Nondimensional Scaling Laws for Controlling Pharmaceutical Spray Uniformity: Understanding and Scale-Up

ARIEL R. MULIADI,[1] PAUL E. SOJKA[2]

[1]School of Chemical Engineering, Purdue University, West Lafayette, Indiana 47907

[2]Maurice J. Zucrow Laboratories, School of Mechanical Engineering, Purdue University, West Lafayette, Indiana 47907

Received 8 November 2011; revised 23 January 2012; accepted 2 February 2012

Published online 14 March 2012 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/jps.23088

ABSTRACT: Spatially resolved drop size, drop velocity, and spray volume flux measurements for sprays produced by a commonly used pharmaceutical coating nozzle were performed in this study. Results showed three distinctive spray patterns: Gaussian, homogeneous, and dumbbell shaped. We found that transition from a dumbbell-shaped to a homogeneous pattern is related to the shaping air-induced breakup of already formed drops: depending on the drop size upstream of the location where the shaping air flows meet (i.e., the "junction" point), the drop viscosity, and the magnitude of the shaping air velocity, the shaping air can either pinch the spray or cause additional drop breakup. When the former outweighs the latter, the dumbbell-shaped pattern occurs; the homogeneous pattern is present when the opposite occurs. A corollary to this experimental interpretation is that whether additional drop breakup homogenizes the sprays or pinches, it is related to a Weber number (*We*) that is calculated using drop sizes upstream of the junction point, drop viscosity and surface tension, and the shaping air velocity at the junction point. With this idea in mind, we propose a *We*-based scaling method for optimizing the uniformity of air-assist spray patterns. © 2012 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 101:2213–2219, 2012
Keywords: Tablet; Coating; Unit operations; Viscosity; Processing; Formulation; Spray; Uniform; Patternation; PDA

INTRODUCTION

Most pharmaceutical tablets have a thin (10–20 µm) film coating on their surface. The coating is often of significant importance as it may mask taste, improve tablet mechanical properties, separate reacting ingredients within the tablet, seal the tablet from moisture to improve shelf life, and control drug release rate and location within the patient (enteric).

The film coat is typically applied by subjecting tablets to an atomizer-produced spray while tumbling them inside a rotating cylindrical drum. The outcome of this process depends heavily on two aspects: the wetting characteristics exhibited by the drops when they strike the tablets[1,2] and the amount of coating each tablet receives each time it passes through the spray zone.[3]

Correspondence to: Paul E. Sojka (E-mail: sojka@purdue.edu, Phone: 765-494-4665, Fax: 765-494-0530).

Journal of Pharmaceutical Sciences, Vol. 101, 2213–2219 (2012)
© 2012 Wiley Periodicals, Inc. and the American Pharmacists Association

Surface wetting encompasses the degree to which the drop spreads over the tablet surface (e.g., "blobbing" vs. splashing), to which the drop penetrates into the tablets, and the mechanical stresses that develop within the film coat because of spreading and penetration. These phenomena in turn influence the physical characteristics of the film coat. Their relation to spray operating parameters is evident from the following studies:

- Kim et al.[4] and Rowe and Forse,[5] who reported that incidences of logo infilling ("bridging") increased as coating liquid supply rate increased.
- Twitchell,[1] Twitchell et al.,[6] and Reiland and Eber,[7] who found that increasing the atomizing air pressure or decreasing the gun-to-target distance resulted in a smoother film coat.
- Twitchell,[1] who noted that a decrease in gun-to-target distance decreased film surface roughness.
- Ruotsalainen et al.,[8] who determined that film surface roughness increased with an increase in liquid supply rate.

- Fisher and Rowe[9] and Rowe,[10] who observed that film-to-tablet adhesion decreased as liquid viscosity increased.

A more comprehensive discussion of this topic is presented in the recent review paper by Muliadi and Sojka.[11]

Of equal importance to film coat physical properties is intertablet film coating uniformity—to minimize intertablet coating variations, the amount of coating each tablet receives each time it passes through the spray zone has to be essentially equal to that received by all the other tablets. As such, the spray coverage area and the homogeneity of the spray pattern (mass distribution) need to be optimized.[12–15]

Flat-shaped air-assist (twin-fluid) sprays have the capability to meet such requirements. They are therefore widely used in pharmaceutical tablet coating processes. Several studies,[1,16] however, have highlighted the challenges of producing homogeneous flat sprays. While the spray boundary, or outline, remains essentially elliptical, small variations in typical scale-up variables (e.g., liquid supply rate, liquid viscosity, etc.) have been found to alter the spray pattern. Often referred to as patternation—that is, the distribution of the sprayed liquid mass flux—it can shift from Gaussian, to uniform, to dumbbell shaped.[16]

Because the conditions that lead to the production of these different spray patterns have not been identified, quantitative guidelines to optimize sprays for tablet coating applications are not available. Instead, vendor-supplied "manuals" typically require operators to iteratively adjust a combination of spray process operating parameters while capturing droplets on a piece of paper until an acceptable spray pattern results. Such a method has obvious failings. Apart from being intrusive to the sprays, it gives only a qualitative indication of how drops of different sizes are distributed across a spray cross-sectional area. More importantly, it cannot provide quantitative information about the spray pattern and its corresponding local spray flux values. This is unfortunate because these are the properties which most strongly affect intertablet coating uniformity.

As a result of existing spray characterizations being imprecise and/or of limited accuracy, it is not uncommon for production tablet coating processes to be carried out using suboptimal (dumbbell- or Gaussian-shaped) spray patterns. This can lead to film thickness variations as high as 57% from one tablet to another.[3] This is a significant problem—all the more so when the film coat serves an enteric function.

This study provides a partial solution to these shortcomings (1) by providing a comprehensive understanding of why the various flat spray patterns develop and (2) by providing quantitative scaling guidelines that allow pharmaceutical engineers and scientists to operate their sprays at conditions that produce optimal tablet coating.

MATERIALS AND METHODS

Spray Nozzle

Measurements were performed on sprays produced by a Schlick 930/7-1-S35 nozzle (Schlick GmbH, Coburg, Germany). It is equipped with a flat-shaped air cap and an antibearding liquid cap (ABC). Unlike conventional units, ABC-type caps protrude several millimeters past the atomizing air outlet. This feature is intended to prevent clogging due to coating liquid buildup at the atomizing air outlet. The nozzle also features separate shaping and atomizing air channels, a design commonly found in modern coating units. This allows the shaping air flow to be completely shut off, thereby producing sprays with a circular pattern. Spray conditions are listed in Table 1.

Test Liquids

Spray tests were performed using water and aqueous HPCM E-5 (Dow Chemical Company, Midland, Michigan) solutions of varying concentrations (1.5, 2.5, and 3.5%, w/w). The viscosity of all test liquids was measured using a dynamic shear rheometer (StressTech; ATS RheoSystems, Bordentown, New Jersey), their densities were determined by weighing (using digital scale) a known volume (as reported by a graduated cylinder), whereas their surface tensions were found using a standard ring tensiometer (CENCO-DuNOÜY model 70535, Central Scientific Company, Chicago, Illinois). Measurement results are listed in Table 2. Note that, here, viscosity values are reported for a shear rate of 632 1/s.

Table 1. Spraying Conditions

Spray Conditions	P_{AA} (kPa)	P_{SA} (kPa)	m_{liq} (g/min)	Gun-to-Target Distance (cm)	Liquid Type
1	205	140	80	14	H_2O
2	275	140	80	14	H_2O
3	275	210	80	14	H_2O
4	275	140	110	14	H_2O
6	275	140	80	14	1.5% HPMC-E5
7	275	140	80	14	2.5% HPMC-E5
8	275	140	80	14	3.5% HPMC-E5

 DOI 10.1002/jps

Download English Version:

https://daneshyari.com/en/article/2485750

Download Persian Version:

https://daneshyari.com/article/2485750

Daneshyari.com