

UNIVERSITI TEKNOLOGI MARA

**CRYSTALLIZATION OF L-
ISOLEUCINE WITH THE
INFLUENCE OF ELECTRIC FIELD**

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ABSTRACT

Problems encountered in crystallization when the end-product does not meet particular requirement for industry specifically in pharmaceutical and fine chemical production. Good quality crystals are defined as crystals with uniform size, shape and correct polymorphic form. Various methods have been established in attempt to achieve the good quality crystal by enhancing the metastable zone width region with external influence. Electric field was chosen in this study to solve the issues. In this study, L-isoleucine was the main material used meanwhile glycine is the other material due to the interesting characteristic of amino acids to exist as zwitterions in solution. Mechanism of this work is known as effect of electric field in crystallization. Investigations of this study focus on speciation behaviour of L-isoleucine in solution and crystallization of the amino acid in distilled water, acidic and basic solutions with the presence of electric field for selected temperatures; 10, 25, 40, 55 and 70°C. From speciation analysis, it is observed that the pKa values increases with the increases of applied electric field demonstrating obstacles added to the system to dissociate H⁺ from both -COOH and -NH₃⁺. Crystallization of L-isoleucine in distilled water in the presence of electric field depicted the presence of new phase of the crystal structure proven by XRPD with consistent new peak at 2θ of 31.0°. This result was supported by thermal properties of DSC data showing the presence of new melting temperature at 380°C. Findings from FTIR proved no proton transfer occurrence when crystallization is induced by electric field. Crystallization of glycine in distilled water with the influence of electric field demonstrates no change of polymorphic form proven by XRPD, DSC and FTIR data. Influence of pH condition in the presence of electric field demonstrated changes in L-isoleucine morphologies as well as the crystals properties.

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CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND STUDY

In order to achieve developed nation status in 2020, Malaysia government has provided a structured and thorough program that is Economic Transformation Program (ETP), as part of National Transformation Program (NTP) (Overview of ETP). The Vision 2020 was firstly initiated by former Prime Minister, Tun Dr Mahathir Mohamad. The ETP aimed to increase the nation's gross national income (GNI) per capita from RM 23,700 in 2009, the year of ETP was firstly introduced, to RM 48,000 in 2020. This growth with six percents per annum would enable to achieve the targets set under Vision 2020. One of parts in ETP is National Key Economic Areas (NKEA). This plan is intentionally to induce economic activity to sector areas that has the electric field to directly and materially contribute a quantifiable amount of economic growth to the Malaysian economy (Overview of ETP). The affected industries cover both sectors; public and private, specifically on healthcare sector. The government has presented few key strategies to increase GNI as much as RM 35.5 billion from the healthcare sector between 2010 and 2020 (Market watch 2012: The healthcare sector in Malaysia). Increasing demand in healthcare sector is due to the increasing number of elderly civilians, consumer awareness in healthcare services as well as urbanization in Malaysian's lifestyle which lead to developed-country illness.

Three subsectors in healthcare including pharmaceutical, health services and medical technology products. Reports have specifically related the challenges faced by healthcare sector with increasing cost of medicine leading to contribution of pharmaceuticals sectors on chemical products (Pharmaceutical industry: Boost efforts to make our own drugs). Pharmaceutical sector is at most turnover and profitability when it comes to fine chemical that form basic ingredients for products that widely sold in market (Carpenter & Wood, 2004). Globally, pharmaceutical industry is expected to increase in growth from 2009 to 2014 as shown in Figure 1.1 whereby the analysts have forecasted that total value will increase until US\$ 900 billion in 2014 (Global pharmaceutical industry market, 2013). Meanwhile, Malaysia government has