Introduction

Inhalable microparticles can be designed and engineered to enhance properties such as general morphology, dispersibility, dosage uniformity, and chemical or physical stability. Large-scale empirical studies can be minimized by employing process and numerical models to effectively design microparticles [1]. To this end, a monodisperse droplet chain in combination with a numerical model was developed to determine the effects of process parameters of co-solvent systems over a droplet’s drying kinetics and on the morphology of the final dried microparticles. Refer to the poster titled “Interaction of Evaporating Multicomponent Microdroplets with Humid Environments” for more information on the numerical model used in this study [2].

Droplet Chain

The Droplet Chain is a set of monodisperse droplets being injected into a laminar drying gas.

The drying behavior of the falling droplets was studied using a camera, a high magnification lens and a collimated light source.

Two thermocouples at the inlet and outlet of the flow tube and a hygrometer allowed monitoring of the temperature and humidity of the drying gas.

The monodisperse dried particles can be collected at the end of the flow tube on aluminum SEM stubs for further microscopy and spectroscopy analysis.

Experiments were conducted at various ratios of ethanol/water mixtures with leucine as the excipient, where only 3 ml of solution was required per experiment with a production rate of about 50 µg/hr solid particles.

Advantages:

- Good for fast evaporation rates
- Can collect solid particles
- Minimal amount of sample needed

Results and Discussions

The drying kinetics of three different compositions of water/ethanol mixtures evaporating in dry air at 21 °C are shown here.

The droplet size histories for these cases are shown below. The experimental data show great agreement with the results of the numerical model.

The following can be inferred from these figures:

- The evaporation rates increase by increasing the ethanol content.
- There is a change in evaporation rate during the drying for the 50% water:50% ethanol case.
- At 30% water:70% ethanol, azeotropic behavior is observed at room temperature and there is no sensible change in the evaporation rates.

A monodisperse droplet chain can be used to measure evaporation rates of co-solvent systems for a variety of drying gas parameters to assist formulation and process development of inhalable pharmaceutical particles.

Monodisperse microparticles with the same morphology can be collected for microscopy and spectroscopy analysis.

This approach uses minimal sample quantities suitable for assaying formulations with expensive actives early in development.

This technique combined with the in silico model has the potential to lower risk and reduce costs in early development of inhalable pharmaceuticals.

References