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COMMUNICATIONS

The effect of the shape of fine particles on the formation of ordered mixtures

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Abstract—A study has been made of the effects of the shape of fine particles on the formation and stability of some ordered mixtures using a specially constructed Y mixer. Irregular particles adhere to indentations on the surface of the carrier particles and form stable ordered mixtures.

The mixing of two materials with free-flowing particles of similar size and density usually produces a random mixture. In contrast, when one or both components are cohesive, ordered mixtures may be formed (Hersey 1975; Yeung & Hersey 1979). Ordered mixtures, consisting of a microfine drug adsorbed onto coarser particles of an excipient, offer significant advantages in the manufacture of certain solid dosages (Hersey 1975), particularly those containing very small quantities of the drug.

The mixing of particles is influenced by their size (Crooks & Ho 1976), size distribution (Thanomkiat et al 1979), shape (Ridgway & Rupp 1970), flow properties (Hersey 1979) and other variables (Hersey 1979). Meloy (1984) demonstrated that, in powders produced by comminution, the smaller the particles the more irregular their shape.

The object of the present work was to investigate the effect of the shape of fine particles on the formation and stability of some ordered mixtures.

Little quantitative work has been done on this particular topic due to the difficulty of sorting fine powders into different shape fractions when the particles are below 30 μm in diameter (Pang & Ridgway 1980).

Materials and methods

Lactose EPD10 (supplied by Forum Chemicals Ltd) was chosen as the excipient. The 500–710 μm size fraction obtained by sieving was shape sorted on a Jeffrey Gallion shape sorting table (Ridgway & Rupp 1969) and essentially spherical particles were collected from pots 1, 2 and 3. Two grades of calcium carbonate SH and SL from Sturge Chemicals were used as model drugs (Nikolakakis & Pilpel 1985).

Both the lactose and the calcium carbonate were dried at 60 °C for 6 h to ensure a moisture content below 1% w/w. The particle densities of the powder ρ_s, g cm^{-3}, were determined with a Beckman air comparison pycnometer (Beckman instrument model 930); their surface areas, S_w m^2 g^{-1}, were measured with a sorptometer (Perkin Elmer model 212 C). The shape coefficient, α, was calculated from the equation (Nikolakakis & Pilpel 1985)

$$\alpha = \rho_s S_w d_e + N \quad (1)$$

where d_e is the Heywood equivalent diameter

$$= \frac{(4 \times 0{\cdot}77 \times B \times L)^{\frac{1}{2}}}{\pi} \mu m$$

and N is the elongation ratio

$$= \frac{\text{length, L}}{\text{breadth, B}}.$$

The properties of the calcium carbonate are given in Table 1.

Table 1. Properties of calcium carbonate.

	Material and code	
	Calcium carbonate SH (precipitated aragonite)	Calcium carbonate SL (precipitated calcite)
Particle density ρ_s g cm^{-3}	2·66	2·66
Mean Heywood diameter d_e μm	3·7	4·0
Elongation ratio N	1·4	1·3
Specific surface area m^2 g^{-1} S_w	5·0	3·5
Average shape coefficient α	50·6	38·5

Calcium carbonate (1 g) was mixed with 200 g of the lactose granules in a small Y cone mixer. This consists of a metal cylinder with a wedge-shaped knife at one end (see Fig. 1). The mixer was operated at 45 rev min^{-1}. During mixing, ten 250 mg samples were removed at time intervals of 1, 2, 5, 10, 15, 30 and 60 min using a sampling thief, taking five samples from the surface and another five from near the bottom of the container. The concentration of calcium carbonate in each sample was determined by atomic absorption spectroscopy (Instrumentation Laboratory Inc. USA Model I.L. 151). At the end of the mixing period the residual material was subjected to 60 min vibration on a Fritsch Laborette vibrator, after which ten samples were taken as described above, and the calcium carbonate in each sample was determined.

Results and discussion

Fig. 2 is the graph of the standard deviation of the samples' concentration of calcium carbonate σ, plotted against the time of mixing. The acceptable standard deviation σ_A with 95% confidence within $\pm$10% of the mean χ calculated using equation 2 (Crooks & Ho 1976) was included on the ordinate of the graph.

$$1{\cdot}96\ \sigma_A = \pm 0{\cdot}10\chi \quad (2)$$

It is seen that during the 1 h period of mixing, the standard deviation profiles for the two samples of calcium carbonate were similar. Both required about 10 min to reach the acceptable standard deviation, σ_A. However, after the final mixtures had been subjected to continuous vibration for 1 h, the standard deviation for sample SL was much higher (i.e. 0·69) than that of SH (0·28). This shows that the mixture containing the calcium carbonate SH is more stable towards mechanical vibration.

Figs 3 and 4 are photomicrographs of individual particles of calcium carbonate SL and SH, and show that the latter is much

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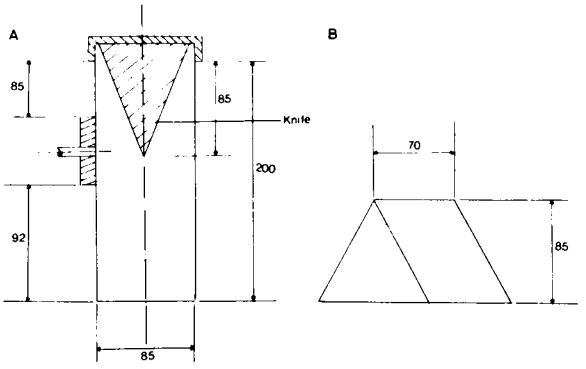

FIG. 1(A) Section view of the Y mixer (all dimensions in mm).

FIG. 1(B) Side view of the wedge-shaped knife (all dimensions in mm).

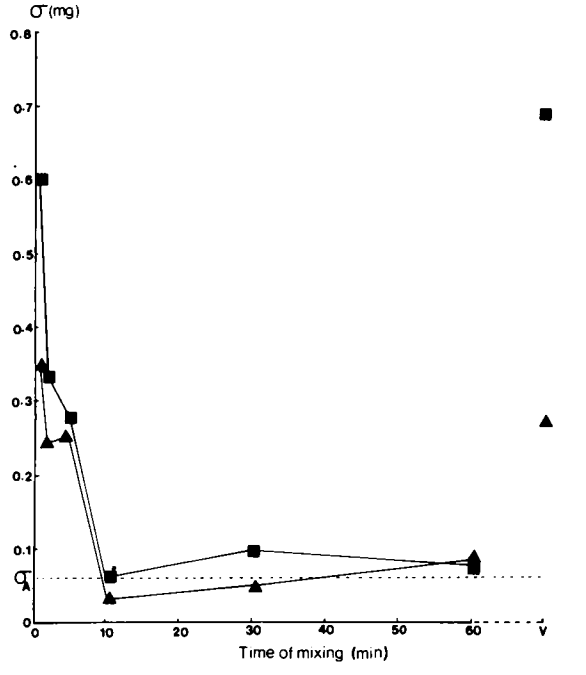

FIG. 2. Standard deviation σ versus time of mixing of lactose and calcium carbonate. (Standard deviation of calcium carbonate ■ SL, ▲ SH). V denotes after 1 h vibration.

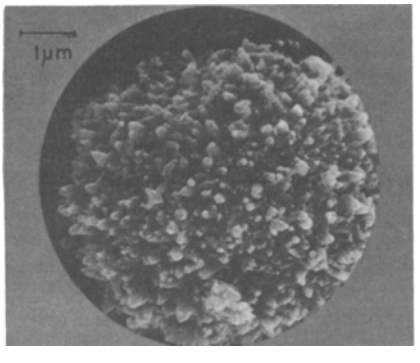

FIG. 3. Individual particle of calcium carbonate SL.

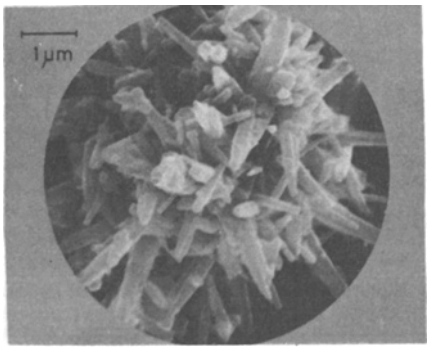

FIG. 4. Individual particle of calcium carbonate SH.

more irregular than the former, and therefore has more adhesive contact points with the lactose carrier. This explains why, after the mixture had been vibrated, the standard deviation for sample SH was much lower than that of sample SL, indicating greater stability of the mixture towards segregation.

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