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Mini Review

Ayahuasca: The Good, the Bad and the Worse

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Abstract

The decoction of bark and stems of *Banisteriopsis caapi* together with leaves of *Psychotria viridis* has been done for centuries, producing a brew named Ayahuasca. While *P. viridis* is rich in the psychoactive agent N, N-dimethyltryptamine (DMT), *B. caapi* contains monoamine oxidase inhibitors (MAOIs), which modulates the availability of monoaminergic neurotransmitters (serotonin, noradrenaline and dopamine) in the synaptic cleft. Ayahuasca moderate consumption is associated with the activation of brain areas related to emotions and memory, and users have reported improved concentration, higher performance in cognitive tasks and enhanced sense of meaning in their lives. Recently, studies have approached ayahuasca as an alternative drug for treating mental disorders such as anxiety, depression, and memory loss, because of the limited effectiveness of traditional medicine. However, the beneficial and detrimental effects that Ayahuasca may have on physiological functioning of the brain and other tissues are not thorough understood, and many cases of over consumption leading to mortality and comorbidities are appearing worldwide. This brief review approaches the goods and the bads in Ayahuasca consumption, and points out the necessity for current guidelines for the usage of Ayahuasca based on the scientific understanding of the brew effects on animals and human models.

Keywords: *Entheogen; Consumption Patterns; Overdose; Anxiety; Depression; Guideline*

Introduction

The Ayahuasca (in Quechua 'vine of the souls') brew is a hallucinogen beverage originally used in religious rituals by Amazonian indigenous groups [1]. After that, new other religious sects emerged, combining ritualistic consumption of ayahuasca and elements of other religion doctrines, such as Christianity and Spiritualism [2,3].

The most common Brazilian ayahuasca sects are *Santo Daime, Uniao do Vegetal* (UDV), and *Barquinha Church* [4,5]. Currently, these religious groups are spread around the globe, in countries such as Peru, Ecuador, United States and some regions of Europe, Oceania, and Asia [4]. It is estimated that nearly 20000 people worldwide are members of some kind of religious sect that makes use of ayahuasca during cerimonies. However, epidemiological data on recreational use is still scarce [6]. In South America, the use of plant-based psychoactive substances is becoming common outside the religions creeds [7].

Ayahuasca infusion is prepared through the decoction of *Banisteriopsis caapi* stalks and the leaves of *Psychotria viridis*; its psychedelic property depends on the interaction between components of both plants [8]. While *P. viridis* contains N,N-dimethyltryptamine (DMT), a psychoactive agent that present similar structure to that of serotonin, the oral administration lead to total inactivation through the activity of MAO (monoamine oxidase) from the liver and intestines. However, when taken in combination with *B. caapi* that contains beta-carboline alkaloids (harmine, harmaline and tetrahydroharmine) and inhibits MAO functioning, DMT becomes capable of acting in the organism, including the nervous system [8,9]. In the brain, ayahuasca causes increased serotonergic activity by both increasing serotonin

availability at the synaptic cleft (inhibition of serotonin reuptake through tetrahydroharmine - THH) and activating serotonin receptors 5-HT2A and 5-HT2C, in a manner similar to serotonin (agonist activity) [10]. In addition, ayahuasca changes GABA and glycine concentrations in a dose-dependent manner, and also affects levels of monoamines, such as serotonin, dopamine and noradrenalin [10].

Neuroimaging studies show that ayahuasca affects different brain regions, causing activation of the prefrontal cortex [11], increased blood flow in the parahippocampal gyrus, anterior cingulate cortex, insula, subgenual area, nucleus accumbens and the amygdala [11-13]. These areas are related to episodic memory, contextual associations, regulation of mood and emotions. In rodent models, ayahuasca exposure increase activity of the amygdala and hippocampus, brain structures associated with memory and emotional learning [10].

The frequency of ayahuasca consumption is dependent on the religious group, varying from two to eight exposures per month; experienced individuals can make use of the drug in higher frequency [14,15]. The effects of ayahuasca begin between 35 and 40 minutes after ingestion, reaching the maximum intensity between 90 and 120 minutes and ceasing 4 to 6 hours after administration [16]. Ayahuasca users describe diverse effects after consumption [17], from sensory, cognitive and affective changes [18] to mystical, entheogenic encounters and near death experiences [19]. A common reaction to the brew intake is dream-like images visions with closed eyes [13] involving scenes of past and future events [20].

Regular users of ayahuasca claim to acquire several benefits from the brew, and many studies investigate the therapeutic potential of ayahuasca to treat psychopathologies that traditional medicine has failed to treat.

However, its use is still controversial: several studies have reported both positive and negative results on cognitive and emotional functions, and many of them can't disconnect ayahuasca physiological effects from those related to religiosity and personality, making it difficult to discriminate the goods and the bads from the drug exposure.

The Good

The ceremonial ingestion of Ayahuasca is associated with positive life style changes. Participants of the rituals usually report mind healing, increased self-knowledge, sense of life meaning and persistent good mood states. Many describe facing deep feelings and memories, which offer to the users the opportunity to re-valuate their negative choices and behavior, sometimes culminating in profound changes in their life perspectives and expectations [21,22].

The psychological enhancement associated with ayahuasca was proposed to be derived from long-term use (years), which is observed both during the drug exposure and in a drug-off state. Furthermore, suggestions on the safety and tolerability of the ayahuasca use were based on reports from users for more than 30 years with no evidence of impaired health [14,16,17,23]. For instance, volunteers from the Santo Daime Church were tested 1 hour after ayahuasca ingestion and presented low scores of panic and hopelessness [24]. Other groups from the same sect were evaluated when out of the effects of ayahuasca, showing low scores in psychopathological dimensions, such as anxiety, depression and obsessive-compulsive behavior [15]. The same authors repeated the sampling one-year later and observed similar results. Individuals from another sect, the UDV church, showed high scores of agreeableness on the Big Five Factors of personality [25], a trait related to cooperation and social harmony [26].

Considering the benefits promoted by the brew, the interest in its therapeutic potential is crescent. Ayahuasca has been suggested as an alternative treatment for disorders related to anxiety, depression and addiction. According to Osório., *et al*. among ayahuasca advantages are the fast response to the treatment, prolonged effect after use and no addictive potential.

Regarding depression and anxiety, studies with animal models and humans showed that the administration of ayahuasca, or its isolated components, seems to attenuate the disorder's symptoms [28]. In rats, harmine reduced immobility and increased activity when the animal is submitted to forced swimming test, a commonly used paradigm to access anxiety-like behavior [29]; this alkaloid also reversed anhedonia in animals submitted to chronic mild stress paradigm [30]. While disruption of the serotonergic system is one of the proposed causes of depression [31], drugs that quickly increase available serotonin and maintain the system normal functioning might be tested as potential treatment. In this sense, DMT enhances the activation of 5-HT receptors (agonist effect) and results in similar effects as the serotonin itself [32], while THH (tetrahydroharmine) is a serotonin reuptake inhibitor similar to many antidepressants currently available [33]. DMT is also an agonist of Sigma-1 receptors leading to antidepressant results [34]. Together, DMT and the monoamine oxidase inhibitors (MAOI) present in ayahuasca also provoke increment in BDNF levels [33], which seems to be related to amelioration of depressive conditions. In animal models, the administration of BDNF reduces depressant-like behaviors [35].

Concerning drug addiction, the regular consumption of ayahuasca is concomitant with the reduction of addictive substances [36-38]. One of the theories for drug addiction relates to the high levels of dopamine in the mesolimbic pathway, also known as the reward pathway [39]. Evidences show that ayahuasca causes reduced level of dopamine in this area through its action on 5-HT receptors. In fact, 5-HT2A receptors stimulation on dopaminergic neurons reduce dopamine release and excites GABA interneurons, causing GABA also to inhibit dopamine release [40]. It was observed that participants of ayahuasca rituals decrease significantly or even cease the consumption of drugs of abuse, including, cigarettes, alcohol and cocaine [25,37,41]. In mice, ayahuasca was shown to prevent and reverse sensitization to alcohol [42], corroborating its potential to inhibit alcohol abuse.

Besides the therapeutic property, some studies demonstrate that ayahuasca can enhance cognitive performance in both animal models and humans. For instance, acute ayahuasca exposure improved mice performance in objects discrimination task [43], long-term ayahuasca exposure improved fear-conditioning response in rats [9], a single dose of ayahuasca increased amygdala and hippocampus activity in rats [10] and administration of harmine alone increased early genes expression in mice's hippocampus [44]. Experienced users of ayahuasca have been shown positive results in neuropsychological tests involving attention, working memory and planning under drug effect and also in off-drug state [11,15]. In accordance to Riba., et al. [12], the improved cognitive skills in cognitive tests are related to the ayahuasca activation of the prefrontal cortex functioning.

The evidences briefly discussed here suggest that ayahuasca carry diverse therapeutic benefits. Moreover, other studies are adding to the ayahuasca potential, showing its neuroprotective effects [28] and capacity to increase creative divergent thinking and mindfulness [38]. The consumption of the brew and the practice of the religious ritual create a powerful and positive change in one's life, which can go from better life habits to healing body and psychological problems. Beyond the ceremonial consumption of ayahuasca, it can be used as alternative treatment to common modern society disorders, such as anxiety and depression (as discussed above in regard to DMT and harmine effects). Moreover, the physiological effects on serotonergic and dopaminergic systems together with the psychological and behavioral changes put ayahuasca in the place of a potential treatment to drug addiction, a disease that has abated the actual society. However, studies show that the positive effects of ayahuasca are dose-dependent and related to the duration of consumption. Therefore, it is important to consider possible side effects and consequences of the occasional and long-term use for recreational or treatment purposes.

The Bad

Although many scientific and anecdotal reports show benefits from long-term consumption of ayahuasca, occasional experiences could be accompanied by negative consequences. The first events of ayahuasca intake are usually associated with cognitive impairment and psychological problems, besides altered physiological responses such as tachycardia and vomiting. Despite many consume ayahuasca in supervised ceremonies, sporadic recreational use also occurs [45], and the absence of guidance and supervision by trained people may result in negative experience and potential psychological disturbance.

One can easily find ayahuasca powder (amazon.com), recipes (soul-herbs.com) and videos on how to prepare the brew (many videos on youtube), and also the already prepared brew (ayahuascahealings.com) on the Internet [4].

Many web sites describe the expected effects and how to identify the plants in nature, making the consumption easy to anyone, anywhere. These available tools to get ayahuasca are facilitating its use, and to our knowledge there is no reports on who buys (if underage, pregnant woman, drug-users, etc) and the consequences of the widespread intake of the drug.

It is important to highlight that recent studies have pointed out detrimental effects of ayahuasca. Animal model studies showed that ayahuasca recurrent exposure may lead to toxic and cognitive-impairment effects, such as neuronal loss [46,47], increased serotonergic activity that induces to neurodegeneration [48] and decreased performance in discriminative tasks (unpublished data).

Bouso., *et al.* [11] found that less experienced individuals have poor performances in cognitive tests that demand high mental skills, such as executive process. These authors also showed that less experienced users present impairment in verbal working memory task. Hallucinogens that act as 5-HT agonist can disrupt cognitive performance in animal models, causing impaired attention [49], deficits in spatial navigation and memory retrieval [50], and fasten fear-conditioning extinction [51].

Some recent researches have presented marked deleterious effects of ayahuasca use. Studies by Bouso., *et al.* [52] have shown that long-term ayahuasca use cause massive loss in posterior cingulated cortex. Favaro., *et al.* [9] showed that 30 days ayahuasca treatment affect contextual association of emotional events in rats, and suggested that the brew activates brain areas related to these processes. It is in accordance with finding from Bouso., *et al.* [52], who showed that the regular intake of ayahuasca could lead to structural changes in

brain areas, which ultimately can alter one's personality. Besides that, ayahuasca seems to also disrupt physiological parameters, such as blood pressure, heart rate, rectal temperature, and other autonomic functions [16,53].

Alvarenga., *et al.* [45] tested high doses of ayahuasca combined with sleep loss in rats, and showed increased sexual impairment, and reduced levels of testosterone and progesterone, while Savoldi., *et al.* (unpublished data) presented both anxiolytic effects of low doses of ayahuasca and very increased anxiogenic effects of medium to high doses of the drug in zebrafish acutely exposed. Indeed, it seems that different doses lead to completely different results. Ayahuasca brew preparation slightly differ among sects and even within the same sect, due to coaction time, substance accumulation in the plants' parts and forms of storing, leading to different concentration of the final product. Because DMT can reach increased levels in the brew and also in the blood, attention should be taken to its toxicity. Actually, DMT is considered a controlled substance in Brazil [54] and also in other countries, under the1971 United Nations Convention on Psychotropic Substances (CPS). Therefore, the combined DMT - MAOIs that produce notable hallucinogenic effects [55,56], also induce physiological alterations potentially dangerous to many users. Hence, it is important to invest in studies on ayahuasca in order to elucidate its toxicological impact.

The Worse

As said above, ayahuasca is brewed with plants that produce MAOI and DMT, the former being the main active compound of the drink. DMT is found in several plants, animals and also in the human body [57]. It is a psychedelic molecule suggested to be produced in the pineal gland of mammals [58] and released during some phases of sleep, near death episodes and during mystical experiences [59,60]. However, the amount of endogenous DMT is very small and rapidly broken down by the action of monoamine oxidase (MAO). Thus, in search for mystical experiences, many people that intake large amounts of DMT usually present DMT levels far from the physiological. Body metabolism by MAO is not enough to break down such amount, and its administration in combination with monoamine oxidase inhibitors (MAOI) make it available for a longer period.

The effects of the combined substances include deeply spiritual experiences, clairvoyant episodes, hallucination, communication with spirits or extraterrestrial beings, altered perception of time, experience of its own death, high euphoria, etc. For many people, these experiences are well accepted and one can keep its normal life, sometimes simply changing ways of living or facing ordinary life dilemmas in a health manner. However, those that have experiences incongruent with their culture, values and worldview may undergo severe distress. Lewis [61] reported cases of strong crisis following ayahuasca experience, including anxiety, apprehensiveness and affliction.

Without any guidance and support from the shamans (who studied several years and has been trained to conduct ayahuasca ceremonies), many users reported fear of profound mental ill after the acute distress experienced during ayahuasca exposure [61]. Mystical experiences that cause dramatically changes in view and perspectives of one's life, lead to increased stress and problems to deal with jobs, social life, daily life and fear for its own sanity [61]. The cases of confusion, instability and mental disorders following psychedelic drugs experience became such increased that a new diagnostic category was included in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), under the category of religious or spiritual problems (Code V62.89) [62].

In fact, ayahuasca and its expected mystic and spiritual encounter have called attention of westerns, and travel packages with the promise of a genuine indigenous restorative experience with "native shamans" have been sold worldwide[63]. In many cases, the shamans are charlatans that pretend to know how to proceed and take advantage of people searching for healing. Shamans should have several years of study, profound knowledge in psychology and instruments to deal with psychological crisis. Since ayahuasca is considered a tool for the "spiritual world" access [64,65], it induces to altered conscientious states in which one may feel an altered pattern of mental functioning [66]. This experience has deeply impact in the user's life [67] and depending on the vivid experience the user go through (for instance, near death experience) one can get positive lessons and change the way he/she is living, or take it as a bizarre experience and develop psychological crisis [68]. Therefore, the shaman's guidance is very relevant on the consequences and importance of the user ex-

perience. Thus, it seems that training in religious and spiritual experiences is required to proper form a shaman [61]. Moreover, therapists focused in treating spiritual crises are an alternative for ayahuasca users make meaning of their experience.

It is worth pointing out that ayahuasca brews are not always the same and admixture of plants can produce a beverage with huge DMT amounts or even other substances with psychoactive action. High doses of DMT per se may lead to toxic effects, already reported in several fatal cases from the abuse of the triptamine [69-76]. When other psychoactive plants are combined to produce a brew with increased power, several side effects may appear.

Recent reports have shown that some ceremonies use ayahuasca prepared from *Banisteriopsis caapi* and *Psychotria viridis* together with *Brugmanisa sp*. Shamans prepare the brew with the "plus" plant (brugmansia) to get a stronger liquor that even ingested in small volumes cause powerful psychological alterations. According to Rosengren [77], people that used the "empowered brew" present symptoms of high psychological distress. This author commented that while ayahuasca users communicate, move and behave in a normal way, those under the influence of brugmansia completely loss responsiveness. Also, if the amount of brugmansia becomes high, it has toxic effects, leading to delirium, convulsion, and coma [78]. Although no scientific reports were shown on the deleterious effects of ayahuasca with brugmansia, various websites address events where the brew was used, and even present cases of death after the substance exposure.

Therefore, caution should be taken in regard to the origin of the brew, the background/trustworthiness of the sect and ceremony that offers the drug and also the possibility of psychological and medical support in cases of counterproductive results. For that, the regulation of ayahuasca, establishing rules, norms and ethical procedures during rituals and recreational use are urgent. In Brazil, the CONAD's (Conselho Nacional de Políticas sobre Drogas) 2010 Resolution is a recent adoption to guide ayahuasca use and users, and this normative affected judicial and administrative decisions in other countries, stimulating international regulatory issues [2,79]. The theme is very delicate because it superposes religious liberty and a world war against drugs, but however, it should be faced sooner or later in order to establish the best procedures and avoid harmful consequences [2].

Conclusion

Ayahuasca is a vegetal psychoactive infusion with similar properties to those of serotonin and known to provoke alternate states of conscience. Despite some positive results on the treatment of anxiety/depression conditions, and suggested potential to improve cognitive ability and promote mindfulness, ayahuasca is still a drug and should be seen as a drug, not a remedy. In uncontrolled use (admixtures, high doses, lack of psychological guidance), ayahuasca can cause deleterious outcomes, such as psychological crisis, intoxication, and even death. Thus, before ayahuasca prescription as a medicine for several disorders, much investment should be given to its scientific study, pharmacological processing and determination of therapeutic window. For that, proper legislation is determinant to establish secure use, avoid dangerous employment and allow its correct use to treat disorders that the current treatments are limited or inadequate.

Bibliography

1 RG dos Santos., *et al.* "The current state of research on ayahuasca: A systematic review of human studies assessing psychiatric symptoms, neuropsychological functioning, and neuroimaging". *Journal of Psychopharmacology* 30.12 (2016): 1230-1247.

2 BC Labate and K Feeney. "Ayahuasca and the process of regulation in Brazil and internationally: Implications and challenges". *International Journal of Drug Policy* 23.2 (2012): 154-161.

3 MG Blainey. "Forbidden Therapies: Santo Daime, Ayahuasca, and the Prohibition of Entheogens in Western Society". *Journal of Religion and Health* 54.1 (2015): 287-302.

4 KW Tupper. "The globalization of ayahuasca: Harm reduction or benefit maximization?". *International Journal of Drug Policy* 19.4 (2008): 297-303.

5 BC Labate., *et al.* "Brazilian ayahuasca religions in perspective, Ayahuasca, Ritual Religion". Brazil (2010): 1-20.

6 V Cakic., *et al.* "Dimethyltryptamine (DMT): Subjective effects and patterns of use among Australian recreational users". *Drug Alcohol Depend* 111 (2010): 30-37.

7 Report of the International Narcotics Control Board for 2016. UNITED NATIONS, New York, 2017, n.d.

8 DJ McKenna. "Clinical investigations of the therapeutic potential of ayahuasca: Rationale and regulatory challenges". *Pharmacology and Therapeutics* 102.2 (2004): 111-129.

9 VM Favaro., *et al.* "Effects of Long-Term Ayahuasca Administration on Memory and Anxiety in Rats". *PLOS Genetics* 10.12 (2015): 1-10.

10 EF De Castro-neto., *et al.* "Changes in aminoacidergic and monoaminergic neurotransmission in the hippocampus and amygdala of rats after ayahuasca ingestion". *Journal of Psychopharmacology* 4.4 (2013): 141-148.

11 JC Bouso., *et al.* "Acute effects of ayahuasca on neuropsychological performance: Differences in executive function between experienced and occasional users". *Psychopharmacology (Berl)* 230.3 (2013): 415-424.

12 J Riba., *et al.* "Increased frontal and paralimbic activation following ayahuasca, the pan-amazonian inebriant". *Psychopharmacology (Berl)* 186.1 (2006): 93-98.

13 DB de Araujo., *et al.* "Seeing with the eyes shut: Neural basis of enhanced imagery following ayahuasca ingestion". *Human Brain Mapping* 33.11 (2012): 2550-2560.

14 CS Grob., *et al.* "Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brazil". *The Journal of Nervous and Mental Disease* 184.2 (1996): 86-94.

15 C Bouso., *et al.* "Personality, Psychopathology, Life Attitudes and Neuropsychological Performance among Ritual Users of Ayahuasca: A Longitudinal Study". *PloS Genetics* 7.8 (2012): e42421.

16 J Riba., *et al.* "Human Pharmacology of Ayahuasca: Subjective and Cardiovascular Effects, Monoamine Metabolite Excretion, and Pharmacokinetics". *Journal of Pharmacology and Experimental Therapeutics* 306.1 (2003): 73-83.

17 J Riba., *et al.* "Subjective effects and tolerability of the South American psychoactive beverage Ayahuasca in healthy volunteers". *Psychopharmacology (Berl)* 154.1 (2001): 85-95.

18 D Almeida Prado., *et al.* "Effects of the Amazonian psychoactive plant beverage ayahuasca on prefrontal and limbic regions during a language task: a fMRI study". *European Neuropsychopharmacology* 19 (2009): S314-S315.

19 B Shanon. "Altered states and the study of consciousness-The case of ayahuasca". *The Journal of Mind and Behavior* 24.2 (2003) 125-153.

20 E Dominguéz-Clavé., *et al.* "Ayahuasca: Pharmacology, neuroscience and therapeutic potential". *Brain Research Bulletin* 126 (2016): 89-101.

21 E Frecska and LE Luna. "Enhancement of Creative Expression and Entoptic Phenomena as After-Effects of Repeated Ayahuasca Ceremonies". *Journal of Psychoactive Drugs* 44.3 (2012): 191-199.

22 E. Frecska., *et al.* "The Therapeutic Potentials of Ayahuasca: Possible Effects against Various Diseases of Civilization". *Frontiers in Pharmacology* 7 (2016): 1-17.

23 JC Callaway., *et al.* "Pharmacokinetics of Hoasca alkaloids in healthy humans". *Journal of Ethnopharmacology* 65.3 (1999): 243-256.

24 RG Santos., *et al.* "Effects of ayahuasca on psychometric measures of anxiety, panic-like and hopelessness in Santo Daime members". *Journal of Ethnopharmacology* 112.3 (2007): 507-513.

25 PC Barbosa., *et al.* "Psychological and neuropsychological assessment of regular hoasca users". *Comprehensive Psychiatry* 71 (2016): 95-105.

26 MS Allen and EE Walter. "Personality and body image: A systematic review". *Body Image* 19 (2016): 79-88.

27 FL Osório., *et al.* "Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report". *Revista Brasileira de Psiquiatria* 37.1 (2015): 13-20.

28 G dos Santos., *et al.* "Effects of the Natural β -Carboline Alkaloid Harmine, a Main Constituent of Ayahuasca, in Memory and in the Hippocampus: A Systematic Literature Review of Preclinical Studies Effects of the Natural β -Carboline Alkaloid Harmine , a Main Constituent of". *Journal of Psychoactive Drugs* 0 (2016): 1-10.

29 JJ Fortunato., *et al.* "Acute harmine administration induces antidepressive-like effects and increases BDNF levels in the rat hippocampus". *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 33.8 (2009): 1425-1430.

30 J Fortunato and GZ Re. "Chronic administration of harmine elicits antidepressant-like effects and increases BDNF levels in rat hippocampus". *Journal of Neural Transmission* 117.10 (2010): 1131-1137.

31 Y Yoshimura., *et al.* "Roles of 5-HT 1A receptor in the expression of AMPA receptor and BDNF in developing mouse cortical neurons". *Neuroscience Research* 115 (2017): 13-20.

32 RA Rabin., *et al.* "5-HT2A receptor-stimulated phosphoinositide hydrolysis in the stimulus effects of hallucinogens". *Pharmacology Biochemistry and Behavior* 72 (2002): 29-37.

33 RG dos Santos., *et al.* "Antidepressive and anxiolytic effects of ayahuasca: A systematic literature review of animal and human studies". *Revista Brasileira de Psiquiatria* 38.1 (2016): 65-72.

34 X Guitart., *et al.* "Sigma receptors: biology and therapeutic potential". *Psychopharmacology (Berl)* 174.3 (2004): 301-319.

35 S Cai., *et al.* "New hypothesis and treatment targets of depression: an integrated view of key findings". *Neuroscience Bulletin* 31.1 (2015): 61-74.

36 JM Fábregas., *et al.* "Assessment of addiction severity among ritual users of ayahuasca". *Drug and Alcohol Dependence* 111.3 (2010): 257-261.

37 G Thomas., *et al.* "Ayahuasca-Assisted Therapy for Addiction: Results from a Preliminary Observational Study in Canada". *Current Drug Abuse Reviews* 6.1 (2013): 30-42.

38 J Soler., *et al.* "Exploring the therapeutic potential of Ayahuasca: acute intake increases mindfulness-related capacities". *Psychopharmacology (Berl)* 233.5 (2016): 823-829.

39 TE Robinson and KC Berridge. "The neural basis of drug craving: an incentive-sensitization theory of addiction". *Brain Research Reviews* 18.3 (1993): 247-291.

40 MB Liester and JI Prickett. "Hypotheses Regarding the Mechanisms of Ayahuasca in the Treatment of Addictions". *Journal of Psychoactive Drugs* 44.3 (2012): 200-208.

41 RG Santos., *et al.* "Ayahuasca e redução do uso abusivo de psicoativos: Eficácia terapêutica?". *Psicologia: Teoria e Pesquisa* 22.3 (2006): 363-370.

42 AJ Oliveira-lima., *et al.* "Physiology & Behavior Effects of ayahuasca on the development of ethanol-induced behavioral sensitization and on a post-sensitization treatment in mice". *Physiology and Behavior* 142 (2015): 28-36.

43 DJ Moura., *et al.* "Effects of β -carboline alkaloids on the object recognition task in mice". Life Sci. 79 (2006).

44 D He., *et al.* "Effects of harmine, an acetylcholinesterase inhibitor, on spatial learning and memory of APP/PS1 transgenic mice and scopolamine-induced memory impairment mice". *European Journal of Pharmacology* 768 (2015): 96-107.

45 T Alvarenga., *et al.* "Can Ayahuasca and sleep loss change sexual performance in male rats?". *Behavioural Processes* 108 (2014): 110-116.

46 ARM Figueroa. "Avaliação dos efeitos neurotóxicos do chá ayahuasca". (2012).

47 A Pic-Taylor., *et al.* "Behavioural and neurotoxic effects of ayahuasca infusion (Banisteriopsis caapi and Psychotria viridis) in female Wistar rat". *Behavioural Processes* 118 (2015): 102-110.

48 XL Jiang., *et al.* "Potentiation of 5-methoxy-N, N-dimethyltryptamine-induced hyperthermia by harmaline and the involvement of activation of 5-HT<inf>1A</inf> and 5-HT<inf>2A</inf> receptors". *Neuropharmacology* 89 (2015): 342-351.

49 J Daumann., *et al.* "Neuronal correlates of visual and auditory alertness in the DMT and ketamine model of psychosis". *Journal of Psychopharmacology* 24.10 (2010): 1515-1524.

50 L Rambousek., *et al.* "The Effect of Psilocin on Memory Acquisition, Retrieval, and Consolidation in the Rat". Frontiers in Behavioral Neuroscience 8 (2014): 1-7.

51 BJ Catlow., *et al.* "Effects of psilocybin on hippocampal neurogenesis and extinction of trace fear conditioning". *Experimental Brain Research* 228.4 (2013): 481-491.

52 JC Bouso., *et al.* "Long-term use of psychedelic drugs is associated with differences in brain structure and personality in humans". *European Neuropsychopharmacology* 25.4 (2015): 483-492.

53 S RJ and Q CR. "Dose-response study of n, n-dimethyltryptamine in humans: I. neuroendocrine, autonomic, and cardiovascular effects". *Archives of General Psychiatry* 51.2 (1994): 85-97.

54 Portaria SVS/MS no◦ 344 da ANVISA Ordinance SVS/MS n. 344 from the National Health Surveillance Agency. (1998, May 12). Brasília, n.d.

55 J Ott. "Pharmepena-psychonautics: Human intranasal, sublingual and oral pharmacology of 5-methoxy-N, N-dimethyl-tryptamine". *Journal of Psychoactive Drugs* 33 (2001): 403-407.

56 AL Halberstadt. "Behavioral and pharmacokinetic interactions between monoamine oxidase inhibitors and the hallucinogen 5-methoxy-N, N-dimethyltryptamine". *Pharmacology Biochemistry and Behavior* 143 (2016): 1-10.

57 D Fontanilla., *et al.* "The hallucinogen N, N-Dimethyltriptamine (DMT) is an endogenous sigma-1 receptor regulator". *Science* 323.5916 (2009): 934-937.

58 SA Barker., *et al.* "LC/MS/MS analysis of the endogenous dimethyltryptamine hallucinogens, their precursors, and major metabolites in rat pineal gland microdialysate". *Biomedical Chromatography* 27.10 (2013): 1690-1700.

59 JC Callaway. "A proposed mechanism for the visions of dream sleep". *Medical Hypotheses* 26.2 (1988): 119-124.

60 LJ Wichlinski. "Possible involvement of an endogenous benzodiazepine receptor ligand of the inverse agonist type in the regulation of rapid-eye movement (REM) sleep: A hypothesis". *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 20.1 (1996): 1-44.

61 SE Lewis. "Ayahuasca and spiritual crisis: Liminality as Space for Personal Growth". *Anthropology of Consciousness* 19.2 (2008): 109-133.

62 AP Association. "DSM-IV-TR: Diagnostic and statistical manual of mental disorders, text revision, Washington, DC". *American Psychiatric Association* 75 (2000).

63 C Elton. "Day trippers". Outside. 24 (1999): 34.

64 BC Labate and WS Araújo. "O uso ritual da ayahuasca". (2002).

65 EJB Macrae. "Guiado pela lua: xamanismo e uso ritual da ayahuasca no culto do Santo Daime". Editora Brasiliense (1992).

66 CT Tart. "States of consciousness and state-specific sciences". *Science* 176.4040 (1972): 1203-1210.

67 AM de Almeida and F Lotufo Neto. "Diretrizes metodológicas para investigar estados alterados de consciência e experiências anômalas". *Revista de Psiquiatria Clínica* 30.1 (2003): 21-28.

68 D Lukoff., *et al.* "Toward a more culturally sensitive DSM-IV: Psychoreligious and psychospiritual problems". *The Journal of Nervous and Mental Disease* 180.11 (1992): 673-682.

69 K Björnstad., *et al.* "Bioanalytical and clinical evaluation of 103 suspected cases of intoxications with psychoactive plant materials". *Clinical Toxicology* 47.6 (2009): 566-572.

70 D.E. Brush., *et al.* "Monoamine oxidase inhibitor poisoning resulting from Internet misinformation on illicit substances". *Journal of Toxicology: Clinical Toxicology* 42.2 (2004): 191-195.

71 Y Fuse-Nagase and T Nishikawa. "Prolonged delusional state triggered by repeated ingestion of aromatic liquid in a past 5-methoxy-N, N-diisopropyltryptamine abuser". *Addiction Science and Clinical Practice* 8.1 (2013): 9.

72 SL Hill and SHL Thomas. "Clinical toxicology of newer recreational drugs". *Clinical Toxicology* 49.8 (2011): 705-719.

73 AA Muller. "New drugs of abuse update: foxy methoxy". *Journal of Emergency Nursing* 30.5 (2004): 507-508.

74 D Sklerov *et al.* "A fatal intoxication following the ingestion of 5-methoxy-N, N-dimethyltryptamine in an ayahuasca preparation". *Journal of Analytical Toxicology* 29.8 (2005): 838-841.

75 S Smolinske., *et al.* "Foxy methoxy: a new drug of abuse". *American College of Medical Toxicology* 1.1 (2005): 22-25.

76 K. Tanaka., *et al.* "A fatal poisoning with 5-methoxy-N, N-diisopropyltryptamine, Foxy". *Forensic Science International* 163 (2006): 152-154.

77 D Rosengren. "Cultivating spirits: On Matsigenka notions of shamanism and medicine (and the resilience of an indigenous system of knowledge)". *Nueva Época* 2002: 85-108.

78 V De Feo. "The ritual use of Brugmansia species in traditional Andean medicine in northern Peru". *Economic Botany* 58 (2004): S221-S229.

79 Resolução n. 01 Resolution no. 01. (2010, Jan. 25). Brasília: CONAD, n.d.

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