ISOLATION, STRUCTURE DETERMINATION AND ANTIMALARIAL ACTIVITY OF 10'HYDROXYUSAMBARENSINE: A NEW BISINDOLE ALKALOID FROM THE ROOTS OF *STRYCHNOS USAMBARENSIS*.

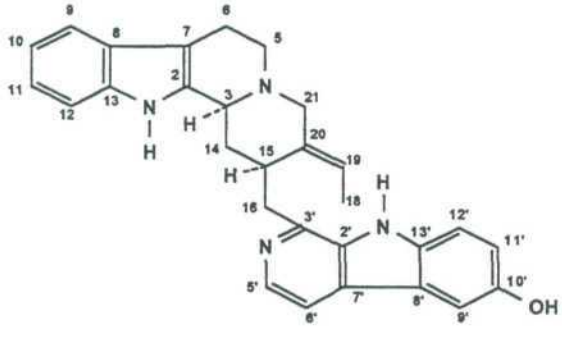
M. Frédérich[1,2], M. Tits[1], M.P. Hayette[2], V. Brandt[1], J. Penelle[1], P. DeMol[2], G. Llabrès[3], and L. Angenot[1].

1 Laboratory of Pharmacognosy, Institute of Pharmacy, University of Liège, CHU, Tour 4, Avenue de l'Hôpital 1, B-4000 Liège, Belgium, 2 Laboratory of Medical Microbiology, University of Liège, CHU, Tour 3, Avenue de l'Hôpital 1, B 4000 Liège, Belgium, and 3 Laboratory of NMR, Institute of Physics, Sart Tilman, B 4000 Liège, Belgium.

Strychnos usambarensis Gilg (Loganiaceae) is a tree used traditionally by people of the Banyambo tribe who live along the Akagera river on the border between Rwanda and Tanzania as the main ingredient of a curarizing arrow poison[1]. A number of tertiary alkaloids found in the root bark showed antiplasmodial, antigiardial, antiamoebic and antimitotic activities[2,3]. In a continuation of our search for potential antiplasmodial compounds from the roots of *Strychnos usambarensis* and other *Strychnos* species[2], we have isolated a new antimalarial usambarensine derivative, 10'-hydroxyusambarensine (**1**).

10'-Hydroxyusambarensine has been extracted by EtOAC in a Soxhlet apparatus and purified by liquid column chromatography with $CHCl_2$ / MeOH and by preparative TLC. The structure and stereochemistry of the substance were determined by detailed spectroscopic methods (UV, CD, IR, ESI and HRFAB MS, ^1H and ^{13}C 1D and 2D NMR).

10'OH Usambarensine and Usambarensine were tested *in vitro* on two strains of *P. falciparum* (see table). 10'-Hydroxyusambarensine was slightly more active than usambarensine against the two strains (IC_{50} < 0.5 µg/mL). The two compounds were more active against the resistant clone than the susceptible one and the activity of **1** against the resistant clone was comparable to these of quinine and chloroquine.



10'-hydroxyusambarensine

References:

(1) Angenot, L. *Ann. Pharm. Franç.* **1971**, *29*, 353.
(2) Wright, C.W.; Allen, D.; Cai, Y.; Zhenping, Ch.; Phillipson, D.; Kirby, G.C.; Warhurst, D.; Tits, M. and Angenot, L. *Phytother. Res.* **1994**, *8*, 149-152.
(3) Bonjean, K.; De Pauw, MC; Quetin-Leclerq, J.; Angenot, L. and Bassleer, R. *Anticancer Res.* **1996**, *16*, 1129-1138.

Table: IC_{50} Values of 10'OH-usambarensine and usambarensine on two *Plasmodium falciparum* clones.

	FCA 20 GHANA (chloroquine sensitive strain)	W2 INDOCHINA (chloroquine resistant strain)
10'-Hydroxy-usambarensine	0.480 ± 0.014 µg/mL	0.160 ± 0.016 µg/mL
Usambarensine	0.655 ± 0.013 µg/mL	0.265 ± 0.023 µg/mL

This research was supported by the Belgian National Fund for Scientific Research (FNRS) [grant N° 3451997 and fellowship of one of us, MF].