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Reabsorption from the Biliary System as a Factor Influencing the Biliary Excretion of Organic Anions

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Although the mechanism of biliary excretion is obscure (Sperber, 1959; Schanker, 1968; Wheeler, 1968), much is known about the properties of the compounds that are eliminated in the bile. Molecular size, polarity and structural features are important factors in determining the extent of biliary excretion of organic molecules (Abou-El-Makarem, Millburn, Smith & Williams, 1967; Millburn, Smith & Williams, 1967a,b; Hirom, Millburn, Smith & Williams, 1969). Thus large organic anions (mol.wt. > 300) are usually extensively excreted in the bile of the rat whereas small ones (mol.wt. < 300) are not. It would seem reasonable to suppose that this difference may be related in some way to the mechanism of bile formation. It has been suggested that bile, during its passage down the biliary tract, may be modified in composition possibly by secretion and reabsorption of water and solutes (Andrews, 1955; Brauer, 1959; Sperber, 1959; Goldfarb, Singer & Popper, 1963; Wheeler, 1968). However, evidence for a reabsorption process in bile formation is scanty (Leong, Holloway & Brauer, 1955; Barber-Riley, 1963; Mallet-Guy, Michoulier & Baev, 1965). If small organic anions are reabsorbed from the primary bile this might explain their low biliary excretion. Therefore we have investigated the reabsorption from the biliary tree of small anions (mol.wts. 179–285), which are poorly eliminated in bile, and larger anions (mol.wts. 445–752), which are extensively excreted in the bile of the rat.

Aqueous solutions of the compounds (20 μ moles/kg.) were administered by retrograde injection during 1–2 min. into a short cannula inserted in the common bile duct of anaesthetized rats. After the infusion, the bile was collected for 30 min. and analysed. With the small anions (hippuric acid, 3-aminophenyl sulphate, succinylsulphanilamide and 2-aminophenyl glucuronide) only 7–15% of

the infused compounds was recovered in the bile whereas 50–60% was found in the urine collected from the bladder. However, with the larger anions (stilboestrol glucuronide, phenolphthalein glucuronide, phenolphthalein disulphate and Indocyanine Green) 50–80% was recovered in the bile and less than 2% in the urine. Thus small but not large organic anions appear to be readily absorbed from the biliary tree after their retrograde injection.

These observations suggest that the low biliary excretion of small organic anions may be due to their reabsorption from the primary bile.

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Bile Secretion in Relation to Decreases in Liver Adenosine Triphosphate Concentration in the Rat

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The relationship between the concentration of ATP in liver and bile secretion has been studied. In this paper the effects on bile flow of two agents that decrease the concentration of ATP in rat liver *in vivo* will be considered.

2,4-Dinitrophenol was studied since it is an active uncoupling agent *in vitro* and was expected to decrease liver ATP concentration after parenteral administration. Intraperitoneal doses up to 70 mg./kg. body wt., however, had little effect either on

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