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Note

Pharmacology of the Alkaloids of *Excavatia coccinea* (Tejsmann and Binnendijk) Mgf.

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The taxonomic status of the genera of the sub-tribe Ochrosiinae of the Apocynaceae is not clear. According to Pichon the genus *Ochrosia* Juss., includes the *Lactaria, Pseudochrosia, Bleckeria* and *Excavatia* of other authors.[1] One member of the group was described as *Lactaria coccinea* by Tejsmann and Binnendijk (1867), *Ochrosia coccinea* by Miquel (1868–9) and finally as *Excavatia coccinea* (T. and B.) Mgf. comb. nov. by Markgraf (1928). In the absence of other information this name for this species appears to be valid.* Crude alkaloids of some of the species classified as *Ochrosia* are reported to be cardiotoxic.[1]

Recently we conducted preliminary pharmacological assays on two fractions representing the total crude alkaloids of the bark and on another sample of the total crude leaf alkaloids of this plant. The presence of reserpine-like activity in these alkaloids, later corroborated by chemical evidence, represents, to our knowledge, the first report of the presence of reserpine in this section of the family.

The weakly basic resinous bark alkaloids were administered to mice in oral doses ranging from 1·0 to 500 mg/kg. The most striking change observed was a CNS depressant action associated with marked or complete ptosis of 1–5 days' duration depending on the dose. In cats anaesthetized with pentobarbital sodium a cumulative dose of 7·5 mg/kg of the crude material i.v. produced a 52 per cent fall in blood pressure with a duration of > 30 minutes.

* We are indebted to Mr. J. Womersley, Chief Botanist, Forestry Department, Lae, Territory of New Guinea, for information about this plant; herbarium specimen N.G.F. 9537, collected at Bulolo, July 1957.

Treatment with standard indicators of autonomic action (epinephrine, furtrethonium, 1,1-dimethyl-4-phenylpiperazinium iodide (DMPP), and peripheral vagal stimulation) before and after drug treatment indicated that hypotension was produced without evidence of peripheral autonomic action. Only after relatively large doses of 11·0 mg/kg i.v. in chloralosed vagotomized cats was the pressor response to bilateral carotid occlusion inhibited. Cumulative acute doses of between 1–5 mg/kg intravenously completely inhibited the central pressor response of central vagal stimulation for over two hours in suitably prepared dogs anaesthetized with pentobarbital sodium. Oral administration of 5 to 25 mg/kg to cats produced marked and prolonged miosis and moderate to marked ptosis. At 10 and 25 mg/kg, some relaxation of the nictitating membrane was evident in the animals. These results are similar to those obtained, in comparable experiments, with reserpine.

Accordingly a sample of the resin was assayed for reserpine and a small amount of crystalline material was obtained* for which the ultraviolet spectrum and paper chromatographic behaviour were identical to those given by an authentic specimen of reserpine.[2] This was later confirmed by its isolation in 0·04 per cent yield from the stem bark of the plant.[3] The mother liquors gave evidence of the presence of eight other alkaloids when examined by paper chromatographic techniques but pharmacological evaluation demonstrated only weak biological activity.

The second fraction of yellow, crystalline bark bases produced moderate CNS depression at high doses (350–2000 mg/kg) but gave only weak evidence of reserpine-like activity. This activity was concentrated in the resinous mother liquors after three crystallizations of the bases from methanol–chloroform. The crystalline portion then showed no evidence of ptosis when administered to mice in doses as high as 1000–2000 mg/kg orally although the animals were quite depressed after doses as low as 500 mg/kg. Slight to moderate hypotension of short duration was produced in pentobarbitalized cats at doses between 1–10 mg/kg but cardiac irregularities appeared at the higher dose level.

The total leaf bases demonstrated pharmacological properties

* These experiments were done by Dr. I. J. Pachter of these Laboratories whose assistance is gratefully acknowledged.

similar to those of the crystalline bases of the bark. Only weak evidence (decreased motor activity, ptosis, hypersensitivity to touch) of the presence of reserpine-like substances was obtained. The detailed chemistry of the plant will be published elsewhere.[3]

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References

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