Ayahuasca is a Brazilian word for a decoction made from the woody liana (vine) *Banisteriopsis caapi* and leaves of *Psychotria viridis*. The beverage is also known as *ayahuasca*, *caapi*, *daime*, *yagé*, and *natem*. The term *ayahuasca* is more commonly used, and will be substituted for ayahuasca in this summary. Indigenous and urban populations living throughout the river regions of Brazil, Bolivia, Ecuador, and Peru commonly drink the beverage. The primary components of the beverage are the harmala alkaloids—harmine, harmaline, and tetrahydroharmine (THH)—from *B. caapi*. Harmine and harmaline provide their effects by a specific and reversible inhibition of monoamine oxidase A (MAO-A). THH acts by weakly inhibiting the uptake of serotonin at presynaptic sites, and possibly by acting as a weak inhibitor of MAO-A, thus contributing to the overall MAO-inhibition effect. The researchers’ data indicates that this action is not that important for THH, since the other harmala alkaloids are much more potent. Together, these alkaloids cause an increase in the concentration of serotonin. The beverage also contains N,N-dimethyltryptamine (DMT) from the *P. viridis* leaves. DMT is a potent psychedelic agent, which binds to serotonergic sites in the brain. DMT, by itself, is not orally active because it is inactivated by MAO in the gut and liver before it reaches its active sites in the brain. In the presence of the MAO-inhibiting harmala alkaloids, however, DMT is protected from this degradation by peripheral MAO and crosses the blood-brain barrier in the active form. This synergistic combination — of MAO-inhibiting harmala alkaloids from *B. caapi*, and hallucinogenic DMT from the key admixture plant, *P. viridis* — forms the pharmacological basis for the psychedelic activity of ayahuasca. This paper reports on the pharmacokinetics and pharmacodynamics of ayahuasca ingestion in healthy volunteers.
One of the paper’s authors, Dennis J. McKenna, Ph.D., an ethnopsycho-
pharmacologist and member of ABC’s scientific advisory board, told HerbClip,
“Although there may well be potential medical applications of ayahuasca
(e.g., in the treatment of addiction, depression, alcoholism etc.), this initial
study was not an attempt to establish those uses. Rather, since there had
been previously no studies at all on the human pharmacology of ayahuasca,
this study was an effort to gather some basic data on its mechanisms of ac-
tion, its metabolism, toxicity or lack of toxicity, and its effect on basic physi-
ological processes such as blood pressure and various parameters that are
known to be modulated by serotonin. The study objective was to collect
some very basic information as there had been none before. Such data is
needed in order to make an assessment of its safety, toxicity, short- and long-
term effects. All of this needs to be understood before we can seriously dis-
cuss any potential medical applications. The results of the study indicated
that ayahuasca is well-tolerated and relatively safe; there are some long-term
changes in serotonin receptors not discussed in this paper (J.C. Callaway,
M.M. Airaksinen, D.J. McKenna, G.S. Brito, & C.S. Grob Platelet serotonin
uptake sites increased in drinkers of ayahuasca. Psychopharmacology,
1994, Vol. 116, pp. 385–387) that may be indicative of positive (in the sense
of beneficial) long-term changes in serotonin receptors.”

Fifteen volunteers (aged 26–48 years) who typically consume ayahuasca
once every other week, ingested 2 ml/kg of ayahuasca prepared by the inves-
tigators. The volunteers were male, and all had used ayahuasca for at least
10 years on a regular basis, in the context of their practice as members of the
UDV, a Brazil-based ayahuasca-centered religious movement. Women were
excluded form this initial study to minimize variables; a future study, which will
include women subjects, is planned, pending funding. Blood samples were
drawn prior to ingestion, and at time 0, 20, 40, 60, 90, 120, 180, 240, 360,
and 480 minutes after ingestion. One final measurement was taken 24 hours
after ingestion. Plasma levels of harmine, harmaline, THH, growth hormone,
and prolactin were measured. The psychotropic effect of ayahuasca was
measured using a hallucinogenic rating scale. According to McKenna, this
scale was developed by neuroscience researcher Dr. Rick Strassman, in
connection with his studies of the human pharmacology of intravenously ad-
ministered DMT. Strassman’s studies were conducted several years ago at
the University of New Mexico. The rating scale was translated into Portu-
guese and modified for the ayahuasca study. As it turned out, McKenna
notes, this scale was not a very useful assessment tool since intravenous
DMT and orally activated DMT are very different in their effects. Heart rate,
blood pressure, respiration, oral temperature, and pupillary diameter were
measured in this study, obvious parameters that should be measured when
assessing any CNS-active agent, especially serotonergic ones.

The freshly prepared ayahuasca used in the study was verified to be typical of
the ayahuasca usually consumed. Chemical analysis revealed that the aya-
uhasca was 1.70 mg/ml harmine, 0.20 mg/ml harmaline, 1.07 mg/ml THH,
and 0.24 mg/ml DMT. The volunteers found the dose to be mild in effect.
Volunteers received a dose of 2 ml/kg of body weight of this test preparation.
McKenna said, “It might be worth mentioning that, at a typical body weight of 75 kg (ca. 165 pounds), the dose of DMT was on the order of 36 mg, which is considered a low to moderate dose when parenterally administered (i.e., injected).”

Peak DMT plasma levels were associated with intricate, colored eyes-closed visual imagery, complex thought processes and a general state of heightened awareness. All 15 volunteers experienced these subjective effects at this dosage. Plasma harmine levels peaked approximately 20 min after ingestion and returned to baseline by 480 minutes. In contrast, THH peaked at 180 min and remained elevated significantly above baseline at 480 minutes Twenty-four hours after ayahuasca ingestion, THH was detected at low levels in three of the volunteers. Plasma growth hormone, prolactin, and cortisol levels transiently increased after ayahuasca consumption. Heart rate, blood pressure, respiration, oral temperature, and pupillary diameter all transiently increased after ayahuasca ingestion.

McKenna clarifies, “The neuroendocrine effects (growth hormone, prolactin, cortisol) and the physiological responses measured are correlated with the subjective effects, and are indicative that the response to ayahuasca is primarily mediated by serotonergic interactions. Similar changes in these parameters were measured in Strassman’s study with I.V. DMT.”

All of the neurological, physiological, and neuroendocrine responses are attributed to ayahuasca’s causing an increase in the levels of serotonin. Various degrees of nausea, vomiting, and diarrhea are common and depend on individual variability, dosage, and the alkaloid composition of ayahuasca.

The authors suggest that this preliminary data provide direction for future investigations. Further, they suggest that by investigating human reactions to psychotropic agents such as ayahuasca, researchers can generate greater understanding of neurochemistry and cognition.

Dr. McKenna also offered the context of an earlier study by the same authors that gives a more adequate perspective on the present article. McKenna said, “This study is only half the picture; this is the physiological, pharmacological, biochemical part of the study that is reported in this article. In order for its relevance to be fully understood, it should be viewed as a companion piece to our previous study published in the Journal of Nervous and Mental Disease (C.S. Grob, D.J. McKenna, J.C. Callaway, G.S. Brito, E.S. Neves, G. Oberlender, O.L. Saide, E. Labigalini, C. Tacla, C.T. Miranda, R.J. Strassman, K.B. Boone. Human pharmacology of hoasca, a plant hallucinogen used in ritual context in Brasil. Journal of Nervous & Mental Disease. 1996, Vol. 184, pp. 86–94), which focused primarily on psychological measurements and subjective effects, both short- and long-term. Viewed by itself, this paper is interesting but inconsequential. It only begins to make sense when considered in conjunction with the earlier paper.”

—Heather S. Oliff, Ph.D.
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