Effect of malaria infection and endotoxin-induced fever on the metabolism of antipyrine and metronidazole in the rat

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http://hinari-gw.who.int/whalecomwww.ncbi.nlm.nih.gov/whalecom0/pubmed/8466545
http://erepository.uonbi.ac.ke:8080/xmlui/handle/123456789/31108
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Abstract:

Antipyrine and metronidazole were administered as a cocktail to young (4 weeks old) male Wistar rats (N = 12 for each treatment) to investigate the effect of malaria infection due to the rodent parasite Plasmodium berghei and Escherichia coli endotoxin-induced fever on the metabolism of the two compounds in vivo. Control rats received normal saline. Antipyrine and metronidazole clearances were estimated from a single saliva sample while the formation clearances of their metabolites (in malaria-infected and control rats) were estimated from the product of clearance of parent drug and the fraction of the administered dose excreted as metabolites in urine in 24 hr. Rats treated with endotoxin produced no urine during this period. Malaria infection had no effect on clearance of antipyrine or on formation clearance of any of its metabolites. However, the clearance of metronidazole was reduced by approximately 20% compared with controls as a result of decreased formation of hydroxymetronidazole. Fever decreased clearance of both antipyrine and metronidazole by approximately 36% and 23%, respectively. These results demonstrate that both malaria infection and fever can influence P450-dependent drug metabolism and the effects seen appear to be isozyme-selective.