UNIVERSITI TEKNOLOGI MARA

THE PHASE TRANSFORMATION ASSESSMENT OF IBUPROFEN-CITRIC ACID COCRYSTAL IN PROPANOL AND ETHANOL SOLUTION

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ABSTRACT

Co-crystallization is an alternative method to combine two or more components within the same crystal lattice where the components are interact via non-ionic interactions and in neutral state (Rajesh Thipparaboina, 2016). Nowadays, pharmaceutical co-crystal has received great attention for the development of the drug as it can alter the physichochemical properties of active pharmaceutical ingredients (API) by increasing the solubility of the API thus lead to the improvement of the efficiency of a dosage form. The objectives of this research are to determine the phase transformation assessment of Ibuprofen-Citric Acid co-crystal in ethanol and propanol solution and to analyse the formation of ibuprofen-citric acid co-crystal using analytical equipment such as XRPD, DSC, ATR-FTIR and optical microscope. The stability and bioavailability of the Active Pharmaceutical Ingredients (API) are important for the product performance. However, a few drugs available in the market have low solubility and dissolution rate problem. In this study, Ibuprofen will be selected as material of interest as it has low solubility. The solubility of Ibuprofen can be increased by cocrystallization of Ibuprofen-Citric Acid in ethanol and propanol solution. Based on the solubility of Ibuprofen, nine mole ratios between Ibuprofen and Citric Acid from 0.5 : 1 until 4.5 : 1, with 0.5 step size are used in this study. The phase transformation of Ibuprofen-Citric Acid cocrystal in propanol and ethanol solution is analysed by slow-cooling method. The cocrystallization will be assessed using analytical equipment such as powder x-ray diffraction (PXRD), differential scanning calorimetry (DSC), attenuated total reflection fourier-transform infrared spectroscopy (ATR-FTIR) and optical microscopy. In this study, the crystal formed has no pattern in term of ratio. The crystal formed showed plate-like shape whenever tested using the optical microscope. No new functional group formed in the crystals as compared to the pure components whenever analysed using the FTIR. The result of differential scanning calorimetry shows that all of the crystals formed are mixture instead of co-crystal. From this result, we can conclude that slow-cooling method is not suitable for co-crystallization of ibuprofen-citric acid.

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CHAPTER 1

INTRODUCTION

1.1 RESEARCH BACKGROUND

Cocrystallization is an alternative method to mix two or more components within the same crystal lattice where the components interact via non-ionic interactions and are in neutral state (Rajesh Thipparaboina, 2016). In order to improve the pharmaceutical properties, the researchers regularly consider the alternative solid state forms to a free drug compound like polymorphs or salts. Unfortunately, some of the compounds do not have suitable site (basic or acidic) for proton transfer. Here where co-crystal can become practical alternative in drug formulation as co-crystals do not involve in proton transfer (Rosli, 2014). This method can help to increase the solubility of the active pharmaceutical ingredients (API). Over the years, co-crystals have been described of various organic substances and given various name such as molecular complexes, heteromolecular co-crystals and addition compound (Rajesh Thipparaboina, 2016). The intermolecular interaction occurred in co-crystal including hydrogen bonds, van der Waals, and π-π staking and the most agreeable geometry will point to a supramolecular network (Ushma Kotak, 2015). There are many methodologies for co-crystal screening is employed. As the examples is the solvent evaporation, slurry conversion and grinding technique (Ushma Kotak, 2015). In this study, co-crystallization is introduced to Ibuprofen to increase the solubility of Ibuprofen using slow-cooling method. Citric acid is used as the co-former and the ethanol and propanol solution as the solvent.

Ibuprofen with molecular formula of $C_{13}H_{18}O_2$ is a non-steroidal anti-inflammatory drug largely used as antipyretic, analgesic and in the arthritis treatment. It has 206.29 g/mol molecular weight (Shui Wang, 2010). Recently, co-crystallization between Ibuprofen and nicotinamide has been done using analytical tools such as mid-infrared (ATR-FTIR), differential scanning calorimetry (DSC), X-ray diffraction (XRPD) and Raman spectroscopy. There are some studies shown that the bioavailability and mechanic stability of Ibuprofen has changed because of the