Depressed Hepatic Uptake and Low Biliary Excretion of Certain Foreign Organic Compounds during Oral Administration of Carbon Tetrachloride or Chloroform to Rats*

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Succinylsulphathiazole or phenolphthalein disulphate tripotassium salt (20mg/kg body wt.) was injected intravenously to bile-duct-cannulated Wistar albino rats. Bile was collected for the next 3h. The amounts excreted in bile were 34% of administered dose for succinylsulphathiazole and 56.6% for phenolphthalein disulphate. The compounds excreted in bile were chromatographically identical with the administered substances (Abdel Aziz et al., 1971).

Oral administration of CCl₄ (50mg/kg body wt., suspended in 2.5ml of olive oil) to rats daily for 7 successive days before operation was performed on the animals lowered the biliary excretion of succinylsulphathiazole to 20.8% and that of phenolphthalein disulphate to 23.8% of the given dose.

Penetration of compounds into the liver and their accumulation is an important step before they are excreted in bile (Wheeler et al., 1958; Billing et al., 1964; Abou-El-Makarem et al., 1968). Distribution studies (determination of phenolphthalein disulphate in plasma, liver and bile at various intervals after its intravenous injection) were

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Fig. 1. Distribution of phenolphthalein disulphate between plasma, liver and bile of the rat

Phenolphthalein disulphate (20mg/kg) was administered intravenously to rats as an aqueous solution of the tripotassium salt. The concentration of phenolphthalein disulphate is expressed as µg/ml for plasma and as µg/g for liver and bile. Results are the means of five experiments. (a) Normal rats; (b) rats after oral administration of CCl₄ for 7 successive days; (c) rats after oral administration of CHCl₃, for 7 successive days.○, Plasma; △, liver; □, bile.
carried out in normal rats and in rats after oral administration of CCl₄ for 7 days. The concentration of phenolphthalein disulphate in normal rat liver was 4–10 times that in plasma. The concentration of the compound in bile increased to 5 times that in the liver, i.e. 20–50 times that in plasma. During oral administration of CCl₄ to rats the liver concentration of phenolphthalein disulphate was 2–4 times that in plasma and the bile concentration was 3–4 times that in the liver, i.e. 6–16 times the plasma concentration.

Previous reports indicated that most of the compounds excreted in bile are generally bound to hepatic proteins (Priestly & O'Reilly, 1966; Levi et al., 1969). Yet in CCl₄-treated rats the binding capacity of liver homogenate protein for succinylsulphathiazole or phenolphthalein disulphate was similar to that in normal rats.

The present results suggested that CCl₄ depressed the capacity of the hepatocytes to concentrate phenolphthalein disulphate from plasma. However, the hepatotoxic agent did not interfere with the binding capacity of liver proteins. Further, it seemed that its effect was not marked on the concentrative mechanism of the hepatocytes through the bile. This finding supports a previous suggestion that both hepatic uptake and biliary excretion involve various mechanisms (Preisig, 1972).

Further evidence supporting the previous idea was obtained in a study on the effect of CHCl₃, another well-known hepatotoxic agent (50mg/kg body wt., suspended in 2.5ml of olive oil, given orally for 7 successive days). Biliary excretion of succinylsulphathiazole or of phenolphthalein disulphate was lowered. Also, depression of hepatic uptake and lowered concentrations of phenolphthalein disulphate in the liver and bile were obtained compared with normal rat liver and bile (Fig. 1).

A single high dose of CCl₄ (250mg/kg body wt., suspended in 2.5ml of olive oil) was administered orally to another group of rats. Measurements of biliary excretion of phenolphthalein disulphate or succinylsulphathiazole as well as distribution studies were made for the 24h after administration of the hepatotoxic agent. The amounts of compound excreted in bile were 3.6 or 2.6% of administered dose respectively. The liver concentration of phenolphthalein disulphate was near to the plasma concentration. Yet the concentration of the compound in bile was nearly double that in liver homogenate. In addition, this high dosage of CCl₄ did not interfere with the binding capacity of liver homogenate protein so far as these two compounds are concerned.


Isomerization of all-trans-Retinal to 11-cis-Retinal in Isolated Frog Retinæ

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Ever since the discovery of rhodopsin by Boll (1877), efforts have been made to gain a thorough understanding of the visual process. As a result it is now well established that rhodopsin consists of a protein opsin linked via a Schiff base to 11-cis-retinal (Akhtar et al., 1967; Bownds, 1967). It is also known that on activation by light a visual impulse originates in the retinal photoreceptors and concomitant with this is the breakdown of...