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Dry powder aerosols based on mucus-penetrating nanocomposite microparticles for pulmonary antibiotics delivery

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Pulmonary antibiotic delivery is increasingly recommended as maintenance therapy to prolong the interval between pulmonary exacerbations and to slow the progression of lung disease in cystic fibrosis (CF) patients with chronic *Pseudomonas aeruginosa* infection due to its capability to achieve high drug concentrations at the site of infection and to minimize the risk of systemic toxicity and drug resistance. Currently used inhaled formations so far include the nebulization of drugs such as tobramycin which are regarded as inconvenient due to the long administration time and limited portability for chronic drug therapy in daily life of patients. Dry powder formulations of tobramycin have many advantages over nebulizers including faster delivery, easy use, portability, reduced need for cleaning and room temperature storage. However, minimal studies have been completed to control its drug release rate. Besides, the abnormally thick and sticky mucus in respiratory tract of CF patients impairs efficient mucus penetration and limits the range of antibiotics for inhalation.

To overcome the obstacles of pulmonary antibiotic delivery, we developed nanocomposite microparticles (nCμP) for pulmonary delivery of antibiotics in the form of dry powder aerosols. Our system consists of a microparticle carrier comprised of mannitol aimed on targeted delivery with drug-loaded nanoparticles entrapped in the carrier. The drug-loaded nanoparticles contain tobramycin as a model drug and the polymer acetalated dextran which provides a controlled drug release rate. The nanoparticle is coated by a Vitamin E poly (ethylene glycol) (PEG) 5000 layer which has been shown to improve the stability and mucus penetrating rate of nanoparticles. Upon synthesis of the tobramycin-loaded nanoparticles via nanoprecipitation, they were loaded into the mannitol carrier via advanced spray drying techniques. The resulting nCμP were then characterized for their shape, drug loading, thermodynamic stability, mucus-penetrating, and aerosol characteristics. Scanning electron microscopy and dynamic light scattering showed approximately 150 nm nanoparticles entrapped in 1 – 2 μm microparticles with smooth morphology. The system effectively entrapped 12% of the loaded nanoparticles and further studies are underway.

This nCμP system sheds a light on dry powder-based antibiotic delivery due to its features including targeted delivery, rapid mucus penetrating rate, and controlled drug release. It can be applied as a promising alternative of the nebulized antibiotic treatment by providing high efficacy of the delivery, more convenient administration, more flexible storage condition and lower risk of contamination in the device.

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