Liver Damage, Carbon Tetrachloride, Cytochrome P450

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.