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Inhalable Lipid-Coated-Chitosan Nano-Embedded Microdroplets of an Antifungal Drug for Deep Lung Delivery

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Abstract : Respiratory microbial infections being among the top leading cause of death worldwide are difficult to treat as the microbes reside deep inside the airways, where only a small fraction of drug can access after traditional oral or parenteral routes. As a result, high doses of drugs are required to maintain drug levels above minimum inhibitory concentrations (MIC) at the infection site, unfortunately leading to severe systemic side-effects. Therefore, delivering antimicrobials directly to the respiratory tract provides an attractive way out in such situations. In this context, current study embarks on the systematic development of lung lia pid-modified chitosan nanoparticles for inhalation of voriconazole. Following the principles of quality by design, the chitosan nanoparticles were prepared by ionic gelation method and further coated with major lung lipid by precipitation method. The factor screening studies were performed by fractional factorial design, followed by optimization of the nanoparticles by Box-Behnken Design. The optimized formulation has a particle size range of 170-180nm, PDI 0.3-0.4, zeta potential 14-17, entrapment efficiency 45-50% and drug loading of 3-5%. The presence of a lipid coating was confirmed by FESEM, FTIR, and X-RD. Furthermore, the nanoparticles were found to be safe upto 40µg/ml on A549 and Calu-3 cell lines. The quantitative and qualitative uptake studies also revealed the uptake of nanoparticles in lung epithelial cells. Moreover, the data from Spraytec and next-generation impactor studies confirmed the deposition of nanoparticles in lower airways. Also, the interaction of nanoparticles with DPPC monolayers signifies its biocompatibility with lungs. Overall, the study describes the methodology and potential of lipid-coated chitosan nanoparticles in futuristic inhalation nanomedicine for the management of pulmonary aspergillosis.

Keywords : dipalmitoylphosphatidylcholine, nebulization, DPPC monolayers, quality-by-design
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