Effect of malaria infection on the pharmacokinetics of paracetamol in rat

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Abstract:

1. Paracetamol (P; 50 and 300 mg/kg i.v.) was administered to the control and malaria-infected (MI) male Wistar rat in order to assess the effect of MI on the metabolism of paracetamol to its glucuronide (PG) and sulphate (PS) conjugates and their excretion in urine. 2. At a dose of 50 mg/kg, neither total clearance (ClT) (controls, 20.3 +/- 0.5; MI, 19.9 +/- 0.9, ml/min/kg; mean +/- SD, $p > 0.05$) nor the renal clearance of P (ClR) were affected by MI. Although the formation clearance of PG (Clf PG) was decreased by about 40% (controls, 6.6 +/- 1.1; MI, 3.9 +/- 0.9, ml/min/kg, $p < 0.05$), the formation clearance of PS (Clf PS) was increased by 30% in the MI rat (controls, 8.8 +/- 0.9; MI, 11.2 +/- 1.7, ml/min/kg, $p < 0.05$), and therefore Clm (controls, 19.7 +/- 0.5; MI, 19.2 +/- 0.8, ml/min/kg, $p > 0.05$) was unchanged by MI. 3. At a dose of 300 mg/kg, MI produced a significant decrease in the total clearance of P (ClT) (controls, 16.9 +/- 1.0; MI, 11.9 +/- 0.9, ml/min/kg, $p < 0.05$), metabolic clearance (Clm) (controls, 15.9 +/- 1.4; MI, 11.3 +/- 0.9, ml/min/kg, $p < 0.05$) and the formation clearance of PG (Clf PG) (controls, 7.9 +/- 1.3; MI, 4.7 +/- 1.5, ml/min/kg, $p < 0.05$) without affecting Clf PS and ClR of P. 4. These findings indicate that MI impairs the glucuronidation of paracetamol in rat in vivo at both the low and high doses of P. Increased sulphate formation appeared to compensate for decreased glucuronidation at the lower dose