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EFFECTS OF PHENETHYLISOTHIOCYANATE ON THE INDUCTION OF GLUTATHIONE-S-TRANSFERASES AND HEPATOTOXICITY INDUCED BY ACETAMINOPHEN

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Phenethylisothiocyanate (PEITC), a constituent of cruciferous vegetables, has been shown to inhibit the metabolism and carcinogenicity of nitrosamines and polycyclic aromatic hydrocarbons in various organs of the rats and mice. The mechanisms of cancer protection by this agent are not clear, but may involve the modulation of the enzyme systems responsible for the activation or detoxification of chemical carcinogens. In this study we have investigated the effects of PEITC on the expression of hepatic glutathione-S-transferases (GSTs) and the capacity of GSH conjugation in rats, and determined whether hepatotoxicity of acetaminophen (AA) can be inhibited through the induction of GSTs expression in mice. The hepatic GST activity and GSTs (Ya, Yb_1, Yb_2 and Yc) protein levels elevated in dose-dependent manner after treatment of PEITC (0, 3.16, 10, 31.6, 100 and 200㎎/kg, 3 days) in Sprague-Dawley rats. A single dose of PEITC (0, 3.16, 10, 31.6, 100 and 200㎎/kg) enhanced markedly the mRNA levels of Ya and Yb_1 at 100 and 200㎎/kg after 24h treatment. The hepatic GSH content was slightly decreased at 3.16 and 10㎎/kg of PEITC, but gradually recovered by a significant increase to 200% of control at 200㎎/kg of PEITC. The pretreatment of PEITC 100㎎/kg enhanced significantly the biliary excretion of AA-GS conjugates to 2-fold, whereas treatment with 200㎎/kg of PEITC did not affect the excretion of AA-GS in bile. When pretreated to ICR mice, PEITC (100 and 200㎎/kg) decreased markedly the lethality and hepatotoxicity caused by AA. These results indicate that 1) the induction of GSTs by PEITC is presumably under the transcriptional regulation, 2) the decrease of AA hepatotoxicity by PEITC may be brought about partly by inducing GSTs.