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Amazonian ethnobotany and the search for new drugs

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Abstract. Tropical rain forests offer enormous prospects for the discovery of new drugs for use in Western medicine. The Amazon supports 80 000 species of higher plants and a diverse Indian population. Focusing attention on those plants used as medicines by indigenous peoples is the most efficient way of identifying the plants that contain bioactive compounds. There is an urgent need for more ethnobotanists and ethnopharmacologists to be trained to document as much information as possible before it and the plants are lost through destruction of the rain forest and acculturation of the indigenous peoples. Ethnobotanical studies have identified plants documented by early travellers; these include *Paullinia yoco* and *Ilex guayusa* which are used as stimulants and have been shown to be rich in caffeine. Studies of the hallucinogen prepared from *Banisterioposis caapi* have shown that the native people know which plants to add to the mixture to lengthen and intensify the intoxication produced by the β-carboline alkaloids in the plant. Three major snuffs are used in the Amazonia; the plants from which they are derived have been identified. One of the snuffs also has antifungal and curare-like activities; chemical analysis on the active principles has not been done. Several plants are considered as prime candidates for scientific study as sources of useful chemicals for medicine or industry. These include some used to prepare teas or other infusions for treatment of various symptoms of senile dementia.

1994 Ethnobotany and the search for new drugs. Wiley, Chichester (Ciba Foundation Symposium 185) p 106–115

There are numerous definitions of ethnobotany. The usual and simplest definitions suggest that it is the study of the uses of plants in primitive societies in both modern and ancient times. Given the many rapidly expanding subdivisions of this interdisciplinary field, a more inclusive definition seems to be necessary. It would encompass the study of the uses, technological manipulation, classification, indigenous nomenclature, agricultural systems, magico-religious concepts, conservation techniques and general sociological importance of the flora in primitive or pre-literate societies (Schultes 1992).

One of the most active aspects of ethnobotanical research is the search for potentially valuable medicinal material with chemical constituents from which

new curative agents may be created for modern pharmacopeias and for the benefit of all mankind. This aspect is often termed ethnopharmacology.

Tropical rain forests, with their exuberant vegetation, which is usually extremely rich in species but incompletely studied, offer the greatest possibilities for the discovery of promising new drugs. The Amazon is an exellent example: 2 722 000 square miles, containing the largest drainage area in the world and one-sixth of the fresh water of the globe, support 80 000 species of higher plants or approximately 15% of the world's flora and an extraordinarily diverse Indian population speaking some 500 languages. The flora increases in complexity and richness towards the western parts near the eastern Andean slopes.

If chemists expect to obtain by random collecting sufficient quantities of 80 000 species and all their ecotypes from this area of such difficult travel and transportation, the task may never be completed. It would be more productive to concentrate on those plants that the indigenous peoples have found, over millennia of experimentation, to be bioactive and which they have used in their medicine as ameliorators, stimulants or curative or psychoactive agents.

An Indian will naturally not seek out a plant, prepare it and imbibe or otherwise employ it to lessen pain or 'cure' ills, unless it produces some physiological effect. If a plant has any physiological or psychic effect, it must have at least one bioactive chemical constituent. We should learn what the constituents are. They may never be useful in our medicine; they may—as in the case of tubocurarine or rotenone—be put to a wholly different use; or, rarely, they may be employed—as quinine has been—for the same purpose as amongst the natives. Occasionally, the chemical structure may be manipulated by the synthetic chemist to produce new semi-synthetic molecules, some of which might be of interest.

That the Amazonian flora represents an extraordinarily rich and hitherto neglected chemical laboratory cannot be doubted. A few years ago, I surveyed five annual volumes of several phytochemical journals and discovered that, in that period, some 250 new alkaloids from Amazonian species had been reported. Since alkaloids represent only one type of the numerous secondary organic compounds in plants, the chemical wealth that lies awaiting in this vegetal laboratory is at once obvious.

Urgency for ethnobotanical conservation

There is an urgency to train many more field ethnobotanists. This precious knowledge seems in many regions to be doomed to extinction with the rapidly increasing acculturation and Westernization resulting from construction of roads, airstrips and dams, with consequent tribal displacement, missionary pressure, warfare, tourism, industrial penetration, local greed on the part of settlers and even well-intentioned governmental efforts to 'civilize' the natives. Loss of this knowledge—and even the physical annihilation of whole

tribes—hinders not only the search for new drug plants but also our efforts to conserve the environment and the flora. Realization of this impending loss has recently given a sense of urgency to the need for ethnobotanical conservation.

Examples of ethnobotanical contributions to the search for new drugs

During my 47 years of field work and that of my students amongst the Indians of the north-west Amazonia, especially in Colombia, some 1600 species employed by the natives as medicines, hallucinogens or poisons have been collected and identified (Schultes & Raffauf 1990). Although only a few have ever been chemically analysed, a number of extremely interesting and unexpected results have come from the botanical and chemical studies of these bioactive plants.

Yoco is a wild forest liana from the bark of which is prepared a stimulating drink of great importance to numerous tribes of the Putumayo of Colombia and adjacent Ecuador (Schultes 1942). References to its domestic and medicinal uses in reports of travellers and missionaries going back to the 17th century (Patino 1967) mention its importance in tribal life and include much ethnobotanical information (Schultes 1979).

The bark of *yoco* was analysed by French scientists (Rouhier & Perrot 1926) and found to have a high concentration of caffeine. The plant was not identified botanically, however, until 1942, when it was described as a new species of the Sapindaceae: *Paullinia yoco*. It is the only caffeine-rich species the bark of which is the part used for its bioactive effects (Schultes 1942).

Another caffeine-rich plant the identity and properties of which ethnobotanical studies have clarified is the cultivated *Ilex guayusa*. This is used by numerous tribes in Ecuador as a morning stimulant and as a vomitive before magico-religious ceremonies (Schultes 1972b). It was described botanically in 1901 from sterile material and was believed never to flower. There was some uncertainty that it was a species, until ethnobotanical investigation found fertile trees in Provincia Pastaza, Ecuador, in 1979 (Shemluck 1979).

The most important hallucinogen in the western and south-western Amazonia of Bolivia, Brazil, Colombia, Ecuador, Peru and Venezuela is a drink prepared basically from the bark of a malpighiaceous liana (Naranjo 1953, 1986, Schultes & Raffauf 1992). It was identified in 1852 by the British plant explorer and ethnobotanist, Richard Spruce (1978, 1908). It is known variously as *ayahuasca*, *caapi*, *natema*, *pinde* and *yajé*. Spruce, unlike most botanists of the last century, wrote a detailed ethnobotanical report on this psychoactive plant, including his experiences in participating in an Indian ceremony and partaking of the intoxicating brew. He collected and described the liana as *Banisteria caapi* (now called *Banisteriopsis caapi*). Furthermore, unlike botanists of his time, he even collected material for chemical analysis. This was lost in transit but eventually arrived at the Royal Botanic Gardens, Kew. The analysis was not done until 1969 (Schultes et al 1969).

Ethnobotanical studies of this hallucinogen have led to the discovery of significant aboriginal knowledge of the appropriate plant additives to use as admixtures with the original drink from *Banisteriopsis*. Many different plants—mostly themselves toxic—are employed by various tribes as additives, but two are pre-eminent and widely used: leaves of the rubiaceous *Psychotria viridis* and of the malpighiaceous *Diplopterys cabrerana* (formerly known as *Banisteriopsis rusbyana*) (Instituto Indigenista Interamericano 1986, Rivier & Lindgren 1972, Schultes & Hofmann 1980). These additives lengthen and intensify the intoxication produced by the *B. caapi* plant. The active constituents of *B. caapi* are β-carboline alkaloids (Deulofeu 1967), harmine, harmaline and tetrahydroharmine. The alkaloids in the leaves of *Psychotria* and *Diplopterys* are tryptamines, which are inactive when taken orally unless taken with a monoamine oxidase inhibitor. The β-carbolines in *B. caapi* are in effect inhibitors of this enzyme. The aboriginal discovery of these two most important additives from a flora of 80 000 species indicates the depth of Indian understanding of the properties of plants in their ambient vegetation. How much more can ethnobotanical research learn of value, if it be intensified in such regions as the Amazonia?

Recent ethnobotanical research has clarified earlier confusion in the anthropological literature concerning the snuffs of the Amazonia (Cooper 1949). We know now that three major snuffs are involved: tobacco, *yopo* (*Anadenanthera peregrina*) and the recently identified *nakwana*, *epena* or *yakee* from several species of the myristicaceous genus *Virola*.

Tobacco is widely employed in the western Amazonia in the form of snuff or *ambíl* (a concentrated liquid placed in the mouth over the gums); it is rarely smoked except in certain ceremonies. *Yopo* is historically the most important snuff; it is used mainly in the northernmost parts of Brazilian Amazonia and the Orinoquia of Colombia and Venezuela. It was formerly employed in the West Indies where it was called *cohoba* (von Reis Altschul 1972, Safford 1916).

A snuff long confused with *yopo* is widely prepared in the Orinoquia of Venezuela and Colombia, the Vaupés of Colombia and the north-western part of the Brazilian Amazon. The source of this hallucinogenic snuff is the red, resin-like exudate of the inner bark of *Virola calophylla, Virola calophylloidea* and especially *Virola theiodora*; other species of this genus may be employed locally. The source of this snuff was definitively identified from ethnobotanical research in 1954 (Schultes 1954). The hallucinogenic activity is due to high concentrations of several tryptamines, in some preparations as high as 11% (Schultes & Holmstedt 1968).

Several discoveries resulted from my ethnobotanical research into the source of the *Virola* snuffs. The primitive Waika Indians in Brazil, who employ the snuff with unusual frequency, value the resinous exudate on darts as a weak kind of curare for hunting small animals. The other interesting use amongst these people is the application of the 'resin' over 10 to 15 days in the treatment

of fungal infections of the skin with apparent success, whether as a cure or suppressant is still not known. Studies have not yet been carried out on the active principles for the curare-like or the antifungal effects.

The interesting point here is the frequency with which ethnobotanical research on one aspect of the use of a plant leads to other unexpected utilitarian aspects that may present new opportunities for phytochemical or other investigations.

Suggested Amazonian plants worthy of study for new drugs

Of the 1600 species reported as medical or toxic plants in the north-west Amazonia, several appear to be worthy of scientific study as sources of useful chemicals either in medicine or industry. Those of top priority, in my opinion, are the following.

The Indians of the Colombian Amazonia have a reputation for caring as much as possible for the aged and infirm. In my ethnobotanical field work, I found 23 species of plant employed in one way or other in treating senile dementia. Of these 23, the following seem to be outstanding and worthy of technical investigation in view of the direct statements of native informants (Schultes 1993).

Mandevilla steyermarkii (Apocynaceae) is a strict endemic: the roots of this beautiful plant are decocted for administration 'to the sick and aged'. *Tabernaemontana heterophylla* (Apocynaceae) is used by Tukano Indian medicine men; they prepare a tea of the leaves for 'old folk who are slow and forgetful'. The fruit of *Gnetum nodiflorum* (Gnetaceae) is boiled by the Kubeo to make a tea, which is prescribed for three or four days for elderly men 'who cannot walk straight and totter and fall'. *Vismia tomentosa* (Guttiferae) is also made into a tea by the Yukunas and Makunas. They believe that the elderly 'who suffer difficulty in understanding instructions and have physical degeneration and difficulty in talking' are helped by a week-long administration of a tea of the leaves. *Piper schultesii* (Piperaceae) is valued by the Karijonas, who gather leaves from the Sierra de Chiribiquete and dry them for use. The plant material is allowed to stand in water for a day and may be put into *chicha* (a fermented drink of maize) for the elderly who 'sit without talking all day, staring into space'.

The Tikunas of the Río Loretoyacu boil the leaves of *Tournefortia cuspidata* (Boraginaceae) to prepare a tea given twice daily over two weeks to the elderly who 'shake all over'. Several species of *Souroubea* (Marcgraviaceae)—*S. crassipetala*, *S. guianensis* var. *corallina* and *S. guianensis* var. *cylindrica*—are frequently employed by Indians in the Colombian Vaupés to make a leaf tea to calm extremely nervous elderly people and to hasten sleep when taken warm in the evening (Schultes & Raffauf 1990).

The leaves of *Caryocar microcarpum* (Caryocaraceae) appear to be toxic to the leaf-cutting ant, killing the ants when they attempt to cut the leaves. Since

these insects cause great crop losses in the tropics, the responsible chemical constituent could be a boon to agriculture.

Conclusion

The intensification of ethnobotanical field research is urgently needed because of acculturation in most areas where people of primitive societies are living and because of the increasing devastation and destruction of rain forests in the tropics. From both points of view, an incredible chemical laboratory still practically untouched by scientific investigation for new therapeutic agents is awaiting urgent attention.

I end with a plea that all scientists involved make every effort possible to encourage the training of more ethnobotanists or ethnopharmacologists willing to carry on field work with people who still have the knowledge of plants and their properties which they have inherited from generations unnumbered.

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DISCUSSION

King: Virola is well known to many scientists. We have looked at its antifungal activity; it does suppress the growth of skin and other fungal pathogens, but it's not fungicidal. The compounds are known and have been published (Gottlieb 1979). It works and it may not be a good drug for Western markets but it's quite efficacious in local applications.

Jain: Training is something that we should think about very seriously. Compared with laboratory training in pharmacology or tissue culture or genetics, it is not expensive to train ethnobotanists. Particularly, because the need for training of ethnobotanists is greater in developing countries, where usually things are still inexpensive and training can be done at less cost. We have been conducting a training course in ethnobotany in Lucknow in India in alternate years since 1986. This lasts for a week or 10 days and there are about 30 students in each group. Of the 120 who have been trained in the last seven years, about 70% have taken up ethnobotany as a profession. The responsibility for training

should not fall only on educational institutions, or government or research institutions; it should also fall on people like those here who in the future want the phytopharmaceutical industry to benefit from ethnobotanical findings.

Lozoya: There are numerous definitions of ethnobotany, but I disagree absolutely with the definition of Professor Schultes. He is ignoring 20 years of very important discussions by many of the people who are sitting around this table. In Latin America, we have been fighting for 20 years to replace language that refers to us as primitive societies. Mexican traditional medicine is not primitive. I propose that we use one of the common definitions of ethnobotany already used by American, French, German, Mexican, Brazilian, Chinese and Japanese universities, that give us a better perspective for the end of the 20th century.

Balée: Professor Schultes' definition of ethnobotany is still the Harshberger's definition, to a large extent, of the 19th century in that the focus is on 'primitive' or non-literate societies. Schultes tries to amplify the importance of the definition in other ways, and I agree with the topical material. We could more broadly define ethnobotany as the total relationship between people and plants. It need not be, for example, non-literate societies only that have ethnobotanical systems. What about Chinese ethnomedical systems, Ayurvedic ethnobotany in India or Mayan ethnobotany, all of which are based on literate traditions?

The big question is whether ethnobotany is seen as a science or not. Are non-Western therapeutic uses of medicinal plants, for example, in the materia medica of China, India and ancient Greece before there was 'real' science, to be considered as ethnobotany or not? Or does ethnobotany simply involve the study of relationships between plants and people? Ethnobotany should not be limited to one or another kind of society; it should be applicable to humankind generally, wherever plants are used and are present in the environment.

Jain: This is not the forum for a discussion on the definition of ethnobotany but certainly the word primitive should be deleted. Ethnobotany is now considered almost unanimously all over the world as the direct relationship between human beings and plant resources. Many advanced human societies in the world have very poor direct relationships with plants, relationships or uses which do not fall into the category of economic botany or medical botany. Therefore a direct relationship between plants and human societies is ethnobotany.

Iwu: We should state clearly that some words are insensitive and should not be used. We should not describe a people's culture without any respect. Professor Schultes has made a wonderful contribution to this discipline, but I take strong exception to the continued use of the term primitive in describing non-European cultures or ethnobotanical work.

Peter: Professor Schultes applied the term 'primitive' to communities that are still rooted in nature. It is not limited to any specific region and could apply to rural communities in many parts of the world. However, since it can easily

be (mis)interpreted as a demeaning cultural qualification, it should not be used any more in the context of ethnobotany.

Cragg: Professor Schultes has a tremendous respect for the people with whom he has worked for decades. I don't think he would have meant this in a demeaning sense at all; it is an unfortunate choice of words.

Martin: Ethnobotany is not just about the people we are studying, it's also about the plants and the ecosystems where we work. Professor Schultes concentrates on tropical humid forest, primary forest at that. Ethnobotany also focuses on temperate forests, arid areas and on secondary vegetation. In fact, the majority of useful plants are found in secondary vegetation. Professor Craveiro's presentation showed that medicinal plants come, not just from tropical humid vegetation, but also from arid areas (Craveiro et al 1994, this volume). We can expand the definition of ethnobotany to include the people other than indigenous people and plants beyond those found in primary tropical forest.

Iwu: I agree. The problem with Professor Schultes' definition is not just the choice of words, it is the whole line of thinking that has governed ethnobotany up till now. Walter Lewis mentioned dividing the forest into three zones: the core region, the buffer zone and an outer, more interactive zone (Lewis & Elvin-Lewis 1994, this volume). It is difficult to get any foreign conservation group, such as The World Wide Fund for Nature or the British Overseas Development Agency to agree to explore areas where the human interaction takes place. Everybody is interested in so-called travel book wilderness—'where no man has ever gone before'. In our cultural system, those areas are already protected, because we don't go there. So the area where there is very high intensity of human use, where ecological conservation is needed, is not studied.

The type of ethnobotany described by Professor Schultes was very useful work but for a different era. It is an era that has gone and the old school needs to re-educate itself. This brings us to the issue of training. How suitable are the programmes offered in Western institutions to meet the demands of ethnobotany? We have just conducted a training programme for ethnobotanists. This took 10 weeks and was for graduates who had already worked in the field. They need to learn about our value systems, about our religion, about our cosmology. These are people who grew up in Nigeria and they still need 10 weeks of intensive training to be able to interview and talk with the local people. Imagine for how much longer a foreign ethnobotanist needs to be educated before being able to enter my world.

I am happy that the New York Botanical Garden is doing a random screen of the USA's own flora. Nobody has ever done any serious study of the flora in their own backyard, because it doesn't fit into what we call ethnobotany. We have to clarify this concept because it gives the impression in Third World countries that ethnobotany is a colonial exercise—that people are coming to get the remnants of what is left in our culture and they are putting nothing back. Some people don't want the lifestyle of the Indians they are studying to be better because that means change.

Posey: I totally agree, even to the point one can say that the concept of ethnobotany is an oxymoron. Traditional peoples do not separate plants from ecosystems; that is all integrated. We ought to be finding some basis for the re-integration of science, not the particularization of it. We have to start seeing all of this in a much larger ecological context—plants in the context of the environment.

McChesney: Plants are utilized in very broad ways. This symposium has focused on pharmaceuticals—new drugs. The outcome of research on plants depends primarily on how we ask the question relative to the biological activity. Will that biological activity address a disease state or will it address an agricultural application, for example? There is increasing concern over the environment, in the developed world as well as in the developing world, for example over the persistence of our current pesticides in the environment and their potential toxicity. We need new approaches to maintain the productivity of agriculture. Plant products and natural products hold real promise in that area and those issues ought to be addressed as well as issues directly affecting health.

Martin: Professor Schultes mentioned the urgency for ethnobotanical conservation. He has played a really critical role since the 1930s in bringing to our attention the importance of local knowledge and the fact that it is a tradition which should continue into the future.

Conservation is a difficult term to use for holding on to peoples' knowledge. I would prefer to use a term which stresses the continuing development of ethnobotanical knowledge. When we think about conservation of forests, we know there's a division between *ex situ* and *in situ* conservation. If you take things out of the forest and preserve them in botanical gardens, or practise other forms of *ex situ* conservation, you take a very small sample of genetic diversity. The tendency now is towards *in situ* conservation, so that the ecosystem can continue evolving and continue to develop with new speciation. Let's extend that metaphor to the knowledge about plants. If we just extract the knowledge and put it in books, which is a kind of *ex situ* conservation of that knowledge, it won't grow and develop. We should be aiming for *in situ* development of this knowledge, so that ethnobotany can be a living tradition, not just an academic tradition.

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