## Revisiting Ayahuasca: Vine of the Soul of the Amazon

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A case report published in the PCC described a young woman who developed psychosis following avahuasca use in a ceremonial setting.1 This case highlights the need for increased research on acclaimed phytoceuticals (plant-based medicines) including the traditional Amazonian drink ayahuasca. The market for plant therapies has burgeoned over the years due to a preference for natural substances.<sup>2</sup> Ayahuasca consumption has expanded from the Amazon to Europe and North America for spiritual, religious, and recreational reasons.3

Avahuasca is a ritual psychedelic decoction used in South America for centuries by native healers.2 Two Brazilian religions, União de Vegetal and Santo Daime, practice ayahuasca rituals with branches spread throughout the world.4 Ayahuasca is a unique combination of monoamine oxidase inhibitors (MAOIs) present in harmala alkaloids (derived from the stem bark of Banisteriopsis caapi vine) with N,N-dimethyltryptamine (DMT) from the Psychotria viridis shrub. Without MAOIs, DMT will get inactivated by gut and liver MAOs and will be unable to reach cortical 5-HT<sub>2A</sub> receptors.3,5 Endogenous DMT found in the pineal gland is hypothesized to play a role in near-death, extracorporeal experiences and mystical states.5,6

The common motivations for ayahuasca (exogenous DMT) use are facilitation for finding direction in life, spirituality, self-discovery, and healing.<sup>2,3</sup> Ayahuasca experience begins about 40 minutes after use, peaking between 1 and 2 hours with effects subsiding in 4 hours.<sup>3</sup> There are 3 phases of use: the first phase with visual imagery and nausea/vomiting (purging effect), the second phase in which users report receiving lessons from spiritual entities, and the third phase involving fading of visuals and physical exhaustion.<sup>3</sup>

Studies have shown ayahuasca's efficacy in treatment-refractory depression with potency comparable to ketamine.<sup>4</sup> Other proposed benefits include treatment of anxiety, eating disorders, trauma, alcohol and cocaine addiction, and opioid withdrawal.<sup>2,3</sup>

A lethal dose of ayahuasca is 50 times the dose used in religious settings.<sup>3</sup> Adverse effects are mild, with gastrointestinal side effects being the most common.<sup>6</sup> By acting as an MAOI, it augments the risk of serotonin syndrome.<sup>4</sup> Psychosis induced by ayahuasca, though rare, seems to involve mainly action on 5-HT<sub>2A</sub> receptors, although there is a possible dopaminergic involvement present as well.<sup>5</sup> This is evident through successful treatment using serotonin and dopamine antagonists.<sup>5</sup>

Ayahuasca tourism has skyrocketed in the Amazon. Its effects depend on the origin, development, and ratio of specific plants used and methods of preparation.<sup>6</sup> There are reports of toxic plants being used as adulterants and tourists being sexually/financially exploited by sham "ayahuasqueros" (equivalent to doctors of ayahuasca) in the Amazon.<sup>7</sup> The darknet is the most common source for buying ingredients outside the Amazon.<sup>3</sup> Uncontrolled intake of nontraditional ayahuasca preparations in unsupervised settings is dangerous.<sup>6</sup>

Collaboration between health care researchers and reputable practitioners in the Amazon is required to provide a safe and legitimate ayahuasca experience.<sup>7</sup> Currently, we do not have ideal treatments for addiction and mental health. It will not hurt to keep our minds open to new possibilities. Presently, ayahuasca is labeled Schedule 1. Relaxing government restrictions will help to facilitate clinical trials and register the risks/ benefits of ayahuasca with clinical databases.<sup>6</sup> Further research is warranted to better understand ayahuasca.<sup>2</sup>

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