

Amorphous Pullulan Trehalose Microparticle Platform for Respiratory Delivery

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Spray drying consists of liquid atomization into droplets in a high flow of hot drying gas to evaporate the solvent and generate solid microparticles from the solutes. Relative to liquid dosage forms, solid dosage forms of spray dried powder tend to have improved thermal stability and lower storage space requirements, potentially allowing for widespread distribution to developing countries without cold chain infrastructure. Recently, it has been demonstrated that use of pullulan and trehalose as excipients outperformed use of leucine and trehalose for stabilizing *Campylobacter* bacteriophage in spray dried powder. Here, spray drying is used to generate inhalable pullulan trehalose powder that is characterized in terms of manufacturability, physical stability, device compatibility, and aerosol performance. Reasonable spray drying yield and powder flowability demonstrate the manufacturability. Short-term physical stability was evident as the powder maintained its amorphous phase during ambient temperature storage in a dry box and 40°C storage in pressurized metered-dose inhaler canisters containing commercial propellants HFA 134a and HFA 227, and subsequent actuation. The powder was theoretically predicted and experimentally supported to have a higher glass transition temperature near the surface, where biologics are expected to reside, than in the interior. Accurate predictions of particle diameter could be made using a newly developed particle formation model. The powder had suitable aerosol performance from a commercial dry powder inhaler as demonstrated by high dispersibility, optimal size for inhalation, and adequate total lung dose, exceeding many commercial inhalation devices. The non-reducing sugar-only and fully amorphous pullulan trehalose platform thus appears promising for respiratory delivery.