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Suppression of agglomeration in fluidized bed coating. II. Measurement of mist size in a fluidized bed chamber and effect of sodium chloride addition on mist size

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Abstract

It has been reported that the degree of particle agglomeration in fluidized bed coating is greatly affected by the spray mist size of coating solution. However, the mist size has generally been measured in open air, and few reports have described the measurement of the mist size in a chamber of the fluidized bed, in which actual coating is carried out. Therefore, using hydroxypropylmethyl cellulose (HPMC) aqueous solution as a coating solution, the spray mist size of the coating solution in a chamber of the fluidized bed was measured under various coating conditions, such as the distance from the spray nozzle, fluidization air volume, inlet air temperature and addition of sodium chloride (NaCl) into the coating solution. The mist size in the fluidized bed was compared with that in open air at various distances from the spray nozzle. Further, the relationship between the spray mist size and the degree of suppression of agglomeration at various NaCl concentrations during fluidized bed coating was studied. The mist size distribution showed a logarithmic normal distribution in both cases of the fluidized bed and open air. The number-basis median diameter of spray mist (D_{50}) in the fluidized bed was smaller compared with that in open air. D_{50} increased with the increasing distance from the spray nozzle in both cases. In the fluidized bed, D_{50} decreased with the increasing fluidization air volume and inlet air temperature. The effect of NaCl concentration on the mist size was hardly observed, but the degree of suppression of agglomeration during coating increased with the increasing NaCl concentration in the coating solution. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Mist size; Fluidized bed; Coating; Agglomeration; Hydroxypropylmethyl cellulose; Sodium chloride

1. Introduction

Film-coating of pharmaceuticals with polymeric materials are useful for prevention of their denat-

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uration and deterioration due to moisture adsorption and oxidation, and for masking their bitter taste and offensive smell. Recently, aqueous coating has been widely used in place of organic solvent-based coating, which leaves the organic solvent in the pharmaceuticals, causes environmental pollution by evaporation of the solvent and entails a risk of explosion during the coating process (Chang et al., 1987; McGinity, 1990; Motoyama, 1991; Watano et al., 1994).

For coating, the fluidized bed has been widely used for the reasons of the short coating time due to drying by fluidization air, prevention of contamination due to the closed structure of its apparatus and simplicity of multi-layering of particles (Motoyama, 1991; Fukumori, 1997). It is known, however, that in the coating process with this apparatus, agglomeration is liable to happen due to the slow current of particles caused by the property of the apparatus. In particular, in coating fine particles, agglomeration and/or granulation happen very frequently (Motoyama, 1991; Fukumori et al., 1992).

It has been reported that agglomeration of particles in fluidized bed coating results from liquid bridges formed between particles, and depends that the degree of agglomeration on the size of spray mist of the coating solution (Schœfer and Wørts, 1977; Fukumori et al., 1992; Sakamoto, 1994; Watano et al., 1996). The mist size is generally measured in open air, but it does not sufficiently represent the size in the actual coating process. Measurement of the mist size in the fluidized bed has not been reported in the field of pharmacy, except for a study on the scale-up of agitation fluidized bed by Watano et al. (1995). There is no report describing the comparison of the mist size measured in the fluidized bed with that in open air.

Fukumori et al. (1993) have found that particle agglomeration is reduced by adding NaCl to the aqueous coating solution of HPC during coating of fine particles in the Wurster process. We studied the effect of NaCl concentration in the coating solution on the suppression of particle agglomeration, and found that the suppression of agglomeration was related to the reduction in the viscosity of the coating solution caused by salting-out of the polymeric membrane materials (Yuasa et al., 1997).

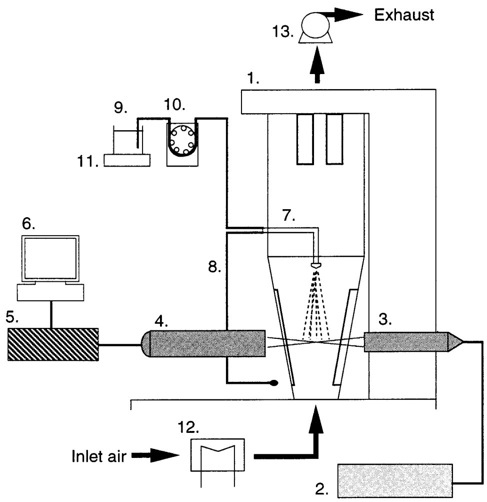

Fig. 1. Scheme of experimental set-up for measurement of mist size in fluidized bed. 1, fluidized bed; 2, helium-neon laser; 3, transmitter; 4, receiver; 5, signal processor; 6, computer; 7, spray nozzle; 8, compressed air; 9, spray solution; 10, peristaltic pump; 11, electronic balance; 12, heater; blower.

Therefore, in this paper, we measured the mist size in a chamber of the fluidized bed, examined the effects of the fluidization air volume, inlet air temperature, distance from the spray nozzle and addition of NaCl in the coating solution on the mist size, and studied the effect of the mist size on the suppression of agglomeration by adding NaCl.

Table 1
Measurement condition for measuring mist size

Spray solution	
HPMC (%)	3
NaCl (%(w/v))	0–1.5
Water	q.s.
Spray condition	
Spray rate (g/min)	13
Spray air pressure (kg/cm^2)	2
Spray air volume (m^3/h)	1.9
Nozzle insert diameter (mm)	1.2

Table 2
Formulation for coating

	Without NaCl	Concentration of NaCl (%(w/v))				
		0.15	0.3	0.5	1.0	1.5
Core particle						
CP (g)	500	←	←	←	←	←
Spray solution						
HPMC (g)	50	←	←	←	←	←
NaCl (g)	–	2.50	5.00	8.25	16.50	25.00
Water (ml)	1650	←	←	←	←	←

2. Materials and methods

2.1. Materials

HPMC (TC-5R, kinematic viscosity 6 mm^2/s, Shin–Etsu Chemical, Japan) and NaCl (Kanto Chemical, Japan) were used as coating material and additive, respectively. As core particles, spherical granules made of crystalline cellulose (CP; Celphere™, CP203, mean particle diameter 240 μm number–basis, Asahi Chemical Industry, Japan) were used.

2.2. Measurement of spray mist size

The mist size of coating solution in a chamber of fluidized bed (MP-01, Powrex, Japan) was measured with a Phase Doppler Particle Analyzer (PDPA; TSI/Aerometrics, USA) at various distances from the spray nozzle, fluidization air volumes and inlet air temperatures. In the actual coating process using CP, we confirmed that the spray mist adhered to the fluidized bed chamber wall within about 20 cm of the spray nozzle, showing that the wet spray mist covered this distance. Therefore, the measuring position of distance was set at 4, 8, 12 and 18 cm from the spray nozzle. Fig. 1 illustrates the PDPA and the experimental set-up for measurement of the mist size. In open air, that is to say, outside the chamber under room temperature and humidity, too, measurement of the mist size was performed with the PDPA at various measuring positions. Formulations of the coating solution and spray conditions are listed in Table 1. The number–basis median diameter of spray mist (D_{50}) and its number–basis geometric standard deviation (SDg) were determined from about 10 000 mist sizes.

Table 3
Operating conditions for coating

Inlet air temperature (°C)	70
Outlet air temperature (°C)	36.0–39.0
Inlet air volume (m^3/h)	80
Spray pressure (kg/cm^2)	2
Spray rate (g/min)	13.0–13.2
Spray air volume (m^3/h)	1.9
Nozzle insert diameter (mm)	1.2

2.3. Coating operation

The coating operation was carried out using the fluidized bed with top spraying. Five grams of the coated particles were collected every 30 min from the start of coating after preheating, and once more after the coating was finished. The formulation and conditions for the coating are listed in Tables 2 and 3, respectively.

2.4. Measurement of particle diameter

The particle diameters of CP and coated particles were calculated by the image analysis method using an image-analyzing package, WinROOF (Mitani, Japan), from about 500 particles. The mean of the horizontal Ferret diameters was regarded as the mean particle diameter number–basis.

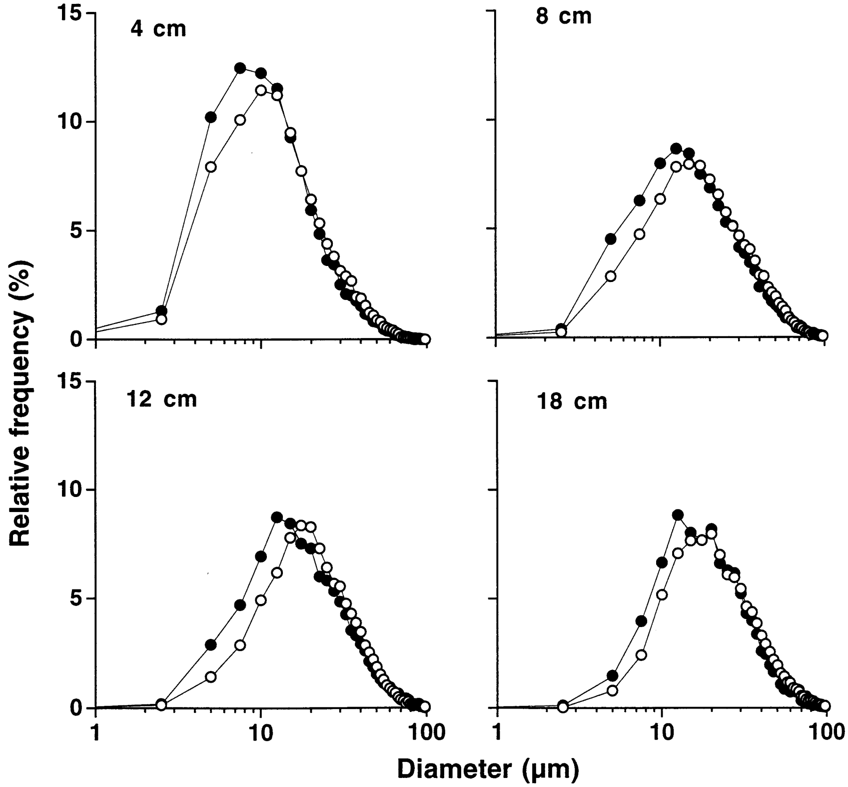

Fig. 2. Mist size distribution of 3%HPMC coating solution in fluidized bed and open air at various distances. (○) in open air, (●) in fluidized bed.

2.5. Observation of surface of CP and samples

A scanning electron microscope (SEM; Type S-2250N, Hitachi, Japan) was used to observe the surface of CP and coated particles.

3. Result and discussion

3.1. Effect of operating conditions of fluidized bed coating on spray mist size

Firstly, in order to compare the mist size in the chamber of the fluidized bed used for actual coating with that in open air where the mist size has been generally measured the mist size was measured at various measuring positions from the spray nozzle. The mist size distributions of 3%HPMC aqueous coating solution are shown in Fig. 2. In the fluidized bed, the inlet air temperature was maintained at 25°C, the same as the temperature in open air, and the fluidization air volume was maintained at 80 m^3/h, the same air volume as in coating. In both cases of the fluidized bed and open air, the mist size distribution showed a logarithmic normal distribution at any distance from the spray nozzle. The peak tops of mist size distribution in the fluidized bed were located in smaller positions compared with those in open air. D_{50} and SDg of the mist sizes in the fluidized bed and open air are listed in Table 4. It was found that D_{50} in the fluidized bed was smaller than that in open air at every distance from the spray nozzle. These results may have been caused because the rate of water evaporation from the surface of spray mist was enhanced by fluidization air. In addition, D_{50} increased and SDg decreased with the increasing distance from

Table 4
D_{50} and SDg of 3%HPMC coating solution in fluidized bed and open air at various distances

Distance from spray nozzle (cm)	Fluidized bed		Open air	
	D_{50} (μm)	SDg	D_{50} (μm)	SDg
4	13.18	2.16	14.96	2.20
8	19.95	2.13	22.00	2.04
12	21.13	2.02	23.71	1.87
18	21.88	1.97	24.27	1.93

the spray nozzle in both cases. The coalescence of the spray mists (Sakamoto, 1995) and disappearance of the smaller spray mists through water evaporation may have caused this. In the case of the fluidized bed, this may have happened also because the smaller spray mists in the measuring area were blown out by fluidization air and disappeared.

Subsequently, the effect of coating conditions, such as fluidization air volume and inlet air temperature, on the mist size was studied by measuring it in the fluidized bed. Fig. 3 shows the effect of fluidization air volume on the mist size distribution at the inlet air temperature of 25°C and the measuring position of 8 cm from the spray nozzle. The relative frequency below about 10 μm increased and that above 10 μm slightly decreased as fluidization air volume increased. D_{50} and SDg at various fluidization air volumes are listed in Table 5. D_{50} decreased with the increasing fluidization air volume. This result may have been due to an increase in the rate of water evaporation from the mist when fluidization air volume increased.

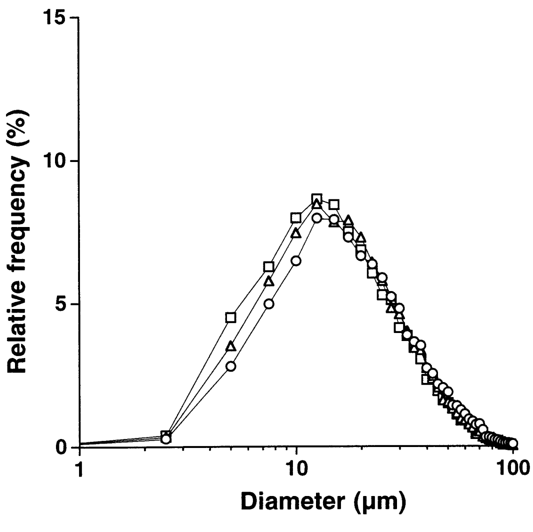

Fig. 3. Effect of fluidization air volume on mist size distribution of 3%HPMC coating solution. fluidization air volume (m^3/h) ((○) 40, (△) 60, (□) 80).

Fig. 4 shows the effect of inlet air temperature on the mist size distribution at the fluidization air volume of 80 m^3/h and the measuring position of 8 cm from the spray nozzle. D_{50} and SDg are listed in Table 6. D_{50} decreased with the increasing inlet air temperature. This may have been caused by an increase in the rate of water evaporation from the mist when inlet air temperature was raised.

3.2. *Effect of sodium chloride addition on spray mist size*

In our previous paper, we reported that particle agglomeration was suppressed by adding NaCl into an aqueous coating solution. Therefore, the effect of addition of NaCl on the mist size in the fluidized bed was studied. Fig. 5 shows the mist size distributions at various NaCl concentrations

Table 5
D_{50} and SDg of 3%HPMC coating solution at various fluidization air volumes

Fluidization air volume (m^3/h)	D_{50} (μm)	SDg
40	22.39	2.05
60	20.65	2.01
80	19.95	2.13

Table 7
D_{50} and SDg of 3%HPMC coating solution at various NaCl concentrations

	Without NaCl	Concentration of NaCl %(w/v)				
		0.15	0.30	0.50	1.00	1.50
D_{50} (μm)	16.98	16.79	15.85	16.22	15.94	16.22
SDg	2.08	2.16	2.11	2.16	2.16	2.14

NaCl concentrations. Fig. 7 shows the effect of NaCl concentration on the size of coated particles. The degree of increase in the particle size was reduced with the increasing NaCl concentration in the coating solution. This result showed that the degree of agglomeration of particles was suppressed with the increasing NaCl concentration, although the mist size was hardly affected by the change of NaCl concentration, as mentioned above.

The SEM photographs of the surface of CP and coated particles are shown in Fig. 8. The surface was smooth in the case of no NaCl addition. The surface became rougher, however, with the increasing concentration of NaCl. In our previous study on HPC aqueous solution, we found that salting-out occurred at a slighter rise in temperature and a lower condensation of the solution by water evaporation with the increasing NaCl concentration, resulting in a reduction in the viscosity of the liquid phase (supernatant fluid; Yuasa et al., 1997). HPMC solved in the coating solution may precipitate by salting-out at a high concentration of NaCl, similarly to HPC. In the case of addition at a lower NaCl concentration, the rate of precipitation of HPMC was low enough for the spray solution to spread uniformly. On the other hand, in the case of that at a higher concentration, the rate of precipitation of HPMC was high, causing HPMC to be precipitated ununiformly and localized quickly after the spray mist of the coating solution adhered to the particles. As a result, the surface became rough.

These results indicate that the mist size was not affected by a change in NaCl concentration in the coating solution, and that the degree of suppres-

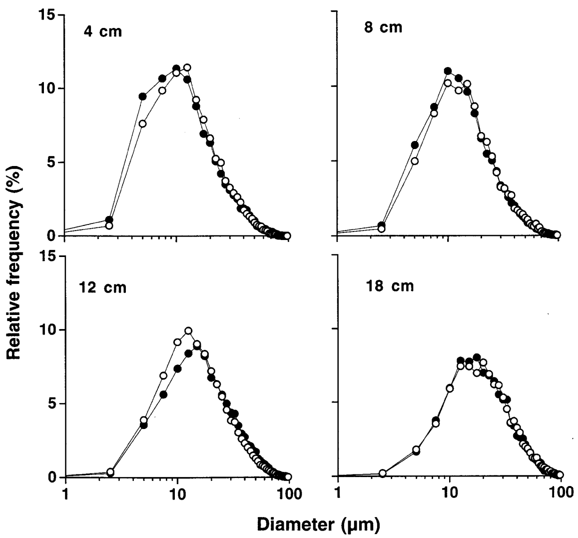

Fig. 6. Effect of addition of NaCl on mist size distribution of 3%HPMC coating solution at various distances from spray nozzle. (○) without NaCl, (●) 1.5%(w/v) concentration of NaCl.

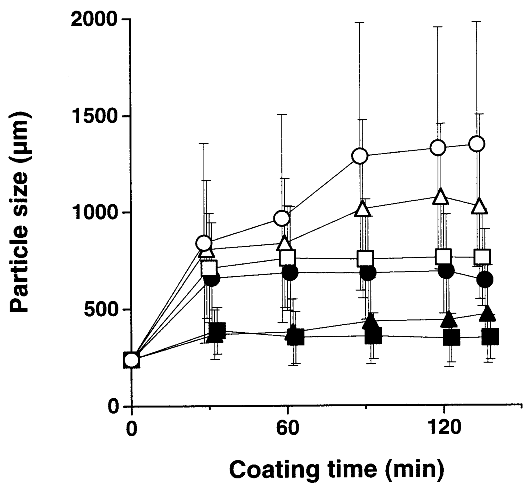

Fig. 7. Effect of NaCl concentration on coated particle size during coating. (○) without NaCl, concentration of NaCl%(w/v) ((△) 0.15%(w/v), (□) 0.3%(w/v), (●) 0.5%(w/v), (▲) 1%(w/v), (■) 1.5%(w/v)).

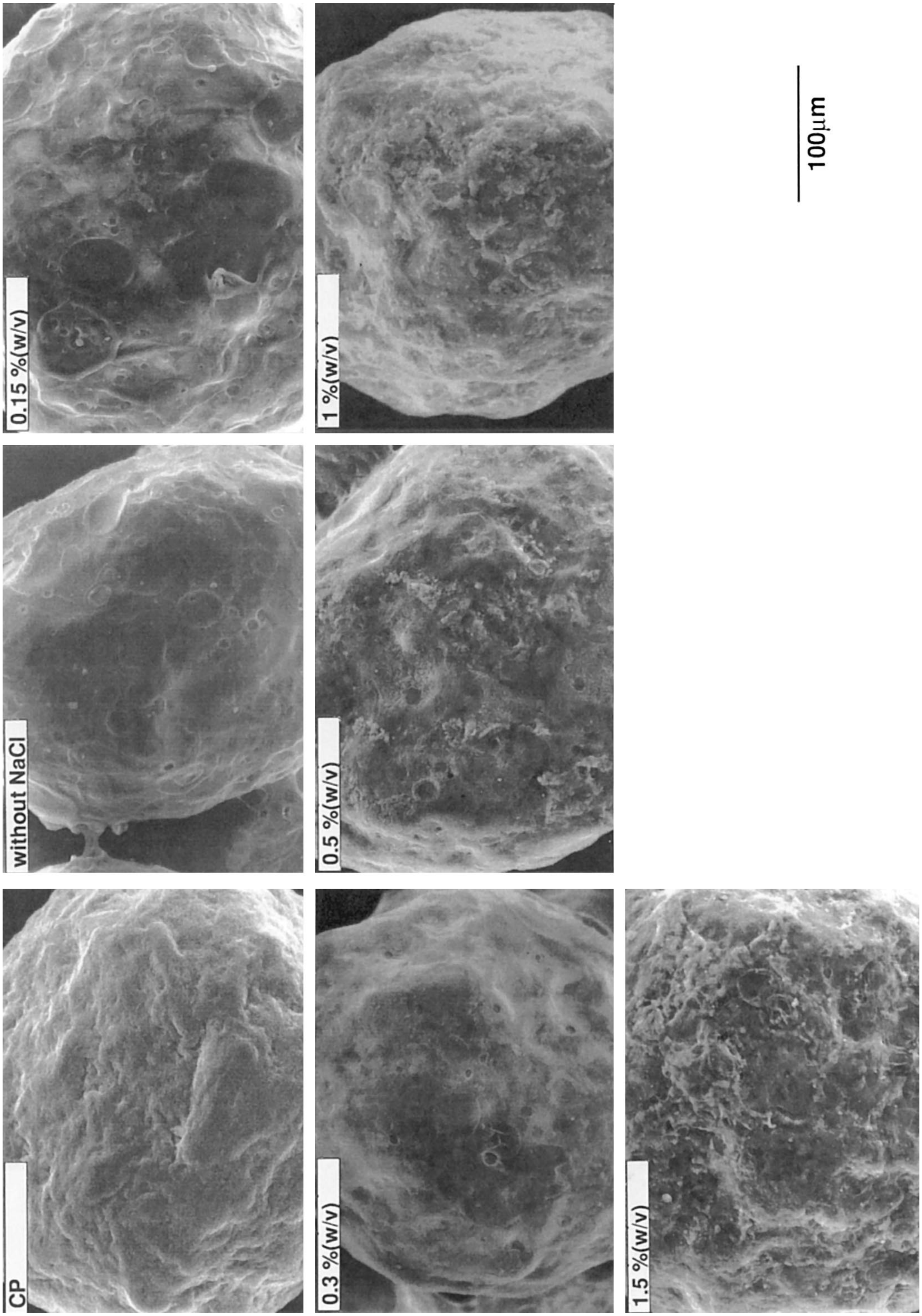

Fig. 8. SEM photographs of CP and particles coated with 3%HPMC coating solution at various NaCl concentrations.

Table 8
D_{50} and SDg of 3%HPMC coating solution with or without NaCl at various distances

Distance from spray nozzle (cm)	Without NaCl		1.5%(w/v) of NaCl concentration	
	D_{50} (μm)	SDg	D_{50} (μm)	SDg
4	15.05	2.14	14.45	2.33
8	16.98	2.08	16.22	2.14
12	18.20	2.07	20.07	2.07
18	23.17	1.95	22.78	2.00

sion of agglomeration increased with the increasing NaCl concentration. Therefore, the variation in the degree of the suppression was hardly related to a change in the spray mist size caused by the addition of NaCl, but was related to a decrease in the viscosity of the liquid phase (supernatant fluid) of the coating solution caused by salting-out by addition of NaCl, as we have reported in our previous paper (Yuasa et al., 1997).

4. Conclusion

The mist size was measured in a chamber of the fluidized bed used for coating. It was found that the mist size distribution in the fluidized bed showed a logarithmic normal distribution, that D_{50} in the fluidized bed was smaller compared with that in open air, and that D_{50} increased with the increasing distance from the spray nozzle, but decreased with the increasing fluidization air volume and inlet air temperature in the fluidized bed. From these results, the effects of coating conditions on the mist size of coating solution were observed, and it is proposed that adhering the spray mist to particles in the vicinity of the spray nozzle and higher fluidization air volume and inlet air temperature are preferable in order to suppress the particle agglomeration by liquid bridges in the actual fluidized bed coating.

The effect of NaCl concentration on the mist size in the fluidized bed was hardly observed, but in the actual fluidized bed coating, an increase was observed in the degree of suppression of agglomeration with the increasing NaCl concentration in the coating solution. Therefore, it has been indicated that, as we have previously reported, the suppression of agglomeration is related to a reduction in the viscosity of the coating solution through salting-out by the addition of NaCl, rather than to a change in the spray mist size by addition of NaCl.

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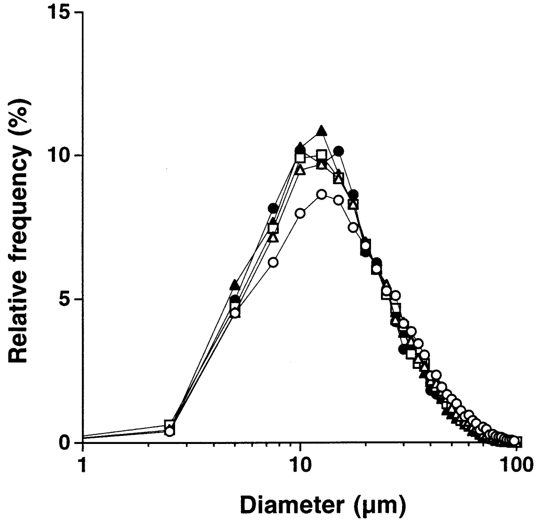

Fig. 4. Effect of inlet air temperature on mist size distribution of 3%HPMC coating solution. inlet air temperature (°C) ((○) 25, (△) 40, (□) 60, (●) 70, (▲) 90).

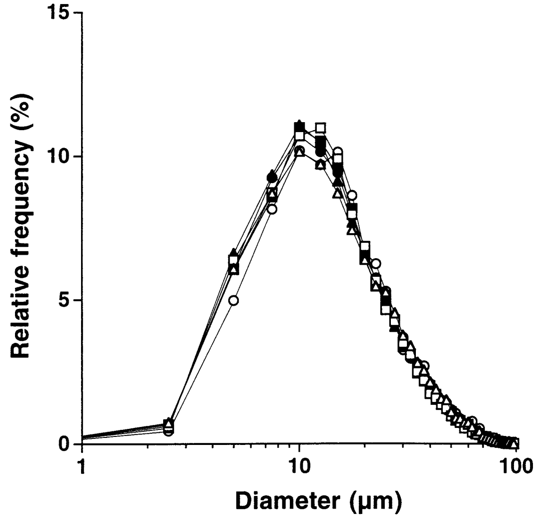

Fig. 5. Effect of NaCl concentration on mist size distribution of 3%HPMC coating solution. (○) without NaCl, concentration of NaCl%(w/v) ((△) 0.15%(w/v), (□) 0.3%(w/v), (●) 0.5%(w/v), (▲) 1%(w/v), (■) 1.5%(w/v)).

in the coating solution at the measuring position of 8 cm from the spray nozzle. The measuring conditions were the same as the actual coating operating condition; inlet air temperature and fluidization air volume were 70°C and 80 m^3/h, respectively. The mist size distributions showed a logarithmic normal distribution and no significant difference was observed at any NaCl concentration. D_{50} and SDg are listed in Table 7. At all the concentrations of NaCl, D_{50} and SDg were about 16 μm and 2.14, respectively, and the effect of NaCl concentration on the mist size was hardly observed.

Then, the mist size of 3%HPMC coating solution with or without NaCl at various distances from the spray nozzle was measured. NaCl concentration was 1.5%(w/v), which was the highest concentration in this study. The inlet air temperature and fluidization air volume were 70°C and 80 m^3/h, respectively. The results are shown in Fig. 6, and D_{50} and SDg are listed Table 8. Almost the same mist size distributions were observed at every distance. In both cases of no NaCl addition and with 1.5%(w/v) concentration of NaCl, D_{50} increased and SDg decreased with the increasing distance from the spray nozzle. This may have been caused by the coalescence of the spray mists (Sakamoto, 1995) and disappearance of the smaller spray mists through water evaporation and blowing out, in a similar manner as that mentioned above. D_{50} and SDg of 1.5%(w/v) concentration of NaCl was the same as that of no NaCl addition at every distance from the spray nozzle, indicating little effect of NaCl addition on the mist size.

Table 6
D_{50} and SDg of 3%HPMC coating solution at various inlet air temperature

Inlet air temperature (°C)	D_{50} (μm)	SDg
25	19.95	2.13
40	18.09	2.13
60	17.48	2.09
70	16.98	2.08
90	16.78	2.11

3.3. Effect of addition of sodium chloride on particle agglomeration during fluidized bed coating

Fluidized bed coating was performed with 3%HPMC aqueous coating solution at various