Compression Characteristics of Some Pharmaceutical Materials

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A commercial single-punch tablet machine (Manesty E 2) fitted with 1/2-in. punches was instrumented with strain gauges to monitor the forces simultaneously on the upper punch and the die-wall. The complete pressure cycles of a number of pharmaceutical materials at various levels of compression have been studied. The materials were sucrose granules and crystals, acetaminophen granules, aspirin crystals, and sodium chloride crystals. It has been found that these materials conform to three different types of compression pattern. The results indicate that materials which laminate on compression behave like a Mohr's body, *e.g.*, acetaminophen granules without binder. Granulation of acetaminophen with polyvinylpyrrolidone altered the compression pattern to that of a body with a constant yield stress. Aspirin compacts were found to exhibit elastic properties. Compression patterns are given for 20/40 mesh and 40/60 mesh crystals and granules of sucrose. No significant differences due to particle size were found, but differences were noted between the crystals and granules. The poisson ratios of these materials are given.

MEASUREMENTS of radial pressures exerted on the die-wall during uniaxial compression of materials to form compacts have been described by Nelson (1), Long (2), Windheuser (3), and Higuchi (4).

Nelson (1) and Higuchi (4), using load cells and strain gauges, respectively, mainly studied the transmission of forces to the die-wall, during the application of axial pressure, *i.e.*, on axial loading. The investigations failed to cover the relaxation/dissipation of pressure during removal of the compressional forces, *i.e.*, during unloading. Long (2) used a split die to measure the radial pressures. He studied the complete pressure cycles during loading and unloading of materials used in powder metallurgy and a theory was put forward regarding the nature of the residual radial pressure. No attention was paid to the effect of particle size, moisture content, and different physical forms.

The object of the present investigation was to find out the type and nature of the pressure cycles involved during compression of different pharmaceutical materials in granular and crystalline form. It was of particular interest to find out whether the ability of a material to form a "good" or "bad" tablet (particularly with respect to capping) was manifested in its pressure cycles.

APPARATUS

A Manesty E2 single-punch tableting machine, fitted with 1/2-in. plain punches was instrumented with strain gauges to monitor the forces involved during a compression cycle. The die-plate was suitably modified to house the die and the wires from the transducers without interfering with the movement of the upper punch and the hopper. To monitor the upper punch force and lower punch force, 1/4-in. linear foil gauges (Saunders Roe, resistance 120Ω, gauge factor 2.2) were used. Three foil gauges were bonded to the three slots around the lower punch holder, and connected in series, to form one active arm of a Wheatstone bridge. Three dummy gauges were used for the compensating arm as described by Shotton (5). In both cases, the transducers were connected as a half-bridge circuit with the resistors in the carrier amplifiers completing the circuit.

Silicone gauges (type 2A-1A-250 P)[1] were used to monitor the die-wall pressure. A 1/2-in. die was cut away on opposite sides, leaving a wall thickness of 1/8 in. on the die. One silicone gauge was bonded on either side of the cut-away surface. A silicone rubber solution was used to fill in the cut-away portions. With the solution hardened, the circumference of the die conformed to its original shape and size. The two silicone gauges formed opposite arms of a Wheatstone bridge. A full bridge was completed by using two resistors.

Type 2506 Carrier amplifiers[2] were employed to activate the transducers on the upper punch and lower punch holder. The oscillator frequency was set at 5 Kc./sec. and the output voltage was 3 v. A low gain amplifier (CA31)[2] of frequency 3 Kc./sec. and output adjusted at 6 v., powered by a power unit PU21,[2] was employed to energize the semiconductors.

The signals from the transducers were received in a 4 channel U.V. recorder (type 1706 Visicorder),[2] using suitably damped galvanometers (BB 250A)[2] and recorded at a chart speed of 6 mm./sec.

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[1] Ether Langham Thompson Ltd.

[2] Honeywell Controls Ltd.

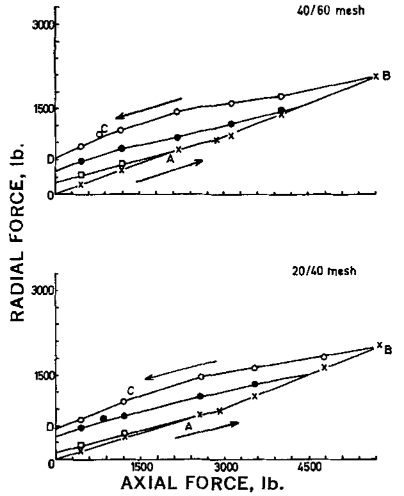

Fig. 1—Compressional cycle of sucrose granules.

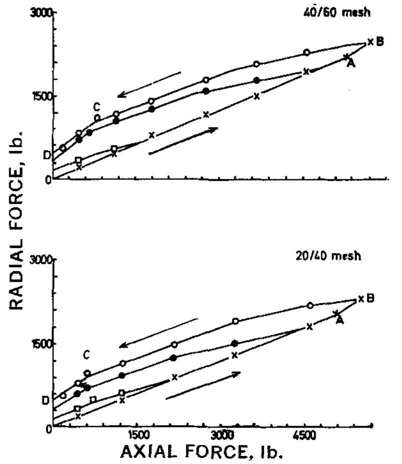

Fig. 2—Compressional cycle of sucrose crystals.

CALIBRATIONS

The upper punch and lower punch were calibrated by the method of Shotton and Ganderton (5). The die was calibrated by two different methods. First, it was clamped between two plates. Water, under pressure, was forced into the die. The height of the water column within the die was 0.16 in. This was of the same height as the tablets to be compressed. A linear relationship was obtained between the hydraulic pressures and the galvanometer deflections. A second calibration was carried out using a rubber plug as a confirmation. The die-wall response was of the same order as before.

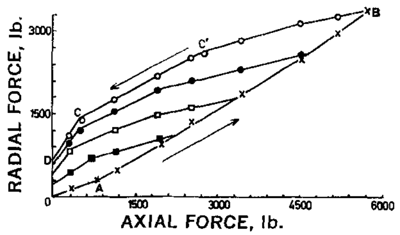

Fig. 3—Compressional cycle of sodium chloride (20/40 mesh).

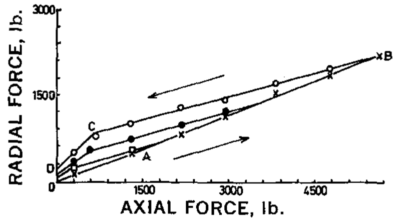

Fig. 4—Compressional cycle of acetaminophen granules (20/40 mesh).

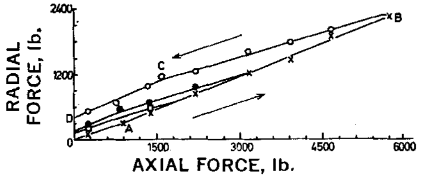

Fig. 5—Compressional cycle of acetaminophen granules and 3% PVP (20/40 mesh).

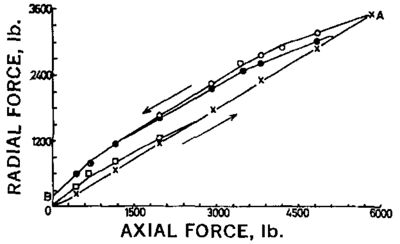

Fig. 6—Compressional cycle of aspirin crystals (20/40 mesh).

EXPERIMENTAL

To investigate the type and nature of pressure cycles exhibited by different forms of the same material, sucrose granules and sucrose crystals were chosen. Two different sizes of each (20/40 mesh; 40/60 mesh) were compressed to investigate the effect of particle size.

The materials used were: sucrose granules (20/40 mesh, 40/60 mesh); sucrose crystals (20/40 mesh, 40/60 mesh); aspirin crystals (20/40 mesh); sodium chloride crystals (20/40 mesh); acetaminophen granules (20/40 mesh); and acetaminophen granules (97% acetaminophen, 3% polyvinylpyrrolidone (20/40 mesh).

The sucrose granules were prepared using distilled water. Acetaminophen granules were prepared using acetone. Granules of 97% acetaminophen and 3% polyvinylpyrrolidone (PVP) were prepared by moist granulation with the PVP in acetone. The granules were dried at 85° overnight. The

TABLE I—SLOPES

Material	Mesh Size	Slope of OA	Slope of AB	Slope of BC	Slope of CD	Max. Axial Load, lb.
Sucrose crystals	40/60	0.45	0.82	0.43	0.84	5600
Sucrose crystals	20/40	0.45	0.81	0.43	0.84	5600
Sucrose granules	40/60	0.36	0.42	0.36	0.42	5600
Sucrose granules	20/40	0.36	0.42	0.36	0.40	5600
Aspirin crystals	20/40	0.53	0.62			
Acetaminophen granules + 3% PVP	20/40	0.33	0.43	0.36	0.43	5600
Acetaminophen granules	20/40	0.38	0.42	0.38	1.00	5600
Sodium chloride crystals	20/40	0.40	0.70	0.48	1.41	5600
					0.70	2200

TABLE II—POISSON RATIOS (ν)

Material	Mesh Size	ν
Sucrose crystals	40/60	0.31
Sucrose crystals	20/40	0.31
Sucrose granules	40/60	0.27
Sucrose granules	20/40	0.27
Aspirin crystals	20/40	0.38
Acetaminophen + PVP granules	20/40	0.24
Acetaminophen granules	20/40	0.29
Sodium chloride crystals	20/40	0.30

two fractions, 20/40 mesh and 40/60 mesh, were obtained by sieving, using a test sieve shaker[3].

All materials were further dried over silica gel in an oven at 50° and stored over P_2O_5 in a desiccator prior to compression. The moisture content of each sample was determined by loss of weight after drying at 95° for 45 min. using infrared heat. Weight loss was found to be below 0.3% in each case.

All samples were lubricated with 0.5% magnesium stearate (100 mesh) and tumbled in a jar for 5 min. (A lubricant was included, because the object of this investigation was to determine the nature of the pressure cycles rather than die-wall friction.) The weight of material compressed in each case was such that a compact of 0.16 in. (height to diameter ratio 0.32) was obtained at the maximum loading. Each sample was weighed to the nearest mg. The compression cycle extended over 30 sec. for the loading and 30 sec. for the unloading. Loading and unloading were carried out evenly over the entire cycle. Five samples of each material were taken up in stages to load levels of approximately 2000, 3000, 4000, 5000, and 5600 lb. on separate occasions before unloading was commenced from these levels.

RESULTS

Figures 1–6 show the relationship between the radial forces and axial forces of the materials during a complete pressure cycle, *i.e.*, during loading and unloading. The slopes of OA, AB, BC, and CD are given in Table I.

Figure 1 shows the nature of the pressure cycles between two different sizes (20/40 and 40/60 mesh) of sucrose granules. Figure 2 shows the nature of the pressure cycles between different sizes (20/40 mesh and 40/60 mesh) of the sucrose crystals.

Table II gives the poisson ratio of the materials. Figure 4 shows the pressure cycle of acetaminophen granules which cap and laminate on compression, while Fig. 5 is the pressure cycle for the same material, granulated with 3% polyvinylpyrrolidone where capping and lamination were absent.

DISCUSSION

In general, a force acting on one part of a body will be transmitted across the section to the other part. This force may be resolved into two components, one normal to the body and the other in the tangential direction. The former is a normal stress and the latter a shearing stress (6). The normal component is consistent with volume changes, whereas the shearing forces (couples) are sources of, or response to, deformation of a body.

When granules or crystals are compressed within a die by means of two opposing punches, the axial load that is applied through the upper punch is transmitted to the die as a shearing force. In addition, force is transmitted radially to the die-wall. The pattern and magnitude of this latter force is governed by the elastic or plastic behavior of the compact. In studying the pressure transmitting characteristics of materials during tableting, using a single punch machine, it must be noted that although the forces involved in the sequence 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 moment that the compact is sufficiently firm, the upper punch force and the die-wall force can be recorded simultaneously. From this stage onward, the compact behaves more or less like a solid body and follows certain characteristics of solid bodies under uniaxial compression.

Consider the three following examples of solid bodies under uniaxial compression within a die. It is assumed that the die is perfectly rigid and that die-wall friction is absent. In the first case, it is assumed that the body is perfectly elastic. When an axial loading is applied, the transmitted radial force is of the same magnitude and the relationship is of the order:

$$\sigma = \nu\,(\tau) \qquad \text{(Eq. 1)}$$

where σ = axial force, τ = radial force, and ν = the poisson ratio.

Figure 7 shows this relationship in graphical form. This will be valid up to the elastic limit of the material. If the elastic limit has not been

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[3] Pascall Inclyno.

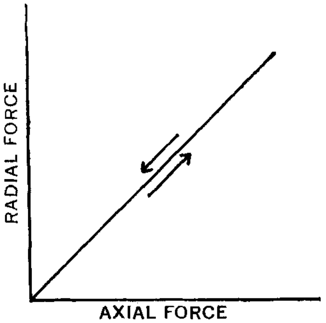

Fig. 7—Compressional cycle of an ideal elastic body.

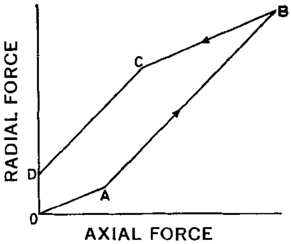

Fig. 8—Compressional cycle of a body with constant yield stress in shear.

exceeded, on unloading, the radial force will dissipate at the rate of ν times the axial force. When the axial force returns to zero, there will be no residual radial force exerted on the die-wall and the body will be free to move out from the die.

In the second case, the axial force is increased above the yield point (A) of the material, when the body starts to deform. The relationship between the axial and radial forces will now depend on the conditions of yield of the material. In this example it is assumed that the body has a constant yield stress in shear, independent of the magnitudes of the principal stresses to which it is subjected. Friction is assumed absent. The principal stresses are σ and τ. After yield has taken place, the following equation applies (2)

$$\sigma - \tau = 2S \qquad \text{(Eq. 2)}$$

S = yield stress in shear, and graphically it follows the course AB (Fig. 8). After a point B has been reached, if the axial force is allowed to fall, the body is no longer forced to yield. The radial force will fall at ν times the rate of fall of the axial force, following the course BC. The slope of the line BC = OA. Provided that the maximum axial loading has been sufficiently large, the point C will be reached at which the radial force is greater than the axial force by an amount equal to $2S$. Yield will again occur. The difference between the radial force and axial force $(\tau - \sigma)$ will again be constant, and the relationship will follow the course CD. Taking this example, it is evident that after the upper punch has been withdrawn, the body will exert a residual radial force of $2S$ on the die-wall. Because of this force, the body will be constrained at the die-wall and will not be free to move out from the die. Whether this value is reached will depend on the maximum axial loading on the body. If this load is not large enough, the difference $(\tau - \sigma)$ will not attain a value as high as $2S$. The change of the slope at C, the yield point on unloading, will not be evident from the graph of the pressure cycle.

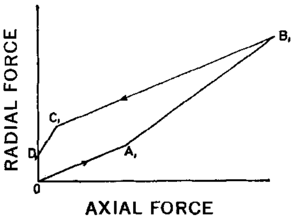

Fig. 9—Compressional cycle of a Mohr's body.

Consider the third case, where the body is also rigid, but after yield has taken place, the shearing stress (Mohr's theory) (7) in a plane of slip depends on the value of the normal stress σ_n acting in the same plane. In other words, the yield stress in shear is a function of the normal stress on the plane of shear. In the simple case where the body yields when:

$$\text{shearing stress} = S + \mu\sigma_n \qquad \text{(Eq. 3)}$$

the term μ is similar to a friction force, and the proportionality factor μ may be interpreted as a coefficient of internal solid (Coulomb type) friction. In this case, the normal stress on the plane of shear $= (\sigma + \tau)/2$ and the shearing stress $= (\sigma - \tau)/2$ (computed from Mohr's circle for principal stresses).

At yield from Eq. 3:

$$\sigma - \tau = 2S + \mu(\sigma + \tau) \qquad \text{(Eq. 4)}$$

$$\therefore \tau = [(1 - \mu)\sigma - 2S]/(1 + \mu) \qquad \text{(Eq. 5)}$$

On unloading, providing the axial loading has been sufficiently large (B′), the radial force will diminish according to the equation $\tau = \nu\sigma$, and then when the material yields again at the point C′,

$$\tau = [(1 + \mu)\sigma + 2S]/(1 - \mu) \qquad \text{(Eq. 6)}$$

The slope A′B′ $= (1 - \mu)/(1 + \mu)$. The final slope C′D′ $= (1 + \mu)/(1 - \mu)$. The typical pressure cycle for this case takes the form shown in Fig. 9.

It must be realized that the pressure cycles described above are for models of solid, isotropic bodies under uniaxial compression, assuming that die-wall friction is absent. Compressing materials within a die to form a compact would obviously be somewhat different, as in this case, die-wall friction cannot be overlooked. In addition, the shape and size of the material (granules/crystals) could modify the pressure cycles.

Comparing the graphs of the pressure cycles of sucrose granules, sucrose crystals, aspirin crystals, sodium chloride crystals, acetaminophen granules, and acetaminophen granules with 3% polyvinylpyrrolidone (PVP), with the pressure cycles described, it can be seen that the cycles have certain features in common and certain analogies may be drawn. The pressure cycles of sucrose crystals, sucrose granules, sodium chloride crystals, and acetaminophen granules with 3% PVP are similar to the behavior of a solid body with a constant yield stress in shear, under uniaxial compression. Acetaminophen granules alone share a striking resemblance to that of a Mohr's body. It is interesting to note that the Mohr's body type pressure cycle of acetaminophen changes to that of a body with a constant yield stress in shear when granulated with 3% PVP. It is well known that acetaminophen on compression tends to cap and laminate. However, when granulated with 3% PVP no capping or lamination is evident. The aspirin compact appears to have a very low yield stress. It behaves more like an elastic body. The hysteresis loss is comparable to that of an elastic body. On completely removing the axial load, the radial force dissipates almost completely. The small residual radial force that is recorded may be due to some die-wall friction.

With all the materials investigated, the axial loading was taken up to various levels from 1000–5600 lb. on separate occasions before unloading was commenced. However, in the plot of the axial-radial pressure cycles shown, only three loading levels (about 2200, 4000, and 5600 lb.) for each material are illustrated. Except in the case of aspirin crystals, it appears that after yield has started, the pressure cycles conform to the same pattern. However, the residual radial force increases with the increase in the axial loading. With aspirin crystals, the residual radial force appears to have reached a limiting value at an axial loading of about 4000 lb. This illustrates the behavior of the compact at different levels of axial loading and seems to support the assumption that the solid aspirin compact behaves like an elastic body. The direct relationship between the residual radial force and axial force of the materials (except for aspirin) may be attributed to the permanent deformation of the compacts after yield has started. It is probably significant that the ratio of height to diameter (0.32) of the aspirin compact remained constant after an axial loading of about 4000 lb. Since all the materials were lubricated with the same amount of lubricant, the difference in behavior would indicate a fundamental difference in the materials.

Table I shows the slopes of the lines corresponding to OA, AB, BC, and CD of Figs. 1–6. The slopes of the lines OA and BC are similar in the case of sucrose granules, sucrose crystals, sodium chloride crystals, and acetaminophen granules granulated with 3% PVP, having values ranging from 0.36 to 0.57. These slopes are directly related to poisson's ratio where the proportionality constant is the same for tablets of the same dimensions. The slopes of the lines BC and CD for sucrose granules, sucrose crystals, and acetaminophen granules with 3% PVP are more or less the same in each case as expected, for materials with a constant yield stress in shear.

The behavior of sodium chloride crystals is rather interesting. At an axial loading of about 2000 lb. it behaves almost like a perfect model of a body with a constant yield stress in shear. At the maximum axial loading of about 5600 lb., although the values of OA and BC are still the same, there is a break in the unloading curve at C′. After the yield point C has been exceeded in the unloading cycle, the radial force exerted is larger than the axial force.

In the three models described (Figs. 7–9) the yield points in each half of the cycle (representing loading and unloading) are clearly defined. With the materials under investigation this is not always the case. For instance, with sodium chloride it is seen that the slope of the line in the first half of the cycle is not constant. The initial change of the line may be taken as the yield point for the material. The subsequent change may be due to either (*a*) closer packing of the compacts, or (*b*) crystal slip or crystal twinning (*i.e.*, a shifting of the position of the lattice in a part of a crystal into a second position, so that the second part is in a symmetrical position relative to the first part and some plane of symmetry). It is likely that both phenomena contribute. On unloading the compact of sodium chloride, the slope of the line changes gradually down to the point C′ before it corresponds to the initial slope in the first half of the cycle (corresponding to poisson's ratio). This may be due to an "after flow" effect.

Comparing the behavior of sucrose granules with the crystals, it is seen that in the case of the crystals, the yield point A is higher and it has just been reached before unloading was commenced at B. The poisson ratio of the crystals is also higher than that of the granules. The residual radial pressure of the granules is, however, higher. After the yield point has been exceeded, the crystals appear to transmit more radial force. The slope of the line changes from 0.42 initially to 0.82, as compared with 0.36 to 0.42 in the case of the granules. The pressure cycles of the two sizes of sucrose granules are almost identical. However, the smaller of the sucrose crystals seem to have a higher yield point (A) at 5000 lb. compared to 4700 lb. for the larger crystals. This is to be expected as the yield point would depend more on the particle size of the material, but once a compact is formed the original particle size would not play a great role in its behavior, as the body now becomes a homogeneous isotropic mass.

Acetaminophen granules appear to behave like a Mohr's body. In this case, the final slope of the line C′D′ is 1. From the slope of A′B′ the value μ (coefficient of internal friction) is found to be 0.40.

The present investigation reveals significant differences between different granular and crystalline materials. Taking the case of acetaminophen it is seen that the change from a freely capping and laminating compact to a solid one is associated with the transformation from a Mohr's body type of pressure cycle to one with a constant yield stress in shear. It is perhaps more than coincidence that the materials which form firm and solid compacts exhibit the pressure cycle of a body with a constant yield stress in shear. At this stage, although no definite conclusion may be drawn, reasonable evidence exists that the classification of materials that form "good" or "bad" tablets may be carried out by an analysis of their pressure cycles, rather than from surmise. Admittedly, a wider range of materials will have to be investigated before any definite form of behavior can be predicted. No account has been taken in this investigation of the crystal shape. Indeed the crystal shape (anisotropy or isotropy) would modify the pressure cycles to a great extent. Further work is being conducted on the effect of lubrication on the pressure cycles.

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