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## 6. Possible risks and interactions of the consumption of ayahuasca and cannabis in humans

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**Abstract.** There is not much literature regarding the possible effects and interactions of the pan-Amazonian hallucinogenic brew ayahuasca and cannabis, except for some anthropological research. One specific Brazilian religious group had used both substances as sacraments in the past, so here it is reported a brief theoretical scientific overview of the possible interactions and risks between those two substances in humans. The main risks were found to be associated with the possible occurrence of cardiac problems, anxiety and panic reactions, and also psychotic reactions. Nevertheless, some “positive” and neutral interactions are also commented.

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## 1. Introduction

Ayahuasca and cannabis are psychoactive substances that have been used for therapeutic and ritual objectives by different human groups. Nevertheless, cannabis had been used ritually by one branch of the Santo Daime religion, a Brazilian ayahuasca religious group[1-3]. This branch, called CEFLURIS, used to call cannabis as *Santa Maria* (Saint Mary or Holly Mary).

The use of Santa Maria, it should be noted, is officially forbidden within the rituals of this group since the 1980s in Brazil, because in this country cannabis is illegal. In this specific religious group, it is important to say that, according to one of its leaders, ayahuasca works with the spiritual male energy of Christ, and cannabis represents the female energy of the Virgin.

## 2. Possible psychological, psychiatric and neuropsychological interactions

Up to this moment, there are limited studies about the possible risks or “positive” interactions between ayahuasca and cannabis. It is possible, however, to consider some characteristics of each substance.

One possibility is that the effects of cannabis would potentiate the psychoactive properties of ayahuasca, producing an experience with more hallucinogenic properties, since both substances can produce these kinds of effects[4,5]. In fact, in pre-clinical studies, there is lack of cross-tolerance between  $\Delta^9$ -tetrahydrocannabinol (THC), cannabis extract, mescaline and lysergic acid diethylamide (LSD-25 or LSD)[6]. Also, in clinical studies, there is lack of cross-tolerance between THC and LSD[7]. Mescaline, LSD and DMT have similar mechanism of action[8]. According to these data, it is possible to speculate that a lack of cross-tolerance would also happen between ayahuasca and cannabis. Finally, consumption of ayahuasca and cannabis have been considered by members of CEFLURIS to produce “very good effects”, and, according to them, the consumption of cannabis after ayahuasca would propitiate “visions”[1].

It is also possible to speculate that the consumption of cannabis could alleviate some possible anxiety produced by some kinds of ayahuasca experiences[9,10], since cannabis can produce relaxation[11,12]. The consumption of cannabis after ayahuasca in the CEFLURIS context have been described to “lead to a felling of ‘unblocked’” and act as a “soother in moments of difficulty”[1]. Nevertheless, the consumption of both substances could produce cases where people would feel extremely anxious, or with panic, or even with psychotic symptoms, especially, but not exclusively,

those with genetic or psychological predisposition. This hypothesis is based on several arguments.

First, there are several studies that suggest that the most common adverse reactions to hallucinogens are anxiety episodes, or even panic episodes and, in rare cases, prolonged psychotic reactions[13-18]. In the case of ayahuasca, the incidence of psychopathology seems to be rare, in adults or even in adolescents[19-24]. Nevertheless, Lima and collaborators[20,21] showed data from 951 ayahuasca consumers, from three Brazilian cities, on the period from 1995 to 2000, and registered 20 psychiatric events (2.1% in the total population), where 7 cases were psychotic reactions (0.73% in the total population). Other study[23] reported that in a period of five years, a Brazilian ayahuasca religious group registered, in an estimated 25000 ayahuasca doses, 13 to 24 cases (0.052-0.096%) where ayahuasca might have contributed in a psychotic episode.

Second, other studies showed that ayahuasca can produce, in some people, anxiety and feelings of “suspiciousness” and “threat”, even in a controlled setting[9,10]. Like with other hallucinogens, those episodes seem to be rare and can be controlled without the necessity of medical intervention[16].

Third, some investigations suggest that cannabis can also produce acute episodes of anxiety, panic, or even experiences with psychotic symptoms, especially in people with predispositions or in novice consumers, and other studies speculate that the chronic use of cannabis can even produce psychosis, although a causal relations is still controversial[4,25-32].

Finally, there is one case report where the consumption of ayahuasca and cannabis produced a psychotic episode[33].

From a neuropsychological perspective, the chronic consumption of cannabis can produce some subtle deficits, especially in memory[31,34-36,]. In the case of ayahuasca, studies with adults or even with adolescents did not found any neuropsychological deficit[19,37]. In fact, the adult study showed that ayahuasca consumers produced better results than the controls in one of the memory tests[19].

The consumption of ayahuasca in combination with cannabis could produce, for example, no ill effects at all, and ayahuasca could, maybe, act as a “neuroprotector” against the effects of cannabis. In fact, there is evidence that the hallucinogens 5-methoxy-*N,N*-dimethyltryptamine (5-MeODMT) and 2,5-dimethoxy-4-iodoamphetamine (DOI), which have a mechanism of action similar to DMT, attenuated the THC-induced impairment of spatial memory[38]. Moreover, the authors even suggested that this kind of drugs could be effective in the treatment of THC-induced memory deficits. Of

course, this is just a hypothesis, and further studies are urgent needed to clarify this topic.

Finally, regarding the potential to produce a dependence syndrome, there is no evidence that ayahuasca can produce it[39]. In fact, there is some limited evidence that ayahuasca can be used to treat dependence[2,19]. In the case of cannabis, it is suggested that about 10% of its users will become dependent on it[28,31]. Considering these factors, there is no apparent reason to assume that ayahuasca might enhance the dependence potential of cannabis. On the other hand, the ritual use of ayahuasca might, maybe, protect against the dependence potential of cannabis[2]. Of course, further studies are needed to better explore this topic.

### 3. Possible physiological interactions

On the clinical level, one obvious possibility is that the antiemetic properties of cannabis[12,40,41] would alleviate or even eliminate the nausea and the emetic properties of ayahuasca[5,42]. In Colombia ayahuasca is known as *la purga* (“the purge”).

Still on a clinical level, Riba et al.[10] assessed the effects of ayahuasca in a single-blind placebo-controlled clinical study in which three increasing doses of encapsulated freeze-dried ayahuasca (0.5, 0.75, and 1 mg DMT/kg body weight) were administered to six healthy male volunteers with prior experience in the use of the brew. The laboratory analyses conducted after each session did not find any clinically relevant alterations in hematological indices or biochemical indicators of liver function or other standard analytical parameters (cellular counting, plasmatic bilirubin, and hepatic enzymes).

Another clinical evaluation did not show any clinically relevant findings among long-term (at least 10 years) consumers of ayahuasca in all organic systems evaluated: neurosensory, endocrine, circulatory (cardiac/respiratory), gastrointestinal (digestive), hepatic and renal, suggesting the absence of any injurious effect induced or caused by long-term ritual use of ayahuasca[43]. Compared to the controls, there were no significant differences in the blood analysis in several parameters tested – hemoglobin, hematocrit, total leukocytes, glycemia (during fasting), creatinine, sodium, potassium, calcium, bilirubin (total, direct and indirect), alkaline phosphatase, glutamic oxalacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), lactate dehydrogenase (LDH) and cholesterol (total and HDL fraction) – except for the platelets, which, although significantly higher in the control group (359.000/mm<sup>3</sup> compared to 271.000/mm<sup>3</sup>;  $p < 0.05$ ), were all inside the normality limit.

In this same study, seven electrocardiographic alterations were found in the ayahuasca group: one case of right branch bundle block, one of left branch bundle block, one of diffuse ventricular repolarization disturbance, and four of sinus bradycardia. Among the controls, there was only a case of sinus bradycardia. Although these alterations were not clinically relevant, and even considering the possibility that the cases of right and left branch bundle block could be attributed to other factors not evaluated in the study (such as Chagas' disease), more studies are needed to better clarify these findings.

Riba and Barbanoj[44] reported that in their pilot and final study combined [10,45], two volunteers showed systolic blood pressure values above 140 mm Hg at some point and four showed diastolic blood pressure values above 90 mm Hg, the diagnostic criteria for hypertension. One volunteer showed heart rate values above 100 bpm, the diagnostic criterion of tachycardia. The maximum values recorded at any time point were 146 mm Hg for systolic blood pressure, 96 mm Hg for diastolic blood pressure and 101 bpm for heart rate. Other study also showed that the acute cardiac effects of ayahuasca are moderate, although in this study there were also values of diastolic blood pressure above 90 mm Hg[46].

Riba and Barbanoj[44] concluded in view of the moderate cardiovascular effects found in their studies that ayahuasca seems relatively safe from a cardiovascular point of view, but they also reported that the results refer only to single dose administrations in young healthy volunteers and recorded in the absence of any physical exercise. They suggested that the cardiovascular picture could be different following repeated dose administration, while performing physical exercise such as dancing, if ayahuasca were ingested by older individuals or by those with cardiovascular conditions/dysfunctions.

Repeated administration, dancing, and older people taking ayahuasca is a very common practice in ayahuasca religions. Nevertheless, there is no published data on clinically relevant cardiovascular alterations associated with acute or even long-term ayahuasca consumption. Indeed, the evidence available suggests its safety in long-term adult use[43].

In the case of cannabis, the consumption of this substance, even in a chronic way, does not seem to commonly produce clinically relevant alterations[12,28,31,40]. Nevertheless, the act of smoking cannabis produces an acute, rapid, and consistent rise of 20-100% in heart rate, which begins around 10 minutes after smoking and lasts for two to three hours[28,47,48]. After repeated use, there is the development of tolerance for this effect, although it disappears rapidly after stop smoking[28,31,47]. Cardiac alterations of clinical value are not common among cannabis consumers;

although there are some rare cases where serious cardiac problems were documented[31,47].

Taking into consideration these data, it is possible to speculate that the cardiac effects of cannabis could potentiate the moderate cardiac effects of ayahuasca. This effect could be even more intense considering that in some ayahuasca rituals there is dancing for several hours.

Finally, it must be considered that there are some adverse reactions that can potentially happen when people present some health conditions that are not indicated when consuming a monoamine oxidase inhibitor (MAOI): severe damage to the liver or kidneys, hypertension, cardiac problems, and brain pathologies[49]. Some of these same preoccupations also can be applied to cannabis consumption, and, of course, for the consumption of both substances together.

## 4. Conclusions

Even considering the positive descriptions of some users of ayahuasca and cannabis[1], these cases and studies are very limited in number and do not present hard evidence, from a scientific point of view. Also, the majority of interactions described here were not investigated rigorously, so the evidence points only to speculative potential risks of the combination of ayahuasca with cannabis.

The main risks appear to be the production of anxiety reactions, panic attacks, psychotic episodes, and cardiac problems. Nevertheless, except for the case of a psychotic episode, where there is a case report published[33], all the other risks are only hypothetical.

It would be wise to advise people with predisposition to psychotic symptoms not to consume ayahuasca with cannabis. It is also important to note that the ayahuasca religious have their own guidelines to prevent people with psychological/psychiatric problems to consume the brew[20,21,50].

Finally, it must be acknowledged that some of the people who consume ayahuasca with Santa Maria also enjoy this combination[1].

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