SLOW COOLING COCRYSTALLIZATION OF IBUPROFEN AND GLUTARIC ACID IN ETHANOL AND PROPANOL SOLVENT

NURUL NABILAH BINTI KAMALRUZZAMAN

This thesis is submitted in fulfillment of the requirements for Degree of Bachelor of Eng. (Hons) Chemical and Bioprocess

FACULTY OF CHEMICAL ENGINEERING UNIVERSITI TEKNOLOGI MARA SHAH ALAM 2016

ABSTRACT

Cocrystallization is a technique used to improve the physicochemical properties of an active pharmaceutical ingredients (APIs). Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that is usually used as pain relieve medicine or to reduce fever that has low solubility limitation in gastrointestinal tract despite its high permeability. The aim of this research project is to investigate the cocrystal formation between ibuprofen and glutaric acid at different ratio in the ethanol and propanol solvent by using slow cooling of cocrystallization technique in order to enhance the solubility of the ibuprofen. The characteristic of the cocrystal was determined by using optical microscopy, differential scanning calorimetry (DSC), powder x-ray diffraction (PXRD) and fourier infrared spectroscopy (FTIR). The result in DSC showed new melting point indicating there was presence of cocrystal. The result showed in XRD result also corresponding with the DSC result where there are presence of new peak at 2θ . Meanwhile, result showed in FT-IR also corresponding to the DSC and XRD result except there is presence of hydroxyl alcohol group shown for ibuprofen-glutaric acid cocrystal for ratio 1:2 in propanol solvent indicating the sample is solvate.

ACKNOWLEDGEMENT

Firstly I wish to thank God for giving me the opportunity to embark on my degree and for completing this long journey successfully. My special gratitude goes to my parents for their prayers, encouragement, support and this thesis is dedicated to them for the vision and determination to educate me.

A special appreciation to my supervisor Mr. Muhammad Fitri Bin Othman that consistently giving guidance, encouragement and continued support towards completing this study to success. I also would like to sincerely thank my co-supervisor Dr. Nornizar Anuar for her guidance and also valuable discussions during our meeting together. Besides that, my appreciation also goes to Miss Umi Rafiah and also Miss Nik Salwani for assistances in teaching and helping me during the experiment and also for helping me in tabulating my characteristic data.

Finally I also would like to wish thank you to my friends for their support either technically or morally through this one year. For my group members in crystal group are thanked for the many discussions that gave me new information and knowledge and also to Miss Amalina Taiffudin for her assistance during the experiment and also in completing my report.

Table of Contents

DECLARATION	i
SUPERVISOR'S CERTIFICATION	ii
Accepted	iii
ABSTRACT	v
ACKNOWLEDGEMENT	vi
LIST OF FIGURE	x
LIST OF TABLE	xiii
CHAPTER ONE	1
INTRODUCTION	1
1.1 BACKGROUND RESEARCH	1
1.2 PROBLEM STATEMENT	3
1.3 OBJECTIVES	4
1.4 SCOPE OF RESEARCH	4
CHAPTER 2	
LITERATURE REVIEW	5
2.1 IBUPROFEN	5
2.2 GLUTARIC ACID	6
2.3 INTRODUCTION TO COCRYSTALLIZATION	7
2.4 PHARMACEUTICAL COCRYSTAL	8
2.5 Comparison of cocrystal with other solid modification techniques	10
2.5.1 Polymorphs	
2.5.2 Salts	
2.5.3 Solvates	13
2.5.4 Hydrates	
2.5.6 Amorphous	
2.6 DESIGN OF COCRYSTAL	
2.7 SELECTION OF COFORMER	
2.8 SELECTION OF SOLVENT	
2.9 PHYSICOCHEMICAL PROPERTIES OF COCRYSTAL	
2.10 SCREENING OF COCRYSTALLIZATION	

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND RESEARCH

According to world health organization (WHO) guideline, active pharmaceutical ingredients (APIs) can be defined as any material or mixture of materials used in a finished pharmaceutical product (FPP), intended to supply pharmacological activity to have direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have direct effect in restoring, correcting or modifying physiological functions in human beings (Kopp, 2011). The APIs can be obtained either by chemical synthesis or by biotechnologically synthesis.

Drugs can be defined as a substance that has the physiological effect when ingested or introduced into the body. According to Babu and Nangia the Biopharmaceutical Classified System (BCS) classified drug into four categories which are Class I, Class II, Class III and Class IV drug which are classified based on their solubility and permeability. The seminal work of Amidon showed that the gastrointestinal (GI) absorption is controlled by the membrane permeability and solubility/dissolution rate (Babu & Nangia, 2011).

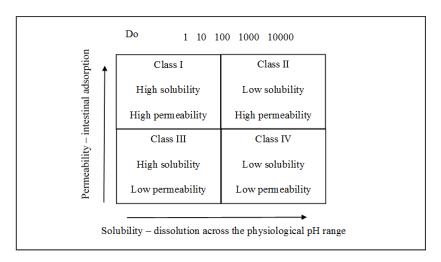


Figure 1. 1: The Biopharmaceutical Classification System of drugs according to intestinal absorption and oral administration parameters (Babu & Nangia, 2011)