ICEERS INTERNATIONAL CENTER FOR ETHNOBOTANICAL EDUCATION RESEARCH & SERVICE

Ayahuasca

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1. What is ayahuasca?

Ayahuasca is the Quechua word referring to a liquid produced by the slow decoction of the Amazonian *Banisteriopsis caapi* vine – as well as to the vine itself – which contains harmine, harmaline and tetrahydroharmine. It is traditionally used throughout the Northwestern Amazon, originating from indigenous cultures that have used it for hundreds of years for medicinal and ritual purposes. At the beginning of the last century, syncretic religions combining Amerindian shamanism, African religiosity, European esotericism, and Christianity began to use ayahuasca. In the 1980s, these churches expanded from the Amazon into Brazilian urban centers (Labate 2004) and, since the 1990s, globally (Labate & Jungaberle, 2011).

Based on the intended use of the decoction of the vine called ayahuasca, Amazonian group or healer with experience using ayahuasca, adds different plants to the decoction with the objective of communicating with a specific spirit depending on the disease to be healed or ritual to be performed. Ethnographic studies suggest that there are more than 5000 different recipes of ayahuasca (Fericgla, 1997) and more than 200 admixture plants to ayahuasca, all using *B. caapi* as their base (McKenna et al., 1986). Some of the traditional recipes involving ayahuasca, considering both the indigenous cultures and the religions that use ayahuasca as their sacrament (or “ayahuasca religions”), include adding leaves of the *Psychotria viridis* bush, which contains DMT (N,N-Dimethyltryptamine), along with the *B. caapi vine* (Schultes & Hofmann, 1992). Ayahuasca is currently being popularized as the combination of *B. caapi* and *P. viridis*, likely because the international expansion of ayahuasca practices was initiated by these churches (Sánchez y Bouso, 2015).

The precise historical beginning of ayahuasca use is unknown. The oldest traces of possible ayahuasca use have been found in the Azapa desert in the north of Chile, where harmine residues have been found in hair analyzed from mummies from the Tiwanaku period between 500 and 1000 C.E. The *B. caapi* vine does not grow in the Azapa valley, nor do any other harmine-containing plants, which suggests well-established commerce between the ancient populations of the Andes and the Amazonian peoples; probably the former provided the latter with salt and the latter provided the former with medicines, among them ayahuasca. Among Amazonian ethnic groups, the use of ayahuasca decoctions that also contain plants with DMT seems to be a more recent phenomenon (Brabec de Mori, 2011).

Ayahuasca is considered a sacred drink by innumerable indigenous Amazonian groups and a medicine by mestizo healers in several parts of South America. The traditional and modern use of ayahuasca extends from Panama to Bolivia, including Peru, Ecuador, Colombia, and Brazil – countries in which its medicinal use is present also in urban centers (Luna, 1986, 2011). A

pioneering 1986 work that brought together all the scientific information on ayahuasca available at that time found more than 400 bibliographical references on the ethnography of ayahuasca (Luna, 1986b), references to more than 70 different Amazonian ethnic groups where it was used traditionally, and more than 40 vernacular names given to the decoction (Luna, 1986c). Ayahuasca is currently being used as a medicine in ceremonies officiated by indigenous peoples, mestizos, and diverse professionals who have learned to use it in its places of traditional origin (Labate & Bouso, 2013; Labate & Cavnar 2014a; Labate, Cavnar & Gearin, 2017; Labate et al., 2009; Luna, 2011).

2. The legal status of ayahuasca

As noted above, ayahuasca is typically produced by the slow decoction of two plants – *B. caapi* and *P. viridis*. The latter of these two plants contains DMT (N,N-dimethyltryptamine), a tryptamine alkaloid listed in the 1971 Convention on Psychotropic Substances, and many countries therefore also include it in their national legislation. Although DMT is listed in Schedule 1 in the Conventions (the most restrictive category), the International Narcotics Control Board (INCB), a quasi-judicial control body for the implementation of the United Nations drug conventions, has stated on several occasions that ayahuasca – as well as other psychoactive plants – are not subject to international control.

In their 2010 Annual Report, the INCB stated that "[…] although some active stimulant or hallucinogenic ingredients contained in certain plants are controlled under the 1971 Convention, no plants are currently controlled under that Convention or under the 1988 Convention. Preparations[1] (e.g. decoctions for oral use) made from plants containing those active ingredients are also not under international control" (paragraph 284, INCB, 2010).

The alkaloids present in the *B. caapi* vine are also not subject to international control. In 2008, ayahuasca was declared Cultural Patrimony of Peru, due to its ancestral use as a traditional medicine (Instituto Nacional de Cultura, 2008) and its use for religious purposes is firmly established and legalized in Brazil (Labate et al., 2009). The religious use of ayahuasca on the part of certain churches is also legally protected and regulated in Holland and the United States, and the churches in which ayahuasca is considered a sacrament and is consumed for that purpose

[1] The Article 1 from the 1971 Convention, which is dedicated to specify the terms used in the treaty, understands as preparation: "1) Any solution or mixture, in whatever physical state, containing one or more psychotropic substances, or 2) One or more psychotropic substances in dosage form." Therefore, since ayahuasca is a decoction of plants that are not controlled, and not a mixture of active principles, then the term "preparation," according to the definition of the treaty, is not appropriate when referring to ayahuasca (Art. 1, f) i)).

have expanded internationally into numerous European, American, and Asian countries (Labate et al., 2009; Labate & Feeney, 2012; Sánchez & Bouso, 2015).

In terms of Spain, upon the request of lawyers working on ayahuasca-related cases, the Spanish Agency of Medicinal Products and Medical Devices (AEMPS) issued letters confirming that although DMT is a controlled substance according to the 1971 Convention on Psychotropic Substances, ayahuasca is not subject to control by Spanish legislation (e.g. AEMPS, 2013).

3. The pharmacology of ayahuasca

The mechanism of action by which ayahuasca produces its effects is highly sophisticated. The harmala alkaloids (harmine, harmaline and tetrahydroharmine) have the property of acting as inhibitors of monoamine oxidase (MAO), an enzyme present in the gastrointestinal tract that degrades monoamines. As DMT is a monoamine, if it is ingested orally, the endogenous MAO deactivates it, preventing it from reaching the brain. At some point in the remote past, the indigenous people of the Amazon Basin discovered that adding the leaves of *Psychotria viridis* (which, as previously mentioned, contain DMT) to a decoction of *Banisteriopsis caapi* (which contains harmala alkaloids), makes the DMT bioactive. This is due to the harmala alkaloids, which, acting as MAO inhibitors (MAOIs), block the MAO present in the gastrointestinal tract and in this way the DMT present in the leaves of P. viridis can reach the brain (Mckenna et al., 1984; Riba et al., 2003). Pure DMT on its own is inactive when consumed orally (Riba et al., 2015). This sophisticated indigenous discovery was only recently rediscovered by science in the 1980s. DMT is found in its natural form in many animal species (Shulgin & Shulgin, 1997) and in human urine, blood, and cerebrospinal fluid (Barker et al., 2012). Its physiological role remains unknown.

During the last few decades, clinical trials have been carried out on humans where both DMT (in purified form, administered intravenously) and ayahuasca (administered orally) have been administered in a laboratory context, and their acute effects have been characterized both at the psychological and somatic levels. In these studies, it has been demonstrated that DMT and ayahuasca have very different pharmaco-dynamics. The acute effects of DMT appear in an intense and almost immediate way after its intravenous administration (Strassman & Qualls, 1994; Strassman et al., 1994), while ayahuasca produces effects in a slower and more progressive way, beginning from 45 to 60 minutes after administration, reaching maximum effects after 2 hours, which disappear after 4 to 6 hours (Riba, 2003; dos Santos, 2011). The maximum intensity of the effects of DMT is approximately two times that of ayahuasca at equivalent doses (Grob et al., 1996), which makes the global effects of ayahuasca much more controllable than pure DMT. In addition, since ayahuasca is a decoction made with plants there are also other compounds (beta-

carbolines) that may modulate the effects and thus make them significantly different from pure DMT.

4. The effects of ayahuasca

Ayahuasca, whether administered in a laboratory context or ingested in a traditional context, produces transitory modifications in emotion, thought content, perception and somatic sensations – as evaluated through questionnaires to measure its subjective effects – while the capacity of the individual to interact with its surroundings is significantly preserved (Grob et al.,1996; Riba et al, 2001, 2003; dos Santos et al, 2011, 2012), even to the point of being able to carry out complex cognitive performance tests (Bouso et al., 2013). The volunteers in these studies also describe the effects of ayahuasca as "well tolerated" (Riba et al., 2001, 2003; dos Santos et al., 2011, 2012). The curve of effects that ayahuasca produces corresponds with the curve of the presence of DMT and harmalines (MAOIs) in plasma, which disappears from the organism after eight hours (Riba et al., 2003; Schenberg et al., 2015).

Studies have been published where neuroimaging techniques were used to determine which cerebral areas are activated after the ingestion of ayahuasca. Two studies showed that ayahuasca activates the cortical and paralimbic areas. Specifically, in the first of these studies (Riba et al., 2006), bilateral increments in cerebral perfusion were found in the inferior frontal gyrus and the anterior insula, the activity being most intense in the right hemisphere. Activations in the anterior cingulate and medial frontal cortex in the right hemisphere, areas involved in awareness of interoceptive and emotional processes, as well as emotional arousal, were also found. Increased cerebral blood flow in the ventral anterior cingulate gyrus and the subcallosal was also recorded, structures that are related to decision-making and emotions. The left amygdala, a structure involved in the processing of potentially threatening stimuli, and the parahippocampal convolution, a structure associated with the hippocampus and intimately involved in the processing of memories, also showed higher blood perfusion compared to placebo. No differences were found compared to placebo in any other area of the brain.

In another second neuroimaging study performed with Functional MRI (fMRI), activation in primary visual areas was also found, and when subjects under the influence of ayahuasca were remembering a photograph its magnitude was comparable to baseline activation levels recorded with the presentation of a natural image with eyes open (de Araujo et al., 2011). According to the authors, this effect causes the brains of volunteers to interpret the ayahuasca experience as if it was "real," not in the sense of a hallucinatory experience, but by the experiential endowment of conscious experience. This overall pattern of activation may be at the base of the introspective

processes, memories of past experiences charged with emotional connotations, and complex cognitive processes, which are so prototypical of the ayahuasca experience (Shanon, 2002).

In fact, a recent fMRI study showed a deactivation of a neural network known as the Default Mode Network (DMN) (Palhano-Fontes et al., 2015). This network, which includes different brain structures, is thought to be involved in internal mental processes, such as the sense of "I," or the mental imagery produced when a person is in a state of relaxation. Abnormal increases in DMN activity were observed in a wide spectrum of neurological disorders such as autism, Parkinson's and Alzheimer's disease, and psychiatric disorders such as schizophrenia and depression. In this study, it was observed that ayahuasca decreased DMN activity, a finding also observed with other substances of similar psychoactivity, such as psilocybin (Carhart-Harris et al., 2012).

When considered together, these cerebral, cognitive, and emotional phenomena could explain why ayahuasca is considered an ethnobotanical tool with psychotherapeutic potential (Labate & Cavnar, 2014b). In fact, one study found that ayahuasca reduced panic and hopelessness scores in experienced users (Santos et al., 2007).

5. Long-term effects

Studies of medium- and long-term ayahuasca use have shown evidence of either neuropsychological or psychopathological alterations associated with the continuous use of ayahuasca. One prospective study conducted among people that ingested ayahuasca for the first time showed improvements on mental health measures and physical pain reduction for six months after initiation to ceremonial ayahuasca use (Barbosa et al., 2005, 2009). Other studies have shown better indicators of psychopathology and higher psychosocial wellness among regular ayahuasca users (Bouso et al., 2012; Halpern et al., 2008) and three studies did not find neuropsychological alterations measured with cognitive performance tests among regular users of ayahuasca after years of continuous use (Grob et al., 1996; Barbosa et al., 2016; Bouso et al., 2012; Bouso et al., 2015). One of these studies compared 127 ayahuasca users with a history of ritual ayahuasca use of at least 15 years with 115 controls, and observed better scores on psychopathological measures and in some neuropsychological tests among the ayahuasca users – results that remained consistent in two evaluations separated by one year (Bouso et al., 2012). Studies with adolescent members of a Brazilian UDV church also failed to observe any neuropsychological or psychiatric alterations associated with ritual ayahuasca use (da Silveira et al., 2005: Doering-Silveira et al., 2005b).

Finally, a recent neuroimaging study with Spanish members of the Santo Daime church with participants who had a history of ayahuasca use of at least 50 occasions in the past two years found differences on cortical thickness among the ayahuasca users compared to a control group. Differences in cortical thickness were only correlated with the personality variable “Self-Transcendence,” suggesting that ayahuasca may produce brain alterations that could manifest as increased spiritual tendencies (Bouso et al., 2015). Ayahuasca users in this study had similar scores to the control group of non-users on psychopathological tests and on neuropsychological function, showing that the structural changes possibly associated with ayahuasca use did not relate to brain toxicity, but to personality changes that simply reflect a “different,” but not pathological, way of being, as has been shown in several previously cited studies (Grob et al., 1996; Barbosa et al., 2009 Barbosa et al., 2016; Bouso et al., 2012; da Silveira et al., 2005; Doering-Silveira et al., 2005b; Halpern et al., 2008). These kinds of brain alterations are also known to be produced through training and practice in numerous activities, such as learning music, and are known as cerebral plasticity – a normal phenomenon that occurs in our brains continuously throughout our lives.

6. Adverse effects

Some adverse effects associated with ayahuasca administration in laboratory contexts have been reported, although these were rare and isolated cases that were resolved without the need for intervention (Riba & Barbanoj, 2005). There are some cases describing psychiatric symptomatology in ritual contexts, although these cases are rare (Lima & Tófoli, 2011; dos Santos & Strassman, 2011) and their occurrence seems to be below the prevalence of psychiatric problems in the general population. In any case, these data suggest that ayahuasca is, in principle, contraindicated for people with grave psychiatric disorders, particularly those individuals prone to psychosis.

Although ayahuasca is psychoactive, this does not mean that the doses that are usually ingested in sessions produce organic or brain toxicity. In this sense, and according to toxicology science, the minimum psychoactive dose should not be equivalent to the toxic dose, if toxicity is considered the capacity of a substance to induce harm to an organism by means of its chemical properties after being in contact with the organism (Baños & Farré, 2002). Regarding the effects of ayahuasca in the organism, studies performed with volunteers both in the laboratory (Riba, 2003; dos Santos, 2011) and in natural contexts (McKenna, 2004) show that ayahuasca is physiologically safe. The impact of ayahuasca on the cardiovascular system is minimal, producing only slight increases in blood pressure and heart rate that have no clinical implications (Riba et al., 2001, 2003; dos Santos et al., 2012). It was also observed that ayahuasca induces transitory increases

in the levels of the hormones prolactin, cortisol, and growth hormone (dos Santos et al., 2011, 2012), and with regards to the immune system, ayahuasca time-dependently reduces subpopulations of CD4 and CD3 lymphocytes and increases natural killers (NK) cells (dos Santos et al., 2011, 2012). These transitory physiological effects do not seem to have negative consequences – in studies where general blood analysis were performed in subjects before and after the participation in the trials, no hematological or biochemical alterations were found (Riba et al., 2001; Riba & Barbanoj, 2005).

The main adverse effects produced by ayahuasca are nausea and vomiting (Callaway, et al., 1999; Riba et al., 2001; Riba, 2003; Riba & Barbanoj, 2005; dos Santos, 2011; dos Santos et al., 2012). The emetic action of ayahuasca is related first to the organoleptic properties of the decoction, and second to its serotonergic action (Callaway et al., 1999). These are not considered important adverse reactions by session participants, where they are understood as potential therapeutic effects and called “la purga” (“the purge”) in traditional Amazonian medicine (Luna, 1986, 2011) or “limpeza” (cleansing) in the context of the Brazilian ayahuasca religions (Labate, 2004). In traditional contexts, the “purge” is understood as a physical and psychological cleansing from internal conflicts that may distress the participant, and is considered an essential part of the therapeutic benefits (Luna, 1986, 2011). The emetic effects of ayahuasca suggest that ayahuasca is likely one of the main reasons it does not have a potential for recreational use.

7. The abuse potential of ayahuasca

Studies with healthy volunteers showed that ayahuasca does not produce tolerance (dos Santos et al., 2012), thus it is not necessary to increase the dose to achieve the desired effects, which, together with the emetic effects, protect consumers from overdose.

Regarding the abuse potential of ayahuasca, in the neuroimaging studies with healthy volunteers described above, no activation of brain areas related to the reward systems was observed – the brain areas activated by drugs with potential for abuse. Moreover, the available evidence suggests that ayahuasca could be used as a tool for the treatment of drug dependence (Bouso & Riba, 2014). Indeed, there are several clinics in South America that specialize in the treatment of drug dependence using ayahuasca, the most well-known being Takiwasi, in Peru (Mabit, 2007). In a recent study conducted with patients with severe depression, researchers found that ayahuasca activates a reward system in the brain called the nucleus accumbens, creating an effect that the authors of the study found to be unique to patients with depression – a finding that contributes to explaining the anti-depressant effects of ayahuasca in patients with severe depression.

One of the first human studies on ayahuasca use showed that many participants of UDV church rituals stopped using alcohol and other drugs, such as cocaine, as a result of their participation in church rituals (Grob et al., 1996). These findings were also found in a subsequent study with members of the Santo Daime church in Oregon, USA (Halpern et al., 2008). Another study with a large number of participants, which compared 127 ayahuasca consumers with 115 controls – failed to find evidence of drug dependence according to the biopsychosocial criteria of the ASI scale (Addiction Severity Index, the standard scale to assess drug dependence), or evidence that the continuous ritual use of ayahuasca was associated with harmful biopsychosocial consequences related to drugs of abuse. Moreover, the ayahuasca group consumed less alcohol and other drugs compared to the control group, and these scores on the biopsychosocial criteria for drug dependence were replicated a year later, confirming the consistency of the results (Fábregas et al., 2010). A study with adolescent members of the UDV church also found that the ayahuasca group consumed less alcohol than the control group, concluding that rather than being associated with drug dependence, ayahuasca use seemed to act as a protective factor regarding alcohol consumption (Doering-Silveira et al., 2005a).

8. Therapeutic potential of ayahuasca

The therapeutic properties of ayahuasca are related to its effects on the brain – it activates cerebral areas associated with memories of personal events (called episodic memory) and with the conscious experience of emotions and internal sensations (Riba et al., 2006; de Araujo et al., 2011). From a psychological perspective, a recent study showed that the therapeutic potentials of ayahuasca might be related to its ability to increase what is called in clinical psychology “decentering” (Soler et al., 2016), or the capacity to observe thoughts and emotions as transitory events of the mind without being trapped by them. This process is considered important in clinical psychology, because it can produce psychological changes in patients.

If ayahuasca does not have potential for recreational use or abuse, there must be other reasons why people use it. Personality studies performed among Brazilian and Spanish ayahuasca users did not find higher scores on a scale known as Novelty Seeking (Grob et al., 1996; Bouso et al., 2012; Bouso et al., 2015), a personality trait for which users of drugs of abuse have high scores. Nevertheless, ayahuasca users scored higher than controls on a personality trait called Self-Transcendence (Bouso et al., 2012; Bouso et al., 2015), or the tendency to have a transcendent concept of life, not necessarily associated with a religious affiliation. Taken together, these personality studies have found that people who use ayahuasca do so for reasons that are related to personal development, the search for psychological wellbeing, and adapting better to their environment. Indeed, these studies reported that ayahuasca users are people perfectly adapted

and integrated in their social, working, and familiar environments and that ayahuasca is used as a tool for personal and spiritual improvement – findings that are similar to those observed among people who practice meditation or other techniques for personal development and wellbeing (Soler et al., 2016; Palhano-Fontes, 2015).

There are some studies that have explored the therapeutic potential of ayahuasca in psychiatric populations. A recent study reported anti-depressant effects of ayahuasca in patients with major depression, effects that were sustained for 21 days after the administration of a single dose (Osório et al., 2015; Sanches et al., 2016). This therapeutic effect was associated with brain changes measured with neuroimaging techniques, thus providing an objective demonstration of therapeutic change (Sanches et al., 2016). Another more recent study confirmed the anti-depressant effect of a single dose of ayahuasca within one day of the session, when compared with a placebo (Palhano-Fontes et al., 2017). Other recent studies showed preliminary evidence of efficacy in the treatment of drug dependence (Fernández et al., 2015; Labate y Canvar, 2014b; Loizaga-Velder y Verres, 2014; Thomas et al., 2013). Although the research on the therapeutic effects of ayahuasca is still nascent, several authors propose that ayahuasca could also be used to treat posttraumatic stress disorder (PTSD) (Nielson and Megler, 2014) or antisocial behavior, among other disorders (Frecksa et al., 2016).

Conclusion

In conclusion, both the currently available scientific evidence on the acute and long-term effects of ayahuasca and the studies that employed it as a therapeutic tool with psychiatric populations suggest that ayahuasca is a substance with an acceptable physiological and psychological safety profile and with therapeutic potential (McKenna, 2004; Gable, 2007; Bouso & Riba, 2011; Barbosa et al., 2012; dos Santos, 2013).

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Signed by:

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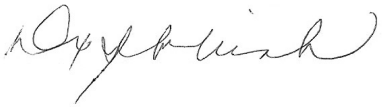

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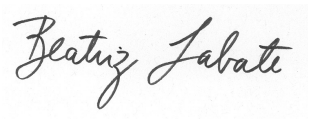

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References

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS). 2013. N. de Registro: 26803 / RG 50172.

Baños, J.A. & Farré, M. 2012. Principios de Farmacologia Clínica. Barcelona: Masson.

Barbosa, P.C.; Giglio J.S. & Dalgalarrondo, P. 2005. Altered states of consciousness and short-term psychological after-effects induced by the first time ritual use of ayahuasca in an urban context in Brazil. *Journal of Psychoactive Drugs*, 37 (2): 193-201.

Barbosa, P.C.; Cazorla, I.M.; Giglio, J.S. & Strassman, R. 2009. A six-month prospective evaluation of personality traits, psychiatric symptoms and quality of life in ayahuasca-naïve subjects. *Journal of Psychoactive Drugs*, 41 (3): 205-12.

Barbosa, P.C.; Mizumoto, S.; Bogenschutz, M.P. & Strassman, R.J. 2012. Health status of ayahuasca users. *Drug Testing & Analysis*, 4 (7-8): 601-9.

Barbosa PC, Strassman RJ, da Silveira DX, Areco K, Hoy R, Pommy J, Thoma R, Bogenschutz M. 2016. Psychological and neuropsychological assessment of regular hoasca users. Compr Psychiatry. 71:95-105.

Barker, S.A.; McIlhenny, E.H. & Strassman, RJ. 2012. A critical review of reports of endogenous psychedelic *N, N*-dimethyltryptamines in humans: 1955-2010. *Drug Testing & Analysis*, 4 (7-8): 617-35.

Bouso, J.C. & Riba, J. 2011. An overview of the literature on the pharmacology and neuropsychiatric long term effects of ayahuasca. In: R.G. dos Santos (Ed.). *The Ethnopharmacology of Ayahuasca*. Trivandrum: Transworld Research Network. http://www.trnres.com/ebook/uploads/rafael/T_12998350813%20Rafael.pdf.

Bouso, J.C & Riba, J. 2014. Ayahuasca and the Treatment of Drug Addiction. In: B.C. Labate & C. Cavnar (Eds.).: The Therapeutic Use of Ayahuasca. Berlin: Springer, pp: 95-109.

Bouso, J.C.; González, D.; Fondevila, S.; Cutchet, M.; Fernández, X.; Barbosa, P.C.R.; Alcázar-Córcoles, M.Á.; Araújo, W.S.; Barbanoj, M.J.; Fábregas, J.M. & Riba, J. 2012. Personality, psychopathology, life attitudes and neuropsychological performance among ritual users of ayahuasca: A longitudinal study. *PLOS ONE*, 7 (8): e42421.

Bouso, J.C.; Fábregas, J.M.; Antonijoan, R.M.; Rodríguez-Fornells, A. & Riba, J. 2013. Acute effects of ayahuasca on neuropsychological performance: differences in executive function between experienced and occasional users. *Psychopharmacology*. doi: 10.1007/s00213-013-3167-9.

Bouso JC, Palhano-Fontes F, Rodríguez-Fornells A, Ribeiro S, Sanches R, Crippa JA, Hallak JE, de Araujo DB, Riba J. Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans. Eur Neuropsychopharmacol. 2015 Apr;25(4):483-92.

Brabec de Mori, B. 2001. Tracing hallucinations: Contributing to a critical ethnohistory of ayahuasca usage in the Peruvian Amazon. In B. C. Labate & H. Jungaberle (Eds.), The internationalization of ayahuasca. Zürich: Lit Verlag, p: 23-47.

Callaway, J.C.; McKenna, D.J.; Grob, C.S.; Brito, G.S.; Raymon, L.P.; Poland, R.E.; Andrade, E.N.; Andrade, E.O. & Mash, D.C. 1999. Pharmacokinetics of hoasca alkaloids in healthy humans. *Journal of Ethnopharmacology*, 65 (3): 243-56.

Carhart-Harris, R.L.; Erritzoe, D.; Williams, T.; Stone, J.M.; Reed, L.J. et al. (2012) Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. PNAS, 109: 2138–2143.

de Araujo, D.B.; Ribeiro, S.; Cecchi, G.A.; Carvalho, F.M.; Sanchez, T.A.; Pinto, J.P.; de Martinis, B.S.; Crippa, J.A.; Hallak, J.E. & Santos, A.C. 2011. Seeing with the eyes shut: Neural basis of enhanced imagery following ayahuasca ingestion. *Human Brain Mapping* 33 (11): 2550-60.

da Silveira, D.X.; Grob, C.S.; Dobkin de Rios, M.; Lopez, E.; Alonso, L.K.; Tacla, C. & Doering-Silveira, E. 2005. Ayahuasca in adolescence: A preliminary psychiatric assessment. *Journal of Psychoactive Drugs*, 37 (2): 129-33.

Doering-Silveira, E.; Grob, C.S.; Dobkin de Rios, M.; Lopez, E.; Alonso, L.K.; Tacla, C. & da Silveira, D.X. 2005a. Report on psychoactive drug use among adolescents using ayahuasca within a religious context. *Journal of Psychoactive Drugs*, 37 (2): 141-44.

Doering-Silveira, E.; Lopez, E.; Grob, C.S.; Dobkin de Rios, M.; Alonso, L.K.; Tacla, C.; Shirakawa, I.; Bertolucci, P.H. & da Silveira, D.X. 2005b. Ayahuasca in adolescence: A neuropsychological assessment. *Journal of Psychoactive Drugs*, 37 (2): 123-28.

dos Santos, R.G. 2011. *Ayahuasca: Physiological and subjective effects, comparison with d-amphetamine, and repeated dose assessment*. Doctoral thesis, Universitat Autònoma de Barcelona, Barcelona, Spain. http://www.tdx.cat/handle/10803/83979.

dos Santos, R.G. 2013. Safety and side effects of ayahuasca in humans - An overview focusing on developmental toxicology. *Journal of Psychoactive Drugs*, 45 (1): 68-78. 2013.

dos Santos, R.G. & Strassman, R. 2011. Ayahuasca and psychosis. In: R.G. dos Santos (Ed.). *The Ethnopharmacology of Ayahuasca*. Trivandrum: Transworld Research Network. http://www.trnres.com/ebook/uploads/contentrafael/T_14049717087%20Rafael.pdf

dos Santos, R.G.; Landeira-Fernandez, J.; Strassman, R.J.; Motta, V. & Cruz, A.P. 2007. Effects of ayahuasca on psychometric measures of anxiety, panic-like and hopelessness in Santo Daime members. *Journal of Ethnopharmacology*, 112 (3): 507-13.

dos Santos, R.G.; Valle, M.; Bouso, J.C.; Nomdedéu, J.F.; Rodríguez-Espinosa, J.; McIlhenny, E.H.; Barker, S.A.; Barbanoj, M.J. & Riba, J. 2011. Autonomic, neuroendocrine and immunological effects of ayahuasca. A comparative study with *d*-amphetamine. *Journal of Clinical Psychopharmacology* 31 (6): 717-26.

dos Santos, R.G.; Grasa, E.; Valle, M.; Ballester, M.R.; Bouso, J.C.; Nomdedéu, J.F.; Homs, R.; Barbanoj, M.J. & Riba, J. 2012. Pharmacology of ayahuasca administered in two repeated doses. *Psychopharmacology*, 219 (4): 1039-53.

Fábregas, J.M.; González, D.; Fondevila, S.; Cutchet, M.; Fernández, X.; Barbosa, P.C.; Alcázar-Córcoles, M.Á.; Barbanoj, M.J.; Riba, J. & Bouso, J.C. 2010. Assessment of addiction severity among ritual users of ayahuasca. *Drug and Alcohol Dependence*, 111 (3): 257-61.

Fericgla, J.M. 1997. Al Trasluz de la Ayahuasca. Antropología cognitiva, oniromancia y conciencias alternativas. Barcelona: La Liebre de Marzo.

Frecska, E.; Bokor, P. & Winkelman M. 2016. The Therapeutic Potentials of Ayahuasca: Possible Effects against Various Diseases of Civilization. Front Pharmacol. 7: 35.

Gable, R.S. 2007. Risk assessment of ritual use of oral dimethyltryptamine (DMT) and harmala alkaloids. *Addiction*, 102 (1): 24-34.

Grob, C.S.; McKenna, D.J.; Callaway, J.C.; Brito, G.S.; Neves, E.S.; Oberlaender, G.; Saide, O.L.; Labigalini, E.; Tacla, C.; Miranda, C.T.; Strassman, R.J. & Boone, K.B. 1996. Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brazil. *Journal of Nervous and Mental Disease*, 184 (2): 86-94.

Halpern, J.H.; Sherwood, A.R.; Passie, T.; Blackwell, K.C. & Ruttenber, A.J. 2008. Evidence of health and safety in American members of a religion who use a hallucinogenic sacrament. *Medical Science Monitor*,14 (8): SR15-22.

Instituto Nacional de Cultura. 2008. *Declaración Patrimonio Cultural de la nación a los conocimientos y usos tradicionales de la ayahuasca practicados por comunidades nativas amazónicas*. Resolución Directoral Nacional, no. 836. Lima, Peru.

Junta Internacional de Fiscalización de Estupefacientes (JIFE). 2010. *Informe Anual 2010 de la Junta Internacional de Fiscalización de Estupefacientes (JIFE).* New York: United Nations. http://www.incb.org/documents/Publications/AnnualReports/AR2010/AR_2010_Spanish.pdf.

Junta Internacional de Fiscalización de Estupefacientes (JIFE). 2012. *Informe Anual 2012 de la Junta Internacional de Fiscalización de Estupefacientes (JIFE).* New York: United Nations. http://www.incb.org/documents/Publications/AnnualReports/AR2012/AR_2012_S.pdf.

Labate, B.C. (Ed.). 2004. A reinvenção do uso da ayahuasca nos centros urbanos. Campinas: Mercado de Letras.

Labate, B.C. & Bouso J.C. (Eds.). 2013. *Ayahuasca y Salud*. Barcelona: Los Libros de La Liebre de Marzo.

Labate, B. C. & Cavnar, C.(Eds). 2014a. *Ayahuasca Shamanism in the Amazon and Beyond.* New York, NY: Oxford University Press.

Labate, B.C. & Cavnar, C. (Eds.). 2014b. *The Therapeutic Use of Ayahuasca*. Berlin/Heidelberg: Springer-Verlag.

Labate, B.C. & Feeney, K. 2012. Ayahuasca and the process of regulation in Brazil and internationally: implications and challenges. Int J Drug Policy. 23(2): 154-61.

Labate, B.C. & Jungaberle, H. (Eds.). 2011. *The Internationalization of Ayahuasca*. Zurich/Berlin: Lit Verlag.

Labate, B.C.; Rose, I.S. & dos Santos, R.G. 2009. *Ayahuasca Religions: A Comprehensive Bibliography and Critical Essays*. Santa Cruz, CA: Multidisciplinary Association for Psychedelic Studies.

Labate, B. C., Cavnar, C., & Gearin, A. K. (Eds.). 2017. *The world ayahuasca diaspora: Reinventions and controversies.* Abingdon, England: Routledge.

Lima F.A.S. & Tófoli, L.F. 2011. An epidemiological surveillance system by the UDV: mental health recommendations concerning the religious use of hoasca. In: B.C. Labate & H. Jungaberle (Eds.). *The Internationalization of Ayahuasca*. Zurich/Berlin: Lit Verlag.

Llagostera, A.; Torres, C.A. & Costa, M.A. 1988. El complejo psicotrópico en Solcor-3 (San Pedro de Atacama). *Estudios Atácamenos*, 9: 61-98. MChAP (Museo Chileno de Arte Precolombino).

Luna, L.E. 1986a. *Vegetalismo shamanism among the mestizo population of the Peruvian Amazon*. Stockholm Studies in Comparative Religion #27. Stockholm: Almqvist and Wiksell International.

Luna, L.E. 1986b. Bibliografía sobre el ayahuasca. América Indígena, 46(1): 235-245.

Luna, L.E. 1986c. “Apéndices”. América Indígena, 46(1): 247-251.

Luna, L.E. 2011. Indigenous and mestizo use of Ayahuasca. An overview. In: R.G. dos Santos (Ed.) *The Ethnopharmacology of Ayahuasca*. Trivandrum: Transworld Research Network. http://www.trnres.com/ebook/uploads/rafael/T_12998349951%20Rafael.pdf.

Mabit, J. 2007. Ayahuasca in the treatment of addictions. In:. M.J Winkelman & T. B. Roberts (Eds.). *Psychedelic Medicine: New Evidence for Hallucinogenic Substances as Treatments*, vol. 2. Westport: Praeger.

McKenna, D.J. 2004. Clinical investigations of the therapeutic potential of ayahuasca: rationale and regulatory challenges. *Pharmacology and Therapeutics*, 102 (2): 111-29.

McKenna DJ, Luna LE, Towers GHN. 1986. “Ingredientes biodinamicos en las plantas que se meszclan al ayahausca. Una farmacopea tradicional no investigada.” America Indigena. 46:73-101. (Spanish with English abstract).

Nielson, J.L. & Megler, J.D. 2014. Ayahuasca as a Candidate Therapy for PTSD. In: B.C. Labate & C. Cavnar (Eds.).: The Therapeutic Use of Ayahuasca. Berlin: Springer, pp: 41-58.

Ogalde, J.P.; Arriaza, B.T. & Soto, E.C. 2009. Identification of psychoactive alkaloids in ancient Andean human hair by gas chromatography/mass spectrometry. *Journal of Archaeological Science*, 36 (2): 467-72.

Osório Fde L, Sanches RF, Macedo LR, Santos RG, Maia-de-Oliveira JP, Wichert-Ana L, Araujo DB, Riba J, Crippa JA, Hallak JE. 2015. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report. Rev Bras Psiquiatr, 37(1):13-20.

Palhano-Fontes, F.; Andrade, K.C.; Tofoli, L.F.; Santos, A.C.; Crippa, J.A.; Hallak, J.E.; Ribeiro, S. & de Araujo, D.B. 2015. The psychedelic state induced by ayahuasca modulates the activity and connectivity of the default mode network. PLoS One. 10(2): e0118143.

Palhano-Fontes, F.; Barreto, D.; Onias, H.; Andrade, K.C.; Novaes, M.; Pessoa, J.; Mota-Rolim, S.; Osorio, F.L.; Sanches, R.; dos Santos, R.; Tofoli, T.; Silveira, G.; Yonamine, M.; Riba, J.; Santos, F.R.R.; Silva-Junior, A.A.; Alchieri, J.; Galvao-Coelho, N.; Lobao-Soares, B.; Hallak, J.; Arcoverde, E.; Maia-de-Oliveira, J. & de Araujo D.B. 2017. Rapid antidepressant effects of the psychedelic ayahuasca in treatment-resistant depression: a randomised placebo-controlled trial. BioRxiv. doi: https://doi.org/10.1101/103531.

Riba, J. 2003. *Human pharmacology of Ayahuasca*. Doctoral thesis, Universitat Autònoma de Barcelona, Barcelona, Spain. http://www.tdx.cat/handle/10803/5378.

Riba, J. & Barbanoj, M.J. 2005. Bringing ayahuasca to the clinical research laboratory. *Journal of Psychoactive Drugs*, 37 (2): 219-30.

Riba, J. & Barbanoj, M.J. 2006. Ayahuasca. In: J.C. Peris; J.C. Zurián; G.C. Martínez & G.R. Valladolid (Eds.) *Tratado SET de Transtornos Adictivos*. Madrid: Ed. Médica Panamericana.

Riba, J.; Rodríguez-Fornells, A.; Urbano, G.; Morte, A.; Antonijoan, R.; Montero, M.; Callaway, J.C. & Barbanoj, M.J. 2001. Subjective effects and tolerability of the South American psychoactive beverage ayahuasca in healthy volunteers. *Psychopharmacology*, 154 (1): 85-95.

Riba, J.; Valle, M.; Urbano, G.; Yritia, M.; Morte, A. & Barbanoj, M.J. 2003. Human pharmacology of ayahuasca: subjective and cardiovascular effects, monoamine metabolite excretion, and pharmacokinetics. *Journal of Pharmacology and Experimental Therapeutics*, 306 (1): 73-83.

Riba J.; Romero, S.; Grasa, E.; Mena, E.; Carrió, I. & Barbanoj, M.J. 2006. Increased frontal and paralimbic activation following ayahuasca, the pan-amazonian inebriant. *Psychopharmacology*, 186 (1): 93-8.

Riba, J.; McIlhenny, E.H.; Bouso, J.C. & Barker, S.A. 2015. Metabolism and urinary disposition of N,N-dimethyltryptamine after oral and smoked administration: a comparative study. Drug Test Anal, 7 (5): 401-6.

Sanches, R.F.; de Lima Osório, F.; Dos Santos, R.G.; Macedo, L.R.; Maia-de-Oliveira, J.P.; Wichert-Ana. L.; de Araujo, D.B.; Riba, J.; Crippa, J.A. & Hallak, J.E. 2016. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A SPECT study. J Clin Psychopharmacol, 36 (1): 77-81.

Sánchez Avilés, C. & Bouso, JC. 2015. Ayahuasca: From the Amazon to the Global Village. Drug Policy Briefing, No. 43. Transnational Institute / ICEERS Foundation.

Schenberg, E.E.; Alexandre, J.F.; Filev, R.; Cravo, A.M.; Sato, J.R.; Muthukumaraswamy, S.D.; Yonamine, M.; Waguespack, M.; Lomnicka, I.; Barker, S.A. & da Silveira, D.X. 2015. Acute Biphasic Effects of Ayahuasca. PLoS One. 10(9): e0137202.

Schultes, R.E. & Hofmann, A. 1992. *Plants of the Gods: Their Sacred, Healing, and Hallucinogenic Powers*. Rochester: Healing Arts Press.

Shanon, B. 2002. *The Antipodes of the Mind: Charting the Phenomenology of the*

Ayahuasca Experience. Oxford/New York: Oxford University Press.

Shulgin, A. & Shulgin, A. 1997. *Tihkal: The Continuation*. California: Transform Press.

Strassman R.J. & Qualls C.R. 1994. Dose-response study of *N,N*-dimethyltryptamine in humans. I. Neuroendocrine, autonomic, and cardiovascular effects. *Archives of Geneneral Psychiatry*, 51 (2): 85-97.

Soler, J.; Elices, M.; Franquesa, A.; Barker, S.; Friedlander, P.; Feilding, A.; Pascual, J.C.; Riba, J. 2016. Exploring the therapeutic potential of Ayahuasca: acute intake increases mindfulness-related capacities. Psychopharmacology (Berl). 233(5):823-9.

Strassman, R.J; Qualls, C.R.; Uhlenhuth, E.H. & Kellner, R. 1994. Dose-response study of *N,N*-dimethyltryptamine in humans. II. Subjective effects and preliminary results of a new rating scale. *Archives of General Psychiatry*, 51 (2): 98-108.

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