Induction and suppression of renal and hepatic cytochrome P450-dependent monooxygenase by acute and chronic streptozotocin diabeties in hamsters.

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摘要

Abstract

The acute and chronic effects of streptozotocin diabetes on kidney and liver microsomal monooxygenases were studied using hamsters 2 days and 6 weeks following treatment with the diabetogen, respectively. Acute diabetes increased aniline hydroxylation and N-nitrosodimethylamine demethylation, decreased pentoxyresorufin O-dealkylation, without affecting benzo(a)pyrene hydroxylation and 7-ethoxycoumarin O-deethylation in kidney and liver microsomes. The effects of chronic diabetes on the microsomal monooxygenases were similar to the effects of acute diabetes, except that the chronic diabetic condition markedly decreased benzo(a)pyrene and 7-ethoxycoumarin oxidations in kidney microsomes. Total cytochrome P450 content and NADPH-cytochrome P450 reductase activity in kidney and liver microsomes of the diabetic hamsters were similar to the controls. Gel electrophoresis of microsomes from control and streptozoptocin treated hamster tissues revealed that diabetes enhanced the intensity of protein band(s) in the P450 molecular weight region. Immunoblotting of microsomal proteins showed that acute and chronic streptozotocin diabetes induced proteins immunorelated to P450s 2E1 and 1A in kidney and liver. In marked contrast, the acute and chronic diabetic conditions decreased the level of a P450 2B-immunorelated protein(s) in kidney and liver. The present study demonstrates that acute and chronic streptozotocin diabetes has the ability to induce P450 2E1 and 1A and suppress P450 2B in hamster kidney and liver and that the hamster monooxygenase responds to diabetes differently from the rat enzyme.