

Ayahuasca Tea in the United States: Why and how?

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Abstract:

Ayahuasca Tea is available through numerous venues. We are developing traditional Ayahuasca Tea for the group treatment of several mental health indications, including major depression, anxiety, addiction, PTSD, and unresolved grief (U.S. FDA path). We are engaging with Amazonian traditional Ayahuasceros and shamans to learn how best to develop this medicine with respect for indigenous healing rituals. Our research group has chosen to develop traditional Ayahuasca Tea—as opposed to synthesized alkaloids, or what is known as "pharmahuasca." Challenges inherent in botanical drug development as well as historical, cultural, and legal issues are discussed. The concept of reciprocity is introduced, and the Ayahuasca Tea reciprocity imperative is discussed.

Disclosure:

LS, JG, and VH are employees of Sacred Medicines, a mission-driven Delaware Public Benefit Corporation

INTRODUCTION

We are developing Ayahuasca Tea (FDA path) for the group treatment of a number of mental health indications, including major depression, anxiety, addiction, PTSD, and unresolved grief. Our goal is to provide potent and contaminant-free Standardized Ayahuasca Tea. We produce the Tea based on traditional South American ethnomedical methods of combining the vine of *Banisteriopsis caapi* (monoamine oxidase [MAO] inhibitors) and the leaves of *Psychotria viridis* (dimethyltryptamine [DMT]). We are committed to developing Standardized Ayahuasca Tea for clinical, neuroscientific, and consciousness science research.

The FDA has granted Breakthrough Drug Designation to MDMA and psilocybin based on Phase 2 clinical trial results for PTSD and depression, respectively. Psychedelic medicines are poised to contribute significantly to the psychiatric pharmacopeia, as many new companies have formed in this new sector: <https://money.usnews.com/investing/stock-market-news/articles/more-psychedelic-companies-are-going-public>

The psychedelic medicines currently in development are synthetic monotherapies (MDMA, psilocybin, LSD, ibogaine, mescaline, 5-methoxy DMT). The development of psychedelic combinations can be expected to

follow after FDA approval of monotherapies; Ayahuasca Tea is a combination of psychedelic and, to our knowledge, is the only botanical psychedelic being developed through FDA.

We take this opportunity to explain some differences between the botanical Ayahuasca Tea and synthetic (chemical) psychedelic medicines. We believe that Ayahuasca Tea offers a uniquely holistic experience: whole plant medicine, ceremony, group administration of medicine and group psychotherapy, shamanic practitioner facilitation, an extended immersive experience, all drawing from centuries of indigenous use. Our goal is to support the introduction of Ayahuasca Tea into Western society while respecting and honoring its origins and indigenous traditions.

TRADITIONAL USE

Ayahuasca Tea is a sacred indigenous medicine used for physical and spiritual healing. The psychoactive plant preparation is indigenous to the peoples of the Amazon basin. The plants that comprise the tea were found in a 1,000-year-old pouch in Bolivia (radiocarbon dating), representing the earliest known evidence of Ayahuasca preparation ^[1]. Further, we know that Catholic priests went to extreme measures to limit access to Ayahuasca

in South America in the 17th and 18th centuries [2], providing more evidence that this medicine has been used for centuries. Currently, in 2021, we engage with traditional Amazonian healers (Ayahuasceros, Shaman, Taitas) in order to adapt and optimize the provision of this offering to Westerners, balancing respect for indigenous culture with feasibility and acceptability to FDA.

AYAHUASCA HUMAN USE OBSERVATIONAL STUDIES

While Ayahuasca Tea has been well-studied, most, if not all, research has been conducted outside of the U.S. A 2021 PubMed search revealed 240 peer-reviewed publications on the use of ayahuasca in humans that included 23 randomized controlled trials in 329 human volunteers, 11 observational studies involving 2300 people, studies of the pharmacology, EEG, fMRI, and psychological effects of Ayahuasca Tea, including three observational studies of 152 adolescents who participated in Ayahuasca Tea ceremonies in South America.

The safety of Ayahuasca Tea in group ceremonies has been well established in multiple studies conducted in South America, where ayahuasca is legal. The Hoasca Project was the first study conducted to assess the long-term effects of Ayahuasca Tea in humans [3]. From 1991 to 1996, the multinational cooperative effort involved researchers from nine universities and research institutions from Brazil, the U. S. and Finland. Psychological assessment of 15 long-term members of the União de Vegetal Church that utilizes Ayahuasca Tea as a legal, psychoactive sacrament as well as 15 matched controls with no prior history of Ayahuasca ingestion. The team reported the remission of psychopathology following the initiation of Ayahuasca use along with no evidence of personality or cognitive deterioration.

Subsequent studies have confirmed the safety of Ayahuasca Tea when used in a ceremonial setting. Bousa et al. [4] studied Brazilian Ayahuasca church users (N = 127) in order to measure the impact of repeated Ayahuasca use on psychological well-being, mental health, and cognition, in regular and controls (n = 115) at baseline and one year later. Controls were active participants in non-Ayahuasca religions. Users showed higher scores in Self-Transcendence and lower Harm Avoidance and Self-Directedness. The study found no evidence of psychological or mental health deterioration or cognitive impairment in the Ayahuasca group.

Spanish researchers studied 380 long-term participants in Ayahuasca Tea ceremonies in Spain and reported that long-term use of ayahuasca was associated with higher self-reported health and lifestyle. Those who drank Ayahuasca Tea more than 100 times scored high in self-reported mental health again showed reductions in depression and improvement in mental health [5,6].

Multiple observational studies conducted on diverse groups of ceremonial Ayahuasca Tea drinkers suggest that this therapy may reduce alcohol and drug addiction [7].

AYAHUASCA TEA AND DEPRESSION

An open-label clinical study found significant therapeutic benefits among patients with treatment-resistant major depressive disorder [8], even after a single dose of ayahuasca in patients with recurrent depression [9]. Palhono-Fontes et al. [10] reported rapid antidepressant effects of ayahuasca in treatment-resistant depression in a placebo-controlled randomized controlled trial conducted in Brazil (N = 29). The anxiolytic effects of the Tea have also been documented [11,12].

WHOLE PLANTS

We are undertaking the challenge of botanical drug development through the FDA because we believe in the principle of whole plant medicine, perhaps better known in the US with Traditional Chinese Medicines. Plants have polymolecular profiles with hundreds, if not thousands, of bioactive molecules. We hypothesize that the biological and psychological effects of Ayahuasca Tea made from two different species of plants differ and are more complex than simply DMT and harmine. Similarly, we hypothesize that the biological and psychological effects of whole *Psilocybe* mushrooms fruiting body and mycelium differ from and are more complex than the molecule psilocybin. Interestingly, harmine has recently been discovered in *Psilocybe* mushrooms [13].

The first step in our work was to study with and learn from traditional Ayahuasca healers to cultivate and sustainably harvest the two plants. We make the Tea based on traditional South American ethnomedical methods of decocting the vine of *Banisteriopsis caapi* (harmala alkaloids such as harmine) and the leaves of *Psychotria viridis* (DMT); when mixed in a hot water decoction, these produce Ayahuasca' Tea.' It is a challenge in the 21st century to improve on the established method of preparation developed by indigenous healers who have successfully used this medicine for centuries.

There exists a body of data demonstrating that DMT alone shows significantly different pharmacodynamics when compared to the DMT-containing plant brew [14]. The *entourage effect* is postulated as a viable principle applicable to cannabinoids' effects on the endocannabinoid system [15,16,17] and *Psilocybe* mushrooms [18]. The synergistic and multi-targeted actions of complex plant preparations may modulate the delivery, efficacy, pharmacokinetics, and toxicity of single constituents [19].

An example of the potential for synergism when comparing *B. caapi* extracts with isolated harmine and harmaline was reported by Schwartz et al. [20], who measured *in-vitro* dopamine release from rat striatal slices and inhibition of MAO-A activity. *B. Caapi* extracts produced a significantly higher signal in both methods when compared to individual alkaloids used at the same concentration, suggesting a "synergism" among extract compounds or the presence of other active compounds in the extract. Standardized plant medicine formulations are required to expand the understanding of botanicals, so we are making standardized Ayahuasca Tea for U.S. clinical trials.

Similarly, we hypothesize that traditional Ayahuasca Tea, because its other constituents, including terpenes, flavonoids, tannins, catechins, procyanidins, and polysaccharides, have other salutary biologic consequences that would not be provided by DMT alone. Further research is needed to explore these hypotheses.

WHY NOT 'PHARMAHUASCA'?

Often, we are asked, why not just make pharmahuasca with pure chemicals DMT and harmine? Modern reductionistic western medicine has excelled at developing potent single-molecule drugs from plants (digitalis from foxglove, the statins from the fungus *Aspergillus terreus*, paclitaxel (Taxol) from the Yew Tree, morphine from the poppy, and up to half of the oncology drugs from various plants [21]. It is of interest to note that Marinol (dronabinol, enantiomer form (-)-trans- Δ^9 -tetrahydrocannabinol) has not been of significant utility for many patients relative to consumption of whole plant or oil extracts of cannabis.

Other companies are developing DMT alone, administered through various routes and rates of administration

(<https://www.technologynetworks.com/neuroscience/news/world-first-clinical-trial-explores-safety-and-efficacy-of-dmt-for-major-depression-343822>). Our path is to honor and invite the botanical complexity of a natural product because it has demonstrated efficacy in indigenous Amazonian communities for centuries. Plant medicines are not just quaint relics from the past, containing only one medically 'useful' substance.

PURGATIVE

One of the qualities that many people are familiar with is the purgative effects of Ayahuasca Tea. The Tea is known to be an emetic/purgative, and the nausea, vomiting, and diarrhea that occur are expected responses, not side effects. Longitudinal studies of users of ceremonial Ayahuasca Tea and have reported few adverse outcomes. Nevertheless, many Westerners view nausea and vomiting as an undesirable outcome to be avoided, while individuals who know this medicine well insist that vomiting is important [22,23]. In a Western context, does purging make the Tea unsafe? No. Traditional Ayahuasca healers and the Santo Daime and União do Vegetal Churches embrace these effects as providing both emotional and physical purging.

Does vomiting result in under-dosing of DMT? In most ceremonies, participants have the opportunity to drink multiple cups of Tea to direct and control the depth of their psychedelic experience. Will Westerners want to consume this purgative Tea? Some people will avoid the medicine because of its inherent nausea and vomiting—traditional Ayahuasqueros view vomiting as a core element of an Ayahuasca Tea treatment. Purging is viewed as a desired outcome that enables those who partake to discharge negativity through purgation and reset their lives [24]. We accept that catharsis is an important psychological element of the healing process, as

understood in the context of the indigenous tradition, and Dennis McKenna (personal communication) has suggested that the "biters" present in Ayahuasca Tea must be tasted in order to elicit the full therapeutic effect, including purging. The medical benefit of emesis has not been well explored and is underappreciated in the West. Because pharma-huasca typically does not induce purging [25], it may not exhibit this important therapeutic property.

MICROBIOME

The gastrointestinal effects of Ayahuasca Tea are unique among psychedelics [26]. The Tea impacts the human microbiome [27], and thus it may have beneficial effects in individuals with chronic diseases linked to dysbiosis. LJS has observed clinical improvement in people with chronic gastrointestinal disorders (including Crohn's disease, IBS, and ulcerative colitis) who have participated in Ayahuasca ceremonies. The Tea may also have direct immunological effects. For example, the DMT in the Tea binds to serotonin receptors present on the surface of T cells throughout the lymphatic tissue that surrounds the gut from mouth to rectum [28]. A grant to study microbiome effects of ayahuasca was recently awarded to a nonprofit that provides the Tea to American veterans with PTSD (<https://markets.businessinsider.com/news/stocks/ubiome-awards-grant-to-nonprofit-heroic-hearts-project-to-study-the-effect-of-psychedelic-based-therapies-on-the-gut-microbiome-in-veterans-with-mental-illness-1028030860>).

SHAMAN-LED SACRED CEREMONY

The platform that most people access to receive Ayahuasca Tea is a shamanic ceremony. We believe that this medicine is powerful not just because of its pharmacology but also shamanic healing, which is not well

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understood by western science. True shamans are of indigenous lineage, whereas so-called 'neo-shamanic' practitioners (Westerners) are often trained by these indigenous spiritual leaders [29]. Many people seek out Ayahuasca ceremonies for spiritual healing, another concept that is foreign to Western healers. We seek the finest South American traditional Ayahuasca healers (Taitas, Curanderos, Ayahuasceros) to work with us in order to certify capabilities and train Westerner shamanic practitioners to administer the medicine ceremonially in our group clinical trials. We view Ayahuasca Tea's therapeutic effects and the skillfully led ceremony as interdependent, though we appreciate the challenges, this may pose to the FDA. We believe that the healing potential of Ayahuasca Tea is potentially compromised by omitting a skilled ceremony leader, as he/she is a key aspect of set and setting.

GROUP ADMINISTRATION AND THERAPY

We consider the group aspect of Ayahuasca Tea ceremonies to be essential, and to the best of our knowledge, this medicine is the first psychedelic to be developed with the group model. The 12 Step Program for addiction recovery owes much of its success and its low cost in treating addiction using a daily group therapy model. Further, we envision significantly reduced cost to patients who participate in group medicine administration compared to single-subject sessions with 1-2 therapists. Research on the group effect of psychedelic therapy is already underway [30]. MEDICARE presently reimburses licensed credentialed clinical providers to provide group therapy. (<https://www.ehealthmedicare.com/medicare-coverage-articles/medicare-coverage-therapy-mental-health-services/>).

Most Ayahuasca Tea ceremonies are prefaced with an 'intention setting' in which each participant articulates their specific psychological or physical issue, hopes, and intentions for the ceremony. Imperial College researchers have developed and validated the 'Communitas Scale' in order to investigate the psychosocial mechanisms that are relevant to psychedelic ceremonies [31]. Inter-subject interactions among the group members predicted enduring positive changes in well-being and social connectedness. We endorse the practice of intention setting within groups prior to ceremonies and honor the essential role of group integration psychotherapy following ceremonies.

EXTENDED IMMERSIVE EXPERIENCE

Ayahuasca Tea provides a prolonged immersive experience due to selective, reversible MAO-A inhibition by harmala alkaloids such as harmine [32,33,34]. Without enzyme inhibition, the DMT half-life when inhaled or by intravenous (IV) administration is short, lasting only minutes [35]. Gallimore and Strassman [14] argue that the short duration of DMT effects makes it a poor method to study its psychological effects. High acute doses of inhaled or intravenous DMT typically produce delirium, and users are sometimes unable to recall details of the experience. We hypothesize that forming and retaining clear memories of the psychedelic drug experience is important for the therapeutic process and is facilitated by a longer experience with these medicines.

WHY SEEK FDA APPROVAL FOR AYAHUASCA?

We believe that the FDA path provides the best way to educate physicians and other health practitioners about the efficacy and safety of Ayahuasca Tea. As most other

Schedule 1 substances are pursuing the FDA path, clinicians and scientists will then have the ability to compare Ayahuasca Tea to other psychedelic medicines.

There are some risks associated with bringing ayahuasca through the FDA, including medicalizing a sacred medicine. As noted above, our development plans do not involve single patient medicine experiences; we intend to preserve the ceremony and shamanic practitioner aspects of this medicine.

Botanical drug development through FDA presents a lack of precedent of psychoactive whole plant medicine. The few examples of FDA-approved botanical drugs reflect the emphasis of modern drug development on single-molecule discoveries and the lack of plant chemistry expertise and interest among western drug developers. We believe that it is possible to entangle the sacred and the scientific without commodifying a powerful sacramental medicine.

Rescheduling of psychedelic medicines is encompassed in the FDA's review of these medicines at the NDA (New Drug Application) stage, all of which are now Schedule 1 substances. Failure to develop Ayahuasca Tea through FDA would likely leave the Tea with Schedule 1 status. Even when psychedelics are no longer highly controlled as Schedule 1 drugs, psychiatrists, psychiatric ARNPs, NDs, MDs, and DOs will want to prescribe FDA-approved medicines that they know are of high quality, potent, safe, and efficacious.

There are several reasons to pursue FDA approval of Ayahuasca Tea:

- U.S. psychiatry and mental health services will adopt psychedelic therapy options for their patients only after FDA approval.
- Insurance coverage generally requires proof of efficacy and safety through the FDA.

- FDA approval may reduce travel to South America, thus limiting carbon footprint and depletion of wild plants.

It is important to note that FDA approval of Ayahuasca Tea will not prevent the UDV and Santo Daime churches from serving Ayahuasca Tea in their religious ceremonies.

We know that plant medicine presents chemistry and standardization challenges. However, these are not insurmountable. FDA provides expert botanical medicine guidance to botanical drug sponsors. In December 2016, FDA released its updated 'Botanical Drug Development: Guidance for Industry' (<https://www.fda.gov/files/drugs/published/Botanical-Drug-Development--Guidance-for-Industry.pdf>). Bloomberg News states that FDA had more than 500 botanical applications pending in 2012, the majority derived from Traditional Chinese Medicine [36].

MEDICAL PLURALISM

We believe in medical pluralism. There will be and should be multiple access paths for psychedelic medicines in the U.S. All pathways are worthwhile. Americans have a choice of how, where, and with whom to receive Ayahuasca Tea, and options will only expand in the future:

1. Church Tea: within the two currently legal U.S. Ayahuasca churches, the Santo Daime and UDV. New non-denominational Ayahuasca churches are beginning to form in the U.S.
2. Decriminalized tea: traditional *legal* shamanic ceremony in the U.S, after the decriminalization movement expands.
3. Amazonian Tea: Adventurers will continue to travel to the Amazon basin for medicine journeys led by indigenous shaman and immersed in nature.

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4. Underground Tea: illegal Tea ceremonies are prevalent in the U.S. and will likely continue.
5. FDA approved Tea: Tea served in authorized U.S. clinics to groups of patients with psychiatric diagnoses (Ayahuasca Tea is investigational at this time).

MEDICALIZATION OF AYAHUASCA TEA

One could question why psilocybin is being developed by two companies (Usona.org and Compasspathways.com) when psilocybin mushroom decriminalization and legalization are spreading rapidly through the US. Likewise, will we need FDA-approved Ayahuasca Tea once psychedelic medicines are decriminalized? One reason to proceed with FDA development is to ensure the quality of the Tea served.

Kaasik and Kreegipuu ^[37] have determined that some Ayahuasca Tea served in the EU is counterfeit, mostly associated with neo-shaman ceremonies but not with EU churches. Some analogs of Ayahuasca vine (*Peganum harmala*, *Mimosa hostilis*) were substituted. Shockingly, 2 of the 102 samples contained moclobemide (a pharmaceutical MAOI), psilocin, high concentrations of DMT, and very low concentrations of *B caapi* alkaloids. We are developing standardized Ayahuasca Tea so that prescribers and users can know that their medicine is authentic and pure. Further, we intend to sell authentic Ayahuasca Tea in jurisdictions with appropriate decriminalization legal structures in place in support of harm reduction. We will offer an Ayahuasca Tea assay service in support of harm reduction efforts.

SUSTAINABLE AGRICULTURE

As the use of Ayahuasca Tea is expanding rapidly, and plant source sustainability is of

significant concern. A study published by the American Botanical Council in 2018 concludes that *B. caapi* (Ayahuasca vine) cultivation is necessary now for the viability of the vine due to its use in ritual ceremonies that are increasingly popular around the world (<http://herbalgram.org/resources/herbalegram/volumes/volume-16/number-7-july/a-preliminary-sustainability-report-of-ayahuasca-vine-in-the-peruvian-amazon/a-preliminary-sustainability-report-of-ayahuasca-vine-in-the-peruvian-amazon/>).

There is no evidence of plans for sustainable *B. Caapi* vine farming in the Amazon, so depletion of these invaluable species is inevitable as a result of its popularity with westerners. A sacred tropical plant preserves using Peruvian cultivars was created by three pioneering American visionaries, Kathleen Harrison, Terence McKenna, and Dennis McKenna, nearly 50 years ago on the Big Island in Hawaii. We exclusively source our plants from this resource that was specifically designed to alleviate the overuse and depletion of sacred plants in the Amazon basin.

RECIPROCITY

It has been suggested that developing Ayahuasca tea through the FDA may be *cultural misappropriation* of a sacrament, and we remain very sensitive to this issue. In 2008, the government of Peru declared ayahuasca a national treasure and "one of the fundamental pillars of the identity of Amazonian peoples." In 1992, the government of Brazil officially exempted ayahuasca and its constituent plants from their list of illegal drugs. The Convention on Biological Diversity adopted the Biodiversity Treaty in 1992 and was signed by 150 government leaders at the Rio Earth Summit (<https://www.cbd.int/convention/>)

We have instituted several reciprocity initiatives to address these assertions:

- Shamanic practitioner-led ceremonies
- A shamanic practitioner certification program designed by indigenous healers
- Community-designed and implemented local reciprocity programs
- A sustainable agriculture program in Hawaii

CONCLUSION

Ayahuasca Tea, served in a group ceremony, is being developed through the U.S. FDA for various psychiatric conditions. The tea ceremonies will be preceded by group intention setting and followed by group integration therapy with ayahuasca certified psychotherapists. Human Ayahuasca brain research will be facilitated by access to an FDA-approved standardized Ayahuasca Tea botanical drug formulation. Where possible, Amazonian Shaman is being engaged to advise on the development of this medicine with respect for indigenous healing rituals.

We suggest that there are two parallel modern scientific paths towards the study and clinical applications of psychedelic substances--single molecules and whole plant medicines. Whole plant botanical medicine is not old-fashioned. Plant medicines have an important scientific and medical future - right alongside reductionistic single-molecule medicine. Sacred plant medicines deserve to be scientifically validated, and the FDA route provides definitive proof of efficacy and safety.

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Standish, L.J.; Giménez, J.; Hale, V. (2021, March). Ayahuasca Tea in the United States: Why and how? *The Journal of Psychedelic Psychiatry*, 3(1).

ACKNOWLEDGEMENTS

Funding for this work was supported by a grant to the Multidisciplinary Association for Psychedelic Studies made by Robin Wechkin and Bill Bolosky. Grateful acknowledgement to Dr. Dennis McKenna for critical review and Rebecca Mains and Chelsey Peat for assistance with manuscript preparation.

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