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Synthesis and biological characterisation of ester and amide derivatives of Fusidic acid as antiplasmodial agents

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Abstract: A series of novel fusidic acid (FA) derivatives was synthesized by replacing the carboxylic acid group with various ester and amide groups and evaluated *in vitro* for their antiplasmodial activity against the chloroquine-sensitive NF54 and multidrug-resistant K1 strains of the malarial parasite *Plasmodium falciparum*. Most of these derivatives showed a 4-49 and 5-17 fold increase in activity against NF54 and KI strains, respectively, as compared to FA and had a good selectivity index. These derivatives are stable over the incubation period and do not appear to be prodrugs of fusidic acid.

Malaria persists as a major public health problem, resulting in 214 million cases and causing 438,000 deaths worldwide in 2015.[1] The disease, transmitted by female Anopheles mosquitoes, is caused by five different species of the protozoan *Plasmodium* parasite, namely: *P.falciparum*, *P.vivax*, *P.malariae*, *P.ovale*, and *P.knowlesi* that infect and destroy red blood cells leading to high fever, anaemia, cerebral malaria, and possibly death. Of these, *P. falciparum* is the most lethal as well as the most prevalent in sub-Saharan Africa and is responsible for high mortality rates especially amongst young children and pregnant women. As there is no available vaccine, the control of the disease relies largely on the use of bed nets, other individual protection against mosquito bites, and the successful drug treatment of