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Original Research Paper

Effects of the centrifugal coating and centrifugal fluidized bed coating methods on the physicochemical properties of sustained-release microparticles using a multi-functional rotor processor

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ABSTRACT

The purpose of the present study was to examine the effect of coating processes on the physicochemical properties of sustained-release microparticles prepared by centrifugal coating (CC) and centrifugal fluidized bed coating (CFC) using a multi-functional rotor processor. Acetaminophen (APAP)-loaded microparticles (DP) were coated with 30% *w/w* aqueous polymer dispersion of Eudragit® RS (RS) by CC or CFC methods with the apparatus until a dry polymer weight gain of 30%, 60%, 150% and 200% *w/w* was achieved, and these coated microparticles were abbreviated as CC-DP-RS and CFC-DP-RS, respectively. Both coated microparticles had similar physicochemical properties, but some differences in the drug dissolution behaviors of CC-DP-RS and CFC-DP-RS at lower coating levels were observed. That is, the coated microparticles prepared by CC showed faster release than that by CFC. As a result of dissolution study using Talc seal-coated microparticles and thermal study using differential scanning calorimeter, the rapid dissolution behaviors from CC-DP-RS at the lower coating levels of RS might be due to APAP migration to the coating film during coating due to the weak drying efficacy of the CC method. These findings suggest for the first time that CFC is a suitable method for the coating of functional polymers at lower polymer coating levels, whereas, for the CC method, adjustment of operational conditions (e.g., product temperature, inlet air volume and liquid flow rate) would be required.

1. Introduction

Microparticle coating using functional polymers is a method in which functionalities such as sustained or delayed release can be added to particles containing drugs with a particle size less than 200 μm. The use of particles of this size, in general, ensures that a feeling of "roughness" in the mouth is avoided. The coating of microparticles is often carried out using the top-spray [1], bottom-spray (Wurster-type) [2] or side-spray [3] fluidized bed coating method. These coating mechanisms and processes are quite different [4–6]. Hence, the physicochemical properties, such as particle size distribution, flowability, and dissolution behavior of the coated particles prepared by these methods are also expected to be different.

Yang et al. [7] reported that, when comparing the top- and bottom-spray fluidized bed coating methods with tangential-spray centrifugal coating by attaching a spray nozzle to the side wall of the fluidized bed apparatus, the spray position and the chamber geometry are the most important factors affecting the drug dissolution behavior of coated particles. In addition, Takei et al. [8] reported that, when comparing diagonal-top-spray and tangential-spray centrifugal coating methods with the top-spray fluidized bed coating method, the spray position also affected the coating efficiency and surface structures as well as the drug dissolution behavior of coated particles. However, these comparisons were carried out under different operational conditions, such as inlet air flow volume, liquid flow rate, and product temperature and/or different types of fluidized bed apparatus. That is, although the particle circulation pattern and the drying capacity of the apparatus might (in a practical sense) be involved in the particle properties and the drug dissolution behavior, reports focusing on these concerns are lacking. Therefore, if it is possible to directly compare coating processes using an apparatus under identical operational conditions, new insights into the effect of the coating process on particle properties and its drug dissolution behavior could be obtained.

Abbreviations: APAP, acetaminophen; CC, centrifugal coating; CFC, centrifugal fluidized bed coating; CT, computed tomography; DP, drug layered particles; DSC, differential scanning calorimeter; HPC, hydroxypropylcellulose; RS, Eudragit® RS; SEM, scanning electron microscopy; T_g, glass transition temperature.

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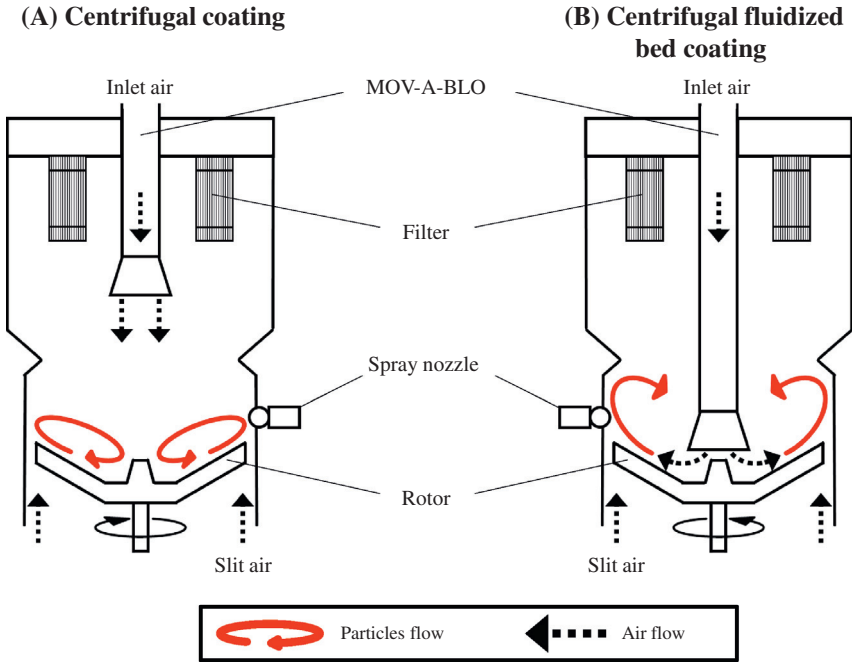

Fig. 1. Schematic diagram of (A) centrifugal coating and (B) centrifugal fluidized bed coating using a multi-functional rotor processor.

Table 1
Operational conditions.

	Drug layering	Seal coating	Polymer coating	
Core material	Nonpareil®	DP	DP	DP-Talc
MOV-A-BLO state	Lower	Lower	Upper, lower	Upper, lower
	CFC	CFC	CC, CFC	CC, CFC
Rotor speed (rpm)	300	300	300	300
Air flow rate (L/min)	400	400	400	400
Inlet air temperature (°C)	40–50	40–50	45–55, 40–50	45–55, 40–50
Product temperature (°C)	30	30	30	30
Spray air pressure (MPa)	0.3	0.3	0.3	0.3
Liquid flow rate (g/min)	8.0	4.0	3.0	3.0

Table 2
Particle properties of DP-RS prepared by CC and CFC methods.

Coating level	30%		60%		150%		200%	
	CC	CFC	CC	CFC	CC	CFC	CC	CFC
Yield (%)	90.0	91.3	94.2	93.2	96.3	95.9	99.3	98.3
Median diameter (μm)	115	115	118	118	149	149	160	159
Bulk density (g/cm^3)	0.689 ± 0.001	0.691 ± 0.003	0.698 ± 0.001	0.697 ± 0.001	0.690 ± 0.001	0.689 ± 0.003	0.697 ± 0.006	0.700 ± 0.002
Coating efficiency (%)	102.7 ± 4.2	97.86 ± 2.5	96.9 ± 1.7	99.1 ± 1.7	91.1 ± 0.3	91.2 ± 1.7	90.4 ± 0.6	89.3 ± 1.0

Against this background, we focused on a multi-functional rotor processor (Granurex®; GX-20; Freund Industrial Co., Ltd., Tokyo, Japan; abbreviated as GX-20; Fig. 1). This apparatus enables to carry out centrifugal coating (CC; Fig. 1A) and centrifugal fluidized bed coating (CFC; Fig. 1B) without changing the spray position (the tangential-spray mode) because an up-and-down drying device (MOV-A-BLO) was equipped in the middle of the apparatus. Fundamentally, CC allows the particles to tumble onto a rotor, whereas CFC allows the particles to tumble on the rotor and become fluidized by the air flow from the MOV-A-BLO which can be positioned near the rotor. The purpose of the present study was to examine the effect of the coating processes, CC and CFC, on the physicochemical properties and drug dissolution behaviors of sustained-release microparticles.

2. Experimental

Nonpareil®-108 (100) (Freund Industrial Co., Ltd.) was layered with 70% *w/w* ethanol aqueous solution containing 20% *w/w* acetaminophen (APAP; Iwaki Pharmaceutical Co., Ltd., Tokyo, Japan) and 2% *w/w* hydroxylpropylcellulose (HPC-L; Nippon Soda Co., Ltd., Tokyo, Japan) by CFC method with GX-20, and 30% *w/w* APAP-loaded microparticles (drug layered particles; DP) were finally obtained. In addition, DP were coated with an aqueous dispersion containing 10% *w/w* talc (Matsumura industrial Co. Ltd., Tokyo, Japan) and 1% *w/w* HPC-L by CFC method with GX-20, until a weight gain of 10% *w/w* was achieved, and talc seal-coated microparticles (DP-Talc) were obtained. The prepared DP or DP-Talc were then coated with 30% *w/w* aqueous polymer dispersion of