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Near-field dynamics of high-speed spray dryer coannular two fluid nozzle: Effects of operational conditions and formulations

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ABSTRACT

The scaling-up of spray drying processes is an important and challenging step in commercializing specialty products with an ensured quality because it mandates a comprehensive understanding of several steps in the process such as atomization, efficient solvent removal, and particle segregation. The formation of needed particle sizes and shapes is impossible without appropriate atomization through spray dryer nozzles. Hence, research is discussed that investigates the atomization mechanism for a pilot scale externally-mixed, two-fluid nozzle spray dryer by using time resolved particle-image velocimetry to study the behavior of droplets in the near-field of the nozzle tip. Important near-field dynamics of droplets emanating from the nozzle are described, and particle formation characteristics are discussed for several formulations which are widely used in the pharmaceutical industry. Spray angle, droplet breakup length, and droplet sizes and velocity distributions are characterized. Understanding these parameters assists the interpretation of particle formation and enables the modeling of the spray drying process.

1. Introduction

Pharmaceutical spray drying is a commonly used tool to make an amorphous solid dispersion of a drug by combining with polymers and other functional excipients like surfactants [1]. The steps in a pharmaceutical spray drying process include [2]: i) preparation of a feed solution using solvent(s) with high capacity for the drug, polymer and other functional excipients; ii) atomization of the feed solution into the drying chamber where it is mixed with heated drying gas; iii) evaporation of a fine droplet spray to create solid particles; and iv) subsequent separation of the processing gas and particles in a cyclone placed downstream to the main spray drying chamber. The formation of the liquid binder droplets by atomization is a critical step during spray drying. It directly influences the size [3] and porosity of the resultant spray dried, fine powder particles, their ability to adhere to one another and form agglomerates [4], and even their spatial chemical homogeneity [5]. Understanding spray characteristics like breakup regime transitions, spray angles, and velocity and size distributions of the formed droplets under different conditions aids in optimizing and controlling the operation of spray dryers.

Pharmaceutical production use spray drying [6], spray-freeze drying [7], tablet coating [8] and fluidized bed granulation [9,10]. Upon injection of a feed solution through a fine nozzle, atomization of the solution occurs in which the liquid jet transitions from an unstable stream or sheet to ligaments and subsequently to droplets. Regardless of the operating conditions, atomization occurs very close to the nozzle tip [11]. By understanding this breakup length and the influences of the cone angle, it is possible to avoid erratic changes in droplet size distributions further downstream of the spray nozzle and to control droplet flow patterns and therefore the drying process [12,13]. As an example, Oakley et al. [13] studied the scaling-up of spray dryers using computational fluid dynamics (CFD) and experimentation. They showed that dramatic changes in the air flow pattern in a spray dryer chamber occurred when the angle of the swirl vanes for feeding the drying air was increased from 25 to 30°. Particle residence time, final powder moisture content, and the spray dryer outlet temperature were dramatically affected by this angle [12].

Commonly used during spray drying is a coannular two-fluid nozzle in which the pharmaceutical solution emanates from the center nozzle tip and gas flows from a separate nozzle which surrounds the solution nozzle tip. The relative velocities between the liquid and gas can be varied; where it has been found that the momentum flux ratio per unit volume of gas-to-liquid is a main driving force for atomization [14]. However, liquid capillary and viscous forces within the solution resist atomization [15]. To achieve an optimum outcome for needed particle sizes, size distributions and moisture contents, it is necessary to carefully control the operating conditions at the spray nozzle and the characteristics of the solution to be spray dried. It is possible to

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achieve this control by carefully understanding the relative magnitudes of the momentum flux ratio, capillary and viscous forces. As an example, increasing the air to liquid velocity difference at the nozzle outlet by either lowering the liquid flow rate or raising the air pressure will result in smaller solution droplets and hence, smaller particle sizes.

Atomization is the vital link between liquid issuing from a nozzle and the subsequent spray drying process which affects the final powder microscale characteristics. Despite the bulk atomization literature in other industry sectors [16], atomization mechanisms are still poorly understood for pharmaceutical two-fluid nozzles. Quantitative observations of the attributes of the near field spray near a nozzle are difficult to accomplish and often suffer from large uncertainties. For example, the dependence of the droplet size on the gas velocity as described by a Sauter mean diameter of the droplets has been approximated by a power law correlation of the velocity with an exponent ranging between −0.7 to −2.1 [17,18]. Aside from this rather poor agreement on what the exponent should be, no decisive physical explanation has been proposed for why the mean droplet sizes should even obey a power-law. Hence, extrapolating data from one study to another when using even an identical same spray design is fraught with uncertainty. Despite various semi-empirical correlations in the literature that were customized for various operating conditions [18,19], the designs and conditions for using a two-fluid nozzle to atomize widely used pharmaceutical formulations is not clear.

One meaningful way of interpreting the atomization process is by relating operational conditions and formulation properties to spray attributes using non-dimensional analysis [15] in which a few non-dimensional parameters are employed to describe the underlying physics behind the breakup phenomena. This non-dimensional approach is used herein to relate atomization break-up length and spray angle and to provide insight into atomization of typical pharmaceutical formulations.

In addition, the experimental study of the spray anatomy in a spray dryer using a two-fluid nozzle, high-speed particle image velocimetry (PIV) was applied to shadowgraph images of droplets emanating from the nozzle to analyze instantaneous droplet sizes and velocity vector fields along with droplet breakup characteristics. Cross-correlations between successive droplet images with a short time delay between exposures was employed along with particle tracking velocimetry (PTV) to determine velocities for individual droplets. A statistical description of the discrete PIV images and PTV results were subsequently used to estimate particle displacements as a function of the spatial resolution [20]. The time-resolved PIV at sampling rates sufficient to resolve the flow provided an accurate measure of the 2D temporal liquid flow field emanating from the nozzle. Although the concept of PIV is relatively simple, its application is not necessarily straightforward because the factors to be considered during its design, implementation, and eventual interpretation are numerous. These variables are discussed and related to uncertainties in the measurements which may arise.

2. Materials and methods

2.1. Materials

Poly vinylpyrrolidone-*co*-vinylacetate (PVP-VA) 64 and hydroxypropylmethylcellulose acetate succinate H-grade (HPMCAS-H) were selected as model polymers because they are often used during the preparation of amorphous solid dispersions with poorly soluble APIs. These polymers are also commonly used in the preparation of solid dispersions able to maintain a supersaturated drug concentration in vivo that prolongs time for optimal absorption [21]. Methanol was used as a model solvent and has a high capacity to dissolve these polymers. PVP-VA was obtained from International Specialty Products (Wayne, NJ, USA) and HPMC-AS (HF grade) from Shin-Etsu Chemical Co., Ltd. (Tokyo, Japan). Methanol was obtained from Sigma-Aldrich, St. Louis, MO. PVP-VA and HPMCAS were then added to methanol and mixed using a magnetic stir bar until completely uniform. Two solutions with 5% by weight of PVP-VA and HPMC-AS in methanol were prepared.

2.2. Methods

Viscosity, surface tension and density of the solvent/solutions were measured [22]. Viscosity measurements were performed on a Brookfield DV-III+ Rheometer (Massachusetts, USA) using spindle CPA-40z at different angular speeds. All the examined formulations except the solutions with HPMC-AS showed a Newtonian behavior; at an angular speed of 30 rpm, the HPMC-AS solutions showed pseudoelastic behavior. Surface tension was measured using a Surface Tensiometer (Fisher Scientific, PA, USA). All the measurements were performed at room temperature (~23 °C), the results of which are presented in Table 1.

Full cone sprays were produced with an external mixing two-fluid nozzle with liquid orifice diameter, d_L, of 0.5 mm. This is the standard nozzle configuration used in a pilot-scale B-290 spray dryer (Buchi, Flawil, Switzerland) having a cap diameter of 1.5 mm (see Fig. 1(b)). A PHD 4400 Hpsi Programmable syringe pump (Harvard Apparatus, MA, USA) with a 50 ml syringe capacity was used to control the liquid flow rate. The liquid volumetric flow rate range was 30–80 ml/min and gas mass flow rate was varied from 0.288 to 0.864 g/s for these experiments. The entire studied cases with their associated operation conditions are listed in the Appendix.

High speed shadowgraph images were acquired using a Phantom V611 CMOS high speed camera, and the experimental set-up is shown in Fig. 1. An Intertek 500 W floodlight was used as the illumination source. Since the droplets were translucent, only the edge of the droplets were darkened within the images because of scattering and refraction that occurred at the air-droplet interface. The acquisition frame rate was 49 kHz, leading to an exposure time of 20 μs and pixel dimensions of 352 (high) × 256 (wide). The projected spatial resolution of the images was 15 pixels/mm. Although this resolution sufficiently resolves the droplets for this study, other experiments may need to resolve smaller droplet sizes. In this case higher resolution images can be acquired by utilizing a different optical system. However, the processing technique described below can still be used.

A multipass algorithm was developed in MATLAB to identify droplets prior to vector processing. The algorithm utilized a dilation operation to approximate the background of each image by spatially enlarging the background which was subsequently subtracted from the original image to give only the droplets. A threshold was then set to identify the droplets. The hydraulic diameter of the droplets was obtained from a count of the pixels inside the binarized droplets, i.e. the area of the droplets, divided by the inscribed perimeter of the droplets. Subsequently, the area was multiplied by four and divided by the perimeter to obtain droplet diameters.

The raw images were multiplied by the binarized images as inputs into the PIV software to provide a sufficient computed correlation map. Velocity vectors were calculated using LaVision Davis 8.3 utilizing the multipass cross correlation algorithm which successively worked from 64 × 64 down to 16 × 16 pixel interrogation window sizes. Therefore, the vector resolution was 1.07 mm for the full velocity field. The PTV algorithm was also used to determine individual droplet velocities, leading to single velocity vectors for each droplet.

Table 1
Physical properties of the liquid solutions.

Property	DI water	Pure methanol	5%PVPVA-methnaol	5%HPMCAS-methanol
Density (kg/m^3)	999	792	793	793
Surface tension (N/m)	0.072	0.0227	0.0228	0.0228
Viscosity (mPa·s)	1.05	0.6	1.66	9.35