

**UNIVERSITI TEKNOLOGI MARA**

**ALKALOIDS, STYRYL LACTONES,  
AND ACETOGENIN FROM THE  
ROOTS OF *Goniothalamus lanceolatus*  
Miq. AND THEIR  
ANTIPROLIFERATIVE ACTIVITY**

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Thesis submitted in fulfilment  
of the requirement for degree of  
**Doctor of Philosophy**  
**(Science)**

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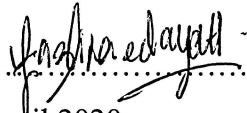
**April 2020**

## 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 results 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.

I, hereby, acknowledge that I have been supplied with Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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## ABSTRACT

*Goniothalamus lanceolatus* Miq., locally known as selukai or getimang is an ethnomedicinal plant indigenous to Sarawak. It is used traditionally to treat cancer. Phytochemical investigation on the roots of *G. lanceolatus* Miq. was conducted with the objective of comprehensively analyse the chemical constituents present in the roots of *G. lanceolatus*, especially the ones potentially active as antiproliferative agents. The roots of *G. lanceolatus* Miq. was extracted successively using hexane, dichloromethane, and methanol. The hexane and dichloromethane extracts showed antiproliferative activity against colorectal and lung cancer cell lines with percentage viability of cell less than 15%. Among the two extracts, the HPLC-DAD profile of the dichloromethane extract revealed the presence of more active UV components, and thus selected for further investigation. Mass-based dereplication strategy using in-house and online mass database system successfully identified 24 constituents comprising of styryl lactones, alkaloids, and acetogenins in the dichloromethane extract. Isolation and purification from the active antiproliferative fractions, M2 to M7 led to characterization of ten styryl lactones, five alkaloids, and one acetogenin, where six dereplicated compounds were verified. All the structures were elucidated using 1D- and 2D-NMR spectroscopy. Absolute configurations of the styryl lactones were established by ECD analysis through comparison of the experimental and theoretically calculated ECD spectra, while stereochemistry of the alkaloids were established using the single X-ray crystallography data. The known *S*-goniothalamine and parvistone D, are reported for the first time from *Goniothalamus* genus. Two new styryl lactones *5R,6R*-5-hydroxy-6-styryltetrahydropyran-2-one and gonioanceolatin E, and five new styryl lactone diastereomers, *5R,6R*-5-acetylgoniothalamine, *5R,6R*-5-hydroxygoniothalamine, goniofupyrone B, deoxygonioppyrone B, and gonioanceolatin A, along with a known pyrano-pyrone, *1S,5S,7R,8S,3-exo,7-endo*(+)-8-*epi*-9-deoxygonioppyrone are described. The *6S/1S*- styryl lactones isolated in this work are new discoveries in *Goniothalamus* species. Biogenesis pathway of these *6S/1S* styryl lactones are proposed. In addition, two new alkaloids, (-)-gonioanceolactam and 2-acetyl-3-amino-1,4-naphthoquinone were also identified along with the known alkaloids, 2-acetyl-3-amino-5-hydroxy-1,4-naphthoquinone, cleistopholine and liriodenine, and the acetogenin, annonacin. *S*-Goniothalamine, (-)-gonioanceolactam and annonacin exhibited potential antiproliferative activity against all tested cancer cell lines with the IC<sub>50</sub> values of less than 10.0 μM. The alkaloids, 2-acetyl-3-amino-1,4-naphthoquinone and 2-acetyl-3-amino-5-hydroxy-1,4-naphthoquinone, as well as liriodenine demonstrated antiproliferative against HCT116, A549, and NCI-H23 cell lines with IC<sub>50</sub> values ranging between 4.5 to 10.3 μM. *5R,6R*-5-hydroxygoniothalamine showed selective activity against lung cancer cell lines, A549, and NCI-H1299, with the IC<sub>50</sub> values of 8.0 and 8.9 μM, respectively. Other styryl lactones exhibited only weak activity. All isolated compounds were non-toxic to normal cell lines except for annonacin.

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# TABLE OF CONTENTS

	<b>Page</b>
<b>CONFIRMATION BY PANEL EXAMINERS</b>	<b>ii</b>
<b>AUTHOR'S DECLARATION</b>	<b>iii</b>
<b>ABSTRACT</b>	<b>iv</b>
<b>ACKNOWLEDGEMENT</b>	<b>v</b>
<b>TABLE OF CONTENTS</b>	<b>vi</b>
<b>LIST OF TABLES</b>	<b>ix</b>
<b>LIST OF FIGURES</b>	<b>xii</b>
<b>LIST OF SYMBOLS</b>	<b>xv</b>
<b>LIST OF ABBREVIATIONS</b>	<b>xvi</b>
<b>LIST OF COMPOUNDS</b>	<b>xviii</b>
<b>CHAPTER ONE: INTRODUCTION</b>	<b>1</b>
1.1 Plant as Source of Therapeutic Agents for Cancer	2
1.2 Problem Statement and Significance of Study	4
1.3 Objectives of Study	5
1.4 Scope of Study	5
<b>CHAPTER TWO: LITERATURE REVIEW</b>	<b>7</b>
2.1 Cancer Chemopreventive Agents from Plants	7
2.2 Botanical and Morphological Description of Annonaceae Family and <i>Goniothalamus</i> Genus	10
2.3 Ethnomedicinal Uses of Annonaceae Family and <i>Goniothalamus</i> Genus	12
2.4 Biological Activities of <i>Goniothalamus</i> Extracts	15
2.5 Chemical Diversity and Pharmacological Significance	16
2.5.1 Styryl Lactones	17
2.5.2 Alkaloids	33
2.5.3 Acetogenins	40