Fluid Bed Nozzle Spray Characterization of an Aqueous Ethylcellulose Dispersion for Particle Taste-Masking Applications

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Purpose

Taste-masking of unpleasant or bitter tasting drug formulations is essential to improve patient compliance especially in the pediatric and geriatric population. Additionally, there is a rising trend to formulate drugs in the form of orally disintegrating dosage forms due to their easy ingestion and absorption process.[1] Moreover, taste-masking and high palatability can provide a competitive advantage, especially in the case of over-the-counter consumer products.

Various taste-masking techniques have been used to improve patient compliance including barrier coating, microencapsulation, and granulation alone, or in combination with sweeteners and flavorants. Coating is one of the most efficient and commonly used taste-masking technologies.[2] Insoluble polymers, such as ethylcellulose, alone or in combination with other polymers have been shown to provide effective taste-masking properties for unpalatable pharmaceutical actives.

The spray droplet characteristics produced by a pneumatic nozzle can have significant impact on the uniformity of a barrier membrane film coating and a risk of agglomeration when applied to particles of active pharmaceutical ingredients (APIs) in a fluid-bed operation. The goal of this study was to determine optimal coating spray conditions for the application of an aqueous ethylcellulose dispersion (Surelease® Ethylcellulose Dispersion Type B), applied as a taste-mask coating, from both laboratory and production scale pneumatic spray nozzles, for the purposes of taste masking.

Methods

Droplet size and velocity of the Surelease dispersion spray, from both Schlick 970 (laboratory scale) and 0/4 (production scale) series spray nozzles, were characterized using phase-Doppler technique. A central composite, quadratic, three-factor experimental design was developed using design of experiment (DoE) software (Fusion Pro, S-Matrix Corporation) to examine both the individual and interactive effects of three process variables on droplet characteristics generated from the spray nozzles. Process variables studied and ranges examined are summarized in Table 1.

Table 1. Experimental Process Variables

Variable Name	Units	970-series Nozzle		0/4-series Nozzle	
		Low Level	High Level	Low Level	High Level
Liquid Delivery Rate	g/min	10	30	150	500
Atomizing Air Pressure	Bar	1.0 / 1.5 / 2.0		1.5 / 2.0 / 2.5	
Dispersion Solids	%	10	15	10	15

Response variables examined were mean droplet size (µm) and droplet velocity (m/s). Seventeen measurements, including three replicates, for determining experimental error, were conducted for both the laboratory and production scale nozzles.

Surelease® (E-7-19040) and Opadry® complete film coating system, clear, non-pigmented formulation, both from Colorcon Inc. (West Point, PA, USA) were used at an 80:20 ratio in all experiments. Viscosity of the spray dispersion was determined by rotational viscometer (Brookfield Engineering) at each of the solids content examined prior to spray testing.

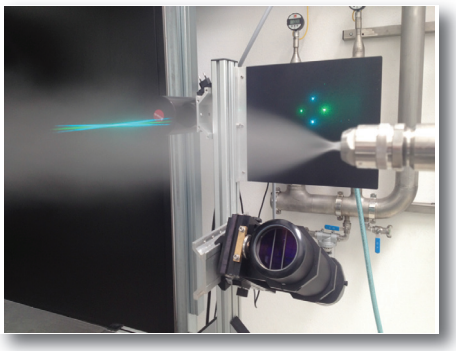
Experimental constants and air consumption values for each nozzle and air pressures tested are summarized in Table 2.

Table 2. Experimental Process Constants and Recorded Air Volumes

Variable Name	Units	970-series Nozzle	0/4-series Nozzle
Liquid Nozzle Insert	mm	1.0	2.2
Tip Protrusion	mm	0.5	Flush
Gun to Laser Distance	cm	15	20
Spray Width	mm	50	150
Atomizing Air Volume	m^3/hr	1.3 / 1.6 / 2.1	30 / 35 / 43

Phase-Doppler analysis (PDA) is a single point optical measuring technique which enables the velocity of droplets or particles conveyed by a fluid flow to be measured in a non-intrusive, real time manner.[3] With this technique, droplet velocity can be determined by analyzing the Doppler equivalent frequency shift of the laser light scattering by the droplets within the flow. The scattering is manifest by intensity modulations within the crossed-beam probe volume, and droplet size is determined by measuring the phase difference between two Doppler bursts detected by two detectors at different angular positions.[4] PDA equipment used for all testing is shown in Figure 1.

Figure 1. Image of PDA system (Schlick Test Center, Düsen-Schlick GmbH).



Results

Examination of residual plots and r-square values did not reveal any unwanted patterns, indicating unbiased results and goodness-of-fit of data to predicted values. A summary of data range obtained for each response variables examined is shown in Table 3.

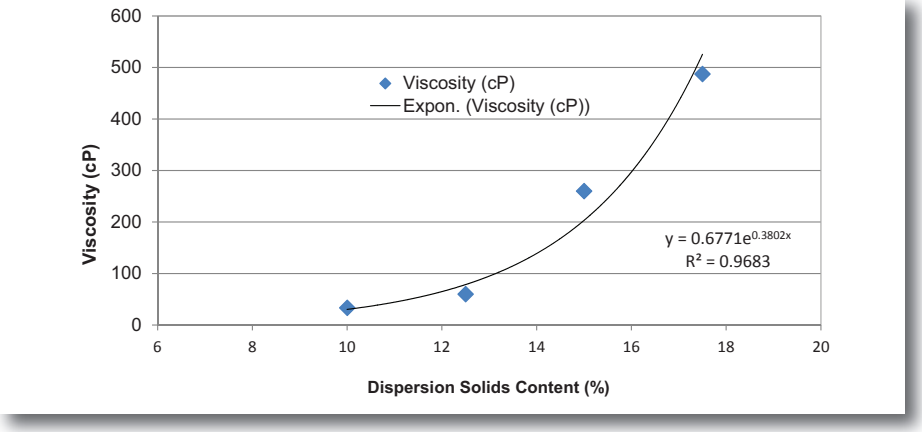
Table 3. Summary of Ranges in Values of Response Variables Obtained

	970-series Nozzle		0/4-series Nozzle	
	Center Point	All Points	Center Point	All Points
Droplet size (µm)				
D(10)	9.2 - 14.8	9.5 - 16.9	10.0 - 15.6	10.6 - 16.3
D(30)	13.4 - 20.6	14.7 - 24.6	14.7 - 23.5	16.2 - 27.7
D(32)	18.7 - 28.1	20.2 - 34.9	21.3 - 35.4	24.1 - 45.6
Droplet Velocity (m/s)				
Mean	9.0 - 18.5	7.4 - 13.2	24.5 - 47.8	14.4 - 26.9
rms	2.3 - 4.7	2.6 - 6.2	6.5 - 11.8	8.6 - 17.6

Recorded Values: Arithmetic or number mean diameter D(10), volume mean diameter D(30), volume/surface mean D(32) usually referred to as Sauter mean diameter, velocity (mean) and velocity root mean square (rms)

Surelease dispersions are two-phased structured fluids that exhibit non-Newtonian elasticity due to the presence of submicron ethylcellulose particles dispersed within a continuous aqueous phase. The stability of the Surelease dispersion is governed by steric and electrostatic forces. Rotational viscosity values of the Surelease and Opadry dispersion at solids content examined in the study are plotted in Figure 2.

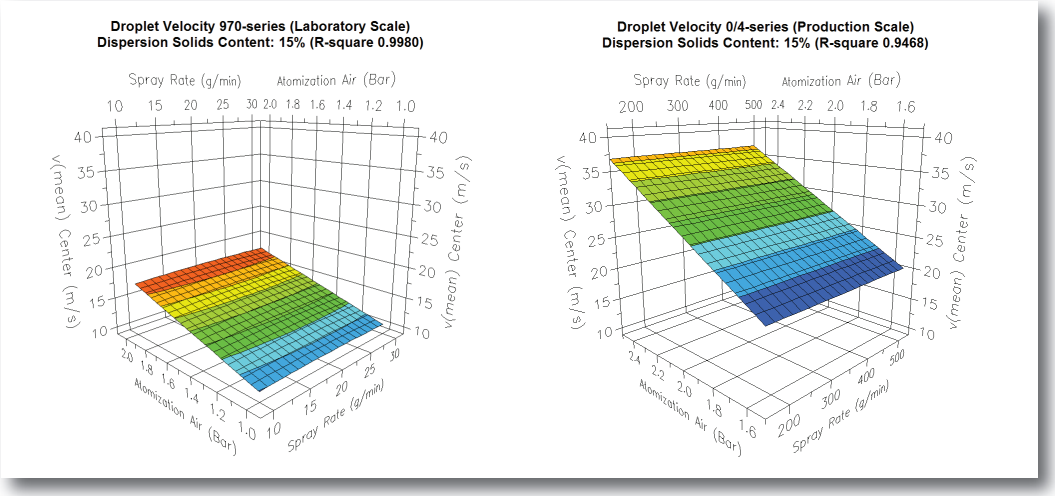
Figure 2: Viscosity of Spray Dispersion at Various Solid Contents Examined (Surelease E-7-19040 and Opadry Clear YS-1-19025-A at 80:20 ratio).



Droplet velocity was primarily affected by atomization air pressure with the highest velocities being measured at the center of the spray and lowest at the edge of the spray. Surprisingly, changes in dispersion solids content, and resulting viscosity, did not prove to be critical to mean droplet velocity.

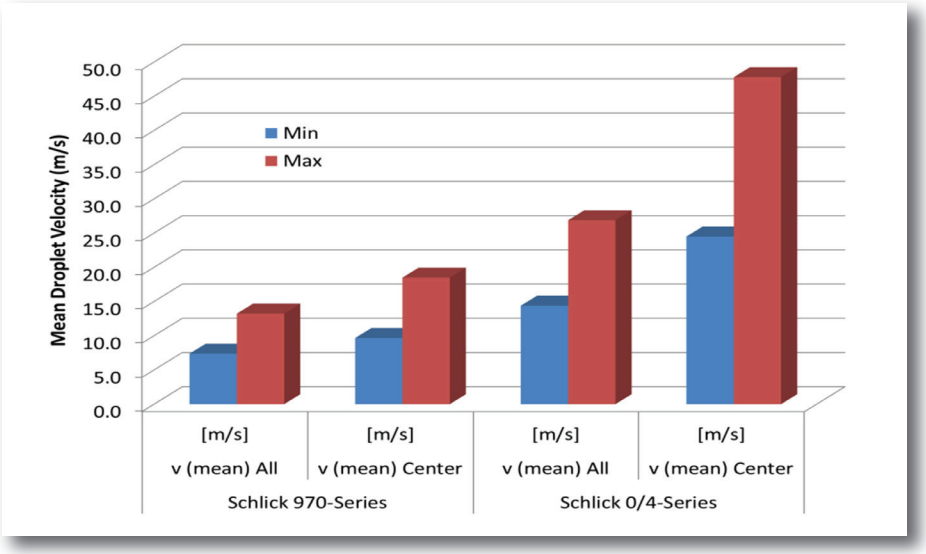
Increases in atomization air pressure resulted in increases in droplet velocity at both laboratory and production scale as shown in Figure 3.

Figure 3. Mean Droplet Velocity (v) for Laboratory and Production Scale Nozzles at Center of Spray Zone



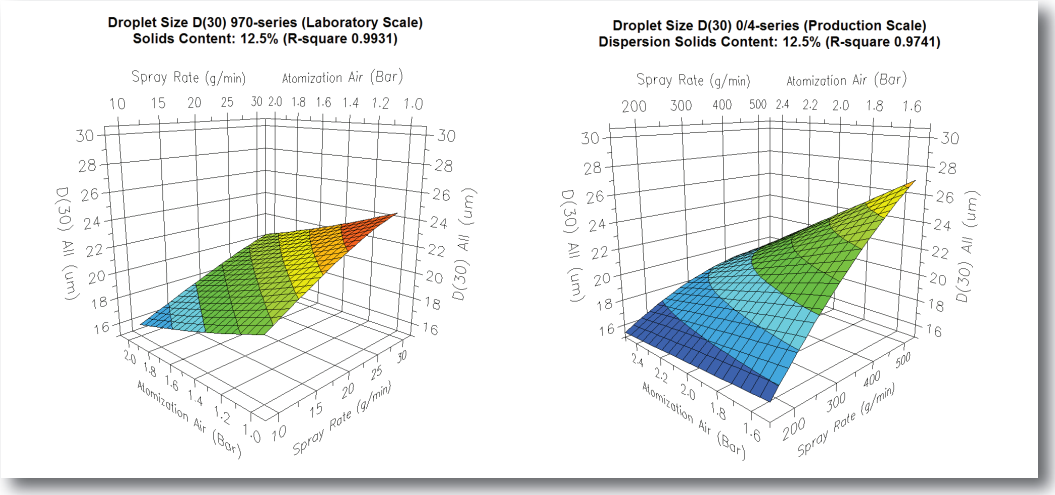
Increases in atomization air pressure, from 1.0 to 2.0 bar at laboratory scale and 1.5 to 2.5 bar at production scale, resulted in an increase in droplet velocity at the center of the spray from 9.7 to 17.4 and 24.5 to 47.8 m/s respectively. As seen in Figure 4, mean droplet velocity for the laboratory and production scale nozzle did not overlap under any test conditions.

Figure 4. Minimum and Maximum Droplet Velocity Values at Both the Center and Across the Width of Spray for All Conditions Tested



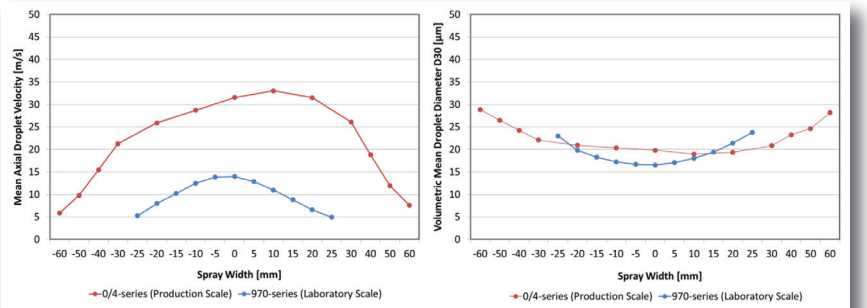
Analysis of data indicated that both the individual and interactive effects of spray rate and atomization air pressure accounted for greater than 60% of the effects on mean droplet size. As expected, an increase in spray rate resulted in an increase in mean droplet size, while increasing atomization air pressure resulted in a decrease in droplet size. These effects were more predominant at moderate to high spray rates, particularly for the production scale nozzle as show in Figure 5.

Figure 5. Average Volume Mean Diameter D(30) for Laboratory and Production Scale Nozzles Across Spray Zone



Overlay plots of axial droplet velocity and volumetric droplet diameter, Figure 6, highlights achievable spray characteristics from both laboratory and production scale spray nozzles. Similar droplet velocity from the nozzles tested is unattainable due to differences in air volume consumption. However, it can be seen that similar droplet size can be achieved across broad spray widths.

Figure 6. Overlay of Mean Axial Droplet Velocity and Volumetric Mean Droplet Diameter for Laboratory and Production Scale Nozzle



970-series (Laboratory Scale): 20 g/min; 1.5 bar; 15% solids content
0/4-series (Production Scale): 325 g/min; 2.0 bar; 15% solids content

Conclusions

Phase-Doppler analysis was successfully used to characterize the droplet size and velocity profiles generated from a both laboratory and production scale fluid-bed nozzle. This technique exhibits good accuracy and repeatability as evidenced by low standard deviation for repeated measurements and low percent error within replicate groups.

The DoE study demonstrates that all three input parameters studied (spray rate, atomizing air pressure and dispersion solids content) have significant influence on droplet velocity and size.

Coating of small particles for the purposes of masking unpleasant or bitter tasting APIs can be challenging. Coating conditions must be optimal in order to maximize coating uniformity and process efficiency in order to achieve effective taste-masking while avoiding unwanted agglomeration and growth of particles that can result in gritty mouth feel. Data from this study can be utilized to determine optimal spray conditions for the taste-masking of particles of various sizes in a fluid-bed coater at both laboratory and production scale.

References

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