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Spray dried hyaluronic acid nanoplexes conjugated with chitosan and its derivatives for the pulmonary administration as dry powder inhalers for tuberculosis

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The current therapies fail to deliver the drug to the alveolar macrophages in lungs, where causative agent resides, for the treatement of tuberculosis [1]. Hence, the ineffective drug delivery approaches lead to the drug toxicity and organ damage. Dry powder inahlers (DPIs) have recently shown promising results for the site specific drug delivery in the infectious diseases. Therefore, we developed nanoplexes based DPIs comprised of biocompatible polymer hyaluronic acid (HA) complexed with chitosan (CS), thiolated chitosan (TC) and mannsosylated chitosan (MC) individually to explore their affinity for alveolar macrophages to achieve higher drug deposition in deeper tissues of lungs. Nanoparticles were prepared by ionic gelation method [2] and later optimized by Design of Experiment (DoE), Box-Behnken design, prior to spray-drying to obtain nano-DPIs encapsulated with isoniazid. The size, morphology, physico-chemical properties, *in-vitro* release profile, *in-vitro* permeation, aerodynamic profile and i*n-silico* drug deposition of the nano-powders were promising. Furthermore, biocompatibility assay revealed the safety profile of nanoplexes. Moreover, spray drying enhanced the rheological properties of nano-powders. Altogether, DPIs highlighted promising results based on the preliminary fundamental outcomes with enhanced drug encapsulation efficiency and drug deposition profile.

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