

Abstract

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Project Title : Effect of glutathione depletion on the expression of hepatic cytochrome P450

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Abstract:

Glutathione (GSH) is a homeostatically controlled antioxidant system of human and animals. Increase of toxicants or pollutants in the current environment is able to disturb the level of GSH. Hepatic cytochrome P450s (CYP) is the main enzyme for drug and toxicant metabolism. This study aimed to determine the effects of GSH depletion on the expression of CYP, especially cancer-related CYP isoforms namely CYP1A1, CYP1A2, and CYP1B1, and drug metabolizing enzyme CYP2E1 and CYP3A activities. Male ICR mice were intraperitoneally injected daily with 150 or 300 mg/kg/day of styrene oxide (SO), or 175 or 350 mg/kg/day of diethyl maleate (DEM), or 300 or 600 mg/kg/day of N-acetylcysteine (NAC) for 7, 14, and 28 days. Plasma ALT, AST, hepatic GSH profiles and *Cyp1* expression were evaluated. Plasma ALT and AST were significantly increased by SO and DEM while GSH contents were suppressed. *Cyp1a1*, *Cyp1a2*, and *Cyp1b1* were induced by SO or DEM at 7, 14, and 28 days, corresponding with the induction of EROD and MROD activities. Moreover, SO and DEM also increased CYP2E1 and CYP3A activities. Because *Cyp1* gets involved in the pro-carcinogen activation of some compound such as poly aromatic hydrocarbons and dioxins, leading to DNA adduct and carcinogenesis. Therefore, people who work with these solvents should be aware the risk of carcinogenesis via GSH depletion with the *Cyp1* induction. In addition, drug interaction via CYP2E1 and CYP3A4 should be aware.

Keywords : GSH, styrene oxide, diethyl maleate, liver injury, CYP