POTENTIALITES ANTIPALUDIQUES DES ALCALOIDES INDOLIQUES

POTENTIAL ANTIMALARIAL ACTIVITY OF INDOLE ALKALOIDS

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Malaria is the major parasitic infection in many tropical and subtropical regions, leading to more than one million deaths out of 400-500 million cases year (WHO world malaria report 2005).

Discovering new drugs in this field is therefore a health priority. The challenge in malaria chemotherapy is to find safe and selective agents whose potencies will not be compromised by plasmodial resistance.

In this context, the search for antiprotozoal compounds from terrestrial plants and marine organisms could provide new leads to antimalarial drugs. The natural active principles are detected either after bioguided isolation from species with a reputation for use in traditional medicine or after screening campaign involving in vitro or in vivo bioassay procedures.

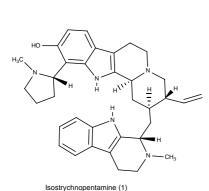
This lecture will be mainly illustrated with references to selected antiplasmodial compounds :

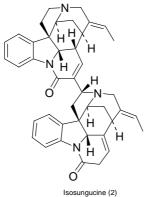
- indole alkaloid analogues of emetine (usambarensine and isostrychnopentamine (1) from *Strychnos usambarensis*, tubulosine from *Pogonopus tubulosus* ...)
- other bisindole alkaloids (isosungucine (2)-, matopensine- and longicaudatine types isolated from African *Strychnos* species, villalstonine from Asiatic *Alstonia* species, voacamine from *Tabernaemontana* (*Peschiera*) *fuchsiaefolia* stem and root bark, ...)
- indoloquinolines (cryptolepine and analogues from *Cryptolepis sanguinolenta*)
- indolo [2,1-b] quinazoline-6,12-diones and derivatives (tryptanthrins) from *Strobilanthes cusia* and other sources
- 1-aminopolycyclic beta-carbolines (manzamines) isolated from Indo-Pacific sponges.

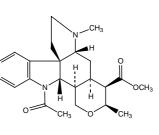
The structural diversity of these compounds with good (micromolar and lower) activity may be a reflection of the varied targets present in the plasmodia.

Finally, the lecture will be shortly focused on the design of chemosensitizers that are capable of reversing in vitro chloroquine resistance in Plasmodium.

Moreover, malagashanine (3) (N_b - C_{21} -secocuran alkaloid isolated from *Strychnos myrtoides*) marked also in vivo chloroquine potentiating action. It might be profitable to carry on further work on other mono-indole alkaloids (e.g. isoretuline from *Strychnos variabilis*) which showed a higher in vitro chemosensitizing action that malagashanine.







Malagashanine (3)