Journal of Applied Pharmaceutical Science Vol. 5 (06), pp. 078-082, June, 2015
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2015.50613
ISSN 2231-3354

Virtual screening of co-formers for ketoprofen co-crystallization and the molecular properties of the co-crystal

S. Siswandi[1,2], Taofik Rusdiana[1], Jutti Levita[3*]

[1]Department of Pharmaceutics and Formulation Technology Faculty of Pharmacy, Universitas Padjadjaran Jl. Raya Bandung-Sumedang km.21 Jatinangor Sumedang, Indonesia. [2]Indonesian Airforce Pharmaceutical Institution Jl.Abdurachman Saleh, Lanud Husein Sastranegara, Bandung, Indonesia.
[3]Department of Pharmaceutical Analysis and Medicinal Chemistry Faculty of Pharmacy, Universitas Padjadjaran Jl. Raya Bandung-Sumedang km.21 Jatinangor Sumedang, Indonesia.

ARTICLE INFO

Article history:
Received on: 02/02/2015
Revised on: 23/02/2015
Accepted on: 17/03/2015
Available online: 27/06/2015

Key words:
Anti-inflammatory agent; co-crystal; co-former; ketoprofen; molecular docking; saccharin.

ABSTRACT

Ketoprofen or [2-(3-benzoylphenyl)propionic acid] is a nonsteroidal antiinflammatory and analgesic agent. The positive qualities of ketoprofen are based on optimal physicochemical and structural characteristics, its ability to penetrate into and accumulate in the inflammation centers and compatibility with other classes of drugs. This compound is practically insoluble in water, therefore as most of NSAID drugs, it is categorized as *Biopharmaceutics Classification System* (BCS) class II. A widely used to enhance the solubility of poorly water soluble drugs is co-crystallization. A co-crystal is a multi-component crystal which involves non-covalent interactions between API and its co-formers. In this work, we developed virtual screening of co-formers for ketoprofen by employing molecular docking method. AutoDock was used for docking. Parameters observed were type and energy (Ei) of interaction. The work was continued by co-crystallization process and solubility assay of the mixtures according to Higuchi and Connor method using UV spectrophotometer. Based on molecular docking, the best co-former is saccharin (Ei = -3.14 kcal/mol). The docking result fits the solubility assay of the ketoprofen-saccharin co-crystal (300.62 µg/mL in water or 256.54% increasing of solubility compared to ketoprofen). Ketoprofen co-crystal shows better curve (90.15 % in 60 minutes) than ketoprofen (78.87 % in 60 minutes). Co-crystallization of ketoprofen with saccharin increases the dissolution profile of ketoprofen.

INTRODUCTION

Ketoprofen (Fig.1) or [2-(3-benzoylphenyl)propionic acid] is a nonsteroidal antiinflammatory and analgesic agent. The positive qualities of ketoprofen are based on optimal physicochemical and structural characteristics, its ability to penetrate into and accumulate in the inflammation centers and compatibility with other classes of drugs (Khormosh, 2009). Ketoprofen is soluble in ethanol, chloroform, and ether. It is practically insoluble in water, therefore as most of NSAID drugs, this compound is categorized as *Biopharmaceutics Classification System* (BCS) class II, i.e. drugs with low solubility and high permeability character (Hussain, 2002). Various techniques have been widely used to enhance the solubility of poorly water soluble drugs; co-crystallization is one amongst them.

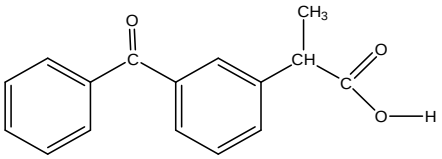

Fig.1 2D structure of ketoprofen ID 3693

A co-crystal is a multi-component crystal which all components are solid at room temperature in a stoichiometric ratio and it involves non-covalent interactions such as hydrogen bonds, van-der Waals bonds, ionic bonds in a crystal lattice (Shan, 2008; Patel, 2012). The selection of co-formers is based on their ability to form reversible or non-covalent interaction with the API.

* *Corresponding Author*
Jutti Levita, e-mail: jutti.levita@unpad.ac.id
Mobile: +628156043663, Office: +62227796200