

# PHARMACOKINETIC STUDY OF THE INTERACTION BETWEEN RIFAMPICIN AND MEFLOQUINE IN HUMANS

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## ABSTRACT

Since mefloquine is a quinolinemethanol compound structurally related to quinine, and quinine is metabolised mainly by human CYP3A4, whereas CYP3A4 is the major isozyme induced by rifampicin there is the possibility of a pharmacokinetic interaction between mefloquine and rifampicin. Therefore, the objective of this study is to examine the effect of coadministration of rifampicin and mefloquine on the pharmacokinetics of mefloquine in healthy volunteers. The pharmacokinetic parameters of mefloquine were determined in 7 healthy male volunteers after receiving mefloquine 500 mg as an oral single-dose in 2 occasions : (a) mefloquine alone, (b) after pretreatment with rifampicin 600 mg given orally once daily for 7 days prior to mefloquine administration and on days 1 through 7 after rifampicin pretreatment, then 600 mg rifampicin twice-weekly on days 8 through 56. The plasma mefloquine and mefloquine metabolite concentrations during 56 days were measured using High Performance Liquid Chromatography (HPLC). Statistical analysis using Student's *t* test indicated that when mefloquine and rifampicin were coadministered, the oral clearance of mefloquine increased by about 4-fold ( $0.0214 \pm 0.0038$  vs  $0.08 \pm 0.03$  l/hr/kg), the  $t_{1/2}$  was shorter about 2.5-fold

( $305.31 \pm 47.15$  vs  $113.43 \pm 49.71$  hr), the  $C_{\max}$  decreased significantly difference ( $855.63 \pm 168.00$  vs  $695.67 \pm 56.63$  ng/ml) and the AUC decreased about 3-fold ( $373.73 \pm 57.47$  vs  $119.77 \pm 54.94$  mg/l.hr). In addition, the  $t_{1/2}$  of mefloquine metabolite decreased about 1.5-fold ( $506.66 \pm 127.64$  vs  $307.45 \pm 56.90$  hr) and  $T_{\max}$  decreased about 4-fold ( $220.62 \pm 69.75$  vs  $52.48 \pm 28.81$  hr). The alteration in mefloquine pharmacokinetic parameters may be mainly due to the induction of CYP 3A4 isozyme by rifampicin and may lead to reduce efficacy of mefloquine in malarial treatment. Therefore, mefloquine and rifampicin should not be coadministered in order to maximise therapeutic efficacy and prevent a risk of resistant of *P. falciparum*.

Keywords: Rifampicin, mefloquine, pharmacokinetics, drug interaction

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