

# Particle slippage and rearrangement during compression of pharmaceutical powders

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Compression data from different size fractions of lactose, chloroquine diphosphate, stearic acid and calcium carbonate have been analysed using the Walker and the Heckel compression equations. Points of inflection in graphs of log applied pressure *vs* the reciprocal of the packing fraction at low pressures corresponded closely to figures for theoretical packing conditions for equisized spheres and are attributed to a change in the stage of compression. The degree of particle slippage and rearrangement taking place during compression has been shown to increase as the particle size of the powder decreases and to be more extensive for powders composed of non-spherical particles. In addition, three types of compression behaviour have been distinguished for the four powders studied.

The several stages that occur during the compression of powders have been identified by a number of authors (Seelig & Wulff, 1946; Train, 1956; Heckel, 1961a, b; Cooper & Eaton, 1962; Hersey & Rees, 1972) although it is recognized that the different mechanisms may overlap as compression takes place (Cole, Rees & Hersey, 1975) and that no single equation adequately describes the process for all powders. The stages can be listed as follows: (i) filling of the die; (ii) densification by particle slippage and rearrangement; (iii) elastic and plastic deformation of particles; (iv) cold welding, with or without fragmentation.

Although numerous studies have been carried out analysing pressure/density relations, little attention has been paid to investigating and quantifying the initial stages (i) and (ii) of compression. These stages have therefore been examined in detail and the effect of particulate physical properties such as particle size, shape and surface morphology on these mechanisms studied.

The representative pharmaceutical powders examined were four size fractions of each of lactose, chloroquine diphosphate and stearic acid and three size fractions of calcium carbonate. Pressure/density data were analysed using two compression equations which have been successfully applied to distinguish the stages occurring during compression of powders—the relation proposed by Walker (1923) and subsequently modified by Bal'shin (1938), and the Heckel equation (1961a, b).

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## MATERIALS AND METHOD

### *Materials*

The powders used were  $\alpha$ -lactose monohydrate (Whey Products Ltd., Crewe, U.K.), chloroquine diphosphate (ICI U.K.), stearic acid (BDH Chemicals Ltd., Poole, U.K.) and calcium carbonate (J. & E. Sturge Chemicals Ltd., U.K.).

The lactose 0–10  $\mu\text{m}$  fraction was produced by micronizing the supplied powder at 100 lb in<sup>-2</sup> (6.9 MN m<sup>-2</sup>). The remaining fractions of lactose, and those of chloroquine diphosphate and stearic acid were obtained using an air jet sieve with appropriate sieve meshes. The calcium carbonate fractions were classified using an Alpine classifier (by courtesy of the Warren Spring Laboratory, Stevenage, U.K.). Particle density determinations were made using the specific gravity bottle technique.

Before carrying out experiments, powders were dried in a hot air oven at appropriate temperatures to achieve a moisture content less than 0.1% w/w then stored in desiccators over silica gel.

### *Method*

An accurately weighed 2.5 g sample of powder was carefully layered into a 19.0 mm diameter stainless steel die which rested on a flat stainless steel plate. The compression apparatus and procedure previously reported (York & Baily, 1977) was employed, the height of the powder bed being recorded at different applied pressures. The volume of powder under known applied pressures was determined and the packing fraction ( $\rho_p$ ) calculated using the expression  $\rho_p = \rho_B/\rho_B$ , where  $\rho_B$  is the bulk density

and  $\rho_p$  is the effective particle density. Allowance was made for the elastic strain in the apparatus by carrying out preliminary experiments without a powder sample in the die and punch unit. Before each compression, the surfaces of the die and punch were lightly brushed with a 1% w/v suspension of magnesium stearate in carbon tetrachloride to act as lubricant. A minimum of ten compressions were carried out for all size fractions of the powders examined.

#### RESULTS AND DISCUSSION

The compressional data has been analysed using the Walker equation (Walker, 1923) and the Heckel equation (1961a, b).

The Walker equation, as modified by Bal'shin (1938), is given in equation (1), expressing the density in terms of the packing fraction ( $\rho_F$ ):

$$\log P_A = a \frac{1}{\rho_F} + b \quad \dots \quad (1)$$

where  $P_A$  = applied pressure, a, b = constants.

Fig. 1 illustrates plots of  $\log P_A$  vs  $1/\rho_F$  for the smallest size fraction of each of lactose, chloroquine diphosphate, stearic acid and calcium carbonate. The representative graphs show two linear sections with different slopes and this behaviour is observed for all size fractions of the powders. For the stearic acid fractions, a third linear section can be distinguished.

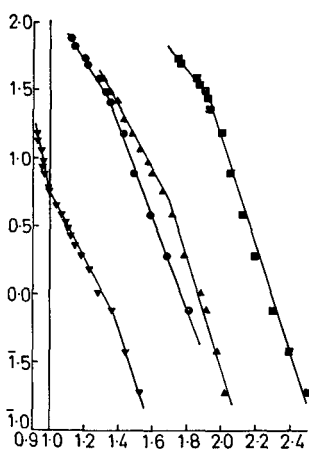


FIG. 1. Relation between the logarithm of applied pressure and the reciprocal of the packing fraction for one size fraction of each of lactose, chloroquine diphosphate, stearic acid and calcium carbonate. ● = lactose 0-10  $\mu\text{m}$ . ▲ = chloroquine diphosphate 0-45  $\mu\text{m}$ . ▼ = stearic acid 0-45  $\mu\text{m}$ . ■ = calcium carbonate 0-3  $\mu\text{m}$ . Ordinate: Logarithm applied pressure ( $P_A$ ) ( $\text{MNm}^{-2}$ ). Abscissa: Reciprocal of packing fraction.

Following Train's interpretation that the point of inflection at low applied pressure corresponds to a change in the stage of compression from interparticular slippage and rearrangement to elastic and plastic deformation (Train, 1956), Table 1 lists values of packing fraction ( $\rho_{F1}$ ) and applied pressure ( $P_{A1}$ ) at this point. Theoretical packing fractions for equisized spheres in regular arrangement (Graton & Fraser, 1935) corresponding most closely to the experimental value of  $\rho_{F1}$  are also given in Table 1.

Table 1. Packing fraction ( $\rho_{F1}$ ) and applied pressure ( $P_{A1}$ ) at change in slope in  $\log \rho_A$  vs  $1/\rho_F$  plots, corresponding theoretical packing fractions, and values of pressing modulus.

Powder and fraction size ( $\mu\text{m}$ )	$\rho_{F1}$	$P_{A1}$ ( $\text{MN m}^{-2}$ )	Theor. packing fraction	Pressing modulus
<b>Lactose</b>				
0-10	0.741	25.12	0.74 (hex.)	1.92
0-45	0.704	13.80	0.70 (rhom.)	2.03
105-150	0.690	9.55	0.70 (rhom.)	2.13
210-295	0.714	8.71	0.70 (rhom.)	2.29
<b>Chloroquine diphosphate</b>				
0-45	0.588	4.73	0.60 (tet.)	2.22
45-125	0.599	3.63	0.60 (tet.)	2.24
125-180	0.595	2.24	0.60 (tet.)	2.34
180-250	0.588	1.91	0.60 (tet.)	2.38
<b>Stearic acid</b>				
0-45	0.741	0.84	0.74 (hex.)	2.34
45-53	0.750	0.79	0.74 (hex.)	2.40
53-75	0.746	0.76	0.74 (hex.)	2.48
75-125	0.730	0.71	0.74 (hex.)	2.52
<b>Calcium carbonate</b>				
0-3	0.521	26.61	0.52 (cubic)	1.55
3-5	0.510	16.60	0.52 (cubic)	1.58
8-12	0.513	11.48	0.52 (cubic)	1.78

Before the slippage and rearrangement of powder particles can take place as pressure is applied, interparticular attractive forces, predominately friction and cohesion, must be overcome. A recent investigation using an instrumented tablet machine has indicated that for unlubricated powder samples, force transmission to the lower punch remained at zero until a certain value of applied pressure had been exceeded (de Blaey, 1972). This suggests that the applied force is initially used to overcome interparticular friction and cohesion, since the loss

of force to the die wall is generally small at low applied pressures (Shotton & Obiorah, 1975). The magnitude of frictional forces will depend on the force required to shear contact points between particles (Bowden & Tabor, 1954). As the applied pressure is raised the frictional force will increase from a minimum and reach a limiting value, at which point sliding will occur (Brown & Richards, 1970). The value of the applied pressure required to effect sliding, and thereby slippage and rearrangement, will be related to the surface structure and size of the particles. Values of  $\rho_{F_1}$  for the two powders containing angular and rough surfaced particles—lactose and chloroquine diphosphate—(see Fig 2a and b respectively) are 0.741 for lactose 0–10  $\mu\text{m}$ , 0.699 (average) for lactose 0–45  $\mu\text{m}$ , 105–150 nm and 210–295  $\mu\text{m}$ , and 0.593 (average) for the four fractions of chloroquine diphosphate. The low figure for the chloroquine diphosphate fractions is

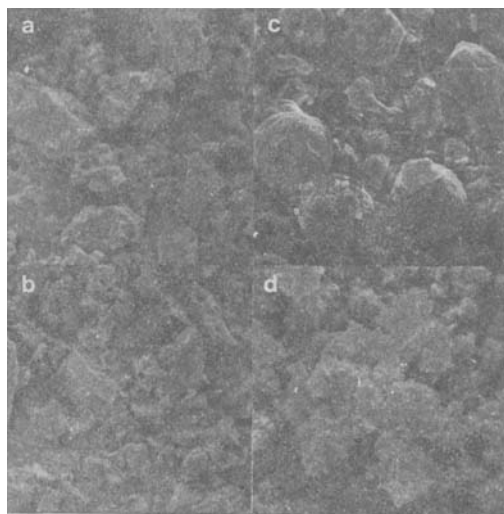


FIG. 2. Electronscanning microscope photograph of A—lactose size fraction 0–45  $\mu\text{m}$  (about  $\times 2200$ ). B—chloroquine diphosphate size fraction 0–45  $\mu\text{m}$  (about  $\times 855$ ). C—stearic acid size fraction 0–45  $\mu\text{m}$  (about  $\times 1900$ ). D—calcium carbonate size fraction 0–3  $\mu\text{m}$  (about  $\times 6500$ ).

attributed to the irregular surfaces which oppose further slippage and rearrangement. The higher figures for lactose, representing close packing conditions, are explained by the fragmentation of particles which has been shown to occur at low applied pressures for this powder (Hardman & Lilley, 1970; Hersey & Rees, 1971). The smaller fragmented particles would tend to occupy the interparticular voids increasing the packing fraction. The lactose 0–10  $\mu\text{m}$  fraction, which attains a packing fraction corresponding to a hexagonal

arrangement, was prepared using a micronizer and this process might produce more spherical particles with smaller surface irregularities thereby facilitating closer packing conditions when pressure is applied.

The high average figure for  $\rho_{F_1}$  of 0.742 for the stearic acid fractions is anticipated from the smooth spherical structure of the particles (see Fig. 2c).

Although calcium carbonate particles exhibit a general spherical structure with a degree of surface irregularity (see Fig. 2d) a low average value of  $\rho_{F_1}$  is observed. The small sized fractions of calcium carbonate have been shown to exhibit high cohesive and frictional forces (Kokova & Pilpel, 1971) which would oppose particle slippage and rearrangement and account for the low observed figure.

Considering  $P_{A_1}$ , it can be seen from Table 1 that the values increase as the particle size of the fraction decreases. This finding is consistent with the fact that there is a larger number of contact points per unit area for small particles compared with large.

The later stages of compression can be analysed from equation (1) by estimating the pressing modulus which is defined as:

$$\log \frac{P_{A_0}}{P_A} \\ \frac{1}{\rho_F} - 1$$

where  $P_{A_0}$  is the extrapolated intercept at the  $\frac{1}{\rho_F}$  axis (Huffine & Bonilla, 1962) and is taken as the gradient of the second linear portion of the graphs shown in Fig. 1. During this section, elastic and plastic deformation are thought to be taking place (Train, 1956).

The values of pressing modulus obtained (see Table 1) increase with increase in particle size. This observation is consistent with previous reports (Huffine & Bonilla, 1962; Fell & Newton, 1971) indicating a larger change in volume for a given pressure increase for the finer powders.

The third linear section observed for the stearic acid fractions at packing fractions greater than unity (explained by extrusion of small amount of material; Lewis & Train, 1965) is attributed to particle rebonding resulting from the creation of fresh surfaces during elastic and plastic deformation (Train, 1956). These changes also reflect the compressibility of the solid material.

The experimental data have also been analysed using the Heckel relation (Heckel, 1961a, b), given in equation (2), in an attempt to distinguish

further the several stages of compression and to determine the degree of densification by particle slippage and rearrangement for the different powders.

$$\ln \frac{1}{1 - \rho_F} = KP_A + A \quad \dots (2)$$

where  $K = \frac{1}{P_Y}$ , where  $P_Y$  is the mean yield pressure

$A = \text{constant}$ .

Graphical representation of equation (2) is shown in Fig. 3 with the initial curvature attributed to particle slippage and rearrangement and the

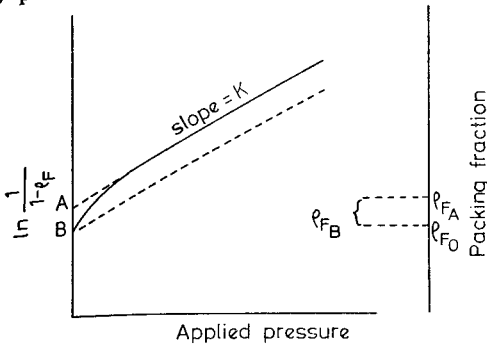


FIG. 3. Graphical representation of the Heckel equation, illustrating derivation of equation constants.

linear section representing compression by elastic and plastic deformation. Use of the packing fraction scale enables the components of the constant,  $A$ , to be distinguished— $\rho_{F_A}$ , densification due to die filling and particle slippage and rearrangement;— $\rho_{F_O}$ , initial powder packing fraction; and  $\rho_{F_B}$ , densification due to particle slippage and rearrangement ( $\rho_{F_B} = \rho_{F_A} - \rho_{F_O}$ ). Representative graphs of  $\ln 1/(1 - \rho_F)$  vs  $P_A$  are illustrated in Fig. 4 for the smallest size fraction of the four powders. The estimated values of  $\rho_{F_A}$ ,  $\rho_{F_O}$  and  $\rho_{F_B}$ , listed in Table 2, indicate that  $\rho_{F_O}$  decreases and  $\rho_{F_B}$  increases as the powder particle size decreases, which is in agreement with other published work for pharmaceutical powders (Fell & Newton, 1971; Hersey & Rees, 1972). Lower values of  $\rho_{F_O}$  are anticipated for smaller sized particles since a larger number of contact points per unit area and higher interparticulate cohesive forces exist at zero pressure which oppose dense packing conditions. Where particles have smooth surfaces this particle size effect might be expected to be reduced and this is substantiated by the similar values of  $\rho_{F_O}$  for the different stearic acid fractions.

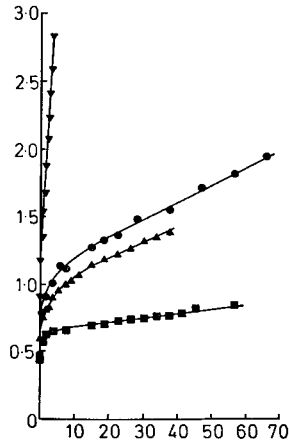


FIG. 4. Relation between natural logarithm  $1/(1 - \rho_F)$  and the applied pressure for one size fraction of each of lactose, chloroquine diphosphate, stearic acid and calcium carbonate. Key as in Fig. 1. Ordinate:  $\ln 1/(1 - \rho_F)$ . Abscissa: Applied pressure ( $\rho_A$ ) ( $\text{MN m}^{-2}$ ).

Particle shape also influences the magnitude of  $\rho_{F_B}$ . The fact that the values decrease as the particles become more spherical supports the concept that  $\rho_{F_B}$  represents the densification due to particle slippage and rearrangement since spherical particles

Table 2. Values of  $\rho_{F_A}$ , densification due to die filling and particle slippage and rearrangement;  $\rho_{F_O}$ , initial powder packing fraction;  $\rho_{F_B}$ , densification due to particle slippage and rearrangement, and mean yield pressure ( $P_Y$ ).

Powder fraction size ( $\mu\text{m}$ )	$\rho_{F_A}$	$\rho_{F_O}$	$\rho_{F_B}$	Mean yield pressure ( $\text{MN m}^{-2}$ )
Lactose				
0-10	0.670	0.375	0.295	183
0-45	0.670	0.426	0.244	176
105-150	0.716	0.490	0.226	150
210-295	0.711	0.576	0.135	168
Chloroquine diphosphate				
0-45	0.640	0.452	0.188	195
45-125	0.676	0.501	0.175	185
125-180	0.680	0.510	0.170	166
180-250	0.698	0.520	0.168	162
Stearic acid				
0-45	0.632	0.604	0.028	} 4.5
45-53	0.654	0.632	0.022	
53-75	0.632	0.606	0.026	
75-125	0.632	0.612	0.019	
Calcium carbonate				
0-3	0.457	0.353	0.104	540
3-5	0.462	0.409	0.053	505
8-12	0.496	0.479	0.027	435

pack densely when placed in a die and exhibit little movement as pressure is applied.

The compressional behaviour of the powders at higher pressures can be elucidated from the Heckel equation by estimating the mean yield pressure,  $P_Y$ , from the reciprocal of the slope of the linear sections in Fig. 4, and derived values are listed in Table 2. This equation distinguishes three groups of powder compressional behaviour—termed Types A, B and C (Hersey & Rees, 1971; York & Pilpel, 1973). In Type A parallel graphs are observed at high applied pressures for different size fractions of a powder, whilst for Type B, particulate fragmentation at low pressures eliminates particle size effects and the graphs become coincident. Type C behaviour is characterized by a small initial curved section, a low value of mean yield pressure and rapid approach to unit packing fraction at low pressures when the Heckel relation becomes invalid.

The average figure for the mean yield pressure of lactose,  $175 \text{ MN m}^{-2}$ , is similar to that quoted in a previous report (Fell & Newton, 1971) but the extensive variation in values for different size fractions (Hersey, Cole & Rees, 1972; Hersey, Rees & Cole, 1973) is not observed. The tendency to coincidence of the graphs above  $25 \text{ MN m}^{-2}$  for the

four size fractions of lactose confirms Type B compressional behaviour (Hardman & Lilley, 1970; Hersey & Rees, 1971).

Unlike the lactose powder, the chloroquine diphosphate fractions exhibit approximately parallel linear sections above  $20 \text{ MN m}^{-2}$ , suggesting Type A behaviour. Graphs for the stearic acid fractions show only a small curved portion before the linear section and are coincident above  $2 \text{ MN m}^{-2}$  with a low mean yield pressure of  $4.5 \text{ MN m}^{-2}$ , indicating the onset of plastic deformation at extremely low applied pressures. These results are consistent with the soft, waxy nature of the material and confirm Type C classification for this powder (York & Pilpel, 1973).

The calcium carbonate fractions which exhibit linear parallel relations above  $10 \text{ MN m}^{-2}$  show Type A behaviour with the estimates of mean yield pressure— $486 \text{ MN m}^{-2}$  (average)—the highest observed for all the powders examined.

For lactose, chloroquine diphosphate and calcium carbonate the mean yield pressure shows a general decrease as particle size decreases, which is expected from the Griffiths theory of particle breakage (Griffiths, 1920).

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