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Studies on Powder Plug Formation Using a Simulated Capsule Filling Machine

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Abstract

Using an apparatus which simulates the action of a Macofar 13-2 dosating-type capsule-filling machine, the variation in plug weight and density with changing machine parameters has been studied.

The piston ejection speed has no effect on plug properties. However increase in compression speed leads to a less consolidated powder plug and hence reduced plug weight. Application of higher pressures reduces plug weight changes, but would be expected to affect release characteristics.

Comparison of axial and radial pressures generated by plugs of Starch 1500 and lubricated lactose show significant differences which can be explained by the different consolidation and elastic properties of the two solids.

Many capsule-filling machines work on the principle of a dosating tube plunging into a bed of powdered or granular material. The dosator contains a piston which may apply a small force or tamp to compress the powder. A plug of powder thus forms within the dosating tube, and is retained within it as the tube is withdrawn from the powder bed. The plug is then ejected into the capsule shell by further extension of the piston. Examples of this type of machine include the Macofar MT 13-2 and MT 5, the Zanasi AZ20 and LZ64, and the mG2. Some machines of the dosating type have been fitted with transducers, and this field has been reviewed by Augsburger (1988).

A simulated mG2 machine has been described by Jolliffe et al (1982) and used extensively by Tan & Newton (1990a). A necessary prerequisite of any simulator is that the pattern of movement of components of the parent machine are faithfully reproduced. It is also advantageous if small quantities of powdered material can be used. Britten & Barnett (1991) and Britten et al (1995) have described a pneumatically operated simulator which imitates the movement of a Macofar MT 13-2 capsule-filling machine, and the forces generated therein. The simulator measures powder-bed movement (equivalent to dosator movement), piston movement, and the forces exerted by the piston and detected at the tip of the dosator. It can operate in three modes, all at a range of dosator and piston speeds.

For precompression simulation, the powder plug is formed solely by the dosator as it descends into the powder bed. No additional compression (tamping) is applied.

For constant displacement simulation, the powder has already been partially precompressed as described above but an additional tamp is applied by the dosator piston. The displacement of the piston is accurately controlled so as to be constant stroke after stroke.

For constant pressure simulation, powder has been precompressed as above and the piston is allowed to travel as far as possible until the resistance of the powder to undergo further consolidation equals the applied compression pressure.

The following information can be collected for each plug: compression pressure, the pressure acting on the dosator piston as the powder consolidates inside the funnel during precompression or compression; radial pressure, the pressure transmitted radially to the funnel wall as powder consolidates during precompression or compression; residual axial pressure, the pressure transmitted to the piston after the plug has had time to undergo particle rearrangement or elastic recovery before ejection; residual radial pressure, the pressure transmitted radially after the plug has had time to undergo partial rearrangement or elastic recovery before ejection; axial ejection pressure, the pressure exerted by the piston during the ejection of the plug from the dosator funnel; radial ejection pressure, the pressure transmitted radially as the piston ejects the powder plug.

In addition the following data can be collected by a combination of physical and electronic measurements: plug weight, plug density (before and after ejection), plug length (before and after ejection) and powder bed density. These can then be related to the pressure and displacement data.

Materials and Methods

The construction and operation of the simulator has been fully described elsewhere (Britten & Barnett 1991; Britten et al 1995).

Materials

Starch 1500 (Colorcon, Orpington, UK), lactose EP (Grade 200, DMV International, Veghel, The Netherlands),

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magnesium stearate (Mallinckrodt, USA) were used as received.

The lubricated lactose blend was prepared by mixing 1980 g lactose with 20 g magnesium stearate for 3 min in a 7-L Y-cone blender (Apex Construction Ltd, Dartford, UK). The tapped bulk densities of the Starch 1500 and lubricated lactose were measured using a jolting volumeter (Jencons Scientific Ltd, Leighton Buzzard, UK).

Powder-bed preparation and plug sampling

The preparation of a powder bed of reproducible density was an essential prerequisite of this work. The target bed density was 0·690 g mL^{-1} ± 3% for both Starch 1500 and lubricated lactose, this being the range encountered during preliminary experiments with a Macofar machine. Two bed depths (16 mm and 30 mm) were used. Beds were prepared as follows. For a bed depth of 16 mm, about half the calculated quantity of powder was weighed into the bowl. The powder was levelled off with a card scraper and then compacted by twisting a consolidating disk backwards and forwards, five times through a small angle. The disk was fitted with 200 g steel weights to provide a standard consolidating load. The remainder of the powder was then added and consolidation repeated. (For a bed depth of 30 mm, the powder was added in four approximately equal portions, consolidation being applied after each addition). A lid was then placed on the powder bed. The simulator bowl was divided into 16 segments, each of which was sampled successively. The depth of the powder bed of each segment was measured with callipers, and portions of the bed withdrawn by means of a cylindrical sampling tool. From a knowledge of bed depth, the plug weight and the internal radius of the sampler, the bed density could be calculated. Coefficients of variation of the density of 2% or less were achieved, both from replicate samples from the same bed and from samples taken from different beds. These are quoted in Tables 1, 2 and 3.

Post ejection measurements

The length and weight of each plug was measured, and the bulk density of the plugs (ρ_p) and the powder bed (ρ_b) determined.

Consolidation was calculated according to the formula:

$$[(\rho_p - \rho_b) \times 100\%]/\rho_b \qquad (1)$$

Results and Discussion

Accurate and reproducible fills are essential attributes of any capsule-filling machine. Plug weight and density data for both fill materials are shown in Tables 1, 2 and 3 the simulator operating in precompression, constant-displacement and constant-pressure modes, respectively. All experiments are two-factor, two-level factorial designs using precompression velocity (i.e. the velocity of the powder bed) and piston ejection velocity as variables. Since the dosator tube is filled volumetrically, variation in the density of the powder bed will cause corresponding differences in the fill weight.

The rate of ejection of the plug from the dosator has no significant effect on the mean plug weight, plug density, and variation in plug weight. However the precompression rate has a significant effect ($P < 0·05$) on the plug weight for both powders when the simulator is in precompression and in constant-displacement modes, increase in speed causing a fall in weight. The heavier plug is reflected in increased plug density, which in turn gives rise to higher compression pressures acting on the piston.

It is possible that at higher bowl velocities, more particles find their way past the piston and collect behind the piston tip. It is thought that this is unlikely since this would be expected to give greater weight variation.

Two reasons are thought to be more likely. At higher speeds, powder is pushed ahead of the dosator nozzle rather than entering it, thereby accounting for the lower plug

Table 1. Plug weight and density data, using the simulator in precompression mode.

Simulator settings Starch 1500	Powder bed density (g cm^{-3}) (CV%)	Compression pressure (MPa) (CV%)	Mean plug weight (mg) (CV%)	Mean plug density (g cm^{-3}) (CV%)	Mean plug volume (cm^3)	Consolidation (%)
P_LE_L	0·679 (0·6)	4·15 (6·9)	251·4 (1·9)	1·040 (1·9)	0·242	53·2
P_LE_H	0·688 (1·8)	3·97 (5·4)	250·0 (1·6)	1·040 (1·6)	0·241	51·2
P_HE_L	0·695 (1·7)	3·37 (10·3)	248·6 (1·4)	1·030 (1·4)	0·241	48·2
P_HE_H	0·691 (1·8)	3·36 (9·4)	246·3 (1·9)	1·020 (1·9)	0·242	47·6
Lubricated lactose						
P_LE_L	0·698 (1·8)	4·26 (11·4)	280·0 (1·7)	1·159 (1·7)	0·242	66·0
P_LE_H	0·701 (2·0)	4·36 (11·1)	281·0 (1·7)	1·163 (1·7)	0·242	65·9
P_HE_L	0·694 (1·6)	3·06 (12·1)	269·3 (1·3)	1·115 (1·3)	0·242	60·7
P_HE_H	0·695 (1·6)	3·27 (11·6)	270·9 (1·6)	1·121 (1·6)	0·242	61·3

P_L: Precompression velocity 0·24 m s^{-1}, P_H: Precompression velocity 0·48 m s^{-1}, E_L: Ejection velocity 0·27 m s^{-1}, E_H: Ejection velocity 0·62 m s^{-1}. Powder bed determinations: n = 3, all other determinations: n = 10.

Table 2. Plug weight and density data, using the simulator in constant displacement mode.

Simulator settings Starch 1500	Powder bed density ($\mathrm{g\,cm^{-3}}$) (CV%)	Compression pressure (MPa) (CV%)	Mean plug weight (mg) (CV%)	Mean plug density ($\mathrm{g\,cm^{-3}}$) (CV%)	Mean plug volume ($\mathrm{cm^3}$)	Consolidation (%)
$P_L E_L$	0·691 (0·6)	5·26 (7·2)	249·2 (1·8)	1·090 (1·9)	0·229	57·7
$P_L E_H$	0·687 (1·5)	5·30 (6·6)	250·3 (2·2)	1·100 (2·2)	0·228	60·1
$P_H E_L$	0·681 (0·9)	5·96 (7·2)	245·3 (1·4)	1·080 (1·9)	0·227	58·6
$P_H E_H$	0·686 (0·6)	5·57 (6·8)	244·5 (1·4)	1·070 (1·6)	0·229	56·0
Lubricated lactose						
$P_L E_L$	0·694 (1·4)	5·06 (10·1)	277·5 (1·7)	1·264 (1·9)	0·220	82·1
$P_L E_H$	0·696 (1·8)	5·32 (10·6)	278·9 (0·7)	1·280 (2·1)	0·219	83·9
$P_H E_L$	0·689 (2·0)	4·64 (11·9)	270·2 (1·7)	1·241 (1·5)	0·218	80·1
$P_H E_H$	0·697 (2·5)	4·65 (5·2)	268·8 (0·9)	1·237 (0·7)	0·217	82·2

P_L: Precompression velocity 0·24 $\mathrm{m\,s^{-1}}$, P_H: Precompression velocity 0·48 $\mathrm{m\,s^{-1}}$, E_L: Ejection velocity 0·27 $\mathrm{m\,s^{-1}}$, E_H: Ejection velocity 0·62 $\mathrm{m\,s^{-1}}$, powder bed determinations: $n = 3$, all other determinations: $n = 10$.

weight. Such an effect was noted by Woodhead (1980). Alternatively, it may be that at high compression speeds, less consolidation of the powder takes place. There is no significant difference in plug volume, but consolidation is significantly greater at lower speeds. A similar observation was made by Armstrong & Palfrey (1989) with tablet compression, especially with Starch 1500. Although pressures are much lower in this case, the dosator and piston speeds are greater than those achieved by the punches in many tablet presses (Armstrong 1989).

This effect of precompression velocity disappears when the simulator is used in constant pressure mode. Furthermore there is no evidence that higher pressures have a significant effect on the uniformity of plug weight, as described by Tan & Newton (1990a). Thus if reproducible and predictable plug weight is the prime aim, then a relatively high tamping pressure is indicated. However this may cause an increase in the physical strength of the plug. It is known (Mehta & Augsburger 1981) that the strength of the plug can influence drug release characteristics, and so for any given formulation, an optimum pressure must be sought.

Jolliffe et al (1980) have pointed out that for the plug to be retained in the dosator tube, a stable arch must form at the nozzle outlet. The strength needed in a powder bed for arch formation is dependent on the friction and the bulk density of the powder bed (Walker 1966). It follows that application of a compressive force will increase bulk density and thereby facilitate arch formation.

No plugs fell out of the dosating tubes in the present study

Table 3. Plug weight and density data, using the simulator in constant compression pressure mode.

Simulator settings Starch 1500	Powder bed density ($\mathrm{g\,cm^{-3}}$) (CV%)	Compression pressure (MPa) (CV%)	Mean plug weight (mg) (CV%)	Mean plug density ($\mathrm{g\,cm^{-3}}$) (CV%)	Mean plug volume ($\mathrm{cm^3}$)	Consolidation (%)
$P_L E_L$	0·699 (1·1)	8·76 (0·3)	258·0 (1·5)	1·173 (1·5)	0·210	67·8
$P_L E_H$	0·695 (1·0)	8·73 (0·5)	254·8 (1·3)	1·173 (1·0)	0·217	68·8
$P_H E_L$	0·699 (1·1)	8·76 (0·45)	256·4 (1·6)	1·189 (0·8)	0·216	70·1
$P_H E_H$	0·696 (1·2)	8·83 (0·6)	254·8 (1·7)	1·177 (0·7)	0·217	69·2
Lubricated lactose						
$P_L E_L$	0·691 (2·0)	8·82 (0·2)	275·4 (1·8)	1·269 (1·7)	0·217	83·6
$P_L E_H$	0·700 (2·0)	8·68 (0·7)	281·4 (2·5)	1·279 (1·6)	0·220	82·7
$P_H E_L$	0·691 (2·2)	8·82 (0·3)	281·6 (1·2)	1·287 (2·1)	0·219	86·3
$P_H E_H$	0·700 (2·2)	8·78 (0·6)	288·6 (2·1)	1·300 (1·9)	0·222	85·7

P_L: Precompression velocity 0·24 $\mathrm{m\,s^{-1}}$, P_H: Precompression velocity 0·48 $\mathrm{m\,s^{-1}}$, E_L: Ejection velocity 0·27 $\mathrm{m\,s^{-1}}$, E_H: Ejection velocity 0·62 $\mathrm{m\,s^{-1}}$, Powder bed determinations: $n = 3$, all other determinations: $n = 10$.

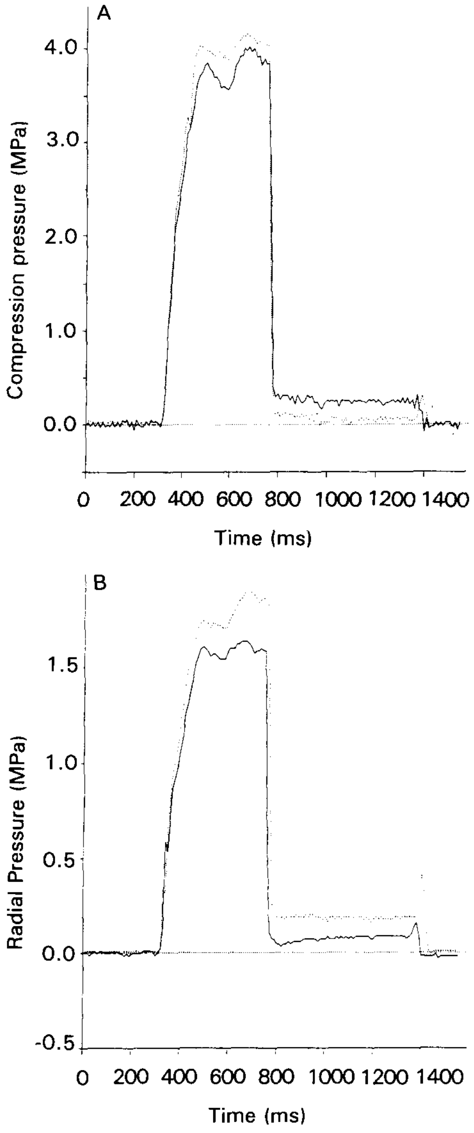

FIG. 1. The change of (A) compression pressure, (B) radial pressure with time with the simulator in precompression mode. Continuous line. Starch 1500: dotted line, lubricated lactose.

before active ejection by the piston, yet, the residual radial pressures are extremely low, especially for Starch 1500. The lowest pressure applied to this substance is about 3 MPa, and this results in a residual radial pressure of only 0·01 MPa, yet plug retention is maintained. It follows that from the point of view of plug retention, high compression pressures are not required, a view also expressed by Tan & Newton (1990b).

Axial and radial pressures for the two substances are shown in Fig. 1, the simulator being in its precompression mode when no additional tamping force is applied to the powder by the piston. The compression pressures generated are similar for the two substances, but the corresponding radial pressures show a larger difference.

Starch 1500 exhibits higher radial pressures than lubricated lactose during compression, but when the compressive stress is removed, the residual radial pressure falls significantly and a residual axial pressure is detected by the piston. Conversely, there is no residual axial pressure for lactose, although a significant radial pressure remains. These differences can be explained by the degree of elastic recovery which each material undergoes.

Before plug ejection occurs, the lower end of the dosator funnel is unconfined, and so the plug is free to recover elastically. Lactose is a highly compressible powder, and its ejected plugs are only 10% longer than the length of the compressed material inside the dosator funnel. This lack of elastic recovery manifests itself in a distinct residual radial pressure and the absence of any residual axial pressure. A measurable ejection pressure (about 7% of the compression pressure) is needed to eject the plug.

Starch 1500 plugs, on the other hand, exhibit considerable elastic recovery, increasing in length by about 22% after ejection. This explains the residual axial pressure detected for this material. This effect has been noted previously by other workers (Cole & May 1975; Small & Augsburger 1977), who referred to it as retention force. The residual radial pressure is lower than that for lactose and the ejection pressure is undetectable, being less than the residual axial pressure. However, like lactose, a radial pressure is detected by the funnel strain gauges as the piston applies ejection pressure to the plug. At this stage, the radial pressure plus wall friction is preventing the plug falling out of the dosator funnel and must be overcome during the ejection phase. Whilst ejection pressure is developing, the plug, restrained by wall friction, experiences some radial expansion which in turn creates pressure on the funnel wall. This is at least partially relieved when the plug begins to move.

The low ejection pressures observed with both materials suggest that magnesium stearate (1%) is a satisfactory lubricant for lactose, and confirms the finding by Small & Augsburger (1978) that Starch 1500 does not need the addition of a lubricant.

If the simulator is used in the constant-displacement mode, pressure-time relationships as shown in Fig. 2 are obtained. The additional movement of the piston (0·5 mm for Starch 1500 and 0·7 mm for lubricated lactose) causes an increase in compaction pressure beyond that achieved by precompression alone. The percentage elastic recovery for Starch 1500 plugs increases from 22% for precompression alone to 28%, and for lactose, the increase is 10 to 18%. The increase in elastic recovery has little effect on residual axial pressure. It is suggested that any extra expansion of the plug is offset by the overall decrease in length brought about by the additional compression force (pressure). Whilst radial pressure, residual radial pressure and radial ejection pressure are virtually unchanged, Starch 1500 now requires a measurable ejection pressure to eject the plug.

The greater elastic recovery of the lubricated lactose now creates a small residual axial pressure together with increases in radial pressure, residual radial pressure and radial ejection pressure. Ejection pressure is virtually unchanged, again suggesting that lubrication is more than adequate.

These results invite comparison with work in the tablet field. Plugs produced in this part of the work are created by the dosator piston penetrating a constant distance into the powder, which is analogous to punch penetration into the die of an eccentric tablet press. To produce a satisfactory

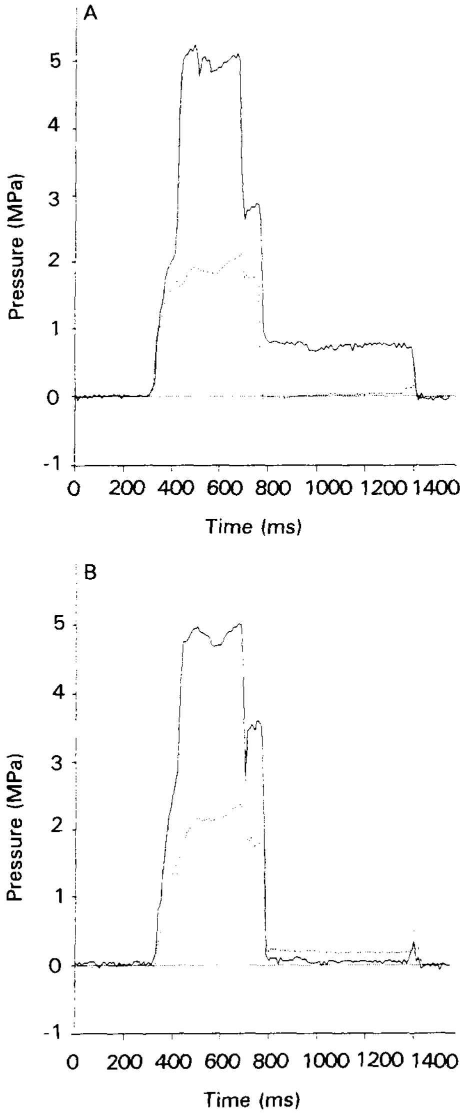

FIG. 2. The change of compression pressure (continuous line) and radial pressure (dotted line) with time with the simulator in constant displacement mode (A) Starch 1500: (B) lubricated lactose.

tablet, residual elastic stresses must be eliminated or substantially reduced by the addition of plastically deforming excipients. In cases where the radial die-wall stress diminishes rapidly upon removal of the compressive stress, tablet failure often occurs with ejection. Starch 1500, which produces negligible residual radial stress gave soft dusty plugs which occasionally broke into pieces on ejection. On the other hand, lactose produced firm dust-free plugs which resisted the stresses of handling.

Use of the simulator in its third mode, constant pressure, permits the application of known pressures to the powder via the dosator piston up to a maximum of 9 MPa.

Fig. 3 shows the relationship between compression pressure and ejection pressure, residual axial pressure and residual radial pressure for both Starch 1500 and lubricated lactose. As anticipated, the ejection pressure increases linearly with compression pressure up to approximately 6 MPa. This confirms earlier work by Small & Augsburger (1978). Beyond 6 MPa, the behaviour of each material differs. With lactose the slope increases whereas for Starch 1500, it decreases slightly.

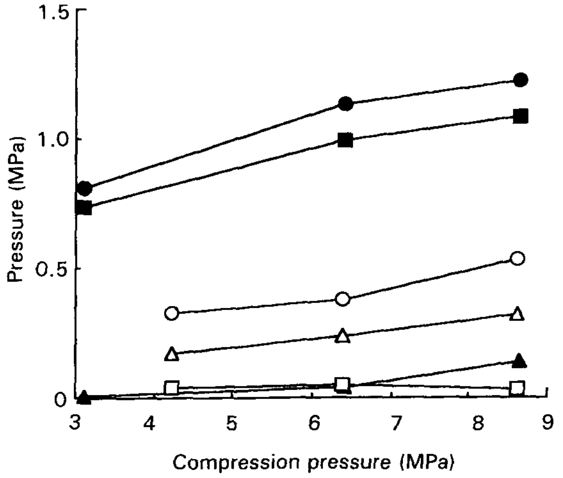

FIG. 3. The relationship between compression pressure and axial ejection pressure (●, ○), residual axial pressure (■, □) and residual radial pressure (▲, △). Closed symbols, Starch 1500: open symbols, lubricated lactose.

The plot of residual axial pressure against compression pressure for both materials demonstrates the much greater elasticity of the starch product. A linear relationship between compression pressure and residual radial pressure exists for lubricated lactose, but for Starch 1500, there is a change in the slope of the graph suggesting a possible change in behaviour from almost totally elastic to some degree of plastic deformation. It is of interest to note that the slope of the residual axial pressure curve decreases over the same compression-pressure range.

In conclusion, changes in dosator velocity and applied pressure can have a significant effect on plug properties such as weight, density and residual pressure. The magnitude of these changes is dependent on the powder involved, and machine parameters must be kept constant if a uniform product is to be obtained.

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