Biochemical Pharmacology, Vol. 17, pp. 2487–2488. Pergamon Press. 1968. Printed in Great Britain

SHORT COMMUNICATIONS

Identification of two new β-carboline alkaloids in South American hallucinogenic plants

(*Received* 20 *July; accepted* 24 *July* 1968)

THE CHEMICAL constituents of snuffs inhaled by some South American indians to produce hallucinations have been investigated by several authors.[1, 2] 5-Methoxy-*N,N*-dimethyltryptamine, *N,N*-dimethyltryptamine and harman alkaloids have been found to be the main active constituents of these snuffs. The botanical origins of some of the snuffs still remain obscure, although several are known to be derived from *Anadenanthera* (*Piptadenia*) *peregrina*.[1, 2]

Recently it was shown[1] that *Virola calophylla*, a source of the snuff called "yakée", contained 5-methoxy-*N,N*-dimethyltryptamine and *N,N*-dimethyltryptamine. We have now investigated *Virola theiodora* Warb., used for the preparation of the snuffs called "epéna" and "nyakwána"[3] and *V. rufula* (A.DC.) Warb. and found them to have an unusually high content of 5-methoxy-*N,N*-dimethyltryptamine. *V. venosa* (Benth.) Warb. and *V. multinervia* Ducke contain only minute amounts of 5-methoxy-*N,N*-dimethyltryptamine.[4]

MATERIAL AND METHODS

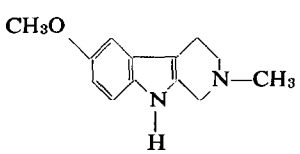
Voucher collections for the chemical analyses are deposited in the Economic Herbarium of Oakes Ames in the Botanical Museum of Harvard University. *Anadenanthera peregrina* (L.) Speg., Schultes 24625—Boa Vista, Brazil. *Virola multinervia*, Schultes 24614—Manáos, Brazil. *Virola rufula*, Schultes 24612—Manáos, Brazil. *Virola theiodora*, Schultes 24626—Rio Tototobí, Brazil. *Virola venosa*, Schultes 24613—Manáos, Brazil.

Gas chromatographic and mass spectrometric methods are described earlier.[2]

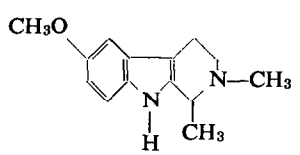
Compound I[5] and compound II[6] were prepared from 5-methoxy-*N*-methyltryptamine by condensation[7] with formaldehyde and acetaldehyde respectively.

In *V. theiodora* and in the snuff prepared from the resin of this plant and in *V. rufula* a new alkaloid was found. A m.wt. of 216 (M^+) was determined for this compound by mass spectrometry. The mass spectrum of this alkaloid was similar to that of 2-methyltetrahydro-β-carboline.[8] From the mass spectrometric, UV and fluorescence data it was assumed to possess the formula I. This structure, 2-methyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline, was proven correct by comparison with a synthetic reference compound.

The same β-carboline was also encountered as a minor constituent in *Anadenanthera peregrina* (L.) Speg., together with another compound having a m.wt. of 230 (M^+). The mass spectrum of the latter compound is similar but not identical to that of tetrahydroharmine.[2] By comparison (GLC, MS, UV and fluorescence data) with a synthetic reference compound, formula II, 1,2-dimethyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline,[6] was established for this alkaloid.



I



II

The occurrence of the β-carbolines together with hallucinogenic tryptamines is interesting, since β-carbolines are known monoamine oxidase inhibitors[9] and may thus potentiate the hallucinogenic effects of the tryptamines. However, the tetrahydro-β-carbolines are less active inhibitors than the corresponding fully aromatic β-carbolines.[9, 10]

Acknowledgement—This investigation was supported by grant MH 12007 (B.H.) from the National Institute of Mental Health and by grant LM-GM 00071-01 (R.E.S.) from the National Institutes of Health. The collection of the plant material was made possible through the participation of two of us (B.H. and R.E.S.) in the R/V Alpha Helix expedition Phase C, 1967. We wish to express our gratitude to the National Science Foundation, the Scripps Institute of Oceanography, La Jolla, Cal., and to the Chief Scientist of our part of the expedition Prof. Carroll M. Williams of Harvard University.

Department of Toxicology,
Swedish Medical Research Council,
Karolinska Institutet,
104 01 *Stockholm* 60

S. AGURELL
B. HOLMSTEDT
J.-E. LINDGREN

Botanical Museum,
Harvard University,
Cambridge 38, *Mass.*

R. E. SCHULTES

REFERENCES

1. B. HOLMSTEDT, *Archs int. Pharmacodyn. Thér.* **156**, 285 (1965).
2. B. HOLMSTEDT and J. E. LINDGREN, *Ethnopharmacologic Search for Psychoactive Drugs*, p. 339. Workshop Series of Pharmacology, N.I.M.H. No. 2, Public Health Service Publication No. 1645. Government Printing Office, Washington, D.C. (1967).
3. R. E. SCHULTES and B. HOLMSTEDT, *Rhodora* **70**, 113 (1968).
4. S. AGURELL, B. HOLMSTEDT and J. E. LINDGREN, *Acta Chem. Scand.* Submitted for publication.
5. S. GHOSAL and B. MUKHERJEE, *J. org. Chem.* **31**, 2284 (1966).
6. R. G. TABORSKY and W. M. MCISAAC, *J. mednl Chem.* **7**, 135 (1964).
7. S. AKABOW and K. SAITO, *Chem. Ber.* **63**, 2245 (1930).
8. S. AGURELL, B. HOLMSTEDT and J. E. LINDGREN, *Am. J. Pharm.* in press.
9. S. UDENFRIEND, B. WITKOP, B. C. REDFIELD and H. WEISSBACH, *Biochem. Pharmac.* **1**, 160 (1958).
10. W. M. MCISAAC and V. ESTEVEZ, *Biochem. Pharmac.* **15**, 1625 (1966).

Biochemical Pharmacology, Vol. 17, pp. 2488–2489. Pergamon Press. 1968. Printed in Great Britain

Central actions of ibotenic acid and muscimol

(*Received* 10 *July* 1968; *accepted* 24 *July* 1968)

THE BIOLOGICAL activity of ibotenic acid and muscimol,[1] two isoxazoles found in mushrooms of the genus *Amanita*, and the structural similarities with glutamic acid and γ-aminobutyric acid (GABA), prompted an investigation of their possible action on central neurones. Experiments were carried out on spinal interneurones and Renshaw cells in cats (decerebrate or sodium pentobarbitone anaesthetized) using multibarrelled micropipettes for drug administration and recording.[2]

Ibotenic acid, administered electrophoretically as an anion from 0·2M pH 7 solutions (NaOH), was a more powerful excitant of spinal interneurones and Renshaw cells than L-glutamic acid (2M, pH 7). The excitant action, which was comparable to that of DL-homocysteic acid (0·2M, pH 7), was of slower onset and more prolonged duration than that of L-glutamic acid. If the taste enhancing properties of monosodium glutamate stem from a depolarization of taste receptors, a similar effect by ibotenic acid presumably accounts for the observation that the taste of this substance is apparently more intense than that of the glutamic acid salt.[1]

Muscimol, administered as a cation from 0·5M, pH 3 solutions (HCl), was a strong depressant of the spontaneous or chemically evoked firing of spinal interneurones and Renshaw cells. The activity of muscimol as a depressant was similar to that of GABA (0·5M, pH 3) and glycine (0·5M, pH 3)