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The effect of some binding agents on the mechanical properties of granules and their compression characteristics

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The modulus of elasticity and the crushing strength of cylindrical granules prepared by a template method, and the friability of conventional granules were measured and the effect of the binding agents, PVP, methyl cellulose and maize starch examined. These properties were related to the compression characteristics of the granules and to the crushing force of the subsequent tablets. According to the base material two cases were observed. With dicalcium phosphate little plastic flow was evident and low radial stress transmission was noticed, the softest granules led to the weakest compacts. With paracetamol more plastic flow occurred giving a greater axial to radial conversion of force and the softest granules produced the strongest tablets. The extent of further generated contact area played the major role. Generally, due to the better bonding capacity, dicalcium phosphate gave stronger compacts than paracetamol, although lower radial transmission ratios were recorded. A good conversion of axial to radial force was thus proved not to be the main factor in obtaining good tablets, as was also confirmed by the paracetamol powder alone. With paracetamol the residual pressure on the die wall was greater with the formulations producing satisfactory tablets than with paracetamol alone which gave rise to capping.

Most studies involving binders are concerned with the properties of the final products (Elowe, Higuchi & Busse, 1954; Lehrman & Skauen, 1958; Mendes & Brannon, 1968; Kristoffersson & Krogerus, 1969; Van Oudtshoorn, Potgieter & others, 1971; Sakr, Elsabbagh & others, 1974). Few of them have included a friability test on the granules (Willis, Banker & Dekay, 1965; Davies & Gloor, 1972). Gold, Duvall & others (1971) and Kurup & Pilpel (1976) have investigated the physical properties of granules without reference to their compression.

Some authors (Nelson, Arndt & Busse, 1957; Varsano & Lachman, 1966; De Blaey, Van Oudtshoorn & Polderman, 1971; and Obiorah & Shotton, 1976) tried to relate the strength of the compacts, as affected by the nature of the binder, to the compression characteristics of the granules.

The only investigation comparing the mechanical properties of the granules, the crushing force of the tablets and the compression behaviour, is that of Edwards (1971). Unfortunately, because of the large scatter of the results attached to the asymmetry of the granules prepared in a conventional way, no definitive conclusion could be drawn.

To obviate this difficulty a template method was used to obtain cylindrical granules. The effects of three binding agents, namely polyvinylpyrrolidone (PVP), maize starch (MS) and methylcellulose (MC), associated with two base materials, dicalcium phosphate dihydrate and paracetamol have been investigated in this work.

MATERIALS AND METHODS

Materials

Dicalcium phosphate dihydrate (O Grade, milled) (Albright and Wilson, Oldbury) had a mean particle diameter $d_{vs} = 4{\cdot}0\,\mu m$*. Paracetamol (Koch-Light Laboratories Ltd., Colnbrook Bucks) had a mean particle diameter $d_{vs} = 14{\cdot}5\,\mu m$‡., Maize starch B.P. (BDH Chemicals Ltd., Poole). Polyvinylpyrrolidone (BDH Chemicals Ltd., Poole) mol. wt approximately 44 000. Methylcellulose (Celacol M20) (British Celanese Ltd., Spondon, Derby).

Granulation

The trituration was carried out in a mortar by adding a suitable amount of the granulation solution

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‡ Determined by Fisher Subsieve Sizer, at 0·625 porosity.

to 100 g of base material in order to incorporate in all formulations 4% w/w of binder calculated on the dry base. For 100 g dicalcium phosphate, 33·3 ml of a 12% w/v solution was used and for 100 g paracetamol 26·7 ml of a 15% w/v solution was added.

Half of the mass was granulated by filling the holes of a perforated steel template with a spatula to obtain cylindrical granules. The metal template (65 mm × 50 mm) contains 100 holes of 1500 μm diameter and 1400 μm thickness. After both faces had been scraped with a razor blade, the still moistened granules were expelled by pressing the template on a plate with pegs coincident with the holes.

The remaining half of the wet mass was fed into a rotating granulator (Erweka type FAG, Germany) fitted with a No. 24 cutting disk. The granules were dried for 2 h in an air oven at 50° and were sieved on an Endecott shaker for 15 min. Two fractions were studied; the $-1{\cdot}70 + 1{\cdot}40$ mm fraction because it approximately corresponds to the size of the cylindrical granules obtained by the template method, and the $-500 + 355$ μm fraction which is more commonly used in tableting.

All the granules were conditioned for a minimum period of 48 h in a container maintained at 44% relative humidity before testing or tableting as this corresponded approximately to ambient conditions.

Testing of granules

Modulus of elasticity. The modulus of elasticity of the cylindrical granules was obtained from stress-strain measurements using the micro-tensile testing machine (Techne Ltd., Duxford, Cambridge), Marsh (1961), and modified by Ridgway, Glasby & Rosser (1969) to work in compression. Each of 20 granules was gradually loaded on its diameter up to 6·5 N in ten increments. The modulus of elasticity was computed from the slope of the straight part of the stress *vs* strain graphs (usually from 1·3 to 6·5 N). Loads (P) were converted into tensile stress (σ) using the equation $\sigma = 2P/\pi td$ where t and d are respectively the thickness and the diameter of the cylindrical granule.

Crushing force. Twenty cylindrical granules were individually tested for their diametral crushing strength. The load was applied by means of a manually-operated rigid platen and an accurate dial gauge (Carry, Le Locle, Switzerland) was adjusted to record the inflexion of an interchangeable spring platen. True tensile failure was seen to occur along the entire diameter of the cylindrical granule.

Friability. The strength of the granules in bulk was assessed by determining the resistance to abrasion of the $-1{\cdot}70 + 1{\cdot}40$ mm Erweka granules using a modified friabilator, Baba & Sugimoto (1965). Five g of granules were fed into the inner Perspex cylinder as well as 10 polyethylene balls of 8 mm diameter, and the whole apparatus was driven at 33 rev min^{-1}. The amount of fines, in mg, less than 500 μm was weighed every 100 revolutions, up to 600 revolutions. The slope of the straight line relations between the cumulative weight of fine powder and the accumulated number of revolutions was taken as an index of friability. This represents a better characterization than a one point type of experiment.

Tableting

The granules and the base materials alone were compressed on a single punch machine instrumented as described by Shotton & Ganderton (1960) and Shotton & Obiorah (1975). Eight tablets were prepared from each formulation at approximately 120 MNm^{-2}, and the setting of the machine was kept constant for every batch of the same base material. The weight for each formulation was calculated from its true density to provide a tablet of 3 mm height at zero porosity using a 12 mm diameter punch and die set. To condition the die it was lightly dusted with magnesium stearate using a small camel-hair brush and the machine was run for about three cycles. The excess of lubricant was then wiped from the surfaces of both punches by means of a paper tissue. The die was filled by hand and the porosity of the tablets was derived from the weight of the tablets and their dimensions immediately after ejection.

Testing of tablets

The crushing force of the tablets was determined after 24 h using the diametral crushing strength apparatus described by Shotton & Ganderton (1960). An attempt was made to measure the Brinell hardness and the modulus of elasticity of the tablets according to Ridgway, Aulton & Rosser (1970), but no consistent results were obtained because of the irregular nature of the surface.

RESULTS

Dicalcium phosphate

Two batches of each formulation (quoted as -1 or -2) were examined. We arbitrarily called batch no. 2

the strongest batch of each formulation. Table 1 presents all the mechanical properties of the granules and those of the resultant tablets.

Table 1. *Mechanical properties of dicalcium phosphate granules and resultant tablets prepared with various binders**.

	Cylindrical granules				−1·70 + 1·40 mm fraction		−500 + 355 μm fraction
Binder batch No.	Porosity %	E MNm⁻²	Fcg N	Fct N	Friability mg × 10³ × rev⁻¹	Fct N	Fct N
PVP-1	41·7	1404	1·8	115	30	120	118
PVP-2	40·5	1963	3·2	125	20	122	133
MC-1	39·6	2310	8·3	129	7	145	150
MC-2	41·5	2531	8·4	144	3	149	154
MS-1	42·9	2178	6·4	166	21	172	184
MS-2	42·0	3073	9·0	172	13	187	198

* E, Fcg are respectively the modulus of elasticity and the crushing force of the cylindrical granules; Fct values refer to the crushing force of the corresponding tablets. PVP for polyvinylpyrrolidone, MS for maize starch and MC for methylcellulose.

Values for modulus of elasticity follow the sequence found by Healey, Rubinstein & Walters (1974) for films made from similar binders alone.

That the values of the elastic modulus and crushing force of cylindrical granules show a strict parallelism is not surprising because in both tests the granule undergoes a tensile stress. Thus, a very simple crushing test can be used to assess the 'strength' of the granules provided their shape is well defined.

The high batch to batch variations probably arise from the difficulty of getting a reproducible consistency of the mass during trituration and this leads to differences in the filling of the template. This is confirmed by the small differences in porosity of no. 1 and no. 2 batches. For the −1·70 + 1·40 mm mesh fraction all friability figures of the second batches are also lower. Generally these values do not follow the same rank order as that of the cylindrical granules. This is not unexpected because the resistance to abrasion is initially dependent upon the surface hardness. The two lots of MC granules showed the lowest friability. Table 1 also gives the crushing force for the three resulting groups of tablets corresponding to the different granules.

Here the same sequence MS<MC<PVP is observed in each batch. However, the second batches of tablets were always slightly harder showing that the strength of the granules has a little effect on the final compacts.

For all binders, the crushing strength of the tablets was generally in the following order according to the type of granules used, −500 + 355 μm fraction > −1·70 + 1·40 mm fraction > cylindrical granules. This is probably due to the increase of contact area between particles during tableting.

Since no detectable difference between the compression cycles of two batches of similar formulation was noticed, we only report in Table 2 the value of the second batch of each granule fraction.

Table 2. *Compression characteristics of dicalcium phosphate granules**.

Binder	Pa MNm⁻²	Pr MNm⁻²	Pres MNm⁻²	R	Fd N	Fe N	Fc N	Porosity %
			Dicalcium phosphate powder					
	122·6	42·6	18·4	0·927	1003	414	127	27·4
			Cylindrical granules					
PVP	108·6	43·6	13·9	0·909	1112	366	125	26·0
MC	113·8	45·6	15·5	0·912	1124	376	144	26·7
MS	120·2	46·1	16·8	0·917	1125	396	172	27·3
			−1·70 + 1·40 mm					
PVP	109·8	42·4	14·6	0·912	1088	369	122	26·4
MC	113·8	46·7	16·6	0·917	1065	393	149	26·8
MS	122·1	48·5	17·6	0·922	1069	406	187	27·6
			−500 + 355 μm fraction					
PVP	109·4	44·3	15·2	0·904	1054	327	133	26·3
MC	112·1	46·4	16·0	0·915	1076	374	154	26·8
MS	122·6	47·8	17·9	0·916	1154	399	198	27·7

* Pa, Pr, Pres, Fd, Fe, Fc are applied pressure, radially transmitted pressure, residual die wall pressure, force lost to the die wall, ejection force and crushing force respectively. R is the ratio of axially transmitted pressure to the applied pressure.

To facilitate comparison we have included the crushing force of some tablets already quoted in Table 1.

As an example, the pressure cycles for all −500 + 355 μm fractions as well as the base material itself are illustrated in Fig. 1.

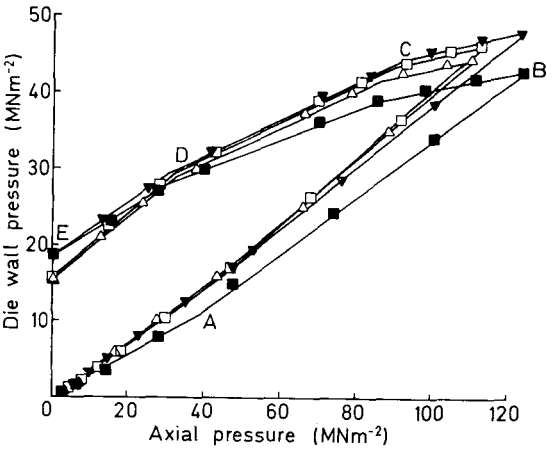

FIG. 1. Pressure cycles for dicalcium phosphate powder and −500 + 355 mm granulations. ■—Dicalcium phosphate powder, △—PVP granules, ▼—maize starch granules, □—methylcellulose granules.

Consideration of the effects of the binding agents for all kinds of granules shows the greatest applied pressure at one machine setting to be obtained with MS, then MC and PVP. A similar grading was noted for the radially transmitted pressure, for the residual die wall pressure and for R values and ejection force. All these parameters parallel the crushing strength of the No. 2 batches of granules and resultant tablets.

No consistent change in the force lost to the die wall was noted. Looking at the influence of the granule fraction used, a trend was noticed showing a slight increase in both the radial stress and the residual die wall pressure from the cylindrical granules to the $-1{\cdot}70 + 1{\cdot}40$ mm and finally to the $-500 + 355\,\mu$m granule fraction. High values, especially that of residual pressure, were recorded for the base material alone which also led to satisfactory compacts.

Paracetamol

Table 3 contains the values for the mechanical properties of the three kinds of granules and tablets for paracetamol.

Table 3. *Mechanical properties of paracetamol granules and resultant tablets prepared with various binders*.*

Binder	Cylindrical granules			$-1{\cdot}70 + 1{\cdot}4$ mm fraction		$-500 + 355\,\mu$m fraction
	Porosity %	F_{cg} N	F_{ct} N	Friability mg × 10^2 × rev^{-1}	F_{ct} N	F_{ct} N
PVP	26·5	6·8	111	86	109	107
MS	27·5	7·4	81	69	84	84
MC	25·5	9·0	91	22	93	98

* For symbols see Table 1.

The strength of the cylindrical granules and the friability values of the $-1{\cdot}70 + 1{\cdot}40$ mm fraction are roughly in the same sequence as for dicalcium phosphate granules. The rank order of the crushing force of the tablets was reversed for paracetamol granules, the weakest granules (PVP) leading to the strongest compacts. This sequence was confirmed at an applied pressure of 70 MNm^{-2}. The pressure cycles of the $-500 + 355\,\mu$m fraction are illustrated in Fig. 2 and all the parameters are reported in Table 4. To allow direct comparison the corresponding values of crushing of the tablets are repeated.

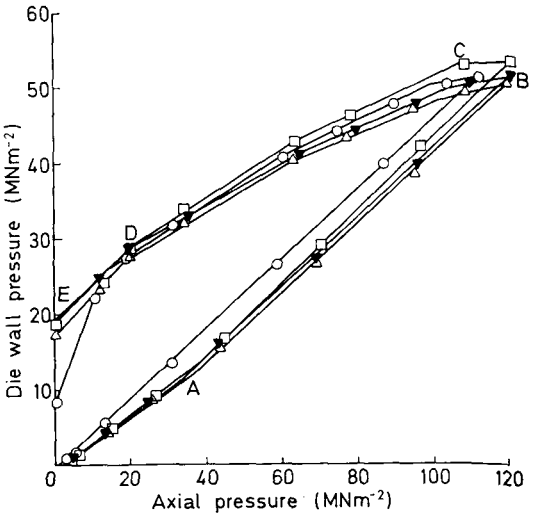

FIG. 2. Pressure cycles for paracetamol powder as $-500 + 355\,\mu$m granulations. ■—Paracetamol powder, △—PVP granules, ▼—maize starch granules, □—methylcellulose granules.

Whereas paracetamol alone yields compacts that cap, satisfactory tablets were obtained when 4% of binder was added.

Differences in applied pressure are small, but significant. Their rank order is similar to that observed for dicalcium phosphate. The same sequence applies to the residual die wall pressure and R values. In addition the radially transmitted stresses parallel the strength of the granules. Paracetamol powder alone is characterized by a low residual die wall pressure indicating capping on ejection.

DISCUSSION

Effect of binders on the maximum applied pressure and the radially transmitted pressure

For a same machine setting, a greater axial pressure Pa should be recorded for materials which are more

Table 4. *Compression characteristics of paracetamol granules*.*

Binder	Pa MNm^{-2}	Pr MNm^{-2}	Pres MNm^{-2}	R	Fd N	Fe N	Fc N	Porosity %
	Paracetamol powder							
	111·9	51·4	8·1	0·87	1637	351	capping	—
	$-500 + 355\,\mu$m fraction							
PVP	118·5	50·3	17·2	0·852	1966	732	107	16·0
MC	119·9	53·9	18·9	0·853	1983	702	98	16·6
MS	120·7	51·7	19·6	0·859	1915	642	84	16·9

* For symbols see Table 2.

difficult to deform (Shotton & Obiorah, 1975). This also holds true for granulations, but this does not prejudge the strength of the compact.

On the other hand, Windheuser, Misra & others (1963) came to the conclusion that materials which permit good conversion of normal pressure to lateral pressure would tend to form good tablets. Later the same team (Higuchi, Shimamoto & others, 1965), stated that the ratio of maximum die wall pressure to maximum upper punch pressure reflects the hardness of crystals employed. This was proved to be true for various crystalline materials (Ridgway & others, 1969), but the order of crushing strength of the compact was more dependent on the inherent bonding force of the particles. However, with different crystal forms of the same material, a higher transmission ratio always corresponded to a stronger tablet (Summers, 1972; Shotton & Obiorah, 1973, 1975).

From our results with dicalcium phosphate granules, probably because of little plastic flow, the radial component of the applied force seems to be the determining factor rather than the relatively small generated area of contact. Thus, the weakest granules do not lead to strong tablets.

For paracetamol granulations, which show more plastic flow (compare segment CD of Figs 1 and 2), greater Pr values are recorded, but again the softest granules (PVP) give the lowest transmission of radial stress, although producing the strongest compact.

It must be emphasised that a good radial transmission of force alone is not sufficient to obtain good tablets as exemplified by paracetamol powder.

Effect of binders on the residual die wall pressure and the ejection force

According to Long (1960, 1962) the residual die wall pressure due to elastic recovery should not be influenced by the maximum applied pressure, but only by the yield stress in shear of the material, Obiorah & Shotton (1976) found an increase in residual pressure with increasing applied force. This is probably due to the fact that at the maximum applied force they used, the compression cycles were not complete to fulfill Long's theory. Our experiments show a similar trend. On the other hand, for paracetamol, the strongest compacts are not associated with the highest value of the residual die-wall pressure. A similar relation was noted by Summers (1972) for different polymorphic forms of sulphathiazole and barbitone.

However, the residual die-wall pressure is particularly useful to detect laminating or capping (Obiorah & Shotton 1976), as shown in Table 4 in 'Pres', between paracetamol powder with and without binder present.

The assertion made by Higuchi & others (1965) that higher residual die wall pressure leads to higher ejection force was only confirmed with dicalcium phosphate granulations.

Relations between granule strength and tablet strength

The tensile strength of a tablet depends upon both the bonding force existing between particles and their area of contact. The latter is expected to be greater for a soft material which readily undergoes crushing and plastic flow. In a comparison of the effect of various binding agents on the strength of tablets of nearly identical porosity, the inherent degree of interaction between base material and binder should predominate. After compression, two possibilities can be envisaged. The specific bonding force continues to be dominant, as exemplified by dicalcium phosphate tablets, or, when more plastic flow and crushing occur, as with paracetamol, the increase in the area of contact can reverse the effect. Thus, the weakest granules using dicalcium phosphate produced the weakest compacts and in the second case the strongest ones.

Additionally, to eliminate a possible effect of moisture on the rank order observed for the tablet strength, a sample of each $-500 + 355\ \mu m$ granule fraction was dried (2 h in air oven at 50° and stored over P_2O_5) then compressed. No change was found in the compression properties.

Conclusions

All granule formulations gave the Mohr-type body of the compression cycle and produced satisfactory compacts. Only paracetamol powder showed capping, as detected by a low residual pressure.

The strength of granules of identical porosity is primarily dependent on the inherent bonding properties of the materials involved, but can be modified by the granulating conditions (Ganderton & Hunter, 1971). In addition, after compression, according to the increase in the area of contact produced by plastic flow and fragmentation, the strength of tablets may have the same rank order (dicalcium phosphate) or be reversed (paracetamol).

Paracetamol granulations, in undergoing more plastic flow, gave higher radial transmission ratios, but at the same time weaker tablets. Thus, for

powders, as well as for granulations, a higher radial transmission is not sufficient to ensure good tablets but must be accompanied by bonding properties that can absorb elastic recovery without rupture.

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