

UNIVERSITI TEKNOLOGI MARA

**IDENTIFICATION AND
DISTRIBUTION OF
ACETYLCHOLINESTERASE
INHIBITORY ALKALOIDS FROM
DIFFERENT LOCATIONS IN
PENINSULAR MALAYSIA**

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ABSTRACT

A series of *Lycopodium* alkaloids, namely 6 β -hydroxyhuperzine A (**96**), 16-hydroxyl huperzine A (**318**) and huperzine A (**93**), have been isolated from *Huperzia phlegmaria*. Their structure and relative stereochemistry were elucidated on the basis of their spectral data and chemical correlations. A simple and reliable high performance liquid chromatography (HPLC) method has been established for the analysis of the isolated compounds. The recovery rates were between 91 – 111 %. The within- and between-day precisions, expressed as R.S.D ranged from 0.5 % to 2.6 %. Good linear regression was observed, $r^2=0.999$. The results demonstrate that this method is simple and suitable for quality control of this traditional Chinese medicinal herb. Additionally, the acetylcholinesterase inhibitory activity of isolated compounds was evaluated. The inhibition of cholinesterase activity was determined based on Ellman's colorimetric method. Colorimetric measurements were measured with a microplate reader at a wavelength of 405 nm. Galanthamine was used as a positive control. In conclusion, 6 β -hydroxyhuperzine A (**96**) exhibited weak acetylcholinesterase inhibitory activity, while 16-hydroxyl huperzine A (**318**) did not show inhibitory effect (>200 μ M) compared to huperzine A (**93**).

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TABLE OF CONTENT

	Page
CONFIRMATION BY PANEL OF EXAMINERS	ii
AUTHOR'S DECLARATION	iii
ABSTRACT	iv
ACKNOWLEDGEMENT	v
TABLE OF CONTENT	vi
LIST OF TABLES	ix
LIST OF FIGURES	xi
LIST OF PLATES	xiii
LIST OF SYMBOLS	xiv
LIST OF ABBREVIATIONS	xv
LIST OF NOMENCLATURES	xvi
CHAPTER ONE: INTRODUCTION	1
1.1 Background	1
1.2 Alzheimer's disease	1
1.2.1 Neuropathology of Alzheimer's Disease	3
1.2.2 Pharmacological Treatment of Alzheimer's Disease	4
1.3 Problem Statement	7
1.4 Objective	7
1.5 Significance of Study	7
1.6 Outline of the study	7
CHAPTER TWO: LITERATURE REVIEW	8
2.1 Introduction	8
2.1.1 Lycopodine Class	11
2.1.2 Lycodine Class	22
2.1.3 Fawcettimine class	30
2.1.4 Miscellaneous group	44
2.2 Bioactivities of Lycopodium Alkaloids	54

CHAPTER ONE

INTRODUCTION

1.1 Background

Natural products as an alternative medicine have been widely researched by the scientists throughout the world. This is because of the concern towards safety of synthetic drugs as medicines practice for the core treatment today. Natural product discovery is not anything new, it started from discovery of digoxin, morphine, aspirin and penicilin but later this discovery method is de-emphasized by the development of powerful technologies using artificial biochemical assay (Rishton, 2008). However, through analysis, introduction of new drug by this high-throughput screening discovery method shows a declining trend (Butler, 2004; Grabowski & Wang, 2006). Recently, the interest of natural product-based drugs have been renew with evidence of 19 natural product-based drugs have been approved between 2005-2010 (Gilani & Atta-ur-Rahman, 2005; Mishra & Tiwari, 2011).

1.2 Alzheimer's disease

Alzheimer's disease (AD) is one of the most common diseases in the world that affect the elderly people and the third major cause of death after cardiovascular disease and cancer in developed countries (Ma and Gang, 2008). One of the syndrome or a set of syndrome and signs occur due to an AD is dementia (Reddy *et al.*, 2010). There are about 46.8 million cases of dementia reported worldwide in 2015 and it is expected to increase by 131.5 million cases in 2050 as world populations continue to age. Dementia also has a huge economic impact. Nowadays, the total estimated cost of dementia worldwide is US\$ 818 billion, and eventually it will become a trillion dollar disease rising to US\$ 2 trillion by 2030. These new estimation were 12-13 % higher than those made for the World Alzheimer Report 2009. This means that if global dementia care were a country, it would be the world's 18th largest economy exceeding the market values of corporate companies such as Apple (US\$ 742 billion), Google (US\$ 368 billion) and Exxon (US\$ 357 billion) (Prince *et al.*, 2015).