

UNIVERSITI TEKNOLOGI MARA

**PHARMACOKINETIC PROFILE OF α -
TOCOPHEROL IN THREE DIFFERENT NANO-
EMULSION FORMULATIONS IN RATS**

MURNIATI BINTI MAZRI

**Dissertation submitted in partial fulfillment of the requirements for
the degree of Bachelor of Pharmacy**

Faculty of Pharmacy

October 2006

ACKNOWLEDGEMENT

In the name of Allah S.W.T., the Most Gracious, Most Merciful and Most Compassionate. Alhamdulillah praise to Allah S.W.T. for giving me strength and ability to complete this thesis (PHM 555). I would never miss the opportunity to express my thanks to all those people that provided me with the information, guidance, comments, ideas, and skilled needed.

First of all, I would like to express my deepest gratitude and warmest appreciation to my supervisor, Mr. Tommy Julianto Bustami Effendi for his willingness to supervise, whose suggestion, and editorial expertise gave this research its present shape. A special debt of gratitude is expressed to him. A special thanks is addressed to Rosa Elizabeth Pereira for her great support, advice and suggestion. Also thank to my subject coordinator, Dr. Kalavathy for her encouragement and guidance that she gave in completing and assuring the success of my project.

To my beloved family members, especially to my parents, for their faith, encouragement, support, and their constant prayer for me. May Allah S.W.T. grant us His guidance.

I also would like to take this opportunity to sincerely thanks to all the faculty's staffs, lab officers, lab assistants and research assistants, especially to Cik Nor Asmah Hashim, Cik Liza Salleh and Encik Rahmat Mohamed Razali for their cooperation and helps.

Last but not least, my gratitude extending to all my friends, especially to my labmates; Adilah Mohd Fazli and Nurul Hayati Abdul Jamal, and my classmates (PH210 part 07 Jul-Nov2006) for their encouragement, critics and support for this project.

Thank you very much.

TABLE OF CONTENTS

| | Page |
|--|------|
| TITLE PAGE | |
| APPROVAL SHEET | |
| ACKNOWLEDGEMENT | ii |
| TABLE OF CONTENTS | iii |
| LIST OF TABLES | vi |
| LIST OF FIGURES | vii |
| LIST OF ABBREVIATIONS | viii |
| ABSTRACT | ix |
| CHAPTER ONE (INTRODUCTION) | 1 |
| 1.1 Introduction | 1 |
| CHAPTER TWO (LITERATURE REVIEW) | 6 |
| 2.1 Pharmacokinetic studies | 6 |
| 2.2 Bioavailability of lipophilic drug | 7 |
| 2.3 Nano-emulsions as method to improve lipophilic drug absorption | 8 |
| 2.4 General pharmacology of vitamin E | 10 |
| 2.5 Pharmacokinetic parameters of vitamin E | 11 |
| 2.6 Analysis of plasma α -tocopherol | 12 |
| CHAPTER THREE (MATERIALS AND METHODS) | 13 |
| 3.1 Materials | 13 |
| 3.2 Instrumentation | 13 |
| 3.3 Research methods | 14 |
| 3.3.1 Particle size measurements | 14 |
| 3.3.2 Sample preparation | 14 |

ABSTRACT

This study was designed to compare the absorption profiles of nano-emulsion containing α -tocopherol formulated with three different oils, i.e. palm oil, soybean oil and VCO in Sprague-Dawley rats. The plasma concentration of α -tocopherol was determined at specific intervals up to 36 hours post administration of formulations with a dose of 30 IU/kg of tocopherol. The peak heights were obtained by direct injection of plasma samples into the High Performance Liquid Chromatography (HPLC), after being deproteinized. The total absorption of the α -tocopherol, calculated as the total area under the plasma concentration time curve ($AUC_{0-\infty}$), was markedly greatest for the palm oil, followed by soybean oil and VCO formulation. This study also showed a rapid absorption of α -tocopherol from oils containing long chain fatty acids (palm oil and soybean oil) compared to the medium chain triglyceride oil (VCO). Although apparently $AUC_{0-\infty}$ and C_{max} of nano-emulsion of α -tocopherol formulated in palm oil is higher than in soybean oil and in VCO, they were not significantly different when analysed by a one-way analysis of variance (ANOVA). From the results obtained, it can be concluded that palm oil provides better absorption of α -tocopherol when being formulated as nano-emulsion, when compared to other oils (soybean oil and VCO).

CHAPTER 1

INTRODUCTION

1.1 Introduction

Poorly water-soluble drugs are increasingly becoming a problem in terms of obtaining the satisfactory dissolution within the gastrointestinal tract that is necessary to obtain good bioavailability. Thus, for such compounds, including vitamin E, modification of the physicochemical properties, such as salt formation and particle size reduction of the compound may be one approach to improve the dissolution rate of the drug (Gursoy and Benita, 2004). In addition, other formulation strategies have been adopted including the use of cyclodextrins, nanoparticles, solid dispersions and permeation enhancers.

This study is focused on nano-emulsions-based formulations. Nano-emulsions are colloidal dispersions formed by a liquid phase dispersed in a second phase in form of droplets. Due to their small droplet size below 500 nm that causes a large reduction in gravity force, nano-emulsions may appear transparent and translucent to the naked eye (Solans *et al.* 2005) (Fig. 1.1). The Brownian motion seems to be sufficient to overcome the effect of gravity. Thus, upon storage, no sedimentation or creaming occurs offering increased stability (Tadros *et al.*, 2004).