Smart hybrid drug delivery systems for the treatment of lung diseases

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Pulmonary drug delivery for the treatment of lung diseases offers high local drug concentration, rapid onset of therapeutic action, and better therapeutic control respect to other administration routes. On the other hand, nanomedicines are very promising in the local treatment of lung diseases, by designing proper carriers to allow mucus penetration, macrophagic escape/uptake and pulmonary surfactant corona inhibition. Size control and charge tuning, surface modification, co-delivery of mucolytic agents, and decoration with surface ligands could offer many opportunities to achieve the desired in vivo fate of the drug-loaded carriers. Polymeric nanoparticles or liposomes are the most promising nanomedicine thanks to versatile drug loading and controlled release, high cellular uptake, storage and biological stability of nanoparticles, and excellent biocompatibility and long circulation half-life of liposomes. Recently, to overcome some of their limitations, such as structural disintegration and drug leakage of liposomes, lipid-polymer hybrid nanoparticles (LPHNPs) were designed, which core-shell structures guarantees high structural integrity and biocompatibility, ability to load multiple therapeutic/imaging agents, targeting, and well-defined drug release kinetics. Moreover, with appropriate design, LPHNPs can be administered by the pulmonary route, optimizing the bioavailability, and reducing the undesirable systemic effects of carried drugs given by conventional dosage forms.

On the basis of several evidences supporting the use of inhibitors of the mammalian target of rapamycin (mTOR) complex, such as Rapamycin, as potential therapeutic intervention in almost chronic lung diseases, such as chronic obstructive pulmonary disease (COPD), and being mannose receptors highly expressed on alveolar macrophages, which are increased in number and defective in COPD, we have recently realized and characterized inhalable Nano into Micro (NiM) particles for the Rapamycin – based inhalation therapy, which showed suitable aerosolization properties, low interaction with mucus, and macrophage targeting of Rapamycin-loaded mannosylated LPHNPs.