A High-throughput Electrospray Nozzle for Nanoparticle Production

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Introduction

• Electrospray, or electrohydrodynamic atomization, operated in the stable cone-jet mode (right figure), produces nano- to micron-scale particles in a narrow size distribution. In electrospray, particles are generated in a single step under ambient temperature and pressure. Chemical or biological properties of the particles are preserved without degradation due to heat or mechanical stresses.

• The scaling challenge is to overcome the 0.6-3 mg/h particle output limit that a single capillary nozzle produces. Traditional means have typically involved increasing the number of capillaries into an array (e.g., see Deng et al.[1]). While logical, translating a simple array of capillary nozzles into a commercially scalable system presents formidable fabrication and operating hurdles. This called for a radically different approach. Nanocopoeia accomplished this by modifying the nozzle design to allow higher flow rate while maintaining the same particle output.

Objectives

• Design, fabricate, and evaluate a novel, multiple cone-jet high throughput electrospray nozzle for producing nanoscale drug formulations.

• Integrate multiple high throughput nozzles in a prototype commercial scale modular electrospray system and demonstrate robust performance.

• Demonstrate the capability of controlling both particle size and morphology using the modular electrospray system with high throughput nozzle.

Nanocopoeia’s Technology

Nanocopoeia is a drug delivery company providing nano-enabled particle design and API formulation services to the pharmaceutical industry. Our patented ElectroNanospray™ (ENS) process is a non-destructive process which produces homogenous nanoparticles in a unique one-step continuous process at ambient temperature and pressure. The ENS process leverages the advantages of electrospray, while increasing the throughput approximately 200 times by using temperature and pressure. The ENS process leverages the advantages of homogenous nanoparticles in a unique one

Nozzle Design

Building upon a design by D. Chen[2], Nanocopoeia designed a proprietary high throughput nozzle that eliminates the capillary structure as the key functional unit. Instead, an open-channel architecture is used. Spray fluid is delivered from a single feed source to a smooth-surfaced open channel, which carries the fluid to the spray region as a sheet of fluid. The spray region consists of a series of projections. A spray plume emits from each of the surface projections, which serve as the functional “nozzles”. The throughput can be further improved by increasing the number of nozzlettes per nozzle.

System Integration with High Throughput Nozzle

The main functional components of the platform, including particle generation system, particle capture system, environmental system, monitoring and control system, etc., are designed in modules to facilitate rapid changes. Spray capacity was increased by mounting different numbers of nozzles into the platform. Figures on the right show four and eight D-24 nozzles in linear arrays, with the unique spray pattern from each nozzle. Our standard working platform contains eight D-24 nozzles, with a throughput of over 0.5 grams of active pharmaceutical ingredient (API) per hour (assuming a 1% API concentration of the spray solution).

Results - Control of Particle Size (Cont.)

Even though our D-series nozzle forms spray from a liquid film instead of a liquid filament like most of other electrospray nozzles, the size distribution of particles produced by these two different nozzles are similar. Figure on the right shows particle size distribution from real-time sampling from particle stream using scanning mobility particle size. The narrow distribution, together with SEM images, demonstrates the capability of our D-nozzle in generating particles. The most significant difference between the D-series nozzle and a traditional single capillary nozzle is that the throughput of the D-series nozzle is increased over 10 to 20 times.

Results - Control of Particle Morphology

Kollidon® was used to study the effect of molecular weight (Mw) and type of solvent on particle morphology. Three samples which were listed in the following table were compared for their morphology.

Materials. Model drugs were griseofulvin (GF) and iraconazole (ITZ), both selected for their poor water solubility. Polymers included polyvinylpyrrolidone (PVP, Kollidon®) and polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft co-polymer (Soluplus®, SP). Different solvents, including ethanol, methanol, ethanol/acetone mixture, and methanol/tetrahydrofuran (THF) mixture were used to prepare feed solutions at solid concentrations ranging from 1% to 10% (w/v). All spray operations were conducted at ambient conditions. Solution feed flow rates per nozzle were controlled by syringe pumps. An electric field was applied to achieve stable cone-jet operation on each nozzle. A stainless steel plate was placed at 2° to 5° below the nozzle to collect particles.

Results - Control of Particle Size

The size of particles generated by an electrospray process is controlled by the properties of the spray solution and critical machine operation parameters. SEM images below show monodisperse spherical particles of various sizes.

Conclusions

• ElectroNanospray™ is a flexible, low-cost, single-step spray process that produces nanoparticles in a narrow, targeted-size distribution.

• Our revolutionary nozzle design enables the scale-up capability of electrospray technology while leveraging the advantages of traditional capillary nozzles.

• The process is capable of controlling particle size and morphology.

• The modular equipment design allows for easy entry at R&D scale moving to pilot and full scale production.

References

