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Original Research Article

Simvastatin-nicotinamide co-crystal: design, preparation and preliminary characterization

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Abstract

Purpose: *To improve the solubility of simvastatin (SV) by co-crystallization using nicotinamide (Nic) as co-crystal agent (co-former).*
Methods: *In silico molecular modeling of Nic counter to SV were investigated using Auto Dock 4.2. Co-crystal of Nic-SV was obtained by solvent evaporation (SE) using an equimolar ratio of Nic and SV. Co-crystal of SV-Nic was evaluated by scanning electron microscopy (SEM), saturated solubility, intrinsic dissolution, x-ray powder diffraction (XRPD), differential scanning calorimetric (DSC), infrared spectrophotometry (FT-IR), binary phase diagram, and for stability at 40 oC and relative humidity (RH) 75% in one month.*
Results: *In silico results showed that the interaction of Nic with SV took place through hydrogen bonding as the synthon agent. The solubility and intrinsic dissolution properties of the co-crystal improved significantly compared to pure SV. Characterization of the co-crystal SV: Nic (1: 1) by SEM, XRPD, DSC, FT-IR, and binary phase diagram indicate the formation of a new solid phase that was different from either SV or Nic. Furthermore, the cocrystal of SV: Nic remained stable for one month.*
Conclusion: *Co-crystallization using Nic has the potential to enhance drug solubility, intrinsic dissolution, and the stability of solution.*

Keywords: *Simvastatin, Co-crystal, Nicotinamide, Solubility, Dissolution*

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INTRODUCTION

The effectiveness of drug delivery to a target organ or system in the body depends on the capability to produce suitable formulation of the drug. Deficiencies in the possessions of the solid pharmaceutical ingredient, such as solubility and bioavailability, have proved to be a major stumbling block in the successful manufacturing of medicines. The bioavailability of an oral preparation depends on its solubility which determines how quickly it is absorbed in the gastrointestinal tract and its permeability over cell membranes [1]. In pharmaceutical practice, many drugs show poor solubility in water, leading to problems with regard to dissolution and bioavailability [2]. Several drugs, including BCS class II and intravenous (IV) drugs like simvastatin (SV), have problems with solubility.

SV is an inhibitor of A (HMG-CoA) reductase; it belongs to the class of statins. Statins are the drugs of choice for the management of hypercholesterolemia due to their recognized