Gozali et al., IJPSR, 2016; Vol. 7(4): 1450-1455. E-ISSN: 0975-8232; P-ISSN: 2320-5148

IJPSR (2016), Vol. 7, Issue 4 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 09 November, 2015; received in revised form, 12 December, 2015; accepted, 05 February, 2016; published 01 April, 2016

VIRTUAL SCREENING OF COFORMERS FOR ATORVASTATIN Co-CRYSTALLIZATION AND THE CHARACTERIZATIONS OF THE Co-CRYSTALS

D. Gozali [1], S. Megantara [1], J. Levita *[1], H.H. Bahti [2], S.N. Soewandhi [3] and M. Abdassah[1]

Faculty of Pharmacy [1], Universitas Padjadjaran, Jl. Raya Bandung-Sumedang km. 21 Jatinangor Sumedang, Indonesia
Department of Chemistry [2], Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran Jl. Raya Bandung-Sumedang km.21 Jatinangor Sumedang, Indonesi
School of Pharmacy [3], Bandung Institute of Technology, Jl. Ganesha 10 Bandung

Key words:

Aspartame, Cholesterol, co-crystallization, HMG CoA-reductase, Hypercholesterolemia, Statin

Correspondence to Author:
Jutti Levita

Department of Chemistry , Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jl. Raya Bandung-Sumedang km.21 Jatinangor Sumedang, Indonesia

E-mail: jutti.levita@unpad.ac.id

ABSTRACT: Atorvastatin calcium (ATC) is very slightly soluble in water and it is classified under BCS class II drugs. A widely used method to enhance the solubility of drugs is co-crystallization. In this work, we screened six co-formers for ATC by employing molecular docking method. The work was continued by co-crystallization process using slurry method, solubility assay of the mixtures using HPLC, and characterization of the co-crystal by PXRD, DSC and SEM. Based on molecular docking, the best co-former is aspartame (Ei = -4.70 kcal/mol). The docking result fits the solubility assay of the ATC-aspartame co-crystal (136.77% increasing of solubility compared to ATC). ATC-aspartame co-crystal shows better dissolution profile (91.62 % in 60 minutes) than ATC (73.54 % in 60 minutes). The characteristic peaks of ATC and aspartame were gone, whilst new peaks appeared after slurry process. The ATC-aspartame characterization by PXRD, DSC and SEM positively confirmed that the co-crystallization of ATC-aspartame using slurry method was successful.

INTRODUCTION: Atorvastatin (PubChem CID 60823), or its IUPAC name is (3R,5R)-7-[2-(4-fluorophenyl)-3-phenyl-4-(phenylcarbamoyl)-5-propan-2-ylpyrrol-1-yl]-3,5 dihydroxy heptanoic acid (**Fig.1**), is in a group of drugs called HMG-CoA reductase inhibitors. Atorvastatin calcium (ATC), a hemi-calcium salt, is very slightly soluble in water, phosphate buffers at pH 7.4, and acetonitrile, freely soluble in methanol.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.7(4).1450-55

Ar cle can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7 (4).1450-55

According to the Biopharmaceutical Classification System (BCS), ATC is classified under BCS class II drugs that exhibit poor aqueous solubility and high permeability. The intestinal permeability of atorvastatin is high at the physiologically intestinal pH (6–6.5). However, it is reported that the absolute bioavailability of atorvastatin is 12% after a 40 mg oral dose [1-3].

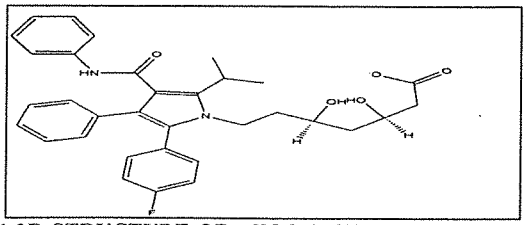

FIG.1 2D STRUCTURE OF ATORVASTATIN CHEMSPIDER ID 54809
(downloaded as *mol* format from www.chemspider.com)