202d Preparing Porous Polymeric Particles by Localized Solvent Implosion for Pulmonary Drug Delivery Applications

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The pulmonary system has gained increasing interest as a convenient and non-invasive route for drug delivery to the systemic circulation. The lungs have served as a targeted organ for the treatment of respiratory diseases, such as asthma and cystic fibrosis, all of which serve to treat local conditions in the lung tissue. Systemic applications (formulations for non-respiratory complications) hold enormous potential, as the lungs provide a vast surface area (100 - 140 m2) for drug absorption along with a rich blood supply. However the success of systemic pulmonary drug delivery relies on the particles ability to reach the deep lungs. Particles capable of achieving this typically have diameters ranging from 2 - 5 μ m.

Aerosol efficiency can be enhanced by the fabrication of highly porous particles with low mass densities. Additionally, by increasing their size (> 5 μ m), these large but light particles can be deposited more efficiently than smaller, nonporous particles. This can be attributed to two main factors - aerodynamic diameter and particle-particle interaction. Increasing the particle diameter reduces the van der Waals forces and decreasing the mass density, alters the particles aerodynamic diameter. Therefore, large, porous particles can behave like smaller particles in the 2 - 5 μ m range, by simple adjustment of their mass density. In coupling this delivery route with a controlled release polymeric carrier, the opportunity for prolonged and enhanced therapeutic delivery can be provided.

Poly (lactic) acid (PLA) has been thoroughly investigated and established as an effective drug carrier, with the ability to provide a tunable release profile by modifications in the polymer molecular weight. However, its hydrophobic surface can lead to rapid opsonization and clearance by alveolar phagocytic cells. Incorporating, the hydrophilic polyethylene glycol (PEG) into the polymer backbone will provide "stealth" properties and render the particles less susceptible to immediate phagocytosis.

Here we present research on techniques to fabricate polymeric particles that are made porous by inducing localised solvent-implosion. Copolymers of PLA-PEG with varying molecular weights are synthesized by ring-opening polymerization in the presence of stannous octanoate [Sn(Oct)2]. The effects of solvent/cosolvent ratios, temperature and polymer molecular weight on particle morphology, size and density are studied. Surface characterization is performed using scanning electron microspoy (SEM) and specific surface area is determined by BET surface area analysis. Surface charge and size distribution is measured by Zetasizer. Future work will evaluate loading efficiency, protein release, in vitro degradation, and respirable fraction by cascade impaction.