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The scale-up of spray coating processes for granular solids and tablets

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Abstract

Important issues pertaining to the scale-up of non-reactive coating processes occurring in fluidized bed and rotating drum-coating equipment, used primarily in the pharmaceutical and food industries, are discussed. A description of the scale-up methodology relating to the operation of the coating equipment is presented. For both types of equipment, the physical and chemical characteristics of the solids (tablets or pellets) must remain constant for all scales of equipment. Important issues in fluidized bed coating operations and scale-up such as air flow, product uniformity, air dew-point control, distributor plate design, attrition, atomizing air pressure, coating time, and batch charge are addressed. Specific issues affecting coating operations in rotating perforated pans including coating and drying cycles, air conditioning, rotation rates, batch charge, and nozzle location are also covered.

Keywords: Coating; Fluid bed; Rotating drum; Scale-up; Nozzle

1. Introduction

Coating materials can be applied to a wide variety of substrates ranging from sub-micron particles to very large objects. The processes covered in this paper are those in which nonreacting coatings are applied to particles between approximately 50 μm and a few centimeters. In particular, processes utilizing fluidized beds and rotating drum coating equipment will be discussed.

The coating of pharmaceutical, agricultural, and food products has been practiced for hundreds of years using techniques as diverse as applying coatings by hand to individual tablets to the application of millions of tablets using fluidized beds or rotating drum coating devices [1]. The scale-up of gas–solid contacting equipment from bench- to industrial-scale has also been studied for many years [2,3]. One approach is to devise bench-scale experiments that contain solids of different size and density than those of interest in the final application. The size and density of the solids along with other operating parameters such as gas flow and gas composition, temperature, and pressure are manipulated so that dimensionless numbers, which characterize the system of interest, are held constant in going from one size of equipment to the next. This application of dimensionless analysis is common practice in the chemical industry and has been used successfully for many years. For example, the scale-up of power requirements for mixing equipment and the characterization of heat and mass transfer coefficients through the use of Reynolds, Prandtl, and Nusselt number, etc., are well known. However, when considering coating processes, with particular emphasis on the pharmaceutical and food industries, the process of scale-up must take into account the fact that, in general, only "standard" equipment of predetermined size are available for processing. For this reason, the use and availability of discrete-sized equipment will be taken as given in the development presented in this paper. In addition, samples from all sizes of equipment must be tested, often through in vitro analysis and/or on human subjects, and must meet all in-process controls and finished product specifications. Therefore, the same quality of solid product (size, density, drug loading, etc.) must be produced at each phase of the scale-up process.

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2. Fluidized bed processes

The term fluidized/fluid bed is used to describe a variety of processes in the Pharmaceutical Industry. The term covers conventional, spouted, and rotating fluidization phenomenon. There are basically three configurations that fluidized bed coating equipment can take. The first and most common configuration used for film coating is the “Wurster-Column” coater [4,5], in which a draft tube insert (Wurster partition or column) is placed co-axially in the bed to aid the circulation of particles. This configuration is illustrated in Fig. 1. A nozzle is placed at the center of the distributor plate. Coating material is atomized through the nozzle and is deposited on the particles as they pass upward through the draft tube. Each particle receives a small amount of coating each time it passes through the spray zone. The repeated movement of particles through the spray leads to the formation of a coherent and relatively uniform coating layer on the particles. One of the main disadvantages of this process is the high erosion of solids, which increases with the size of the particles (tablets or pellets) because of the higher air velocity needed to circulate them. A second disadvantage is the clogging of the nozzle(s) that cannot be remedied easily since removal of the nozzle during a run is almost impossible.

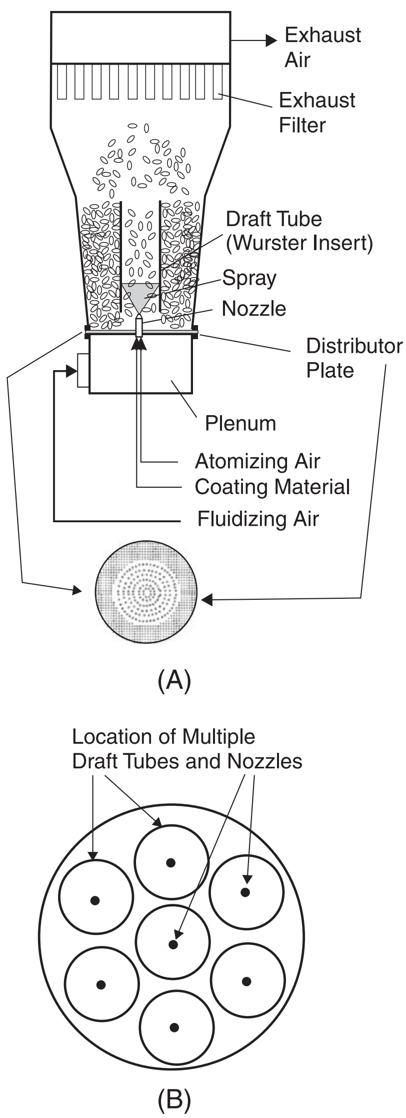

Fig. 1. Schematic diagram of bottom spray fluidized bed coater with “Wurster Column” (draft tube insert); (A) diagram of bed and distributor plate; (B) top view of bed showing configuration when multiple (seven in case shown) draft tubes are used.

The second fluidized bed configuration is known as the top-spray mode, which is illustrated in Fig. 2. For this type of operation, no draft tube is used, but instead, the nozzle is placed in the freeboard above the bed and coating material is sprayed downwards onto the top surface of the bed. The uniformity of the product is worse than for bottom-spraying but this method has the advantage that the nozzle may be cleaned and replaced during the course of a run. This mode of operation is commonly used for granulation and for hot melt coating operations.

The third fluidized bed coating operation is the so-called rotary fluidized bed in which a special rotor is made to spin just above the gas distributor. This configuration is illustrated in Fig. 3. Air enters the bed between a slot between the rotor and the inner wall of the product container. The combination of the fluidizing air and the movement of the rotor causes the bed of particles to form a twisting rope-like structure that moves circumferentially around the bottom of the bed. Coating material is then sprayed tangentially into this moving “rope” of particles. This equipment is preferred when a powder coating or layering process is to be performed. Spray coating is the most common pharmaceutical coating process and this paper will concentrate on the development of scale-up strategies for fluidized beds using the so called “Wurster-Column” design.

3. Scale-up of fluid bed coaters containing draft tube (Wurster columns or partition) inserts

According to Mehta [6] there are over 20 variables that may affect the coating process. These variables may be categorized as follows:

3.1. Product or substrate variables

These include the properties of the solid to be coated, for example, its hardness, size, shape, and friability. The following list outlines common issues for substrate variables.

- Pellets or beads, which are often non-pareils made of sucrose and microcrystalline cellulose, are in the size range of 50 μm to 2 mm. On the other hand, tablets usually range from 2 to 10 mm.
- Substrates having a low friability may give acceptable results in small lab-scale equipment. However, when scaling up to commercial sized equipment, problems