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The action of colloidal silicon dioxide as a glidant for lactose, paracetamol, oxytetracycline and their mixtures

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Anomalies are observed in some of the physical and mechanical properties of mixtures of lactose, paracetamol and oxytetracycline when small amounts of colloidal silicon dioxide are added to them. Owing to its differing propensities to coat the particles of the host powders, the silicon dioxide acts as a glidant for the lactose and paracetamol, but as an antiglidant for the oxytetracycline.

Glidants are frequently employed in the handling and processing of cohesive powders in order to improve their flow properties. Those used in Pharmacy include colloidal silicon dioxide, talc, calcium phosphates and various metallic stearates (Burak, 1966; Pilpel, 1971).

Several workers have investigated the addition of glidants to a variety of single powders and mixtures of powders and measured the changes produced in their flow-ability, angle of internal friction, angle of repose, porosity, bulk density, shear and tensile strength (Craik & Miller, 1958; Pecht, 1961; Tawashi, 1963; Nash, Leiter & Johnson, 1965; Ohodaira, 1965; Jones & Pilpel, 1966; Gstirner & Pick, 1969; Ogawa, Hirayama & Nakajima, 1970; Kristensen, 1971; Pelez & Mannheim, 1973).

The effects produced by different glidants depend: (a) on their chemical nature in relation to that of the host material, i.e. on the presence of unsaturated valency, ionic or hydrogen bonds on their respective surfaces which could interact chemically and (b) on physical factors. These include the size and shape distributions of both the glidant and host particles, the moisture content, temperature and the amount of consolidation that may be applied to the sample (Pilpel, 1971).

In general, hydrophilic glidants tend to be more effective on hydrophilic powders than on hydrophobic powders and the opposite occurs with hydrophobic glidants (Burak, 1966).

For any particular system there is usually an optimum concentration above which the glidant may start to act as an antiglidant (Kristensen, 1971). This optimum depends amongst other things on the moisture level in the sample and it may be related to the glidants' propensity to act also as an anticaking agent (Burak, 1966).

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We recently showed (Varthalis & Pilpel, 1976) that anomalies occurred in the properties of certain powders—in their apparent particle size, tensile strength and angle of internal flow—when a second component was added to them in increasing amounts This was ascribed to a rearrangement of the particles and a change in their packing structure.

Since one of the mechanisms which appears to be involved in the action of a glidant is a change in the packing arrangement of the particles, we have investigated whether the addition of a typical glidant to some of the powders previously examined might also produce anomalies in their properties.

An objective of the present work was to see whether any connection could be established between anomalous behaviour and the amount of glidant required to produce optimum flowability in a powder.

Colloidal silicon dioxide was selected as a representative glidant. It was added in amounts up to 1·5% (w/w) to several powders and mixtures of powders and certain of their physical and flow properties were then measured.

MATERIALS AND MIXTURES

The materials used were paracetamol B.P. microcrystalline powder from Bush Ltd., oxytetracycline dihydrate B.P. microcrystalline powder from ICI Ltd., lactose B.P. fine powder from Whey Products and colloidal silicon dioxide (Cab-o-cil M5) from the Cabot Corporation.

Free water was removed by heating the materials to constant weight at 60°. Some of their relevant properties are listed in Table 1.

Mixtures containing up to 1·5% added silicon dioxide, with the compositions shown in Table 2, were prepared by mixing the ingredients for 0·5 h in a rotating bottle. The progress of the mixing was monitored by successive measurements of the particle size until it became constant, corresponding

Table 1. *Properties of materials.*

Material	Mean particle diam. d_{vs}(μm)	Range of diam. μm	Wt. loss (2 h at 60°) % dry basis	*Appar. true dens. kg m^{-3} × 10^{-3}
Lactose(L)	23	5–50	0·5	1·55
Paracetamol(P)	20	0–40	1	1·29
Oxytetracycline(OTC)	16	0–40	2	1·45
Colloidal silicon dioxide M5(A)	0·01	0–0·1	1	2·20

* Determined by liquid displacement.

to a particular degree of mixing. This degree of mixing was checked by analysis and was found generally to be >0·95 after 0·5 h.

Apparatus and procedure

The surface volume particle diameters, d_{vs}, of the samples were determined with a Fisher sub sieve sizer at porosities between 0·4 and 0·5 (Allen, 1975). The tensile strengths of their compressed beds were measured in a tensile tester (Ashton, Cheng & others, 1965) at different packing fractions, Pf, and the values were extrapolated to a fixed packing fraction of 0·5.

The packing fractions or porosities E = (1-Pf) were also measured after subjecting the samples to various numbers of taps in a cylindrical container (British Standard, 1460) and the results were converted to values of angle of internal flow.

Fuller details of the experimental procedure and of the derivation of the parameters d_{vs}, T and Θ are given by Varthalis & Pilpel (1976).

RESULTS

Fig. 1 shows how the measured particle diameter of a typical mixture P25 + 0·5A (see Table 2) varied with mixing time, the limiting value of d_{vs}, attained after about 0·5 h corresponding to a degree of mixing >0·95. This type of behaviour has been

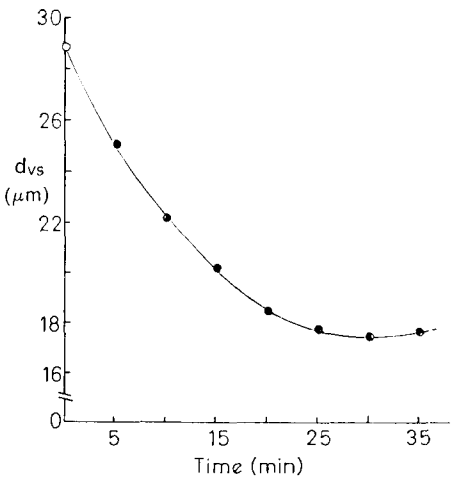

FIG. 1. Mean particle size d_{vs} (μm) versus time of mixing for P25 + 0·5A. ● Measured. ○ Measured on unmixed ingredients layered in correct proportion.

observed in other mixtures (see e.g. Fig. 6 in Varthalis & Pilpel, 1976) and can be explained as due to a gradual change in the packing arrangement of the particles.

Additions of up to 1% of silicon dioxide to the lactose, to the paracetamol and to the lactose/paracetamol mixtures caused decreases in their measured particle size, in their tensile strengths (at the fixed Pf = 0·5) and in their angles of internal flow. But with more silicon dioxide, the values tended to increase again and typical results are illustrated in Figs 2–4.

The silicon dioxide produced similar effects on the particle diameters of all the oxytetracycline mixtures, see Fig. 5, but when these mixtures contained more than 25% of antibiotic, there was a change in the pattern of behaviour of the other parameters so that both the tensile strength and the

Table 2. *Composition of mixtures.*

System		Notation: Silicon dioxide (A) % in system 0	0·5	1·0	1·5
Lactose L		L	L + 0·5A	L + 1A	L + 1·5A
Paracetamol	P	P	P + 0·5A	P + 1A	P + 1·5A
75%	L 25%	P75	P75 + 0·5A	P75 + 1A	P75 + 1·5A
50	50	P50	P50 + 0·5A	P50 + 1A	P50 + 1·5A
25	75	P25	P25 + 0·5A	P25 + 1A	P25 + 1·5A
Oxytetracycline	OTC	OTC	OTC + 0·5A	OTC + 1A	OTC + 1·5A
75%	L 25%	OTC75	OTC75 + 0·5A	OTC75 + 1A	OTC75 + 1·5A
50	50	OTC50	OTC50 + 0·5A	OTC50 + 1A	OTC50 + 1·5A
25	75	OTC25	OTC25 + 0·5A	OTC25 + 1A	OTC25 + 1·5A

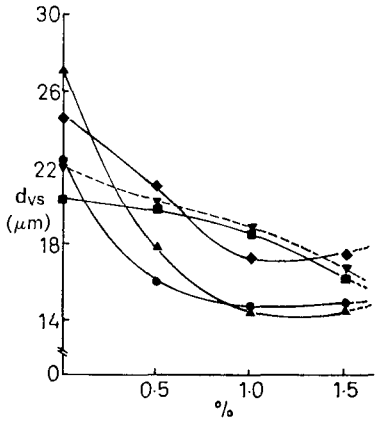

FIG. 2. Mean particle size d_{vs} (μm) versus % silicon dioxide for paracetamol/lactose mixtures. ● = L. ▲ = P25. ◆ = P50. ▼ = P75. ■ = P.

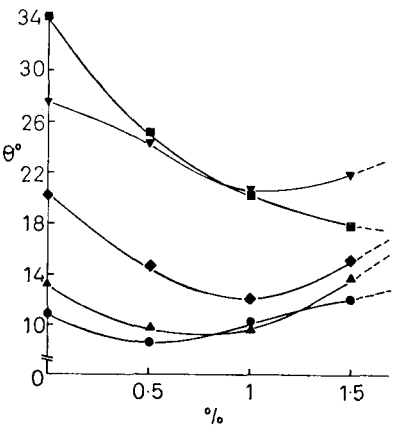

FIG. 4. Angle of internal flow (Θ) versus % silicon dioxide for paracetamol/lactose mixtures. ● = L. ▲ = P25. ◆ = P50. ▼ = P75. ■ = P.

angle of internal flow increased with increasing additions of the silicon dioxide (Figs 6 and 7).

In passing it may be mentioned that the same relation between tensile strength, Θ and the number of taps applied in the tapping experiments (i.e. equation 9 Varthalis & Pilpel, 1976) was found to apply to the present three component mixtures containing silicon dioxide as to the previously investigated two component mixtures.

DISCUSSION

It is apparent from the results that the silicon dioxide produces essentially different effects on the tensile and flow properties (though not on the measured particle sizes) of lactose, paracetamol and mixtures of lactose/paracetamol on the one hand and on oxytetracycline and the mixtures of it with lactose containing more than 25% of antibiotic on the other.

On the former systems, the silicon dioxide is acting as a glidant, causing a decrease in their tensile strength and angle of internal flow. The maximum glidant effect occurs at a concentration between 0·5 and 1·0% (somewhat higher for paracetamol alone, presumably because of its smaller particle size and therefore larger surface area to be coated—see Table 1).

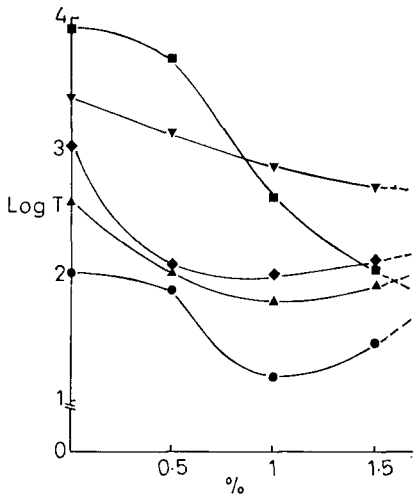

FIG. 3. Log T versus % silicon dioxide for paracetamol/lactose mixtures ● = L. ▲ = P25. ◆ = P50. ▼ = P75. ■ = P.

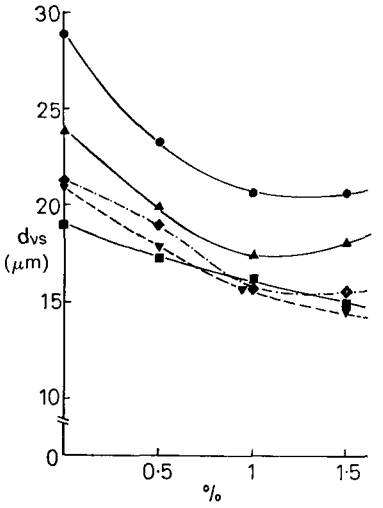

FIG. 5. Mean particle size d_{vs} (μm) versus % silicon dioxide for OTC/lactose mixtures. ● = L. ▲ = OTC 25. ◆ = OTC 50. ▼ = OTC 75. ■ = OTC.

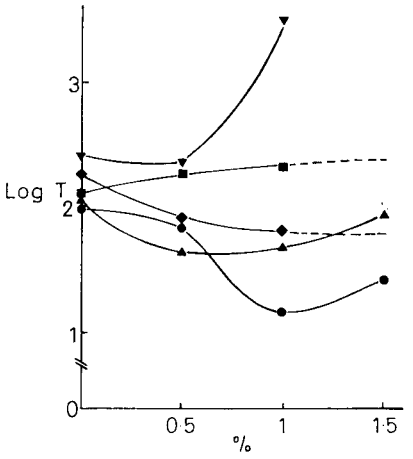

FIG. 6. Log T versus % silicon dioxide for OTC/lactose mixtures at Pf = 0·5. ● = L. ▲ = OTC 25. ◆ = OTC 50. ▼ = OTC 75. ■ = OTC.

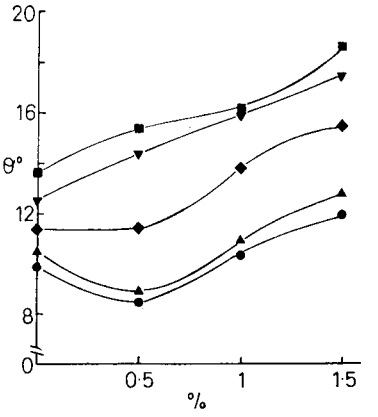

FIG. 7. Angle of internal flow Θ versus % silicon dioxide for OTC/lactose mixtures. ● = L. ▲ = OTC 25. ◆ = OTC 50. ▼ = OTC 75. ■ = OTC.

But in the oxytetracycline systems (with the exception of the most dilute i.e. OTC 25) the silicon dioxide is acting in the opposite sense, as an anti-glidant and is actually making the mixtures less free flowing than before, so that Θ increases.

It is believed that silicon dioxide acts as a glidant by covering the surface of the host powder, filling irregularities, reducing the cohesive and frictional forces between the particles and altering their packing arrangement.

Part of its action may also be to reduce the amount of capillary bonding which could arise from adsorbed films of moisture in the host powder even after drying (Krupp, 1967).

The extent to which the silicon dioxide will adhere to and coat the surfaces of powders or powder mixtures will depend on whether these are hydrophilic or hydrophobic. Cab-o-cil M5 is essentially hydrophilic, due to the presence of hydroxyl and hydrogen bonded hydroxyl groups on its otherwise hydrophobic siloxane surface. It appears to be compatible with paracetamol and with lactose, both of which are essentially hydrophilic. But it seems less able to spread uniformly over the surface of oxytetracycline and therefore act as a glidant because this material has a more hydrophobic surface, as demonstrated by its very much lower solubility in water and its behaviour as seen in electron micrographs.

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