

Thesis Title	<i>In Vitro</i> Drug Interaction of Mefloquine and Quinine Against <i>Plasmodium falciparum</i>		
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ABSTRACT

This study was designed to study the blood schizontocidal activities (pharmacodynamic effect) of the combination of mefloquine (MQ) and quinine (QN) against *Plasmodium falciparum* (K₁) assayed *in vitro*, using a standard microtechnique (microtest) with modifications. Blood schizontocidal activity of the combined regimen (MQ+QN) was investigated in sera collected at intervals, from seven healthy male Thais after the pretreatment of a single oral dose of 750 mg MQ, followed by a single oral dose of 600 mg QN at 24 hours later. In addition, blood schizontocidal activities of MQ alone and QN alone

were investigated in the same subjects after administration of a single oral dose of 750 mg MQ, and a single oral dose of 600 mg QN.

The results of undiluted serum samples showed that the effects of MQ+QN on blood schizontocidal activity against *P. falciparum* were observed at the beginning of QN (24 hours after MQ administration; 0-h) throughout the end of the observation (72-h), indicated by no normal rings found in those wells. When the same subjects were given with QN alone regimen, the effects of QN on blood schizontocidal activity against *P. falciparum* were observed after 30 minutes of QN administration (0.5-h) throughout day-1 (24-h). There was no activity at the beginning of QN administration (0-h), day-2 (48-h) and day-3 (72-h), indicated by the appearance of normal rings in the wells with the medians (range) of 514 (405-570), 451 (402-533) and 458 (398-568) respectively. For MQ alone regimen, the activity was observed at the beginning time (24 hours after MQ administration; 0-h) throughout the end of the observation (72-h).

Moreover, the results of microdilution assessment showed that the MIC of QN of the combined regimen (MQ : QN) ranged between 21.25 and 73.5 $\mu\text{g/l}$, whereas the MIC values of QN alone regimen were significantly higher ($p < 0.0001$), ranging between 118 and 150 $\mu\text{g/l}$ at 0.5-h through 24-h. The

MIC of MQ of the combined regimen (MQ+QN) ranged between 17 and 9.12 $\mu\text{g/l}$, whereas the MIC values of MQ alone regimen were significantly higher ($p < 0.003$), ranging between 24.4 and 26.8 $\mu\text{g/l}$ at 0-h through 24-h.

This study provided *in vitro* evidence that blood schizontocidal activities against *P. falciparum* of the sera collected at various time-intervals from healthy subjects after administration of MQ+QN regimen were significantly superior to those collected after administration of MQ alone and QN alone regimens at all time-intervals of serum collection. This finding indicated that the MIC values of MQ and QN of the combined regimen were lower than that of MQ alone as well as QN alone regimens. Furthermore, the results revealed that the administration of the combined regimen has longer inhibitory effect (100% inhibition) against *P. falciparum* than QN alone regimen, but it is not different from MQ alone regimen.