ICEERS INTERNATIONAL CENTER FOR ETHNOBOTANICAL EDUCATION RESEARCH & SERVICE

Technical Report about
Ayahuasca

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Ayahuasca is a liquid produced by the slow decoction of the *Banisteriopsis caapi* vine, which contains harmine, harmaline and tetrahydroharmine, and the leaves of the *Psychotria viridis* shrub, which contains DMT (Schultes & Hofmann, 1992). Ayahuasca is considered a sacred drink by an uncountable number of indigenous Amazonian groups and a medicine by mestizo healers in much 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 intensely present in urban centers (Luna, 1986, 2011). Ayahuasca is presently used as a medicine in ceremonies officiated by Indians, mestizos, and diverse professionals who have learned to use it in its places of traditional origin (Labate et al., 2009; Labate & Jungaberle, 2011; Luna, 2011; Labate & Bouso, 2013). The therapeutic properties of ayahuasca are due to its action on the brain: it activates the cerebral areas related to episodic memory and awareness of emotions and internal sensations (Riba et al., 2006; de Araujo et al., 2011).

The antiquity of ayahuasca use is unknown. The oldest traces of possible use of ayahuasca have been found in the Azapa desert in the north of Chile, where residues of harmine have been found in hair analyzed from mummies from the Tiwanaku period between 500 and 1000 C.E. In the Azapa valley *Banisteriopsis caapi* does not grow, nor does any other harmine-containing plant, which suggests an intense commerce between the ancient populations of Chile and the Amazonian peoples; probably the former provided the latter with salt and the latter provided the former with medicines, among them ayahuasca. It is also known that the ancient inhabitants of the north of Chile (Azapa and Atacama deserts) were inveterate consumers of DMT-type hallucinogens: the most ancient remains of paraphernelia for consuming hallucinogens have been found precisely in excavations carried out in the Atacama desert and dated at 480 C.E +/- 60 years. (Llagostera et al., 1988) and today many of these artifacts can be contemplated, among other places, in the Chilean Museum of Precolumbian Art in the city of Santiago. The use of hallucinogens like DMT was considered a sacred practice among the ancient Chilean citizens.

DMT is on the list of substances subject to international control by the United Nations, but neither ayahuasca nor any plant that contains DMT, nor any plant preparation made with plants that contain DMT is subject to control. (JIFE, 2010, 2013). The alkaloids present in the *Banisteriopsis 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, Canada, and the United States and the churches in which ayahuasca is considered a sacrament and is consumed for that purpose have expanded internationally into numerous European, American and Asian countries (Labate et al., 2009; Labate & Jungaberle, 2011).

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 monoamineoxidase (MAO), an enzyme present in the gastrointestinal tract which serves to degrade monoamines. As DMT is a monoamine, if it is ingested orally, the endogenous MAO deactivates it, keeping it

from reaching the brain. At some moment in the remote past, the indigenous people of the Amazon Basin discovered that adding leaves of *Psychotria viridis*, which. as already mentioned, contain DMT, to a decoction of *Banisteriopsis caapi* (which contains harmala alkaloids), turns the DMT bioactive. This is due to the harmala alkaloids, which, acting as MAOIs, block the MAO present in the gastrointestinal tract and in this way the DMT present in the leaves of *Psychotria viridis* can reach the brain (Mckenna et al., 1984; Riba et al., 2003). This sophisticated indigenous discovery has been uncovered by science only recently, in the decade of the 1980s of the last century. 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 is still unknown today, although there are those who speculate that it may be at the base of dreams and other spontaneous altered states of consciousness (Callaway, 1988; Strassman, 2001).

During the last decades, clinical trials have been carried out on humans in which both DMT in purified form (administered intravenously) and ayahuasca (administered orally) have been administered in a laboratory context, and its acute effects have been characterized both at a psychological and a somatic level. 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 exercises its effects in a slower and more progressive way, beginning at 45 to 60 minutes after administration, reaching its maximum effects after 2 hours and disappearing after 4 to 6 hours (Riba, 2003; dos Santos, 2011). The maximum intensity of the effects of DMT is approximately double the maximum effect of ayahuasca at equivalent doses (Grob et al., 1996), which makes the global effects of ayahuasca much more controllable than pure DMT.

Ayahuasca, whether administered in a laboratory context or ingested in a traditional context, produced, as evaluated with questionnaires to measure its subjective effects, transitory modifications in emotion, thought content, perception and somatic sensations (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 tests of cognitive performance (Bouso et al., 2013). The volunteers in these studies also describe the effects of ayahuasca as "I like the medicine" and "good effects" (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 in the plasma, disappearing from the organism after 8 hours (Riba et al., 2003).

Studies have been published in which neuroimaging techniques have been used in order to determine the cerebral areas that activate after the ingestion of ayahuasca. Both studies show 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 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 the memory, also showed higher blood perfusion compared to placebo. No differences were found compared to placebo in any other brain area.

In the second neuroimaging study (de Araujo et al., 2011), performed with Functional MRI (fMRI) activation in primary visual areas were also found, its magnitude when a photograph was being remembered by subjects under the influence of ayahuasca being comparable to baseline activation levels recorded with the presentation of a natural image with eyes open. According to the authors, this effect causes the brains of volunteers to interpret the ayahuasca experience as if it were "real," not in the sense of a hallucinatory experience, but with the experiential endowment of sense 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 such prototypical experiences with ayahuasca (Shanon, 2002). These brain and cognitive phenomena may explain why ayahuasca is considered a potential psychotherapeutic ethnobotanical tool (Cavnar & Labate, 2013). Indeed, one study found that, under the effects, ayahuasca reduced the scores of panic and hopelessness in ritual users (Santos et al. , 2007). Another study found antidepressant effects of ayahuasca in patients with major depression (Osório et al., 2011).

Some side effects after the administration of ayahuasca in the laboratory have been described, but they are localized and isolated (Riba et al., 2001; Riba & Barbanoj, 2005, 2006; dos Santos et al., 2011, 2012). Cases in which psychiatric effects have appeared in the context of ayahuasca ritual use have also been documented, although their occurrence is rare (Lima & Tofoli , 2011). This suggests that ayahuasca, in principle, is contraindicated for people with serious psychiatric disorders.

As far as the effects of ayahuasca on the organism, clinical trials carried out with volunteers, both in laboratory conditions and natural contexts, suggest that ayahuasca is physiologically very safe (Riba, 2003; dos Santos, 2011). The impact of ayahuasca on the cardiovascular system is minimal, producing light increases in blood pressure and cardiac rate. (Riba et al., 2001, 2003; dos Santos et al., 2011, 2012). It has also been shown to transiently increase concentrations of the hormones prolactin, cortisol and growth hormone (dos Santos et al., 2011, 2012) and in regard to the immune system, it decreases in a time-dependent manner the subpopulations of CD4 and CD3 lymphocyte cells and increases the "*natural killers*" (NK) (dos Santos et al., 2011, 2012). These transitory physiological changes do not seem to have negative effects: in the general blood analyses carried out before and after on volunteers in clinical trials, no changes in hematological and biochemical functions were observed (Riba et al., 2001; Riba & Barbanoj, 2005).

The principal side effect that ayahuasca induces is 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 action of ayahuasca on vomiting is due, first, to the specific organoleptic properties of the decoction, and secondly, to its serotonergic action (Callaway et al., 1999). In any case, this is not an adverse reaction considered

important by the participants in the sessions but rather as something understood as a potential therapeutic effect called "the purge" in traditional Amazonian medicine (Luna, 1986, 2011). "The purge," in the contexts of traditional use, is understood as a physical and psychological cleansing of internal conflicts that can afflict the participant, and is considered an essential part of the therapeutic benefits (Luna, 1986, 2011).

It has also been shown in clinical trials that ayahuasca does not produce tolerance (dos Santos et al., 2012). As far as its potential for abuse, in the neuroimaging studies cited earlier, no active areas have been found in the reward centers. Rather, in this sense, the existing evidence indicates that ayahuasca can be a useful tool in the treatment of addictions (Bouso & Riba, 2013). In fact, there are various clinics in South America that specialize in the treatment of drug addiction, the most important of these being Takiwasi, in Peru (Mabit, 2007).

One of the first studies carried out in humans showed how many participants in ritual ayahuasca sessions had abandoned the consumption of alcohol and other drugs, such as cocaine, as a consequence of their participation in the rituals (Grob et al., 1996). This finding has been found again in later studies (Halpern et al., 2008). A recent study, in which 127 users of ayahuasca in traditional contexts were evaluated and compared with 115 controls, no evidence was found of criteria of addiction according to the biopsychosocial indicators evaluated with the ASI (Addiction Severity Index) nor was it found that the continued use of ayahuasca was associated with the noxious biopsychosocial effects occasioned by drugs of abuse. Rather, the groups of ayahuasca users consumed less alcohol and other drugs than the control subjects and these high scores on the biopsychosocial indicators of addiction were replicated a year later, confirming the consistency of the results (Fábregas et al., 2010). One study, carried out with adolescents belonging to a Brazilian ayahuasca church, found that they consumed significantly less alcohol than the controls, concluding that ayahuasca, far from producing abuse or dependency, for these adolescents was a protecting factor against the consumption of alcohol (Doering-Silveira et al., 2005a).

Medium-term and long-term studies have also been carried out in which there has been no evidence of neuropsychological or psychopathological alterations derived from the continued consumption of ayahuasca. A prospective study carried out with people who drank ayahuasca for the first time has found improvements in measures of mental health and reductions in physical pain six months after initiating the ritual consumption of ayahuasca (Barbosa et al., 2005, 2009). Other studies have found lower indices of psychopathology and greater psychosocial integration in habitual users of ayahuasca (Bouso et al., 2012; Halpern et al., 2008) and two other studies have found no neuropsychological alterations, evaluated through tests of neuropsychological performance, in habitual users of ayahuasca after 10 to 15 years of continuous consumption (Grob et al., 1996; Bouso et al., 2012). One of these studies evaluated 127 users of ayahuasca with a history of a minimum of 15 years of consumption, and compared them with 115 controls, finding better scores in psychopathological tests and in some of the neuropsychological tests, results that showed themselves to be consistent in each of the evaluations separated by a year that was carried out on the subjects (Bouso et al., 2012). Studies with adolescent members of ayahuasca churches have also not found

neuropsychological or psychiatric alterations associated with the ritual consumption of ayahuasca (da Silveira et al., 2005: Doering-Silveira et al., 2005b).

In conclusion, in the literature on the short-term, medium-term, and long-term effects,it is shown that ayahuasca is a substance that is physiologically and psychologically acceptably safe (McKenna, 2004; Gable, 2007; Bouso & Riba, 2011; Barbosa et al., 2012; dos Santos, 2013).

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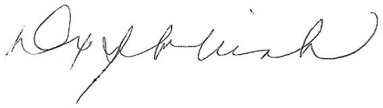

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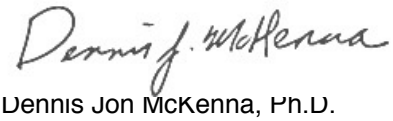

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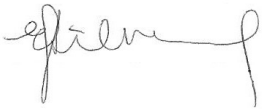

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