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BIOLOGICALLY ACTIVE ALKALOIDS FROM MADAGASCAN FROGS (MANTELLA).

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Skins of amphibians contain a wide range of biologically active substances, that in some instances have been utilized in folk medecine, as poisons, and as modern research tools. Poison frogs of the family Dendrobatidea are the source of a wide range of alkaloids including quinolizidines, indolizidines, a pumiliotoxin(PTX)-A class of 6-alkylidene-8-hydroxy-8-methyl-1-azabicyclo 14.3.0.Inonanes and a PTX-A subclass having a 7-hydroxy group(1). Madagascan ranid frogs of the genus Mantella have been found to contain such "dendrobatid" alkaloids (2) and in addition new alkaloids. Analysis has been by gas Chromatography-Mass spectrometry and Infrared spectroscopy. Four populations of M. madagascariensis all had major amounts of a quinolizidine. Three of the populations had substantial amounts of a 13,14-dihydroalloPTX-B (M.W. 325). All populations had either a 13,14-dihydroPTX-A (M.W. 309) or PTX-A (M.W. 307). Two of populations had a new alkaloid. M. aurantiaca (?) did not contain the 217,231 or 235 quinolizidines but instead an alkaloid ($C_{12}H_{23}NO$, M.W. 235) of unknown structure. This specie contained a number of known PTX alkaloids, namely 267C, PTX-A, PTX-B and alloPTX 323B, an unknown ketonic PTX (M.W. 305) and an unknown indolizidine (M.W. 295). Many of these alkaloids have activity at nerve and muscle.

(1). J. W. DALY and T. F. SPANDE, Offprints from Alkaloids : chemical and biological perspectives, vol. 4, edited by S. W. Pelletier, John Wiley & Sons, Inc., Chapter one 1-274(1986).

(2). J. W. DALY, R. J. HIGHET and C. W. MYERS, Toxicon 22, 905 (1984).

T.2/4

FROM ETHNOBOTANICAL USES OF STRYCHNOS HENNINGSII TO ANTIINFLAMMATORIES, ANALGESICS AND ANTISPASMODICS

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As regards the pharmacology of Strychnos, emphasis in the past was on the investigation of the tetanizing or curarizing species. However, it is evident from the ethnobotany that the rôle of other species as medicinal and useful plants is not a minor one. The present work relates to some uses of *S. henningsii* GILG in African Pharmacopoeia

- in case of rheumatism;
- against stomach and abdominal complaints;
- and for snake-bite treatment (1).

The pharmacology of several alkaloids of *S. henningsii* from Zaïre was considered (2). Moreover, isoretuline - easily derived from strychnine - was also tested (3).

a) Antiinflammatory action - (Iso)-retuline reduces experimental edemas in rats (ED 50 = 40 mg/kg i.p.);
b) Analgesic action - Isoretuline possesses an activity with respect to the nociceptive action of phenyl-paraben/oquinone in mice (ED 50 = 20 mg/kg per os);
c) Antispasmodic effect - Isoretuline reduces the stimulation of the ileum of rats by histamine and bradykinin (IC = 10^{-6} to 10^{-4} M);
d) Intravenous acute toxicity in mice - (Iso)-retuline, having an LD 50 of 70 mg/kg, is much less toxic than strychnine, whose LD 50 is 0.5 mg/kg i.v.
e) Oral toxicity - In intragastric administration in mice, LD 50 of (iso) retuline is about 300 mg/kg. The animals receiving lower doses show no lesions, especially at the gastro-intestinal level.

Our results demonstrate that some of the reported folk-medicinal applications of *S. henningsii* can be at least partially explained by the presence of retuline-like alkaloids, whose use could lead to new anti-nociceptive and antispasmodic drugs.

1. N.G. Bisset, Lloydia, 33, 201-243 (1970)
2. L. Angenot and M. Tits, Planta Med., 41, 240-243 (1981)
3. Université de Liège, PCT WO 89/05301.