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Research Papers

POSSIBLE PREDICTION OF COMPRESSION CHARACTERISTICS FROM PRESSURE CYCLE PLOTS

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SUMMARY

The possibility of evaluating compressibility of materials from pressure cycles was studied with a wide range of pharmaceutical powders. The initial transmission of axial pressure to the die wall was very small in each case where unsatisfactory tablets resulted. The pressure cycle that can be constructed from the measurement of the axial pressure and the corresponding die wall pressures offers information that is useful in the formulation of tablets. The main difference between the poorly compressible materials and those yielding sound tablets lies in the greater values of initial slopes and residual die wall pressures obtained for these latter substances. The poorly compressible samples yielded pressure cycles which were similar to those of an elastic body while those for the readily compressible materials were akin to a Mohr body. Low values for Poisson ratio and residual radial pressure for materials would be an indication the compact had recovered axially and contracted radially. Plotting of pressure cycles could thus be a useful research tool in that information obtained from them could be used to identify those materials capable of direct compression.

INTRODUCTION

Windheuser et al. (1963) studied the transmission of pressure to the die wall during tablet compression. Strain gauges were used to monitor die expansion and this was related to the transmitted pressure. These authors concluded that materials which permit good conversion of axial pressure to radial pressure tend to form good tablets.

Using a single punch tablet machine instrumented with strain gauges, Leigh et al. (1967) studied the complete pressure cycles of several pharmaceutical materials at various levels of compression to determine from the pressure cycle whether the material would form satisfactory tablets. The pressure exerted by various substances on the die wall during and after compression of tablets was measured by Higuchi et al. (1965). They

reported that this information could be related directly to the ease of formation and ejection of tablets. These workers also found that the die wall pressure decayed at a measurable rate after the normal compression force was abruptly removed.

MATERIALS AND METHODS

The following materials were used: sodium chloride (cubic[1] and dendritic[2]) crystals, direct compression paracetamol (acetaminophen)[3], paracetamol[4], phenacetin[5], spray-dried lactose[6] and crystalline lactose[7]. Lactose granules with the following composition by weight were also used: lactose 50%, sucrose 33%, maize-starch 16%, and magnesium stearate 1%.

A vibratory sieving machine was used to obtain 30–40 mesh of the various crystalline materials and lactose granules. An air jet sieve was used to obtain a 75 μm fraction of direct compression paracetamol. The 40–45 μm fraction of the spray-dried and crystalline lactose powders was separated using a zig-zag classifier[8]. All materials were dried at 60°C for 4 h in a hot air oven and stored in wax-sealed screw-capped jars.

Compression was carried out at four machine settings, which gave approximately 45, 90, 140 and 180 MN m^{-2}, on an instrumented single punch tablet machine.

The top and bottom punches were instrumented as described by Shotton and Ganderton (1961). The radial pressure was measured by inserting a piezoelectric transducer[9] through the die wall. Recordings for pressure applied to the top punch and the corresponding pressures exerted on the die wall were made continuously during the down and up strokes of the top punch by UV spot galvanometer on photographic paper. The die wall pressure was then plotted against the corresponding axial pressure to obtain the pressure cycle. Different granule formulations of paracetamol and phenacetin containing moisture, Byco[10] were also compressed as above.

RESULTS AND DISCUSSION

Compacts that showed signs of capping or that were too fragile were regarded as unsatisfactory. Whilst tablets produced from plain paracetamol and phenacetin were unsatisfactory, those from the other materials and formulations were satisfactory. Table 1 shows the values of initial slope of the first portion of the compression cycle and those for the maximum pressure exerted on the die wall, residual pressure exerted on the die wall, as well as the axial pressure for the various materials. The compression cycle plots

[1] British Drug Houses.
[2] Direct Salt Supplies (Ruislip) Ltd.
[3] Graesser Salicylates Ltd.
[4] Graesser Salicylates Ltd.
[5] Monsanto Ltd.
[6] McKesson and Robbins Ltd.
[7] Thomas Kerfoot and Co. Ltd.
[8] Alpine.
[9] Kistler, 601H.
[10] Cold-water soluble protein supplied by Croda Food Products Limited, England.

TABLE 1

DETAILS OF TABLETTING PARAMETERS [a] FOR VARIOUS MATERIALS

Material	Mesh or Particle size	Pa	Pd	Pdr	OA
Spray dried lactose	40–45 μm	170	60	25	0.22
Crystalline lactose	40–45 μm	160	58	22	0.27
Lactose granules	−30 + 40	180	54	15	0.41
Dendritic sodium chloride	−30 + 40	179	70	52	0.33
Cubic sodium chloride	−30 + 40	168	58	45	0.26
Direct compr. paracetamol	200 mesh	175	65	20	0.23
Paracetamol crystals	−30 + 40	160	58	5	0.10
Paracetamol powder	60 μm	180	78	8	0.14
Paracetamol + 4% Byco	60 μm	185	79	28	0.17
Paracetamol + water	60 μm	180	78	15	0.20
Phenacetin crystals	−30 + 40	150	50	7	0.22
Phenacetin powder	75 μm	172	80	5	0.16
Phenacetin + 4% Byco	75 μm	175	80	23	0.17
Phenacetin + water	75 μm	170	76	8	0.18

[a] Pa, Pd, and Pdr are applied pressure, die wall pressure and residual die wall pressure, respectively, expressed in MN m^{-2}. OA is slope of first part of compression cycle.

for the various materials from 45 Mn m^{-2} to 180 MN m^{-2} are illustrated in Figs. 1–5. The compression cycles for sodium chloride, lactose powders and granules as well as direct compression paracetamol and various formulations of paracetamol and phenacetin had the same general form and seem to indicate that these materials behave similarly to a Mohr body as described by Long (1960). The shape of the cycles obtained for plain paracetamol and phenacetin differed in some respects. The residual pressure on the die

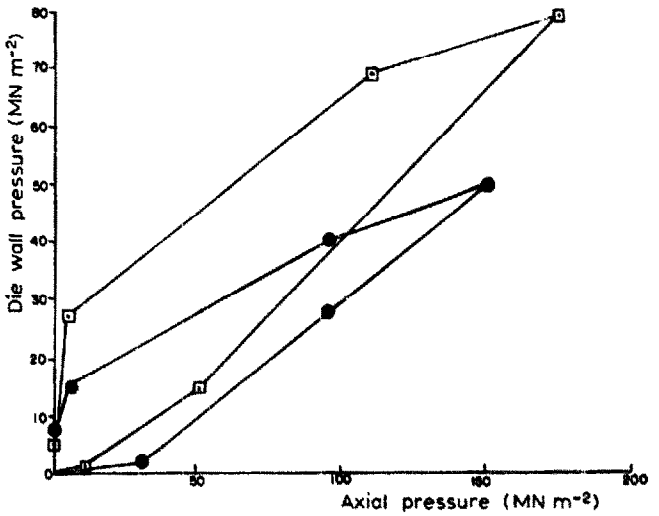

Fig. 1. Compression cycles for phenacetin. Filled circles, crystals −30 + 40 mesh; dotted squares, powder d_m = 75 μm.

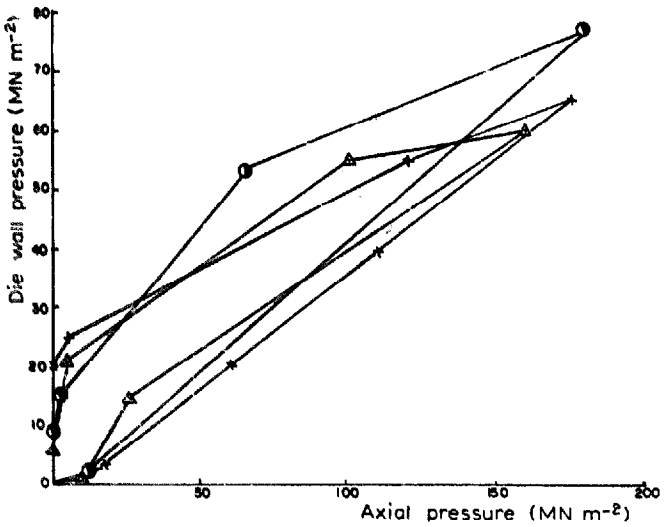

Fig. 2. Compression cycles for paracetamol. Crosses, direct compression paracetamol; triangles, crystals −30 + 40 mesh; half-filled circles, powder d_m = 60 μm.

wall after the axial pressure returned to zero was lower than with the other materials studied. None of the materials gave a pressure cycle similar to that of a body with constant yield stress in shear since the value of the second upward slope of the line would be constant and equal to 1 for such a material.

With the crystalline paracetamol and phenacetin, the initial transmission of axial pressure to the die wall was very small, probably due to difficulties encountered by the particles to rearrange. This is an indication that although the forces involved in the sequence

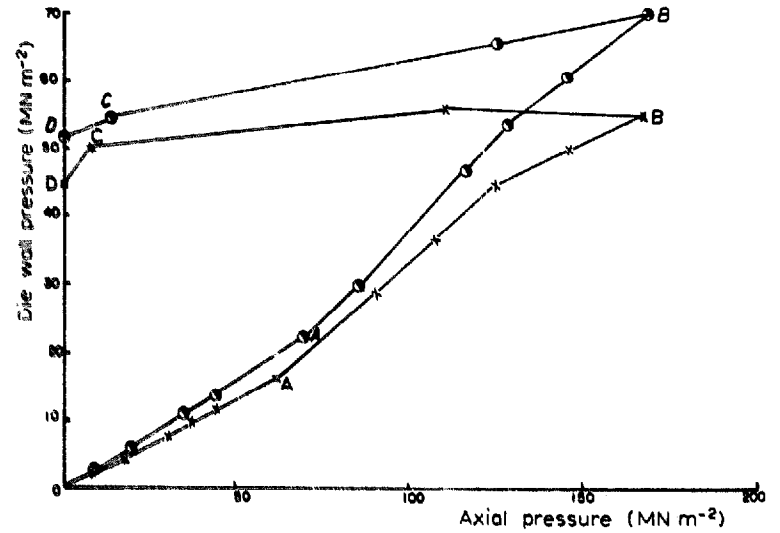

Fig. 3. Compression cycles for sodium chloride. Half-filled circles, dendritic crystals −30 + 40 mesh; crosses, cubic crystals −30 + 40 mesh.

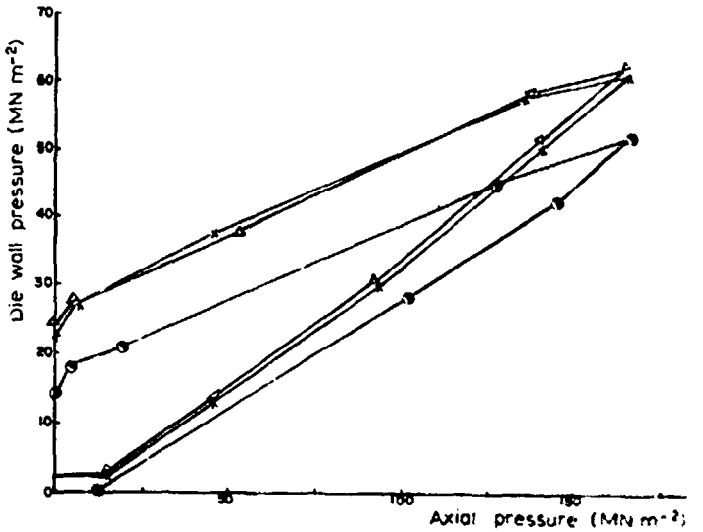

Fig. 4. Compression cycles for lactose. Half-filled circle, spray dried 40–50 μm; crosses, crystalline 40–45 μm; triangles, granules −30 + 40 mesh.

starting from loose material to close packing to compact formation are being monitored from the moment the upper punch enters the die, these forces cannot be recorded until the material forms a sufficiently firm compact to offer resistance to the downward movement of the upper punch. The powder forms of both the paracetamol and phenacetin as

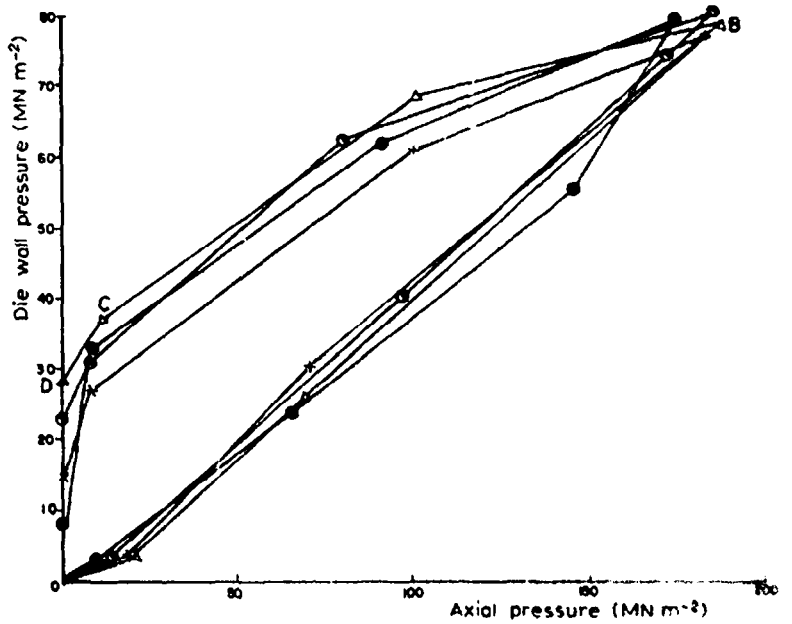

Fig. 5. Compression cycles for granulations of paracetamol and phenacetin. Crosses, paracetamol with water; triangles, paracetamol with 4% Byco; filled circles, phenacetin with water; half-filled circles, phenacetin with 4% Byco.

well as direct compression paracetamol showed a transmission of pressure to the die wall from the beginning of the compression. The initial slope, OA, in the first half of the plot is very low for paracetamol and phenacetin, reaching a value of 0.16–0.18. As had been reported earlier (Shotton and Obiorah, 1973) for sodium chloride, the values for the initial slopes were broadly in agreement with the Poisson ratio of the materials. The initial slope for the direct compression paracetamol was much higher than for the others, reaching a value of 0.23. The Poisson ratio determines the degree of lateral expansion a body subjected to a normal axial force would undergo. Because of the low values of the Poisson ratio obtained for paracetamol and phenacetin, these materials would be expected to exhibit small radial expansion. When the forming pressure is removed, the compact is free to expand in the axial direction whilst contracting radially. This would induce considerable strains within the compact. The residual die wall pressure recorded with these two materials was very low. This indicates a substantial axial relaxation. Mohr's theory of failure can be used to explain the process here. An isotropic solid material fails during compression by slip along a certain surface when shear stress acting along the surface reaches a limiting value which would depend on the major principal stress. The radial pressure can be regarded as a normal component when the axial pressure has been returned to zero. This would be the major principal stress acting on the periphery to the compact and when this exceeds a critical value, failure will occur along the direction of the shearing stress, in accordance with the Mohr theory. The direction of failure is similar to capping in a tablet. The distribution and direction of the stresses during recovery could account for the capping and lamination which occurred with paracetamol and phenacetin. This explanation assumes that failure occurred while the compact was still in the die. The substantial transmission of axial pressure to the die wall right from the beginning of compression and the greater value obtained for the slope OA, in the case of direct compression paracetamol, indicate a greater plastic deformation with this material. Thus the main difference between the compression cycle plots of the other materials and those for plain paracetamol and phenacetin lies in the values of the initial slope, OA, and the amount of residual die wall pressure, which were much greater than for these latter materials. This suggests that the dissipation of radial pressure with the plain paracetamol and phenacetin was much greater than for the others. The greater pressure left on the die wall after the forming pressure had returned to zero obtained for materials that yielded sound tablets, indicates that such materials had been subjected to more permanent deformation than the other materials which gave unsatisfactory tablets. It is also possible that with the direct compression paracetamol, gelatin films may help bonding and the bonds may yield under elastic recovery to give relaxation at the bond and not across the crystal. The inability of plain paracetamol and phenacetin to form lasting interparticulate linkages is probably due to the absence of any significant signs of plastic deformation characteristics during compaction. When the axial pressure is released the high elastic recovery inherent in these materials may force the bonds to rupture. This tendency would be increased by the direction and magnitude of the stresses during release of the forming pressure when the radial pressure becomes greater than the axial stresses. The addition of 4% hydrolyzed gelatin to paracetamol in the direct compression paracetamol seems to have increased the degree of lateral expansion of the material. An indirect evidence for this is the increase in the initial slope OA for this material. It has been stated that this slope is proportional to the

Poisson ratio which determines the degree of lateral expansion.

Varsano and Lachman (1966) found a direct proportionality between binding and the contact area of the solid surfaces on which these forces play a role. Materials such as sodium chloride, which showed plastic flow from the pressure cycles, gave correspondingly good tablets due to a greater contact area being formed whereas plain paracetamol and phenacetin, in which recovery was mainly elastic, produced weak tablets. Leigh et al. (1967) reported that materials giving the Mohr-type body of pressure cycle are prone to capping and lamination. In this study, there was no tendency to cap or laminate at the pressure used for sodium chloride and the other materials that gave pressure cycles akin to a Mohr body.

The plain paracetamol and phenacetin gave pressure cycles which were more similar to those of an elastic body. The low values for the Poisson ratio and the residual die wall pressure for these two substances indicate the compact had recovered axially and contracted radially. This would induce considerable strain within the compact, because during the recovery process the tablet was subjected to a residual pressure acting from the die wall and friction restricted peripheral movement. Under these conditions, separation or capping can occur along the stress loci.

Certain predictions can be made by evaluating the die wall pressures. In every case, a satisfactory tablet resulted when there was a good conversion of applied pressure to the die wall. In such cases the residual die wall pressure, after the compression pressure returned to zero, was greater than that for the materials yielding unsatisfactory tablets. Thus, sodium chloride, lactose and direct compression paracetamol gave satisfactory tablets. Similarly, tablets prepared from granules of paracetamol and phenacetin containing binder, as well as from these materials containing gelatin hydrolyzate (Byco), and moisture were satisfactory. Also, those materials which showed plastic flow from the pressure cycles gave correspondingly good tablets due to a greater contact area being formed whereas plain paracetamol and phenacetin, in which recovery was mainly elastic, produced weak tablets.

Plotting of pressure cycles could thus be a useful research tool in that information obtained from them could be used to identify those materials capable of direct compression.

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