ELSEVIER International Journal of Pharmaceutics 123 (1995) 247–256

international journal of pharmaceutics

Droplet size measurement: I. Effect of three independent variables on droplet size distribution and spray angle from a pneumatic nozzle

Laura Juslin [a,*], Osmo Antikainen [a], Pasi Merkku [b], Jouko Yliruusi [a]

[a] *Pharmaceutical Technology Division, Department of Pharmacy, P.O. Box 56, University of Helsinki, FIN-00014 Helsinki, Finland*
[b] *Leiras Oy, Pharmaceutical R&D, P.O. Box 415, FIN-20101 Turku, Finland*

Received 1 December 1994; accepted 20 February 1995

Abstract

The effect of three independent variables (atomizing air pressure, flow rate of binder solution and polyvinylpyrrolidone concentration) on the droplet size distribution from a pneumatic nozzle was studied using a normal 3^3 factorial design. The droplet sizes and size distributions were determined by laser diffractometry. The effect of the same variables on the spray angle and cross-sectional area of spray cone (describes the area of wetted bed in a fluidized bed granulator) was also evaluated. The dependence of these latter response variables on the independent variables was studied by a multilinear stepwise regression analysis. It was noted that increasing the amount of polyvinylpyrrolidone in binder solution decreased the number of bimodal distributions and increased the width of the distributions. A high pressure with water as a binder solution resulted in a pronounced bimodality and a narrow width of distribution. Increasing the flow rate had no clear effect on the shape of distributions (uni- or bimodal), but the width of distributions increased. The atomizing air pressure was the most significant factor affecting the spray angle and the cross-sectional area of the spray cone. Increasing the pressure led to a decline in the spray angle and to a decreased area. The effect of PVP concentration was opposite to that of pressure. The effect of flow rate was controversial because, according to the regression analyses, it affected inversely the spray angle and the area.

Keywords: Pneumatic nozzle; Laser diffractometry; Atomizing air pressure; Binder solution flow rate; PVP concentration; Volume droplet size distribution; Spray angle

1. Introduction

During the last few decades, the function and characteristics of different nozzles have been studied extensively within mechanical engineering. Tate and Marshall (1953) studied centrifugal pressure nozzles in order to correlate mean drop size, drop size uniformity and cone angle with the liquid velocity and orifice diameter. Drop size measurements with pneumatic nozzles have been made by Gretzinger and Marshall (1961) and by

* Corresponding author. Tel. +358-0-708 59145; fax +358-0-708 59144.

SSDI 0378-5173(95)00081-X

Kim and Marshall (1971). Atomization by pneumatic nozzles is based on the effect of high-velocity gas upon a liquid jet (Gretzinger and Marshall, 1961; Kim and Marshall, 1971). Pneumatic nozzles are suitable for producing fine sprays of an average drop diameter below 30 μm (Gretzinger and Marshall, 1961). When using pneumatic nozzles the flow rate of both liquid and air can be controlled independently and they are well suited for atomization of viscous liquids (Kim and Marshall, 1971).

The methods used for droplet size determination have usually been based on taking photomicrographs of droplets and counting them by microscopic methods. Only few studies concerning droplet size measurements have been carried out within pharmaceutical technology as part of fluidized bed granulation studies. In fluidized bed granulation the binder solution is sprayed on starting materials through a pneumatic nozzle. Hence, the droplet size of binder solution affects the final granule size; one of the first to report this was Thurn (1970). The most important study was that of Schæfer and Wørts (1977a) who measured the droplet size of atomized binder solutions from a pneumatic nozzle. The droplet size was analysed by taking a photomicrograph of the droplet sample collected in viscous lubricating oil and counting about 1000 droplets. Aulton and Banks (1979), Waldie et al. (1987) and Yliruusi et al. (1992) used laser diffraction for measurement of spray droplet size.

In this paper, a complete 3^3 factorial design was used to evaluate the effects of three independent variables (atomizing air pressure, flow rate of binder solution and polyvinylpyrrolidone concentration) on the droplet size distribution of atomized binder solution. Droplets were produced by a pneumatic nozzle used in a laboratory scale fluidized bed granulator. The droplet size distributions were measured by laser diffractometry which offers an easy and rapid analysis compared to techniques used earlier. Furthermore, some effort was made to determine the spray angles when different atomizing air pressures, flow rates and PVP concentrations were used. The spray angle is important because it is a major factor affecting the area of wetted bed in a fluidized bed granulator. According to our knowledge, no attempts have been made to determine the effect of these variables on the spray angle. Schæfer and Wørts (1977b), however, presented some approximations for spray angles with three different positions of air dome setting.

Table 1
Levels and dimensions of independent variables

Variable	Level			Dimension
	−1	0	+1	
Atomizing air pressure (P)	1.0	1.5	2.0	(bar)
Flow rate of binder solution (Q)	100	150	200	(g/min)
PVP concentration (C)	0	10	20	(%)

2. Materials and methods

2.1. Study design

The droplet size distribution was determined using a 3^3 factorial design. The independent variables used were atomizing air pressure (bar), flow rate of binder solution (g/min) and polyvinylpyrrolidone (PVP) concentration (%). The levels of each variable are shown in Table 1 and the matrix of experiments in Table 2. Each measurement was repeated twice. Parallel tests were performed three times in the central point and once in the corner points. The total number of experiments was thus 38.

2.2. Regression analysis

Multilinear stepwise regression analysis was used to study the dependence of response variables (spray angle and cross-sectional area of spray cone at 15 cm distance from nozzle tip) on the independent variables atomizing air pressure (P), flow rate of binder solution (Q) and PVP concentration (C).

The regression model for three independent variables (P, Q and C) can be presented in a general form:

$$Y = \alpha + \beta_1 P + \beta_2 Q + \beta_3 C + \beta_4 PQ + \beta_5 PC + \beta_6 QC + \beta_7 P^2 + \beta_8 Q^2 + \beta_9 C^2 + \beta_{10} PQC \quad (1)$$

where $\beta_1 ... \beta_{10}$ represent regression coefficients and α is a constant. When the equation is presented with coded values, the magnitude of the regression coefficient details how much the factor affects the dependent factor according to the model, and the sign indicates the trend of the change. The model was simplified with a backward selection technique which means that some terms are removed from the model in order to increase the explanation degree (R^2). Before any term was removed from the model, its significance was assessed by Student's *t*-test to ensure that only non-significant terms were rejected. Modelling was performed by Design-Expert Software (v. 3.0.6c, Stat-Ease, Inc., USA). The surface plots were drawn by Graftool (v. 3.3, Graphical Analysis System, 3-D Visions Corp., USA).

2.3. Materials

The binder solutions used were purified water and 10 and 20% aqueous dispersions of polyvinylpyrrolidone (PVP) (Kollidon® K25, BASF, Germany). Water was chosen as a reference low-viscosity solution for the study even though pure water is not commonly used as a binder solution in fluidized bed granulation.

2.4. Determination of droplet size distribution

The droplet size distributions from a pneumatic nozzle (Schlick Model 940-943, Form 7-1, Gustav Schlick GmbH, Germany) were measured by laser diffractometry (Malvern 2600C Droplet and Particle Sizer, Malvern, UK). The focal lens length was 300 mm. The nozzle used had a liquid orifice diameter of 1.2 mm and the air dome was kept constant. A schematic diagram of the measurements is presented in Fig. 1. A suction system was constructed in order to collect binder solution droplets after they had passed through the laser beam. The atomizing air pressure was controlled by the automatic system built in the Glatt WSG 5 fluidized bed granulator (Glatt GmbH, Germany) described earlier (Merkku et al., 1992). The droplet size measurement was started when the atomizing air pressure had reached the target value. The flow rates of the binder solutions were controlled manually by adjusting the revolution speed of the pump because the automatic control was not stable enough. Even manually it was impossible to keep the flow rates accurately at the target values (100, 150 and 200 g/min) but the real flow rates could be calculated from the process data collected during the determination. The distributions were calculated by the liquid droplet spray (LDS) method and presented as volume distributions fitted by the model-independent routine. Some results were also fitted to the Rosin-Rammler distribution. The distributions were drawn as means of three measurements.

2.5. Determination of spray angle and cross-sectional area of spray cone

Sprays of purified water and 10 and 20% aqueous solutions of PVP were photographed (Olympus OM 10 super zoom 35-105, Olympus, Japan).

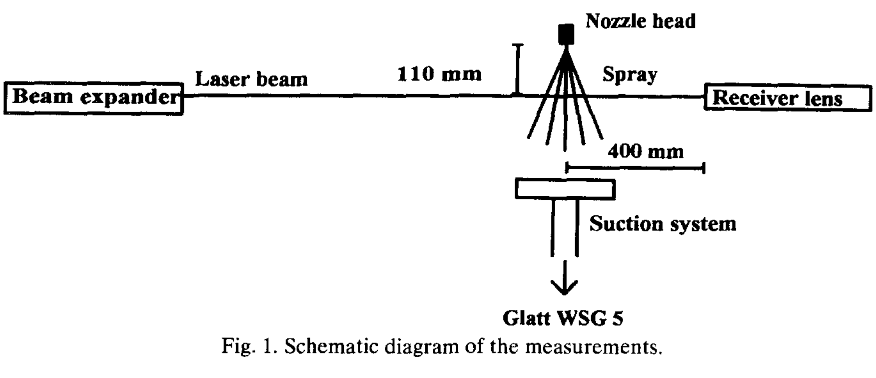

Fig. 1. Schematic diagram of the measurements.

Table 2
Matrix of experiments

Experiment	Variables		
	C	*P*	*Q*
1	−1	−1	−1
2	−1	0	−1
3	−1	+1	−1
4	−1	−1	0
5	−1	0	0
6	−1	+1	0
7	−1	−1	+1
8	−1	0	+1
9	−1	+1	+1
10	0	−1	−1
11	0	0	−1
12	0	+1	−1
13	0	−1	0
14	0	0	0
15	0	+1	0
16	0	−1	+1
17	0	0	+1
18	0	+1	+1
19	+1	−1	−1
20	+1	0	−1
21	+1	+1	−1
22	+1	−1	0
23	+1	0	0
24	+1	+1	0
25	+1	−1	+1
26	+1	0	+1
27	+1	+1	+1
Corner point parallel test			
28	−1	−1	−1
29	−1	+1	−1
30	−1	−1	+1
31	−1	+1	+1
32	+1	−1	−1
33	+1	+1	−1
34	+1	−1	+1
35	+1	+1	+1
Central point parallel tests			
36	0	0	0
37	0	0	0
38	0	0	0

The atomizing air pressures and the target values of flow rates were the same as in the droplet size measurements. Because the main purpose was to evaluate the effects of different variables on the spray angle, the air dome was kept constant (number 3). The spray angles were measured with a geometric triangle from original size slides projected on the screen. Also, the diameter of the spray cone at 15 cm distance from the nozzle tip was measured and hence the cross-sectional area of the spray cone was calculated. This latter response variable was calculated in order to estimate the area of wetted bed. The other factor affecting the wetted bed area in addition to the spray angle is the nozzle height. In this case the 15 cm distance from the nozzle tip was chosen for practical reasons: the greater the distance, the more unclear the outlines of the spray cone. Because different people are likely to obtain slightly different results, the angles and the diameters were measured independently by two persons in a random order, and averaged values were used.

3. Results and discussion

3.1. Effect of model fitting on droplet size distribution

The droplet size distributions (Fig. 2–4) are only presented for Expts 1–27 (Table 2); the parallel tests 28–38 are included in Table 3. Reproducibility of the consecutive measurements was quite good (Table 3). In the literature (Aulton and Banks, 1979; Malvern Instruments, 1986), the Rosin-Rammler (RR) distribution is recommended for spray droplet size distributions. Also in this study, some measurements were fitted to the RR distribution, but finally this fitting was rejected because it removed the bimodal shape of distributions discussed later and since log diff values were almost the same as with model-independent fitting. It has been reported earlier that droplet size distribution from a pneumatic nozzle does not follow any usual distribution functions such as normal, log-normal or square root normal functions (Kim and Marshall, 1971; Schæfer and Wørts, 1977a).

3.2. Effect of different variables on the shape of distributions

In general, it is evident that the shape of some droplet size distributions is bimodal (Fig. 2–4). Because all distributions were more or less bi-

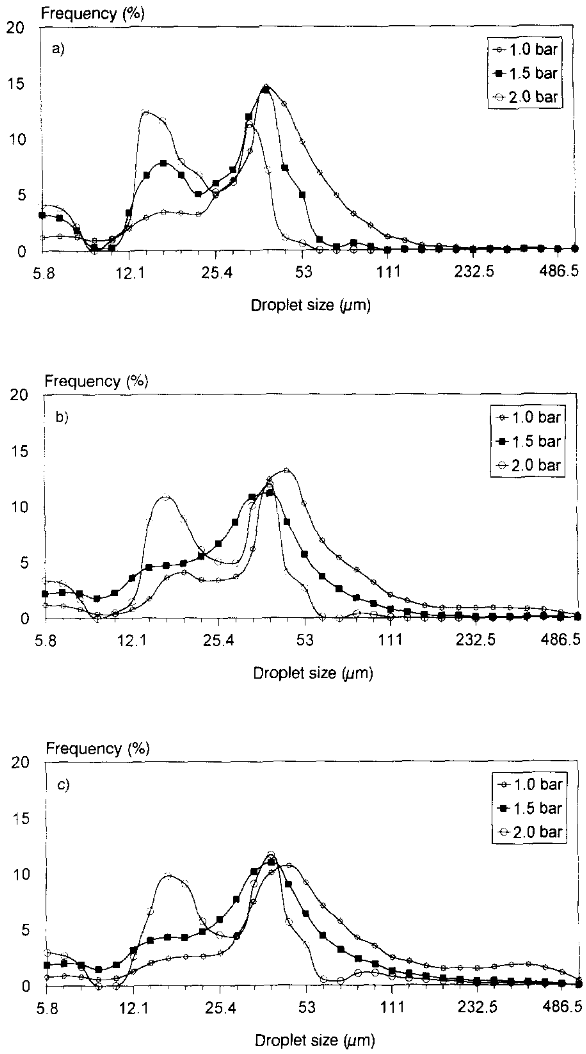

Fig. 2. Droplet size distributions for water from a pneumatic nozzle at different flow rates and atomizing air pressures. Flow rate: (a) 100 g/min, (b) 150 g/min and (c) 200 g/min.

modal, only a clear bimodality of distribution (a clear second peak) is presented in Table 3. With increasing PVP concentration the number of bimodal distributions decreases (Table 3) and the bimodality of water distributions is most evident with the greatest atomizing air pressure (Fig. 2). On the basis of these observations, we assume that the shape of distributions (uni- or bimodal) is determined by a sum of at least two factors: the atomizing air pressure and PVP concentration. Because pressure is defined as a force towards a certain area, it is rational that increasing the pressure causes the binder solution to atomize in smaller drops (see median of droplet sizes, Table 3) due to increased dynamic force of atomizing air. This is seen in droplet size distributions as an increased volume of small droplets causing a pronounced bimodality (Fig. 2). No obvious explanation was found for the bimodal distribution seen in Fig. 3c with an atomizing pressure of 1.5 bar.

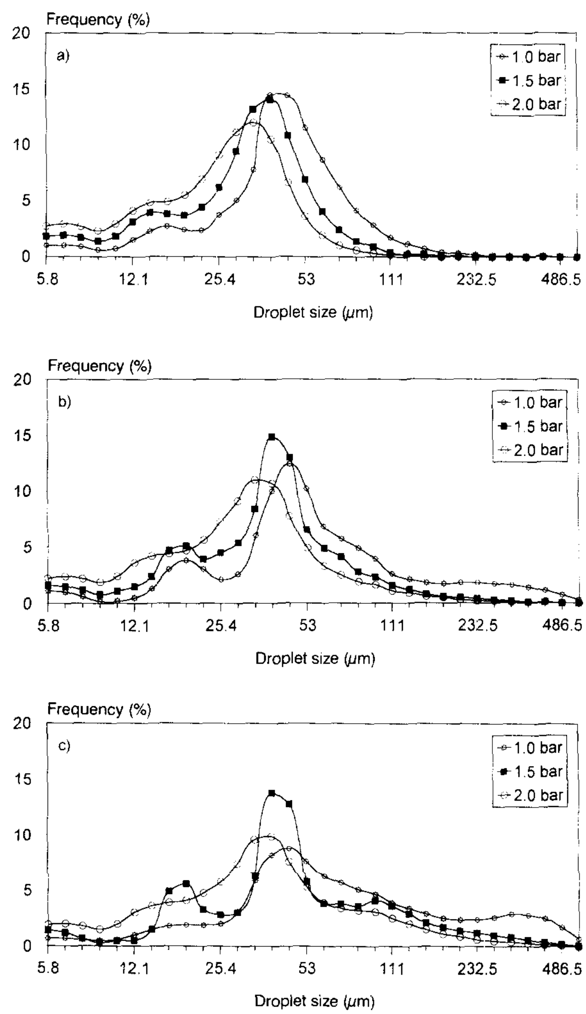

Fig. 3. Droplet size distributions for 10% PVP binder solution from a pneumatic nozzle at different flow rates and atomizing air pressures. Flow rate: (a) 100 g/min, (b) 150 g/min and (c) 200 g/min.

For 20% PVP, on the other hand, the shape of distributions is unimodal and almost identical despite the atomizing air pressure used (Fig. 4, except for one distribution in Fig. 4c discussed later). This could be due to the effect of higher viscosity with increasing PVP concentration: the viscosity of Kollidon® K25 in water (25° C) is 1, 4 and 15 mPa s at 0, 10 and 20% PVP concentrations, respectively (Kollidon® Marken, 1985). With increasing viscosity the ability of binder

Table 3
Parameters describing the droplet size distributions

Amount of PVP (%) in solution	Atomizing air pressure (bar)	Target flow rate of binder solution (g/min)	Median of droplet size (μm) $x \pm \epsilon$ [a]	Width of distribution 90–10% (μm) $x \pm \epsilon$ [a]	Maximum site of second peak (μm)	Height of second peak (%)
0	1.0	100	37.1 ± 0.9	55.9 ± 2.2	–	–
0	1.5	100	24.3 ± 0.3	37.9 ± 0.3	16.3	7.8
0	2.0	100	15.4 ± 0.2	30.0 ± 0.2	14.1	12.4
0	1.0	150	41.6 ± 0.2	89.7 ± 0.7	–	–
0	1.5	150	28.6 ± 0.2	48.0 ± 0.2	–	–
0	2.0	150	17.7 ± 0.1	34.2 ± 0.1	16.3	10.9
0	1.0	200	45.1 ± 0.3	178.9 ± 2.0	–	–
0	1.5	200	31.5 ± 0.1	62.7 ± 0.5	–	–
0	2.0	200	19.4 ± 0.2	42.4 ± 0.4	16.3	9.8
10	1.0	100	40.5 ± 0.2	60.8 ± 0.7	–	–
10	1.5	100	31.2 ± 0.1	42.8 ± 0.1	–	–
10	2.0	100	24.7 ± 0.4	36.1 ± 0.3	–	–
10	1.0	150	45.9 ± 0.3	161.7 ± 11.3	–	–
10	1.5	150	35.7 ± 0.3	64.4 ± 0.4	–	–
10	2.0	150	28.4 ± 0.4	53.8 ± 4.0	–	–
10	1.0	200	56.0 ± 0.5	258.5 ± 0.7	–	–
10	1.5	200	39.4 ± 0.4	110.6 ± 5.5	18.9	5.6
10	2.0	200	32.4 ± 0.2	86.9 ± 0.2	–	–
20	1.0	100	41.4 ± 0.4	64.6 ± 8.3	–	–
20	1.5	100	35.5 ± 0.2	49.9 ± 0.3	–	–
20	2.0	100	31.9 ± 0.3	43.7 ± 1.2	–	–
20	1.0	150	45.5 ± 0.7	150.5 ± 19.0	–	–
20	1.5	150	37.5 ± 0.5	87.6 ± 13.9	–	–
20	2.0	150	34.7 ± 0.7	104.0 ± 3.6	–	–
20	1.0	200	59.5 ± 3.5	315.7 ± 20.0	362.0	4.5
20	1.5	200	43.8 ± 0.7	185.1 ± 8.7	–	–
20	2.0	200	38.9 ± 0.7	133.7 ± 2.3	–	–
Corner point parallel tests						
0	1.0	100	38.0 ± 0.2	55.1 ± 1.7	–	–
0	2.0	100	16.2 ± 0.1	30.2 ± 0.1	14.1	12
0	1.0	200	45.3 ± 0.2	213.2 ± 12.8	–	–
0	2.0	200	21.0 ± 0.1	37.9 ± 0.3	18.9	12
20	1.0	100	42.4 ± 0.0	64.7 ± 0.4	–	–
20	0.2	100	31.4 ± 0.1	38.5 ± 0.4	–	–
20	1.0	200	51.4 ± 0.8	244.0 ± 7.9	–	–
20	2.0	200	34.1 ± 0.3	55.7 ± 0.8	–	–
Central point parallel tests						
10	1.5	150	35.2 ± 0.8	53.0 ± 2.8	–	–
10	1.5	150	34.8 ± 0.7	53.4 ± 1.1	–	–
10	1.5	150	34.0 ± 1.0	54.0 ± 4.3	–	–

In case of a bimodal distribution the maximum site and height of the second peak (usually the lower) are presented.
[a] x is the mean and ϵ denotes the maximum error calculated as $1/2(\max - \min)(n = 3)$.

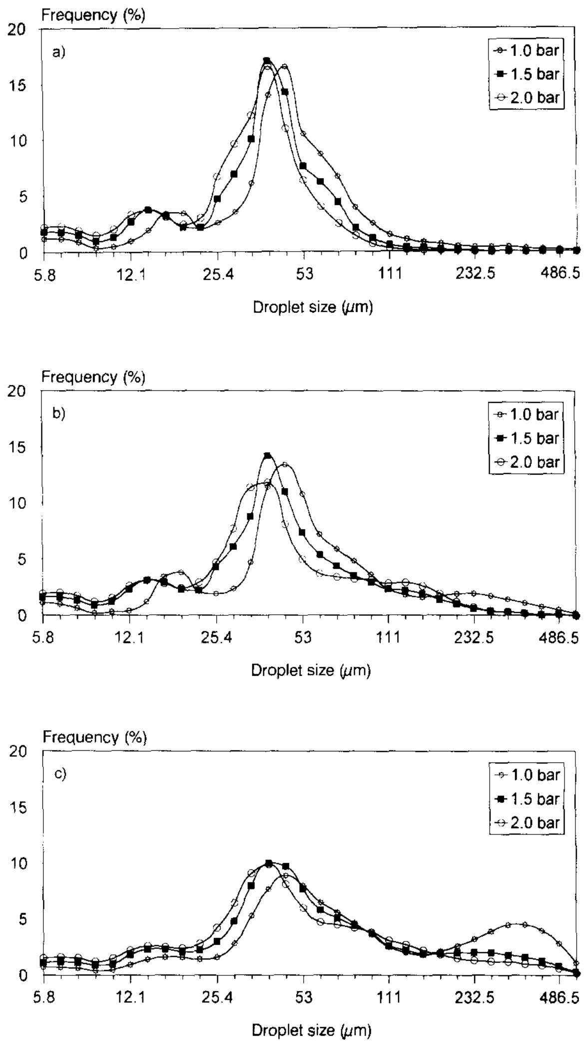

Fig. 4. Droplet size distributions for 20% PVP binder solution from a pneumatic nozzle at different flow rates and atomizing air pressures. Flow rate: (a) 100 g/min, (b) 150 g/min and (c) 200 g/min.

solution to resist the dynamic force of atomizing air increases. This, in turn, leads to a larger droplet size (see median of droplet sizes, Table 3) and thus the bimodality caused by small droplets decreases. The second peak seen in Fig. 4c with a large droplet size can be explained by the fact that a low atomizing air pressure (1.0 bar) is not able to atomize the fast flowing (200 g/min) viscous binder solution so effectively, leading to increased volume of large droplets.

The flow rate of binder solution had no clear effect on the shape of distributions but did affect the frequencies of different droplet sizes. For example, the volume of large water droplets is greater with the highest flow rate as compared to the lowest rate (Fig. 2a,c).

3.3. Effect of different variables on the width of droplet size distributions

Table 3 shows the systematic dependence of the width of the distribution on the atomizing air pressure: the higher the pressure, the narrower the distribution. This can be explained by the steep fall in the number and volume of large droplets with higher pressure. Aulton and Banks (1979) reported that the pressure exerted only a slight influence on the width of the RR droplet size distribution. In contrast, increasing the flow rate or PVP concentration increases the width of distributions (Table 3). This is caused by the increasing amount of large droplets the higher the above-mentioned variables are. It is also seen that the maximum error of width of distribution is usually higher with 20% PVP concentration compared to lower concentrations (Table 3). The pneumatic atomizer is, probably, not able to produce with high-viscosity PVP solution as reproducible droplet sizes as with low-viscosity solutions. In some experiments the difference between the width of distribution of the original and parallel test is remarkable. This could be an indication of poor compatibility of values of independent variables, for example, 20% PVP concentration, high flow rate (200 g/min) and low pressure (1.0 bar).

3.4. Effect of different variables on the spray angle and on the cross-sectional area of spray cone

Fig. 5 shows that the shape of spray is conical and therefore also the diameter of the spray cone was measured in addition to the spray angle. It can be assumed that the independent variables have a stronger effect on the angle as compared to the diameter (d) because with increasing distance the air resistance also gradually affects the diameter of the spray cone.

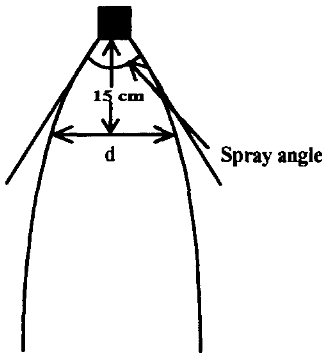

Fig. 5. Schematic presentation of the shape of the spray from a pneumatic nozzle showing the spray angle and the diameter (d) used in cross-sectional area calculations.

The spray angles and the cross-sectional areas of spray cone are listed in Table 4. The interpretation of results is facilitated if the effect of different variables on the spray angle is studied by regression analysis. The following equations were created by the regression analysis:

$$\text{angle mean}\ (P,Q,C) = 49.7 - 5.44P + 1.00Q + 0.890C + 1.33P^2 + 1.17PC \quad (2)$$

$$\text{angle mean}\ (P,Q,C) = 77.6 - 29.2P + 0.0200Q - 0.261C + 5.33P^2 + 0.233PC \quad (3)$$

Eq. 2 shows the regression model in terms of coded factors. The effect of different variables on

Table 4
Spray angles and cross-sectional areas of the spray cone at 15 cm distance from the nozzle tip with different values of independent variables

Amount of PVP (%) in solution	Atomizing air pressure (bar)	Target flow rate of binder solution (g/min)	Spray angle (° C)	Diameter (d) of the spray cone (cm) 15 cm from the nozzle tip	Cross-sectional area of the spray cone $A = \pi(d/2)^2$ (cm^2) [a]
0	1.0	100	55	11.0	95
0	1.5	100	45	9.4	69
0	2.0	100	43	8.2	53
0	1.0	150	58	11.1	97
0	1.5	150	47	9.8	75
0	2.0	150	44	8.5	57
0	1.0	200	58	11.9	111
0	1.5	200	51	9.6	72
0	2.0	200	43	8.8	61
10	1.0	100	58	12.3	119
10	1.5	100	50	9.1	65
10	2.0	100	46	8.7	59
10	1.5	150	49	10.2	82
10	1.5	150	49	10.2	82
10	2.0	150	46	8.7	59
10	1.0	200	54	10.2	82
10	1.5	200	52	9.5	71
10	2.0	200	48	8.7	59
20	1.0	100	54	12.8	129
20	1.5	100	50	10.6	88
20	2.0	100	45	9.3	68
20	1.0	150	55	10.5	87
20	1.5	150	51	9.7	77
20	2.0	150	47	10.1	80
20	1.0	200	58	11.1	97
20	1.5	200	52	10.1	80
20	2.0	200	48	9.8	75

[a] For area calculations the cross-sectional area of the spray cone was supposed to be circle-shaped.

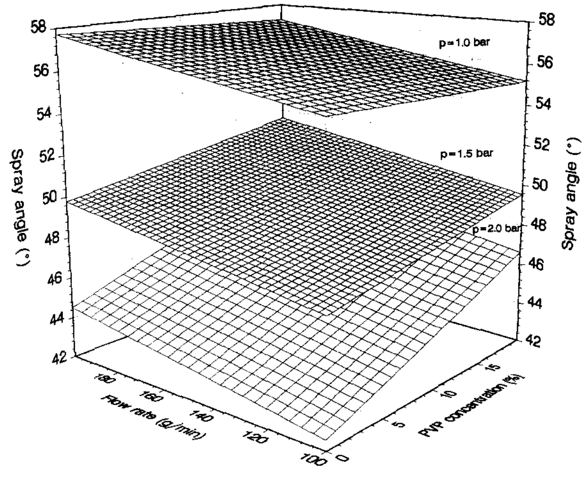

Fig. 6. Dependence of the spray angle on independent variables.

the response variable can be compared directly from this equation. Eq. 3 reveals the model in terms of actual factors. In this study it was used to create the three-dimensional response surface plots. The squared multiple regression coefficient was 0.917. The terms were included in the model if their significance level was at least 5%. The first equation shows clearly that the atomizing air pressure which has the highest regression coefficient is the most important factor affecting the spray angle. The model reveals that the other two variables (Q and C) also affect the spray angle somewhat and that the pressure only has a quadratic effect. Furthermore, a quite marked interaction between pressure and PVP concentration is noted.

The response surface plots drawn on the basis of Eq. 3 by giving a constant value to the pressure show that with increasing pressure the spray angle decreases (Fig. 6). To understand this, we must consider the construction of the nozzle: liquid is drawn from the central tube and broken up by the surrounding air. Increasing the pressure increases the dynamic force of atomizing air forcing the forming droplets to fall in a narrow spray. In contrast, increasing the PVP concentration enlarges the angle, but this effect is quite minimal.

The following equations (first with coded and second with actual values) were created when studying the effect of different factors on the cross-sectional area of spray cone at 15 cm distance from the nozzle tip ($A_{15\text{cm}}$):

$$A_{15\text{ cm}}(P,Q,C) = 75.6 - 18.6P - 2.04Q + 5.02C + 6.61P^2 + 5.70PQ - 4.98QC \quad (4)$$

$$A_{15\text{ cm}}(P,Q,C) = 228 - 151P - 0.283Q + 1.99C + 26.4P^2 + 0.228PQ - 0.00995QC \quad (5)$$

The explanation degree for the model was 81%. Only the statistically significant terms ($p \leq 0.10$) were accepted in the model unless hierarchy of the model required otherwise. The 10% level was selected in this case because the application of the common 5% level would have led to a clear fall in the explanation degree. The model shows that the atomizing air pressure is the most important factor affecting the area. Comparing Eq. 2 and 4, it can be seen that increasing the flow rate apparently enlarges the spray angle but decreases the area. This result is probably due to inaccuracy of the latter model and the measured values.

It can be seen (Fig. 7) that the cross-sectional area of the spray cone changes from 50 to 120

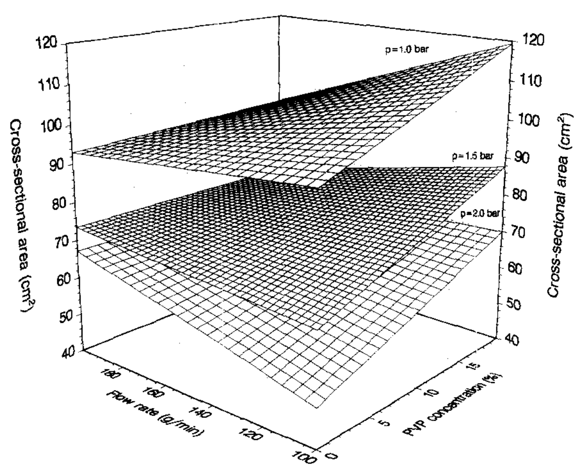

Fig. 7. Dependence of the cross-sectional area of the spray cone at 15 cm distance from the nozzle tip on independent variables.

cm^2, depending on the sizes of independent variables. Decreasing the pressure or increasing the PVP concentration results in a larger area. The effect of flow rate is controversial as stated earlier.

Acknowledgements

This study was supported by the Technology Development Centre in Finland (TEKES). The authors wish to thank Jyri Menna B.Sc. (Eng.), Pirjo Kinnunen M.Sc. (Eng.) and Tanja Ikonen, laboratory assistant, for help.

References

Aulton, M.E. and Banks, M., The measurement of spray droplet size distributions. *J. Pharm. Pharmacol.*, 31 (Suppl.) (1979) 102P.

Gretzinger, J. and Marshall, W.R., Jr, Characteristics of pneumatic atomization. *AIChE J.*, 7 (1961) 312–318.

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

Kollidon® Marken, Polyvinylpyrrolidon für die Pharmazeutische Industrie, BASF Feinchemikalien, 1985, p. 9.

Malvern Instruments Particle Sizer Reference Manual, version 3.0, July 1986.

Merkku, P., Yliruusi, J. and Hellén, L., Testing of an automated laboratory scale fluidized bed granulator using different bed loads. *Acta Pharm. Fenn.*, 101 (1992) 173–180.

Schæfer, T. and Wørts, O., Control of fluidized bed granulation: I. Effects of spray angle, nozzle height and starting materials on granule size and size distribution. *Arch. Pharm. Chem. Sci.*, 5 (1977b) 51–60.

Schæfer, T. and Wørts, O., Control of fluidized bed granulation: II. Estimation of droplet size of atomized binder solutions. *Arch. Pharm. Chem. Sci.*, 5 (1977a) 178–193.

Tate, R.W. and Marshall, W.R., Jr., Atomization by centrifugal pressure nozzles. *Chem. Eng. Progr.*, 49 (1953) 169–174.

Thurn, U., Mischen, Granulieren und Trocknen Pharmazeutischer Grundstoffe in Heterogenen Wirbelschichten. Ph.D Thesis, Eidgenössische Technische Hochschule, Zürich (1970).

Waldie, B., Wilkinsson, D. and Zachra, L., Kinetics and mechanisms of growth in batch and continuous fluidized bed granulation. *Chem. Eng. Sci.*, 42 (1987) 653–665.

Yliruusi, J., Merkku P. Antikainen, O. and Kristoffersson, E., Effect of atomizing air pressure and surfactant concentration on the droplet size in a fluidized bed granulator. *Pharm. Res.*, 9 (1992) S-124.