MAL2

New chloroquine-ferrocene hybrids upgraded with azathia heterocycle as promising antiplasmodial agents

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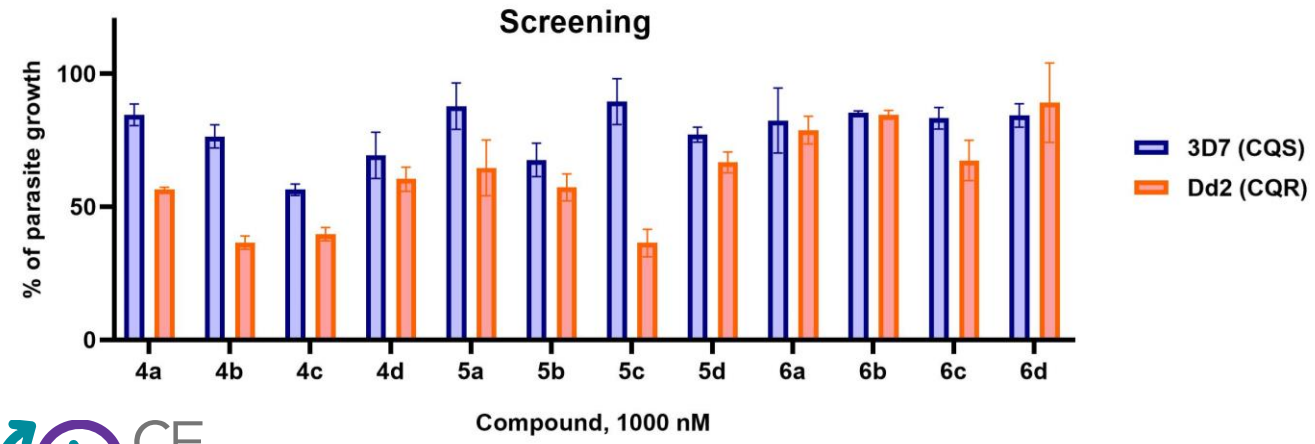
Due to **climate change** and **mass human migration**, autochthonous cases of malaria are increasingly appearing in countries or regions in which the disease was considered eradicated. *Plasmodium* **parasites** are developing **resistance to nearly all conventional antimalarials**, *Anopheles* **vectors** are becoming **resistant to insecticides**, and **no vaccine** exists to date. There is an urgent need for **new antimalarial compounds**.

In vitro evaluation of the antimalarial activity of the compounds was performed using the colorimetric **LDH assay** in cultures of both **3D7**, CQ-sensitive (**CQ^S**) and **Dd2**, CQ-resistant (**CQ^R**) strains of *P. falciparum*. Screening was done at a concentration of **1000 nM** (three replicates per compound for each strain) and those that showed a minimum of 50% parasite growth inhibition were further **titrated to determine their IC_{50} value**. CQ was used as a positive control.*



Compound	3D7 (CQ^R), IC50 nM			
	1	2	3	Mean
4a	171,4	186,1	178,6	178,7
4b	349,6	579,4	571,8	500,3
4c	260,2	301,8	222,5	261,5
5c	446,4	229,6	296,8	324,3
CQ	287	201,7	137,3	208,7

Better *in vitro* activity against the CQ^R strain of two compounds is highly relevant, since the primary goal of new treatment options is **to overcome parasite resistance**. The next step in this study would be to evaluate their anti-inflammatory effects in several *in vitro* macrophage-based models.

*Compounds were tested for **cytotoxicity** on rat peritoneal macrophages and **shown nontoxic** at a concentration lower than 10 μM.

CE for Food and Vector-borne Zoonoses

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