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Research paper

Application of mercury porosimetry in evaluation of extrusion-spheronisation process

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Abstract

In this study we evaluated the applicability of mercury porosimetry on the properties of extrudates and pellets. We investigated the effect of thickness of the screen, speed of the agitator and spheronisation time as well as the effect of re-extrusion. The extruder variables had no systematic effect on the porosity parameters of the pellets. Spheronisation was such a drastic process that it eliminated differences in the porosity parameters of extrudates. With increasing spheronisation time, the total pore volume and mean pore diameter of the pellets decreased significantly. Due to the loose structure of the extrudates, the centrifugal force caused the wet mass to migrate towards the surface. This contributed to the formation of a cavity inside the pellets which became larger with increasing spheronisation time. Due to re-extrusion, the volume of the large pores decreased and that of the small pores increased. Although all the porosity parameters studied were useful in characterising the pore structure of pellets, the most sensitive parameter was the pore-volume size distribution. The use of microscopy in the interpretation of mercury porosimetry results is recommended. © 1997 Elsevier Science B.V.

Keywords: Mercury porosimetry; Extrusion; Spheronization; Porosity; Extrudate; Pellet

1. Introduction

Extrusion-spheronisation is a multistage, and therefore a multivariate process for production of pellets. Extrusion is an important densifying stage. The extrusion process has not been investigated as intensively on a production scale as the final stage of the pelletisation, spheronisation. The theory of extrusion, however, has been thoroughly studied by Fielden and Newton [1] and by Harrison et al. [2]. Extrusion with an instrumented laboratory scale ram extruder was investigated by Harrison et al. [3,4].

Rowe [5] classified extruders into two groups according to the type of the feeder mechanism: screw extruders and gravity-feed extruders. With screw extruders, the screen can be arranged either cylindrically around the screw or in the form of a plate at the end of the screw. The arrangement of radial screen extruder has the advantages of high throughput, low heat generation and avoidance of water gradient formation. Due to the construction of this type of extruder, the extrudates produced are less dense than those produced with axial screw extruders. Brittle extrudates may cause problems during the spheronisation stage: extrudates may be smashed and in addition the particle size distribution of pellets becomes wide [6]. The deformation of extrudates during spheronisation is first of all dependent on the mechanical properties of the wet mass [1] assumingly related to the degree of porosity [7]. One common

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method for changing the density of extrudates is to vary the thickness of the extruder screen [8]. Another possible method is re-extrusion, which has not been thoroughly investigated previously.

The influence of the various process variables on the main characteristics of pellets have been widely investigated; pelletisation can be optimised to produce pellets that have a narrow size distribution, spherical shape, sufficient density and low friability. Less attention has been paid to detailed evaluation of the microstructure of dried pellets and extrudates. The amount and quality of the granulation liquid [9], the binder concentration [10,11], and both the quality and amount of filler or active drug [12] have been found to affect the porosity of pellets. The microstructure of pellets can be influenced during the manufacturing process by changing the pressure used in extrusion or due to the effect of mechanical forces during spheronisation. In addition, the method used to dry wet pellets and possible shrinkage during the drying stage might markedly affect the final structure of pellets [13–15].

One method for determination of the porosity parameters and pore size distributions of solid dry samples is mercury porosimetry. With this method, information about pores 7 nm–220 μm in diameter can be obtained. High pressure porosimetry has been used to study the porosity of pellets. With porosimetry it is possible to investigate the drug-release mechanisms—pore size, in particular, affects the rate of drug release from pellets [12,16]. Another possible method for the characterisation of the microstructure of pellets is a spin echo Nuclear Magnetic Resonance (NMR) technique [17]. The advantage of mercury porosimetry is the wide measuring range of the pore diameter. The applicability of mercury porosimetry in characterisation of extrudates has not been investigated previously.

In this study, we evaluated the applicability of mercury porosimetry in determining the effect of the extrusion-spheronisation process on the properties of pellets. The aim was to investigate the effect of screen thickness and agitator speed on the microstructure of extrudates and pellets and the effect of spheronisation time on the microstructure of pellets. Furthermore, we also studied how additional application of pressure in the form of re-extrusion affected the porosity parameters of extrudates and pellets.

2. Materials and methods

2.1. Materials

The pellets used contained 40% propranolol hydrochloride (Knoll AG, Minden, Germany) and 60% microcrystalline cellulose (Avicel PH 102, FMC, Wallingstown, Ireland). Distilled water was used as the granulation liquid; on the basis of dry weight, the amount of water was 67%, i.e. 40% of the wetted mass.

2.2. Preparation of extrudates and pellets

Extrudates were prepared using a Nica system consisting of a continuously working granulator (Nica M6L, Nica System AB, Mölndal, Sweden), a radial screen extruder (Nica E140) and a spheroniser (Nica S320).

The premixed powders were moistened in the granulator. During wet mixing the set-ups were kept constant. The speed of the powder feeder was 35 rpm, corresponding to 1360 g/min, and the speed of the liquid pump was 152 rpm, corresponding to 910 g/min. The size of the granule outlet was 15 mm measured from the lower side of the outlet. The moisture content of freshly wet granules, determined by an infra-red dryer (Sartorius Thermo Control YTC 01 L, Sartorius, Göttingen, Germany) varied between 40 and 42%.

The moist mass was extruded immediately after wet mixing. The functioning of the Nica extruder is based on the feeder and the agitator, which rotate in opposite directions pressing the material through the vertical screen. The variable levels were chosen with the pretests and the process was optimised to produce pellets that were similar enough in size (0.71–1.00 mm in diameter) and in sphericity. The process variables studied were speed of the agitator (25, 75 and 125 rpm), thickness of the screen (1.00, 1.25 and 1.50 mm) in the extruder, and spheronisation time (1, 4 and 7 min).

In all the above-mentioned screens, the diameters of the dies were 1.00 mm. The number of dies was 30 cm^{-2}, and the perforated area made up 24% of the total screen area. The speed of the feeder was kept constant at 50 rpm. The moisture content of the extrudates immediately after processing was 40–41% regardless of process variables. The load in the spheroniser was 300 g and the speed of the friction plate was 700 rpm (12 ms^{-1} at the periphery of the plate).

In the re-extrusion study, the wet granules were extruded and the fresh extrudate was immediately re-extruded prior to spheronisation. Three different screens (1.00, 1.25 and 1.50 mm) were used. Both the speed of the agitator (75 rpm) and the spheronisation time (4 min) were kept constant. Otherwise, the process was similar to that mentioned above.

For mercury porosimetry analysis, the extrudates and the pellets were dried on trays at room temperature in ambient humidity for at least 48 h. An approximation was made, that drying has only a negligible effect on the differences between extrudate samples, which allows comparison of samples.

Table 1
Porosity parameters of extrudates measured by low-pressure porosimetry corresponding to pore diameter range of 14–220 μm ($n = 3$, standard deviation in brackets)

Screen size (mm)	Speed of agitator (rpm)	Total pore volume (ml g^{-1})	Mean pore diameter (μm)
1.00	25	0.147 (0.039)	39 (3)
1.00	75	0.177 (0.018)	32 (3)
1.00	125	0.118 (0.044)	31 (5)
1.25	25	0.064 (0.009)	28 (4)
1.25	75	0.088 (0.046)	29 (4)
1.25	125	0.072 (0.010)	29 (3)
1.50	25	0.109 (0.018)	35 (1)
1.50	75	0.058 (0.012)	30 (4)
1.50	125	0.104 (0.021)	33 (2)

2.3. Porosity

For low-pressure porosimetry, a filling apparatus (Quantachrome Corp., Syosset, NY) was used. The pressure range used was 6–97 kPa, which corresponded to pore diameters in the range 14–220 μm. The pressure range of the high-pressure porosimeter (Autoscan 33, Quantachrome Corp., Syosset, NY) was 0.1–227 MPa and corresponded to pore diameters in the range 6.5 nm–14 μm. The contact angle of mercury (Θ) was approximated to be 140°, and according to the supplier of the equipment, the surface tension (γ) was 480 mN/m (Quantachrome Corp., Syosset, NY). The volume of the sample cell was 3.5 cm^3 and the volume of the capillary stem 0.5 cm^3. The amount of sample was 0.3 g for the extrudates and 0.6 g for the pellets, and the scanning speeds were 270 Pa/s for the low-pressure method and 250 kPa/s for the high-pressure method. Measurements were made in triplicate. Total intruded volume of mercury, i.e. total pore volume (V_{tot}), total pore surface area (S), mean pore diameter, and $D_v(d)$ volume pore-size distribution function were calculated from the intrusion data with Quantachrome Autoscan PORO2PC Software, Version 2.17. Distribution $D_v(d)$ is defined as the pore volume per unit interval of pore diameter (d): dV/dd. The total surface area of pores is calculated by Eq. (1), assuming that pores are cylindrical and open at both ends:

$$S = \frac{1}{\gamma|\cos\theta|}\int_0^{V_{tot}} p\,dV \quad (1)$$

where p is the pressure and V is the volume of intruded mercury.

The mean pore diameter (d_{mean}) was calculated according to Eq. (2):

$$d_{mean} = 4\cdot\frac{V_{tot}}{S} \quad (2)$$

For a better understanding of the porosity parameters, both the outer surface of extrudates and pellets and the surface of cross section were examined with scanning electron microscopy (Jeol JSM-840A, Jeol, Tokyo, Japan). Intrusion of mercury into the pellet core was confirmed by optical microscopy (Olympus Stereo Zoom Microscopy, SZH-ILLK, Tokyo, Japan). The two-way analysis of variance (ANOVA) together with Fisher's Protected Least Significant Difference (PLSD) as a post-hoc test including interactions [18] were determined for porosity parameters using the Statview statistical program for Macintosh (Version 4.0, Abacus Concepts Inc., Berkeley, CA).

3. Results and discussion

3.1. Extrudates

3.1.1. Effect of screen thickness and agitator speed

The total pore volume in the pore diameter range 14–220 μm was largest when a screen of 1.00 mm in thickness was used (Table 1). The total pore volumes of extrudates processed with a 1.00 mm screen differed significantly from those processed with 1.25 mm and 1.50 mm screens ($P < 0.001$). According to ANOVA, the total pore volume of the extrudates produced using 1.25 and 1.50 mm screens did not differ significantly. With longer contact time caused by increasing length of die, the surface of the extrudates became smoother and more dense (Fig. 1a–c). However, when the die length increased from 1.25 to 1.50 mm, the effect was no longer detectable. As seen in Fig. 1a–c, screen thickness affected the pores larger than 14 μm in diameter, which explained why the differences were seen with low-pressure porosimetry. As found in a previous study, the screen thickness also clearly affected the surface of the mannitol-based extrudates [19]. Sharkskinning was found to occur in extrudates prepared with a 1.00 mm screen. In this study also, sharkskinning was the reason for the high total pore volume of the extrudates. With thicker screens (1.25 and 1.50 mm), the surface of extrudates became more dense, all of them becoming equally smooth. The behaviour of the formulation used

in this study and of that used previously [19] are clearly similar.

The changes in pore surface area and in mean pore diameter with increasing screen size correlated with the changes in total pore volume (Table 1). However, the differences in the mean pore diameters of extrudates

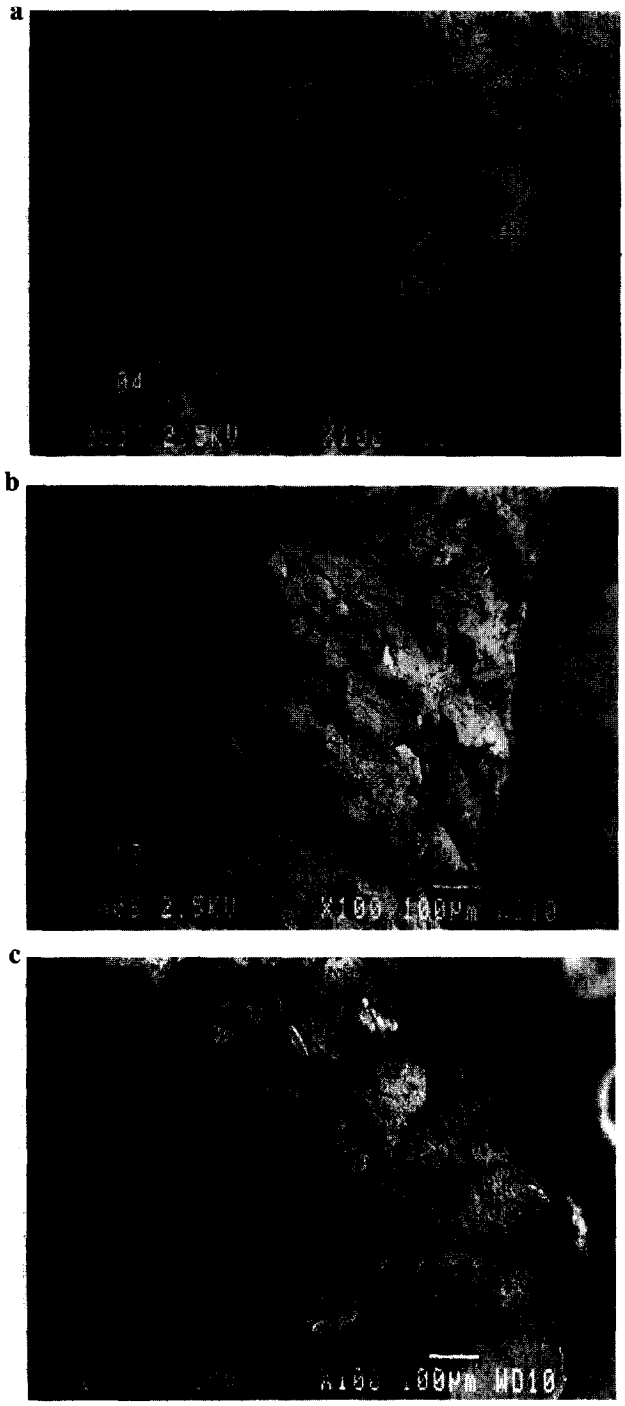

Fig. 1. Scanning electron micrographs of extrudates produced with different screens: die length (a) 1.00 mm (b) 1.25 mm and (c) 1.50 mm. The speed of the agitator was 75 rpm. The bars represent 100 μm.

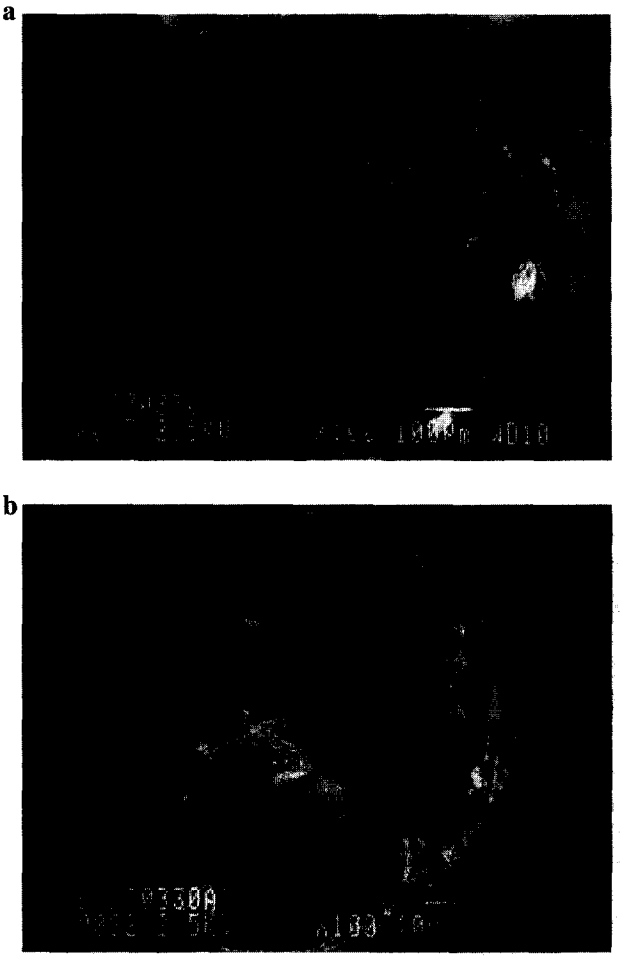

Fig. 2. Scanning electron micrographs of the cross-section of extrudates produced using the screen 1.00 mm in thickness and an agitator speed of 75 rpm: (a) extruded once and (b) extruded twice. The bars represent 100 μm.

produced with different screen thicknesses were not statistically significant. The large variation of results was caused by the inhomogeneous length of dried extrudates.

In a previous study, an increase in the speed of agitator increased the total pore volume of mannitol-based pellets [20]. Thus, it could be expected that in the present study the response to extrudates would be similar. However, for this formulation, speed of the agitator had no clear influence on the total pore volume of extrudates measured in the low-pressure range.

The process variables in the range studied had no effect on the porosity parameters measured in the high-pressure range. This was due to the gentleness of this extrusion process. In the Nica extruder, the mass is under much less pressure than, e.g. in axial screw extruders. Thus, the densification of mass in this system, and at least with this formulation, does not contribute to changes in the structure of pores 6.5 nm–14 μm in diameter.

3.1.2. Effect of re-extrusion

Only with a screen thickness of 1.00 mm did re-extrusion decrease the total pore volume measured in the low-pressure range (from 0.137 to 0.067 mlg^{-1}). As observed in Fig. 1, the surface of 1.00 mm extrudates was clearly the roughest showing deep holes which were measurable in the low-pressure range. The structure of these extrudates was obviously loose enough to densify further during re-extrusion, which diminished the volume of pores that were 14–220 μm in diameter (Fig. 2).

With all the screens used, re-extrusion clearly diminished the total pore volume measured in high-pressure range (Table 2). With increasing die length, the decrease in the total volume of pores in re-extrusion increased from 14 to 20%. Re-extrusion with the longest die was the most effective. Total pore volume of the extrudates processed with a screen thickness of 1.00 mm was clearly larger than that of extrudates processed with longer dies (Table 2, $P < 0.002$ according to Fisher's PLSD).

Mean pore diameter decreased with re-extrusion (Table 2). Also in the case of this parameter the change was most drastic with the 1.00 mm screen extrudates. After the first extrusion, the structure of these extrudates was least dense. Therefore, re-extrusion was able to densify the structure of these extrudates the most.

3.2. Pellets

3.2.1. Effect of screen thickness, agitator speed and spheronisation time

As seen in the scanning electron micrographs, the surface of the pellets was smooth, except for some propranolol hydrochloride crystals (Fig. 3a and b). No pores larger than 14 μm were detected. Thus, in the case of these pellets, at the low-pressure range used for determining pores larger than 14 μm, porosimeter analysis was unnecessary, unlike in the case of the extrudates. Use of high-pressure porosimetry in characterisation of the microstructure of pellets is therefore appropriate.

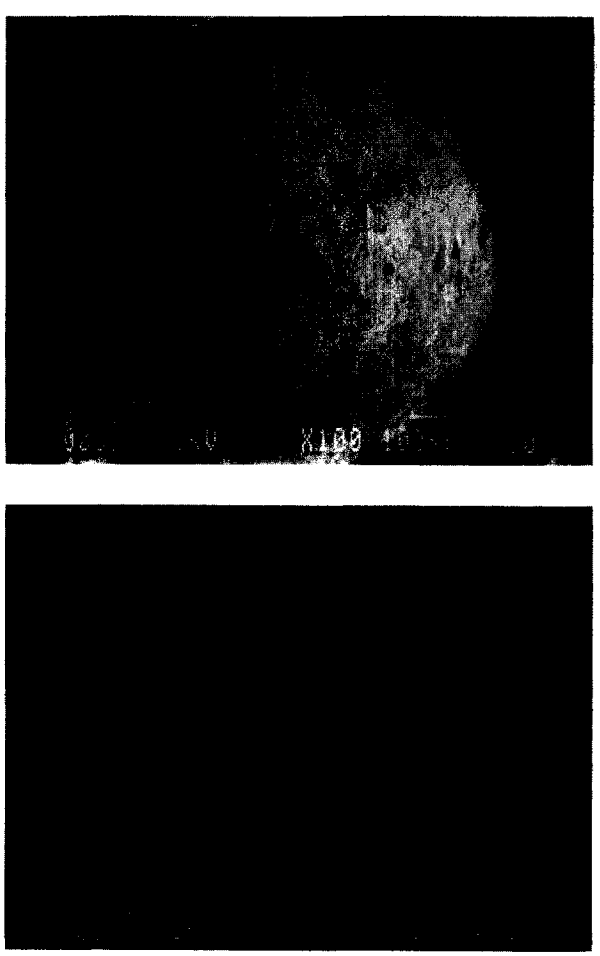

Fig. 3. Scanning electron micrograph of the surface of a pellet (screen thickness 1.00 mm, speed of agitator 125 rpm and spheronisation time 7 min). The bars represents (a) 100 μm and (b) 10 μm.

When the spheronisation time increased from 1 to 7 min, in the case of pellets prepared from the extrudate produced with the shortest die, the total pore volume of pellets decreased approximately 30%. When the longest die was used, the decrease was about 20% (Table 3, $P < 0.0001$). The greatest difference in the pore volume of pellets was found between spheronisation times of 1 and 4 min. With increasing spheronisation time, large pores disappeared, decreased in size or formed smaller pores; all of this contributed to the increase in the number of very small pores. This was also detected by an increased total surface area of the pores in pellets and by a marked decrease in mean pore diameter (Table 3, $P < 0.001$). The changes in the pore structure were also seen in the pore-volume size distributions: Firstly, due to the stage of spheronisation, the large

Table 2
Porosity parameters of once and twice processed extrudates measured by high-pressure porosimetry, corresponding to pore diameter range of 6.5 nm–14 μm

Screen size (mm)	Total pore volume (ml g^{-1})	Mean pore diameter (nm)
1.00 once extruded	0.349 (0.006)	158 (4)
1.00 twice extruded	0.300 (0.012)	114 (14)
1.25 once extruded	0.323 (0.004)	159 (33)
1.25 twice extruded	0.264 (0.009)	129 (27)
1.50 once extruded	0.336 (0.011)	131 (12)
1.50 twice extruded	0.269 (0.006)	121 (6)

The speed of agitator was 75 rpm ($n = 3$, standard deviation in brackets).

Table 3
Effect of screen thickness (S), speed of agitator (A) and spheronisation time (T) on the porosity parameters of pellets ($n = 3$, standard deviation in brackets, *replicate batch)

S (mm)	A (rpm)	T (min)	Total pore volume (TPV) (ml g^{-1})	Total pore surface area (m^2 g^{-1})	Mean pore diameter (nm)
1.00	25	1	0.168 (0.006)	8.6 (0.3)	78 (4)
1.00	25	4	0.130 (0.004)	7.6 (0.7)	69 (4)
1.00	25	7	0.123 (0.002)	10.2 (0.4)	48 (1)
1.00	75	1	0.169 (0.004)	7.6 (1.2)	91 (12)
1.00	75	4	0.139 (0.003)	8.2 (0.5)	67 (6)
1.00	75	7	0.123 (0.002)	8.8 (0.3)	56 (2)
1.00	125	1	0.182 (0.009)	8.5 (0.5)	86 (2)
1.00	125	4	0.126 (0.009)	9.1 (1.3)	55 (4)
1.00	125	7	0.129 (0.007)	10.5 (0.6)	49 (1)
1.25	25	1	0.158 (0.003)	8.9 (0.9)	71 (6)
1.25	25	4	0.143 (0.002)	8.9 (0.4)	65 (3)
1.25	25	7	0.127 (0.004)	10.1 (0.8)	50 (5)
1.25	75	1	0.148 (0.001)	7.3 (1.3)	83 (17)
1.25	75	4	0.138 (0.008)	9.2 (0.7)	61 (5)
		*	0.136 (0.004)	9.8 (0.7)	56 (3)
1.25	75	7	0.138 (0.003)	9.1 (0.7)	61 (5)
1.25	125	1	0.158 (0.016)	8.3 (0.1)	76 (7)
1.25	125	4	0.127 (0.004)	10.0 (1.2)	51 (7)
1.25	125	7	0.125 (0.003)	11.3 (0.4)	44 (1)
1.50	25	1	0.163 (0.001)	7.6 (0.4)	86 (5)
1.50	25	4	0.136 (0.001)	10.1 (0.4)	54 (2)
1.50	25	7	0.121 (0.002)	11.1 (1.1)	44 (5)
1.50	75	1	0.153 (0.003)	8.2 (0.5)	75 (4)
1.50	75	4	0.130 (0.004)	9.8 (0.2)	53 (2)
1.50	75	7	0.125 (0.005)	11.0 (0.4)	54 (3)
1.50	125	1	0.161 (0.006)	8.0 (0.4)	81 (6)
1.50	125	4	0.135 (0.006)	10.1 (1.7)	55 (11)
1.50	125	7	0.128 (0.004)	10.7 (0.2)	48 (1)

pores (> 1 μm) of the extrudates disappeared, and the volume of pores with a diameter of 200–1000 nm increased (Fig. 4). Secondly, with increasing spheronisation time, the volume of pores with a diameter of 200–1000 nm was reduced, which also showed up as an decrease in total pore volume (Table 3). The increase in spheronisation time and also in the speed of the friction plate was previously found to result in changes in density and in the porosity of pellets made of lactose and microcrystalline cellulose [13,14].

When the spheronisation time was shortest (1 min), the cross-section of the pellet was loose (Fig. 5a). With longer spheronisation time, a cavity was formed and the exterior solid part of the pellet was relatively dense (Fig. 5b). A cavity was formed in all pellet batches that were spheronised for 4 or 7 min. With increasing spheronisation time, the hole inside the pellet became larger and simultaneously the outer part of the pellet became denser. The use of a radial screen extruder and thin screens may partly cause this formation of a cavity. These extruders exert only a slight gentle pressure on the wet mass and produce either rough or shark-skinned highly porous extrudate [1,6]. During the following stage in the process, spheronisation, the centrifugal forces cause migration of water and movement of the wet mass towards the pellet surface [21]. In the case of porous extrudate, this contributes to the creation of a cavity inside the pellet. Another mechanism for the formation of a cavity has been presented by Baert et al. [22]. In their case, the cavity was formed through rope folding and twisting of extrudate, dumb-bell formation and rupture of the dumb-bells. After this rupture, the outlet of a cavity could be seen clearly, but with increasing spheronisation time, the cavity was closed. In our study, no such outlet was observed.

Intrusion of mercury into the cavity was confirmed with optical microscopy. On the basis of Fig. 6a, it can be stated that even at a pressure of 25 MPa (pore diameter approx. 60 nm), mercury intruded into the core of the pellet, even though the outer part of the pellet appeared to be free of mercury. When the pressure was increased to 227 MPa, both the cavity and the small pores of the exterior part were filled with mercury (Fig. 6b). Thus, the total pore volume measured also included the volume of the cavity and therefore described the total volume of the empty space in the entire pellet, not only in the exterior layer.

Agitator speed and screen thickness did not systematically affect the total pore volume, total pore surface area, mean pore diameter or pore-volume size distribu-

tions of the pellets (Table 3). Spheronisation was such a drastic process that it eliminated the observed differences in the microstructure of the extrudates (Table 1). Due to the loose and easily deformable construction of the extrudates, spheronisation for even as short as 1 min neutralised the differences in their pore structures.

3.2.2. *Effect of re-extrusion*

The effect of re-extrusion on the pore characteristics of pellets has not been investigated previously. In this study, the total pore volume of pellets prepared from the twice-processed extrudates was clearly smaller than that in pellets prepared from the single-processed extrudates (Table 4). No effect was observed on total pore surface area or on mean pore diameter. However, pore-volume size distribution, a more sensitive parameter, revealed that re-extrusion affected the pore structure of the pellets (Fig. 7). For pellets prepared from the single-processed extrudates, the volume of pores larger than 400 nm in diameter was higher than for pellets prepared from the twice-processed extrudates. Thus, due to re-extrusion, the volume of the above-mentioned pores decreased and the volume of the smaller pores (< 400 nm) increased. This indicated greater densification of the pellet surface.

The thickness of the extruder screen affected the pore-volume size distribution of pellets prepared from the twice-processed extrudates (Fig. 8). For pores with a diameter larger than 1 μm, the pore volume of pellets prepared from the extrudates produced with the thinnest screen was smallest. On the other hand, the pore volume of those pores with diameter smaller than 1 μm was greatest. Obviously, with the thinnest screen,

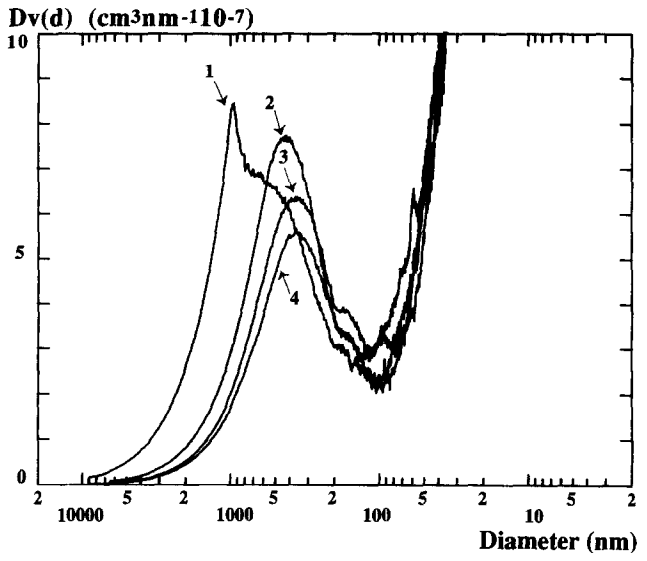

Fig. 4. Pore-volume size distributions ($D_v(d)$) of extrudate (1) prepared with a 1.00 mm screen and at the agitator speed of 75 rpm and pellets spheronised from that extrudate for 1 min (2), 4 min (3) and 7 min (4).

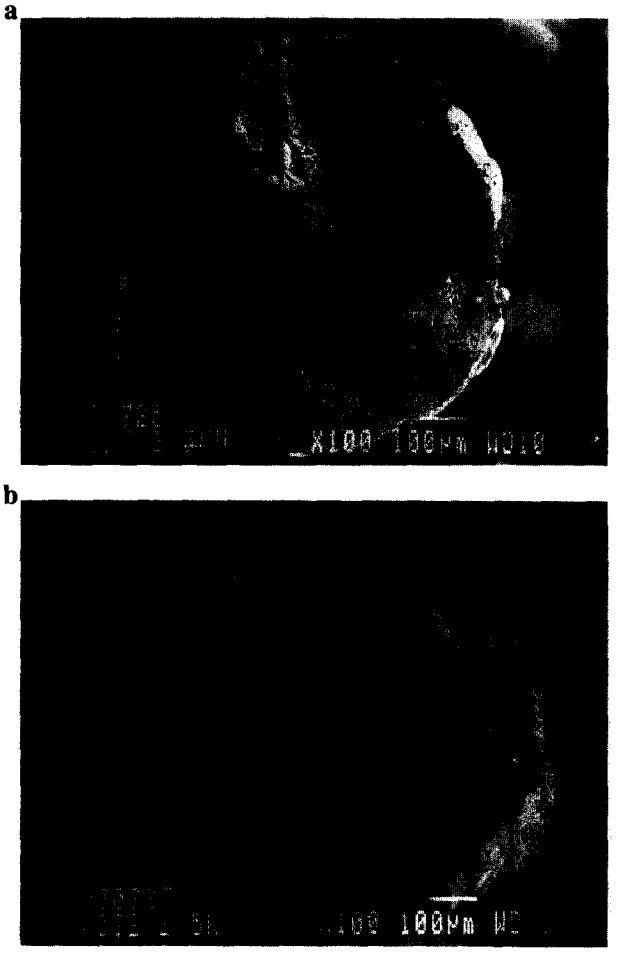

Fig. 5. Scanning electron micrograph of the cross-section of a pellet prepared with the thickest screen, 1.50 mm, and with a spheronisation time of (a) 1 min and (b) 7 min (speed of agitator 125 rpm).

the extrudate was least dense and was more readily deformable into a pellet which had the smallest number of large pores and the largest number of small pores. Re-extrusion through the thickest screen lead to a less deformable extrudate and to a pellet with a larger volume of large pores and smaller number of small pores.

4. Conclusions

With mercury porosimetry, it was possible to detect differences between extrudates produced with different screens and number of extrusions. According to the results of this study, in the case of gentle extrusion such as the Nica process, low-pressure porosimetry appeared to be a suitable method for evaluating the effect of extruder variables. According to the re-extrusion study, re-extrusion might be preferable in radial screen extrusion, when the extrudates are too brittle and therefore causing problems during spheronisation. Using re-extrusion with the radial screen extruder, denser extru-

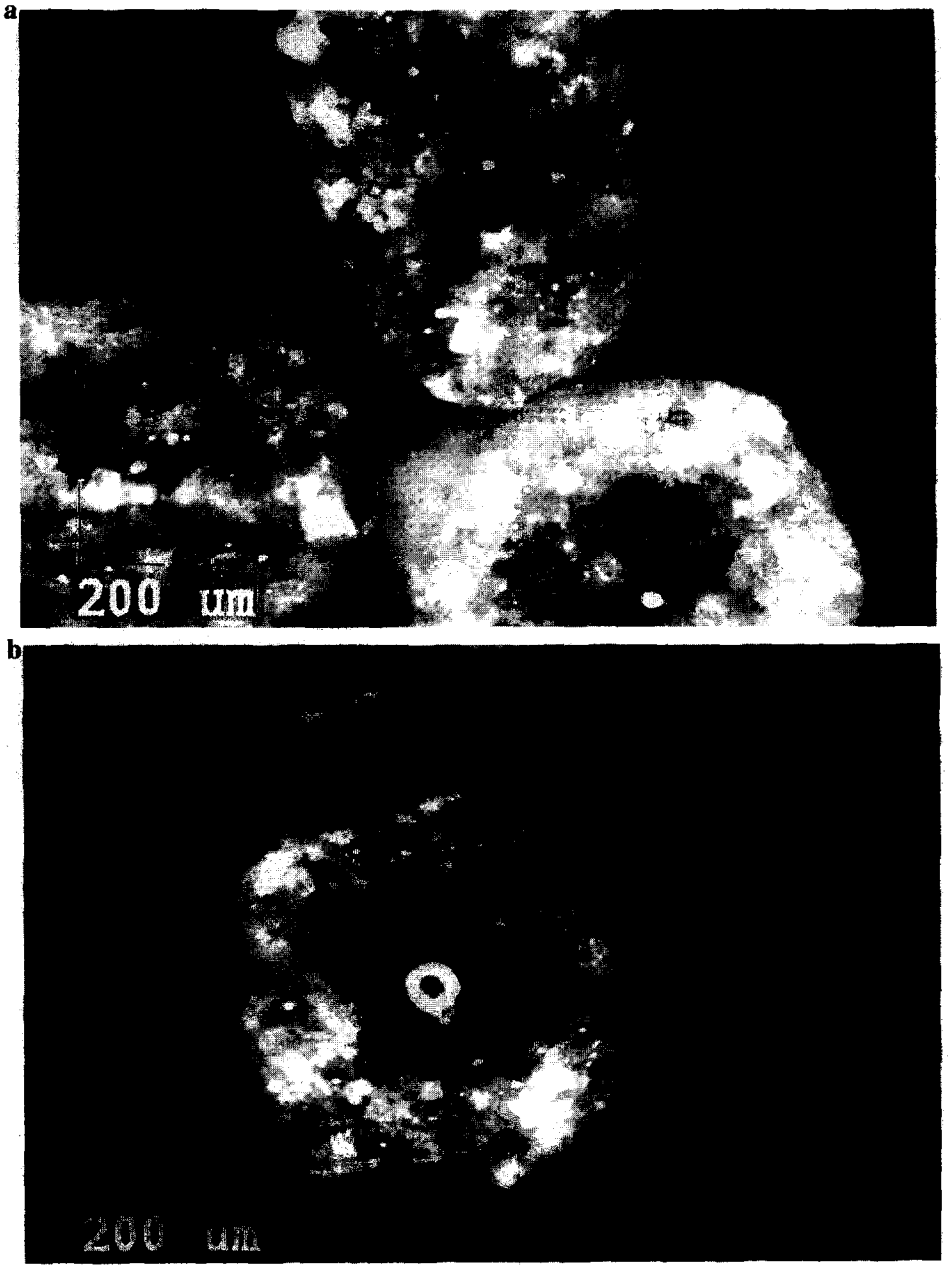

Fig. 6. Cross-section of pellets (optical microscopy) which have been in porosimetry analysis up to (a) 25 MPa and (b) 227 MPa (thickness of screen 1.00 mm, speed of agitator 125 rpm, spheronisation time 7 min). Bars represent 200 μm.

dates can be produced but heat increase and the resulting moisture evaporation can still be avoided. With all screens, re-extrusion decreased the total pore volume of extrudates measured in the high-pressure range (7 nm–14 μm). Contrary to the situation when extruder variables were studied, the differences in porosity parameters after re-extrusion were observed more clearly with high-pressure porosimetry. This was due to further compaction of extrudates, which resulted in smaller pores.

The variables of the radial screen extruder and the properties of the extrudate did not significantly affect the porosity parameters of the pellets. With this formulation, differences in the porosity parameters of extrudates were eliminated by spheronisation. Increasing the spheronisation time, the pore structure on the surface of pellets was changed. Collisions and frictional forces contributed to the disappearance of large pores and the formation of small pores on the pellet surface. With increasing spheronisation time, due to centrifugal forces, the water and wet mass migrated to the outer surface of the pellets, forming a cavity inside.

Re-extrusion facilitated the formation of slightly denser pellets. However, after 4 min spheronisation, this effect was no longer found. With single-processed extrudates and with the longest spheronisation time, the total pore volumes of the pellets were the same.

Table 4
Effect of screen thickness on the porosity parameters of pellets prepared from twice-processed extrudates ($n = 3$, standard deviation in brackets)

Screen thickness (mm)	Number of extrusions	Total pore volume (TPV) (ml g^{-1})	Total pore surface area (m^2 g^{-1})	Mean pore diameter (nm)
1.00	1	0.139 (0.003)	8.2 (0.5)	67 (6)
1.00	2	0.123 (0.003)	9.4 (0.9)	52 (5)
1.25	1	0.138 (0.008)	9.2 (0.7)	61 (5)
1.25	2	0.128 (0.005)	9.4 (0.8)	55 (5)
1.50	1	0.130 (0.004)	9.8 (0.2)	53 (2)
1.50	2	0.119 (0.009)	9.6 (1.0)	50 (7)

Speed of agitator 75 rpm and spheronisation time 4 min.

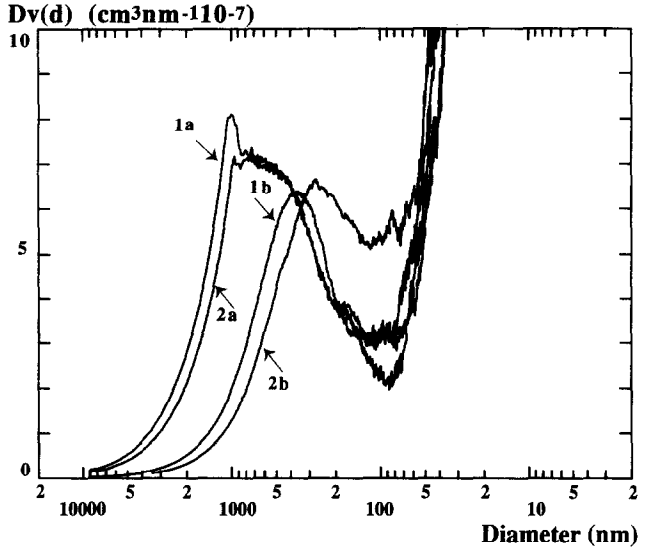

Fig. 7. Pore-volume size distributions ($D_v(d)$) of single (1) and twice (2) processed extrudates (a) and corresponding pellets (b). Agitator speed was 75 rpm, screen thickness 1.00 mm and spheronisation time 4 min.

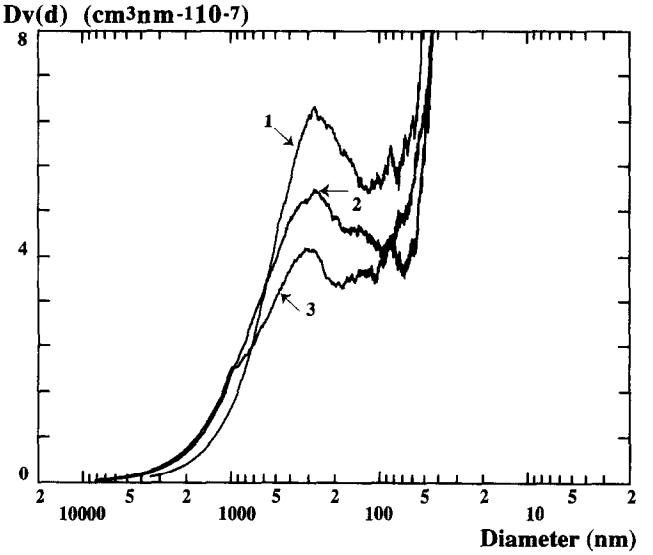

Fig. 8. Pore-volume size distributions ($D_v(d)$) of pellets prepared from twice-processed extrudates produced with screens of 1.00 mm (1), 1.25 mm (2) and 1.50 mm (3) in thickness. Agitator speed was 75 rpm and spheronisation time 4 min.

In the case of re-extrusion, the effect of screen thickness was clearly detected in pore-volume size distributions. For coating, the number of large pores on the surface of pellets should be minimal. This can be achieved by re-extrusion using the thinnest screen or with one extrusion using the longest spheronisation time.

In the case of pellets that are relatively homogeneous in size and shape, the microstructure of the pellets is a good parameter to use for evaluating the quality of the pellet. Pore-volume size distribution appears to be the parameter that reveals the differences most sensitively. However, the size distribution is presented versus the unit interval of the diameter of the pore opening. Therefore, microscopy of the cross-section was needed for the detection of the cavity inside the pellets. Thus, the combination of these two techniques is recommended for the evaluation of the microstructure of pellets.

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