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Compaction studies on pellets I. Uncoated pellets

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Summary

Pellets made from microcrystalline cellulose, plus dicalcium phosphate dihydrate, lactose and propranolol HCl were compacted on an Integrated Compaction Research System. Several methods including porosity changes, Heckel equation, total work of compaction and average power consumption were used to compare the compaction behavior of the pellets with that of the powders from which they were formed. The effect of external additives and punch velocity on the compaction properties of the pellets was also studied. Significant differences between the compaction properties of the pellets and the powders were observed. It was found that the powders examined compacted by plastic deformation and produced strong compacts, whereas, their pellets exhibited elastic deformation and brittle fragmentation which resulted in compacts of lower tensile strength.

Introduction

The phenomena and mechanisms involved during the compaction of pharmaceutical powders (Nelson et al., 1955; Hersey and Rees, 1971) and granules (DeBlaey and Polderman, 1970) have been the subject of numerous publications during the last four decades. However, there are not many published reports on the compaction characteristics of pellets (Lehmann, 1984).

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The densification of powders with increasing compaction pressure has often been described by the Athy-Heckel equation (Athy, 1930; Heckel, 1961; Rue and Rees, 1978; Geoffroy and Carstensen, 1991), which can be expressed:

$$\log E^{-1} = KP + A \quad (1)$$

where E is porosity, P denotes applied pressure, and K and A are constants.

Heckel (1961) postulated that in the equation, constant A represents the degree of packing at low pressures during particle rearrangement and the value of K is related to the yield strength of the material. The latter is regarded as a material constant, and has been used to characterize the

consolidation mechanisms of powders (Hersey and Rees, 1971).

In order to assess the consolidation behavior of pharmaceutical materials, many researchers have attempted to measure the energy (work) involved during the compaction of tablets (De Blaey and Polderman, 1970; Carstensen et. al., 1981; Ragnarson and Sjogren, 1983). Energy transferred by the upper and lower punches is utilized for particle rearrangement, elastic-plastic deformation and/or brittle fracture of the material. The amount of the total energy applied to the material during compaction can be estimated from the area under an appropriate force-displacement curve. Çelik and Marshall (1989) estimated the total work of compaction (TWC) using the following equation, in which the contributions of the upper and lower punches to the total work are calculated separately:

$$\mathrm{TWC} = \int_{x=0}^{x=x_{\max}(\mathrm{up})} F_{\mathrm{up}}\, \mathrm{d}x_{\mathrm{up}} + \int_{x=0}^{x=x_{\max}(\mathrm{lp})} F_{\mathrm{lp}}\, \mathrm{d}x_{\mathrm{lp}} \tag{2}$$

where F_{up} and F_{lp} are the forces on the upper and lower punches, respectively; x_{up} and x_{lp} are the contributions of the upper and lower punches, respectively, to the decrease in distance between them; $x = 0$ is the point at which $E = E_0$ (E_0 is the initial porosity) and the maximum applied load is reached at x_{max}(up) and at x_{max}(lp).

Since the rate of compaction is known to affect the consolidation process, some researchers have turned their attention to an alternative way where the energy data are presented using a power profile which includes the time parameter (Armstrong et al., 1983; Çelik and Marshall, 1989). Çelik and Marshall (1989) used the following relationship to calculate the 'Average' power consumption (APC) (units: W):

$$\mathrm{APC} = \int_{x=0}^{x=x_{\max}} \frac{F\, \mathrm{d}x}{t} \tag{3}$$

where $x = 0$ and $x = x_{max}$ are the points at which $E = E_0$ and $E = E_m$ (E_m is the porosity at maximum applied load), respectively. The parameter t is the time during which the material has been compressed.

The strength of compacts is commonly measured by the diametral compression method which involves their tensile failure. This type of failure is often referred to as the crushing stength of the tablet. However, the crushing strength of compacts of varying dimensions is not comparable, due to non-uniform distribution of stress and density. Fell and Newton (1968) applied the following equation which allows comparison of tensile strength (T_s) of compacts of different sizes, since it includes the normalizing factors of diameter (d_e) and thickness (H_e):

$$T_s = \frac{2F_c}{\pi d_e H_e} \tag{4}$$

where F_c is the force required to break the compact.

The aim of the present work is to study the compaction behavior of pellets, to compare their deformation characteristics with those of the powders from which formed, and to investigate the effect of external additives and punch velocity on the compaction properties of the pellets.

Materials and Methods

Microcrystalline cellulose (Emcocel 50M, E. Mendell Co.), lactose (Fast-Flo, Foremost Whey Products), dicalcium phosphate dihydrate (Emcompress, E. Mendell Co.), and propranolol HCl (Byron Chemicals) were the materials used to prepare the pellets. Magnesium stearate (Fisher Scientific), pregelatinized starch (Starch 1500, Colorcon), and soy polysaccharide (Emcosoy, E. Mendell Co.) were used as the external additives. All the powders were used as received.

A 1 kg Glatt rotor granulator was employed to make the pellets from microcrystalline cellulose alone and from two formulations. One of the latter consisted of 80% w/w microcrystalline cellulose, 10% w/w lactose, and 10% w/w propranolol HCl, while the other contained 80% w/w

TABLE 1

Moisture content of the pellets and their powders forms

Materials	Moisture content (%)
Powders	
Microcrystalline cellulose	4.28
F-I	4.10
F-II	4.38
Pellets	
Microcrystalline cellulose	4.34
F-I	4.15
F-II	4.26

microcrystalline cellulose, 10% w/w dicalcium phosphate, and 10% w/w propranolol HCl. Throughout the study, the former formulation was designated as F-I and the latter as F-II. Moisture content of the powders were determined using Karl Fisher (Metro-HM, 658KF processor, 665, Bosimet). The data summarized in Table 1 indicate that the moisture contents of the powders varied between 4.10 and 4.38%. Deionized water was used as the pelletizing agent. During pelletization samples were withdrawn at regular intervals and their moisture content was determined. Pellets were dried until their moisture content reached a constant value of 4.25 $\pm 0.15\%$, which was comparable to that of their powders. Typical size distribution of the pellets used in this study is presented in Table 2.

The true densities of the materials were measured using a helium pycnometer (Quantachrome Multipycnometer, model MVF-I), and the amount of material to be compacted was calculated to give a pre-determined true volume of 0.2 cm^3 which was kept constant for all the materials used throughout this study. An Integrated Compaction Research System (Mand Testing Ltd., Stourbridge, U.K.), also known as a 'compaction simulator' (Çelik and Lordi, 1991), fitted with 10.3 mm diameter, flat-faced, round BB tooling was employed for the compaction studies.

TABLE 2

Particle size distribution of the pellets

Mesh no.	Size (μm)	Frequency (%)
18	1000	2.14
20	840	42.86
25	695	32.14
30	595	17.86
35	500	5.00

Most of the compaction tests were carried out using a double-ended compaction profile with a constant punch velocity of 100 mm/s per punch up to the maximum applied load. A punch velocity of 1 mm/s was also applied in order to investigate the effect of rate of force application on the compaction characteristics of the materials. The maximum applied pressure was varied from one material to another to produce compacts at a pre-determined final porosity of 3 $\pm 0.3\%$ within the die.

The fidelity of displacement measurements during a compaction event, which influences the accuracy of the results obtained from subsequent data analysis, such as Heckel plots and porosity changes, depends on whether these measurements are properly corrected for the system deformation, i.e., the deformation of the punches, die and other associated machine components. In this study, the distortion of the system was determined by bringing the upper and lower punches into contact with no material in the die and applying loads up to 40 kN. The distortion factors were then calculated statistically and incorporated into the compaction data evaluation process.

The compaction data, consisting of the forces on and the displacement of the upper and lower punches, were collected using a digital storage oscilloscope (Nicolet model 440) at a speed of 5000 data/s per channel. The acquired data were subsequently analyzed using a program written in a combination of Microsoft Basic and RPL (a macro language used in a conjunction with RS1, a statistical data analysis tool) to obtain Heckel profiles and plots of porosity vs pressure, force vs displacement, TWC vs pressure and APC vs pressure.

The post-compaction tests performed on the ejected tablets included the determination of weight, thickness and diameter, friability (Erweka friabilator, type TAP, Germany), and crushing strength (Schleuniger, type 2E, Germany) of the

compacts, as well as their disintegration (Pharmatest, type PTZ1, Germany), and dissolution (Pharmatest, type PTWII, Germany) properties.

All pre-compaction, compaction and post-compaction tests were performed on at least five replicates.

Results and Discussion

Compacts of microcrystalline cellulose powder and pellets

In the present work, the materials were subjected to a varying applied pressure until a predetermined compact porosity was reached. One of the main advantages of this method is that some of the post-compaction test parameters, such as tensile strength and drug release profiles, can be compared directly without any need for normalization for the differences in the porosities of the compacts. However, the ejected compacts of different materials can exhibit some differences in their final porosities since the amount of elastic expansion during decompression and after ejection may vary significantly from one material to another. The difference between the applied pressures needed to cause a reduction in porosity to 3% within the die for different materials also gives a measure of their compressibility. Table 3 presents the maximum pressure applied to the materials in order to obtain compacts with this predetermined in-die porosity.

TABLE 3

Comparison of the maximum applied pressure required to produce compacts with 3% in-die porosity, and the tensile strength values of those compacts

Compacts	Maximum pressure (MPa)	Tensile strength (MPa)
Powders		
Microcrystalline cellulose	348	10.70
F-I	431	8.89
F-II	418	8.28
Pellets		
Microcrystalline cellulose	165	0.52
F-I	169	0.56
F-II	177	0.54

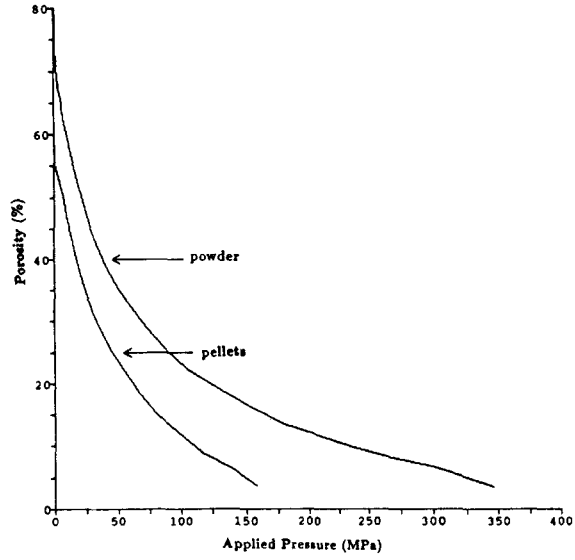

Fig. 1. Porosity vs pressure plots for the compacts of microcrystalline cellulose powder and pellets.

The following equation was used for the determination of percentage porosity:

$$E(\%) = \left(1 - \frac{V_t}{V_c}\right) \times 100 \qquad (5)$$

where V_t is the true volume of the material and V_c is the volume of the compact at a given pressure. The accuracy of the in-die porosity measurement depends on the precision of the weight, true density, and punch displacement determinations.

The porosity changes, as a function of compaction pressure for the compacts made from the powder and pellet forms of microcrystalline cellulose, are shown in Fig. 1. Microcrystalline cellulose powder exhibited a higher initial porosity change at low pressures than that of its pellets. This could be attributed to the higher initial porosity of the powder (geometric mean diameter, $d_g = 50\ \mu m$) which required low pressures to undergo repacking whereas pellets ($d_g = 650\ \mu m$) being spherical and relatively denser, exhibited shorter particle rearrangement stage and proceeded to the subsequent steps of compaction.

On compaction, the pellets required lower pressures than the powder to obtain the same porosities. The differences between the magnitude of the applied pressures to achieve the corresponding porosities increased as they approached the minimum porosity. However, the tensile strength of the ejected compacts of powder form was significantly higher than that of the pellets (Table 3). Therefore, the ability of this material to reduce in volume when compressed does not ensure the formation of a stronger compact.

The porosity data obtained for the compacts of microcrystalline cellulose powder and pellets were also used in the Heckel equation (Eqn 1) which is another method of studying the density-pressure relationship during compaction. The slopes of the linear portion of Heckel profiles (proportional to 1/yield pressure) differed for the powder and pellet forms (Fig. 2). This suggests that changing the shape and size of the microcrystalline cellulose particles may have affected the compaction properties (such as degree of bonding) of this material. When using the porosity function according to Heckel to describe the compaction mechanisms, as evaluated from slope of the linear

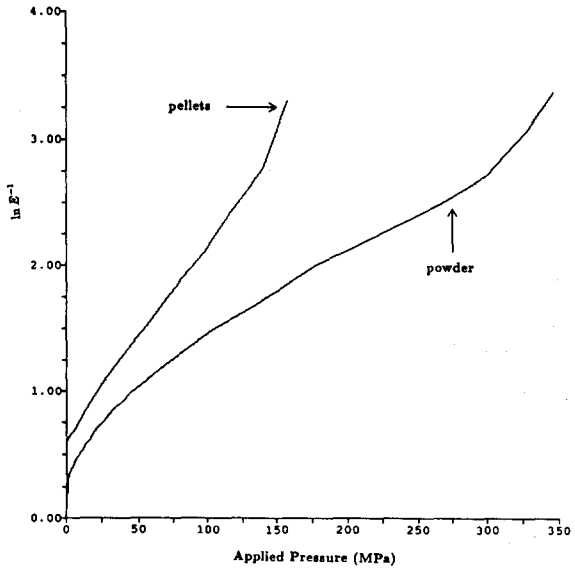

Fig. 2. Heckel plots for the compacts of microcrystalline cellulose powder and pellets.

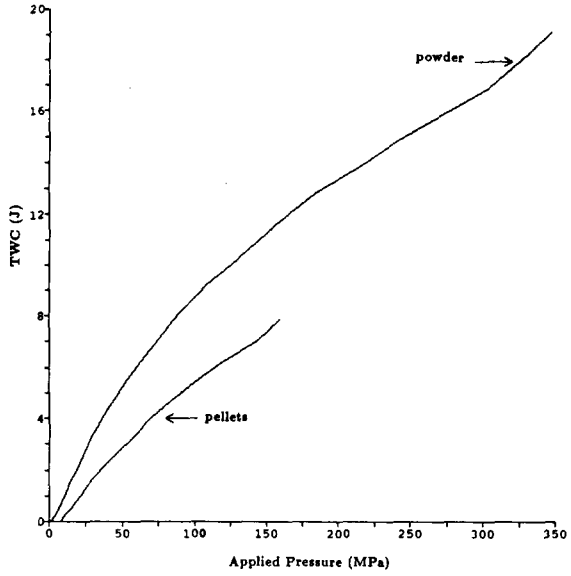

Fig. 3. Total work of compaction (TWC) vs pressure plots for the compacts of microcrystalline cellulose powder and pellets.

portion of the profile, it is difficult to distinguish between elastic and plastic deformation. According to Duberg and Nystrom (1986) density values 'at pressure' contain both elastic and plastic components, therefore, the yield pressure, determined from the slope of the linear portion of Heckel profiles, reflects the particles total ability to deform.

Materials with different packing characteristics and different deformational properties will absorb varying amounts of energy (Krycer et al., 1982) and the work involved in compaction correlates well with the strength of the resulting compacts (Çelik and Marshall, 1989). In this study, such a correlation was observed between the TWC (Fig. 3) and tensile strength (Table 3) values for the compacts of powders and pellets of microcrystalline cellulose. The work involved in the compaction and the tensile strength values of their compacts were both significantly less than those of the powder form, suggesting that the degree of bonding of this material has been considerably affected by the changes in its shape, size and also possibly by the reduction in the number of its potential bonding sites due to the pelletization process. Pellets, which are large and spheri-

cal in shape as compared to the small, irregular powder particles, have a low surface to volume ratio, and this might have resulted in a decreased area of contact between the particles as they consolidated.

APC values of the compacts of the microcrystalline powder and pellets were calculated using Eqn 3 and were plotted as a function of applied pressures (Fig. 4). A material exhibiting higher APC values at corresponding pressures usually produces relatively stronger compacts (Çelik and Marshall, 1989). However, the results in the present work (Fig. 4) were found to be in contrast with this statement. The compacts of the pellets exhibited higher APC values at corresponding pressures than those of powder form. This can be attributed to the shorter contact time (the time during which the upper punch remained in contact with the material) due to the absence of particle rearrangement stage which was observed in case of powder form.

Compacts of powder formulations and their pellets

The maximum pressure required to achieve the pre-determined porosity was lower for microcrystalline cellulose powder than that required

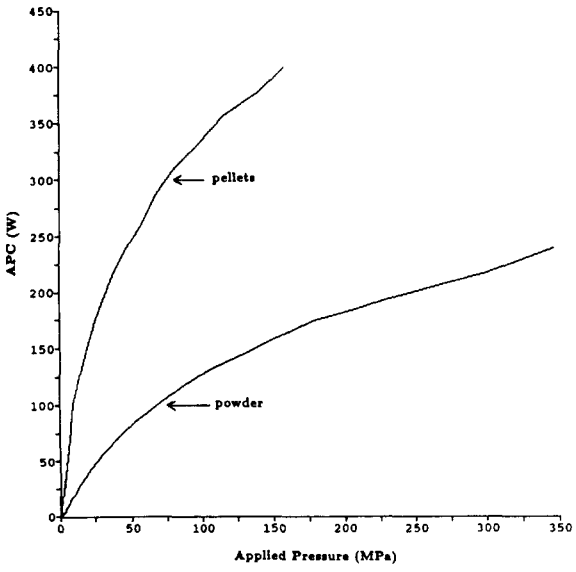

Fig. 4. Average power consumption (APC) vs pressure plots for the compacts of microcrystalline cellulose powder and pellets.

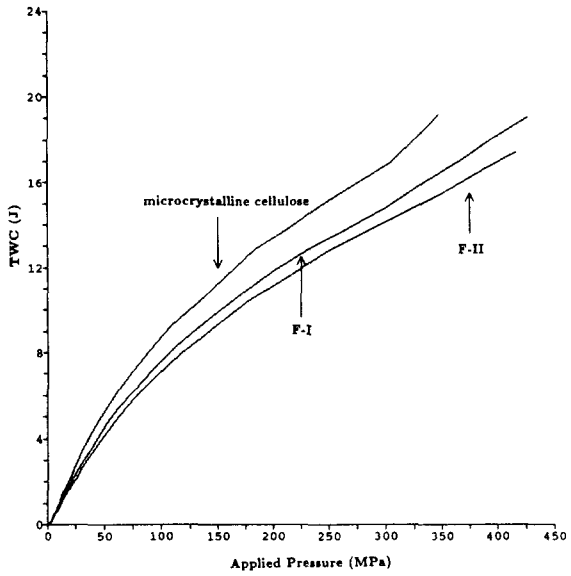

Fig. 5. Total work of compaction (TWC) vs pressure plots for the compacts of microcrystalline cellulose, F-I, and F-II powders.

for the two powder formulations (F-I and F-II) used in the study (Table 3). This indicates that addition of lactose or dicalcium phosphate dihydrate and propranolol HCl decreased the compressibility of the microcrystalline cellulose.

Fig. 5 presents TWC vs pressure plots for the compacts made from these powders. It can be suggested from the data given in this figure and Table 3, that stronger compacts are produced where a higher TWC has been involved. Therefore, the rank order for the calculated work and the tensile strength of compacts made from different materials in powder form is the same and as follows: microcrystalline cellulose > F-I powder formulation > F-II powder formulation.

Fig. 6 shows a comparison between the TWC vs pressure plots obtained from the materials in powder form and their pellets. The compacts of the powders exhibited higher values of TWC at corresponding pressures than that of the pellets. Compacts made from the powder formulation containing lactose (F-I) exhibited relatively higher TWC values at corresponding pressures and the tensile strength (Table 3) than that of the compacts made from the formulation containing dicalcium phosphate dihydrate (F-II). The tensile

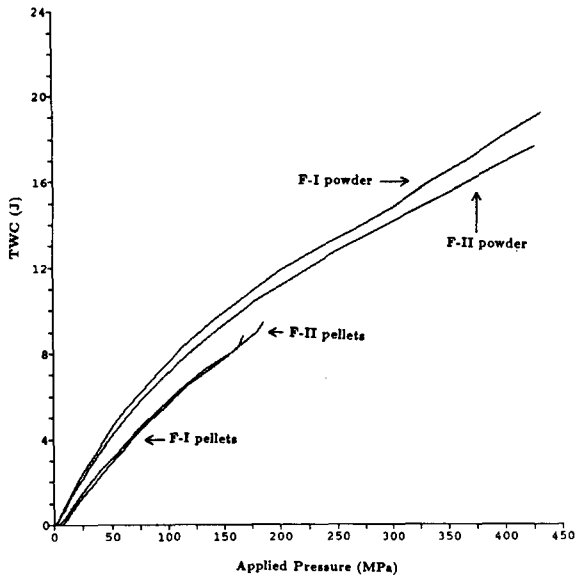

Fig. 6. Total work of compaction (TWC) vs pressure plots for the compacts of powder formulations and their pellets.

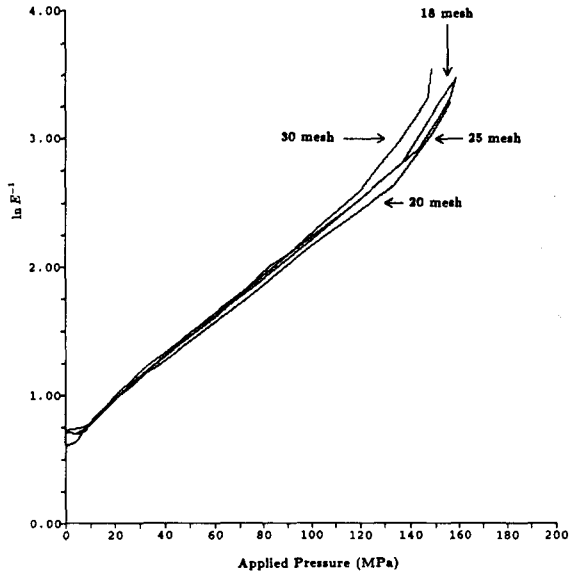

Fig. 7. Heckel plots for the compacts made from different particle sizes of F-I pellets.

strength and TWC values of the compacts made from microcrystalline cellulose pellets, F-I pellets, and F-II pellets did not differ significantly. Since F-I and F-II pellets used in the study contained 90% w/w of the same ingredients (80% w/w microcrystalline cellulose and 10% w/w propranolol HCl), they exhibited similar compaction properties. Therefore, for the purposes of clarity F-II pellets were omitted from the subsequent figures.

Hersey and Rees (1971) stated that the slopes of Heckel profiles of the materials that readily undergo time dependant deformation during compaction are significantly influenced by the particle size and initial bed porosity. On the other hand the materials that consolidate by brittle fragmentation exhibit a single relationship above a certain pressure irrespective of the initiated bed density. In the present work the Heckel equation was also applied to investigate the compaction characteristics of different particle sizes of the F-I pellets. Fig. 7 shows that the curves representing the compacts made from different size fractions of the pellets almost overlapped suggesting that, to a certain extent, brittle fragmentation might have occurred during compaction of the pellets. This view can be supported by scanning electron micrographs of the pellets before (Figs 8 and 9) and after (Figs 10 and 11) compaction in which there is evidence for some fragmentation. However, it should be noted that the particle size range (50–1000 μm) selected in this work may not be wide enough to conclude whether the brittle fragmentation is the dominant compaction mechanism for the pellets.

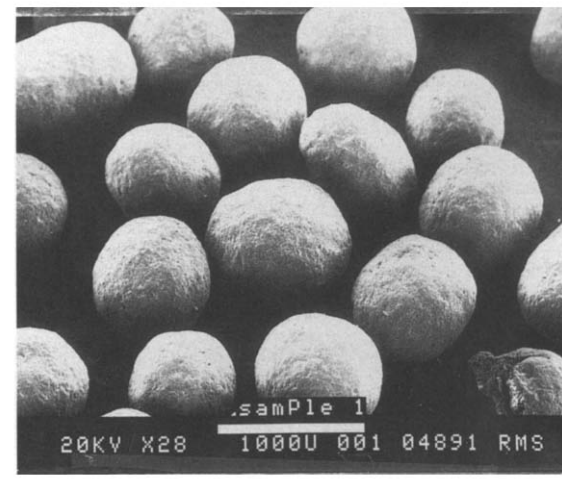

Fig. 8. Scanning electron micrograph of F-I pellets.

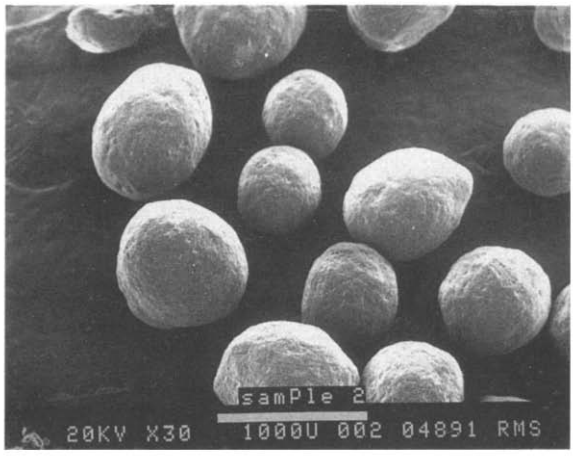

Fig. 9. Scanning electron micrograph of F-II pellets.

The measurement of the degree of elastic recovery that the compacts undergo on ejection is important due to the disruptive effects that the stored elastic expansion may have on the final strength of the compacts. Armstrong and Haines-Nutt (1970) determined the elastic recovery (ER_o) as:

$$ER_o(\%) = \frac{H_e - H_c}{H_c} \times 100 \quad (6)$$

where H_e and h_c are the thicknesses of the compact after ejection and at maximum load in the die, respectively.

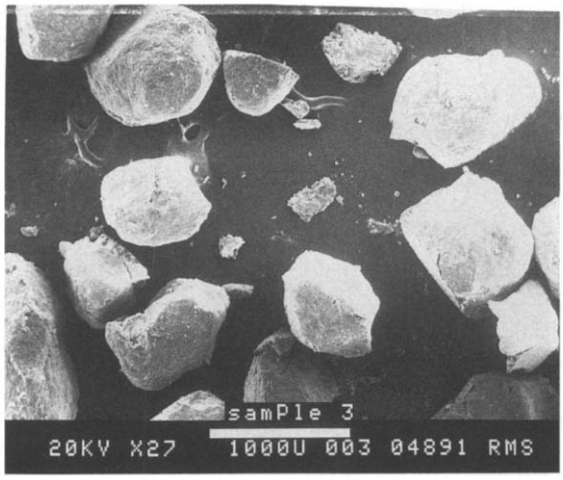

Fig. 10. Scanning electron micrograph of the broken compacts of F-I pellets.

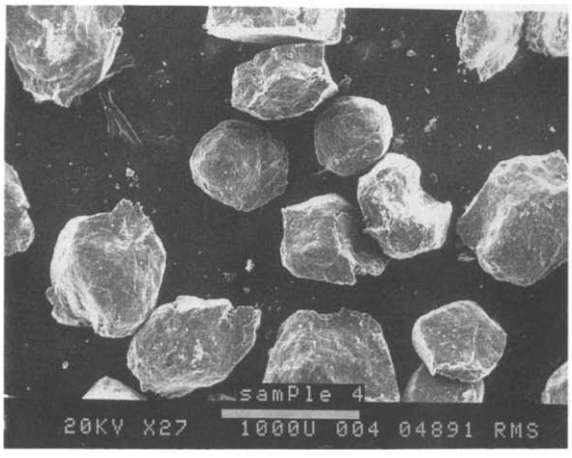

Fig. 11. Scanning electron micrograph of the broken compacts of F-II pellets.

The above equation, however, does not take into account the radial expansion of the compact. In the present study this parameter was also taken into consideration and the following equation was utilized while computing the elastic recovery indices.

$$ER(\%) = \frac{d_e^2 H_e - d_c^2 H_c}{d_c^2 H_c} \times 100 \quad (7)$$

where d_e and d_c are the diameters of the compacts after ejection and at maximum load in the die, respectively.

Eqn 7 is applicable only for the cylindrical compacts obtained by using flat faced punches. Assuming that there is negligible die expansion under applied load, the diameter of the die may be used as d_c. Table 4 presents the ER values of the compacts made from F-I and F-II formulations and their pellets. The compacts of pellets had higher ER values than those made from corresponding powder formulations. This must be due to the greater expansion of the compacts of pellets during decompression and ejection phase of the compaction event. Many of the bonds formed during compaction did not survive these phases, resulting in the lower tensile strength of their compacts.

A number of workers (Roberts and Rowe, 1985; Armstrong and Palfrey, 1989) have shown

TABLE 4

ER values for the compacts of powder formulations and their pellets

Compacts	ER (%) value
Powder formulations	
F-I	4.14
F-II	4.32
Pellets	
F-I	7.64
F-II	8.23

that the consolidation mechanism of a material is significantly influenced by changes in the rate of force application. Figs 12 and 13 present the Heckel curves for the compacts made from the powder and pellet forms of F-I and F-II at two different punch velocities. The tensile strength and yield pressure values of these compacts are given in Table 5. The yield pressure was calculated from the reciprocal of slope of the linear portion of the curves and the linearity was assumed between ln E^{-1} values of 1.5 and 2.5. It is clear from these data that an increase in punch velocity from 1 to 100 mm/s resulted in lower tensile strength and higher yield pressure values for the compacts of the powder form. The difference in the values at two different punch velocities were found to be significant indicating that the powders consolidated primarily by time dependant deformation mechanisms. On the contrary, the yield pressure and tensile strength values of the compacts made from pellets of this formulation did not differ significantly at different punch velocities.

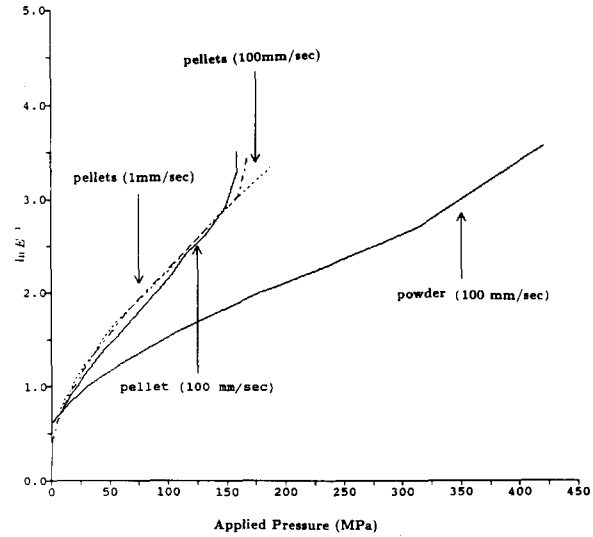

Fig. 12. Heckel plots for the compacts made from powder and pellets of F-I at two different punch velocities.

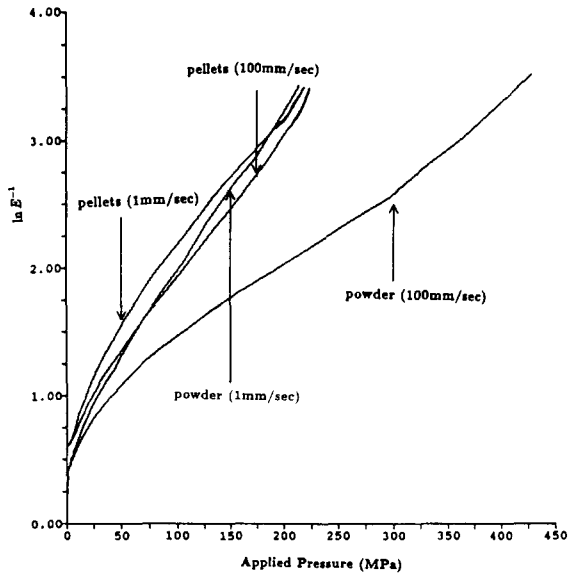

Fig. 13. Heckel plots for the compacts made from powder and pellets of F-II at two different punch velocities.

The following equations (Eqns 8 and 9) were used to compare the relative changes in the K and tensile strength values of the compacts at 1 and 100 mm/s punch velocities, respectively:

$$A(\%) = \frac{K_1 - K_{100}}{K_1} \times 100 \qquad (8)$$

A is the percentage change in the slope of Heckel curves relative to K_1 where K_1 and K_{100} are the slopes of Heckel plots for the compacts made at 1 and 100 mm/s punch velocities, respectively.

$$B(\%) = \frac{T_{s1} - T_{s100}}{T_{s1}} \times 100 \qquad (9)$$

B is the percentage change in tensile strengths relative to T_{s1} where T_{s1} and T_{s100} are the tensile

strength values of the compacts made at 1 and 100 mm/s punch velocities, respectively.

When the K and tensile strength values determined at different punch velocities were normalized, the compacts made from the powder form exhibited significantly higher A and B values (Table 5) than those of pellets. Therefore, for any given force, a reduced degree of compaction is achieved with a corresponding reduction in compact tensile strength with increasing punch velocities. This finding also supports the view that the pellets compressed by elastic deformation and brittle fragmentation, thereby showing very little dependance on the force application rates.

Compacts of pellets with external additives

The effect of the addition of a lubricant (0.5% w/w of magnesium stearate) on the compactional properties of F-I and F-II pellets was investigated. 99.5 g of the pellets were blended with 0.5 g of magnesium stearate (sieved through no. 40 mesh) for about 30 s in a laboratory scale mixer (Turbula, TC2, Glen Mills).

Porosity vs pressure plots for the unlubricated and lubricated F-I pellets were compared in Fig. 14. The compacts of unlubricated pellets required higher pressures to obtain the same porosities than the compacts of lubricated pellets. This can be attributed to the fact that magnesium stearate reduced the friction between the die-wall and the material during compaction. On addition of magnesium stearate, the pellets were almost completely coated with the lubricant resulting in compacts with zero tensile strength, i.e., no coherent compacts were formed (Table 6), and relatively lower TWC values at corresponding pressures (Fig. 15).

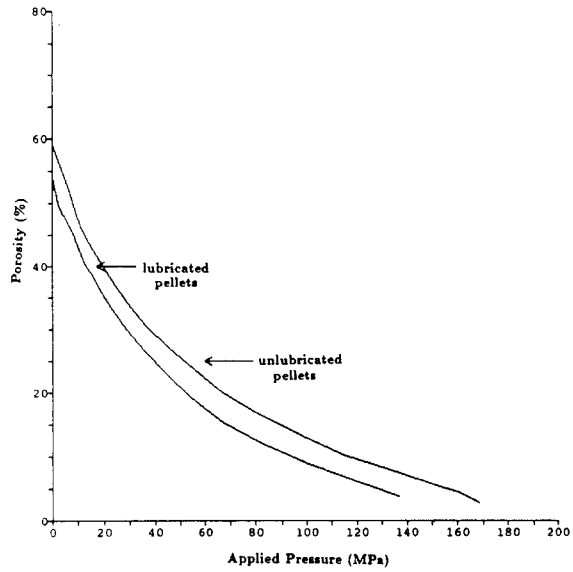

Fig. 14. Comparison of the porosity vs pressure plots for the compacts of lubricated and unlubricated F-I pellets.

The APC vs pressure plots in Fig. 16 indicate clearly that the compacts of unlubricated pellets produced higher APC values than the compacts of lubricated pellets. This finding is in agreement with the view expressed by Çelik and Marshall (1989), and suggests that materials exhibiting higher APC values produce relatively stronger compacts, provided that the materials are subjected to the same contact time during the compaction event.

TABLE 5

Comparison of the 1 / K (yield pressure) and tensile strength values of the compacts made from powder and pellet forms of F-I and F-II at two different punch velocities

Compacts	$1/K$		Tensile strength (MPa)		A (%)	B (%)
	1 mm/s	100 mm/s	1 mm/s	100 mm/s		
Powder						
F-I	74.66	140.24	10.540	8.800	46.76	15.65
F-II	84.60	146.21	9.910	8.280	42.13	16.45
Pellets						
F-I	73.76	74.80	0.565	0.562	1.39	0.53
F-II	88.97	91.07	0.542	0.540	2.31	0.37

TABLE 6

Comparison of the maximum applied pressure required to produce compacts from unlubricated and lubricated (with 0.5% w/w magnesium stearate) F-I and F-II pellets at 3% in-die porosity, and the tensile strength values of the compacts

Compacts	Maximum pressure (MPa)	Tensile strength (MPa)
F-I pellets		
Unlubricated	169	0.56
Lubricated	138	0.00
F-II pellets		
Unlubricated	177	0.54
Lubricated	129	0.00

In order to assess the effect of the addition of other external excipients on the compaction mechanisms of pellets, the F-I pellets were compacted with additives including soy polysaccharide, microcrystalline cellulose, and pregelatinized starch. The addition of external additives to the pellets resulted in an increase in the pressures required to obtain the same porosities within the die, and this effect was found to be dependent on the nature and the amount of external excipients added (Table 7). The external excipients, being small and irregular particles, when added to the pellets increased the duration of the particle rearrangement stage during compaction, and possibly, introduced new bonding sites. Pellets with microcrystalline cellulose as external additive were found to be more compressible and produced stronger compacts than the pellets con-

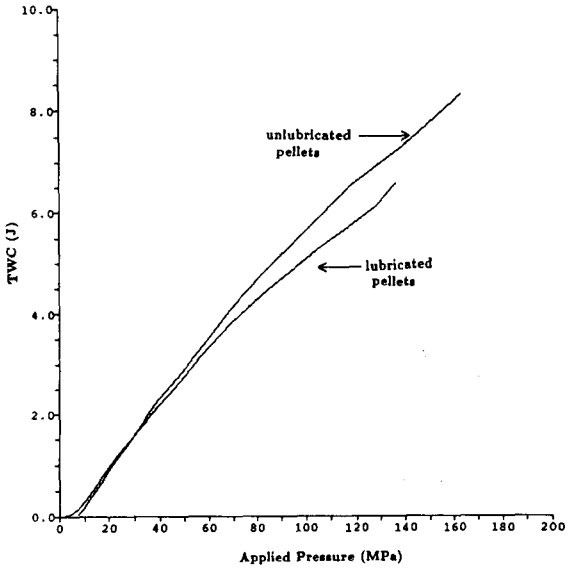

Fig. 15. Comparison of the total work of compaction (TWC) vs pressure plots for the compacts of lubricated and unlubricated F-I pellets.

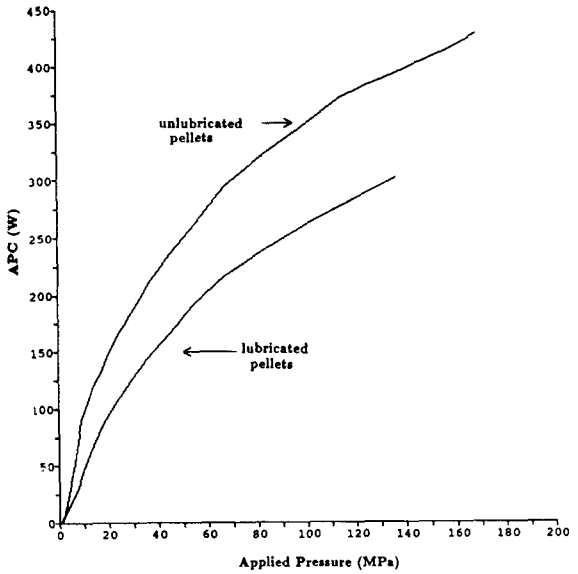

Fig. 16. Comparison of the average power consumption (APC) vs pressure plots for the compacts of lubricated and unlubricated F-I pellets.

TABLE 7

Comparison of the maximum applied pressure required to produce compacts from F-I pellets with external additives at 3% in-die porosity, and the tensile strength values of those compacts

Compacts	Maximum pressure (MPa)	Tensile strength (MPa)
10% w/w microcrystalline cellulose	203	1.61
20% w/w microcrystalline cellulose	228	2.18
10% w/w pregelatinized starch	256	chipped
20% w/w pregelatinized starch	277	chipped
10% w/w soy polysaccharide	220	0.47
20% w/w soy polysaccharide	239	0.45
10% w/w soy polysaccharide and 0.5% w/w magnesium stearate	198	0

taining pregelatinized starch or soy polysaccharide as external additives. Since pellets constitute 80% w/w of microcrystalline cellulose, the addition of microcrystalline cellulose as external additive to them during compaction caused an increase in the number of potential cohesive and adhesive bonds, thereby producing relatively strong compacts (Table 7).

Fig. 17 and Table 7 indicate that the addition of soy polysaccharide to the pellets caused a slight reduction in TWC and tensile strength values of the resulting compacts, respectively. The overlapping curves (b and c) in Fig. 17 suggest that the addition of 10 or 20% w/w soy polysaccharide produced a similar effect on the compaction characteristics of the pellets. Lower TWC values (curve d in Fig. 17) and compacts with zero tensile strength (Table 7) values resulted on addition of 0.5% w/w magnesium stearate to the pellets containing 10% w/w soy polysaccharide as an external additive. As soy polysaccharide was incapable of forming strong adhesive bonds with the pellets during compaction, its addition as external excipient did not result in compacts with improved tensile strength values.

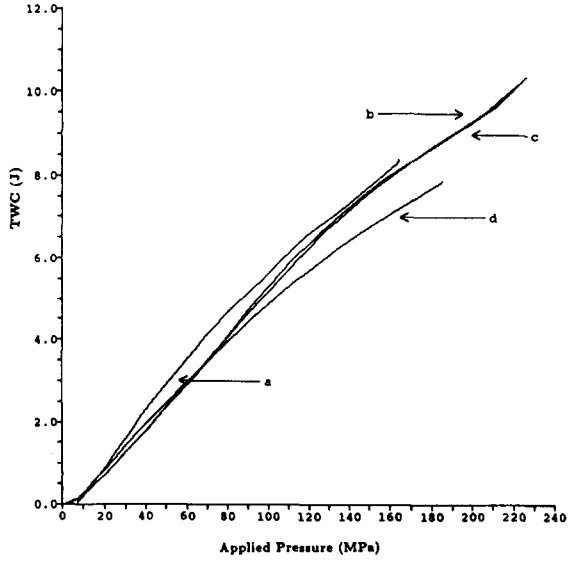

Fig. 17. Total work of compaction (TWC) vs pressure plots for the compacts of F-I pellets with soy polysaccharide as external additive. (a) Pellets; (b) pellets and 20% soy polysaccharide; (c) pellets and 10% soy polysaccharide; (c) pellets and 10% soy polysaccharide; (d) pellets, 10% soy polysaccharide and 0.5% magnesium stearate.

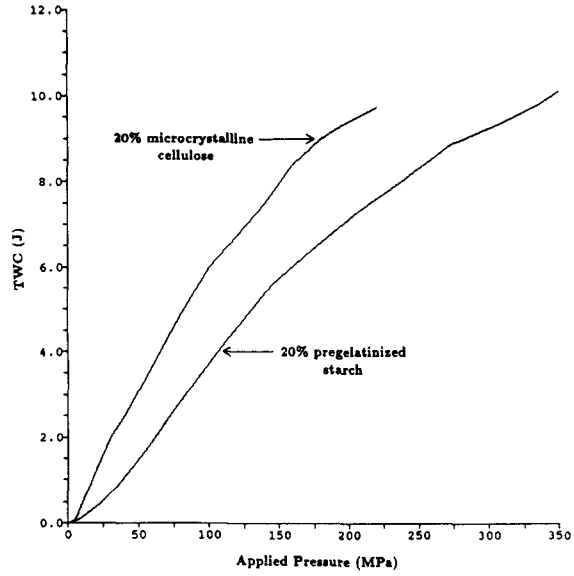

Fig. 18. Total work of compaction (TWC) vs pressure plots for the compacts of F-I pellets with two different external additives (10% w/w).

The compacts of F-I pellets containing 20% w/w microcrystalline cellulose exhibited higher TWC values at corresponding pressures (Fig. 18) than those made from pellets containing 20% w/w pregelatinized starch as external additive. The compacts made with pregelatinized starch as external additive exhibited chipping, possibly, due to the flat-faced punches and/or disruptive effects of the frictional force on their mechanical strength during ejection.

The compacts made from powder formulations exhibited long disintegration times with a rank order of microcrystalline cellulose (28 min) > F-II (25 min) > F-I (22 min). Despite their higher tensile strength, the compacts of F-I powder formulation exhibited shorter disintegration time than that of F-II powder formulation. This may be attributed to the osmotic pressure exerted by lactose and its solubility in water. The compacts made from the pellets were highly friable and disintegrated within 5 s. Addition of 20% w/w of microcrystalline cellulose to the pellets resulted in compacts with low friability values and longer disintegration times (64 s).

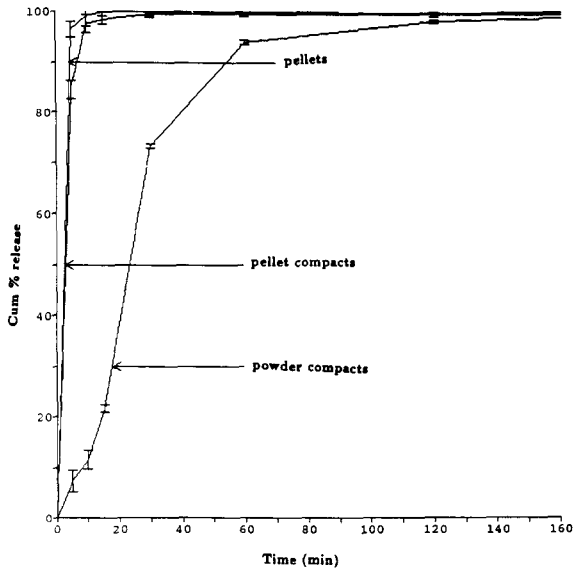

Fig. 19. Dissolution profiles of the F-I pellets and compacts of F-I powder and pellet forms.

In dissolution studies of F-I in water show that the pellets and their compacts exhibited similar dissolution profiles in which 95% of the drug was released within 5 min (Fig. 19). The cumulative percentage release of propranolol HCl from the compacts of pellets with different external additives was similar to that of the compacts made from pellets alone. The compacts of the powder formulations, on the other hand, released 95% of the drug at 60 min.

Conclusions

The work described here demonstrates that the size and shape of the particles and their potential bonding sites affect the compaction characteristics of the pharmaceutical materials. It was found that the powders examined compacted primarily by plastic deformation and produced strong compacts, whereas, their pellets exhibited elastic deformation and brittle fragmentation which resulted in compacts of lower tensile strength. However, further studies may be needed in order to assess the dominant compaction mechanism of these pellets.

When compacted under the same experimental conditions, the tensile strength of the compacts made from the powder and pellets correlated well with their ER and TWC values.

The inclusion of external additives to the pellets affected their compaction characteristics. The mechanical strength of their compacts increased with the presence of microcrystalline-cellulose, and decreased with the inclusion of either pregelatinized starch, soy polysaccharide or magnesium stearate as external additives.

Glossary

Symbol	Meaning
E	bed porosity of the material at given pressure
K	constant in Heckel equation
A	constant in Heckel equation
TWC	total work of compaction
APC	average power consumption
P	applied pressure
F_{up}	force on upper punch
F_{lp}	force on lower punch
E_o	initial bed porosity
E_m	bed porosity at maximum pressure
t	time during which the material has been compressed
T_s	tensile strength of the compact
T_{s1}	tensile strength of the compact made at 1 mm/s punch velocity
T_{s100}	tensile strength of the compact made at 100 mm/s punch velocity
F_c	force required to break the compact
d_e	diameter of the ejected compact
H_e	thickness of the ejected compact
V_t	true volume of the material
V_c	volume of the compact at given pressure
d_g	geometric mean diameter
d_c	diameter of the die
H_c	thickness of the compact at maximum load in the die
ER_o	elastic recovery calculated using Eqn 6
ER	elastic recovery calculated using Eqn 7
K_1	slope of the Heckel curve for the compact made at 1 mm/s punch velocity
K_{100}	slope of the Heckel curve for the compact made at 100 mm/s punch velocity

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