

## Ayahuasca: From Ethnobotany to Pharmacology

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(Received 26 March 2012; Revised 27-29 March 2012; Accepted 31 March 2012)

### ABSTRACT

Several studies have reported the ethnobotany characteristics and pharmacological properties of *ayahuasca*, beverage prepared from decoction of two Amazon forest native species, the vine *Banisteriopsis caapi* and the bush *Psychotria viridis*. This beverage, in which its use date from pre-Columbian period, has been employed in religious cults by many south-American populations situated in the Brazilian Amazon and in the region comprised between Panamá and Peru. Considered the keystone of Amazon medicine, its composition presents a series of psychoactive substances capable to generate visionary experiences in healers, shamans and followers. In this review, it will be addressed the main aspects related to aims and ways of using *ayahuasca*, its chemical compounds and action mechanisms. Besides, it will be briefly discussed the regulatory aspects involved in its use and the approach that this beverage have been taken by international scientific community during the last years.

**Keywords:** *Ayahuasca*; Daime; *Banisteriopsis caapi*; *Psychotria viridis*.

### INTRODUCTION

*Ayahuasca* is a beverage obtained from decoction of two typical Amazon plant species, the liana *Banisteriopsis caapi* and the bush *Psychotria viridis* (Schultes and Hofmann, 1979). The term *ayahuasca* – also spelled as *ayawaska* – have a Quechua origin and derives from *aya* (= spirit, ancestral) and *huasca* (= vine). It can refer to others beverages produced from a vine added with several plant species; however, in contemporary literature, the term refers specifically to the beverage obtained from the above-mentioned species and is commonly used in religious cults by some communities in the region between Peru, Bolivia, Brazil and parts of Ecuador (Luna, 2011). The range of its translation to *spirit vine* is an indicative of *ayahuasca* properties: its consumption generates complex psychoactive effects like those observed when hallucinogens as LSD and other similar drugs are ingested. For conceptual reasons, we will refer to this beverage as entheogen (Ott, 1996) – which means “that comes from inside” – and not hallucinogen, due the recurrent pejorative use of the term. The first scientific reports on *ayahuasca*, its components and

psychoactive properties come from the beginning of the Twentieth century, and reveal the surprise on the fact of having no register of the narcotic potential of Malpighiaceae family species in that time (Spruce, 1908). Its use, however, is much more ancient. It is believed that communities utilized the beverage more than 3000 years ago in sacred rituals as a way to reach the divine and seek the cure to various diseases (Naranjo, 1979). Although the main action mechanisms of chemical compounds present in *ayahuasca* had already been elucidated, its consumption by certain South American populations still arouses interest of scientific community, in whose studies dialog with classical and contemporaneous issues in ethnobotany, pharmacology, anthropology, psychiatry and even arts (Labate and Cavnar, 2011). The present review aims to summarize the main ethnobotany and pharmacology knowledge on *ayahuasca*, discuss some regulatory aspects of its use by communities nowadays and evaluate the scientific focus given in the last years concerning its consumption, contributing with a better understanding and demystification of the beverage.

### ETHNOBOTANY

Since the pre-hispanic period to the present days, indigenous have used natural substances with psychoactive properties as auxiliary to immersion in supernatural realms, that is, as facilitating agents for induction of religious trance and cure rituals (Smet, 1983). In this ambit, the figure of the shaman has an important role in the understanding the origin of the use of this kind of drink during the time. Shamans are visionaries responsible for maintain contact with the supernatural world and perform different functions in the community. During the shamanistic ritual, they go into deep trance-called altered states of consciousness – and, in the name of the society to which they serve, establish relations with spirituals entities in order to help their communities through the provision of diagnosis and treatment of certain illnesses or riddles and prophecies (MacRae, 1992). From the traditional knowledge of shamans from Amazon region, it was created the professor plant concept – plants capable to generate knowledge. The two plant species utilized for *ayahuasca* production are considered in this concept (Luna, 1984). The *ayahuasca* use seems to go back to pre-Columbian period. Archaeological data from 3000 years ago found by several researchers in Sixties decade show the utilization of various artifacts related to the ceremonial utilization of entheogen beverages, such as small vase, images of non-human beings possibly seen during their use, sculptural objects that symbolize divinities similar to those observed in other ancestral communities and places possibly designed as the central base to the realization of religious rituals (Naranjo, 1979). Currently, its utilization is concentrated mainly in South America by indigenous and crossbred communities. In all Amazon regions, it is estimated that about 70 indigenous groups use *ayahuasca* (Goulart, 2011). The context of its use practices vary considerably, going beyond the forest borders and reaching the majors urban centers in the last decades (MacRae, 2004). In Brazil, *ayahuasca* started to gain notoriety from Seventies decade with the hippie movement, discovered by artists, intellectuals and curious seeking the cure. In the beginning of Eighties decade, its consumption passed to be adopted by a parcel of medium class of the big urban centers. In Nineties decade, two ayahuasca religions, the *Santo Daime* and the *União do Vegetal* (UDV) expanded beyond American continent; nowadays, the *Santo Daime* has centers in at least 21 countries in four different continents, while UDV has officials representatives in United States and Spain, and incipient centers in 4

European countries, disputing space with other religions and transiting among different symbolic, economic and cultural frontiers (Labate, et al., 2008). The *Santo Daime* was founded in 1930 by the rubber tapper Raimundo Irineu Serra-known as Mestre Irineu-in the city of Rio Branco, capital of Acre state (Brasil), after years of contact with *ayahuasca* in the border region between Brazil, Peru and Bolivia (MacRae, 1992). Its origins are related with three diverse cultural matrix, as the European (influence of Catholicism and esoterism), the afro-brazilian (presence of afro entities), and the indigenous or amazon (through utilization of the beverage, ways of preparing, consumption and ritualistic aspects) (Labate, 2005). For *daimistas*- the followers of *Santo Daime*- the use of *ayahuasca* allows the development of a spiritual life, as well the contact with divine, providing knowledge, power and welfare. The beverage is consumed in a ritual where hymns are sung and a ball is danced, accompanied by vigorous percussion instruments (De Rios and Rumrill, 2008). The second *ayahuasca* religion emerged in Brazil is known as *A Barquinha*, created in 1945 by Daniel Pereira Mattos. Also known as Mestre Daniel, he attended the cult of Mestre Irineu (*Santo Daime*) for a decade and after founded *A Barquinha*, in the city of Rio Branco (Goulart, 2004). Known firstly as a *rezador* (prayer specialist), he helped travelers, hunters and rubber tapper that passed by the forest. There, he began his spiritual activities and gained some followers of his teachings. With the time, he mixed to these activities the consumption of *ayahuasca*, being one of the most striking characteristic of this new religion the practice of rituals similar to those in Umbanda, an afro-brazilian religion (Labate, et al., 2010). Finally, we have the *União do Vegetal* (UDV). It is the biggest and most widespread Brazilian *ayahuasca* religion. Founded in 1961 by the rubber tapper José Gabriel da Costa-also known as Mestre Gabriel-in the city of Plácido de Castro, in Acre state, UDV has in Porto Velho (capital of Rondônia state) its main activity center (MacRae, 2004). The main influence comes from spiritism, incorporating aspects of other afro-brazilian religions during the time, as the batuque, the umbanda and the macumba. In UDV, the preparing of the drink receives special attention, being considered an extreme important moment for the followers (Goulart, 2004). According to Mikosz (2009), there are different ways to prepare the *ayahuasca*. In some cases, it is not even necessary to boil the plants, being sufficient to maintain them in cold water. The description for the mode of preparation follows that observed by the author in the ambit of UDV, being the most frequent in other religions. The vine is picked, cut, washed and macerated. The bush leaves are washed and put with the vine to boil in a big pan with water, in intercalated layers. Normally it is used the double of vine in relation to the leaf. The decoction consists in a long process, which may last days, depending the beverage quantity and its refinement, until obtain a tea with a hazel colour (between the ochre and brown) with a bitter taste. In some amazon religions, hymns and chants are sung and a ritualistic and respectful posture is adopted during the preparation of the drink. The tasks can be divided among men and women: women wash the bush leaves, commonly associated to the feminine energy and to the light; men work with the vine, associated to the masculine principle and strength. The beverage must to be carefully manipulated; since it has no type of preservative, it can sour rapidly. *Ayahuasca* consumers begin to feel the first symptoms at about 30 minutes after ingestion – situation known among the consumers as *burracheira*, expression probably derived from the Spanish word *borracho* (drunk). In the first ingestion, the bitter is extremely strong and nasty to taste. It can occur nausea and diarrhea, being common the sensation of face disfiguration and other body parts (Mikosz, 2009).

Physiologically, cardiovascular stimulation is occurred, with moderate increase of heart rate and blood pressure (Riba, et al., 2003). The emotional experiences when *ayahuasca* is consumed, such as change in cognitive patterns, are related to the powerful action of the beverage in the central nervous system (Bouso and Riba, 2011). It is noteworthy, however, that the nature of these experiences can not be explained by just one scientific field; the understanding of *ayahuasca* effects go beyond the frontiers of different knowledge fronts, as pharmacology, psychology and anthropology, and reinforce the potential of therapeutic knowledge of indigenous and traditional communities of South America.

### PHARMACOLOGY

The first analytic studies on the chemical composition of *ayahuasca* were published in Seventies decade. Rivier and Lindgren (1972) reveal the presence of  $\beta$ -carbolines and N,N-dimethyltryptamine (DMT) as its majority compounds. Among the main  $\beta$ -carbolines present in *B. caapi* there are harmine, harmaline and tetrahydroharmine (Furst, 1976). *Psychotria viridis* is the main source of DMT, a hallucinogenic triptamine with ultra-rapid action which reach plasmatic concentration spikes in a relative short period of time and in low ingested doses (Callaway, et al., 1999). The harmine is an alkaloid of  $\beta$ -carboline group, commonly found in plant species, as *Grevia bicolor* (*Malvaceae*), *Passiflora incarnata* (*Passifloraceae*) and *Peganum harmala* (*Zygophyllaceae*) (Kartal, et al., 2003; Jaspers, et al., 1986; Cao, et al., 2007). Its pharmacological properties goes from tremorgenic action (Cox and Potkonjak, 1971), depression of cardiac (Carpentier, 1980) and vascular (Berrougui, et al., 2006) muscle, antibacterial activity (Aassila, et al., 2003), antiparasitic (Di Giorgio, et al., 2004), insecticide (Bouayad, et al., 2012), to activities in complex process of bone regeneration (Yonezawa, et al., 2011). But the main studies are focused in the activity of the substance on nervous system, whose properties comprise sedative and ansiolitic activities (Carlini, 2003), antidepressive (Fortunato, et al., 2010) and treatment of mood disorders (Fortunato, et al., 2009). By temporally modify serotonergic neurotransmission, the *ayahuasca* has a powerful action on central nervous system. Its action mechanism constitutes a classical sample of synergism between drugs, where the conjunct ingestion of DMT and  $\beta$ -carbolines is responsible by the unleashing of reactions which constitute the base of user's experience. Therefore, it is particularly interesting that South American indigenous, without any scientific knowledge, discover centuries ago the synergic effect of plant species used in the preparation of *ayahuasca* (Carlini, 2003). The DMT can be found both in plant species, such as *B. capis* (*Malpighiaceae*) and *Mimosa tenuiflora* (*Mimosoideae*) (Gaujac, et al., 2012; Moura, et al., 2010), as in animals, particularly mammals, being considered an endogenous substance, that is, also produced inside the human body (Christian, et al., 1977). It presents a structure similar to serotonin, joining to the same receptors to this neurotransmitter (Smith, et al. 1998), which has functions in different systems, such as cardiovascular, gastrointestinal and central nervous, where acts in motor, sleep, mood, nociception, sensorial perception and cognition activities, among others (Brunton, 2010). The DMT from the bush is rapidly metabolized and inactivated by monoamine oxidase (MAO) presents in liver and intestine, enzyme responsible by degradation of serotonin in case of high levels in organism and that works as serotonergic synaptic activity regulator. However, the vine  $\beta$ -carbolines are able to inhibit MAO, allowing DMT to reach the SNC and act in similar manner to serotonin (Cakic, et al., 2010; Brunton, 2010). Studies prove the

action of DMT in the cerebral cortex, initiating the conscience alterations and visualization of multicolor geometric patterns by *ayahuasca* users, and reinforce the synergic character of the beverage chemical compounds (DMT and  $\beta$ -carbolines) for initiating reactions (Don, et al., 1998; Freedland and Mansbach, 1999). The appearance of psychoactive effects can be described in three distinct stages (Laqueille and Martins, 2008). Firstly, it occurs physiologic alterations more or less intense, such as violent peristaltic contractions with vomit, colic and distorted, disordered and multicolor patterns vision. The second stage is characterized by capacity of individual to control these visions, adjusting to its life personal experiences. This period requires a certain concentration effort, otherwise physical and emotional discomfort can appear. The power of controlling the visualization of multicolor patterns through the opening and closing of the eyes is frequently mentioned by users (Mikosz, 2009), situation in which there are significant alterations in cortical cerebral activity (Don, et al., 1998). Finally, in the third stage, the individual let to be taken by his own thoughts, freely associating them through an introspective disleptic experience highly emotional and that can be easily remembered after the end of drinking activity. Studies show that DMT needed doses to the emerging of psychoactive effects are about 25mg, through parenteral route; if ingested orally, the effects do not appear nor in high concentrations of 1000 mg (Shulgin, 1982), due the intestinal and liver MAO action in the absence of the  $\beta$ -carbolines. The dose of *ayahuasca* ingested during a religious ceremony is very variable. McKenna et al. (1984) found high DMT values (60mg) and of harmine (467mg) in doses of 100ml used by Peruvian communities. Rivier and Lindgren (1972) related that doses of 200ml commonly utilized in Amazonian rituals provide about 25 mg of DMT and 40mg of harmine. These quantities were sufficient for the emerging of drinking psychoactivity, although other studies point alterations in cerebral cortex when more high doses are administrated (approximately 40mg of DMT and 55mg of harmine) (Don, et al., 1998). Obviously, the effects intensity, duration and kinds of reactions can variate from an individual to another. The evaluation of the beverage psychoactive effects on consumers do not followed a defined pattern in the past time. Recently, it has been utilized the Hallucinogen Rating Scale (HRS) for the studies of the subjective effects of *ayahuasca*, considering parameters as somaesthesia (alterations in physiologic process, as visceral and tactile), affection (sensitivity to affective and emotional responses), volition (capacity to interact with the *self*), cognition (alterations in thoughts or content process), perception (vision, hearing, smell and taste alterations), and, lastly, intensity (experience strength) (Riba, et al., 2001). Due the inactivity of DMT by MAO when ingested, recent studies have pointed the employ of others administration methods of the substance, for example the smoke, both of the synthetic DMT and of the extracted from plant species acquired or cultivated by the own users (Cakic, et al., 2010). The action of the smoked DMT is extremely fast, generating short duration episodes very intense (McKenna, et al., 1984). Although elucidated the main action mechanisms of *ayahuasca* chemical compounds, a better understanding of the metabolic routes involved in the psychoactive reactions generated in the individuals has encouraged new researches in this field, bringing more informations about the pharmacokinetic of its active principles (Zhao, et al., 2012).

**Legal aspects in the use of *ayahuasca*:** Recently, a controversy has emerged in global level in relation to the legality in the use of *ayahuasca*, mainly due to the expansion of *ayahuasca* religions to USA and European countries. Public reactions against this

expansion follow a particular pattern and perform an important role in international approach about the legitimacy on the use of psychoactive plants by minorities religious groups (Labate and Feeney, 2012). In this sense, it becomes essential to know the history of the beverage use by traditional communities. An evaluation of regulatory aspects during the time is also necessary for a wider understanding of the legal issue of use. At the time of emergence of Daime, around 1930, it was in the mainstream in Brazil an official politic of repression to sorcery and to the use of “magic”, to the illegal medicine practice and shamanism, reflecting a law valid since Nineteenth century. Some ayahuasca centers, however, were unaffected to police chase due the support of local elite; so to Daime was conferred a religion *status* (MacRae, 1992). In 1971, the DMT, *ayahuasca* psychoactive principle, pass to integrate the list of illicit drugs in International Drug Treaties, in which Brazil is signatory, according to the established in the Convention on Psychotropic Substances (United Nations, 1971). From the dissemination of informations about the beverage psychoactive effects and the expansion of its consumption by urban social classes, the Brazilian Health Ministry conferred to the use of *ayahuasca* a prohibitive character in 1985. The prohibition lasted only 6 months and the pressure of religious groups and Daime doctrine adepts forced to create a new scientific commission to investigate the nocive effects in health related to the beverage consumption (MacRae, 1998). In that same year, it was created a Work Group to examine the issue of production and consumption of substances derivated for plant species which compound *ayahuasca*, in all its aspects (CONFEN, 1985). After 2 years, the referring group recommended the authorization of using the beverage for religious purposes, considering the tradition of its use by ayahuasca religions without any known social injury (CONFEN, 1986). Lately, after 25 years of group acting, its final report published in 2010 recommend the maintenance of the non-prohibition of *ayahuasca* use, decision which seems to finish the polemic in relation to its use, although the DMT compound still remain in the list of prohibid substances in Brazil. In 2006, an important step was given with the authorization of international use of *ayahuasca*: the Supreme Court of the United States granted to the Spirit Center União do Vegetal (UDV) the right to utilize the beverage in religious rituals in American territory (Godoy, 2006). Similar cases in country like Australia, Italy, Holland and Spain reveal the importance of the discussion about the right to the religion freedom (Tupper, 2008). Considering the even more global character of the society, governments of all world will be confronted with this issue, and should be able to deal with the most fair way possible with practices that not always coincide with conventional values, so that the current war against drugs do not damage the minorities religious groups (Labate and Feeney, 2012).

**Current scientific focus on ayahuasca:** The recent works being published in different science areas, such as psychiatry, philosophy, anthropology and arts, in the ambit of *ayahuasca* use, have demonstrate an interesting variety in the scientific focus on the beverage. From the most traditional research about the pharmacological and psychosocial effects of beverage consumption, to the recent artistic approaches, it is possible to realize the great interest of scientific community in the beverage use by present society. Inside psychiatry and pharmacology, long term studies about personality, psychopathology and neuropsychological functions in *ayahuasca* users are essential to determine the implications that the beverage use can bring to the mental health of consumers (Bouso and Riba, 2011). Fábregas et al., (2010) showed that the ingestion practice of *ayahuasca* in religious ceremony have no relation to

psychosocial deleterious effects typically caused by other types of abuse drugs. The controlled administration of known dosages in selected individuals has provided valious information about the impacts of its ingestion on organism and psyche (Bouso and Riba, 2011). Researches have demonstrated the therapeutic potential of *ayahuasca* for treatment of disorders like alcoholism and drugs abuse. Clinical investigations performed in Europe suggest that its use can be done in a safe way in healthy adults. More detailed clinical studies, however, slip into problems in the regulatory and ethics, especially in the United States (McKenna, 2004). In the social ambit, another recent approach about *ayahuasca* comprises the study of recreative beverage use for non-religious purposes, that is, in situations in which the beverage ingestion is decontextualized of its origins (Cakic, et al., 2010). It seems to have a growing beverage use outside the ritualistic ambit, revealing, however, a positive subjective perception of psychotherapeutics and spirituals effects in consumers. Studies also have been directed to the understanding of how the curiosity about the *ayahuasca* entheogen power can affect the amazon communities, mainly due the increasing of spiritual tourism. The tourism of *ayahuasca* is inserted in a paradigm which involves the social-economic gap between the local amazons and the tourists and curious, many times neglecting the impacts caused in tradicional communities (Holman, 2011), since economical, environmental, socioculturals and even political (Bauer, 2008). It should be considered the growth of ecotourism industry in South America, discovering the exploring potential of ayahuasca religions. In countries as Colombia, Peru and Brazil, there are travel agencies which provide tour packages in whose is included the right to visit traditional amazon communities and try the *ayahuasca* (Halpern, 2004). Finally, interesting and recent interdisiciplinary research fronts have addressed how *ayahuasca* induces the formation of Non-Ordinarie State of Conciousness (NOSC), initiating the visualization of various geometrical and multicolor characteristics patterns. In many times these patterns are artistically expressed by visionary art-art which production is conditioned to experiences arising from NOSC (Mikosz, 2009). There are several works produced by ayahuasca artists, and interdisciplinary studies have been realized in order to relate the influence of beverage effect on artistic and cultural expression.

### CONCLUSION

The recent studies on *ayahuasca* in diferente science areas show its importance to international scientific community, interested in raise the knowledge about its properties. A bigger understanding on its origins, action mechanisms and bioactivity will only be reached when the scientific approach gain a wider scope through interdisciplinary studies, which is occouring in the last years, and can reduce the negative character attributed to its consumption in certain societies. The discussion about legality of *ayahuasca* use and the authorization of clinical investigation with consumers is extremely valid, and may have implications in major discussions about the use of abuse drugs, non-conventional therapeutic and religious freedom.

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