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Analysis of extrusion of some wet powder masses used in extrusion/spheronisation

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Abstract

The extrusion flow behaviour of mixtures of lactose, microcrystalline cellulose (MCC) and water in the ratio 5:5:6 by weight has been analysed from data previously obtained by a ram extruder for powder and colloidal grades of MCC. The analysis followed a recent approach of examining the viscous and elastic behaviour of polymers. Results suggest that at low flow rates, mixtures containing colloidal grades of MCC have significantly higher shear viscosities than powder grades. The present analysis also shows that shear thickening of some mixtures occurs. Elongational flow was also examined together with entry flow to the die. The results of the analysis indicate that: (a) particle size of the MCC is not important, (b) the greatest extrudate distortions occur for systems having relatively low shear viscosities at low flow rates. There appears to be an optimal elasticity for the formation of satisfactory spheres in the spheronisation stage, i.e. they must neither be too elastic nor have low elasticity.

Keywords: Extrusion/spheronisation; Microcrystalline cellulose; Shear/elongation flow; Entry flow; Viscous/elastic behaviour

1. Introduction

Pellets of reproducible quality can be prepared by the process of extrusion/spheronisation. However, not all wet powder masses can be prepared by this process. Extensive studies have shown that a number of factors must be considered to produce satisfactory spheroids (Newton, 1994). In particular, the wet masses must have a certain consistency, i.e they must have an optimal rheological behaviour. It has been found that the initial mixing to form the uniform wet mass is not a matter for concern if extrusion involves the use of long dies (e.g., Chapman, 1985), as such extrusion involves relatively high forces. Extrusion is the forcing of a material through a cylinder or other cross-sectional container (barrel) through a smaller cross-section (a die). This has been used in the plastics and metal industries for many years. In the past the flow through barrel and die was assumed to be entirely viscous, largely shear-dominated and involving simple flow patterns (e.g., Dealy and Wisbrun, 1990). For polymeric melt flows, literature exists on these matters and some of the features taken from this literature are of concern in the present paper.

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An important feature of pharmaceutical pastes is the presence of surface defects or imperfections on the extrudate surfaces after exiting the die. This has been addressed by Harrison et al. (1985), who found that surface defects do occur for certain lactose/microcrystalline cellulose/water mixtures under certain conditions of extrusion. Thus the problem is formulation and process-dependent. Gross surface defects will influence the formation of a uniform size distribution of pellets. Recently, Chohan (1994) has carried out extensive studies on the extrusion of polymer melts, showing that such materials are both viscous and elastic. Certain parameters were utilised to look at the elastic, elongational and shear behaviour of the flow using capillary rheometry (Chohan, 1994). The purpose of the present work is to analyse some pharmaceutical systems data following this approach. To this end data set out by Raines (1990) have been utilised.

1.1. Shear and elongational flow

The flow of materials through the die of an extruder is normally assumed to occur with zero boundary flow, i.e. the material at the wall of the extruder is immobile. The flow properties of the material are then characterisable by the common parameters: shear stress, shear rate, shear viscosity. By necessity, any material being extruded has to undergo flow reorganisation when going from the wider cross-section barrel to the small cross-section die. This converging flow has been the subject of much discussion and research effort in the polymeric literature (e.g., Chohan, 1994). Both shear and elongational (i.e. stretching) flow occurs in this region. It has been observed that vortices form just above the entrances to the die for a number of materials. The size of these vortices is material dependent (see, e.g., Dealy and Wisbrun, 1990). Further, a pressure drop is required for the material to flow through this entrance region, and this is known as the entrance pressure drop (referred to as EP below). According to certain theories, this entrance pressure drop is relatable to elastic behaviour (e.g., Cogswell, 1972). A concise review of the phenomenon appears in Dealy and Wisbrun (1990).

The flow of melts through a capillary rheometer or extruder is described by Cogswell (1972). As material flows from the barrel into the die, the flow streamlines converge and accelerate, which results in extensional flow. Attempts have been made to interpret such flows as stretching, which also allows the elongational properties to be deduced. In his analysis, Cogswell (1972) separates the flow field into one due to shear deformation and the other due to tensile deformation. Following further analysis, the equations below are derived:

$$\mathrm{TS} = (3/8)(n+1)P \quad (1)$$

$$\mathrm{ESR} = 4\tau\gamma/[3(n+1)P] = (\gamma/2)\tan\theta \quad (2)$$

$$\mathrm{EV} = \mathrm{TS}/\mathrm{ESR} \quad (3)$$

where TS, ESR and EV are the tensile (i.e. stretching) stress, the tensile stretch rate and the apparent extensional (or elongational) viscosity, respectively, and n, P, τ, γ and θ are the power law index, the entrance pressure drop, the shear stress at the die wall, the shear strain rate and the half angle of natural flow convergence at the die entry, respectively. Therefore, knowing shear stress, shear rate, the power law index and the entrance pressure drop, it is possible to calculate the elongational characteristics following the approach of Cogswell (1972). The use of such an approach may not be applicable to wet powder masses if their flows 'are dominated by wall slip' and not representable by the power law analysis. Numerous extrusions of pharmaceutical pastes by the ram extruder have indicated that, whilst slip has been observed, the flow is dominated by wall adhesion (i.e. zero slip flow). It has also been found that the power law model is satisfactorily approximated in a number of cases. Hence the Cogswell (1972) model will be applied here.

In the extrusion of polymers, certain parameters have assumed importance as far as the elastic behaviour of materials is concerned when flowing through the entrance regions. Two parameters that have been used (Dealy and Wisbrun, 1990; Chohan, 1994) are:

(a) the recoverable shear, RS:

$$\mathrm{RS} = P/4\tau \quad (4)$$

Table 1
Grades of powdered microcrystalline cellulose

	Average particle size	Median diameter (μm)	Moisture content (%)
Avicel PH101	50	37	<5
Avicel PH102	100	62	<5
Avicel PH103	50	36	<3
Avicel PH105	20	25	<5
Emcocel	56		<5
Unimac MG100	38		<5
Unimac MG200	105		<5

(b) the 'Compliance', C:

$$C = P/4\tau\ \tau \quad (5)$$

These have been discussed and have been utilised by Chohan (1994) to study the flow of branched polyethylene melt. At low flow rates these equations indicate a measure of elasticity. It is not known what is exactly implied by these terms at high stretch rates, but there is little doubt that the elastic behaviour of the material influences their value. The object of the current work is to look at these parameters for some wet powder masses and to attempt to relate the postprocessing values to operations, such as sphere production.

2. Materials and methods

Raines (1990) has carried out an extensive series of experiments using mixtures of lactose, microcrystalline cellulose and water. These were prepared in the ratio 5:5:6 by weight. Only one type of lactose was used of median particle size 18 μm. The type of microcrystalline cellulose was varied. Powder and colloidal grades of microcrystalline celluloses were employed. Table 1 and Table 2 list the characteristics of these materials as provided by the supplier. The materials were extruded through a ram extruder of the design of Ovenston and Benbow (1968) attached to a mechanical tester (Instron Model TT-CM, High Wycombe, Bucks.).

Entry pressures were determined by extrapolating total extrusion pressures obtained with dies having different length/diameter ratios. Shear stresses were calculated in the usual way (from the slope of capillary pressure as a function of the length/diameter ratio of the die). Power law indices were determined by fitting the shear stress and shear strain data to a logarithmic scale.

The systems will be referred to by the microcrystalline grade used as this is the parameter differentiating the samples. The RC501 showed no surface impairment. Low surface impairment was associated with RC581, RC591 and CL611. Medium surface distortion was indicated in PH101, PH105, PH103, PH102 and Emcocel. Severe surface impairment was exhibited by MG200 and MG100.

The spheronised exrudate quality of these systems is described by Newton et al. (1992). PH102 produced a satisfactory product; PH101 was slightly inferior, whilst PH103 and PH105 gave slightly elongated pellets. The Emcocel, MG100 and MG200 tended to produce large agglomerates, while the RC and CL grades failed to produce spheres.

3. Results and discussion

Fig. 1 shows the shear stress–shear rate data for all the systems. The least variation of stress with shear rate is shown by RC501 which had no extrudate surface defects. The largest variation is associated with MG100 and MG200 which had the most severe extrudate surface defects. RC581 and RC591 show the largest stresses but RC501 tends to have relatively lower stresses of the colloidal grades at most shear rates. It is clearly seen that all the colloidal grades produced higher shear stresses at low shear rates. All the powdered

Table 2
Grades of colloidal microcrystalline cellulose

	NaCMC (%)	Relative NaCMC content	% colloidal	Method of drying
Avicel RC501	8.5	Medium	30	Bulk
Avicel RC581	11.0	Medium	70	Bulk
Avicel RC591	11.0	Medium	70	Spray
Avicel CL611	15.0	Low	70	Spray

grades gave the greatest variation in stress for the shear rate range studied. RC581 and RC591 have practically identical behaviour. Table 2 shows that they have identical sodium carboxymethylcellulose content and they only differ by the method of drying. It appears, therefore, that the method of drying of the cellulose material is not significant for these grades. For the powdered grades, PH101 and PH103 have identical cellulose particle sizes but they have significant difference in their flow behaviour. Emcocel also has similar particle size to these two grades but it also differs in its shear stress-shear rate characteristics. It appears that there are characteristics other than particle size which have a greater significance in terms of rheological behaviour. The MG100 and MG200 celluloses are of different particle size; at low shear, MG100 has a lower shear stress and at higher shear the opposite is the case. The shear viscosities of the systems as a function of shear rate on a logarithmic scale are shown in Fig. 2. At low flow rates the powdered and colloidal grades give distinctly different behaviour. The powdered grades appear to settle down to a constant viscosity at low shear rates (this is analogous to the Newtonian viscosity for polymer melts especially linear polyethylenes). However, the colloidal grades show quite high viscosities at low flow rates, which suggest that they probably have high yield values, as found by Raines (1990) when analysed by the method of Benbow et al. (1987). If the slopes are taken at the low shear rates and extrapolated to zero flow, it can be seen that the order of decreasing viscosity at zero flow is RC501, RC581, RC591, C611; then followed by the powdered grades PH103, PH102, PH105, PH101, Emcocel, MG100, MG200. This corresponds to the degree of surface defects. The results also seem to suggest that Emcocel, MG100 and MG200 exhibit shear thickening.

The elongational viscosities calculated by the method of Cogswell (1972) (Eq. (3) above) are presented in Fig. 3. The materials seem to behave quite similarly in terms of elongation flow but there are some subtle differences. At the highest stretch rates, MG100 and MG200 have the lowest elongational viscosities, whilst PH101 through to 105 have the highest and quite similar viscosities.

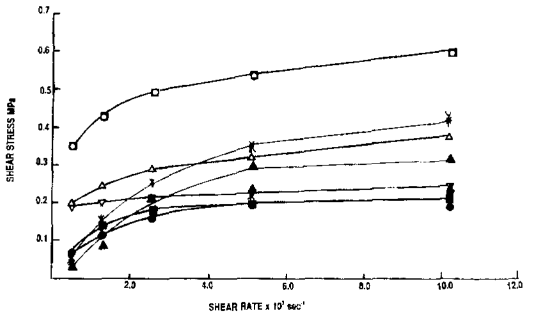

Fig. 1. Shear stress-shear rate relationships for pastes containing different grades of MCC and lactose. (●) PH101, (■) PH102, (◆) PH103, (▼) PH105, (▲) Emcocel, (X) MG100, (x) MG200, (▽) RC501, (□) RC581, (O) RC591, (△) CL611.

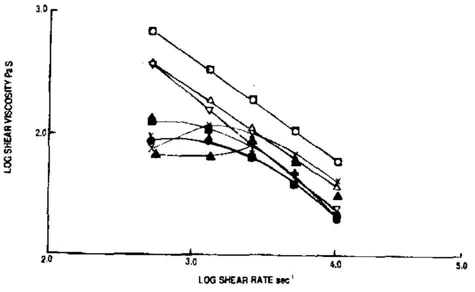

Fig. 2. Shear viscosity-shear rate relationships for the pastes of MCC and lactose (symbols as Fig. 1).

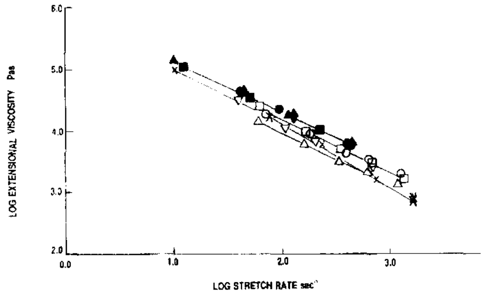

Fig. 3. Extensional viscosities of the pastes of MCC and lactose (symbols as Fig. 1).

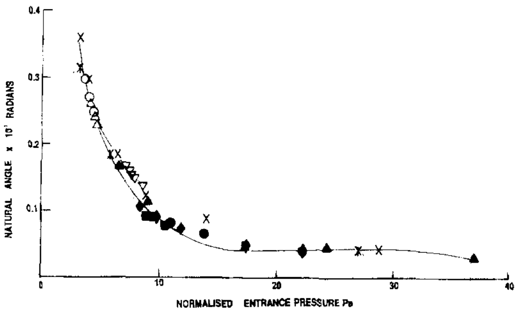

Fig. 5. Natural angles for the pastes of MCC and lactose (symbols as Fig. 1).

The largest variation of the elongational viscosities is shown by MG100 and MG200, whilst the smallest variation is that for the PH grades.

The entry pressures as a function of the shear stress data are shown in Fig. 4. The results indicate that, of the colloidal grades, the RC501 stands out from the other three (RC581, RC591 and CL611) which mostly lie away from the other data, including those for the powder grades. The highest entry pressures at high flow rates are for RC581 and RC591 and the lowest for MG100 and MG200. Despite their difference in particle size, MG100 and MG200 give similar entry pressures and are largely independent of shear stress. On the other hand, all the powdered cellulose grades give large changes in entry pressures with shear stress. As for shear rate/shear stress values, the entry pressures for RC581 and RC591 are quite similar. RC501 gives the highest entry pressure of all the colloidal grades for equivalent shear stresses; it also has the lowest colloid content, suggesting that larger colloidal grades in the presence of sodium carboxymethylcellulose enhance the entry pressures. Emcocel, which has a similar cellulose particle size, has significantly different entry pressure characteristics.

The natural angle θ, calculated from Eq. (2), plotted against normalised entrance pressure (the entry pressure divided by the shear stress) is shown in Fig. 5. The PH grades and more RC grades all lie on one general curve. The grade RC501 is again distinctly different from the other grades. MG100 and Emcocel show a wider range of natural angles. It has also been found that such plots give results independent of material type for a class of polymer melts (Shroff et al., 1977). The results in Fig. 5 indicate that natural flow angles are quite small for the present systems, suggesting that quite large vortices exist.

For clarity the 'elastic' results for the powdered and colloidal grades, calculated from Eqs. (4) and (5), are presented separately. Fig. 6 shows the recoverable shear (Eq. (4)) for the colloidal grades against shear stress. The RC501 data clearly lie

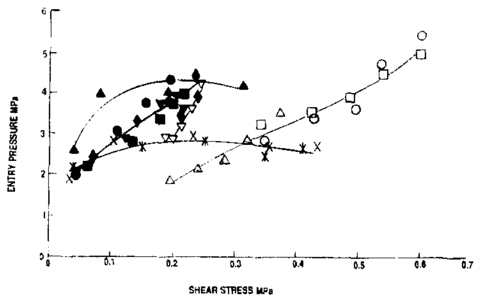

Fig. 4. Entry pressure variation with shear stress for the pastes of MCC and lactose (symbols as Fig. 1).

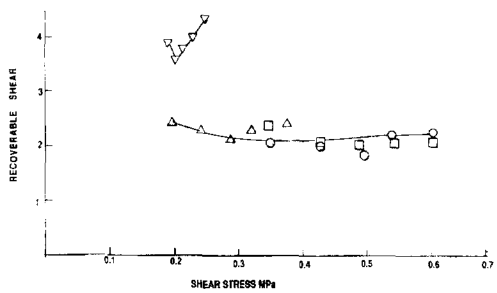

Fig. 6. Recoverable shear for pastes with colloid grades of MCC and lactose (symbols as Fig. 1).

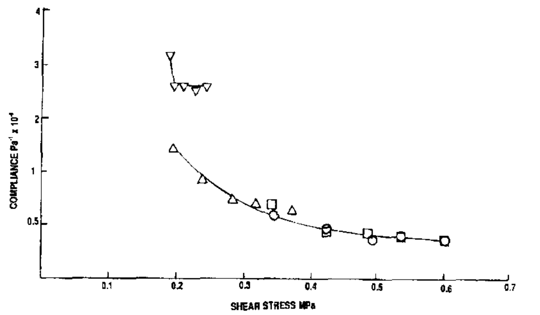

Fig. 7. Compliance of the pastes having colloidal grades of MCC and lactose (symbols as Fig. 1).

away from the other three which are generally similar. This suggests that the level of colloidal content of the microcrystalline cellulose is most important in the elastic behaviour of the materials. Fig. 7 shows the compliance (Eq. (5)) against shear stress for these materials. Again the RC501 data stand out whilst the other three are similar. Both this and the last figure suggest that RC501 is more elastic at low stresses. These and the results in Fig. 6 also appear to indicate that similar colloidal content materials give quite similar elastic behaviour even if there are differences in NaCMC levels and their method of drying.

The recoverable shear (RS) data against shear stress for the powdered grades are shown in Fig. 8. The values of recoverable shear are the highest for Emcocel, MG100 and MG200 at low stresses but they fall rapidly compared to the other materials. In fact, at high stresses the values for MG100 and MG200 are the smallest. The least variation in the value of recoverable shear is

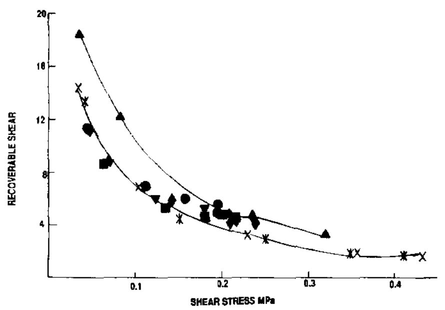

Fig. 8. Recoverable shear for pastes having powder grades of MCC and lactose (symbols as Fig. 1).

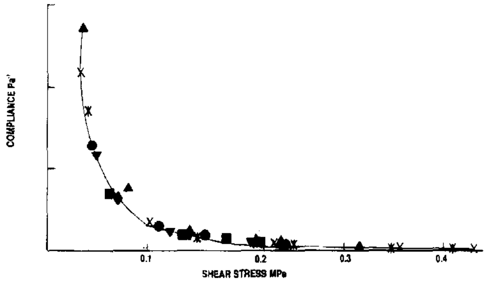

Fig. 9. Compliance of pastes having powder grades of MCC and lactose (symbols as Fig. 1).

shown by PH102 closely followed by the other powdered Avicel grades; the greatest variation is shown by MG100, MG200 and Emcocel. Except for low shear stresses, the values of RS for the powdered grades tend to lie on a single curve. Despite their differences in particle size, MG100 and MG200 give similar elastic behaviour. PH101 and PH103 have similar elastic levels but Emcocel, with a similar particle size, gives much higher elasticity levels at low shear stresses. The compliance for the powdered grades of MCC is shown in Fig. 9. At low stresses the highest values of compliance are for Emcocel, MG100 and MG200. The smallest variation is that shown by PH103 and the largest variation that by Emcocel. PH101 and PH105 have similar values of compliance despite different particle sizes. PH101 and PH103, despite similar particle size, have quite different elasticities at low flow rates. MG100 and MG200 have quite similar elastic levels despite their considerable particle size difference. It appears that particle size may be less critical in determining elasticity levels than other factors, such as differences in the physical-chemical characteristics of the source cellulose materials from which these excipients were derived, resulting in different interactions with water. At low shear stresses the powdered grades have much higher values of recoverable shear than colloidal grades. At high stresses the values of recoverable shear for Emcocel, MG100 and MG200 are similar to those of the colloidal grades (except RC501). The values for MG100 and MG200 lie on a single curve.

Superposition of all the compliance data shows that, at low shear stresses, the highest values of compliance are for Emcocel, MG100 and MG200. Except at low stresses, all the data tend to lie on a single curve. The values of compliance achieved by the colloidal grades, except for RC501, show that they are not very sensitive to shear stress.

Examination of the actual values of the recoverable shear data shows that the values for RC501 are similar to those of the non-colloidal grades showing little variation with shear stress. Other colloidal grades also show little sensitivity to the shear stress but at lower stresses their values are much lower than the powder grades. The reason for the difference in behaviour of RC501 from the other colloidal grades is probably because it has a 30% colloidal content whilst the others have a much larger value of 70%. As pointed out earlier, at low stresses the highest values of RS are for Emcocel, MG100 and MG200. This is also the case for the values of compliance. This suggests that these three are the most elastic at lower stresses.

The greatest extrudate surface distortions occur for pastes having relatively low shear viscosities at low shear rates, relatively low elongational viscosities at high stretch rates. The natural angles for similar materials lie on one curve. The values for these suggest that the half angles of convergence are small (about 20°). Earlier work by Harrison et al. (1985) suggests these orders of magnitude occur for the natural angles when determined experimentally.

The results here suggest that particle size of the microcrystalline cellulose may not be as important as other characteristics in determining the shear flow behaviour or their elastic behaviour. It appears that the physico-chemical characteristics of the source cellulose and the level of colloidal content have a significant effect on the flow and the elastic behaviour. The level of colloidal content is an important parameter as materials with low colloidal content will behave more like powdered grades systems while similar colloidal content tends to have similar behaviour, even if differences in surface characteristics exist.

The elastic parameter results suggest that the pastes should have optimal elasticity for satisfactory spheres, i.e. they must neither be too elastic nor have too low elasticity. Relatively more elastic materials such as Emcocel tend not to give satisfactory spheres as is the case for relatively inelastic materials such as the colloidal grades of MCC.

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