297b Dry Powder Aerosols for Multi-Drug Resistant Tuberculosis (Mdr-Tb) Treatment

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Multi-drug resistant TB (MDR-TB) is emerging as a significant public health threat, creating an unmet medical need that requires the development of new treatment approaches. To begin addressing this need, we are developing new dry powder aerosols for the direct, topical delivery of antibiotics to infected lungs. Our primary goal is to target high drug doses to the site of primary infection for rapid sterilization of the lung mucosa and reduction in the duration of MDR-TB therapy. We have designed dry powder aerosols containing 50-80% of an injectable hydrophilic TB drug molecule, that exhibit similar physical and aerosolization properties. Aerosols with geometric diameters ranging from 2-10 μm and aerodynamic diameters in the 5-6 μm range were formed by spray drying. Optimization of processing parameters increased powder yields up to 60% prior to large batch scale-up. The aerosols show excellent storage capacity at refrigerated, room temperature, and accelerated (40°C) conditions, with both the chemical and physical properties remaining stable for up to 3 months of storage. A pharmacokinetic (PK) study is now underway in a guinea pig model to evaluate the bioavailability of the drug delivered via the lung, compared to injection. We expect this work to lead to a drug formulation that will be further tested in toxicology studies, in support of future clinical trials. This approach represents a new paradigm for treating and limiting the spread of respiratory infectious diseases such as TB, severe acute respiratory syndrome (SARS), influenza, and small pox.