

Sipping on Serotonin: A Quick Fix with Ayahuasca for Treating Depression

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Depression is a mental illness with a prevalence of 300 million people in 2017, as reported by the World Health Organization (Palhano-Fontes et al., 2019). The main depressive symptoms include feelings of sadness and suffering, trouble concentrating and often having pessimistic thoughts. Depression is associated with biological changes in the brain, where especially an imbalance in monoamines such as serotonin, dopamine and norepinephrine contributes to depressive symptoms (Osório et al., 2015). Finding the right medication to treat depression is often difficult, since one-third of the diagnosed people are non-responsive to the prescribed medication and it usually takes two weeks to test its effectiveness (Palhano-Fontes et al., 2019). Alternative medications may be helpful to fill this gap, since more people are being attracted to this kind of medical practices (Jiménez-Garrido et al., 2020). Ayahuasca can address these limitations of present treatments, because of its quick and significant effect on depression scores (Palhano-Fontes et al., 2019; Osório et al., 2015; Sanches et al., 2016).

Originally, Ayahuasca is a Brazilian psychoactive brew, that was used for religious purposes (Ruffell et al., 2021). Since the 1980s, its use has spread to cities and other countries for healing and spiritual processes. Nowadays, it is mainly used for these purposes as well and is used by a wider public to experience the special effects of Ayahuasca. The non-clinical setting of the Ayahuasca intake is mostly in a group, led by an Ayahuasca expert to guide you safely through the experience. The Ayahuasca experience itself is caused by the special ingredients and preparation of the brew. Essentially, Ayahuasca is made from two kinds of plants with effective substances, growing in the Amazon area (Ruffell et al., 2021). These plants are the *Banisteriopsis caapi* and the *Psychotria viridis*. The combination of these two plants will give people a mystical psychedelic experience and emotional healing that is often accompanied by insights in their current lives. To fully understand the contribution of Ayahuasca as a potential treatment of depression, it is helpful to understand its chemical

composition, which has been shown to have similar modulation in the brain as certain other antidepressant medication (Palhano-Fontes et al., 2019).

The effective substances of the plants are monoamine oxidase inhibitors (MAOI) and N,N-dimethyltryptamine (DMT), which independently have a psychoactive effect on users as well (Palhano-Fontes et al., 2019). Especially the agonistic behaviour of DMT on the serotonin receptor, has promising results regarding anti-depressive effects. The combination of the substances during Ayahuasca will result in the experience lasting for 4-6 hours due to the MAOis that prevent the inactivation of DMT, enabling DMT re-uptake in the brain areas rich in serotonin receptors, causing the psychedelic effect of the experience in both healthy and depressive participants (Jiménez-Garrido et al., 2020).

In line with traditional claims about Ayahuasca’s effectiveness, Ruffel et al. (2021) concluded that Ayahuasca has a positive impact on mental health when analyzing this in a ceremonial setting. Especially reductions in depression scores were associated with improved well-being. Earlier scientific studies have been conducted to explore the effectiveness of ayahuasca in a clinical setting to address its effects on well-being (Palhano-Fontes et al., 2019; Osório et al., 2015; Sanches et al., 2016; Jiménez-Garrido et al., 2020).

Osório et al. (2015) conducted an open-label preliminary study on Ayahuasca’s antidepressant effects, finding significant improvements multiple times after administration in all participants, regardless of the severity of their depression before the experiment. Since this was a preliminary study, the sample size was small, no long term effects were measured and their experiment was not controlled or blindly executed.

Regarding the limitation of the small sample size, Sanches et al. (2016) studied the same antidepressant effects by using a larger sample and also studying brain effects associated with intake of Ayahuasca in a SPECT study. In line with the study of Osório et al. (2015), fast and consistent anti-depressive effects in response to the Ayahuasca were found, as well as brain activation in regions connected to mood and emotional states, which are associated with anti-depressive effects.

Elaborating on these findings, Dos Santos et al. (2018) studied the lasting effects of the experience in a qualitative study after a 5-year period. Most participants rated the Ayahuasca experience as one of the most important events in their lives, although they reported no further reduction in depressive symptoms a months after the Ayahuasca experience.

The same effect of Ayahuasca was investigated by Palhano-Fontes et al. (2019) using a randomized, double-blind, placebo-controlled design. They concluded that Ayahuasca appears to have a fast and increasing impact on antidepressant effects compared to the placebo group up to seven days post-dosing, implicating that the observed antidepressant effects are solely caused by Ayahuasca.

These previous studies mainly focused on the effects of Ayahuasca on novice users who are diagnosed with depression and are treatment-resistant. Jimenez et al. (2020) compared (non-)diagnosed novice and experienced Ayahuasca users in an observational study. Most importantly, they found that depression scores

were significantly improved in novice users and were consistent up to 6-months after the Ayahuasca experience. They suggested that continuous use might be beneficial as well. Non-clinical settings in addition to clinical settings make it plausible to generalize the outcomes to a wider use.

Van Oorsouw et al. (2022) conducted a study in a non-clinical setting, confirming long-lasting improvements in depression. In this study, the researchers tested clinically depressed participants with prior experience in Ayahuasca, but were novice users of an analogue of Ayahuasca, which is chemically similar to the origin.

In conclusion, the high prevalence of depression and the limitations of current treatments require studies investigating alternative therapies, such as Ayahuasca, with similar therapeutic benefits for depression. Preliminary studies have shown promising results regarding rapid and sustained antidepressant effects as well as activated areas in the brain associated with anti-depressive effects (Sanches et al., 2016; Osório et al., 2015). Palhano-Fontes et al. (2019) strengthens these results with a placebo-controlled group. Furthermore, long-term non-clinical studies elaborated on these previous findings, adding proving for long-term sustained and generalizing effects. Overall, the existing studies suggest that Ayahuasca could offer a fast-acting, prolonging and effective treatment for depression. Although these results are promising for treating depression, future research should include well-designed control groups and aim for larger and more diverse sample sizes.

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