Cluster Formation and Drag Reduction—Proposed Mechanism of Particle Recirculation within the Partition Column of the Bottom Spray Fluid-Bed Coater

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Received 14 August 2014; revised 12 November 2014; accepted 2 December 2014

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/jps.24323

ABSTRACT: Bottom spray fluid-bed coating is a common technique for coating multiparticulates. Under the quality-by-design framework, particle recirculation within the partition column is one of the main variability sources affecting particle coating and coat uniformity. However, the occurrence and mechanism of particle recirculation within the partition column of the coater are not well understood. The purpose of this study was to visualize and define particle recirculation within the partition column. Based on different combinations of partition gap setting, air accelerator insert diameter, and particle size fraction, particle movements within the partition column were captured using a high-speed video camera. The particle recirculation probability and voidage information were mapped using a visiometric process analyzer. High-speed images showed that particles contributing to the recirculation phenomenon were behaving as clustered colonies. Fluid dynamics analysis indicated that particle recirculation within the partition column may be attributed to the combined effect of cluster formation and drag reduction. Both visiometric process analysis and particle coating experiments showed that smaller particles had greater propensity toward cluster formation than larger particles. The influence of cluster formation on coating performance and possible solutions to cluster formation were further discussed. J Pharm Sci

Keywords: coating; fluid bed; image analysis; processing; particle size; drying; high-speed imaging; cluster formation; particle recirculation; visiometrics

INTRODUCTION

Bottom spray fluid-bed (BSFB) coating is commonly used for small particles in the manufacture of multiparticulate drug delivery systems.[1–3] In general, the coating process within the BSFB is achieved by using air flow to fluidize, suspend, and convey particles while depositing atomized coating fluid droplets onto the particles' surface. The rapid drying process is achieved by individually suspending particles in an atmosphere of heated air. Compared with fluid-bed dryers, the design of BSFB coaters includes the addition of partition column and specially designed air distribution plate.[4] The perforated area of the air distribution plate directly beneath the partition column has a much higher porosity compared with the periphery, resulting in a higher velocity air stream within the partition column. As such, the particles in the staging annular bed at the periphery are drawn by the Venturi suction into the partition column through the partition gap and are conveyed upward by the air stream. A two-fluid nozzle is usually located centrally below the partition column to atomize the coating fluid feed. Particles are coated by the deposition of atomized coating fluid droplets onto their surfaces. Upon exiting at the top of the partition column, the particles start to decelerate outward and fall onto the annular bed because of the decreased air velocity caused by the vertically expanding cross-sectional area of the BSFB container. The particles in queue then gradually flow back into the partition column through the partition gap and the coating cycle repeats.

Fundamental studies using positron emission particle tracking of particle movement within the BSFB revealed that wide-particle cycle–time distribution is mainly attributed to particle recirculation within the partition column.[5,6] Wide-particle cycle–time distribution often yields non-uniform coat layer.[7–11] Thus, under the quality-by-design framework, particle recirculation within the partition column can be a major variability source causing coat non-uniformity in the BSFB coating process.[12] However, the mechanism of particle recirculation within the partition column is still largely unclear, impeding further improvement of the BSFB process.

As particles within the partition column move at high speeds, high-speed imaging is a useful tool for capturing individual particles' motion and investigating particle recirculation within the partition column. Therefore, the purpose of this study was to visualize and elucidate the mechanism of particle movement within the partition column by mapping individual particles' trajectories with a high-speed video camera. Particle recirculation probability and voidage were quantified using the visiometric process analyzer developed by Liew et al.[12,13] The impact of partition gap, air accelerator insert (AAI) diameter, and particle size fraction on particle recirculation within the partition column was investigated because of their potential influences on fluid dynamics. The extent of spray drying effect for the three different size fraction particles was measured to examine the contact efficiency between particles and the atomized coating fluid. Moreover, air velocity and boundary layer

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Journal of Pharmaceutical Sciences

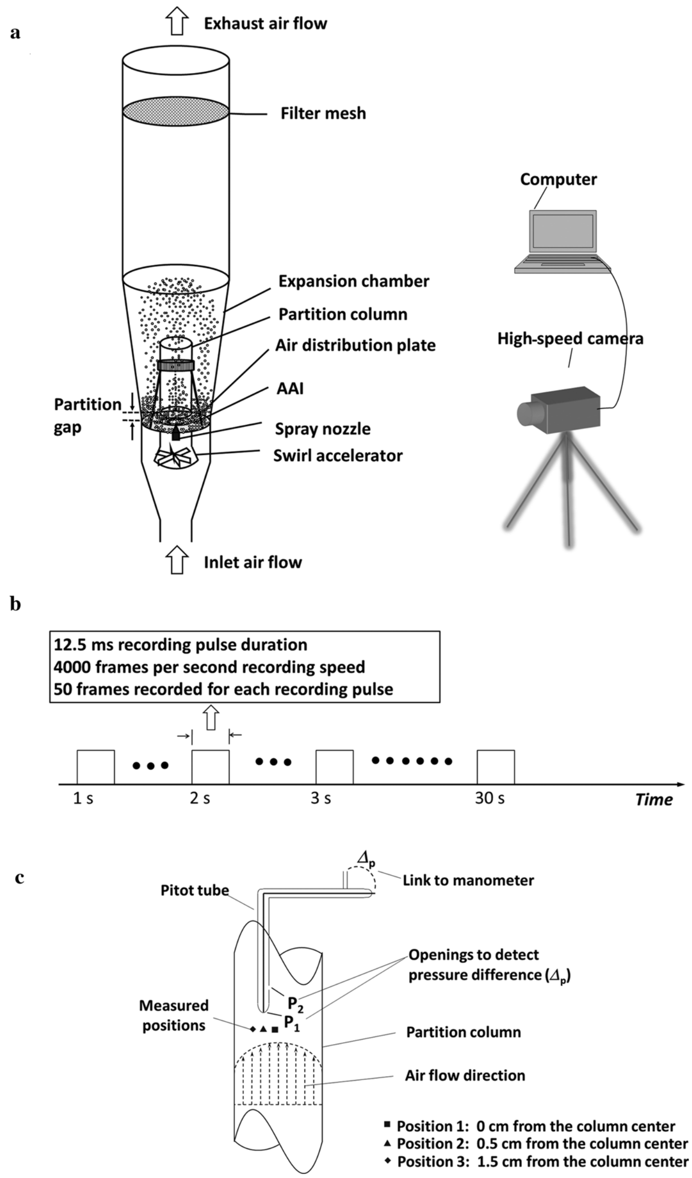

Figure 1. Schematic diagram of (a) high-speed imaging, (b) time sequence for video recording, and (c) air velocity measurement.

thickness within the partition column were also estimated to obtain fundamental fluid dynamics profile within the partition column.

EXPERIMENTAL

Materials

Sugar pellets (1.72 g/cm^3 density; Hanns G Werner's, Tornesh, Germany) of three different size fractions (355–425, 500–600, and 710–850 μm) were used as model particles. Hydroxypropyl methylcellulose (HPMC; Methocel E3-LV; The Dow Chemical, Midland, Michigan) was employed to pre-coat the particles to protect their integrity and to coat particles for assessment of the extent of spray drying effect during coating. HPMC aqueous solution (10%, w/w) was obtained by dispersing in hot water and then hydrating in the refrigerator overnight.

Table 1. Process Conditions for High-Speed Imaging

Process Parameters	Values
Air flow rate	90 m^3/h
Atomizing air pressure	2.0 bar
AAI diameter	20, 24, 30, and 40 mm
Partition gap	5, 10, 15, 20, and 25 mm
Particle size fraction	355–425, 500–600, and 710–850 μm

High-Speed Imaging

Pre-coated particles amounting to 1 kg were charged into the product chamber of the BSFB coater (Precision coater, Multiprocessor-1; GEA Aeromatic-Fielder, Eastleigh, UK). Both the partition column and product chamber of the coater were made of transparent acrylic such that the high-speed movement of particles in the partition column (Fig. 1a) could be recorded by a high-speed video camera (MotionPro HS-3; Redlake, Tallahassee, Florida). The camera was programmed and controlled using Matlab (R2007b; The Mathworks, Natick, Massachusetts) to acquire video clips on a pulse mode. The recording speed was 4000 frames per second with a resolution of 248 pixels by 744 pixels. For each combination of process parameters, 30 video clips were recorded, with each video clip comprising 50 frames recorded in the first 12.5 ms of each second; this was achieved by using pulse recording mode of the high-speed video camera (Fig. 1b). Compared with previously published methods,[12,13] the current study used larger imaging area and pulse recording mode, which helped to capture the particle motion within the partition column. The combinations of process parameters used for the high-speed imaging experiments are listed in Table 1.

Quantification of Particle Recirculation Probability and Estimation of Voidage within the Partition Column

The high-speed images were analyzed using the previously developed visiometric process analyzer for quantifying particle recirculation probability within the partition column.[12]

Voidage (ε) within the partition column was estimated using the following equation:

$$\varepsilon = 1 - \frac{N_p V_i}{V_c} \tag{1}$$

where N_p is the average number of particles on the image, V_i is the volume of a single particle, and V_c is the total volume captured by the high-speed camera. The number of particles (N_p) on the image was determined by the morphological image processing method developed previously.[13]

Air Velocity Measurement

A Pitot tube (160–12; Dwyer Instruments, Unanderra, Australia) linked to a micro barometer (DP-8705; TSI, Shoreview, Minnesota) was used to measure air velocities in the partition column. Air velocity was measured at positions 1, 2, and 3, that is, 0, 0.5, and 1.5 cm away from the center of the partition column, respectively (Fig. 1c). The AAI diameter was kept the same as in the high-speed imaging experiments and the partition gap was set at 10 mm. Twenty measurements were taken and averaged for each set of process conditions.