

UNIVERSITI TEKNOLOGI MARA

**STUDY ON DISSOLUTION BEHAVIOUR OF
SACCHARIN IN ONE MOLECULE OF ETHANOL
USING MOLECULAR MODELLING METHOD**

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ABSTRACT

Saccharin is a Food and Drug Administration (FDA)-approved sweetener and the most popular used as co-former in producing new pharmaceutical co-crystal for the development of drug. The Molecular Dynamic (MD) method was applied to analyze the behavior of five main Saccharin crystal facets with one molecule of ethanol; (1 0 0), (1 1 0), (1 0 -2), (1 1 -1), (0 1 1). The interaction of each molecule in one unit cell of the crystal was then analyzed based on Radial Distribution Function (RDF) graph and the dissolution behavior was determined by Mean Square Displacement (MSD) graph. For the RDF analysis, the highest peak of $g(r)$ for the facet (1 0 0), (1 1 0), (1 0 -2), (1 1 -1) are from the molecules 2 at the radius of 5.91, 5.53, 5.41 and 5.19 Å respectively while for the facet (0 1 1), the highest peak was molecule 4 (SAC m4) at radius of 4.95 Å and the interactions are mainly caused by the Coulomb and Van Der Waals. The MSD results concluded that the molecule 1 (1 1 -1) facet had the largest D value while disproportionally, the molecule 4 (0 1 1) facet had the least D value. The m1 for the facet (1 1 -1) has the largest D value while the m4 of facet (0 1 1) has the least D value which indicates that the ethanol and SAC molecules diffuses more on facet (1 1 -1).

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CHAPTER ONE

INTRODUCTION

1.1 RESEARCH BACKGROUND

Pharmaceutical drug or we simply called as medicine is a drug that usually used to prevent or cure a disease. There are two types of solid state form that the drug could survive which are amorphous and polymorphs. It is important to have drugs with various properties such as biological properties, in the latest development of them (Pindelska et al., 2017). However, a significant number of drug getting approvals have poor biopharmaceutical properties during drug the process. Therefore, it is useful for the pharmaceutical industry to manipulate and testing the properties of drug during the drug development process (Khadka et al., 2014).

Nowadays, many of the pharmaceutical industry having a problem with poor solubility and lower bioavailability of the drug resulting in drug delivery system in the human body. The drug solubility becomes one of the issues in pharmacological industry. Thus, there are many techniques that have been used to improve the performance characteristic of Active Pharmaceutical Ingredients (APIs) as well as the solubility of drug such as pharmaceutical co-crystal, salt formation, micronization, emulsification, and complexation (Lee et al., 2013). One of the most popular and gained an interest for pharmaceutical research is pharmaceutical co-crystal technique because it have an ability to improve physicochemical characteristics of an API.

For the separation and purification of intermediate compounds and active pharmaceutical ingredients (APIs), an important unit operation is crystallization processes. Downstream processing as well as the product performance such as bioavailability will be effected (Richard, 2018). Pharmaceutical co-crystal is a multi-component compound that combined from an active pharmaceutical ingredients (APIs) and appropriate co-former with specific stoichiometric coefficient by several