UNIVERSITI TEKNOLOGI MARA

PREDICTION OF DISSOLUTION BEHAVIOUR OF FUMARIC ACID (FORM A) USING MOLECULAR MODELLING

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ABSTRACT

In this study, a dissolution prediction of fumaric acid (Form A) in ethanol solvent was investigated using molecular dynamic simulation. Five important facets were selected for this study which are (0 2 0), (1 0 0), (0 1 1), (-1 1 0) and (1 1 -1). The dissolution prediction of fumaric acid (Form A) was analysed using radial distribution function (RDF) for molecular interactions analysis and mean square displacement (MSD) for diffusion coefficient values, D. Based on the analysis, facet (0 1 1) is the fastest facet to dissolve in ethanol and (1 0 0) facet is the last facet to dissolve in solvent. The correlation between radial distribution function and mean square displacement is the lower peak for RDF indicated the distance of fumaric acid for unrigid atom is closed with reference atom which exist with hydrogen bond. The MSD is proved that hydrogen bond is more difficult to break and display lower diffusion coefficient, D in the system.

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CHAPTER ONE

INTRODUCTION

1.1 Summary

This chapter explained about the material used which are Fumaric acid (Form A) as co-former and ethanol as solvent using Material Studio version 7.0 and discussed about the background of the research, problem statement, aim that need to be achieved and the scope of study.

1.2 Research Background

Oral ingestion is the most convenient technique of drug delivery because of its not difficult to control, high patient consent, which is necessary for patient to agree before undergoes the treatment after knowing the benefit, the risk of the treatment. Oral ingestion also has the least sterility constraint and can design in several of the dosage form. Therefore, more pharmaceutical company produces bioequivalent oral drug products (Krishnaiah, 2010). However, commonly design of oral dosage forms has to deal with high challenge because of their poor bioavailability. There are several factors will affect oral bioavailability such as aqueous solubility, drug permeability, dissolution rate to give a homogenous system, first-pass and pre-systemic metabolism and perceptivity to efflux mechanisms. Low oral bioavailability commonly occurs because of poor solubility and low dissolution rate of solute (poorly soluble drug) in the solvent (gastrointestinal fluids) particularly for class II so that increase the solubility will increase the bioavailability of drugs (K. T. Savjani, Gajjar, & Savjani, 2012).

Fumaric acid or in synthetic name called trans-butenedioic acid is intermediate in the tricarboxylic acid cycle for organic acid biosynthesis in humans and mammals, therefore it is the most important agents in the food industry (Dallos, Hajós-Szikszay, & Liszi, 2000). Furthermore, fumaric acid has essential practical packages within the polymer industry and in medicinal drug, especially as antifungicides and as a counter