

POSTER PRESENTATION

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Substituted flavones: a promising scaffold in the fight against malaria

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From Challenges in malaria research: Core science and innovation
Oxford, UK. 22-24 September 2014

Background

Ever since 2008, when evidence of artemisinin resistant malaria was highlighted in Western Cambodia [1], the need for new drugs with an original structure and novel mechanisms of action is even more pressing. The study of traditional remedies such as Cinchona bark or Artemisia aerial parts led to the discovery of the most potent antimalarials, bearing out that nature is still an incredible source of inspiration. Based on this approach, we are developing new synthetic antimalarial agents with an original structure inspired by nature.

Material and methods

In vitro antiplasmodial activity is evaluated against two strains of *P. falciparum* (multiresistant K1 and chloroquino-resistant 7G8) with two different methods: the inhibition of ³[H]-hypoxanthine incorporation assay and the Plasmodium-LDH immunoassay detection kit. Cytotoxicity assays are performed on two murine cell types (L6 and Hepa) in order to estimate the selectivity index, with two different viability tests: the resazurine assay and an MTT-based approach. *In vivo* activity is performed according to Peters' experiment [2] on *P. berghei* ANKA murine model at a dosing regimen of 100 mg/kg intraperitoneally.

Results

The isolation of an *in vitro* active biflavonoid from *Campno-sperma panamense* (Anacardiaceae, IC₅₀ = 480 nM, *P. falciparum* K1), led us to the development of simplified synthetic analogs (MR series) with improved pharmacological and pharmacokinetic profiles. Notably one of them (MR70) exhibits a partial *in vivo* antimalarial activity with a reduction of parasitaemia by 45% on day 4.

Conclusion

We described here the first substituted flavone showing an *in vivo* antimalarial activity in a murine model. This scaffold should be promising in the fight against malaria. To understand its mechanism of action, we are currently running differential metabolomics analysis by solid NMR (coll. Pr. J. I. Namer, Strasbourg, France) to highlight some potential impact on Plasmodium metabolic pathways.

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Published: 22 September 2014

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doi:10.1186/1475-2875-13-S1-P64

Cite this article as: Nardella et al.: Substituted flavones: a promising scaffold in the fight against malaria. *Malaria Journal* 2014 **13**(Suppl 1):P64.

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