Amgen Seminar Series in Chemical Engineering

in

Cherry Auditorium, Kirk Hall, 1 PM

Presents on October 3, 2013

Inhalable PEGylated Phospholipid Lipospheres Containing Paclitaxel for Targeted Pulmonary Delivery for Lung Cancer Applications

By

Professor Samantha A. Meenach
Department of Chemical Engineering
University of Rhode Island

Despite the significant advances in the treatment of lung cancer, it is a disease that still signifies poor prognosis due to the challenges in implementation of treatment. Targeted pulmonary inhalation drug delivery offers many advantages for lung cancer patients in comparison to conventional systemic chemotherapy. These include the potential to deliver local therapeutically effective concentrations of drug directly to the lung, minimized side effects due to limited systemic delivery, and ease of use for the patient. Inhalable dry powder formulations of nanoparticles and microparticles (lipospheres) containing a chemotherapeutic are advantageous in their ability to deliver drug deep in the lung via optimally sized particles, higher local drug dose delivery, and long-term storage capability. In this work, novel advanced spray-dried inhalable PEGylated phospholipid liposphere powders containing the chemotherapeutic paclitaxel were successfully designed and produced via dilute organic solution advanced spray drying under various conditions. Fixed ratios of dipalmatoylphosphatidylcholine (DPPC) and dipalmatoylphosphatidylethanolamine poly(ethylene glycol) (DPPE-PEG) at three different polymeric chain lengths were combined with various ratios of paclitaxel in a dilute methanol solution. Upon optimization of the spray drying conditions (e.g. pump rate), the physicochemical characterization of the particles was completed. Scanning electron microscopy (SEM) images showed the spherical particle morphology of the inhalable particles. The size of the particles was statistically analyzed using these images SigmaScan software, and these particles were determined to be 600 nm – 1.2 μm in diameter, which is optimal for efficient targeting of the deep lung alveolar and small airway regions for enhanced local deposition. Differential scanning calorimetry (DSC) and X-ray powder diffraction (XRPD) were performed to analyze solid-state transitions and long-range molecular order, respectively, and allowed for the confirmation of the presence of phospholipid bilayers and/or paclitaxel and their phase transition behavior. The water content of the particles was very low as quantified analytically via Karl Fisher titration. The composition of the particles was confirmed using attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy. Confocal Raman microspectroscopy was employed in chemical imaging to assess particle composition and miscibility. The amount of paclitaxel loaded into the particles was analyzed via high performance liquid chromatography (HPLC), and their aerosol performance was evaluated using the Next Generation Impactor (NGI) and an approved dry powder inhaler (DPI) device for human use to determine the emitted dose, respirable dose, fine particle fraction and mass median aerodynamic diameter. Overall, these results demonstrate this novel therapeutic nanomedicine platform as one capable of effectively delivering paclitaxel directly to the lung in high local concentration for the treatment of lung cancer.

This series at the University of Rhode Island is made possible through the generosity of Amgen, West Greenwich, R.I.

Refreshments provided by the Joseph Estrin Endowment.