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COMMUNICATIONS

The flow properties of microcrystalline cellulose powders

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Conflicting opinions have been expressed on the flow properties of microcrystalline cellulose powders. Fox, Richman & others (1963) using a commercial grade of microcrystalline cellulose, Avicel (F.M.C. Corporation, Marcus Hook, Pa.), concluded that these powders were free flowing. Later work (Mendell, 1972; Bolhuis & Lerk, 1973) showed that two grades of Avicel, PH 101 and PH 102, possessed very poor flow properties.

To clarify this situation, we have examined the flow properties of the tableting grades of Avicel, the two mentioned in the previous paragraph and grades PH 103 and PH 105, by three different techniques. A direct measurement, simulating conditions in feeding the dies of a tablet machine, namely that of the vertical flow of the powder through an orifice, was used. From this the minimum aperture size through which flow would take place was determined. An indirect method of measurement, the Jenike shear cell, was also used. This enabled the coefficient of internal friction, the cohesiveness and the Jenike flow factor to be found. This factor indicates the resistance to flow once this has been initiated and decreases in value as the cohesiveness of the powder increases. Our procedure for the determination of the angle of repose of these powders was based essentially on that of Train (1958) and used the fixed height and fixed base techniques. As the Avicels would not flow freely, Train's original method had to be slightly modified in that the powder was allowed to flow from a tube 38 mm diameter for the fixed height method. No simple reproducible technique could be found for the fixed base method using pure Avicel powders, but it was successful at a later stage when studying Avicel/spray dried lactose mixtures.

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The results obtained are given in Table 1. The results for spray dried lactose, conditioned as for the Avicels, are included for comparison.

From Table 1 it can be seen that none of the Avicels are free flowing. These powders have been previously characterized (Marshall & Sixsmith, 1974) and from a consideration of their particle sizes and shapes, their order of cohesiveness is as would be expected. Avicel PH 102 consisting of large irregular masses of particles forming a granular type of powder would be expected to be the least cohesive. PH 102 would flow more freely than grades PH 101 and PH 103 which are composed of a mixture of smaller irregular masses and rod shaped particles. The differences between PH 101 and PH 103 are caused by their different initial moisture contents. These grades would be expected to flow more freely than Avicel PH 105 which is composed almost entirely of small rod like particles, interlocking of which would create a great resistance to flow. All the Avicels are more cohesive than spray dried lactose, whose excellent flow properties are attributable to its large regular shaped particles.

It has also been reported (Fox & others, 1963) that Avicel, in concentrations above 50% w/w exhibits glidant properties. We have studied the effect of lower concentrations of Avicel on the flow properties of Avicel PH 101/spray dried lactose mixtures using the vertical flow of powder through an orifice, Jenike shear cell and angle of repose techniques mentioned previously.

The results of this investigation are given in Table 2. These show that addition of up to 4% w/w Avicel PH

Table 1. *The flow characteristics of the Avicels.*

Avicel PH grade	Median Stokes diameter (μm)	Co-efficient of internal friction			Cohesiveness kN m^{-2}	Flow factor	Blocking aperture size (cm)
		Fixed height	Fixed base	Shear cell			
102	62	1·19	—	0·65	0·113	9·2	Irregular flow
101	37	1·28	—	0·73	0·112	6·9	None would flow from the largest diameter orifice available (2·5 cm)
103	36	1·28	—	0·73	0·112	5·4	
105	25	1·43	—	0·83	0·320	2·8	
Spray dried lactose	136	0·90	1·32	0·52	0·047	12·4	1·0

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	Powder will not flow through largest diameter orifice (2·5 cm)

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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REFERENCES

BOLHUIS, G. K. & LERK, C. F. (1973). *Pharm. Weekblad.*, **108**, 469–481.
FOX, C. D., RICHMAN, M. D., REIER, G. E. & SHANGRAW, R. (1963). *Drug Cosmet. Ind.*, **92**, 161–164; 258–261.
MARSHALL, K. & SIXSMITH, D. G. (1974). *Drug Development Communications*, **1**, 51–71.
MENDELL, E. J. (1972). *Mfg. Chem. Aerosol News*, **43**, 43–46.
TRAIN, D. (1958). *J. Pharm. Pharmac.*, **10**, *Suppl.* 127T–137T.

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–