

UNIVERSITI TEKNOLOGI MARA

**INVESTIGATION OF SOLUTION
THERMODYNAMICS AND SOLUTE
CHARACTERIZATION OF CITRIC ACID
POLYMORPHS**

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Thesis submitted in fulfillment
of the requirements for the degree of
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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.


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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.

TABLE OF CONTENTS

	Page
AUTHOR'S DECLARATION	ii
ABSTRACT	iii
ACKNOWLEDGEMENTS	iv
LIST OF TABLES	vii
LIST OF FIGURES	viii
LIST OF ABBREVIATIONS	x
1.0 CHAPTER ONE : INTRODUCTION	1
1.1 Introduction	1
1.2 Problem Identification	3
1.3 Research Objectives	4
1.4 Scope of Study	5
1.5 Expectation of the Research	5
2.0 CHAPTER TWO : LITERATURE REVIEW	6
2.1 Introduction	6
2.2 The Fundamental of Crystallization	7
2.2.1 Solubility and Thermodynamic Study	7
2.2.2 Mathematical Modelling	12
2.2.3 Polymorph Screening	13
2.3 Molecular Modeling – Material Studio®	18

3.0	CHAPTER THREE : RESEARCH METHOD	21
3.1	Introduction	21
3.2	Materials	21
3.3	Methods	23
3.3.1	Solubility determination	23
3.3.2	Thermodynamic Study	24
3.3.3	Mathematical Modelling	25
3.3.4	Polymorph Screening	28
3.3.5	Polymorph Screening Analysis	31
3.3.5.1	Microscopic Camera	31
3.3.5.2	X-ray Powder Diffraction (XRPD)	31
3.3.5.3	Differential Scanning Calorimetry (DSC)	32
3.3.6	Molecular Modeling – Material Studio®	32
4.0	CHAPTER FOUR : RESULTS AND DISCUSSION	36
4.1	Solubility Determination	36
4.2	Thermodynamic Study	38
4.3	Mathematical Modelling	44
4.4	Polymorph Screening	48
4.4.1	Microscopic Camera	48
4.4.2	X-ray Powder Diffraction (XRPD)	51
4.4.3	Differential Scanning Calorimetry (DSC)	57
4.4	Molecular Modeling – Material Studio®	61
5.0	CONCLUSIONS	66
	REFERENCES	68
	APPENDICES	73