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USE OF AYAHUASCA IN THE TREATMENT OF DEPRESSION

AYAHUASCA USE IN TREATMENT OF DEPRESSION

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Summary

Depression is a chronic psychiatric illness that causes deep sadness and a strong feeling of hopelessness. In this sense, new therapies are being approached. Ayahuasca tea is an example, a drink made from the ayahuasca vine.*Banisteriopsis caapi*. and the leaves of *Psycotria viridis*frequently used in religious rituals such as santo-daime, and which has also been shown to be effective in the treatment of depression and other mental disorders. The study investigates findings on the use of the plant in the treatment of depression. The work is based on a literary review collected mainly by articles in Portuguese and English aimed at an analysis of the pharmacological effects highlighted in clinical and pre-clinical trials. The results presented a series of promising data on the use of the drink to treat depression. Standing out for containing bioactive compounds such as Betacarboline and Dimethyltryptamine (DMT) that interact synergistically, causing changes in the perception of reality and emotions. The research revealed a very significant increase in serotonin in the individuals evaluated, which demonstrated a constant and effective pharmacological effect as a therapy. The tests were very consistent, implying the need for more research to understand the interactions due to ayahuasca, in order to guarantee safety and effectiveness and thus disseminate the treatment in the near future. **Key words:**Santo-daime. Dimethyltryptamine. Betacarboline. Synergism.

Abstract

Depression is a chronic psychiatric illness that causes deep sadness and a strong feeling of hopelessness. In this sense, new therapies are being approached. Ayahuasca tea is an example, a drink made from the vine of the Banisteriopsis caapi. and the leaves of Psycotria viridis often used in religious rituals such as santo-daime, and which has also been shown to be effective in

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the treatment of depression and other mental disorders. The study investigates findings about the use of the plant in the treatment of depression. The work starts from a literature review collected mainly by articles in Portuguese and English, aimed at an analysis of the pharmacological effects highlighted in trials and pre-clinical studies. The results provide a range of promising data on the use of drinking for the treatment of depression. Standing out for containing bioactive compounds such as Betacarboline and Dimethyltryptamine (DMT) that interact synergistically, causing changes in the perception of reality and emotions. The research revealed a significant increase in serotonin in the highly acquired, it did not express a constant and effective pharmacological effect as a therapeutic. The tests were very consistent, implying the need for more research into the proper interactions of ayahuasca, in order to guarantee the safety and efficacy and thus spread the treatment in the near future.
Keywords: Santo-daime. Disorders. Dimethyltryptamine. Betacarboline.

1. Introduction

The word Ayahuasca*Aya*means "dead person, spirit soul" and*waska*means "rope, liana, vine or wine". So the translation, into Portuguese, would be something like "rope of the dead" or "wine of the dead", (LABATE; ARAÚJO, 2002). Ayahuasca is a drink traditionally used for spiritual healing purposes by indigenous populations of the Amazon Basin (LUNA, 2011; SPRUCE and WALLACE, 1908). Tea is made from a mixture of two plants found in the Amazon Rainforest: the leaves of the bush*Psychotria viridis*and the vine*Banisteriopsis caapi*(LABATE; ARAÚJO, 2002; MACREA, 1992).

Several species of the genus*Psychotria,*are popularly known for their medicinal properties (TEIXEIRA*et al.,*2012), and, according to Riba*et al*. (2012), the genre*Psychotria* stands out for its characteristic action on the nervous system. How is the use of sheets of*P. viridis*in the preparation of the psychoactive drink Ayahuasca, together with the vine of *Banisteriopsis caapi*(Malpighiaceae). (Riba*et al*. 2012).

A*Psycotria viridis*family plant*Rubiaceae*, has in its composition the indolic alkaloid derivative N, N-dimethyltryptamine (DMT) in a concentration of 0.1% to 0.66% that acts on serotonin receptors (MCKENNA*et al*., 1998).

The vine*Banisteriopsis caapi*It's family*Malpighiaceae*, native to the Amazon and the Andes. It has MAO inhibitor β-carboline alkaloids in its composition, the highest concentrations of which are: harmine, harmaline, tetrahydroharmaline. The concentration of these alkaloids varies from 0.05% to 1.95% (MCKENNA et al., 1998).

Generally in syncretic churches, the ayahuasca drink is prepared as follows: fragments (shells) of*B. caapi*are collected and bathed in water, beaten with a hammer

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of wood and carefully placed in a cauldron, alternating with washed leaves of*P. viridis.* Water is then added until the plant material is covered and the combination is boiled and concentrated for at least 8 hours to produce several liters. The resulting extract is basically dark. In most of the experimental and clinical studies carried out, a similar method of preparing ayahuasca is used, obtaining a decoction for oral administration (120 to 125 ml/patient) during the rituals, in accordance with the traditional practices of each region. (CALLAWAY, MCKENNA, GROB, BRITO, RAYMON, POLAND, ANDRADE ANDRADE, MASH).

Although the tradition of the drink is common among different tribes in much of South America, such as Peru, Colombia, Venezuela, Bolivia and Ecuador, only in Brazil were non-indigenous religions that use Ayahuasca developed. These religions reworked ancient traditions with influences from Christianity, Kardecist spiritualism and Afro-Brazilian religion (LABATE; ARAÚJO, 2002).

In Brazil, the religions that use ayahuasca in rituals are: Santo Daime, Barquinha and União do Vegetal (UDV). These religions were self-regulated as a result of investigations by the federal government, which began in the 1980s. These investigations on several occasions found that these religions collaborate in a favorable way for the communities in which they are included (LABATE, 2003), which led to the authorization, but also its recognition as: cultural heritage, of public utility and in certain cases historical heritage. (LABATE; GOLDSTEIN, 2009).

Religious use in the country was legalized in 1986, as stated in the opinion of the Working Group of the Federal Council on Narcotic Drugs – CONFEN. According to Federal Government investigations into Ayahuasca, these religions contribute in a beneficial way to society and are cultural and historical heritage. The psychiatrist member of CONAD who regulated the use of the drink in Brazil argues that expanding consciousness does not mean having a hallucination. These concepts are separated by the capacity for reflection. (SANTOS, 2006).

In recent years, there has been a growing search for the consumption of the drink in several regions of Brazil, driving the growth of extractivism of these species in the Amazon region (SÉRPICO; CAMURÇA, 2006).

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2 Objectives

2.1 General objectives

This study aims to discuss the various pharmacological effects of the Ayahuasca drink and its therapeutic potential in the treatment of depression, highlighting the physical-chemical activities of the compounds.

2.2 Specific Objectives

Among the specific objectives, the research explores:

• Identify aspects of the pharmacological and biochemical process of Ayahuasca.

• Discuss clinical and pre-clinical findings in the treatment of depression.

3 Justification

The search for new therapies with the potential to treat mental disorders such as depression indicates the need to seek to understand the particularities of the complexes, and thus demystify their proper properties. This research is precisely about justifying the tests through the other aspects highlighted by the Ayahuasca plant. Therefore, analyzing the pharmacokinetic and pharmacodynamic processes of this, reveals to be an important step to apply more experimental studies regarding anda posteriori, possibly be disseminated for treatment, thereby improving the patient's condition.

4 Theoretical Foundation

Through the analysis of several articles and texts referring to ayahuasca tea, pointing out evidence related to the treatment of depression. In this context, pharmacological aspects of the other psychoactive compounds were outlined. According to Winkelman (2005), among the main motivations of individuals presented for the search: is the search for a better perception of life; emotional healing; and contact with sacred nature, deities, spirits and natural energies caused by ayahuasca.

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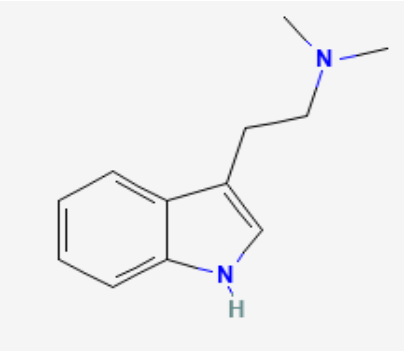
4.1 Ayahuasca and its compounds

The drink is rich in a substance with hallucinogenic potential called dimethyltryptamine (DMT) and other bioactive compounds that facilitate its pharmacological action. There is evidence that Ayahuasca provides benefits in the treatment of some mental disorders, such as depression. (LABATE; GOLDSTEIN, 2009).

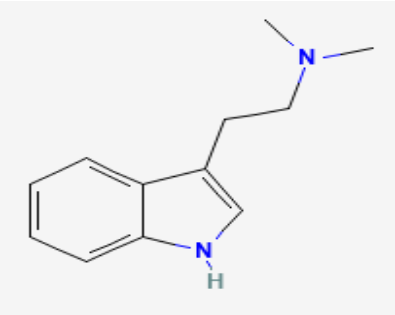
Figure 3 - Structural formula of Dimethyltryptamine.



Source: Pubchem (2021)

DMT is a potent 5-HT receptor agonist, being inhibited by intestinal and hepatic MAO activity. Beta-carbolines are compounds with molecular structures similar to serotonin that have primary sedative effects when administered orally (PIRES, 2009).

Figure 4 - Structural formula of Betacarboline.



Source: Pubchem (2021)

It has been established that signs associated with anxiety, panic and depression are considerably alleviated by serotonergic agonists such as serotonin reuptake inhibitors and MAO-A (WIKINSKI, 2004; NASH; NUTT, 2005;

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STARCEVIC, 2006). The fact that the alkaloids present in ayahuasca block the reuptake of serotonin (THH) and MAO-A (harmine, THH and harmaline) (MCKENNA, 2004) and effect a direct serotonergic agonist (DMT) action (SMITH et al., 1998) proposes that ayahuasca can alleviate emotional conditions regulated by the serotonergic system. Previous studies recommend that ayahuasca has a therapeutic role in cases of depression and anxiety (GROB*et al.*, 2004).

4.2 Pharmacological effects presented by the drink

The acute psychological effects of ayahuasca last about four hours and include intense perceptual, cognitive, emotional and affective changes. (SHANON, 2002; RIBA*et al.*, 2003; FRECSKA*et al.*, 2016). Although nausea, vomiting and diarrhea are constantly reported, mounting evidence points to ayahuasca's positive safety profile. For example, ayahuasca is not addictive and is not associated with psychopathology, personality or cognitive deterioration, promoting only sympathomimetic effects. (GROB*et al.*, 1996; CALLAWAY*et al.*, 1999; DOS SANTOS *et al.*, 2011; BOUSO*et al.*, 2012; BARBOSA*et al.*, 2016).

Over the past two decades, mental health assessments of ayahuasca consumers have shown preserved cognitive function, increased well-being, reduced anxiety and depressive symptoms when compared to non-ayahuasca consumers. (GROB*et al.*, 1996; BOUSO*et al.*, 2012; BARBOSA*et al.*, 2016). Furthermore, a recent study observed that a single dose of ayahuasca increased capabilities (SOLER*et al.*, 2016), related to mindfulness and meditation practices have been associated with antidepressant effects. (SEGAL *et al.*, 2010).

4.2.1 Ayahuasca: Pharmacological aspects.

There is pre-clinical evidence that Ayahuasca has anxiolytic, antidepressant and reducing effects on the consumption of psychoactive substances. Depressive symptoms may be associated with a reduction in neurotransmitters, such as serotonin and norepinephrine. (PALHANO-FONTES*et al.*, 2019) The pharmacological mechanisms of action already elucidated show that the effects of Ayahuasca are due to DMT, which interacts with

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serotonergic receptors, and β-carbolines, alkaloids with inhibitory potential on monoamine oxidase (MAO), this enzyme is capable of metabolizing DMT and serotonin. Thus, a synergistic interaction occurs between bioactive compounds that favor the increase of serotonergic activity in the brain (CALLAWAY; MCKENNA; GROB; BRITO; RAYMON; POLAND; ANDRADE; ANDRADE; MASH, 1999).

The alkaloid when isolated from *B. caapi* turned out to be harmine (Deshayes P. Psychotropes. 2002). Indole alkaloids known as β-carbolines of *P. harmala*, harmaline and tetrahydroharmine, are also present in *B. caapi* (MR EVANS; A. HOFOMANN; TITTARELLI R; MANNOCHI G; PANTING F; ROMOLO FS LEDIAK AD; MUSAH RA, 2018, 2015, 2016). The drink that contains DMT in the leaves *P. viridis*, which was initially discovered from *Mimosa tenuiflora*, a compound subclassified as a simple tryptamine (CALLAWAY; GROB, 1998). The chemical analysis of the ayahuasca drink through various experiments has been driven by specific scientific interest in the search for natural resources, clinical research and the need to identify possible drugs of abuse associated with such components (CALLAWAY, *et al.*, 1996).

The active ingredients generated by ayahuasca depend on the synergistic interaction between the compounds. β-Carbolines are potent reversible MAOIs (MCKENNA, TOWERS, AND ABBOTT 1984) and can raise your serotonin levels by blocking its deamination. The main activity of ayahuasca is to protect DMT from peripheral degradation, preventing oxidative deamination of DMT when ingested and allowing it to reach the central nervous system (RIBA *et al.,* 2003, MCKENNA; TOWERS; ABBOTT, 1984). DMT being a substrate for cell surface serotonin uptake transporters (SERTs) and neuronal vesicle monoamine transporters (VMAT2). Therefore, high intracellular and vesicular concentrations of DMT can reach inside neurons and interact with intracellular sigma-1 receptors located in the endoplasmic reticular membrane (organelle exclusive to eukaryotic cells) together with the mitochondria (SU, HAYASHI, AND VAUPEL 2009). Thus, DMT will be released into the synaptic cleft after vesicular fusion, which will interact with the sigma-1 receptors at the ends of the cells or post-synaptic serotonin receptors present (COZZI *et al.*, 2009).

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5 Methods

Aiming to report the various pharmacological effects of Ayahuasca tea and its therapeutic potential in the treatment of depression, a literature review was carried out in databases from the Scientific Electronic Library Online (SciELO), The National Institutes of Health (PubMed), Europe PMC and for the Springer Nature . In order to gather information necessary for the production of this scientific work, we have articles in Portuguese and English, from 1984 to 2020. The applied studies are based on reviews of pre-clinical and clinical studies evaluating the use of the plant in the treatment of depression.

6 Results and Discussions

6.1 Ayahuasca: Mechanisms of action

The action of ayahuasca infers the synergistic interaction between such components. β-Carbolines are potent reversible MAOIs (Mckenna; Towers; Abbott, 1984) and can elevate serotonin levels by blocking deamination. The main action in ayahuasca is the protection of DMT from peripheral degradation, preventing oxidative deamination of DMT when ingested and thus allowing it to reach the central nervous system (RIBA*et al.*, 2003; MCKENNA; TOWERS; ABBOTT, 1984). The pharmacological effects of DMT may vary when there is an interaction with the serotonergic system. DMT is the substrate for cell surface serotonin uptake transporters (SERTs) and neuronal vesicle monoamine transporters (VMAT2) (STRASMA, 2001).

The β-carboline alkaloids, harmine and harmaline (found in the vine) inhibit the MAO enzyme, after which the serotonin neurotransmitter will undergo molecular modifications at the enzymatic level until it becomes the hallucinogenic molecule 5-MeO-DMT (MCKENNA, 2004). It will initially be in the pineal gland of the brain that this cascade of neurochemical and enzymatic processes will take place in the formation of this psychotropic molecule (SALIM, 1987; MCKENNA et al., 1989; 2004).

The interaction of these actions occurs through two serotonergic agonist mechanisms – inhibition of MAO and serotonin reuptake – which can lead to increased levels of

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serotonin (LUNA, 2005; MCKENNA; CALLAWAY; GROB, 2006). DMT, being a serotonergic agonist, can cause an increase in brain levels of serotonin, which may interfere with the psychoactivity of DMT, as serotonin competes with DMT for serotonergic binding sites (OTT, 2006). However, inhibition of serotonin reuptake can generate an expansion in the half-life of DMT (MCKENNA; CALLAWAY; GROB, 2006).

Serotonin is so important that it appears to be the substance that most closely predominates among the neurotransmitters related to depressive disorders. The role of serotonin in the CNS is to connect with that of noradrenaline, thus, with these substances, they intervene in the regulation of states of wakefulness, in the active process of sleep, attention, in motivational processes (antidepressant), in the regulation of mood states, in addition of the inhibitory stimulus to appetite (FONTANILLA*et al.*, 2009; SU*et al.*, 2009).

If there is free space to react, with MAO temporarily out of the way due to the excess beta-carbolines present, DMT will act on neurons by binding to them in their own receptor sites. Thus, serotonergic 5-HT receptors$_{1A}$5-HT$_{2A}$and 5- HT$_{2C}$in which serotonin (5-HT) - one of the neurotransmitters responsible for our mood state - would commonly bind if it did not have DMT in its path as a competitor (CALLAWAY *et al.*, 1999; FONTANILLA*et al.*, 2009; SU*et al.*, 2009). This results in a cascade of neurochemical effects that modify the normal patterns of our perception, being the definition of what we commonly understand as "real" (MAYFRANK*et al.*, 1998; FISCHBACH, 1992; SANTOS, 2009).

The first effects of the tea appear approximately half an hour after ingestion and last for approximately four hours. However, the most intense visionary and physical effects ever reported were between 60 and 120 minutes after ingestion (MCKENNA*et al.*, 1998; CALLAWAY*et al.*, 1999; DE SOUZA, 2006). Among the variations in the degrees of nausea, vomiting and, occasionally, in some cases, simultaneous diarrhea can be common and are related to the hallucinogenic experiences themselves (OTT, 1999). Such effects vary according to the individual's physiological predisposition, dosage and composition of alkaloids in the tea (MCKENNA*et al.*, 1984). It is also common to observe some side effects such as nausea or drowsiness, which tend to ease even if use continues. It is assumed that some type of physiological adaptation is occurring, although it is still little reported

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about these present mechanisms (STRASSMAN*et al*., 1994; CALLAWAY*et al*., 1999; MCKENNA*et al*., 1998; 2004; SANTOS, 2007a).

6.2 Pre-clinical and clinical evidence of Ayahuasca in the treatment of depression.

Preclinical trials are essential in biomedical research to understand the pathophysiology of diseases and new treatments, including surgical interventions, medications and vaccines. Within experimental psychopharmacology, the forced swimming test is a preliminary test used to evaluate substances with antidepressant potential. The rodents (rats or mice) are placed in a cylinder of water, with no possibility of escape, and after some time trying to escape they acquire an immobile posture. This behavior can be understood as depressive-like behavior. The time spent trying to escape or climb the cylinder can be extended with the use of antidepressants (NUNES et al, 2014). Some studies have shown that ayahuasca and harmine alone were able to reduce this immobility time in rats subjected to the forced swimming test, showing an antidepressant-like effect (FORTUNATO et al, 2010; PIC-TAYLOR et al, 2015)

As a result of studies with non-human primates (*Callithrix jacchus*) who were subjected to an experimental depression protocol, with a single dose of tea capable of reducing behaviors associated with depression and reversing endocrine changes in marmosets, for 14 days (SILVA; 2019).

For Silva and*such*. (2019) the results were based on: Investigating the effects of chronic social isolation and the antidepressant Nortriptyline on physiological parameters (cortisol and weight) and behavioral in juvenile males and females of*Callithrix jacchus*, to validate this species of non-human primate as a translational model of juvenile depression. To evaluate the antidepressant potential of Ayahuasca tea in reversing the depressive state previously induced by chronic social isolation (60 days) in juvenile males and females of *Callithrix jacchus*.

In this study by Silva*et al*. (2019), after analyzing the possible variables studied, it was evidenced that at the end of the CI, there was a significant decrease in cortisol levels, an increase in*self-grooming*, itching and drowsiness, as well as reductions in food and sucrose intake. All assessments were independent of gender.

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A pilot study carried out by Costa, Figueiredo and Cazenave (2005) in São Paulo, where 6 volunteers received a dose of Ayahuasca and showed an improvement of up to 72% on the Hamilton Depression Rating Scale in 7 days, also showing that Ayahuasca was able to generate an effect faster than traditional antidepressants.

A clinical trial was conducted at a University Hospital in Natal-RN, where 29 volunteers diagnosed with resistant depression received a dose of Ayahuasca or placebo and changes were observed in the depression assessment scales. When compared to the placebo group, patients who received Ayahuasca showed a 64% reduction in disease severity. Some adverse effects such as nausea, vomiting and restlessness were observed, but they were short-lived. The use of the plant required specific care. Its side effects had to be minimized, such as hallucinations, dizziness and nausea, patients received the drink in the hospital. The environment was suitable to provide them with tranquility, decorated with plants and illuminated by natural light. After ingesting, the participants, accompanied by two study researchers, were instructed to remain silent, thinking about their own bodies with their eyes closed. The effect occurred gradually (PALHANO FONTES*et al.*, 2019).

The therapeutic possibilities for ayahuasca are numerous in the article by Domínguez (2016), evidence indicates that ingesting ayahuasca helps the individual to overcome diseases and symptoms related to acceptance and the ability to have changes in consciousness. The authors confirm that tea can be a therapy that allows safe exposure to emotional events, such as in the treatment of impulse disorders, personality disorders, substance abuse, in addition to the treatment of post-traumatic stress.

In Gobret's experimental research*et al.* (1996) cited by Meneguetti & Meneguetti (2014), using the Tridimensional Personality Questionnaire (TPQ), showed differences between the UDV – União do Vegetal examinees and the control individuals. The test evaluates pathological characteristics such as anxiety, impulsivity, ability to feel pleasure, persistence, self-direction, cooperation and self-transcendence. The work of Meneguett and Meneguetti (2014) consisted of several reviews published on the topic that aim to define the beneficial effects of ingesting ayahuasca on human health, and its neuropsychological, immunophysiological, microbiological and parasitic actions. It was carried out within the religious and social context of the communities. In this sense, the studies carried out at UDV, even considering scientific, medical and pharmaceutical aspects of ayahuasca, continue

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in the religious context that in terms of the results of ingestion, it improves chemical dependency and disorders, such as depression.

Barbosa (2001, apud GUIMARAES, 2006) found a decrease in psychiatric symptoms with a general improvement in the emotional state in research participants without previous contact with tea. According to Guimarães, the results of his work show that ayahuasca showed a significant attenuating effect on the relative signs of panic. The beta-carbolines present in ayahuasca, such as tetrahydroharmine (THH), can selectively inhibit the reuptake of serotonin and chemical components such as harmine and harmaline, which can selectively inhibit MAO, especially MAO-A, which preferentially inhibit noradrenaline and serotonin. .

In another article by Osório*et al*. (2016), the research carried out with six patients in a psychiatric unit at the University of São Paulo: 2 men and 4 women with Major Depressive Disorder undergoing medication transition, as the latter had failed. Two of them were experiencing a mild depressive episode, three were experiencing moderate episodes and one was experiencing severe depression, all of whom did not present psychotic symptoms. The work was carried out before changing the medication. Patients were admitted to the psychiatric unit weeks before the first dose of Ayahuasca, during which they remained without psychotropic medication. The doses were 120-200 ml obtained by a daimista community to guarantee the appropriate composition, that is, not adulterated in relation to the dosage culturally used in ayahuasca rituals.

Patients ingested AYA under observation on days 1, 7, 14 and 21. The application was 10 minutes before ingestion (-10) and 40, 80, 140, 180 minutes after (+40), (+80), (+140) and (+180) by an experienced clinical psychoanalyst trained in using such scales. On the first day, 62% of the symptoms presented were alleviated, using the appropriate tests. On the seventh day, there was a 72% reduction. On the fourteenth day, the reduction was still visible, but to a lesser extent. There was a large increase on the twenty-first day, obtaining better scores in the score.

The action of ayahuasca infers the synergistic interaction between such components. β-carbolines are potent reversible MAOIs (MCKENNA; TOWERS; ABBOTT 1984) and can elevate serotonin levels, blocking deamination. The main action in ayahuasca is to protect DMT from peripheral degradation, thus preventing oxidative deamination of DMT when ingested orally and thus allowing it to reach the system.

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central nervous system (RIBA et al., 2003; MCKENNA; TOWERS; ABBOTT, 1984). The pharmacological effects of DMT may vary when there is interaction with the serotonergic system. DMT is the substrate for cell surface serotonin uptake transporters (SERTs) and neuronal vesicle monoamine transporters (VMAT2). Unlike drugs that are absorption inhibitors, DMT is transported to the cytosol or vesicle by SERT or VMAT2, respectively (COZZI et al., 2009). Therefore, high intracellular and vesicular concentrations of DMT can be affected within neurons and can interact with intracellular sigma-1 receptors present in the endoplasmic reticular membrane along with the mitochondria (SU; HAYASHI; VAUPEL, 2009). Thus, DMT released into the synaptic cleft after vesicular fusion to react with cell surface sigma-1 receptors or postsynaptic serotonin receptors (COZZI*et al.*, 2009).

The effects of ayahuasca are heterogeneous and encompass sensory, cognitive and affective changes (RIBA, RODRIGUEZ-FORNELLS,*et al.*, 2001), rich visual experiences (SHANON, 2002b, SHANON, 2002a) and entheogenic experiences (SHANON, 2003). These effects begin between 35 and 40 minutes after tea ingestion, reaching a peak between 90 and 120 min, and lasting approximately 4 h (RIBA, RODRIGUEZ-FORNELLS,*et al.*, 2001). To date, all studies have demonstrated the safety of ayahuasca, with reports from individuals who have used it for more than 30 years with no evidence of harm to health (CALLAWAY*et al* ., 1999, GROB*et al*. 1996, RIBA, RODRIGUEZ-FORNELLS,*et al.*, 2001, RIBA*et al.*, 2003) and does not cause significant changes in systolic, diastolic and mean blood pressure and heart rate (RIBA*et al*. 2003). Furthermore, it was shown that the ritual use of tea is not associated with the psychosocial problems that are generally found with other drugs (FÁBREGAS*et al*. 2010).

6.2.1 Acute effects of ayahuasca

Most studies carried out with ayahuasca have investigated its acute effects, almost all on individuals with previous experience with ayahuasca and/or other psychedelics. In a recent systematic review of the literature, 28 published works were found, until December 2016, that evaluated changes caused by the ingestion of ayahuasca by humans, of this total, 18 are about acute effects (DOS SANTOS*et al.*, 2016).

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The characterization of these acute effects largely occurs through the application of psychometric scales (questionnaires) sensitive to certain characteristics of the psychedelic state, such as, for example, changes in visual perception. A*Hallucinogenic Rating Scale*(HRS) is one of them (GROB*et al*. 1996; CALLAWAY*et al*., 1999; RIBA, RODRÍGUEZ-FORNELLS,*et al*., 2001; RIBA, RODRIGUEZ-FORNELLS;*et al*., 2001; MCKENNA 2005; ALONSO*et al*. 2015). It was initially proposed to characterize the effects caused by intravenous administration of N,N-DMT in experienced volunteers (STRASSMAN*et al*. 1994). It is divided into six subscales, somatic effects, affect, volition, cognition, perception and intensity, and has been used in several studies with different psychedelics (RIBA*et al*. 2003, STRASSMAN*et al*. 1994, Ross*et al* . 2016, GRIFFITHS et al., 2016).

The first study to use the HRS as an instrument for evaluating the acute effects of ayahuasca was carried out with experienced members of the UDV, one of the churches that uses ayahuasca as a sacrament (GROB*et al*. 1996). The results show a significant increase in all HRS subscales (GROB*et al*. 1996). These results are consistent with other controlled studies with experienced volunteers, which also found a significant increase in the six HRS subscales during the acute effects of freeze-dried ayahuasca (ALONSO et al., 2015, RIBA, RODRIGUEZ-FORNELLS, BARBANOJ, 2002; RIBA, RODRÍGUEZ-FORNELLS, et al., 2001). The effects are dependent on the dose of N,N-DMT contained in the formulation. In five of the six HRS subscales (with the exception of volition), the higher the dose, the greater the effects detected by the HRS (RIBA; RODRIGUEZ-FORNELLS;*et al* ., 2001; RIBA; RODRIGUEZ-FORNELLS; BARBANOJ, 2002/2003). On the other hand, the administration of consecutive doses of ayahuasca, each containing 0.75 mg of N,N-DMT/kg, suggests a lack of tolerance and

awareness (DOS SANTOS*et al*. 2012).

Neuropsychological tests have also been used to evaluate the acute effects of ayahuasca. One of these studies compared the performance of occasional and experienced users, under the effect of a single dose of ayahuasca, in three neuropsychological tests:*Stroop*,*Sternberg*and Tower of London (Bouso*et al*. 2013). In both groups, an increase in the number of errors in the task was observed.*Sternberg*, decreased reaction time and maintenance of task accuracy*Stroop*. In the Tower of London test, there was a significant increase in execution times, resolution times, and the number of movements performed by inexperienced volunteers, but not by experienced volunteers. Furthermore, a correlation was observed

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significant inverse between the worsening of performance in the Tower of London and time using ayahuasca, that is, the more experienced, the less the degradation of the response (BOUSO*et al.* 2013).

The identification of neural correlates of the acute effects of ayahuasca has been carried out, mainly, by different functional neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) (DE ARAUJO et al. 2012, PALHANO-FONTES *et al.*, 2019).

SPECT assessment during the effects of ayahuasca in experienced individuals suggests a significant increase in blood flow bilaterally in the anterior insula, right anterior cingulate/frontomedial cortex, left amygdala and left parahippocampal gyrus. The results showed significant activation of the frontal and paralimbic brain. The authors concluded that ayahuasca interacts with neural systems that are central to introspection and emotional processing, increasing serotonergic neurotransmission in these processes. (RIBA*et al.*, 2006).

Final considerations

The study addressed biochemical and pharmacological aspects of Ayahuasca and also provided information on the use of tea in the treatment of mental disorders, in addition to several tests carried out with the plant. The results are very promising as a therapy, with the need for more studies with the aim of demystifying the use of psychedelic/ hallucinogenic substances and ensuring safety and effectiveness for patients so that the therapeutic potential of ayahuasca can be explored and applied. pharmacological medicine.

Although there are many positive reports about the use of tea, it is necessary to take into account the lack of information about the guarantee of use and the possible undesirable effects that are not completely clarified.

Most studies and articles address the use of ayahuasca, in a ritual context, as being beneficial for followers. In studies and experiments, tea consumption guarantees an increase in serotonin in the brain, where a deficit of this neurotransmitter is related to diseases, for example, depression.

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