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Enhanced Solubility and Dissolution of Cilnidipine Nanocrystals for Oral Administration: Fabrication and Evaluation

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Extended Abstract

Objectives:

The current study aimed to fabricate and characterize cilnidipine (CLN) nanocrystals (NCs) to enhance CLN oral bioavailability by enhancing its dissolution rate and solubility. Being a BCS class II drug, CLN has dissolution and solubility-limited oral absorption [1, 2]. Therefore, the objective of this project was to utilize sonoprecipitation technique to produce CLN NCs capable of enhancing CLN dissolution rate and solubility.

Keywords:

Cilnidipine (CLN); Nanocrystals (NCs); Oral bioavailability improvement; Solubility enhancement; Sonoprecipitation.

Scope:

The CLN nanocrystal formulation was optimized by varying different formulation parameters including stabilizer (PVP K30), cryoprotectant (mannitol), and CLN concentrations. Moreover, different high-speed mixing and drug solution flow rates were investigated. The optimized formulation was evaluated for zeta potential, particle size, polydispersity index (PDI), morphology (SEM), crystallinity (XRD, DSC), and in vitro drug release and solubility.

Research Gaps:

While nanocrystallization has proven effective for other hydrophobic drugs [3, 4], limited studies exist on CLN NCs prepared specifically by sonoprecipitation. This study addresses this gap by exploring the sonoprecipitation method, a combination of antisolvent precipitation with high-speed homogenization and ultrasonication [5], known for its scalability and efficiency [6].

Methods:

Sonoprecipitation was used to prepare CLN NCs. Briefly, the organic phase (CLN dissolved in acetone) was added to the antisolvent phase (PVP K30 and mannitol dissolved in HPLC water) under high-speed homogenization (2200 rpm) at different organic phase flow rates (0.5 or 0.062 ml/min). The resulting suspension was centrifuged, and the solid was lyophilized [5]. The prepared NCs were characterized using various techniques: particle size and zeta potential were measured; morphology was examined via SEM; crystallinity was assessed by XRD and DSC; and in vitro drug release and saturation solubility were determined aided by UV-Vis spectroscopy.

Results and Discussion:

The sonoprecipitation method successfully produced CLN NCs with optimal formulation particle sizes ranging from 16.2 nm to 121.7 nm, depending on the formulation parameters. The smallest particle size (16.2 nm) was achieved with 0.25% w/v PVP K30, 40mg/ml drug concentration, and a flow rate of 0.062 ml/min. XRD analysis confirmed the crystalline nature of CLN in the NCs, although peak intensities were reduced, suggesting a decrease in crystallinity due to particle size reduction and the presence of PVP K30 [7]. DSC analysis showed a slight shift in the melting point of CLN in the NCs, indicating an interaction between CLN and PVP K30 [8]. FTIR analysis suggested hydrogen bond formation between the NH moiety of CLN and the hydroxyl and carbonyl groups of PVP K30 [9]. In vitro dissolution studies demonstrated a significant enhancement in CLN release from the NCs (95%) compared to bulk CLN (24%) and the physical mixture (50%). The saturation solubility of CLN in the NCs also increased threefold compared to bulk CLN. Therefore, the nanocrystallization significantly enhanced CLN's solubility and dissolution.

Conclusion:

In the work presented herein, CLN NCs were successfully prepared using the sonoprecipitation technique. The optimized formulation significantly enhanced CLN release and saturation solubility, holding great potential for improving CLN oral bioavailability and therapeutic efficacy. Such in vitro findings warrant further in vivo studies for confirmation.

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