Optimizing Excipient Formulation and Spray Freeze Drying Conditions to produce Nanoparticulate Aerosols with Good Morphology and Aqueous Re-dispersibility

Poly-caprolactone (PCL) nanoparticles loaded with antibiotics can be inhaled to treat infections of the respiratory tract, like tuberculosis. These nanoparticles must first aggregate to form nano-aggregates before delivery into the respiratory tract. The aggregates must have an aerodynamic diamemter of approximately 2-4μm and must have high re-dispersibility in aqueous media. These characteristics depend largely on the formulation of excipients used to consolidate the nanoparticles to form the nano-aggregates. Excipients used in this study are mannitol, leucine, PVA, PEG, lactose, trehalose and pluronic. The excipients are mixed with PCL nanoparticles in various ratios to form a feed solution, which is then spray-freeze dried to obtain dry-powder nano-aggregates. Lactose and trehalose aggregates are unstable as they absorb moisture and collapse easily. PEG has poor redispersibility while pluronic has an aerodynamic size of greater than 4μm. PVA, leucine and mannitol are then used in subsequent runs in various ratios to determine the effect of these 3 excipients on the effective density, dg, da and aqueous re-dispersibility of the nano-aggregates produced. The most favourable ratio is the PCL:mannitol:leucine ratio of 1:6:1 at total solid concentration of 5.5% w/v and atomization flow rate of 443L/h.