Dry Powder Inhaler of Physically Improved Pulmospheres for Peptide Delivery

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Abstract

The aim of the present investigation was to develop and evaluate physically improved dry powder inhaler of peptide colistin sulfate (CS) using pulmosphere technology. CS can improve the infectious condition if given in the form of pulmospheres as Dry powder inhaler (DPI) dosage form. Fourier transform infrared spectroscopy (FTIR) had employed to study drug-excipient incompatibility. Analytical method was performed using UV spectrophotometer. DPI of CS pulmospheres was successfully prepared with CS (22.8 mg), poly (lactide-co-glycolide) acid (PLGA) (227.2 mg), sodium deoxycholate (1.5%w/v), mannitol (1%w/w) and magnesium stearate (0.028%w/w) by solvent emulsification followed by spray drying method and evaluated for particle size, percent drug entrapment, surface morphology, flow property, aerosol performance, *in-vitro* drug release study, antimicrobial study and stability study. Optimization of process parameter was done by Box behnken design (BBD) using Design Expert software. Drug and excipients were found to be compatible to each other which was confirmed by FTIR study. Optimization study of process parameter shows that batch prepared with inlet temperature 65°C, aspiratory rate 25 Nm^3/hr, feed flow rate 1 ml/min considered as optimum condition for spray drying. Particle size was found to be 3.67 ± 0.015 µm for optimized batch. Scanning Electron Microscopy (SEM) study indicates that the particles were found to be in spherical shape and porous in nature. Carr's index, hausners ratio and angle of repose were found to be 11.17 ± 0.67%, 1.13 ± 0.008 and 26.2 ± 0.155° respectively which show good flow property of pulmospheres. Percent drug entrapment and *in-vitro* drug

release were found to be 91.66 ± 0.4084% and 92.78 ± 0.44% respectively for optimized batch. A fine particle fraction (FPF), fine particle dose (FPD), Mass median aerodynamic diameter (MMAD) and Geometric standard deviation (GSD) were found to be 66.98%, 66.04%, 2.54 µm and 1.67 respectively for optimized batch. CS shows most promising antimicrobial activity and it is as effective as CS marketed formulation. Stability study shows DPI containing CS pulmospheres was stable at accelerated condition. The present study demonstrated that, a spray-dried powder is suitable for respiratory deposition and hold great potential for treating diseases that require direct lung delivery.

***Keywords*:** Colistin Sulfate; Cystic Fibrosis; Pulmospheres; Dry Powder Inhaler; Box Behnken Design; Spray Drying.