diagnostic of the enema ceremony. Robicsek's book describes the effects of smoking a Mesoamerican cigar.

11. PETAL BOUQUETS on long sticks are held by lords and attendants in several throne scenes where enema jugs are nearby. That they are in fact pleasantly scented flowers is suggested by a little bird hovering over a bouquet on Grolier 28 (not an enema scene) and also by one vase where the lord seems to be sniffing at the bouquet. Did the Maya also take stimulating snuff? If so, they consumed drugs through every opening of their body except their ears. Their ears received stimulants from pulsating drum and rattles. The traditional tendency in Maya academia to render conservative interpretations is inappropriate in a situation such as the highly evolved Maya rituals which involved a total chemical assault on every sense organ from a wide variety of stimulants administered in sequence. We must also remember that certain of these drinking and injecting rituals took place before the bloody sacrifice of babies (Hellmuth 1978: 212 and two other vases, unpublished, Hellmuth Photo Archive) as well as of adults followed by a gory dance of crazed priests and ritual attendants.

12. BUMP OUTLINED DECORATIONS ON WOMEN'S HUIPILS are

noticeable on enema related scenes (Hellmuth Photo Archive A–358a; 456981–66 (West Berlin); and 48667–2). Some stylized water lilies (in other, unrelated scenes) have the water lily pad with the same pattern of bumps around the edge.

13. CONGLOMERATE MONSTER GOD HUT is a special construction seen three times in front of enema rituals, on the Whipple Vase (Fig. 18a), on the other side of Fig. 22 (Hellmuth Photo Archive A–358a); and on the other side of Fig. 21 (Hellmuth Photo Archive 486667–2). This hut is composed of a stack of monster faces. Whereas the Whipple Vase is totally overlined and partially re–created in Miami, discovery of the other two untouched Maya paintings in original condition certifies reality of the overall layout of the Whipple Collection scene.

PARTICIPANTS

Standardized enema ceremony participants include:

(a) Water Lily Jaguar is as frequent in enema jug scenes as he is in Dance after Decapitation paintings though his costume may be different in each situation. For the Dance after Decapitation he wears a red or orange scarf. For the enema ritual he wears a turban–bib. Several Tepeu 1 multiple resist style paintings show one of each feline together (private collection, Zurich), demonstrating that the two costumes are both separate yet can be worn in a combined ritual – an enema associated with sacrifice. That it is a human actor wearing a costume is clear from another vase where the celebrant's head sticks out from his feline costume (Hellmuth 1978:210, upper left).

(b) Spider Monkey is as common in enema jug scenes as he is in Dances after Decapitation. In death ceremonies, though, the monkey conflates with a deer, and may wear a red or orange scarf, or carry a fruit–like object. In enema scenes the monkey more likely has an enema turban–bib and may wear a loincloth (Figs. 13a–e). The deer is not as prominent in enema scenes as is the monkey, except where God D is present.

(c) Drug bird is distinguished by a beak with fat, out–turned end. This beak is unlike any real bird yet this avian character is present in at least four enema scenes. Hellmuth 1978:210 illustrates one. On a matched set of two nearly identical Late Classic Petén plates an anthropomorphic dancer in net weave body stocking (yet not in this case a God N) has one of these special bird beaks attached to his face. Of the many different birds in enema rituals, this is the easiest character to recognize.

(d) Enema birds in general are more common in highland Guatamalan paintings (Fig. 9), but birds do occur on Petén plates together with enema jug drinking scenes. One Late Classic plate in the

Denver Art Museum has highland type bird celebrants next to enema jugs. Some of the birds shake musical rattles, just as on the series of highland vases (one of which is in the American Museum of Natural History, New York). Altogether at least five different species of birds are represented in this group of highland vase paintings and other species are sure to be recognized as additional vases become available for study. Whereas birds in Dance after Decapitation scenes tend to be raptorial, have slit stomachs, or carry snakes, enema birds tend to be simplier and more anthropomorphic. Birds also occur in lowland paintings, as on a Red Band style bowl (Fig. 12b).

(e) Big lipped frogs are dominant personages on one Tepeu 1 enema scene (Fig. 13a). One holds a giant water lily in his lap. The frogs on this one bowl have large, round eyes and thick, almost bird-beak like lips. Other frogs, but differing in anatomical and mythical detail, appear on the Vase of the 31 gods (Grolier 37). In some of these 7th-8th century paintings it is hard to distinguish between toads and frogs, or even iguanas.

(f) Other animals appear in enema scenes. One may be an armadillo (Fig. 12b). The Vase of the 31 Gods (Grolier 37) pictures other beasts. Since every rendering is a little bit different it is difficult to ascertain whether the differences are stylistic or anatomical.

(g) Rain Beast is the name given by Coe to the officiating deity on the Whipple Vase. He is generally considered to be GI (though Coe keeps them separate).

(h) God N or devotee is the principal celebrant. A full-fledged God N is elderly and wears a conch shell (or turtle shell or snail shell). A devotee may be of any age, and shows his devotion to the God N cult by wearing net weave napkin headdress (Figs. 7a-b; 9b). God N, and devotees, appear in many other ceremonies besides those related to enemas.

(i) God D (Fig. 14c), especially when seated on a planetary band throne often has enema jugs associated with him (Fig. 15). This elderly slouching god may have a rabbit or young woman (the Moon Goddess most likely) on the throne behind him. God D appears in many scenes other than those related to enemas. He appears himself, rather than in the guise of devotees.

(j) Women wearing huipils decorated with bump-outlined forms are diagnostic of enema attendants.

DISTINCTIVE RITUAL TYPES WHICH EMPLOYED ENEMAS AS PART OF LONGER ENACTMENTS.

There is not really just one "enema ritual." Actually, enemas were taken in:

A) plain palace settings with minimal special costumes and pagentry (Figs. 16; 35).
B) multi-actor settings but still with minimal costumes (Fig. 36).
C) With God N devotees, often with the Cauac Monster God Hut, and female attendants (Figs. 7; 11; 18; 19; 20; 21; 22; 23).
D) As complex enema rituals, generally with animals (Figs. 5; 12; 13; 17; 24 [Type E also]; 34).
E) As part of the Dance after Decapitation Sacrifice (Figs. 24 [aspects of Type D]; 27; 28; 31; 32; 33; 40; 42).
F) By God D (Figs. 14; 15; 38 [God D is on other side]).

As catologing of photographs continues additional categories of enema ritual can be classified.

Based on more than 50 Late Classic scenes, I propose the following hypothetical reconstruction of the ceremony, Type C, which shares many features with Type D.

Two specially dressed men seat themselves on either side of a giant enema jug, often with an attractive young female attendant. A clyster and drinking cup are ready on top of the container of special drink. With small cups the celebrants dip into the jugs, fill their containers, and drink. They keep drinking to a state of intoxication. 16th-17th century Spanish chroniclers document that such alcohol consumption was a standard part of Maya rituals. One purpose was to induce visions, a form of communication with their gods. Celebrants or attendants costumed as deer, felines, and spider monkeys dance in bearing additional jugs in tumblines. Other bizarrely costumed characters also appear.

All of this interaction takes place in front of a Monster Face Conglomerate "God Hut," a ceremonial structure of perishable material. Inside the hut reigns the supervising or honored deity, in two cases GI (Whipple Vase and the vase of Fig. 22 [on the other side]); in one case a God K-like supernatural, (Fig. 21, other side, Hellmuth Photo Archive 486667-2). In the background a musical group plays, with gourd rattles, turtle carapace rasped with deer antler, and small drums. Women attend to the pre-enema preparation, fanning, undressing, massaging, costuming, and applying make-up to the men who will receive the clyster. Two paintings picture the women holding the bib-turban ready to dress the man nearby. All the while the men continue drinking from cups dipped into the enema jugs. The participants also make use of

special little "cookies" and "U-things" (either another edible or make-up material). Flower-like bouquets are offered and sniffed and potent cigars are smoked continuously. At a certain point the God N devotees parade near their enema jugs, with the female attendants behind them, getting ready to take off their loincloth apron. The devotees render obsequience to the god in the conglomorant hut. As a final event, the men recline and bend over to receive the enema, administered themselves, or by the women.

The Vase of the 31 Gods (Grolier 37) depicts a variant, and even more complicated enema ritual, featuring God D (though not a sky band God D type enactment). The multiple-resist Tepeu 1 vases (Figs. 31; 32) and the same ceremony on vases of other styles (Figs. 24; 25; 27; 28; 42), present the combined enema ritual together with the Dance after Decapitation Sacrifice. Figs. 16 and 35 show the simpler, Type A enema administration.

I feel it is a fair conclusion from the frequency of drinking scenes on Maya pottery, combined with Landa's and Margil de Jesus' comments on native Maya alchoholic consumption in religious rituals to recognize that drinking in the Maya palace reached high levels comparable to that of ancient Greece and Rome, if not more. The Cholti-Lacandon of Sac Balam, Chiapas (Nuestra Senora de los Dolores de Lacandon, 1694-ca.1710) had attendants whose job it was to keep the caciques drinking and intoxicated four days in a row for a single ceremony (Margil de Jesus 1984). And the Maya were religious all year long. Considering that at the same time the Maya were smoking native cigars of considerable potency in nicotine alone, not to mention other stimulants not found in a Havanna puro or in a Marlboro, eating pellets and balls of potential stimulating action, and then injecting chemical substances directly into their body through an enema clyster, would certainly affect them. We cannot discount the effect of music and dance. Ecstatic states can be obtained through suggestive music and dance alone, and bare breasted young females may not have gone entirely unnoticed either. Imagine what condition they were in on the morning after a four day ceremony. Aztec excesses are simply better documented. Maya polychrome paintings at last make available for the Maya what Spanish chronicles and Aztec codices long ago provided for central Mexico.

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APPENDIX C

A PICTORIAL APPROACH TO ENEMA SCENES ON ANCIENT MAYA POTTERY

[All plates originate from the archive of the Foundation for Latin American Anthropological Research (St.Louis, Missouri), except plate 3 (Peter Furst), plate 40 (Royal Museums of Art and History, Bruxelles) and plate 41 (John Justeson). Where possible, information on time period, (tentative) provenance, present location and condition is given on basis of personal communications by Nicholas Hellmuth in 1984. Previous publications are sometimes indicated, but no attempt has been made to be exhaustive.]

PLATE 1. Painted polychrome Maya cylindrical tripod.
Time period: Early classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Condition: feet are broken off.
Description: Both sides show a personage bending forward, who is giving himself an enema (1a, 1b).

PLATE 2. Painted polychrome Maya tripod bowl.
Time period: Early classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publication: Robicsek 1978.
Description: A personage bending forward is giving himself an enema (cf. plate 1).

PLATE 3. Painted polychrome Maya pot.
Time period: Late classic, probably Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publication: Furst and Coe 1977.
Description: Plate 3a shows the actual shape of the vase. Plate 3b is a painting of the whole vase by Diane Peck. It shows seven pairs of a male and a female. One of the females is inserting a syringe into the anus of her companion (bottom middle), and a second male is himself performing this task (top right). Two other males have an enema syringe tucked into the belt (top left and bottom right). Between the couples, there are nine jugs with painted dots at their mouth. Several males have a bib around their neck, and some of them are wearing this garment as a head-dress. Most females are holding an U-shaped object in the hand,

and some of them offer a bib to their companion. Between the top and bottom, a glyph appears in a repetitive band. Coe (1978) suggests that this glyph may be the sign for the enema ritual, and adds the speculative notion that it represents an anal sphincter muscle.

PLATE 4. Carved Maya bowl.
Time period: Late classic.
(Tentative) provenance: Yucatan, Mexico.
Present location: private collection.
Description: A personage is pouring black-eyed circular forms out of a jug.

PLATE 5. Painted polychrome Maya bowl.
Time period: Late classic, Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A jug emitting scrolls is flanked by an indeterminate creature (left) and a Water Lily Jaguar (right).

PLATE 6. Painted polychrome Maya bowl.
Time period: Late classic, probably Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A seated figure is surrounded by two large jugs, which are emitting dotted lines.

PLATE 7. Painted polychrome Maya bowl (Red Band style).
Time period: Late classic, Tepeu 1.
(Tentative) provenance: Petén or Motagua, Guatemala.
Present location: Museo Popol Vuh, Guatemala City.
Previous publication: Robicsek 1978.
Description: The scene shows large jugs with an U-shaped object on top, which are flanked by two males wearing bibs (7a, 7b). On one side of the bowl, the right male is holding a second U-shaped object, and there is also an enema syringe on top of the jug (7a).

PLATE 8. Painted polychrome Maya bowl.
Time period: Late classic.
(Tentative) provenance: Campeche or Yucatan, Mexico.
Present location: private collection.
Description: The scene shows a large jug with a probable syringe on top (8a) and seated figures holding a bowl full of large black-eyed forms (8a, 8b).

PLATE 9. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Highlands, Guatemala.
Present location: private collection.
Condition: possibly repainted.
Description: A bird-like creature holding a probable enema syringe (9a) is being offered a cup by a second bird-like creature (9b). A large jug is shown between them.

PLATE 10. Painted Maya vase (Codex style).
Time period: Late classic.
(Tentative) provenance: ?
Present location: private collection.
Description: A large jug with a syringe on top of it is flanked by a canine creature (left) and by a male holding a drinking cup (right).

PLATE 11. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén or adjacent area, Guatemala.
Present location: private collection.
Description: There is a large jug with a probable enema syringe on top of it. A male is painted on the jug or sitting in front of it. According to Coe (pers. commun. 1985), this personage is probably God N.

PLATE 12. Painted polychrome Maya bowl (Red Band Style).
Time period: Late classic, Tepeu 1.
(Tentative) provenance: Guatemala.
Present location: private collection.
Previous publication: Robicsek 1978.
Description: The centre of the scene shows a large jug with small circular forms on top of it, and dotted lines are coming out of it (12b). A personage is either painted on the jug or sitting next to it. The jug is flanked by a large black bird (left) and another animal (right). Left of this scene, two males are gathered around a huge enema syringe, out of which evidently something is pouring (12a), while the right part shows a smaller jug, again with small circular forms on top (12c). It is surrounded by two males, the left one holding a possible enema syringe.

PLATE 13. Painted polychrome Maya bowl.
Time period: Late Classic, Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publications: Anonymous 1976b; Hellmuth 1978; Robicsek 1978; Torres 1984.
Description: The scene shows three Water Lily Jaguars with objects that might be small jugs at the tip of their tail (13a middle; 13c middle; 13e left). Out of the objects the same scrolls are coming as out of the cigarette held by one of the Jaguars, who also has a jug in front of him with a possible syringe on top (13d right). Besides the Jaguars, there are four monkeys, each of them with a cigarette from which scrolls are being emitted (13b middle; 13c left; 13d middle; 13e right). One of the smoking monkeys seems to hold up an enema syringe, while the figure in front of him is conspicuously holding his hand near his anus (13e middle). There are four of such indeterminate creatures in the scene (13b left; 13b right; 13c right; 13e middle). Hellmuth (1978) suggests that they are frogs, but this view is not shared by Robicsek (1978). One of them is holding something that might be a water lily flower in his hand (13b left). Several personages are wearing a bib.

PLATE 14. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publications: de Smet 1981b, 1984.
Description: The scene shows two males (14a, 14b), who are kneeling in fornt of God D on a throne (14c). The left male has a cup in his hand and a cigarette in his mouth (14a). The other one is holding a deer antler in his left hand. He is kneeling next to a jug with a probable enema syringe on top of it. Besides the jug, there is a plate filled with segmented rectangular forms (14b).

PLATE 15. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: Museum of the American Indian, New York.
Description: God D is seated on a throne (cf. plate 14c). Under the throne, jugs are depicted with plume-like forms coming out of them.

PLATE 16. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publications: Torres 1984.
Description: Two large jugs are standing next to a throne, on which a male with a large enema syringe in his hand is seated (16a). A female companion is offering a bowl to the male (16c), and there is a smaller jug under the throne (16b).

PLATE 17. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: Two persons are sitting around a jug, filled with bundles of stick-like forms (cf. plate 14b). The left person is holding an enema syringe. Above the enema jug stands a tripod full of large circular forms (cf. plate 18d).

PLATE 18. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Campeche, Mexico or Petén, Guatemala.
Present location: private collection.
Condition: repainted.
Previous publications: Coe 1978; Hellmuth 1978.
Description: In the left part of the central scene (18b), there are two pairs of a male and a female. The females have their hands tucked under the armpits of the companion. In front of the males, there are two jugs with enema syringes on top, and scrolls are being emitted from one of the syringes (bottom). The right part of the central scene (18c) shows two female servants (left side), who are facing two males (middle), accompanied by two other females (right). The upper male is fanned by his servant. He has a jug in front of him and the female behind him offers him a bib. The lower servant holds up a mirror to the male who is apparently painting his face. He has an U-shaped object in his left hand, possibly a paintpot. Coe (1978) identifies all the four males as God N.

Behind the central figures, three monsters are playing a musical instrument (18d). They are almost identical to the one, who is sitting in a hut on the left (18a), and who seems to be their conductor. According to Coe (1978), they may represent Rain Beasts. The orchestra instrumentarium consists of a rattle (top), a drum (bottom left), and a turtle shell struck with a deer antler (bottom left). There is a jug with a syringe on top, out

of which scrolls are coming, behind the rattle player. A tripod filled with oval forms is shown in front of him.

PLATE 19. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Condition: repainted.
Previous publications: Robicsek 1978; Torres 1984.
Description: A male is standing in front of a large jug with a syringe and a drinking cup on top of it (19a), while a female companion is untying his loincloth (19b). The netted head-dress of the males indicates that they represent God N's or his devotees. This vase painting is one of a series, all of which show females undressing males (plates 19–23).

PLATE 20. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Guatemala.
Present location: private collection.
Condition: possibly repainted.
Description: Both sides of the vase show a male standing in front of a jug with a drinking cup on top (20a, 20b). The male is followed by a female, who appears to untie his loincloth (cf. plate 19).

PLATE 21. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Guatemala.
Present location: private collection.
Description: A male is standing in front of a jug, out of which scrolls are being emitted (21a). Behind him a female is standing, apparently untying his loincloth (21b) (cf. plate 19).

PLATE 22. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: Both sides of the vase show males standing in front of a jug (22a, 22b). They are followed by females, who appear to untie their loincloth (cf. plate 19).

PLATE 23. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: ?
Present location: private collection.
Condition: repainted.
Description: A male is standing in front of a jug, followed by a female, who appears to untie his loincloth (cf. plate 19).

PLATE 24. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publication: Coe 1982.
Description: This part of the vase shows a bird (top), an animal with canine and rodent features (middle), and a male vomiting over an enema syringe (bottom). Coe (1982) identifies this latter personage as God A'.

PLATE 25. Painted polychrome Maya bowl.
Time period: Late classic, Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: Museo Popol Vuh, Guatemala City.
Previous publication: Hellmuth 1978.
Description: A jug with a possible enema syringe on top is surrounded by a vomiting creature (left) and a Water Lily Jaguar (right).

PLATE 26. Painted polychrome Maya bowl.
Time period: Late classic, probably Tepeu 1.
(Tentative) provenance: ?
Present location: private collection.
Condition: repainted.
Description: A bib-wearing male has his hand in a large jug, apparently to fill up a drinking cup or enema syringe.

PLATE 27. Painted polychrome Maya vase.
Time period: Late classic, probably Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A vomiting Water Lily Jaguar with a bib around his neck is standing next to a jug with a cup on top of it.

PLATE 28. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A Water Lily Jaguar is wearing a bib and holding a drinking cup.

PLATE 29. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A Water Lily Jaguar (29b) is standing in front of a large jug full of stick-like forms, on top of which there are circular forms (29a).

PLATE 30. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: One side of the vase shows a male holding a brush or some other flexible object in each hand. He is seated in front of a jug (30a). The other side shows a giant toad- or frog-like monster, characterized by the 'ear' with three dots. There is a vaguely painted jug in front of him (30b).

PLATE 31. Painted polychrome Maya vase (Multiple Resist).
Time period: Late classic, Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: One side of the vase shows a Water Lily Jaguar wearing a bib (31a), while the other side displays a Dance after Death Jaguar, characterized by his red-orange scarf (31b). The latter character is a common participant in scenes representing a special dance performed after human sacrifice. This vase therefore raises the possibility of a relation between the enema ritual and the dance after death ritual (cf. plate 32).

PLATE 32. Painted polychrome Maya vase (Multiple Resist).
Time period: Late classic, Tepeu 1.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: On one side of the vase, a smoking male is seated, who has tucked a jug under his left arm (32a). The other side shows a Water Lily Jaguar (32b). He is wearing a red-orange scarf, which is characteristic of a Dance after Death Jaguar (cf. plate

31), but under this scarf, he may be wearing a bib. In his left hand, he carries a portable jug which is commonly seen in Dance after Death scenes, and in his right hand he is holding a possible enema syringe. The simultaneous occurrence of objects characteristic for the enema scenes and for Dance after Death scenes raises the possibility of a relation between the two rituals (cf. plate 31).

PLATE 33. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Previous publication: Hellmuth 1978.
Description: A bib-wearing jaguar is carrying a jug full of pointed forms in his backpack. A possible enema syringe is sticking out of his belt.

PLATE 34. Painted polychrome Maya plate.
Time period: Late classic.
(Tentative) provenance: Campeche, Mexico or Petén, Guatemala.
Present location: Denver Art Museum, Denver.
Condition: repainted.
Description: The middle of the plate shows a male on a throne, who is being offered a probable cup by a servant. The rim shows jugs with things sticking out of them and personages holding drinking cups. One of the jugs is flanked by musicians with rattles and a drum (rim left).

PLATE 35. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A man who is sniffing or closely looking at a bouquet-like object, is standing next to a large jug with a row of things on top of it.

PLATE 36. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: The scene shows large jugs (36a, 36b) and a man holding a bouquet-like object close to his face (36a far left).

PLATE 37. Painted Maya vase (Codex style).
Time period: Late classic.
(Tentative) provenance: ?
Present location: private collection.
Previous publication: Robicsek and Hales 1981.
Description: A large jug appears to be tumbling over, thereby spilling its contents.

PLATE 38. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: Mint Museum of Art, Charlotte.
Condition: possibly repainted.
Description: A female holding an animal is seated on a throne. Hellmuth (pers. commun. 1984) identifies her as the Moon Goddess holding a rabbit, her sexual companion. A jug is standing in front of her and other jugs are seen under the throne. The latter ones show black-eyed circular forms on top of smaller plain ones.

PLATE 39. Painted polychrome Maya vase.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A female is carrying a jug.

PLATE 40. Painted polychrome Maya vase.
Time period: Late classic.
(Tentative) provenance: ?
Present location: Royal Museums of Art and History, Bruxelles.
Description: An animal is carrying a small jug.

PLATE 41. Painted Maya vase.
Time period: Late classic.
(Tentative) provenance: Highlands or Motagua, Guatemala.
Present location: ?
Description: A large jug with protruding rod-like objects (41b) is surrounded by an animal personage (41a) and a human figure (41c) with a cup in their hand.

PLATE 42. Painted polychrome Maya bowl.
Time period: Late classic, Tepeu 2.
(Tentative) provenance: central Petén, Guatemala.
Present location: Museo Popol Vuh, Guatemala City.
Previous publication: Hellmuth 1978.
Description: On the right, a jaguar is carrying a syringe and a jug.

PLATE 43. Painted polychrome Maya bowl.
Time period: Late classic.
(Tentative) provenance: Petén, Guatemala.
Present location: private collection.
Description: A mammal is jumping out of a jug.

APPENDIX D

PROCEDURE FOR THE PLASMA LEVEL DETERMINATIONS OF CAFFEINE

by

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Extraction procedure

100 µl of plasma was brought in a centrifuge tube of 5 ml. 100 µl of the internal standard solution (D4030 50 mg/l in water), 100µl of water, 100 µl of ammonium sulphate solution (saturated) and 3.0 ml of dichloromethane were added. The tube was vortexed for 2 min and centrifuged for 5 min at 4900 t.p.m. The water phase was removed, and the organic layer was transferred to a centrifuge tube with a conical bottom and evaporated at 55°C under nitrogen. The residue was resolved in 1000 µl of the mobile phase by vortexing for 30 sec. 10 µl was injected into the HPLC system.

High Performance Liquid Chromatography (HPLC)

The HPLC system consisted of the following components: Pump: Waters, type M45; Detector: Waters, Model 441 U.V. 280 nm R=0.01; Injection sytem: Waters, wisp 710B; Integrates: Spectra Physics, SP 4100; Column: Merck, Hibar column packed with Lichrosorb Si-60-5 µm, catalogue number: 50388, length: 250 mm, I.D.: 4.0 mm.

The sample was concentrated with the aid of the sample concentrator type SC-3 of Techne.

The chromatographical conditions were: room temperature; flow rate: 1.0 ml/min.; pressure: 1300 p.s.i.; composition of mobile phase: chloroform 55%, n-heptane 41%, methanol 4%, and acetic acid 0.05%.

APPENDIX E
PROCEDURE FOR THE PLASMA LEVEL DETERMINATIONS OF HARMINE

by
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and
Pierre Baumann
[Psychiatric University Clinic, Lausanne, Switzerland]

Extraction procedure

Typically, 1 ml of plasma was diluted with 1 ml of water and 50 ng of harmane added as internal standard. The pH of the water was brought to 9 with 2N NaOH and 1 ml of a toluene/isoamyl alcohol mixture (85:15) was added. The toluene/isoamyl alcohol fraction was reduced to 50 µl and 3 µl were injected into the GC–MS system.

Gas chromatography/mass spectrometry (GC–MS)

Analyses were carried out on a combined GC–MS instrument (Model 5985A, Hewlett–Packard, Palo Alto). Typical GC conditions used throughout were: SE–54 WCOT fused silica capillary column (25 m x 0.3 mm i.d.). The column was connected directly to the MS source and the carrier gas flow rate (helium) was 1.5 ml/min at 200°C through the end of the column. Temperature conditions were: initial oven temperature 155°C for 0 min; heating rate 30°C/min; final temperature 260°C for 10 min. Injection port for splitless injections was maintained at 280°C and the tranfer line and ion source were 250°C and 200°C, respectively. For allowing the sensitivity and specificity necessary for accurate harmane and harmine quantifications, Selective Ions Monitoring (SIM) or Mass Fragmentography was used. Using this mode, the MS was set up for detecting 4 ions representative of the molecules (182.0 for harmane and 169.0, 197.0 and 212.0 for harmine). Each ion was measured for 100 msec. Calibration curves were obtained by proceeding standard solutions in the same way as the plasma samples.

The calibration curve obtained by SIM with harmane as internal standard indicated that the response of the detector was linear over the 0 to 50 ng/ml levels.

The limit was set up to 2 ng/ml as it was from such a level that a clear signal emerging from the noise could be measured. It was found that harmane is a good internal standard as no signal at all could be detected at the place of emergence when drug free

plasma was used. This is not the case for norharmane (*).

(*) Baumann,P., Rivier,L. and Perey,M. (1983) In: A.Frigerio (Ed.) Recent Developments in Mass Spectrometry in Biochemistry, Medicine and Environmental Research, Vol.8, pp.7–18

APPENDIX F

SOME RITUAL PLANTS AND REPUTED BOTANICAL INTOXICANTS OF NEW GUINEA NATIVES (*)

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Acalypha insulana (Euphorbiaceae)			is also known as Acalypha hellwigii; New Guinea natives are sometimes said to smoke the leaves of var. mollis (1,41)	Leaves are also used as tobacco wrapper (26)
Acorus calamus (Araceae)	api	IAI—people	Rhizome is eaten in certain ceremonies, whereafter the participants feel able to contact spirits (48)	
		Raiapu Enga	Huntsmen spit chewed sweet flag into the nose of their dogs to promote their ability to locate game (10)	North American Sioux Indians spit masticated sweet flag into the mouth of a puppy to make it a fierce watchdog (23)
Alocasia sp. (Araceae)		Baining	Participants in dancing ceremonies are said to eat Colocasia esculenta or tubers of Alocasia indica, followed by Laportea leaves to counteract the poisonous action (19,20)	The New Guinea flora does not include the Javanese A.indica, but other Alocasia species (41); in Australia, juice of Alocasia macrorhiza is considered an antidote for Laportea gigas (25)
		Wewäk—Boikin	Malevolent sorcerers may start with eating a 'gombi' mixture which includes wild taro, wild lemon, grated coco—nut, bark of the 'mali' tree, and several kinds of ginger (12)	

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Amaracarpus sp. (Rubiaceae)		Gimi	Vide Elaeagnus sp.	
Amaranthus sp. (Amaranthaceae)	tumeni	Orokaiva	'Tumeni' and 'siroru' (flame-coloured coxcomb) are included in a mixture intended to provoke a ceremonial shaking-fit (44)	
Archontophoenix sp. (Palmae)		New Britain	Nut is chewed as intoxicant (26)	The collection of the State Herbarium in Leiden contains only Archontophoenix from Australia (41)
Beaumontia sp. (Apocynaceae)		Lake area or Kema valley	Smoked instead of tobacco (22)	Misspelled as 'Bomoncia'; said to occur among the Australian Arunta as well (22)
Bubbia sp. (Winteraceae)	kikisira	Gimi	Man of power smokes tobacco with 'kikisira' bark to pass into a dream-like state during a healing ceremony (13)	
Capparis sp. (Capparaceae)	kara	Western islands Torres Straits	To become a magician, the novice must eat the unripe fruit; leaves and root are eaten by magicians wanting to be wild (15)	

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Castanopsis acuminatissima (Fagaceae)	kawang	Banz area	Seed is said to have similar intoxicating effects as certain mushrooms, when steamed and eaten in quantity (16)	Against the advice of their parents, children sometimes persist in eating the raw kernels, because of their pleasant taste; this often leads to emaciation, anaemia and mouth ulceration (7,17)
Cinnamomum sp. (Lauraceae)		Mailu island	Death sorcerer may chew cinnamon bark to become 'hot' or powerful (29)	Mixture of tobacco and cinnamon is sometimes claimed to cause marihuana-like effects in the New World (28)
	kai-yau-kwera	Kukukuku	Cinnamon leaves are mixed with dog's food to make it a good hunter (8)	
Citrus hystrix (Rutaceae)	tadi	Marind-anim	To become a sorcerer, the novice must take a mixture of various ingredients, including the leaves of Citrus hystrix, Codiaeum variegatum, Cordyline fruticosa, Crinum asiaticum and several unidentified plants (46)	
Citrus sp. (Rutaceae)	ximbung	Wewäk-Boikin	Vide Alocasia sp.	
		Marind-anim	Leaves of the wild lemon tree are used to induce ecstasy (46); sometimes even their smell is claimed to be sufficient (40)	
Codiaeum variegatum (Euphorbiaceae)	kundama	Marind-anim	Vide Citrus hystrix	

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Colocasia esculenta (Araceae)		Baining	Vide Alocasia sp.	
Cordyline fruticosa (Liliaceae)	ngasi	Marind-anim	Vide Citrus hystrix	
Costus sp. (Zingiberaceae)	jangun, jangun fagata	Adzera	Fruit is chewed as substitute for betel nut (18)	
Crinum asiaticum (Amaryllidaceae)	jarangar	Marind-anim	Vide Citrus hystrix	
Cryptocarya aromatica (Lauraceae)	a seren-gachi	Baining	Aromatic massoibark is chewed with lime and a species of betel leaf as substitute for betel nut (21,24)	
	oa	Sentani sea	Bark is chewed during various ritual actions, for instance by media who want to contact supernatural beings (47)	
Curcuma longa (Zingiberaceae)	söuwaa	Pawaia	Before young men are admitted to the circle of adults, they must drink a beverage prepared from the rhizome (48)	
Cycas circinalis (Cycadaceae)	baibai, bebai	Gunantuna	Pollen are used as a narcotic (33)	Cycas pollen or male bracts are also reputed to be narcotic in India (38,43)

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Cycas sp. (Cycadaceae)	budzamar	Western islands Torres Straits	Young leaf shoots are eaten by sorcerers wanting to be wild (15)	
Diospyros sp. (Ebenaceae)	kubilgim	Western islands Torres Straits	To become a magician, the novice must inter alia chew this plant (15)	
Elaeagnus sp. (Elaeagnaceae)		Gimi	In divination rites, a mixture of tobacco with leaves of Elaeagnus sp. and Amaracarpus sp. is smoked to pass into a trance-like state (13)	
Endospermum moluccanum (Euphorbiaceae)		Jimi or Mt. Hagen	Used in a ritual context to make young warriors fierce (26)	
Euodia cf. bonwickii (Rutaceae)	kilt	Mt. Hagen-people	Bark is chewed by men during dancing feasts (37)	
Ficus subnervosa (Moraceae)		Rossel Island	Leaves are chewed as substitute for betel nut (17)	
Galbulimima belgraveana (Himantandraceae)	agara	Okapa area	Natives chew a mixture of 'agara' bark and 'ereriba' leaves (Homalomena sp.) to provoke premonitory visions; sometimes the rhizome of 'kaine' (Zingiber zerumbet) is added as well; direct observation of an user has revealed violent tremor with miosis, followed after an hour by calmness and euphoria, and thereafter drowsiness (5,6)	Is also used in a ritual context to make young warriors fierce (26,42)

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Galbulimima belgraveana (continued)		Gimi	For divination, men may pass into a trance-like state by chewing the bark (13)	
Homalanthus sp. (Euphorbiaceae)		New Britain	Used in a ritual context to make young warriors fierce (26)	Indicated as Omalanthus, which is a synonym (41)
Homalomena sp. (Araceae)	ereriba	Okapa area	Leaves are used, sometimes together with Galbulimima bark, to provoke dreams and visions, followed by serious neurological symptoms resembling Parkinson's disease (4,5)	
Kaempferia galanga (Zingiberaceae)	maraba	Okapa area	Root is said to be hallucinogenic (6)	
Lactuca indica (Asteraceae)	kuntigea kada-a	Kukukuku	Seeds are chewed as substitute for betel mixture (8)	
Laportea sp. (Urticaceae)	a mingual, a mangarai	Baining	Laportea leaves of the large-leaved 'a mingual' and of the small-leaved 'a mangarai' are taken by dancers after the ingestion of Alocasia tubers (vide supra) (20)	
	salak	Komba	Death sorcerer eats leaves of a stinging nettle (Laportea sp.?) to become 'hot' (33)	
Palmeria sp. (Monimiaceae)	boma kan	Chimbu	Leaves are eaten by men as a stimulant in time of war (36)	Leaves are also eaten by women as an abortivum (34,36)

Scientific name	Vernacular name	Tribe or area	Uses	Additional remarks
Pandanus sp. (Pandanaceae)	amugl keja	Chimbu	Natives are said to become 'long long' (mad) in the beginning of the year, when pandanus fruits are ripe; this temporary folly is reputed to be provoked by the ingestion of raw or immature nuts of the pandanus tree or even by the smell of its rotting fruit shells (6,16,27,34,42)	The nuts are said not to be from local trees, but from Jimi valley (16); pandanus leaves are used in New Guinea as a cigarette wrapper (22,26)
	tayuaka, hamanga	Kukukuku	Fruit is eaten by boys in puberty ceremony (8)	
Ptychococcus paradoxus (Palmae)		Barriai	Fruit is used as substitute for betel nut (11)	
Pueraria phaseoloides (Leguminosae)		New Britain	Leaves are used as intoxicant (26)	
Strychnos minor (Loganiaceae)			Bark is crushed with ginger and fed to dogs, to stimulate them for hunting (17)	
Zornia gibbosa (Leguminosae)			Used for sorcery (30)	Leaves of Zornia latifolia are smoked in Brazil as substitute for Cannabis (30)

Notes:

(*) Specific exclusions from the table are:

- well-known plants and preparations like tobacco (14,22,33,39), betel (32,33,48), kava (31,33,48), ginger (33,48), alcoholic beverages (26), opium (2) and hemp (35);
- psychoactive plants which are merely reported to have caused unintentional poisoning, such as hallucinogenic Brugmansia species (7,9,17);
- certain mushrooms, which are possibly associated with a native frenzy (16,27);
- plants which are merely used as cigarette wrappers, such as Donax canniformis, Ficus sp., Hibiscus sp., Kleinhovia hospita, Macaranga sp., Myrmecodia brassii and Rubus moluccanus (22,26,36);
- plants without botanical identification, such as the kevo tree in the Bismarck Mountains (3), the kumani creaper in the western islands of the Torres Straits (15), the nong'n plant of the Danga (27),the sota and tsinimp leaves of the Adzera (18) and the yiragai herb of the Kutubu (45).

References:
(1) Airy Shaw 1980 (2) Anonymous 1920 (3) Aufenanger and Höltker 1940 (4) Barrau 1957 (5) Barrau 1958 (6) Barrau 1962 (7) Bell 1973 (8) Blackwood 1940 (9) Bridgewater 1968 (10) Feachem 1972-73 (11) Friederici 1912 (12) Gerstner 1954 (13) Glick 1967 (14) Haddon 1946 (15) Haddon and Seligmann 1904 (16) Heim and Wasson 1965 (17) Henty 1980 (18) Holzknecht 1971 (19) Laufer 1946-49 (20) Laufer 1963-64 (21) Laufer 1965-66 (22) Le Roux 1948 (23) Morgan 1980 (24) Parkinson 1907 (25) Plowman 1969 (26) Powell 1976 (27) Reay 1960-61 (28) Reko 1949 (29) Saville 1926 (30) Schultes and Hofmann 1980b (31) Serpenti 1962 (32) Seyfarth 1981 (33) Sterly 1970 (34) Sterly 1973 (35) Sterly 1978-79 (36) Sterly, pers. commun. 1985 (37) Stopp 1963 (38) Thieret 1958 (39) Van Nouhuys 1932 (40) Vertenten 1916 (41) Vink, pers. commun. 1983 (42) Webb 1960 (43) Whiting 1963 (44) Williams 1928 (45) Williams 1941-42 (46) Wirz 1925 (47) Wirz 1928 (48) Wolff-Eggert 1977.

APPENDIX G

MULTIDISCIPLINARY TABLE ON SOME REPUTEDLY PSYCHOACTIVE FUMIGATORIES AMONG MIDDLE AND SOUTH AMERICAN NATIVES (*)

Scientific name	Area	Ethnobotany (**)	Phytochemistry (***)	Psychopharmacology	Efficacy of smoking
Amanita muscaria (Amanitaceae)	Valley of Puebla, Mexico	A curandero is reputed to smoke dried A.muscaria mixed with tobacco as an intoxicant and to perform ritual diagnoses (17)	Muscimol, ibotenic acid (15)	Evidence for hallucinogenic activity is less impressive than in the case of psilocybian mushrooms (15,39)	-
Anadenanthera colubrina var. cebil (Leguminosae)	Paraguay and Argentina	Aboriginal smoking of çevil pods is mentioned in an early source on Paraguay (18), and Argentinian natives are said to smoke jatáj (=cebil) mixed with tobacco (8). Botanical identifications are not given, but such preparations are associated with A. colubrina var. cebil (53,63)	DMT, 5-OH-DMT in the seed and in the seed pod (26)	True hallucinogenic activity is definitely established for DMT, but not for 5-OH-DMT (15)	DMT is claimed to be effective, when smoked (6)
Anadenanthera peregrina (Leguminosae)	British Guiana	Aboriginal smoking of the pulverized seeds is mentioned in an early source (52)	DMT, 5-MeO-DMT, 5-OH-DMT in the seed (15)	True hallucinogenic activity is definitely established for DMT and 5-MeO-DMT, but not for 5-OH-DMT (15)	The smoking of 6-10 mg 5-MeO-DMT is effective (15). DMT is claimed to be effective, when smoked (6)

Scientific name	Area	Ethnobotany (**)	Phytochemistry (***)	Psychopharmacology	Efficacy of smoking
Calea zacatechichi (Asteraceae)	State of Oaxaca, Mexico	Chontal curanderos prepare an infusion and a cigarette from the dried leaves for clarification of the senses (17,31)	Caleines and zexbrevin in aerial parts (25,44)	–	C.zacatechichi was mildly psychoactive, when inhaled and ingested in an uncontrolled study (17)
Cannabis sativa (Cannabaceae)	Brazil	The Tenetehara Indians smoke the dried flower and leaf as a recreational stimulant (64). Among Mexican natives like the Tepehua Indians, the principal way of Cannabis use is oral administration (23,68)	Delta-9-tetrahydrocannabinol and many other cannabinoids (60)	The mild hallucinogenic activity is well established (36,53)	Well established (2,38)
Cytisus canariensis (Leguminosae)	Northern Mexico	This plant is also known as Genista canariensis (53). A Yaqui shaman prepares cigarettes from the dried blossoms (19)	Cytisine, N-methylcytisine and anagyrine in the leaf (69)	Cytisine and N-methylcytisine have similar peripheral effects as nicotine, but their central activity may be different (1,70)	C.canariensis was mildly psychoactive, when smoked in an uncontrolled study (19)

Scientific name	Area	Ethnobotany (**)	Phytochemistry (***)	Psychopharmacology	Efficacy of smoking
Datura sp. (Solanaceae)	Mexico	Spiked ceramics might be associated with Datura use (30), so finds of archaeological clay pipes with spiked bowls should be mentioned here (43), but substantial evidence for pre-Hispanic Datura smoking in Mexico is lacking. Contemporary data are limited to a vague statement that dried toloachi leaves are added to tobacco cigarettes in the Guanajuato region (46), but this may be a non-aboriginal practice	Scopolamine, hyoscyamine in the leaf (24,53)	The deliriant activity is well established (15)	Well established (56,67)
Erythroxylum sp. (Erythroxylaceae)	Peru	Aboriginal smoking is reported for the Omagua Indians (7), but no primary reference is given. The non-aboriginal smoking of coca paste is well documented (27)	cocaine in the leaf (47)	The psychostimulating properties are well established (21)	Well established (40,41)

Scientific name	Area	Ethnobotany (**)	Phytochemistry (***)	Psychopharmacology	Efficacy of smoking
Lobelia tupa (Campanulaceae)	Chile	The Mapuche Indians are said to smoke the leaves as an intoxicant (32)	Lobeline, lobelanidine, norlobelanine in the leaf (28)	Lobeline has similar peripheral effects as nicotine, but its central activity may be different (49,59)	Recent references on the efficacy of smoking have not been found; there is merely a report associating a smoking mixture of Lobelia inflata and Datura stramonium with the sudden death of an asthmatic (35)
Nicotiana spp. (Solanaceae)	Widespread	Tobacco is undoubtedly the most common fumigatory of Middle and South American aboriginals. The principal species are N.tabacum and N.rustica in Middle America and N.tabacum in South America (48,66)	Nicotine in the leaf (15)	The psychostimulating properties are well established (15,59)	Well established (4,5)
Psilocybe sp. (Strophariaceae)	Mexico	The contemporary smoking of psilocybian mushrooms by a Yaqui Indian has been described (9, 10), but the authenticity of this report is very gravely doubted (14,57). The ancient Aztecs smoked mushrooms as an admixture to tobacco (50), but the botanical identity is unkown	Psilocybin, psilocin (53)	The hallucinogenic activity is well established (15)	The availability of psilocybin is said to be compromised by pyrolytic degradation and by condensation, when it is smoked in a pipe (57)

Scientific name	Area	Ethnobotany (**)	Phytochemistry (***)	Psychopharmacology	Efficacy of smoking
Quararibea funebris (Bombacaceae)	Mexico	The Aztecs used poyomatli, the flower of the cacauaxochitl plant, as an admixture to smoking tobacco (50,51). One of the suggested identifications is Q.funebris (33,65).	funebrine (45)	–	–
Tagetes lucida (Asteraceae)	Sierra Madre, Mexico	The Huichol Indians smoke the dried leaves and flowers, either alone or mixed with Nicotiana rustica (58)	The root contains BBT (11); various non-alkaloidal constituents have been reported for the genus (17,53)	–	–
Trichocereus pachanoi (Cactaceae)	Las Aldas, Peru	This plant is also known as Echinopsis pachanoi (53). Archaeological excavations have yielded what appear to be cigars made from a cactus thought to be T.pachanoi (55)	Mescaline (13)	The hallucinogenic activity is well established (15)	–
Trichocline spp. (Asteraceae)	Argentina	The Chaco Indians smoke the powdered root of T.reptans, either alone or mixed with tobacco. Other species said to be used are T. auriculata, T.dealbata, T.exscapa and T.incana (20,63,71)	Isopimpinellin, phellopterin and trichoclin in T.incana (37)	–	–

Scientific name	Area	Ethnobotany (**)	Phytochemistry (***)	Psychopharmacology	Efficacy of smoking
Virola sebifera (Myristicaceae)	Venezuela	Witch doctors are reputed to smoke the inner bark to cure fevers (53,63)	DMT and 5-MeO-DMT in the bark (12, 34)	The hallucinogenic activity is well established (15)	The smoking of 6-10 mg 5-MeO-DMT is effective (15). DMT is claimed to be effective, when smoked (6)
Virola sp. (Myristicaceae)	Brazil	The bark of an indeterminate Virola species reportedly is smoked by witch doctors as an additive to tobacco (34)	A collected bark sample was devoid of alkaloids (34)	-	-

Notes:

(*) Reported North American Indian fumigatories other than tobacco include Achillea millefolium (61), Arctostaphylos uva-ursi (62), Cornus stolonifera (29), Datura meteloides (3) = D.innoxia? (24,53), Eriogonum sp. (58), Eupatorium solidaginifolium (62), Leptotaenia californica (22), Lobelia inflata (61), Rhus glabra (61), Sassafras officinale (61), Verbascum thapsus (61), Viburnum opulus (61)

(**) Since their use as a fumigatory is or may be non-aboriginal, the following plants have been excluded : Canavalia maritima (16), Cestrum laevigatum (53), Leonurus sibiricus (16), Myristica fragrans (54), Salvia divinorum (16), Sida acuta (16), Stropharia cubensis (42), Zornia latifolia (53)

(***)The following abbreviations are used to indicate constituents:

DMT = N,N-dimethyltryptamine
5-OH-DMT = 5-hydroxy-N,N-dimethyltryptamine
5-MeO-DMT = 5-methoxy-N,N-dimethyltryptamine
BBT = 5-(3-buten-1-ynyl)-2,2'-bithienyl

References:

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SUMMARY

The general outline of the thesis is given in the preface. The first two chapters review the ethnobotany, phytochemistry and psychopharmacology of ritual intoxicating enemas and snuffs among the aboriginal inhabitants of the western hemisphere. They are supplemented by a third chapter, which gives a general outlook on some factors to be taken into consideration in the multi-disciplinary approach to ritual intoxicating plants.

Chapter one is an overview of intoxicating enema rituals in the western hemisphere.

Part one discusses ethnobotanical, chemical and psycho-pharmacological aspects. The following categories of ritual enema ingredients arise from this multidisciplinary approach:

1) It is well established that the plant provides one or more psychoactive principles and the Indian use of the plant as a ritual enema ingredient is confirmed or is quite probable: Agave, Anadenanthera, Brugmansia.
2) It is well established that the plant provides one or more psychoactive principles, but the Indian use of the plant as a ritual enema ingredient is not well recorded or is even unlikely: Banisteriopsis, Datura, Ilex guayusa, Lophophora williamsii, Nicotiana.
3) The Indian use of the plant as a ritual enema ingredient is confirmed or is quite probable, but it is not well established that the plant provides one or more psychoactive principles: none.
4) The Indian use of the plant as a ritual enema ingredient is not well recorded, and it is not well established that the plant provides one or more psychoactive principles: Capsicum.

Part two discusses the rectal pharmacokinetics and efficacy of possible ritual enema constituents. The literature yields convincing clinical evidence that caffeine and nicotine are effective following rectal application. A good rectal efficacy could also be expected from mescaline and from tropane alkaloids, but this is a hypothetical view which still awaits experimental confirmation.

In self-experiments, ethyl alcohol produced substantial blood levels via the rectal route, but dimethyltryptamine did not

produce any effect when parenterally active quantities were taken as an enema. First-pass elimination is the most likely explanation for the observed inactivity of dimethyltryptamine via the rectal route.

Part three reports the chemistry of paricá seeds of the Brazilian Maué Indians. These seeds date from the first half of the 19th century, and seem to be the only ethnobotanical material from the western hemisphere, which has ever been directly associated with ritual rectal intoxication. Despite their considerable age, the seeds still yielded as much as 15 mg/g of the Anadenanthera alkaloid bufotenin. This analytical finding supports the botanical view that the seeds are Anadenanthera seeds.

Part four discusses enema scenes on classic Maya pottery. These scenes undoubtedly represent rituals and may very well indicate that the ancient Maya took intoxicating enemas in a ritual context. This idea is quite contrary to the traditional view that the ancient Maya were a contemplative people, who did not indulge in ritual ecstasy. The occasional display of vomiting actors would seem to provide a plausible reason why the Maya opted for rectal application. Some scenes present a fair amount of evidence that an alcoholic beverage may have been taken rectally. Other scenes open up the possibility that tobacco and the water lily may have served as an enema ingredient. It is sometimes speculated that the latter plant is hallucinogenic, but pharmacological confirmation of this view is still awaited.

Chapter two is an overview of intoxicating snuff rituals in the western hemisphere.

Part one discusses ethnobotanical, chemical and psycho-pharmacological aspects. The following categories of ritual snuff ingredients arise from this multidisciplinary approach:

1) It is well established that the plant provides one or more psychoactive principles and the Indian use of the plant as a ritual snuff ingredient is confirmed or is quite probable: Anadenanthera, Erythroxylum, Nicotiana, Virola.
2) It is well established that the plant provides one or more psychoactive principles, but the Indian use of the plant as a ritual snuff ingredient is not well recorded or is even unlikely:
   Banisteriopsis, Cannabis, Datura, Ilex guayusa.

3) The Indian use of the plant as a ritual snuff ingredient is confirmed or is quite probable, but it is not well established that the plant provides one or more psychoactive principles: Justicia pectoralis, Pagamea macrophylla, Tanaecium nocturnum.
4) The Indian use of the plant as a ritual snuff ingredient is not well recorded, and it is not well established that the plant provides one or more psychoactive principles: Acorus calamus, Capsicum, Maquira sclerophylla, Piper interitum.

Part two discusses the nasal pharmacokinetics and efficacy of possible ritual snuff constituents. The literature yields convincing clinical evidence that atropine, cocaine, nicotine and scopolamine are effective following nasal application, but experimental confirmation of the efficacy of nasal tryptamine alkaloids is still awaited. This seems to be due, at least in the case of dimethyltryptamine, to the testing of low and therefore inadequate doses.

In self-experiments, caffeine produced substantial plasma levels via the nasal route, but harmine, when 40 mg was taken as a nasal powder, did not produce measurable plasma levels. Without additional experiments, it is difficult to give a definite explanation for this negative result.

Part three reports the chemistry of two yopo snuffs of the Venezuelan Piaroa Indians. One snuff yielded 10 mg/g of bufotenin, and the other one contained traces of harmine and of bufotenin. The isolation of harmine is quite significant, since this Banisteriopsis alkaloid is only rarely found in South American snuffs.

Chapter three provides a general outlook on the multidisciplinary approach to native ritual plants by reviewing some botanical, chemical and pharmacological factors, which should be taken into consideration with this approach.

With respect to botanical aspects, emphasis is laid on the importance of voucher specimens, on the usefulness of material in museum collections, on geographical predilection, and on non-pharmacological terminology in ethnobotanical references.

Significant chemical factors are a careful selection of the studied material, and the specificity, sensitivity and reactivity of the analytical procedure.

The pharmacological discussion focuses on experimental design and on common differences between native and experimental drug

taking: clinical data are mostly obtained by testing an isolated constituent instead of the whole indigenous dosage form and this constituent may be administered in another dose and by another route of administration. It is argued that ethnopharmacology deserves a branch called ethnopharmacokinetics which must be aimed at the fate of indigenous drug constituents in the body.

Some points in chapter three are illustrated by separate appendices.

Appendix F provides an ethnobotanical survey of the ritual plants and reputed botanical intoxicants of New Guinea natives. The enumeration of thirty-seven different genera suggests that New Guinea practices are underrepresented in those general reviews on ritual botanical intoxication, which do not use pharmacological validity as a strict criterion for inclusion.

Appendix G gives multidisciplinary information on fifteen different genera, all of which are established or suggested ingredients of ritual fumigatories in Middle and South America. Taken together with chapter one and chapter two, this appendix demonstrates the enormous variety in non-oral ritual intoxication among Latin American aboriginals.

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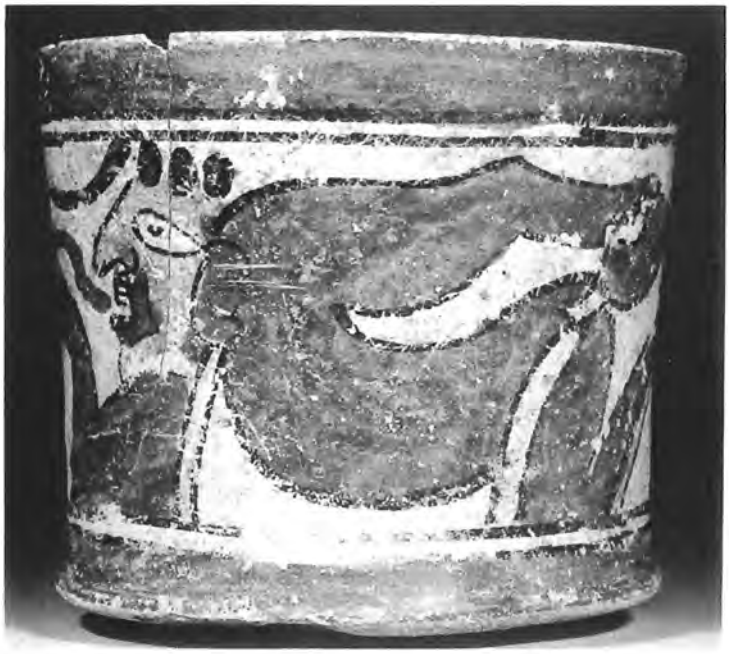

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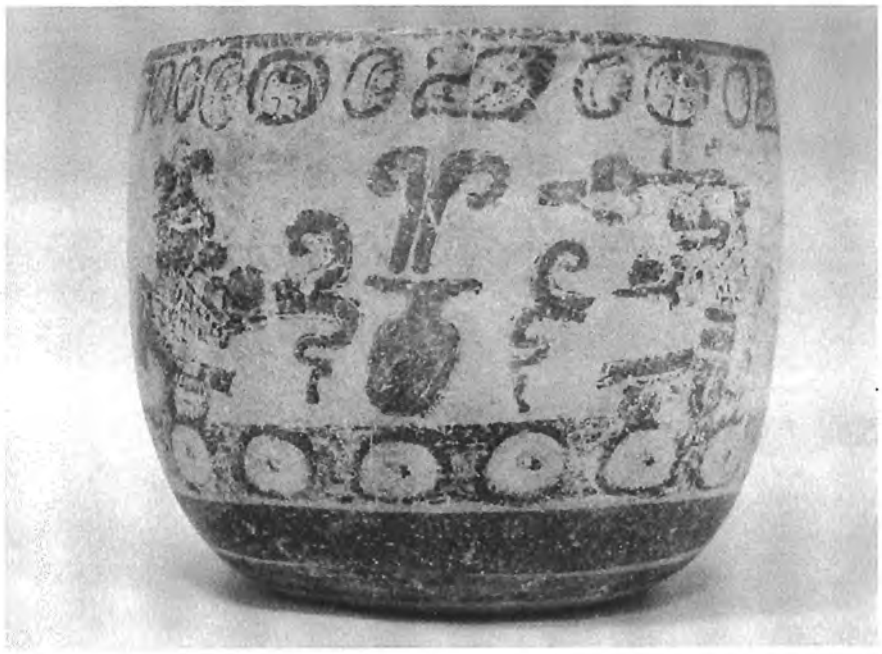

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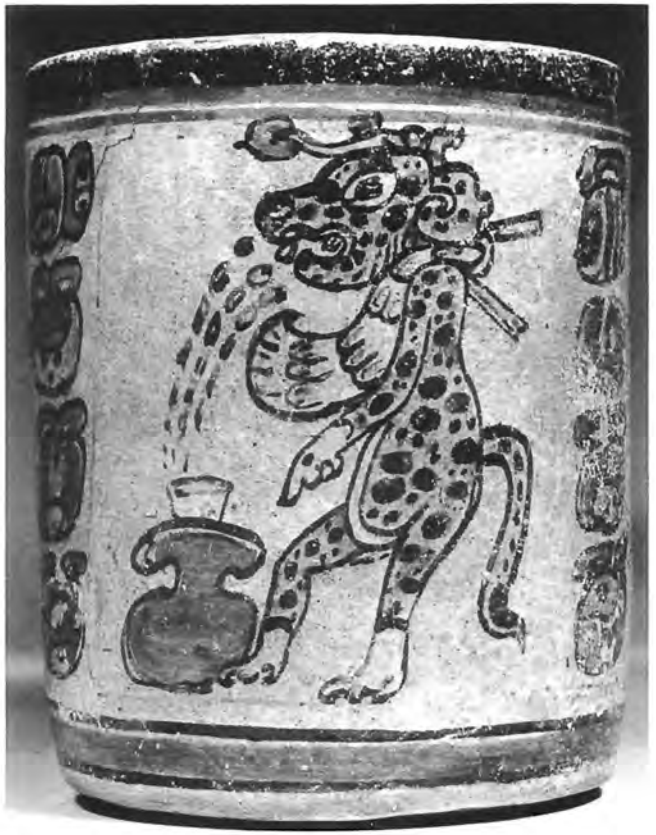

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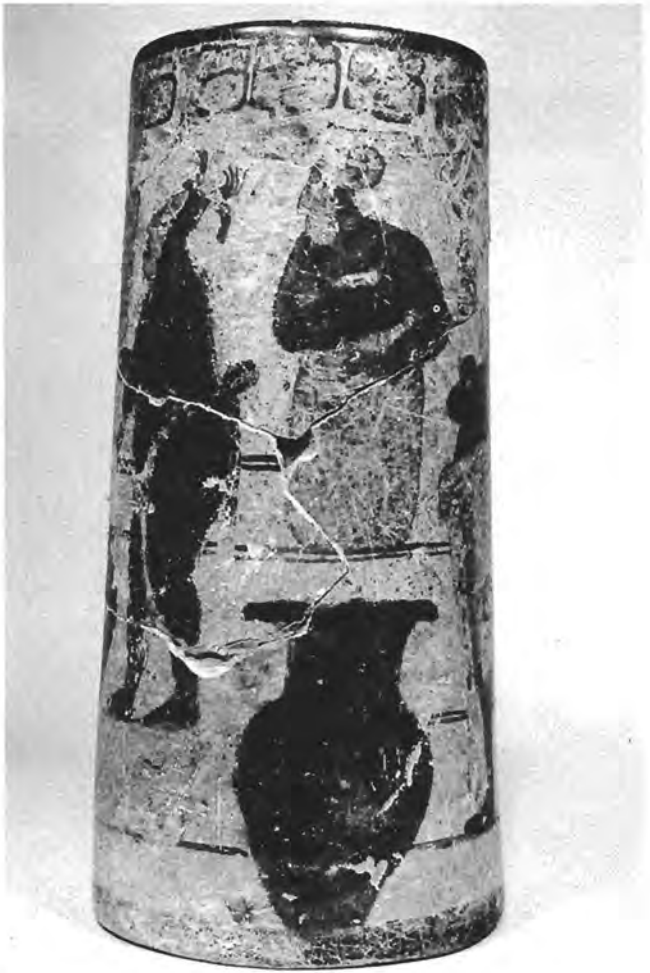

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