UNIVERSITI TEKNOLOGI MARA

MORPHOLOGY PREDICTION AND DISSOLUTION BEHAVIOR OF A-SUCCINIC ACID IN ETHANOL SOLUTION USING MOLECULAR DYNAMIC SIMULATION

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Thesis submitted in fulfillment
of the requirements for the degree of
Bachelor of Engineering (Hons.) Chemical and Process

Faculty of Chemical Engineering

June 2018

ACKNOWLEDGEMENT

First and foremost, I would like to express my indebtedness to my supervisor, Mr Muhammad Fitri bin Othman, lecturer of Faculty of Chemical Engineering, Universiti Teknologi Mara for giving me the opportunity to carry out this research project . His constant guidance and advice played the vital role in helping me completing my thesis.

Appreciation also goes to my research group member in Universiti Teknologi Mara, Miss Nik Salwani Md. Azmi, Miss Vannessa Shalomy Darrell and Madam Umi Rafiah Shukri for their willingness to assist me on using Material Studio software and also their valuable advice on my work. Special thanks to my colleagues and friends for helping me with this project.

Finally, I would like to thank to my dear family for their full support, prayers and encouragement to weather on degree level journey.

ABSTRACT

Succinic acid is a potential co-former to produce co-crystal, thus an understanding of the dissolution behavior of succinic acid crystal is crucial for designing the co-crystal. In this works, α-succinic acid was chosen as a model compound for this study regardless its attractive crystal chemistry and its diverse surface properties. The aims of this study are to analyze the morphology of succinic acid crystal (form A) and to simulate the dissolution behavior of succinic acid crystal (form A) in the ethanol solution using molecular dynamic simulation. Molecular dynamics simulations have been performed by using Material Studio 4.4 by ACCELERYS. The most suitable morphology of the crystal was found in the combination of ESP charges with CVFF potential function and the morphology shape is elongated hexagonal needle-like shape which gives good agreement with the experimental crystal shape. In this research work, the MD simulation of dissolution of α-succinic acid has been successfully carried out. The less morphological important facet and high attachment energy which located at the tip of the crystal tends to dissolve faster compare to the most morphological important crystalline facet.

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CHAPTER 1

INTRODUCTION

1.1 Research Background

In the medicine and pharmacology field, drug development is the process by which new drugs are found and bring to the market. Drug or medication is used as one of the methods to prevent, diagnose and cure human disease. The pharmaceutical industry has discovered, develops and markets drug as they find drug medicine is an important part of the medical field. For a continual advancement in pharmacology, a research and development for a better drug performance is being developed and continuously perform.

During drugs manufacturing processes especially during drug synthesis, impurity can be produced which can be degradation by-product formed when improper environmental condition exist (A.V. Micheal, 2014). Impurities are substances that can coexist in pharmaceuticals that serve no purpose yet give low purity to the product. Therefore, purification which is the final step in active pharmaceutical ingredients (APIs) step is needed to remove the contaminants or impurities and increase the purity of APIs (Martin Viertelhaus, 2015). Formulation is the next procedure in order to develop a drug product after an API with suitable biological activity was archive. Since formulation for new drug development often has to deal with low bioavailability, the development of co-crystal can be one possibility to improve bioavailability without altering the API per se.

Crystallization has the paramount role in the pharmaceutical industry starting from intermediates separation process and the ending manufacture step of APIs. Crystallization is the main choice for separation and purification process in numerous areas such as the fine chemical, food, agrochemical and pharmaceutical industries. In pharmaceutical cocrystal, usually succinic acid crystal (pure crystal) act as coformer to produce a cocrystal in which will help or increase the dissolution rate of APIs.

Poor solubility remains a main concern for the pharmaceutical industry as it results in inadequate dissolution rate and insufficient bio-availability of APIs to reach its therapeutic effect. Both industry and academic researchers have done many types of researches on the crystal growth and dissolution behaviour of crystals to increase the aqueous solubility of