Strychnogucine A and B, Two New Antiplasmodial Bisindole Alkaloids from *Strychnos icaja*

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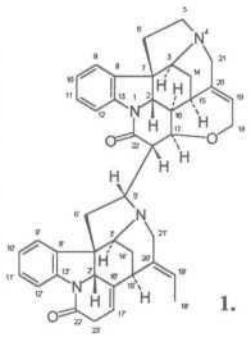
Strychnos icaja Baillon (Loganiaceae), a 20 – 100 m long liana distributed in all central Africa, is the only african *Strychnos* source of strychnine. Roots were principally used for the preparation of arrow and ordeal poisons [1]. Their toxicity is mainly due to the monoindole alkaloids strychnine and hydroxystrychnine isolated from the roots by Sandberg *et al.* [2]. Recently, in a continuation of our search for new potential antiplasmodial compounds from African *Strychnos*, we isolated from *S. icaja* three new sungucine derivatives, named isosungucine, 18-hydroxysungucine and 18-hydroxyisosungucine [3]. These compounds, particularly 18-hydroxyisosungucine, were moderately active against *Plasmodium falciparum*.

Further investigations of *S. icaja* roots resulted in the isolation of two tertiary quasi-symmetrical bisindole alkaloids, named strychnogucine A (**1**) and strychnogucine B (**2**). The structures were established by means of 1D and 2D NMR experiments (^{1}H, ^{13}C, COSY, DEPT, HMQC, HMBC) as well as by UV, IR and (HR)ESI mass spectrometry. Compound **2** was highly and compound **1** moderately active against four strains of *Plasmodium falciparum in vitro*. Compound **2** has the particularity to be more active against the chloroquine resistant strains (CI_{50}: 85±10 nM on W2 strain) than against the chloroquine sensitive one. Strychnogucine B (**2**) shows also a selective antiplasmodial activity with 25 – 180 times greater toxicity towards *Plasmodium falciparum*, relative to cultured human cancer cells (KB) or fibroblasts (WI38).



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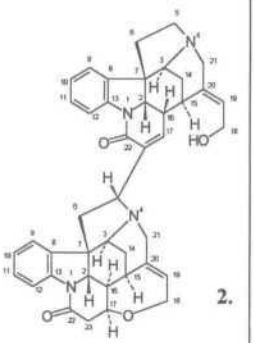

2.

References:

1. Neuwinger, H.D. African Ethnobotany. (1996) Poisons and drugs. Chemistry. Pharmacology. Toxicology. *Chapman et Hall, London*, 569-578.
2. Sandberg, F., Roos, K., Ryrberg, K.J., Kristianson, K. (1968) Tetrahedron Lett. 29: 6217-6218.
3. Frédérich, M., De Pauw, M.C., Llabrès, G., Tits, M., Hayette, M.P., Brandt, V., Penelle, J., De Mol, P., Angenot, L. (2000) Planta Med. 66 : 262-269.