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International Journal of Pharmaceutics 238 (2002) 61–76

international journal of pharmaceutics

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The influence of liquid binder on the liquid mobility and preparation of spherical granules by the process of extrusion/spheronization

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Received 1 August 2001; received in revised form 31 January 2002; accepted 7 February 2002

Abstract

The influence of the type of liquid on the movement of water and the performance of the preparation of pellets by the process of extrusion/spheronization has been studied. Liquid movement was assessed by a pressure membrane technique and by extrusion, while the pellet properties were assessed in the terms of their median size, size range (interquartile range), roundness (by a two-dimensional shape factor) and porosity. The model formulations studied were microcrystalline cellulose (MCC) and mixtures of MCC and barium sulphate at 20, 50 and 80% levels. The liquids were water, a 25% solution of glycerol in water and an anionic surfactant (sodium lauryl sulphate) below its c.m.c. and two concentrations (0.01 and 0.0001%) of a non-ionic surfactant (Pluronic PF68). The presence of the different liquids changed the ease and extent with which the liquid could be removed (drying) and reabsorbed (wetting), resulting in lower levels of saturation with the glycerol solution and considerably increased levels of saturation with the surfactants. Changes in liquid movement during extrusion, were influenced more by the level of liquid and the rate of extrusion, than by its composition. The level of liquid was also an important factor in terms of the force necessary to extrude the different formulations. For a given level of liquid, the glycerol solution tended to increase extrusion force, while the surfactant solutions tended to decrease the extrusion force. The liquid levels, particulate composition and rate of extrusion were important in terms of pellet size, size range, roundness and porosity. The low level of liquid involved produced elongated pellets. The wet formulations produced larger, agglomerated pellets with a wide particle size range and a higher porosity. The lowest porosity pellets were prepared from mixtures with no or a low barium sulphate content while the highest levels of porosity were found with equal parts MCC and barium sulphate. In general, for equivalent liquid contents, pellets made with the glycerol solution were more porous than those prepared with water while the opposite was true for pellets made with surfactants. Although the different liquids influenced water movements, they did not prevent the formation of high quality pellets by the process of extrusion/spheronization.

Keywords: Barium sulphate; Extrusion/spheronization; Glycerol; Microcrystalline cellulose; Pellets; Pressure membrane; Surfactants

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0378-5173/02/$ - see front matter
PII: S0378-5173(02)00064-9

1. Introduction

The presence of a liquid is an essential feature of all formulations used in the preparation of pellets by the process of extrusion/spheronization. The function is to provide a powder mass, which has appropriate rheological properties to allow the preparation of a smooth extrudate and the transformation of this extrudate into spherical pellets on the spheronizer plate (Newton, 1996). Fielden et al. (1992, 1993) have discussed the role of water movement in such formulations, emphasising that if the water is too mobile, the consistency can be changed as water migrates under the forces of both extrusion and spheronization. The movement of liquid could also be influenced by such factors as the viscosity and surface tension, the former influencing the resistance to flow, the latter possible changes in accessibility of the pore structure within the powder bed. Both factors could influence the 'consistency' of the wet powder mass, which in turn would influence the process ability to produce spherical pellets. Before attempting to study the property of 'consistency', it is important to consider the degree of 'mobility 'of the liquid binder in the wet mass as this will considerably influence the rheological conditions used to measure the consistency. To study the problem associated with the accessibility of the liquid to the powder mass and the mobility of the liquid under pressure, four powder compositions have been studied, containing mixtures of barium sulphate and microcrystalline cellulose (MCC) in the ratio 0:10, 2:10, 5:5 and 8:2. The liquid binder has been varied from the basic water system to preparations containing either a 25% glycerol/water mixture or a surfactant solution. The choice of barium sulphate as the model system provided a powder, which was virtually insoluble in any of the fluids, and hence would retain the same particulate form throughout the processes. A pressure membrane technique (Fielden et al., 1992) has been used to assess the movement of liquid within the bed structure, while the identification of the water content during the extrusion process has employed the technique of collection of extrudate fractions (Baert et al., 1992), using a ram extruder. These properties have been compared to the performance of the formulation in terms of pellet properties, when the wet mass was process under standard conditions.

Table 1
Values for contact angles of powders for the liquids used in the preparation of pellets

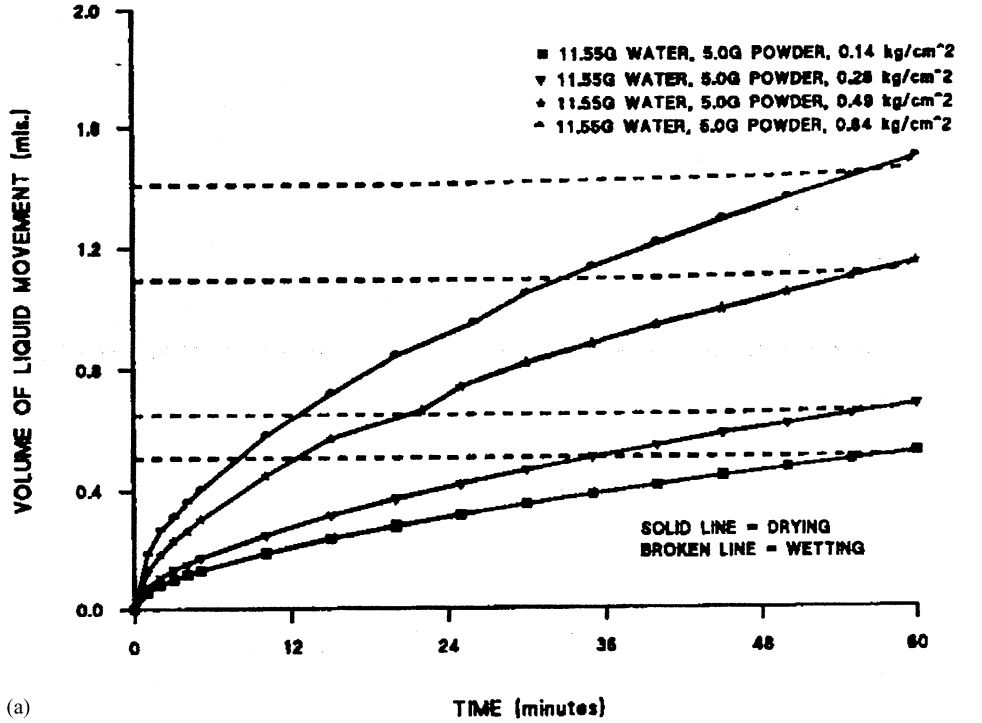
Powder	Liquid	Contact angle
(1)		
Avicel PH101	Water	40.5
Avicel PH101	25% Glycerol	46.1
Avicel PH101	0.1% S.L.S.	24.4
Avicel PH101	0.0001% PF68	18.6
Avicel PH101	0.01% PF68	b.l.d.
(2)		
Barium sulphate	Water	19.6
Barium sulphate	25% Glycerol	28.4
Barium sulphate	0.1% S.L.S.	b.l.d.
Barium sulphate	0.0001% PF68	19.3
Barium sulphate	0.01% PF68	b.l.d.
(3)		
Equal parts of (1)+(2)	Water	35.5
Equal parts of (1)+(2)	25% Glycerol	36.0
Equal parts of (1)+(2)	0.1% S.L.S.	b.l.d.
Equal parts of (1)+(2)	0.0001% PF68	b.l.d.
Equal parts of (1)+(2)	0.01% PF68	b.l.d.

b.l.d., below level of detection; S.L.S., sodium lauryl sulphate; PF68, pluronic PF68.

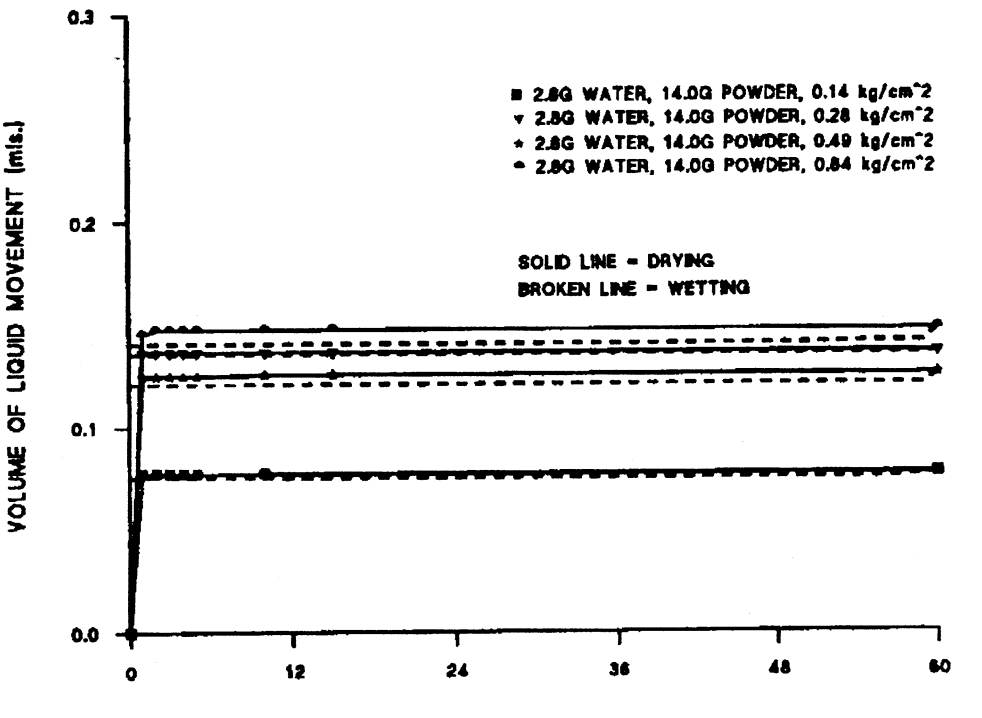
2. Materials and methods

2.1. Materials

Microcrystalline cellulose (MCC) (Avicel PH101) was donated by FMC (Philadelphia, USA). A single batch of barium sulphate EP was supplied by Sachleben Chemie GmbH (Germany) as the XRAH 10 grade, which has a volume mean particle diameter of 10 μm. Sodium lauryl sulphate was specially pure grade (BDH Poole, UK). Pluronic PF68 was obtained from ICI, London, UK whilst the glycerol was Analar grade (BDH Poole).

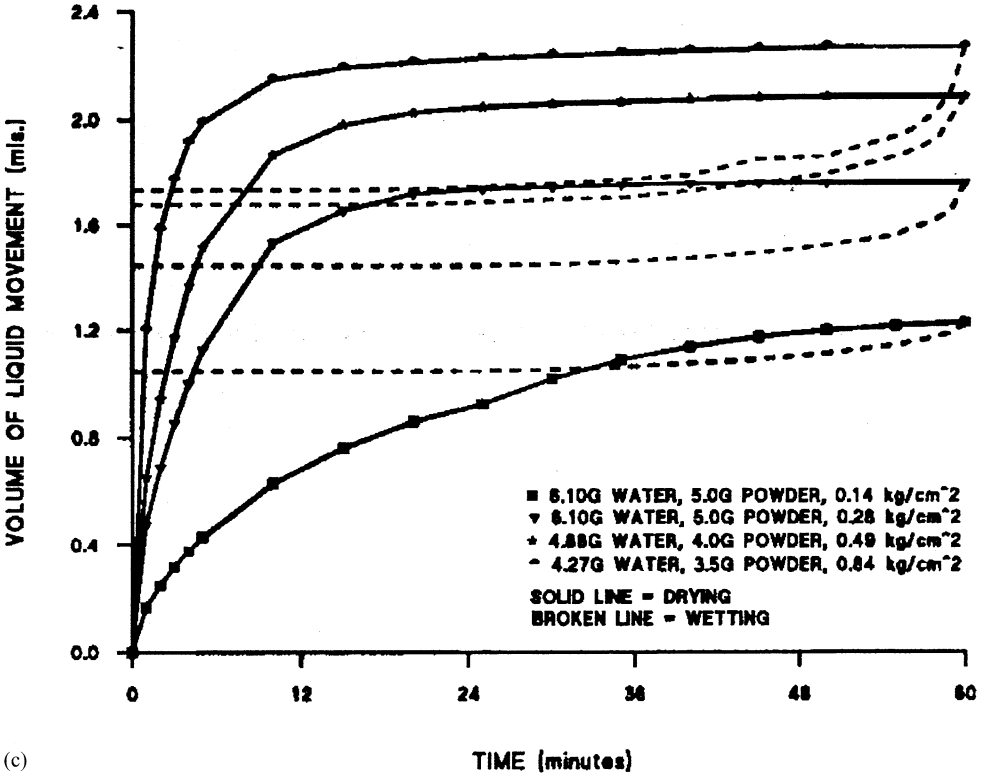


(a)



(b)

Fig. 1. Volume of liquid moved as a function of time at various applied pressures for (a) MCC and water, (b) barium sulphate and water, (c) equal parts by weight of MCC and barium sulphate and water and (d) for MCC and water, 0.1% S.L.S., 0.01 and 0.0001% PF68 at an applied pressure of 0.28 kg/cm^2.



(c)

Fig. 1. (*Continued*)

2.2. Materials characterisation

The surface tensions of solutions of sodium lauryl sulphate and Pluronic PF68 were measured with a dynamic contact angle analyser (DCA 312 Hahn Instruments Inc, USA) with a cleaned glass plate. A concentration of sodium lauryl sulphate of 0.1% was identified as having a surface tension of 47.2 N/m being below the c.m.c. For the non-ionic surfactant Pluronic PF68 two concentrations 0.01 and 0.0001% representing solutions above and below the point of inflection (approximate c.m.c) of the surface tensions concentration curve were identified for use in further experiments. These solutions had surface tensions of 62.54 and 49.46×10^{-3} N/m. The surface tensions of the water and 25% glycerol solution were determined as 72.6 and 71.24×10^{-3} N/m, respectively. The presence of the surfactants did not change the viscosity of water (1.0 mPa s) while the presence of 25% glycerol will increase the viscosity to a value of 2 mPa s (CRC Handbook of Chemistry and Physics, 61st Edition CRC Press, Boca Raton, FL, 1980).

The contact angles formed by these solutions against MCC and barium sulphate equal mixtures were measured with the dynamic contact angle analyser using compacted beams $1.2 \times 6.0 \times 0.2$ cm. The values are presented as an advancing contact angle in Table 1.

2.3. Water movement

The pressure membrane technique described by Fielden et al. (1992) was used following the necessary precautions. Here a mass of powder saturated with the appropriate liquid is placed on a membrane connected to a column of liquid whose volume can be measured accurately. Thus the volume of liquid pushed out (drying) when pres-

sure is applied and the volume of liquid, which is taken back into the bed (wetting) on removal of the pressure is measured as a function of applied pressure. The percentage saturation (volume of liquid in 100 g powder) was determined by estimating the water content at the end of the experiment by drying the wet plug to constant weight, and allowing for the water movement measured by the capillary. The mean hydraulic radius m, as a function of saturation was calculated from the equation:

$$m = \frac{\tau \cos \theta}{P_c}$$

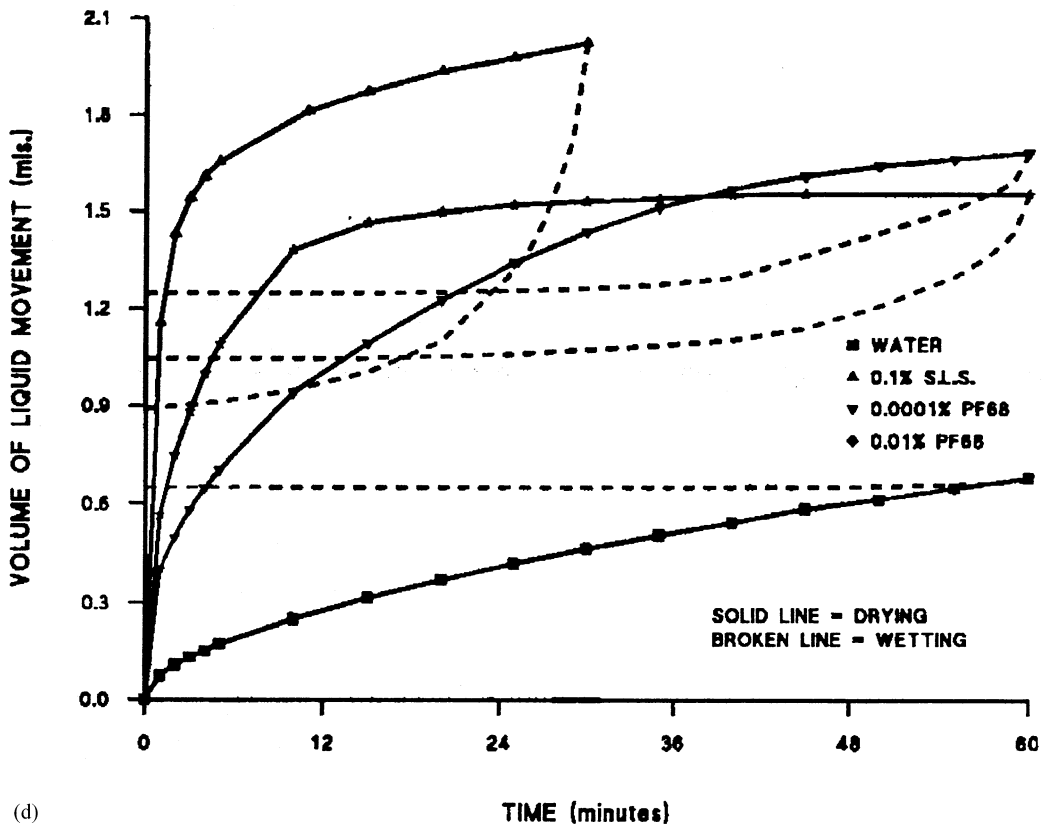
where θ is the appropriate contact angle, P_c, the capillary pressure and τ is the surface tension of the liquid.

2.4. Water content of extrudate

The relative water content of the extrudate issuing from a ram extruder was measured as described by Baert et al. (1992). Successive samples issuing from a ram extruder fitted with a 6 mm long, 1.5 mm diameter die with a ram speed of either 20 or 200 mm/min were collected at fixed time intervals. The samples were weighed and dried to constant weight, providing an estimate of their original water content.

2.5. Preparation of pellets

Pellets were prepared from MCC and mixtures containing different ratios of MCC and barium sulphate with quantities of liquid, which for water



(d)

Fig. 1. (*Continued*)

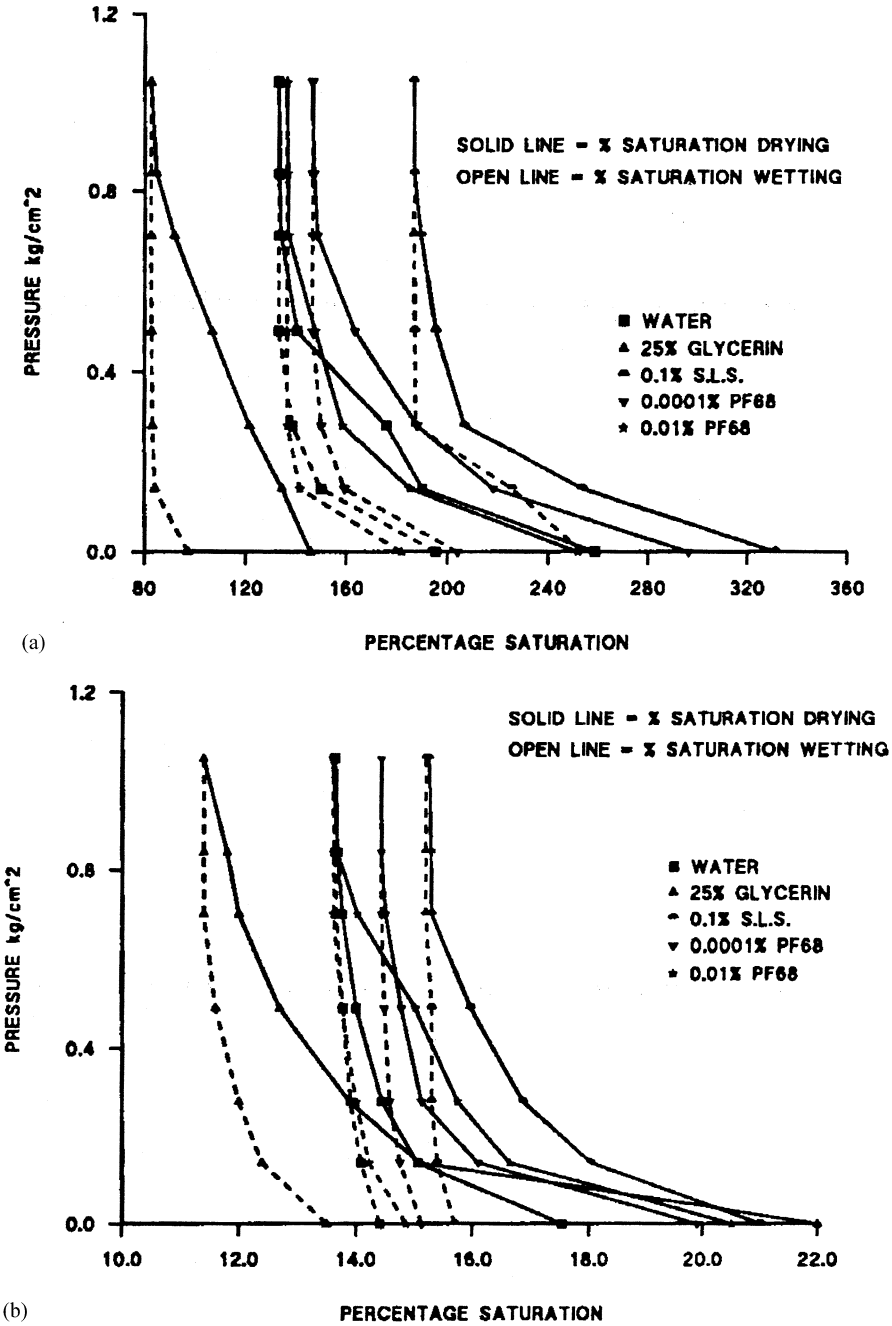


Fig. 2. Applied pressure as a function of saturation for water, 25% glycerol, 0.1% S.L.S., 0.01 and 0.0001% PF68 and (a) MCC, (b) barium sulphate and (c) equal parts by weight of MCC and barium sulphate.

provided a dry, a good and a wet mixture. The former blends generally failed to spheronize, the good produced spherical pellets while the wet mix produced agglomerated pellets. Mixing of powder and liquids was achieved with standardised concentrations in a planetary mixer (Kenwood Ma-

jor, London, UK) and the wet powder mass was extruded through a 1 mm diameter die 6 mm in length of a ram extruder (Harrison et al., 1985) at crosshead speeds of 20 and 200 mm/min by a mechanical testing instrument (Lloyds MX50, Southampton, UK). The extrusion forces involved were recorded for each wet mass.

Three hundred grams of wet extrudate was spheronized in a 20.32 cm diameter radial plate spheronizer (G.B. Caleva Ltd, Dorset, UK) at a plate speed of 1000 rpm for 10 min. The pellets were collected, and dried in a hot air oven (Hotbox, Gallenkamp, London, UK) at 40 °C for 24 h.

2.6. Analysis of pellets

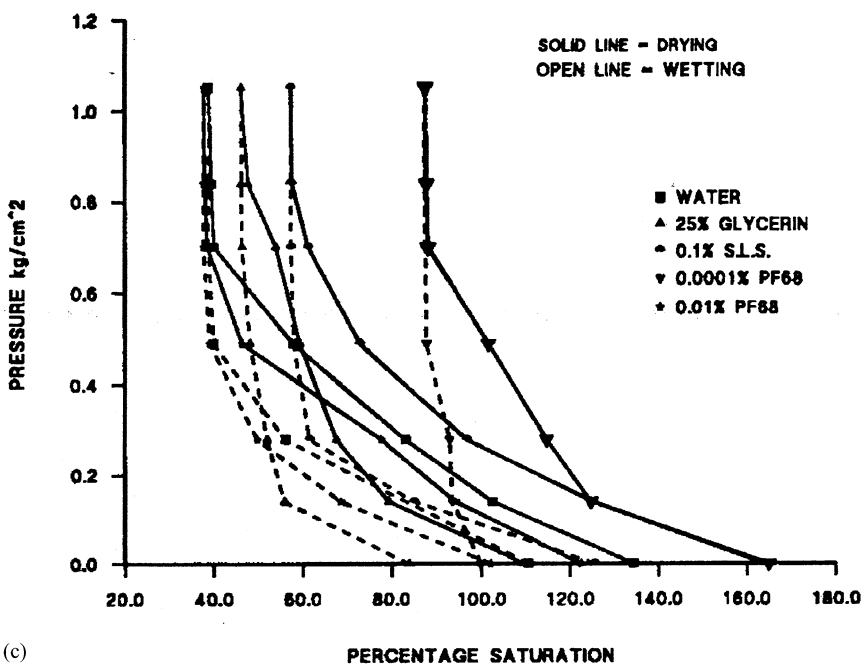
The size distribution of the pellets was determined by sieving analysis with a $\sqrt{2}$ progression of B.S. sieves on a sieve shaker (Endecott Ltd, London, UK). The shape of the pellets was analysed by the method of Podczeck and Newton (1994) using a sample of 50 pellets and an image analyser (Solitaire 512, Seescan, Cambridge, UK) connected to a black and white camera (CDD-4 miniature video camera module Rengo Co., Ltd, Japan) and a zoom lens (18-108/2.5 Olympus, Hamburg, Germany). Each pellet was analysed separately (i.e. using an angle of 1° between each radius measurement). The system also measured aspect ratio and perimeter automatically.

2.7. Density of pellets

The apparent particle density of the powders and the pellets was determined with an air comparison pycnometer model 930 (Beckman, High Wycombe, UK). Porosities of the pellets were estimated by assuming the contribution of the density of each component was additive and comparing with pellet density values.

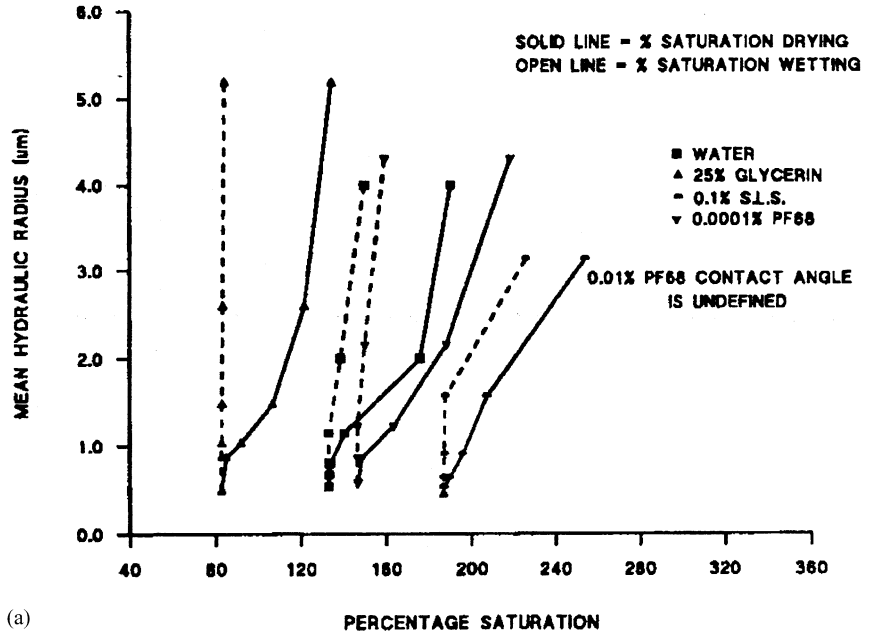
3. Results and discussion

To provide information on the way liquids moved through the wet powder masses, three of the four powder systems were studied, MCC and

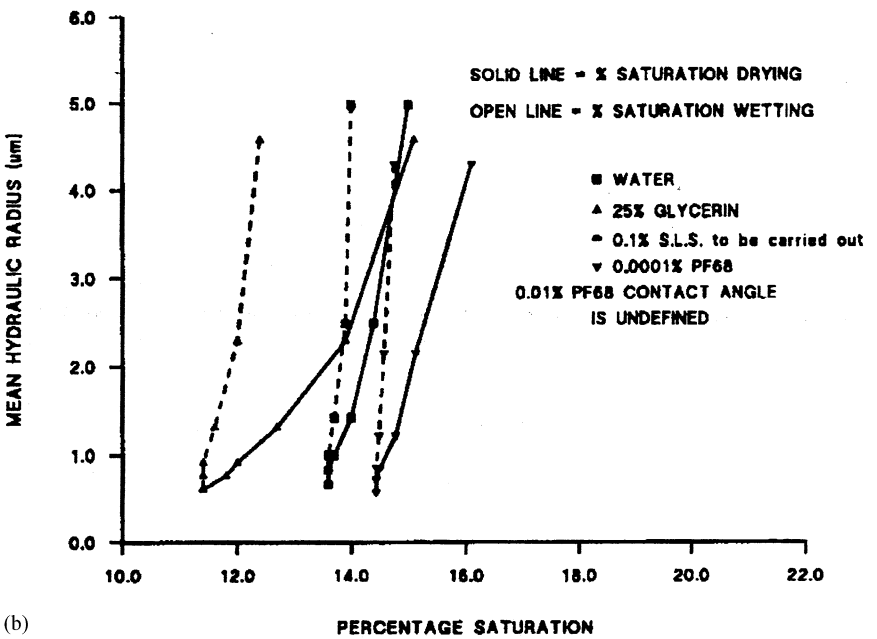


(c)

Fig. 2. (*Continued*)



(a)



(b)

Fig. 3. Mean hydraulic radius of powder beds as a function of percentage of liquid saturation for (a) MCC and water, 25% glycerol, 0.1% S.L.S. and 0.0001% PF68, (b) barium sulphate and water, 25% glycerol and 0.0001% PF68 and (c) equal parts by weight of MCC and barium sulphate and water and 25% glycerol.

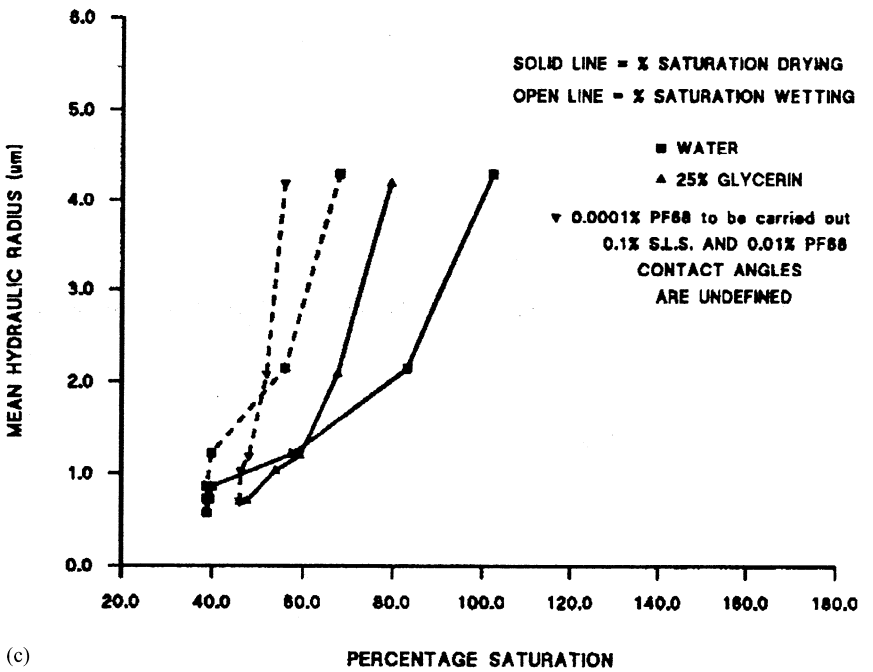
barium sulphate alone and an equal mixture of the two solids. Fig. 1a and b readily illustrate the difference between the MCC and the barium sulphate. The latter, Fig. 1b, responds to the application of pressure by removal of a small amount of water, which reaches rapid equilibrium when the pressure is applied. As the pressure increases, the water removed increases. There is little reabsorp-

tion (wetting) of water when the pressure is removed (wetting curve). MCC on the other hand, Fig. 1a, shows a slow but continuous removal of water (drying) over an hour of the experiment. There is a slight intake of water once the pressure is removed (wetting curve). When the two powders are mixed (Fig. 1c), the powder behaves more like MCC than barium sulphate. As the pressure increases, there is clear evidence of water reabsorption, i.e. distinct wetting, the amount increasing with an increase in drying pressure.

When surfactants are added, for the same applied pressure there is considerably more water removed from the bed of MCC, Fig. 1d. The lower the surface tension, the greater the water removal. There is also a notably higher quantity of water sucked back into the powder bed, especially with the sodium lauryl sulphate solution. Thus with the reduction in surface tension and hence contact angle, the liquid can move to a greater extent through the powder bed.

When these results are represented as pressure/% saturation graphs the significance of the presence of surfactants is clearly demonstrated, Fig. 2. When the powder is just MCC (Fig. 2a), it can be clearly observed that addition of surfactants increases the percentage of saturation (weight of liquid per weight of powder) initially possible up to 330% when sodium lauryl sulphate is used. The inclusion of glycerol, which has a surface tension approximately equal to that of water, reduces by half the level of saturation possible, both when fully wet and after subjecting to pressure. This restriction is presumably associated with the increased viscosity of the system. Fig. 2b clearly illustrates the limited saturation with barium sulphate. Again the presence of surfactants does increase the saturation possible while the presence of glycerol reduces the levels of saturation attainable.

For equal mixtures of MCC and barium sulphate the results show some differences from the individual powders (Fig. 2c). The levels of saturation are reduced from those of MCC but considerably higher than those for barium sulphate. The greatest level of saturation is achieved with a lower concentration of Pluronic PF68. Considerable reductions in saturation are achievable and



(c)

Fig. 3. (*Continued*)

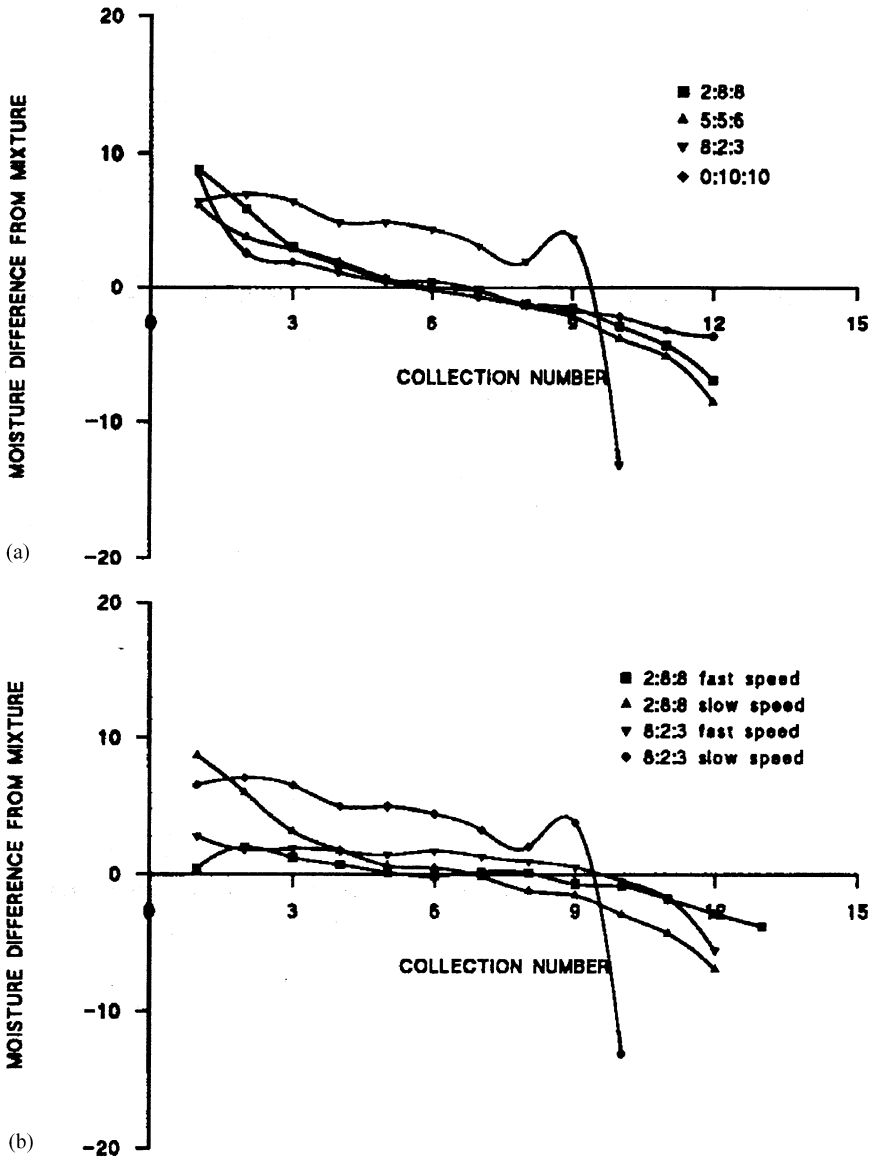
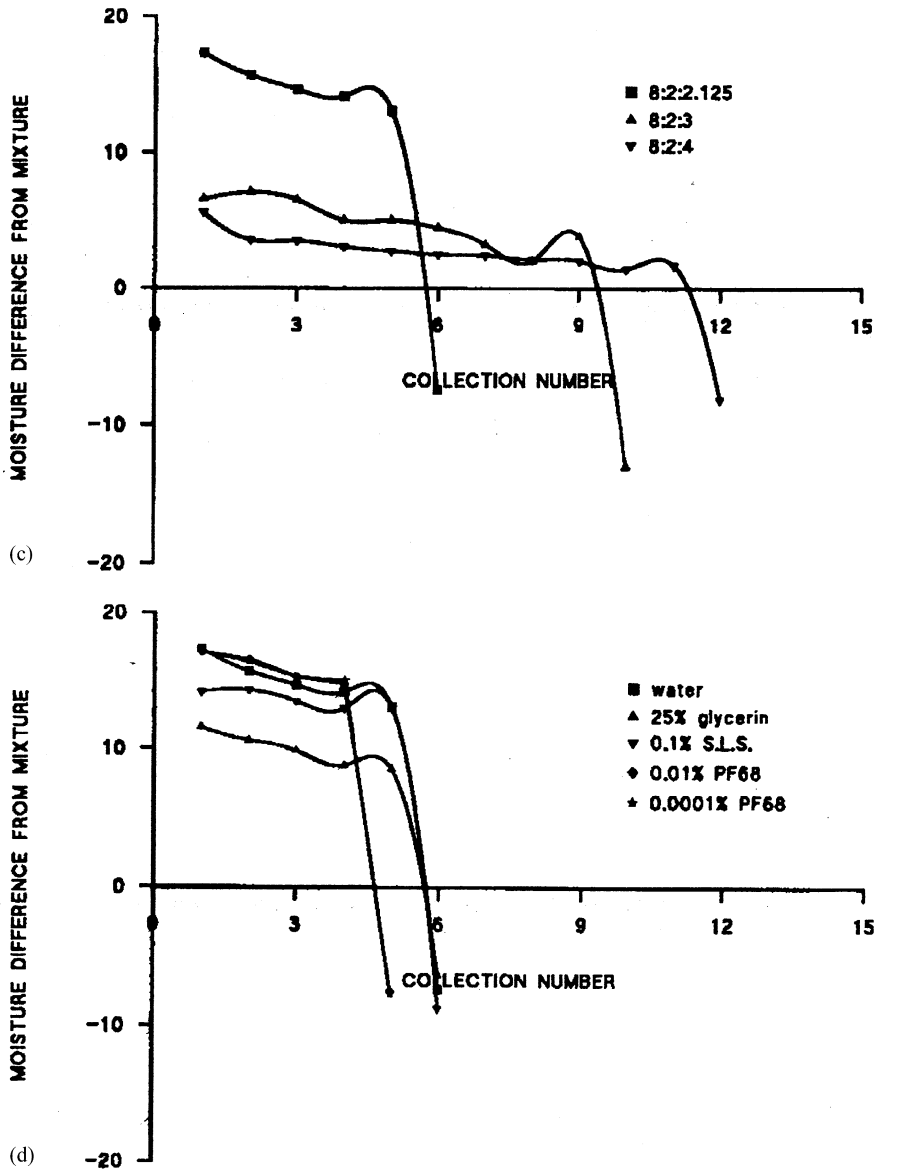


Fig. 4. The influence of various factors on the fluid content of the extrudate as a function of collection sequence relative to the fluid content of the original powder/fluid mass. (a) The influence of MCC to barium sulphate ratio at extrusion speed 20 mm/min. (b) The influence of extrusion speeds of 20 and 200 mm/min for barium sulphate, MCC and water ratios of 2:8:8 and 8:2:3. (c) The influence of water content for a barium sulphate to MCC ratio of 8:2 at an extrusion speed of 20 mm/mm. (d) The influence of liquid binder (water, 25% glycerol, 0.1% S.L.S, 0.01% and 0.0001% PF68) for a barium sulphate, MCC and liquid ratio of 8:2:2.125 at an extrusion speed of 20 mm/min. (e) The influence of liquid binder (water, 25% glycerol, 0.1% S.L.S., 0.01 and 0.0001% PF68) for a barium sulphate, MCC and liquid ratio of 8:2:3 at an extrusion speed of 20 mm/mm. (f) The influence of liquid binder (water, 25% glycerol, 0.01% S.L.S., 0.01 and 0.0001% PF68) for a barium sulphate, MCC and liquid ratio of 8:2:4 at an extrusion speed of 20 mm/mm.

liquid can be taken back to give wetted saturation above 100%. The presence of glycerol appears less distinctive than when with MCC alone.

Calculation of the results to illustrate mean hydraulic radius of the pores involved, shows that even at different levels of saturation, the pore

radii are similar (Fig. 3a, b and c). They appear to be in the range 1–5 μm. The extent of hysteresis between the wetting and the drying curves is clearly demonstrated. These results clearly show that by adding glycerol and surfactant the interaction between the liquid and the powder is changed. There is an indication that surfactant solutions could be more readily mobile, while the presence of glycerol would limit movement of liquid. The first stage of the process where this could be evident is that of extrusion. Hence this will be considered next. There are two aspects of the process that are important. Any formulation which is too dry is more prone to water mobility in the ram extruder as the system tries to push water through the powder bed to the die entrance to try to reduce the resistance to flow. This results in the initial extrudate being wetter than the orig-



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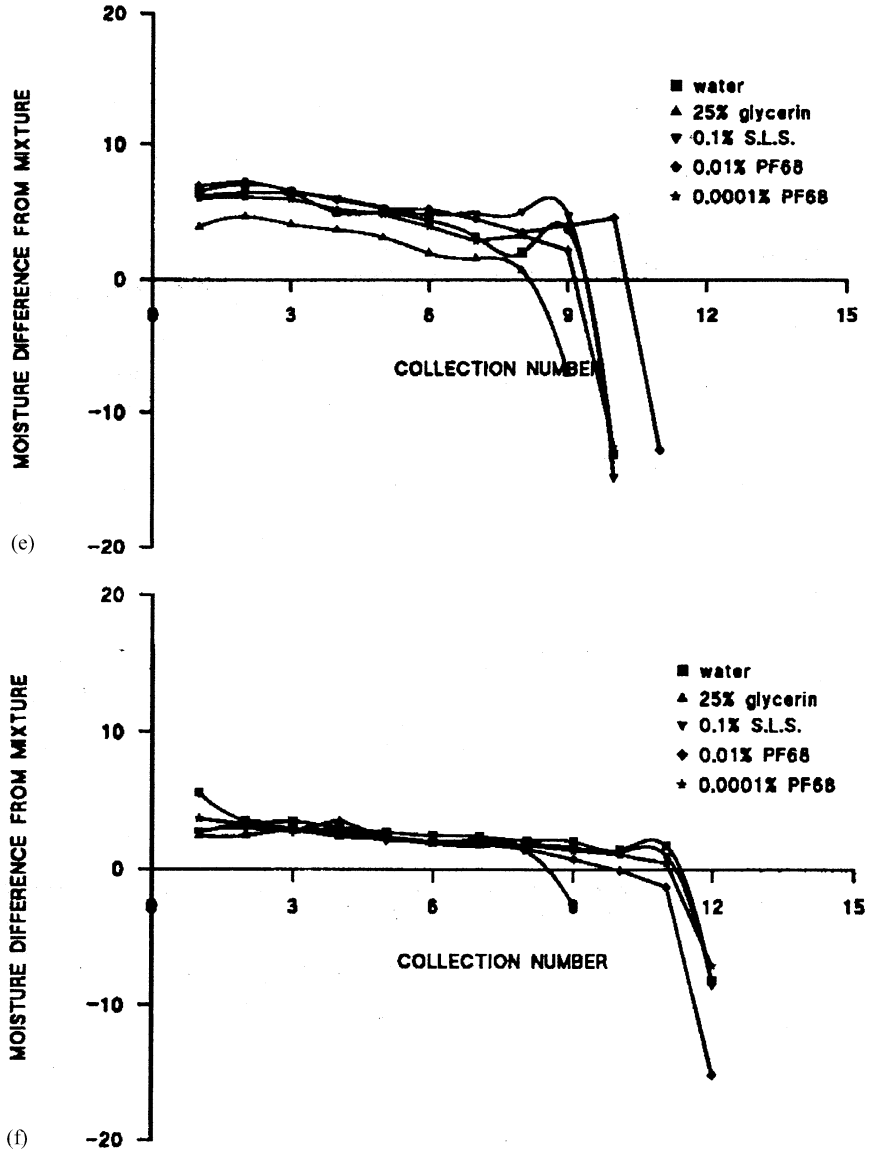

Fig. 4. (*Continued*)

inal level while the later stages will obviously be less wet, due to early loss of water. Such effects are exaggerated by extruding slowly. If for the apparently correct water content, surfactants change water mobility then an additional effect will be added to this mobility. The influence of having a range of water levels for the same solid ratio (8:2 barium sulphate/MCC) is shown in Fig. 4a. The driest formulation (0.2–17.5 parts water) shows the typical curve for a dry formulation. This is not improved by any of the surfactants Fig. 4b. For the middle water content (3.0), the addition of surfactants does tend to extend the period of constant water level slightly, while the presence of glycerol shortens this period (Fig. 4c). When the formulation becomes quite wet (Fig. 4d), there is little difference between the excess presence of liquid dominating the effect. This

technique illustrates that gross effects can be detected, but the changes in water measurement demonstrated with the press-membrane technique are not so clearly differentiated. Formulations, which are too dry are readily identified.

The influence of the water movement will also manifest itself in the extrusion forces involved. If there are gross changes in water content, as seen in Fig. 4a, then steady state extrusion forces will not be obtained; force flow will be clearly evident. To add to the results for the collection of extrudate, extrusion forces were recorded at two crosshead speeds, 20 and 200 mm/min. The four formulations were tested at each of three water levels for water, a 25% glycerol solution in water, 0.1% sodium lauryl sulphate and 0.0001 and 0.01% Pluronic PF68. The results are tabulated in Table 2. At the extrusion rate of 200 mm/min, a steady state level was always obtained for all combinations of powders and all added liquids, except for the 8:2:2.125 system, where the level of MCC is obviously important. In all cases, the formulations containing 25% glycerol show the highest extrusion force corresponding to the lowest level of water movement. The extent of the increase in the extrusion force is not always the same, indicating that it is not just the doubling of the viscosity of the binder liquid produced by the use of a 25% solution of glycerol, which influences the value of the extrusion force. Generally, the systems containing 0.1% sodium lauryl sulphate show the lowest steady state extrusion force, reflecting the apparent greater ease of movement of liquid seen in the pressure membrane measurements. Even when there is a range of forces at low extrusion speeds, the range of extrusion forces tends to be lowest for this system.

Table 2
The steady state extrusion force or force range (kN) for the extrusion of formulations containing barium sulphate (B), Avicel PH101 (A), and various liquids in ratio set out in column 1

Mixture B:A:LIQ	Speed (mm/min)	Liquid binder				
		Water	25% Glycerol	0.1% S.L.S	0.0001% PF68	0.01% PF68
0:10:8.17	200	12.81	17.74	12.34	13.79	13.79
0:10:8.17	20	3.61–16.74	6.00–19.10	1.88–14.46	1.88–16.98	1.57–17.10
0:10:10.0	200	6.44	9.03	6.44	6.36	5.73
0:10:10.0	20	1.37–8.0	3.60–8.80	0.78–7.50	1.96–8.80	1.00–6.30
0:10:12.0	200	2.75	4.41	2.75	3.18	4.24
0:10:12.0	20	2.16	2.36	1.25	1.30–4.30	0.90–6.30
2:8:6.5	200	15.56	15.99	13.99	16.15	14.93
2:8:6.5	20	1.88–19.69	4.90–19.60	4.20–17.45	1.60–19.80	2.20–19.72
2:8:8.0	200	7.58	9.74	6.87	8.09	6.32
2:8:8.0	20	1.57–9.82	2.80–12.90	1.53–9.15	2.00–8.80	1.76–7.98
2:8:10.5	200	2.24	2.65	2.24	2.67	2.35
2:8:10.5	20	1.49	1.80–3.40	0.82–2.63	1.17–3.20	1.06
5:5:4.5	200	14.46	14.30	13.20	14.54	15.48
5:5:4.5	20	2.79–20.00	5.20–17.80	2.75–19.96	2.30–20.00	2.30–19.40
5:5:6.0	200	5.73	7.74	4.87	6.60	5.20
5:5:6.0	20	1.88–7.80	4.50–9.10	1.49–2.31	1.50–8.20	1.88
5:5:8.0	200	1.21	2.39	1.21	1.92	1.84
5:5:8.0	20	0.90	1.50–2.40	0.70	0.66	0.86
8:2:2.125	200	13.08–20.00	17.71–20.00	12.70–20.00	14.20–20.00	12.40–20.00
8:2:2.125	20	5.58–20.00	4.40–20.00	5.03–20.00	2.50–20.00	6.20–20.00
8:2:3.0	200	7.54	9.82	6.99	7.07	6.72
8:2:3.0	20	1.72–20.00	2.60–20.00	1.70–20.00	2.30–20.00	1.76–20.00
8:2:4.0	200	2.71	4.20	1.84	2.04	2.47
8:2:4.0	20	0.92–9.20	2.04–10.30	0.55–7.40	0.80–11.00	0.60–7.80

S.L.S., sodium lauryl sulphate; PF68, pluronic 68.

Table 3
The influence of the ratio of barium sulphate (B), Avicel (A) and liquid (LIQ) on the median pellet size (μm) and interquartile range (μm) for different binder solutions (water, 25% glycerol, 0.1% sodium lauryl sulphate 'S.L.S.', and 0.0001 and 0.01% pluronic PF68)

Mixture B:A:LIQ	Speed (mm/min)	Liquid binder				
		Water	25% Glycerol	0.1% S.L.S.	0.0001% PF68	0.01% PF68
0:10:8.17	200	863 (326)	1155 (246)	911 (359)	1004 (354)	1097 (307)
0:10:8.17	20	1193 (247)	1155 (318)	1282 (431)	1205 (210)	1193 (222)
0:10:10.0	200	733 (258)	1155 (246)	742 (246)	927 (419)	1032 (371)
0:10:10.0	20	1226 (258)	869 (181)	1492 (484)	1234 (269)	1169 (230)
0:10:12.0	200	1613 (710)	1639 (508)	1201 (234)	1314 (464)	2060 (803)
0:10:12.0	20	1685 (701)	2115	1565 (415)	1540 (657)	2064 (803)
2:8:6.5	200	879 (334)	1139 (296)	919 (331)	1064 (338)	1084 (315)
2:8:6.5	20	1242 (286)	1164 (279)	1161 (210)	1222 (254)	1266 (371)
2:8:8.0	200	693 (250)	1290 (226)	685 (258)	980 (443)	838 (275)
2:8:8.0	20	1285 (306)	1295 (250)	1476 (496)	1298 (448)	1391 (286)
2:8:10.5	200	1855 (723)	2229 (863)	1661 (455)	1814 (653)	1688 (496)
2:8:10.5	20	2242 (839)	2278 (863)	2032 (816)	1891 (705)	1685 (460)
5:5:4.5	200	1121 (254)	1139 (269)	1129 (246)	1161 (214)	1169 (210)
5:5:4.5	20	1443 (504)	1655 (343)	1605 (355)	1512 (484)	1576 (487)
5:5:6	200	685 (258)	1123 (336)	726 (258)	1032 (364)	1130 (295)
5:5:6	20	1661 (298)	1606 (383)	1645 (298)	1649 (318)	1169 (306)
5:5:8	200	>2800	>2800	>2800	>2800	>2800
5:5:8	20	>2800	>2800	>2800	>2800	>2800
8:2:2.125	200	1629 (346)	1680 (310)	1726 (387)	1661 (318)	1673 (137)
8:2:2.125	20	2379 (407)	2155 (875)	2362 (395)	2096 (1218)	>2800
8:2:3.0	200	1193 (206)	1704 (322)	1153 (242)	1665 (306)	1655 (306)
8:2:3.0	20	>2800	2008 (544)	>2800	1673 (310)	1669 (137)
8:2:4.0	200	>2800	2133 (302)	>2800	1677 (302)	1669 (133)
8:2:4.0	20	>2800	2360 (415)	>2800	>2800	2435 (455)

Table 4
The influence of the ratio of barium sulphate (B), Avicel (A) and liquid binder (LIQ) and extrusion speed on the shape factor, E_r, and aspect ratio, AR, of pellets

Mixture B:A:LIQ	Liquid binder	Extrusion speed (mm/min)	Mean E_r	Mean AR
2:8:6.5	Water	200	0.35	1.17
2:8:8.0	Water	200	0.42	1.10
2:8:10.5	Water	200	0.52	1.08
5:5:4.5	Water	200	0.36	1.31
5:5:4.5	Water	20	0.31	1.32
5:5:6.0	Water	200	0.47	1.08
5:5:6.0	Water	20	0.55	1.06
5:5:8.0	Water	200	0.51	1.09
5:5:8.0	Water	20	0.42	1.15
8:2:2.125	Water	200	0.54	1.09
8:2:3.0	Water	200	0.57	1.06
8:2:4.0	Water	200	0.57	1.06
5:5:6.0	25% Glycerol	200	0.47	1.11
5:5:6.0	0.1% S.L.S.	200	0.53	1.07
5:5:6.0	0.0001% PF68	200	0.50	1.07
5:5:6.0	0.01% PF68	200	0.51	1.07

Those formulations showing a rising extrusion force will contain extrudate which is of different water content, hence such formulations will probably show the tendency to agglomerate, on spheronization, as some extrudate is too wet and some too dry. A wider size distribution will result as the extrudate will vary in water content and hence consistency. The results for the spheronization stage are shown in Table 3 for the median pellet diameter and Table 4 for the spread of pellet size, represented by the interquartile range. In general for all formulations, as the water content increases, the median pellet size increases, as does the value for the interquartile range. For some formulations, e.g. formulation (5:5:8) the mixtures were all too wet and gross agglomeration occurred in all cases. 'Dry' formulations tended to give larger pellet sizes when surfactants and glycerol were present, if the extrudate was formed at the higher rate of ram movement. 'Wet' formulations tended to produce smaller pellets when surfactants were present and the extrudate had been produced at the faster rate, but all formulations tended to be larger than 'good' formulations. 'Good' formulations are still good when glycerol and surfactants are present, but there is a tendency to produce larger size pellets when surfactants or glycerol are present. The range of sizes is not, however, grossly extended.

When making pellets by extrusion/spheronization, size and size range alone should not be the only criteria of quality. The roundness of the pellets should be considered. Only those processes, which produce round pellets should be accepted, as irregular shapes tend to indicate a process, which is out of control. Confirmation that the pellets are spherical is provided by a measure of the roundness by the shape factor E_r

Table 5
The influence of the ratio of barium sulphate (B), Avicel (A) and liquid (LIQ) on the porosity of pellets for different binder solutions (water, 25% glycerol, sodium lauryl sulphate (S.L.S.) and 0.0001 and 0.01% pluronic PF68)

Mixture B:A:LIQ	Speed (mm/min)	Liquid binder				
		Water	25% Glycerol	0.1% S.L.S.	0.0001% PF68	0.01% PF68
0:10:8.17	200	0.01	0.02	0.03	0.00	0.00
0:10:8.17	20	0.08	0.03	0.12	0.06	0.06
0:10:10.0	200	0.03	0.08	0.09	0.04	0.04
0:10:10.0	20	0.03	0.08	0.20	0.03	0.03
0:12:12.0	200	0.05	0.06	0.09	0.03	0.05
0:12:12.0	20	0.05	0.07	0.09	0.02	0.05
2:8:6.5	200	0.20	0.20	0.18	0.16	0.17
2:8:6.5	20	0.21	0.23	0.26	0.21	0.21
2:8:8.0	200	0.21	0.21	0.24	0.20	0.21
2:8:8.0	20	0.21	0.25	0.23	0.20	0.20
2:8:10.5	200	0.21	0.24	0.24	0.19	0.20
2:8:10.5	20	0.21	0.24	0.24	0.19	0.19
5:5:4.5	200	0.25	0.29	0.24	0.25	0.25
5:5:4.5	20	0.26	0.31	0.25	0.26	0.26
5:5:6.0	200	0.24	0.32	0.24	0.25	0.24
5:5:6.0	20	0.25	0.32	0.24	0.25	0.24
5:5:8.0	200	0.28	0.34	0.24	0.27	0.25
5:5:8.0	20	0.28	0.33	0.23	0.27	0.26
8:2:2.125	200	0.17	0.23	0.16	0.16	0.15
8:2:2.125	20	0.16	0.25	0.16	0.17	0.14
8:2:3.0	200	0.18	0.25	0.16	0.15	0.15
8:2:3.0	20	0.17	0.24	0.16	0.15	0.15
8:2:4.0	200	0.16	0.25	0.16	0.16	0.14
8:2:4.0	20	0.16	0.26	0.17	0.16	0.15

reported by Podczeck and Newton (1994) and aspect ratio, of a range of pellets produced from different formulations, with different binders and extruded at different rates, Table 5. 'Dry' formulations prepared with water show values of E_r generally less than 0.4 and aspect ratios greater than 1.10, indicating poor spheres. Good formulations prepared with water show values of E_r above 0.5 indicating relatively good spherical pellets. The addition of glycerol or surfactants does not change these values greatly, hence they do not detract from the formation of good spheres.

A further factor, which might be influenced by the presence of surfactants is the packing of the particles within the pellets as a result of different liquid/solid interactions. Hence the porosity of the pellets was calculated from their apparent pellet density and the apparent particle density of its component mixtures. The results in Table 5 do in fact show some general tendencies. The use of Pluronic solutions tends to give pellets which are less porous than those produced with water. Pellets produced with glycerol are generally less porous. The sodium lauryl sulphate, which had the greatest effect on water movement, appears to have less influence on porosity, which is somewhat surprising. Pellets, which do not contain barium sulphate have the lowest porosities, while those containing equal parts of barium sulphate and MCC the highest. This tends to indicate these were the systems, which had the strongest tendency to agglomerate. Hence the pellets were probably formed by a different mechanism than those of the smaller pellet. Agglomeration could result in pellets formed from smaller pellets, which would be incapable of packing to high density and hence low porosity.

Acknowledgements

J.S.B. expresses her thanks for the grant from the EPSRC and the authors thank FMC Corporation for the gift of microcrystalline cellulose.

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