RESEARCH NOTE

ASSESSMENT OF *IN VITRO* ANTIMALARIAL INTERACTIONS BETWEEN DIHYDROARTEMISININ AND FOSMIDOMYCIN

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Abstract. Malaria remains one of the leading causes of morbidity and mortality in the tropics with an annual estimate of 500 million clinical cases and 2 million deaths. The treatment and control of malaria is becoming increasingly difficult due to *Plasmodium falciparum* resistance to commonly used antimalarials. Combination therapy is currently the strategy for combating multi-drug resistant falciparum malaria, through exploiting pharmacodynamic synergistic effects and delaying the emergence of drug resistance. The combination of artemisinin derivatives with fosmidomycin, which have different modes of action, appears to be one of the most promising combinations. The objective of the present study was to investigate the antimalarial interactions between dihydroartemisinin and fosmidomycin *in vitro*, against chloroquine-resistant (K1) and chloroquine-sensitive (G112) *P. falciparum* strains. Concentration-response analysis was performed based on an *in vitro* schizont maturation inhibition test. The fixed concentration ratios of dihydroartemisinin: fosmidomycin used were 0:5,000, 2:4,500, 6:3,500, 10:2,500, 14:1,500, 18:500 and 20:0 nM. The highest final concentrations of dihydroartemisinin and fosmidomycin were 20 and 5,000 nM, respectively. Results showed IC_{50} (drug concentration which produced 50% schizont maturation inhibition) medians (range) for dihydroartemisinin against K1 and G112 strains to be 1.6 (1.2-2.0) and 2.5 (2.4-2.6) nM, respectively. The IC_{50} medians (range) for fosmidomycin against K1 and G112 strains were 1,347 (1,068-1,625) and 786 (737-834) nM, respectively. An isobologram revealed an increasing trend for the fraction IC_{50} (FIC), which indicates marked antagonism of this drug combination against both chloroquine resistant and chloroquine sensitive strains.

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