

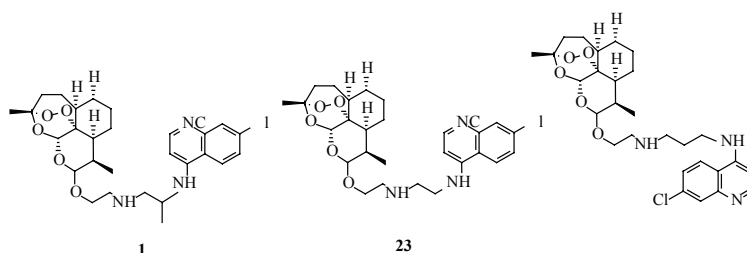
Potent in vivo antimalarial activity of artemisinin-quinoline hybrids

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Plasmodium falciparum displays tolerance against the recommended artemisinin combination therapies (ACT), which emphasizes the urgent need for safer and newer classes of antimalarial drugs. Artemisinin-aminoquinoline hybrids 1-3 were evaluated to ascertain whether the potent low nanomolar *in vitro* antiplasmodial activity displayed against the chloroquine resistant strain Dd2, would be carried over in vivo against *Plasmodium vinckei*.

Plasmodium vinckei infected mice were treated with hybrids 1-3 for four days at a dosage of 0.8 mg/kg, 2.5 mg/kg, 7.5 mg/kg or 15 mg/kg intraperitoneally (ip), and 2.7 mg/kg, 8.3 mg/kg, 25 mg/kg or 50 mg/kg orally (per os) using artesunate as reference drug. Hybrids 1, 2 and 3 displayed potent in vivo antimalarial activity with ED₅₀ values of 1.1, 1.4 and <0.8 mg/kg by the ip route, and 12, 16 and 13 mg/kg per os, respectively. Long-term monitoring of parasitaemia showed a complete cure of mice (without recrudescence) at 15 mg/kg *via* ip route and at 50 mg/kg by oral route for hybrid 1 and 2, respectively, whereas artesunate was only able to provide a complete cure at 30 mg/kg by ip and 80 mg/kg per os. These hybrids were able to cure malaria in mice at very low dosages, thus, stand as good drug candidates to be further investigated. It will be interesting to conduct a comprehensive pharmacokinetic study including metabolite identification in order to ascertain which pharmacophore governs their antimalarial activity.



Biography

David D. N'Da has completed his Ph.D. at the age of 34 years from the University of the Witwatersrand, Johannesburg, and postdoctoral studies from the North-West University, Potchefstroom, South Africa. He is currently Research Associate Professor in Medicinal Chemistry at the Center of Excellence for Pharmaceutical Sciences (PharmacEn). He has published more than 30 papers in reputed journals and has been serving as an ad hoc articles reviewer for several international peer-reviewed journals. His research activity focuses on the discovery of new antimalarial drugs.

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