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A Novel of Cocrystalization to Improve Solubility and Dissolution rate of Simvastatin

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Abstract : Simvastatin (SV) is the drug of choice for hypercholesterolemia, which belong to the BCS class II as very troubled with drug solubility. We report the novelty of increased solubility and dissolution rate of simvastatin with cocrystallization methods, using Malic acid (MA) as coformer with molar ratios (1:1). Simulation modeling of molecules against MA and SV has performed with in silico using auto dock 4.2. Synthesis of cocrystal has done with Liquid-Assisted Grinding (LAG). Cocrystal formed subsequently confirmed by tests of saturated solubility, invitro dissolution, Scanning electron microscope (SEM), Powder X-ray Diffraction (PXRD), Fourier Transformations Infrared Spectrophotometry (FTIR), and Differential Scanning Calorimetry (DSC). Insilico evaluation against the interactions between the MA and SV has demonstrated the existence of hydrogen bonding interactions. Tests of saturated solubility and invitro dissolution of Cocrystal SV: MA (1:1) was indicating an increase in the solubility and dissolution rate of the better as a result of the formation of cocrystal SV: MA (1:1). All characterization against cocrystal SV: MA (1:1) has indicated the formation of a new solid crystalline phase, which differs with SV, MA, and physical mixtures (SV: MA). Cocrystalization has can be used as a method to improve the solubility and dissolution rate of SV.

Keywords : cocrystallization, Simvastatin, Solubility, dissolution.

Introduction

Drugs that quite soluble in water will demonstrate good oral absorption and show a good biological availability. Approximately 40% of drugs on the market showed less soluble in water, this causes the drug to be absorbed more slowly so that the levels of which enter the blood lower than should be[1]. In the pharmaceutical industry, the poor nature of biopharmaceutical includes toxicity and lack of efficacy of the drug is 1% of the major cases of a drug on the market[2]. An effectiveness of drug therapy is highly dependent on the levels of a drug in the blood, thus, the most important nature biopharmaceutical drugs have solubility properties[3]. Approximately 70% of drugs nominee had problems with solubility, so this is a challenge in the pharmaceutical manufacturing to develop drugs and preparations for better solubility especially for oral preparations [4]. Based on the solubility and permeability properties in the biopharmaceutical classification system (BCS) is classified into four classes of drugs, including drugs with low solubility is class II, like SV. SV is the drug of choice of