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HUMAN PHARMACHOLOGY OF AYAHUASCA

OBJECTIVE: The goal of my study is Ayahuasca, known as one of the most hallucinogenic drugs of the world. I have focused on its pharmacology and effects.

METHODS: I have studied this drug by consulting different scientific articles.

AYAHUASCA

***N,N*-dimethyltryptamine** (DMT)
From *Psychotria viridis* (Rubiaceae) and *Diplopterys cabrerana* (Malpighiaceae)

ß-carboline alkaloids
From *Banisteriopsis caapi* (Malpighiaceae)

HARMINE | **HARMALINE**

TETRAHYDROHARMINE

HARMOL | **HARMALOL**

ABSTRACT: Ayahuasca is known as a hallucinogenic beverage from extremely potents psychoactive plants used by shamans. DMT, structurally related to the neurotransmitter serotonin (5-HT), binds to its receptors. ß-carboline alkaloids contribute to the overall effects of Ayahuasca by blocking monoamine oxidase activity (MAO). That is how it prevents DMT degradation. Ayahuasca causes dramatic modifications in perception, the sense of self and reality and can be very intense but relatively short in duration. The drug performs notorious cardiovascular, autonomic, neuroendocrine and neurological effects.

CONDITIONING FACTORS

The quality and the quantity of the brew, the psychosomatic state of the patient, the degree of familiarity with the drug and so a bad diet are conditioning factors. Our position within time and space, identification of what is real or not, what is ours or somebody else's, the sense of ourselves, discrimination of movements, volumes, bodily equilibrium etc., can be altered.

ENVIRONMENTAL EFFECTS: The lighting, odors, posture, sounds, etc., are conditions that allow or not the consumer to capture stimuli which were previously subliminal. These conditions can provoke a hallucinogenic intoxication.

INTERFERENCES BETWEEN PARTICIPANTS: During the session, the continuity of relationships between consumers decreases, but there are some exchanges between all of them called "energies". The eviction of those called "energies" can be at an emotional level, at a mental level, or at a physical level.

INFLUENCE OF THE THERAPIST: The healer is, perhaps, the most important conditioning factor. The shaman's role consists of controlling, modulating and harmonizing the "energies" of each particpant.

MECHANISM OF ACTION

MAO-A inhibition by ß-carboline alkaloids facilitates DMT absorption by preventing its metabolism, so its elimination decreases. This action allows the activity of DMT when it is taken orally.

The effects caused by DMT are due to the interactions at the central serotonin receptors site 5-HT2A , 5-HT2C and 5-HT1A .

ß-carboline alkaloids generally bind to 5-HT2A and to 5-HT2C. THH inhibits 5-HT uptake.

The increased level of 5-HT compete with DMT for the receptors and the metabolism of the last mentioned becomes even slower.

PHARMACOKINETICS

DMT

Deamination via MAO-A → 3-Indoleactic acid (3-IAA)

N-oxidation → DMT-N-Oxide (DMT-NO) → Cyclation → methyl-1,2,3,4-tetrahydro-ß-carboline (2-MTHßC).

N-demethylation → N-methyltryptamine (NMT) → Cyclation → methyl-1,2,3,4-tetrahydro-ß-carboline (2-MTHßC).

N-methyltryptamine (NMT) → Deamination via MAO-A → 3-Indoleactic acid (3-IAA)

Rapid disappearance from plasma.

ß-carboline alkaloids

Rapid disappearance from plasma.

O-demethylation of harmaline: cytochromes P450 1A1, 1A2 and 2D6.

Major urinary metabolites: harmol sulfate and harmol glucoronide.

O-demethylation of harmine: cytochromes CYP1A1, CYP1A2, CYP2C9, CYP2C19, and CYP2D6.

Harmine disappears rapid from plasma, but there are significant concentrations of THH, Harmol and Harmalol.

EFFECTS

Cardiovascular effects: increases in blood pressure and so in heart rate.

Autonomic effects: stimulation of intestinal motility, vomits, tremors and increases on rectal temperature and pupil diameter.

Neuroendocrines effects: increased growth hormone, cortisol, corticotrophin and ß-endorphin levels.

Neurological levels: Alpha-2, delta and beta frequency bands are reduced over the temporo-parieto-occipital junction whilst theta is decreased in the temporomedial and frontomedial areas.

CONCLUSIONS

The Ayahuasca brew contains both ß-carboline and tryptamine alkaloids, which are necessary for the psychoactive effects of the drug. *P.viridis* and *D.cabrerana* are rich in DMT and *B.caapi* in ß-carboline alkaloids.
DMT has a rapid metabolism by MAO-A, so its interaction with ß-carboline alkaloids, which act as MAOi, allows its absorption preventing its rapid elimination.

Main references:
Callaway JC, McKenna DJ, Grob CS, et al. Pharmacokinetics of *Hoasca alkaloids in healthy humans. Journal of Ethnopharmacology 1999;65:243-256.*
1Riba J, Valle M, Urbano G, Yritia M, Morte A, Barnanoj MJ. Human pharmacology of Ayahuasca: Subjective and Cardiovascular Effects, Monoamine Metabolite Excretion, and Pharmacokinetics.
The Journal of Pharmacology and Experimental Therapeutics 2003;306:78-83.