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Research paper

Powder and capsule filling properties of lubricated granulated cellulose powder

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Abstract

Granulated powdered cellulose was studied in terms of powder bulk properties and capsule filling performance on a tamp-filling machine with and without the addition of various concentrations of magnesium stearate. Carr's compressibility reached its minimum value at 0.4% magnesium stearate suggesting an improvement of powder flow compared to the unlubricated material. However, shear cell measurements and the use of a powder rheometer indicated that the addition of 0.2% magnesium stearate and more impairs powder flow and does not reduce interparticulate friction. When capsules were filled into hard gelatine capsules at a zero-compression setting, the fill weight and plug density could be predicted from Carr's compressibility index and from the maximum bulk density. The decrease in one and simultaneous increase in the other bulk property with increasing magnesium stearate concentration caused both fill weight and plug density to go through a minimum at a lubricant concentration of 0.4%. When the capsules were filled at maximum compression, however, the addition of lubricant increased the coefficient of fill weight variation significantly, and the plug density remained constant for any added concentration of magnesium stearate. These findings were in agreement with the shear cell and powder rheometer results. However, the optimum lubricant concentration in terms of ease of machine function, which was identified from tamping pressure measurements, was found to be 0.8% magnesium stearate, which was not an optimal concentration for the powder bulk properties. © 2000 Published by Elsevier Science B.V.

Keywords: Capsule filling; Granulated powdered cellulose; Powder bulk properties; Tamp filling machine

1. Introduction

Granulated powdered cellulose is recommended specially for capsule filling as diluent and flow agent. Its comparatively large particle size results in overall acceptable flow properties, and due to its rough surface texture it should be useful for the manufacture of interactive powder mixtures used in capsule filling of low dose drugs. The material is highly compressible and swells to twice its original volume at contact with water [1].

Although the powder properties of granulated cellulose powder and capsule filling performance suggest that such products could be filled without the addition of lubricants [2], the presence of a drug substance and the function principle of high-speed tamp-filling capsule machines will most certainly require the addition of some lubricant to the formulation.

The aim of this work was to identify a suitable magnesium stearate concentration for powder flow and capsule filling of granulated cellulose powder, and to identify relationships between the individual properties measured.

2. Materials and methods

2.1. Materials

Granulated powdered cellulose (GPC, Vivacel A300, batch 070809111, Rettenmeier & Sons, Ellwangen–Holzmühle, Germany) and magnesium stearate (MgSt, batch 1691198, Medex Pharmaceuticals, Naseby, Northamptonshire, UK) were employed in this study. The geometric mean particle size and geometric standard deviation of the GPC were found to be 190 μm and 1.3, respectively, whereby less than 0.01% of the powder particles were larger than 500 μm (sieve analysis, $n = 3$). The mean particle size of the magnesium stearate powder was 2.7 ± 1.8 μm with 90% of the particles being smaller than 5 μm. The particles were of plate-like shape, and the loss on drying was found to be 4.5%.

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2.2. Methods

MgSt and GPC were mixed for 5 min in a Y-cone blender (Erweka Apparatebau, Heusenstamm, Germany). Two kilograms of each mixture was produced.

The flow and packing properties of the powders were determined using an automatic tap volumeter (Jencons Scientific Equipment, Radon Industrial Electronics, Worthing, UK) with a lift height of 30 mm and a tapping frequency of 30 taps/min. About 200 ml powder was carefully filled into a mounted measuring cylinder with known tare. The powder bed was levelled with a spatula, and the maximum bulk volume was read. A single tap was employed, and the volume was read again. This procedure was repeated, thereby gradually increasing the number of taps between individual readings, until three consecutive replicates of 200 taps did not reduce the powder volume further. Hence the minimum powder volume (to give the maximum bulk density) had been reached. The measuring cylinder was then weighed to determine the powder mass. The powder density was evaluated as a function of the number of taps using the models described by Mohammady and Harnby [3]

$$\rho_n = \rho_t - (\rho_t - \rho_a)e^{-n/T} \quad (1)$$

and Varthalis and Pilpel [4]

$$\frac{np^2}{1-p} = \tan(\text{AIF})n \quad (2)$$

where ρ_n is the powder density after n taps, ρ_t is the maximum bulk density, ρ_a is the minimum bulk density, T is the compaction constant, p is the powder porosity, and AIF is the angle of internal flow.

Carr's compressibility index [5] was also calculated

$$\text{CI} = \frac{\rho_t - \rho_a}{\rho_t} \times 100\ (\%) \quad (3)$$

All experiments were performed in triplicate.

The Zero–Torque–Limit (ZTL) of a 60 g powder column was determined using the FT3 Process Rheometer (Freeman Technology, Bourne End, Buckinghamshire, UK) in compaction mode employing a series of helix angles (2, 5 and 8°) and blade tip speeds (10, 30, 50, 70 and 90 mm/s) as described in [6,7].

The angle of wall friction was measured in an annular shear cell (Technigraphic, Bristol, UK) against a polished stainless steel plate as described in [8] using 30 g of powder mixture, whereas the angle of internal friction (δ) and cohesion coefficient (τ_0) [9] were determined using 50 g of powder mixture, carefully packed into the cell in layers of 10 g each. Four consolidation loads (2.20, 2.46, 2.83 and 3.34 MPa) were always used, and a fresh powder sample was employed for each run. Jenike's flow factor [10] was determined as defined, from the reciprocal of the slope of the unconfined yield strength (f_c) as a linear function of the major principal stress (σ_m) obtained for various consolidation loads (σ), with [11]

$$f_c = \frac{2\tau_0}{(1+\tan^2\delta)^{0.5} - \tan\delta} \quad (4)$$

$$\sigma_m = (\tan\delta\cdot\sigma + \tau_0)\left(\tan\delta + \left(\tan^2\delta + 1\right)^{0.5}\right) + \sigma \quad (5)$$

The powders were filled into clear hard gelatine capsules (Shionogi Qualicaps, SA, Alcobendas, Madrid, Spain) size 1 on a Bosch GKF 400S tamp-filling machine (Robert Bosch GmbH, Waiblingen, Germany) with a 19.6 mm dosing disk. The tamping forces were recorded with an instrumented pneumatic tamping head [12]. Capsules were filled on the basis of pure flow (cumulative tamping distance of the pins as defined in [13]: CTD = 0 mm) and maximum compression (CTD = 18 mm). A further increase in CTD caused overfilling of the capsules.

To determine the capsule fill weight and the coefficient of fill weight variation (CFV), 50 capsules were weighed on an analytical balance to ±0.1 mg (Sartorius, Göttingen, Germany). The weights were corrected for the mean weight and standard deviation of the empty capsule shells, exploiting the additivity of arithmetic mean values and variances [14].

None of the filling conditions provided a firm plug, which could be pulled out of the capsules, and the powder filled the inner volume of the capsules completely. Hence, the plug density was determined from the fill weight and the volume of the capsules. To determine the latter, the closing length of the capsules was obtained using an image analysis system (Sonata, Seescan, Cambridge, UK). The closing length was 19.56 ± 0.05 mm for all batches of filled capsules.

3. Results and discussion

The powder properties obtained from tap density measurements and Jenike's flow factor are summarized in Table 1 as a function of the MgSt concentration used.

Carr's compressibility index indicates moderate flow properties for the unlubricated GPC. Addition of 0.4% MgSt enhances powder flow considerably to result in a Carr's compressibility index of about 16%. Further increase in MgSt appears not to improve this parameter, because all further values, although smaller than 16%, are in terms of statistics not significantly different (ANOVA, $P = 0.05$).

Table 1
Results from tap density and shear cell experiments

MgSt (%)	CI (%)	AIF (°)	T	ρ_t (g/ml)[a]	FF
0	23.1 ± 0.8	51.7 ± 0.2	19.4 ± 2.0	0.501 ± 0.003	8.47
0.2	19.6 ± 1.6	53.2 ± 0.2	12.6 ± 1.0	0.502 ± 0.001	3.89
0.4	16.6 ± 0.6	52.4 ± 0.2	20.6 ± 2.7	0.521 ± 0.002	2.40
0.6	15.1 ± 1.1	52.4 ± 0.2	22.8 ± 3.4	0.529 ± 0.003	1.32
0.8	15.8 ± 1.2	51.2 ± 0.2	22.6 ± 3.2	0.530 ± 0.003	4.42
1.0	15.7 ± 0.9	51.5 ± 0.2	22.8 ± 3.2	0.535 ± 0.003	2.49

[a] Values are the arithmetic mean and standard deviation of 3 replicates.

The angle of internal flow, which is related to interparticulate friction, appears unaffected by the addition of MgSt in the range of concentrations tested. This indicates that incomplete coverage of individual particles with the lubricant occurred. The compaction constant T has a distinct minimum at 0.2% MgSt, but remains otherwise little affected. The maximum bulk density increases above a concentration of 0.2% MgSt, indicating a reduction in interparticulate friction. This appears to be in contrast to the values for the angle of internal flow. However, the latter is a parameter quantifying dynamic behaviour, whereas the maximum bulk density represents a property of the powder when at rest. Jenike's flow factor decreases sharply when adding small amounts of MgSt. Although there appears an initial trend for this property to have a minimum at 0.6% MgSt, the fluctuations observed at higher MgSt concentrations allow no definite conclusion about the influence of MgSt above 0.2% on the flow factor. It is hence assumed here, that an addition of MgSt in concentrations between 0.2 and 1.0% has a similar influence on the flow properties of GPC.

The results obtained from the powder rheometer indicate a significant change in powder properties after addition of as little as 0.2% MgSt (Fig. 1). When the results for the unlubricated GPC were excluded, there is a strong linear relationship between the ZTL and the operating conditions (Eq. (6) and Fig. 2)

$$\text{ZTL} = 80.863 + 0.087 \times \text{helix angle} \times \text{blade tip speed} \quad (6)$$

$$(r = 0.934;\ \text{RMS} = 3.86\%)$$

These results suggest that in a range between 0.2 and 1.0% of MgSt added to GPC such powder mixtures respond proportional to all process variables causing powder movement, but that the amount of MgSt added is not important in this respect. The only property of the powder mixtures listed in Table 1, which shows a fairly similar pattern, is Jenike's flow factor.

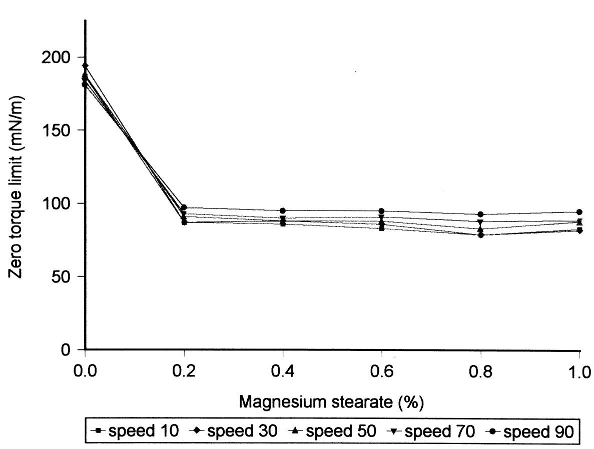

Fig. 1. ZTL as a function of the MgSt concentration for different blade tip speeds and a helix angle of 2° (profiles are similar for helix angles 5 and 8°).

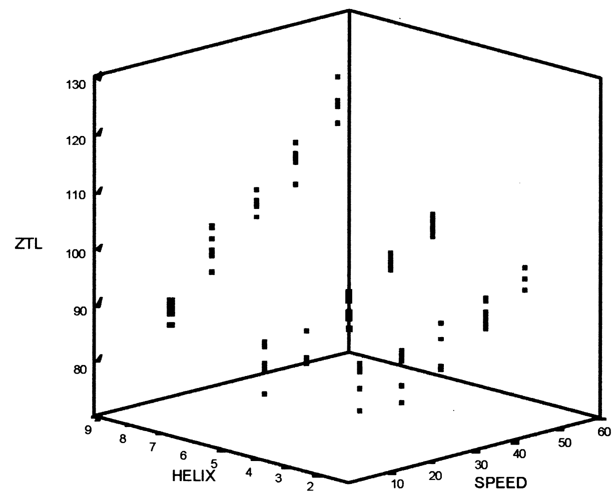

Fig. 2. ZTL as a function of the blade tip speed and the helix angle for lubricated GPC (the clouds of points represent the comparatively small effect of an increased concentration of MgSt between 0.2 and 1% on the property measured).

The angle of wall friction decreases with an increase in MgSt at lower normal loads (Fig. 3). At higher normal loads the tendency for the angle of wall friction to decrease with an increase in MgSt concentration is also observable except for the addition of 0.2% MgSt, which causes an increase in this property compared to the unlubricated GPC.

The relevant capsule filling parameters are compared in Tables 2 and 3. When filling the capsules without pin penetration into the dosing disk (CTD = 0 mm), i.e. on the basis of pure flow, the fill weight drops considerably when adding MgSt. However, the CFV has an apparent optimum at 0.4%, and there is a minimum value for the fill weight and plug density at this concentration. At 0.4% MgSt Carr's compressibility index has reached its limiting value of about 16% (see Table 1), and the tapped density starts to increase. Multiple regression analysis was able to show that two of these capsule filling properties could be predicted from the

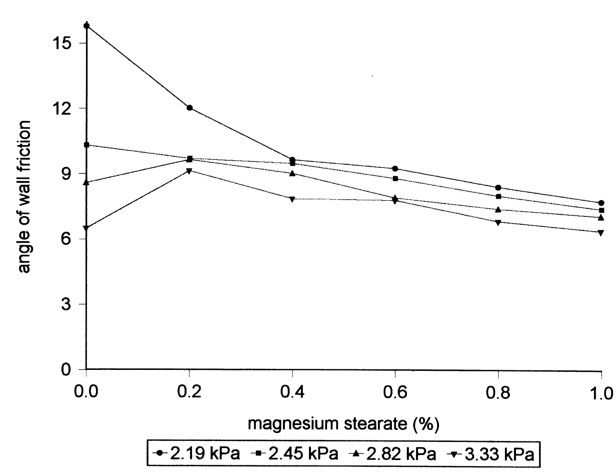

Fig. 3. Angle of wall friction as a function of the MgSt concentration at different normal loads.

Table 2
Results obtained from capsule filling on the basis of flow (CTD = 0 mm)

MgSt (%)	TF[a] (N)	Fill weight (mg)	CFV (%)	PD (g/ml)
0	<57	266.6 ± 6.1	2.28	0.496
0.2	<57	229.5 ± 4.8	2.07	0.427
0.4	<57	224.4 ± 3.8	1.68	0.418
0.6	<57	234.9 ± 4.1	1.74	0.437
0.8	<57	235.8 ± 5.1	2.18	0.439
1.0	<57	237.4 ± 4.2	1.76	0.442

[a] TF, tamping force – the minimum value to be reached to overcome the inner chamber pressure was set to 57 N (see [11] for details).

values of Carr's compressibility index CI and the tapped density ρ_t as follows

$$\text{Weight} = 10.0 \times \text{CI} \times 1498.9 \times \rho_t - 716.9 \quad (R^2 = 0.889;\ \text{RMS} = 2.06\%) \tag{7}$$

$$\text{Plug density} = 0.02 \times \text{CI} \times 2.80 \times \rho_t - 1.34 \quad (R^2 = 0.892;\ \text{RMS} = 2.02\%) \tag{8}$$

The MgSt concentration as a factor was statistically insignificant ($P > 0.05$) and hence was excluded from the equations. There is obviously a strong interaction between these two powder properties with respect to the observed filling performance. However, inclusion of an interaction term into the equations did not improve the quality of the fit and the significance of the independent variables. An increase in either property increases the fill weight and plug density, but because of the fact that with increasing concentration of MgSt, Carr's compressibility index decreases, whereas ρ_t increases, the capsule fill weight and plug density must have a minimum at an intermediate MgSt concentration.

The mean fill weight increases at 0.2% MgSt compared to unlubricated GPC, when using high compression during tamping (CTD = 18 mm). In contrast, the CFV increases threefold. However, a further increase in MgSt concentration does not influence the capsule fill weight or the CFV. This finding appears similar to the results obtained using the powder rheometer (Fig. 1), and to Jenike's flow factor (Table 1). Hence, when using compression during tamping, the MgSt concentration can be kept at a minimum. The tamping forces decrease proportionally to the increase in MgSt concentration up to 0.8%. A similar pattern was observed for the angle of wall friction (Fig. 3). A reduced tamping force is in the first instance an expression of an easier machine operation with reduced friction between the moving metal parts. Between 0.2 and 1.0% MgSt, the plug density remains constant (Table 3), and hence to improve the compression properties of GPC only 0.2% of MgSt are required. The results suggest that an increase in MgSt is favourable for the machine function, yet is not necessarily helpful in reducing fill weight variability. However, in the tests undertaken here, all coefficients of fill weight variation were within acceptable limits.

To understand the apparent discrepancy between the influence of the magnesium stearate concentration on the flow properties and the machine function, the physics of lubrication needs to be considered. According to Tabor [15], the three basic elements of friction are (1) the area of true contact between the moving particles or between the sliding particles and the machine tools, (2) the type and strength of the attractive forces between the contacting surfaces, and (3) the shearing and rupture properties of the materials at the contact points and the surrounding area during sliding. The last point is of major importance, because magnesium stearate can form a film covering the machine tools and the asperities of the GPC particles. The coefficient of friction between two materials is defined as the ratio between the shear strength of the formed adhesion junctions and the yield pressure of the softer material [16]. In the absence of a lubricant these two parameters are those characteristic for the unlubricated powder and the metal used to make the machine tools. In the presence of a lubricant film the shear strength of the adhesion junctions formed is reduced, and the normal pressure is reduced inversely proportional to the lubricant concentration due to an increasing distance between the surface of the film, where shearing occurs, and the surface of the particles [17]. Hence, the value of the ratio between shear stress, which remains constant, and the normal pressure will increase with increasing lubricant concentration. As soon as this ratio becomes larger than that for the unlubricated state, a further increase in film thickness will result in increased friction and thus in a decrease in powder flow, and/or an increase in tamping force. The different effects observed for the flow properties and the tamping force hence first suggest that the shear stress at the contact between individual GPC particles is much smaller than the shear stress at the contact of the GPC particles and the machine tools. Secondly, an increase in MgSt concentration appears to result in a steady increase of the lubricant film thickness surrounding the machine tools. Obviously, with concentrations up to 1%, the ratio between shear stress and normal pressure is always smaller than that observed between unlubricated granules and machine tools. Hence, the tamping force decreased with an increase in MgSt

Table 3
Results obtained from capsule filling on the basis of compression (CTD = 18 mm)

MgSt (%)	TF (N)	Fill weight (mg)	CFV (%)	PD (g/ml)
0	64.04 ± 0.09	309.6 ± 1.2	0.39	0.577
0.2	59.39 ± 0.22	321.3 ± 4.0	1.26	0.598
0.4	58.69 ± 0.15	321.3 ± 3.7	1.15	0.598
0.6	58.50 ± 0.13	324.0 ± 3.4	1.06	0.603
0.8	58.06 ± 0.09	322.6 ± 3.3	1.03	0.601
1.0	58.12 ± 0.13	322.9 ± 3.8	1.19	0.601

concentration over the whole range of lubricant concentrations tested. On the other hand, the GPC particles comprise an irregular surface texture with clefts and groves, in which lubricant particles could be trapped, and therefore would not participate in the lubrication process. The flow properties observed suggest that the addition of only 0.2% MgSt was sufficient to cover all asperities with a lubricant film able to lower the ratio between shear stress and normal pressure significantly. This resulted in some improvement in powder flow. A further increase in lubricant concentration, however, only filled the clefts and groves of the GPC particles and hence was ineffective with respect to powder flow. Machine vibrations during capsule filling might have dislodged some of these particles, thus increasing the amount of lubricant particles available to cover the surfaces of the machine tools proportional to the MgSt concentration.

4. Conclusion

Powder properties and capsule filling performance of granulated cellulose powder can be modified by adding a lubricant such as magnesium stearate. The filling properties are better at lower MgSt concentrations, whereas the machine performance improves with an increase in MgSt up to 0.8%.

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Appendix A. List of Abbreviations

AIF, angle of internal flow;
ANOVA, analysis of variance;
CFV, coefficient of fill weight variation;
CI, Carr's compressibility index;
CTD, cumulative tamping distance;
f_c, unconfined yield strength;
FF, Jenike's flow factor;
GPC, granulated powdered cellulose;
MgSt, magnesium stearate;
n, number of taps;
p, powder porosity;
P, error probability (ANOVA);
PD, plug density;
R^2, determinant (regression analysis);
RMS, root mean square deviation (residual analysis);
T, compaction constant;
TF, tamping force;
ZTL, zero–torque–limit;
δ, angle of internal friction;
ρ_a, minimum (aerated) bulk density;
ρ_t, maximum (tapped) bulk density;
σ, consolidation load;
σ_m, major principal stress;
τ_0, cohesion coefficient.

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