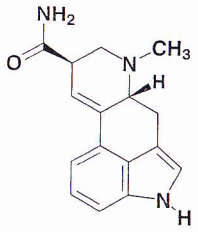
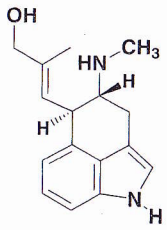
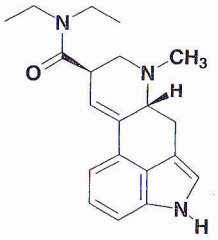
Lysergol



Lysergamide = ergine



Chanoclavine I



LSD

8. BIBLIOGRAPHY

Borowiak, K.S., Ciechanowski, K. and Waloszczyk, P. (1998). Psilocybin Mushroom (*Psilocybe semilanceata*) Intoxication with Myocardial Infarction, *J. Toxicol. - Clin. Toxicol.*, **36**, 47-49.

Desmarchelier, C., Gurni, A., Ciccia, G. and Giulietti, A.M. (1996). Ritual and Medicinal Plants of the Ese'ejas of the Amazonian Rainforest (Madre de Dios, Perú), *J. Ethnopharmacol.*, **52**, 45-51.

De Smet, P.A.G.M. (1995). Considerations in the Multidisciplinary Approach to the Study of Ritual Hallucinogenic Plants, *in* "Ethnobotany - Evolution of a Discipline", (Schultes, R.E. and von Reis, S., Eds.), p. 369-382, Chapman & Hall, London.

See also, in the same book:

1. Lindgren, J.E., Amazonian Psychoactive Indoles: A Review, p. 343-348 ;

2. McKenna, D.J., Luna, L.E. and Towers, G.N., Biodynamic Constituents in *Ayahuasca* Admixture Plants: An Uninvestigated Folk Pharmacopeia, p. 349-361,

Furbee, R.B., Curry, S.C., Kunkle, D.B. (1991). Ingestion of *Argyreia nervosa* (Hawaiian Baby Woodrose) Seeds, *Vet. Hum. Toxicol.*, **33**, 370.

Grob, C.S., McKenna, D.J., Callaway, J.C., Brito, G.S., Neves, E.S., Oberlaender, G., Saide, O.L., Labigalini, E., Tacla, C., Miranda, C.T., Strassman, R.J. and Boone, K.B. (1996). Human Psychopharmacology of Hoasca, a Plant Hallucinogen Used in Ritual Context in Brazil, *J. Nerv. Ment. Dis.*, **184**, 86-94.

Merlin, M.D. and Allen, J.W. (1993). Species Identification and Chemical Analysis of Psychoactive Fungi in the Hawaian Islands, *J. Ethnopharmacol.*, **40**, 21-40.

Strassman, R.J., Qualls, C.R., Uhlenhuth, E.H. and Kellner, R. (1994). Dose-Response Study of *N,N*-Dimethyltryptamine in Humans, *Arch. Gen. Psychiatry*, **51**, 98-108.

Wills, S. (1993). Drugs and Substance Misuse. (4) Plants, *Pharm. J.*, **251**, 227-229.

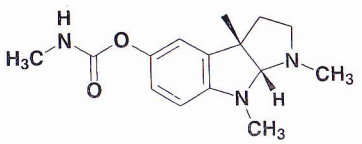
Calabar Bean Alkaloids

● **CALABAR BEAN,**
Physostigma venenosum Balf., Fabaceae

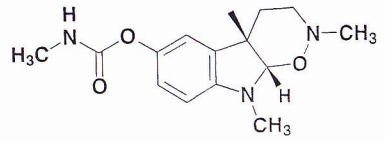
The seed of this vine was formerly official. It is a source of physostigmine, a cholinesterase inhibitor (also known as eserine). Recently, it was established that this alkaloid can also be obtained by fermentation: it is produced, with a yield that can reach 0.88 g/L, by a *Streptomyces* (*S. griseofuscus* NRRL 5324).

The Plant, the Drug. This climbing vine whose trifoliolate leaves are reminiscent of a creeping bean grows wild along the rivers of the Gulf of Guinea (Nigeria, Cameroon, Gabon). The seed is 2-3 cm long and 12-15 mm wide, and has a shiny brown tegument. It is odorless, tasteless, very hard, and marked on its convex side with a lighter groove which is 2-3 mm wide.

Chemical Composition. The seeds contain alkaloids (0.2-0.3%), chiefly represented by (–)-physostigmine (= eserine), occurring alongside norphysostigmine, eseramine, physovenine, geneserine, and unidentified substances. Physostigmine is unstable and is rapidly oxidized when exposed to air and light. In solution, its urethane group is rapidly hydrolyzed: it is converted to eseroline. In the presence of ammonia, a blue phenoxazone is formed.



Physostigmine (eserine)

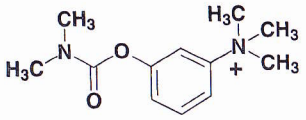


Geneserine

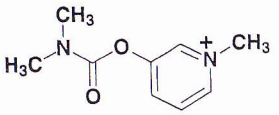
Properties and Uses. Traditionally, Calabar beans were used, in the regions where the plant grows wild, as an ordeal poison. They were pulverized and administered to individuals suspected of having committed some crime: only the innocents were to survive, and death was considered proof of guilt. In fact, if vomiting failed to begin rapidly, the subjects (innocent or guilty!) died by respiratory arrest.

Physostigmine is a reversible cholinesterase inhibitor: its affinity for the enzyme is 10,000 times greater than that of acetylcholine. It behaves as a parasympathomimetic, causing myosis, sialorrhea, rhinorrhea, bradycardia, hypotension, bronchospasms, nausea, vomiting, abdominal cramps, and central effects. It normalizes striated muscle contraction by facilitating nerve impulse transmission at the motor end-plate (hence the fasciculations and convulsive movements observed at toxic doses—and the use of synthetic derivatives to treat myasthenia).

Physostigmine can be used as an antidote for parasympatholytic poisoning (e.g., by Solanaceae such as stramonium or belladonna). Many authors emphasize that this treatment must be applied with good judgement, because of the risk of overdose and severe side effects.



Neostigmine



Pyridostigmine

Other Derivatives. In therapeutics, physostigmine has been replaced by synthetic anticholinesterases, neostigmine and pyridostigmine, which retain as part of their structure, the methylurethane group characteristic of the naturally-occurring alkaloids. The therapeutic indications of these compounds are myasthenia, post-operative intestinal or bladder atony, stubborn constipation, and post-operative recovery after curarization with a competitive neuromuscular blocking agent. Asthma, parkinsonism, and obstruction of the digestive or urinary tract are contraindications.

The salicylate of eserine oxide (eseridine, INN) is used in granules or drops to treat the symptoms of dyspepsia (to enhance vagal tone and therefore motility and secretions).

Potential Uses of Physostigmine. Like other cholinesterase inhibitors, physostigmine has been tested to treat the impairment of cognitive skills characteristic of Alzheimer's senile dementia. The results were rather contradictory. The most recent clinical trials show a small but significant improvement of performance in some subjects. The short half-life and low bioavailability of physostigmine have led to the preparation of synthetic analogs that have undergone—and continue to undergo—preclinical and clinical studies. For example, derivatives as eptastigmine * (p. 978) (with a carbamoyl-heptyl group instead of a carbamoyl-methyl group) have a longer half-life and larger therapeutic margin.