UNIVERSITI TEKNOLOGI MARA

EVALUATION OF POLYMORPHIC FORMS OF MEFENAMIC ACID CRYSTALS FROM SOLUTION: MODELLING AND EXPERIMENTAL APPROACH

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Thesis submitted in fulfilment
of the requirements for the degree of
Master of Science

Faculty of Chemical Engineering

February 2016

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, University Teknologi MARA, regulating the conduct of my study and research.

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Faculty	:	Chemical Engineering
Thesis Title	:	Evaluation of Polymorphic Forms of Mefenamic Acid Crystals From Solution: Modelling and Experimental Approach
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ABSTRACT

Mefenamic acid (MA) is an active pharmaceutical drug (API), used widely as an antipyretic analgesic and anti-rheumatic drug. However it is practically insoluble in water, restricting its utility in clinical trials. It exhibits two polymorphs that show different solubility and stability where form II is more soluble than form I, thus preferable for pharmaceutical production. Hence, it is the objective of this thesis to assess the polymorphic forms of MA crystals produced using crystallization process in different process conditions. Molecular modelling simulation was also done to study the molecular interactions of the crystal in order to increase the level of understanding of the factors affecting the produced crystal. XRPD, DSC and FTIR results reveal that different solvent (acetone and dimethylformamide (DMF)) produces different polymorphic forms; form Iand form II respectively, with different morphologies. Solubility test was carried out which shows that form II is more soluble than form I. HPLC result reveals that there is small inclusion of solvent in the crystals. The prediction of MA crystal morphology and the effect of solvent on crystal were studied using molecular modelling technique. Predicted morphology reveals similarity with the experimental morphology with low percentage errors of lattice energy between modelling and experimental values (0.07% for form I and 0.72% for form II). Assessment of solvent interaction on MA crystal reveals that both solvents are favorable to attach on the crystal, validating the HPLC result. However, DMF is more favourable to attach on form II than acetone on form I. Detail observations revealthat molecular packing of MA crystal plays an important role in the morphological difference between form I and form II, hence different polymorph, thus explaining the experimental result.

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