

Pathogenesis of Carbon Tetrachloride-Induced Hepatocyte Injury

Bioactivation of CCl₄ by Cytochrome P450 and Effects on Lipid Homeostasis

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The CCl₄-induced development of liver damage was studied in monolayer cultures of primary rat hepatocytes:

(1) CCl₄ caused accumulation of triglycerides in hepatocytes following cytochrome P450 induction with β -naphthoflavone or metyrapone. Ethanol or a high dose of insulin plus triiodothyronine had the same effect. (2) CCl₄ increased the synthesis of fatty acids and triglycerides and the rate of lipid esterification. Cholesterol and phospholipid synthesis from acetate was also increased. (3) CCl₄ reduced β -oxidation of fatty acids as assessed by CO₂-release and ketone body formation. Hydrolysis of triglycerides was also reduced. (4) The content of unsaturated fatty acids in microsomal lipids was decreased by almost 50% after incubation with CCl₄, while saturated fatty acids increased slightly. (5) CCl₄ exerted a pronounced inhibitory effect on the exocytosis of macromolecules (albumin), but did not affect secretion of bile acids from hepatocytes.