Spray-Drying of Proteins for Pulmonary Delivery

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Purpose: Developing and applying theoretical and experimental tools to control and optimize product performance of protein particles produced by a spray-drying process for pulmonary delivery,

Methods: Particles are produced with custom spray-drying hardware, using an air-assist atomizer for droplet production and a cyclone collection system. Atomizer performance is measured with a Phase-Doppler-Particle-Analyzer. Temperature and flow fields in the spray-dryers are calculated using a CFD model. A numerical model of the droplet evaporation process predicts the internal distribution of components during the lifetime of the droplet. The particle formation process is studied experimentally on monodisperse droplets, which are evaporated in an idealized, well-controlled environment. A custom-built, high-sensitivity Raman spectrograph is used to characterize solid state and protein conformation in the final dry particles.

Results: Air-assist atomizers can be used to produce droplets with a mean droplet diameter < 10 μm, which allows maintaining a small, commercially attractive scale even for the production of large quantities of powder. During the drying process proteins are protected from overheating by the hot gas via evaporative cooling. Theoretical and experimental results on the evaporation and particle formation process are in good agreement, showing the process has time constants on the order of milliseconds and the internal distribution of components is controlled by diffusion. This information can be used to control particle parameters such as particle density by adjusting the processing conditions. All polymorphs and the amorphous fraction of mannitol in protein formulations were discriminated and determined semi-quantitatively by dispersive Raman spectroscopy.

Conclusions: The results show that significant product improvements can be achieved by appropriate control of the spray drying process based on thorough understanding of the underlying physicochemical processes.