Induction and inhibition of cytochrome P450-dependent monooxygenase in hamster tissues by ethanol.

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摘要

Abstract

The effects of ethanol on hamster hepatic and extrahepatic monooxygenases were determined in the present study. Chronic ethanol administration increased cytochrome P-450 (P-450) content and monooxygenase activities towards aniline, N-nitrosodimethylamine, and 7-ethoxyresorufin. In contrast, benzphetamine and benzo(a)pyrene oxidation rates were decreased 21-24% by ethanol. In kidney, ethanol pretreatment increased P-450 content, aniline and N-nitrosodimethylamine oxidation activities. In lung, ethanol ingestion selectively increased aniline hydroxylation without affecting other monooxygenase activities. Intestinal monooxygenase activity was refractory to ethanol induction. Immunoblotting of the microsomal proteins showed that ethanol induced a protein cross-reactive with rabbit antibody raised against human P-450 2E1 in hamster liver, kidney, and lung. Immunoblotting analysis using mouse monoclonal antibody 1-12-3 raised against scup P-450 1A1 revealed that ethanol induced an immunorelated protein in hamster liver, kidney, and lung. Induction of P-450 2E1 and 1A was not observed with intestinal protein blots. Immunoblotting analysis using mouse monoclonal antibody 2-66-3 against rat P-450 2B1 showed inhibition of an immunorelated protein in ethanol-treated hamster liver. The inhibitory effect on P-450 2B was not observed with extrahepatic tissues. These results suggest that ethanol has the ability to induce P-450s 2E1 and 1A and to inhibit P-450 2B in hamster tissues.