UNIVERSITI TEKNOLOGI MARA

STUDY ON CO-CRYSTAL FORMATION OF IBUPROFEN AND OXALIC ACID VIA SLOW COOLING TECHNIQUE

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Thesis Submitted in Fulfilment
of The Requirements for The Degree of
Bachelor of Engineering (Hons) Chemical and Bioprocess

Faculty of Chemical Engineering

July 2017

ABSTRACT

Pharmaceutical co-crystals can improve the solubility, physicochemical properties as well as their chemical properties. In this study, the interaction between Active Pharmaceutical Ingredients (API) Ibuprofen (IBP) and oxalic acid (OXA) to crystallize into a newly formed drug is experimented viz slow cooling method with the cooling rate of 0.5°C/min by decreasing the temperature from 60°C to 20°C. The mol ratio of IBP:OXA ranging from 1:0.5 to 1:4.5 in both solvents, ethanol and propanol. However, co-crystal formation is limited to 1:2.5 to 1:4.5 in ethanol and 1:1.5 to 1:4.5 in propanol. IBP-OXA co-crystals are then analysed using optical microscopy, Fourier Transform Infrared Spectroscopy (FTIR), Powder X-Ray Diffractometer (PXRD) and Differential Spectrometer Calorimetry (DSC). Morphology obtained are long rod-shaped crystals. The PXRD analysis shows that the co-crystals produced are in impure state. The IR spectra and thermal analysis using FTIR and DSC proves the existence of co-crystals. This indicates that the cocrystallization of Ibuprofen and Oxalic Acid can be conducted by using slow cooling method to increase its bioavailability in the pharmaceutical industry.

ACKNOWLEDGEMENT

Firstly, all praises to Allah for giving me the opportunity to complete this study. I would like to say my utmost gratitude to everyone involved in this study especially to my parents for their unconditional love and understanding.

I would also like to thank my very kind supervisor, En. Muhamad Fitri bin Othman who has helped me with knowledge and skills throughout this study. Not forgotten to both Dr. Nornizar binti Anuar and Dr. Siti Nurul 'Ain binti Yusop who have also been so cooperative and helpful during to share problems and knowledge.

Apart from that, to all staff and lab assistants who have guided me and also to all my friends, thank you so much.

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CHAPTER 1

INTRODUCTION

1.1 Background Study

In the pharmaceutical industry, less than 1% of active pharmaceutical ingredients (API) are in the market because of its poor biopharmaceutical properties, as compared to its toxicity or its inefficiency (Aakeroy et al., 2007). The main issue which relates the biopharmaceutical properties is the solubility and it had been one of the challenges the pharmaceutical industry has to overcome (Blagden et al., 2007; Qiao et al., 2011). Hence, various methods have been used to manipulate the solid state of pharmaceutical materials on specific drug formulation problems. Among the techniques used in the pharmaceutical industry to improve the solubility and stability of problematic drugs is by crystallization, either into salts and hydrates (Chow et al., 2012). These days, there are a few drugs that have been studied like carbamazepine, itraconazole, piroxicam, norfloxacin, fluoxetin, caffein and others (Zhang et al., 2015). Since each of the APIs studied are different in its molecular structure and component, different results are expected. Co-crystals, as defined by Aakeröy and Salmon (2005) is structurally homogeneous crystalline materials containing two or more components present in definite stoichiometric amounts. Another definition of pharmaceutical co-crystal is a co-crystal which its constituent element is made up of as an Active Pharmaceutical Ingredient (API) and the coformers (Aakeroy et al., 2005)

Before any co-crystals are produced physically, the formation on the co-crystals is predicted. The Cambridge Structural Database (CSD) is used for the analysis on the existing crystals, which acts as the first step in co-crystal predictions. Technically, the CSD facilitates statistical analysis of packing motifs and thereby provides empirical information concerning similar functional groups and how they interact in molecular association, that is, which explains the supramolecular synthons formation (Vishweshar et al., 2005). Another explanation on co-crystal packing motifs as explained by Desiraju (1995), supramolecular synthons are the structural units within supramolecules in which synthetic operations can form or create by manipulating its intermolecular interactions.