

## Fine particle coating by a novel rotating fluidized bed coater

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### Abstract

Fine particle coating has been conducted by using a novel rotating fluidized bed coater. The coater consists of a plenum chamber and a horizontal porous cylindrical air distributor, which rotates around its axis of symmetry inside the plenum chamber. Cohesive fine cornstarch (mass median diameter of 15  $\mu\text{m}$ ), a Geldart Group C powder, was used as core particle and an aqueous solution of hydroxypropylcellulose (HPC-L) was sprayed onto the cornstarch to generate a film coating. Fine particle coating was conducted under various coating levels (wt.% HPC-L) and the particle size distribution of the coated particles, release rate of an aqueous pigment (food blue No. 1), which had been pre-coated onto the initial cornstarch, and the degree of agglomeration were investigated. The relationship between the coating level and the physical properties of the coated particles was analyzed. The results indicated that coating of cohesive fine cornstarch with HPC-L could be achieved, producing a favorable prolonged release property with almost maintaining the individual single particle.

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### 1. Introduction

In the pharmaceutical industry, fine powders have become of major interest lately. Many potential pharmaceutical applications, such as asthma treatment by inhalation, cancer treatment by transcatheter arterial embolization and others, use fine powders in a drug delivery system.

Fluidization is one of the most promising techniques for handling fine powders because of its advantages of high heat and mass-transfer rates, temperature homogeneity and high flowability of particulate materials. However, as pointed out by Geldart [1] in his classification map, fine powders in Group C (small particle size and low particle density) fluidize poorly due to their strong interparticle cohesive forces, exhibiting channeling, lifting as a plug and forming “rat holes” when aerated. Therefore, the development of reliable techniques to improve the fluidization of cohesive fine powders is required. Several external devices based on

using vibration [2] and mechanical agitation [3] have been suggested to improve the flowability of cohesive fine powders. Despite the use of these devices, handling of fine powders is still extremely difficult and wet processing, such as coating and granulation of fine powders has been regarded as nearly impossible. Only Ichikawa et al. [4] reported the possibility of fine powder coating by using a draft tube in a (Wurster type) fluidized bed and succeeded in coating fine cornstarch powder with composite latex without generating agglomeration; however, sufficient prolonged release properties could not be obtained.

In this study fine particle coating was conducted using a novel rotating fluidized bed coater. Fine cohesive cornstarch powder was coated by a hydroxypropylcellulose (HPC-L) aqueous solution and the coated particles were evaluated at different coating levels, depending on the amount (wt.%) of (HPC-L) that was sprayed onto them.

The size distribution, degree of agglomeration and release rate of an aqueous pigment (food blue #1), used to represent a model drug which was pre-coated onto the initial cornstarch, were investigated. The performance of the rotating fluidized bed as a fine particle coating system was also evaluated.

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## 2. Experimental

### 2.1. Equipment

A schematic diagram of the experimental apparatus is shown in Fig. 1. A novel rotating fluidized bed [5] was used for fine particle coating. The rotating fluidized bed consists of a plenum chamber and a porous cylindrical air distributor (ID  $400 \times D$  50 mm) made of stainless sintered mesh with 20- $\mu\text{m}$  openings. The horizontal cylinder (air distributor) rotates around its axis of symmetry inside the plenum chamber. There is a stationary concentric cylindrical metal filter (ID  $140 \times D$  100 mm, 40- $\mu\text{m}$  openings) inside the air distributor to retain any elutriated fine powder.

A binary spray nozzle mounted on the metal filter sprays mist of coating material (volume based median diameter of spray mist size measured by a laser diffraction method is 7  $\mu\text{m}$ ) into the powder bed. A pulse air-jet nozzle is also placed inside the metal filter, which cleans the surface of the metal filter in order to prevent it from clogging. An air knocker is installed outside the plenum chamber to prevent powder adhesion onto the air distributor mesh and the front cover. Pressure taps are mounted on the inlet and exhaust air pipes and on the metal filter, so that the manometer (1) measures the pressure drop across the powder bed and air distributor, while manometer (2) measures pressure drop

across the metal filter. In this study, the pressure drop across the powder bed,  $\Delta P$ , is defined by Eq. (1).

$$\Delta P = P_1 - P_2 \quad (1)$$

Where  $P_1$  is the pressure drop across the powder bed and air distributor measured during the experiments and  $P_2$  is the pressure drop across the air distributor measured during idling without powder, respectively. By measuring the relationship between pressure drop across the powder bed and supplied air velocity, a minimum fluidization velocity,  $u_{mf}$ , was obtained [5]. The same procedures were conducted under various centrifugal accelerations and then finally the relationship between the minimum fluidization velocity and centrifugal acceleration was obtained. The detailed information was described previously [5].

Fig. 2 compares the fluidization mechanism in a rotating fluidized bed with that in a conventional fluidized bed. In a conventional fluidized bed, the air distributor is mounted horizontally and the powder samples are introduced onto the distributor. Powders are lifted up by a vertical airflow (drag force and buoyancy against the gravity force). In a rotating fluidized bed, powder samples are introduced inside the air distributor and are forced to the wall by centrifugal force due to the rotation of the distributor. Air flows radially inward through the air

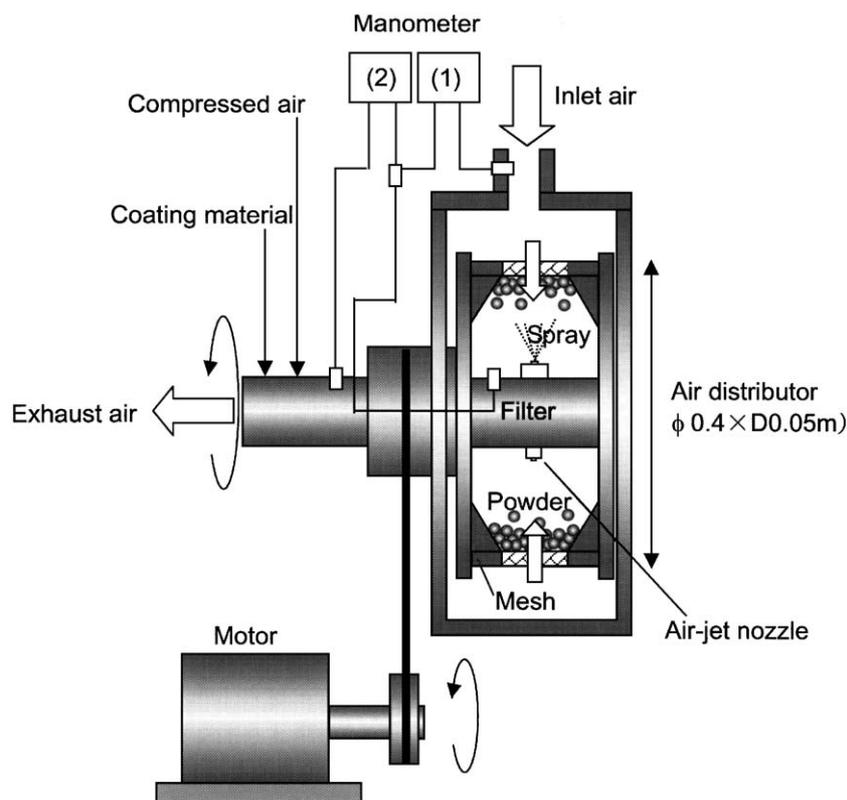


Fig. 1. Schematic diagram of the rotating fluidized bed coater.

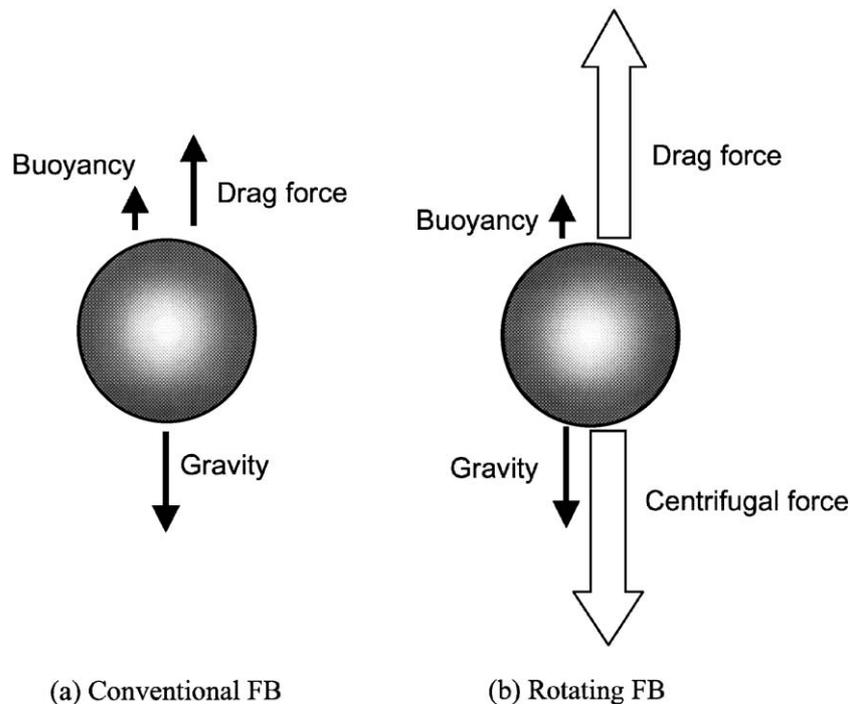


Fig. 2. Fluidization mechanisms.

distributor, and the forces on the powder are balanced by the airflow (drag force and buoyancy) and the centrifugal force. Unlike a conventional fluidized bed, a rotating fluidized bed can impart a high centrifugal force and therefore the drag force needed to lift the particles (fluidize them) also becomes large to satisfy the force balance. These large forces enable fine particles, which normally behave as a Geldart Group C powder, to behave as a Geldart Group A powder [6].

By increasing the rotational speed or the diameter of the distributor, the centrifugal force can be made very large as compared to other mechanical forces such as vibration, mechanical agitation, etc. This implies that the rotating fluidized bed can uniformly fluidize much finer powders than conventional fluidized beds, even when they are equipped with these mechanical devices. Theoretically, if the distributor rotates at a high enough speed and the airflow increases correspondingly to keep a uniform fluidization, the adhesion (interparticle) force between powders can be neglected as compared to the centrifugal and drag forces.

## 2.2. Powder sample

Cornstarch with a mass median diameter of 15  $\mu\text{m}$  was used in this research. This cohesive, poorly flowing powder belongs to Geldart Group C [1]. A mass of 0.3 kg of cornstarch powder (Nihon Shokuhin Kako) was charged into the equipment, which gave a bed height of approximately 0.02 m. Aqueous pigment food blue No. 1 (Izumiya Shikiso) was used as a model drug and was pre-coated (0.05 wt.%) onto the cornstarch powder. For

the coating material, a 5% aqueous solution of hydroxypropylcellulose (HPC-L, Nippon Soda) was used. The solution was sprayed onto the cornstarch powder through a binary nozzle. Coated particles were prepared with different amounts of HPC-L (coating level). The sprayed amount (coating level) was 3, 5 and 9 wt.%, respectively (solid base).

## 2.3. Experimental procedure and operating conditions

Table 1 lists the operating conditions used in the experiments. Coating experiments were conducted as follows:

- (1) The powder sample (pre-coated cornstarch with aqueous pigment food blue No. 1) was fed into the cylindrical air distributor (vessel).
- (2) The air distributor was rotated and fluidization air was supplied.
- (3) Coating liquid was sprayed onto the powder bed.
- (4) After a predetermined amount of coating material was sprayed to produce a specific coating level, drying and curing of coated particles was conducted for 1 h at an air temperature of 353 K.

Table 1  
Operating conditions

Rotational speed	7.88 rps (50 G) <sup>a</sup>
Airflow rate	0.805 m/s ( $u/u_{mf}=2.5$ )
Air temperature	333 K
Spray air pressure	0.55 MPa
Liquid feed rate	0.75 g/min

<sup>a</sup> 1 G = 9.8 m/s<sup>2</sup> (gravity acceleration).

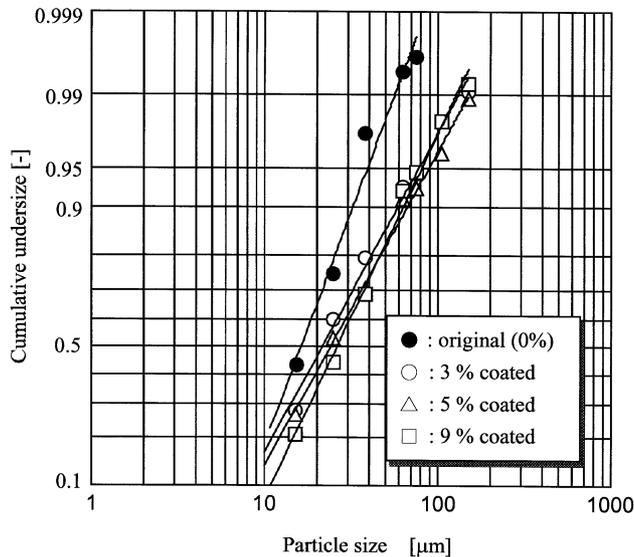


Fig. 3. Size distributions of coated particles for different coating levels.

#### 2.4. Evaluation of coated particles

The size and size distribution of the coated particles were measured by sieve analysis using a vibration-sieving machine. A log-normal distribution was used to calculate the 50% median particle size and the geometric standard deviation (size distribution). Since the original cornstarch powder contains only 0.6 wt.% of the fraction larger than 63  $\mu\text{m}$ , the degree of agglomeration (coarse fraction generated by agglomeration) was defined as the wt.% of the fraction larger than 63  $\mu\text{m}$ .

The amount of drug (aqueous pigment food blue No. 1) release was measured as follows: 1.0 g of the coated particles was put into a JP dissolution test vessel [7] with 900 ml of water kept at 310 K and agitated by a paddle at 100 rpm. The amount of the drug (food blue No. 1, absorbance wavelength of 630 nm) released from the coated particles was continuously analyzed by measuring absorbance of the dissolution water at the wavelength of 630 nm

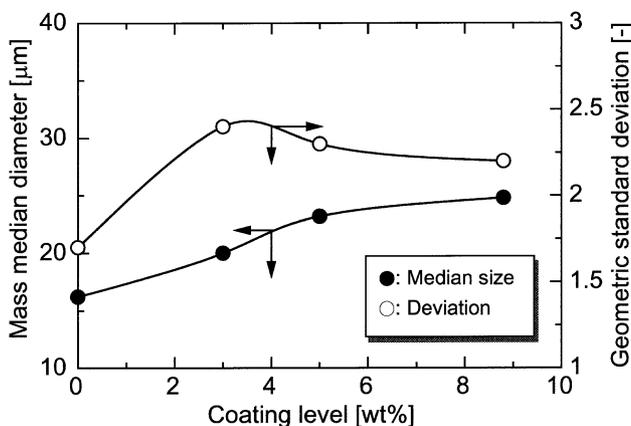


Fig. 4. Mass median diameter and geometric standard deviation of coated particles.

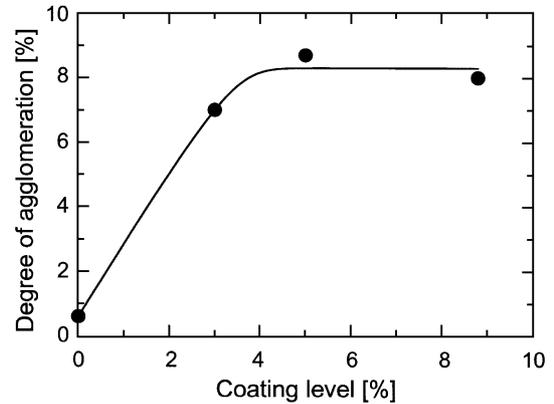


Fig. 5. Degree of agglomeration vs. coating level.

(absorbance wavelength of the food blue No. 1) via a UV spectrophotometer (UV-1200, Shimadzu). The drug release (%) was defined as the ratio of the amount of the drug actually released from the coated particles to the total amount of the drug really coated onto the particles, which was measured by 24-h dissolution test.

### 3. Results and discussions

Figs. 3 and 4 show size distributions of the coated particles prepared at different coating levels. Fig. 4 also shows the evolution of the mass median diameter and the geometric standard deviation of the coated particles. As seen in Fig. 3, the fine particle fraction tended to adhere at the initial stage of the coating (coating level of 3%), which shifted the size distribution to the right. This also caused a wider particle size distribution (large geometric standard deviation in Fig. 4). However, at coating levels above 3%, the size distribution did not shift to the right anymore. This is confirmed in Fig. 4, which shows that the geometric standard deviation decreased gradually above a coating level of 3%. The mass median diameter also increased slightly with an increase in the coating level. At a coating level of 9%, the mass median diameter was 22.8  $\mu\text{m}$ . Considering the size increase due to the coating layer (thickness was

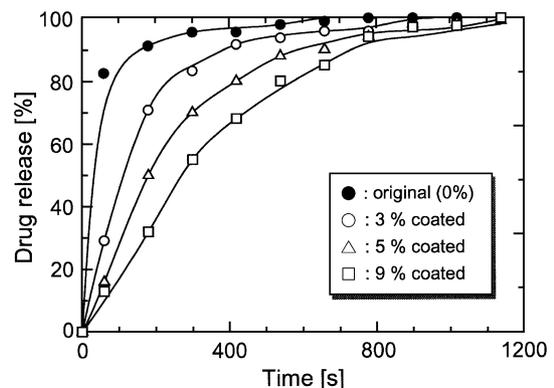
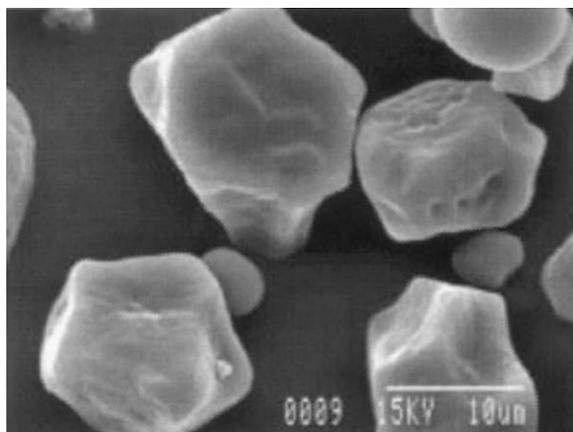
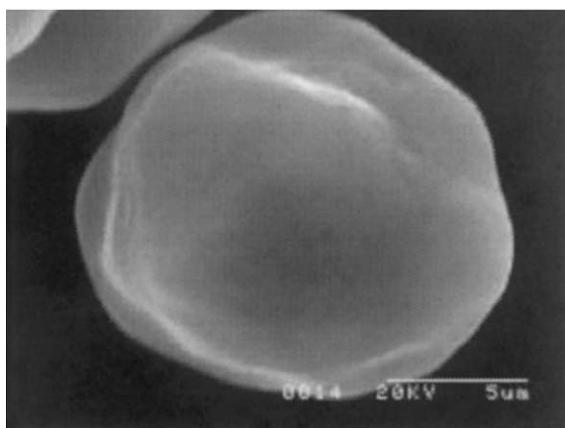


Fig. 6. Drug release vs. coating level.



(a) Initial cornstarch



(b) 9% coated particle

Fig. 7. SEM photographs of initial cornstarch and coated cornstarch.

1.0–1.5  $\mu\text{m}$ , roughly measured of the particle cross section by Scanning Electron Microscopy (SEM)), the size increase due to agglomeration is very small, and most of the cornstarch was coated as individual particles.

Fig. 5 shows the evolution of the degree of agglomeration. The mass (wt.%) fraction larger than 63  $\mu\text{m}$ , which was defined as the degree of agglomeration, increased at low coating levels and then remained almost constant. After the fine particle fraction adhered to larger particles in the initial coating stage, there did not appear to be any further adhesion between particles.

Fig. 6 shows the release amount of the model drug (aqueous food blue No. 1) as a function of the coating level. Without the coating, the release amount was 80% after just 1 min of the dissolution test. With an increase in coating levels, the drug release amount was much longer. At the 9% coating level, the 80% drug release took 10 min and showed a favorable prolonged release property.

Fig. 7 shows the Scanning Electron Microscopy (SEM) photographs of the uncoated and coated cornstarch particles. The initial cornstarch has a rough surface and an irregular shape. By contrast, the 9 wt.% coated particle shows a very smooth surface with a rounded shape.

Based on the results obtained in Figs. 6 and 7, it appears that individual cornstarch particles were fluidized inside the vessel and their surfaces were uniformly covered by the coating material. Thus, we have successfully developed a method for fine particle coating of cohesive fine powders, which resulted in a favorable prolonged drug release property without generating agglomeration.

It is noteworthy that the spraying material (5% HPC-L) is a very viscous aqueous solution and therefore should readily lead to particle agglomeration. Despite the use of such a highly viscous liquid spray, fine particle coating can be conducted in the rotating fluidized bed due to the high centrifugal force and therefore the large amount of air required to keep the particles uniformly fluidized, which results in a correspondingly large shear force on the particles. This shear force is strong enough to prevent agglomeration between the particles and produce a smooth film coating on the particles' surface. This method can be extended to modify and tailor other surface properties and to improve the handling and processing of fine cohesive powder.

#### 4. Concluding remarks

A novel rotating fluidized bed coater has been developed and applied to coating fine cohesive powder (cornstarch having a mass median diameter of 15  $\mu\text{m}$ ), which is normally categorized as a Geldart Group C powder. Favorable surface property modifications and a prolonged drug release property were achieved without causing serious particle agglomeration.

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