UNIVERSITI TEKNOLOGI MARA

STUDY OF COCRYSTALLIZATION BETWEEN IBUPROFEN AND GLUTARIC ACID VIA SLOW EVAPORATION TECHNIQUE

FARAH ALIA BINTI RAHAMAT

BEng

July 2017

ABSTRACT

Active Pharmaceutical Ingredients (APIs) are known as active chemical agent that delivers the effect of the substances into the body such as pharmaceutical drugs. These drugs can be administered through oral ingestion into the body system of the patients. However, less than 40% of these drugs are water soluble, particularly ibuprofen which is categorized in BSC Class II drugs. Thus, cocrystallization has emerged as one of the novel ways to overcome this dilemma. Pharmaceutical cocrystal can be defined as multi-component crystal that consists of two or more solid compounds under ambient condition where at least one of the compound is neutral API and the coformer is pharmaceutically accepted ion or molecules. Cocrystallization has become a promising method used nowadays to enhance the solubility, bioavailability and stability of most of the APIs. Cocrystallization between ibuprofen (API) and glutaric acid (coformer) has been studied in this research paper through slow evaporation technique with two solvents which are ethanol and propanol. The cocrystallization was conducted with nine different molar ratios starting from 0.5 to 4.5 moles with step size of 0.5. Pure ibuprofen and glutaric acid were mixed and heated until they were completely dissolved before being left at room temperature for slow evaporation process. The cocrystal characterizations were performed using four different equipment which are optical microscope (OM), Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC) and X-ray Diffraction (XRD). Based on the results obtained, glutaric acid is a suitable coformer for ibuprofen to undergoes cocrystallization technique. However, it was revealed that lower molar ratios are more suitable for this process both for ethanol and propanol (within range 0.5 – 3.0). Therefore, it can be concluded that glutaric appears to be a suitable coformer for ibuprofen in lower molar ratios.

ACKNOWLEDGEMENT

Firstly, I wish to thank God for giving me the opportunity to experience this research progress. I would like to express my gratitude to my supervisor, Mr. Muhamad Fitri bin Othman for all the guidance and knowledge given through the completion of this research project. I would also like to express a special thanks to all the faculty crystal communities which comprises of Chief Department, Dr. Nornizar Anuar, fellow lecturers, postgraduate and undergraduate members for their guidance and support.

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 RESEARCH BACKGROUND

Active Pharmaceutical Ingredients (API) are known as active chemical agent that delivers the effect of the substances into the body such as pharmaceutical drugs. These drugs can be administered through oral ingestion into the body system of the patients. Oral ingestion is one of the most convenient method for drug delivery system as it can be administered easily, fewer sterility constrictions as well it is able to obtain high approval from patients (Savjani, Gajjar et al. 2012). Through this method, development of the dosage form has also become more flexible where solid form products are majorly produced nowadays. However, (Savjani, Gajjar et al. 2012) has stated that less than 40% of these drugs are water soluble which means pharmaceutical drug developers are still facing the low solubility drug dilemma.

One of the challenges in formulation of drug molecules includes low solubility and dissolution rate in biological liquid which has become a wide concern on the drug delivery system as it lowers the therapeutic effect of the drugs. Therefore, various methods have been developed in order to enhance the APIs solubility which includes micronization (lessening of particle size), solid dispersion with appropriate hydrophilic transferors, nanosuspension and micellar solubilization (Savjani, Gajjar et al. 2012). Yet, the exact physicochemical properties of the studied molecules defines the success of the methods stated above according to (Qiao, Li et al. 2011). Hence, designation of pharmaceutical cocrystals has been a growing interest following this few decades.

Pharmaceutical cocrystal can be define as multi-component crystal that consists of two or more solid compounds under ambient condition as stated by (Pathak, Savjani et al. 2013) where at least one of the compound is neutral API and the co-former is pharmaceutically accepted ion or molecules. Cocrystallization has become a promising technology used nowadays to enhance the solubility, bioavailability and stability of most of the APIs. Where drug molecules are more stable, reproduceable and amendable to purification, cocrystallization is the best approach to overcome issues in pharmaceutical drugs as stated above.