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SYNTHESIS AND ANTIMITOTIC EFFECTS OF ISORETULINAL, A MAIN ALKALOID ISOLATED FROM STRYCHNOS VARIABILIS

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In Central Africa, the root bark of *S. variabilis* is said to be a violent poison (1). Bearing in mind that the study of the toxic plants increases the probability of discovering new drugs, we have isolated 23 alkadoids from this material (2), and we have tested them on the culture media of different strains of cancer cells. At doses of 1 and 10 µg of alkaloid per ml of culture, no effect was detected for the alkaloids, with the exception of isoretulinal which showed a weak but useful antimitotic effect. Isoretulinal is the main component of diastereomeric equilibrating alkaloids (3). We have developed a semi-synthetic method for the preparation of this compound. The last stage of this method is the quantitative oxidation of the alcohol group of isoretuline with pyridinium chlorochromate (4).

Biological properties of isoretulinal:

a) Cytotoxicity: against melanoma B16, isoretulinal reduces the mitoses by a factor of eight at a concentration of 10 µg/ml, and by a factor of twenty at a concentration of 50 µg/ml. At the latter concentration, a necrosis of the cells is however evident.

b) Analgesic action: isoretulinal possesses an analgesic activity with respect to the nociceptive action of phenyl-parabenzoquinone in mice (ED 50 = 20 mg/kg per os)

c) Intravenous acute toxicity in mice: isoretulinal, having an LD 50 of 30 mg/kg, is sixty-fold less toxic than strychnine.

Our investigations corroborate the idea that if future work on the alkaloids of Strychnos is to have any meaning, it will be essential to associate it with a pharmacological screen (5).

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