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Review

Mathematical modeling of the coating process

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A B S T R A C T

Coating of tablets is a common unit operation in the pharmaceutical industry. In most cases, the final product must meet strict quality requirements; to meet them, a detailed understanding of the coating process is required. To this end, numerous experiment studies have been performed. However, to acquire a mechanistic understanding, experimental data must be interpreted in the light of mathematical models. In recent years, a combination of analytical modeling and computational simulations enabled deeper insights into the nature of the coating process.

This paper presents an overview of modeling and simulation approaches of the coating process, covering various relevant aspects from scale-up considerations to coating mass uniformity investigations and models for drop atomization. The most important analytical and computational concepts are presented and the findings are compared.

Contents

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1. Introduction

Coating of tablets or particles is one of the oldest and most common unit operations in the pharmaceutical industry. Generally speaking, coating is a repeated exposure of particles (tablets, granules, etc.) to a spray, containing solute and solvent. As a particle moves through the spray zone, it receives a partial coating with a local distribution and amount depending on the local conditions on the particle's way through the spray zone. The liquid coating spreads to some extent over the particle and, in some cases, penetrates it. It also may be transferred to other particles. After being sprayed, the particle moves into a region where the partial coating is solidified, typically via evaporation of the solvent facilitated by heated drying air. This cycle of spraying and drying is repeated multiple times until the desired coating mass and/or uniformity are reached (Turton, 2008).

Although coating systems are quite diverse, the underlying principle of most of the modern systems is the same (Fig. 1). Differences primarily relate to the way particles move between spray and drying zones and the way of removing the solvent. Since most solid dosage forms are coated using either a fluidized bed or a rotation drum, they were the focus of this work, with an emphasis on drum coating of tablets, for which an extensive body of literature exists. However, because the underlying principle is similar, findings are generally applicable to coating of particles in general.

1.1. Drum coating

Drum coating of tablets is a very common coating method in the pharmaceutical industry. Tablet cores are placed in a rotating drum, where the rotation promotes their radial and axial mixing (Fig. 2).

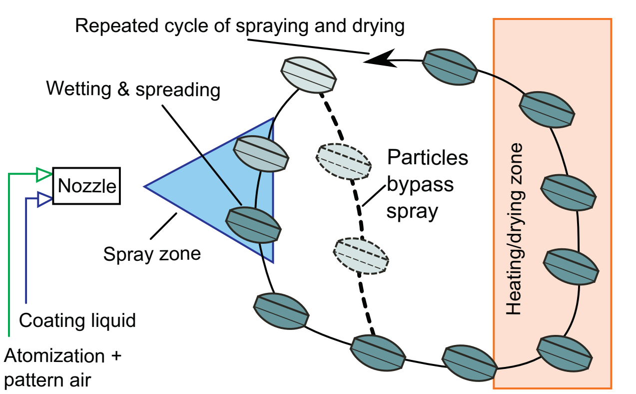

Fig. 1. General principle of a particle coating process. This cycle (coating in the spray zone – transportation and drying – re-enter the spray) appears in most types of coating apparatus.
From Turton (2008).

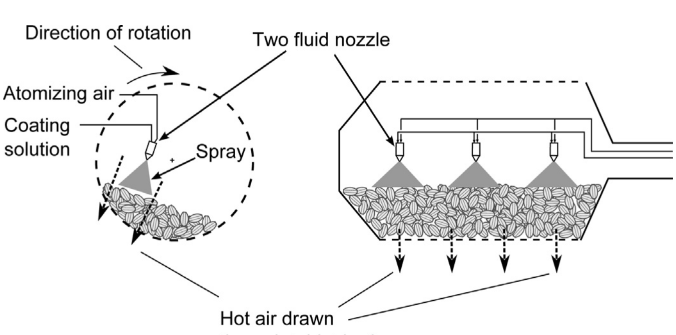

Fig. 2. Schematic representation of a typical drum coating apparatus.
From Turton and Cheng (2005).

Typically, axial mixing is slower, and is often facilitated by installing baffles in the drum (Muliadi and Sojka, 2010). Drum coaters are available in different designs, distinguished mainly by the drying air flow through the drum and by the baffle arrangement. However, all of them operate similarly, with particles cascading down the top of the bed and some passing through the spray zone. The spray zone is formed by one or more spray nozzles mounted atop and spraying down onto the tablet bed.

For the coating quality, dominant factors are the movement of the tablet and locally the tablet-drop interaction. The relative effect of droplet size, impact and frequency, liquid spreading, drying and the ensuing solid-state transformations determine the morphology and quality of the coating (Bolleddula et al., 2010; Suzzi et al., 2010).

During a pan-coating process, operational parameters can be divided into two groups: pan-and-tablet-related and spray-related (Pandey et al., 2006c; Porter, 2012; Ruotsalainen et al., 2002).

Important pan and tablet parameters are:

- pan diameter and depth
- pan speed
- pan load
- core shape, size, and mass
- baffle setup
- number of spray nozzles
- pan perforation
- mechanic tablet properties (e.g. hardness, friability, friction coefficient)

Important spray-related parameters are:

- spray rate
- inlet air flow rate
- inlet/outlet air temperature
- inlet/outlet air humidity
- atomizing air
- solution properties
- nozzle-to-bed distance
- coating time

To achieve a deeper understanding of the coating process, experimental investigations studied the influence of process parameters on the outcome (Mueller and Kleinebudde, 2007a; Patel et al., 2009; Sandadi et al., 2004). Both inter- and intra-tablet uniformities were measured (Tobiska and Kleinebudde, 2003), with a trend toward novel non-destructive techniques, such as Terahertz-Pulse Imaging (Brock et al., 2012; Ho et al., 2007) or Optical Coherence Tomography (Koller et al., 2011; Mauritz et al., 2010; Zhong et al., 2011).

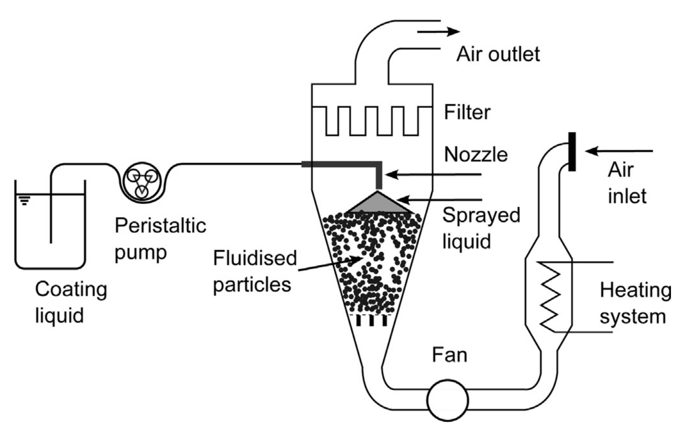

Fig. 3. Schematic representation of a top spray fluid bed granulator or coater.
From Teunou and Poncelet (2002).