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The characterization of wet powder masses suitable for extrusion/spheronization

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The characterization of the flow of wet powder masses has been achieved using a ram extruder. Force/displacement curves obtained when material is forced through dies of varying length were found to exhibit three stages: (1) compression (2) steady state flow and (3) forced flow. To provide high quality extrudate it was found preferable to ensure that the compression stage was as short as possible and that steady state flow predominated. To produce these conditions, an optimum composition, die length and ram speed were required. The implications of these findings in relation to the provision of suitable formulations and production conditions for the preparation of spherical granules are discussed.

The ability to shape a material by its passage through a die has been utilized by the pharmaceutical industry in the extrusion/spheronization process. This process has been described in detail by Reynolds (1970), and involves the extrusion of a wet powder mass to produce a cylindrical extrudate (approximately 1 mm diameter), which is fed onto a rotating friction plate (spheronizer). The extrudate is broken into short lengths by the friction plate and then rounded into the granules (spheroids). The final diameter of spherical granules formed has been found to approximate to the diameter of the extrudate produced. Conine & Hadley (1970) suggested that if regular spherical granules are to be formed by this process then the extrudate produced must be able to break into short segments that are sufficiently plastic to be rounded by spheronization. The consistency or plasticity of a formulation can be assessed during formation of the extrudate by studying the flow material through the extruder. Unfortunately flow criteria cannot easily be quantified by instrumenting commercial extruders. Because extrusion entails the conversion of a suitable material of specific cross-section by forcing it from a large diameter reservoir through an orifice of small diameter (ram extrusion), a system consisting of a die of small diameter attached to a barrel of large diameter, through which a piston can pass to enable the material to be forced through the die, suffices as a model for production systems. Miyake et al (1973) reported that microcrystalline cellulose exhibited the elasticity required for extrusion/spheronization, whereas corn starch and lactose could not be extruded and spheronized when mixed with various quantities of water. Harrison (1982) attempted to determine rheological parameters to characterize the plasticity exhibited by microcrystalline cellulose alone or in combination with the water soluble diluent lactose when mixed together with a suitable quantity of water. While rheological parameters could not be obtained, a method was developed that enabled both a qualitative and quantitative assessment of wet extrusion of materials used in extrusion/spheronization to be made. It is the purpose of this work to describe this method of assessment and to outline any pertinent properties exhibited in the wet powder extrusion that may be important in the extrusion/spheronization process.

THEORY

When a material flows through a die under steady state conditions the force tending to retard flow (the viscous drag) will be exactly balanced by the pressure gradient created between the ends of the die. By equating the two opposing forces it is possible to derive the following equation

$$\tau_w = \Delta P R/2L \qquad (1)$$

where τ_w = wall shear stress, L = die length, R = die radius, ΔP = pressure difference between ends of the die.

The pressure exerted at the plane of entry to the die is not generally monitored because of the difficulties in defining the true entry point. The pressure is more usually monitored as the pressure

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† Correspondence.

exerted by the piston of the ram extruder and will thus include the finite pressure drop in the barrel of the extruder.

The pressure drop along the barrel can be estimated by determining piston pressure values at varying die lengths, then plotting these piston values against the length to radius ratio of the die and extrapolating to zero. A finite pressure loss at zero die length can thus be estimated and this is equivalent to the pressure drop along the barrel. Thus equation (1) can be modified to include this finite pressure loss as follows:

$$\tau_w = [(P - P_0)R]/2L \qquad (2)$$

where P = piston pressure, P_0 = upstream pressure loss. From this equation, two rheological parameters can be determined: the wall shear stress (τ_w) within the die and the pressure drop along the barrel, commonly described by the term 'upstream pressure loss'.

These flow dependent variables can be used in conjunction with a qualitative assessment of the extrusion profiles (load applied by the piston versus displacement of the piston in the barrel) and the quality of the extrudate produced, to aid in the selection of suitable formulations for extrusion/spheronization.

MATERIALS

Three formulations containing either (i) microcrystalline cellulose (Avicel PH101 – FMC Corporation), (ii) lactose (regular grade, Unigate), or (iii) microcrystalline cellulose/lactose in equal quantities, were mixed in planetary mixer (Hobart) with sufficient water to form a granule. This wet powder mass was passed through a 2·84 mm screen to remove large lumps. Approximately 50 g of the granulate (the amount was not critical and depended upon the moisture content of the mix) was packed into the barrel of the ram extruder to a constant volume by applying a hand pressure after the appropriate die had been attached. The filled barrel was then mounted on a support in the form of a metal 'C-piece' and aligned underneath the piston which was attached to the crosshead of a servo-hydraulic press (Dartec Ltd, Model M1000/RE) via a calibrated load cell. The crosshead was lowered by manual control until the piston reached the packed wet mass in the barrel, and then lowered by machine control at the preselected speed. The force exerted by the piston was recorded as a function of displacement on an X–Y recorder (Bryans Instruments Ltd, Model 29000 A3). The force displacement profiles at each crosshead speed (0·5–6·0 mm s^{-1}), for each die diameter (1·0–2·0 mm), die length (2–20 mm) and material mix were recorded at various length to diameter ratios of the die. The extrudate produced was then examined for quality in terms of its surface texture (Harrison et al 1985).

RESULTS AND DISCUSSION

The force/displacement profile as shown in Figs 1–5 consisted of three distinct regions:

1. *Compression stage*. Before extrusion, the wet mass, initially packed into the barrel by a hand pressure, consolidated further with only a slight application of pressure.

The extent of the consolidation was estimated as an apparent density value by determining the weight and volume of the plug of material in the barrel of the extruder after extrusion had commenced. The estimated values for apparent density were approximately equal to the apparent particle density of the wet powder masses (Harrison 1982). This agrees with the results of Shepphard & Clare (1972) who found that a metal powder consolidated its apparent particle density before flow in a ram extruder, implying that interparticulate voidage had been eliminated before the commencement of flow. This does not necessarily imply that extrusion cannot take place before all the interparticulate voidage has been eliminated. If the force/displacement profiles are examined, it can be seen that the build-up in ram force immediately before extrusion, occurs over a negligible displacement of the piston. The length of the compression stage for microcrystalline cellulose (Fig. 1) can be seen to be moisture content depen-

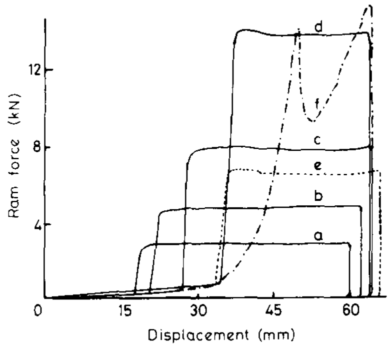

FIG. 1. Force/displacement profiles at various moisture contents of mixtures of microcrystalline cellulose and water: a–d: microcrystalline cellulose–lactose–water (5:5:6): e: and lactose–water (8:2): f; at a ram speed of 4 mm s^{-1}, a die diameter of 1·0 mm and a length-to-radius ratio of 12. Moisture content of microcrystalline cellulose–water mixtures, %; a = 59.4, b = 54·8, c = 51·1, d = 45.

dent with the pressure build-up before extrusion taking place over a greater displacement. The hand pressure applied before extrusion presumably eliminated more voidage at higher moisture contents. It can also be inferred that at higher moisture content it would be possible to obtain flow in the extruder before all the interparticulate voidage has been eliminated. In contrast, the microcrystalline cellulose/lactose mix shows no dependency on moisture content (Fig. 2) presumably because the material is less sensitive to hand pressure and is therefore less compressible.

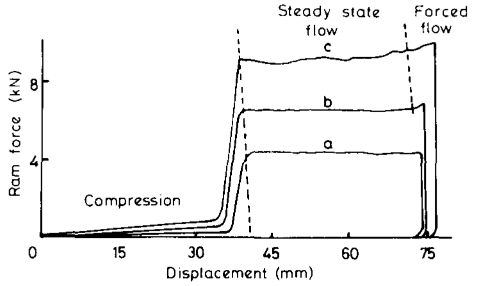

FIG. 2. Force/displacement profiles at various moisture contents of microcrystalline cellulose–lactose–water mixtures at a ram speed of 4 mm s^{-1}, a die diameter of 1·5 mm and a length-to-radius ratio of 12. Microcrystalline cellulose–lactose–water ratios: a = 5:5:7, b = 5:5:6, c = 5:5:5.

The length of the compression stage and its sensitivity to moisture content therefore may give information on the compressibility of the material selected for extrusion/spheronization. Ideally, for manufacturing purposes, the compression stage should be minimal to increase the throughput of semi-continuous commercial extruders. In general, formulations should be adjusted to give short compression stages with rapid build-up to extrusion pressure.

2. *Steady state flow.* Once the material in the barrel and die of the ram extruder has begun to flow, the applied pressure required to maintain the flow will remain constant provided that the flow pattern created in both the barrel and the die remain constant. This concept of steady state flow has been supported by monitoring the flow pattern with coloured material (Harrison et al 1984). Ideally, all product extrusion should take place under these steady state conditions so that the product is formed under uniform loading. The force/displacement profiles indicate that microcrystalline cellulose mixtures at all moisture contents were extruded under steady state conditions (Fig. 1), whereas those for microcrystalline cellulose/lactose mixtures show that the length of the plateau was dependent upon the moisture content of the mix (Fig. 2) and the extrusion rate (Fig. 3) but not die diameter (Fig. 5). Lactose mixtures did not exhibit a plateau (Fig. 1). In conclusion, the force required for extrusion should ideally be independent of displacement and this can be achieved by increasing the amount of readily deformable materials such as microcrystalline cellulose by increasing the moisture content of the mix, or by increasing the ram speed and hence the extrusion rate. The actual magnitude of the constant force will differ with the material and operating conditions.

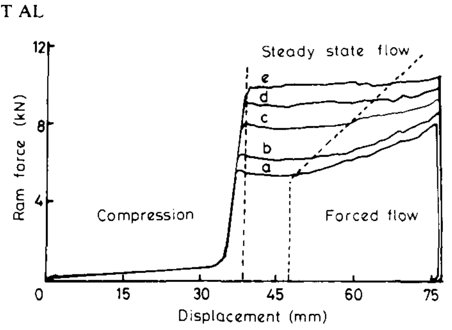

FIG. 3. Force/displacement profiles at various ram speeds for microcrystalline cellulose–lactose–water (5:5:6) with a die diameter of 1·5 mm and a length-to-radius ratio of 12. Ram speeds mm s^{-1}; a = 1·5, b = 2·0, c = 3·0, d = 4·0, e = 6·0.

3. *Forced flow stage.* At this stage increasing force is required to maintain extrusion from the die. This stage occurs because the flow patterns within the mass in the extruder alter in an attempt to maintain extrusion. These changes in the flow pattern result in an increasing ram force (Figs 1–5). The end point of this stage is cessation of flow, when the applied force can no longer induce flow in the material by the established flow pattern or the total possible displacement of the ram has been reached. The lactose/water mixture in Fig. 1 exhibited only forced flow; a steady state flow pattern was not created. The resultant extrudate produced was of poor, variable quality and depended on the applied load. When the moisture content of the wet mass of the various systems was determined during extrusion in the forced flow stage, a moisture gradient was found between the material in the barrel and that leaving the die of the extruder. The extrudate always had a higher moisture content than the material remaining in the barrel. The extent of the forced flow region was found to increase with a reduction in ram speed (Fig. 3). This was thought to occur for microcrystalline cellulose/lactose mixtures because the moisture

gradient created during forced flow was more likely to occur at lower ram speeds. Thus, at low speeds, a moisture gradient will be set up in the ram extruder, resulting in the loss of steady state flow patterns. It can therefore be surmised that extrusion should improve when the extrusion rate is increased. In practice, this is acceptable provided that the ram force at the higher extrusion rate does not affect the quality of the extrudate produced. The ideal extrusion profile should exhibit no forced flow stage and formulations should be designed to minimize the extent of this by the methods outlined to maximize the steady state flow region. In summary, qualitative examination of the force/displacement profile enables adjustments to be made to the formulation to improve the quality of the extrudate.

Quantitative comparisons can be made between formulations by measuring the ram force required to maintain steady state flow extrusion under selected experimental conditions. The results in Figs 1–5 show that the ram force during steady state flow increased with increasing length-to-radius ratio of the die. The velocity of the throughput decreased with increasing die diameter and moisture content and varied with changes in the material mix. Work with metals showed that ram force was independent of die length in the presence of lubricants (Sheppard & Clare 1972). Hence the dependency of ram force on length to radius ratio (Fig. 4) suggests that the presence of a lubricating film of water is not the only factor controlling extrusion. The mean frictional force at the die wall per unit length (the mean wall shear stress) was estimated as the slope of a plot of the steady state flow piston pressure values against the length-to-radius ratio of the die according to equation 2. This plot was found to be linear up to a length-to-radius ratio of 16 (Fig. 6), above which a moisture gradient was created in the die itself. It is therefore necessary to ensure that the length of the die in commercial extruders is not of sufficient length to create a moisture gradient in the die. The intercept of such a plot represents the piston pressure at zero die length and will be equivalent to the upstream pressure loss. The two values of mean wall shear stress and upstream pressure loss can be used to compare different formulations at particular ram speeds. These values of upstream pressure loss and mean wall shear stress can also be related to the quality of the spherical granules (in terms of particle size range and shape) by spheronizing the extrudate produced from ram extruders. Unfortunately, no specific rheological parameters independent of ram speed can be derived for the particular mixtures tested; examples of the extrusion rate dependency of these rheological parameters evaluated and their sensitivity to formulation changes are in Table 1. The magnitude of these values allows quantitative comparisons to be made between formulations and process variables. Clearly mean wall shear stress and upstream pressure loss decrease with water content and ram speed.

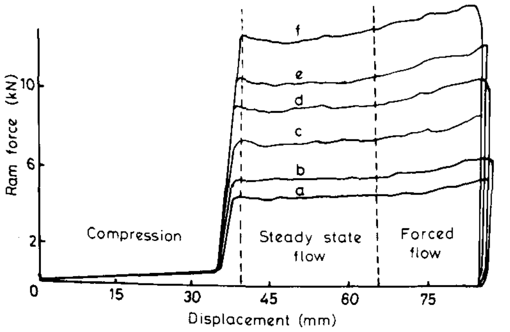

FIG. 4. Force/displacement profiles at various length-to-radius ratios (L/R) for microcrystalline cellulose–lactose–water (5:5:5) at a ram speed of 4·0 mm s^{-1} and die diameter of 1·5 mm. L/R ratios; a = 2, b = 4, c = 8, d = 12, e = 16, f = 20.

Table 1. Upstream pressure loss (P_o) and wall shear stress (τ_w) values (kNm^{-2}) at selected ram speeds for (A) microcrystalline cellulose mixtures and (B) microcrystalline cellulose–lactose mixtures. Die diameter 1·0 mm.

A

Ram speed mm s^{-1}	Moisture content (% w/w) 45·3 τ_w	45·3 P_o	51·1 τ_w	51·1 P_o	54·7 τ_w	54·7 P_o
6·0	927	8840	522	3440	151	1590
3·0	822	7570	479	3070	211	1560
1·5	601	7070	356	2820	277	1510
6·75	—	—	268	2800	323	1460

B

	Moisture content (% w/w) 34·0		37·4		40·8	
6·0	563	9370	309	6430	224	3250
3·0	413	11200	275	5110	207	2710
1·5	—	—	215	4930	175	2470
0·75	—	—	—	—	135	2390

(—) No steady state flow values could be obtained at these extrusion rates.

It has also been reported (Harrison et al 1985) that extruder die design affects the quality of the extrudate produced by ram extrusion. The smooth extrudate normally produced becomes sharkskinned at short length to radius ratios (less than 4) and becomes rough at high extrusion rates (Harrison

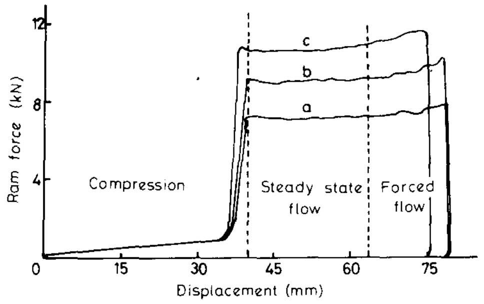

FIG. 5. Force/displacement profiles at various die diameters for microcrystalline cellulose-lactose-water (1 : 1 : 1) at a ram speed of 4 mm s^{-1} and a length-to-radius ratio of 12. Die diameter mm: a = 2·0, b = 1·5, c = 1·0.

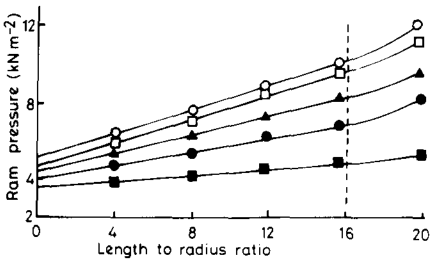

FIG. 6. Ram pressure as a function of length-to-radius ratio at various ram speeds for microcrystalline cellulose-lactose-water mixes (5 : 5 : 6) at a die diameter of 1·0 mm. Ram speeds mm s^{-1}: ■ 0·5, ● 1·0, ▲ 2·0, □ 4·0, ○ 6·0.

et al 1985). Die design can be adjusted to ensure that a smooth extrudate is produced. This is a necessary requirement for good spheronization.

It is unfortunate that the rheological parameters derived from ram extrusion through a die are dependent on extrusion rate. To achieve a term independent of extrusion rate, the extrusion system must be modified. When a material flows along a tube of sufficient diameter to reduce flow differentials to a minimum, the force required to maintain a 'plug flow' in the tube will be equivalent to the wall friction. This wall friction will be an assessment of the flow properties of the material tested. The force required to maintain plug flow in the ram extruder was estimated by removing the die and recording the force that was required to initiate flow of a known length of the plug of material that remained in the barrel of the ram extruder, after steady state extrusion. This is termed the ejection force, and was found to be independent of ram speed of ejection. The measured values of this ejection stress observed from the ejection force and area of contact between the wall and the plug at various moisture contents for microcrystalline cellulose, microcrystalline cellulose/lactose and lactose mixes are shown in Fig. 7. This

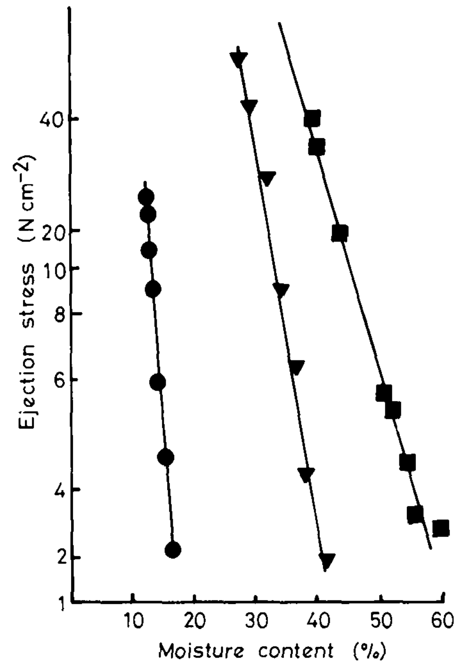

FIG. 7. The relation between the mean ejection stress and the moisture content of the mixtures. ■ Microcrystalline cellulose, ● lactose, ▼ microcrystalline cellulose and lactose.

Figure shows that the ejection stress is moisture-dependent and the relative sensitivity of ejection stress to moisture content is material-dependent. Microcrystalline cellulose, a material that has the ability to take up water into its intraparticulate voidage and become readily deformable (Battista 1975), is relatively insensitive to moisture concentration changes when compared with the water-soluble crystalline material, lactose. It would be an advantage to produce a formulation for extrusion/spheronization that is not particularly sensitive to moisture concentration. Therefore, formulations for extrusion/spheronization should exhibit the least possible gradient when ram extrusion ejection stress values determined by the method outlined are plotted against moisture content. Thus this simple extrusion parameter, the ejection stress, can be determined independent of extrusion rate, and can be used to characterize a particular wet powder mass extrusion process.

CONCLUSION

A ram extruder can be used in the extrusion/spheronization process for small-scale production of spherical granules. By monitoring the ram force during extrusion it is possible to assess the formulation by examining the resultant force/displacement profile. It is also possible to determine two rheological parameters, the 'upstream pressure loss' and the 'mean wall shear stress' that are both extrusion rate-dependent. These two can be related to the quality of spherical granules produced by extrusion/spheronization. A further rheological parameter, the ejection stress required to eject the material remaining in the extruder barrel, can be determined and used to evaluate the sensitivity of a particular formulation to moisture content.

The method of ram extrusion, therefore, provides a system which can be used on a small scale to develop and improve formulations for extrusion/spheronization.

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