

สารต้านมาลาเรียจาก *GONIOHALAMUS TENUIFOLIUS*

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สถาบันวิทยบริการ
วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
จุฬาลงกรณ์มหาวิทยาลัย

ภาควิชาเคมี

บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2539

ISBN 974-636-392-1

ลิขสิทธิ์ของบัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

**ANTIMALARIAL COMPOUNDS FROM
*GONIOTHALAMUS TENUIFOLIUS***



Miss Lalita Wirasathien

**A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Pharmacy**

Department of Pharmacognosy

Graduate School

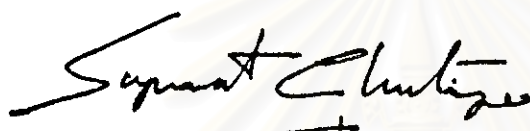
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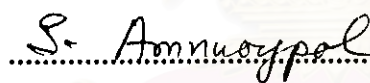
ISBN 974-636-392-1

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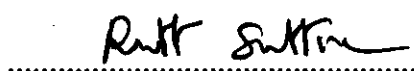
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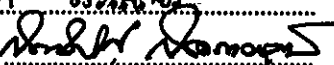
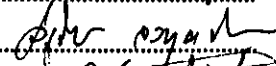

ลลิตา วีระเสถียร : สารต้านมาลาเรียจาก *Goniolothalamus tenuifolius* (Antimalarial compounds from *Goniolothalamus tenuifolius*) อ. ที่ปรึกษา : ผศ.ดร. กิตติศักดิ์ ลิขิตวิทยาวุฒิ, อ. ที่ปรึกษาร่วม : ผศ. วิเชียร จงบุญประเสริฐ และรศ.ดร. จิระพันธ์ กริ่งไกร, 172 หน้า. ISBN 974-636-392-1

การค้นหาสารต้านมาลาเรียจาก *Goniolothalamus tenuifolius* สามารถแยกได้ aristolactam alkaloids จำนวน 4 ชนิด ได้แก่ aristolactam BI, aristolactam BII, velutinam, และ ariatolactam AII นอกจากนี้ยังได้แยกสารในกลุ่ม 4,5-dioxoaporphines จำนวน 1 ชนิด ได้แก่ norcepharadione B และสารอีกหนึ่งชนิดซึ่งมีโครงสร้างสารอนุพันธ์เป็น ethyl ester ของ 2,4-dihydroxy-6-methylbenzoic acid การพิสูจน์เอกลักษณ์ทางกายภาพและการหาสูตรโครงสร้างทางเคมีของสารทั้งหมดนี้ทำโดยวิเคราะห์ข้อมูลจาก spectrum ของ UV, IR, MS and NMR นอกจากนี้ยังได้ศึกษาคุณสมบัติทาง NMR ของคาร์บอนทุกอะตอมในสารเคมีที่แยกได้ การศึกษาฤทธิ์ต้านมาลาเรียจากเชื้อ *Plasmodium falciparum* T₉₀₄ ของสารเคมีที่สกัดโดยใช้วิธี radioisotope microdilution technique พบว่าสารอนุพันธ์ ethyl ester ของ 2,4-dihydroxy-6-methylbenzoic acid, aristolactam BI, aristolactam BII, velutinam, aristolactam AII และ norcepharadione B แสดงฤทธิ์ต้านมาลาเรียโดยมีค่า EC₅₀ = 33, 10.5, 11, 7.5, 7.5 and 9.5 µg/ml ตามลำดับ เมื่อเปรียบเทียบกับ chloroquine และ pyrimethamine ซึ่งมีค่า EC₅₀ = 0.03 และ 2.8 µg/ml ตามลำดับ การศึกษาฤทธิ์ต้านมาลาเรียของสารกลุ่ม aristolactam alkaloids ไม่เคยมีผู้ได้ศึกษามาก่อน งานวิจัยชิ้นนี้นับเป็นรายงานชิ้นแรก

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..... 

C875365 : MAJOR PHARMACOGNOSY

KEY WORD: ANTIMALARIAL / *GONIOTHALAMUS TENUIFOLIUS* / ARISTOLACTAM

LALITA WIRASATHIEN : ANTIMALARIAL COMPOUNDS FROM
GONIOTHALAMUS TENUIFOLIUS. THESIS ADVISOR : ASSISTANT PROFESSOR
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PROFESSOR JERAPAN KRUNGKRAI, Ph.D. 172 pp. ISBN 974-636-392-1

In the search for antimalarial compounds from *Goniothalamus tenuifolius*, four aristolactam alkaloids, namely aristolactam BI, aristolactam BII, velutinam and aristolactam AII were isolated along with a 4,5-dioxoaporphine alkaloid named norcepharadione B, and an ethyl ester of 2,4-dihydroxy-6-methylbenzoic acid. The structure identifications of all of the isolated compounds, including their unequivocal ^{13}C NMR assignments, were achieved by analysis of their UV, IR, MS and NMR data. All compounds were evaluated for their antimalarial activity against *Plasmodium falciparum* T₉₇₉₄ by radioisotope microdilution technique. The ethyl ester of 2,4-dihydroxy-6-methylbenzoic acid, aristolactam BI, aristolactam BII, velutinam, norcepharadione B and aristolactam AII showed EC₅₀ values of 33, 10.5, 11, 7.5, 7.5 and 9.5 $\mu\text{g/ml}$, respectively, whereas those of chloroquine and pyrimethamine were 0.03 and 2.8 $\mu\text{g/ml}$, respectively. This investigation is the first report of antimalarial activity of aristolactam alkaloids.

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ACKNOWLEDGEMENTS

I wish to express my deepest appreciation and grateful thank to my thesis advisor, Assistant Professor Kittisak Likhitwitayawuid of the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University for his concern, encouragement and valuable advice throughout my period of study.

I would like to express my grateful thank to my co-advisor, Associate Professor Jerapan Krungkrai of the Department of Biochemistry, Faculty of Medicine, Chulalongkorn University for his valuable advice. I also thank Mrs. Sudarat Krungkrai for her concern and valuable suggestions.

I would like to express my gratitude to my co-advisor, Assistant Professor Vichien Jongboonprasert of the Department of Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University for the plant collection and botanical verification.

I would like to thank the thesis committee for their kind attention and useful advice.

I am very grateful to Professor Norio Aimi, Associate Professor Hiromitsu Takayama and Assistant Professor Mariko Kitajima of the Laboratory of Molecular Structure and Biological Function, Faculty of Pharmaceutical Sciences, Chiba University, Japan, for their helpful assistance in NMR experiments, their concerns and valuable advice. I also thank several Ph.D. students at Chiba University for their assistance in EIMS experiments and useful advice.

I would like to thank the University Development Commission (UDC) and Faculty of Pharmaceutical Sciences, Srinakharinwirot University, for the scholarship throughout my two years of study.

I would like to thank the Graduate School of Chulalongkorn University for granting partial support to conduct this investigation.

Finally, I wish to express my infinite gratitude to my family and my friends for their love, understanding and encouragement.



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สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

LIST OF ABBREVIATIONS

br	=	broad (for NMR spectra)
°C	=	degree Celcius
chloroform- <i>d</i>	=	deuterated chloroform
cpm	=	count per minute
cm	=	centimeter
¹³ C NMR	=	carbon-13 nuclear magnetic resonance
d	=	doublet (for NMR spectra)
dd	=	doublet of doublets (for NMR spectra)
ddd	=	doublet of doublets of doublets (for NMR spectra)
DEPT	=	Distortionless Enhancement by Polarization Transfer
DMSO	=	dimethylsulfoxide
DMSO- <i>d</i> ₆	=	deuterated dimethylsulfoxide
δ	=	chemical shift
EIMS	=	Electron Impact Mass Spectrum
EC ₅₀	=	effective concentration at 50 % inhibition of parasite growth
g	=	gram
μg	=	microgram
h	=	hour
¹ H NMR	=	Proton Nuclear Magnetic Resonance
HMBC	=	¹ H-detected Heteronuclear Multiple Bond Coherence
HMQC	=	¹ H-detected Heteronuclear Multiple Quantum Coherence
HSQC	=	¹ H-detected Heteronuclear Single Quantum Coherence
Hz	=	hertz
IR	=	Infrared spectrum
<i>J</i>	=	coupling constant
kg	=	kilogram

L	=	Liter
μl	=	microliter
λ_{max}	=	wavelength at maximal absorption
ε	=	molar absorptivity
M⁺	=	molecular ion
mg	=	milligram
mCi	=	millicurie
ml	=	milliliter
MHz	=	megahertz
min	=	minute
m/z	=	mass to charge ratio
MS	=	mass spectrometry
nm	=	nanometer
NMR	=	Nuclear Magnetic Resonance
NOE	=	Nuclear Overhauser Effect
NOESY	=	Nuclear Overhauser Effect Correlation Spectroscopy
ppm	=	part per million
pyridine-<i>d</i>₅	=	deuterated pyridine
ν_{max}	=	wave number at maximal absorption
s	=	singlet (for NMR spectra)
TLC	=	Thin Layer Chromatography
UV	=	ultraviolet