Table 2. *The flow properties of Avicel PH 101/spray dried lactose mixtures.*

Avicel PH 101 % w/w	Coeff. of int. frict.	Cohesiveness kN m^{-2}	Flow factor	Blocking aperture size (cm)
0	1·32	0·047	12·4	1·0
2	1·28	0·040	13·9	0·6
4	1·28	0·035	16·4	0·5
8	1·60	0·055	11·6	2·2
16	1·80	0·060	10·0	Powder will not flow through largest diameter orifice (2·5 cm)
32	2·06	0·065	8·6	

101 improves the flow properties of the mixtures. Above this concentration, the effect is reversed and increase in Avicel content worsens the flow characteristics.

From these results Avicel appears to have glidant properties at concentrations below 4% w/w. As the concentration of Avicel increases above this level, however, a continuous microcrystalline cellulose matrix is formed within the mixture. The flow characteristics then become more dependent on the flow properties of the Avicel than the spray dried lactose and so the flow of the mixtures becomes worse.

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Biliary reabsorption of ^{35}S-sulfobromophthalein sodium under T_m-conditions

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It has been suggested that during its passage down the biliary tract bile may be altered in composition by reabsorption and secretion of water and solutes (Brauer, 1959; Goldfarb, Singer & Popper, 1963; Wheeler, 1968). In studies of the biliary uptake of organic compounds of large molecular weight in the rat, the possibility of some, albeit poor, absorption of representative compounds from the biliary tract was suggested by Clark, Hirom & others (1971). Czok & Dammann (1972) supported this suggestion by demonstrating that sulfobromophthalein sodium was absorbed from the bile duct into the hepatocytes of the rat after retrograde intrabiliary injection. Whilst this technique can be used to measure absorption of a retrogradely injected compound it can do so only if the volume in which the compound is administered is less than the distended capacity of the rat biliary tree. In this study a volume of 40 μl was used because it did not interfere with the biliary tree capacity. Up till now there have been two measurements available for the distended state (Barber-Riley, 1963; Fujimoto, 1975). Fujimoto (1975) found a distended biliary tree capacity of 37 μl for a rat liver weighing 10 g. Since in our study the average liver weight was 14·4 $\pm$ 1·2 g the distended capacity could have been about 53 μl.

The present work was undertaken to investigate the possibility of biliary reabsorption of sulfobromophthalein sodium (^{35}S-BSP) from the rat biliary tree against a concentration gradient after retrograde injection. Unlabelled sulfobromophthalein was intravenously infused at a constant rate of 0·96 mg min^{-1} rat^{-1} until the biliary excretion of BSP indicated that T_m—values were established. When T_m—values are observed BSP serum and liver concentrations are about 0·5 μmol ml^{-1} and 2·25 μmol g^{-1} liver respectively (Grote, Schmoldt & Dammann, 1975). Thus, when 4·8 nmol ^{35}S-BSP dissolved in 20 μl was retrogradely administered, a high concentration gradient was established against both the hepatocytes and the bloodstream. No concentration gradient was found when 12 μmol ^{35}S-BSP was injected retrogradely. Biliary fistulae were prepared and retrograde injection was made in male Wistar rats, 350–

Table 1. *Group 1–4: % recoveries of 4·8 nmol (Group 1,3) and 1·2 μmol (Group 2,4) [^{35}S]sulfobromophthalein sodium dissolved in 20 μl 0·9 % w/v NaCl solution after retrograde intrabiliary injection.* The doses were washed in with 20 μl of isotonic NaCl solution (0·9 % w/v). Group 3 and 4 received an intravenous infusion of unlabelled sulfobromophthalein sodium (0·96 mg min^{-1} rat^{-1}) performed until T_m-values were observed before retrograde injection. Each value is the mean with s.d. of 5 or more rats.

Group n	0–2·5 min	2·5–5 min	5–10 min	10–15 min	15–30 min	Total
1	48·4 ± 4·8	9·4 ± 2·6	14·6 ± 1·5	8·8 ± 1·5	10·4 ± 2·1	89·0 ± 3·5
2	43·4 ± 3·0	3·2 ± 0·1	6·3 ± 1·2	4·7 ± 1·1	6·6 ± 1·4	64·3 ± 0·5
3	46·8 ± 4·2	1·2 ± 0·3	3·6 ± 0·8	3·8 ± 0·7	8.3 ± 1·0	63·9 ± 4·4
4	47·2 ± 4·2	1·0 ± 0·8	1·9 ± 0·2	2·4 ± 0·5	6·9 ± 1·3	59·3 ± 4·1

420 g, as described by Dammann & Czok (1975). ^{35}S-BSP was administered by the retrograde biliary route using a Hamilton micrometer syringe joined to the bile duct cannula. The technique guarantees accurate administration of microlitre quantities and allows free bile flow to be restarted 3–5 s after the injection. In all sets of experiments bile flow was re-established immediately after the retrograde injection. Bile samples were collected 0–2·5 min, 2·5–5 min, 5–10 min, 10–15 min, and 15–30 min after administration of the dye. Blood samples were collected 25 min after injection. The radioactivity in each sample of bile and blood was estimated by counting in a liquid scintillation spectrometer. Since bile flow in the first 2·5 min after retrograde administration (75–102 μl rat^{-1}) surpasses biliary tree capacity three—to fourfold (Häcki & Paumgartner, 1973), it is suggested that percent recoveries in the first 2·5 min after retrograde injection of ^{35}S-BSP reflect also the amount of reabsorbed dye, i.e. the difference between administered ^{35}S-BSP (4·8 nmol and 1·2 μmol respectively) and percent recoveries in the first 2·5 min after retrograde administration indicates the extent of reabsorption.

According to the results summarized in Table 1, a constant intravenous infusion of unlabelled BSP within the T_m-range had no effect on the biliary reabsorption of ^{35}S-BSP given retrogradely at either 4·8 nmol or 1·2 μmol. Interestingly, regarding the percent recoveries in the first 2·5 min after retrograde injection, no difference in the extent of biliary reabsorption of 4·8 nmol ^{35}S-BSP could be detected when this dose was administered retrogradely under T_m-conditions, i.e. when a concentration gradient against hepatocytes and bloodstream has been established. A significant concentration of ^{35}S-BSP was found in the plasma 2·5 min after administration of 4·8 nmol and 1·2 μmol ^{35}S-BSP by the retrograde biliary route.

Whether these findings may be an approach to the concept of an active transport-system which carries ^{35}S-BSP rapidly out the biliary system can only be supposed. Little is known about the site of absorption after the retrograde injection. According to histological findings when india ink is used as a marker most probably only the ductular region is reached after retrograde injection of microlitre quantities (Dammann, Süssenbach & Czok, 1976). Thus, if bile ducts and ductules ought to be the main site of reabsorption, whether a concentration gradient against the ductular epithelium is achieved under the experimental conditions used remains unresolved. Furthermore it cannot be ruled out that after retrograde injection a leakage of the compound into the systemic circulation occurs depending on the increased intrabiliary pressure occurring during the course of injection (Fujimoto, 1975).

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