Difference between in vivo and in vitro effects of propofol on defluorination and metabolic activities of hamster hepatic cytochrome P450-dependent monooxygenases.

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摘要

Abstract

We have compared the in vivo and in vitro effects of propofol on cytochrome P450-dependent monooxygenase activities in hamster liver microsomes. Propofol (Diprivan) 10 mg/100 g body weight was injected i.p. twice a day for 2 weeks to induce cytochrome P450 enzymes. Liver microsomes were prepared by differential centrifugation. Metabolism of the cytochrome P450-dependent mono-oxygenase system was evaluated by measuring aniline hydroxylation, benzphetamine demethylation and benzo(a)pyrene hydroxylation. Defluorination of enflurane was assayed by detecting free fluoride metabolites. At similar concentrations as in the in vivo group, propofol in vitro exhibited concentration-dependent inhibition of metabolism of benzphetamine and benzo(a)pyrene. Aniline hydroxylation and defluorination of enflurane were inhibited to 78% of control with propofol 0.25 mmol litre-1. In propofol-treated hamsters, there was only minimal inhibitory or inductive effects on either mono-oxygenase activities or capacity for defluorination. This difference between the in vitro and in vivo effects of propofol on cytochrome P450 mono-oxygenase activities emphasizes the need for care when comparing in vitro and clinical data.