ฟลาโวนอยด์ที่มีฤทธิ์ทางชีวภาพจากเมล็ดมันแกวและเปลือกต้นขะเจาะ

นางสาว อำไพ พฤติวรพงศ์กุล

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BIOACTIVE FLAVONOIDS FROM *PACHYRRHIZUS EROSUS* SEEDS AND *MILLETTIA LEUCANTHA* VAR. *LEUCANTHA* STEM BARK

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Thesis Title	Bioactive flavonoids from *Pachyrrhizus erosus* seeds and *Millettia leucantha* var. *leucantha* stem bark
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อำไพ พฤติวรพงศ์กุล: ฟลาโวนอยด์ที่มีฤทธิ์ทางชีวภาพจากเมล็ดมันแกวและเปลือกต้นขะเจาะ (BIOACTIVE FLAVONOIDS FROM *PACHYRRHIZUS EROSUS* SEEDS AND *MILLETTIA LEUCANTHA* VAR. *LEUCANTHA* STEM BARK) อาจารย์ที่ปรึกษา: รศ. ดร. นิจศิริ เรืองรังษี, อาจารย์ที่ปรึกษาร่วม: รศ. ดร. วิมลมาศ ลิปิพันธ์, PROFESSOR DR. TSUTOMU ISHIKAWA, 221 หน้า. ISBN 974-17-2001-7

จากการศึกษาทางพฤกษเคมีของเมล็ดมันแกว สามารถแยกสารที่เคยมีรายงานมาแล้วได้ทั้งหมด 8 ชนิด คือ dehydroneotenone, dolineone, (+)-12a-hydroxydolineone, (+)-12a-hydroxypachyrrhizone, (-)-12a-hydroxyrotenone, neotenone, pachyrrhizin และ (+)-pachyrrhizone และได้ทำการพิสูจน์พร้อมทั้งรายงานตำแหน่งทาง NMR ของสารที่แยกได้อย่างสมบูรณ์ สำหรับการศึกษาทางพฤกษเคมีของเปลือกต้นขะเจาะสามารถแยกสารได้ 11 ชนิดซึ่งเป็นสารใหม่ 2 ชนิด คือ 2,4,6,β-tetramethoxy-3',4'-methylenedioxychalcone และ 2',4',6'-trimethoxy-3,4-methylene dioxydihydrochalcone และสารที่พบครั้งแรกในธรรมชาติอีก 2 ชนิด คือ 2',4'-dimethoxy-3,4-methylenedioxychalcone และ 2',4',6'-trimethoxy-3,4-methylenedioxychalcone นอกจากนี้ยังพบสารที่มีรายงานมาแล้วอีก 7 ชนิด ได้แก่ desmethoxykanugin, dihydromilletenone methyl ether, 2'-hydroxy-3,4,4',6'-tetramethoxychalcone, karanjin, lanceolatin B, 3',4'-methylenedioxy-5,7-dimethoxyflavone และ 3',4'-methylenedioxy-7-methoxyflavone การพิสูจน์โครงสร้างทางเคมีของสารทั้งหมดที่แยกได้อาศัยการวิเคราะห์เชิงสเปคตรัมของ UV, IR, MS และ NMR ร่วมกับการเปรียบเทียบข้อมูลของสารที่ทราบโครงสร้างแล้ว นอกจากนี้ ยังได้นำสารที่แยกได้ไปทดสอบฤทธิ์ทางชีวภาพ ได้แก่ ฤทธิ์ต้านจุลชีพ, ฤทธิ์ต้านไวรัสเริม, ฤทธิ์ยับยั้งเอนไซม์ cyclooxygenase-2 และฤทธิ์ความเป็นพิษต่อเซลล์ พบว่า (+)-12a-hydroxydolineone และ (+)-12a-hydroxypachyrrhizone จากเมล็ดมันแกว และ dihydromilletenone methyl ether และ 2',4',6'-trimethoxy-3,4-methylene dioxydihydrochalcone จากเปลือกต้นขะเจาะมีฤทธิ์ปานกลางในการยับยั้งเชื้อไวรัสเริม ขณะที่ desmethoxykanugin มีฤทธิ์ปานกลางในการยับยั้งเอนไซม์ cyclooxygenase-2 และยังพบว่า 2',4'-dimethoxy-3,4-methylenedioxychalcone และ 2',4',6'-trimethoxy-3,4-methylenedioxychalcone มีฤทธิ์เป็นพิษต่อเซลล์มะเร็ง NCI-H460 อย่างมีนัยสำคัญ ส่วนการตรวจสอบฤทธิ์ต้านจุลชีพนั้นพบว่า ไม่มีสารใดแสดงความสามารถในการต้านการเจริญของจุลชีพทดสอบ

ภาควิชาเภสัชเวท
สาขาวิชาเภสัชเคมีและผลิตภัณฑ์ธรรมชาติ
ปีการศึกษา 2545

ลายมือชื่อนิสิต.....
ลายมือชื่ออาจารย์ที่ปรึกษา.....
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

4176961933 MAJOR: PHARMACEUTICAL CHEMISTRY AND NATURAL PRODUCTS
KEY WORD: *PACHYRRHIZUS EROSUS*/ *MILLETTIA LEUCANTHA*/ FLAVONOIDS/ ANTI-HERPES SIMPLEX VIRUS ACTIVITY/ CYCLOOXYGENASE-2 INHIBITORY ACTIVITY/ CYTOTOXIC ACTIVITY

AMPAI PHRUTIVORAPONGKUL: BIOACTIVE FLAVONOIDS FROM *PACHYRRHIZUS EROSUS* SEEDS AND *MILLETTIA LEUCANTHA* VAR. *LEUCANTHA* STEM BARK. THESIS ADVISOR: ASSOCIATE PROFESSOR NIJSIRI RUANGRUNGSI, Ph.D., THESIS CO-ADVISOR: ASSOCIATE PROFESSOR VIMOLMAS LIPIPUN, Ph.D., PROFESSOR TSUTOMU ISHIKAWA, Ph.D., 221 pp. ISBN 974-17-2001-7

Phytochemical study on the seeds of *Pachyrrhizus erosus* revealed the presence of eight known compounds including dehydroneotenone, (+)-dolineone, (+)-12a-hydroxydolineone, (+)-12a-hydroxypachyrrhizone, (-)-12a-hydroxyrotenone, neotenone, pachyrrhizin and (+)-pachyrrhizone. All isolates were identified and completed ^{1}H- and ^{13}C-NMR data. Additionally, eleven compounds were obtained from the phytochemical investigation of the stem bark of *Millettia leucantha* var. *leucantha*. These included two new compounds, 2,4,6,β-tetramethoxy-3',4'-methylenedioxychalcone and 2',4',6'-trimethoxy-3,4-methylenedioxydihydrochalcone, two new natural products, 2',4'-dimethoxy-3,4-methylenedioxychalcone and 2',4',6'-trimethoxy-3,4-methylenedioxychalcone, and other seven known compounds, namely desmethoxykanugin, dihydromilletenone methyl ether, 2'-hydroxy-3,4,4',6'-tetramethoxychalcone, karanjin, lanceolatin B, 3',4'-methylenedioxy-5,7-dimethoxyflavone and 3',4'-methylenedioxy-7-methoxyflavone. The structure determination of all isolates were accomplished by spectroscopic analyses (UV, IR, MS and NMR) and compared with the literary data of known compounds. The isolated compounds were also subjected for biological activities evaluation, involving antimicrobial, anti-Herpes Simplex Virus (HSV), cyclooxygenase-2 (COX-2) inhibitory and cytotoxic activities. (+)-12a-Hydroxydolineone and (+)-12a-hydroxypachyrrhizone from *P. erosus*, and dihydromilletenone methyl ether and 2',4',6'-trimethoxy-3,4-methylenedioxydihydrochalcone from *M. leucantha* showed moderate anti-HSV activity, whereas desmethoxykanugin demonstrated moderate COX-2 inhibitory activity. Furthermore, 2',4'-dimethoxy-3,4-methylenedioxychalcone and 2',4',6'-trimethoxy-3,4-methylenedioxychalcone showed significant cytotoxic activity against NCI-H460 cell line. This work verified that no isolated compound showed antimicrobial activity.

Field of Study Pharmaceutical Chemistry and Natural Products
Academic year 2002

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LIST OF ABBREVIATIONS AND SYMBOLS

α	=	Alpha
$[\alpha]^{27}_{D}$	=	Specific rotation at 27° and sodium D line (589 nm)
β	=	Beta
BSA	=	Bovine serum albumin
°C	=	Degree Celsius
calcd	=	Calculated
CA	=	Chemical Abstract
CC_{50}	=	50% Cytotoxic Concentration
$CDCl_3$	=	Deuterated chloroform
C_5D_5N	=	Deuterated pyridine
CF_3COOH	=	Trifluoroacetic acid
CFU	=	Colony forming unit
$CHCl_3$	=	Chloroform
CH_2Cl_2	=	Dichloromethane
cm^{-1}	=	Reciprocal centimeter (unit of wave number)
^{13}C NMR	=	Carbon-13 Nuclear Magnetic Resonance
CO_2	=	Carbon dioxide
COX	=	Cyclooxygenase
COX-1	=	Cyclooxygenase-1
COX-$1^{-/-}$	=	Cyclooxygenase-1 null cell
COX-2	=	Cyclooxygenase-2
COX-$2^{-/-}$	=	Cyclooxygenase-1 null cell
CPMA	=	Count per minute average
2-D NMR	=	Two Dimensional Nuclear Magnetic Resonance
d	=	Doublet (for NMR spectra)
dd	=	Doublet of doublets (for NMR spectra)
DEPT	=	Distortionless Enhancement by Polarization Transfer
DMEM	=	Dulbecco's modified medium
DMSO	=	Dimethyl sulfoxide
DMSO-d_6	=	Deuterated dimethyl sulfoxide
δ	=	Chemical shift

LIST OF ABBREVIATIONS AND SYMBOLS (continued)

EIMS	=	Electron Impact Mass Spectrometry
ESIMS	=	Electrospray Ionization Mass Spectrometry
EtOAc	=	Ethyl acetate
EtOH	=	Ethanol
Et_3SiH	=	Triethylsilane
g	=	Gram
GC	=	Gas Chromatography
hr	=	Hour
^1H NMR	=	Proton Nuclear Magnetic Resonance
HMBC	=	^1H-detected Heteronuclear Multiple Bond Coherence
HMQC	=	^1H-detected Heteronuclear Multiple Quantum Coherence
^3H-PGE_2	=	Tritium prostaglandin E_2
H_2O	=	Water
HRFABMS	=	High Resolution Fast Atom Bombardment Mass Spectrometry
HSV-1	=	Herpes Simplex Virus type 1
HSV-2	=	Herpes Simplex Virus type 2
Hz	=	Hertz
IC_{50}	=	Median Inhibitory Concentration
IR	=	Infrared Spectrum
J	=	Coupling constant
Kg	=	Kilogram
KH_2PO_4	=	Potassium biphosphate
K_2HPO_4	=	Potassium phosphate
l	=	Liter
μg	=	Microgram
μl	=	Microliter
μM	=	micromolar
λ_{max}	=	Wavelength at maximal absorption
ε	=	Molar absorptivity

LIST OF ABBREVIATIONS AND SYMBOLS (continued)

M^+	=	Molecular ion
m	=	Multiplet (for NMR spectra)
MHA	=	Mueller Hinton agar
MeOH	=	Methanol
mg	=	Milligram
$[M+H]^+$	=	Protonated molecular ion
MHz	=	Megahertz
min	=	Minute
ml	=	Milliliter
MW	=	Molecular weight
m/z	=	Mass to charge ratio
MS	=	Mass Spectrometry
NaCl	=	Sodium chloride
$NaHCO_3$	=	Sodium bicarbonate
nm	=	Nanometer
NMR	=	Nuclear Magnetic Resonance
NOE	=	Nuclear Overhauser Effect
NS-398	=	N-(2-[Cyclohexyloxy]-4-nitrophenyl)methanesulfonamide
NSS	=	Normal saline solution
PFU	=	Plaque forming unit
PGE_2	=	Prostaglandin E_2
ppm	=	Part per million
pyridine-d_5	=	Deuterated pyridine
RIA	=	Radioimmunoassay
SDA	=	Sabouraud dextrose agar
spp.	=	Species
ν_{max}	=	Wave number at maximal absorption
s	=	Singlet (for NMR spectra)
TLC	=	Thin Layer Chromatography
UV-VIS	=	Ultraviolet and Visible Spectrophotometry