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ACKNOWLEDGMENTS AND ADDRESSES

Received October 3, 1974, from the *Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206*

Accepted for publication December 12, 1974.

Presented at the Pharmaceutical Analysis and Control Section, APhA Academy of Pharmaceutical Sciences, New Orleans meeting, November 1974.

The authors are grateful to Mr. G. E. Drummond and Mr. H. F. Hugar for technical assistance.

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PHARMACEUTICAL TECHNOLOGY

Effect of Physical Properties on Compression Characteristics

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Abstract □ The transmission of force to the die wall was measured by a piezoelectric sensor, and the compression cycles of lactose granules of different shapes were compared. In addition, a nearly spherical fraction of spray-dried lactose was similarly compared with a crystalline sample. Better tablets were formed when the conversion of axial to radial pressure was high and the residual pressure on the die wall remained after removal of the top punch. With acetaminophen and phenacetin, the pressure on the die wall was low, as was the residual pressure, and capping occurred in both cases. With direct compression acetaminophen, higher die wall pressure was produced and capping did not occur. It is considered that these results can be explained by the ease with which the more nearly isodiametric particle can rearrange under pressure and by the elastic properties of the solid.

Keyphrases □ Lactose granules—effect of physical properties on compression characteristics □ Compression of lactose granules—effect of physical properties compared □ Die wall pressures—compared for various lactose granules, effect on tablet compressibility

The effect of crystal habit and particle shape upon the properties of cubic and dendritic crystals of sodium chloride and the tablets produced from these crystals was previously examined (1). For any particular material, the difference between applied and lower punch pressure depends on the coefficient of friction at the die wall and on the radial pressure.

Working with sodium chloride, aspirin, and hexamine (methenamine), Shotton and Ganderton (2) postulated that capping of hexamine was due to the failure of the material induced by axial elastic recovery after compression force was removed, and this capping occurred when the interparticulate bonds were sufficiently strong to resist separation of the crystals.

EXPERIMENTAL

The following materials were used: phenacetin[1], acetaminophen[2], direct compression acetaminophen[3], spray-dried lactose[4], and crystalline lactose[5]. Lactose granules[6] 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 lactose granules, acetaminophen crystals, and phenacetin crystals, and an air jet sieve was used to obtain a 75-μm fraction of direct compression acetaminophen. The 40–45-μm fraction of the spray-dried and crystalline lactose powders was separated using a zig-zag classifier[7]. All materials were dried at 60° for 4 hr in a hot air oven and stored in wax-sealed screw-capped jars.

Different shape fractions of the lactose granules were obtained from the shape-sorting table described by Ridgway and Rupp (3). In Table I, 1, 4, 8, and 12 refer to the fractions obtained at these stations of this machine. The smaller the number of the station, the more spherical was the shape of the particles; the larger the number of the station, the more angular were the particles. The shape coefficient for the shape fractions of lactose granules was calculated from the average values of the particle volume, surface area, and projected diameter using the method of Heywood (4) as modified by Ridgway and Rupp (3).

Shape factor determinations were not carried out for the lactose powders because it was not possible to count accurately such fine particles. Microscopic examinations, however, showed that the spray-dried lactose was composed of spheroidal particles and that the crystalline lactose was highly angular. The shape-sorting table was unsuitable for the needle-shaped crystals of acetaminophen and phenacetin because these were broken down by vibration. The values of shape coefficient for lactose granules are presented in Table II.

[1] Monsanto Ltd.
[2] Paracetamol crystals BP, Graesser Salicylates Ltd.
[3] Graesser Salicylates Ltd.
[4] McKesson and Robbins Ltd.
[5] Whey Products Ltd.
[6] Thomas Kerfoot and Co., Ltd.
[7] Alpine.

Table I—Details of Tableting Parameters[a] at Highest Machine Setting

Material	Sieve or Particle Size	*Fa*	*Fb*	*Fd*	*Fe*	*Fc*	Porosity	*R*
Spray-dried lactose	40—45 μm	19,044	18,400	644	878	82	15.8	0.9662
Crystalline lactose	40—45 μm	17,638	16,844	794	822	78	16.1	0.9550
One lactose granules	−30—+40	21,120	20,795	325	685	72	13.8	0.9894
Four lactose granules	−30—+40	21,096	20,756	340	703	65	13.9	0.9559
Eight lactose granules	−30—+40	20,584	20,184	400	722	63	13.9	0.9479
Twelve lactose granules	−30—+40	20,298	19,858	440	745	61	13.8	0.9422
Acetaminophen crystals	−30—+40	17,246	14,527	2719	567	—	—	0.8423
Phenacetin crystals	−30—+40	17,950	14,826	3124	573	—	—	0.8260
Direct compression acetaminophen	+200 mesh	19,713	18,005	1708	721	19	15.5	0.9134

[a] *Fa, Fb, Fd, Fe,* and *Fc* are applied force, transmitted force, force lost to the die wall, ejection force, and crushing force, respectively, expressed in newtons (N). Porosity values are expressed in percentage. Punch diameter is 12 mm. *R* is the ratio of *Fb/Fa.*

Table II—Values of Shape Coefficient for Lactose Granules (30—40 mesh)

Station[a]	Shape Coefficient
1	14.5
4	15
8	17
12	21.5

[a] Refers to the stations from the shape-sorting table; a sphere would have a shape coefficient of 6.

The powders were compressed in an instrumented single-punch machine. The top and bottom punches were instrumented as described by Shotton and Ganderton (5). The radial pressure was measured by inserting a piezoelectric transducer[8] through the die wall, and forces were recorded as previously described (1). Five tablets were prepared from each powder sample at approximately 45, 90, 135, and 180 MN m^{-2} compression pressures. Once the tableting pressure had been chosen for a particular material, the same machine setting was used for the compression of different shape fractions or forms where applicable.

To condition the die, the first two tablets of any compression exercise were rejected. The weight of material in each case, calculated from its true density, was sufficient to give a tablet of 4-mm length at zero porosity using a 12-mm diameter punch and die set. The material was introduced by hand into a die previously lubricated by applying, with a small camel-hair brush, a 2% solution of stearic acid in a mixture of equal parts of acetone and carbon tetrachloride and the solvents were allowed to evaporate.

The porosity of the tablet was obtained from the dimensions of the ejected tablet. In all cases, the crushing strength of the tablet was determined after 24 hr using the diametral crushing strength test described by Shotton and Ganderton (6).

RESULTS

Compacts that showed signs of capping or that were too fragile to be measured were regarded as unsatisfactory. Both the crystalline acetaminophen and phenacetin yielded unsatisfactory tablets, so it was not possible to determine the values of crushing strength and porosity. Tablets produced from direct compression acetaminophen, lactose powders, and lactose granules were satisfactory.

The results for the different tableting parameters at the highest compression pressure used are presented in Table I. With lactose, at the highest machine setting, greater values of applied force *(Fa)* were obtained for the spheroidal spray-dried powder than with the crystalline form. Similarly, the lactose granules gave greater values of applied force for the more nearly spherical particles than for the more angular ones. Also, the more spherical-shaped lactose granules and the spheroidal spray-dried lactose gave stronger tablets on compression than the more irregular granules and the crystalline powder.

[8] Kistler, 601H.

The force lost to the die wall *(Fd)* increased with increasing departure from the spherical, *i.e.*, increasing shape coefficient; thus, lower values of *R*, the ratio of transmitted and applied force, *Fb/Fa*, were obtained for the less spherical particles (Table I). The values obtained at four axial pressures are shown in Fig. 1 for the four shape fractions of lactose granules. These findings show that the force lost to the die wall $[Fd = (Fa - Fb)]$ increases as the particles depart increasingly from the spherical.

However, for the lactose powders, the crystalline form, which was highly angular, gave a smaller value for the ejection force *(Fe)*. The converse was true for the lactose granules.

The compression cycle plots for the various materials are illustrated in Figs. 2–4.

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 a UV spot galvanometer on photographic paper. The die wall pressure was then plotted against the corresponding axial pressures to obtain the pressure cycle. The compression cycles for the lactose powders and granules as well as for direct compression acetaminophen had the same general form and seem to indicate that the crystals behave similarly to a Mohr body as described by Long (7).

The shape of the cycles obtained for acetaminophen and phenacetin crystals differed in some respects. The residual pressure on the die wall after the axial pressure returned to zero was lower than with lactose granules and powder and with direct compression acetaminophen. 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.

DISCUSSION

In cases where a greater axial force, *Fa*, is recorded, the particles are probably more difficult to deform. Data obtained by Higuchi *et al.* (8) show that materials associated with high residual die wall pressure give correspondingly high ejection force. They concluded that residual elastic compressional energy remaining after partial recovery in the die appears to determine the amount of work required to remove the finished tablet. This conclusion is in agreement with friction theory.

Train and Hersey (9) postulated that the value of the force lost to the die wall *(Fd)* is the product of the shear strength of the compressed material and the true area of contact between compact and the die wall. Carrington (10) showed that a maximum value for *Fd* can only be obtained when the whole compact is moved relative to the die at the point of maximum compression.

In every case, a satisfactory tablet resulted when there was a good conversion of the 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, lactose powders and granules and direct compression acetaminophen gave satisfactory tablets. Versano and Lachman (11) found a direct proportionality between binding and the contact area of the solid surfaces on which these forces play a role. Materials such as lactose, which showed plastic flow from the pressure cycles, gave correspondingly good tablets due to a greater contact area being formed whereas acetaminophen and

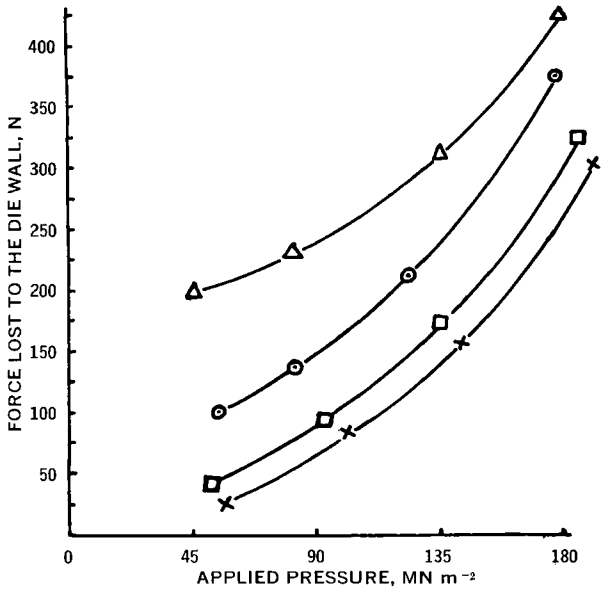

Figure 1—*Force lost to die wall for lactose granules at four machine settings. Key: ×, No. 1 shape fraction; □, No. 4 shape fraction; ○, No. 8 shape fraction; and △, No. 12 shape fraction.*

phenacetin crystals, in which recovery was mainly elastic, produced weak tablets. Also, the acetaminophen and phenacetin crystals were essentially needle-like and could be readily fractured.

None of the materials used gave pressure cycles identical with the theoretical pressure cycles described by Long (7), since these pressure cycles were for models of solid, isotropic bodies under uniaxial compression, assuming that die wall friction was absent. Leigh *et al.* (12) 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 lactose and direct compression acetaminophen, although these behaved like a Mohr body.

With the crystalline acetaminophen and phenacetin, the pressure cycles were more akin to those of an elastic body. With these latter materials, the initial transmission of pressure to the die wall was very small, probably due to difficulties encountered by the particles to rearrange. The values for the initial slopes were broadly in agreement with the Poisson ratio of the materials, and this ratio determines the degree of lateral expansion a body undergoes when subjected to a normal axial force. The values for the Poisson ratio obtained for acetaminophen and phenacetin from the slope were low, and the residual pressure on the die wall was also low after the axial pressure was removed. Thus, the compact had recovered axially and contracted radially, inducing considerable strain within the compact, because during the recovery process the

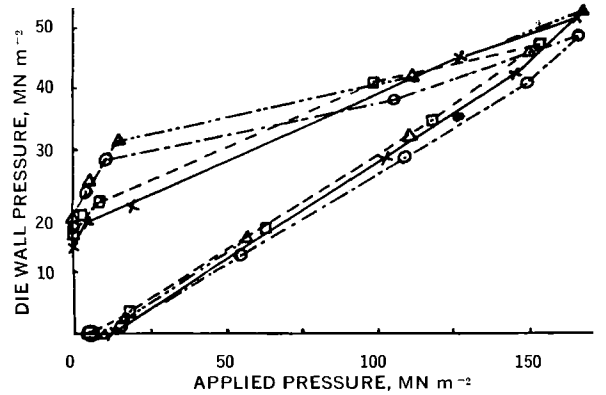

Figure 2—*Pressure cycles for four shape fractions of lactose granules (30–40 mesh) at the highest machine setting. Key: ×, No. 1 shape fraction; □, No. 4 shape fraction; ○, No. 8 shape fraction; and △, No. 12 shape fraction.*

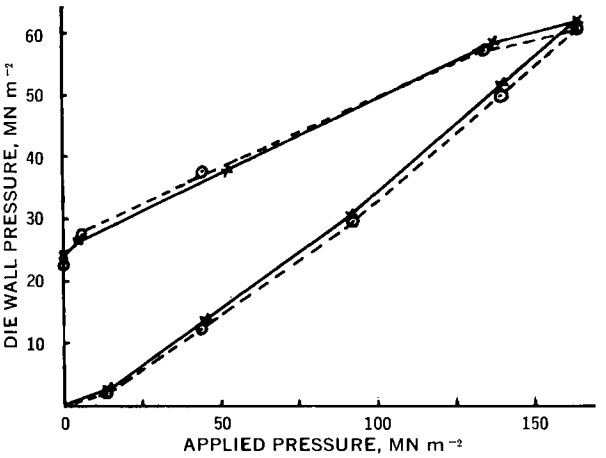

Figure 3—*Pressure cycles for spray-dried and crystalline lactose, 40–45 μm, at the highest machine setting. Key: ×, spray-dried lactose; and ○, crystalline lactose.*

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.

Mohr's theory of failure can be used to explain this process. 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 depends on the major principal stress. The radial pressure is the major stress when the axial pressure returns to zero. This assumes that failure occurs initially while the compact is still in the die.

The dissipation of radial pressure for acetaminophen and phenacetin was greater than for the direct compression acetaminophen and was probably due to a greater axial recovery. This finding also indicates that the direct compression acetaminophen was subjected to more permanent deformation than the crystals; with the direct compression material, it is possible that the gelatin films may interfere with the bonding between the solid particles and that the gelatin films may yield under elastic recovery to give relaxation at the bond.

CONCLUSIONS

Certain predictions can be made by evaluating the die wall pressures. The indications are that materials that permit good conversion of applied pressure to the die wall yield satisfactory tablets. This finding may prove to be a useful tool in the search for materials that can be directly compressed to yield tablets. Furthermore, materials giving a low residual die wall pressure yield tablets that are too weak or that cap on ejection.

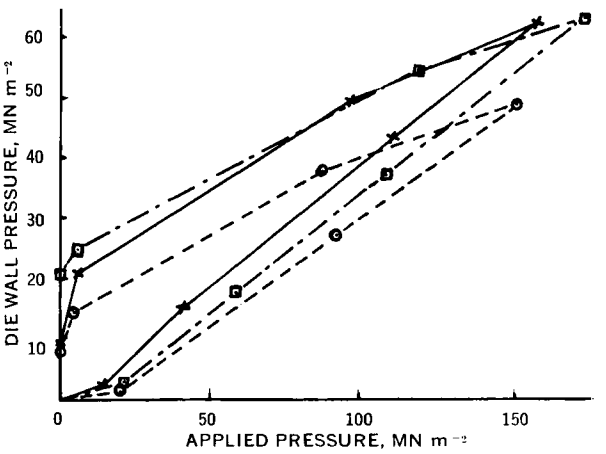

Figure 4—*Pressure cycles for direct compression acetaminophen, acetaminophen crystals, and phenacetin crystals. Key: ○, phenacetin (30–40 mesh); ×, acetaminophen (30–40 mesh); and □, direct compression acetaminophen.*

The acetaminophen and phenacetin crystals, which are essentially needle shaped, have a tendency to fracture easily and yield weak tablets. Investigations must be conducted with a much wider range of materials.

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ACKNOWLEDGMENTS AND ADDRESSES

Received August 5, 1974, from the *Department of Pharmaceutics, School of Pharmacy, University of London, Brunswick Square, London, WC1N 1AX, England.*

Accepted for publication December 4, 1974.

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Application of Powder Failure Testing Equipment in Assessing Effect of Glidants on Flowability of Cohesive Pharmaceutical Powders

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Abstract □ Powder failure testing equipment was used successfully to study the effect of glidants on the flowability of two cohesive pharmaceutical powders, lactose and calcium hydrogen phosphate, using the flow factor as the flowability parameter. Fine silica, magnesium stearate, and purified talc were investigated as glidants; for each host powder–glidant mixture, an optimum concentration of glidant was observed beyond which no further increase in flowability occurred. The order of efficiency of glidants for both host powders was fine silica > magnesium stearate > purified talc. The mode of action of the three glidants is discussed.

Keyphrases □ Flow properties of cohesive powders—application of powder failure testing equipment (shear cell and tensile tester) □ Glidant—effect on flow factor for powder mixtures, optimum concentration, mode of action □ Powders—effect of glidants on flowability determined using powder failure testing equipment

Over recent years the increasing use of fine powders has emphasized the need for more information regarding their handling and mechanical properties. Fine powders, in general, exhibit nonfree-flowing (*i.e.*, cohesive) properties, which can cause serious problems such as caking of powders in storage and bridging in hoppers. Such problems can lead to the uneven flow of powders and to difficulties in filling operations in various pharmaceutical processes.

To improve the flowability of powders and granulations, a small amount of a second agent, or glidant (1, 2), is often added, usually in powder form. Examples of glidants commonly used in the pharmaceutical industry are talc, magnesium stearate, starch, and fine silica (3). Several postulates have been proposed to explain the mechanism of action of glidants:

1. Removal of electrostatic charges on the surface of the host powder (3, 4).

2. Distribution of glidant through the host powder, and the collection of very fine cohesive host particles onto glidant particle surfaces (5).

3. Selective adsorption of gases and vapors otherwise adsorbed onto the host powders (5).

4. Reduction of van der Waals forces by separation of host powder particles (3).

5. Reduction of interparticular friction and surface rugosity by glidant particles adhering to the surface of the host powder (3, 4).

Several techniques have been employed to study the effects of the addition of glidant to host powders and granulations. Several investigators measured the rate of flow of powder particles from hoppers through circular orifices and measured the flow rate under dynamic conditions (6–8). Other methods have included tablet weight variation (9), vibrating funnel (10), and angle of repose (6, 11, 12). In the latter test, the maximum angle between the surface of a heap of powder and the horizontal plane is measured and values reflect the magnitude of the static coefficient of friction between particles.

All of these tests are most successfully employed for assessing the flowability of relatively coarse powders and granules in the 100–400-μm range (13), and optimum glidant concentrations were derived for particular systems (3, 14). However, the results obtained are significantly affected by the conditions of the test. Angular tests, such as the angle of repose, only provide a qualitative basis for assessing the flow of powders (14). In addition, these techniques do not lend themselves to the study of the flowability of fine cohesive powders, because the measurements become inaccurate (5).

The mechanical properties of cohesive powders can