DEVELOPMENT OF POROUS HYALURONIC ACID BASED DRY POWDER INHALATION SYSTEM OF TOPOTECAN HYDROCHLORIDE USING SPRAY DRYING TECHNIQUE

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Abstract:

The aim of the present investigation was to prepare and evaluate porous hyaluronic acid based dry powder inhalation system of topotecan HCl using spray drying technique. Topotecan Hydrochloride can improve the cancerous condition if given in the form of porous hyaluronic acid microparticles as dry powder. Porous Hyaluronic Acid based dry powder inhalation system of topotecan hydrochloride was evaluated for particle size, percent drug entrapment, flow property, zeta potential, surface morphology, aerosol performance, *in-vitro* drug release study and stability study. Optimization of formulation parameter and process parameter were done by 3^2 full factorial design and Box Behnken Design (BBD) using Design Expert software. FTIR study shows that neither drug decomposition nor drug-excipients and excipient-excipient interactions occurred in the formulation. Porous Hyaluronic Acid based dry powder inhalation system of topotecan hydrochloride was successfully prepared using Topotecan hydrochloride(0.5%w/w), Hyaluronic acid (1%w/w), Polystyrene latex (4%w/w), Respitose SV001 (89.95%w/w), Magnesium stearate (0.028%w/w). Optimization study of process parameter shows that batch prepared with inlet temperature 100°C, aspiratory rate 50 Nm^3/hr, feed flow rate 2 ml/min considered as optimum condition for spray drying. Particle size, zeta potential, and percent drug entrapment were found to be 2.41 µm, -57.5 mV and 84.57 ± 0.40%. Scanning electron microscopy study indicates that the particles were found to be in spherical shape with porous structure. Carr's index, hausner's ratio and angle of repose were

found to be 13.71 ± 0.24%, 1.15 ± 0.01 and 27.98 ± 0.68° respectively which show good flow property of porous dry powder. I*n-vitro* drug release of optimized batch was found to be 97.28 ± 1.01 % up to 24 hr. A fine particle fraction (FPF), fine particle dose (FPD), Geometric standard deviation (GSD) and mass median aerodynamic diameter (MMAD) were found to be 86.55%, 16.73 mg, 1.68 and 2.95 µm respectively for optimized batch. Stability study shows dry powder containing topotecan hydrochloride porous dry powder was stable at accelerated condition. The present study demonstrated that, a porous hyaluronic acid based dry powder inhalation system is suitable for respiratory deposition and hold great potential for deep lung targeting.

***Keywords*:** Cancer Targeting; Hyaluronic Acid; Topotecan Hydrocholride; Lung Cancer; Porous microparticles; Dry Powder Inhaler; Box Behnken Design; Spray Drying.