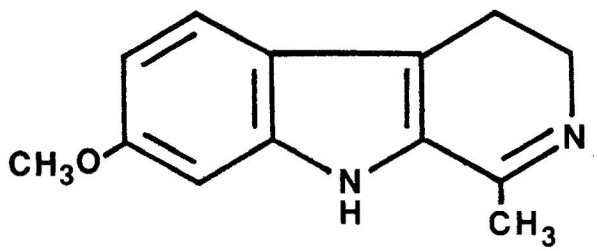
Profiles of Psychedelic Drugs



4. HARMALINE

Description and Properties: Harmaline, 4,9-dihydro-7-methoxy-1-methyl-3H-pyrido-[3,4-b]-indole, 7-methoxy-1-methyl-3,4-dihydro-β-carboline, harmaline, is a colorless solid with a large number of crystal habits with melting points recorded between 230° and 260° (with decomposition), and with a low solubility in water and ether. The hydrochloride salt is bright yellow (m.p. 212°) and is soluble in water and alcohol. Its solutions are highly fluorescent.

History: Harmaline was first isolated from plant sources in 1841, but its structure was not correctly established until 1919; it was first synthesized eight years later. This alkaloid is a component of a number of plants of well-established pharmacological activity. A number of species of the genus *Banisteriopsis* (in particular *caapi* and *inebrians*) are used in the preparation of the hallucinogenic drink known as *ayahuasca* or *yajé* employed by several tribes of South American Indians in puberty rituals and in the initiation of shamans. It is a principle alkaloid in the seed of the Syrian rue (*Peganum harmala*) which has been used as an intoxicant. Close biosynthetic relatives of harmaline (harmine and tetrahydroharmine) are known components of plants of several other genera which have medical use but no reputation as hallucinogens; e.g., *Passiflora* (*P. incarnata*, the passion flower) and species of *Leptactine*, *Zygophyllum* and *Cabi*.

Human Biochemistry and Pharmacology: The β-carboline alkaloids are of particular interest metabolically, as they are potent enzyme inhibitors and they can be easily synthesized from well-established neurochemicals under physiological conditions. Harmaline itself is an effective amine-oxidase inhibitor. It may thus play two roles in native drug decoctions, not only as an active agent *per se*, but also as a protective factor for drugs which might otherwise be inactivated. Field specimens of *ayahuasca* contain quantities of DMT as a result of the routine addition of leaves of plants of the genus *Psychotria* (which are, by themselves, orally inactive). In the search for possible endogenous factors associated with mental illness, it has been observed that serotonin metabolites such as melatonin (a normal pineal gland factor) and 0-methyl serotonin can be readily converted to 6-methoxytetrahydroharman, a positional isomer of reduced harmaline and itself an effective hallucinogen in man. Tryptamine and serotonin can undergo similar chemical conversions. There is as yet no evidence that these reactions occur in the intact human brain. The metabolic fate of harmaline is unknown although animal studies have shown the occurrence of extensive demethylation (to harmalol) and oxidation (to harmine).

Human Psychopharmacology: The effective dose range of harmaline in man is 70-100 mg i.v., or 300-400 mg orally. The initial effects are noted about one hour following oral administration and persist for about 6 hours (following i.v. administration the effects are noted within seconds, and are of much shorter duration). The indicators of physical toxicity are common and often severe. Paresthesias of hands, feet, or face are almost always present with the onset of effects, and are usually followed by the sensation of numbness. There can be isolated symptoms such as pressure in the head or chest, nausea and distressful vomiting, dizziness, and general malaise. Mydriasis and pressor effects are never seen. The anxiety and general discomfort encourages a withdrawal

from social contact, and a quiet dark environment is preferred by most subjects. The modality most consistently affected by harmaline is the visual sense. There can be vivid images generated, often in the form of meaningful dream-like sequences, and frequently containing subject matter such as wild animals or jungle scenes. Other reported visual syntheses are limited to the generation of geometric patterns which are entertaining but not felt to be of any intrinsic significance. In psychotherapeutic studies, harmaline has often been used in conjunction with other psychedelic drugs (e.g., MDA, LSD, and mescaline) in which the effects of the latter appear greatly prolonged, and qualitatively modified.

Legal Status: Harmaline is not included in the Federal Controlled Substances Act.

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