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Growth mechanisms in melt agglomeration with a low viscosity binder

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Abstract

Lactose monohydrate was melt agglomerated in an 8-l high shear mixer using stearic acid as meltable binder. The impeller speed was varied at six levels, and the temperature of the heating jacket was varied at three levels. The agglomerate growth mechanisms were found to be different from those observed in previous melt agglomeration experiments. This is attributed to the low viscosity of the molten stearic acid. A higher impeller speed and a higher jacket temperature resulted in an agglomerate growth that was markedly affected by comminution and accordingly gave rise to agglomerates of a wider size distribution and a higher porosity. A lower impeller speed and a lower jacket temperature resulted in smoother and more spherical agglomerates. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Binder viscosity; Comminution; Porosity; Melt agglomeration; High shear mixer; Agglomerate growth mechanisms

1. Introduction

Agglomerate growth proceeds by nucleation, growth by coalescence and/or by layering, and ball growth (Sherrington and Oliver, 1981). The growth represents a balance between size enlargement and size reduction (Kristensen, 1995; Tardos et al., 1997). In melt agglomeration processes, two mechanisms for nucleation, i.e. immersion and distribution, have been identified (Schæfer and Mathiesen, 1996a). The distribution mechanism was found to dominate at a low binder viscosity. The mechanisms for the subsequent size enlargement were found to be coalescence (Schæfer et al., 1992b; Knight, 1993), and eventually ball growth arising from an uncontrollable coalescence between agglomerates (Schæfer, 1996b; Schæfer and Mathiesen, 1996c). Size reduction caused by breakage of agglomerates is promoted if the strength of the agglomerates is low (Keningley et al., 1997) or the disruptive forces are high (Kristensen, 1995). The strength of the dynamic liquid bridge within an agglomerate is dominated by viscous forces (Mazzone et al., 1987). A low viscosity (Schæfer and Mathiesen, 1996c; Keningley et al., 1997) and a high porosity (Kristensen et al., 1985; Knight et al., 1998) reduce the strength of an agglomerate and make it more susceptible to comminution (Eliasen et al., 1998). Densification of agglomerates is promoted by high collisional

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forces (Ennis et al., 1991) and a low binder viscosity (Ennis et al., 1991; Schæfer and Mathiesen, 1996c; Keningley et al., 1997). However, if the strength of the agglomerates is low, high collisional forces will promote comminution of the agglomerates. A simultaneous agglomerate formation and comminution will inhibit the densification of the agglomerates (Eliasen et al., 1998).

Most of the previous studies on the agglomerate growth mechanisms involved in melt agglomeration in high shear mixers have been carried out with polyethylene glycols as meltable binders (Schæfer et al., 1992b; Knight, 1993; Schæfer and Mathiesen, 1996c). The rather high viscosities of the PEGs, being in the range 80–26 500 mPa·s, give rise to a high agglomerate strength. Consequently, comminution of agglomerates takes place initially in the process only, where large, loose agglomerates were broken down (Schæfer et al., 1992a; Schæfer and Mathiesen, 1996b).

Agglomerate growth mechanisms are supposed to be much more affected by comminution if a meltable binder of a viscosity below approximately 50 mPa·s is used (Eliasen et al., 1998). In the case of a low viscosity binder, therefore, the balance between agglomerate growth and comminution is assumed to be affected by small changes in viscosity and impeller speed. Most hydrophobic binders used for melt agglomeration of prolonged release products have viscosities below 50 mPa·s (Thomsen et al., 1994).

The aim of the present experiments was to study the effects of the impeller speed and the product temperature on the agglomerate growth mechanisms using a meltable binder with a viscosity of approximately 10 mPa·s, i.e. lower than the viscosities of the meltable binders used in previous studies of agglomerate growth mechanisms.

2. Materials and methods

2.1. Materials

Lactose 450 mesh (α-lactose monohydrate, DMV, the Netherlands) was used as starting material. Stearic acid (BP 93 grade, Jahress Fabrikker, Norway) was used as the meltable binder. Stearic acid was used as flakes.

The size distribution by volume of the lactose was determined by a Malvern 2601Lc laser diffraction particle sizer (Malvern Instruments, UK). The median particle diameter and the span were found to be 23 μm and 2.3. The span is the difference between the diameters at the 90 and the 10 percentage points relative to the median diameter.

The BET multipoint surface area of the lactose, determined by a Gemini 2375 Surface Area Analyzer (Micromeritics, USA), was 0.80 m^2/g.

The true densities of the materials were determined by an AccuPyc 1330 gas displacement pycnometer (Micromeritics, USA) using helium purge. The density was 1.551 g/cm^3 for the lactose and 0.991 g/cm^3 for the stearic acid. The density of the molten binder was estimated at 52, 56, 60, 70, and 80°C as previously described (Eliasen et al., 1998). All results are mean values of three estimations.

The water content on a wet-weight basis, i.e. the water content corresponding to the loss on drying, was estimated by volumetric titration as previously described (Schæfer and Mathiesen, 1996b). The water content was found to be 5.0% for the lactose and 0.0% for the stearic acid.

The melting range of the stearic acid was estimated by a Perkin Elmer DSC 7 differential scanning calorimeter as previously described (Schæfer and Mathiesen, 1996b) and was found to be 46–56°C with a peak temperature of 55°C.

The viscosity of the molten stearic acid was estimated at 56, 60, 70, and 80°C by a rotation viscosimeter, Rotovisco RV 12 (Haake, Germany), with a NV sensor system. The viscosity values used are the results obtained at 256 rpm.

The surface tension of the stearic acid was estimated at 70 and 80°C by a Digital Tensiometer K 10 ST (Krüss, Germany). The results are mean values of four estimations.

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 employed in the experiments.

2.3. Mixing procedure

The load of the mixer was 1 kg of lactose. The concentration of the stearic acid was kept constant at 23% m/m of the amount of lactose. In all the experiments, an impeller speed of 1300 rpm was applied until the product temperature reached 58°C after which the impeller speed was lowered to the predetermined value, and the massing was continued for 4.5 min. 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, 1996a).

A relative air humidity of approximately 80%, achieved by evaporation of water, at a temperature of 22–24°C was maintained in the room during processing to reduce generation of static electricity (Eliasen et al., 1999).

2.4. Granule characterization

2.4.1. Size distribution

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. A series of 12 ASTM standard sieves in the range of 180–2000 μm was vibrated for 10 min by a Fritsch analysette 3 vibrator (Fritsch, Germany). The mass median diameter and the span were calculated.

2.4.2. Density

Granules within the size range 355–2000 μm were milled in a coffee mill (Braun AG 4041, Braun, Spain) in 10 s followed by 10 s of rest. The procedure was repeated until the granules were milled for 30 s in total. The true densities of the milled granules were determined by an AccuPyc 1330 gas displacement pycnometer (Micromeritics, USA) using helium purge. The true density was used in the calculations of the intragranular porosity of the granules.

2.4.3. Intragranular porosity

The intragranular porosity of the granules within the size range 355–2000 μm was estimated by a mercury immersion method as previously described (Schæfer et al., 1992a), and the liquid saturation was calculated (Eliasen et al., 1998).

2.4.4. Water content

The water content on a wet-weight basis of the granules within the size range 355–2000 μm was estimated by volumetric titration as previously described (Schæfer and Mathiesen, 1996b).

2.4.5. Image analysis

The granules within the size range of 1120–1400 μm were placed on an illuminated desk, and measurements were carried out as previously described (Eliasen et al., 1998). Two hundred agglomerates were used for one analysis. The shape of the agglomerates was characterized by the aspect ratio (length/width) and by the two-dimensional shape factor, e_R, devised by Podczeck and Newton (1994).

2.4.6. Scanning electron microscopy

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

2.5. Experimental design

A series of 30 experiments was carried out in which the impeller speed was varied at 200, 400, 600, 800, 1000 and 1200 rpm, and the temperature of the heating jacket was varied at 35, 60 and 85°C. The combinations of impeller speed and jacket temperature that were applied in the experiments are shown in Table 1. All the 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 analyzed by analysis of variance.

3. Results and discussion

3.1. Binder characteristics

The viscosity and the density of the stearic acid at different temperatures are shown in Fig. 1. The surface tension of stearic acid was 28.2 and 27.8 mN/m at a temperature of 70 and 80°C, respectively. As to be expected, a rise in temperature reduces the viscosity, the density, and the surface tension of the stearic acid. The reduction in the viscosity and the density is more pronounced at

Table 1
Experimental design

Jacket temperature (°C)	Impeller speed (rpm)					
	200	400	600	800	1000	1200
35	+	+	+	+	+	+
60	+	+	+	+	+	−
85	+	+	+	+	−	−

temperatures within or slightly above the melting range. The surface tension and the viscosity of the stearic acid could not be estimated at temperatures below 70 and 56°C, respectively, due to an uneven solidification of the binder in the measuring chamber.

A good wetting of the lactose particles by the stearic acid was indicated by a fast penetration and subsequent sedimentation of the lactose particles when lactose was sprinkled over the surface of molten binder.

A constant binder concentration of 23% m/m was applied. As a consequence of the temperature dependency of the binder density, the binder concentration obtained at the lowest and the highest final product temperature corresponded to 25.8 and 27.3% v/m, respectively.

3.2. Product temperature

In Fig. 2, the final product temperature is seen to increase significantly by a rise in the impeller speed ($P < 0.001$) as well as by a rise in the temperature of the heating jacket ($P < 0.001$). A rise in the impeller speed increases the product temperature due to development of heat caused by friction. At each temperature of the heating jacket, a linear relationship between the product temperature and the impeller speed is obtained. The parallel curves indicate that the energy input from the impeller rotation is converted completely into heat in the mass (Holm et al., 1985). A product temperature exceeding the pre-set temperature of the jacket can thus be obtained due to the action of the impeller. This is seen in all the experiments with a jacket temperature of 35°C and in the experiments with a jacket temperature of 60°C at the three highest impeller speeds.

In previous melt pelletization experiments with lactose monohydrate, evaporation of water of crystallization was found to commence at product temperatures between 80 and 90°C (Schæfer and Mathiesen, 1996b). This evaporation of water of crystallization alters the characteristics of the agglomerates and thereby affects the agglomerate

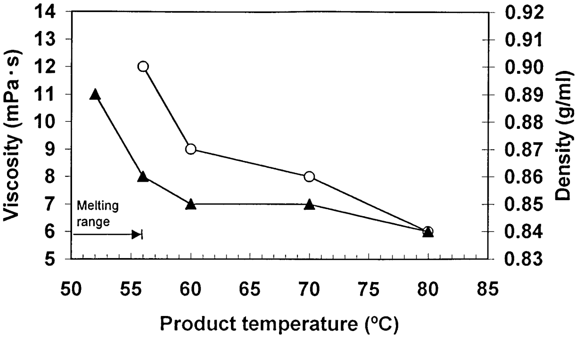

Fig. 1. Effect of temperature on the viscosity (○) and density (▲) of the stearic acid.

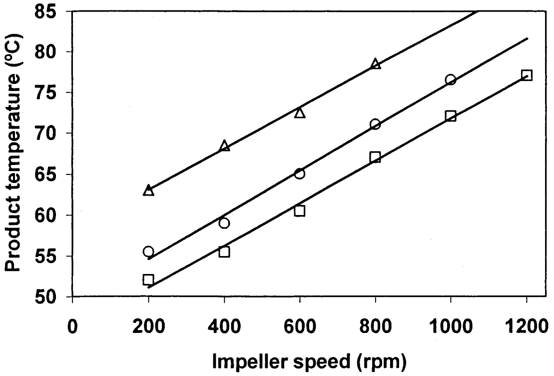

Fig. 2. Effect of impeller speed on the product temperature at different jacket temperatures. Jacket temperature: (□) 35°C, (○) 60°C, (△) 85°C.

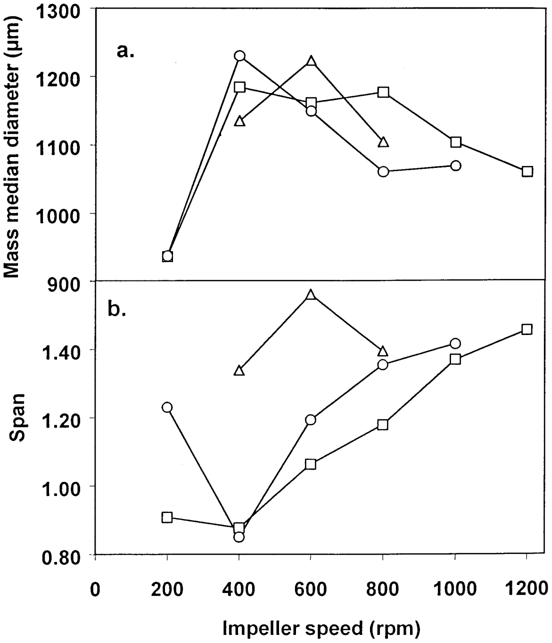

Fig. 3. Effect of impeller speed on the mass median diameter (a) and the span (b) at different jacket temperatures: (□) 35°C, (○) 60°C, (△) 85°C.

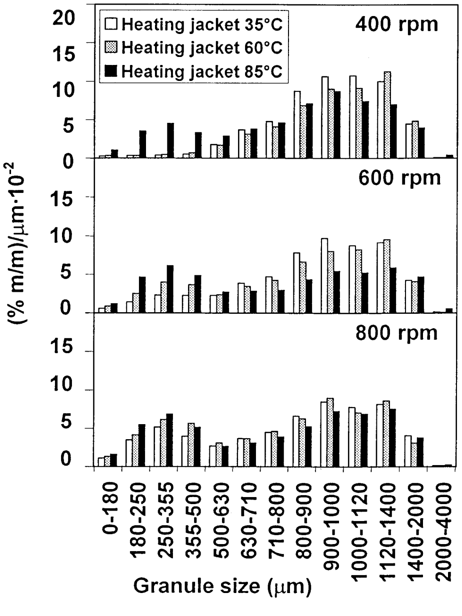

Fig. 4. Effect of jacket temperature on the granule size distribution at different impeller speeds.

growth. In the present experiments, the experimental conditions were chosen so that the product temperature could be kept below 80°C (Fig. 2) in order to avoid that the agglomerate growth was affected by an evaporation of water of crystallization.

3.3. Agglomerate size and size distribution

Fig. 3 shows the effects of the impeller speed and the temperature of the heating jacket on the mean granule size and the granule size distribution in terms of the mass median diameter and the span, respectively. The geometric mean diameter and the geometric standard deviation, which have been used in previous investigations to characterize the size distributions (Eliasen et al., 1998), were not applicable in the present experiments, because several size distributions deviated markedly from the log-normal distribution.

Fig. 3 demonstrates that a change of the impeller speed from 200 to 400 rpm gives rise to significantly larger ($P < 0.001$) and more uniformly sized granules ($P < 0.001$). This is in accordance with results on the effects of the impeller speed reported from previous melt agglomeration experiments (Kinget and Kemel, 1985; Schæfer et al., 1993b; Thomsen et al., 1993). Contrary to previous results, a further rise in impeller speed causes a significant ($P < 0.001$) increase in the span of the size distribution and no significant change in the median size.

The highest temperature of the jacket gives rise to a significantly wider granule size distribution ($P < 0.001$) in accordance with previous results (Thomsen et al., 1993), whilst no significant effect of the temperature of the jacket on the mean granule size was found. The differences in the agglomerate growth are not sufficiently explained by the median diameter and the span due to the different profiles of the size distributions from which they were calculated. Therefore, detailed analyses of the size distributions are necessary in order to interpret the effects of impeller speed and jacket temperature on the agglomerate growth mechanisms.

The effects of the temperature of the jacket on the granule size distribution at different impeller speeds are shown in Fig. 4. At an impeller speed of 400 rpm, the highest temperature of the jacket results in a higher content of granules within the smaller size fractions, which indicates breakage of agglomerates (Knight et al., 1998). Consequently, a higher temperature must cause a reduction in the agglomerate strength. The strength of the dynamic liquid bridges within an agglomerate is dominated by viscous forces (Mazzone et al., 1987), but is additionally affected by capillary forces which depend on the surface tension of the binder (Ennis et al., 1991; Tardos et al., 1997). A higher product temperature resulting from the higher jacket temperature reduces the strength of the agglomerates by reducing the viscosity and the surface tension of the stearic acid. It is surprising, however, that the slight reduction in viscosity, i.e. from 12 to 8 mPa·s, which corresponds to the rise in jacket temperature from 35 to 85°C, and the slight reduction in surface tension to be expected clearly augment the comminution of the agglomerates. The continuous formation and comminution of agglomerates seen at a low agglomerate strength inhibit the densification of the agglomerates (Eliasen et al., 1998) and result in agglomerates of a higher porosity (Fig. 7b). At the highest temperature of the jacket, therefore, comminution of agglomerates is more pronounced as a consequence of a lower agglomerate strength caused by a higher porosity (Kristensen et al., 1985) as well as a lower strength of the liquid bridge.

At an impeller speed of 600 and 800 rpm, relatively high contents of agglomerates in the smaller size fractions are obtained irrespective of the jacket temperature (Fig. 4). However, at a higher jacket temperature, the contents of agglomerates in the smaller size fractions increase indicating that comminution is more pronounced. A higher impeller speed results in a higher product temperature causing a lower agglomerate strength, because of a combination of a higher porosity (Fig. 7b) and a reduction in the viscosity and the surface tension of the stearic acid. The lower agglomerate strength combined with the higher shear forces explains why a comminution becomes more pronounced at a higher impeller speed.

Table 2
Effects of jacket temperature and impeller speed on % m/m of agglomerates within the sieve fraction 2000–4000 μm

Jacket temperature (°C)	Impeller speed (rpm)		
	400	600	800
35	1.7	2.4	2.3
60	2.1	1.7	2.7
85	7.1	11.3	4.7

At the highest temperature of the jacket, irrespective of the impeller speed, the content of agglomerates in the size fraction 2000–4000 μm increases (Table 2), and the amount of agglomerates greater than 4 mm was found to be slightly higher ($P < 0.05$). The fact that the amount of smaller as well as larger agglomerates increases at the same time indicates that the dominant growth mechanism is crushing and layering (Hoornaert et al., 1998). Small particles will be preferentially captured by larger ones (Tardos et al., 1997). Consequently, those agglomerates that by densification have gained sufficient strength to resist comminution are supposed to grow in size by layering of particles or small fragments formed by crushing of other agglomerates. This is in accordance with fundamental agglomeration studies showing that growth by crushing and layering is the dominating agglomerate growth mechanism in case of relatively weak agglomerates (Kapur, 1971; Linkson et al., 1973). The process was found to be sensitive to random variations in the experimental conditions since one of the repeated experiments performed at a jacket temperature of 35°C and an impeller speed of 800 rpm had to be interrupted due to ball growth, i.e. an uncontrollable formation of very large agglomerates.

The amount of adhesion to the bowl lining was generally found to be higher at the highest temperature of the jacket ($P < 0.05$). In the experiments performed at a jacket temperature of 85°C, all the material adhered to the bowl at an impeller speed of 200 rpm whilst at higher impeller speeds, the amount of adhesion varied between 3 and 22%. At the lower temperatures of the jacket, the amount of adhesion varied between 3 and 12%. Generally, repeated experiments gave rise to a similar size distribution despite variations in the amount of adhesion.

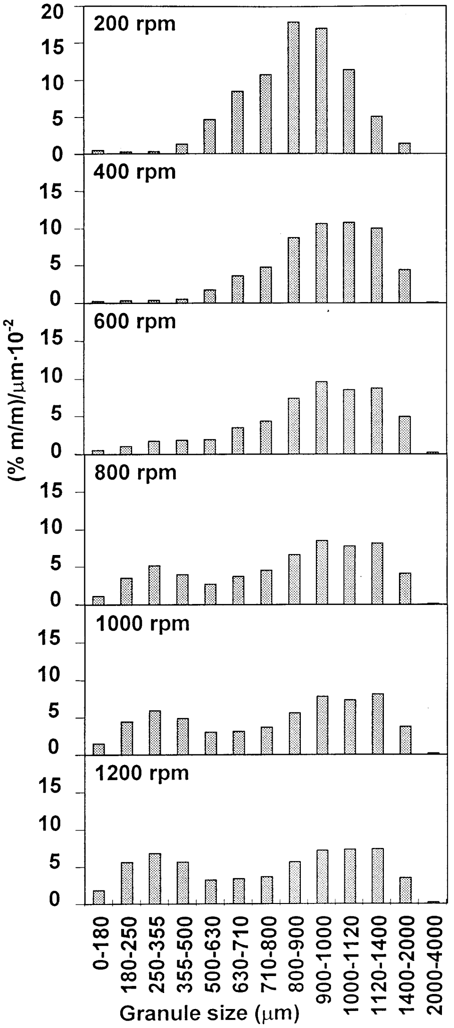

Fig. 5. Effect of impeller speed on the granule size distribution. Jacket temperature: 35°C.

In Fig. 5, the effect of the impeller speed on the size distribution at a jacket temperature of 35°C is shown. When the impeller speed is raised from 200 to 400 rpm, the content of agglomerates within the larger size fractions increases, indicating that agglomerate growth is promoted. This is due to an increased deformability of the agglomerates at collisions (Adetayo et al., 1993; Schæfer and Mathiesen, 1996b). At an impeller speed of 600 rpm, there is a slight increase in the contents of the agglomerates in the smaller size fractions. This becomes even more evident when the impeller speed is raised to 800 rpm which indicates that breakage of the agglomerates becomes more dominant. A further rise in the impeller speed increases the content of agglomerates in the smaller size fractions whilst the contents of agglomerates in the larger size fractions decreases. This means that the higher agglomerate growth to be expected at the higher impeller speed is counteracted by an increased comminution.

Fig. 6 shows the effect of the impeller speed on the size distribution at combinations of jacket temperature and impeller speed giving rise to approximately constant temperatures of the product. Consequently, the effect of the shear forces can be estimated since the agglomerate strength is supposed to be approximately constant at a constant temperature. At a product temperature of 56°C, i.e. within the melting range of the binder, a rise in the impeller speed causes an increased amount of agglomerates within the larger size fractions.

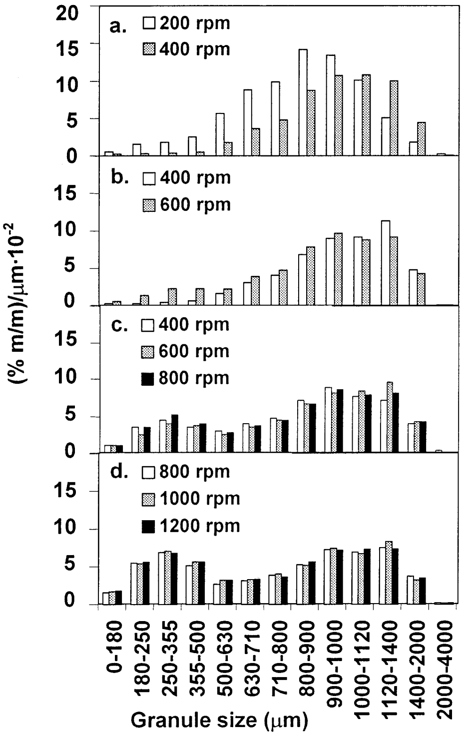

Fig. 6. Effect of the impeller speed on the granule size distribution at different temperatures of the product. Product temperature: 56°C (a); 60°C (b); 65°C (c); 77°C (d).

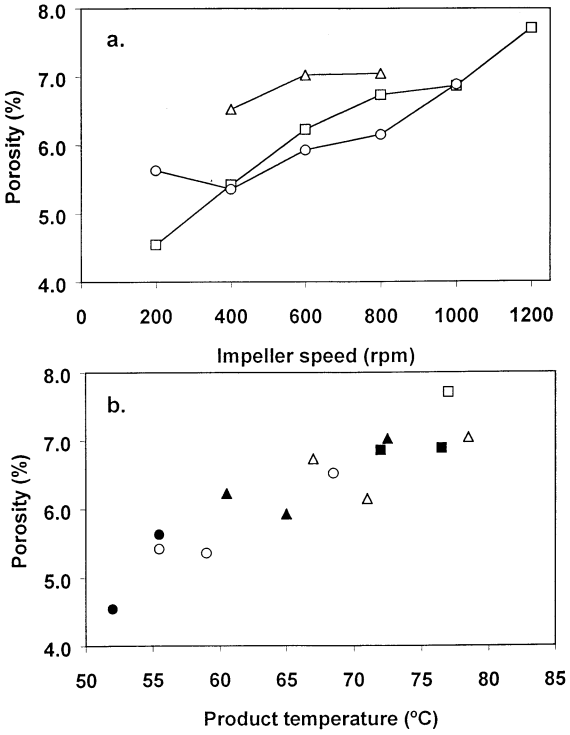

Fig. 7. a: Effect of impeller speed on the intragranular porosity at different jacket temperatures: (□) 35°C, (○) 60°C, (△) 85°C. (b): Effect of product temperature on the intragranular porosity at different impeller speeds: (●) 200 rpm, (○) 400 rpm, (▲) 600 rpm, (△) 800 rpm, (■) 1000 rpm, (□) 1200 rpm.

At this temperature, the agglomerates possess sufficient strength to withstand the increased risk of comminution associated with the higher shear forces at the higher impeller speed. Therefore, agglomerate growth is promoted by a higher impeller speed. At a product temperature of 60°C, comminution of the agglomerates is initiated at an impeller speed of 600 rpm, whilst an impeller speed of 400 rpm is sufficient to cause a comminution of the agglomerates at a product temperature of 65°C because of the decrease in agglomerate strength at a higher temperature. In previous melt agglomeration experiments, the higher agglomerate strength, caused by the higher viscosity of the meltable binders applied, explains why a rise in the impeller speed was found to increase agglomerate growth instead of causing comminution (Schæfer et al., 1992a,c; Thomsen et al., 1994). A similar size distribution arises if a similar equilibrium state between growth and comminution is obtained. This might explain why the size distributions are independent on the impeller speed at product temperatures of 65 and 77°C.

3.4. Intragranular porosity and liquid saturation

Fig. 7(a) shows that a significantly higher intragranular porosity is obtained at a higher impeller speed ($P < 0.001$) and at a jacket temperature of 85°C ($P < 0.01$), whilst a similar porosity is obtained at jacket temperatures of 35 and 60°C. The densification of agglomerates is eased by a lower binder viscosity and by higher collisional forces (Ennis et al., 1991). This implies that a lower intragranular porosity of the agglomerates would generally be expected at a higher impeller speed and at a higher temperature of the jacket. However, higher impeller speeds and higher temperatures of the jacket simultaneously promote a comminution of the agglomerates. A simultaneous formation and comminution of agglomerates result in loose agglomerates unable to densify (Eliasen et al., 1998). This explains why a higher porosity is obtained at a higher jacket temperature as well as a higher impeller speed.

Fig. 7(b) shows that the porosity increases almost linearly with the temperature of the product. At a constant product temperature, a similar porosity, therefore, is obtained despite differences in the impeller speed. This indicates that the higher porosity to be expected at a higher impeller speed, due to an increased comminution of agglomerates, is counteracted by an increased densification due to the higher collisional forces.

Fig. 8 shows that a significant reduction in the liquid saturation of the agglomerates is obtained at a higher impeller speed ($P < 0.01$) and at a jacket temperature of 85°C ($P < 0.05$). The differences in the intragranular porosity are reflected in the liquid saturation, a higher porosity giving rise to a lower liquid saturation. At higher impeller speeds as well as higher temperatures of the jacket, the fall in the liquid saturation that has to be expected at an increasing porosity is partly counteracted by the thermal expansion of the binder liquid caused by an increasing product temperature. At higher liquid saturations, the deformability of the agglomerates and the amount of binder liquid squeezed to the surface at collisions between agglomerates increase. Therefore, the potential for agglomerate growth by coalescence is increased at a higher liquid saturation. The lack of an effect of the impeller speed on agglomerate growth at speeds exceeding 400 rpm might partly be a consequence of the fall in the liquid saturation.

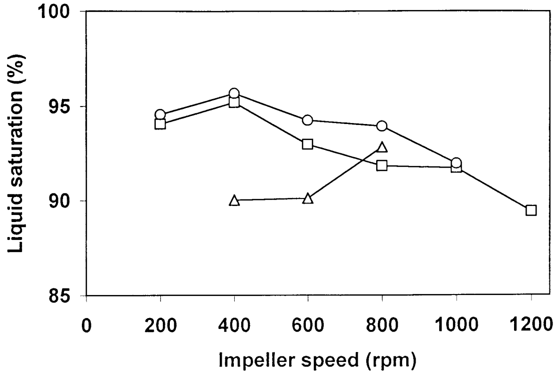

Fig. 8. Effect of impeller speed on the liquid saturation of the agglomerates at different jacket temperatures. Jacket temperature: (□) 35°C, (○) 60°C, (△) 85°C.

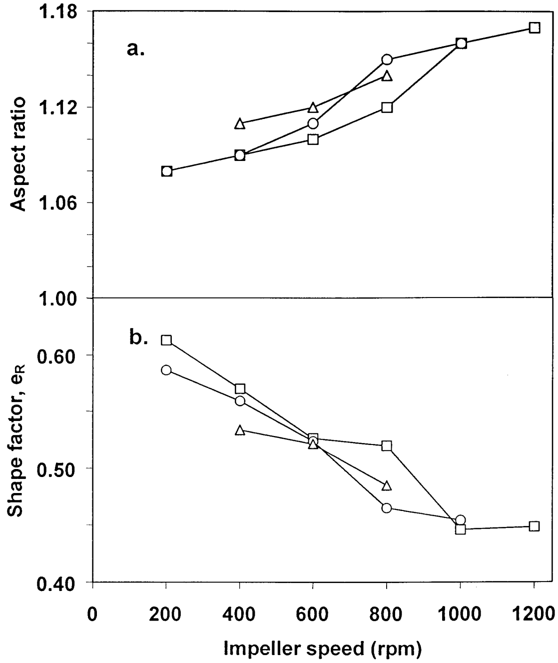

Fig. 9. Effect of impeller speed on the aspect ratio (a) and the shape factor (b) of the agglomerates at different jacket temperatures. Jacket temperature: (□) 35°C, (○) 60°C, (△) 85°C.

3.5. Agglomerate shape and smoothness

The aspect ratio (Fig. 9(a)) describes the deviation of shape from a circle towards an ellipse whilst the shape factor (Fig. 9(b)), e_R, considers both ellipticity and surface roughness (Podczeck and Newton, 1994). A circle will theoretically give rise to a value of 1 of the aspect ratio as well as the shape factor.

It is seen that the agglomerates become more spherical and smoother at a lower impeller speed ($P < 0.001$) (Figs. 9 and 10), whilst a lower temperature of the jacket gives rise to only slightly more spherical agglomerates ($P < 0.05$; Fig. 9(a)). The values of the shape factor are assumed to be acceptable since two sets of apparently spherical pellets produced by extrusion/spheronization gave shape factor values of 0.568 and 0.416 (Podczeck and Newton, 1994).

At a lower impeller speed, the higher liquid saturation aids the rounding of the agglomerates due to a higher deformability of the agglomerates (Schæfer and Mathiesen, 1996c) and a higher surface plasticity caused by the higher amount of liquid at the surface (Pinto et al., 1992; Wan et al., 1993; Watano and Miyanami, 1995; Schæfer and Mathiesen, 1996c). At a higher impeller speed as well as a higher temperature of the jacket, the viscosity of the stearic acid becomes reduced as a consequence of the higher product temperature obtained. This increases the surface plasticity of the agglomerates, which is supposed to promote a spheronization (Schæfer and Mathiesen, 1996c). However, the spheronization of the agglomerates is counteracted by the continuous formation and comminution of agglomerates caused by the lower agglomerate strength obtained at a higher product temperature. Thus, the final effects of impeller speed and jacket temperature on the sphericity and the smoothness of the agglomerates depend

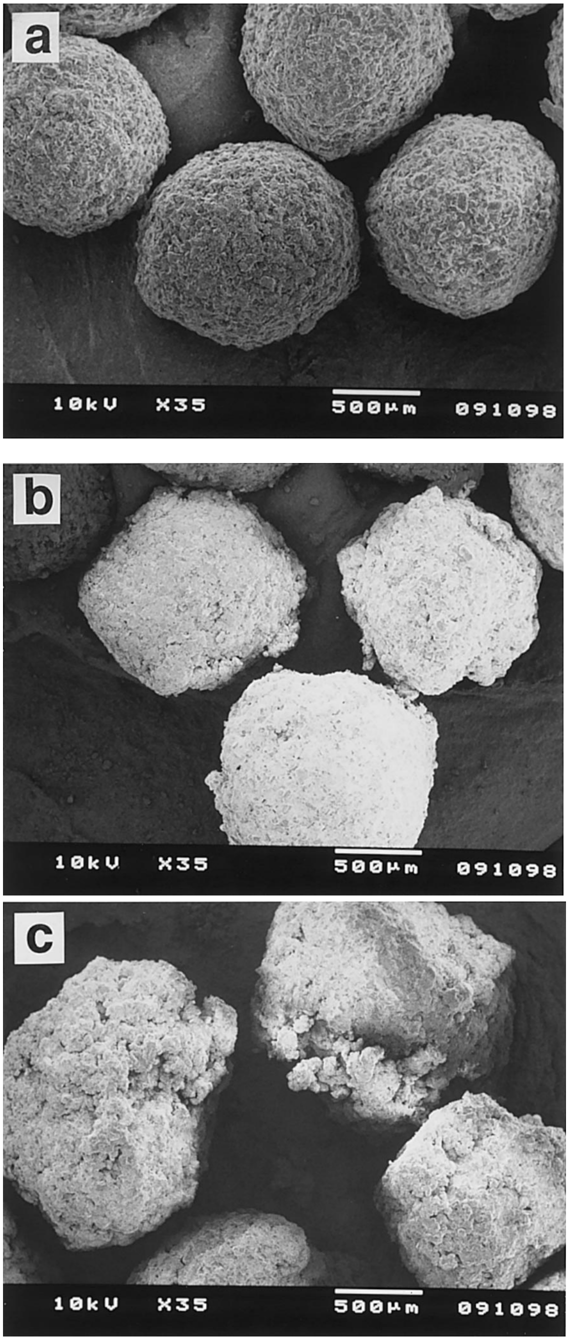

Fig. 10. SEM photographs of agglomerates produced at different impeller speeds. Impeller speed: 200 rpm (a), 600 rpm (b), and 1200 rpm (c). Jacket temperature: 35°C.

on the balance between the effects of liquid saturation, surface plasticity and comminution.

4. Conclusions

In granulation of pharmaceutical products, agglomerate growth is indicated to occur primarily by nucleation and coalescence, because the starting materials are usually fine powders with wide particle size distributions which produce strong agglomerates (Kristensen, 1995). The present experiments, however, gave rise to clearly different agglomerate growth mechanisms since agglomerate growth was found to be markedly dependent on the balance between coalescence of agglomerates and breakdown of agglomerates. This is ascribed to a low agglomerate strength caused by the low viscosity and the low surface tension of the stearic acid. The simultaneous coalescence and comminution of agglomerates were found to inhibit the densification of the agglomerates which further decreased the agglomerate strength. The low agglomerate strength explains, why crushing and layering was found to be a probable agglomerate growth mechanism concurrently with coalescence. Because of the low agglomerate strength, the agglomerate growth was much more sensitive to slight variations in binder viscosity than that seen in previous agglomeration experiments. Even a minor reduction in the viscosity caused by a higher product temperature was able to reduce the agglomerate strength sufficiently to increase the comminution of the agglomerates.

Further, a higher impeller speed was found to increase the comminution of the agglomerates. A higher impeller speed could be applied at a lower product temperature before breakage of the agglomerates occurred. This indicates that the impeller speed required to break the agglomerates was affected by slight differences in the strength of the agglomerates. In contrast to previous melt agglomeration experiments, a lower impeller speed was found to give rise to smoother and more spherical agglomerates. At a higher impeller speed, the spheronization of the agglomerates was counteracted to a larger extent by the continuous formation and comminution of the agglomerates.

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