UNIVERSITI TEKNOLOGI MARA

MOLECULAR DYNAMIC INVESTIGATION ON THE DISSOLUTION BEHAVIOUR OF FUMARIC ACID CRYSTAL (FORM B) IN ETHANOL SOLUTION

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ABSTRACT

Nowadays, co-crystal had been used in pharmaceutical industry. Co-crystal is the combination of active pharmaceutical ingredient (API) and co-former. The dissolution rate of API can be improved by the co-former and it is very important to select suitable co-former for the formation of co-crystal. Fumaric acid is belong to dicarboxylic acid group can act as co-former. It is also very crucial to study the properties of the crystal before we can choose it as a co-former. So, the objectives of this study are to analyse the morphology of fumaric acid crystal (form B) and to access dissolution behaviour of fumaric acid crystal (form B) in ethanol solution. For this study, we used molecular dynamic simulation approach by using Material Studio 4.4 by ACCELERYS to achieve our objectives. The combination of dreiding forces and hirshfeld charges give the morphology of fumaric acid (form B) crystal. The shape is small needle like. There are ten important facet from the morphology which are (0 1 0), (0 1 -1), (1 -1 0), (0 0 1), (1 2 1), (1 0 0), (1 -2 0), (1 0 -1), (0 2 -1) and (1 -3 1). RDF and MSD analysis show that facet (0 1 -1) is interact and dissolve first in ethanol solution.

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CHAPTER 1

INTRODUCTION

1.1 Research Background

A crystal can be defined by the arrangement of atoms, molecules or ions in a solid material. The arrangement of crystal is organized in a repeating pattern. Crystal is divided into four types which are ionic, covalent, molecular and metallic. The types of crystal are formed based on their bond in its atom. Nowadays, crystal has been widely used in pharmaceutical industry and there a lot of research that was carried out to improve the crystal functions in this industry.

In pharmaceutical, co-crystals have gain many considerations in pharmaceutical industry due to their ability to improve the biological properties and physicochemical of free active pharmaceutical ingredient (API). (X. Zhang et al. 2016). A co-crystal is the combination of two or more different molecules that are in solid state at room temperature in a crystal lattice and the hydrogen bond help to stabilised the structure. (Tomaszewska et al. 2013). Generally, there are few methods to form the co-crystal, such as melt crystallization, crystallization from solution, co-milling and slurry conversion. The co-crystal formation can be achieved by introducing different molecular component into the crystal lattice and in pharmaceutical this can be refer to the APIs and co-crystal former (CCF) or conformer. One of the examples for conformer is fumaric acid crystal.