Formulation and optimization of sildenafil citrate-loaded PLGA large porous microparticles using spray freeze-drying technique: A factorial design and in-vivo pharmacokinetic study

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Abstract

The oral administration of sildenafil citrate (SC) for the treatment of pulmonary arterial hypertension is associated with several drawbacks. The study aimed to design and formulate SC-loaded inhalable poly (lactic-co-glycolic acid) [PLGA] large porous microparticles (LPMs) for pulmonary delivery. A factorial design was used to study the effect of the composition of LPMs on physicochemical properties. The study also evaluated the effect of glucose and L-leucine concentration on the formulation. The developed LPMs demonstrated an acceptable yield% (≤48%), large geometric particle size (>5µm) with a spherical and porous surface, and sustained drug release (up to 48 h). Increasing the concentration of poly (ethyleneimine) from 0.5% to 1% in SC-loaded LPMs led to an increase in entrapment efficiency from ~3.02% to ~94.48%. The optimum LPMs showed adequate aerodynamic properties with a 97.68 ± 1.07% recovery, 25.33 ± 3.32% fine particle fraction, and low cytotoxicity. Intratracheal administration of LPMs demonstrated significantly higher lung deposition, systemic bioavailability, and longer retention time ($p < 0.05$) compared to orally administered Viagra® tablets. The study concluded that SC-loaded LPMs could provide better therapeutic efficacy, reduced dosing frequency, and enhanced patient compliance.

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