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Melt pelletization with polyethylene glycol in a rotary processor

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Abstract

The purpose of this study was to investigate the effect of the airflow, the binder concentration, the massing time, the friction plate rotation speed, and the surface structure of the friction plate on melt pelletization in a laboratory scale rotary processor. Lactose monohydrate was melt agglomerated with polyethylene glycol (PEG) 3000 as meltable binder. The study was performed as a full factorial design. An increase in agglomerate size was found when the binder concentration, the massing time, or the friction plate rotation speed was increased. The agglomerate size was also increased when increasing the shearing forces by using a friction plate with a different surface structure. The size distribution of the agglomerates was significantly narrowed when the binder concentration or the shearing forces caused by the friction plate were increased. An increase in the adhesion of material to the friction plate was found when the shearing forces of the friction plate were increased either by the rotation speed or by the surface structure. Generally, the rotary processor was found to be a suitable alternative to melt pelletization in a high shear mixer.

Keywords: Rotary processor; Melt agglomeration; Polyethylene glycol; Spheronization; Friction plate

1. Introduction

Melt agglomeration is a type of wet agglomeration that requires the addition of a molten binder or a solid binder, which melts during the process. A suitable binder for melt agglomeration should be solid at room temperature, and the melting range of the binder should at least be 20–30 °C above room temperature (Schæfer, 2001). Examples of binders applied for melt agglomeration are glycerides, fatty acids, polyethylene glycols, and waxes. The process of melt agglomeration requires furthermore materials that are stable at temperatures above the melting range of the binder. In order to control the process, the product temperature must be controlled since the viscosity of the molten binder affects agglomerate growth (Seo et al., 2002). The end product from a melt agglomeration process might be either irregular granules of a wide size distribution or spherical granules of a narrow size distribution, i.e. pellets.

Melt agglomeration has primarily been carried out in high shear mixers. High shear mixers are capable of producing granules as well as pellets. A higher shearing force and a longer massing time have been found to promote the formation of pellets (Kinget and Kemel, 1985; Schæfer et al., 1992a; Heng et al.,

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2000; Seo and Schæfer, 2001). Heating jackets are applied to control the product temperature. It is difficult, however, to keep the temperature constant, because the shearing forces raise the product temperature due to heat of friction (Hamdani et al., 2002). Also formulation variables such as the concentration of the binder (Kinget and Kemel, 1985; Schæfer et al., 1992c; Heng et al., 2000), the viscosity of the binder (Kinget and Kemel, 1985; Schæfer and Mathiesen, 1996b; Johansen and Schæfer, 2001; Heng et al., 2003), and the particle size of the binder (Schæfer and Mathiesen, 1996a) and filler (Schæfer et al., 1992c; Heng et al., 2000; Johansen and Schæfer, 2001) have been found to affect the sphericity of the final product. The end point of a melt agglomeration process in a high shear mixer can be determined by measuring the power consumption of the impeller (Schæfer et al., 1992b; Royce et al., 1996; Heng et al., 1999).

Fluid bed granulators have also been used for melt agglomeration (Abberger and Henck, 2000; Yanze et al., 2000; Abberger, 2001; Abberger et al., 2002; Kidokoro et al., 2002; Seo et al., 2002). Because of the low shearing forces in fluid beds, it is difficult to obtain spheronization of the agglomerates (Schæfer, 2001; Seo et al., 2002). The fluid bed granulator has an advantage compared to the high shear mixer in a better control of the product temperature. This enables the product to be formed at an elevated temperature and subsequently to be cooled down to room temperature in the same equipment. This simplifies the melt agglomeration process in a fluid bed granulator compared to a high shear mixer. Furthermore, it keeps the movement of the product during cooling, which reduces the amount of clusters of agglomerates (Ukita and Murakami, 1994; Seo et al., 2003). However, the fluid bed granulator lacks a simple way to determine the end point of the agglomeration process.

A rotary processor is a fluid bed granulator equipped with a rotating friction plate, which increases the shearing forces. The rotary processor has been used for wet agglomeration and wet pelletization. It has been shown that the rotation speed of the friction plate (Holm et al., 1996; Vertommen and Kinget, 1997; Kristensen et al., 2000a), the wet massing time (Wan et al., 1994; Vertommen and Kinget, 1997), and the ratio between the starting materials and water (Vertommen and Kinget, 1997; Kristensen et al., 2000b) affect the sphericity of the agglomerates produced. Furthermore, it has been shown that torque measurements from the rotor shaft can be used as an end point control (Kristensen et al., 2000a,b). Since melt pelletization in a rotary processor combines the good temperature control of the fluid bed granulator with the higher shearing forces and the possibility of end point control of the high shear mixer, it is supposed that it could be an easier and more controllable way to produce pellets by melt pelletization.

Reo and Roche (1996) have reported a few selected formulations that were applicable for melt agglomeration in a rotary processor. However, no systematic investigations of the effects of equipment, process, and formulation variables on melt agglomeration in a rotary processor have been published.

The present work was based on the hypothesis that melt pelletization could be performed in a rotary processor by a simple and controllable process. The purpose of this study was to test this hypothesis by investigating the effect of selected equipment, process, and formulation variables on the melt pelletization process in a rotary processor, and to compare the results from the rotary processor with previous results from fluid bed granulators and high shear mixers.

2. Materials and methods

2.1. Materials

Lactose 350 mesh (α-lactose monohydrate, DMV, The Netherlands) was used as filler. The sieve fraction >250 μm of polyethylene glycol (PEG) 3000P (powder) (Clariant, Germany) was used as meltable binder.

2.2. Methods

2.2.1. Primary characterization of materials

The particle size distributions by volume of the lactose and the PEG 3000 were determined in triplicate by a Malvern Mastersizer S laser diffraction particle sizer (Malvern Instruments, UK) fitted with a dry powder feeder operating at 3 bar. The span is defined as the difference between the volume diameters at the 90 and the 10 percentage points relative to the volume median diameter.

The BET multipoint surface area of the lactose was determined in duplicate by a Gemini 2375 Surface Area Analyzer (Micromeritics, USA).

The pycnometric densities of lactose and PEG 3000 were determined in duplicate by an AccuPyc 1330 gas displacement pycnometer (Micromeritics, USA) using helium purge. The poured and tapped densities of lactose and PEG 3000 were determined in duplicate according to the test of apparent volume (European Pharmacopoeia, 2002).

The density of the molten PEG 3000 was determined in triplicate at 60 and 70 °C as previously described (Eliasen et al., 1998).

The melting range and the melting peak temperature of the PEG 3000 were estimated in triplicate by a Perkin-Elmer DSC 7 differential scanning calorimeter (Perkin-Elmer, USA). A sample of about 4 mg was sealed in a 40-μl aluminum pan with holes and scanned between 45 and 70 °C at a heating rate of 4 °C/min.

The viscosity of the melted PEG 3000 was determined in duplicate by a RV20 Rotovisco (Haake, Germany) with a NV sensor system and a measuring system M. The viscosity was determined as the slope of the linear part of the obtained flow curve. The analyses were performed at 60 and 70 °C.

2.2.2. Agglomeration equipment

The melt agglomeration experiments were performed in a rotary processor (Glatt GPCG-1, Glatt, Germany) connected to a personal computer, which monitored and recorded the product temperature, the inlet and outlet fluidizing air temperature, the fluidizing airflow, the fluidizing air gap pressure difference, and the torque of the rotating friction plate. Further, an additional temperature sensor was inserted into the product chamber at a lower position than the original temperature sensor (Fig. 1). Readings from the lower sensor were recorded manually every 30 s and were used to monitor the product temperature. The rotary processor was fitted with one of three different friction plates (Fig. 2) with a diameter of 28 cm.

2.2.3. Agglomeration procedure

The rotary processor was set to preheat with the friction plate rotating until the product temperature reached 50 °C. In order to prevent adhesion to occur during loading, the central cone was not installed during the preheating. Lactose and PEG were manually mixed and then placed at the center of the plate. The fluidizing airflow was set to the specified value according to the experimental design, and the rotary processor was started. Then the fluidizing air gap pressure difference was adjusted to 2000 Pa and the rotation of the friction plate was started.

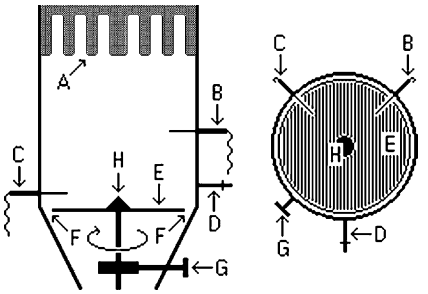

Fig. 1. Schematic drawing of the rotary processor: (A) exhaust air filter, (B) upper product temperature sensor, (C) lower product temperature sensor, (D) sample thief, (E) friction plate, (F) air gap, (G) friction plate elevator, and (H) cone.

During a period of approximately 5 min some 2–3 min before the massing time was started, the container was frequently tapped on by a hammer to loosen the starting build up of adhesion to the wall of the container.

The start of the massing time was defined as the point where the product temperature reached 60 °C. At the end of massing time, the cooling of the product was started. The cooling was initiated by opening a valve, which conducted unheated air of room temperature into the container. Then the fluidizing airflow was increased to approximately 100 m^3/h, the speed of the friction plate was reduced to 500 rpm, and the air heater was turned off. After 3 min of cooling, the rotary processor was stopped, and the product was removed from the product container and weighed.

2.2.4. Agglomerate characterization

2.2.4.1. Yield. The yield was calculated as the total amount of end product expressed as a percentage of the amount of starting materials.

2.2.4.2. Adhesion. The adhesion of material to the friction plate was determined as the difference between the weight of the friction plate after the process and the weight of the clean friction plate. The

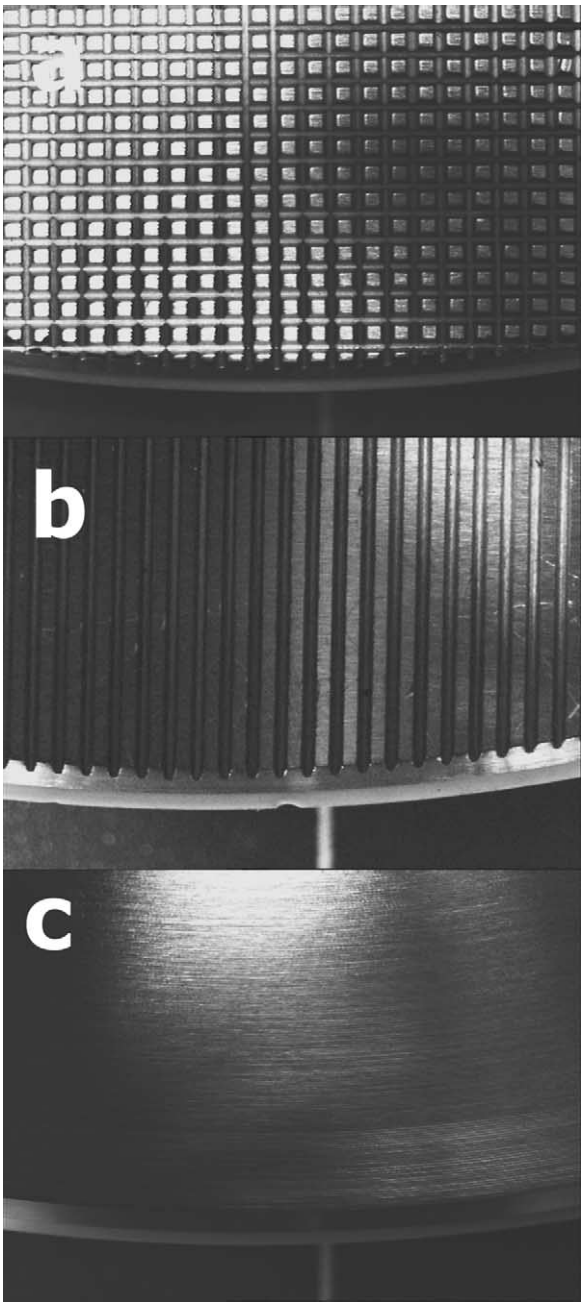

Fig. 2. Photographs of the three different surface structures of the friction plates: (a) crosshatched grooved, (b) longitudinal grooved, and (c) smooth.

adhesion was expressed as a percentage of the amount of starting materials.

2.2.4.3. Size distribution. The amount of agglomerates >4 mm was determined as the retained fraction after vibration sieving of the agglomerates for approximately 10 s by a Jel-Fix 50 (J. Engelsmann, Germany). The result was expressed as a percentage of the total amount of end product.

Sieve analyses were performed on samples of approximately 45 g of the agglomerates <4 mm. The samples were prepared by a Laborette 27 automatic rotary sample divider (Fritsch, Germany) and added to a series of 14 standard ASTM sieves ranging from 75 to 2000 μm. The sieves were vibrated permanently for 10 min with a vertical amplitude of 6 mm. The agglomerate size distributions were in good agreement with the log-normal distribution. The geometric weight mean diameter (d_{gw}) and the geometric standard deviation (s_g) were calculated from the sieve analysis data.

2.2.4.4. Differential scanning calorimetry. The melting peak of PEG 3000 in samples from selected experiments was estimated by a Perkin-Elmer DSC 7 differential scanning calorimeter (Perkin-Elmer, USA). A sample of about 3–4 mg was sealed in a 50-μl aluminum pan with holes and scanned between 50 and 60 °C at a heating rate of 2 °C/min.

2.2.4.5. PEG content. The content of PEG 3000 from selected experiments was determined indirectly as the difference between the weighed amount of agglomerates and the amount of lactose determined colorimetrically as previously described (Thomas, 1984). The content of PEG was expressed as a percentage of the amount of lactose.

2.2.4.6. Image analysis. Agglomerates from the size fraction 500–630 μm were placed on an illuminated desk. Pictures were taken with a digital camera (MTI CCD72EX, DAGE-MTI, USA) connected to a 60 mm lens (Mikro-Nikkor, Nikon, Japan) (1 pixel = 17 μm). Image analyses were performed on the pictures using imaging processing and analysis software (Global Lab Image /2, Data Translation Inc., USA). Approximately 140 agglomerates were used for each analysis. The shape of the agglomerates was described by the

Table 1
The levels of the independent variables in the complete 2^4 factorial design

Independent variable	Low level	Center point	High level
Fluidizing airflow (m^3/h) (A)	50	70	90
Binder concentration (%) (B)	22	24	26
Friction plate rotation speed (rpm) (C)	700	1000	1300
Massing time (min) (D)	7.0	9.5	12.0

two-dimensional shape factor (e_R) (Podczeck et al., 1999) as well as the aspect ratio calculated as the maximum length divided by the maximum width found at a 90° angle to the length.

2.2.4.7. Scanning electron microscopy. Pictures of the size fraction 500–630 μm from selected experiments were taken by a scanning electron microscope (SEM) (JSM 5200, JEOL, Japan). The agglomerates were sputtered with gold (E5200 Auto Sputter Coater, BioRad, UK) for 120 s before microscopy.

2.3. Experimental design

On the basis of results obtained from preliminary experiments, a complete 2^4 factorial design with one genuine repetition and eight center points was performed giving a total of 40 experiments. The experiments were performed in a partially randomized order, and five experiments always including one center point were performed each day. The experimental design is shown in Table 1. All the experiments in Table 1 were performed with the crosshatched friction plate. The binder concentration is indicated as the amount of PEG 3000 in percent of the amount of lactose.

By performing an additional four experiments with the friction plate with the smooth surface structure and four experiments with the friction plate with the longitudinal surface structure at center point settings, the effect of the surface structure of the friction plate was evaluated. These additional experiments were performed in a randomized order.

The response variables were the geometric weight mean diameter (d_{gw}), geometric standard deviation (s_g), the yield, the adhesion to the friction plate, the two-dimensional shape factor (e_R), and the aspect ratio. The results from the experiments were analyzed by analysis of variance (ANOVA) using the STATISTICA version 6.0 software (StatSoft Inc., OK, USA).

3. Results and discussion

3.1. Material properties

It is seen from Table 2 that the PEG 3000 has a rather narrow size distribution. This is because the particles ≤250 μm were removed by sieving as mentioned above.

3.2. Preliminary investigations

The equipment, process, and formulation variables to be investigated in the final experiments and the range of these variables were selected on the basis of preliminary experiments. It was found that the highest fluidizing airflow, at which the rotary processor could be operated without blocking the product filters, was around 100 m^3/h, and that the lowest fluidizing airflow should be around 50 m^3/h to maintain a sufficient fluidization of the powder bed. The friction plate rotation speed should be no less than 500 rpm to prevent the powder bed from caking at the friction plate. A binder concentration below 20% was found insufficient to form agglomerates of the desired size, and a binder concentration around 28% gave rise to

Table 2
The physical properties of the materials

Material	Volume median diameter (μm)	Span	Specific surface area (m^2/g)	Pycnometric density (g/ml)	Poured density (g/ml)	Tapped density (g/ml)	Density molten (g/ml)		Melting (°C)		Viscosity (mPa s)	
							60 °C	70 °C	Range	Peak	60 °C	70 °C
Lactose	33	2.43	0.78	1.55	0.53	0.74	–	–	–	–	–	–
PEG 3000	370	1.14	–	1.23	0.63	0.68	1.09	1.09	57–61	59	267	194

uncontrollable agglomerate growth. A massing time of around 10 min was chosen, because a longer massing time might cause an uncontrollable agglomerate growth. The batch size was varied between 600 and 840 g. A larger batch size gave smaller pellets in accordance with a previous study of wet pelletization in a rotary processor (Kristensen et al., 2000a). An inlet air temperature of 70 °C was found to be suitable to maintain a product temperature around 60–70 °C. Furthermore, it was found that using unfractionated PEG 3000 resulted in a poor reproducibility because of an increased adhesion to the wall of the product container. By using the size fraction of PEG 3000 >250 μm, the reproducibility was improved.

The levels of the fluidizing airflow, the friction plate rotation speed, the binder concentration, and the massing time in the final experiments (Table 1) were chosen in such a way that all combinations of the variables gave agglomerates of a mean size within 300–1000 μm.

3.3. Size and size distribution

The variation in the results of the eight center point experiments (Table 3) is a measure of the reproducibility of the process. The agglomerate size is seen to range from 473 to 629 μm, and the standard deviation was calculated to 63 μm. The variation between repeated experiments explains the rather low r^2-values (Table 4) for the fit between the data and the models illustrated in Figs. 3 and 4. Similar reproducibilities were seen in high shear mixers where melt pelletization experiments with PEG 3000 resulted in standard deviations ranging from 20 to 84 μm (Schæfer et al., 1993; Schæfer and Mathiesen, 1996b). From repeated wet pelletization experiments in a rotary processor (Kristensen et al., 2000a) a standard deviation of 40 μm was calculated. By a *F*-test, this was not found to be significantly different from the standard deviation of the present melt pelletization experiments.

A narrow size distribution is desirable when producing pellets. The lowest geometric standard deviation obtained in the rotary processor is seen to be 1.30 (Table 3). Melt pelletization with PEG 3000 in high shear mixers resulted in similar size distributions, the lowest geometric standard deviations being 1.2–1.3 (Schæfer et al., 1992a,c; Schæfer and Mathiesen, 1996b). The standard deviation of the geometric standard deviation of the center point experiments (Table 3) was calculated to 0.11 compared with 0.02–0.03 in high shear mixer experiments (Schæfer et al., 1993; Schæfer and Mathiesen, 1996b). Fluid bed granulators have been shown to give a slightly narrower size distribution in melt agglomeration experiments with PEG 3000 with geometric

Table 3
Effects of the independent variables in the factorial design in Table 1 on agglomerate size (d_{gw}) and size distribution (s_g)

Run no.	Level[a]	d_{gw} (μm)	s_g
30	A	402	1.66
8	A	480	1.66
11	AB	546	1.58
13	AB	542	1.52
21	AC	344	1.80
12	AC	397	1.76
37	AD	431	1.67
36	AD	382	1.82
4	ABC	572	1.39
33	ABC	613	1.44
25	ABD	561	1.33
5	ABD	527	1.50
1	ACD	377	1.83
29	ACD	430	1.53
38	ABCD	682	1.45
35	ABCD	733	1.49
27	1	379	1.85
23	1	406	1.75
18	B	542	1.43
10	B	395	1.84
39	C	447	1.61
6	C	353	1.92
2	D	432	2.08
34	D	395	1.71
17	BC	564	1.37
24	BC	508	1.45
16	BD	535	1.52
15	BD	553	1.45
19	CD	455	1.66
28	CD	371	1.64
32	BCD	877	1.58
9	BCD	597	1.36
31	0	501	1.52
3	0	620	1.31
26	0	480	1.56
14	0	599	1.36
40	0	531	1.41
7	0	629	1.30
22	0	473	1.49
20	0	523	1.40

[a] Capital letters indicate high level, '1' indicates all low levels, and '0' indicates center point.

Table 4
The results of the statistical analysis on the geometric weight mean diameters (d_{gw}) and the geometric standard deviations (s_g) from the factorial design in Table 1

Factors and interactions	d_{gw} (μm) ($r^2 = 0.7540$)		s_g ($r^2 = 0.4847$)	
	Effect	P	Effect	P
Constant	504.6	0.0000	1.6	0.0000
Fluidizing airflow (m^3/h) (1)	13.1	0.5710	0.0	0.3772
Binder concentration (%) (2)	179.1	0.0000	−0.3	0.0000
Friction plate rotation speed (rpm) (3)	50.8	0.0347	−0.1	0.2259
Massing time (min) (4)	53.0	0.0280	0.0	0.6451
(1) × (2)	12.5	0.5894	0.0	0.8307
(1) × (3)	−16.1	0.4870	0.1	0.2703
(1) × (4)	−24.6	0.2912	0.0	0.9731
(2) × (3)	67.4	0.0064	0.0	0.8307
(2) × (4)	44.9	0.0598	0.0	0.7614
(3) × (4)	37.5	0.1124	0.0	0.9910

standard deviations of 1.1–1.2 (Abberger et al., 2002; Seo et al., 2002).

The maximum amount of meltable binder that can be incorporated in the agglomerates depends on the intragranular voids and thus on the densification of the agglomerates. With lactose 350 mesh and PEG 3000, the approximate maximum binder concentration in the present experiments in the rotary processor was found to be 28% compared with 22% in a high shear mixer (Schæfer et al., 1992c) and 30% in a fluid bed granulator (Seo et al., 2002). This reflects the difference in the magnitude of the shearing forces in the equipments. Higher shearing forces result in more densification and thus in a lower maximum binder concentration.

The effect of the process on the crystallinity and crystal form of the meltable binder was determined by comparing the melting point of PEG 3000 expressed as the peak value of the DSC thermogram for the raw material and agglomerate samples stored for 24 h and 11 months after the production. The melting points were found to be 57.0 °C for the raw material, 57.4 °C for the agglomerate sample stored for 24 h, and 57.2 °C for the agglomerate sample stored for 11 months. The fact that the melting points are similar indicates that no changes in either crystallinity or crystal form have occurred during the agglomeration and storage (Craig and Newton, 1991).

Table 4 shows that the massing time, the binder concentration, the friction plate rotation speed, and the interaction between the two latter have a statistically significant effect ($P < 0.05$) on the agglomerate size. Fig. 3a shows that an increase in the massing time increases the agglomerate size, and that there is no significant effect of increasing the fluidizing airflow. Fig. 3b shows that increasing the binder concentration or the friction plate rotation speed will increase the agglomerate size. Furthermore, the variables are seen to interact, the effect of the binder concentration or the friction plate rotation speed being more pronounced at a higher friction plate rotation speed or binder concentration, respectively. These results are in good accordance with previous melt pelletization experiments with PEG in high shear mixers where an increased massing time, binder concentration as well as impeller speed were found to increase the agglomerate size (Kinget and Kemel, 1985; Schæfer et al., 1992a; Heng et al., 2000).

From Table 4 it can also be seen that only the binder concentration has a statistically significant effect on the geometric standard deviation of the agglomerates. A higher binder concentration results in a narrower size distribution (Fig. 4). Although previous melt agglomeration experiments in high shear mixers (Schæfer et al., 1992a; Heng et al., 2000) and wet agglomeration experiments in rotary processors (Holm et al., 1996; Liew et al., 2002) have shown that a higher rotation speed and a longer massing time caused a narrower size distribution, no significant effect of neither friction plate rotation speed nor massing time is found in the present experiments.

Table 5 shows the significant effects of the surface structure of the friction plate. The largest agglomerate

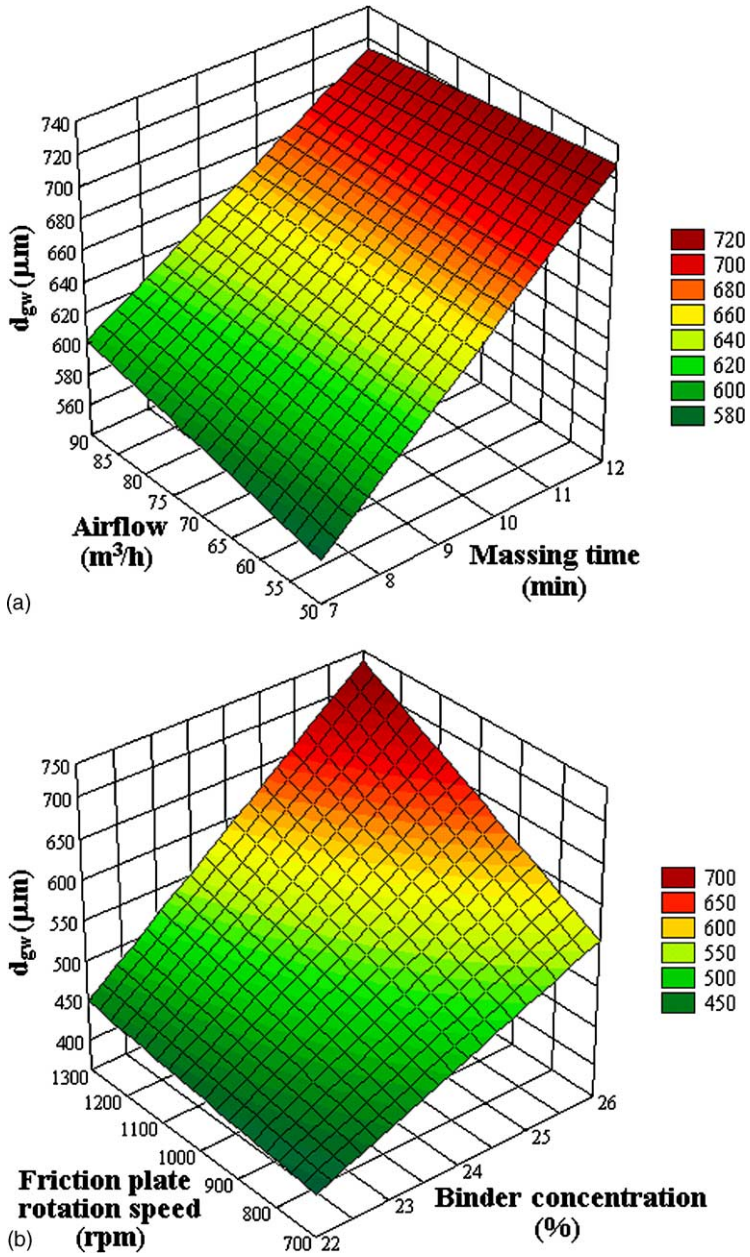

Fig. 3. Effects of independent variables on agglomerate size (d_{gw}). (a) Effects of fluidizing airflow and massing time. Friction plate rotation speed: 1300 rpm; binder concentration: 26%. (b) Effects of friction plate rotation speed and binder concentration. Fluidizing airflow: 50 m^3/h; massing time: 12 min.

size and the narrowest size distribution are obtained, when the friction plate with the crosshatched surface structure is used, and the opposite is seen when using the friction plate with the smooth surface structure. This is because the crosshatched plate gives the highest, the smooth plate the lowest, and the longitudinal plate intermediate shearing forces. This complies with wet agglomeration experiments in a rotary processor,

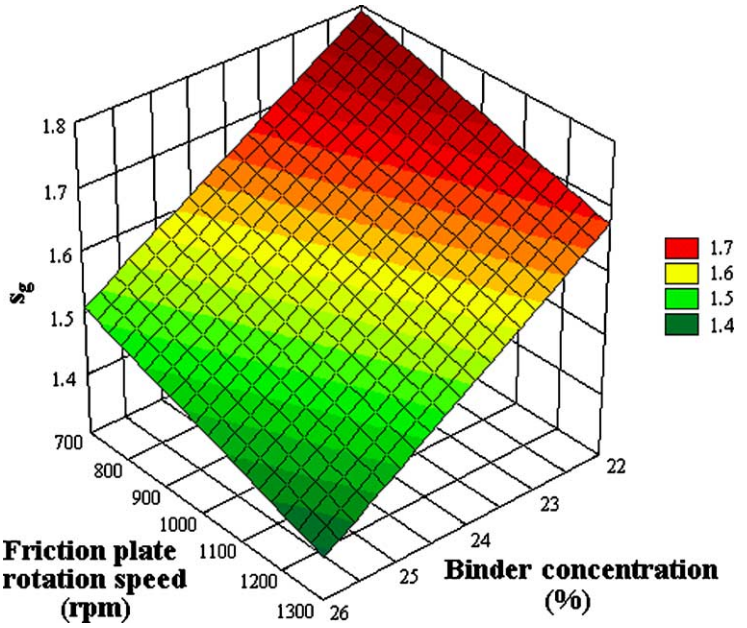

Fig. 4. Effects of friction plate rotation speed and binder concentration on agglomerate size distribution (s_g). Fluidizing airflow: 50 m^3/h; massing time: 12 min.

Table 5
Effects of the surface structure of the friction plate on the response variables

Response variable	Surface structure	Mean	S.D.	*P*
d_{gw} (μm)	Smooth	389	47	0.0009
	Longitudinal	458	14	
	Crosshatched	545	63	
s_g	Smooth	1.69	0.06	0.0016
	Longitudinal	1.56	0.08	
	Crosshatched	1.43	0.11	
Adhesion (%)	Smooth	0.2	0.1	0.0000
	Longitudinal	3.8	0.5	
	Crosshatched	4.5	0.5	
Yield (%)	Smooth	94	1	0.0160
	Longitudinal	92	1	
	Crosshatched	91	1	
Shape factor (e_R)	Smooth	0.350	0.040	0.0008
	Longitudinal	0.448	0.009	
	Crosshatched	0.435	0.032	
Aspect ratio	Smooth	1.273	0.041	0.0021
	Longitudinal	1.187	0.014	
	Crosshatched	1.193	0.032	

which showed that increasing the shearing forces by changing the surface structure of the friction plate increased the agglomerate size and narrowed the size distribution (Heng et al., 2002).

Table 5 shows that the friction plate with the longitudinal surface structure results in a lower standard deviation of the agglomerate size than the two other friction plates. More experiments are needed, however, to decide whether the reproducibility is really improved with the longitudinal plate.

There was found no significant effects on the amount of agglomerates >4 mm, which generally was between 0.0 and 0.7%. Optimized melt pelletization experiments with PEG 3000 in a high shear mixer showed similar low values of the amount of agglomerates >4 mm (Schæfer et al., 1992a).

It was tried to correlate the agglomerate growth to the torque increase since wet pelletization experiments have shown a clear correlation between torque increase and agglomerate size (Kristensen et al., 2000a,b). No clear correlation was found, however, in the present experiments. This might be because of the differences in binder addition and binder viscosity between the actual melt and wet pelletization processes.

3.4. Adhesion to the friction plate

The adhesion to the friction plate varied between 0.0 and 8.5%. The 2^4 factorial analysis showed that only the friction plate rotation speed had a significant effect ($P = 0.0028$) on the adhesion. A higher friction plate rotation speed was found to give more adhesion.

Furthermore, the adhesion was significantly influenced by the surface structure of the friction plate (Table 5). The friction plate with the smooth surface structure gave rise to almost no adhesion, whereas the friction plates with the longitudinal and the crosshatched surface structures gave rise to more adhesion. This is in accordance with wet agglomeration experiments in a rotary processor (Heng et al., 2002).

A preferential adhesion of PEG to the friction plate would result in a PEG content in the product being lower than the nominal content. No indications of a preferential adhesion were found since the PEG content in selected experiments with a nominal PEG content of 24% was found to be within 23.5–24.5%.

3.5. Yield

The yield of the experiments was within 85–95%. In the 2^4 factorial analysis no significant effect was found of the variables on the yield.

The surface structure of the friction plate had a significant effect on the yield (Table 5). The highest yield is obtained with the friction plate with the smooth surface structure and the lowest with the friction plate with the crosshatched surface structure. Thus, the yield seems simply to be correlated to the adhesion to the friction plate. Also wet agglomeration experiments in a rotary processor showed that the yield was increased when the shearing forces of the friction plate were decreased by changing the friction plate surface structure (Heng et al., 2002).

3.6. Shape

The sphericity of the agglomerates was described by the aspect ratio and the two-dimensional shape factor (e_R) (Podczeck and Newton, 1994). The ideal value for e_R is 1.0, and it is influenced by the deviation of shape from a circle towards an ellipse as well as the surface irregularities. The e_R-values reported for a set of apparently spherical pellets produced by extrusion–spheronization were 0.416 and 0.568 (Podczeck and Newton, 1994). The e_R and the aspect ratio were calculated to be within 0.31–0.47 and 1.16–1.31, respectively, for all the present experiments. No statistically significant effects on e_R or aspect ratio were found in the 2^4 factorial analysis. The same was seen in a similar study on wet pelletization in a rotary processor, where no significant effects were found on the aspect ratio, which was in the range of 1.08–1.12 (Kristensen et al., 2000a).

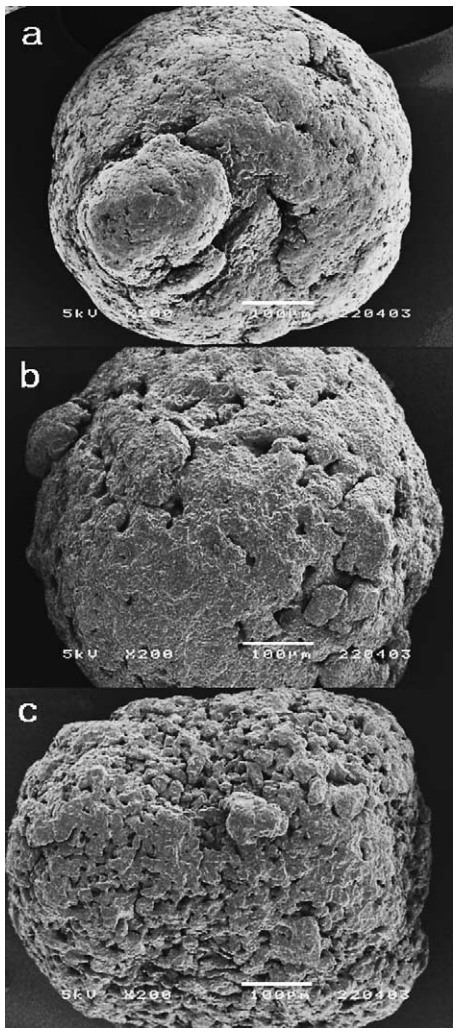

Fig. 5. SEM pictures of agglomerates produced with friction plates with different surface structure: (a) crosshatched, (b) longitudinal, and (c) smooth.

However, the surface structure of the friction plate had a significant effect on the sphericity (Table 5). In accordance with a wet agglomeration study in a rotary processor (Heng et al., 2002), it is seen that the friction plate with the smooth surface structure gives the least spherical agglomerates. Furthermore, Fig. 5 shows that the crosshatched friction plate gives smoother and denser agglomerates than the smooth friction plate. Fig. 5 also shows that the smooth friction plate causes a larger deviation from the ideal round shape than the other two plates.

Melt pelletization experiments with different formulations in a high shear mixer have reported e_R-values up to and slightly above 0.6 (Schæfer, 1996; Eliasen et al., 1999). The more spherical agglomerates obtained in a high shear mixer are most likely due to the higher shearing forces but might also be ascribed to the different formulations.

A comparison of Fig. 5 with SEM pictures of agglomerates obtained in fluid bed granulators with PEG 3000 and lactose 350 mesh (Abberger et al., 2002; Seo et al., 2002) shows that the rotary processor is capable of producing more spherical agglomerates than the fluid bed granulator. Furthermore, it is seen that when the crosshatched and the longitudinal friction plates are used, the rotary processor is capable of producing denser agglomerates with a smoother surface than the fluid bed granulator. The fluid bed granulators lower shearing forces explain these differences.

4. Conclusions

The study showed that melt pelletization is possible in a rotary processor, and that the process is simple and controllable. The surface structure of the friction plates was found to significantly influence the properties of the agglomerates and the yield of the process. The friction plate with the smooth surface structure was found least suitable for melt pelletization because of insufficient shearing forces. The crosshatched and the longitudinal friction plates were both found suitable for melt pelletization. However, to make a clear distinction between these plates more experiments with the longitudinal friction plate are needed.

The binder concentration was found to be the most important variable influencing the agglomerate size and size distribution. Of the process variables studied, the friction plate rotation speed and the massing time were found to influence the agglomerate size.

Compared to high shear mixers, the rotary processor has shown to be an alternative in the choice of equipment for melt pelletization. The process is simplified in the rotary processor since a fast cooling of the agglomerates in the equipment is possible. The agglomerates produced by the rotary processor were of a similar size and size distribution and with a similar reproducibility as those produced by a high shear mixer. The high shear mixer, however, is able to produce agglomerates, which are more spherical than those from the rotary processor due to the higher shearing forces. On the other hand, the rotary processor produces more spherical agglomerates than a conventional fluid bed granulator, which seems to be unsuitable for pelletization even though the fluid bed granulator has been shown to produce slightly narrower size distributions.

Because of the lower shearing forces in the rotary processor, it is capable of incorporating more binder in the agglomerates than the high shear mixer but less than the fluid bed granulator. This might make the rotary processor more suitable than the high shear mixer for incorporating solid dispersions in agglomerates by melt pelletization.

Meltable binders of a lower viscosity and addition of a molten binder might improve the reproducibility and result in more spherical agglomerates in the rotary processor. Further experiments with different types of meltable binders are necessary, therefore, in order to evaluate the general applicability of the rotary processor for melt pelletization.

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