

# Metabolism of caffeine and theophylline in rats with malaria and endotoxin-induced fever

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## Abstract:

1. The effects of malaria infection due to *Plasmodium berghei* and *Escherichia coli* endotoxin-induced fever on the metabolism of orally-administered caffeine (CA: 10 mg/kg) to its primary metabolites (theobromine (TB), paraxanthine (PX) and theophylline (TH)) were studied in 5-week-old male Wistar rats (n = 5 for each treatment). In separate experiments, the effects of malaria and endotoxin-induced fever on the clearance of i.v.-administered theophylline (TH; 15 mg/kg) were studied in another group of rats. 2. The ratios of CA to the three primary metabolites (TB/CA, PX/CA, PH/CA) determined in a single plasma sample obtained 3 h after CA administration were significantly reduced ( $p < 0.05$ ) both by malaria and fever compared with control (saline) treatment. The clearance of TH determined from the concentration of TH in a single plasma sample obtained 6 h after TH administration was significantly reduced ( $p < 0.05$ ) by fever but not malaria (4.0 +/- 0.7 ml/min/kg in controls; 4.2 +/- 0.5 in malaria; 2.4 +/- 0.4 in fever). 3. These results suggest that malaria and fever have different effects on CA and TH metabolism in vivo, probably as a result of different effects on the hepatic isozymes involved.