Melt pelletization in a high shear mixer. VIII. Effects of binder viscosity

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Abstract

Lactose monohydrate and anhydrous lactose were melt pelletized in an 8-l high shear mixer using polyethylene glycol (PEG) 2000, 3000, 6000, 8000, 10000, or 20000 as meltable binder. The maximum impeller speed had to be applied in order to avoid an uncontrollable agglomerate growth with the highly viscous types of PEG. A higher binder viscosity resulted in a lower initial agglomerate growth and in a higher subsequent growth rate. The effect of binder viscosity on agglomerate growth was reflected in the power consumption of the impeller motor. A lower binder viscosity gave rise to more spherical pellets.

Keywords: Binder viscosity; Polyethylene glycols; Melt pelletization; High shear mixer; Power consumption; Agglomerate growth mechanisms

1. Introduction

In wet granulation processes, agglomeration is usually caused by the addition of a binder solution of a rather low viscosity, typically within the range of 2–300 mPa·s. In a fluidized bed granulator, however, a marked evaporation of the solvent occurs during the process. This will increase the viscosity of the binder solution, and the liquid bridges within the agglomerates might become immobile (Jäger and Bauer, 1984).

In fluidized bed granulation experiments, an increase in the viscosity owing to a higher initial viscosity of the binder solution (Jäger and Bauer, 1984; Massoud and Bauer, 1989), or to a gelation during the process (Schæfer and Wørts, 1978) resulted in a larger agglomerate size.

The effect of the viscosity of the binder liquid is less pronounced by agglomeration in a high shear mixer, because the shearing forces are higher, and the evaporation of solvent is less than in a fluidized bed. Experiments in a high shear mixer with five binders in different concentrations (Ritala et al., 1986) did not show any effect of

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viscosity, apart from an effect that was ascribed to gelation. On the other hand, other authors (Hoornaert et al., 1994) found that an increase in viscosity obtained by a doubling of the binder concentration gave rise to a larger mean granule size.

A higher viscosity of the binder liquid will make it more difficult to obtain a uniform distribution of the liquid (Kinget and Kemel, 1985; Visavarungroj et al., 1990; Wan and Lim, 1991; Kokubo et al., 1993). Consequently, a high viscosity might give rise to insufficient agglomeration or to an inhomogeneous size distribution of the agglomerates. Such problems are counteracted by atomizing the binder liquid or by increasing the shearing forces involved in the process.

By melt agglomeration with PEGs, the viscosities of the molten binders are normally higher than the viscosities of the binder solutions used for wet agglomeration. In previous melt agglomeration experiments with PEG 3000 and 6000, a higher viscosity resulted in a smaller agglomerate size (Schæfer et al., 1990, 1992a,b). This was explained by a lower surface plasticity caused by the higher viscosity. It was found, however, that the agglomerate growth rate increased in an uncontrollable way when the viscosity exceeded an upper critical limit, which was dependent on the actual product and process variables (Schæfer and Mathiesen, 1996).

The results described in literature indicate that the effect of the viscosity of the binder liquid on agglomerate growth is rather complex. The purpose of the present work was to obtain further knowledge of the effect of binder viscosity by means of melt pelletization experiments with different types of PEG covering a wide range of viscosities.

2. Theory

The fundamental agglomeration theory of Rumpf (1962) is based upon the tensile strength of liquid bridges which are static. The strength of a static bridge is dominated by the surface tension of the liquid and is independent of the viscosity. In agglomeration processes, the particles are sub-jected to relative movement, and consequently the liquid bridges are dynamic (Mazzone et al., 1987; Ennis et al., 1991).

The force required to separate two moving particles is much higher than that required in static systems, because the viscosity of the liquid resists the motion in the dynamic case (Mazzone et al., 1987). The strength of the dynamic bridge is dominated by viscous forces. Therefore, agglomeration models based upon the strength of static bridges will grossly underestimate the agglomerate size (Mazzone et al., 1987).

Ennis et al. (1991) have developed an agglomeration model, which takes into consideration that the liquid bridges are dynamic. The theory is based upon a dimensionless viscous Stokes' number

$$St_v = \frac{8\rho u_o a}{9\mu} \qquad (1)$$

where ρ is the density of the particle or granule (g/cm^3), u_o is the initial relative granule collisional velocity (cm/s), a is the particle or granule radius (μm), and μ is the binder viscosity (P). The viscous Stokes' number is a measure of the ratio of granule collisional kinetic energy to the viscous dissipation brought about by the binder liquid. In a mixer granulator, u_o is assumed to be equal to $a\omega$, where ω is the impeller rotation speed (1/s). Then Eq. (1) becomes

$$St_v = \frac{8\rho \omega a^2}{9\mu} \qquad (2)$$

Coalescence will occur at collision between particles or granules if St_v is below a critical value, St_v^*, of the viscous Stokes' number. St_v^* is given by

$$St_v^* = (1 + \tfrac{1}{e}) \ln\left(\frac{h}{h_a}\right) \qquad (3)$$

where e is a particle coefficient of restitution, which is 1 in the case of rigid particles, and which is lower, the more deformable the particles or granules are; h is the thickness of the liquid layer on the surface of the colliding particles or granules, and h_a is a characteristic length scale of surface asperities.

Table 1
Physical properties of the PEGs

PEG	True density (g/cm^3)	Water content (%)	Melting range (°C)	Peak temp. (°C)
2000	1.224	0.5	42–53	52
3000	1.221	0.4	48–59	58
6000	1.227	0.2	52–62	61
8000	1.226	0.2	54–63	62
10000	1.226	0.2	57–64	63
20000	1.223	0.2	53–66	64

Agglomerate growth by coalescence is promoted by a low value of St_v and a high value of St_v^*. It appears from Eqs. (2) and (3) that the agglomerate growth rate according to the theory is increased by a lower particle density, a lower impeller speed, a smaller particle size, a higher viscosity, a higher deformability of the agglomerates, an increased thickness of the liquid layer, and by smaller surface asperities.

In practice, it will be difficult to estimate e and h in Eq. (3). They are, however, closely related to the liquid saturation of the agglomerates (Adetayo, 1993). A higher liquid saturation will increase St_v^*. This is in accordance with the fact that liquid saturation is a primary factor controlling agglomerate growth (Kristensen, 1995).

In an agglomeration process, the values of St_v will vary within the mixer, because the velocities of the particles or granules will be different at different locations in the mixer. When all the St_v-values are below the critical value, all the collisions will result in coalescence. The St_v-values increase during the process since the particle size (a in Eq. (2)) increases owing to agglomerate growth. When the St_v-values become equal to the critical value, no further agglomerate growth will occur (Ennis et al., 1991).

Ennis et al. (1991) supported their agglomeration theory by fluidized bed granulation experiments. Further, the theory was found to be suitable for a qualitative description of an agglomeration process in a drum granulator (Adetayo, 1993) as well as in a high shear mixer (Hoornaert et al., 1994).

3. Materials and methods

3.1. Materials

Lactose 450 mesh (α-lactose monohydrate, DMV, The Netherlands) and anhydrous lactose (N.F., impalpable, Quest International, The Netherlands) were used as starting materials.

Polyethylene glycol (PEG) 2000, 3000, 6000, 8000, 10000, and 20000 (Hoechst, Germany) were used as meltable binders. All the PEGs were used as flakes.

The size distributions by volume of the starting materials were determined by a Malvern 2601Lc laser diffraction particle sizer (Malvern Instruments, UK). The median particle diameter and the span were found to be 20 μm and 2.1 for lactose monohydrate and 34 μm and 2.1 for anhydrous lactose. The span is defined as the difference between the diameters at the 90 and the 10 percentage points relative to the median diameter.

The BET multipoint surface areas, determined by a Gemini 2375 Surface Area Analyzer (Micromeritics, USA), were 0.81 m^2/g for lactose monohydrate and 0.71 m^2/g for anhydrous lactose.

The true densities of the materials were determined by an AccuPyc 1330 gas displacement pycnometer (Micromeritics, USA) using helium purge. The densities of lactose monohydrate and anhydrous lactose were 1.547 g/cm^3 and 1.572 g/cm^3, respectively. The densities of the PEGs are shown in Table 1.

The water contents on a wet-weight basis of lactose monohydrate, anhydrous lactose, and the PEGs were estimated by volumetric titration as

previously described (Schæfer and Mathiesen, 1996). The sample size was about 400 mg (lactose monohydrate), about 3 g (anhydrous lactose), and about 1.5 g (PEGs) respectively. The water content was found to be 5.1% for lactose monohydrate and 0.6% for anhydrous lactose. The water contents of the PEGs are shown in Table 1.

The melting ranges of the PEGs were estimated by a Perkin Elmer DSC 7 differential scanning calorimeter (Perkin Elmer, USA) as previously described (Schæfer and Mathiesen, 1996). The melting ranges and the peak temperatures are shown in Table 1.

The viscosities of the molten PEGs were estimated at 70°C, 80°C, and 90°C by a rotation viscosimeter, Rotovisco RV 12 (Haake, Germany), with a MV sensor system and a MV II K rotor. Results obtained at the highest rev./min that gave rise to a deflection within the scale are presented in Table 2. The results did not indicate that the viscosity values were dependent on the rotation speed of the rotor. The correlation between the temperature and the logarithm of the viscosity was found to be linear with correlation coefficients between -0.996 and -1.000. Viscosity values at 100°C and 110°C were extrapolated by means of the regression lines.

3.2. Equipment

The 8-l laboratory scale high shear mixer (Pellmix PL 1/8, Niro A/S, Denmark), described in a previous paper (Schæfer et al., 1993), was employed in the experiments. The temperature of the heating jacket was set to 50°C in all the experiments.

3.3. Mixing procedure

The load of the mixer was 1 kg of lactose monohydrate or anhydrous lactose in all the experiments. The concentration of the PEGs was determined on the basis of preliminary experiments and was kept constant at 23% in the experiments with lactose monohydrate and at 22% in the experiments with anhydrous lactose. The PEG concentration is expressed as the percentage (% m/m) of the amount of lactose.

In all the experiments, the starting material and the PEG were dry mixed at an impeller speed of 1300 rev./min. The impeller speed was increased to 1500 rev./min, 2 min after the melting point of the PEG was observed as an inflection point on the recorded product temperature curve. This inflection point was defined as the start of massing time.

The power consumption of the impeller motor was measured by a power consumption meter, and the energy input was estimated from the power consumption curves as previously described (Schæfer et al., 1993).

The procedures for cooling of the agglomerates and for estimation of the adhesion to the bowl were the same as described in a previous paper (Schæfer, 1996).

3.4. Granule characterization

3.4.1. Size distribution

The amount of lumps larger than 4 mm was determined as previously described (Schæfer, 1996).

The granule size distribution was estimated by a sieve analysis of a sample of about 100 g drawn by scooping from the cooled fraction finer than 4 mm, and the geometric mean diameter (d_{gw}) and the geometric standard deviation (s_g) were calculated. A series of 12 ASTM standard sieves was vibrated for 10 min by a Fritsch analysette 3 vibrator (Fritsch, Germany). Sieves in the range of 75–2000 μm were used for the experiments at massing times of 1 min and 3 min. For the

Table 2
The effect of temperature on the viscosities (mPa·s) of the molten PEGs

PEG	Temperature, °C				
	70	80	90	100	110
2000	101	77	60	(46)	(36)
3000	222	170	132	(102)	(78)
6000	938	701	553	(421)	(323)
8000	1620	1230	909	(683)	(512)
10000	4660	3560	2730	(2080)	(1590)
20000	26 500	19 000	14 900	(10 900)	(8180)

The values in parentheses are extrapolated values.

experiments at massing times of 6, 9, 12, and 15 min the sieves were in the range of 180–2000 μm.

Size fractions including the three sieve fractions closest to the mean diameter were prepared by vibration for 5 min, and these size fractions were applied for the measurements in Section 3.4.2, Section 3.4.3 and Section 3.4.4.

3.4.2. Intragranular porosity

The intragranular porosity was estimated by a mercury immersion method, and the liquid saturation was calculated as previously described (Schæfer et al., 1992a; Schæfer and Mathiesen, 1996).

3.4.3. Water content

The water content on a wet-weight basis was estimated by volumetric titration as previously described (Schæfer and Mathiesen, 1996). A sample of about 1 g was used for the measurements.

3.4.4. Image analysis

The agglomerates were placed on an illuminated desk, and measurements were carried out using a video camera (MTI CCD72EX, DAGE-MTI, USA) connected to a 55-mm lens (Micro-Nikkor, Nikon, Japan), video digitiser software (Media Pro + /HiRes v2.01 +, Rombo Productions, Scotland, UK), and image processing and analysis software (Global Lab. Image Version 2.20, Data Translation Inc., USA); 200 agglomerates were used for one analysis.

3.4.5. Scanning electron microscopy

Photographs were taken by a scanning electron microscope (SEM) (Jeol JSM 5200, Japan).

3.5. Experimental design

A series of 72 factorially designed experiments was carried out with lactose monohydrate. The six types of PEG included in Table 1 were used, and the massing time was varied at 1, 3, 6, 9, 12, and 15 min. All experiments were carried out in duplicate.

A series of 10 experiments was carried out with anhydrous lactose. The massing time was kept constant at 12 min, and experiments were made in

duplicate with PEG 2000, 3000, 6000, 8000, and 10000.

The results shown in this paper are mean values of two experiments unless otherwise stated. The data were analysed by analysis of variance.

4. Results and discussion

4.1. Experiments with lactose monohydrate

In previous experiments (Schæfer and Mathiesen, 1996), PEG 6000 gave rise to an uncontrollable agglomerate growth at an impeller speed of 1200 rev./min. This was ascribed to the high viscosity of the PEG 6000. Preliminary experiments at 1200 rev./min with PEG 8000, 10000, and 20000 showed a similar uncontrollable growth. The uncontrollable growth was prevented by increasing the impeller speed to 1500 rev./min, which is the maximum speed. This is in accordance with Eq. (2), which shows that the potential for agglomerate growth by coalescence is increased at a higher viscosity and is counteracted by a higher impeller speed. Consequently, a very high impeller speed is a condition of using highly viscous binders.

The effects of viscosity and impeller speed are, however, more complex than it appears from Eq. (2), because both factors affect Eq. (3) too. A higher binder viscosity will reduce the deformability of the agglomerates. This will increase the coefficient of restitution, e. Further, the thickness, h, of the liquid layer in the surface is reduced, because less liquid is squeezed to the surface at collisions between agglomerates. Both will counteract the agglomerate growth by decreasing St_v^*. A higher impeller speed will augment the deformability at collisions and will increase the densification of the agglomerates. The latter will squeeze more liquid to the surface, and this will decrease e and increase h in Eq. (3) (Adetayo, 1993). Thus, the impeller speed will promote the agglomerate growth by increasing St_v^*.

The effects of the viscosity and the impeller speed on the ratio St_v/St_v^* will decide whether an increase in viscosity or impeller speed will augment or reduce the agglomerate growth rate. The

Table 3
Results of the repeated experiments with different types of PEG at a massing time of 1 min

PEG	d_{gw} (μm)	s_g	Lumps > 4 mm (%)
2000	629	2.66	15.6
	560	2.77	12.8
3000	569	2.72	13.7
	548	2.78	18.7
6000	413	2.36	6.0
	422	2.38	5.9
8000	384	2.39	6.2
	373	2.41	6.4
10000	466	2.28	3.3
	416	2.29	4.5
20000	185	4.46	0.0
	190	4.61	0.0

Starting material: lactose monohydrate. Impeller speed: 1300 rev./min.

lower the ratio, the higher the growth rate. Several authors (Kinget and Kemel, 1985; Schæfer et al., 1990, 1992a, 1993; Knight, 1993; Thomsen et al., 1993) have found that the agglomerate growth rate increased with a higher impeller speed in melt agglomeration experiments with binders of a rather low viscosity. This indicates that the effect of the impeller speed on St_v^* is larger than the simultaneous effect on St_v when the binder has a low viscosity. On the other hand, the preliminary experiments described above indicate that the effect of impeller speed on St_v will dominate in the case of highly viscous binders, i.e. a higher impeller speed will decrease the growth rate.

The effects of the type of PEG on the mean granule size, the granule size distribution, and the amount of lumps are presented in Table 3 and Fig. 1. After 1 min of massing, the size distributions deviate markedly from the log-normal distribution, and the values of d_{gw} and s_g, therefore, are not directly comparable with the values in Fig. 1. Early in an agglomeration process, the rate of coalescence is controlled by the distribution of the binder (Ennis et al., 1991). A high binder viscosity gives rise to a poor binder distribution and a low deformability of the molten binder droplets. This is why only a slight agglomerate growth is seen with PEG 20000 at 1 min of massing. The PEGs with the lowest viscosities cause a marked ag-

glomerate growth at 1 min. This is reflected in a large mean granule size and a large amount of lumps.

After 2 min of massing, the impeller speed is raised from 1300 rev./min to 1500 rev./min. The higher impeller speed and the prolonged massing result in a breakdown of lumps until 6 min of massing (Fig. 1c). A simultaneous fall in the mean granule size is seen between 1 min and 3 min except for PEG 20000. The distribution of the highly viscous PEG 20000 is improved by prolonged massing, and this will start the agglomerate growth. Between 6 min and 9 min of massing, the agglomerate growth rate is seen to be higher
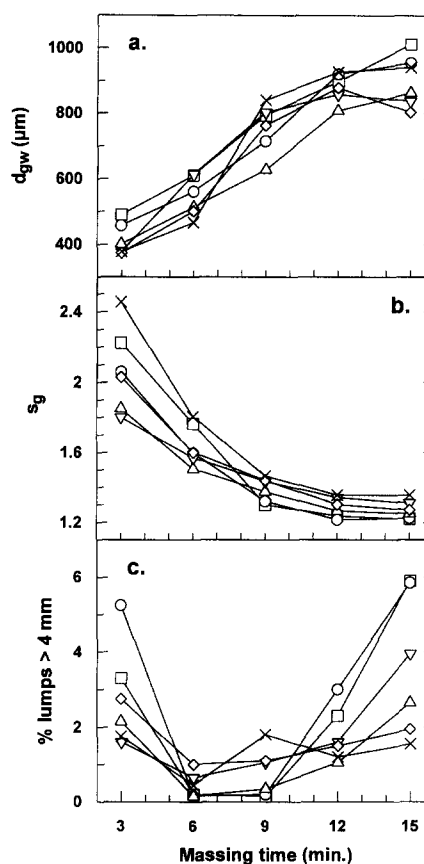

Fig. 1. Effect of type of PEG on the mean granule size (a), the geometric standard deviation (b), and the amount of lumps (c) during massing. Starting material: lactose monohydrate. ($\square$) PEG 2000; ($\bigcirc$) PEG 3000; ($\triangle$) PEG 6000; ($\triangledown$) PEG 8000; ($\diamondsuit$) PEG 10000; ($\times$) PEG 20000.

with PEG 10000 and PEG 20000 than with the PEGs of lower viscosities (Fig. 1a). This delayed agglomerate growth is ascribed to the slower distribution of binders of a high viscosity.

Between 3 min and 12 min, prolonged massing results in a significantly larger mean granule size ($P < 0.001$), whereas no effect of massing time is seen between 12 min and 15 min. The type of PEG was found to have a slight effect ($P < 0.05$) on the mean granule size. PEG 6000 causes the smallest granule size, and the largest granule sizes are obtained with PEG 2000 and PEG 20000. However, this effect is seen at 9 and 12 min of massing only.

Fig. 1b shows that the size distribution becomes significantly narrower ($P < 0.001$) at prolonged massing until 12 min, after which no further narrowing occurs. During the start of the process, PEG 6000 and PEG 8000 give rise to the narrowest size distribution. At the end of the process, a lower viscosity is seen to cause a narrower size distribution. From 3 min of massing, the size distributions were generally found to be in good agreement with the log-normal distribution except for a slight over-representation of larger granules. The agreement with the log-normal distribution was not found to be affected by the binder viscosity.

A minimum in the amount of lumps is seen at 6 min, from which the amount of lumps rises owing to agglomerate growth (Fig. 1c). The amount of lumps becomes larger, the lower the viscosity ($P < 0.01$). This is assumed to be due to the higher deformability of the agglomerates at decreasing viscosity.

Table 4 shows results on the reproducibility of the process. The reproducibility of the variables is generally seen to become poorer late in the process, where the agglomerate growth is more difficult to control. The standard deviation on the mean granule size was previously found to be about 20 μm (Schæfer et al., 1993) in experiments with lactose monohydrate in the same mixer. The standard deviation is higher in the present experiments, because the higher impeller speed makes the process less reproducible. The analysis of variance gave no indication of an effect of binder viscosity on the reproducibility.

Table 4
The reproducibility of the process expressed by the standard deviations of the dependent variables estimated by analysis of variance at varying massing times

Dependent variable	Massing time	
	6 and 9 min	12 and 15 min
d_{gw} (μm)	53	84
s_g	0.020	0.017
Lumps (%)	0.3	1.0
Porosity (%)	0.17	0.26
Liquid satur. (%)	0.7	1.0
Water content (%)	0.074	0.098
Energy input (kJ/kg)	7.6	10.0
Product temp. (°C)	1.0	1.9

Starting material: lactose monohydrate.

Fig. 2a shows a fall in the intragranular porosity until 6 min of massing. A high viscosity delays the densification, and this is why the porosity at 3 min is markedly higher with PEG 20000 than with the other PEGs. The high porosity with the PEG 20000 gives rise to a low liquid saturation, which explains the low initial agglomerate growth rate seen with PEG 20000. After 6 min of massing, the porosity increases, and a simultaneous fall in liquid saturation is seen. This increase in porosity was previously found to be due to evaporation of water of crystallization giving rise to formation of small pores (Schæfer and Mathiesen, 1996).

Fig. 3 shows that water of crystallization escapes during the process. The initial water content of the agglomerates was 4.1–4.2% dependent on the water content of the PEG (cf. Table 1). As can be seen, the evaporation of water is increased by a lower binder viscosity. A lower binder viscosity gives rise to a higher energy input (Fig. 4a). This is due to a higher surface plasticity of the agglomerates which causes a higher power consumption of the impeller motor (Schæfer et al., 1992b). Since the energy input is converted into heat of friction within the mass, a lower binder viscosity will result in a higher product temperature (Fig. 4b) in accordance with previous results (Schæfer et al., 1990, 1992a). The evaporation of water of crystallization is augmented by the higher product temperature, and this is why the evaporation depends on the binder viscosity.
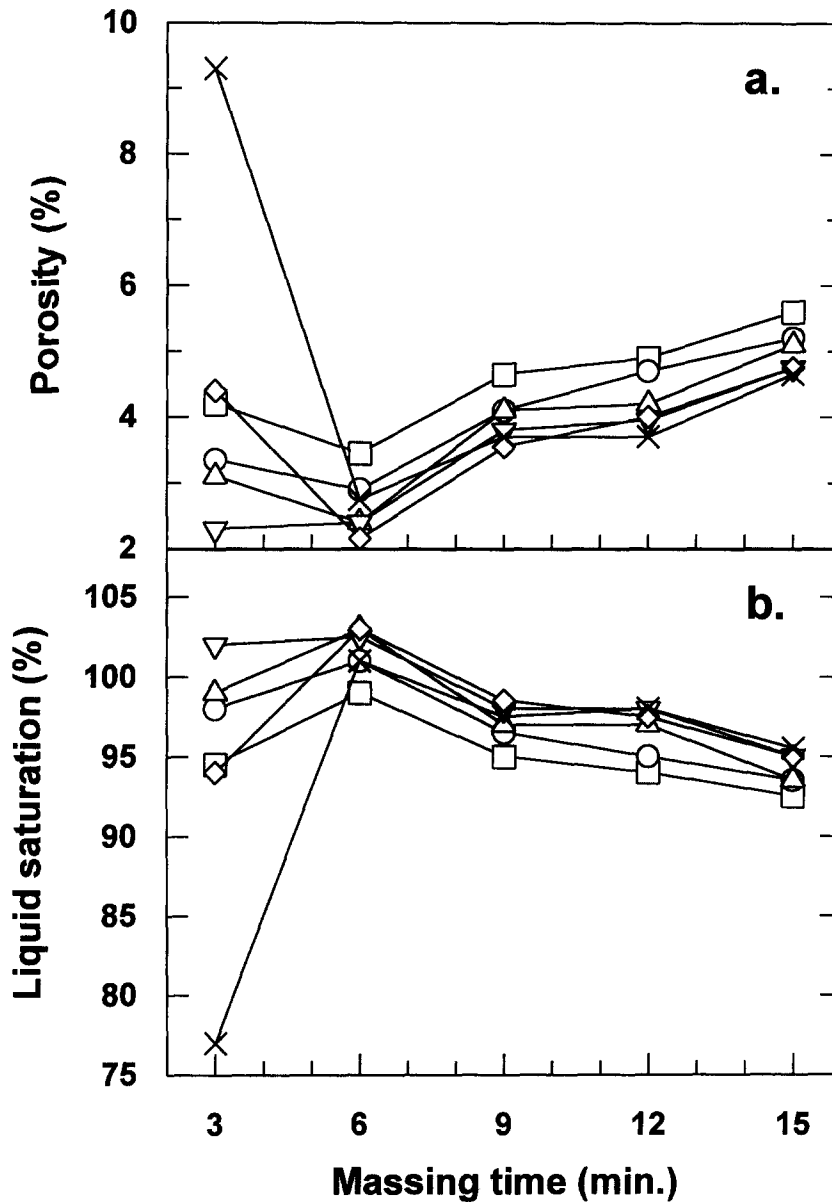
Fig. 2. Effect of type of PEG on the intragranular porosity (a) and the liquid saturation (b) during massing. Starting material: lactose monohydrate. (□) PEG 2000; (○) PEG 3000; (△) PEG 6000; (▽) PEG 8000; (◇) PEG 10000; (×) PEG 20000.

The rise in product temperature is counteracted by a cooling caused by the evaporation of water. This cooling is most pronounced when the evaporation rate is high. That explains why the differences in energy input are not reflected directly in the product temperature after 6 min of massing.

Because of the high impeller speed, a marked rise in the product temperature is observed during the process, and this will cause a pronounced fall in the binder viscosity (cf. Table 2).

The fall in the liquid saturation (Fig. 2b), caused by the evaporation of water of crystalliza-
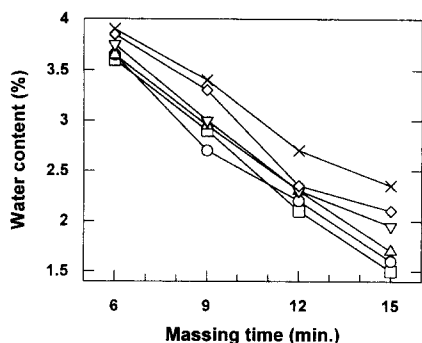
Fig. 3. Effect of type of PEG on the water content of the agglomerates during massing. Starting material: lactose monohydrate. (□) PEG 2000; (○) PEG 3000; (△) PEG 6000; (▽) PEG 8000; (◇) PEG 10000; (×) PEG 20000.

tion, explains why no agglomerate growth occurs between 12 and 15 min of massing (Fig. 1a). The fact that more water evaporates at a lower binder viscosity complicates the interpretation of the effect of binder viscosity on the agglomerate growth since the agglomerate growth will be counteracted to a larger extent at a lower viscosity.
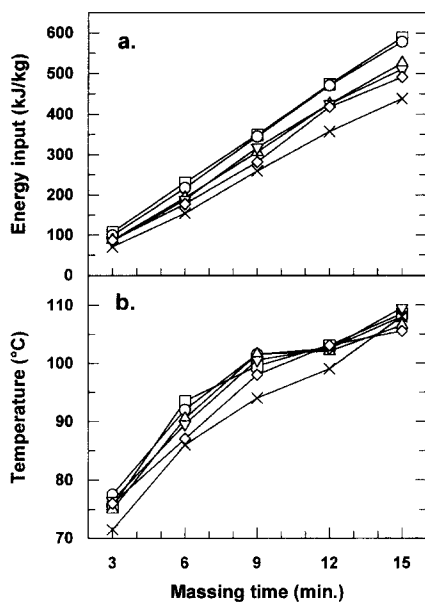

Fig. 4. Effect of type of PEG on the cumulative energy input (a) and the product temperature (b) during massing. Starting material: lactose monohydrate. (□) PEG 2000; (○) PEG 3000; (△) PEG 6000; (▽) PEG 8000; (◇) PEG 10000; (×) PEG 20000.
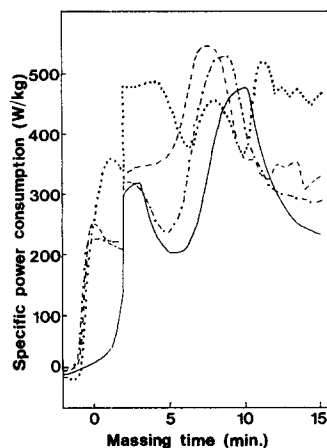

Fig. 5. Effect of type of PEG on the specific power consumption during massing. Starting material: lactose monohydrate. (· · ·) PEG 2000; (- - -) PEG 6000; (-- · --) PEG 10000; (———) PEG 20000.

The agglomerate growth was previously found to be reflected in the power consumption of the impeller motor (Schæfer et al., 1992b; Schæfer, 1996). Fig. 5 shows the changes in power consumption during experiments with four types of PEG. It is clearly seen that the rise in power consumption is delayed at a higher viscosity. This indicates that the distribution of the binder and the densification of the agglomerates are more difficult, the higher the viscosity. In the case of PEG 20000, a steep increase in the power consumption occurs between 6 min and 9 min corresponding to the marked increase in agglomerate growth rate seen at the same time (cf. Fig. 1a). Distinct peaks are seen on the power consumption curves except for PEG 2000. The fall in power consumption is ascribed to the evaporation of water of crystallization, which gives rise to a reduced surface plasticity of the agglomerates. The peak is seen to appear later when the viscosity is higher, because the evaporation is delayed at a high viscosity owing to a lower product temperature.

Knight (1993) studied the granule growth kinetics in melt granulation experiments in a high shear mixer with a binder of a low viscosity, and found that the growth was described by zero order kinetics, i.e. the granule size increased linearly with

Table 5
The results of regression analysis of the linear correlation between time (t, min) and mean granule size (d_{gw}, μm):
$d_{gw} = a + t \times b$

PEG	Mean viscosity (mPa·s)	a (μm)	b (μm/min)	Correlation coefficient
2000	51	348	47	0.989
3000	112	278	51	0.981
6000	473	254	45	0.987
8000	799	255	54	0.913
10000	2570	185	59	0.941
20000	14 700	148	67	0.956

Time interval: 3–12 min. Starting material: lactose monohydrate.

time. In order to evaluate if the growth kinetics in the present experiments was of zero order or of first order, regression analysis was carried out of the linear correlation between time and mean granule size (Table 5) and between time and log mean granule size (Table 6). The results at 15 min are omitted from the regression analysis, since the agglomerate growth between 12 min and 15 min of massing is markedly counteracted by the evaporation of water of crystallization. The mean viscosities stated in Table 5 are the mean values of the viscosities corresponding to the product temperatures at 6 min and 9 min.

Neither the linear model (Table 5) nor the exponential model (Table 6) was rejected by the regression analysis except for PEG 20000, which gave rise to rejection of both models. The rather high standard deviation on the mean granule size (cf. Table 4) explains why it is impossible to decide if the growth kinetics is of zero order or of

Table 6
The results of regression analysis of the linear correlation between time (t, min) and log mean granule size (d_{gw}, μm): log $d_{gw} = \log a + t \times \log b$

PEG	a (μm)	%/min	Correlation coefficient
2000	405	7.2	0.985
3000	357	8.1	0.991
6000	319	8.0	0.993
8000	319	9.5	0.916
10000	284	10.3	0.960
20000	268	11.5	0.960

Time interval: 3–12 min. The percentage increase in d_{gw} per min (%/min) is calculated on the basis of the constant b. Starting material: lactose monohydrate.

first order. In the case of PEG 20000, the viscosity is so high that the agglomerate growth becomes atypical, and, therefore, none of the models can be used for a description of the growth.

It appears from the correlation coefficients in Tables 5 and 6 that the correlation becomes better at the low viscosities, and that the exponential model gives rise to a slightly better correlation than the linear model. The value, a, obtained from the regression lines is the size of the granules at time zero (Knight, 1993). The agglomerate growth rate is expressed in μm/min (Table 5) or in %/min (Table 6). Both models show that a higher binder viscosity results in a smaller initial granule size. This is due to a more difficult distribution of the binder as mentioned above. When the distribution of the binder is finished, however, a higher viscosity is seen to increase the agglomerate growth rate according to Eq. (2). These counteracting effects of binder viscosity on granule size are the cause of the unclear effect of binder viscosity on the final granule sizes in Fig. 1a.

The adhesion of material to the bowl was slightly increased during the process and varied between 6% and 10% at 15 min of massing. The adhesion was significantly greater ($P < 0.001$) at a higher viscosity indicating that the adhesion forces are related to the binder viscosity in accordance with previous results (Ugri-Hunyadvári, 1975a,b; Massoud and Bauer, 1989).

The shape of the pellets was characterized by the aspect ratio (ratio of length to width), which is a suitable measure of the shape, provided that the pellets show a smooth surface (Lindner and Kleinebudde, 1994). This was the case in the

Fig. 6. SEM photographs of pellets produced from lactose monohydrate. Massing time: 15 min. Binder: PEG 2000 (a); PEG 20000 (b).

present experiments as illustrated in Fig. 6. Table 7 shows that the pellets become more spherical (P < 0.001), and that the variation in shape is lower (P < 0.001) when the binder viscosity is lower. The higher surface plasticity at lower viscosity makes the rounding of the agglomerates easier. Fig. 6 shows the difference in shape between pellets produced with PEG 2000 and PEG 20000 respectively. The aspect ratios of the pellets produced with PEG 2000 and PEG 3000 are lower than, or similar to the optimum aspect ratios of pellets previously produced by extrusion/ spheronization (Kleinebudde, 1994; Kleinebudde et al., 1994; Lindner and Kleinebudde, 1994).

4.2. Experiments with anhydrous lactose

The effect of binder viscosity was further investigated in a few complementary experiments with anhydrous lactose in order to avoid agglomerate growth being affected by evaporation of water of crystallization. The results are shown in Table 8.

The mean granule size shows a minimum with PEG 6000 and PEG 8000. The PEGs of lower as well as higher viscosities give rise to a larger granule size. The same tendency, although less clear, was seen in the experiments with lactose monohydrate. A higher binder viscosity causes a narrower size distribution and a larger amount of lumps with anhydrous lactose. The opposite effect of binder viscosity was observed with lactose monohydrate (Fig. 1b,c). The anhydrous lactose generally gives rise to a wider size distribution and to a smaller amount of lumps than lactose monohydrate. In the experiments with PEG 2000, the amount of fines smaller than 250 μm was found by sieve analysis to be about 2%, and fine particles were seen to adhere to the surface of the pellets. Practically no fines were observed in the experiments with lactose monohydrate and in the other experiments with anhydrous lactose.

The strength of the agglomerates produced with anhydrous lactose is lower than the strength of

Table 7
Effect of the type of PEG on the aspect ratios of the pellets estimated by image analysis

PEG	Aspect ratio
2000	1.093 (0.083)
	1.093 (0.071)
3000	1.105 (0.079)
	1.100 (0.072)
6000	1.141 (0.097)
	1.143 (0.095)
8000	1.169 (0.115)
	1.182 (0.109)
10000	1.282 (0.171)
	1.233 (0.149)
20000	1.287 (0.182)
	1.294 (0.188)

Results of repeated experiments are shown with standard deviations in parantheses. Starting material: lactose monohydrate. Massing time: 15 min.

Table 8
Results of the repeated experiments with anhydrous lactose and different types of PEG

Dependent variable	PEG				
	2000	3000	6000	8000	10000
d_{gw} (μm)	973	1163	860	853	1142
	1250	1147	766	819	1104
s_g	1.85	1.43	1.44	1.47	1.34
	1.53	1.46	1.45	1.48	1.33
Lumps (%)	0.3	0.4	0.6	1.3	1.5
	0.6	0.4	0.5	1.4	1.8
Porosity (%)	1.1	1.3	1.2	1.1	1.5
	1.3	1.3	1.2	1.3	1.4
Liquid satur. (%)	111	109	110	110	108
	110	110	110	109	109
Energy input (kJ/kg)	392	378	320	321	339
	398	376	327	328	330
Product temp. (°C)	118	114	111	109	109
	120	116	—	111	112
Aspect ratio	1.164	1.120	1.132	1.140	1.183
	1.161	1.116	1.138	1.132	1.181

Massing time: 12 min.

those produced with lactose monohydrate, because anhydrous lactose has a larger initial particle size (Rumpf, 1962). Agglomeration is a balance between comminution and growth. The weaker the agglomerates, the more comminution will occur. This is why the size distribution becomes wider, and the amount of lumps becomes lower when anhydrous lactose is used instead of monohydrate. The experiments with anhydrous lactose indicate that the strength of the agglomerates is increased by a higher viscosity since less fines, more lumps, and a narrower size distribution are obtained at increasing binder viscosity. This effect is not seen with lactose monohydrate, because the agglomerate strength is high enough to resist comminution at all the binder viscosities examined.

The intragranular porosities of the agglomerates produced with anhydrous lactose are not affected by an evaporation of water of crystallization. The porosities shown in Table 8 are, therefore, lower than those seen in Fig. 2a. The liquid saturations in Table 8 exceed 100% indicating that free binder liquid is present on the surface of the agglomerates. This is because the liquid saturation has to be high in order to promote an agglomer-

ate growth by coalescence, which is sufficient to overcome the tendency to comminution.

The cumulative energy input at 12 min of massing is lower with anhydrous lactose than with lactose monohydrate, because the particles of anhydrous lactose are less cohesive owing to a larger size. Nevertheless, the product temperature becomes higher, because the agglomerates of anhydrous lactose are not cooled by an evaporation of water of crystallization.

The aspect ratios show that the most spherical pellets are obtained with the PEG 3000. The pellets become less spherical at higher viscosities in accordance with the results in Table 7. The effect of binder viscosity on the sphericity is, however, less pronounced with anhydrous lactose, because the agglomerates are more deformable owing to a higher liquid saturation. With the PEG 2000, the lower agglomerate strength causes a deformability that is too high to resist the shearing forces, and this makes the pellets less spherical.

Since the agglomerate growth is reflected in the power consumption of the impeller motor, the power consumption curve gives an indirect indication of the agglomerate growth during the pro-

cess. Fig. 7 shows that the increase in power consumption is delayed at a higher viscosity in accordance with Fig. 5. No fall in power consumption is seen in Fig. 7, because no water of crystallization evaporates. The differences between the power consumption curves in Fig. 7 clearly indicate that a low binder viscosity results in a high initial agglomerate growth followed by a rather low agglomerate growth rate, whereas a high binder viscosity gives rise to a low initial growth and a subsequent high growth rate. This means that the effect of binder viscosity on agglomerate formation and growth is fundamentally the same with lactose monohydrate and anhydrous lactose.

5. Conclusions

A higher binder viscosity will increase the viscous contribution to the force of the dynamic pendular liquid bridges, and this will increase the potential for agglomerate growth by coalescence. However, a higher viscosity will decrease the deformability of the agglomerates simultaneously, and this will reduce the potential for growth. The effect of viscosity on agglomerate growth will depend on the balance between these counteracting effects.
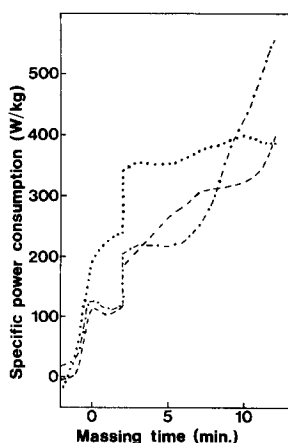

Fig. 7. Effect of type of PEG on the specific power consumption during massing. Starting material: anhydrous lactose. (· · ·) PEG 2000; (- - -) PEG 6000; (– · –) PEG 10000.

This balance is affected by the process variables as well as the other product variables. Thus, the effect of binder viscosity on agglomerate growth interacts with the impeller speed. Impeller speed has to be extremely high in order to counteract an uncontrollable growth if the binder viscosity exceeds an upper critical limit. This limit was found to be of the order of magnitude of 1000 mPa·s in the present experiments.

The effect of the binder viscosity is further affected by the initial particle size of the solid material. If the agglomerate strength is low owing to a large particle size, the amount of fines will be increased, and the size distribution will be widened at a low viscosity. This indicates that the agglomerate strength is augmented by an increasing viscosity.

The distribution of a highly viscous binder is difficult, and this causes a smaller initial growth at an increasing viscosity. From the moment when the distribution is finished, the viscous contribution to the force of the liquid bridges will dominate, and this results in a higher agglomerate growth rate at a higher viscosity. These effects of viscosity are reflected in the power consumption signal from the impeller motor. The agglomeration theory of Ennis et al. (1991) was found to be suitable for a qualitative description of the effect of binder viscosity on the agglomerate growth.

The surface plasticity of the agglomerates becomes lower at a higher viscosity, and this results in agglomerates of an irregular shape. If the binder viscosity is too low, however, the deformability of the agglomerates becomes so high that the pellets become elongated owing to the shearing forces. Therefore, the optimum binder viscosity for the production of spherical agglomerates will depend on the agglomerate strength as well as the impeller speed.

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