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Suppression of agglomeration in fluidized bed coating I. Suppression of agglomeration by adding NaCl

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Abstract

Fluidized bed coating was carried out with aqueous spray solution at various additional amounts of NaCl, using water-soluble hydroxypropyl cellulose (HPC) or hydroxypropylmethyl cellulose (HPMC) as membrane material, and spherical granules made of crystalline cellulose (Celphere™) as core particle. The mean particle diameter, density and surface morphology of the coated particles were studied. The viscosity of the spray solution was studied with a corn-plate viscometer at various additional amounts of NaCl, temperatures and concentrations of the spray solution. Agglomeration of particles was clearly suppressed by adding NaCl to the aqueous spray solution in both cases of HPC and HPMC. The mean particle diameter of the coated particles decreased with the increasing additional amount of NaCl in the spray solution. The viscosity of HPC water solution began to decrease at over 6% (w/v) NaCl concentration at 30°C. The NaCl concentration required to reduce the viscosity of the HPC solution became lower as temperature became higher. When the viscosity of the solution decreased, turbidity and/or precipitate were observed. These results suggest that the suppression of agglomeration was caused by the reduction in the viscosity of the spray solution through salting-out of the polymeric membrane materials. © 1997 Elsevier Science B.V.

Keywords: Fluidized bed; Coating; Agglomeration; Viscosity; NaCl; Salting-out

1. Introduction

Film-coating with polymeric materials for pharmaceuticals are useful for prevention of denaturation and deterioration due to moisture adsorption and also for masking bitter tastes and offensive smells. In recent years, the aqueous coating has been widely used in place of the organic solvent-based coating because of the organic solvent remaining in pharmaceuticals, an environmental pollutant, caused by its evaporation and a risk of explosion in the coating operation (Macginity, 1990; Motoyama, 1991; Watano et al., 1994).

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Table 1
Formulation, yield and density of products in coating with HPC

	Without NaCl	Conc. of NaCl (%(w/v))				
		0.5	1	3	5	8
Core CP (g)	300	←	←	←	←	←
Spray solution						
HPC-L (g)	60	←	←	←	←	←
NaCl (g)	0	5	10	30	50	80
Water (ml)	1000	←	←	←	←	←
Products						
Yield (%)	93.03	91.79	92.57	90.88	87.74	91.00
Density (g/cm^3)	1.38	1.40	1.42	1.44	1.47	1.51

For coating of pharmaceutical particles, fluidized bed has been used by drug manufacturers because of the short coating time, due to drying by fluidizing air and the prevention of contamination due to its closed structure of the apparatus. In the coating process with this apparatus, however, it is known that agglomeration is liable to happen due to the slow current of particles caused by the property of the fluidized bed apparatus. In particular, in the coating with fine particles, agglomeration and/or granulation happen very frequently (Motoyama, 1991). Fukumori et al. (1993) have found that this agglomeration is reduced by adding NaCl to aqueous spray solution of HPC in the coating of fine particles in the Wurster process. However, the details of the cause were not described.

In this paper, the coating in the fluidized bed with aqueous spray solution, added with NaCl, was performed and the mechanism for suppression of the agglomeration was studied.

2. Materials and methods

2.1. Materials

As core particles, spherical granules made of crystalline cellulose (CP) (Celphere™, CP203, number-base mean particle diameter 282 μm, true density 1.48 g/cm^3, Asahi Chemical Industry) were used. As additives, NaCl (true density 2.12 g/cm^3, Kanto Chemical) and as membrane materials, HPC (HPC-L, viscosity 6.0–10.0 cps, true density 1.19 g/cm^3, Nippon Soda) and HPMC (E-6, viscosity 4.8–7.2 cst, true density 1.29 g/cm^3, Nippon Soda) were used.

2.2. Coating operation

The coating operation was carried out using fluidized bed (MP-01, Powrex) with top spray. A binary nozzle with 1.2 mm insert diameter was used. The selected nozzle height was 32 cm from the bottom of the chamber in order to bring the top of nozzle close to fluidized powder bed.

A total of 5 g of the coated particles were collected every 30 min. from the start of coating after preheating and once after coating. The formulation of the spray solution, yields, and densities of the products in the coating with HPC and HPMC are listed in Tables 1 and 2, respectively. The coating conditions are listed in Table 3.

2.3. Measurement of density

The densities of materials were calculated from the volume measured with an Air Comparison Pycnometer (Toshiba-Beckman, Model 930).

2.4. Measurement of mean particle diameter

The number-base mean particle diameters of CP and coated particles were calculated by the picture analysis method, using a picture analyzing package, Win ROOF (Mitani), for about 300 particles. The mean of the horizontal feret diameters was regarded as the mean particle diameter.

2.5. Observation of surface of CP and samples

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

2.6. Measurement of viscosity of spray solution

The viscosity of the spray solutions was determined from the relationship between shear rate and shear stress with a corn-plate viscometer (Brookfield Engineering Laboratories, a digital viscometer model DV-II +), at various concentrations, temperatures of the spray solution and NaCl concentrations.

2.7. Measurement of turbidity

The turbidity of the spray solutions was determined by measuring the transmittance at 600 nm and 30°C, using a spectrophotometer (Ubest-30, Japan Spectroscopic).

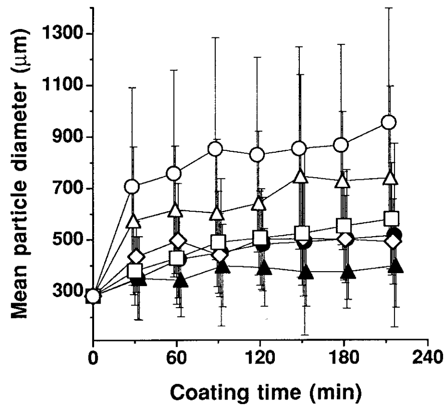

Fig. 1. Effect of NaCl concentration on mean particle diameter during coating with HPC. (○) spray solution of 6% (w/v) HPC water solution without NaCl, concentration of NaCl in 6% (w/v) HPC spray solution ((△) 0.5% (w/v), (□) 1% (w/v), (◇) 3% (w/v), (●) 5% (w/v), (▲) 8% (w/v)).

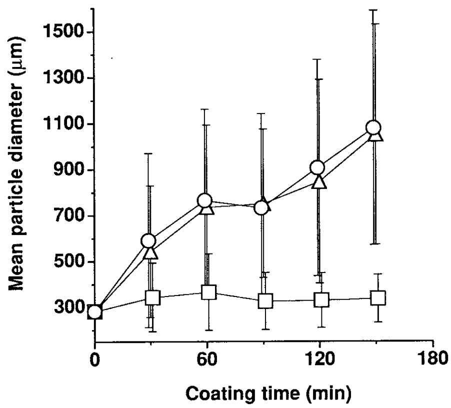

Fig. 2. Effect of NaCl concentration on mean particle diameter during coating with HPMC. (○) spray solution of 8% (w/v) HPMC water solution without NaCl, concentration of NaCl in 8% (w/v) HPMC spray solution ((△) 0.5% (w/v), (□) 5% (w/v)).

Table 2
Formulation, yield and density of products in coating with HPMC

	Without NaCl	Conc. of NaCl (% (w/v))	
		0.5	5
Core CP (g)	300	←	←
Spray solution			
HPMC (g)	42	←	←
NaCl (g)	0	2.625	26.25
Water (ml)	525	←	←
Products			
Yield (%)	93.2	94.47	96.46
Density (g/cm^3)	1.43	1.44	1.50

Table 3
Operating conditions in coating

	HPC	HPMC
Inlet air temperature (°C)	80	80
Outlet air temperature (°C)	34.8–47.8	41.5–53.3
Spray pressure (kg/cm^2)	2	2
Spray rate (g/min)	4.8–5.6	3.9–4.1
Spray air volume (m^3/h)	1.9	1.9
Inlet air volume (m^3/h)	40	40

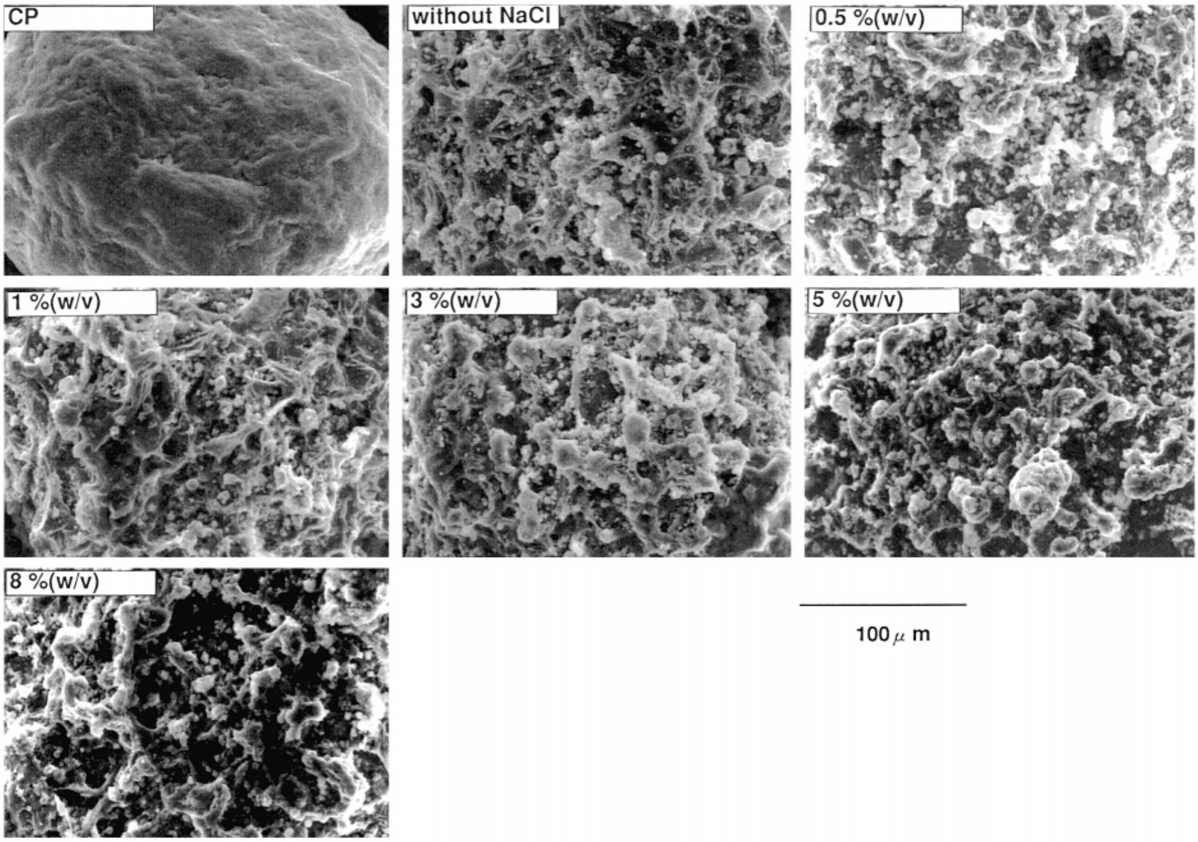

Fig. 3. SEM photographs of surface of CP and particle coated with HPC at various NaCl concentrations

3. Results and discussion

3.1. Effect of adding NaCl on the coating with HPC and HPMC

Fig. 1 shows the effect of NaCl concentration in the HPC spray solution on the mean particle diameter. The degree of increase in the mean particle diameter with the coating was reduced by adding NaCl, so the suppression of agglomeration by adding NaCl was observed as reported by Fukumori et al. (1993). Furthermore, the degree of the suppression became larger as the NaCl concentration became higher.

Fig. 2 shows the effect of NaCl concentration in the HPMC spray solution on the mean particle diameter. At 0.5% (w/v) concentration of NaCl, the decrease in the mean particle diameter was hardly found, and the agglomeration tendency was similar to the case of no addition of NaCl. At 5% (w/v) concentration of NaCl, the mean particle diameter was remarkably reduced compared with the case of no addition of NaCl. Similarly to the case of HPC, the suppression of agglomeration by adding NaCl was found in the coating with HPMC.

SEM photographs of the surface of CP and particles coated with HPC at various additional amounts of NaCl are shown in Fig. 3. Fukumori et al. (1993) reported that the suppression of agglomeration by adding NaCl was caused by the increase in the surface roughness due to NaCl crystallization on the surface of the coated particles. In the photographs, however, the difference in the surface was hardly observed, and the surface was rough in all the coated particles. The surface roughness was thought to be caused by precipitated and evaporated polymer in the absence of NaCl, and also by both NaCl crystal and precipitated and evaporated polymer in the case of NaCl addition. The agglomeration occurred in the coating without NaCl, in spite of the rough surface. These results suggest that the suppression of agglomeration was a result from some other factor, and not the surface roughness.

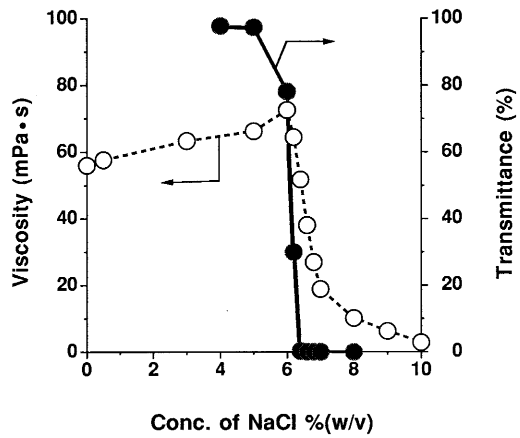

Fig. 4. Effects of concentration of NaCl on viscosity and transmittance of 6% HPC water solution at 30°C. (○) viscosity, (●) transmittance.

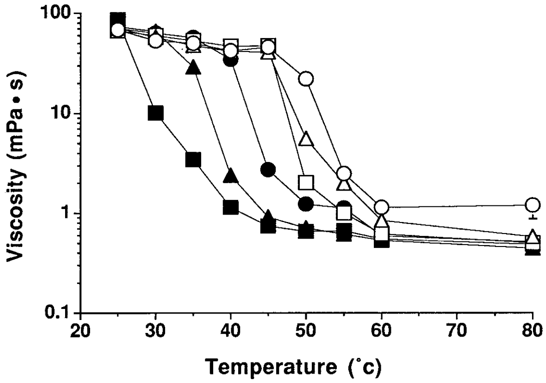

Fig. 5. Relation between temperature and viscosity of 6% (w/v) HPC water solution with or without NaCl. (○) spray solution of 6% (w/v) HPC water solution without NaCl, concentration of NaCl in 6% (w/v) HPC spray solution ((△) 0.5% (w/v), (□) 1% (w/v), (●) 3% (w/v), (▲) 5% (w/v), (■) 8% (w/v)).

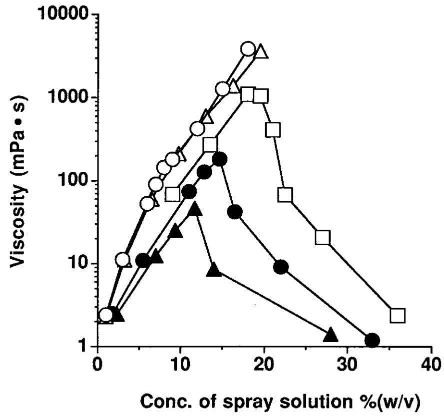

Fig. 6. Effect of concentration of solute (HPC and NaCl) in spray solution on viscosity of HPC/NaCl solution at 30°C. (○) HPC water solution without NaCl, weight ratio of HPC/NaCl in solute ((△) 6/0.5, (□) 6/3, (●) 6/5, (▲) 6/8).

3.2. Effects of NaCl concentration on viscosity and turbidity of HPC water solution

Since the agglomeration of particles is affected by the viscosity of spray solution (Schœfer and Wørts, 1977, 1978), the viscosity of our spray solution was studied. Fig. 4 shows the effects of NaCl concentration on the viscosity and turbidity of the 6% (w/v) HPC spray solution at 30°C. When the NaCl concentration was over 6% (w/v), a remarkable falling of viscosity was observed, and the transmittance was also remarkably decreased, that is, the turbidity increased. In addition, milky precipitates appeared at $\approx 8\%$ (w/v), and the precipitates were qualitatively confirmed as HPC (JP XIII, 1997).

These results will be explained as follows; the electric charge of the hydrophilic colloidal HPC was neutralized and the hydration water of the HPC was dehydrated by adding the electrolyte of NaCl added in abundance. Then, HPC was gelled and precipitated through salting-out (Hans, 1980; Kawashima, 1991).

3.3. Effect of temperature on viscosity of HPC solution with or without NaCl

Hot air was conducted into the chamber of the fluidized bed apparatus from the bottom, for

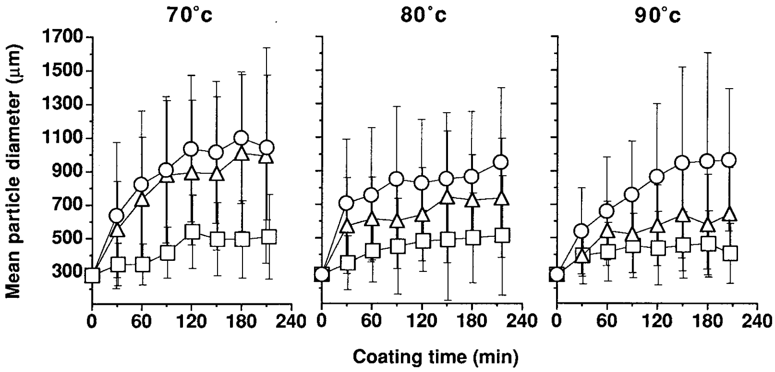

Fig. 7. Effect of NaCl concentration on mean particle diameter during coating at various inlet air temperatures. (○) spray solution of 6% (w/v) HPC water solution without NaCl, concentration of NaCl in 6% (w/v) HPC spray solution ((△) 0.5% (w/v), (□) 5% (w/v)).

fluidizing and drying. Thus, the temperature of the spray solution may vary during the coating operation. Fig. 5 shows the effect of temperature on the viscosity of the HPC spray solution with or without NaCl. When the precipitates were observed due to NaCl addition, the supernatant without the precipitates was measured. The viscosity of the HPC water solution without NaCl remarkably fell due to separating out of HPC when the temperature was over ~45°C, that is, the gelation temperature of HPC (Macginity, 1990). In the case of the HPC solution with NaCl, a lowering was observed in the apparent HPC gelation temperature, and furthermore, decreased in proportion to the increase in the NaCl concentration.

3.4. Effect of concentration of spray solution on viscosity

The concentration of the solute in the spray solution will increase due to moisture evaporation after being sprayed from the nozzle. Fig. 6 shows the effect of the concentration of the solute (HPC and NaCl) in the spray solution and the HPC/NaCl ratio on the viscosity at 30°C. The viscosity suddenly fell at levels over a certain concentration, except with HPC alone and the HPC/NaCl ratio of 6/0. 5. The viscosity fell at the lower concentration with the higher NaCl ratio in the solute.

3.5. Effect of inlet air temperature on suppression ability of agglomeration

From these results, it is speculated as follows. The spray solution temperature and the rate of concentration due to moisture evaporation vary with a change in the inlet air temperature in the actual coating operation. These changes cause variations in the NaCl concentration required for salting-out and gelation of HPC and the viscosity of the spray solution. Thus, the suppression ability of the agglomeration varies.

In order to make sure of this speculation, the coating operation was performed at 70, 80 and 90°C of the inlet temperature with 6% (w/v) HPC spray solution with or without NaCl, using CP as the core. The results are shown in Fig. 7.

In the 5% (w/v) concentration of NaCl, the degree of increase in the mean particle diameter was already low and a remarkable suppression ability of agglomeration was observed at the lowest, 70°C, among the three temperatures. Assuming that the viscosity is singly affected by the temperature of the spray solution and the temperature reaches ~45°C, the viscosity will be about 1 mPa·s, and will not decrease any more with an increase in the temperature, as shown in Fig. 5. This agrees with the result that the mean particle diameter was not changed by the increase in the inlet air temperature.

On the other hand, at 0.5% (w/v) concentration of NaCl, the degree of increase in the mean particle diameter was hardly different from that in the case of no NaCl addition at 70°C, but it decreased compared to that with no NaCl addition, at higher inlet air temperatures (80°C, 90°C). Assuming a case similar to the 5% (w/v) NaCl concentration, if the temperature of the spray solution reaches ~45°C at 70°C of the inlet air temperature, the viscosity will be the same as that of the spray solution without NaCl, and will remarkably decrease with the increase in the temperature, as shown in Fig. 5. This also agrees with the result that the degree of increase in the mean particle diameter decreased with the increase in the inlet air temperature.

Therefore, it is suggested that, in the actual coating process, the degree of the suppression of agglomeration varies due to a change in the viscosity of the spray solution added with NaCl, owing to a change in the inlet air temperature.

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