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Melt pelletization in a high shear mixer.
VII. Effects of product temperature

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Abstract

Lactose monohydrate, anhydrous lactose and anhydrous dicalcium phosphate were melt pelletized in an 8-l high shear mixer using polyethylene glycol (PEG) 3000 or 6000 as meltable binder. The temperature of the heating jacket was varied at two levels giving rise to different product temperatures. The agglomerate growth was affected by the product temperature because a higher temperature caused a lower binder viscosity, a thermal expansion of the binder liquid and more evaporation of water of crystallization. The possibility of controlling the process and the quality of the resulting pellets were found to depend on the physical properties of the materials.

Keywords: Product temperature; Polyethylene glycols; Binder viscosity; Water of crystallization; Melt pelletization; High shear mixer

1. Introduction

By melt granulation or pelletization in high shear mixers, the temperature of the product during the process depends on the energy input owing to the impeller rotation and the heat balance between the heat flow from the heating jacket and the loss of heat to the surroundings. Large differences in temperature are seen because the product temperature is markedly influenced by massing time and impeller speed (Flanders et al., 1987; Schæfer et al., 1992a; Schæfer et al., 1993b). The final product temperature might attain 120–130°C.

The product temperature is likely to affect the agglomeration process because both the density and the viscosity of the molten binder is temperature dependent. The viscosity of the binder liquid might influence the distribution of the binder (Kinget and Kemel, 1985), the granule consolidation and coalescence rate (Ennis et al., 1991) and the deformability of the agglomerates (Schæfer et al., 1992a).

Kinget and Kemel (1985) found no effect of varying the jacket temperature between 60°C and 70°C, probably because of the rather small varia-

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Table 1
Physical properties of the materials

Materials	M.D. (μm)	Span	Tr.D. (g/cm^3)	S.A. (m^2/g)
Lactose monohydrate	19	2.3	1.55	0.67
Anhydrous lactose	6.5	2.1	1.61	1.49
Anhydrous dicalcium phosphate	17	1.7	2.91	1.12

M.D., median particle diameter; Tr.D., true density; S.A., BET surface area.

tion in temperature. Thomsen et al. (1993) reduced the product temperature by discharging the product for cooling before a final massing in the mixer. This cooling reduced the potential for agglomerate growth and gave rise to smoother pellets with a lower release rate, most likely because of a partly solidification of the binder.

The product temperature might further affect thermolabile materials. In previous experiments with lactose monohydrate, the water of crystallization was seen to evaporate at product temperatures about 100°C (Schæfer et al., 1992a; Schæfer et al., 1992b; Schæfer et al., 1993b). It was assumed that this evaporation might increase the agglomerate growth rate.

The purpose of the present work was to elucidate the effect of the product temperature on the agglomerate growth during a melt pelletization process. Experiments at different temperatures of the heating jacket of the mixer were carried out.

2. Materials and methods

2.1. Materials

Lactose 450 mesh (α-lactose monohydrate, DMV, The Netherlands), anhydrous lactose (Pharmatose DCL 21, DMV, The Netherlands) and anhydrous dicalcium phosphate (Budenheim, Germany) were used as starting materials. The same batch of the anhydrous lactose was used in previous experiments (Schæfer, 1996).

Polyethylene glycol (PEG) 3000 and 6000 (Hoechst, Germany) were used as meltable binders. PEG 3000 was used as flakes from two different batches. Batch 1 was applied for the experiments with the lactose monohydrate and batch 2 for the experiments with the anhydrous lactose and the anhydrous dicalcium phosphate. Three different batches of PEG 6000 were used. Batch 1 and 3 were powders, and batch 2 was a fine powder identical to that used in previous experiments (Schæfer, 1996). Batch 1, 2 and 3 were applied for the experiments with the lactose monohydrate, the anhydrous lactose and the anhydrous dicalcium phosphate, respectively.

The size distributions by volume of the starting materials were determined by a Malvern 2601Lc laser diffraction particle sizer (Malvern Instruments, UK). The values of the median particle diameter and the span are shown in Table 1. The span is defined as the difference between the diameters at the 90 and the 10% points relative to the median diameter.

The true densities of the materials were determined by an AccuPyc 1330 gas displacement pycnometer (Micromeritics, USA) using helium purge. The BET multipoint surface areas were determined by a Gemini 2375 Surface Area Analyzer (Micromeritics, USA). The results are shown in Table 1.

The melting range of the PEGs was estimated by a Perkin Elmer DSC 7 differential scanning calorimeter (Perkin Elmer, USA). A sample of about 4 mg was sealed in a 40-μl aluminium pan and scanned between 40°C and 80°C at a heating rate of 2°C per min. The melting range of the PEG 3000 was found to be 47–60°C with a peak temperature of 58°C (batch 1) and 46–59°C with a peak temperature of 57°C (batch 2). The PEG 6000 had a melting range of 50–61°C (batch 1), 54–63°C (batch 2) and 49–62°C (batch 3) with peak temperatures of 60°C, 61°C and 61°C, respectively.

Table 2
The effect of temperature on the viscosities (mPa.s) of the molten PEGs. The values in the parentheses are extrapolated values

	Temperature, °C						
	60	70	80	90	100	110	120
PEG 3000	296	198	158	119	(88)	(66)	(49)
PEG 6000	1235	869	632	474	(343)	(250)	(182)

The viscosities of the molten PEGs were estimated at 60°C, 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 64 rpm are presented in Table 2. The correlation between the temperature and the logarithm of the viscosity was found to be linear with correlation coefficients of −0.994 (PEG 3000) and −0.999 (PEG 6000). Viscosity values at 100°C, 110°C and 120°C were extrapolated by means of the regression lines.

2.2. 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., 1993a), was used in the experiments. The starting temperature of the heating jacket was set to 50°C in all the experiments.

2.3. Mixing procedure

The load of the mixer was 1 kg in the case of the lactose monohydrate or the anhydrous lactose and 1.3 kg in the case of the anhydrous dicalcium phosphate. Varying amounts of PEG were added in a solid state. The concentration of the PEG is expressed as the percentage (% m/m) of the amount of the starting material.

In all the experiments, the starting material and the PEG were dry mixed at an impeller speed of 1300 rpm. The impeller speed was decreased 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 impeller speed was decreased to 1200 rpm in the experiments with the lactose monohydrate, to 900 rpm in the experiments with the anhydrous lactose and to 800 rpm in the experiments with the anhydrous dicalcium phosphate. At the same time, the setting of the jacket temperature was either increased to 120°C or kept at 50°C.

At the end of the process, the amount of agglomerates which flowed from the bowl when tilted was sieved as mentioned below and then spread out in thin layers on trays in order to cool at ambient temperature.

2.4. Granule characterization

2.4.1. Size distribution

The amount of lumps larger than 4 mm, the geometric mean diameter (d_{gw}), and the geometric standard deviation (s_g) were estimated as previously described (Schæfer, 1996).

2.4.2. 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). In the calculation of the liquid saturations, a correction was made for changes in the volume of binder liquid caused by changes in product temperature during the process. The volume of binder liquid was estimated on the basis of data on the densities of the molten PEGs at varying temperatures (Hoechst, 1992). In the experiments with the lactose monohydrate, the size fraction 500–2000 μm was used for the measurements of the porosity. In the experiments with the anhydrous lactose and the anhydrous dicalcium phosphate, a size fraction including the three sieve fractions being closest to the mean diameter was used in order to obtain a representative sample. All results are mean values of two estimations.

2.4.3. *Water content*

The water content on a wet-weight basis was estimated by volumetric titration at 50°C with a Karl Fischer Titrator 701 KF Titrino (Metrohm, Switzerland). Hydranal® Composite 5 (Riedel-de Haën, Germany) was used as the titrant, and methanol as the working medium. A sample of about 700 mg from the size fraction 500–2000 μm was used for the measurements. The sample was ground for 30 sec in a small coffee grinder before the titration. All results are mean values of three titrations.

2.4.4. *Scanning electron microscopy*

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

2.5. *Experimental design*

A series of 32 factorially-designed experiments was carried out with the lactose monohydrate, the anhydrous lactose as well as the anhydrous dicalcium phosphate. The jacket temperature was varied at two levels (50°C and 120°C), two binders were used (PEG 3000 or PEG 6000), and the massing time was varied at four levels. The levels of massing time were 6, 9, 12 and 17 min with the lactose monohydrate, 8, 11, 14 and 17 min with the anhydrous lactose and 7, 10, 13 and 16 min with the anhydrous dicalcium phosphate. All experiments were carried out in duplicate, and the results shown in this paper are mean values of two experiments unless otherwise stated. The data were analysed by analysis of variance. The results of the experiments with the anhydrous lactose at a jacket temperature of 50°C were presented in a previous paper (Schæfer, 1996).

3. Results and discussion

3.1. *Product temperatures*

Fig. 1 shows the effect of jacket temperature on the product temperature during massing in the experiments with the lactose monohydrate (Fig. 1a), the anhydrous lactose (Fig. 1b) and the anhydrous dicalcium phosphate (Fig. 1c). At a jacket temperature of 50°C, the product temperature exceeds 50°C during dry mixing, i.e. the increase in the product temperature after the melting of

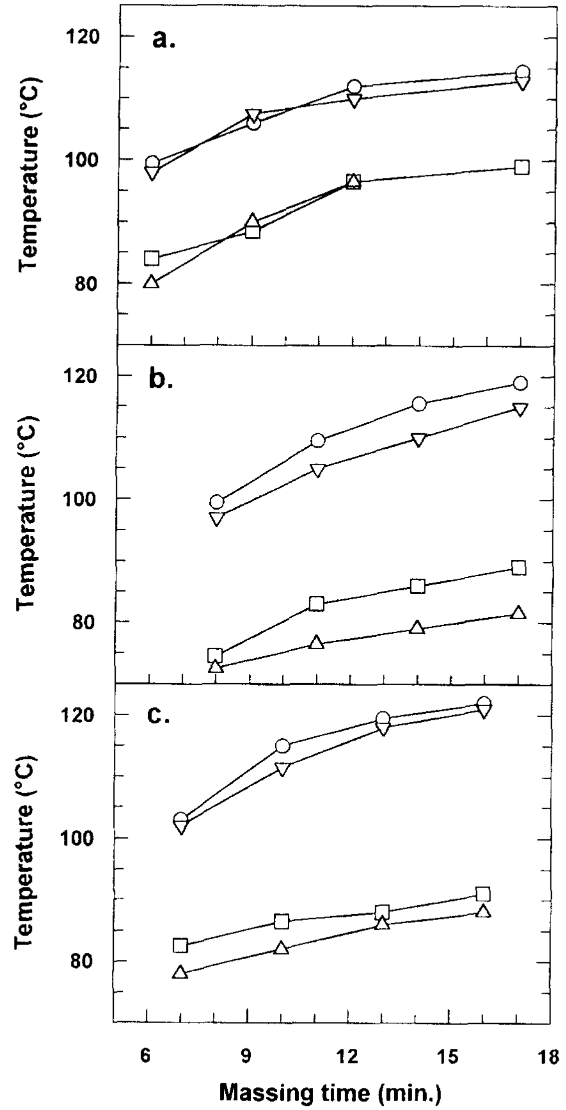

Fig. 1. Effects of jacket temperature and type of PEG on the product temperature during massing. (a) lactose monohydrate; (b) anhydrous lactose; (c) anhydrous dicalcium phosphate. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

the binder is caused by frictional heat owing to the impeller solely. As can be seen, the difference in jacket temperature causes a marked difference in product temperature.

Because of differences in frictional heat between the materials, the impeller speed was chosen to be 1200 rpm (lactose monohydrate), 900 rpm (anhydrous lactose) and 800 rpm (anhydrous dicalcium phosphate) in order to keep the maximum product temperature at about 120°C.

The binder concentration had to be markedly different in order to produce pellets from the different materials. These differences in binder concentration are partly explained by the different densities of the materials. The binder concentrations 23% m/m (lactose monohydrate), 29% m/m or 30.5% m/m (anhydrous lactose) and 11% m/m (anhydrous dicalcium phosphate) correspond to 35.6% m/v, 46.7% m/v, 49.1% m/v and 32.0% m/v, respectively. The higher binder concentration necessary for agglomeration of the anhydrous lactose is ascribed to the smaller particle size, which makes it more difficult to densify the agglomerates. In the experiments with the anhydrous lactose, the concentration of the PEG 6000 had to be higher than that of the PEG 3000 in order to obtain agglomeration (Schæfer, 1996).

Previous experiments (Schæfer et al., 1992a) showed that PEG 3000 gave rise to a higher product temperature than did PEG 6000, and that an increase in binder concentration resulted in a higher temperature. Both effects were ascribed to an increased deformability of the agglomerates because of a lower viscosity and a higher liquid saturation respectively. Fig. 1a shows no significant effect of the type of PEG, whereas PEG 3000 in Fig. 1c results in a significantly ($P < 0.001$) higher temperature than does PEG 6000. Despite a lower binder concentration, the highest product temperature was obtained with PEG 3000 in the experiments with the anhydrous lactose (Fig. 1b).

3.2. Experiments with lactose monohydrate

The effects of jacket temperature on the mean granule size, the granule size distribution and the amount of lumps are presented in Fig. 2. At a jacket temperature of 50°C, PEG 6000 results in an uncontrollable agglomerate growth, which is seen as a high agglomerate growth rate (Fig. 2a), an atypical widening of the size distribution at prolonged massing (Fig. 2b) and a sudden increase in the amount of lumps between 9 and 12 min of massing (Fig. 2c). Experiments, therefore,

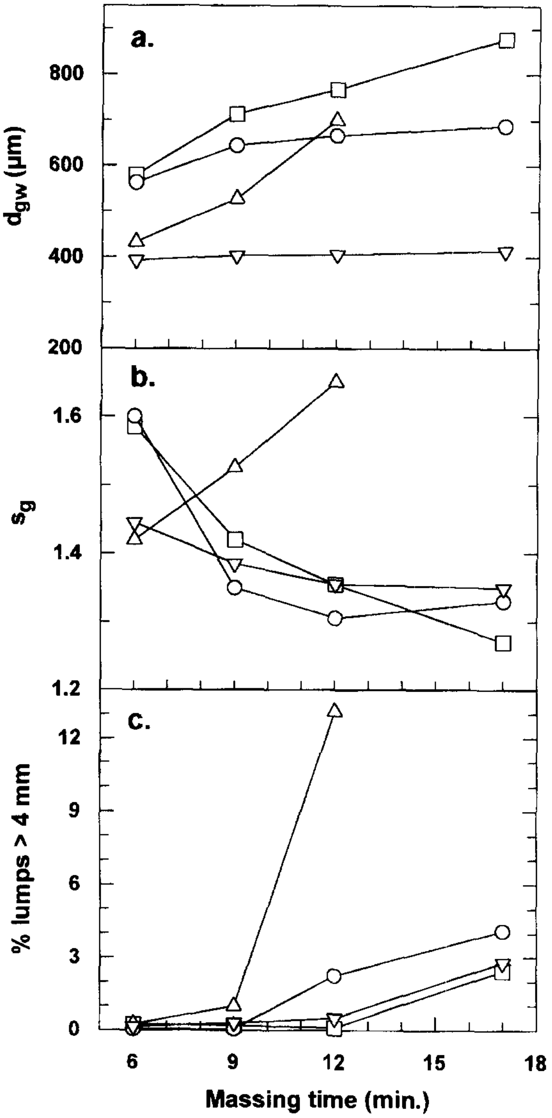

Fig. 2. Effects of jacket temperature and type of PEG on the mean granule size (a), the geometric standard deviation (b) and the amount of lumps (c) during massing. Starting material: lactose monohydrate. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

could not be carried out at a massing time of 17 min. The experiments with PEG 6000 at a jacket temperature of 120°C gave rise to only a slight agglomerate growth (Fig. 2a). The uncontrollable growth is explained by the higher viscosity of the PEG 6000 at the low temperature, which gives an increased potential for growth (Ennis et al., 1991).

Fig. 3 shows pellets produced with the PEG 6000 at the low and the high jacket temperature. It is seen that the surface of the pellets becomes smoother when the jacket temperature is increased, because the smoothing of the surface is favoured by the lower viscosity at the high temperature. With the PEG 3000, smooth pellets were obtained at both jacket temperatures because of the lower viscosity of the PEG 3000.

As can be seen in Fig. 2a, the PEG 3000 gives rise to a significantly ($P < 0.001$) larger mean granule size than does the PEG 6000. In previous experiments (Schæfer et al., 1992a), this effect was explained by an increased potential for agglomerate growth by coalescence owing to a higher deformability caused by the lower viscosity of the PEG 3000. Accordingly, it was to be expected that a higher jacket temperature would cause a larger mean granule size. The opposite effect is seen, however, since the mean granule size is significantly lower ($P < 0.001$) at the high jacket temperature.

A higher jacket temperature causes a significantly ($P < 0.01$) narrower size distribution (Fig. 2b), but this effect is primarily due to the abovementioned uncontrollable growth with PEG 6000 at the low jacket temperature. Apart from the large amount of lumps caused by the uncontrollable growth, no significant effect of jacket temperature and type of PEG on the amount of lumps is seen (Fig. 2c).

Previous experiments (Schæfer et al., 1990; Schæfer et al., 1992a; Schæfer et al., 1993b) showed a decrease in intragranular porosity because of densification at prolonged massing. It is surprising, therefore, to see in Fig. 4a that a jacket temperature of 120°C causes an increase in the porosity during massing. At a jacket temperature of 50°, a decrease in the porosity is seen until 12 min of massing after which the porosity becomes slightly higher. The porosity is significantly ($P < 0.001$) higher at the high jacket temperature. The effect of jacket temperature is most pronounced at a long massing time, which is reflected in a significant ($P < 0.001$) interaction. PEG 6000 gives rise to significantly ($P < 0.001$) higher porosities than PEG 3000 contrary to previous experiments (Schæfer et al., 1992a) where no effect of the type of PEG was found.

The changes in the intragranular porosity are reflected in the liquid saturation of the agglomerates (Fig. 4b). The decrease in liquid saturation corresponding to the increase in porosity is partly counteracted, however, by an expansion of the volume of binder liquid caused by the rise in temperature during massing. The uncontrollable growth in the experiments with the PEG 6000 at the low jacket temperature is seen to be caused by a sudden increase in the liquid saturation. In the other experiments, the liquid saturation decreases after 12 min of massing, and this is why only a slight agglomerate growth is seen in these experiments (cf. Fig. 2a).

It was found in previous experiments (Schæfer et al., 1992b) that evaporation of water of crystallization gave rise to very small holes in the surface of the agglomerates. SEM photographs of pellets from the present experiments showed similar holes, which might cause the observed increase in the porosity. In order to confirm this assumption, the water content of the agglomerates was estimated (Fig. 5). The initial water content of the mixture of lactose and PEG was 4.2%. The escape of water of crystallization commences at a product temperature between 80°C and 90°C. A rise in product temperature causes an increase in the evaporation of water of crystallization, and this is why a longer massing time and a higher jacket temperature give rise to a lower water content ($P < 0.001$). Thus, the unexpected effects of the massing time and the jacket temperature on the intragranular porosity seem to be caused by an evaporation of water of crystallization. The PEG 6000 results in less evaporation than does the PEG 3000 ($P < 0.001$). This is ascribed to the higher viscosity of the PEG 6000, which might delay the evaporation.

In order to further clarify the effect of evaporation of water of crystallization on the agglomerate

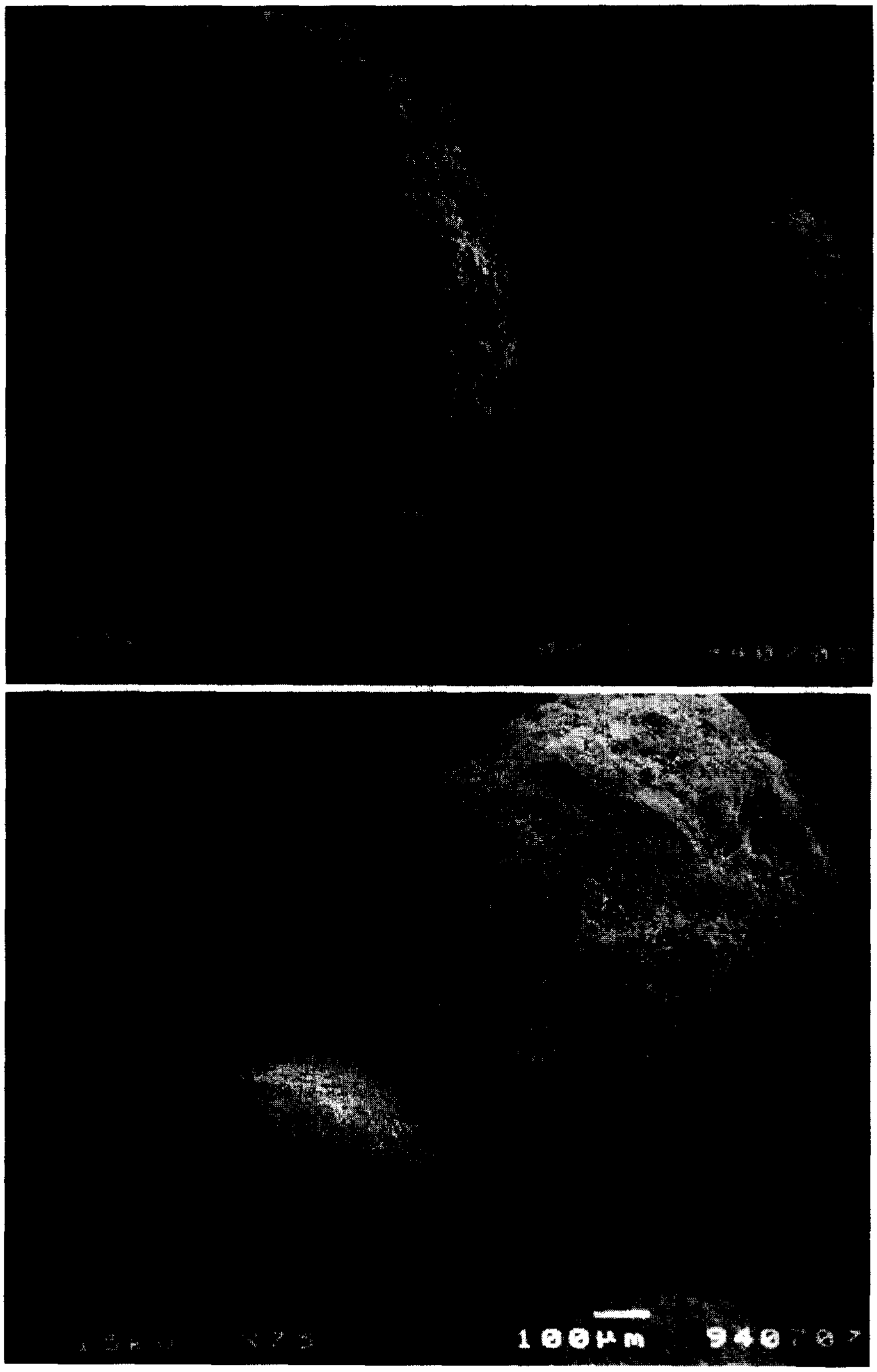

Fig. 3. SEM photographs of pellets produced from lactose monohydrate and PEG 6000. Jacket temperature: 50°C (a) and 120°C (b). Massing time: 12 min.

growth, complementary experiments were carried out with the lactose monohydrate after drying at 130°C for 24 h. By this drying, the water of crystallization became completely removed, and this caused the specific surface area of the lactose to increase from 0.67 m^2/g to 2.19 m^2/g. This confirms the assumption that the porosity of the agglomerates is increased by evaporation of water of crystallization.

Results of some of the experiments with the dried lactose are shown in Table 3. The binder concentration had to be increased to 30–32% in order to obtain an agglomeration similar to that seen in Fig. 2. Although the binder concentration is markedly increased, the liquid saturation does not exceed 100%. This further confirms that the agglomerate growth rate is decreased by the evaporation of water of crystallization.

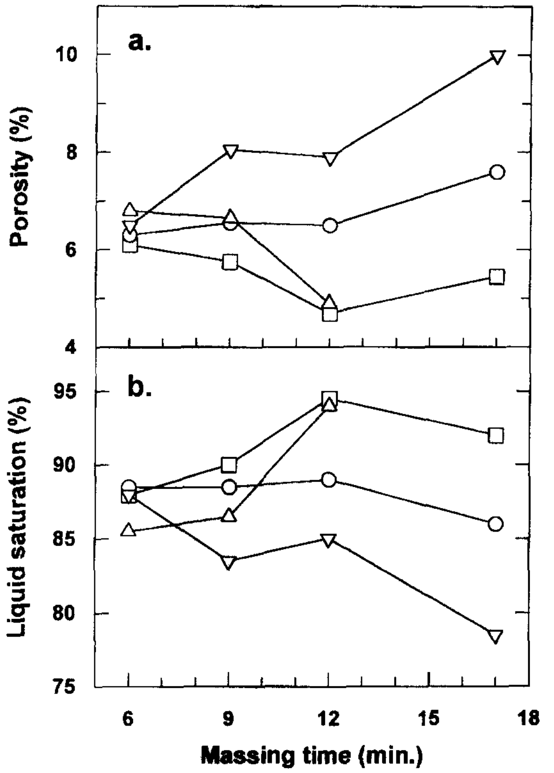

Fig. 4. Effects of jacket temperature and type of PEG on the intragranular porosity (a) and the liquid saturation (b) during massing. Starting material: lactose monohydrate. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

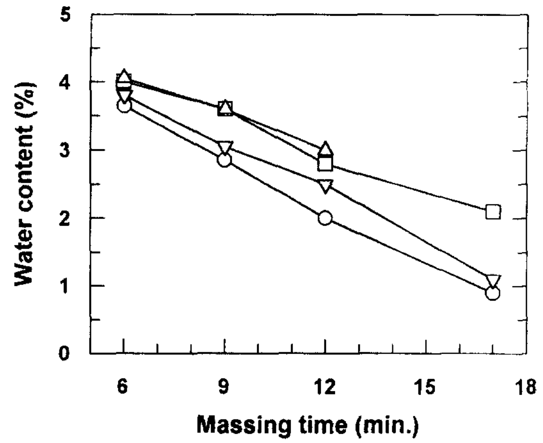

Fig. 5. Effects of jacket temperature and type of PEG on the water content of the agglomerates during massing. Starting material: lactose monohydrate. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

3.3. Experiments with anhydrous lactose

The jacket temperature was found to have a significant effect on the mean granule size with the PEG 3000 ($P < 0.01$) as well as with the PEG 6000 ($P < 0.001$). The effect was dependent on the type of PEG, however. As can be seen in Fig. 6a, the highest jacket temperature results in the largest mean granule size with the PEG 3000, whereas the opposite effect is seen with the PEG 6000.

With the PEG 3000, the jacket temperature had no significant effect on neither the geometric standard deviation nor the amount of lumps. With the PEG 6000, a higher jacket temperature caused a significantly ($P < 0.001$) narrower size distribution (Fig. 6b) and a significantly ($P < 0.01$) lower amount of lumps (Fig. 6c). The effect of jacket temperature with the PEG 6000 is similar to that seen in the experiments with the lactose monohydrate (Fig. 2b and c) since the low jacket temperature results in an increase in s_g and a marked increase in the amount of lumps early in the massing phase. The combination of the cohesive anhydrous lactose and the high viscosity of the PEG 6000 gives rise to an increased potential for agglomerate growth (Schæfer, 1996), which is

Table 3
Results of experiments with lactose monohydrate dried at 130°C for 24 h.

Binder conc. (% m/m)	Massing time (min)	d_{gw} (μm)	s_g	Lumps >4 mm (%)	Porosity (%)	Liquid satur. (%)
30	17	625	1.44	1.5	5.4	98
		658	1.42	1.7	6.0	96
32	11	1188	1.31	4.5	4.9	100
		1475	1.35	4.4	4.7	100

Mixer load: 1000 g of lactose monohydrate corresponding to 946 g of dried lactose. Binder: PEG 3000; jacket temperature: 50°C; impeller speed: 1200 rpm.

close to becoming uncontrollable at the low jacket temperature.

It is further seen that the PEG 3000 results in a narrower final size distribution and a lower amount of lumps than does the PEG 6000; this is because the viscosity of the PEG 3000 is lower. The lower viscosity at the high jacket temperature will increase the deformability of the agglomerates, and this will augment the tendency to a controlled agglomerate growth by coalescence. This explains why a higher jacket temperature gives rise to a larger mean granule size in the case of PEG 3000.

Prolonged massing results in the expected decrease in intragranular porosity (Fig. 7a). The PEG 6000 causes a lower porosity than does the PEG 3000. This was previously ascribed to the finer particle size of the PEG 6000 (Schæfer, 1996). The jacket temperature has no significant effect on the porosity with the PEG 3000, whereas the high jacket temperature gives rise to a significantly higher ($P < 0.01$) porosity with the PEG 6000. This effect is not obvious since a higher viscosity might be assumed to delay densification.

The jacket temperature had no significant effect on the liquid saturation of the agglomerates (Fig. 7b), because the higher porosity at the high jacket temperature was compensated for by an increased volume of binder owing to thermal expansion. As previously discussed (Schæfer, 1996), the liquid saturation has to slightly exceed 100% in order to obtain a deformability sufficiently high for agglomerate growth by coalescence, because the cohesiveness of the anhydrous lactose increases the strength of the agglomerates. This high liquid saturation results in formation of clusters of smaller agglomerates and makes it difficult to control the pelletization process.

3.4. Experiments with anhydrous dicalcium phosphate

A series of experiments was carried out with an anhydrous dicalcium phosphate in order to evaluate the effect of product temperature with an anhydrous material being less cohesive than the anhydrous lactose. Significant effects ($P < 0.001$) on the mean granule size were found of the massing time, the type of PEG as well as the jacket temperature. As can be seen in Fig. 8a, granule size is increased by prolonged massing, by a higher jacket temperature and by using PEG 3000 instead of PEG 6000. The effects of the type of PEG and the jacket temperature on the agglomerate growth are primarily explained by differences in viscosity. As discussed above, a lower viscosity will increase the deformability of the agglomerates and thus promote agglomerate growth by coalescence. Accordingly, an increasing growth rate is seen at decreasing viscosity. At 16 min of massing, large variations in mean granule size between repeated experiments and formation of clusters of smaller agglomerates occurred with the PEG 3000. This indicates an uncontrollable agglomerate growth.

A longer massing time results in a significantly ($P < 0.001$) narrower size distribution (Fig. 8b). Although the Figure indicates that a higher jacket temperature might give rise to a lower s_g value, this effect was not found to be significant.

The intragranular porosity becomes significantly ($P < 0.001$) lower at longer massing time, and the high jacket temperature gives rise to a significantly ($P < 0.05$) lower porosity than the low jacket temperature (Fig. 9a). The latter effect is assumed to be due to the lower viscosity at the high jacket temperature, which promotes the densification of the agglomerates. No significant effect of the type of PEG on porosity was found.

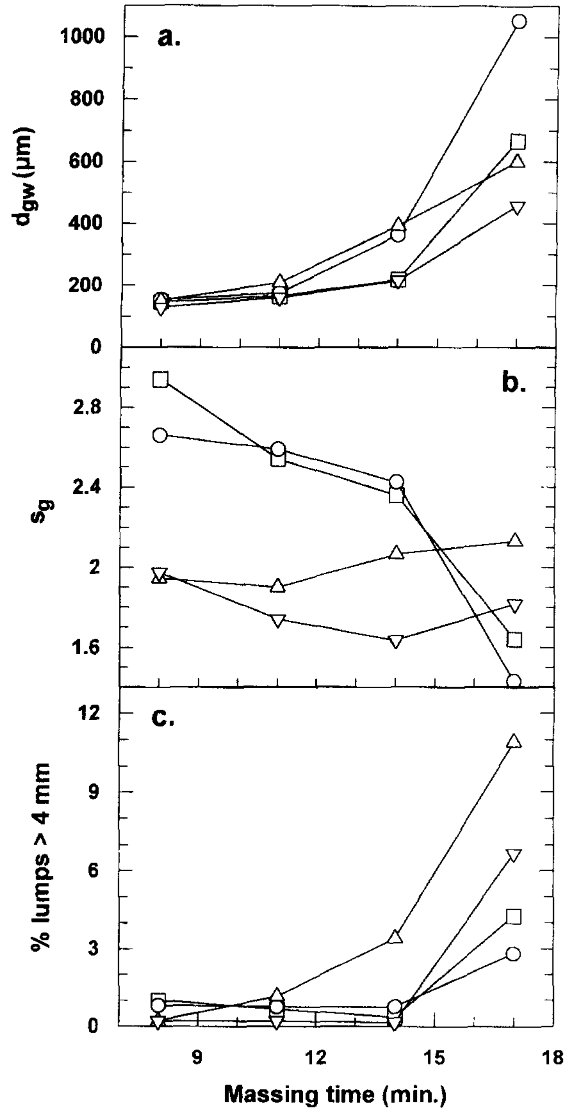

Fig. 6. Effects of jacket temperature and type of PEG on the mean granule size (a), the geometric standard deviation (b) and the amount of lumps (c) during massing. Starting material: anhydrous lactose. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

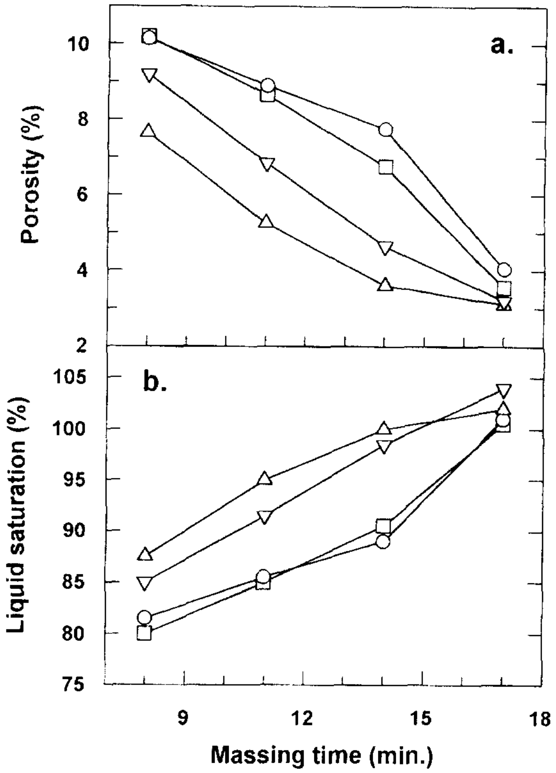

Fig. 7. Effects of jacket temperature and type of PEG on the intragranular porosity (a) and the liquid saturation (b) during massing. Starting material: anhydrous lactose. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

A higher jacket temperature results in a significantly ($P < 0.001$) higher liquid saturation owing to the lower porosity as well as the thermal expansion of the binder liquid. This will contribute to the above-mentioned effect of the jacket temperature on the mean granule size. Fig. 9b shows that the liquid saturation has to exceed 100% in order to obtain a marked agglomerate growth by coalescence. This explains why it is difficult to control the agglomeration of the anhydrous dicalcium phosphate. The density of the anhydrous dicalcium phosphate comes close to being twice that of the two lactose qualities (Table 1). This explains why the liquid saturation has to exceed 100% in order to obtain a sufficient agglomerate growth since the potential for agglomerate growth by coalescence is reduced at a higher density of the material (Ennis et al., 1991).

None of the variables had significant effect on the amount of lumps, which was below 1% in all the experiments except in one experiment with uncontrollable agglomerate growth. It was surprising that the PEG 6000 at the low jacket temperature gave rise to no formation of lumps since large amounts of lumps were formed in the similar experiments with the lactose monohydrate and the anhydrous lactose (Fig. 2c and 6c). The absence of lumps might be explained by a reduced agglomerate strength caused by a smaller amount of binder in the case of the anhydrous dicalcium phosphate. When the binder concentrations are expressed as the amount of PEG per surface area, the concentrations are 0.343 g/m^2 (lactose monohydrate), 0.195 g/m^2 or 0.205 g/m^2 (anhydrous lactose) and 0.098 g/m^2 (anhydrous dicalcium phosphate). The surface irregularities of the particles of the anhydrous dicalcium phosphate are assumed to cause an interlocking of the particles, which reduces the need of binder. Further, the higher density of the anhydrous dicalcium phosphate is supposed to reduce the potential for formation of lumps.

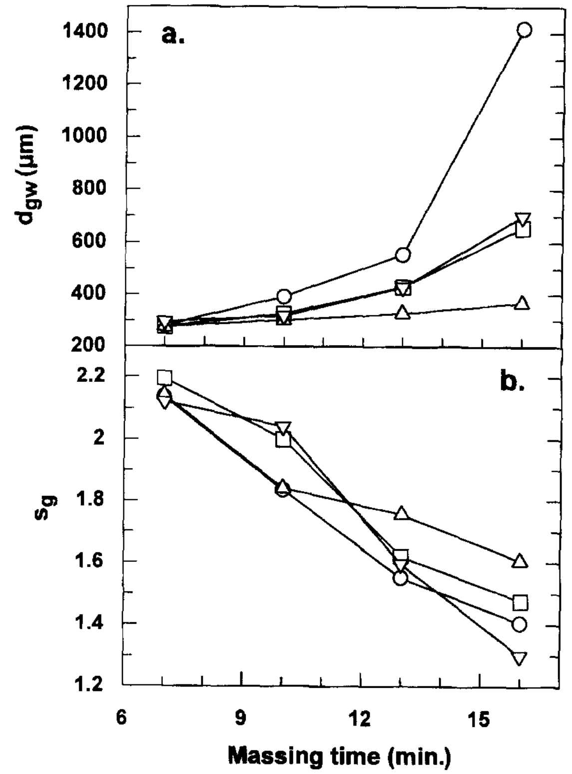

Fig. 8. Effects of jacket temperature and type of PEG on the mean granule size (a) and the geometric standard deviation (b) during massing. Starting material: anhydrous dicalcium phosphate. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

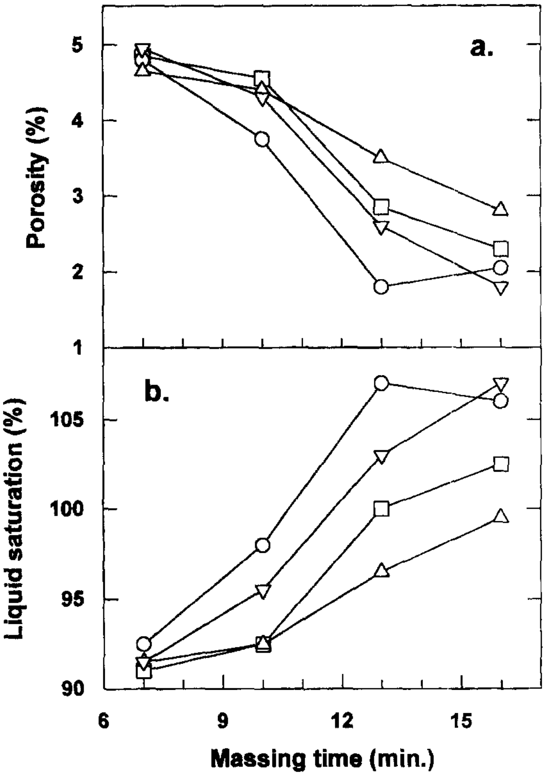

Fig. 9. Effects of jacket temperature and type of PEG on the intragranular porosity (a) and the liquid saturation (b) during massing. Starting material: anhydrous dicalcium phosphate. (□) PEG 3000, 50°C; (○) PEG 3000, 120°C; (△) PEG 6000, 50°C; (▽) PEG 6000, 120°C.

At the high jacket temperature, a pungent smell was observed when the lid was opened at the end of the experiments at massing times of 13 and 16 min. This smell was assumed to be caused by an escape of volatile aldehydes formed by a thermal decomposition of the PEG (Hoechst, 1992). The decomposition was supposed to be catalyzed by the dicalcium phosphate since the smell was not observed in the experiments with the two lactose qualities.

Fig. 10 shows pellets produced with the PEG 3000 at the low and the high jacket temperature. It is seen that the surface of the pellets becomes

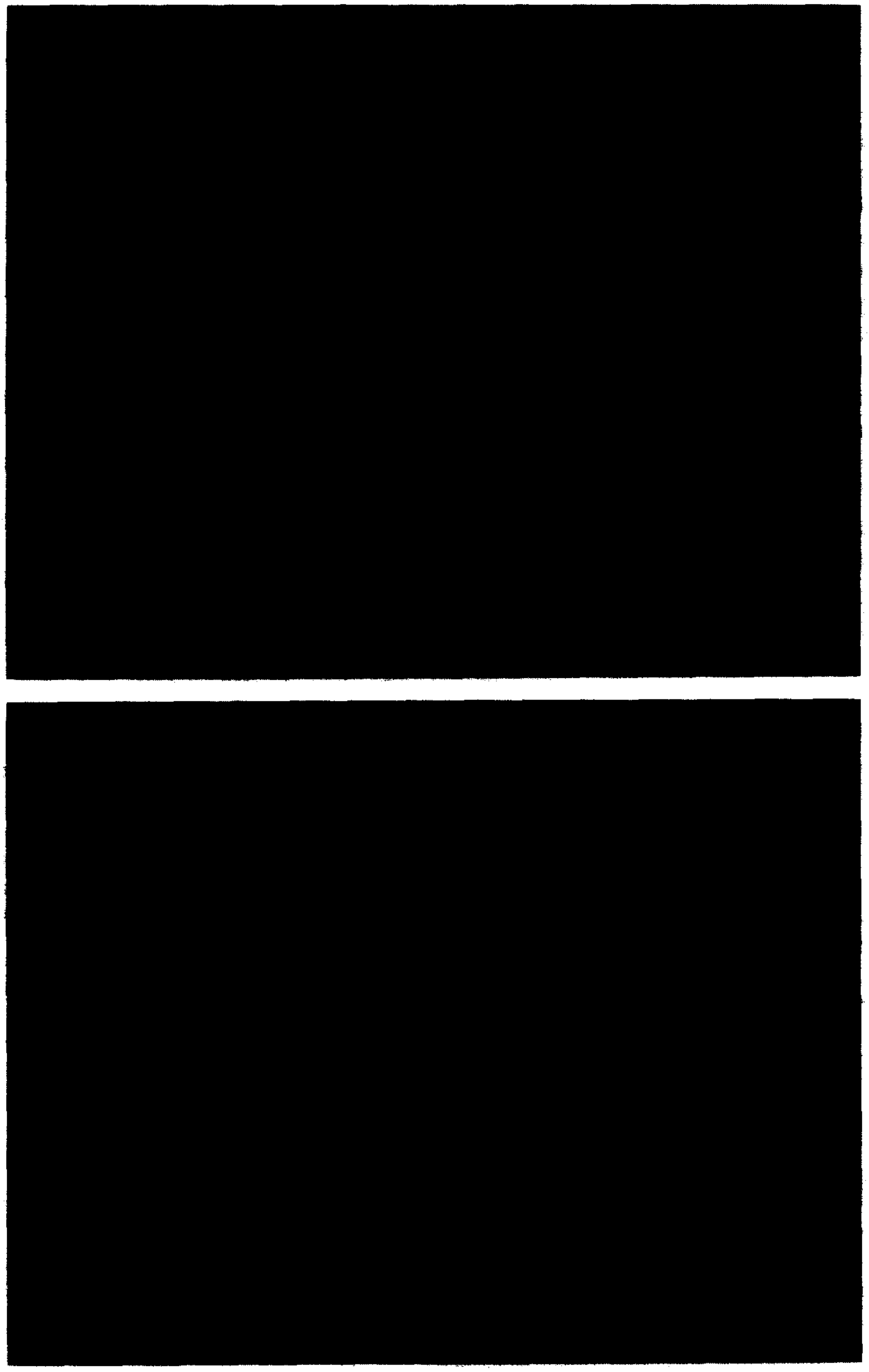

Fig. 10. SEM photographs of pellets produced from anhydrous dicalcium phosphate and PEG 3000. Jacket temperature: 50°C (a) and 120°C (b). Massing time: 16 min.

smoother at a higher jacket temperature. This is assumed to be due to a combination of a lower viscosity and a slightly higher liquid saturation at the high temperature.

4. Conclusions

A melt pelletization process is affected by the product temperature, because a higher temperature will decrease the viscosity of the molten binder and increase the volume of the binder liquid owing to thermal expansion. The lower viscosity will give rise to a higher deformability of the agglomerates and thus promote agglomerate growth by coalescence. The increase in the volume of binder liquid will cause a slight increase in the liquid saturation, which results in a slightly larger agglomerate size. The pellets were normally found to become smoother at a higher product temperature because of a combined effect of a lower viscosity and a higher liquid saturation.

If the viscosity exceeds an upper critical limit, however, the viscous contribution to the force of the dynamic pendular liquid bridges will markedly increase the potential for agglomerate growth by coalescence (Ennis et al., 1991). This will lead to a formation of lumps, which might be uncontrollable. The critical viscosity will depend on other factors influencing the potential for growth and/or affecting the strength of the agglomerates, e.g. the particle size and surface structure, the particle density, the amount of binder and the impeller speed. This explains why the viscosity of the PEG 6000 at the low jacket temperature exceeded the critical limit in the present experiments with the lactose monohydrate and the anhydrous lactose, but not in the experiments with the anhydrous dicalcium phosphate. The viscosity of the PEG 3000 was found to be below the critical limit independent of the jacket temperature.

A serious drawback of increasing the product temperature by a heating jacket is an augmented risk of thermal decomposition of the materials. At a product temperature of about 120°C, the PEG decomposed in a mixture with anhydrous dicalcium phosphate. When the product temperature exceeded about 80°C, water of crystallization started to evaporate from the lactose monohydrate. This evaporation was found to increase the surface area of the lactose and the intragranular porosity of the agglomerates and, consequently, the agglomerate growth became delayed. This might be convenient in order to control the agglomerate growth, but normally an uncontrollable escape of water of crystallization during the process is undesirable. Thus, it will be advantageous that a high shear mixer for melt pelletization is equipped with a jacket that is able to heat as well as to cool the product.

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