Surface Properties Are a Major Factor in Determining the Dispersibility of Protein Dry Powders for Inhalation

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Purpose. To demonstrate the effects of surface properties on the dispersibility of dry powder protein formulations intended for inhalation.

Methods. The surface activity of proteins in solutions was characterized using the Wilhemy plate method. Formulations were prepared by spray drying 1% w/w solutions containing 20 to 95% of trehalose and either hemoglobin (62kDa) or myoglobin(17kDa). Morphology was evaluated from scanning electron microscopy (SEM). The specific surface area was measured using N_2 BET adsorption isotherm. The true density of the powder was measured with a helium pycnometer. The surface composition was assessed using X-ray photon spectroscopy (XPS). The surface energetics were determined using inverse gas chromatography (IGC). The aerosol performance was measured in terms of the fine particle mass (FPM) less than 3μm and emitted dose (ED).

Results. Hemoglobin and myogobin as 0.5% solutions reduced the surface tension of bulk water from 72 to 48 dyne/cm for hemoglobin and 54 dyne/cm for myoglobin. Trehalose was not found to reduce surface tension. The particles produced by spray drying were enriched with protein at the surface as determined by XPS. Formulations containing hemoglobin yielded wrinkled particles with a lower bulk density whereas formulations containing myoglobin yielded smooth spherical particles with large invaginations and a higher bulk density. The aerosol performance (FPM) of the powders from both proteins ranged from 39% to 56%. The dispersive component of surface engery (γ_s^D) determined from the nonpolar probes had a rough correlation with the powder aerosol performance.

Conclusion. During spray drying, protein and trehalose compete for the air-water interface according to their surface activities, diffusion constant based on their molecular weight, and solubility. Although no one factor alone determines the dispersibility of dry powders, control of the surface composition stands out as an important design parameter.