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POTENTIATED MECHANISM OF CARBONTETRACHLORIDE INDUCED HEPATOTOXICITY

BY THINNER INHALATION

BY

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POTENTIATED MECHANISM OF CCl_4 -INDUCED HEPATOTOXICITY BY THINNER
INHALATION IN RATS

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ABSTRACTS

The possible mode of action of thinner on enhancing CCl_4 -induced hepatotoxicity was studied in rats. The animals were housed in a chamber with the continuous flow of thinner vapour at the rate of 1.11 g/liter/hr for 2 hrs prior to administration of CCl_4 (0.1 ml/kg BW) at 18 hrs after thinner inhalation. Thinner inhalation potentiated CCl_4 (0.1 ml/kg BW)-induced hepatotoxicity in a dose-dependent fashion. The maximal enhanced effect was observed at 24 hrs after CCl_4 administration by which the activity of plasma glutamic oxaloacetic transaminase and plasma glutamic pyruvic was significantly increased (3 folds), from transaminase 373 ± 40 to 1366 ± 210 units ($P < 0.001$) and 361 ± 35 to 1127 ± 161 units ($P < 0.001$) respectively. Thinner by itself caused an increase in accumulation of liver triglycerides and it exerted additive action on CCl_4 -induced liver triglyceride accumulation by 2 folds from 13.2 ± 1.2 to 25.6 ± 1.9 mg/kg liver ($P < 0.001$). This finding confirms our previous reported in which thinner given i.g. (4.0 ml/kg) could enhance hepatic necrosis in the rat and two major constituents, methanol (1022 ppm) and toluene (842 ppm) are responsible for this potentiated effect by increasing the activity of PGOT from 373 ± 40 to 1233 ± 40 ($P < 0.001$) and to 990 ± 15 units ($P < 0.005$) respectively. At 18 hr after thinner inhalation or at the time of

CCl_4 administration, the activity of NADPH cytochrome c reductase was markedly increased from 99 ± 6 to 217 ± 21 nmoles/min/mg protein ($P < 0.001$), but no change in the activity of aminopyrine N-demethylase. At 18 hr after thinner pretreatment, thinner was able to increase the binding of $^{14}\text{CCl}_3$ free radical both to the hepatic microsomal protein from 1.0 ± 0.2 to 1.8 ± 0.3 nmoles/mg protein and to the hepatic microsomal lipid from 1.1 ± 0.2 to 1.6 ± 0.3 nmoles/mg protein ($P < 0.001$) and increased the CCl_4 -induced lipid peroxidation from 28.36 ± 3.0 to 40.9 ± 2.8 $\mu\text{g/g}$ liver ($P < 0.001$). These results indicate that thinner pretreatment cause an increase in mixed function oxidases, NADPH-cytochrome c reductase to activate the formation of $^{14}\text{CCl}_3$ free radical which in turn stimulate hepatic damage via lipid peroxidation in the membrane.