As shown in Table 1 in contrast to results obtained in mammals, phenobarbital did not enhance the liver/body weight ratio and depressed rather than stimulated bile secretion. The latter was true whether the drug was administered daily (group A) or as a single dose eight days earlier (group B). No stimulating effects of phenobarbital on MFO pathways were observed in any of the studies. However, three of four MFO pathways were depressed in the operated control fish as compared with nonoperated controls suggesting that either the biliary cannulation or the length of fasting during captivity resulted in diminished microsomal enzyme function. Soluble enzyme activity as assessed by glutathione-S-aryltransferase was not affected in operated fish nor was it altered by phenobarbital administration. These studies indicate that phenobarbital does not stimulate biliary secretion or MFO pathways in the skate as it does in some mammalian species and suggests that the ability of this animal to increase hepatic metabolism and biliary excretion when chronically exposed to xenobiotics may be limited.

1973 #5

SELECTIVE HEPATIC UPTAKE AND BILIARY SECRETION OF ORGANIC ANIONS IN ELASMOBRANCHS *Squalus acanthius* AND *Raja erinacea.*

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^{35}S-bromsulphathalein (BSP) or ^{14}C-Sodium Taurocholate (NaTC) were administered intravenously to free swimming dogfish sharks and to small skates to evaluate the capacity of these marine species to transport organic anions from plasma into bile. Plasma disappearance was determined by sampling blood at 15, 30, 60 and 120 minutes and at eight, 12 and 24 hours. Hepatic bile was obtained utilizing cannulation techniques which permitted intermittent sampling from the free swimming fish (Boyer, Bull. MDIBL 11:4-5, 1971). After 24 hours the fish were killed. Aliquots of plasma, bile, and liver homogenate were added to Scintisol and counted by liquid scintillation spectrometry. Samples of bile containing ^{35}S-BSP were also subjected to cellulose thin layer chromatography (n-butanol: glacial acetic acid: H_2O-40:10:50) to determine the percent of anions excreted as conjugates.

Both ^{35}S-BSP and ^{14}C-NaTC were removed from plasma by the liver and secreted into bile (Table 1). Initial fractional clearance rates of ^{35}S-BSP from plasma were .045 $\pm$ .008 in 6 dogfish and .044 $\pm$ .01 in four small skates while fractional clearance rates for ^{14}C-NaTC were .0319 $\pm$ .0015 and .050 $\pm$ .004 in dogfish and skates respectively. By 24 hours 79.1 percent and 78 percent of the administered doses of ^{35}S-BSP were recovered in the liver and bile of the dogfish and small skates respectively; these values compared favorably with recoveries of 80.5 and 59 percent of administered ^{14}C-NaTC in these two species. Large concentration gradients between plasma and bile were observed for both anions in dogfish and skates, averaging 4057:1 and 1592:1 respectively for ^{35}S-BSP, and 4180:1 and 2071:1 for ^{14}C-NaTC. When conjugates of ^{35}S-BSP were assessed by thin layer chromatography only 12.4 percent of the secreted BSP was metabolized by the dogfish while 24.7 percent of the excreted BSP was in conjugated form in bile from the small skate. Thus conjugation of BSP was not essential for transport into bile in either species.

TABLE 1

HEPATIC CLEARANCE OF ORGANIC ANIONS IN ELASMOBRANCHS

	BILE	LIVER	LIVER & BILE	% CONJUGATES IN BILE	MEAN B/P RATIOS
	(% DPM's at 24 Hours)				
Squalus acanthius					
^{35}S-BSP (5)	50.5 ± 20.7	28.7 ± 12.3	79.1 ± 13.3	12.4 ± 4.1	4057:1
^{14}C-NaTC (2)	75 ± 3.1	5.4 ± 2.7	80.4 ± 5.8	------	4180:1
Raja erinacea					
^{35}S-BSP (3)	48.3 ± 21	30.0 ± 17.4	78.4 ± 10.0	24.7 ± 6.0	1592:1
^{14}C-NaTC (2)	57 ± 18	2.3 ± .25	59 ± 17.5	------	2071:1

Numbers in parenthesis equal # of animals studied.

The mean ± standard deviation are given.

These studies demonstrate that despite the slow rate of biliary excretion of ^{35}S-BSP and ^{14}C-NaTC transport mechanisms exist in an elasmobranch liver which ultimately clear these organic anions from plasma into the liver and excrete them against large concentration gradients into bile. Thus despite the presence of gills and kidneys mechanisms have already evolved in primitive marine vertebrates for selective concentrative transport of these compounds into liver and bile.

1973 #6

BILE SECRETION AND COMPOSITION IN THE LITTLE SKATE, *Raja erinacea*

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Previous studies in the spiny dogfish *Squalus acanthias* (Boyer, Bull. MDIBL 11:4-5, 1971) indicated that continuous collections of hepatic bile could be successfully obtained in the free swimming fish after cannulation of the biliary tree through the gallbladder. These techniques were adopted for use in the little skate *Raja erinacea* in order to assess bile secretion and composition in this species. Male and female skates weighing approximately 1.0 kg were anaesthetized and restrained on a skate board for approximately 15 minutes while the gills were perfused with oxygenated sea water. A ventral incision was made, the gallbladder drained, and a 260 PE cannula inserted through the gallbladder and tied in place. The externalized cannula was attached to readily removable small balloons and the skates were allowed to swim freely in large tanks. Bile composition studies (Table 1) were performed on gallbladder bile removed at the time of cannulation and on hepatic bile obtained during the first 24-hour period of bile collection; these values are compared