THE STRUCTURE OF ISOSTRYCHNOPENTAMINE A, A NEW BISINDOLE MONOTERPENE ALKALOID WITH ANTIMITOTIC PROPETIES

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The leaf of the African plant, *Strychnos usambarensis*, contains numerous bisindole monoterpene alkaloids and also the peculiar alkaloid strychnopentamine (1), which presents considerable pharmacological interest because of its potent antimitotic properties (3,4).

The structure of strychnopentamine ($C_{35}H_{43}N_5O$) was firmly established by crystallographic methods in 1977 (2). Its distinctive feature is the unprecedented joining of a pyrrolidine ring to C_{12} of the tetracyclic indolo [2, 3a] quinolizine moiety, resulting in a molecule with five nitrogen atoms, hence the name strychnopentamine.

Two more compounds from *S. usambarensis*, probably related to strychnopentamine, were briefly mentioned in 1978 (1). We now report that one of these compounds, which was named isostrychnopentamine A, is the $C_{2''}$ epimer of strychnopentamine. The IR, UV, MS, ^{13}C-NMR and CD spectra of the two alkaloids are practically superposable.

However, the 350 MHz ^{1}H-NMR spectra do show for some hydrogens of the pyrrolidine ring minor differences in chemical shift, which provide a basis for structural discrimination, relying for that purpose on an extensive series of 1-D and 2-D COSY 45 experiments. We conclude that the configuration of isostrychnopentamine A is 3*S*, 4*R*, 15*S*, 17*S*, 20*R*, 2"*S*; ($C_{2''}$ being the first atom of the N-methyl-pyrrolidinyl ring).

Isostrychnopentamine A has been tested for its antimitotic activity on cultured melanoma B_{16} cells and compared with strychnopentamine and other bisindolic alkaloids that possess an usambaran skeleton (3). The presence of a N-methyl-pyrrolidine group increases the antimitotic activity of this type of alkaloids. Indeed, strychnopentamine and isostrychnopentamine A exhibit the same activity (ED_{50} on melanoma cells = 5×10^{-1} µg/ml) as that of some antitumor drugs like anthracycline-cytostatics and ellipticine.

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