Thesis Title Effect of Piperine on Carbon Tetrachloride Induced Hepatotoxicity

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ABSTRACT

The effect of piperine on CCl_4-induced hepatotoxicity was investigated in male Wistar rats. The hepatotoxicity was assessed by measuring plasma glutamic pyruvic transaminase (PGPT) and glutamic oxaloacetic transminase (PGOT) levels at 24 h following the CCl_4 administration (0.1 ml/kg BW, i.p.). Piperine had ability to potentiate the hepatotoxicity of CCl_4 whereas piperine itself had no hepatotoxic effect. The maximum potentiation occurred when piperine (100 mg/kg BW) was orally administered 4 h prior to CCl_4 at which the activities of PGPT and PGOT were elevated by 70-80%. Concurrent to the rise in PGPT and PGOT levels, an accumulation of hepatic triglycerides was increased and plasma triglycerides level was decreased. The potentiating effect of piperine on these action of CCl_4

showed a dose-dependent pattern and the maximum dose in producing effect was 100 mg/kg BW, p.o.

The potentiating mechanism of piperine was investigated. Piperine also potentiated the stimulating action of CCl_4 on lipid peroxidation and on NADPH-cytochrome c reductase activity. The extent of potentiation on these two parameters were similar and correlated well with the elevation of plasma transaminase activities.

The effect and mechanism of piperine on CCl_4-induced hepatotoxicity were further explored by modifying schedule of treatment. Piperine pretreatment for 4 h slightly enhanced the in vitro effect of CCl_4 in stimulating lipid peroxidation and activity of NADPH-cytochrome c reductase but there was a statistical difference ($P<0.05$). A similar enhancing effect of piperine on both CCl_4-stimulated lipid peroxidation and NADPH-cytochrome c reductase also significantly occurred when the liver microsomes were exposed to both piperine and CCl_4. The potentiating effect was increased with the concentration of piperine and the presence of piperine in the incubation mixture before adding CCl_4 was essential for producing potentiation. However, the potentiating action of piperine on CCl_4-induced hepatotoxicity in vitro was very much lower than that of in vivo system. From these in vitro studies, it suggests that piperine itself, not its metabolite, exerts the potentiating action. And as the degree of potentiation on various concentrations of

CCl_4 was similar, piperine probably affected the liver function by binding to the liver membrane non-competitively.

Therefore, it is concluded that piperine potentiates CCl_4-induced hepatotoxicity by directly interacting with liver cell. Its mechanism associates with the increase in activity of NADPH-cytochrome c reductase which accelerates biotransformation of CCl_4 to the highly reactive metabolite, thereby increasing lipid peroxidation and enhancing its hepatotoxicity.