UNIVERSITI TEKNOLOGI MARA

INVESTIGATION OF SOLUTION THERMODYNAMICS AND SOLUTE CHARACTERIZATION OF CITRIC ACID POLYMORPHS

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of the requirements for the degree of
Master of Science

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AUTHOR'S DECLARATION

I declare that the work in this thesis/dissertation 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, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Crystallization is an important industrial process used in a multitude of different industries including pharmaceutical-, chemical production-, and food-industry. In pharmaceutical industry, new polymorphs and transition of polymorphs may appear spontaneously from less stable to more stable. The scenario occurs due to the manufacturing process (addition of solvent), changes in the equipment used to dry the final drug substance, and conditions of materials to be stored. The objective of crystallization is to produce high quality crystals with desirable macro- and microscopic properties, shape and desired polymorph and enabling them to be utilized in end user specific applications. The scope of the studies consists of two sections which covers the determination of activity coefficients and behaviour and structure of citric acid. Analytical gravimetric solubility studies of anhydrous and monohydrate citric acid in conjunction with Van't Hoff plots have elucidated specific polymorphic thermodynamic properties; enthalpy, entropy and activity coefficients. The solubility characteristics exhibited infer that the polymorphs undergo transition at TEMPERATURE and are enantiotropically related. Polymorph screening and molecular modeling studies indicate that the addition of impurities to a pure solvent solute system can initiate polymorphic transition. Specifically; the presence of polar molecules appears to initiate transition from the anhydrous to the monohydrate polymorph of citric acid.

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