

องค์ประกอบทางเคมีที่มีฤทธิ์ทางชีวภาพจากนมแมวป่าและงาเงาะ



นางสาว ลลิตา วีระเสถียร

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต

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BIOACTIVE CHEMICAL CONSTITUENTS FROM *ELLIPEIOPSIS CHERREVENSIS* AND
STELECHOCARPUS CAULIFLORUS

Miss Lalita Wirasathien

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By Miss Lalita Wirasathien

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Thesis Advisor Associate Professor Rutt Suttisri, Ph.D.

Thesis Co-Advisor Associate Professor Thitima Pengsuparp, Ph.D.

Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn University in Partial Fulfillment of the Requirements for the Doctor's Degree

.....*Pornpen Premyothin*.....Dean of the Faculty of Pharmaceutical Sciences
(Associate Professor Pornpen Premyothin, Ph.D.)

THESIS COMMITTEE

.....*Ekarin Saifah*.....Chairman
(Associate Professor Ekarin Saifah, Ph.D.)

.....*Rutt Suttisri*.....Thesis Advisor
(Associate Professor Rutt Suttisri, Ph.D.)

.....*Thitima Pengsuparp*.....Thesis Co-Advisor
(Associate Professor Thitima Pengsuparp, Ph.D.)

.....*K. Likhit*.....Member
(Associate Professor Kittisak Likhitwitayawuid, Ph.D.)

.....*VARIMA WONGPANICH*.....Member
(Varima Wongpanich, Ph.D.)

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การศึกษาองค์ประกอบทางเคมีจากใบและต้นของนมแมวป่า (วงศ์ Annonaceae) สามารถแยกสารในกลุ่ม polyoxygenated cyclohexene จำนวน 3 ชนิด คือ ferrudiol, zeylenol และสารอนุพันธ์ชนิดใหม่ คือ ellipsepsol D พร้อมกับ สารในกลุ่ม flavonoid glycoside จำนวน 2 ชนิด คือ tiliroside และ kaempferol-3-*O*-rutinoside รวมทั้งสารกลุ่ม chalcone ที่พบในธรรมชาติเป็นครั้งแรก คือ 2',4'-dihydroxy-3'-(2-hydroxybenzyl)-6'-methoxychalcone และ สารในกลุ่ม alkaloid จำนวน 1 ชนิด คือ lanuginosine สำหรับการศึกษายาองค์ประกอบทางเคมีจากใบและต้นของงำเงาะซึ่งเป็นพืชอีกชนิดหนึ่งในวงศ์ Annonaceae สามารถแยกสารในกลุ่ม lignan จำนวน 4 ชนิด คือ galgravin, licarin A, acuminatin และสารผสมระหว่าง veraguensin และ galgravin ในอัตราส่วน 2:1 พบสารในกลุ่ม alkaloid จำนวน 4 ชนิด คือ aristolactam AII, piperolactam A, piperolactam D และ noraristolodione สารในกลุ่ม flavonoid จำนวน 2 ชนิด คือ engeletin และ astilbin นอกจากนี้ยังพบสารในกลุ่ม sesquiterpene จำนวน 1 ชนิด คือ spathulenol การพิสูจน์โครงสร้างทางเคมีของสารทั้งหมดที่สกัดแยกได้โดยอาศัยการวิเคราะห์เชิงสเปกตรัมของ UV, IR, MS และ NMR ร่วมกับการเปรียบเทียบข้อมูลของสารที่เคยมีการรายงานมาแล้ว พบว่า 2',4'-dihydroxy-3'-(2-hydroxybenzyl)-6'-methoxychalcone, licarin A, piperolactam D แสดงฤทธิ์ต้านวัณโรค ฤทธิ์ต้านไวรัสเริม และฤทธิ์ความเป็นพิษต่อเซลล์มะเร็ง ซึ่งสาร chalcone ชนิดนี้ยังสามารถแสดงฤทธิ์ต้านมาลาเรียด้วย และพบว่า acuminatin แสดงฤทธิ์ต้านวัณโรคและฤทธิ์ความเป็นพิษต่อเซลล์มะเร็ง ในขณะที่ galgravin แสดงฤทธิ์ต้านเชื้อวัณโรคและไวรัสเริม นอกจากนี้ tiliroside, kaempferol-3-*O*-rutinoside, ferrudiol และ zeylenol สามารถกระตุ้นการเพิ่มจำนวนของ lymphocyte ได้ และจากกระบวนการสกัดแยกสารโดยอ้างอิงฤทธิ์ทางชีวภาพ พบว่า engeletin และ astilbin สามารถยับยั้งเอนไซม์ aldose reductase และยับยั้งการสร้าง Advance Glycation End Products ได้

สาขาวิชาเภสัชเคมีและผลิตภัณฑ์ธรรมชาติ

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OXOAPORPHINES

LALITA WIRASATHIEN: BIOACTIVE CHEMICAL CONSTITUENTS FROM
ELLIPEIOPSIS CHERREVENSI AND *STELECHOCARPUS CAULIFLORUS*.

THESIS ADVISOR: ASSOC. PROF. RUTT SUTTISRI, Ph.D., THESIS CO-ADVISOR:
ASSOC. PROF. THITIMA PENGSUPARP, Ph.D., 290 pp. ISBN 974-14-3303-4

Chemical investigation of the aerial parts of *Ellipeiopsis cherrevensis* R. E. Fr. (family Annonaceae) led to the isolation of three polyoxygenated cyclohexenes namely ferrudiol and zeyleol and a new derivative, ellipseiopsol D, along with two flavonoid glycosides, tiliroside and kaempferol-3-*O*-rutinoside, as well as a new natural chalcone, 2',4'-dihydroxy-3'-(2-hydroxybenzyl)-6'-methoxychalcone and one alkaloid, lanuginosine. From the leaves and stems of another annonaceous plant, *Stelechocarpus cauliflorus* R. E. Fr., four lignans namely galgravin, licarin A, acuminatin, and a 2:1 mixture of veraguensin and galgravin, four aporphine alkaloids which are aristolactam AII, piperolactams A and D and noraristolodione, two flavonoids namely engeletin and astilbin, together with one sesquiterpenoid, spathulenol, were isolated. The structure determination of these compounds was accomplished by spectroscopic methods, including UV, IR, MS and NMR, and comparison with previously reported data. 2',4'-Dihydroxy-3'-(2-hydroxybenzyl)-6'-methoxychalcone, licarin A and piperolactam D exhibited antituberculosis, anti HSV-1 and cytotoxic activities, whereas the chalcone also showed antimalarial activity. Acuminatin displayed antituberculosis and cytotoxic activities, while galgravin exhibited antituberculosis and anti HSV-1 activities. Tiliroside, kaempferol-3-*O*-rutinoside, ferrudiol and zeyleol were all able to stimulate lymphocyte proliferation, whereas the latter two cyclohexenes also showed anti HSV-1 and antituberculosis activities. In addition, bioactivity-guided fractionation yielded engeletin and astilbin as inhibitors of aldose reductase enzyme and Advance Glycation End Products formation.

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Student's signature... Lolita Wirasathien

Advisor's signature... Rutt Suttisri

Co-advisor's signature... T. Pengsuparp

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LIST OF ABBREVIATIONS AND SYMBOLS

$[\alpha]^{25}_D$	=	Specific rotation at 25° and sodium D line (589 nm)
α	=	Alpha
Acetone- d_6	=	Deuterated acetone
AGEs	=	Advanced glycation endproducts
AR	=	Aldose reductase
β	=	Beta
Bn	=	Benzyl
br	=	Broad (for NMR spectra)
BSA	=	Bovine serum albumin
Bu	=	Butyl
BuOH	=	Butanol
Bz	=	Benzoyl
c	=	Concentration
°C	=	Degree Celsius
calcd	=	Calculated
$CDCl_3$	=	Deuterated chloroform
CFU	=	Colony forming unit
$CHCl_3$	=	Chloroform
CH_2Cl_2	=	Dichloromethane
CIMS	=	Chemical ionization mass spectrometry
cm	=	Centimetre
cm^{-1}	=	Reciprocal centimeter (unit of wave number)
^{13}C NMR	=	Carbon-13 Nuclear Magnetic Resonance
Con A	=	Concanavalin A
2D NMR	=	Two dimensional 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	=	Dimethyl sulfoxide
DMSO- d_6	=	Deuterated dimethyl sulfoxide

δ	=	Chemical shift
ϵ	=	Molar absorptivity
ED ₅₀	=	Median effective dose
EIMS	=	Electron Impact Mass Spectrometry
ESIMS	=	Electrospray Ionization Mass Spectrometry
ESITOFMS	=	Electrospray Ionization Time of Flight Mass Spectrometry
EtOAc	=	Ethyl acetate
em.	=	emission
ex.	=	excitation
g	=	Gram
hr	=	Hour
¹ H NMR	=	Proton Nuclear Magnetic Resonance
¹ H- ¹ H COSY	=	Homonuclear (Proton-Proton) Correlation Spectroscopy
HMBC	=	¹ H-detected Heteronuclear Multiple Bond Coherence
HMQC	=	¹ H-detected Heteronuclear Multiple Quantum Coherence
HPLC	=	High Pressure Liquid Chromatography
H ₂ O	=	Water
HREIMS	=	High Resolution Electron Impact Mass Spectrometry
HRESIMS	=	High Resolution Electrospray Ionization Mass Spectrometry
HSQC	=	Heteronuclear Single Quantum Correlation
Hz	=	Hertz
IC ₅₀	=	Median Inhibitory Concentration
IR	=	Infrared Spectrum
<i>J</i>	=	Coupling constant
KBr	=	Potassium bromide
Kg	=	Kilogram
L	=	Liter
Me	=	Methyl
μ g	=	Microgram
μ g/ml	=	Microgram per milliliter
μ Ci	=	Micro
μ l	=	Microliter
μ M	=	Micromolar

λ_{\max}	=	Wavelength at maximal absorption
ϵ	=	Molar absorptivity
$[M]^+$	=	Molecular ion
m	=	Metre
<i>m</i>	=	Multiplet (for NMR spectra)
$[M+H]^+$	=	Protonated molecular ion
MeOH	=	Methanol
mg	=	Milligram
MHz	=	Megahertz
MIC	=	Minimum inhibitory concentration
min	=	Minute
ml	=	Milliliter
mM	=	Millimolar
mm	=	Millimeter
mp	=	Melting point
MS	=	Mass Spectrometry
MW	=	Molecular weight
<i>m/z</i>	=	Mass to charge ratio
NaCl	=	Sodium chloride
nm	=	Nanometer
NMR	=	Nuclear Magnetic Resonance
NOESY	=	Nuclear Overhauser Enhancement Spectroscopy
OBz	=	Benzoyloxy
OD	=	Optical Density
PBS	=	Phosphate Buffer Saline
Ph	=	Phenyl
ppm	=	Part-per-million
prep HPLC	=	Preparative High Pressure Liquid Chromatography
<i>s</i>	=	Singlet (for NMR spectra)
ν_{\max}	=	Wave number at maximal absorption
rpm	=	round per minute
SI	=	Stimulation Index
SIMS	=	Secondary Ion Mass Spectrometry

TFA	=	Trifluoroacetic acid
THF	=	Tetrahydrofuran
TLC	=	Thin Layer Chromatography
UV	=	Ultraviolet