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Granule size control and targeting in pulsed spray fluid bed granulation

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ABSTRACT

The primary aim of the study was to investigate the effects of pulsed liquid feed on granule size. The secondary aim was to increase knowledge of this technique in granule size targeting. Pulsed liquid feed refers to the pump changing between on- and off-positions in sequences, called duty cycles. One duty cycle consists of one on- and off-period. The study was performed with a laboratory-scale top-spray fluid bed granulator with duty cycle length and atomization pressure as studied variables. The liquid feed rate, amount and inlet air temperature were constant. The granules were small, indicating that the powder has only undergone ordered mixing, nucleation and early growth. The effect of atomizing pressure on granule size depends on inlet air relative humidity, with premature binder evaporation as a reason. The duty cycle length was of critical importance to the end product attributes, by defining the extent of intermittent drying and rewetting. By varying only the duty cycle length, it was possible to control granule nucleation and growth, with a wider granule size target range in increased relative humidity. The present study confirms that pulsed liquid feed in fluid bed granulation is a useful tool in end product particle size targeting.

1. Introduction

Fluid bed granulation is a commonly used unit operation in the pharmaceutical industry, and has been widely studied since the invention of the technique (Parikh et al., 1997; Faure et al., 2001). It has been shown that the choice of varying operating parameters such as inlet air temperature (Faure et al., 2001; Rambali et al., 2001; Jiménez et al., 2006; Ehlers et al., 2009), liquid feed rate (Faure et al., 2001; Bouffard et al., 2005; Jiménez et al., 2006; Hu et al., 2008; Ehlers et al., 2009) and atomizing pressure (Hemati et al., 2003; Bouffard et al., 2005; Jiménez et al., 2006) have a significant effect on the quality of the end product, especially the particle size distribution. The granule growth mechanisms have in recent years frequently been discussed in the literature, beginning from the onset of wetting and nucleation, consolidation and growth to attrition and breakage (Iveson et al., 2001).

The effect of inlet air relative humidity on agglomerate growth and the particle size of the end product has been addressed by a number of authors, and the importance of this parameter has recently been frequently highlighted. The general understanding is that an increase in relative humidity of the inlet air yields larger granules (Schaafsma et al., 1999; Rambali et al., 2001; Hemati et al., 2003; Närvänen et al., 2008). Changes in inlet air relative humidity are difficult to control, but efforts have been made to deal with this issue (Schaafsma et al., 1999; Lipsanen et al., 2007, 2008; Närvänen et al., 2008). Pulsed spray has been found to be a promising way to compensate for changes in inlet air relative humidity (Schaafsma et al., 1999; Närvänen et al., 2008). During the spraying phase the liquid feed is interrupted in regular sequences, giving the powder mass the possibility to undergo intermittent drying and rewetting, resulting in more versatile applications of different spraying rates and better control of the humidity within the granulation chamber (Schaafsma et al., 1999).

The primary aim of the present study was to further investigate the effects of pulsed liquid feed presented by Närvänen et al. (2008) and Schaafsma et al. (1999) on granule size and granule growth. The secondary aim was to produce granules within a d_{50} range of 100–250 μm. The aim was to increase the knowledge of the possibilities to use this technique as a tool in end product particle size targeting. Furthermore, an additional goal was to bring insight into the effect of inlet air relative humidity on the process and how pulsed liquid feed can be applied in different humidity conditions as a process optimization tool to ensure the targeted particle size range.

2. Materials and methods

2.1. Materials

The materials used in the study were α-lactose monohydrate (Pharmatose 200M, DMV, The Netherlands), anhydrous caffeine

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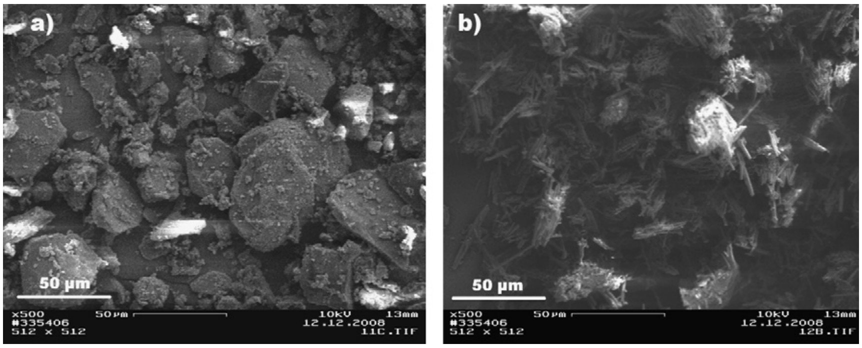

Fig. 1. SEM-micrographs of (a) lactose 200 M and (b) caffein anhydrate.

(Orion Pharma, Espoo, Finland), Povidone K25 (Kollidon® K25, BASF, Germany) and purified water (Fig. 1).

2.2. Granulation

The powders granulated were caffeine and lactose at a ratio of 1:4. For granulation, 100 g of caffeine and 400 g of lactose were sieved through a 1-mm sieve, and placed to acclimatize in the process facilities for 16 h prior to the granulation. The binder liquid used was a 20% (w/w) aqueous solution of Kollidon K-25.

The granulation was performed with an Aeromatic STREA-1 laboratory-scale fluidized bed granulator (Aeromatic AG, Switzerland). The batch size was 500 g. The duration of the mixing phase was 2.5 min, during which the inlet air temperature was increased from ambient room temperature to 40 °C. This was also the process temperature during the spraying phase. The spraying phase was performed as pulsed spray with varying atomization pressures using a Schlick model 970/7-1 two-substance nozzle (Düsen-Schlick GmbH, Germany) mounted on a brass/aluminium tripod situated between the granulation chamber and the oscillating upper sieve. The distance between the nozzle and the perforated bottom plate was 340 mm.

Duty cycle is defined as a sequence during the spraying phase, which begins with the pump being turned on, after which it runs for a predetermined time, turns off and stays off for a predetermined time. The previous duty cycle ends and the next one is initiated as the pump starts again. Repeated duty cycles make the spray pulsed, which as a whole also can be referred to as pulsed liquid feed or spray.

The spray altered automatically between on- and off-positions with a on:off (spray:lag)-ratio of 1:1. This can also be described as having a duty cycle of 50%. During the lag sequences only the pump was switched off, keeping the atomizing pressure and needle air feed unchanged to prevent clogging of the nozzle and irregularities in the level of fluidization. The liquid feed rate during the spray-sequences was 2.5 g/min. The granulation liquid was at ambient room temperature.

The level of fluidization was controlled by keeping the pressure difference between pressure sensors above the oscillating upper sieve and below the perforated bottom plate between 600 and 800 Pa, which required varying fluidizing air velocities between 2 and 12 l/s. The decision to use this method of controlling the level of fluidization instead of a fixed inlet air velocity was made based on preliminary experiments. The moisture content, and thus mass, of the processed powder mass varied during the spraying phase, resulting in a risk over-fluidization in dry conditions and insufficient fluidization in wet conditions.

The inlet air was at ambient relative humidity, which was taken into account by retrospectively including the inlet air relative humidity at 50 g binder liquid consumption into the experimental design as an uncontrolled and unscaled variable. The inlet air relative humidity was measured with a Vaisala HUMICAP© HMT100 humidity and temperature probe (Vaisala Oyj, Helsinki, Finland) as a part of the overall instrumentation of the granulator. The inlet air temperature and humidity probe is situated at the inlet air intake.

The drying phase was initiated after 100 g binder liquid consumption, which occurred after 80 min of spraying time (duty cycle 50%, liquid feed rate 2.5 g/min). The drying temperature was 50 °C, and the drying was continued until the difference between inlet air and outlet air relative humidity stayed below 1% continuously for a whole minute. The moisture content of all batches was analyzed immediately after the process using a Sartorius MA 100 moisture analyzer (Sartorius AG, Germany) and Karl Fischer titrimetry (Mettler DL 35 Karl Fischer Titrator, Mettler Toledo AG, Switzerland).

2.3. Experimental design

The studied variables were duty cycle length and atomization pressure (Table 1). The concept of duty cycle is only related to the function of the liquid feed pump, all other factors determining the spray are unaffected by the concept of duty cycle. The range of the variables was determined based on preliminary experiments. The experimental design used in the present experiment was a randomized central composite design with triplicate centre point runs (batches 9, 10 and 11) to ensure the repeatability of the process. The experiment was built using MODDE for Windows (MODDE 7, Umetrics AB, Sweden). The inlet air relative humidity during the experiments was included in the design as an uncontrolled variable and added retrospectively.

2.4. Granule size measurement

Every batch of granules was divided into eight parts by a vibratory feeder (Fritsch Vibratory Feeder Laborette 24, Germany)

Table 1
Process variables (ATM = atomization pressure [bar]; DC = duty cycle length [s]; RH% = relative humidity), d_{10}, d_{50}, d_{90}-values (µm), undersize percentage (<50 µm) and oversize percentage (>500 µm) of the granulated batches.

Batch	ATM	DC	RH%	d_{10}	d_{50}	d_{90}	Undersize	Oversize
1	0.5	50	55.5	76	162	369	1.2	4.8
2	0.9	50	56.7	70	141	399	1.8	7.0
3	0.5	190	35.6	71	153	308	1.7	1.5
4	0.9	190	33.8	68	126	264	2.1	2.5
5	0.42	120	55.5	71	146	308	1.6	2.5
6	0.98	120	37.0	98	98	210	3.0	1.5
7	0.7	21	44.5	71	161	357	1.8	3.9
8	0.7	219	56.5	75	139	318	1.3	4.8
9	0.7	120	50.5	68	119	292	2.0	3.7
10	0.7	120	56.3	66	118	260	2.4	3.1
11	0.7	120	35.8	66	113	260	2.5	3.3

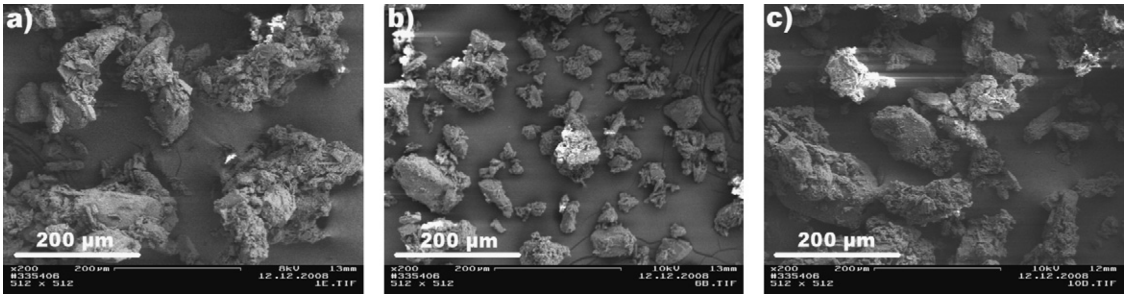

Fig. 2. SEM-micrographs of the granules of batches (a) 1, (b) 6 and (c) 10.

combined with a rotary sample divider (Fritsch Sample Divider Laborette 27, Germany). One-eighth of the batch was divided further, as described above, into 8 new fractions of which two (2/64) were combined into one sample for granule size analysis. The mass of the samples for granule size analysis was 13.0 ± 0.73 g. The samples were analyzed with Spatial Filter Velocimetry using a Parsum Probe (Parsum® IPP 70-Se; Gesellschaft für Partikel-, Strömungs- und Umweltmesstechnik GmbH, Germany) based on the particle size measurement method comparison by Närvänen et al. (2008). Spatial filter velocimetry gives velocimetric, numerical and volumetric information from the particles (Petrak, 2002), of which the volumetric information was used. The raw data was treated to show the d_{10}-, d_{50}- and d_{90}-values, oversize percentage (>500 μm) and undersize percentage (<50 μm). The oversize and undersize limits were decided based on the particle size of ungranulated material and conventional granules. Final d_{50}-values outside these boundaries were to be considered unacceptable.

2.5. Data analysis and modelling

The obtained d_{50}-values were analyzed with stepwise multilinear regression analysis using MODDE for Windows (MODDE 7, Umetrics AB, Sweden). The response surfaces were constructed using SigmaPlot 2000 (Systat Software Inc., USA).

2.6. Scanning electron microscopy

Scanning electron microscope-micrographs were taken on lactose 200 M, caffeine anhydrate, the granule batches with the smallest and largest d_{50}-value and one of the centre point repetitions (batch 10).

3. Results and discussion

3.1. General notices

By using a fixed spray:lag-ratio it was possible to investigate how the duty cycle length affects the granule size, which to the knowledge of the authors has not previously been reported. α-Lactose monohydrate does not absorb water vapor very efficiently, as shown by Airaksinen et al. (2005) and Faqih et al. (2007). Lactose 200 M adsorbs less than 0.3% atmospheric water in conditions between 0% RH and 95% RH (Airaksinen et al., 2005). The main portion of the water is adsorbed above 80% RH, which is outside the range used in the present study. Anhydrous caffeine adsorbs only 0.3% atmospheric water in a range of 0–90% RH (Krzyzaniak et al., 2007). Taken this into account, the experiment singles out the effect of the variables studied quite efficiently.

3.2. Granule size

The granule size of Pharmatose 200 M is by definition under 200 mesh, i.e. <75 μm, and was assumed to be normally distributed. The particle size of the anhydrous caffeine was approximately 5 μm when it came to the primary particles, and 50 μm for the agglomerates (Fig. 1). In the present study, the granule size of all granulated batches (Table 1) show that, considering the particle size of the starting material, the process was able to create granules that undergo only nucleation and very limited subsequent growth in size (Fig. 2) presented as the introduction period by Iveson et al. (2001). This, along with the d_{50}-values of the granules obtained, was in concordance with the goals set out for the present study.

Nucleation starts by liquid bridges forming between particles, known as the pendular state, and continues with the funicular state (Parikh et al., 1997). In these states the liquid saturation of the pores of the nucleus is still not complete, which inhibits extensive growth in size (Iveson and Litster, 1998; Schaafsma et al., 1998). Reaching the capillary- and droplet-state cause menisci to form on the agglomerate surfaces, promoting growth in granule size (Parikh, 1997). In terms of states of liquid content in the formed agglomerates, it can be stated that the agglomerates in the present study experienced the pendular and funicular state, in which the liquid saturation in the pores is not complete, without reaching the capillary- or droplet-state.

In addition, the mechanism by which the nucleation occurs in the present study is through the formation of an ordered mix in the mixing phase (Fig. 3), due to the difference in particle size of

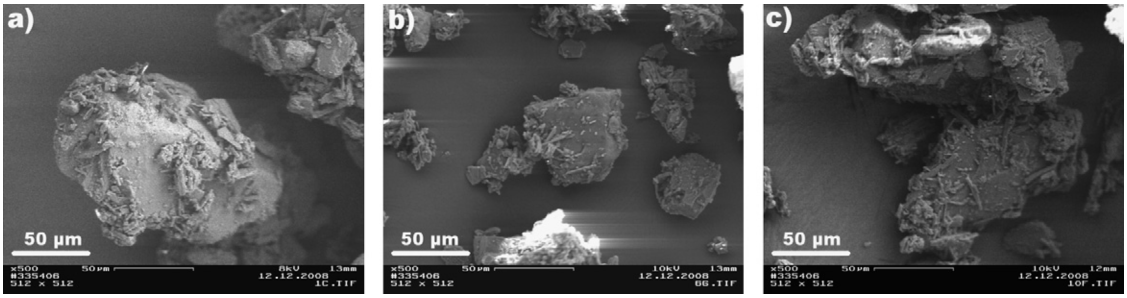

Fig. 3. SEM-micrographs of the binder-strengthened and thin-coated ordered mix formed during granulation.

the starting material (Fig. 1). In the ordered mix lactose particles are considered host-particles and caffeine particles are considered guest-particles. The first event of nucleation is strengthening of the ordered mix with PVP, followed by thin-coating with PVP, as described by Ehlers et al. (2009). This phenomenon can only be present in systems with significant differences in starting material particle size.

The formation of nuclei is an event controlled by the thermodynamics and kinetics of wetting (Iveson et al., 2001; Hapgood et al., 2003). This supports the theory of being able to control particle size growth with liquid feed pulsing (Schaafsma et al., 1999; Närvänen et al., 2008). Furthermore, it must be added that in the case of using pulsed liquid feed the thermodynamics and kinetics of drying can be added to that mentioned above, and also the inlet air relative humidity of the inlet air should be taken into account, making the nucleation and initial agglomerate growth in pulsed spray granulation a far more complex phenomenon than described earlier (e.g. Närvänen et al., 2008; Hapgood et al., 2003; Iveson et al., 2001; Schaafsma et al., 1999).

3.3. Data analysis and modelling

The d_{50}-values of each batch of granules (Table 1) were fitted into a second-order polynomial expression (Table 2). The least significant factors were reduced one by one until the highest possible predictive power (Q^2) of the model was obtained. The model shows both good fit and predictive power, as the R^2 and Q^2 values were 0.997 and 0.909, respectively. The inlet air relative humidity was included in the model by constructing three different response surfaces representing the process at the relative humidity levels 34%, 45% and 56%, projecting the effect of the inlet air relative humidity parallel to the z-axis (Figs. 4 and 5).

Table 2
The scaled coefficients of the factors and their statistical significance (P) in the second-order polynomial model (A is atomizing pressure (bar), D is duty cycle length (s) and RH% is inlet air relative humidity).

Factors	Scaled coefficients	P
Constant	1.16E+02	3.20E−06
ATM	−1.36E+01	5.24E−04
DC	−3.79E+00	2.57E−02
RH%	3.15E+00	5.19E−02
ATM × ATM	N/S	N/S
DC × DC	2.00E+01	3.09E−04
RH% × RH%	N/S	N/S
ATM × DC	−6.32E+00	5.10E−02
ATM × RH%	−5.26E+00	5.96E−02
DC × RH%	−1.03E+01	3.32E−03

The repeatability of the process was studied by examining the d_{50}-values of granule batches 9, 10 and 11, which shared process variables (Table 1). Batch 11 was slightly smaller than batches 9 and 10, which can be considered to be of similar size. The deviation in inlet air relative humidity or a pure sampling or measurement error can be singled out as possible causes of this occurrence. Thus, to be exact the experiment did not have true triplicate centre point runs, as the inlet air relative humidity was uncontrolled and retrospectively added to the design. This, however, can be considered as

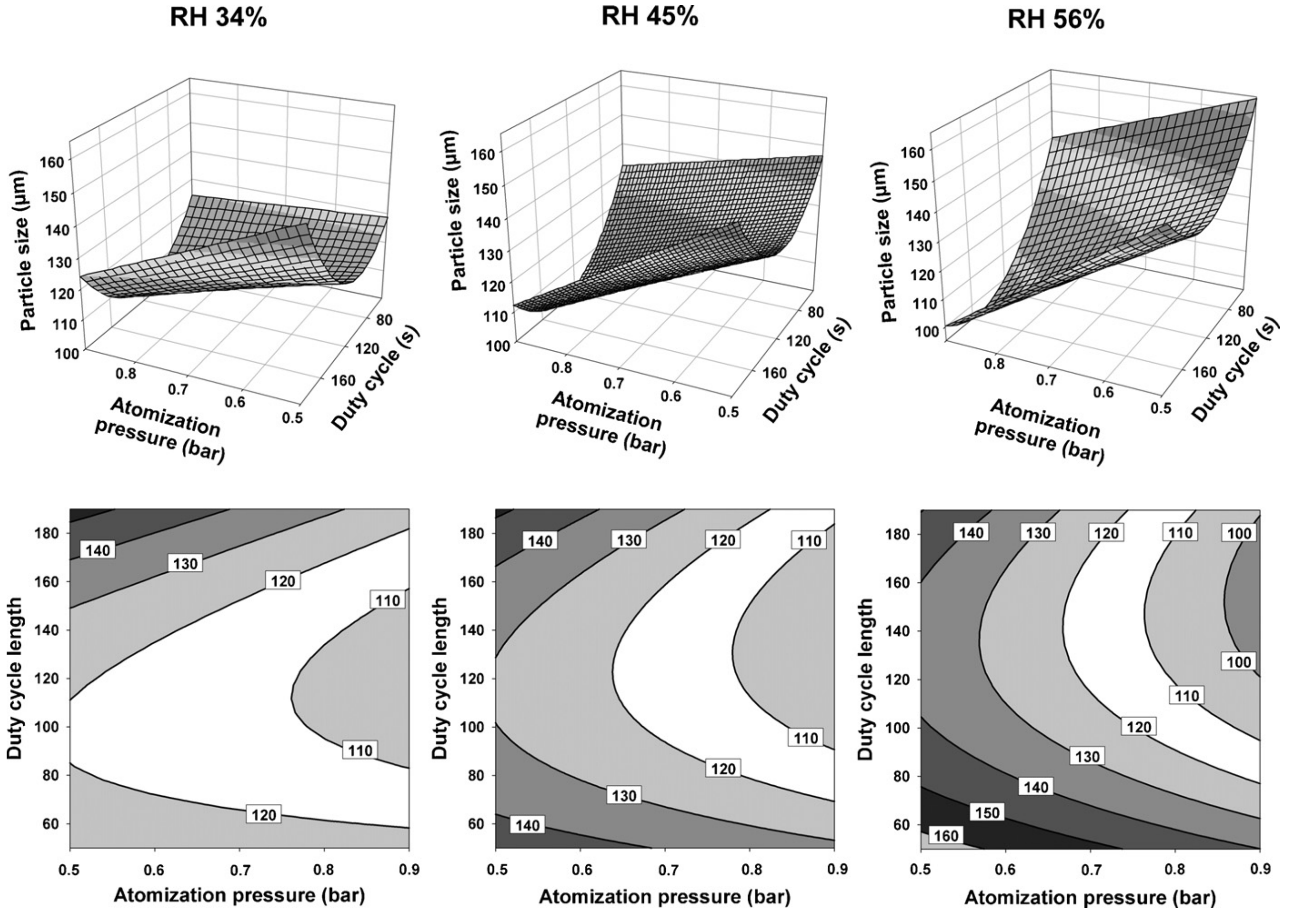

Fig. 4. The granule size ranges achieved at different process conditions and relative humidity (RH%).

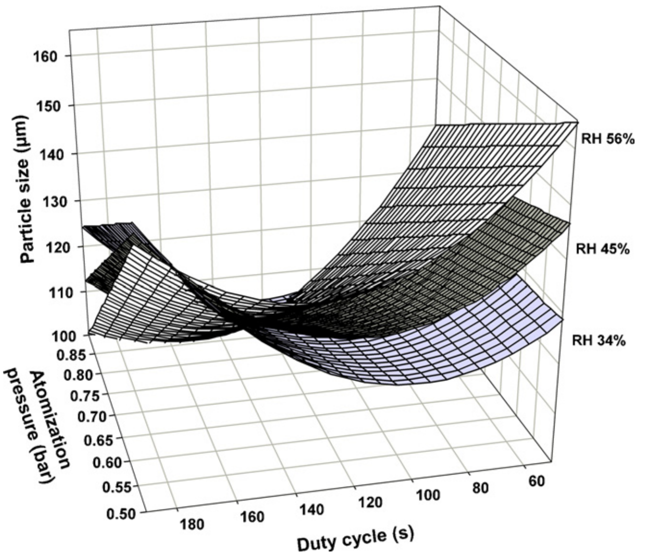

Fig. 5. The effect of pulsed binder application, atomization pressure and relative humidity on granule size in varying relative humidity.

a mere technicality which does neither impair the repeatability nor its assessment.

3.4. The effect of atomization pressure on granule size

The present study confirms that the atomization pressure clearly affected the particle size of the end product (Tables 1, 3 and 4; Figs. 4 and 5). As can be seen in Table 2, the effect of atomization pressure on granule size was linear, in line with previous reports by other authors (e.g. Bouffard et al., 2005; Jiménez et al., 2006). The results of the present study show that atomizing pressure is of critical importance to the particle size of the final product, in concordance to findings by other authors. An increase in atomizing pressure lowers the droplet size, reducing the droplet penetration of the bed which leads to lower moisture content of the bed and a smaller granule size (Bouffard et al., 2005). Smaller droplets are also susceptible to drying to such an extent that the powder is not sufficiently wetted for extensive growth.

The atomizing pressure affects nucleation and early stages of agglomerate growth, as powder is especially sensitive to binder liquid droplet size at these phases in the formation of granules (Schaafsma et al., 2000, 1999). In addition, increased atomization pressure decreases the growth rate of the granules (Hemati et al., 2003). The atomizing pressure also increases the air shear forces within the granulation chamber adding to the breakage of formed granules, which contributes to size reduction of the granules (Bouffard et al., 2005). This phenomenon was heightened in the present study, as only the pump was switched off during the lag-periods leaving the atomizing pressure unchanged throughout the spraying phase.

3.5. The effect of duty cycle on granule size

The granule sizes as a function of duty cycle length forms a second-order equation, as seen in Table 2 and Figs. 4 and 5. This gives rise to the forming of a minimum value, which the chosen duty cycle length range in the experimental design was able to reveal at all inlet air relative humidity levels, as shown in Tables 3 and 4. When the duty cycle length is shorter than the value at the particle size minimum, it can be assumed that the granulate mass is not given the opportunity to dry as extensively as at the minimum, due to the short lag-time. On the contrary, when the duty cycle length is longer than the value at the particle size minimum the granulate mass can be assumed to undergo such an extensive wetting due to the long duration of the spray, that the duration of the lag-time is not long enough to provide sufficient drying. At the particle size minimum the wetting and drying is at such a balance, that the overall wetting is as small as possible. The use of pulsed liquid feed causes repeated intermittent drying of the granulate mass during the spraying phase. This gives each cycle length a specific powder wetting profile, which is reflected in the particle size of the final granules. An increase in bed moisture content results in larger granules (Bouffard et al., 2005). In short, more efficient intermittent drying yields smaller granules.

Table 3
Modelled particle size minimum values (d_{50} [µm]) at atomization pressure 0.5 bar (ATM = atomization pressure [bar]; DC = duty cycle length [s]; RH% = relative humidity).

RH%	ATM	DC	d_{50}
34	0.5	100.4	119.3
45	0.5	114.4	129.3
56	0.5	134.4	136.8

The binder used in the present study is an aqueous povidone-solution with a concentration as high as 20%. The increased viscosity slows down the nucleation kinetics and might cause nucleation by coalescence of several binder droplets (Hapgood et al., 2003). However, the granule size can still remain small if there are sufficient dispersion forces present in the system. As described by Bouffard et al. (2005), the atomizing pressure can be defined as a source of dispersion forces, and as the atomization pressure was unchanged during the lag-periods, the system is subjected not only to increased breakage due to intermittent drying but also to additional granule growth inhibiting forces.

The granule size of the obtained final products in the present study confirms, that the particle size lowering effect of the intermittent lag-periods can partly be due to increased dispersion of wet nuclei. Breakage of the formed granules is thus a phenomenon that is expected to occur during the spraying phase in the present study. The d_{10}-values, d_{90}-values, oversize fractions and undersize fractions in the present study do not reveal any systematic differences in amount of breakage (Table 1).

The drying time of the granulate masses did not show any systematic behavior. This is due to the fact, that the starting criterion of the drying, 100 g binder consumption could be fulfilled at any point of the spraying phase of a duty cycle. The degree of wetting in the beginning of the drying determines the duration of the drying, and as the drying might start at any point of the spraying phase of a cycle and as the length of the duty cycles and inlet air relative humidity vary, it is difficult to clearly assess the degree of wetting at the beginning of the drying. This also affects the breakage behavior of granules during drying.

The breakage of granules can, by Iveson et al. (2001), be divided into breakage of wet and dry granules. Although the understanding of these mechanisms is limited, it can be stated that these affect the end product differently. In the present study both of these breakage types are to be expected during the spraying phase lag-periods, and the degree of wetting at the initiation of a lag period

Table 4
Modelled particle size minimum values (d_{50} [µm]) at atomization pressure 0.9 bar (ATM = atomization pressure [bar]; DC = duty cycle length [s]; RH% = relative humidity).

RH%	ATM	DC	d_{50}
34	0.9	122.8	104
45	0.9	136.8	101
56	0.9	156.4	96

affects the breakage behavior, resulting in differences in final product attributes, namely particle size.

3.6. The effect of inlet air relative humidity on granule size

3.6.1. Atomizing pressure

The effect of changes in atomizing pressure on granule size was small at low inlet air relative humidity, and increased with increasing inlet air relative humidity (Fig. 5). An explanation to this can be found in the droplet velocity. The droplet velocity decreases as the atomizing pressure decreases, which leads to a longer exposure to heated air. Air with low relative humidity causes more pronounced droplet evaporation as a result of the longer exposure time, in comparison to more humid air. The phenomenon of premature droplet evaporation as such is not novel (e.g. Abberger, 2001; Bouffard et al., 2005). However, the relation between droplet evaporation, droplet velocity and inlet air relative humidity combined with quantifying premature droplet evaporation at various droplet velocities and the effect of relative humidity onto this phenomenon needs further research.

The particle size minimum values shift towards longer cycle lengths as the inlet air relative humidity increases at both high and low atomization pressure (Tables 3 and 4; Figs. 4 and 5). This is a clear indicator of the changes in wetting behavior caused by the atomization pressure. Interestingly, the effect of inlet air relative humidity on the final granule size at low atomization pressure is in concordance to findings by other authors, but opposite at high inlet air relative humidity (e.g. Schaafsma et al., 1999; Rambali et al., 2001; Närvänen et al., 2008). This finding will be discussed more thoroughly in the following section.

3.6.2. Duty cycle length

In the present study the effect of the cycle length on particle size seems to be strong at high inlet air relative humidity, and smaller at low inlet air relative humidity (Figs. 4 and 5). Furthermore, changes in cycle length seem to give a larger granule size range at higher inlet air relative humidity, which includes cycle length dependent formation of both larger and smaller granules in high inlet air relative humidity (Fig. 4). The latter is unexpected, as there in the literature only are reports on increasing particle size with increasing inlet air relative humidity, and no reports on the opposite (e.g. Schaafsma et al., 1999; Rambali et al., 2001; Närvänen et al., 2008). It must be pointed out, however, that the studied variables in the mentioned studies were somewhat different to the ones in the present study, no previous reports could be found with a fixed spray:lag-ratio. The use of a fixed spray:lag ratio gives the opportunity to investigate how the length of the cycle affects the wetting and drying of the powder mass during the spraying phase.

An explanation to the unexpected formation of smaller granules could be found in the heat transfer coefficient of the inlet air. At low relative humidity the heat transfer coefficient of air is smaller than at high relative humidity. When the inlet air has a higher heat transfer coefficient, the temperature of the granulate mass is likely to increase faster during the intermittent lag-times, thus enabling more efficient drying of the powdered mass. Wang et al. (2007) have computationally shown that as inlet air relative humidity is elevated, the temperature of the particles in a fluidized bed increases. This finding has been experimentally confirmed by Lipsanen et al. (2007, 2008).

Wang et al. (2007) also imply, that the differences in moisture content as a function of time is small in the timeframe used in the present study. The evaporation rate was found to be very fast in the initial phase of the drying, correlating with the rate of temperature increase. Wang et al. (2007) suggest that the heat supplied to the systems is divided between evaporation of water and heating the particles. All the above-mentioned findings support the proposed theory, that the increase of product temperature at increasing inlet air relative humidity might be the cause of the formation of smaller granules at high inlet air humidity and at an optimal duty cycle length.

It is, however, important to note, that the maximum amount of water vapor in the air is dependent on relative humidity (Parikh et al., 1997). Taking this into consideration, moist air should cause slower drying and thus larger granules. It seems that using pulsed liquid feed with the duty cycles used in the present study, the heat transfer coefficient is of greater importance. Parikh et al. (1997) describe the equation $dw/dt = h(A/H)\Delta T$, with which the evaporation rate of a liquid film surrounding a granule being dried can be calculated. The equation shows that the heat transfer coefficient h and surface area A are of importance to the drying rate. In moist air h is elevated, and by restricting the growth with intermittent drying particle size is decreased and A is elevated. This results in increased drying, which contributes to keeping the particle size small, which then results in again more efficient drying. An increase in temperature difference between the air and the granulate mass, ΔT, also promotes drying, while an increase in latent heat of evaporation, H, decreases the drying rate.

When using pulsed spray this of kind, traditional approaches to thermodynamic description (mass transfer, heat transfer, etc.) of the phenomena present in fluid bed granulation are more difficult to implement, due to the more chaotic nature of pulsed spray granulation compared to traditional granulation, in terms of, e.g. increased temperature fluctuations, pronounced breakage and lack of saturation of nucleus pores. However, as the example above demonstrates, when properly modified and implemented, a thermodynamic approach to the process might provide a powerful tool to explain the observed phenomena.

The particles suspended in air are susceptible to the formation of interparticle electrostatic interactions (Guardiola et al., 1996). An increase in inlet air relative humidity decreases the electrostatic interaction between particles. This results in less particle–particle interaction keeping the starting material particle size small, allowing smaller granules to form (Guardiola et al., 1996; Faqih et al., 2007). In addition, liquid saturation has been found to play an important role in granule formation (Iveson and Litster, 1998; Schaafsma et al., 1998). When a droplet hits the particle surface, it is absorbed into porosity-related voids by capillary forces (Schaafsma et al., 1998). The granule growth rate is greatly affected by the degree of liquid saturation in the pores of the nucleus (Iveson and Litster, 1998; Schaafsma et al., 1998). Pulsed liquid feed is possible to reduce the degree of saturation, which can be enough to overcome the moisture added to the process by increased inlet air relative humidity. As can be seen in Fig. 5, increased inlet air relative humidity offers a greater range of duty cycle length-dependent end product particle size; the end product can reach smaller particle sizes at higher inlet air relative humidity at optimal conditions below the liquid saturation-point of the granule nuclei.

However, strictly from a drying point of view high inlet air relative humidity is likely to increase the drying time (Wang et al., 2007). Still, a theoretical possibility might exist, that the use of pulsed spray enhances the drying at optimal duty cycle lengths to such an extent, that this effect overpowers the granule growth-enhancing effects of the inlet air relative humidity.

4. Conclusions

Pulsed spray fluidized bed granulation has proven to be a useful tool in process control. Pulsed liquid feed provides the opportunity to target the particle size of the end product in fluid bed granulation and is able to compensate for changes caused by changes in inlet air relative humidity. Achieving this effect is possible without altering the spraying rate, spray:lag ratio or inlet air temperature.

The results of the present study imply that in addition to keeping the above-mentioned parameters constant atomization pressure can be kept constant at a high level and particle size can still be effectively down- and up-regulated by controlling the duty cycle length.

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