

ห้องสมุดงานวิจัย สำนักงานคณะกรรมการการวิจัยแห่งชาติ



E46273

CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF  
*Amomum uliginosum* RHIZOMES

WANNAPORN CHATE

MASTER OF SCIENCE  
IN CHEMISTRY

THE GRADUATE SCHOOL  
CHIANG MAI UNIVERSITY  
OCTOBER 2011

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**A THESIS SUBMITTED TO THE GRADUATE SCHOOL IN  
PARTIAL FULFILLMENT OF THE REQUIREMENTS  
FOR THE DEGREE OF  
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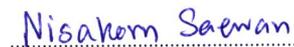
THIS THESIS HAS BEEN APPROVED  
TO BE A PARTIAL FULFILLMENT OF THE REQUIREMENTS  
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IN CHEMISTRY

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27 October 2011

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Wannaporn Chate

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### ABSTRACT

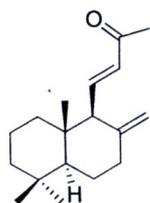
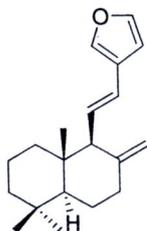
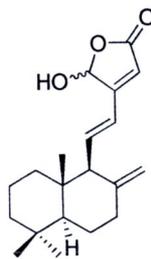
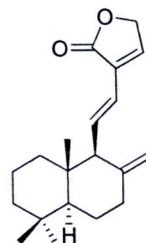
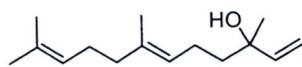
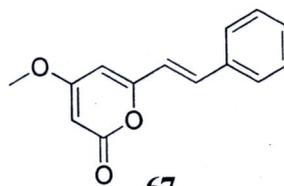
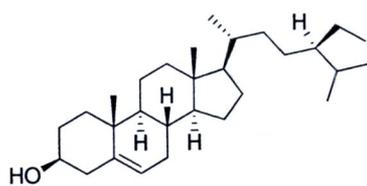
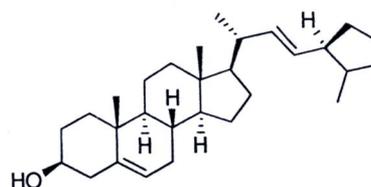
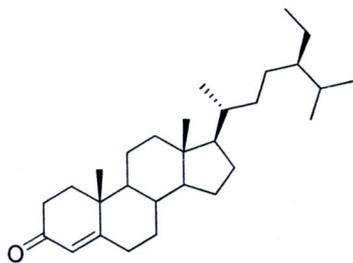
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Phytochemical investigation of the rhizomes of *Amomum uliginosum* resulted in the isolation of four labdane diterpenes ; *E*-15,16-bisnorlabda-8 (17),11-diene-13-one (**27**), coronarin E (**61**), 16-hydroxylabda-8 (17), 11, 13-trien-15, 16-olide (**65**) and villosin (**66**), one sesquiterpenoids; (+)-nerolidol (**21**), one stilbene; 5,6-dehydrokawain (**67**) and two steroids; mixture of  $\beta$ -sitosterol (**62**) and stigmasterol (**63**) and stigmast-4-en-3-one (**64**). Their structures were identified by comparison of spectroscopic and some physical data with those of the reported compounds. All identified compounds were reported for the first time in this plant.

Compounds **27**, **61**, **65** and **66** were tested for antimycobacterial and cytotoxic activities against human oral epidermoid carcinoma (KB), human breast cancer (BC), human small cell lung cancer (NCI-H187) and noncancerous Vero cells. Among the tested compounds, **65** and **61** exhibited moderate activity against *Mycobacterial tuberculosis* with MIC values of 6.25 and 12.50  $\mu\text{g/mL}$ , respectively. For cytotoxic activity, compounds **66** and **65** showed potent activity against the NCI-H187 cells with  $\text{IC}_{50}$  values of 0.12 and 0.72  $\mu\text{g/mL}$ , respectively. Compound **65** also exhibited

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the highest activity against the KB and BC cells with  $IC_{50}$  values of 0.91 and 2.89  $\mu\text{g/mL}$ , respectively and it appeared to be the most potent compound among all tested. However, compound **65** was very toxic to Vero cells ( $IC_{50}$  5.37  $\mu\text{g/mL}$ ) whereas compound **66** was non-cytotoxic.

**27****61****65****66****21****67****62****63****64**

ชื่อเรื่องวิทยานิพนธ์

องค์ประกอบทางเคมีและฤทธิ์ทางชีวภาพของเหง้า

*Amomum uliginosum*

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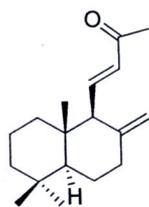
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## บทคัดย่อ

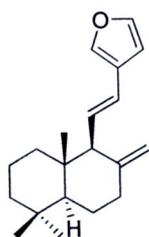
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ในการศึกษาองค์ประกอบทางเคมีจากเหง้ากระวานป่า สามารถแยกสารกลุ่ม labdane diterpenes ได้ 4 ชนิด คือ (*E*)-15,16-bisnorlabda-8(17),11- diene- 13-one (27), coronarin E (61), 16-hydroxylabda-8 (17), 11, 13- trien-15, 16-olide (65) และ villosin (66), กลุ่ม sesquiterpenoids 1 ชนิด คือ (+)-nerolidol (21), กลุ่ม stilbene 1 ชนิด คือ 5,6-dehydrokawain (67) และ กลุ่มสเตอรอยด์ 2 ชนิด คือ สารผสมของ  $\beta$ -sitosterol (62) และ stigmasterol (63) และ stigmast-4-en-3-one (64) โครงสร้างของสารได้จากการเปรียบเทียบข้อมูลทางสเปกโทรสโกปี และข้อมูลทางกายภาพกับข้อมูลของสารที่มีการรายงานไว้แล้ว โดยสารที่แยกได้ทั้งหมดเพิ่งมีการรายงานเป็นครั้งแรกในพืชชนิดนี้

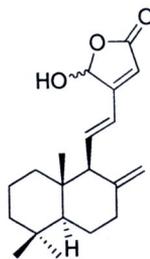
เมื่อนำสาร 27, 61, 65 และ 66 ส่งทดสอบฤทธิ์ในการต้านเชื้อแบคทีเรีย *Mycobacterial tuberculosis* และความเป็นพิษต่อเซลล์มะเร็งเยื่อช่องปาก (KB) เซลล์มะเร็งเต้านม (BC) เซลล์มะเร็งปอด (NCI-H187) และเซลล์ปกติ พบว่าสารประกอบ 65 และ 61 แสดงฤทธิ์ปานกลางในการต้านเชื้อ *Mycobacterial tuberculosis* ด้วยค่า MIC 6.25 และ 12.50  $\mu\text{g/mL}$  ตามลำดับ ในการทดสอบความเป็นพิษต่อเซลล์มะเร็งพบว่าสาร 66 และ 65 แสดงฤทธิ์ในการยับยั้งเซลล์มะเร็งปอดสูงด้วยค่า  $\text{IC}_{50}$  0.12 และ 0.72  $\mu\text{g/mL}$  ตามลำดับ นอกจากนี้สาร 65 ยังมีฤทธิ์สูงสุดในการยับยั้งเซลล์มะเร็งเยื่อช่องปาก และเซลล์มะเร็งเต้านมด้วยค่า  $\text{IC}_{50}$  0.91 และ 2.89  $\mu\text{g/mL}$  ตามลำดับ และสาร 65 เป็นสารที่มีฤทธิ์สูงที่สุดในการทดสอบทั้งหมด อย่างไรก็ตามสาร 65 มีความเป็นพิษต่อเซลล์ปกติสูง ( $\text{IC}_{50}$  5.37  $\mu\text{g/mL}$ ) ในขณะที่สาร 66 ไม่มีความเป็นพิษต่อเซลล์ปกติ



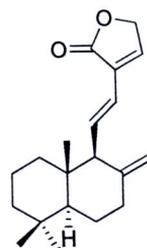
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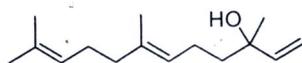
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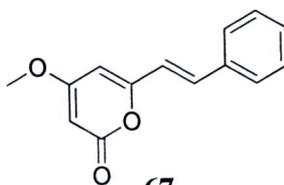
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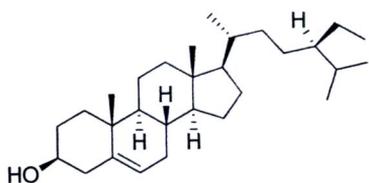
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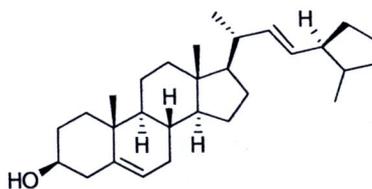
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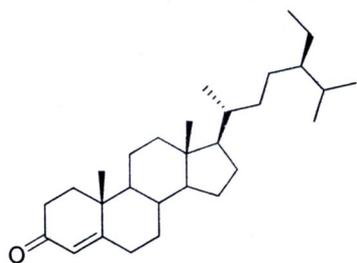
67



62



63



64

**TABLE OF CONTENTS**

	Page
ACKNOWLEDGEMENTS	iii
ABSTRACT (ENGLISH)	iv
ABSTRACT (THAI)	vi
LIST OF TABLES	x
LIST OF FIGURES	xi
ABBREVIATIONS AND SYMBOLS	xv
CHAPTER 1 INTRODUCTION	1
CHAPTER 2 EXPERIMENTAL	15
2.1 Plant Materials	15
2.2 General Method	15
2.2.1 Chromatography	15
2.2.1.1 Column Chromatography (CC)	15
2.2.1.2 Flash Column Chromatography (FCC)	15
2.2.2 Thin Layer Chromatography (TLC)	16
2.2.3 Detection of Chromatographic plate	16
2.2.4 Physical Constants	16
2.2.5 Spectroscopy	17
2.2.5.1 Infrared (IR) Spectra	17

2.2.5.2 Nuclear Magnetic Resonance (NMR) Spectra	17
2.2.5.3 Mass Spectra	17
2.2.5.4 GC/MS	17
2.3 Extraction and Isolation of Bioactive Compounds	18
2.3.1 Hexane Extract	18
2.3.2 CH <sub>2</sub> Cl <sub>2</sub> Extract	26
2.3.3 MeOH Extract	35
2.4 Biological activities	38
2.4.1 Antimycobacterial Assay	38
2.4.2 Cytotoxicity Assays	38
CHAPTER 3 RESULTS AND DISCUSSION	41
3.1 Structure Elucidation of Pure Compounds	41
3.2 Biological Activities	58
CHAPTER 4 CONCLUSIONS	60
REFERENCES	62
APPENDICES	69
CURRICULUM VITAE	102

## LIST OF TABLES

Table	Page
1 Monoterpenoids from <i>Amomum</i> species	4
2 Sesquiterpenoids from <i>Amomum</i> species	7
3 Diterpenoids from <i>Amomum</i> species	8
4 Flavonoids from <i>Amomum</i> species	9
5 Ketones from <i>Amomum</i> species	12
6 Phenolics from <i>Amomum</i> species	13
7 Miscellaneous from <i>Amomum</i> species	14
8 Anti- <i>Mycobacterial tuberculosis</i> (Anti-TB) H37Ra	39
9 Cytotoxic activities	40
10 $^1\text{H}$ , $^{13}\text{C}$ -NMR and HMBC data of compound <b>61</b>	43
11 $^1\text{H}$ , $^{13}\text{C}$ -NMR and HMBC data of compound <b>27</b>	45
12 $^1\text{H}$ - and $^{13}\text{C}$ -NMR data of compound <b>62</b>	47
13 $^1\text{H}$ - and $^{13}\text{C}$ -NMR data of compound <b>64</b>	49
14 $^1\text{H}$ , $^{13}\text{C}$ -NMR and HMBC data of compound <b>65</b>	51
15 $^1\text{H}$ , $^{13}\text{C}$ -NMR and HMBC data of compound <b>21</b>	53
16 $^1\text{H}$ , $^{13}\text{C}$ -NMR and HMBC data of compound <b>66</b>	55
17 $^1\text{H}$ , $^{13}\text{C}$ -NMR and HMBC data of compound <b>67</b>	56

## LIST OF FIGURES

Figure	Page
1 Morphological illustration of <i>Amomum uliginosum</i>	2
2 Selected HMBC correlations of coronarin E ( <b>61</b> )	43
3 Selected HMBC correlations of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	45
4 Selected HMBC correlations of 16-hydroxylabda-8(17), 11,13-trien-15,16-olide ( <b>65</b> )	51
5 Selected HMBC correlations of villosin ( <b>66</b> )	55
6 Selected HMBC correlations of 5,6-dehydrokawain ( <b>67</b> )	57
7 Mass spectrum of (+)-nerolidol ( <b>21</b> )	70
8 IR spectrum of (+)-nerolidol ( <b>21</b> )	70
9 <sup>1</sup> H-NMR of (+)-nerolidol ( <b>21</b> )	71
10 Expansion of <sup>1</sup> H-NMR spectrum of (+)-nerolidol ( <b>21</b> )	71
11 <sup>13</sup> C-NMR spectra of (+)-nerolidol ( <b>21</b> )	72
12 <sup>1</sup> H- <sup>1</sup> H COSY spectrum of (+)-nerolidol ( <b>21</b> )	72
13 HMQC spectrum of (+)-nerolidol ( <b>21</b> )	73
14 HMBC spectrum of (+)-nerolidol ( <b>21</b> )	73
15 Mass spectrum of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	74

16	IR spectrum of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	74
17	<sup>1</sup> H-NMR spectrum of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	75
18	Expansion of <sup>1</sup> H-NMR spectrum of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	75
19	<sup>13</sup> C-NMR spectra of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	76
20	<sup>1</sup> H- <sup>1</sup> H COSY spectrum of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	76
21	HMQC spectrum of of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	77
22	HMBC spectrum of of ( <i>E</i> )-15,16-bisnorlabda-8(17), 11-dien-13-one ( <b>27</b> )	77
23	Mass spectrum of coronarin E ( <b>61</b> )	78
24	IR spectrum of coronarin E ( <b>61</b> )	78
25	<sup>1</sup> H-NMR spectrum of coronarin E ( <b>61</b> )	79
26	Expansion of <sup>1</sup> H-NMR spectrum of coronarin E ( <b>61</b> )	79
27	<sup>13</sup> C-NMR and DEPT 135 spectra of coronarin E ( <b>61</b> )	80
28	HMQC spectrum of coronarin E ( <b>61</b> )	80
29	HMBC spectrum of coronarin E ( <b>61</b> )	81
30	Mass spectrum of $\beta$ -sitosterol ( <b>62</b> )	82
31	Mass spectrum of stigmasterol ( <b>63</b> )	82
32	IR spectrum of $\beta$ -sitosterol ( <b>62</b> ) and stigmasterol ( <b>63</b> )	83

33	<sup>1</sup> H-NMR spectrum of $\beta$ -sitosterol (62) and stigmasterol (63)	83
34	Expansion of <sup>1</sup> H-NMR spectrum $\beta$ -sitosterol (62) and stigmasterol (63)	84
35	<sup>13</sup> C-NMR spectrum of $\beta$ -sitosterol (62) and stigmasterol (63)	84
36	<sup>1</sup> H- <sup>1</sup> H COSY spectrum of $\beta$ -sitosterol (62) and stigmasterol (63)	85
37	HMQC spectrum of $\beta$ -sitosterol (62) and stigmasterol (63)	85
38	HMBC spectrum of $\beta$ -sitosterol (62) and stigmasterol (63)	86
39	Mass spectrum of stigmast-4-en-3-one (64)	87
40	IR spectrum of stigmast-4-en-3-one (64)	87
41	<sup>1</sup> H-NMR spectrum of stigmast-4-en-3-one (64)	88
42	<sup>13</sup> C-NMR and DEPT 135 spectra of stigmast-4-en-3-one (64)	88
43	HMQC spectrum of stigmast-4-en-3-one (64)	89
44	HMBC spectrum of stigmast-4-en-3-one (64)	89
45	Mass spectrum of of 16-hydroxy-labda-8(17),11,13-trien-15,16-olide (64)	90
46	IR spectrum of 16-hydroxy-labda-8(17),11,13-trien-15,16-olide (64)	90
47	<sup>1</sup> H-NMR spectrum of 16-hydroxy-labda-8(17),11,13-trien-15,16-olide (65)	91
48	Expansion of <sup>1</sup> H-NMR spectrum of 16-hydroxy-labda-8(17), 11,13- trien-15,16-olide (65)	91
49	<sup>13</sup> C-NMR and DEPT 135 spectra of 16-hydroxy-labda-8(17), 11,13-trien-15,16-olide (65)	92
50	<sup>1</sup> H- <sup>1</sup> H COSY spectrum of 16-hydroxy-labda-8(17),11,13-trien- 15,16-olide (65)	92
51	HMQC spectrum of 16-hydroxy-labda-8(17),11,13-trien-15,16-olide (65)	93
52	HMBC spectrum of 16-hydroxy-labda-8(17),11,13-trien-15,16-olide (65)	93
53	Mass spectrum of villosin (66)	94

54	IR spectrum of villosin (66)	94
55	$^1\text{H}$ -NMR spectrum of villosin (66)	95
56	Expansion of $^1\text{H}$ -NMR spectrum of villosin (66)	95
57	$^{13}\text{C}$ -NMR spectrum of villosin (66)	96
58	$^1\text{H}$ - $^1\text{H}$ COSY spectrum of villosin (66)	96
59	HMQC spectrum of villosin (66)	97
60	HMBC spectrum of villosin (66)	97
61	Mass spectrum of 5,6-dehydrokawain (67)	98
62	IR spectrum of 5,6-dehydrokawain (67)	98
63	$^1\text{H}$ -NMR spectrum of 5,6-dehydrokawain (67)	99
64	Expansion of $^1\text{H}$ -NMR spectrum of 5,6-dehydrokawain (67)	99
65	$^{13}\text{C}$ -NMR and DEPT 135 spectra of 5,6-dehydrokawain (67)	100
66	$^1\text{H}$ - $^1\text{H}$ COSY spectrum of 5,6-dehydrokawain (67)	100
67	HMQC spectrum of 5,6-dehydrokawain (67)	101
68	HMBC spectrum of 5,6-dehydrokawain (67)	101

## ABBREVIATIONS AND SYMBOLS

<i>br</i>	broad
CC	column chromatography
cm	centimeter
cm <sup>-1</sup>	wave number
<sup>13</sup> C-NMR	carbon 13 nuclear magnetic resonance
CH <sub>2</sub> Cl <sub>2</sub>	dichloromethane
CHCl <sub>3</sub>	chloroform
COSY	correlated spectroscopy
<i>d</i>	doublet
<i>dd</i>	doublet of doublet
<i>ddd</i>	doublet of doublet of doublet
DEPT	distortionless enhancement by polarization transfer
<i>dt</i>	doublet of triplet
EIMS	electron impact mass spectrometry
ESI-MS	electrospray ionization mass spectrometry
EtOAc	ethyl acetate
EtOH	ethyl alcohol
FCC	flash column chromatography
FT-IR	fourier transform infrared spectroscopy
g	gram
Gr	Group

HMBC	heteronuclear multiple bond correlation
HMQC	heteronuclear multiple quantum coherence
$^1\text{H-NMR}$	proton nuclear magnetic resonance
Hz	hertz
$\text{IC}_{50}$	50% inhibitory concentration
$J$	coupling constant (hertz)
Kg	kilogram
m	meter
$m/z$	a value of mass divided by charge
MeOH	methanol
mg	milligram
MHz	megahertz
MIC	minimum inhibitory concentration
mL	milliliter
mm	millimeter
MS	mass spectrometry
<i>Mult</i>	multiplicity
ppm	part per million
$s$	singlet
TLC	thin layer chromatography
$\delta$	chemical shift (ppm)
$\nu_{\text{max}}$	maximum absorption frequency
$\mu\text{g}$	microgram
$[\alpha]_{\text{D}}$	specific rotation