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# The packing characteristics of physical and formulated mixtures of oxytetracycline and lactose powders

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Measurements have been made of the tap densities and angles of internal flow of physically mixed and formulated mixtures of oxytetracycline and lactose powders. The differences between the two types of mixtures are ascribed to differences in the packing and surface morphologies of the particles.

In the present investigation oxytetracycline and lactose powders have either been mixed together in different proportions (physical mixtures) or first mixed and then granulated with water (formulated mixtures). The packing of the two types of mixtures, after milling the particles to less than 50 μm diameter, and containing 1–2 and 3·5–4·5% w/w moisture have been compared by measuring their densities after tapping. The ease with which the particles can move past each other and rearrange their positions has been tested by calculating their angles of internal flow.

*Materials and methods*

*Materials.* The materials used were the same as in a previous investigation (Adeyemi & Pilpel 1984).

*Methods.* Batches of oxtetracycline dihydrate and lactose were dry mixed in various proportions to produce a range of physical mixtures. Further batches were wet granulated to produce formulated mixtures in the same proportions. Each mixture was prepared at two ranges of moisture content (1–2 and 3·5–4·5% w/w) and also milled down to <50 μm in a standardized manner to minimize as far as possible electrical and surface energy effects besides those of surface morphology. All the samples were kept in airtight bottles. Their compositions, code numbers and physical properties have already been given (Adeyemi 1981; Adeyemi & Pilpel 1984). Y denotes oxytetracycline, L lactose, $M_1$–$M_3$ are the physical mixtures containing 25, 50 and 75% (w/w) of lactose, respectively, $M_4$–$M_6$ are the corresponding formulated mixtures.

The packing fractions produced after tapping were measured using the standard apparatus (Scientific Development, Romford) described by Newmann (1967). The packing fraction ($P_F$) was calculated as

$$P_F = \frac{\text{Bulk density}}{\text{Particle density}} \quad (1)$$

taking the mean of four replicates which differed by not more than ± 2 standard deviations (BS 1450, 1948).

*Results and discussion*

Typical results in Fig. 1 show that the tap density (expressed by the packing fraction, $P_F$) becomes constant after about 100 taps, t. At any value of t the formulated mixtures have higher $P_F$ than the corresponding physical mixtures.

The effect of increasing the moisture content from 1–2 to 3·5–4·5% w/w was to reduce $P_F$ for all mixtures on average about 20%. This can be ascribed to the particles becoming more cohesive and thus less able to pack together during tapping.

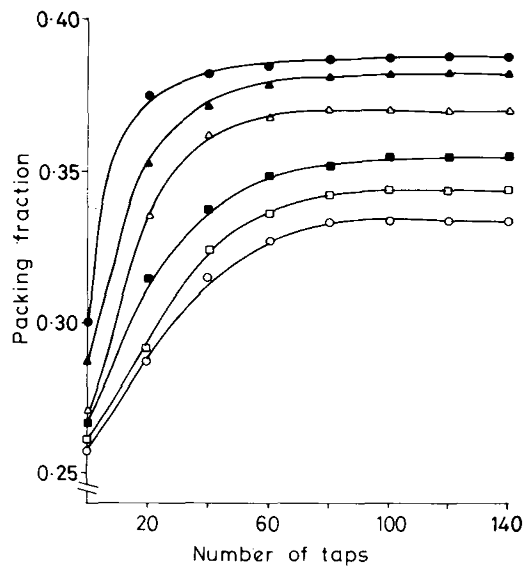


FIG. 1. Packing fraction versus number of taps for physical and formulated mixtures. Moisture content <2% (w/w). Key: ○ Y, □ $M_3$, ● L, ▲ $M_4$, △ $M_1$, ■ $M_6$.

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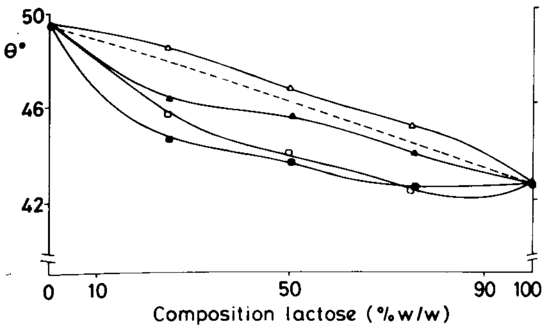


FIG. 2. Angle of internal flow θ versus composition of mixtures (w/w). Physical mixtures, moisture △ 1–2%, ▲ 3·5–4·5%. Formulated mixtures, moisture □ 1–2%, ■ 3·5–4·5%. – – – Theoretical line.

Plotting $(1 - P_F)^2 t/P_F$ versus t yields a series of straight lines from which values of the angle of internal flow, θ were obtained as described by Varthalis & Pilpel (1976). These are plotted against composition in Fig. 2. It is seen that θ deviates from the values calculated by the simple additive rule (shown by – – –) by an amount which depends on the moisture content and this is ascribed to changes in the packing arrangement of the particles as the composition of a mixture is altered (Varthalis 1975). Lactose and oxytetracycline granules have essentially different surface morphologies, as illustrated in Fig. 3a, b. The overall surface in the formulated mixtures is smoother than in the physical mixtures, as shown by comparing Fig. 3c, d. This would explain their higher tap densities and their lower angles of internal flow.

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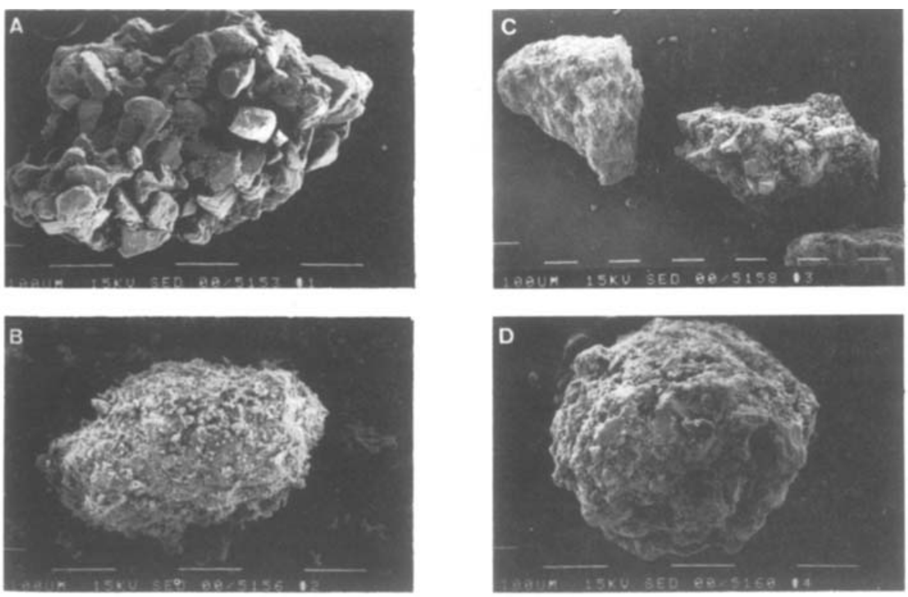


FIG. 3. Electronmicrographs of unmilled granules scale 10 μm. (A) Sample L. (B) Sample Y. (C) Sample $M_3$. (D) Sample $M_6$.