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RESEARCH ARTICLE

Appraisal of Felodipine Nanocrystals for Solubility Enhancement and Pharmacodynamic Parameters on Cadmium Chloride Induced Hypertension in Rats

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Abstract: ***Aims:*** Felodipine (FDP), an antihypertensive drug possesses low water solubility and extensive first-pass metabolism leading to poor bioavailability. This impelled us to improve its solubility, bioavailability, and pharmacodynamic properties through the Nanocrystal (NC) approach.

Methods: FDP-NC were prepared with Poloxamer F125 (PXM) by the antisolvent precipitation method. The experimental setup aimed at fine-tuning polymer concentration, the proportion of antisolvent to solvent, and the duration of ultrasonication for NC formulation.

Results: Optimized formulation was characterized for particle size, solubility, and PDI. Particle reduction of 74.96 times was achieved with a 9X solubility enhancement as equated to pure FDP. The morphology of NC was found to be crystalline through scanning electron microscopy observation. The formation of the crystal lattice in FDP-NC was further substantiated by the XRD and DSC results. Lowering of the heat of fusion of FDP-NC is a clear indication of size reduction. The stability studies showed no substantial change in physical parameters of the FDP-NC as assessed by particle size, zeta potential, and drug content.

Conclusion: The crystalline nature and improved solubility of FDP-NC improve the dissolution profile and pharmacodynamic data. The stability study data ensure that FDP-NC can be safely stored at 25°C. It is revealed that FDP-NC had a better release profile and improved pharmacodynamic effects as evident from better control over heart rate than FDP.

Keywords: Antisolvent precipitation, cadmium chloride, felodipine, heart rate variability, heat of fusion, crystallinity.

1. INTRODUCTION

Nanocrystal (NC), technology is the brightest novel formulation method to enhance the saturation solubility and bioavailability (BA) of low aqueous solubility (BCS Class II) drugs and reducing irregularity during systemic exposure [1, 2].

Felodipine (FDP) is a calcium channel blocker mainly used to deal with hypertension and angina pain. FDP is some-what absorbed from the gastric mucosa, but has an adequate oral BA (15%) which is attributed to low solubility (19.17mg/L) and high first-pass metabolism. NC is an attempt to enhance the solubility of FDP. The reason for formulating NC is to reduce the first-pass metabolism, improve the dissolution profile and thus improve BA as a reduction in the size of FDP leads to a larger surface area [3]. An increase in solubility also affirms the irregular absorption of the drug and improves the bioavailability of drugs with a narrow absorption window [4-8].

The present investigation aims to prepare NC formulation. There are two techniques for the preparation of NC 'top-down' and 'bottom-up' technologies. Top-down includes media milling and HPH, while anti-solvent precipitation is a bottom-up technique. The top-down process requires an extended processing time and is also affected by the contamination of products due to erosion of milling beads [9].

2. MATERIALS AND METHODS

Felodipine gift samples were obtained from IPCA Pharmaceutical Ltd, India. PXM was purchased from Sigma Aldrich, Mumbai, India. Tween 80 was procured from SD Fine Chem. Ltd, Mumbai, India. Methanol,Formaldehyde, and Carboxymethyl cellulose were purchased from LOBA Chemie Pvt. Ltd, Mumbai, India. Chloroform and EDTA dipotassium salt were procured from SD Fine chemical Ltd, Mumbai, India. Distilled water used was obtained through quartz double distillation assembly Infusil India Pvt. Ltd, Bangalore, India.

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