

Thesis Title *In Vitro* Blood Schizontocidal Activity of Plasma
Containing Artemether - Pyrimethamine

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ABSTRACT

Plasma samples collected at intervals from 8 healthy volunteers after administrations of 3 drug regimens (300 mg artemether, 100 mg pyrimethamine, and 300 mg artemether plus 100 mg pyrimethamine) were investigated for their blood schizontocidal activities against K₁ strain and T_{9/94} clone *P. falciparum* *in vitro* by using two different types of media, *i.e.*, RPMI and RPS (low PABA, low folic acid). No antimalarial activity was observed with pyrimethamine containing plasma against K₁ strain *P. falciparum* which is highly resistant to pyrimethamine in both types of media. The presence of

pyrimethamine in the combined regimen was shown to have no effect on activity of artemether against K₁ strain *P. falciparum*. For pyrimethamine sensitive clone of *P. falciparum* (T_{9/94}), though pyrimethamine containing plasma could exert inhibitory effect but synergistic effect with artemether was not observed in combined regimen using RPMI medium. Up to 8 folds of pyrimethamine activity against T_{9/94} *P. falciparum* was obtained by using RPS medium. Only with RPS medium that the MIC_{SEq} of artemether and its derivative (dihydroartemisinin) in combined regimen were found to be significantly lower than those of artemether alone. The present results are likely to indicate the synergistic effect or at least additive effect of the combined drugs. Further study in uncomplicated falciparum patients is encouraged due to the limitation of drug regimens for treatment multidrug-resistant strains of *P. falciparum*.