Formulating Antiviral Drug Combinations Using Spray Drying to Overcome Bioavailability Barriers

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Abstract

Lopinavir and ritonavir are co-administered antiretroviral agents widely used in the treatment of HIV-1 infection. Both are characterized by poor aqueous solubility and limited oral bioavailability, placing them within the Biopharmaceutics Classification System (BCS) Class II. While ritonavir serves primarily as a pharmacokinetic enhancer by inhibiting cytochrome P450 3A4 (CYP3A4), both compounds are susceptible to extensive first-pass metabolism and efflux via P-glycoprotein, necessitating advanced formulation strategies to ensure therapeutic efficacy. This research explores the development of a spray-dried amorphous solid dispersion (ASD) system to improve the solubility, dissolution rate, and bioavailability of lopinavir and ritonavir in a fixed-dose combination.

A series of spray-dried formulations were prepared using hydrophilic polymers, along with surfactants and stabilizers to enhance drug-polymer miscibility and prevent recrystallization. Physicochemical characterization was performed using differential scanning calorimetry (DSC), X-ray powder diffraction (XRPD), Fourier-transform infrared spectroscopy (FTIR), and scanning electron microscopy (SEM) to confirm the amorphous nature of the dispersions and evaluate molecular interactions. In vitro dissolution studies demonstrated a marked improvement in dissolution kinetics compared to crystalline and commercial forms.

Keywords

Lopinavir, Ritonavir, Spray drying, Solubility, Antiviral agents.