

องค์ประกอบทางเคมีและฤทธิ์ทางชีวภาพของเนื้อไม้ชิงชัน *Dalbergia oliveri*
และการสังเคราะห์ไอโซฟลาโวนอยด์ที่คัดเฉพาะ



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CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF THE
HEARTWOODS OF *Dalbergia oliveri* AND THE SYNTHESIS
OF SELECTED ISOFLAVONOIDS

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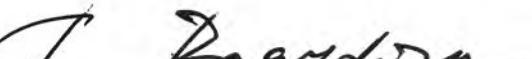
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สุจิตตรา ดีเสมอ : องค์ประกอบทางเคมีและฤทธิ์ทางชีวภาพของเนื้อไม้ชิงชัน *Dalbergia oliveri* และการสังเคราะห์ไอโซฟลาโวนอยด์ที่คัดเฉพาะ (CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF THE HEARTWOODS OF *Dalbergia oliveri* AND THE SYNTHESIS OF SELECTED ISOFLAVONOIDS) อ. ที่ปรึกษา: ศ. ดร. อุตุน กึกผล, อ. ที่ปรึกษาร่วม: ผศ. ดร. วรินทร ชาวศิริ, 198 หน้า. ISBN 974-14-3377-8.

ผลการศึกษาฤทธิ์ทางชีวภาพเบื้องต้นแสดงให้เห็นว่าสิ่งสกัดของเนื้อไม้ชิงชันแสดงฤทธิ์ด้านอนุมูลอิสระ DPPH การศึกษาองค์ประกอบทางเคมีของสิ่งสกัดดังกล่าว แยกสารได้ 3 ชนิดจากสิ่งสกัดเซกเชน ได้แก่ คิโนโน่ต์ตองชนิดอ่อนดัว ของพสมของ triterpenoid ester และ stigmasterol และสารบิสูที 8 ชนิดจากสิ่งสกัดไดคลอโรเมเทน ในขณะที่องค์ประกอบส่วนใหญ่ในสิ่งสกัด เอทิลแอลเซ็ตเดทที่ได้เหมือนกับที่พบในสิ่งสกัดไดคลอโรเมเทน โดยอาศัยสมบัติทางกายภาพและ สเปกโทรสโคปีพบว่าโครงสร้างของสารที่แยกได้คือ *trans-cinnamic acid*, (+)-pterocarpin, (+)-medicarpin, (+)-3,4-*trans*-[3-hydroxy-9-methoxypterocarpan-8-yl]-2',7-dihydroxy-4'-methoxyisoflavan, (\pm)-mucronulatol, formononetin, (\pm)-violanone และ calycosin (+)-medicarpin ซึ่งเป็นองค์ประกอบหลักแสดงฤทธิ์ยับยั้งเชื้อร้า *Fusarium oxysporum* และ *Alternaria brassicicola* และแสดงฤทธิ์ความเป็นพิษต่อเซลล์มะเร็งตับ (+)-pterocarpin และฤทธิ์ความเป็นพิษต่อเซลล์มะเร็งตับด้วยค่า IC_{50} เท่ากับ 2.3 $\mu\text{g/mL}$ นอกจากนี้ (\pm)-mucronulatol และฤทธิ์ด้านอนุมูลอิสระ DPPH ในระดับสูง เช่นเดียวกับฤทธิ์ยับยั้งเชื้อร้า *F. oxysporum* นอกจากนี้ (\pm)-violanone ยังแสดงความเป็นพิษต่อหนอนไข้ผักและลูกน้ำยุงลายด้วยค่า LC_{50} เท่ากับ 92 and 121 ppm ตามลำดับ

ได้สังเคราะห์ไอโซฟลาโวนอยด์เป้าหมาย 3 ชนิดใน 8 ขั้นตอนเป็นครั้งแรก โดยใช้ปฏิกิริยา arylation ของ α -phenylthiochroman-4-one กับ aryllead (IV) triacetate รีเอเจนต์ พลิตกัณฑ์รวมของปฏิกิริยาเมื่อเทียบกับสารตั้งต้นของ 3',7-dihydroxy-2',4'-dimethoxy-isoflavone, -isoflavanone และ -isoflavan คือ 9%, 13% และ 8-13% ตามลำดับ นอกจากนี้ การสังเคราะห์ ไอโซฟลาโวนเป้าหมายโดยการเติมคาร์บอน 1 ยูนิต เข้าไปที่ deoxybenzoin (ผ่าน deoxybenzoin) สามารถทำได้สำเร็จใน 10 ขั้นตอนจาก 2,6-dimethoxyphenol ซึ่งให้ผลิตภัณฑ์รวมของปฏิกิริยา 6% 3',7-dihydroxy-2',4'-dimethoxyisoflavan และแสดงฤทธิ์ความเป็นพิษต่อเซลล์ HBL100 ด้วยค่า IC_{50} เท่ากับ 5.21 μM

ภาควิชา.....เคมี.....	ลายมือชื่อนิสิต.....สุจิตตรา.....กีเสมอ.....
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SUJITTRA DEESAMER: CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF THE HEARTWOODS OF *Dalbergia oliveri* AND THE SYNTHESIS OF SELECTED ISOFLAVONOIDs. THESIS ADVISOR: PROF. UDOM KOKPOL, Ph.D., THESIS CO-ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., 198 pp. ISBN 974-14-3377-8.

The preliminary biological activity results pointed out that the extract of *Dalbergia oliveri* G heartwoods exhibited significant scavenging effect on DPPH radical. The chemical constituent investigation led to the isolation of three substances, long chain saturated ketone, a mixture of triterpenoid ester and stigmasterol from the hexane extract and eight pure compounds from CH_2Cl_2 extract. Most chemical constituents in EtOAc extract were similar to those found in CH_2Cl_2 extract. By means of physical properties and spectroscopic evidences, the structures of isolated compounds could be determined as *trans*-cinnamic acid, (+)-pterocarpin, (+)-medicarpin, (+)-3,4-*trans*-[3-hydroxy-9-methoxypterocarpan-8-yl]-2',7-dihydroxy-4'-methoxyisoflavan, (\pm)-mucronulatol, formononetin, (\pm)-violanone and calycosin. Among the isolated substances, (+)-medicarpin, the major component, displayed significant antifungal activity against both *Fusarium oxysporum* and *Alternaria brassicicola* and cytotoxicity toward HepG2 cells. (+)-Pterocarpin presented high cytotoxicity against HepG2 cells with IC_{50} value of 2.3 $\mu\text{g}/\text{mL}$. In addition, (\pm)-mucronulatol exhibited the highest scavenging activity toward DPPH radical as well as the highest antifungal activity against *F. oxysporum*. Moreover, (\pm)-violanone showed significant cytotoxicity against diamondback moth and mosquito larvae with LC_{50} values of 92 and 121 ppm, respectively.

Three target isoflavonoids were accomplished synthesized for the first time in eight steps using arylation of common α -phenylthiochroman-4-one with aryllead (IV) triacetate reagent as a key step. The total yield of 3',7-dihydroxy-2',4'-dimethoxy-isoflavone, -isoflavanone and -isoflavan over eight steps reaction sequence was 9%, 13% and 8-13%, respectively based on the starting material. In addition, the synthesis of desired isoflavone using the addition of a one carbon unit to a deoxybenzoin (*via* deoxybenzoin) was accomplished in ten steps from 2,6-dimethoxyphenol as starting material, giving total yield of 6%. 3',7-Dihydroxy-2',4'-dimethoxyisoflavan displayed high cytotoxicity against HBL100 cells with IC_{50} value of 5.21 μM .

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LIST OF ABBREVIATIONS

BHA	butylated hydroxyanisole
CDCl ₃	deuterated chloroform
CH ₂ Cl ₂	dichloromethane
CHCl ₃	chloroform
cm	centimeter
cm ⁻¹	unit of wavelength
COSY	correlated spectroscopy
d	doublet (NMR)
dd	doublet of doublet (NMR)
ddd	doublet of doublet of doublet (NMR)
DMSO	dimethylsulfoxide
DPPH	2,2-diphenyl-1-picrylhydrazine
EtOAc	ethyl acetate
EtOH	ethanol
FT	fourier transform
g	gram (s)
h	hour
HMBC	heteronuclear multiple bond correlation experiment
HSQC	heteronuclear multiple quantum coherence experiment
Hz	hertz
IR	infrared
J	coupling constant
m	multiplet (NMR)
mg	milligram (s)
mL	milliliter
mm	millimeter
m.p.	melting point
m/z	mass to charge ratio
M ⁺	molecular ion
MeOH	methanol
MS	mass spectrometry

MW	molecular weight
nm	nanometer (s)
NOE DIFF	nuclear overhauser effect difference
NMR	nuclear magnetic resonance
ppm	part per million
R _f	retardation factor
s	singlet (NMR)
t	triplet (NMR)
TLC	thin layer chromatography
UV	ultraviolet
wt	weight
λ	wavelength
δ	chemical shift
μg	microgram (s)
μM	micromolar
%	percent
°C	degree Celsius