# **UNIVERSITI TEKNOLOGI MARA**

# CHEMICAL CONSTITUENTS FROM THE HEXANE FRACTION OF GONIOTHALAMUS MACROPHYLLUS ROOTS

### NORKAMILAH BINTI MOHAMMED @ ABDULLAH

Thesis submitted in fulfillment of the requirements for the degree of Master of Science

**Faculty of Pharmacy** 

August 2013

#### **AUTHOR'S DECLARATION**

I declare that the work in this thesis 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 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.

Name of Student	:	Norkamilah Binti Mohammed @ Abdullah
Student I.D. No		2008732203
Programme	•	Master of Science
Faculty	•	Faculty of Pharmacy
Title	*	Chemical Constituents from the Hexane Fraction of
		Goniothalamus Macrophyllus Roots.
Signature of Student	;	
Date	:	August 2013

#### ABSTRACT

Goniothalamus is one of the species from the Annonaceae family consisting of 115 species distributed throughout the tropics and subtropics. Goniothalamus macrophyllus is a medicinal plant used widely in Peninsular Malaysia and known by the local name "pokok gajah beranak". Phytochemical studies on Goniothalamus species have led to the isolation and characterization of large number of styryl lactones, acetogenins, alkaloids and flavanoids. Besides, investigation on the biological activities of Goniothalamus species showed the potential usage as an anticancer, antimalarial, antiplasmodial and antimicrobial. The objectives of the study are to isolate compounds from the hexane fraction from the roots of G. macrophyllus and test against brine shrimp assay. Dried roots of G. macrophyllus were ground into fine powder using a cutter mill. The ground roots were soaked in 80 % aqueous methanol at room temperature, filtered and the solvent were removed under reduced pressure to give crude methanolic extract. The crude extract was further suspended in aqueous methanol and sequentially partitioned with n-hexane, chloroform and *n*-butanol. Two known compounds, goniothalamin (13) and linderatone (147) with two new compounds, goniolandrene A (148) and B (149) were isolated and purified from the hexane fraction by using analytical HPLC, preparative HPLC and TLC preparative. The structures were discussed and confirmed by using one (1D) and two - dimensional (2D) NMR, MS-TOF, IR, UV-Vis spectroscopy and comparison with the known compounds. The isolated compounds were tested against Brine Shrimp Lethality assay (BSL).

### TABLE OF CONTENTS

	Page
AUTHOR'S DECLARATION	ii
ABSTRACT	iii
ACKNOWLEDGEMENT	iv
TABLE OF CONTENTS	v
LIST OF TABLES	viii
LIST OF FIGURES	ix
LIST OF SCHEMES	xii
LIST OF ABBREVIATIONS	xiii

CHAPTER ONE : INTRODUCTION		
1.1	Background of Study	1
1.2	Problem Statement	2
1.3	Objectives of Study	2
1.4	Significance of Study	2
1.5	Outline of Study	3

CHA	PTER '	TWO : LI	TERATURE REVIEW	4
2.1	Chemi	Chemical Constituents from Goniothalamus Species		4
	2.1.1	1.1 Styryl Lactones		
		2.1.1.1	Five Membered Ring Styryl Lactones	6
		2.1.1.2	Six Membered Ring Styryl Lactones	7
		2.1.1.3	Eight Membered Ring Styryl Lactones	14
		2.1.1.4	Bis – styryl Lactones	15
		2.1.1.5	Unusual Ring Styryl Lactones	15
2.1.2 A		Acetoger	nins	16
		2.1.2.1	Non-tetrahydrofuran (THF) Ring	16
		2.1.2.2	Mono-tetrahydrofuran (THF) Ring	18
		2.1.2.3	Bis-tetrahydrofuran (THF) Ring	22

2.1.2.4 Tri-tetrahydrofuran (THF) Ring 22

		2.1.2.5	Tetrahydropyran (THP) Ring	23
	2.1.3	Alkaloid	S	23
		2.1.3.1	1- Azaanthraquinone Alkaloids	23
		2.1.3.2	Aporphine Alkaloids	25
		2.1.3.3	Indole Alkaloids	27
		2.1.3.4	Phenanthrene Lactam Alkaloids	27
		2.1.3.5	Unusual Group Alkaloids	29
	2.1.4	Flavanoids		29
		2.1.4.1	Flavones	29
		2.1.4.2	Flavanols	30
		2.1.4.3	Chalcones	30
		2.1.4.4	Flavanones	31
		2.1.4.5	Unusual Skeleton Flavanoids	32
2.2	Chemi	cal Consti	tuents from Goniothalamus Macrophyllus	33
2.3	Biosynthesis Pathway			33
	2.3.1	Biosyntł	nesis Pathway of Goniothalamin(13)	33
	2.3.2	Biosyntł	nesis Pathway of $\alpha$ -Phellandrene	35
2.4	Biological Activities of Goniothalamus Species			37
	2.4.1	4.1 Cytotoxicity Activity		
	2.4.2	Antilarvicidal and Antimalarial Activity		
	2.4.3	Antibac	terial and Antimicrobial Activity	39
CHA	APTER	THREE :	<b>RESEARCH METHODOLOGY</b>	40
3.1	Instrun	nentation	and Chemicals	40
3.2	Plant I	dentificati	on	40
3.3	Extrac	raction and Partition		
3.4	Isolatio	tion and Purification		
3.5	Confir	mation of Goniothalamin (13)		
3.6	Structu	ructural Elucidation		
3.7	Biological Activity			45
	3.7.1	Brine Sl	nrimp Lethality Assay	45
	3.7.2	P388 Bi	oassay	46