International Journal of Pharmaceutics 391 (2010) 148–154

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

In situ droplet size and speed determination in a fluid-bed granulator

Henrik Ehlers[a,∗], Jussi Larjo[b], Osmo Antikainen[a], Heikki Räikkönen[a], Jyrki Heinämäki[a], Jouko Yliruusi[a]

[a] Division of Pharmaceutical Technology, Faculty of Pharmacy, P.O. Box 56 (Viikinkaari 5 E), FI-00014 University of Helsinki, Finland
[b] Oseir Ltd., Alasniitynkatu 30, FI-33560 Tampere, Finland

ARTICLE INFO

Article history:
Received 22 December 2009
Received in revised form 26 February 2010
Accepted 28 February 2010
Available online 6 March 2010

Keywords:
Fluid bed
Droplet size
Droplet speed
High speed imaging
Diode laser stroboscopy
Particle tracking velocimetry

ABSTRACT

The droplet size affects the final product in fluid-bed granulation and coating. In the present study, spray characteristics of aqueous granulation liquid (purified water) were determined *in situ* in a fluid-bed granulator. Droplets were produced by a pneumatic nozzle. Diode laser stroboscopy (DLS) was used for droplet detection and particle tracking velocimetry (PTV) was used for determination of droplet size and speed. Increased atomization pressure decreased the droplet size and the effect was most strongly visible in the 90% size fractile. The droplets seemed to undergo coalescence after which only slight evaporation occurred. Furthermore, the droplets were subjected to a strong turbulence at the event of atomization, after which the turbulence reached a minimum value in the lower halve of the chamber. The turbulence increased as speed and droplet size decreased due to the effects of the fluidizing air. The DLS and PTV system used was found to be a useful and rapid tool in determining spray characteristics and in monitoring and predicting nozzle performance.

1. Introduction

Numerous factors affect the outcome of a process in fluid-bed granulation and coating. Important factors are e.g. inlet air temperature and relative humidity, spray rate, fluidizing air speed, atomization air flow rate, bed temperature and nozzle position (Davies and Gloor, 1971; Faure et al., 2001; Hemati et al., 2003; Jiménez et al., 2006). All of the above mentioned parameters are, however, interrelated, and process control must be approached by controlling all of the above mentioned parameters independently and together, in order to adjust the key parameters bed humidity, binder spreading and droplet size (Faure et al., 2001).

The droplet size affects the final product in both fluidized bed granulation and coating (Davies and Gloor, 1971; Dewettinck and Huyghebaert, 1998; Schaafsma et al., 2000; Hemati et al., 2003; Jiménez et al., 2006; Hede et al., 2008). In pneumatic nozzles the main determining factors of droplet size of the spray are atomization pressure and spray rate (Rambali et al., 2001). More specifically, the atomization air and spray rate mass flow ratio is of key importance in controlling spray characteristics (Kim and Marshall, 1971; Schæfer and Wørts, 1977, 1978b). As the atomization air/liquid flow rate mass flow ratio increases the size of the droplets formed decreases (Schæfer and Wørts, 1977; Chen et al., 2008). In addition to the atomization air/liquid mass flow-ratio (Schæfer and Wørts, 1977, 1978b; Chen et al., 2008) also the type of binder (Schæfer and Wørts, 1978a; Dewettinck et al., 1998), binder viscosity (Schæfer and Wørts, 1977; Juslin et al., 1995a) and spray angle caused by air dome settings and spray rate are of importance in the process of droplet formation.

Spray characterization has previously been performed using laser diffraction (Wan et al., 1995; Schaafsma et al., 1999), sieve analysis and microscopy of solidified droplets (Kim and Marshall, 1971) and microscopy of aqueous droplets collected into viscous oil (Schæfer and Wørts, 1977). Particle tracing velocimetry (PTV) has proven to provide detailed information about droplet size and speed, and can be utilized as a useful tool in spray characterization and process optimization in pan coating processes (Chen et al., 2008). Direct drop-collection methods have a tendency to overestimate the droplet size (Kim and Marshall, 1971), which does not occur with non-intrusive measurement techniques, such as PTV.

The primary aim of the present study was to investigate and gain understanding of the behavior of aqueous spray (droplets) produced by a pneumatic nozzle in a fluid-bed process. Special attention was paid to effects of increased temperature and inlet air flow on the spray characteristics (i.e. droplet size and speed). The secondary aim was to investigate applicability of diode laser stroboscopy (DLS) and particle tracking velocimetry (PTV) system in high speed imaging (monitoring) of aqueous solution droplets and in evaluating nozzle performance in a fluid-bed granulator.

In most earlier studies, the spray characteristics have been studied *ex situ*, i.e. with the nozzle removed from the process itself (e.g. Chen et al., 2008; Wan et al., 1995; Schæfer and Wørts, 1977). This gives valuable information about the spray characteristics and

∗ Corresponding author. Tel.: +358 9 191 59674; fax: +358 919159144.
E-mail address: henrik.ehlers@helsinki.fi (H. Ehlers).

0378-5173/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.ijpharm.2010.02.033

nozzle performance, but fails to identify how the spray behaves and what is the fate of the droplets in the real process. One key objective of the present study was to investigate whether DLS and PTV (SprayWatch) can be utilized for *in situ* spray characterization in a process similar to an actual fluid-bed process. Furthermore, the fate of the spray, namely droplet size and speed, along the central line covering the whole possible working range of the spray, was set out to be studied.

In earlier studies, the spray pattern has been studied stepwise through the spray zone both perpendicular to the central line, creating a cross section of the spray zone at the studied distance from the nozzle (Schaafsma et al., 2006; Wan et al., 1995; Chen et al., 2008), as well as along the central line of the spray (Mueller and Kleinebudde, 2007). In the present study, the spray was continuously monitored along the central line of the spray zone at five different distances, which resulted in detailed information on the behavior of the spray along the central line of the chamber.

2. Materials and methods

2.1. Equipment

The process environment used in the study was a laboratory-scale instrumented Aeromatic STREA-1 fluid-bed granulator equipped with a Schlick 970 7-1 (Düsen-Schlick GmbH, Germany) two-fluid external mixing pneumatic nozzle with an orifice diameter of 0.5 mm. The chamber made of acrylic plastic was perforated with five Ø 25 mm orifices, through which the measurements were performed (Fig. 1). The edges of the orifices were reinforced with a 2 mm thick rubber sheet, which also served as air insulation. The measurements were performed through an extension piece, which protected the measuring window from stray droplets which could affect its optical properties. All orifices were sealed air tight during the measurements. The process conditions are described in Table 1. The liquid temperature was 21.6 ± 0.4 °C and the liquid flow rate was kept constant at 2.5 g/min.

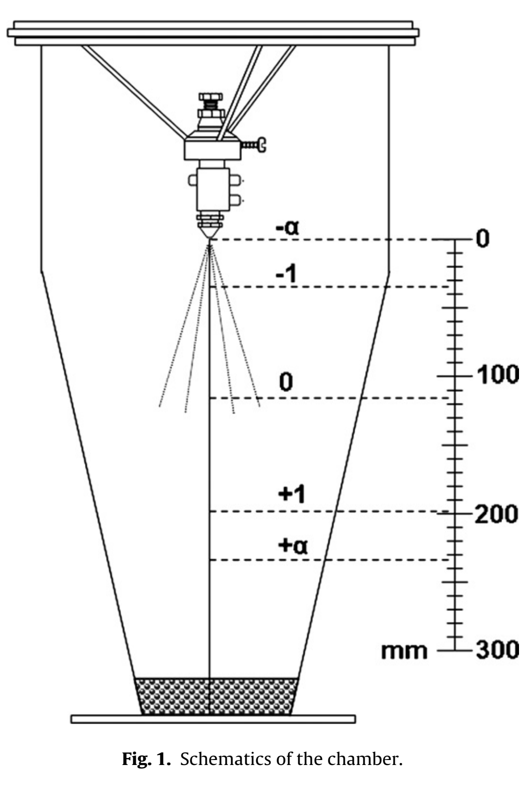

Fig. 1. Schematics of the chamber.

Table 1
Process conditions (mean ± S.D.). Dist. = distance from nozzle [mm]; Atm. = atomization pressure [bar]; RH% = relative humidity [%]; Air flow = inlet air flow rate [l/s]; Air temp. = inlet air temperature [°C].

Experiment	Dist.	Atm.	RH%	Air flow	Air temp.
1	34	0.5	9.8 ± 0.0	5.93 ± 0.2	49.95 ± 0.9
2	198	0.5	10.8 ± 0.0	6.11 ± 0.1	49.79 ± 1.0
3	34	0.9	9.7 ± 0.1	6.05 ± 0.1	50.29 ± 1.0
4	198	0.9	11 ± 0.2	6.10 ± 0.1	50.19 ± 1.0
5	0	0.7	10.1 ± 0.2	6.10 ± 0.2	49.99 ± 0.9
6	232	0.7	10.9 ± 0.0	5.90 ± 0.4	50.59 ± 0.6
7	116	0.42	9.6 ± 0.1	6.04 ± 0.1	50.19 ± 1.1
8	116	0.98	9.5 ± 0.0	6.03 ± 0.1	49.76 ± 0.8
9	116	0.7	9.6 ± 0.1	6.06 ± 0.2	50.31 ± 1.2
10	116	0.7	9.5 ± 0.0	6.06 ± 0.2	50.10 ± 1.1
11	116	0.7	9.3 ± 0.1	6.05 ± 0.1	49.62 ± 0.8
12	0	0.5	9.7 ± 0.0	6.09 ± 0.2	50.43 ± 0.9
13	0	0.9	9.8 ± 0.1	5.84 ± 0.4	50.05 ± 1.1
14	34	0.7	9.9 ± 0.1	5.99 ± 0.2	49.85 ± 1.1
15	116	0.9	9.6 ± 0.1	5.96 ± 0.3	49.93 ± 0.9
16	116	0.5	9.4 ± 0.0	5.91 ± 0.3	49.78 ± 1.0
17	198	0.7	11.0 ± 0.1	6.12 ± 0.2	50.77 ± 0.8
18	232	0.9	10.9 ± 0.0	6.04 ± 0.1	51.25 ± 0.8
19	232	0.5	10.8 ± 0.0	6.03 ± 0.1	50.93 ± 1.2

2.2. Data acquisition

The droplet size and speed were measured with particle tracking velocimetry (PTV) using HiWatch diode laser stroboscopy, DLS (Oseir Ltd, Finland) and a CCD camera (Lumenera, Canada) for droplet detection. The results were processed using Osirec-software (Oseir Ltd, Finland). The droplets were illuminated with three consecutive pulses of laser light with a wave length of 808 nm, resulting in three imprints of a droplet in a single frame. The duration of the pulses was 100–200 ns and the time elapsed between the pulses was 50–80 μs, both depending on the droplet speed observed.

The droplet size was derived from the diameter of the droplets. Henceforth the term droplet size is used to describe the droplet diameter. The droplet speed was calculated based on the droplet displacement in the triplicate imprint and the known time-interval between the laser pulses. The measuring principle is described in more detail by Larjo (2005). The camera lens was positioned 170 mm from the central line of the spray at all distances from the nozzle, and the background was recorded to reduce noise in the images. The size of the studied area was 9.3 mm × 6.95 mm at the vertical central line of the spray zone.

2.3. Materials

In the experiments, 500 g of Ø 10 mm glass beads were used to represent the powder mass of normal powder processing as the use of powders as model material would cause disturbances in the image analysis. The diameter was chosen based on the mass of the beads being sufficient to keep them as an immobile heat reserving air diffuser with the air flow rate used. The liquid used in the experiments was purified water at ambient room temperature.

2.4. Modeling and data analysis

A full Central Composite Design was used as an experimental design. The studied variables were atomization pressure and distance from the nozzle head (Tables 1 and 2). The centre point in the experimental design was measured in triplicate to ensure the repeatability of the process. Furthermore, total 8 additional points not included in the design were measured to further improve the quality of the models. The modeling was performed with MODDE 7-software (Umetrics AB, Sweden) using stepwise multilinear

Table 2
The studied variables.

Abbreviation	Distance from nozzle (mm)	Atomization pressure (bar)
$-\alpha$	0	0.42
−1	34	0.50
0	116	0.70
+1	198	0.90
$+\alpha$	232	0.98

regression analysis (MLR). The terms were stepwise eliminated until the predictive power of the model was at its highest with p-values for the individual terms taken into consideration.

The droplet size (d), speed (v) and trajectory angle (a) 10%-, 50%- and 90%-fractiles as well as droplet amount (n) and sum of droplet mass (m) were fitted into the second degree polynomial expressions

$$d_{10}, d_{50}, d_{90}, a_{10}, a_{50}, a_{90}(D, A) = a_1 \cdot D + a_2 \cdot A + a_3 \cdot D^2 + a_4 \cdot A^2 + a_5 \cdot D \cdot A + a_6 \quad (1)$$

and

$$\log[v_{10}, v_{50}, v_{90}, n, m(D, A)] = a_1 \cdot D + a_2 \cdot A + a_3 \cdot D^2 + a_4 \cdot A^2 + a_5 \cdot D \cdot A + a_6, \quad (2)$$

in which the term D stands for distance from the nozzle (mm) and A stands for atomization pressure (bar). Eq. (1) was used for normally distributed responses and Eq. (2) for distributions skewed to the left in order to transform the data into a more normal shape. The final simplified models are described in Table 3.

3. Results and discussion

3.1. General notices

The results show that the DLS and PTV method (SprayWatch) can be used in rapid and continuous measuring speed and size distribution of droplets produced by a pneumatic granulation/coating nozzle. Measurements of droplet size, speed as well as trajectory angle, were found to be repeatable. The total mass of the droplets at each measuring point was modeled (Fig. 2). The model gave high Q^2- and R^2-values (Table 3). As the area of interest was unchanged throughout all batches the model gives an estimate of the humidity profile along the central axis of the spray. As the atomizing pres-

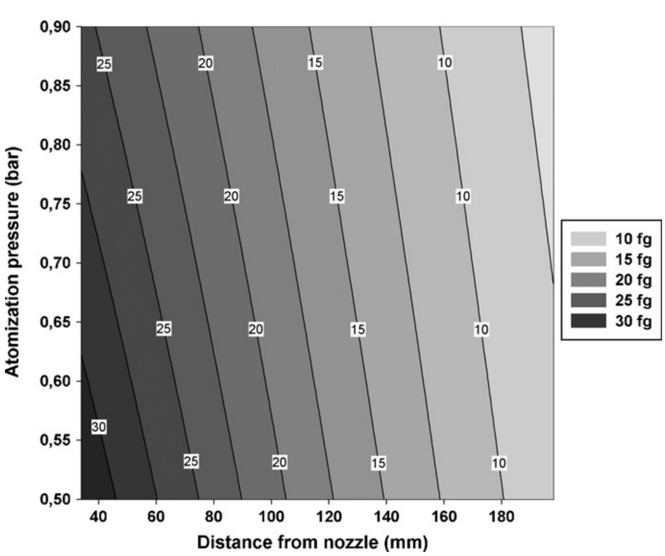

Fig. 2. The sum of the masses (fg) of the individual droplets.

Table 3
The models obtained by multilinear regression analysis (D = distance from nozzle [mm], A = atomization pressure [bar], n = amount of droplets, m = sum of mass (fg), d = droplet diameter (μm), v = droplet speed [m/s], a = droplet trajectory angle [°]).

	n	m	d_{10}	d_{50}	d_{90}	v_{10}	v_{50}	v_{90}	a_{10}	a_{50}	a_{90}
a_1	−3.88E−03***	−1.86E−03***	1.44E−02	2.03E−02	7.79E−02*	4.59E−03	2.13E−03**	1.75E−03**	−6.81E−02***	−3.61E−01***	−7.01E−01**
a_2	N/S	−2.43E−01*	−9.35E−01**	−2.27E+00**	−1.01E+01***	1.58E−01	−2.38E−01*	−1.05E−01*	1.25E+01	3.47E+01	2.86E+01*
a_3	N/S	−7.42E−06*	−5.81E−05***	−8.04E−05***	−2.85E−04***	−2.15E−05***	−2.22E−05***	−1.88E−05***	4.24E−04***	1.85E−03***	3.34E−03***
a_4	N/S	N/S	N/S	N/S	N/S	N/S	N/S	N/S	N/S	N/S	N/S
a_5	N/S	N/S	N/S	N/S	N/S	N/S	3.53E−03**	2.92E−03*	−8.01E−02*	−2.17E−01**	−1.56E−01*
a_6	3.62E+00***	−1.33E+01***	2.14E+01***	2.51E+01***	3.57E+01***	−9.25E−02***	5.02E−01***	6.66E−01***	1.68E+00**	2.10E+01***	6.14E+01***
R^2	0.948	0.954	0.800	0.728	0.785	0.795	0.905	0.857	0.865	0.929	0.974
Q^2	0.933	0.919	0.655	0.537	0.627	0.682	0.794	0.722	0.711	0.850	0.942

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

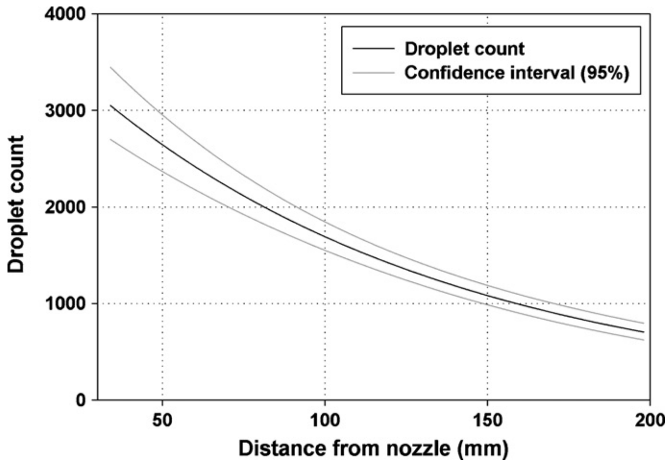

Fig. 3. Droplet count as a function of distance from nozzle (mm).

sure increases, the sum of mass decreases as a result of stronger dispersion of the liquid. This indicates that the most effective part of the spraying zone is close to the nozzle, and lower atomization pressures result in greater wetting of the powder mass and subsequently larger granules. This is in accordance with the general understanding of the effect of the atomizing pressure. The amount of droplets observed was modeled with high R^2- and Q^2-values (Table 3). Atomizing pressure was found not to affect the amount of droplets formed. The amount of droplets decreases more rapidly close to the nozzle head, and the decreasing settles down to a slower rate as the distance increases (Fig. 3). This can be seen as an indication of droplet coalescence before the onset of subtle evaporation.

3.2. Droplet size

The droplet size data followed trends described in Table 3. The relatively low R^2 and Q^2 values were expected, as the environment inside the chamber of a fluid-bed granulator can be described as chaotic. The droplet speed and angle, however, gave significantly stronger models, which indicates that the weaker models observed for droplet size might be due to something else than the chaotic environment. A simple explanation could be surface tension-caused pulsating, stretching and bending of the droplet as a result of the atomization. The detection limit of the present setup was 18 μm, which is somewhat close to the d_{10}-value. The error in the d_{10}-values caused by the proximity of the detection limit is, however, considered small. The detection limit is highly dependent on the optics used.

According to the literature, the droplet diameter depends on density, surface tension and viscosity of the atomized liquid, and the effects of these parameters in addition to liquid and gas speed at the nozzle are described differently by numerous authors (Hede et al., 2008). Mueller and Kleinebudde (2007) measured droplet sizes at the spray center and they suggested that all of these factors affect droplet size. Along the central line of the spray zone the droplets are smaller in size and greater in speed than on the edges of the spray zone (Mueller and Kleinebudde, 2007; Chen et al., 2008). As the present study was performed *in situ* in a downwards narrowing conical chamber, the droplet size was only measured along the vertical central axis of the spray.

The results show that the droplet size was small, with d_{50}-values between 23 μm and 25 μm over the entire studied range (Fig. 4). The most significant changes in droplet size were seen in the d_{90}-values. This finding is in accordance with the results obtained by Juslin et al. (1995a,b). The effect of atomization pressure on the droplet size was found to be linear, and with decreasing droplet

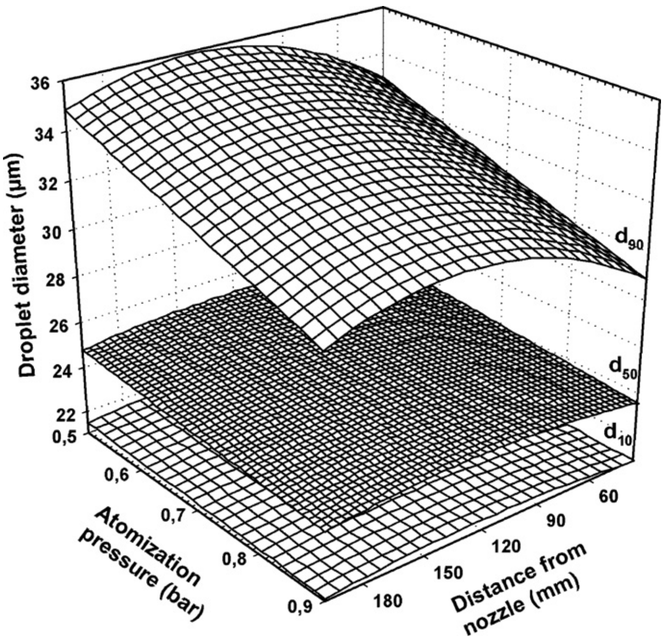

Fig. 4. Droplet diameter (μm).

size with increasing atomization pressure. This is in concordance to the general understanding of the effect of the atomization pressure on droplet size.

In the present study, the liquid was not fully atomized as the plateau stage of the droplet size vs. atomization pressure was not reached. This has been also described by Kim and Marshall (1971) and more recently Chen et al. (2008). After reaching the fully atomized state, atomization pressure cannot be used to control the process, as the droplet size does not decrease with increasing atomization pressure after the threshold value.

After the atomization, the droplet size increased for a distance of 136 mm from the nozzle head (Figs. 1, 4). This can be explained by droplet coalescence and sorting of the droplets; the droplets which are small in size and low in speed are likely to be transported upwards with the fluidizing gas. The droplet size decreased as the droplets reached the distance of 136 mm from the nozzle head, which can be attributed to droplet evaporation and the sorting mentioned above (Fig. 4). Large droplets are reported to evaporate more slowly than small droplets (Davies and Gloor, 1971; Dewettinck and Huyghebaert, 1998; Leclére et al., 2004). The time consumed to evaporate 50% of the liquid decreases linearly with decreasing droplet Sauter mean diameter (Leclére et al., 2004). Evaporation of droplets is an issue that might cause unwanted final product (Jiménez et al., 2006) and compromise the representativeness of samples (Kim and Marshall, 1971).

In the present study, the distance of 136 mm is sufficient to reach the surface of a fluidized particulate mass. This finding indicates that droplet evaporation is not a major factor at the studied process conditions. The results of the present study were opposite to those of Mueller and Kleinebudde (2007), in which gun-to-bed-distance was found not to affect the droplet size. Their experiment was, however, performed *ex situ*, which is a clearly different situation than the one described in the present study.

The droplet size distributions were narrow over the entire range of the studied variables. The droplet size distributions had a slight widening towards higher droplet sizes, but no undisputable bimodality was observed. This is partly in concordance with Juslin et al. (1995a). Droplet size distributions are expected to be bimodal with increased bimodality at higher atomizing pressures (Juslin et al., 1995a). The droplet size distribution width ($d_{90} - d_{10}$) and rela-

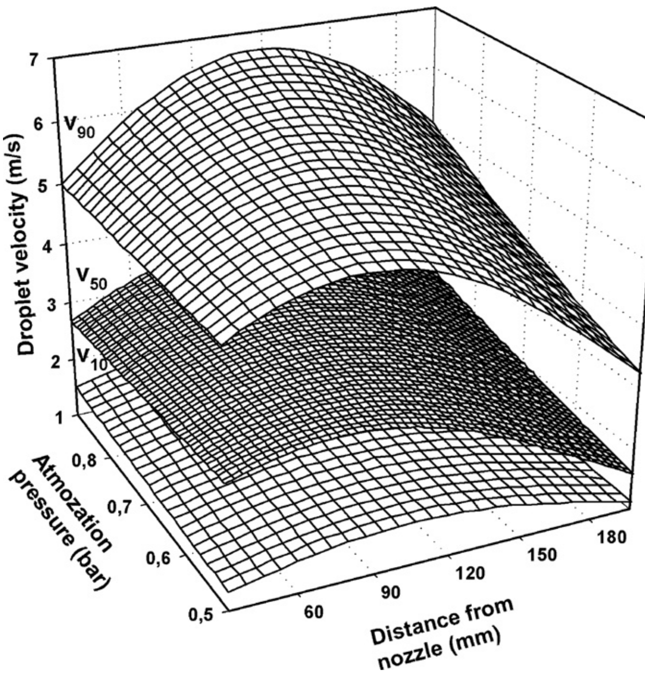

Fig. 5. Droplet speed (m/s).

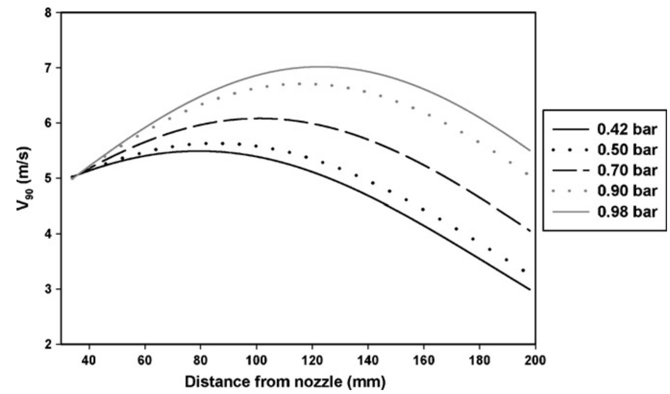

Fig. 6. Droplet speed profiles at different atomization pressures along the central axis of the spray zone.

tive width ($d_{50}/[d_{90} - d_{10}]$) could not be modeled, which indicates that no distinct trends or behavior could be recognized from the obtained data. This finding is in contrast to the results of Juslin et al. (1995a), according to which higher air pressures make the width of the droplet size distribution ($d_{90} - d_{10}$) narrower, explained by a decreased amount of large droplets.

In this study, the influence of spray rate on the droplet size was not investigated. There are several studies available of the effect of spray rate on droplet size. These papers conclude that the influence of spray rate on droplet size at constant atomization pressure is inferior compared to the effect of the atomization air at constant spray (e.g. Schæfer and Wørts, 1977; Wan et al., 1995; Hemati et al., 2003; Chen et al., 2008). According to Juslin et al. (1995a), the flow rate of the solution has no apparent effect on the shape of the droplet size distribution. At lower viscosities the atomization pressure has a higher effect on droplet size (Juslin et al., 1995b). This study was performed with purified water as liquid, which has a lower viscosity than polymer solutions that are used in granulation and coating. It can thus be expected that the effect of atomization pressure on droplet size is slightly smaller when polymer solutions are used.

3.3. Droplet speed

The obtained speed models were satisfactory in both goodness of fit and predictive power (Table 3). The droplet speed increased as the atomization pressure increased (Fig. 5). This is due to the higher force exerted on the liquid at the event of atomization. Similarly to the droplet size, the droplet speed increased as the droplets progress further along the central axis (Figs. 5 and 6), and this may be also due to coalescence of droplets. The droplets underwent a decrease in speed after reaching the maximum speed. This is partially contradictory to the findings of the study (*ex situ*) performed by Mueller and Kleinebudde (2007), who found that the gun-to-bed-distance clearly affected the speed, but the droplets undergo a rapid decrease in speed directly after leaving the nozzle.

The speed at the moment of atomization was vertically identical at all atomization pressures (Fig. 6). The atomization pressure dependent changes in speed occurred on a distance from 0 mm to 79 mm at 0.42 bar and 123 mm at 0.98 bar. The differences in speed-profile could possibly correlate with the distance downwards along the central axis to which the atomizing air is able to reach at different atomization pressures. Atomization air with higher atomization pressures were able to reach further down along the central axis. This was not observed when it comes to droplet size. The results indicate that the used method is able to identify the upper limit in atomization pressure caused by the chamber geometry.

Panda et al. (2001) found that an increase in droplet speed decreased the growth rate of coating, due to differences in the impact between droplet and particle. Link and Schlünder (1997) found that an increase in droplet speed and momentum increase the growth rate of coating to a maximum value, after which the growth rate starts to decrease. In the present study water was used; Panda et al. (2001) and Link and Schlünder (1997) found that polymer solutions behave slightly different than solutions without polymers. The polymer has an impact on viscosity and thus droplet size. Both of these affect the behavior in impact such, that a higher speed is needed for the droplets to bounce back upon impact, resulting in impaired droplet deposition.

The results of the present study confirmed the need of the discussion that has occurred in several publications: also the airflows in the chamber are of importance when it comes to granule formation. The atomization air is a source of shear forces which affect the final granule size (Bouffard et al., 2005), even though granule rupture according to Schaafsma et al. (2000) is not significant at the correct process conditions. The atomization air also has an impact on the temperature in the chamber, which influences the overall process conditions such as bed temperature and droplet evaporation (Dewettinck and Huyghebaert, 1998). When the conditions in the (fluid-bed) chamber promote drying too intensely, the process of granulation or coating might result in a non-acceptable final product (Jiménez et al., 2006). The results of the present study showed how far down the central axis the effect of the atomizing air is able to reach. After reaching the maximum speed the droplets slowed down. This was expected due to the resistance exerted on the droplet by the oppositely directed atomization air. The conical shape of the chamber also increased the probability of slowing down as the droplets move further down the chamber.

The speed distribution width ($\nu_{90} - \nu_{10}$ and $\nu_{50}/[\nu_{90} - \nu_{10}]$) could not be modeled. Though, by visual inspection of the distributions it could be concluded that the distributions seemed to start out narrow at the nozzle and became wider as the distance increases. The distributions started to narrow down as they have reached a maximum width. Compared to the droplet size distributions more pronounced bimodality was observed in the speed distributions. In all, the effect of droplet speed on the final product

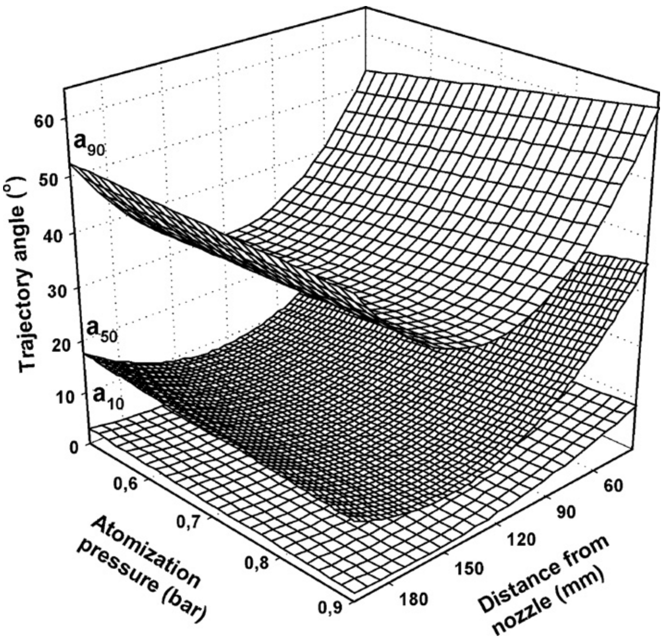

Fig. 7. Droplet trajectory angles (°).

is scarcely studied, and no further conclusions can be made with the obtained data.

3.4. Turbulence

The turbulence-models were satisfactory in both predictive power and goodness of fit (Table 3). The extent of turbulence was calculated by assessing the angle of the droplet trajectory in comparison to the vertical central axis of the spray zone. The method did not provide information on the direction, but gave a vector with an accuracy of ±180°. The angle of the vector pointing downwards was chosen as the measure of turbulence. The error caused by assuming that all droplets move downwards is considered small.

As expected the turbulence was at its highest directly after the atomization (Fig. 7). The turbulence reached a minimum value similarly to the maximum values of the droplet size and speed. This can be explained by the atomization air of the nozzle extending a significant distance away from the nozzle head. The turbulence increased after the minimum value due to the droplets evaporating, slowing down and changing direction to the one of the fluidizing air (Figs. 7 and 8). This can be attributed to the impact of the fluidizing air on the droplets. The turbulence was higher with higher

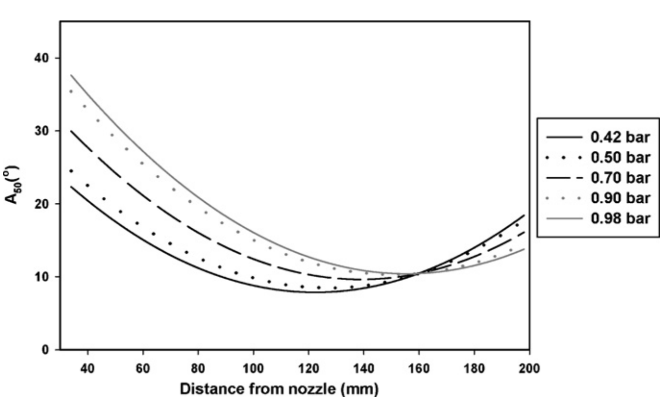

Fig. 8. Droplet trajectory angle (A_{50}) [°] profiles at different atomization pressures along the central axis of the spray zone.

atomization pressures, and reached further away from the nozzle head with increasing atomization pressure. The droplets in a spray are expected to move mostly in the *y*-direction (Mueller and Kleinebudde, 2007). By measuring the trajectory angle along the central axis it is possible to find the distance, at which the droplet trajectories are ideal. In the present study the most uniform movement along the *y*-axis was ranged from 122 mm from the nozzle for 0.42 bar atomization pressure to 155 mm for 0.98 bar (Fig. 8).

4. Summary and conclusions

The aqueous spray characteristics and pneumatic nozzle performance were investigated *in situ* in a laboratory scale fluid-bed granulator. In conclusion, particle tracking velocimetry (PTV) using HiWatch diode laser stroboscopy (DLS) and a CCD camera proved to be a useful and rapid tool in determining atomized spray characteristics. Increased atomization pressure decreased the droplet size linearly, and the effect was most strongly visible in the 90% size fractile. The aqueous droplets produced by a pneumatic nozzle seemed to undergo coalescence before evaporation. The extent of droplet evaporation at the studied fluid-bed process parameters appeared to be small. Droplet speed is a scarcely studied parameter well describing the spray. The droplets produced by a pneumatic nozzle were subjected to a strong turbulence at the event of atomization, after which the turbulence reached a minimum value in the lower half of the chamber. The turbulence within the spray increased as speed and droplet size decreased due to the effects of the fluidizing air. The trajectory angles also revealed at which point the droplet trajectories were most strongly parallel to the central line of the spray zone. Increased knowledge of nozzle function and subsequent spray characteristics increases process understanding.

Acknowledgements

The Finnish Pharmaceutical Society is acknowledged for financial support. Oseir Ltd (Finland) is acknowledged for supplying equipment and expertise. Niina Kivikero, M.Sc. (Pharm.) is acknowledged for fruitful discussions.

References

Bouffard, J., Kaster, M., Dumont, H., 2005. Influence of process variables and physicochemical properties on the granulation mechanism of mannitol in a fluid bed top spray granulator. Drug Dev. Ind. Pharm. 31, 923–933.
Chen, W., Chang, S.-Y., Kiang, S., Early, W., Paruchuri, S., Desai, D., 2008. The measurement of spray quality for pan coating processes. J. Pharm. Innov. 3, 3–14.
Davies, W.L., Gloor, W.T., 1971. Batch production of pharmaceutical granulations in a fluidized bed. I. Effects of process variables on physical properties of final granulation. J. Pharm. Sci. 60, 1869–1874.
Dewettinck, K., Deroo, L., Messens, W., Huyghebaert, A., 1998. Agglomeration tendency during top spray fluidized bed coating with gums. Lebensm.-Wiss. U.-Technol. 31, 576–584.
Dewettinck, K., Huyghebaert, A., 1998. Top-spray fluidized bed coating: effect of process variables on coating efficiency. Lebensm.-Wiss. U.-Technol. 31, 568–575.
Faure, A., York, P., Rowe, R.C., 2001. Process control and scale-up of pharmaceutical wet granulation processes: a review. Eur. J. Pharm. Biopharm. 52, 269–277.
Hede, P.D., Bach, P., Jensen, A.D., 2008. Two-fluid spray atomization and pneumatic nozzles for fluid bed coating/agglomeration purposes: a review. Chem. Eng. Sci. 63, 3821–3842.
Hemati, M., Cherif, R., Saleh, K., Pont, V., 2003. Fluidized bed coating and granulation: influence of process related variables and physicochemical properties on growth kinetics. Powder Technol. 130, 18–34.
Jiménez, T., Turchiuli, C., Dumoulin, E., 2006. Particles agglomeration in a conical fluidized bed in relation with air temperature profiles. Chem. Eng. Sci. 61, 5954–5961.
Juslin, L., Antikainen, O., Merkku, P., Yliruusi, J., 1995a. Droplet size measurement. I. Effect of three independent variables on droplet size distribution and spray angle from a pneumatic nozzle. Int. J. Pharm. 123, 247–256.
Juslin, L., Antikainen, O., Merkku, P., Yliruusi, J., 1995b. Droplet size measurement. II. Effect of three independent variables on parameters describing the droplet size distribution from a pneumatic nozzle studied by multilinear stepwise regression analysis. Int. J. Pharm. 123, 257–264.

Kim, K.Y., Marshall, W.R., 1971. Drop-size distributions from pneumatic atomizers. AIChE J. 17, 575–584.

Larjo, J., 2005. High power diode lasers in spray process diagnostics. Proc. SPIE 5580, 455, doi:10.1117/12.567358.

Leclére, K., Briens, C., Gauthier, T., Bayle, J., Guigon, P., Bergougnou, M., 2004. Experimental measurement of droplet vaporization kinetics in a fluidized bed. Chem. Eng. Proc. 43, 693–699.

Link, K.C., Schlünder, E.-U., 1997. Fluidized bed spray granulation. Investigation of the coating process of a single sphere. Chem. Eng. Proc. 36, 443–457.

Mueller, R., Kleinebudde, P., 2007. Comparison of a laboratory and production coating spray gun with respect to scale-up. AAPS PharmSciTech 8 (Article 3).

Panda, R.C., Zank, J., Martin, H., 2001. Experimental investigation of droplet deposition on a single particle. Chem. Eng. J. 83, 1–5.

Rambali, B., Baert, L., Massart, D.L., 2001. Using experimental to optimize the process parameters in fluidized bed granulation on a semi-full scale. Int. J. Pharm. 220, 149–160.

Schaafsma, S.H., Vonk, P., Kossen, N.W.F., 2000. Fluid bed agglomeration with a narrow droplet size distribution. Int. J. Pharm. 193, 175–187.

Schaafsma, S.H., Kossen, N.W.F., Mos, M.T., Blauw, L., Hoffmann, A.C., 1999. Effects and control of humidity and particle mixing in fluid bed granulation. AIChE J. 45, 1202–1210.

Schaafsma, S.H., Kossen, N.W.F., Vonk, P., Hoffmann, A.C., 2006. A model for the spray zone in early-stage fluidized bed granulation. AIChE J. 52, 2736–2741.

Schæfer, T., Wørts, 1977. Control of fluidized bed granulation. II. Estimation of droplet size of atomized binder solutions. Arch. Pharm. Chem., Sci. Ed. 5, 178–193.

Schæfer, T., Wørts, 1978a. Control of fluidized bed granulation. IV. Effects of binder solution and atomizing on granule size and size distribution. Arch. Pharm. Chem., Sci. Ed. 6, 14–25.

Schæfer, T., Wørts, 1978b. Control of fluidized bed granulation. V. Factors affecting granule growth. Arch. Pharm. Chem., Sci. Ed. 6, 69–82.

Wan, L.S.C., Heng, P.W.S., Liew, C.V., 1995. The influence of liquid spray rate and atomizing pressure on the size of spray droplets and spheroids. Int. J. Pharm. 118, 213–219.