

**Publication****Antimalarial versus cytotoxic properties of dual drugs derived from 4-aminoquinolines and Mannich bases: interaction with DNA****JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)****ID** 524402**Author(s)** Wenzel, N. I.; Chavain, N.; Wang, Y.; Friebolin, W.; Maes, L.; Pradines, B.; Lanzer, M.; Yardley, V.; Brun, R.; Herold-Mende C.; Biot, C.; Toth, K.; Davioud-Charvet E.,**Author(s) at UniBasel** [Brun, Reto](#) ;**Year** 2010**Title** Antimalarial versus cytotoxic properties of dual drugs derived from 4-aminoquinolines and Mannich bases: interaction with DNA**Journal** Journal of Medicinal Chemistry**Volume** 53**Number** 8**Pages / Article-Number** 3214-3226**Mesh terms** Aminoquinolines, pharmacology; Antimalarials, pharmacology; Antineoplastic Agents, pharmacology; Cell Line, Tumor; DNA, metabolism; Drug Resistance; Drug Screening Assays, Antitumor; Hemeproteins, chemistry; Humans; Mannich Bases, pharmacology; Plasmodium falciparum, drug effects; Structure-Activity Relationship

The synthesis and biological evaluation of new organic and organometallic dual drugs designed as potential antimalarial agents are reported. A series of 4-aminoquinoline-based Mannich bases with variations in the aliphatic amino side chain were prepared via a three-steps synthesis. These compounds were also tested against chloroquine-susceptible and chloroquine-resistant strains of Plasmodium falciparum and assayed for their ability to inhibit the formation of beta-hematin in vitro using a colorimetric beta-hematin inhibition assay. Several compounds showed a marked antimalarial activity, with IC(50) and IC(90) values in the low nM range but also a high cytotoxicity against mammalian cells, in particular a highly drug-resistant glioblastoma cell line. The newly designed compounds revealed high DNA binding properties, especially for the GC-rich domains. Altogether, these dual drugs seem to be more appropriate to be developed as antiproliferative agents against mammalian cancer cells than Plasmodium parasites

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