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Effect of particle size on the compaction mechanism and tensile strength of tablets

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The effect of particle size variation on tablet tensile strength for spray-dried lactose, Sta-Rx 1500 and Avicel PH-101 was investigated. Decreasing the particle size of spray-dried lactose and Sta-Rx 1500 resulted in stronger compacts whereas the tablet tensile strength of Avicel PH-101 was unaffected by particle size variation. The Heckel relationship, at two different contact times, was used to examine the predominant compaction mechanism. This was independent of the size fractions studied for all three materials. Angle of repose and Hausner ratio measurements indicated a correlation between the internal forces of friction and cohesion of the sized powders and the tensile strength of compacts formed from them.

Directly compressible materials are widely used as excipients in the pharmaceutical industry. In the present study it was intended to examine the effect of particle size variation on the tensile strength of compacts formed from spray-dried lactose, Sta-Rx 1500 and Avicel PH-101. Furthermore, since changes in particle size distribution might well change the predominant compaction mechanism (Gregory 1962), the Heckel relation was employed to investigate this effect (Heckel 1961).

It has been suggested that powder compaction at higher pressures may be classified into three types, termed A, B and C (York & Pilpel 1973). Type A behaviour is characteristic of a material which consolidates mainly by plastic flow, whereas Type B represents a material which deforms by fragmentation. Type C behaviour is indicated by a low value of mean yield pressure and rapid approach to unit packing fraction at low pressures when the Heckel relation becomes invalid. However, caution is required when attempting to classify compaction behaviour on the basis of changes in the Heckel plots with particle size (Rue & Rees 1978). This is due to variations in the Heckel curves depending on the technique employed. Therefore, Heckel curves have been drawn for two different contact times and the areas under the curves estimated to provide a quantitative measure of the amount of plastic deformation occurring within the materials studied.

MATERIALS AND METHODS

Preparation of powders

Three directly compressible materials, spray-dried lactose (Searle & Co Ltd), Avicel PH-101 (F.M.C. Corp.) and Sta-Rx 1500 (Colorcon Ltd) were used. Sieving was undertaken using a bed of test sieves (Endecott Ltd) on a mechanical vibrator (Pascall Engineering Co Ltd). Particle density determinations were made using the specific gravity bottle method.

Before experimentation, powders were stored in airtight containers. The different particle size ranges were examined for shape variation using the scanning electron microscope.

During processing the powders were handled in a relative humidity of 50–55%. The equilibrium moisture content of the powders under these conditions were as follows; spray-dried lactose 2·4% w/w, Avicel PH-101 6·7% w/w, Sta-Rx 1500 11·7% w/w. Moisture determination was undertaken by drying to constant weight at 100 °C. Higher temperatures tended to cause sample discolouration.

Preparation of tablets

Tablets were produced using an instrumented Manesty F3 single punch machine with flat faced punches (1 cm diameter). When required, lubrication of tooling was undertaken by dusting with magnesium stearate. The rate of compaction was 0·1 cm s^{-1} and the tablets were formed by filling the die with 0·4 g of the required powder. Ten tablets were prepared at each machine setting.

Tensile strength measurements

Tablet crushing strength was determined (after 1 h) using a calibrated Strong-Cobb hardness tester and values were converted into tensile strength using the method of Fell & Newton (1970). The mean of ten determinations was used.

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Heckel plots

Several equations have been used to examine the compaction of powders (Walker 1923; Bal'shin 1938; Heckel 1961). The Heckel relation was used in this study and is given in equation (1):

$$\ln\left(\frac{1}{1 - \rho f}\right) = KP + A \qquad (1)$$

Where P is the applied pressure, A is a constant, K = 1/Py where Py is the mean yield pressure, ρf is the packing fraction and is equivalent to ρ_B/ρ_P where ρ_B is the bulk density and ρ_P is the particle density.

The Heckel plots were determined at two different contact times (1 and 10 s) using the tablet press. The areas under the Heckel curves were estimated using the trapezoidal rule. Tablet density was measured following ejection from the die (after 1 h).

Angle of repose

The powder (30 g) was carefully poured into a dry glass funnel whose sealed tip (diameter 0·75 cm) was suspended 6 cm from the working surface. The seal was removed and the powder allowed to flow onto a sheet of parchment under the force of gravity. The height and diameter of the cone were measured. The mean result of six determinations was used. The angle of repose (α°) can be obtained from equation (2):

$$\tan \alpha^\circ = \frac{h}{0{\cdot}5\,d} \qquad (2)$$

Where h is the height of the cone and d is the diameter.

Hausner Ratio determination

The Hausner Ratio is defined as the ratio of the tap density to the apparent density of a powder mass. It was determined by the method of Hausner (1967).

RESULTS AND DISCUSSION

It was considered that rather than report tablet strength as hardness (i.e. fracture force) it would be better to express these results as tensile strength (Fell & Newton 1970) since the latter is independent of tablet dimensions and is a measure of the compact's strength (Newton et al 1971; Ridgway et al 1972). It is clear from Fig. 1 that particle size variation has a marked effect on the tensile strength of spray-dried lactose tablets. A decrease in particle size caused a concomitant increase in compact strength particularly at higher compressional forces. Above a pressure of approximately 140 MNm^{-2} capping and lamination began to occur. It was noted that the higher tensile strength of the smaller particle size

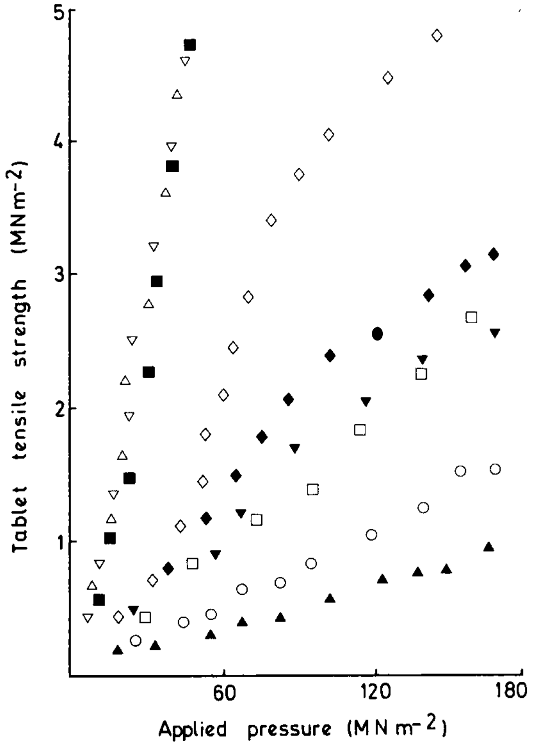


FIG. 1. Relation between applied pressure and tensile strength of tablets prepared from different size fractions of spray-dried lactose, Sta-Rx 1500 and Avicel Ph-101. □ = 0–45 μm, ○ = 90–125 μm, ▲ = 180–250 μm Spray-dried lactose. ◇ = 0–45 μm, ◆ = 90–125 μm, ▼ = 180–250 μm Sta-Rx 1500. ■ = 0–45 μm, ▽ = 90–125 μm, △ = 180–250 μm Avicel PH-101.

compacts was accompanied by a decrease in tablet density (Fig. 2). The Heckel plots, using the 0–45 μm and 180–250 μm size ranges to highlight any variation in the compaction mechanism, indicated that the latter was particle size independent (Fig. 2). Previous workers have suggested that spray-dried lactose deforms mainly by brittle fracture and this theory is supported by the coincidence of the Heckel plots (Fig. 2) for the two different contact times (Hardman & Lilley 1970; Cole et al 1975). The effect of particle size distribution on the angle of repose and Hausner ratio is shown in Table 1. Particle size of spray-dried lactose less than 125 μm exhibited a large increase in the angle of repose. This suggests an increase in cohesive and frictional forces with decreasing particle size (Carstensen 1973) which is further supporting by the concomitant rise in the Hausner ratio. Therefore, it is not surprising, from this point of view, that the smaller particle sizes yield compacts having superior tensile strength. It is possible that the larger particle sizes form the denser compacts

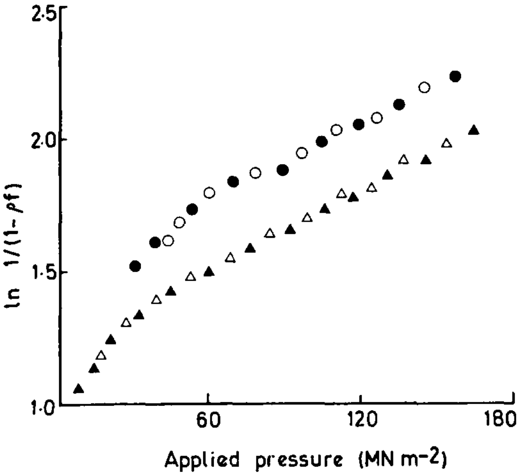
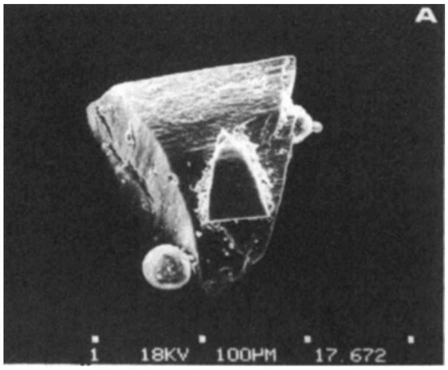


FIG. 2. Relation between natural logarithm $1/(1 - \rho f)$ and applied pressure for two size fractions of spray-dried lactose at two different contact times. ▲ = 0–45 μm, ● = 180–250 μm, contact time 1 s. △ = 0–45 μm, ○ = 180–250 μm, contact time 10 s.

due to shape variations associated with certain size fractions. Fig. 3a and b illustrate the change in particle shape with different size range distributions. It can be seen that the particles tend to become much more spherical in shape with decreasing size. In Fig. 3a the difference in shape between the large and small particles is quite clear. Since the larger particles (180–250 μm) are rather angular in shape

Table 1. Values of α°, angle of repose and Hausner ratio for various size ranges of spray-dried lactose, Sta-Rx 1500 and Avicel PH-101.

Particle size range (μm) Spray-dried lactose	Angle of repose (α°)	Hausner ratio
0–45	38	1·51
45–63	36	1·49
63–90	32	1·38
90–125	24	1·32
125–180	22	1·25
180–250	23	1·19
Sta-Rx 1500		
0–45	36	1·50
45–63	32	1·43
63–90	28	1·37
90–125	27	1·33
125–180	22	1·17
180–250	20	1·09
Avicel PH-101		
0–45	37	1·58
45–63	38	1·50
63–90	38	1·43
90–125	37	1·54
125–180	37	1·43
180–250	38	1·48



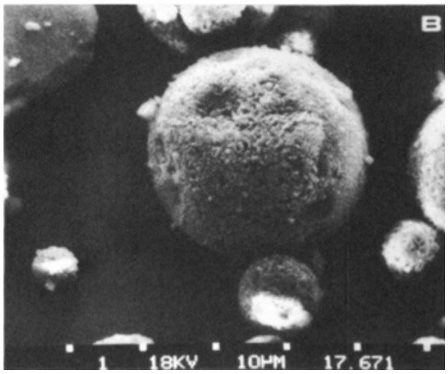


FIG. 3. Electroscanning microscope photographs of (a) spray-dried lactose size fraction 180–250 μm (× 300). (b) spray-dried lactose size fraction 0–45 μm (× 2000).

fragmentation along a variety of slip planes could occur. The smaller fragmented particles would tend to occupy the interparticular voids and thus increase the density of the compact. In contrast, it would be expected that only a relatively small amount of fragmentation would occur in the small particle size fraction (0–45 μm) due to the spherical shape of this material. Furthermore, the increased frictional forces associated with the smaller size ranges would also tend to restrict densification. It might well be argued that increased fragmentation (of the larger size fractions) should result in increased bonding due to the formation of fresh surfaces. However, it has been reported that fragmentation of spray-dried lactose is particularly prevalent close to punch and die surfaces (Hess 1978). This would lead to non-uniform stresses within the compact as well as high levels of static and dynamic die-wall friction during ejection. Under these circumstances although a dense compact would be formed its structural strength would be eroded.

Sta-Rx 1500 exhibited a similar trend to spray-dried lactose. The smallest particle size range

(0–45 μm) gave a marked increase in tablet tensile strength over the entire compression range (Fig. 1). Overall Sta-Rx 1500 yielded harder compacts than spray-dried lactose. Compact density measurements indicated that, in contrast to spray-dried lactose, the smaller particle ranges produced the denser compact. The increase in density is 0–45 μm > 90–125 μm > 180–250 μm. Analysis of the Heckel plots (Fig. 4) indicated that there was no change in compaction mechanism with variation in particle size. However, it can be seen that the material compacted principally by plastic flow (divergence of plots with different contact times). Rue & Rees (1978) have suggested that it is possible to quantify

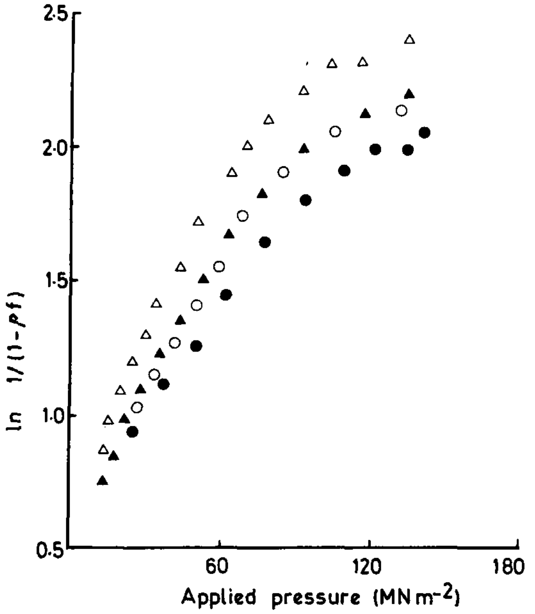


FIG. 4. Relation between natural logarithm 1/(1 − ρf) and applied pressure for two size fractions of Sta-Rx 1500 at two different contact times. Key as in Fig. 2.

the amount of plastic deformation occurring during compaction by measuring the areas under Heckel curves at different contact times. Using this technique it was found that the ratio of areas for the large (180–250 μm) and small (0–45 μm) size ranges was 1:1.38. This implies a greater amount of plastic deformation associated with the smaller particle size range. The angle of repose and Hausner ratio data (Table 1) indicate that there is an increase in interparticulate frictional and cohesive forces with decreasing powder size. These factors could possibly explain the increase in tablet tensile strength with decreasing particle size of Sta-Rx 1500. The concomitant increase in density would result due to the increased amount of plastic flow and packing with decreasing particle size.

The final material which was studied (Avicel PH-101) resulted in observations which were in contrast to those of the previous substances. It can be seen from Fig. 1 that particle size variation had little effect on the tensile strengths of the compacts. Furthermore, Avicel PH-101 exhibited only slight variations in angle of repose and Hausner ratio with changes in particle size (Table 1). These results are somewhat unusual since size distributions normally affect interparticle forces which will influence the angle of repose and Hausner ratio (Nelson 1955; Pilpel 1964). However, in the case of Avicel PH-101 it would appear that cohesion and interparticular frictional forces remain virtually independent of particle size variation. Analysis of the Heckel curves (Fig. 5) indicated that the mechanism of deformation was particle size independent. The slight divergence

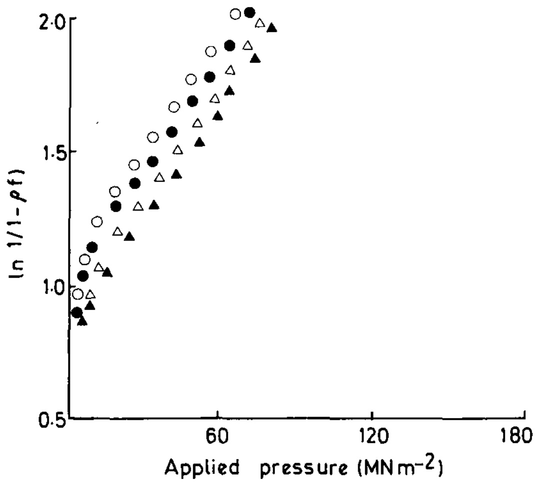


FIG. 5. Relation between natural logarithm 1/(1 − ρf) and applied pressure for two size fractions of Avicel PH-101 at two different contact times. Key as in Fig. 2.

of the curves for the two different contact times indicated plastic flow as the predominant compaction process. Following their stress relaxation studies, David & Augsburger (1977) also suggested that Avicel Ph-101 compacted mainly by plastic flow. It has been proposed that microcrystalline cellulose (e.g. Avicel PH-101) can be visualized as a special form of cellulose fibril in which the crystals are compacted close enough together so that hydrogen bonding can occur (Reier & Shangraw 1966).

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