

Use of South American plants for the treatment of neuropsychiatric disorders

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Two conditions greatly encourage the folk use of plants to cure diseases and alleviate ailments:

- plant biodiversity (the richer the better)
- particular cultural traits of local populations.

Where these conditions are met, local scientific advancement may result from experimentation with and elaboration of folk remedies. Unfortunately, little scientific research has been done on South American plants that may be useful in the treatment of central nervous system (CNS) disturbances.

The 13 countries of South America possess several ecosystems and a rich cultural diversity; the population is descended from pre-Colombian cultures (such as the Maya and Inca ancient civilisations), many other indigenous ethnic groups, African slaves and European colonisers. All these segments of the population have traditionally relied on plants to treat their ailments and had at their disposal a very rich flora. In fact, more than 50% of all plant species are concentrated in tropical forests, in which Brazil and Colombia are particularly rich. For example, taking into consideration only three out of the five main Brazilian ecosystems, it is estimated that nearly 8000 endemic species are present in Atlantic forest, 4400 in the Cerrado and nearly 30000 in the Amazon rain forest (including other South American countries) (Cunningham, 1996). Unfortunately, all this biological and cultural richness has led to only a meagre number of ethnopharmacological (preclinical, clinical and toxicological) research studies.

We scrutinised what research had been published through bibliographical surveys, conducted on databases such as LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) and Medline (PubMed). The keywords for the surveys were: SOUTH AMERICA, each one of its 13 countries and PLANTS or HERBS or EXTRACT or HERBAL or PHYTOTHERAPY and PRECLINICAL or CLINICAL or PHYTOCHEMICAL or PHARMACOLOGY or PHARMACOLOGICAL STUDIES. From the published studies retrieved, only those referring to psycholeptic and psychoanaleptic effects were selected, specifically: antidepressants, memory enhancers, stimulants, antiparkinsonian agents, hypnotics, anxiolytics, anticonvulsants and aphrodisiacs.

After that, another survey was carried out using the same databases, but this time excluding the terms SOUTH AMERICA and the countries. This permitted

us to obtain a similar set of data for all other areas of the world on plants that may have psycholeptic or psychoanaleptic properties. The results of these surveys are shown in Table 1. It may be seen that only 1.3% of world research on plants possibly possessing CNS activity was conducted with South American plants, despite the continent's rich flora.

Although several preclinical studies have been performed under adequate laboratory conditions, very few clinical studies have been carried out under double-blind randomised conditions. Furthermore, these clinical studies generally had a poorly defined patient population, used non-standard measures and had small sample sizes.

Plants tested pharmacologically or phytochemically

Banisteriopsis caapi and *Psychotria viridis*

Although there were 13 articles on the Medline database concerning the pharmacological and phytochemical properties of these species, they were not revealed in our literature search as they have hallucinogenic effects and the terms PSYCHODYSLEPTIC and HALLUCINOGEN were not included as keywords.

Ayahuasca is a beverage derived from these plants (Carlini, 2003; McKenna, 2004). It is consumed by certain Indians in the Amazon area (Brazil, Peru and Colombia) and by some religious cults in the cities of northern Brazil, and the practice is spreading to southern Brazilian cities and other countries.

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Table 1 Number of preclinical, clinical and phytochemical studies reported for some psychoanaleptic and psycholeptic effects of plants, by region of origin

Effect	South America				Other countries	Percentage South American
	Pre-clinical	Clinical	Phyto-chemical	Total		
Antidepressant	3	0	0	3	564	0.5
Memory	3	0	0	3	642	0.4
Stimulant	2	1	1	4	298	1.0
Antiparkinsonian	4	4	2	10	97	9.3
Hypnotics	14	1	1	16	1160	1.3
Anxiolytic	11	4	0	15	863	1.7
Anticonvulsant	8	0	0	8	969	0.8
Aphrodisiacs	2	1	0	3	46	6.1
Total	47	11	4	62	4639	1.3

Ayahuasca is interesting as its pharmacological activity is dependent on a synergism between the two plants. *B. caapi* contains β -carboline alkaloids, mainly harmine and harmaline, whereas *P. viridis* has *N,N*-dimethyltryptamine (DMT) in it.

Rauvolfia serpentina

There were 63 articles on the Medline database concerning the pharmacological and phytochemical properties of this species (common name *sarpagandha*). Reserpine, an alkaloid isolated from *R. serpentina* during the middle of the 20th century, was an important clinical advance in the treatment of schizophrenia. According to the database of the Missouri Botanical Garden, consulted in 2004, there are at least 41 other species from this genus in South America, 17 of them belonging to the Brazilian flora.

After the introduction of reserpine, it was to be expected that other species from this genus would be a target for pharmacological investigation. However, with the exception of *R. canescens*, for which preclinical and clinical investigations have suggested a sedative effect, no other *Rauvolfia* species have been investigated in this way. Furthermore, only four other species have undergone some phytochemical investigation: *R. bahiensis*, *R. macrophylla*, *R. sellowii* and *R. tetraphylla*. In marked contrast, the Medline database refers to 308 studies performed with *Hypericum perforatum* (St John's wort), a plant from Europe with antidepressant properties.

Passiflora incarnata

Thirty articles were found on the Medline database concerning pharmacological and phytochemical studies of this species (common name *maracujá*, or passion flower) (Carlini, 2003). There are nearly 500 *Passiflora* species, most of them occurring in the tropical Americas; among them, *P. incarnata* has received most attention from the scientific community: there are dozens of studies dealing with its ethnopharmacology, as well as clinical and preclinical pharmacological studies. *P. incarnata* is commonly used in association with other species, including *Erythrina mulungu*, *Matricaria chamomilla* and *Valeriana officinalis*.

P. incarnata and other species of the same genus (*P. alata*, *P. coerulea*, *P. edulis*) are widely used in traditional medicine all over Europe and in the Americas for their seemingly sedative and anxiolytic properties.

Several compounds isolated from *Passiflora* species have been suggested as being responsible for the alleged anxiolytic/sedative effects; these include flavonoids (apigenin, vitexin, kampferol, homorientin, chrysin) and pyrone derivatives (malthol), but to date the active principles have not been identified.

Paullinia cupana* var. *sorbilis

Fifteen articles were found on Medline concerning the pharmacological and phytochemical studies of this species (common name *guaraná*) (Carlini, 2003). Found growing in the central region of the

Amazon basin and utilised in folk medicine for cases of physical and intellectual stress, the seeds of *guaraná* contain caffeine (2.5–5%) as well as theophylline and theobromine in small amounts; they also contain large quantities of tannins.

Through its methylxanthine content, *guaraná* is able, among other effects, to block adenosine receptors and to inhibit phosphodiesterase. Because of the latter effect, it enhances the actions of noradrenaline, which can be released from stores by plants containing ephedrine. Therefore, the existence of commercially available herbal mixtures containing ephedrine and *guaraná* as active ingredients is not surprising. One of the mixtures, in a randomised, double-blind, placebo-controlled study, effectively promoted weight loss and fat reduction of overweight men and women. Its effects were accompanied by stimulatory symptoms characteristic of ephedrine and caffeine.

Plants analysed only through ethnopharmacological studies

Plants employed by Colombian Indians for the treatment of senile dementia

Schultes (1993) recorded a total of 25 plants used by Colombian Indians for treatment of the signs and symptoms of senile dementia. In this sense, these 25 plants are administered mostly to older people, mainly those who have motor and mental disturbances. A bibliographical search carried out on the Medline and LILACS databases in 2004 revealed that none of these species had been studied from the pharmacological or phytochemical point of view, despite their undeniable therapeutic potential.

Plants employed by the Brazilian Krahô Indians and by the Quilombolas

A survey among the Krahô Indians (who live in the Cerrado ecosystem) revealed that 64 plants were used in ritual contexts for their seemingly psychoactive properties, including 14 used as anxiolytics, 10 as antidepressants or stimulants and 11 for sleep disorders (Rodrigues & Carlini, 2005). Similarly, work with a group of the Quilombolas (descendants of former African slaves, living in an isolated area of Brazil) revealed the use of 38 plants for the treatment of several CNS disturbances, including three for 'insanity', four as sedatives and another 11 for insomnia, and 11 to 'fortify' the brain (Rodrigues & Carlini, 2004).

Conclusion

It seems that South America possesses a treasury of plants. These have been little researched to date, and may harbour new therapies for psychiatric and neurological disturbances.

References

- Carlini, E. A. (2003) Plants and the central nervous system. *Pharmacology, Biochemistry and Behavior*, **75**, 501–512.

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Cunningham, A. B. (1996) Professional ethics and ethnobotanical research. In *Selected Guidelines for Ethnobotanical Research: A Field Manual* (ed. M. N. Alexiades), pp. 19–51. New York: New York Botanical Garden.

McKenna, D. J. (2004) Clinical investigation of the therapeutic potential of ayahuasca: rationale and regulatory challenges. *Pharmacology and Therapeutics*, **102**, 111–129.

Rodrigues, E. & Carlini, E. A. (2004) Plants with possible action on the central nervous system used by a Quilombola group in Brazil. *Phytotherapy Research*, **18**, 748–753.

Rodrigues, E. & Carlini, E. A. (2005) Ritual use of plants with possible action on the central nervous system by the Krahô Indians, Brazil. *Phytotherapy Research*, **19**, 129–135.

Schultes, R. E. (1993) Plants in treating senile dementia in northwest Amazon. *Journal of Ethnopharmacology*, **38**, 129–135.

POINT OF VIEW

Earthquake 2005: challenges for Pakistani psychiatry

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At 8.52 a.m. on 8 October 2005 an earthquake measuring 7.6 on the Richter scale struck the northern part of Pakistan and devastated large areas of North West Frontier Province and Azad Kashmir. Almost 90 000 people died and many thousands were reported missing. Half the dead were estimated to be children, killed in their classrooms. Some 3.5 million people were rendered homeless. The mountainous terrain made relief work a logistical nightmare.

Mental health issues in disasters

According to the World Health Organization (WHO), 3–4% of survivors are affected by severe mental disorders (psychosis, severe depression or anxiety), and up to 15% can be expected to suffer from mild to moderate mental disorders (Ashraf, 2005). In the context of Pakistan after the earthquake, this would mean between 120 000 and 160 000 in need of treatment for severe mental disorders and up to 600 000 for mild to moderate disorders. It was obvious that mental health services as they existed were grossly inadequate to deal with the scale of the disaster.

Why are mental health services so inadequate in Pakistan?

Pakistan is a country with huge contradictions. On the one hand, it is the sixth most populous country in the world (its population is approximately 150 million), one of the largest Muslim countries and a nuclear power. On the other hand, more than a third of its people live below the poverty line, the literacy rate is around 35% and its national health indicators make sorry reading. As in many other developing countries (Dyer, 2006), corruption has been one of the major impediments to progress. The lack of transparency and accountability coupled with poor governance has led to high failure rates for health initiatives in Pakistan.

Mental health services are poorly developed. Health spending is a pitiable 0.5–1% of gross national product. Mental health does not have a separate budget but is believed to account for 1% of the health budget. There is about 1 psychiatrist to 0.5–1 million of the population, but the distribution is unequal, as most psychiatrists are in large urban centres, while more than 70% of the population live in rural areas.

Government primary health services and the few psychiatric facilities are poorly organised and resourced and are accessed only by the very poor. Most healthcare is out-of-pocket expenditure, with the private sector contributing 77–90% nationally. On the other hand, community-based prevalence studies give very high figures for common mental disorders, with an estimated 25–66% of women and 10–40% of men suffering from them (Mumford *et al*, 2000).

Psychiatry and behavioural sciences are neither taught nor examined as a separate subject on the undergraduate medical curriculum in most medical colleges in Pakistan. Most graduating doctors, therefore, have little exposure to mental health issues.

Programmes galore

After the earthquake, many different psychological programmes were launched by a variety of organisations. Even the computer giant IBM, in collaboration with the Ministry of Social and Population Welfare, flew in two experts from the USA to conduct trauma management workshops. While all these organisations were well intentioned, there was little coordination between them. Some programmes focused only post-traumatic stress disorder (PTSD), and others focused on generic counselling skills. Almost all the programmes had separate training manuals and teaching materials. The target audience was not clearly identified. In many cases the same people ended up in various workshops without any clear idea of how or where they were going to use their newly acquired

The author has been part of a team that has developed and conducted training of health professionals in primary care health centres in Kashmir and North West Frontier Province.