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RESEARCH PAPER

Effect of Compression Force, Compression Speed, and Particle Size on the Compression Properties of Paracetamol

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ABSTRACT

The compression characteristics of two particle size fractions (< 90 μm, 105–210 μm) of paracetamol were examined. Each fraction produced extremely weak tablets and displayed a high tendency to cap. Low correlation coefficients of the initial parts of the Heckel plots, a low strain rate sensitivity, and an increase in mean yield pressure (from 34.2 to 45.5 MPa) with decrease in particle size all confirmed that the main mechanism during the compaction of paracetamol was fragmentation. The 105–210-μm particles underwent more fragmentation than the less than 90-μm powder. Heckel analysis confirmed that the larger size fraction of paracetamol produced denser compacts than the smaller fraction. The 105–210-μm fraction resulted in tablets with lower elastic recoveries and elastic energies. The elastic : plastic energy ratios indicated that the majority of energy involved during the compaction of paracetamol was utilized as elastic energy, indicative of massive elastic deformation of paracetamol particles under pressure.

Key Words: *Compression force; Compression speed; Elastic deformation; Fragmentation; Mean yield pressure; Paracetamol; Plastic deformation*

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INTRODUCTION

Unmodified paracetamol crystals exhibit poor compressibility during compaction, resulting in weak and unacceptable tablets with a high tendency to cap (1). Malamataris et al. (2) noted that the incidence of capping and lamination during production, following ejection of tablets from the die, depended on the plastic and elastic behaviors of the material used. It has been suggested that materials undergoing plastic deformation, in contrast to elastic deformation, display enhanced bond formation and produce strong tablets (3).

In general, the strength of a compact depends on the inherent ability of the powder to reduce in volume during compression and the amount of interparticulate attraction in the final compact. The decrease in compact volume with increasing compression load is attributed normally to particle rearrangement, elastic deformation, plastic deformation, and particle fragmentation. Pharmaceutical materials normally consolidate by more than one of these mechanisms (4,5).

The aim of this study was to investigate the fundamental compression characteristics of paracetamol. Two different particle size fractions of paracetamol were compressed at different compaction forces and compaction speeds. Heckel analysis, elastic recoveries, elastic energies, and plastic energies were determined.

EXPERIMENTAL

Paracetamol powder was obtained from Sterling Organics, Northumberland, UK. Two particle size fractions (<90 and 105–210 μm) were used.

Compression

Compression was carried out using a high-speed compaction simulator (ESH Testing Ltd., Brierley Hill, West Midlands, UK) fitted with 12.5-mm flat-faced punches. A sawtooth time-displacement profile was used to control both upper and lower punches.

The die wall was prelubricated with 4% w/w magnesium stearate in acetone before each compression. Four tablets were produced at compression speeds of 10, 50, 100, or 250 mm s^{-1} up to a maximum of 30 kN compression force. A constant weight of 400 mg was maintained for all the samples. To eliminate the effect of moisture on the compaction properties of paracetamol (6), the sieved fractions were dried in an oven at 55°C for 24 h and stored in tightly closed jars before use.

During a compression cycle, the force and displacement data from the upper and lower load cells and linear variable differential transformers (LVDTs) were captured and analyzed.

Measurement of Elastic and Plastic Energies

For a system in which both punches are mobile, the punch separation may be plotted against the upper punch force. The area under this curve will be the work done or energy used. The net work of compaction (plastic energy) and expansion work of compaction (elastic energy) were measured using energy analysis on the force-punch displacement plots.

Figure 1 illustrates a typical force-punch displacement plot, where A is the punch separation at the first measurable force. B is the peak force at minimal punch separation, C represents the minimum punch separation, and D is the separation after decompression. The area ABC gives the gross energy, and the area under curve CBD corresponds to the decompression energy or elastic energy. The net compaction energy or plastic energy (the area under curve ABD) was determined from the difference between area ABC and area CBD.

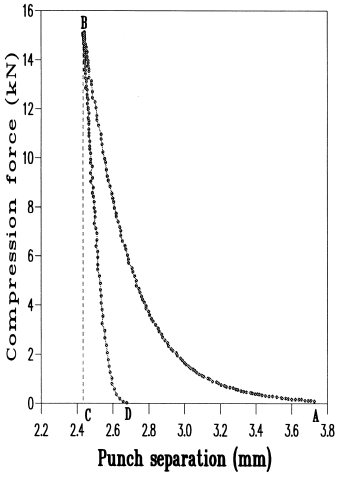

Figure 1. Typical force-punch separation plot for paracetamol (105–210-μm sample) at a compression speed of 10 mm s^{-1}.

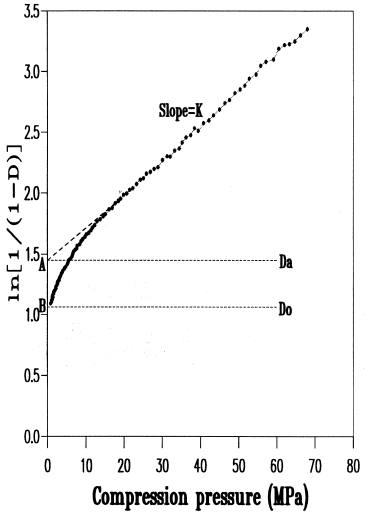

Figure 2. Typical Heckel plot for paracetamol (105–210-μm sample) at a compression speed of 10 mm s^{-1}.

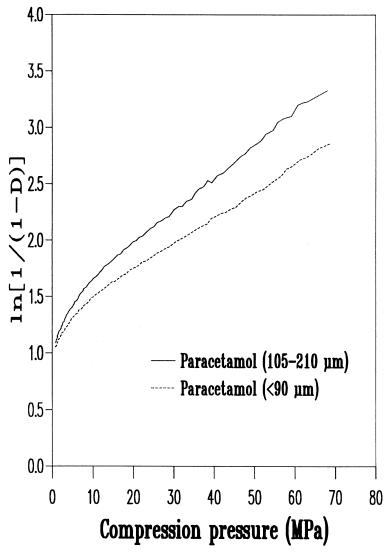

Figure 3. Typical Heckel plots of the size fractions less than 90 μm or 105–210 μm of paracetamol at a compression speed of 10 mm s^{-1}.

Heckel Analysis

A computer program was employed to fit data obtained during compaction to the Heckel equation (Eq. 1) (7,8).

$$\ln[1/(1-D)] = KP + A \quad (1)$$

Figure 2 illustrates a typical Heckel plot. In Eq. 1, D is the relative density of a tablet (the ratio of tablet density to true density of powder) at applied pressure P. K is the slope of the straight-line portion of the Heckel plot, and the reciprocal of K is the mean yield pressure. From the intercept of the linear portion of this plot, A, the total densification of the powder bed due to die filling, was obtained and used to determine the particle rearrangement D_a from Eq. 2.

$$D_a = 1 - e^{-A} \quad (2)$$

From B, the place where the Heckel plot intercepts the $\ln 1/1-D$ axis (Fig. 3), the density of powder at zero pressure D_0 is obtained (Eq. 3). D_0 can be defined as the densification due to die filling or to initial powder packing.

$$D_0 = 1 - e^{-B} \quad (3)$$

The extent of particle slippage and rearrangement D_b is determined by subtracting D_0 from D_a (Eq. 4).

$$D_b = D_a - D_0 \quad (4)$$

Determination of Elastic Recovery of Tablets in the Die

Tablets made from different particle sizes of paracetamol were too weak and capped after ejection, so that it was impossible to handle them and monitor their thickness outside the die. Therefore, the percentage of elastic recovery in the die of each tablet was calculated using Eq. 5.

$$\%\ \text{Elastic recovery} = [(H - H_c)/H_c] \times 100 \quad (5)$$

where H_c and H are the thicknesses of the tablet under maximum pressure and after the compression force has been removed, respectively.

RESULTS AND DISCUSSION

Compression of both particle size fractions of paracetamol at all compression forces, even at the lowest compression speed, produced extremely weak tablets with no measurable strength and with a high tendency to cap, which is indicative of weak interparticulate bonding between paracetamol particles.

Figure 3 shows typical Heckel plots of the different particle size fractions of paracetamol obtained at a compaction speed of 10 mm s^{-1}. This figure indicates that the larger particles (105–210 μm) exhibited higher relative densities for a given applied

pressure than the smaller fraction (< 90 μm). Thus, the degree of densification that occurred during compression was greater for the larger particle size fraction. This can be attributed to increased frictional and cohesive forces associated with the smaller size range, which tend to restrict particle sliding and thus reduce densification (9,10). Furthermore, during compaction, small particles were produced from fragmentation of the larger angular-shaped particles, and there appeared to be a tendency to fill the remaining interparticulate voids between the crystals with the new smaller particles. This could lead to further increase in the relative density of the compacts made from larger particle fractions. In contrast, it would be expected that only a relatively small amount of fragmentation would occur in the smaller particle size fraction (< 90 μm) due to the spherical shape of these particles as reported by McKenna and McCafferty (11) and Roberts and Rowe (10).

Figure 3 exhibits that the slope of Heckel plot for the 105–210-μm fraction was greater than for the fraction less than 90 μm, indicating that the reciprocal of K, which is mean yield pressure, is lower for the larger particle fractions. Table 1 also shows that the mean yield pressures for the particles less than 90 μm and 105–210 μm at a compression speed of 10 mm s^{-1} were 34.2 and 45.5 MPa, respectively.

The correlation coefficients r^* of the initial part of the Heckel plot (0–20 MPa) for the particles 105–210 μm and less than 90 μm were 0.957 and 0.972, respectively, indicating a higher degree of fragmentation for the larger particles than the smaller particles. It has been reported that the correlation coefficient of the initial part of the curve of a Heckel plot serves as a tool that may be used to quantify the tendency of particles to fragment. A linear segment (with a high value of the correlation coefficient) is obtained for nonfragmenting materials such as sodium chloride, whereas a nonlinear curve (with a low correlation coefficient) corresponds to materials that consolidate mainly by fragmentation rather than plastic deformation (e.g., dicalcium phosphate dihydrate) (3,12).

Table 1 also shows that the mean yield pressures for fractions less than 90 μm and 105–210 μm at a compression speed of 10 mm s^{-1} are 34.2 and 45.5 MPa, respectively. A low mean yield pressure (< 50 MPa), obtained for materials such as microcrystalline cellulose, indicates a high degree of plastic deformation under pressure (13,14). York (9) and Duberg and Nystrom (5) reported that the value of mean yield pressure derived from the slope of the linear portion of the Heckel plot depends on the fragmentation and both elastic and plastic deformation of the material under applied load. Therefore, for elastic materials, a false, low mean yield pressure may be obtained (15).

It is difficult to distinguish between elastic and plastic deformation evaluated from the slope of the linear portion of the Heckel plot; therefore, Duberg and Nystrom (5) divided the Heckel plot into compression and decompression phases. During decompression, the elastic propensities of the particles could result in an increase in porosity or a decrease in the density of the tablets. The decompression curve should be approximately horizontal when no elastic deformation is present; that is, the instantaneous elastic expansion of the tablet is negligible. A considerable deviation from the horizontal in the decompression phase indicates an elastic behavior of the material under pressure. In this case, a low value of the mean yield pressure was obtained. Therefore, a low value of mean yield pressure is real and acceptable when the decompression phase of the Heckel plot does not show a large deviation from the horizontal; that is, the tablet does not undergo a massive elastic deformation. Figure 4 shows the whole compression cycle (compression and decompression phases) for the 105–210-μm fraction of paracetamol. The large deviation from the horizontal during the decompression phase is indicative of a high degree of elastic propensity of these particles under pressure. Therefore, the low mean yield pressure found for paracetamol is attributed to its elastic behavior and not to its plastic deformation.

The effects of compression speed on mean yield pressure of the 90 μm and 105–210-μm fractions of

Table 1

Effect of Compression Speed on the Mean Yield Pressures (± SD) of the < 90-μm and 105–210-μm Particle Size Fractions of Paracetamol

Compression Speed (mm s^{-1})	Mean Yield Pressure (MPa)	
	105–210 μm	< 90 μm
10	34.4 ± 2.0	44.5 ± 1.5
50	35.5 ± 1.2	44.8 ± 1.2
100	38.6 ± 0.6	48.7 ± 1.5
250	42.3 ± 1.6	51.5 ± 2.7

crystals are shown in Table 1. As the compaction speed increased, the mean yield pressure for each particle size increased. However, Tukey's test revealed that there were no significant differences ($P > .05$) between the mean yield pressures obtained at 10 and 50 mm s^{-1} for both fractions. In addition, the mean yield pressure obtained at 100 and 250 mm s^{-1} for the fraction less than 90 μm could not be differentiated.

The changes of mean yield pressures with compression speeds can be quantified using Eq. 6, which allows the calculation of percentage strain rate sensitivity (SRS) (16):

$$\text{SRS} = [(P_{y2} - P_{y1})/P_{y2}] \times 100 \quad (6)$$

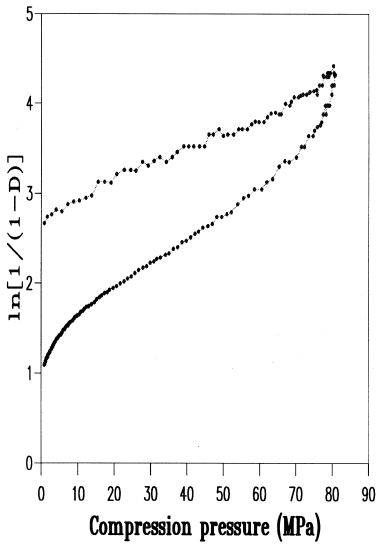

Figure 4. Heckel plot, including compression and decompression phases, of the 105–210-μm fraction of paracetamol at a compression speed of 10 mm s^{-1}.

where P_{y1} and P_{y2} are the mean yield pressures at 10 mm s^{-1} and 250 mm s^{-1} punch velocity, respectively. The SRS values for the fractions less than 90 μm and 105–210 μm of paracetamol were 13.6% and 18.7%, respectively.

The SRS is a useful index that can show the plastic or brittle nature of a material. Due to the time-dependent nature of plastic deformation, the mean yield pressure increases with increasing punch velocity for plastic materials such as Avicel® and sodium chloride, which consequently show high values of SRS (>40%). However, for lactose, which deforms by a combination of particle fracture and plastic deformation, the SRS was about 16% (16,17). The rather low SRS values found for both particle sizes of paracetamol is indicative that fragmentation is the dominant mechanism during compaction.

Table 1 also indicates that, at each punch velocity, the mean yield pressure increased as the particle size decreased. It has been reported that, for plastically deforming materials such as sodium chloride and potassium chloride (12,18), microcrystalline cellulose (10), and starch (11), the measured mean yield pressures were independent of particle size. However, for materials that deform by particle fragmentation such as lactose and calcium carbonate, the mean yield pressures increased with a reduction in particle size (9,10,18). The findings of this part of the study again indicate that paracetamol belongs to the group of materials that predominantly deform by fragmentation. The massive fracture of paracetamol particles under applied load has been also confirmed by other techniques such as permeametry (19).

Table 2 shows the values of D_0, D_a, and D_b derived from Heckel plots at compression speeds of 10 and 250 mm s^{-1}. For each particle size, the values of D_0 and D_a decreased with increasing punch speeds. The decrease of relative densities with

Table 2

Values of D_0, D_a, *and* D_b ($\pm$ *SD*) *of Different Particle Size Fractions of Paracetamol at Compaction Speeds of 10 and 250 mm* s^{-1}

Compression Speed (mm s^{-1})	105–210 μm			<90 μm		
	D_0	D_a	D_b	D_0	D_a	D_b
10	0.667	0.718	0.061	0.645	0.703	0.058
	±0.008	±0.004	±0.008	±0.005	±0.004	±0.004
250	0.620	0.670	0.053	0.593	0.648	0.055
	±0.005	±0.000	±0.004	±0.005	±0.005	±0.005

increasing compaction speed may be either due to an increase in the frictional and adhesive forces between particles or due to restriction of the air escape from the powder bed (16).

Table 2 also indicates that, at each compaction speed, the smaller particle fraction of paracetamol showed apparently lower values of D_0 and D_a than the larger fractions. Two-way analysis of variance showed that there were significant differences ($P < .05$) between the less than 90-μm and the 105–210-μm particle fractions in terms of D_0 and D_a. Decrease in values of D_0 and D_a for smaller particles may be attributed to an increase in the frictional and cohesive forces between the smaller size particles and/or more fragmentation of the 105–210-μm fraction, as discussed above.

The effect of compression force on the elastic recoveries in the die of tablets made from the two size fractions of paracetamol is shown in Fig. 5. Increasing the compaction force resulted in an increase in the elastic recoveries of the tablets. Tablets made from the fraction less than 90 μm exhibited higher elastic recoveries than larger particles. Two-way analysis of variance showed that there were significant differences ($P < .05$) between the elastic recoveries of the tablets made from the fraction less than 90 μm and tablets made from the 105–210-μm fraction. However, there were no significant differences (using Tukey's test) between the elastic recoveries of the tablets made from the two particle sizes at 20 and 25 kN ($P > .05$). Elastic recovery is axial expansion of a tablet following the removal of the compression force. The precise quantification of elastic recovery is useful in elucidation of the dominant mechanisms of powder consolidation. Elastic recovery has been associated with the storage of elastic energy during compression as deformation energy under stress and subsequent release of this energy after removal of axial pressure.

The effects of compression force or compression speed on the elastic energy, plastic energy, and the ratio of elastic energy/plastic energy (EE/PE) of tablets made from paracetamol samples are illustrated in Tables 3 and 4. These data indicate that, at different compaction forces or speeds, the tablets made from the 105–210-μm fraction exhibited lower elastic energies than the fraction less than 90 μm. However, Tukey's test showed that there was no significant difference ($P > .05$) between elastic energies for the two particle fractions at 30 kN compaction force (Table 3) and at 100 mm s^{-1} compaction speed (Table 4). In the present study, the results of elastic recovery were in agreement with the data of

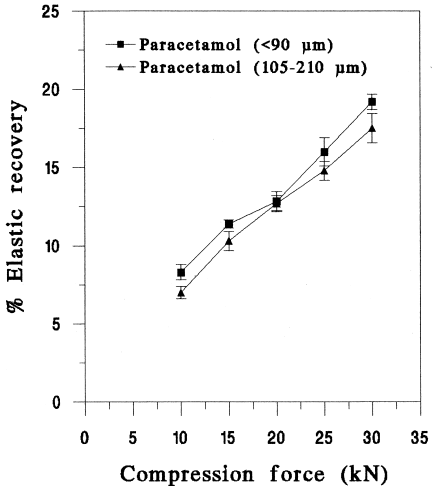

Figure 5. Effect of compression force on the elastic recovery in the die of tablets made from particle size fractions less than 90 μm or 105–210 μm of paracetamol at a compression speed of 10 mm s^{-1}.

Table 3

Effect of Compression Force on the Elastic Energy (EE), Plastic Energy (PE), and Elastic Energy/Plastic Energies Ratio (± SD) of Tablets Made from 105–210-μm or < 90-μm Particle Fractions of Paracetamol at a Compression Speed of 10 mm s^{-1}

Compression Force (kN)	Elastic Energy (J)		Plastic Energy (J)		EE/PE Ratio	
	105–210 μm	< 90 μm	105–210 μm	< 90 μm	105–210 μm	< 90 μm
10	1.0 ± 0.1	1.7 ± 0.2	1.9 ± 0.1	2.2 ± 0.1	0.54 ± 0.05	0.74 ± 0.06
15	2.1 ± 0.2	2.5 ± 0.2	2.3 ± 0.1	2.7 ± 0.1	0.87 ± 0.09	0.92 ± 0.04
20	3.4 ± 0.1	4.1 ± 0.3	2.6 ± 0.1	3.0 ± 0.1	1.31 ± 0.11	1.36 ± 0.14
25	5.1 ± 0.3	5.5 ± 0.2	3.2 ± 0.2	3.4 ± 0.2	1.58 ± 0.18	1.73 ± 0.11
30	6.8 ± 0.2	7.1 ± 0.5	3.6 ± 0.2	4.0 ± 0.2	1.89 ± 0.16	1.78 ± 0.17

Table 4

Effect of Compression Speed on the Elastic Energy (EE), Plastic Energy (PE), and Elastic Energy/Plastic Energies Ratio (±SD) of Tablets Made from 105–210-μm or <90-μm Particle Fractions of Paracetamol at a Compression Force of 15 kN

Compression Speed (mm s^{-1})	Elastic Energy (J)		Plastic Energy (J)		EE/PE Ratio	
	105–210 μm	<90 μm	105–210 μm	<90 μm	105–210 μm	<90 μm
10	2.1 ± 0.2	2.5 ± 0.2	2.3 ± 0.1	2.7 ± 0.1	0.87 ± 0.09	0.92 ± 0.37
50	2.4 ± 0.1	3.1 ± 0.2	2.9 ± 0.1	3.4 ± 0.1	0.75 ± 0.07	0.92 ± 0.08
100	3.7 ± 0.2	4.0 ± 0.2	3.4 ± 0.1	4.0 ± 0.2	1.08 ± 0.08	1.00 ± 0.06
250	4.9 ± 0.3	5.6 ± 0.3	4.3 ± 0.4	4.5 ± 0.3	1.14 ± 0.12	1.24 ± 0.10

the elastic energies. The elastic energies indicated that the tablets made from smaller particles were relatively more elastic than tablets made from larger particles, resulting in an increase in the elastic recovery of tablets made from the fraction less than 90 μm fraction (Fig. 5). The lower elastic recovery and elastic energy of tablets made from larger particles of paracetamol may indicate higher interparticulate bondings for the 105–210-μm fraction compared to the smaller size fraction. In addition, increased fragmentation of the larger particles resulted in an increased interparticulate bonding due to the formation of more fresh and clean particle surfaces for bonding compared to smaller particles with less fragmentation.

Tables 3 and 4 also indicate that, at constant speeds or forces, the plastic energies of tablets made from the fraction less than 90 μm were higher than for tablets made from the 105–210-μm fraction. However, Tukey's test revealed that, at 25 kN compaction force (Table 3) and at 250 mm s^{-2} (Table 4), there were no significant differences ($P > .05$) between the plastic energies of tablets made from the fractions less than 90 μm or 105–210 μm. Plastic energy (net compaction energy) is utilized for die wall friction, interparticle friction, particle slippage and rearrangement, plastic deformation, fragmentation, and formation of bonds during compaction. An increase in plastic energy for smaller particles may be attributed to the increased frictional and cohesive forces between the smaller particles.

The ratios of elastic/plastic energies (EE/PE) at different compaction forces or speeds (Tables 3 and 4) indicate that the majority of the energy involved during compression of paracetamol was consumed as elastic energy at higher compression forces and speeds. These results also show that, with increase in compression force or compression speed, the ratio EE/PE increased; that is, the tablets became more elastic. Garr and Rubinstein (20) reported that the intensity of capping of paracetamol compacts increased with increasing compaction speed. The increase in capping tendencies with compaction speed may be related to the increase in the EE/PE ratio.

CONCLUSIONS

The results of Heckel analyses indicated that the predominant mechanism of compaction of paracetamol was fragmentation. The larger particle fraction of paracetamol underwent more fragmentation than the smaller particles. Heckel analysis also indicated that, for a given applied pressure, the larger particles of paracetamol produced denser compacts than the smaller particles.

The results of elastic/plastic energies ratio indicated that the majority of energy involved during compaction of paracetamol was utilized as elastic energy. This indicated a massive elastic deformation of paracetamol particles under pressure, resulting in weak and capped tablets.

A high degree of elastic behavior of paracetamol particles during compaction was confirmed by the decompression phase of the Heckel plot. This showed a large deviation from horizontal. Therefore, the rather low mean yield pressure obtained for paracetamol was attributed to its high elastic propensity during compaction and not due to plastic deformation.

It was found that larger particles exhibited less elastic recovery and elastic energy compared to smaller particles. This was attributed to increased fragmentation of larger particles, resulting in increased bonding between particles due to the formation of more new, fresh, and clean particle surfaces.

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