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The influence of the extrusion screen on pellet quality using an instrumented basket extruder

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Abstract

The measurement of the power consumption of the extrusion head motor of a basket extruder proved to be a suitable method for monitoring the extrusion process. A comparison of the phase diagrams of β-lactose/Avicel® PH101/water and of dicalcium phosphate dihydrate/Avicel® PH101/water mixtures showed that the zone, where pellets of the desired quality were obtained, outlined with a length-to-radius (L/R) ratio of 2 screen was much smaller compared to the zone outlined with an L/R ratio of 4 screen. This phenomenon was due to the lower densification during extrusion using an L/R ratio of 2 screen. The storage time between granule production and extrusion affected the quality of β-lactose pellets due to the transformation of β-lactose into α-lactose monohydrate while the quality of dicalcium phosphate pellets remained unchanged.

Key words: Extrusion; Spheronisation; Instrumentation; Basket extruder; Pellet quality; Power consumption

1. Introduction

Extrusion-spheronisation is still a popular method for the production of spheres. The quality of the pellets is determined by the process parameters during the different stages of the process: the amount of liquid added during the granulation (Malinowski and Smith, 1975; Bataille et al., 1990a; Bains et al., 1991; Barrau et al., 1992; Baert and Remon, 1993; Hellen et al., 1993a), the speed of extrusion (Hellen et al., 1993d), the speed and time of spheronisation (Woodruff and Nuessle, 1972; Malinowski and Smith, 1975; Chariot et al., 1987; Bataille et al., 1990a,b, 1993; Rahman et al., 1991; Hasznos et al., 1992; Hellen and Yliruusi, 1993; Hellen et al., 1993a,b; Hileman et al., 1993; Wan et al., 1993), and the method of drying (Bataille et al., 1993). In addition to the extrusion speed, the specifications of the extrusion screen are important parameters affecting the quality of the extrudate, and hence of the pellets (Goodhart et al., 1973; Chariot et al., 1987; Hellen et al., 1993c,d; Hileman et al., 1993). In recent years, increasing attention has been paid to the monitoring of a production process. Therefore, some authors in-

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strumented their extruder in order to gain a better insight into the extrusion process (Dietrich and Brausse, 1988; Baert et al., 1991; Elbers et al., 1992; Kleinebudde and Lindner, 1993). The present paper reports on the monitoring of the extrusion process using a basket extruder and on the influence of the extrusion screen specifications on the pellet quality.

2. Materials and methods

2.1. Materials

Three model compounds with different water solubilities were chosen: anhydrous β-lactose (DCL 21) (solubility, 500 g/l (25°C)), α-lactose monohydrate (Pharmatose 200 M) (solubility, 86 g/l (25°C)) and dicalcium phosphate dihydrate (DCP) (solubility, 100 mg/l (25°C)). β-Lactose and α-lactose monohydrate, selected as model compounds for drugs with a high and medium solubility, respectively, were purchased from DMV, Veghel, The Netherlands. DCP, the substitute for an insoluble drug, was purchased from C.N. Schmidt B.V., Amsterdam, The Netherlands.

Microcrystalline cellulose (Avicel® PH101) (FMC Wallingstown, Little Island, Cork, Ireland) was chosen as the filler.

Demineralised water was used as the granulation fluid in all experiments.

A Nica E 140 extruder (Niro-Fielder, Eastleigh, Hants, U.K.) was used to extrude all compositions. Two types of screens were used, one with a length-to-radius (L/R) ratio of 2 (screen thickness 1 mm and perforation diameter 1 mm) the other with an L/R ratio of 4 (screen thickness 2 mm and perforation diameter 1 mm). In both screens 23.1% of the surface was perforated.

2.2. Methods

2.2.1. Instrumentation

The Nica extruder was instrumented with a power consumption meter (WMP 21, MTS, Willemshaven, Germany) connected to the motor driving the extrusion head (Fig. 1). The transducer measured power consumption between 0 and 1000 W and converted this measurement to the corresponding output signal between 0 and 10 V (accuracy, 2.5%). This output signal was recorded during the complete extrusion cycle.

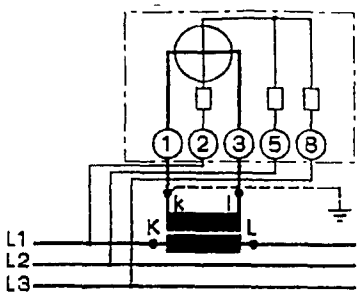

Fig. 1. Scheme with the connection between the motor driving the extrusion head of the extruder and the transducer for measuring the power consumption. One phase watt meter system adapted for three phase. L1, L2 and L3, three phase mains; 1 and 3, current coil; 2, 5 and 8, voltage coils; k, l, K and L, current transformer (optional).

2.2.1.1. Measurement of the power consumption. The average power consumption was calculated between 30 s and 1 min from the start of the extrusion process. During extrusion the rotational speed of the extrusion head dropped depending on the plasticity of the different compositions investigated. A correction was made to obtain the real power consumption at 30 rpm. Therefore, all binary and ternary mixtures were extruded at a rotational speed of 25, 30, 60 and 90 rpm. Each formulation was processed three-fold. After linear regression the x coefficient of the power consumption vs the rotational speed of the extrusion head profile indicated the change in power consumption per rotation. The r^2 coefficient was better than 0.97 in all cases, with an increase of the r^2 value as the amount of water in the formulation increased.

2.2.1.2. Validation of the power consumption measurement. To validate the system six separate batches of three different compositions were prepared and extruded at a rotational speed of 30 and 40 rpm for the extrusion and feeder heads, respectively. A screen with an L/R ratio of 2

Table 1
Average power consumption data (±S.D.) during extrusion of Avicel® PH101/water mixtures

Composition (w/w) Avicel/water	Power consumption (W) (average ($n = 6$) ± S.D.)
450:550	139.9 ± 4.8
500:500	250.2 ± 10.1
550:450	371.3 ± 11.0

Every composition was extruded six times using an L/R ratio of 2 screen at a rotational speed of 30 rpm for the extrusion head and 40 rpm for the feeder head.

was used. After each extrusion the extruder was taken apart and cleaned. The power consumption during extrusion of each batch was calculated and for each mixture the average of the power consumption and the standard deviation were calculated (Table 1).

2.2.2. Compositions of the mixtures

2.2.2.1. Instrumentation. Binary and ternary mixtures were granulated and extruded. The binary mixtures consisted of Avicel® PH101 and water in the following ratios: 60:40, 57.5:42.5, 55:45, 52.5:47.5, 50:50, 47.5:52.5, 45:55 (w/w). The ternary mixtures were prepared containing 0, 5, 10, 15, 20, 25, 30, 40 and 50% of α-lactose monohydrate or β-lactose as model compound. An additional two mixtures were made containing 60 and 70% of β-lactose. Mixtures containing 0, 5, 10, 15 and 20% DCP were also prepared. Besides α-lactose monohydrate, β-lactose and DCP, the remaining part of all mixtures consisted of equal amounts of Avicel® PH101 and water.

2.2.2.2. Influence of the extrusion screen. Different ternary mixtures containing β-lactose or DCP were prepared in order to outline the zones within the phase diagrams.

2.2.3. Preparation of the spheres

2.2.3.1. Granulation procedure. For the ternary mixtures the microcrystalline cellulose was first blended for 10 min with β-lactose, α-lactose monohydrate or DCP in a planetary mixer (Kenwood Chef, Hampshire, UK) at 60 rpm using a K-shaped mixing arm. Next the water was added and the mixture was granulated for 2 min in a planetary mixer (Kenwood Chef, Hants, U.K). at 60 rpm using a K-shaped mixing arm. In all cases a 1 kg batch was prepared.

In order to study the influence of the storage time between granulation and extrusion on the quality of the pellets, four different compositions (DCP/Avicel® PH101/water 100:420:480 and 100 : 450 : 450 (w/w); β-lactose/Avicel® PH101/water 300:375:325 and 300:410:290 (w/w)) were granulated. One mixture was extruded immediately after granulation, the other three batches were stored in well sealed plastic containers and processed with a time interval of 2 h.

2.2.3.2. Extrusion procedure. The granulated mass was extruded in a radial basket extruder (Nica E 140 extruder). The rotational speed of the feeder and extrusion heads was set at 40 and 30 rpm, respectively. The influence of the extrusion speed was studied for some mixtures (β-lactose/Avicel® PH101/water 125 : 500 : 375, 250 : 450 : 300, 400:325:275 (w/w) (compositions to the left of the zone); 100 : 475 : 425, 250 : 425 : 325, 400 : 300 : 300 (w/w) (compositions from the zone); 100:450:450, 250:400:350, 400:275:325 (w/w) (compositions to the right of the zone)) at a rotational speed for the extrusion head of 60 and 90 rpm. The rotational speed of the feeder head was kept at 40 rpm in all cases.

2.2.3.3. Spheronisation procedure. 200 g of the extrudate were spheronised in a spheroniser (Spheroniser model 15, Caleva Ltd, Sturminster Newton, Dorset, U.K.) for 10 min at 750 rpm.

Next the spheres were dried in a fluidized bed (Aeromatic AG, Aeromatic Ltd, Basel, Switzerland) for 20 min at 50°C.

2.2.4. Physical testing of the spheres

2.2.4.1. Particle size distribution, friability and roundness. The particle size distribution, friability and roundness of the pellets were evaluated according to the methods described by Baert et al. (1992a).

Spheres were considered of acceptable quality if 90% of the spheres had a particle size between 710 and 1400 μm, a friability lower than 0.2% and an E value between 1 and 1.20.

2.2.4.2. Bulk density and average pore diameter of the extrudate. The average pore diameter and the bulk density of the extrudate (DCP/Avicel® PH101/water 150:380:470 and 150:400:450 (w/w)) was determined with mercury as the displacement fluid (Autopore II 9220 V3.00, Micromeritics Instrum. Corp., Norcross, GA, U.S.A.).

2.2.4.3. Water content of the granulate. A sample of the granulate (β-lactose/Avicel® PH101/water 300:375:325 and 300:410:290 (w/w); DCP/Avicel® PH101/water 100:420:480 and 100:450:450 (w/w)) was taken and dried for 2 h at 80°C (Mettler LP 16-M Infrared Drying Unit) (Mettler Instruments, Greifensee, Switzerland).

2.2.4.4. Differential scanning calorimetry (DSC) of the granulate. DSC profiles were recorded for dried samples of the granulate (β-lactose/Avicel® PH101/water 300:410:290 (w/w)). The samples were heated to 250°C at a rate of 5°C/min (DuPont 2000, DuPont de Nemours Co., Wilmington, Delaware, U.S.A.).

3. Results and discussion

3.1. Instrumentation of the Nica extruder

Baert et al. (1991) described the instrumentation of a gravity feed extruder and proved that the extrusion process could be monitored by measuring the forces during the extrusion process. Because this instrumentation was not applicable to every type of extruder, the basket extruder was instrumented with a power consumption meter in order to monitor the extrusion process. The average power consumption was measured for the different binary and ternary mixtures and those values were plotted vs the amount of granulation fluid used in the case of the binary mixtures (Fig. 2) and vs the amount of model compound used in the case of the ternary mixtures (Fig. 3). These figures were similar those obtained on a gravity feed (Baert et al., 1991), a twin screw (Baert et al., 1993) and a ram extruder (Baert et al., 1992b) and clearly indicated that the power consumption was dependent on the amount of liquid phase present in the mixtures. Due to the water solubility of both lactose types, an initial decrease in power consumption was observed owing to the increase in fluid phase. The minimum in the curves was observed at the point of maximum solubility of lactose in the granulation liquid (20% for β-lactose and 5% for α-lactose monohydrate). From this point onwards the amount of the liquid phase was reduced and the power consumption increased. The profile of DCP showed no initial decrease in power consumption, as was expected due to the fact that the insoluble DCP did not increase the volume of the liquid phase. These results confirmed previous data obtained on other types of extruders and clearly showed that the instrumentation of a basket extruder with a power consumption meter was suitable to monitor the extrusion process.

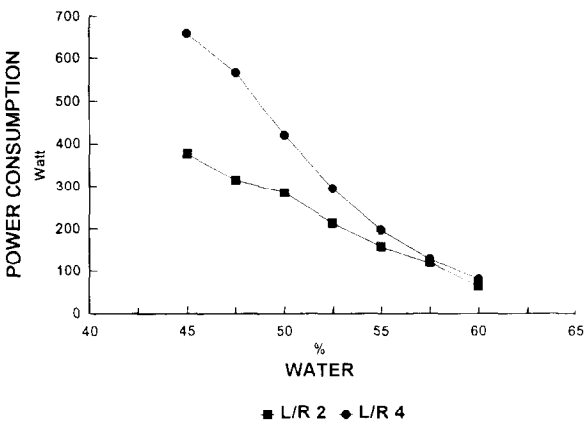

Fig. 2. Influence of the amount of water on the power consumption (W) recorded during extrusion of a mixture of Avicel® PH101 and water.

From Fig. 3A and B the observation made by Baert et al. (1993) was confirmed where, at higher concentrations of α-lactose monohydrate and β-lactose, no increase and even a reduction in the recorded power consumption was measured when

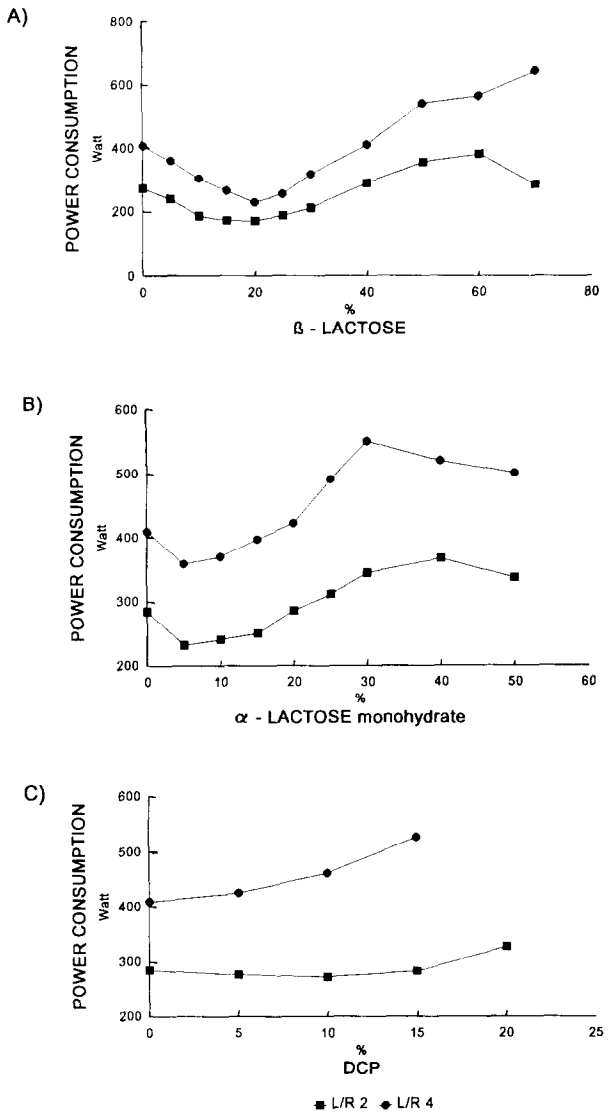

Fig. 3. Influence of the amount of model compound on the power consumption (W) during extrusion of mixtures of lactose/DCP, Avicel® PH101 and water. (A) β-Lactose/Avicel® PH101/water, (B) α-lactose monohydrate/Avicel® PH101/water, (C) DCP/Avicel® PH101/water.

the mass was extruded on a twin screw extruder equipped with an L/R ratio of 1.8 screen. The results shown in Fig. 3B indicate that the drop in power consumption occured not only with an L/R ratio of 2 screen but also with an L/R ratio of 4 screen. In both cases, insufficient water was present in the granulate to obtain the necessary cohesiveness to form a well bound extrudate. This resulted in an 'easier' extrusion process with a lower power consumption but producing only dust and no extrudate. No decrease in power consumption was achieved in the profile of β-lactose extruded with an L/R ratio of 4 screen. Possibly, this decrease in power consumption could occur at higher β-lactose contents, however, the authors were unable to extrude these mixtures without screen damage. Baert et al. (1991) could not detect the above-described second reduction in extrusion forces at a higher content of the different model compounds when the extrusion was performed on a gravity feed extruder equipped with an L/R ratio of 4 screen. A possible explanation could be that on the gravity feed extruder the reduction in power consumption occurs at a concentration level above 40% α-lactose monohydrate or above 60% β-lactose.

3.2. Influence of screen characteritics

The zone where pellets of the desired quality were obtained was dramatically larger when the extruder was equipped with an L/R ratio of 4 screen, this observation being valid for both β-lactose (Fig. 4) and DCP (Fig. 5). It is possible that with an L/R ratio of 4 screen the mass was more densified during extrusion due to the greater length of the die perforations. Due to this greater

Table 2
Average pore diameter and bulk density of the extrudate composed of DCP/Avicel® PH101/water mixtures, extruded using screens with a different L/R ratio

Composition (w/w) DCP/Avicel/water	L/R ratio of screen	Average pore diameter (μm)	Bulk density (g/ml)
150:380:470	4	0.982	1.132
150:400:450	4	0.992	1.211
150:380:470	2	1.249	0.949
150:400:450	2	1.292	0.947

The mixtures were extruded at a rotational speed of 30 rpm for the extrusion head and 40 rpm for the feeder head. All formulations were processed three-fold and the coefficient of variation was less than 3% in all cases.

densification a smooth and well bound extrudate was formed even at lower water contents in contrast with an L/R ratio of 2 screen where a losely bound extrudate with large surface defects was formed (Fig. 6). These data confirm the observations of Hellen et al. (1992) where the extrudate became smoother and more bound as the L/R ratio of the extrusion screen increased and of Gamlen and Eardley (1986) who stated that a extrudate with a very rough surface was formed because the extrusion screen was not thick enough. The difference in extrudate quality has a profound influence on the spheronisation process: while the well bound extrudate broke up evenly during spheronisation, a lot of fines were formed when the loosely bound extrudate was further processed. The extra densification due to the greater length of the die was also demonstrated by the porosity measurements (Table 2). The average pore diameter was definitely smaller for the mixtures extruded with an L/R ratio of 4 screen.

Some mixtures were extruded at a rotational speed of the extrusion head of 60 and 90 rpm,

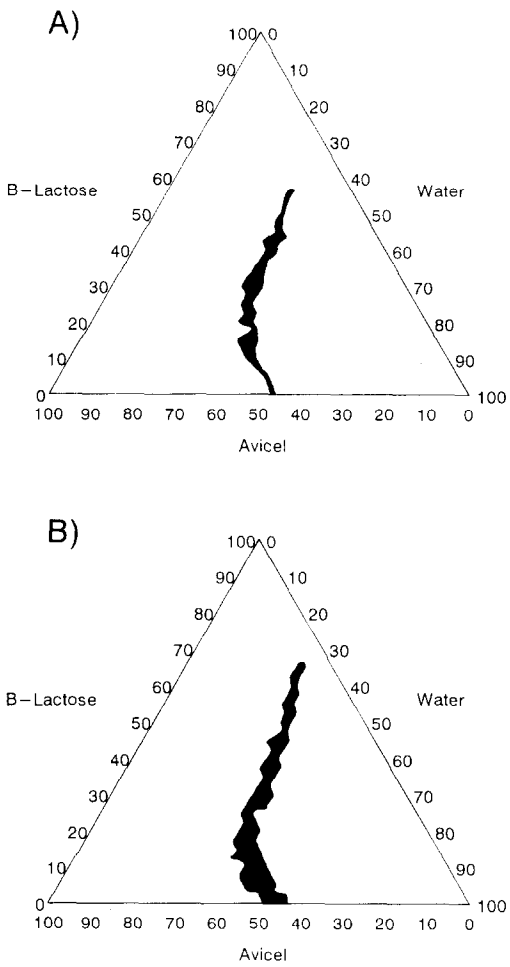

Fig. 4. Phase diagrams indicating the zone where pellets of the desired quality were obtained for β-lactose/Avicel® PH101/water mixtures. (A) Zone outlined with an L/R ratio of 2 screen, (B) zone outlined with an L/R ratio of 4 screen.

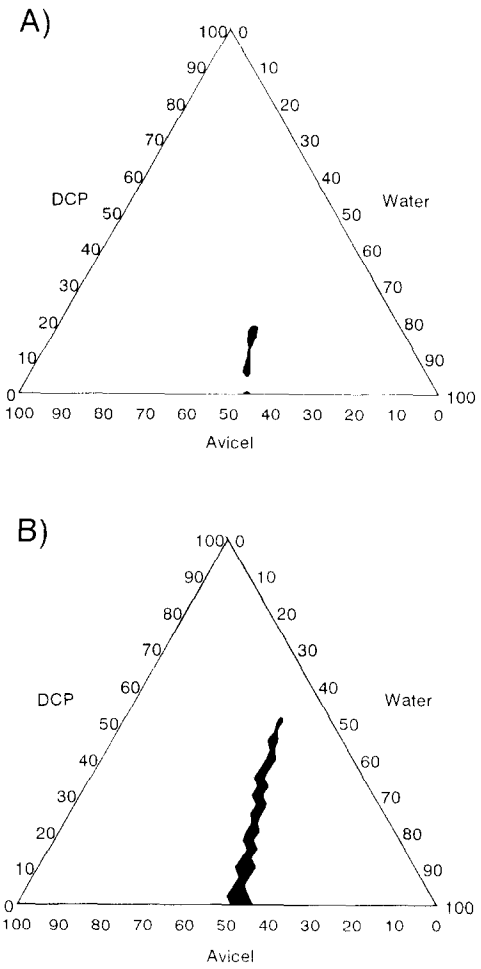

Fig. 5. Phase diagrams indicating the zone where pellets of the desired quality were obtained for DCP/Avicel® PH101/water mixtures. (A) Zone outlined with an L/R ratio of 2 screen, (B) zone outlined with an L/R ratio of 4 screen.

respectively, leading to better energy transfer into the mass and subsequently a possible increase in the binding properties of the particles. The increased strength of the extrudate caused less abrasion during spheronisation. The compositions containing β-lactose just to the left of the zone outlined at an extrusion speed of 30 rpm and with an L/R ratio of 2 screen showed a yield for the 710–1400 μm fraction of about 70%. After extrusion at a higher speed the yield of the 710–1400 μm fraction increased to about 90% (Table 3). From the above results it was concluded that the zone of the L/R ratio of 2 screen was extended to the area of mixtures with a lower water con-

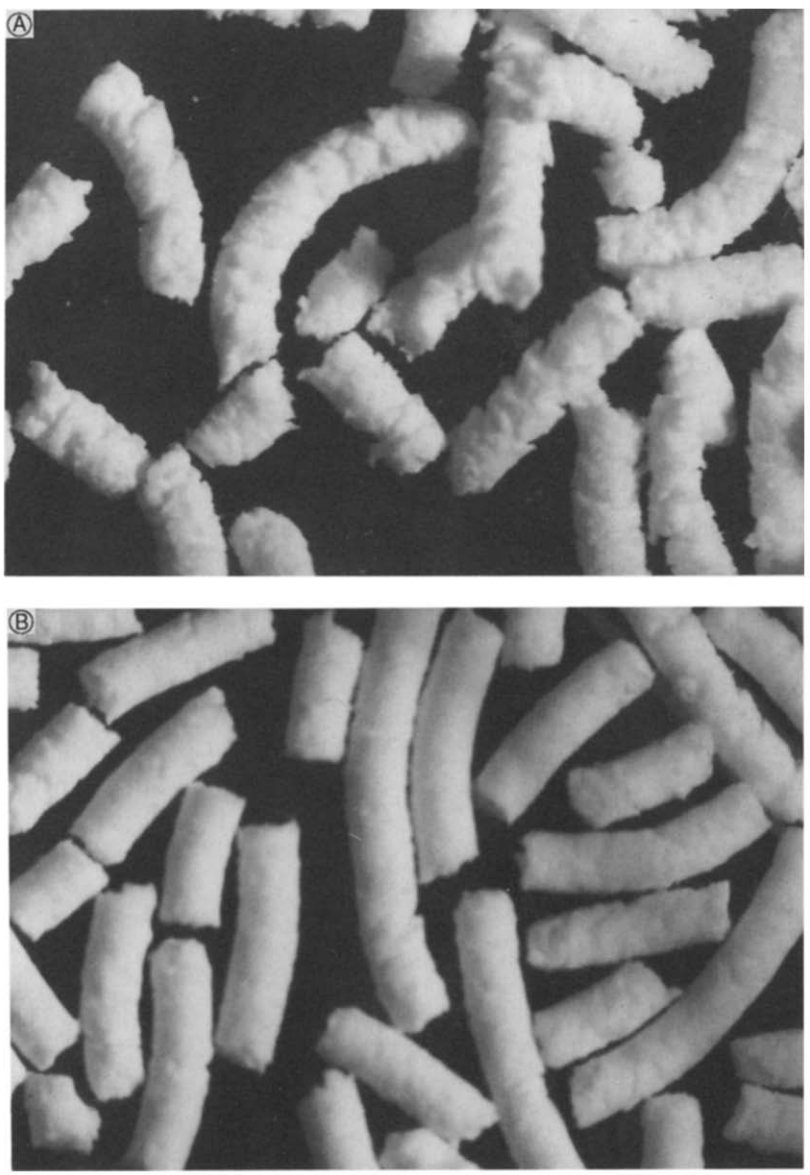

Fig. 6. Photographs of extrudate containing DCP/Avicel® PH101/water (150:380:470 (w/w)). (A) Extrudate produced with an L/R ratio of 2 screen, (B) extrudate produced with an L/R ratio of 4 screen.

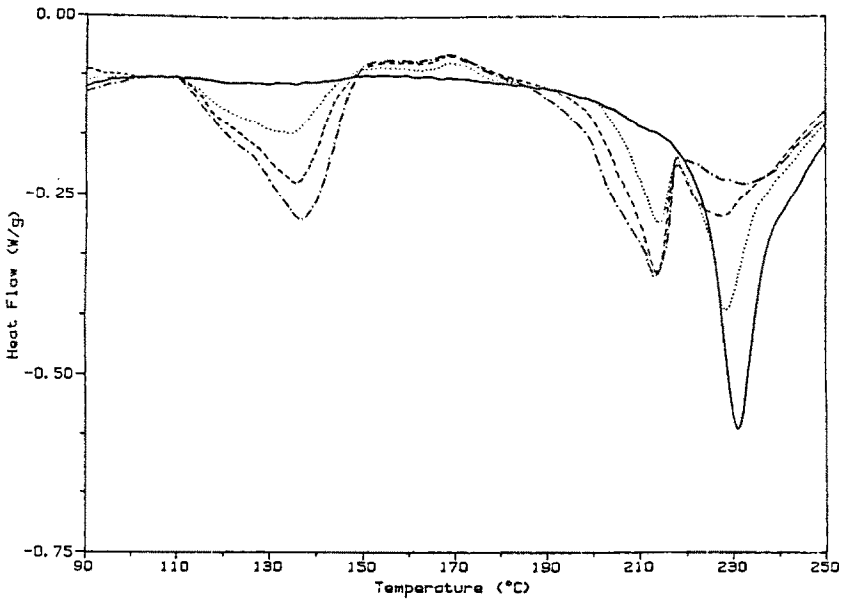

Fig. 7. DSC records of a granulate composed of β-lactose/Avicel® PH101/water (300:410:290 (w/w)) dried after different storage times. (———) 0 h, (· · · · · ·) 2 h, (- - - - - -) 4 h, (· – · – ·) 6 h.

tent when the extrusion was performed at a higher rotational speed of the extrusion head. Mixtures situated on the right and in the zone at 30 rpm remained unaffected by a higher extrusion speed. The extrusion speed had no effect on the extrusion of mixtures extruded with an L/R ratio of 4 screen and the quality of the pellets remained unaffected by the rotational speed of the extrusion head. The extra binding strength induced by the higher extrusion speed was neglible in this case compared to the densification of the mass during the extrusion with an L/R ratio of 4 screen.

Fig. 4 and 5 show that it was possible to prepare pellets with a higher load of β-lactose and of DCP using an L/R ratio of 4 screen. In the case of mixtures containing DCP the maximum content of model compound allowing pellets of the desired quality to be obtained was 50% using an L/R ratio of 4 screen and 20% using an L/R ratio of 2 screen. Using an L/R ratio of 2 screen, the zone showing pellets of good quality was very small, so that the composition of the mass was very critical and the process became less robust.

3.3. Influence of storage time

The influence of storage time between the granulation process and the extrusion phase on the quality of the pellets was studied. Table 4 shows that mixtures containing β-lactose were affected by the storage time. After 6 h of storage in well sealed plastic containers the yield of the 710–1400 μm fraction dropped by about 20% for both compositions containing β-lactose. In contrast, the DCP mixtures remained unaffected after a storage time of 6 h. The E value and the

Table 3
Yield of the 710–1400 μm fraction of mixtures containing β-lactose/Avicel® PH101/water extruded at different rotational speeds of the extrusion head

Composition (w/w) β-Lactose/Avicel/water	Yield of the 710–1400 μm fraction (%)		
	30 rpm	60 rpm	90 rpm
125:500:375	79.5	90.7	89.7
250:450:300	69.9	82.7	87.7
400:325:275	74.8	88.9	90.3

All formulations were processed three-fold and the coefficient of variation was less than 3.5% in all cases.

Table 4
Influence of storage time between granulation and extrusion on the quality of pellets using β-lactose/Avicel® PH101/water and DCP/Avicel® PH101/water mixtures

Composition (w/w) Model/Avicel/water	Fraction yield of 710–1400 μm (%) after				Water content after	
	0 h	2 h	4 h	6 h	0 h	6 h
DCP pellets						
100:420:480	87.1	84.7	88.2	84.0	47.9	48.1
100:450:450	79.4	74.3	78.9	76.4	45.0	44.9
β-Lactose pellets						
300:375:325	97.2	93.1	90.9	77.5	32.3	32.2
300:410:290	80.4	79.7	73.5	56.5	28.9	28.7

All compositions were extruded using an L/R ratio of 2 screen at a rotational speed of 30 rpm for the extrusion head and 40 rpm for the feeder head. All formulations were processed three-fold and the coefficient of variation was less than 3% for the fraction yield and less than 2% for the water content of each formulation.

friability remained unaffected by this kind of handling for β-lactose and DCP. To explain this phenomenon, differential thermal analysis was performed on the different compositions. Fig. 7 shows DSC diagrams of mixtures immediately after granulation and after a storage period of 2, 4 and 6 h. Table 5 lists the corresponding area under the curve for the dehydration endotherm of α-lactose monohydrate and the melting endotherms of α-lactose and β-lactose, respectively. Initially, only a melting endotherm of β-lactose was observed whereas endothermic peaks due to the dehydration of α-lactose monohydrate and α-lactose melting increased as a function of storage time. Simultaneously, the surface of the β-lactose melting endotherm decreased. This observation proved that the β-lactose fraction dissolved in the granulation liquid was progressively transformed into α-lactose monohydrate. Since α-lactose monohydrate has a lower water solubility than β-lactose, it precipitated thereby reducing the total volume of the fluid phase. The granulated mass became dryer and more fines were formed during extrusion. No interference of Avicel® PH 101 with the dehydration endotherm of α-lactose monohydrate and the melting endotherms of α-lactose and β-lactose was observed.

Table 5
Area (J/g) under the curve of the dehydration endotherm of α-lactose monohydrate and of the melting endotherms of α-lactose and β-lactose for the mixtures stored for different periods of time

Storage time (h)	Dehydration of α-lactose monohydrate	Melting endotherm of α-lactose	Melting endotherm of β-lactose
0	0	0	50.6
2	21.6	8.5	31.3
4	36.0	16.3	19.3
6	48.2	21.7	14.0

Composition of the mixture (w/w): β-lactose/Avicel® PH101/water 300:410:290 (w/w).

4. Conclusion

This study clearly indicated that it was possible to follow the extrusion process when a basket extruder was equipped with a power consumption metering device fixed on the motor driving the extrusion head.

Comparison of pellet quality produced after extrusion using screens of different L/R ratios showed that a screen with a high L/R ratio provided a more robust production system. When pellets of low quality were obtained during development the choice of a screen with a high L/R ratio should be investigated prior to formulation modifications.

Finally, it was shown that when using β-lactose as a filler, mutarotation to α-lactose monohydrate occurred during storage of the granulate before extrusion. The influence of storage time conditions of the granulated mass on extrusion and sphere quality should be investigated.

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