องค์ประกอบทางเคมีและฤทธิ์ทางชีวภาพของเอื้องเงินแสด

นางสาวภัทราภา รุ่งวิชานิวัฒน์

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CHEMICAL CONSTITUENTS AND BIOACTIVITIES OF *DENDROBIUM WILLIAMSONII*

Miss Pathrapa Rungwichaniwat

A Thesis Submitted in Partial Fulfillment of the Requirements

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ภัทราภา รุ่งวิชานิวัฒน์ : องค์ประกอบทางเคมีและฤทธิ์ทางชีวภาพของเอื้องเงินแสด (CHEMICAL CONSTITUENTS AND BIOACTIVITIES OF *DENDROBIUM WILLIAMSONII*)
อ. ที่ปรึกษาวิทยานิพนธ์หลัก : รศ. ดร. บุญชู ศรีตุลารักษ์
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การศึกษาทางพฤกษเคมีของสารสกัดหยาบด้วยเมทานอลจากต้นเอื้องเงินแสด (วงศ์กล้วยไม้) สามารถแยกสารบริสุทธิ์ที่เคยมีรายงานมาแล้ว 6 ชนิด ได้แก่ tetratriacontanyl-*p*-coumarate, *trans*-docosanoylferulate, 3,3′-dihydroxy-4,5-dimethoxybibenzyl, moscatilin, apigenin และ vanillic acid สารทั้งหมดนั้นสามารถพิสูจน์โครงสร้างทางเคมี โดยการวิเคราะห์ข้อมูลทางสเปกโทรสโคปี (UV, IR, MS, NMR) ร่วมกับการเปรียบเทียบข้อมูลที่มีรายงานมาแล้ว จากการศึกษาฤทธิ์ต้านอนุมูลอิสระด้วยวิธี DPPH assay พบว่า 3,3′-dihydroxy-4,5-dimethoxybibenzyl, moscatilin, apigenin มีฤทธิ์ยับยั้งอนุมูล DPPH โดยมีค่าความเข้มข้นที่สามารถยับยั้งอนุมูลอิสระได้ร้อยละ 50 (IC_{50}) เท่ากับ 19.56 $\pm$ 1.30 , 8.56 $\pm$ 1.24 และ 19.34 $\pm$ 1.19 ไมโครโมลาร์ ตามลำดับ ชุดควบคุมผลบวกที่ใช้คือvitamin C และ quercetin ซึ่งมีค่าความเข้มข้นที่สามารถยับยั้งอนุมูลอิสระได้ร้อยละ 50 (IC_{50}) เท่ากับ 42.46 $\pm$ 2.31 และ 8.34 $\pm$ 0.47 ไมโครโมลาร์ ตามลำดับ นอกจากนี้ในการศึกษาความเป็นพิษต่อเซลล์พบว่าสาร 3,3′-dihydroxy-4,5-dimethoxybibenzyl และ moscatilin เป็นพิษต่อเซลล์ KB (มะเร็งเยื่อบุช่องปาก) รวมทั้งพบว่า 3,3′-dihydroxy-4,5-dimethoxybibenzyl มีฤทธิ์ต้านไวรัสเริมที่อ่อนต่อเชื้อเฮอร์ปีซิมเพล็กซ์ทั้ง 2 ชนิด

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PATHRAPA RUNGWICHANIWAT: CHEMICAL CONSTITUENTS AND BIOACTIVITES OF *DENDROBIUM WILLIAMSONII*.

ADVISOR: ASSOC.PROF. BOONCHOO SRITULARAK, Ph.D.,

CO-ADVISOR: PROF. KITTISAK LIKHITWITAYAWUID, Ph.D., 139 pp.

Phytochemical study of a MeOH extract prepared from the whole plant of *Dendrobium williamsonii* Rchb.f. led to the isolation of six known compounds, namely, tetratriacontanyl-*p*-coumarate, *trans*-docosanoylferulate, 3,3′-dihydroxy-4,5-dimethoxybibenzyl, moscatilin, apigenin and vanillic acid. Their structures were determined by means of spectroscopic analysis (UV, IR, MS, and NMR), as well as by comparison with previously reported data. These compounds were evaluated for 2.2–diphenyl-1-picryhydrazyl (DPPH) free radical scavenging activity. 3,3′-Dihydroxy-4,5-dimethoxybibenzyl, moscatilin and apigenin exhibited moderate DPPH free radical scavenging activitiy with IC_{50} values of 19.56 $\pm$ 1.30, 8.56 $\pm$ 1.24 and 19.34 $\pm$ 1.19 μM, respectively. Vitamin C and quercetin were used as positive controls with IC_{50} values of 42.46 $\pm$ 2.31 and 8.34 $\pm$ 0.47 μM, respectively. In addition, the isolates were evaluated for cytotoxicity and anti-herpes simplex activity. 3,3'-Dihydroxy-4,5-dimethoxybibenzyl and moscatilin showed cytotoxicity against KB cell line (oral human epidermal carcinoma). Moreover, 3,3'-dihydroxy-4,5-dimethoxybibenzyl showed weak activity against herpes simplex type 1 and type 2.

Department : Pharmacognosy and Pharmaceutical Botany Student's Signature .....

Field of Study : Pharmacognosy Advisor's Signature .....

Academic Year : 2013 Co-Advisor's Signature .....

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ABBREVIATIONS

Acetone-d_6	=	Deuterated acetone
α	=	Alpha
β	=	Beta
br s	=	Broad singlet (for NMR spectra)
C	=	Concentration
°C	=	Degree Celsius
CC	=	Column chromatography
$CDCl_3$	=	Deuterated chloroform
CD_3OD	=	Deuterated methanol
CH_2Cl_2	=	Dichloromethane
cm	=	Centimeter
^{13}C NMR	=	Carbon-13 Nuclear Magnetic Resonance
d	=	Doublet (for NMR spectra)
dd	=	Doublet of doublets (for NMR spectra)
δ	=	Chemical shift
DMSO-d_6	=	Deuterated dimethylsulfoxide
DPPH	=	1,1-Diphenyl-2-picrylhydrazyl
ESIMS	=	Electrospray Ionization Mass Spectrometry
EtOAc	=	Ethyl acetate
g	=	Gram
GF	=	Gel Filtration Chromatography
Glc	=	Glucose
Hr	=	Hour
^1H-NMR	=	Proton Nuclear Magnetic Resonance
HSV-1	=	Herpes Simplex Virus type 1
HSV-2	=	Herpes Simplex Virus type 2
Hz	=	Hertz
IC_{50}	=	Concentration exhibiting 50% inhibition
IR	=	Infrared spectrum
J	=	Coupling constant

Kg	=	Kilogram
L	=	Liter
μL	=	Microliter
λ_{max}	=	Wavelength at maximal absorption
ε	=	Molar absorptivity
$[M]^+$	=	Molecular ion
$[M+H]^+$	=	Pseudomolecular ion
$[M+Na]^+$	=	Sodium adduct molecular ion
m	=	Multiplet (for NMR spectra)
MeOH	=	Methanol
mg	=	Milligram
ml	=	Milliliter
μg	=	Microgram
μg/ml	=	Microgram per milliliter
μL	=	Microliter
μM	=	Micromolar
min	=	Minute
mm	=	Millimeter
MS	=	Mass spectrum
MW	=	Molecular weight
m/z	=	Mass to charge ratio
nm	=	Nanometer
NMR	=	Nuclear Magnetic Resonance
NOESY	=	Nuclear Overhauser Effect Spectroscopy
ppm	=	Part per million
Rha	=	Rhamnose
s	=	Singlet (for NMR spectra)
t	=	Triplet (for NMR spectra)
TLC	=	Thin Layer Chromatography
UV-VIS	=	Ultraviolet and Visible spectrophotometry
VLC	=	Vacuum Liquid Column Chromatography

CHAPTER I

INTRODUCTION

Orchidaceae is a diverse and widespread family. Several plants in this family have been traditionally used as medicinal plants in South-East Asia, China, Japan, Europe, Africa, Australia and America. *Dendrobium* is the biggest genus of the family Orchidaceae. They are epiphytic, lithophytic, polymorphic, deciduous or evergreen. Their stems are vertical rhizomes with one or several nodes. Their flowers are greatly variable in shape and color. Their sizes range from very small to large. They can be found transient or outlive (Guanghua *et al*., 2009). Plants of this genus are commonly used in China under the name "Shi-Hu" for the treatment of many diseases such as kidney and lung disorders, stomach diseases, red tongue, dry mouth, fever, gastritis and diabetes (Hossain M.M., 2011).

The chemical constituents found in the plants in this genus can be classified as flavonoids, phenanthrenes, alkaloids, bibenzyls, sterols, sesquiterpenes and fluorenones. The most significant groups are alkaloids and flavonoids due to their biological activities (Hossain M.M., 2011).

Plants in genus *Dendrobium* are representd by more than 1,100 species, widely distributed throughout Asia, South East Asia and Australia. There are about 150 species of *Dendrobium* in Thailand (Seidenfaden, 1985; Guanghua *et al*.,2009). Some have been identified (Smitinand, 2001) as follows.

Dendrobium acerosum Lindl.	**กล้วยไม้มือนาง** Kluai mai mue nang (Chumphon)
D. acinaciforme Roxb.	**เอื้องยอดสร้อย** Ueang yot soi (Northern)
D. albosanguineum Lindl.	**เอื้องตางัว** Ueang ta ngua (Mae Hong Son)
D. aloifolium (Blume) Rchb.f.	**เอื้องมณี** Ueang mani (Bangkok)
D. anosmum Lindl.	**เอื้องสาย** Ueang sai (Chiang Mai, Peninsular)

D. aphyllum (Roxb.) C.E.C.Fisch.	**เอื้องงวงช้าง** Ueang nguang chang (Mae Hong Son)
D. bellatulum Rolfe	**เอื้องแซะภู** Ueng sae phu
D. bicameratum Lindl.	**เอื้องเข็ม** Ueang khem (Northern)
D. bilobulatum Seidenf.	**กล้วยไม้ก้างปลา** Kluai mai kang pla (General)
D. binoculare Rchb.f.	**เอื้องคำสาย** Ueang kham sai (Northern)
D. brymerianum Rchb.f.	**เอื้องคำฝอย** Ueang kham foi (Northern)
D. capillipes Rchb.f.	**เอื้องคำกิ่ว** Ueang kham kio (Lampang, Phrae)
D. cariniferum Rchb.f.	**เอื้องกาจก** Ueang kachok (Chiang Mai)
D. christyanum Rchb.f.	**เอื้องแซะภูกระดึง** Ueang sae phu kradueng (Loei)
D. chrysanthum Lindl.	**เอื้องสายมรกต** Ueang sai morakot (Bangkok)
D. chrysotoxum Lindl.	**เอื้องคำ** Ueang kham (Northern)
D. compactum Rolfe ex Hackett	**เอื้องข้าวตอก** Ueang khao tok (Northern)
D. concinnum Miq.	**หางเปีย** Hang pia (Narathiwat)
D. crepidatum Lindl. & Paxton	**เอื้องสายน้ำเขียว** Ueang sai nam khiao (General)
D. crocatum Hook.f.	**เอื้องนางนวล** Ueang nang nuan (Peninsular)
D. cruentum Rchb.f.	**เอื้องนกแก้ว** Ueang nok kaeo (Bangkok)
D. crumenatum Sw.	**หวายตะมอย** Wai tamoi (Central, Peninsular)
D. crystallinum Rchb.f.	**เอื้องนางฟ้อน** Ueang nang fon (Chiang Mai)

D. cumulatum Lindl.	**เอื้องสายสี่ดอก** Ueang sai si dok (Northern, Southeastern)
D. dantaniense Guillaumin	**เอื้องเข็ม** Ueang khem (Chiang Mai)
D. densiflorum Lindl.	**เอื้องมอนไข่** Ueang mon khai (Northern)
D. devonianum Paxton	**เอื้องเมี่ยง** Ueang miang (Chiang Mai)
D. dickasonii L.O. Williams	**เอื้องเคี้ยะ** Ueang khia (Chiang Mai)
D. discolor Lindl.	**หวายกลัก** Wai klak (Bangkok)
D. dixanthum Rchb.f.	**เอื้องเทียน** Ueang thian (Northern)
D. draconis Rchb.f.	**เอื้องเงิน** Ueang ngoen (Northern)
D. ellipsophyllum Tang & Wang	**เอื้องทอง** Ueang thong (General)
D. exile Schltr.	**เอื้องเสี้ยน** Ueang sian (General)
D. falconeri Hook.	**เอื้องสายวิสูตร** Ueang sai wisut (Bangkok)
D. farmeri Paxton	**เอื้องมัจฉาณุ** Ueang mat chanu (Bangkok)
D. fimbriatum Hook.	**เอื้องคำน้อย** Ueang kham noi (Chiang Mai)
*D. findlayanu*m Parish & Rchb.f.	**พวงหยก** Phuang yok (Bangkok)
D. formosum Roxb. ex Lindl.	**เอื้องเงินหลวง** Ueang ngoen luang (Chiang Mai)
D. friedericksianum Rchb.f.	**เอื้องเหลืองจันทบูร** Ueang Lueang chantabun (Bangkok)
D. fuerstenbergianum Schltr.	**เอื้องแซะภูกระดึง** Ueang sae phukradueng (Loei)
D. gibsonii Lindl.	**เอื้องคำสาย** Ueang kham sai (Northern)

D. grande Hook.f	**เอื้องแผงใบใหญ่** Ueang pheang bai yai (Peninsular)
D. gratiosissimum Rchb.f.	**เอื้องกิ่งดำ** Ueang king dam (Bangkok)
D. gregulus Seidenf.	**เอื้องมะต่อม** Ueang matom (Chiang Mai)
D. griffithianum Lindl.	**เอื้องมัจฉาณุ** Ueang matchanu (Bangkok)
D. harveyanum Rchb.f.	**เอื้องคำฝอย** Ueang kham foi (Chiang Mai)
D. hendersonii Hawkes & Heller	**หวายตะมอยน้อย** Wai tamoi noi (Peninsular)
D. hercoglossum Rchb.f.	**เอื้องดอกมะเขือ** Ueang dok ma kuea (Bangkok)
D. heterocarpum Lindl.	**เอื้องสีตาล** Ueang si tan (Chiang Mai)
D. indivisum (Blume) Miq. var. *indivisum*	**ตานเสี้ยนไม้** Tan sian mai (Chumphon)
D. indivisum (Blume) Miq. var. *pallidum* Seidenf.	**ก้างปลา** Kang pla (General)
D. infundibulum Lindl.	**เอื้องตาเหิน** Ueang ta hoen (General)
D. intricatum Gagnep.	**เอื้องชมพู** Ueang chom phu (Chanthaburi)
D. jenkinsii Wall. ex Lindl.	**เอื้องผึ้งน้อย** Ueang phueng noi(Chiang Mai)
D. kanburiense Seidenf.	**หวายเมืองกาญจน์** Wai muang kan (Kanchanaburi)
D. leonis (Lindl.) Rchb.f.	**เอื้องตะขาบใหญ่** Ueang ta khap yai (General)
D. lindleyi Steud.	**เอื้องผึ้ง** Ueang phueng (Northern)
D. lituiflorum Lindl.	**เอื้องสายม่วง** Ueang sai muang (Bangkok, Northern)

D. moschatum (Buch.-Ham.) Sw.	**เอื้องจำปา** Ueang champa (Northern)
D. nathanielis Rchb.f.	**เกล็ดนิ่ม** Klet nim (Chantaburi)
D. nobile Lindl.	**เอื้องเค้ากิ่ว** Ueang khao kio (Northern)
D. ochreatum Lindl.	**เอื้องตะขาบ** Ueang ta khap (Chiang Mai)
D. oligophyllum Gagnep.	**ข้าวตอกปราจีน** Khao tok prachin (General)
D. pachyglossum C.S.P.Parish & Rchb.f	**เอื้องขนหมู** Ueang khon mu (Mae Hong Son)
D. pachyphyllum (Kuntze) Bakh.f.	**เอื้องน้อย** Ueang noi (General)
D. palpebrae Lindl.	**เอื้องมัจฉา** Ueang mat cha, **เอื้องมัจฉาณุ** Ueang mat chanu (Bangkok)
D. parcum Rchb.f.	**เอื้องก้านกิ่ว** Ueang kan kio (Bangkok)
D. parishii Rchb.f.	**เอื้องครั่ง** Ueang khrang (Northern)
D. pendulum Roxb.	**เอื้องไม้เท้าฤาษี** Ueang mai thao ruesi (Bangkok, Chiang Mai)
D. pensile Ridl.	**หวาย** Wai (Narathiwat)
D. porphyrophyllum Guillaumin	**เอื้องลิ้น** Ueang lin (Lampang)
D. primulinum Lindl.	**เอื้องสายประสาท** Ueang sai prasat (Bangkok)
D. pulchellum Roxb. ex Lindl.	**เอื้องคำตาควาย** Ueang kham ta khwai (Mae Hong Son)
D. pychnostachyum Lindl.	**เศวตสอดสี** Sawet sot si (Chiang Mai)
D. salaccense (Blume) Lindl.	**เอื้องใบไผ่** Ueang bai phai (Chiang Mai)

D. scabrilingue Lindl.	**เอื้องแซะ** Ueang sae (Mae Hong Son)
D. secundum (Blume) Lindl.	**เอื้องแปรงสีฟัน** Ueang preang si fan (Bangkok)
D. seidenfadenii Rchb.f.	**เอื้องเกี๊ยะ** Ueang kia (Chiang Mai)
D. senile Parish & Rchb.f.	**เอื้องชะนี** Ueang chani (Bangkok)
D. signatum Rchb.f.	**เอื้องเค้ากิ่ว** Ueang khao kio (Chiang Mai)
D. stuposum Lindl.	**เอื้องสาย** Ueang sai (Chiang Mai)
D. sulcatum Lindl.	**เอื้องจำปาน่าน** Ueang champa nan (Bangkok)
D. superbiens Rchb.f.	**หวายคิง** Wai khing (Bangkok)
D. sutepense Rolfe ex Downie	**เอื้องมะลิ** Ueang mali (Chiang Mai)
D. terminale Parish & Rchb.f	**เอื้องแผงโสภา** Ueang phaeng sopha (Peninsular)
D. thyrsiflorum Rchb.f	**เอื้องมอนไข่ใบมน** Ueang mon khai bai mon (Northern)
D. tortile Lindl.	**เอื้องไม้ตึง** Ueang mai tueng (Mae Hong Son)
D. trigonopus Rchb.f.	**เอื้องคำเหลี่ยม** Ueang kham liam (Chiang Mai)
D. trinervium Ridl.	**เทียนลิง** Thian ling (Chumphon)
D. unicum Seidenf.	**เอื้องครั่งแสด** Ueang krang saet (General)
D. uniflorum Griff.	**เอื้องทอง** Ueang thong (Pattani)
D. venustum Teijsm. & Binn	**ข้าวเหนียวลิง** Khao niao ling (Central)
D. villosulum Lindl.	**กล้วยหญ้านา** Kluai ya na (Bangkok)
D. virgineum Rchb.f.	**เอื้องเงินวิลาศ** Ueang ngoen wilat (Northern)

D. wardianum Warner	**เอื้องมณีไตรรงค์** Ueang mani trai rong (Northern)
D. wattii (Hook.f.) Rchb.f.	**เอื้องแซะ** Ueang sae (Northern)
D. ypsilon Seidenf.	**เอื้องแบนปากตัด** Ueang baen pak tat (General)

Dendrobium williamsonii Day & Rchb.f. is known in Thai as Ueang Ngoen Sad (เอื้องเงินแสด). It is also known as Williamson's *Dendrobium*. Its stems are straight, hairy, 12-15 cm, width 5-6 cm, diameter 1-1.5 cm and tightly cluster. The apex of the stem has 3-5 leaves, with elongated shape in the size of 12 cm. These flowers are characterized by white or pale yellow with orange throated lip in the middle. The amount of flowers are 1-3. Flowering period is between March to April. This species is found in Thailand, India, Vietnam, China, Mianmar and South East Asia (ศรีประไพ, 2554). In Yunnan Province of China, the decoction of stems or whole plant from *D. williamsonii* has been used as poultice to treat adynamia, dyspepsia, numbness of limbs, and injuries from falls and fracture (Long C.L., and Li R. 2004).

Our preliminary screening of a methanolic extract of *D. williamsonii* for DPPH free radical scavenging activity revealed a positive result, showing 90 % inhibition at a concentration of 200 µg/ml. The extract was also found to possess anti-Herpes simplex virus activity, with 80 % inhibition at a concentration of 200 µg/ml, as evaluated by plaque reduction assay. According to the literature survey, the chemical constituents and bioactivities of this plant have never been reported. The phytochemical data to be obtained in this study would broaden our knowledge on the chemotaxonomy of this plant family and the biological studies would add more information on the bioactivities of thai medicinal plants.

The main objectives of this research are as follows.

1. Isolation and purification of chemical constituents from *Dendrobium williamsonii.*
2. Determination of the structures of the isolated compounds.
3. Study of the bioactivities of isolated compounds, including the DPPH free radical scavenging activity, anti-herpes simplex virus activity and cytotoxicity.

Figure 1. *Dendrobium williamsonii* Day & Rchb.f.

CHAPTER II

HISTORICAL

Chemical constituents of *Dendrobium*.

According to previous studies, chemical constituents found in plants of the genus *Dendrobium* could be divided into six major groups, including bibenzyls (dihydrostilbenes), phenanthrenes, dihydrophenanthrenes, flavonoids, alkaloids, and miscellaneous compounds (Table 1).

Table 1 Distribution of chemical constituents in the genus *Dendrobium*

Plant and compound	Category	Plant part	Reference
Dendrobium aduncum			
Aduncin [**1**]	Sesquiterpene	Whole plant	Gawell and Leander, 1976
Dendrobium amoenum			
Amoenin [**2**]	Sesquiterpene	Whole plant	Majumder, Guha and Sen, 1999
Amoenumin [**3**]	Phenanthrene	Whole plant	Veerraju *et al*., 1989
Amoenylin [**4**]	Bibenzyl	Whole plant	Majumder *et al.*, 1999
Amotin [**5**]	Sesquiterpene	Whole plant	Majumder *et al.*, 1999
3,4′-Dihydroxy-5-methoxybibenzyl [**6**]	Bibenzyl	Whole plant	Majumder *et al.*, 1999
Flaccidin (Amoenumin) [**3**]	Phenanthrene	Whole plant	Majumder *et al.*, 1999
Isoamoenylin [**7**]	Bibenzyl	Whole plant	Majumder *et al.*, 1999
Moscatilin [**8**]	Bibenzyl	Whole plant	Majumder *et al.*, 1999

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dendrobium aphyllum			
Batatasin III [**9**]	Bibenzyl	Whole plant	Chen *et al.*, 2008a
Coelonin [**10**]	Phenanthrene	Whole plant	Chen *et al.*, 2008a
Dibutyl phthalate [**11**]	Benzoic acid ester	Whole plant	Chen *et al.*, 2008a
Diisobutyl phthalate [**12**]	Benzoic acid ester	Whole plant	Chen *et al.*, 2008a
Flavanthrin [**13**]	Biphenanthrene	Whole plant	Chen *et al.*, 2008a
Gigantol [**14**]	Bibenzyl	Whole plant	Chen *et al.*, 2008a
p-hydroxyphenyl propionic methyl ester [**15**]	Phenylpropa-noid	Whole plant	Chen *et al.*, 2008a
Lusianthridin [**16**]	Phenanthrene	Whole plant	Chen *et al.*, 2008a
Moscatin [**17**]	Phenanthrene	Whole plant	Chen *et al.*, 2008a
Dendrobium aurantiacum **var. *denneanum***			
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Yang, Wang and Xu 2006a
Chrysotoxine [**19**]	Bibenzyl	Stem	Yang *et al.*, 2006a
Coumarin [**20**]	Coumarin	Stem	Yang *et al.*, 2006a
Crepidatin [**21**]	Bibenzyl	Whole plant	Liu *et al*., 2009a
Defuscin [**22**]	Phenylpropa-noid	Stem	Yang *et al.*, 2006a
Dendroflorin [**23**]	Fluorenone	Stem	Yang *et al.*, 2006a
Dengibsin [**24**]	Fluorenone	Stem	Yang *et al.*, 2006a
Gigantol [**14**]	Bibenzyl	Whole plant	Liu *et al*., 2009a
1-[4-(*β*-D-glucopyranosyloxy)-3,5-dimethoxyphenyl]-1-	Phenylpropa-noid	Stem	Xiong *et al.*, 2013

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
propanone [**25**]			
(−)-(7*S*,8*R*,7′*E*)-4-hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-7,9,9′-triol 7,9′-bis-*O*-*β*-D-glucopyranoside [**26**]	Neolignan glycoside	Stem	Xiong *et al.*, 2013
Kaempferol [**27**]	Flavonol	Stem	Yang *et al.*, 2006a
Luteolin [**28**]	Flavone	Whole plant	Liu *et al.*, 2009a
Moscatilin [**8**]	Bibenzyl	Stem	Yang *et al.*, 2006a
Moscatin [**17**]	Phenanthrene	Whole plant	Liu *et al.*, 2009a
Naringenin [**29**]	Flavanone	Stem	Yang *et al.*, 2006a
n-Octacosyl ferulate [**30**]	Phenylpropa-noid	Stem	Yang *et al.*, 2006a
Shashenoside I [**31**]	Phenylpropa-noid	Stem	Xiong *et al.*, 2013
(−)-Syringaresinol-4,4′-bis-*O*-*β*-D-glucopyranoside [**32**]	Lignan	Stem	Xiong *et al.*, 2013
Syringaresinol-4-*O*-*β*-D-monoglucopyranoside [**33**]	Lignan	Stem	Xiong *et al.*, 2013
Stigmasterol [**34**]	Steroid	Whole plant	Liu *et al.*, 2009a
Syringin [**35**]	Phenylpropa-noid	Stem	Xiong *et al.*, 2013
Taraxerol [**36**]	Triterpene	Stem	Yang *et al.*, 2006a
Vicenin-2 [**37**]	Flavonoid	Stem	Xiong *et al.*, 2013

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dendrobium candidum			
Dendrocandin A [**38**]	Bibenzyl	Stem	Li *et al.*, 2008
Dendrocandin B [**39**]	Bibenzyl	Stem	Li *et al.*, 2008
Dendrocandin C [**40**]	Bibenzyl	Stem	Li *et al.*, 2009a
Dendrocandin D [**41**]	Bibenzyl	Stem	Li *et al.*, 2009a
Dendrocandin E [**42**]	Bibenzyl	Stem	Li *et al.*, 2009a
Dendrocandin F [**43**]	Bisbibenzyl	Stem	Li *et al.*, 2009b
Dendrocandin G [**44**]	Bisbibenzyl	Stem	Li *et al.*, 2009b
Dendrocandin H [**45**]	Bibenzyl	Stem	Li *et al.*, 2009b
Dendrocandin I [**46**]	Bisbibenzyl	Stem	Li *et al.*, 2009b
Dendrophenol [**47**]	Bibenzyl	Stem	Li *et al.*, 2008
3,4-Dihydroxy-5,4′-dimethoxybibenzyl [**48**]	Bibenzyl	Stem	Li *et al.*, 2008
4,4′-Dihydroxy-3,5-dimethoxybibenzyl [**49**]	Bibenzyl	Stem	Li *et al.*, 2008
Gigantol [**14**]	Bibenzyl	Stem	Li *et al.*, 2008
3-*O*-Methylgigantol [**50**]	Bibenzyl	Stem	Li *et al.*, 2008
Dendrobium capillipes			
Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-*β*-D-glucopyranoside [**51**]	Flavonol glycoside	Stem	Phechrmeekha, Sritularak and Likhitwitayawuid, 2012
Kaempferol-3-*O*-α-L-rhamnopyranosyl-(1→2)-*β*-D-xylopyranoside [**52**]	Flavonol glycoside	Stem	Phechrmeekha *et al.*, 2012
Quercetin-3-*O*-α-L-rhamnopyranosyl-(1→2)-*β*-D-xylopyranoside [**53**]	Flavonol glycoside	Stem	Phechrmeekha *et al.*, 2012

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Phechrmeekha *et al*., 2012
Chrysotoxine [**19**]	Bibenzyl	Stem	Phechrmeekha *et al*., 2012
Crepidatin [**21**]	Bibenzyl	Stem	Phechrmeekha *et al*., 2012
Gigantol [**14**]	Bibenzyl	Stem	Phechrmeekha *et al*., 2012
Moscatilin [**8**]	Bibenzyl	Stem	Phechrmeekha *et al*., 2012
Dendrobium cariniferum			
Batatasin III [**9**]	Bibenzyl	Stem	Chen *et al*., 2008b
Daucosterol [**54**]	Steroid glycoside	Whole plant	Lui *et al.*, 2009a
Dendronone [**55**]	Phenanthrene	Stem	Chen *et al.*, 2008b
Gigantol [**14**]	Bibenzyl	Stem	Chen *et al.*, 2008b
Stigmasterol [**34**]	Steroid	Whole plant	Lui *et al.*, 2009a
3,3′,5-Trihydroxy bibenzyl [**56**]	Bibenzyl	Whole plant	Lui *et al.*, 2009a
Dendrobium chrysanthum			
7-7′-bis-(4-hydroxy-3,5-dimethoxyphenyl)-8-8′-dihydroxymethyltetrahydrofuran-4β-D-glucoside [**57**]	Lignan	Stem	Ye, Zhao and Qin, 2004
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Yang *et al*., 2006b
Chrysotoxine [**19**]	Bibenzyl	Stem	Yang *et al*., 2006b
Crepidatin [**21**]	Bibenzyl	Stem	Yang *et al*., 2006b

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dehydrodiconiferyl alcohol-4-β-D-glucoside[**58**]	Lignan	Stem	Ye *et al*., 2004
Denchryside B [**59**]	Neolignan glucoside	Stem	Ye *et al*., 2004
Dendrochrysanene [**60**]	Phenanthrene	Stem	Yang *et al*., 2006b
Dengibsin [**24**]	Fluorenone	Stem	Yang *et al*., 2006b
2,5-Dihydroxy-4,9-dimethoxylphenanthrene [**61**]	Phenanthrene	Stem	Yang *et al*., 2006b
Gigantol [**14**]	Bibenzyl	Stem	Yang *et al*., 2006b
Lioniresinol [**62**]	Lignan	Stem	Ye *et al*., 2004
Moscatilin [**8**]	Bibenzyl	Stem	Yang *et al*., 2006b
Moscatin [**17**]	Phenanthrene	Stem	Yang *et al*., 2006b
Dendrobium chryseum			
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Ma *et al*., 1998
Chrysotoxine [**19**]	Bibenzyl	Stem	Ma *et al*., 1998
Confusarin [**63**]	Phenanthrene	Stem	Ma *et al*., 1998
2,6-Dimethoxy benzoquinone [**64**]	Benzoquinone	Stem	Ma *et al*., 1998
β-Sitosterol [**65**]	Steroid	Stem	Ma *et al*., 1998
Dendrobium chrysotoxum			
Antiarol [**66**]	Phenolic compound	Stem	Hu *et al*., 2012
Batatasin III [**9**]	Bibenzyl	Whole plant	Li *et al.*, 2009c
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Hu *et al*., 2012
Chrysotoxol A [**67**]	Phenanthrene	Stem	Hu *et al*., 2012
Chrysotoxol B [**68**]	Phenanthrene	Stem	Hu *et al*., 2012

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Chrysotoxine [**19**]	Bibenzyl	Stem	Hu *et al*., 2012
Confusarin [**63**]	Phenanthrene	Stem	Hu *et al*., 2012
Crystalltone [**69**]	Phenanthrene	Stem	Wang *et al.*, 2009
Daucosterol [**54**]	Steroid glycoside	Whole plant	Li *et al.*, 2009c
Denchrysan A [**70**]	Fluorenone	Whole plant	Chen *et al.*, 2008c
Denchrysan B [**71**]	Fluorenone	Whole plant	Li *et al.*, 2009c
Dendroflorin [**72**]	Fluorenone	Whole plant	Chen *et al.*, 2008c
Dengibsin [**24**]	Fluorenone	Whole plant	Li *et al.*, 2009c
Densiflorol B [**73**]	Phenanthrene	Whole plant	Li *et al.*, 2009c
3,7-Dihydroxy-2,4-di methoxyphenanthrene [**74**]	Phenanthrene	Whole plant	Li *et al.*, 2009c
4,5-Dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene [**75**]	Phenanthrene	Stem	Hu *et al*., 2012
5,6-Dihydroxy-4′-methoxy-flavone [**76**]	Flavone	Stem	Hu *et al*., 2012
Epheranthol B [**77**]	Phenanthrene	Stem	Hu *et al*., 2012
Episyringaresinol [**78**]	Lignan	Stem	Hu *et al*., 2012
Erianin [**79**]	Bibenzyl	Stem	Hu *et al*., 2012
4,9-Dimethoxy phenanthrene-2,5-diol [**61**]	Phenanthrene	Whole plant	Li *et al.*, 2009c
Gigantol [**14**]	Bibenzyl	Whole plant	Li *et al.*, 2009c
Moscatin [**17**]	Phenanthrene	Whole plant	Li *et al.*, 2009c
Stigmasterol [**34**]	Steroid	Whole plant	Li *et al.*, 2009c
Salidrosol [**80**]	Phenylpropa-noid	Stem	Hu *et al*., 2012
β-Sitosterol [**65**]	Steroid	Stem	Hu *et al*., 2012

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Syringoside [**81**]	Phenylpropa-noid	Stem	Hu *et al*., 2012
1,4,5-Trihydroxy-7-methoxy-9H-fluoren-9-one [**82**]	Fluorenone	Whole plant	Chen *et al.*, 2008c
2,4,7-Trihydroxy-5-methoxy-9-fluorenone [**83**]	Fluorenone	Stem	Yang *et al*., 2004
2,4,7-Trihydroxy-1,5-dimethoxy-9-fluorenone [**84**]	Fluorenone	Stem	Yang *et al*., 2004
3,6,9-Trihydroxy-3,4-dihydroanthracen-1-(2*H*)-one [**85**]	Anthracene	Stem	Hu *et al*., 2012
Trigonopol B [**86**]	Bibenzyl	Stem	Hu *et al*., 2012
Tristin [**87**]	Bibenzyl	Stem	Hu *et al*., 2012
Vanillic acid [**88**]	Benzoic acid derivative	Whole plant	Li *et al.*, 2009c
Dendrobium clavatum var. auranteacum			
Aliphatic acids [**89**]	Aliphatic acid	Stem	Chang, Lin and Chen, 2001
Aliphatic alcohols [**90**]	Aliphatic alcohol	Stem	Chang *et al.*, 2001
Alkyl 4′-hydroxy-*trans*-cinnamates [**91**]	Cinnamate	Stem	Chang *et al.*, 2001
Alkyl *trans*-ferulates [**92**]	Cinnamate	Stem	Chang *et al.*, 2001
Campesterol [**93**]	Steroid	Stem	Chang *et al.*, 2001
Coumarin [**20**]	Coumarin	Stem	Chang *et al.*, 2001
Stigmast-4-en-3-one [**94**]	Steroid	Stem	Chang *et al.*, 2001
Stigmasterol [**34**]	Steroid	Stem	Chang *et al.*, 2001

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dendrobium crepidatum			
Crepidatin [**21**]	Bibenzyl	Whole plant	Majumder and Chatterjee, 1989
Dendrobium crystallium			
Apigenin [**95**]	Flavone	Stem	Wang *et al.*, 2009
Crystallinin [**96**]	Sesquiterpene	Stem	Wang *et al.*, 2009
Crystalltone [**69**]	Phenanthrene	Stem	Wang *et al.*, 2009
Dencryol A [**97**]	Bisbibenzyl	Stem	Wang *et al.*, 2009
Dencryol B [**98**]	Bisbibenzyl	Stem	Wang *et al.*, 2009
Dendronobilin B [**99**]	Sesquiterpene	Stem	Wang *et al.*, 2009
6‴-Glucosyl-vitexin [**100**]	Flavone glycoside	Stem	Wang *et al.*, 2009
3-Hydroxy-2-methoxy-5,6-dimethylbenzoic acid [**101**]	Benzoic acid derivative	Stem	Wang *et al.*, 2009
Isoviolanthin [**102**]	Flavone glycoside	Stem	Wang *et al.*, 2009
Palmarumycin JC2 [**103**]	Naphthalene	Stem	Wang *et al.*, 2009
Syringic acid [**104**]	Benzoic acid derivative	Stem	Wang *et al.*, 2009
Dendrobium cumulatum			
Cumulatin [**105**]	Bibenzyl	Whole plant	Majumder and Pal, 1993
Dendrobium denneanum			
9-β-D-allofuranulsyguanine [**106**]	Purine	Stem	Pan *et al*., 2012
Guanosine [**107**]	Purine	Stem	Pan *et al*., 2012
Tachioside [**108**]	Phenol	Stem	Pan *et al*., 2012
Vanilloside [**109**]	Guanine	Stem	Pan *et al*., 2012

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dendrobium densiflorum			
Ayapin [**110**]	Coumarin	Stem	Fan *et al.*, 2001
Cypripedin [**111**]	Phenanthrene	Stem	Fan *et al.*, 2001
Dengibsin [**24**]	Fluorenone	Stem	Fan *et al.*, 2001
Densiflorol A [**112**]	Bibenzyl	Stem	Fan *et al.*, 2001
Densiflorol B [**73**]	Phenanthrene	Stem	Fan *et al.*, 2001
4,7-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene [**113**]	Phenanthrene	Stem	Fan *et al.*, 2001
2,6-Dihydroxy-1,5,7-tri methoxyphenanthrene [**114**]	Phenanthrene	Stem	Fan *et al.*, 2001
Gigantol [**14**]	Bibenzyl	Stem	Fan *et al.*, 2001
Homoeriodictyol [**115**]	Flavanone	Stem	Fan *et al.*, 2001
Moscatilin [**8**]	Bibenzyl	Stem	Fan *et al.*, 2001
Moscatin [**17**]	Phenanthrene	Stem	Fan *et al.*, 2001
Naringenin [**29**]	Flavanone	Stem	Fan *et al.*, 2001
Scoparone [**116**]	Coumarin	Stem	Fan *et al.*, 2001
Scopoletin [**117**]	Coumarin	Stem	Fan *et al.*, 2001
1,4,7-Trihydroxy-5-methoxy-9H-fluoren-9-one [**118**]	Fluorenone	Stem	Fan *et al.*, 2001
Tristin [**87**]	Bibenzyl	Stem	Fan *et al.*, 2001
Dendrobium draconis			
Batatasin III [**9**]	Bibenzyl	Stem	Sritularak, Anuwat and Likhitwitayawuid, 2011a
Gigantol [**14**]	Bibenzyl	Stem	Sritularak *et al.*, 2011a

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Hircinol [**119**]	Phenanthrene	Stem	Sritularak *et al.*, 2011a
7-Methoxy-9,10-dihydro phenanthrene-2,4,5-triol [**120**]	Phenanthrene	Stem	Sritularak *et al.*, 2011a
5-Methoxy-7-hydroxy-9,10-dihydro-1,4 phenanthrenequinone [**121**]	Phenanthrene	Stem	Sritularak *et al.*, 2011a
Dendrobium falconeri			
Dendrofalconerol A [**122**]	Bisbibenzyl	Stem	Sritularak and Likhitwitayawuid, 2009
Dendrofalconerol B [**123**]	Bisbibenzyl	Stem	Sritularak and Likhitwitayawuid, 2009
Docosanoyl (*E*)-ferulate [**124**]	Phenylpropanoid	Stem	Sritularak and Likhitwitayawuid, 2009
p-Hydroxybenzaldehyde [**125**]	Phenolic compound	Stem	Sritularak and Likhitwitayawuid, 2009
p-Hydroxybenzoic acid [**126**]	Phenolic compound	Stem	Sritularak and Likhitwitayawuid, 2009
2-(*p*-Hydroxyphenyl) ethyl *p*-coumarate [**127**]	Phenylpropanoid	Stem	Sritularak and Likhitwitayawuid, 2009
Tetracosyl (*E*)-*p*-coumarate [**128**]	Phenylpropanoid	Stem	Sritularak and Likhitwitayawuid,

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Tetracosyl (*Z*)-*p*-coumarate [**129**]	Phenylpropanoid	Stem	2009 Sritularak and Likhitwitayawuid, 2009
Dendrobium fimbriatum			
Defuscin [**22**]	Phenylpropanoid	Whole plant	Talapatra, Bhaumik and Talapatra,1992
Denfigenin [**130**]	Steroid	Whole plant	Talapatra *et al.*, 1992
Diosgenin [**131**]	Steroid	Whole plant	Talapatra *et al.*, 1992
Dendrobium findlayanum			
Crystallinin [**96**]	Sesquiterpene	Whole plant	Qin *et al.*, 2011
Findlayanin [**132**]	Sesquiterpene	Whole plant	Qin *et al.*, 2011
Dendrobium fuscescens			
Defuscin [**22**]	Phenylpropanoid	Whole plant	Talapatra, Das and Talapatra, 1989
(-)-Shikimic acid [**133**]	Aliphatic acid	Whole plant	Talapatra *et al.*, 1989
Dendrobium gratiosissimum			
Batatasin III [**9**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
Dengraol A [**134**]	Bisbibenzyl	Stem	Zhang *et al.*, 2008a
Dengraol B [**135**]	Bisbibenzyl	Stem	Zhang *et al.*, 2008a

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
3,4-Dihydroxy-5,4′-dimethoxybibenzyl [**48**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
3,4′-Dihydroxy-5-methoxybibenzyl [**6**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
Gigantol [**14**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
Moscatilin [**8**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
3,5,4′-Trihydroxybibenzyl [**136**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
Tristin [**87**]	Bibenzyl	Stem	Zhang *et al.*, 2008a
Dendrobium huoshanense			
6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-galactopyranosyl]apigenin [**137**]	Flavone glycoside	Aerial part	Chang *et al*., 2010
6-*C*-(α-Arabinopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl]apigenin [**138**]	Flavone glycoside	Aerial part	Chang *et al*., 2010
Dimethyl malate [**139**]	Aliphatic acid ester	Aerial part	Chang *et al*., 2010
Isopentyl butyrate [**140**]	Aliphatic acid ester	Aerial part	Chang *et al*., 2010
Isoschaftoside [**141**]	Flavone glycoside	Aerial part	Chang *et al*., 2010

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Malic acid [**142**]	Aliphatic acid	Aerial part	Chang *et al*., 2010
N-phenylacetamide [**143**]	Aromatic compound	Aerial part	Chang *et al*., 2010
6-*C*-[(2-*O*-α-Rhamnopyranosyl)-β-glucopyranosyl]-8-*C*-(α-arabinopyranosyl) apigenin [**144**]	Flavone glycoside	Aerial part	Chang *et al*., 2010
Salicylic acid [**145**]	Hydroxybenzoic acid	Aerial part	Chang *et al*., 2010
Shikimic acid [**133**]	Aliphatic acid	Aerial part	Chang *et al*., 2010
6-*C*-(β-Xylopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl] apigenin [**146**]	Flavone glycoside	Aerial part	Chang *et al*., 2010
Dendrobium loddigesii			
Batatasin III [**9**]	Bibenzyl	Whole plant	Ito *et al.*, 2010
Dehydrovomifoliol [**147**]	Ketone	Whole plant	Ito *et al.*, 2010
Gigantol [**14**]	Bibenzyl	Whole plant	Ito *et al.*, 2010
Hircinol [**119**]	Phenanthrene	Whole plant	Ito *et al.*, 2010
5-Hydroxy-2,4-dimethoxy phenanthrene [**148**]	Phenanthrene	Whole plant	Ito *et al.*, 2010
Loddigesiinol A [**149**]	Phenanthrene	Whole plant	Ito *et al.*, 2010
Loddigesiinol B [**150**]	Phenanthrene	Whole plant	Ito *et al.*, 2010
Loddigesiinol C [**151**]	Bibenzyl	Whole plant	Ito *et al.*, 2010
Loddigesiinol D [**152**]	Bibenzyl	Whole plant	Ito *et al.*, 2010

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Lusianthridin [**16**]	Phenanthrene	Whole plant	Ito *et al.*, 2010
(-)-Medioresinol [**153**]	Lignan	Whole plant	Ito *et al.*, 2010
Moscatilin [**8**]	Bibenzyl	Whole plant	Chen *et al.*, 1994 ; Ito *et al.*, 2010
Moscatin [**17**]	Phenanthrene	Whole plant	Chen *et al.*, 1994 ; Ito *et al.*, 2010
(-)-Pinoresinol [**154**]	Lignan	Whole plant	Ito *et al.*, 2010
Rotundatin [**155**]	Phenanthrene	Whole plant	Ito *et al.*, 2010
Sitostenone [**156**]	Steroid	Whole plant	Ito *et al.*, 2010
β –Sitosterol [**65**]	Steroid	Whole plant	Ito *et al.*, 2010
Stigmasterol [**34**]	Steroid	Whole plant	Ito *et al.*, 2010
Dendrobium longicornu			
Aloifol I [**157**]	Bibenzyl	Stem	Hu *et al*., 2008a
Batatasin [**158**]	Bibenzyl	Stem	Hu *et al*., 2008a
Bis (2-ethylhexyl) phthalate [**159]**	Benzoic acid ester	Whole plant	Li *et al*., 2009d
Dibutyl phthalate [**11**]	Benzoic acid ester	Whole plant	Li *et al*., 2009d
n-Docosyl trans-ferulate [**160**]	Phenylpropanoid	Whole plant	Li *et al*., 2009d
Episyringaresinol [**161**]	Lignan	Stem	Hu *et al*., 2008a
Episyringaresinol 4″-*O*-β-D-glucopyranoside [**162**]	Lignan glycoside	Stem	Hu *et al*., 2008a
Erythro-1-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-1,3-propanediol [**163**]	Lignan glycoside	Stem	Hu *et al*., 2008a

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Ethylhaematommate [**164**]	Phenolic compound	Whole plant	Li *et al*., 2009d
Eugenyl *O*-β-D-glucopyranoside [**165**]	Glycoside	Stem	Hu *et al*., 2008a
Ferulaldehyde [**166**]	Phenylpropanoid	Whole plant	Li *et al*., 2009d
Gallic acid [**167**]	Phenolic compound	Whole plant	Li *et al*., 2009d
Gigantol [**14**]	Bibenzyl	Stem	Hu *et al*., 2008a
5-Hydroxy-7-methoxy-9,10-dihydrophenanthrene-1,4-dione(Dendronone) [**55**]	Phenanthrene	Stem	Hu *et al*., 2008a
4-[2-(3-Hydroxyphenol)-1-methoxyethyl]-2,6-dimethoxyphenol [**168**]	Bibenzyl	Stem	Hu *et al*., 2008a
Longicornuol A [**169**]	Bibenzyl	Stem	Hu *et al*., 2008a
4-Methoxy-9,10-dihydrophenanthrene-2,5,7-triol [**170**]	Phenanthrene	Stem	Hu *et al*., 2008a
3-(3-Methoxy,4-hydroxyphenyl)-1-propanol [**171**]	Phenylpropanoid	Stem	Hu *et al*., 2008a
Methyl β-orsellinate [**172**]	Phenolic compound	Stem	Hu *et al*., 2008a
Moscatilin [**8**]	Bibenzyl	Stem	Hu *et al*., 2008a
Naringenin [**29**]	Flavanone	Stem	Hu *et al*., 2008a
9-β-D-Ribofuranosyl-9H-purin-6-amine [**173**]	Purine nucleotide	Stem	Hu *et al*., 2008a

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
β-Sitosterol [**65**]	Steroid	Stem	Hu *et al*., 2008a
(3S,4S,5R)-3,4,5-trihydroxy-1-cyclohexene carboxylic acid (Shikimic acid) [**133**]	Aliphatic acid	Stem	Hu *et al*., 2008a
3,3′,4-Trihydroxybibenzyl [**174**]	Bibenzyl	Stem	Hu *et al*., 2008a
Tristin [**87**]	Bibenzyl	Stem	Hu *et al*., 2008a
Dendrobium moniliforme			
Acanthoside B [**175**]	Lignan glycoside	Stem	Zhao *et al,* 2003
Daucosterol [**54**]	Steroid glycoside	Stem	Bi *et al.*, 2004
Denbinobin [**176**]	Phenanthrene	Stem	Lin *et al.*, 2001
Dendromoniliside A [**177**]	Sesquiterpene glycoside	Stem	Zhao *et al,* 2003
Dendromoniliside B [**178**]	Sesquiterpene glycoside	Stem	Zhao *et al.*, 2003
Dendromoniliside C [**179**]	Sesquiterpene glycoside	Stem	Zhao *et al.*, 2003
Dendromoniliside D [**180**]	Sesquiterpene glycoside	Stem	Zhao *et al.*, 2003
Dendromoniliside E **[181**]	Bibenzyl glycoside	Stem	Zhao *et al.*, 2003
Dendroside A [**182**]	Sesquiterpene glycoside	Stem	Zhao *et al.*, 2003
Dendroside C [**183**]	Sesquiterpene glycoside	Stem	Zhao *et al.*, 2003
Dendroside F [**184**]	Sesquiterpene glycoside	Stem	Zhao *et al.*, 2003
α-Dihydropicrotoxinin [**185**]	Sesquiterpene	Stem	Bi, Wang and

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
			Xu, 2004
3,4-Dihydroxy-5,4′-dimethoxybibenzyl [**48**]	Bibenzyl	Stem	Bi *et al.*, 2004
Moniliformin [**186**]	Phenanthrene	Stem	Bi *et al.*, 2004
n-Nonacosane [**187**]	Long chain hydrocarbon	Stem	Lin *et al.*, 2001
			Bi *et al.*, 2004
n-Octacosyl ferulate [**30**]	Phenolic compound	Stem	Bi *et al.*, 2004
β-Sitosterol [**65**]	Steroid	Stem	
n-Triacontyl *p*-hydroxy-cis-cinnamate [**188**]	Phenolic compound	Stem	Bi *et al.*, 2004
			Bi *et al.*, 2004
Vanilloside [**189**]	Phenolic glycoside	Stem	Zhao *et al.*, 2003
Dendrobium moscatum			
Moscatilin [**8**]	Bibenzyl	Whole plant	Majumder and Sen, 1987
Dendrobium nobile			
Bulbophyllanthrin [**190**]	Phenanthrene	Stem	Yang, Sung and Kim, 2007
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Zhang *et al*., 2007a
Chrysotoxine [**19**]	Bibenzyl	Stem	Zhang *et al*., 2007a
Coelonin [**10**]	Phenanthrene	Stem	Yang *et al*., 2007 ; Hwang *et al*., 2010
Confusarin [**63**]	Phenanthrene	Stem	Zhang *et al*., 2008b

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Crepidatin [**21**]	Bibenzyl	Stem	Zhang *et al*., 2007a
Denbinobin [**176**]	Phenanthrene	Stem	Yang *et al*., 2007 Ye and Zhao, 2002
Dendrobane A [**191**]	Sesquiterpene	Stem	Zhang *et al*., 2007a
Dendrobin A [**192**]	Bibenzyl	Stem	Wang, Zhao and Che, 1985; Ye and Zhao, 2002
Dendrobine [**193**]	Sesquiterpene alkaloid	Stem	Zhang *et al*., 2007a
Dendroflorin [**23**]	Fluorenone	Stem	Zhang *et al*., 2007b
Dendronobilin A [**194**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin B [**99]**	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin C [**195**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin D [**196**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin E [**197**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin F [**198**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin G [**199**]	Sesquiterpene	Stem	Zhang *et al*., 2007b

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dendronobilin H [**200**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin I [**201**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin J [**202**]	Sesquiterpene	Stem	Zhang *et al*., 2007b
Dendronobilin K [**203**]	Sesquiterpene	Stem	Zhang *et al*., 2008c
Dendronobilin L [**204**]	Sesquiterpene	Stem	Zhang *et al*., 2008c
Dendronobilin M [**205**]	Sesquiterpene	Stem	Zhang *et al*., 2008
Dendronobilin N [**206**]	Sesquiterpene	Stem	Zhang *et al*., 2008c
Dendronobiloside A [**207**]	Sesquiterpene Glycoside	Stem	Zhao *et al*., 2001; Ye and Zhao, 2002
Dendronobiloside B [**208**]	Sesquiterpene glycoside	Stem	Zhao *et al*., 2001; Ye and Zhao, 2002
Dendronobiloside C [**209**]	Sesquiterpene glycoside	Stem	Ye and Zhao, 2002
Dendronobiloside D [**210**]	Sesquiterpene glycoside	Stem	Ye and Zhao, 2002
Dendronobiloside E [**211**]	Sesquiterpene glycoside	Stem	Ye and Zhao, 2002
Dendroside A [**182**]	Sesquiterpene glycoside	Stem	Zhao *et al*., 2001; Ye and Zhao, 2002

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Dendroside B [**212**]	Sesquiterpene glycoside	Stem	Ye and Zhao, 2002
Dendroside C [**183**]	Sesquiterpene glycoside	Stem	Ye and Zhao, 2002
Dendroside D [**213**]	Sesquiterpene glycoside	Stem	Ye, Qin and Zhao, 2002
Dendroside E [**214**]	Sesquiterpene Glycoside	Stem	Ye *et al.*, 2002
Dendroside F [**184**]	Sesquiterpene glycoside	Stem	Ye *et al.*, 2002
Dendroside G [**215**]	Sesquiterpene glycoside	Stem	Ye and Zhao, 2002
4,5-Dihydroxy-3,3′-dimethoxybibenzyl (Dendrobin A) [**192**]	Bibenzyl	Stem	Ye and Zhao, 2002
4,5-Dihydroxy-3,7-dimethoxy-9,10-dihydrophenanthrene [**216**]	Phenanthrene	Stem	Ye and Zhao, 2002
3,4′-Dihydroxy-5,5′-di methoxydihydrostilbene [**217**]	Bibenzyl	Stem	Hwang *et al*., 2010
2,5-Dihydroxy-3,4-di methoxyphenanthrene [**218**]	Phenanthrene	Stem	Yang *et al*., 2007
2,5-Dihydroxy-4,9-di methoxyphenanthrene [**61**]	Phenanthrene	Stem	Zhang *et al*., 2008b
3,7-Dihydroxy-2,4-Di methoxyphenanthrene [**74**]	Phenanthrene	Stem	Zhang *et al*., 2008b

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
2,2′-Dihydroxy-3,3′,4,4′,7,7′-hexamethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene [**219**]	Biphenanthrene	Stem	Yang *et al*., 2007
7,12-Dihydroxy-5-hydroxymethyl-11-isopropyl-6-methyl-9-oxatricyclo [6.2.1.$0^{2,6}$]undecan-10-one-15-*O*-β-D-glucopyranoside (Dendromoniliside D) [**180**]	Sesquiterpene glycoside	Stem	Shu *et al*., 2004
4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene [**220**]	Phenanthrene	Stem	Yang *et al*., 2007
2,8-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene [**221**]	Phenanthrene	Stem	Yang *et al*., 2007
2,8-Dihydroxy-3,4,7-tri methoxyphenanthrene [**222**]	Phenanthrene	Stem	Yang *et al*., 2007
5,7-Dimethoxy phenanthrene-2,6-diol [**223**]	Phenanthrene	Stem	Hwang *et al*., 2010
Ephemeranthol A [**224**]	Phenanthrene	Stem	Yang *et al*., 2007 ; Hwang*et al*., 2010
Ephemeranthol C [**225**]	Phenanthrene	Stem	Hwang *et al*., 2010
Erianthridin [**226**]	Phenanthrene	Stem	Yang *et al*., 2007 ; Hwang *et al*.,2010
Fimbiatone [**227**]	Phenanthrene	Stem	Zhang *et al*., 2008b

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Fimbriol B [**228**]	Phenanthrene	Stem	Yang *et al*., 2007 ; Hwang *et al*., 2010
Flavanthridin [**229**]	Phenanthrene	Stem	Hwang *et al*., 2010
Flavanthrinin [**230**]	Phenanthrene	Stem	Zhang *et al*., 2008b
Gigantol [**14**]	Bibenzyl	Stem	Zhang *et al*., 2007
Hircinol [**119**]	Phenanthrene	Stem	Hwang *et al*., 2010
2-Hydroxy-4,7-dimethoxy-9,10-dihydrophenanthrene [**231**]	Phenanthrene	Stem	Yang *et al*., 2007
3-Hydroxy-2-oxodendrobine [**232**]	Sesquiterpene alkaloid	Stem	Wang, Zhao and Che,1985
4-Hydroxy-3,5,3′-trimethoxybibenzyl [**233**]	Bibenzyl	Stem	Ye and Zhao, 2002
2-Hydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene [**234**]	Phenanthrene	Stem	Yang *et al*., 2007
3-Hydroxy-2,4,7-trimethoxy-9,10-dihydrophenanthrene [**235**]	Phenanthrene	Stem	Yang *et al*., 2007
3-Hydroxy-2,4,7-tri methoxyphenanthrene [**236**]	Phenanthrene	Stem	Yang *et al*., 2007
Lirioresinol A [**237**]	Lignan	Stem	Zhang *et al*., 2008b
Lusianthridin [**16**]	Phenanthrene	Stem	Yang *et al*., 2007 ; Hwang *et al*., 2010
Medioresinol [**153**]	Lignan	Stem	Zhang *et al*., 2008b
Moscatilin [**8**]	Bibenzyl	Stem	Yang *et al*., 2007 ; Hwang *et al*., 2010
Nobilin A [**238**]	Bibenzyl	Stem	Zhang *et al*., 2006
Nobilin B [**239**]	Bibenzyl	Stem	Zhang *et al*., 2006
Nobilin C [**240**]	Bibenzyl	Stem	Zhang *et al*., 2006
Nobilin D [**241**]	Bibenzyl	Stem	Zhang *et al*., 2007a

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Nobilin E [**242**]	Bisbibenzyl	Stem	Zhang *et al*., 2007a
Nobilone [**243**]	Fluorenone	Stem	Zhang *et al*., 2007a
Nudol [**244**]	Phenanthrene	Stem	Yang *et al*., 2007
Pinoresinol [**245**]	Lignan	Stem	Zhang *et al*., 2008b
Plicatol A [**246**]	Phenanthrene	Stem	Yang *et al*., 2007
Protocatechuic acid [**247**]	Phenolic compound	Stem	Ye and Zhao, 2002b
Syringaresinol [**248**]	Lignan	Stem	Zhang *et al*., 2008b
10β,12,14-Trihydroxy-alloaromadendrane [**249**]	Sesquiterpene	Stem	Ye and Zhao, 2002b
2,3,5-Trihydroxy-4,9-dimethoxyphenanthrene [**250**]	Phenanthrene	Stem	Yang *et al*., 2007
3,4,8-Trimethoxy phenanthrene-2,5-diol [**251**]	Phenanthrene	Stem	Hwang *et al*., 2010
Dendrobium ochreatum			
Dendrosteroside [**252**]	Steroid glycoside	Whole plant	Behr and Leander, 1976
Epi-ochreasteroside [**253**]	Steroid glycoside	Whole plant	Behr and Leander, 1976
Ochreasteroside [**254**]	Steroid glycoside	Whole plant	Behr and Leander, 1976
Dendrobium plicatile			
Batatasin [**158**]	Bibenzyl	Stem	Yamaki and Honda, 1996
2,2′-Dimethoxy-4,4′,7,7′-tetrahydroxy-9,9′,10,10′-tetra hydro-1,1′-biphenanthrene [**255**]	Biphenan threne	Stem	Yamaki and Honda, 1996

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
Ephemeranthoquinone [**256**]	Phenanthrane	Stem	Yamaki and Honda, 1996
Epheranthol B [**257**]	Phenanthrane	Stem	Yamaki and Honda, 1996
Erianthridin [**226**]	Phenanthrane	Stem	Yamaki and Honda, 1996
Lusianthridin [**16**]	Phenanthrane	Stem	Yamaki and Honda, 1996
3-*O*-Methylgigantol [**50**]	Bibenzyl	Stem	Yamaki and Honda, 1996
Plicatol A [**246**]	Phenanthrene	Stem	Honda and Yamaki, 2000
Plicatol B [**258**]	Phenanthrene	Stem	Honda and Yamaki, 2000
Plicatol C [**259**]	Phenanthrene	Stem	Honda and Yamaki, 2000
Dendrobium polyanthum			
Batatasin [**158**]	Bibenzyl	Stem	Hu *et al.*, 2009
Corchoionoside C [**260**]	Sesquiterpene	Stem	Hu *et al.*, 2009
Daucosterol [**54**]	Steroid glycoside	Stem	Hu *et al.*, 2009
9,10-Dihydromoscatin [**261**]	Phenanthrene	Stem	Hu *et al.*, 2009
9,10-Dihydrophenanthrene-2,4,7-triol [**262**]	Phenanthrene	Stem	Hu *et al.*, 2009
Gigantol [**14**]	Bibenzyl	Stem	Hu *et al.*, 2009
Moscatilin [**8**]	Bibenzyl	Stem	Hu *et al.*, 2009
Moscatin [**17**]	Phenanthrene	Stem	Hu *et al.*, 2009

Table 1 (continued)

Plant and compound	Category	Plant part	Reference
β-Sitosterol [**65**]	Steroid	Stem	Hu *et al.*, 2009
3,6,9-Trihydroxy-3,4-dihydroanthracen-1(2*H*)-one [**263**]	Anthracene	Stem	Hu *et al.*, 2009
Dendrobium pulchellum			
Chrysotobibenzyl [**18**]	Bibenzyl	Stem	Chanvorachote *et al*., 2013
Chrysotoxine [**19**]	Bibenzyl	Stem	Chanvorachote *et al*., 2013
Crepidatin [**21**]	Bibenzyl	Stem	Chanvorachote *et al*., 2013
Fimbiatone [**227**]	Phenanthrene	Stem	Chanvorachote *et al*., 2013
Liriodendrin [**264**]	Lignan glycoside	Stem	Chanvorachote *et al*., 2013
Moscatilin [**8**]	Bibenzyl	Stem	Chanvorachote *et al*., 2013
(−)- Shikimic acid [**133**]	Aliphatic acid	Stem	Chanvorachote *et al*., 2013
Dendrobium rotundatum			
Batatasin III [**9**]	Bibenzyl	Whole plant	Majumder and Pal, 1992
2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene [**265**]	Phenanthrene	Whole plant	Majumder and Pal, 1992
2,7-Dihydroxy-3,4,6-tri methoxyphenanthrene [**266**]	Phenanthrene	Whole plant	Majumder and Pal, 1992

Table 1 (continued)

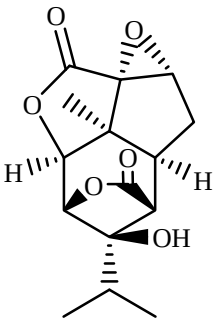
Plant and compound	Category	Plant part	Reference
Moscatin [**17**]	Phenanthrene	Whole plant	Majumder and Pal, 1992
Nudol [**244**]	Phenanthrene	Whole plant	Majumder and Pal, 1992
Rotundatin [**155**]	Phenanthrene	Whole plant	Majumder and Pal, 1992
Dendrobium secundum			
Brittonin A [**267**]	Bibenzyl	Stem	Sritularak, Duangrak and Likhitwitayawuid 2011b
Ferulic acid [**268**]	Phenylpropanoid	Stem	Sritularak *et al.*, 2011b
5-Hydroxy-3,4,3′,4′,5′-pentamethoxybibenzyl [**269**]	Bibenzyl	Stem	Phechrmeekha, Sritularak and Likhitwitayawuid, 2012
Kaempferol-3,7-*O*-di-α-L-rhamnopyranoside [**270**]	Flavonol glycoside	Stem	Phechrmeekha *et al*., 2012
Kaempferol-3-*O*-α-L-rhamnopyranoside [**271**]	Flavonol glycoside	Stem	Phechrmeekha *et al*., 2012
Quercetin-3-*O*-α-L-rhamnopyranoside [**272**]	Flavonol glycoside	Stem	Phechrmeekha *et al*., 2012
Moscatilin [**8**]	Bibenzyl	Stem	Sritularak *et al.*, 2011b
Syringaresinol [**248**]	Lignan	Stem	Sritularak *et al.*, 2011b

Table 1 (continued)

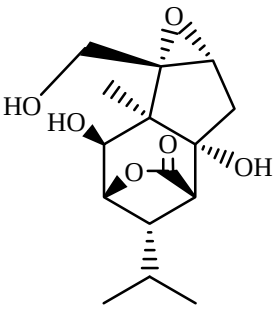
Plant and compound	Category	Plant part	Reference
4,5,4′-Trihydroxy-3-3′-dimethoxybibenzyl [**273**]	Bibenzyl	Stem	Sritularak *et al.*, 2011b
4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene [**274**]	Phenanthrene	Whole plant	Chen *et al*., 2013
4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene [**275**]	Phenanthrene	Whole plant	Chen *et al*., 2013
Dendrobium thyrsiforum			
Chrysophanol [**276**]	Anthraquinone	Stem	Zhang *et al*., 2005
Daucosterol [**54**]	Steroid glycoside	Stem	Zhang *et al*., 2005
Denthyrsin [**277**]	Coumarin	Stem	Zhang *et al*., 2005
Denthyrsinin [**278**]	Phenanthrene	Stem	Zhang *et al*., 2005
Denthyrsinol [**279**]	Biphenanthrene	Stem	Zhang *et al*., 2005
Denthyrsinone [**280**]	Biphenanthrene	Stem	Zhang *et al*., 2005
Emodin [**281**]	Anthraquinone	Stem	Zhang *et al*., 2005
Physcion [**282**]	Anthraquinone	Stem	Zhang *et al*., 2005
Scoparone [**116**]	Coumarin	Stem	Zhang *et al*., 2005
β-Sitosterol [**65**]	Steroid	Stem	Zhang *et al*., 2005
Dendrobium trigonopus			
Gigantol [**14**]	Bibenzyl	Stem	Hu *et al.*, 2008b
Hircinol [**119**]	Bibenzyl	Stem	Hu *et al.*, 2008b
3-(4-Hydroxy-3-methoxy phenyl)-2-propen-1-ol [**283**]	Phenylpropanoid	Stem	Hu *et al.*, 2008b
Moscatin [**17**]	Phenanthrene	Stem	Hu *et al.*, 2008b
Naringenin [**29**]	Flavanone	Stem	Hu *et al.*, 2008b
(-)-Syringaresinol [**248**]	Lignan	Stem	Hu *et al.*, 2008b
Trigonopol A [**284**]	Bibenzyl	Stem	Hu *et al.*, 2008b

Table 1 (continued)

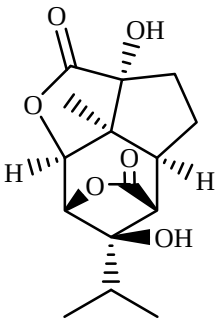
Plant and compound	Category	Plant part	Reference
Trigonopol B [**86**]	Bibenzyl	Stem	Hu *et al.*, 2008b
Tristin [**87**]	Bibenzyl	Stem	Hu *et al.*, 2008b
Dendrobium wardianum Warner			
Dendrobane A [**191**]	Sesquiterpene	Stem	Fan *et al*., 2013
Dendronobilin I [**201**]	Sesquiterpene	Stem	Fan *et al*., 2013
Dendrowardol A [**285**]	Sesquiterpene	Stem	Fan *et al*., 2013
Dendrowardol B [**286**]	Sesquiterpene	Stem	Fan *et al*., 2013
Dendrowardol C [**287**]	Sesquiterpene	Stem	Fan *et al*., 2013
10β,12,14-trihydroxyalloaromadendrane [**288**]	Sesquiterpene	Stem	Fan *et al*., 2013



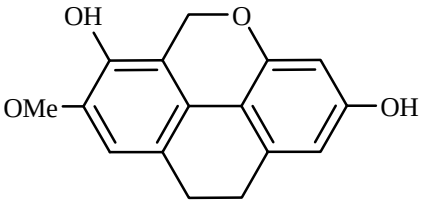
[**1**] Aduncin



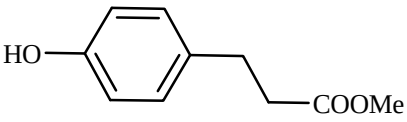
[**2**] Amoenin



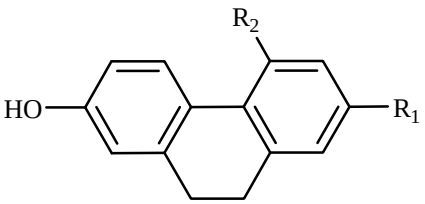
[**5**] Amotin



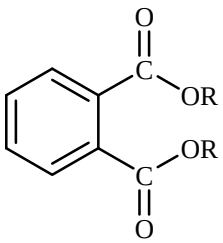
[**3**] Amoenumin



[**15**] *p*-Hydroxyphenyl propionic methyl ester

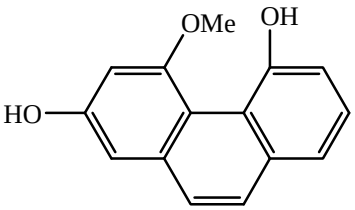


	R_1	R_2
[**10**] Coelonin	OH	OMe
[**16**] Lusianthridin	OMe	OH

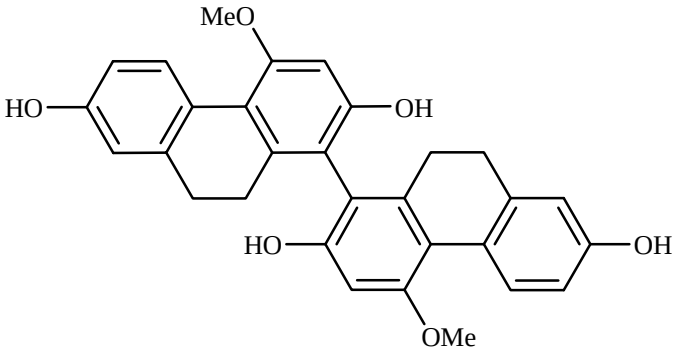


[**11**] Dibutyl phthalate
R = $(CH_2)_3CH_3$

[**12**] Diisobutyl phthalate
R=$CH_2CH(CH_3)_2$

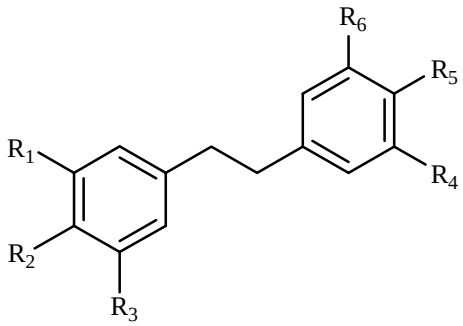


[**17**] Moscatin



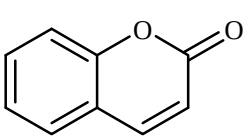
[**13**] Flavanthrin

Figure 2 Structures of compounds previously isolated from *Dendrobium* species

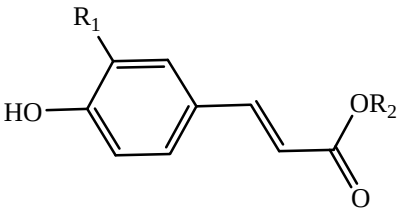


	R_1	R_2	R_3	R_4	R_5	R_6
[**4**] Amoenylin	OMe	OH	OMe	H	OMe	H
[**6**] 3,4'-Dihydroxy-5-methoxybibenzyl	OH	H	OMe	H	OH	H
[**7**] Isoamoenylin	OMe	OMe	OMe	H	H	OH
[**8**] Moscatilin	OMe	OH	OMe	H	OH	OMe
[**9**] Batatasin III	OMe	H	OH	H	H	OH
[**14**] Gigantol	OMe	H	OH	H	OH	OMe
[**18**] Chrysotobibenzyl	OMe	OMe	OMe	OMe	OMe	H
[**19**] Chrysotoxine	OMe	OH	OMe	OMe	OMe	H
[**21**] Crepidatin	OMe	OMe	OMe	OMe	OH	H
[**56**] 3,3′,5- Trihydroxy bibenzyl	H	H	OH	OH	H	OH
[**79**] Erianin	OMe	OMe	OMe	H	OMe	OH
[**87**] Tristin	OH	H	OH	H	OH	OMe
[**105**] Cumulatin	OMe	OMe	OH	OH	OMe	OMe
[**157**] Aloifol I	OMe	OH	OMe	OH	H	H
[**158**] Batatasin	OMe	H	H	OH	H	OH
[**174**] 3,3′,4- Trihydroxy bibenzyl	OH	OH	H	H	H	OH
[**181**] Dendromoniliside E	OGlc	OGlc	OMe	H	OMe	H
[**217**] 3,4′-Dihydroxy-5,5′-dimethoxydihydrostilbene	OH	H	OMe	OMe	OH	H

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

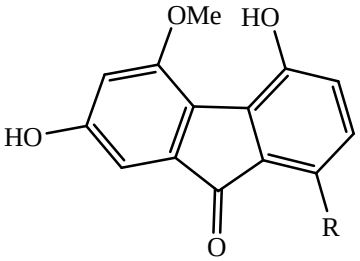


[**20**] Coumarin



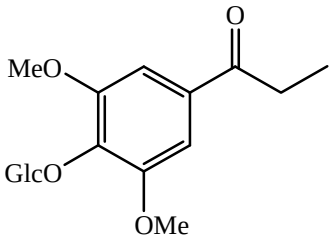
[**22**] Defuscin R_1= OMe, R_2= $(CH_2)_{27}CH_3$

[**30**] *n*-Octacosyl ferulate R_1= H, R_2= $(CH_2)_{29}CH_3$

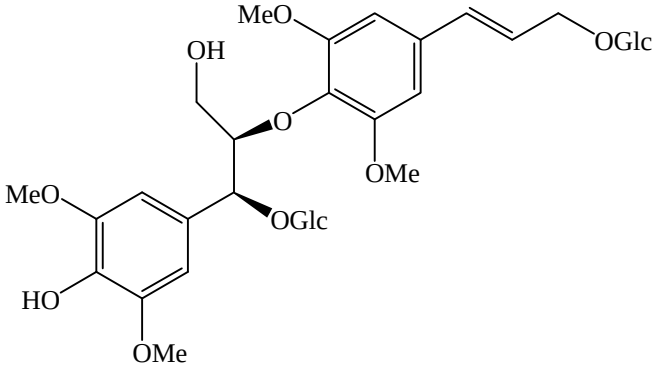


[**23**] Dendroflorin: R= OH

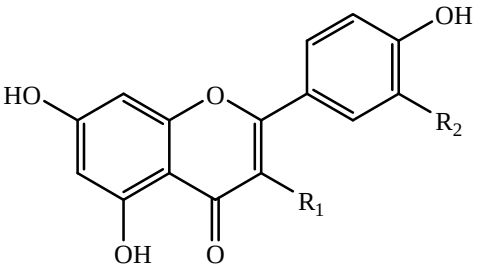
[**24**] Dengibsin: R= H



[**25**] 1-[4-(*β*-D-glucopyranosyloxy)-3,5-dimethoxyphenyl]-1- propanone

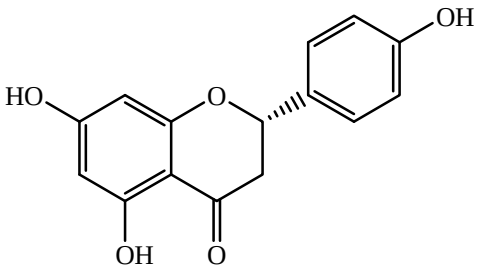


[**26**] (–)-(7*S*,8*R*,7′*E*)-4-hydroxy-3,3′,5,5′-tetramethoxy-8,4′-oxyneolign-7′-ene-7,9,9′-triol 7,9′-bis-*O*-*β*-D-glucopyranoside



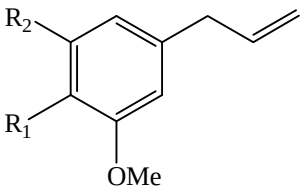
[**27**] Kaempferol: R_1= OH, R_2 = H

[**28**] Luteolin: R_1= H, R_2 = OH



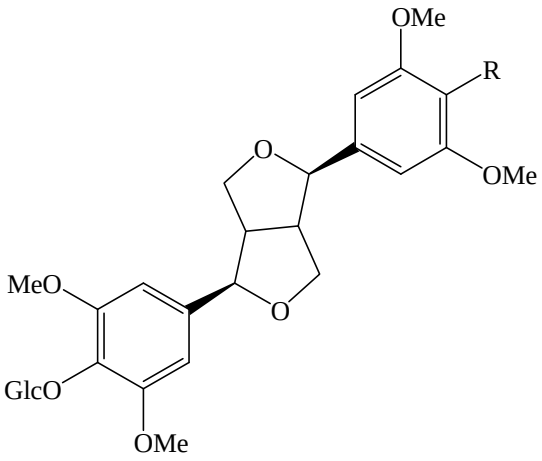
[**29**] Naringenin

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



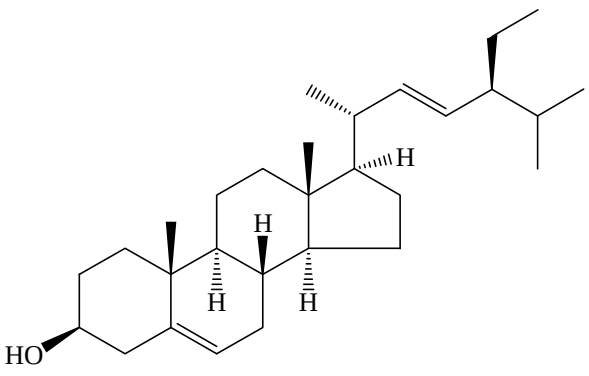
[**31**] Shashenoside I R $_1$= OGlc, R_2 = OGlc

[**35**] Syringin R $_1$= OGlc, R_2 = OMe

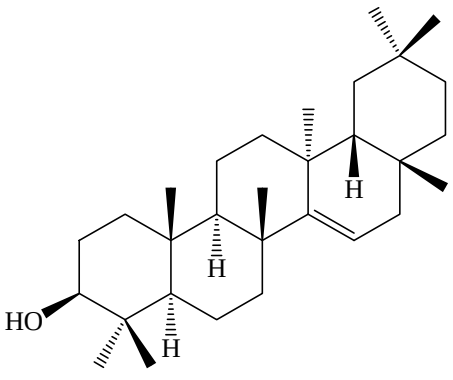


[**32**] (–)-Syringaresinol-4,4′-bis-*O*-*β*-D-glucopyranoside R: OGlc

[**33**] Syringaresinol-4-*O*-*β*-D-monoglucopyranoside R: OH

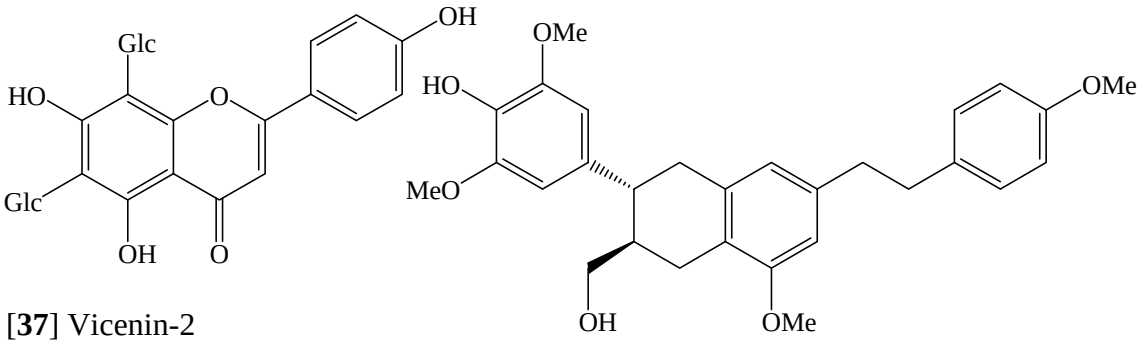


[**34**] Stigmasterol



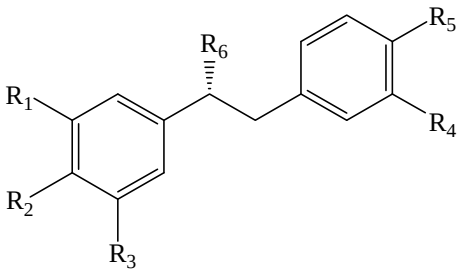
[**36**] Taraxerol

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

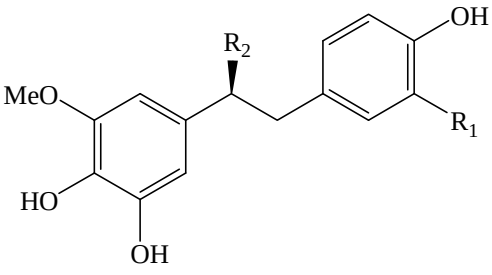


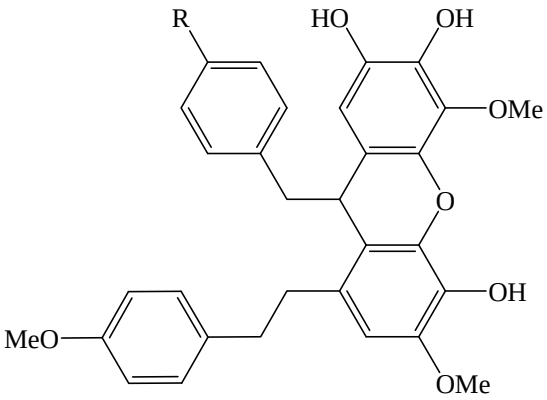
[**37**] Vicenin-2

[**39**] Dendrocandin B



	R_1	R_2	R_3	R_4	R_5	R_6
[**38**] Dendrocandin A	OMe	OH	OH	H	OMe	OMe
[**47**] Dendrophenol	OMe	OH	OMe	OH	OH	H
[**48**] 3,4-Dihydroxy-5,4′-dimethoxybibenzyl	OH	OH	OMe	H	OMe	H
[**49**] 4,4′-Dihydroxy-3,5-dimethoxybibenzyl	OMe	OH	OMe	H	OH	H
[**50**] 3-*O*-Methylgigantol	OMe	H	OH	OMe	OMe	H



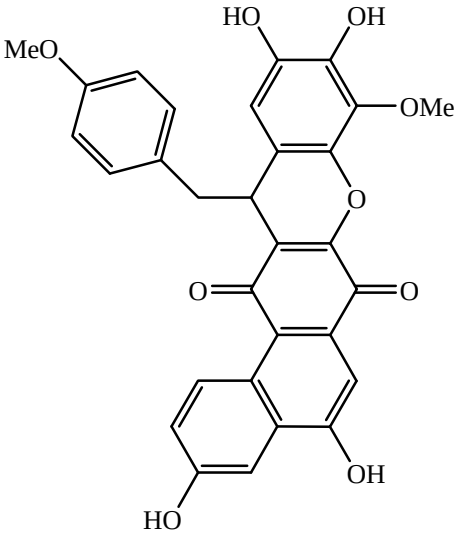


[**40**] Dendrocandin C: R_1=H, R_2 = OMe

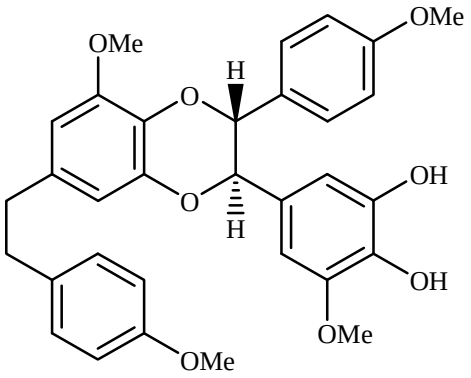
[**41**] Dendrocandin D: R_1=H, R_2 = OCH_2CH_3 [**43**] Dendrocandin F: R = OMe

[**42**] Dendrocandin E: R_1=OH, R_2 = H [**44**] Dendrocandin G: R = OH

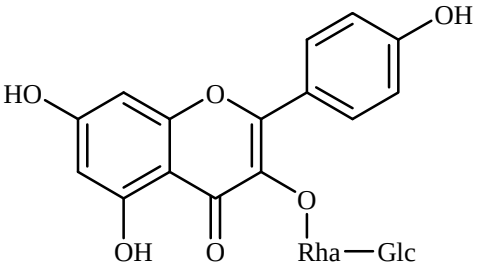
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



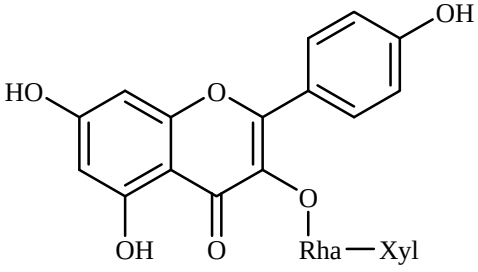
[**45**] Dendrocandin H



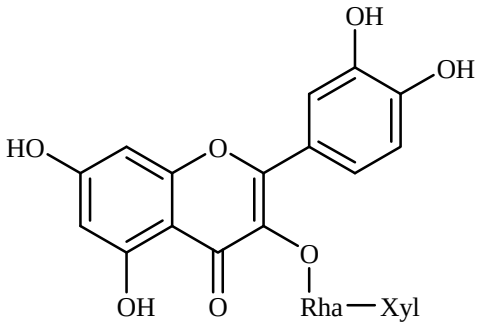
[**46**] Dendrocandin I



[**51**] Kaempferol-3-*O*-α-L-rhamno pyranosyl-(1→2)-*β*-D-glucopyranoside

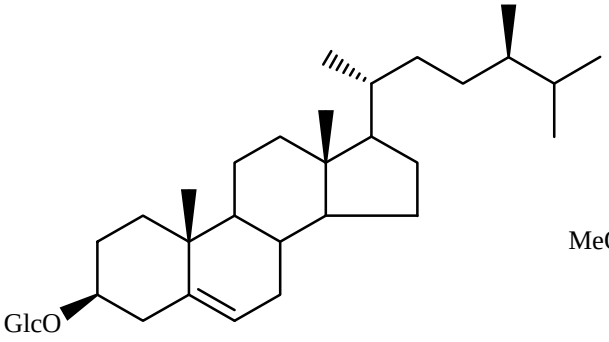


[**52**] Kaempferol-3-*O*-α-L-rhamno pyranosyl-(1→2)-*β*-D-xylopyranoside

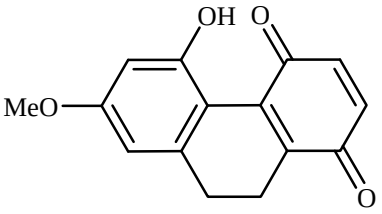


[**53**] Quercetin-3-*O*-α-L-rhamnopyranosyl-(1→2)-*β*-D-xylopyranoside

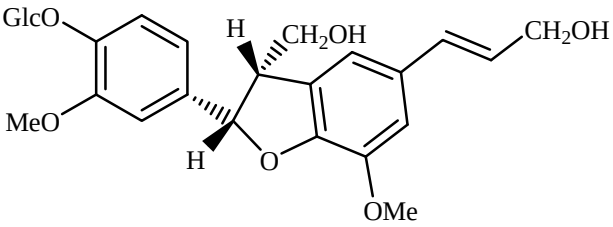
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



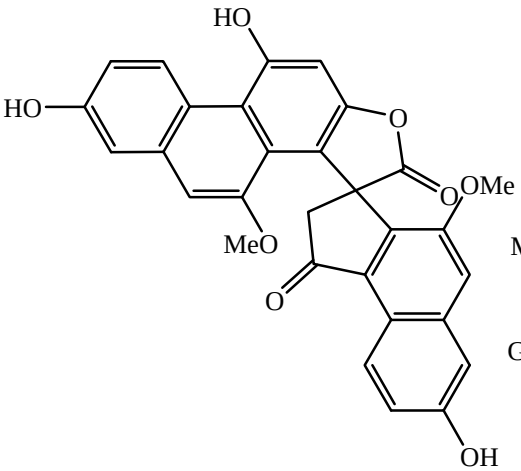
[**54**] Daucosterol



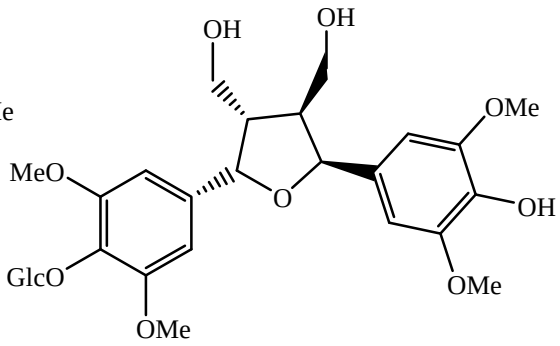
[**55**] Dendronone



[**57**] 7,7′-bis-(4-hydroxy-3,5-dimethoxyphenyl)-8,8′-dihydroxymethyltetrahydrofuran-4β-D- glucoside

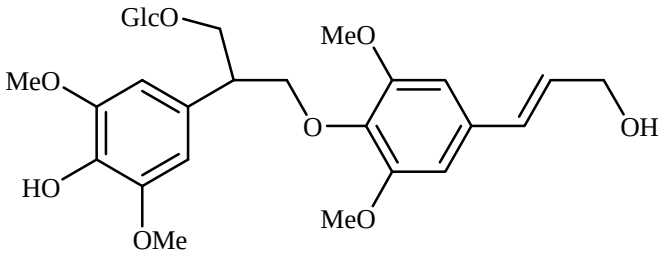


[**60**] Dendrochrysanene

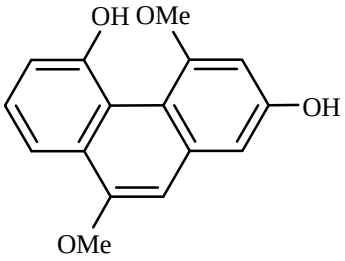


[**58**] Dehydrodiconiferyl alcohol-4-β-D-glucoside

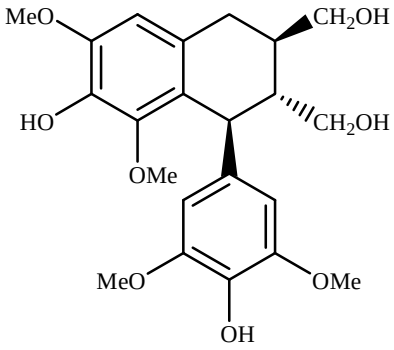
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



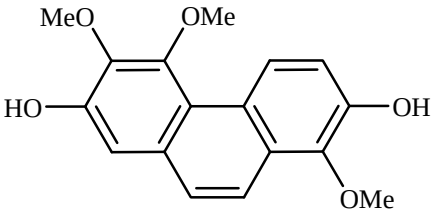
[**59**] Denchryside B



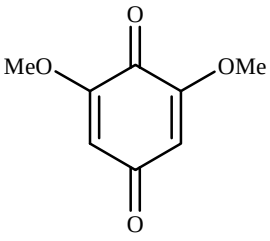
[**61**] 2,5-Dihydroxy-4,9-dimethoxylphenanthrene



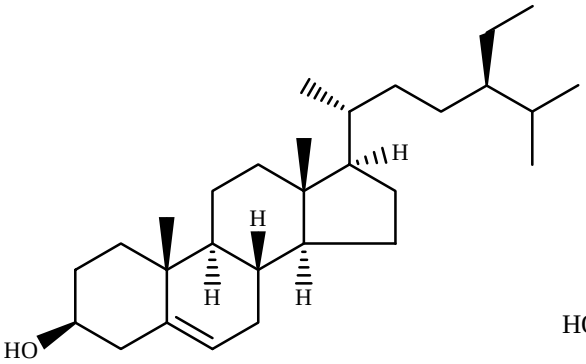
[**62**] Lioniresinol



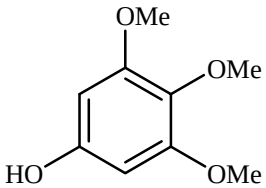
[**63**] Confusarin



[**64**] 2,6-Dimethoxybenzoquinone

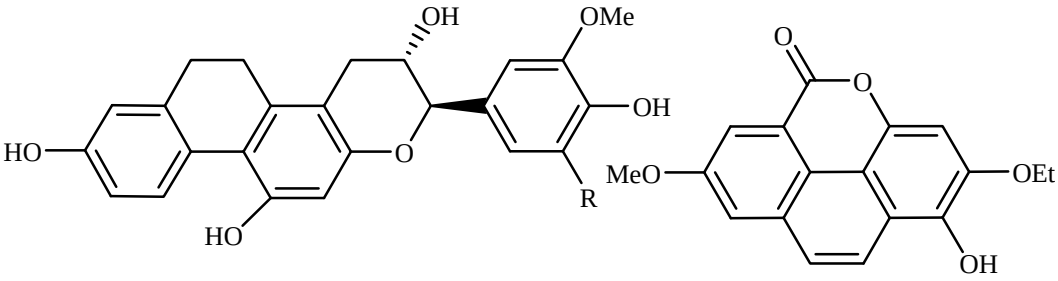


[**65**] β-Sitosterol



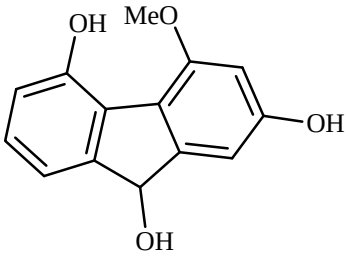
[**66**] Antiarol

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

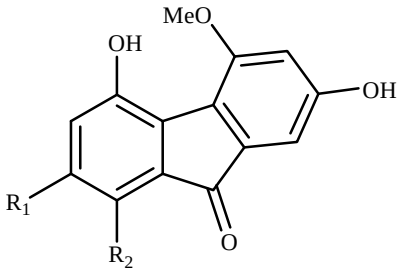


[**67**] Chrysotoxol A: R=H
[**68**] Chrysotoxol B: R= OMe

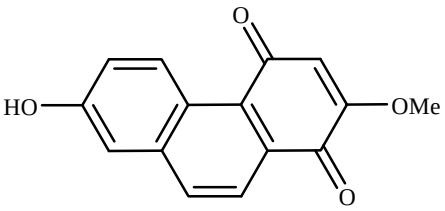
[**69**] Crystalltone



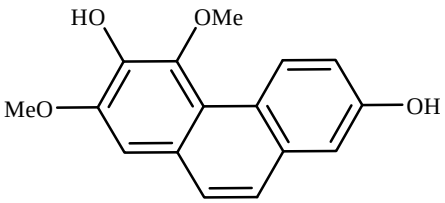
[**71**] Denchrysan B



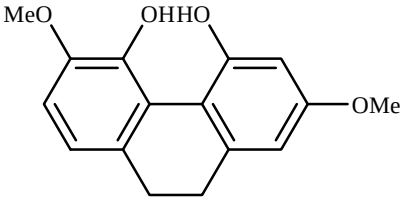
[**72**] Dendroflorin: R_1=H, R_2=OH
[**70**] Denchrysan A: R_1=OH, R_2=H



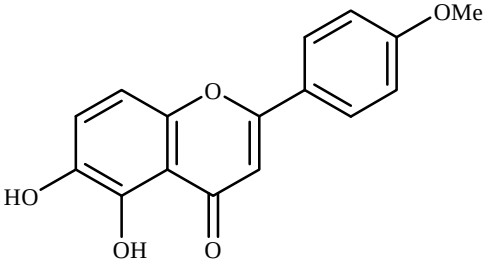
[**73**] Densiflorol B



[**74**] 3,7-Dihydroxy-2,4-dimethoxyphenanthrene

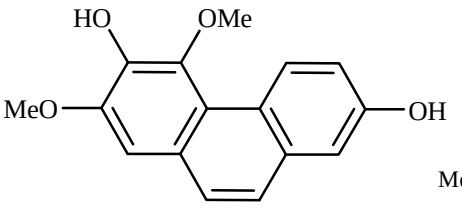


[**75**] 4,5-Dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene

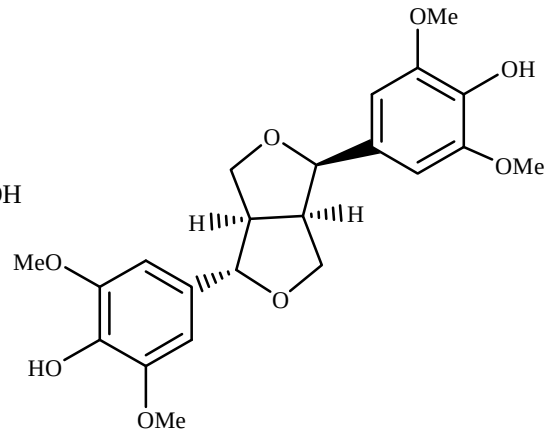


[**76**] 5,6-Dihydroxy-4′-methoxy-flavone

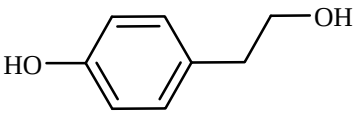
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



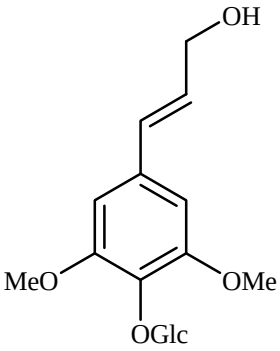
[**77**] Epheranthol B



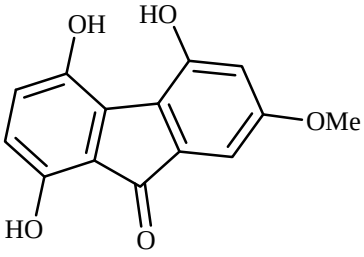
[**78**] Episyringaresinol



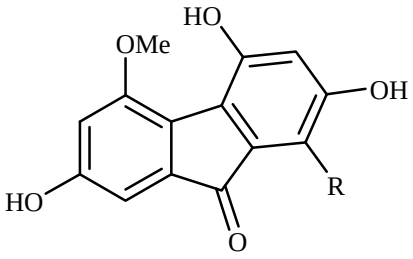
[**80**] Salidrosol



[**81**] Syringoside



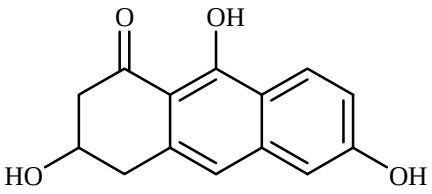
[**82**] 1,4,5-Trihydroxy-7-methoxy-9*H*-fluoren-9-one



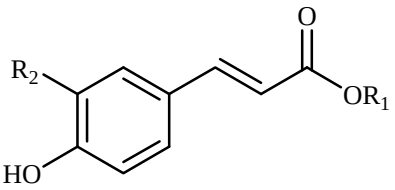
[**83**] 2,4,7-Trihydroxy-5- methoxy 9- fluorenone:R=H

[**84**] 2,4,7-Trihydroxy-1,5-dimethoxy-9-fluorenone:R=OCH_3

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



[**85**] 3,6,9-Trihydroxy-3,4-dihydro anthracen-1-(2*H*)-one

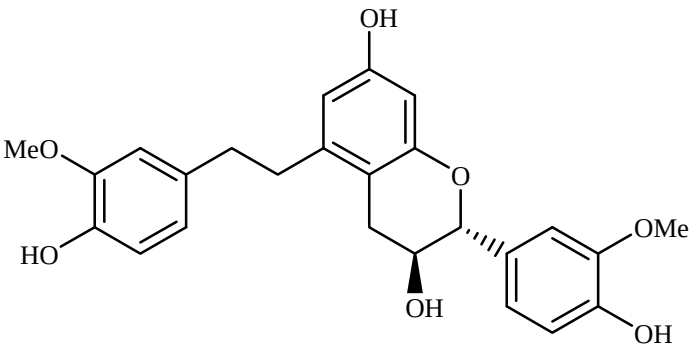


[**91**] Alkyl 4′-hydroxy-*trans*-cinnamates:

$R_1 = C_nH_{2n+1}$, n = 22-32, R_2 = H

[**92**] Alkyl *trans*-ferulates:

$R_1 = C_nH_{2n+1}$, n = 18-28, 30, R_2 = OMe



[**86**] Trigonopol B

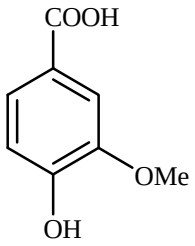
$CH_3(CH_2)_nCH_2R$

[**89**] Aliphatic acids:

R = COOH, n = 19-31

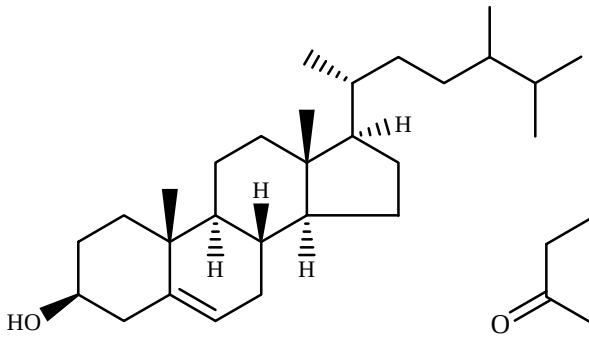
[**90**] Aliphatic alcohol:

R= OH, n=22-32

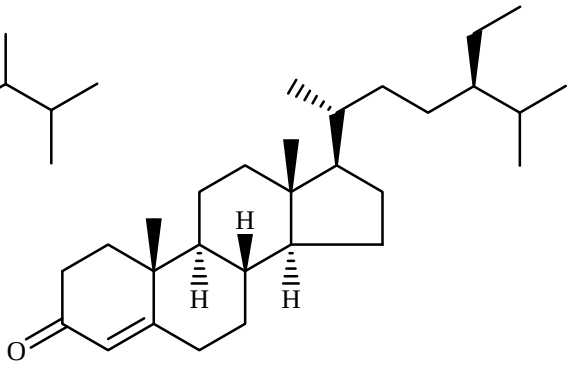


[**88**] Vanillic acid

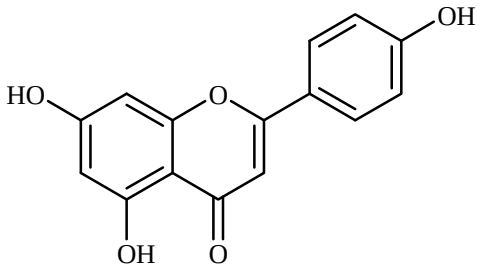
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



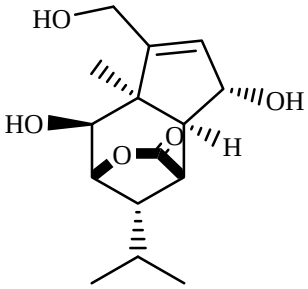
[**93**] Campesterol



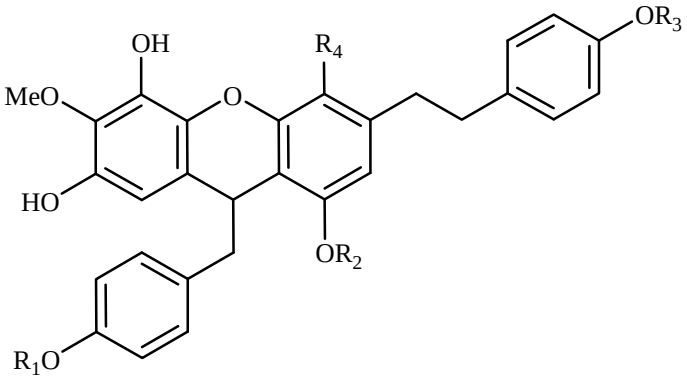
[**94**] Stigmast-4-en-3-one



[**95**] Apigenin

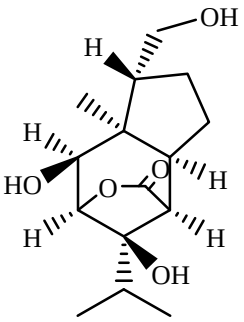


[**96**] Crystallinin

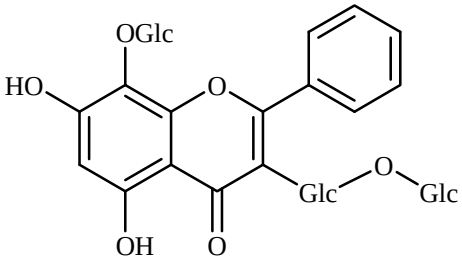


	R_1	R_2	R_3	R_4
[**97**] Dencryol A	Me	H	H	H
[**98**] Dencryol B	H	Me	Me	OH

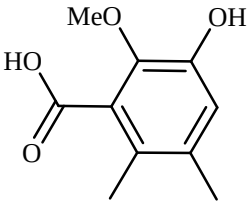
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



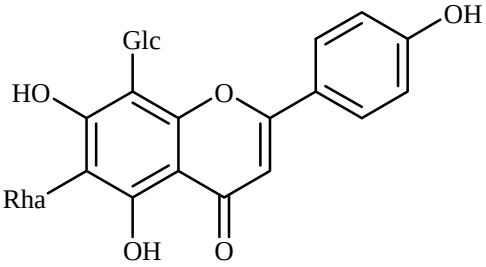
[**99**] Dendronobilin B



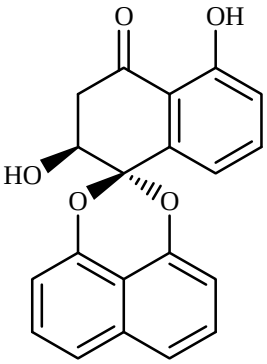
[**100**] 6′′′- glucosyl-vitexin



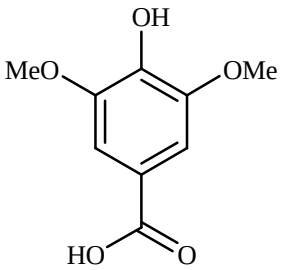
[**101**] 3-Hydroxy-2-methoxy-5,6-dimethylbenzoic acid



[**102**] Isoviolanthin

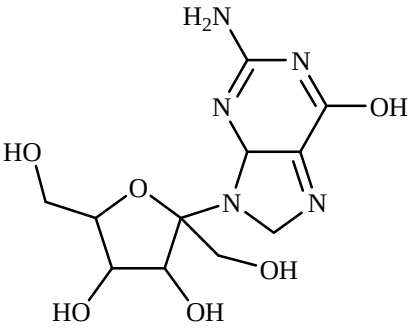


[**103**] Palmarumycin JC2

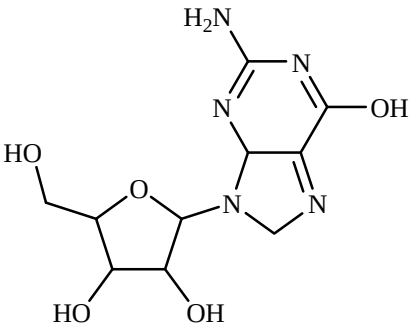


[**104**] Syringic acid

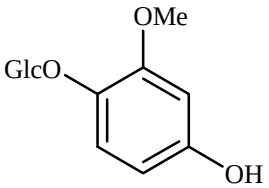
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



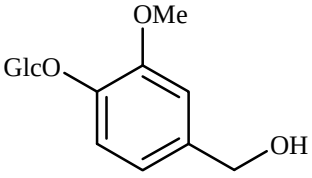
[**106**] 9-*β*-D-allofuranulsyguanine



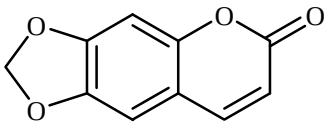
[**107**] Guanosine



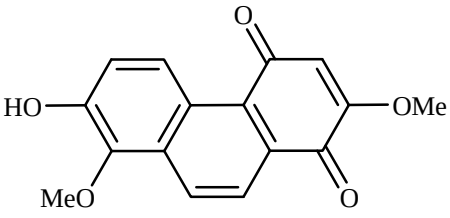
[**108**] Tachioside



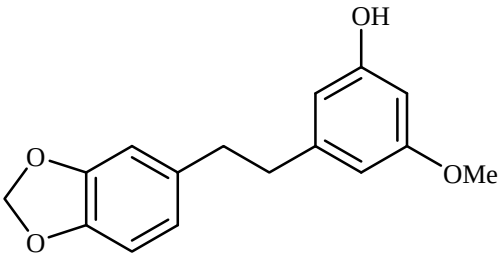
[**109**] Vanilloside



[**110**] Ayapin

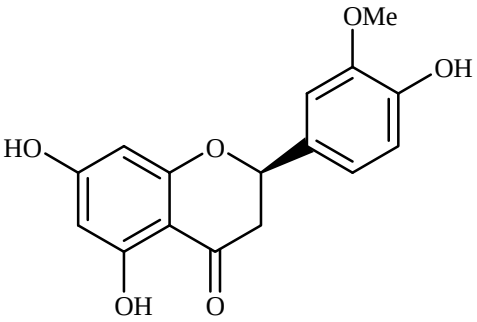


[**111**] Cypripedin

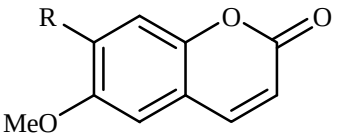


[**112**] Densiflorol A

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

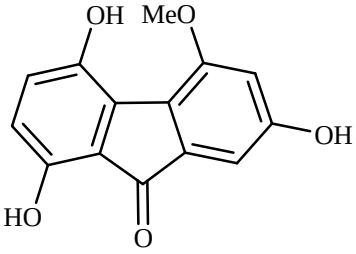


[**115**] Homoeriodictyol

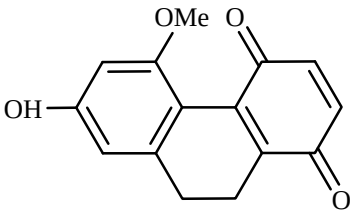


[**116**] Scoparone: R=OMe

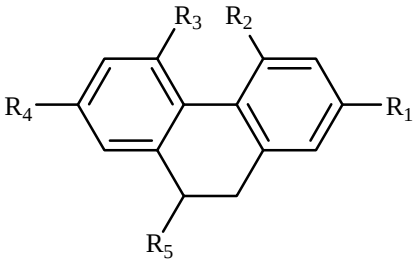
[**117**] Scopoletin: R= H



[**118**] 1,4,7-Trihydroxy-5-methoxy -9H-fluoren-9-one

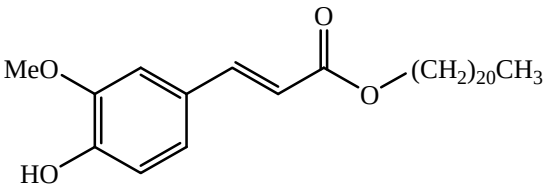


[**121**] 5-Methoxy-7-hydroxy-9,10-dihydro-1,4-phenanthrenequinone

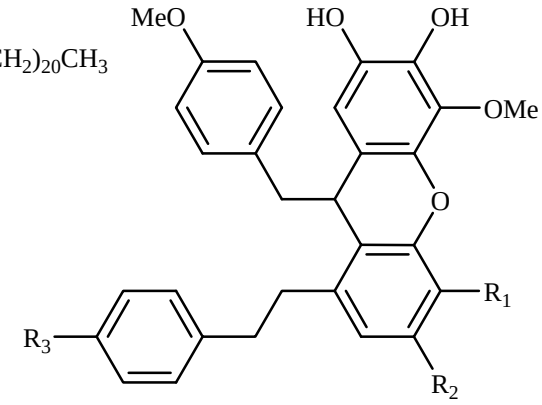


	R_1	R_2	R_3	R_4	R_5
[**113**] 4,7-Dihydroxy-2-methoxy-9,10 –dihydrophenanthrene	OMe	OH	H	OH	H
[**119**] Hircinol	OH	OMe	OH	H	H
[**120**] 7-Methoxy-9,10-dihydro phenanthrene 2,4,5-triol	OH	OMe	OH	OH	H
[**155**] Rotundatin	OH	OMe	OH	H	OH

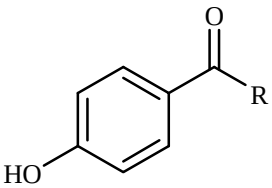
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



[**124**] Docosanoyl (*E*)- ferulate

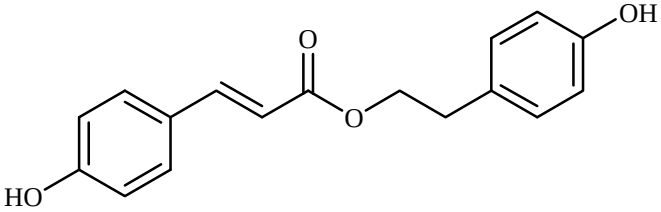


	R_1	R_2	R_3
[**122**] Dendrofalconerol A	OH	OMe	OMe
[**123**] Dendrofalconerol B	H	OH	OH

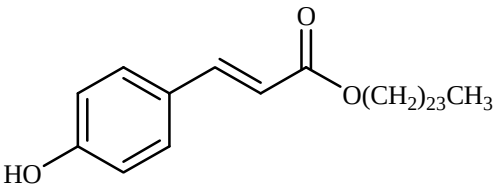


[**125**] *p*- Hydroxybenzaldehyde: R=H

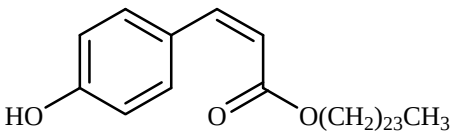
[**126**] *p*- Hydroxybenzoic acid: R= OH



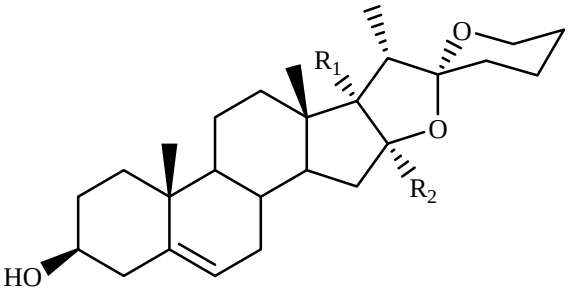
[**127**] 2-(*p*- Hydroxyphenyl) ethyl *p*-coumarate



[**128**] Tetracosyl (*E*)-*p*-coumarate

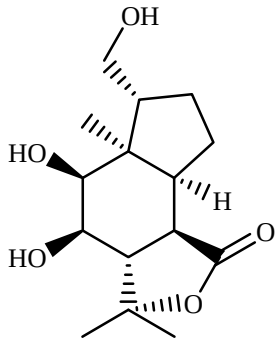


[**129**] Tetracosyl (*Z*)-*p*-coumarate



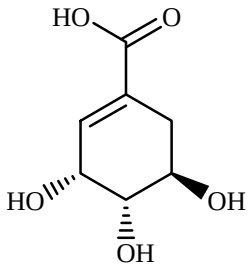
[**130**] Denfigenin: R_1=R_2=OH

[**131**] Diosgenin: R_1=R_2=H

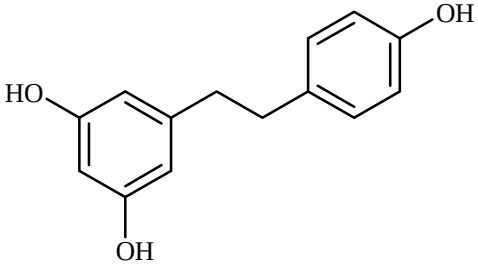


[**132**] Findlayanin

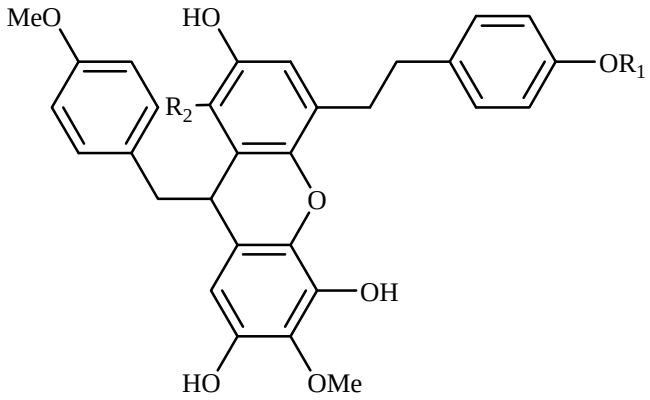
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



[**133**] (–)-Shikimic acid

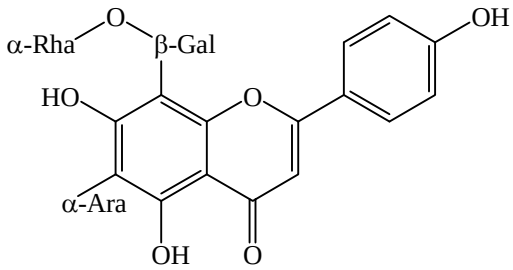


[**136**] 3,5,4′ Trihydroxybibenzyl

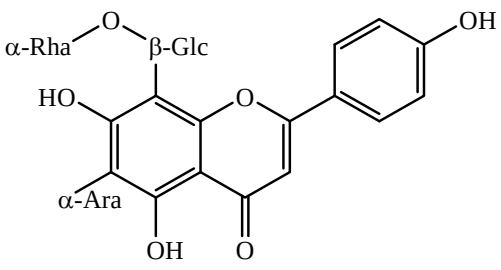


[**134**] Dengraol A: R_1,R_2=H

[**135**] Dengraol B: R_1=Me, R_2=OMe

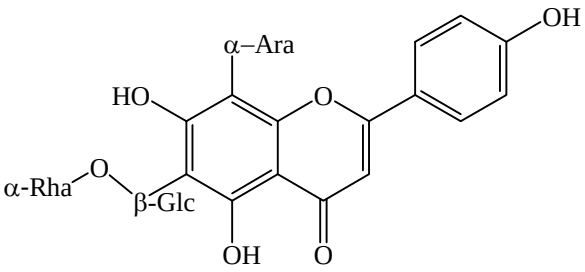


[**137**] 6-*C*-(*α*-Arabinopyranosyl)-8-*C*-[(2-*O*-α rhamnopyranosyl) -*β*-galactopyranosyl]apigenin

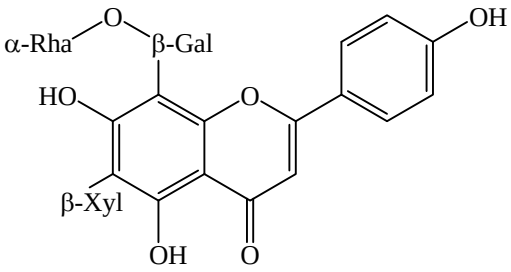


[**138**] 6-*C*-(*α*-Arabinopyranosyl)-8-*C*-[(2-*O*-α rhamnopyranosyl) -*β*-glucopyranosyl]apigenin

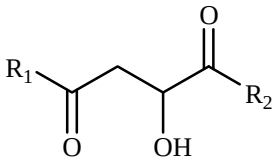
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



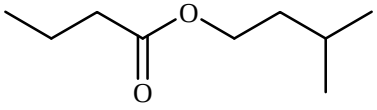
[**144**] 6-*C*-[(2-*O*-α-rhamnopyranosyl)-*β*-glucopyranosyl]-8-*C*-*α*-arabino pyranosyl]apigenin



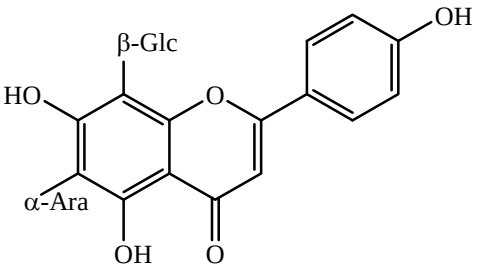
[**146**] 6-*C*-(β-Xylopyranosyl)-8-*C*-[(2-*O*-α-rhamnopyranosyl)-β-glucopyranosyl] apigenin



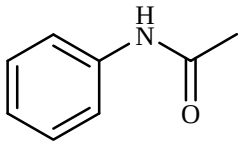
[**139**] Dimethyl malate:$R_1 = R_2 = OMe$
[**142**] Malic acid: $R_1 = R_2 = OH$



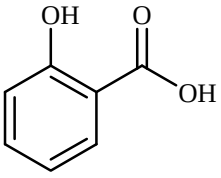
[**140**] Isopentyl butyrate



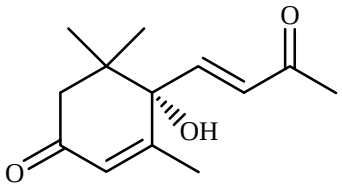
[**141**] Isoschaftoside



[**143**] *N*-Phenylacetamide

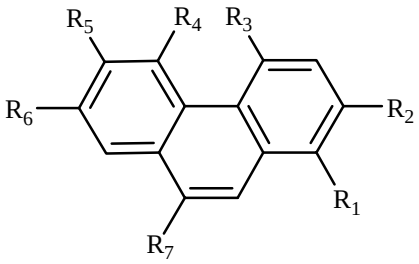


[**145**] Salicylic acid

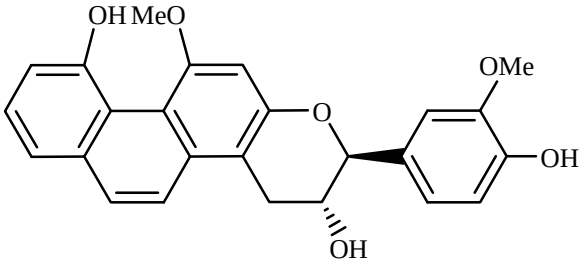


[**147**] Dehydrovomifoliol

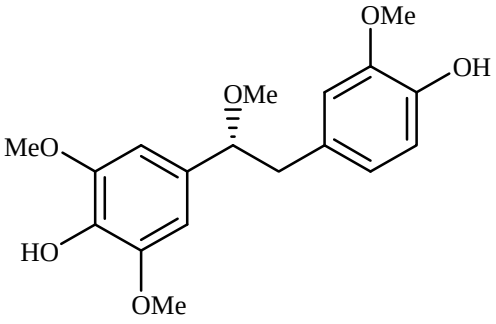
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



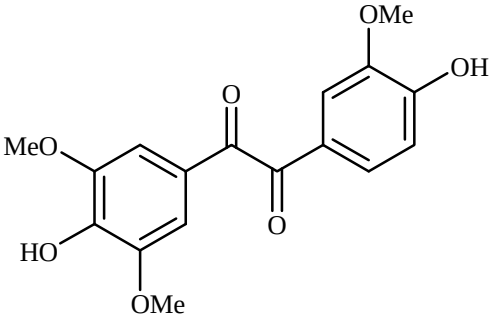
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**114**] 2,6- Dihydroxy-1,5,7-trimethoxyphenanthrene	OMe	OH	H	OMe	OH	OMe	H
[**148**] 5-Hydroxy-2,4-dimethoxyphenanthrene	H	OMe	OMe	OH	H	H	H
[**149**] Loddigesiinol A	H	OH	OMe	OMe	H	H	OH



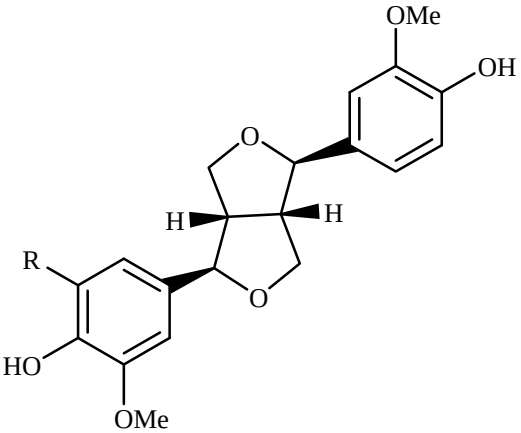
[**150**] Loddigesiinol B



[**151**] Loddigesiinol C



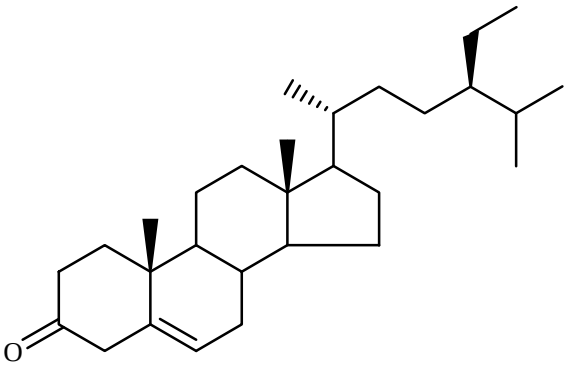
[**152**] Loddigesiinol D



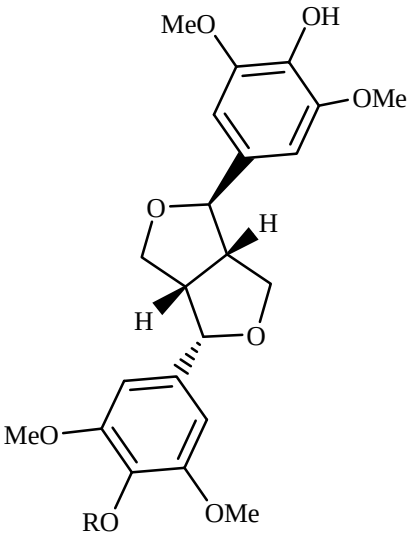
[**153**] (–)-Medioresinol: R = OMe

[**154**] (–)-Pinoresinol: R = H

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

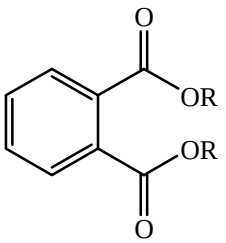


[**156**] Sitostenone



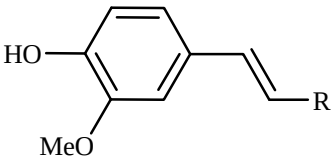
[**161**] Episyringaresinol: R=H

[**162**] Episyringaresinol 4′′-*O*-β-D-glucopyranoside: R = β-D-Glucose



[**159**] Bis(2-ethylhexyl)phthalate:

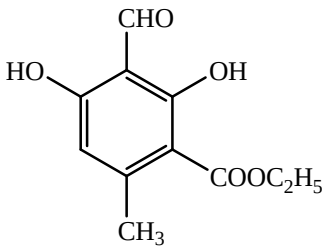
R =$CH_2CH(C_2H_5)(CH_2)_3CH_3$



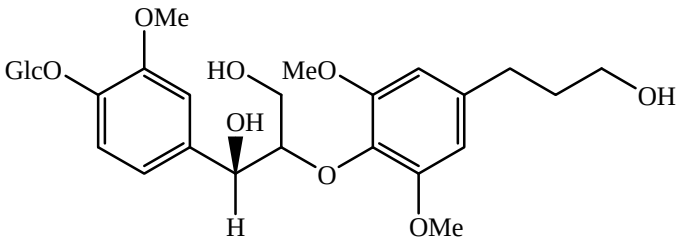
[**160**] *n*-Docosyl *trans*-ferulate:

R=$COOCH_2(CH_2)_{20}CH_3$

[**166**] Ferulaldehyde: R = CHO

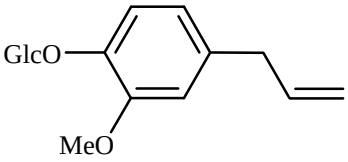


[**164**] Ethylhaematommate

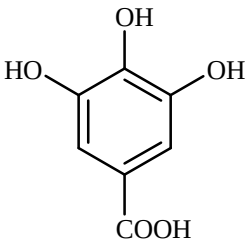


[**163**] Erythro-1-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)-2-[4-(3-hydroxypropyl)-2,6-dimethoxyphenoxy]-1,3-propanediol

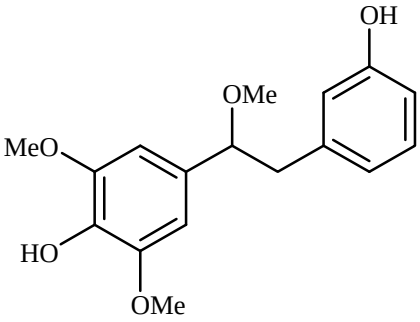
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



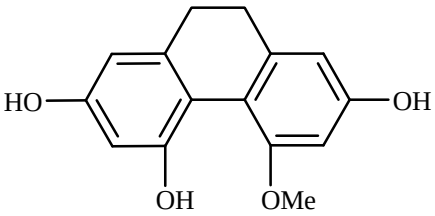
[**165**] Eugenyl -*O*-β-D-glucopyranoside



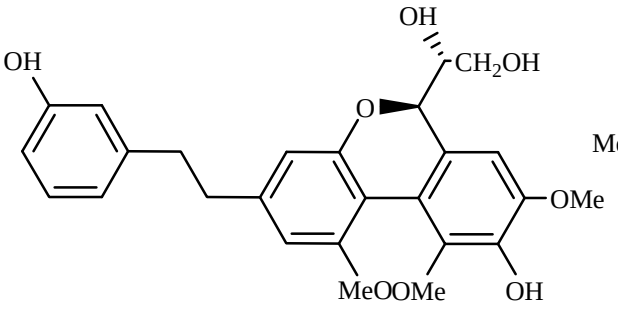
[**167**] Gallic acid



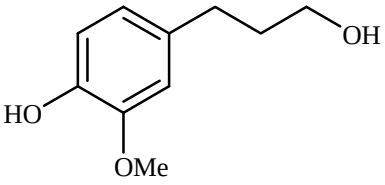
[**168**] 4-[2-(3Hydroxyphenol)-1-methoxyl]-2,6-dimethoxyphenol



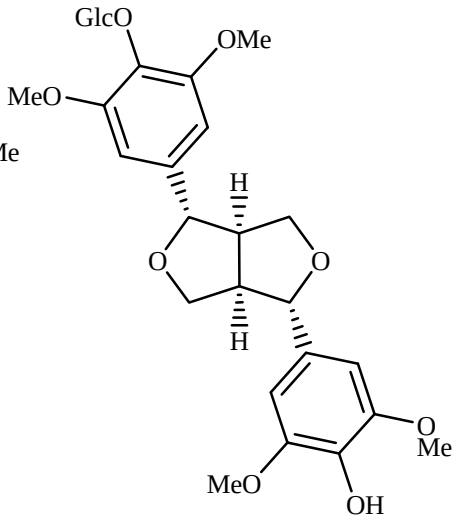
[**170**] 4-Methoxy-9,10-dihydro phenanthrene-2,5,7-triol



[**169**] Longicornuol A

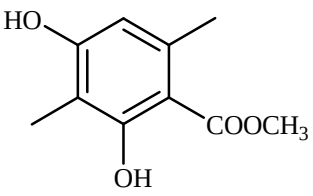


[**171**] 3-(3-Methoxy,4-hydroxyphenyl)-1-propanol

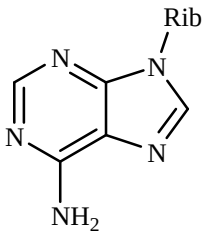


[**175**] Acanthoside B

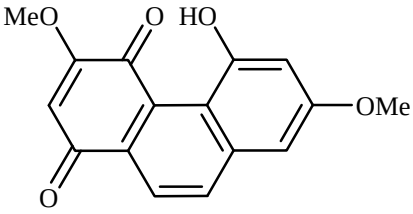
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



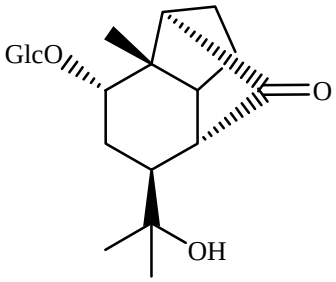
[**172**] Methyl *β*- orsellinate



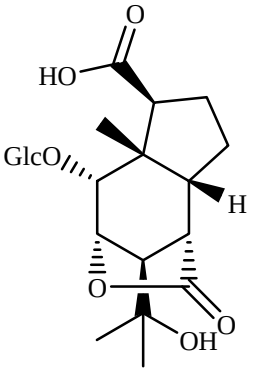
[**173**] 9-β-D-Ribofuranosyl-9H-purin-6- amine



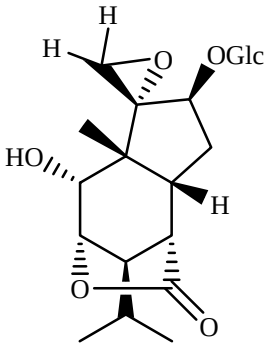
[**176**] Denbinobin



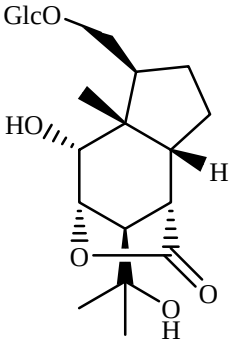
[**177**] Dendromoniliside A



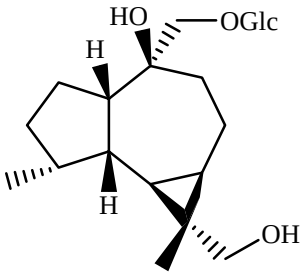
[**178**] Dendromoniliside B



[**179**] Dendromoniliside C

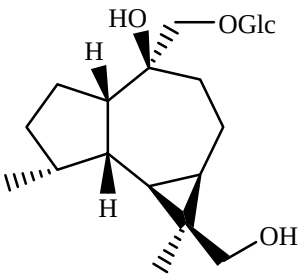


[**180**] Dendromoniliside D

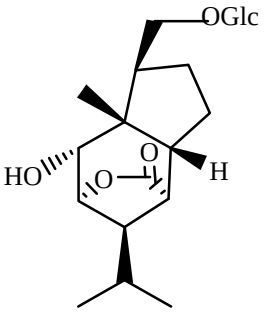


[**182**] Dendroside A

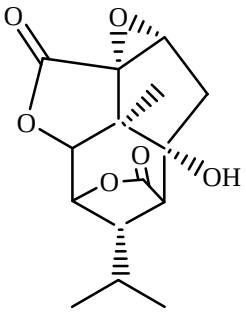
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



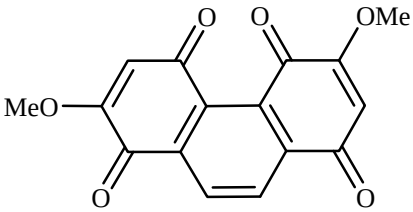
[**183**] Dendroside C



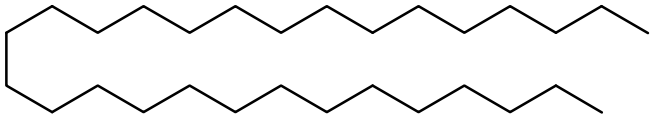
[**184**] Dendroside F



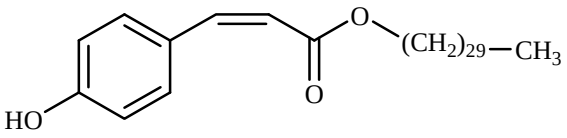
[**185**] α-Dihydropicrotoxinin



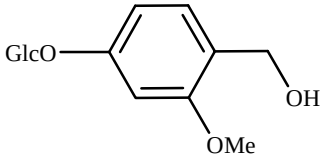
[**186**] Moniliformin



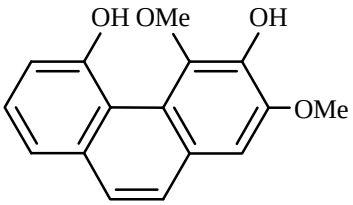
[**187**] *n*-Nonacosane



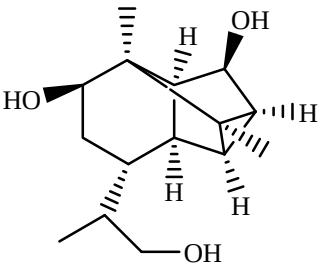
[**188**] *n*-Triacontyl *p*-hydroxy-cis-cinnamate



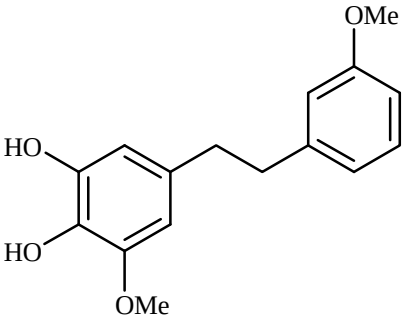
[**189**] Vanilloside



[**190**] Bulbophyllanthrin

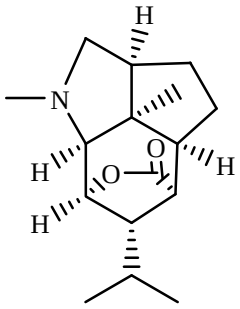


[**191**] Dendrobane A

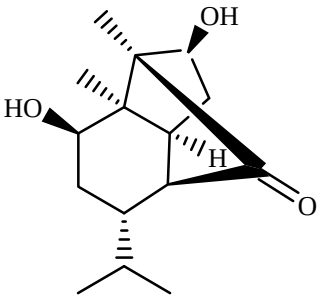


[**192**] Dendrobin A

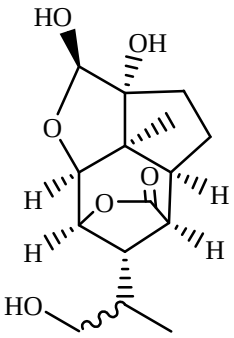
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



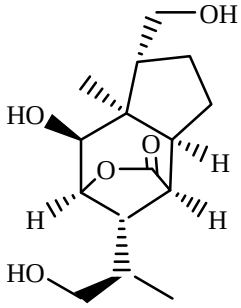
[**193**] Dendrobine



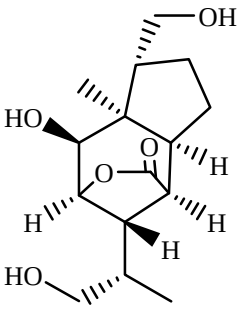
[**194**] Dendronobilin A



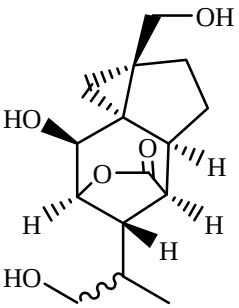
[**195**] Dendronobilin C



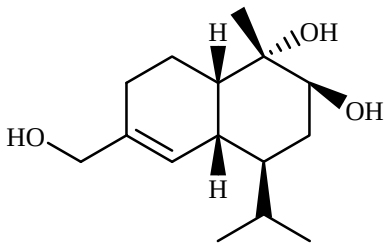
[**196**] Dendronobilin D



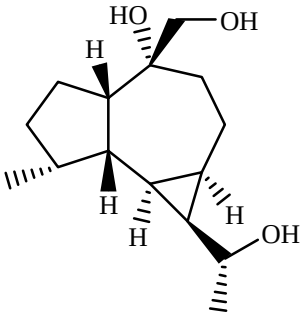
[**197**] Dendronobilin E



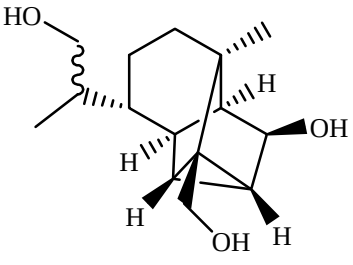
[**198**] Dendronobilin F



[**199**] Dendronobilin G

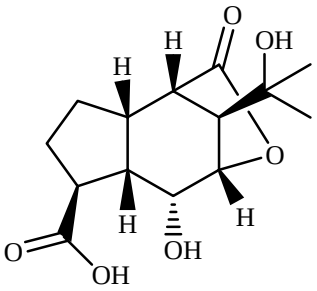


[**200**] Dendronobilin H

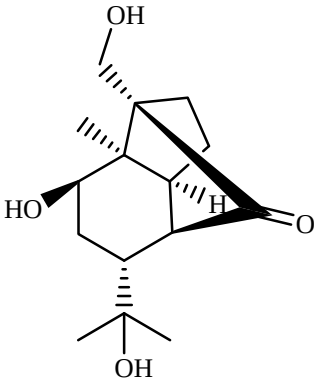


[**201**] Dendronobilin I

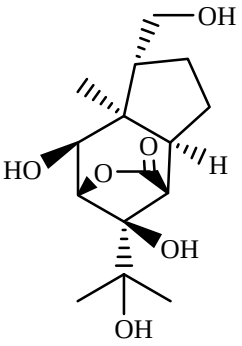
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



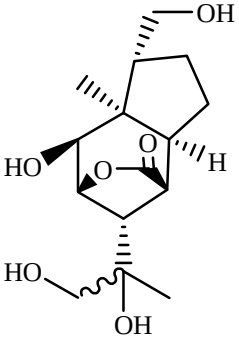
[**202**] Dendronobilin J



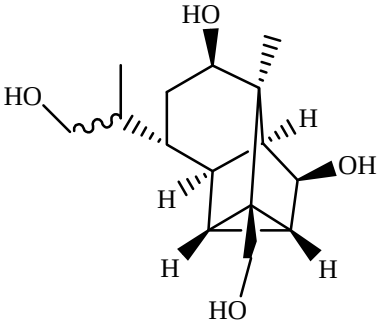
[**203**] Dendronobilin K



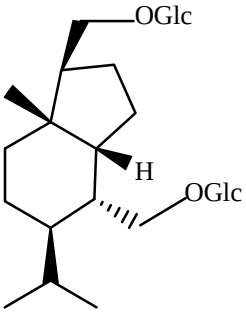
[**204**] Dendronobilin L



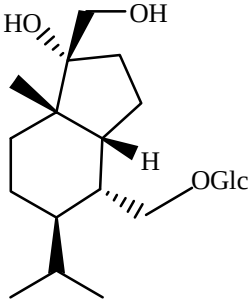
[**205**] Dendronobilin M



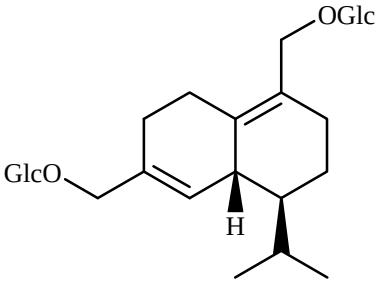
[**206**] Dendronobilin N



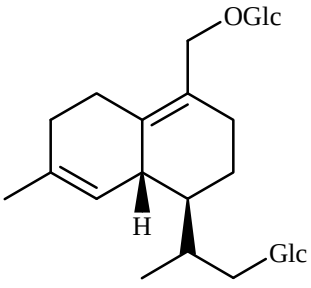
[**207**] Dendronobiloside A



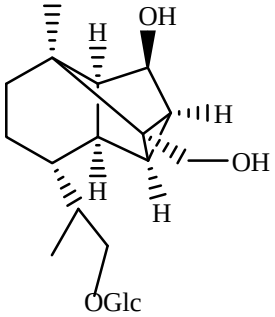
[**208**] Dendronobiloside B



[**209**] Dendronobiloside C

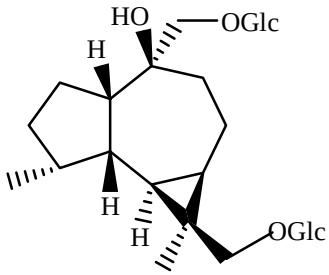


[**210**] Dendronobiloside D

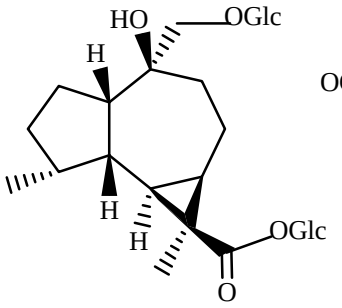


[**211**] Dendronobiloside E

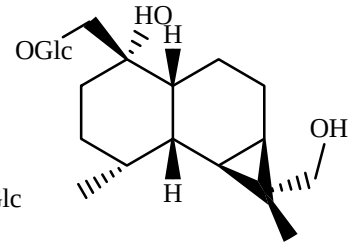
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



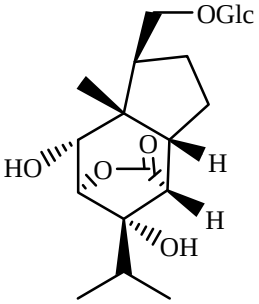
[**212**] Dendroside B



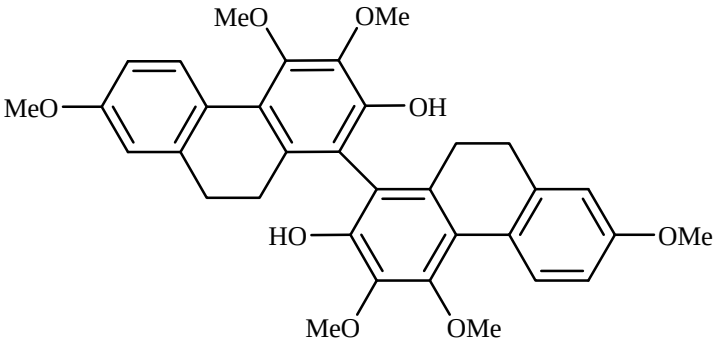
[**213**] Dendroside D



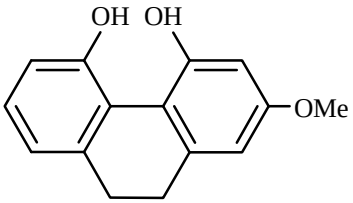
[**214**] Dendroside E



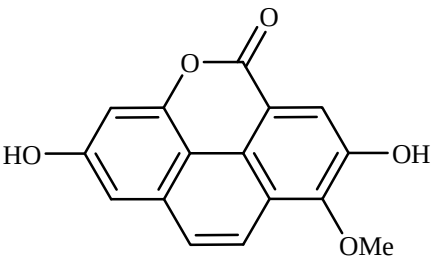
[**215**] Dendroside G



[**219**] 2,2′-Dihydroxy-3,3′,4,4′,7,7′-hexamethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene

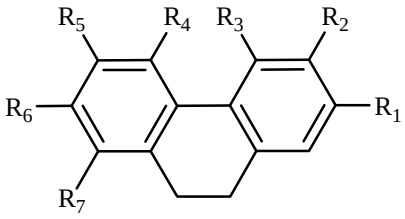


[**220**] 4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene

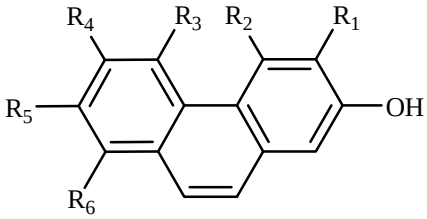


[**227**] Fimbiatone

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

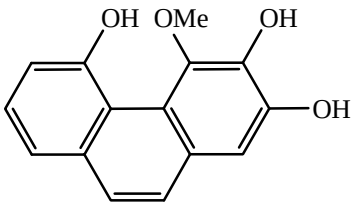


	R_1	R_2	R_3	R_4	R_5	R_6	R_7
[**216**] 4,5- Dihydroxy-3,7-dimethoxy -9,10-dihydrophenanthrene	H	OMe	OH	OH	H	OMe	H
[**221**] 2,8-Dihydroxy-3,4,7-trimethoxy -9,10-dihydrophenanthrene	OH	OMe	OMe	H	H	OMe	OH
[**224**] Ephemeranthol A	OH	H	H	OH	OMe	OMe	H
[**225**] Ephemeranthol C	OH	OH	OMe	OH	H	H	H
[**226**] Erianthridin	OH	OMe	OMe	H	H	OH	H
[**229**] Flavanthridin	OH	H	H	OMe	OH	OMe	H

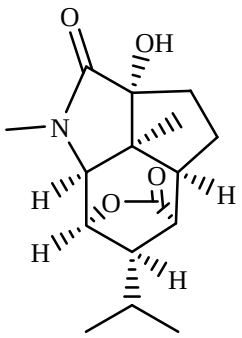


	R_1	R_2	R_3	R_4	R_5	R_6
[**218**] 2,5-Dihydroxy-3,4-dimethoxy phenanthrene	OMe	OMe	OH	H	H	H
[**222**] 2,8-Dihydroxy-3,4,7-trimethoxy phenanthrene	OMe	OMe	H	H	OMe	OH
[**223**] 5,7-Dimethoxy phenanthrene-2,6-diol	H	H	OMe	OH	OMe	H
[**231**] 2-Hydroxy-4,7-dimethoxy-9,10-dihydrophenanthrene	H	OMe	H	H	OMe	H
[**234**] 2-Hydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene	OMe	OMe	H	H	OMe	H

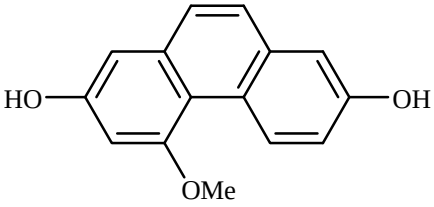
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



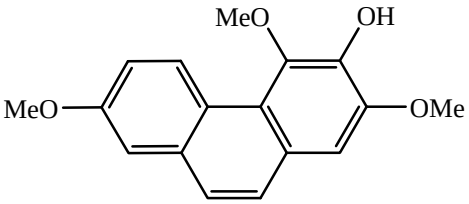
[**228**] Fimbriol B



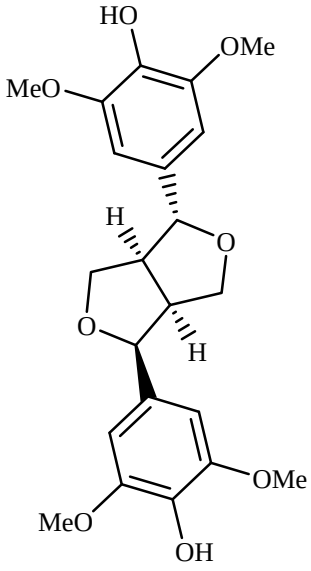
[**232**] 3-Hydroxy-2-oxodendrobine



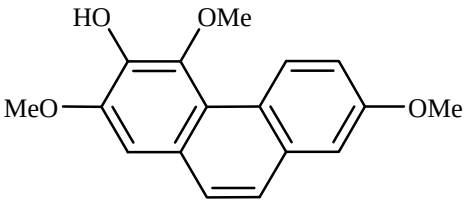
[**230**] Flavanthrinin



[**235**] 3-Hydroxy-2,4,7-trimethoxy -9,10-dihydrophenanthrene

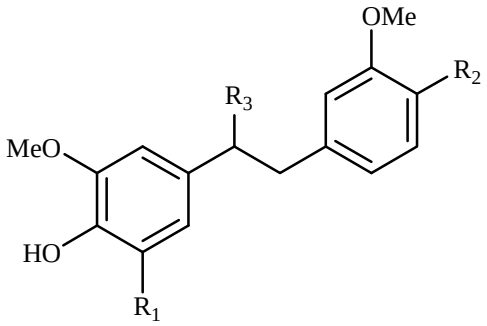


[**237**] Lirioresinol A

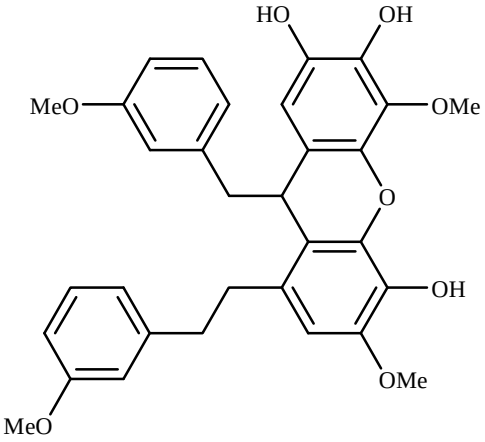


[**236**] 3-Hydroxy-2,4,7-trimethoxyphenanthrene

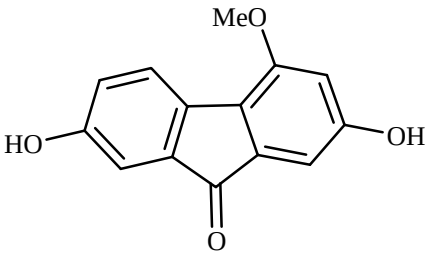
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



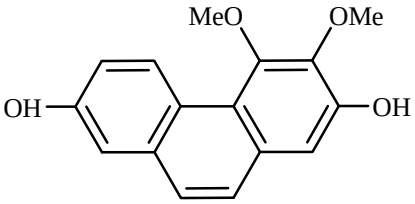
	R_1	R_2	R_3
[**233**] 4-Hydroxy-3,5,3′-trimethoxy bibenzyl	OMe	H	H
[**238**] Nobilin A	OH	H	OMe
[**239**] Nobilin B	OMe	OH	OMe
[**240**] Nobilin C	OMe	OMe	OMe
[**241**] Nobilin D	OMe	OH	OH



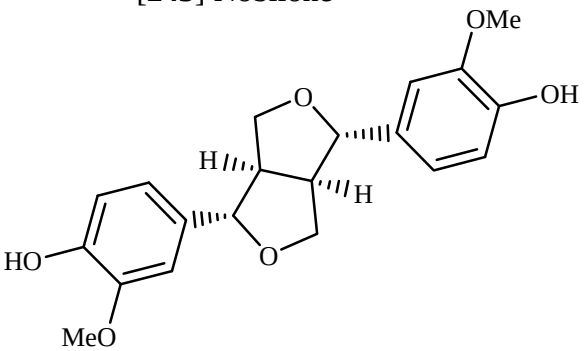
[**242**] Nobilin E



[**243**] Nobilone

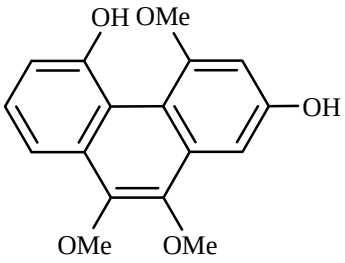


[**244**] Nudol

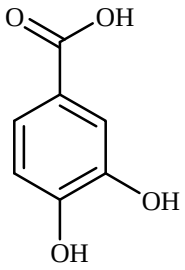


[**245**] Pinoresinol

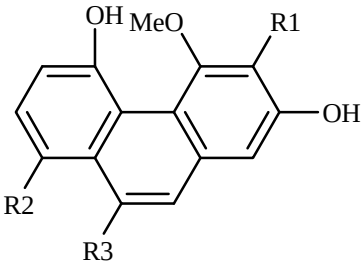
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



[**246**] Plicatol A

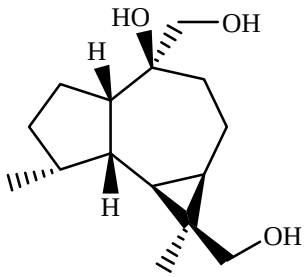


[**247**] Protocatechuic acid

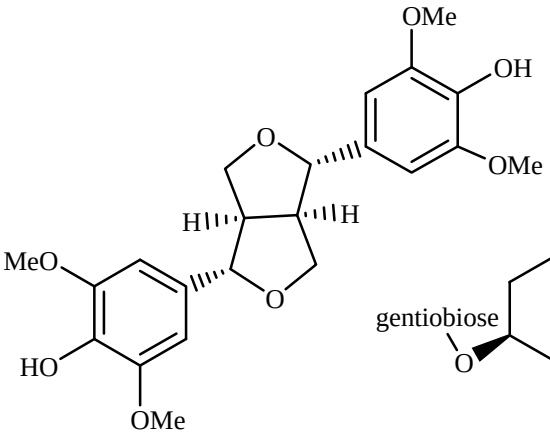


[**250**] 2,3,5-Trihydroxy-4,9-dimethoxy phenanthrene: R_1= OH, R_2 = H, R_3 = OMe

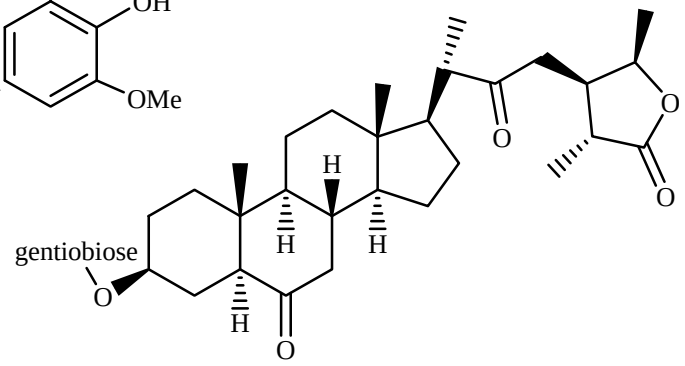
[**251**] 3,4,8-Trimethoxyphenanthrene-2,5-diol: R_1= OMe, R_2 = OMe, R_3 = H



[**249**] 10β,12,14-Trihydroxy alloaromadendrane

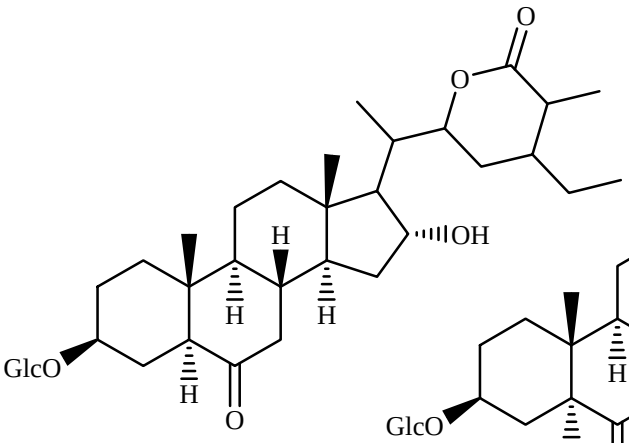


[**248**] Syringaresinol

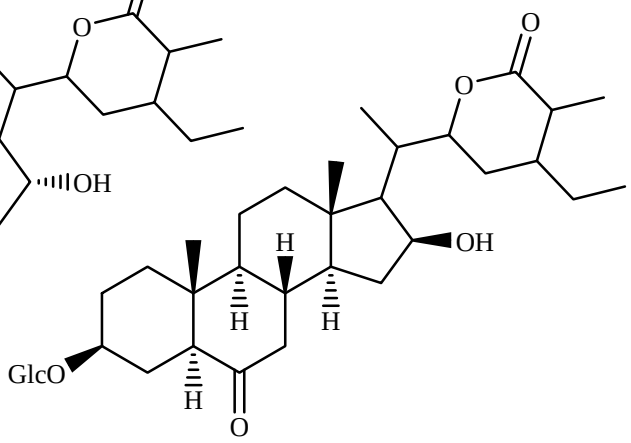


[**252**] Dendrosteroside

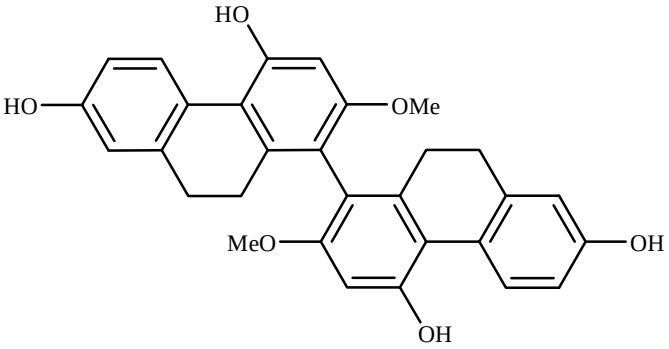
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



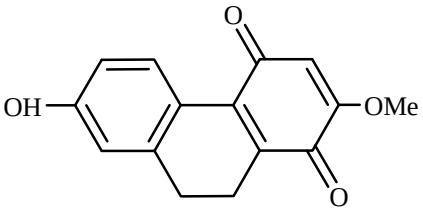
[**253**] Epi-ochreasteroside



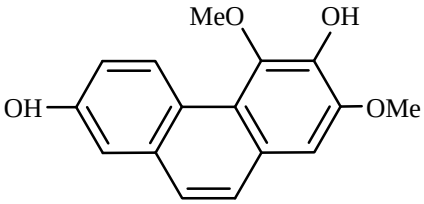
[**254**] Ochreasteroside



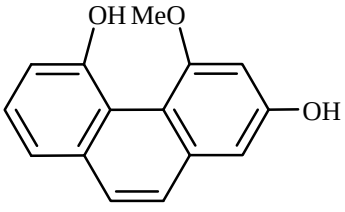
[**255**] 2,2′-Dimethoxy-4,4′,7,7′-tetrahydroxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene



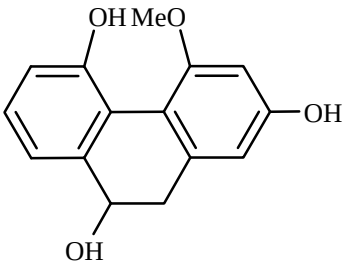
[**256**] Ephemeranthoquinone



[**257**] Epheranthol B

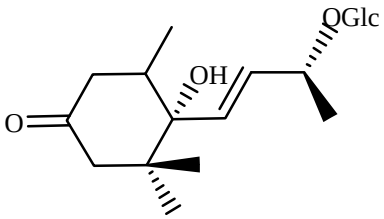


[**258**] Plicatol B

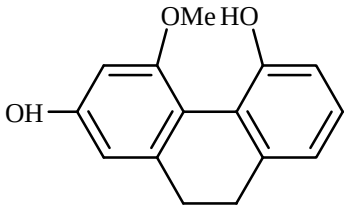


[**259**] Plicatol C

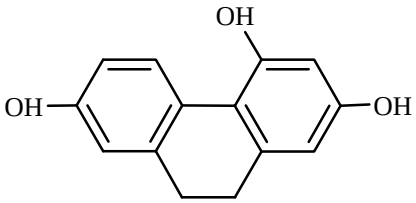
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



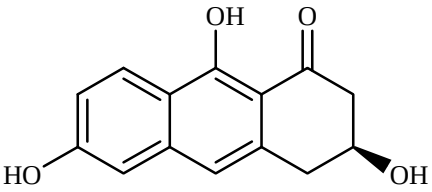
[**260**] Corchoionoside C



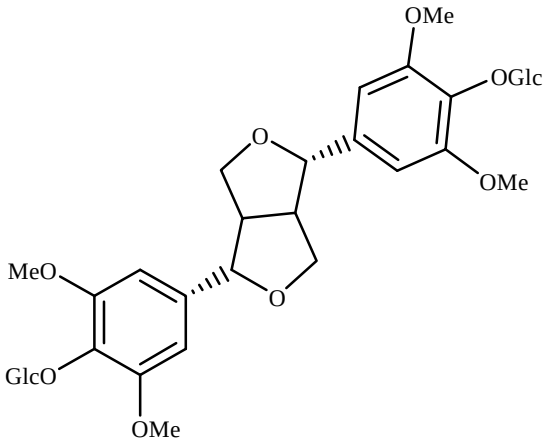
[**261**] 9,10-Dihydromoscatin



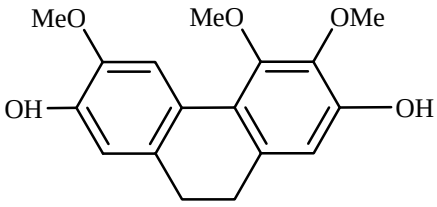
[**262**] 9,10-Dihydrophenanthrene-2,4,7-triol



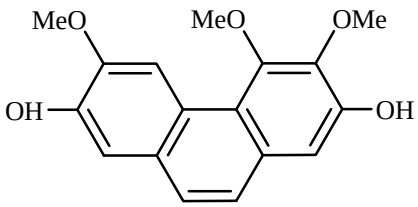
[**263**] 3,6,9-Trihydroxy-3,4-dihydro anthracen-1(2H)-one



[**264**] Liriodendrin

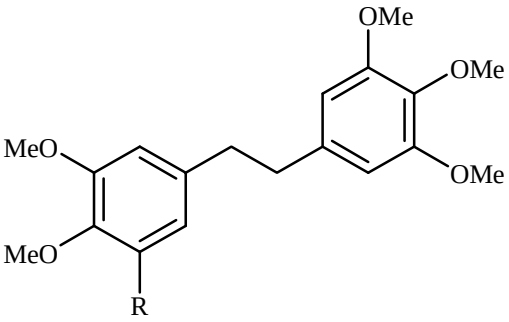


[**265**] 2,7-Dihydroxy-3,4,6-trimethoxy -9,10-dihydrophenanthrene



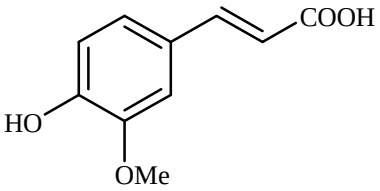
[**266**] 2,7-Dihydroxy-3,4,6-trimethoxyphenanthrene

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

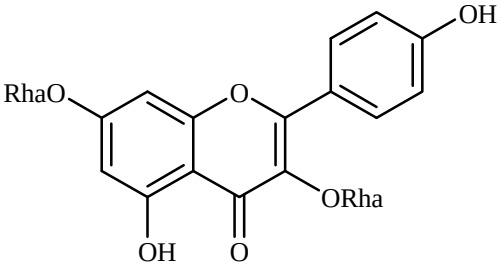


[**267**] Brittonin A: R= OMe

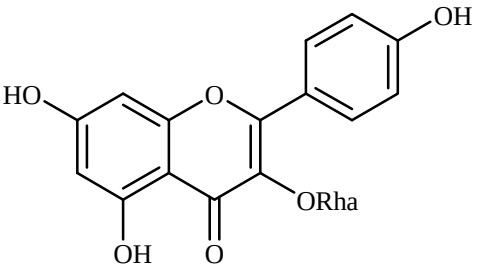
[**269**] 5-Hydroxy-3,4,3′,4′,5′-pentamethoxybibenzyl: R= OH



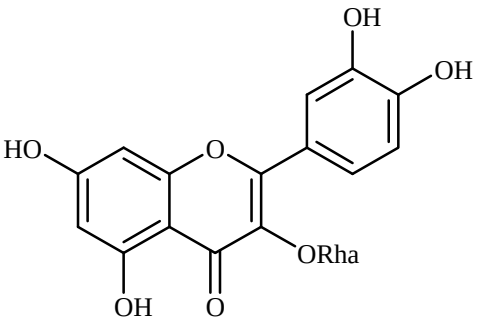
[**268**] Ferulic acid



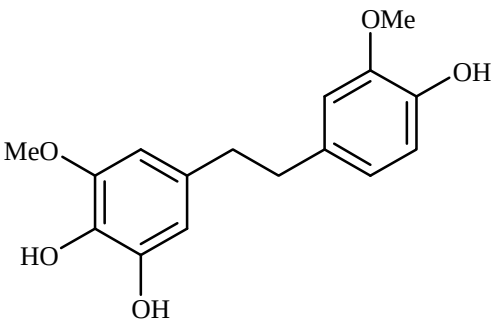
[**270**] Kaempferol-3,7-*O*-di-α-L-rhamnopyranoside



[**271**] Kaempferol-3-*O*-α-L-rhamnopyranoside

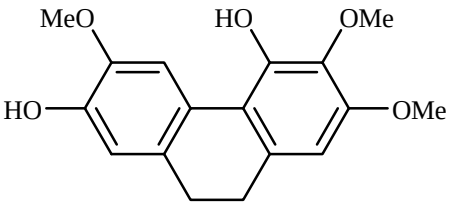


[**272**] Quercetin-3-*O*-α-L-Rhamnopyranoside

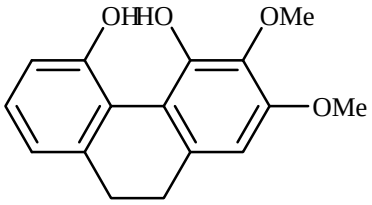


[**273**] 4,5,4′-Trihydroxy-3-3′-dimethoxybibenzyl

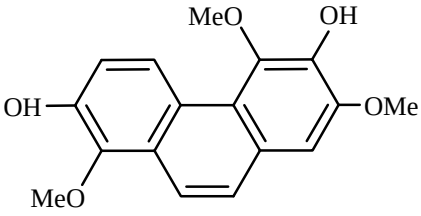
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



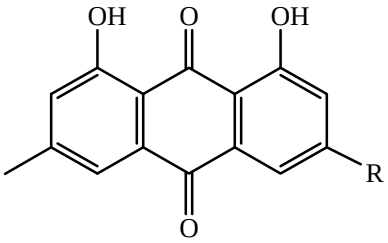
[**274**] 4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene



[**275**] 4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene



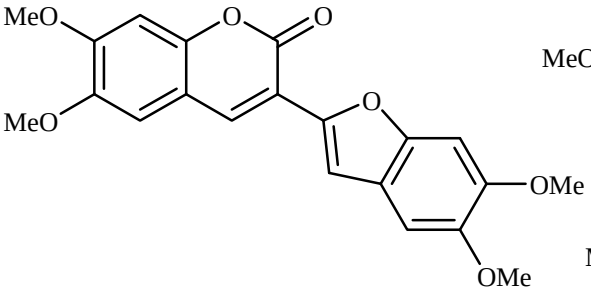
[**278**] Denthyrsinin



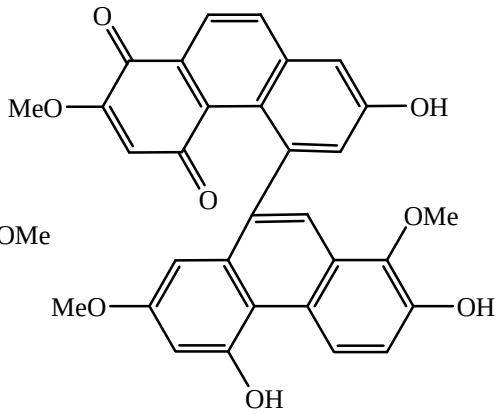
[**276**] Chrysophanol: R = H

[**281**] Emodin: R = OH

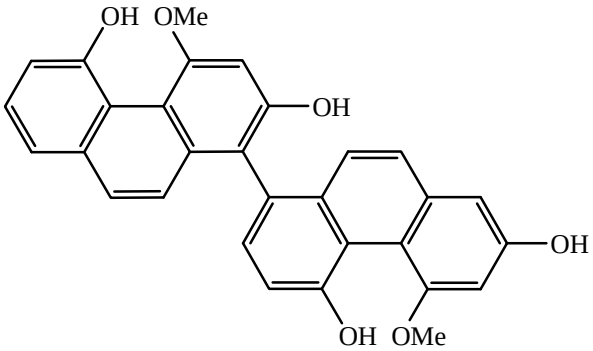
[**282**] Physcion : R= OMe



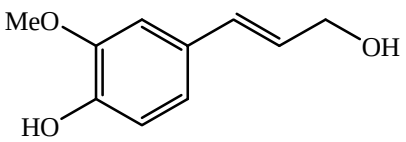
[**277**] Denthyrsin



[**280**] Denthyrsinone

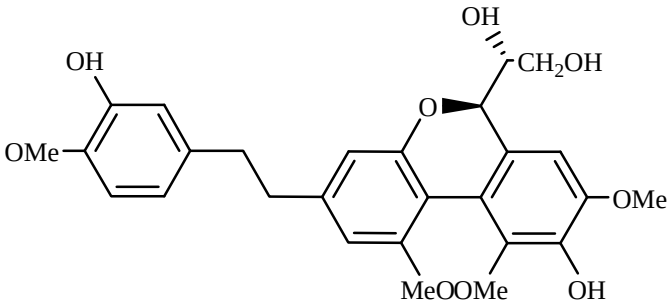


[**279**] Denthyrsinol

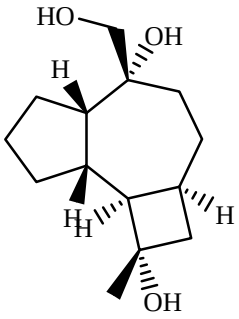


[**283**] 3-(4-Hydroxy-3-methoxyphenyl)-2- propen-1-ol

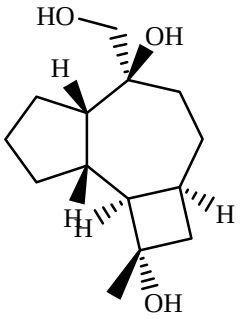
Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)



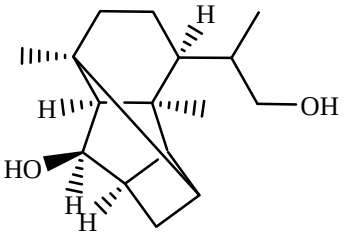
[**284**] Trigonopol A



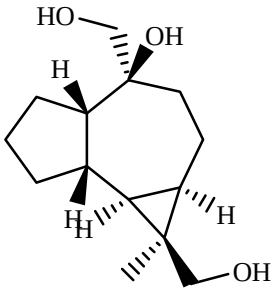
[**285**] Dendrowardol A



[**286**] Dendrowardol B



[**288**] 10*β*,12,14-trihydroxy alloaromadendrane



[**287**] Dendrowardol C

Figure 2 Structures of compounds previously isolated from *Dendrobium* species (continued)

2. Traditional uses and biological activities of *Dendrobium* species.

Previous pharmacological studies have shown that many plants from this genus exhibited a number of biological activities, such as antiplatelet aggregation (Fan *et al*., 2001), antioxidant activity (Ono *et al*., 1995), anti-inflammation (Lin *et al*., 2001) and cytotoxicity (Zhang *et al*., 2005, Yang *et al*., 2007). Interestingly, in the DPPH assay , crepidatin, chrysotoxine, moscatilin, nobilin D and nobilin E showed very strong activities, which were nearly equivalent to that of vitamin C (Zhang *et al*., 2007a). Moreover, in a cytotoxicity study, moscatilin, a bibenzyl found in many plants in this genus, showed potent cytotoxicity, and this compound has been further studied in preclinical trials (Tsai *et al*., 2010, Ho and Chen *et al*., 2003).

In China, several species of *Dendrobium* have been used in traditional medicine. They are also used to treat kidney and lung disorders and stomach diseases, red tongue, swelling, dry mouth, fever, hyperglycemia and diabetes (Hossain, 2011). For example, “Shi-Hu” (Herba Dendrobii) are used as a Yin tonic to promote the production of body fluid, supply the stomach and reduce fever (Bensky and Gamble, 1993).

Chemical constituents including dihydrostilbenes (bibenzyls), phenanthrenes, dihydrophenanthrenes, flavonoids, flavonoid glycosides, alkaloids, fluorenones and coumarins have been previously isolated from *Dendrobium* species (Bensky and Gamble, 1993). Many biological activities of plants in this genus have been reported including antioxidant, anti-inflammatory, cytotoxic, antiplatelet aggregation and immunomodulatory activities.

The bibenzyl derivatives, phenanthrenes, lignans and fluorenones obtained from *Dendrobium nobile*, including chrysotoxin [**19**], moscatilin [**8**], crepidatin [**21**], nobilin D [**241**], nobilin E [**242**], confusarin [**63**], syringaresinol [**248**] and dendroflorin [**23**], showed potent activity in DPPH assay with IC_{50} values of 14.0, 14.5, 21.8, 19.9, 21.0, 12.9, 9.8 and 16.2 μM, respectively (Zhang *et al*., 2007a; Zhang *et al*., 2008b). Furthermore, in the DPPH scavenging and ORAC assays, crepidatin [**21**], moscatilin [**8**] and chrysotoxin [**19**] exhibited activity stronger than or equivalent to vitamin C (Ono *et al*.,1995).

In an anti-inflammatory study, erianthridin [**226**], ephemeranthol A [**224**], ephemeranthol C [**225**], coelonin [**10**] and lusianthridin [**16**] isolated from *Dendrobium nobile* exhibited inhibitory effects on the lipopolysaccharides induced nitric oxide production in macrophage cells (RAW 264.7) with IC_{50} values of 19.5, 12.0, 17.6, 10.2, 9.6 µM, respectively (Hwang *et al*., 2010).

Regarding cytotoxicity, it was reported that denthyrsin [**277**], denthyrsinol [**279**], denthyrsinone [**280**] and denthyrsinin [**278**] from *Dendrobium thyrsiflorum* exhibited cytotoxicity against several cancer cell lines such as Hela, K-562 and MCF-7 (Zhang *et al*., 2005). Moreover, coelonin [**10**] and denbinobin [**176**] from *Dendrobium nobile* could inhibit the proliferation of hepatic stellate cells (HSCs-T6) (Yang *et al*., 2007). In addition, moscatilin [**8**], which was obtained from several plants of this genus, exhibited potent cytotoxic effect against lung and stomach cancer cells (Ho and Chen, 2003). Furthermore, this compound induced apoptosis in human colorectal cancer cells through tubulin depolymerization and DNA damage through the activation of C-Jun NH_2- terminal protein kinase (JNK) and mitochondria involved intrinsic apoptosis pathway (Chen *et al*., 2008a). Additionally, it suppresses tumor angiogenesis and growth in vitro and in vivo (Tsai *et al*., 2010). Three fluorenones isolated from *Dendrobium chrysotoxum* including dendroflorin [**23**], denchrysan A [**70**] and 1,4,5- trihydroxy-7-methoxy-9-fluorenones [**82**] demonstrated cytotoxicity against human hepatoma (BEL-7402) with IC_{50} values of 0.97, 1.38 and 14.9 µg/ml, respectively (Chen *et al*., 2008b).

For antiplatelet aggregation studies, the compounds isolated from *Dendrobium densiflorum* such as moscatilin [**8**], gigantol [**14**], homoeriodictyol [**115**], scoparone [**116**] and scopoletin [**117**] were found to exhibit antiplatelet aggregation activity on rat platelets *in vitro* (Fan *et al*., 2001). In addition, moscatilin [**8**] and moscatin [**17**] strongly inhibited both arachidonic acid and collagen induced platelet aggregations (Chen *et al*., 1994).

Sesquiterpenes glycosides isolated from *Dendrobium nobile* including dendroside A [**182**] and dendrosides D-G [**213**, **214**, **184**, **215**] were found to stimulate significantly the generation of mouse T and B lymphocytes *in vitro* (Zhao *et al*., 2001 and Ye *et al*., 2002).

CHAPTER III

EXPERIMENTAL

1. Source of plant materials

Whole plant samples of *Dendrobium williamsonii* were purchased from Jatujak market, Bangkok, in July 2010. Plant identification was done by Associate Professor Thatree Phadungcharoen, together with comparison with botanical information from Kluaymai Muangthai book (อบฉันท์ ไทยทอง, 2549). A voucher specimen (BS-DW-072553) is deposited at the Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University.

2. General techniques

2.1 Analytical thin-layer chromatography (TLC)

Technique	:	One dimension, ascending
Absorbent	:	Silica gel 60 F_{254} (E. Merck) precoated plate
Layer thickness	:	0.2 mm
Distance	:	6.5 cm
Temperature	:	Laboratory temperature (30-35^{o}C)
Detection	:	1. Ultraviolet light at wavelengths of 254 and 365 nm 2. Spraying with anisaldehyde reagent (0.5 ml *p*-anisaldehyde, 10 ml glacial acetic acid, 85 ml methanol and 5 ml conc. sulfuric acid) and heating at 105 ^{o}C for 10 min

2.2 Column Chromatography

2.2.1 Vacuum liquid chromatography (VLC)

Adsorbent	:	Silica gel 60 (No. 7734) particle size 0.063-0.200 mm (E. Merck)
Packing method	:	Dry packing
Sample loading	:	The sample was dissolved in a small amount of

organic solvent, mixed with a small quantity of the adsorbent, triturated, dried and then gradually placed on top of the column.

Detection : Each fraction was determined by TLC under UV light at the wavelengths of 254 and 365 nm.

2.2.2 Column chromatography (CC)

Adsorbent : Silica gel 60 (No. 9385) particle size 0.040-0.063 mm (E. Merck)

Packing method : Wet packing

Sample loading : The sample was dissolved in a small amount of the organic solvent, mixed with a small quantity of the adsorbent, triturated, dried and then gradually applied on top of the column.

Detection : Fractions were examined in the same way as described in section 2.2.1

2.2.3 Medium pressure liquid chromatography

Adsorbent : Silica gel 60 (No. 9385) particle size 0.040-0.063 mm (E. Merck)

Packing method : Dry packing

Sample loading : The sample was dissolved in a small amount of organic solvent, mixed with a small quantity of adsorbent, triturated, dried and then gradually placed on top of the column.

Detection : Fractions were examined in the same way as described in section 2.2.1

2.2.4 Gel filtration chromatography

Adsorbent : Sephadex LH-20 (Pharmacia)

Packing method : An appropriate organic solvent was used as the eluent. Gel filter was suspended in the eluent, left standing

about 24 hours prior to use and then was poured into the column and allowed to set tightly.

Sample loading : The sample was dissolved in a small amount of the eluent and then was gradually distributed on top of the column.

Detection : Fractions were determined in the same way as described in section 2.2.1

2.3 Spectroscopy

2.3.1 Ultraviolet (UV) absorption spectra

UV (in methanol) spectra were obtained on a Shimadzu UV-160A UV/VIS spectrophotometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.3.2 Infrared (IR) spectra

IR spectra were obtained on a Perkin-Elmer FT-IR 1760X spectrophotometer (Scientific and Technology Research Equipment Center, Chulalongkorn University).

2.3.3 Mass spectra

Mass spectra were recorded on a Bruker microTOF or a Micromass LCT mass spectrometer (National Center for Genetic Engineering and Biotechnology).

2.3.4 Proton and carbon-13 nuclear magnetic resonance (^{1}H and ^{13}C-NMR) spectra

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker Avance DPX-300 FT-NMR spectrometer (Faculty of Pharmaceutical Sciences, Chulalongkorn University).

^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a JEOL JMN-A 500 NMR spectrometer (500 MHz) (Scientific and Technology Research Equipment Center, Chulalongkorn University).

Deuterated solvents for NMR spectra were used, including deuterated chloroform ($CDCl_3$), deuterated methanol (CD_3OD), deuterated acetone (acetone -

d_6). Chemical shifts were reported in ppm scale using the chemical shift of the solvent as the reference.

2.4 Solvents

All organic solvents used throughout this work were of commercial grade and were redistilled prior to use.

3. Extraction and isolation

3.1 Extraction

The whole plants (1kg) were dried, powdered and then macerated with methanol (3×5L) for 72 hours three times. The methanol extract was concentrated under rotary evaporation to give 165.9 g of a crude extract.

3.2 Separation of methanol extract

Crude extract (165.9 g) was first separated by vacuum liquid chromatography (VLC). The procedure was performed as described in section 2.2.1. Silica gel (No.7734, 600 g) was used as the stationary phase and a step gradient of *n*-hexane-EtOAc (100:0 to 0:100) and EtOAc-Methanol (100:0 to 0:100) as the mobile phase. The eluates were collected about 500 mL per fraction and examined by TLC (silica gel, *n*-hexane-EtOAc 6:4) to yield eighty fractions. Fractions with similar chromatographic patterns were combined to give six fractions, including fractions A (1.71g), B (3.27 g), C (2.37 g), D (9.18 g), E (1.65 g) and F (93.05 g).

3.2.1 Isolation of compound DW1 (tetratriacontanyl-*p*-coumarate)

Fraction D (9.18 g) was further separated by column chromatography (CC) on silica gel (No. 9385) with gradient elution (*n*-hexane-EtOAc 100:0 to 0:100). Eighty fractions were obtained and combined in accordance with their TLC patterns (silica gel, *n*-hexane-EtOAc 7:3) to give ten fractions: D1(363 mg), D2 (244 mg), D3 (650 mg), D4 (388 mg), D5 (794 mg), D6 (1746 mg), D7 (863 mg), D 8 (1869 mg), D9 (584 mg) and D10 (773 mg).

Fraction D3 (650 mg) was separated by CC using silica gel (No. 9385) as the stationary phase with gradient elution (*n*-hexane-CH_2Cl_2 100:0 to 0:100). Thirty three fractions were obtained and combined according to their TLC patterns (silica gel, *n*-hexane- CH_2Cl_2 8:2) to give six fractions: D3a (140 mg), D3b (30 mg), D3c (50 mg), D3d (60 mg), D3e (120mg), and D3f (30 mg).

Fraction D3d (60 mg) was purified on a Sephadex LH-20 column, eluted with CH_2Cl_2: MeOH 1:1, to give compound DW1 as a white powder (38 mg, R_f 0.38, silica gel, *n*-hexane- CH_2Cl_2 2:8). It was identified as tetratriacontanyl-*p*-coumarate [**289**].

3.2.2 Isolation of compound DW2 (*trans*-docosanoylferulate)

Fraction D3b (30 mg) was purified on a Sephadex LH-20 column, eluted with CH_2Cl_2: MeOH 1:1, to give compound DW2 as a white powder.
(3 mg, R_f 0.46, silica gel, *n*-hexane- CH_2Cl_2 2:8). It was identified as *trans*-docosanoylferulate [**124**].

3.2.3 Isolation of compound DW3 (3,3′-dihydroxy-4,5-dimethoxybibenzyl)

Fraction D5 (794 mg) was separated by CC using silica gel (No. 9385) as the stationary phase with a step gradient of *n*-hexane-EtOAc (100:0 to 0:100). Fifty fractions were obtained and combined according to their TLC patterns (silica gel, *n*-hexane-EtOAc 6:4) to give four fractions: D5a (30 mg), D5b (300 mg), D5c (210 mg) and D5d (30 mg).

Fraction D5b (300 mg) was purified on a Sephadex LH-20 column, eluted with CH_2Cl_2: MeOH 1:1 to give compound DW3 as a brown amorphous solid (20 mg, R_f 0.33, silica gel, *n*-hexane-EtOAc 8:2). It was identified as 3,3′-dihydroxy-4,5-dimethoxybibenzyl [**290**].

3.2.4 Isolation of compound DW4 (moscatilin)

Fraction D6 (1746 mg) was separated by CC using silica gel (No. 9385) as the stationary phase with a step gradient of *n*-hexane-EtOAc (100:0 to 0:100). Forty fractions were obtained and combined according to the similarity of their TLC patterns (silica gel, *n*-hexane-EtOAc 6:4) to give seven fractions: D6a (100 mg), D6b (130 mg), D6c (70 mg), D6d (60 mg), D6e (50 mg), D6f (80 mg), and D6g (50 mg).

Fraction D6e (50 mg) was purified on Sephadex LH-20, eluted with CH_2Cl_2: MeOH 1:1 to give four fractions with different TLC patterns (silica gel, *n*-hexane-EtOAc 6:4): D6e1 (10 mg), D6e2 (5 mg), D6e3 (7 mg), and compound DW4 as white-yellowish needle crystals (3 mg, R_f 0.14, silica gel, *n*-hexane-EtOAc 6:4). It was identified as moscatilin [**8**].

3.2.5 Isolation of compound DW5 (apigenin)

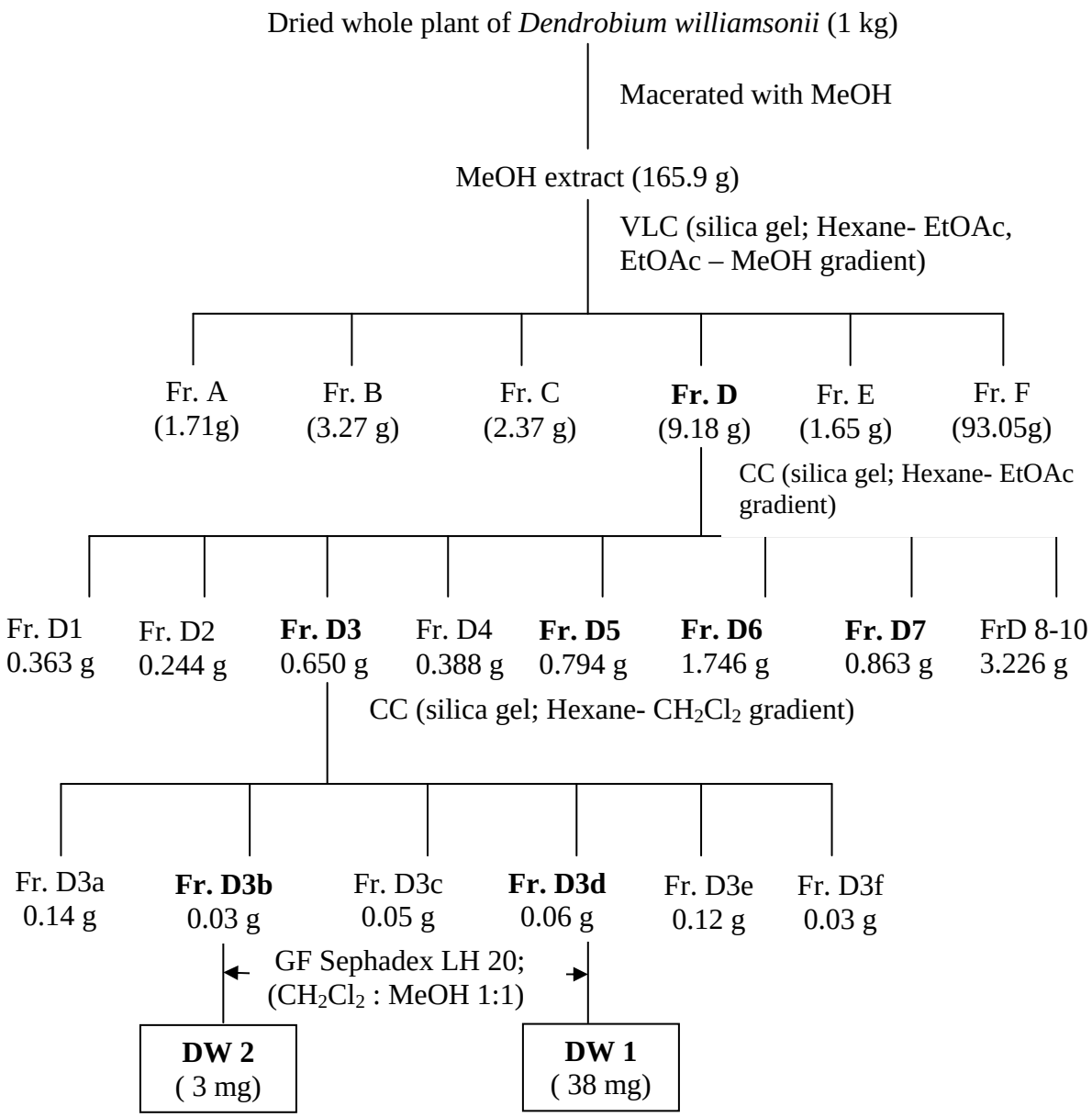
Fraction D6g (50 mg) was purified on Sephadex LH-20, eluted with CH_2Cl_2: MeOH 1:1 to give twenty fractions. Fractions with similar TLC patterns (silica gel, *n*-hexane-EtOAc 6:4) were combined to yield eight fractions: D6g1 (10 mg), D6g2 (5 mg), D6g3 (25 mg), D6g4 (8 mg), D6g5 (5 mg), D6g6 (5 mg), D6g7 (2 mg), and D6g8 (2 mg).

Fraction D6g3 (25 mg) was further separated by CC using silica gel (No. 9385) as the stationary phase with a step gradient of CH_2Cl_2- MeOH (100:0 to 0:100) to give compound DW5 as a yellow powder (5 mg, R_f 0.46, silica gel, *n*-hexane-EtOAc 6:4). It was identified as apigenin [**95**].

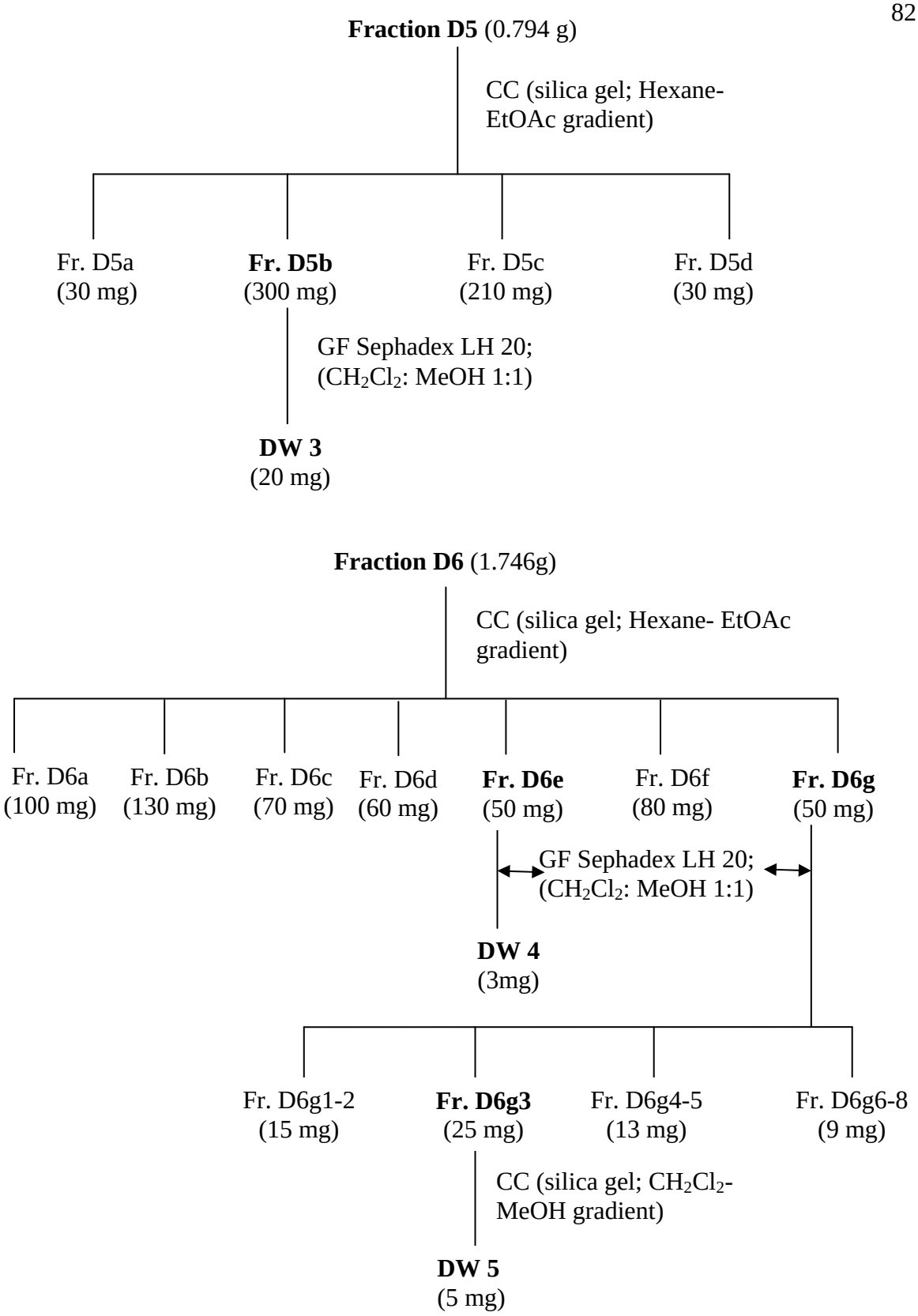
3.1.2.6 Isolation of compound DW6 (vanillic acid)

Fraction D7 (863 mg) was separated by MPLC using silica gel (No. 9385) as the stationary phase with a step gradient mixture of CH_2Cl_2- acetone (100:0 to 0:100). Sixty fractions were obtained and then combined according to their TLC patterns (silica gel, CH_2Cl_2-EtOAc 8:2) to give ten fractions: D7a (5 mg), D7b (22 mg), D7c (90 mg), D7d (48 mg), D7e (36 mg), D7f (4 mg), D7g (72 mg), D7h (100 mg), D7i (19 mg) and D7j (99 mg).

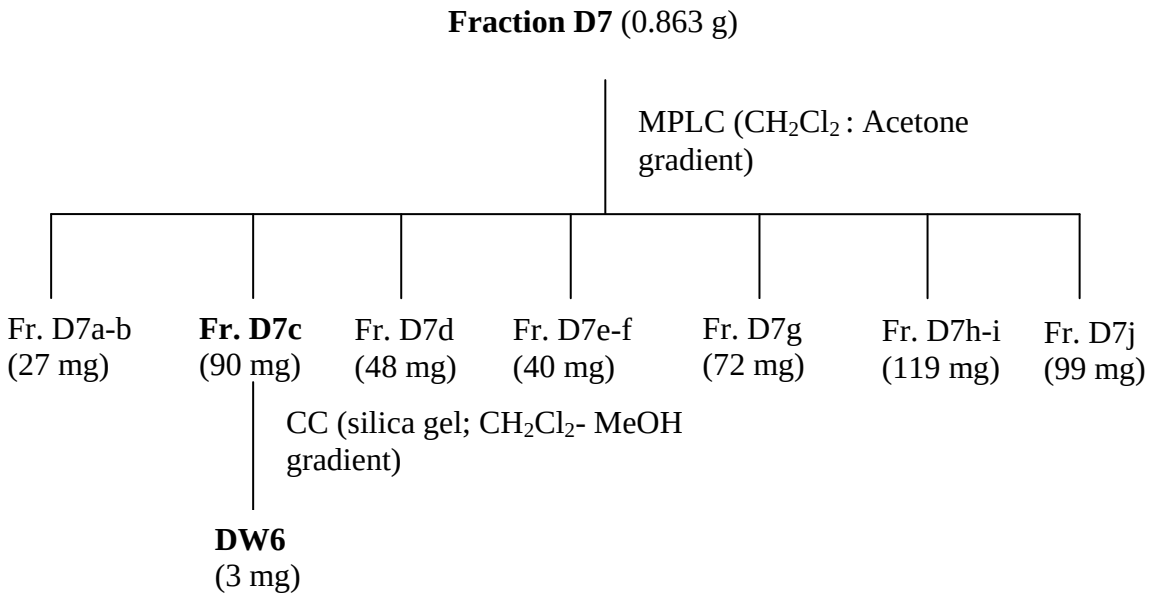
Fraction D7c (90 mg) was further separated by CC using silica gel (No. 9385) as the stationary phase with a step gradient of CH_2Cl_2- MeOH (100:0 to 0:100) to give compound DW6 as a colorless powder (3 mg, R_f 0.16, silica gel, CH_2Cl_2-EtOAc 8:2). It was identified as vanillic acid [**88**].



Scheme 1. Seperation of the MeOH extract of *Dendrobium williamsonii*



Scheme 1 Seperation of the MeOH extract of *Dendrobium williamsonii* (continued)



Scheme 1 Seperation of the MeOH extract of *Dendrobium williamsonii* (continued)

4. Physical and spectral data of isolated compounds

4.1 Compound DW1 (Tetratriacontanyl-*p*-coumarate)

Compound DW1 was obtained as a white powder, soluble in CH_2Cl_2 (38 mg, 3.8×10^{-3} % based on dried weight of whole plants).

ESI-MS **:** $[M+Na]^+$ ion at *m/z* 663 ($C_{43}H_{76}O_3$); Figure 3

FT-IR **:** υ_{max} cm^{-1}: 3390, 2920, 1710, 1603, 1469, 1170, 918, 720; Figure 5

UV **:** λ_{max} nm (log ε), in methanol: 226 (3.12), 312 (3.36)**;** Figure 4

^{1}H NMR **:** δ ppm, 500 MHz, in $CDCl_3$; see Table 2, Figure 6

^{13}C NMR **:** δ ppm, 125 MHz, in $CDCl_3$; see Table 2, Figure 7

4.2 Compound DW2 (*trans*-Docosanoylferulate)

Compound DW2 was obtained as a white powder, soluble in CH_2Cl_2 (3 mg, 3.0×10^{-4} % based on dried weight of whole plants).

ESI-MS **:** $[M+Na]^+$ ion at *m/z* 525 ($C_{32}H_{54}O_4$); Figure 8

FT-IR **:** υ_{max} cm^{-1}: 3425, 2953, 2918, 2850, 1712, 1633, 1604, 1594, 1517, 1467, 1430, 1271, 1210, 1170, 1031, 785; Figure 10

UV **:** λ_{max} nm (log ε), in methanol: 220 (3.14), 235 (3.16), 325 (3.30); Figure 9

^{1}H NMR **:** δ ppm, 500 MHz, in $CDCl_3$; see Table 3, Figure 11

^{13}C NMR **:** δ ppm, 125 MHz, in $CDCl_3$; see Table 3, Figure 12

4.3 Compound DW3 (3,3′-Dihydroxy-4,5-dimethoxybibenzyl)

Compound DW3 was obtained as a brown amorphous solid, soluble in CH_2Cl_2 (20 mg, 2.0×10^{-3} % based on dried weight of whole plants).

ESI-MS **:** $[M+H]^+$ ion at *m/z* 275.13 ($C_{16}H_{18}O_4$); Figure 13

FT-IR **:** υ_{max} cm^{-1}: 3400, 2935, 1709, 1593, 1455, 1234, 1103, 998, 779, 696; Figure 15

UV **:** λ_{max} nm (log ε), in methanol: 220 (3.19), 275 (2.52)**;** Figure 14

^{1}H NMR **:** δ ppm, 300 MHz, in $CDCl_3$; see Table 4, Figure 16

^{13}C NMR **:** δ ppm, 75 MHz, in $CDCl_3$; see Table 4, Figure 17

4.4 Compound DW4 (Moscatilin)

Compound DW4 was obtained as a brown amorphous solid, soluble in CH_2Cl_2 (3 mg, 3.0×10^{-4} % based on dried weight of whole plants).

ESI-MS **:** $[M+H]^+$ ion at *m/z* 305 ($C_{17}H_{20}O_5$); Figure 20

FT-IR **:** υ_{max} cm^{-1}: 3410, 1609, 1517, 1463, 1227, 1115; Figure 22

UV **:** λ_{max} nm (log ε), in methanol: 219 (3.21), 280 (2.74); Figure 21

^{1}H NMR **:** δ ppm, 300 MHz, in $CDCl_3$; see Table 5, Figure 23

^{13}C NMR **:** δ ppm, 75 MHz, in $CDCl_3$; see Table 5, Figure 24

4.5 Compound DW5 (Apigenin)

Compound DW5 was obtained as a yellow amorphous powder, soluble in acetone (5 mg, 5.0×10^{-4} % based on dried weight of whole plants).

ESI-MS **:** $[M+H]^+$ ion at *m/z* 271.06 ($C_{15}H_{10}O_5$); Figure 25

FT-IR **:** υ_{max} cm^{-1}: 3390, 2920, 1655, 1608, 1453, 1156, 829; Figure 27

UV **:** λ_{max} nm (log ε), in methanol: 269 (2.72), 220 (2.95); Figure 26

^{1}H NMR **:** δ ppm, 300 MHz, in acetone- d_6; see Table 6, Figure 28

^{13}C NMR **:** δ ppm, 75 MHz, in acetone- d_6; see Table 6, Figure 29

4.4 Compound DW6 (Vanillic acid)

Compound DW6 was obtained as a colorless powder, soluble in acetone (3 mg, 3.0×10^{-4} % based on dried weight of whole plants).

ESI-MS **:** $[M+H]^+$ ion at *m/z* 169 ($C_8H_8O_4$); Figure 30

FT-IR **:** υ_{max} cm^{-1}: 3485, 2923, 1680, 1597, 1434, 1377, 1279, 764, 758; Figure 32

UV **:** λ_{max} nm (log ε), in methanol: 220 (2.71), 260 (2.36), 287 (2.3); Figure 31

^{1}H NMR **:** δ ppm, 500 MHz, in acetone- d_6; see Table 7, Figure 33

^{13}C NMR **:** δ ppm, 125 MHz, in acetone- d_6; see Table 7, Figure 34

5. Determination of DPPH free radical scavenging activity

5.1 Preparation of test sample

The test compound (0.5 mg) was dissolved in 1 mL of methanol (or suitable solvent) and diluted with methanol until a suitable range of concentration (mg/mL) was obtained. The final concentration was expressed as μM. For example, DW3 (MW 274) at 0.5 mg/1 mL was equal to 1825 μM [(0.5 mg x 10^3 x 1000 mL)/274)]. For each well, the test solution (20 μL) was added to the reaction mixture to furnish the total volume of 200 μL. The final concentration was calculated by the formula below (Braca *et al*., 2002).

$$N_1V_1 = N_2V_2$$

N_1 = Beginning concentration (μM)

V_1 = Beginning volume (μL)

N_2 = Final concentration (μM)

V_2 = Final volume (μL)

Thus, the final concentration of DW3 solution = 1825 μM x 20 μL/ 200 μL

= 182.5 μM

5.2 Preparation of DPPH solution (100 μM)

DPPH (2 mg) was dissolved in 100 mL of methanol, and the solution was stirred for 30 min.

5.3 Measurement of activity

The test sample (20 μL) was added to 180 μL of DPPH solution (100 μM) in 96-well plate. The solution mixture was incubated at 37ºC for 30 min in the dark place, and then the absorbance of each well was measured at 510 nm on a SpectraMax M5 Microplate reader (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University). The DPPH solution (180 μL) mixed with methanol (20 μL) was used as negative control and vitamin C and quercetin were used as positive controls (Arabshahi and Urooj 2007; Amarowicz *et al*., 2010).

5.4 Calculation of percent inhibition of DPPH scavenging activity

The percentage of DPPH reduction was calculated as follows.

% DPPH reduction = [A-(B-C)] x 100 / A

A = The absorbance of DPPH solution and methanol after incubation 30 min at 510 nm

B = The absorbance of DPPH solution and sample after incubation 30 min at 510 nm

C = The absorbance of sample and methanol after incubation 30 min at 510 nm

For IC_{50} value determination of pure compounds, a graph showing concentrations of the sample versus % inhibition DPPH was plotted. The IC_{50} value was calculated from the graph obtained from 3 separate experiments.

6. Determination of anti-herpes simplex virus activity

6.1 Viruses and cells

HSV strains used were HSV-1 (KOS) and HSV-2 (Baylor186). Vero cells (ATCC CCL81) were grown and maintained in Eagle's minimum medium supplemented with 10% fetal bovine serum.

6.2 Plaque reduction assay

Anti-HSV activity of test compound was determined by the plaque reduction assay modified from the previously reported method (Chansriniyom *et al*., 2009; Lipipun *et al*., 2003). Briefly, in the post-treatment assay, Vero cells, in 96-well tissue culture plate, were infected with 30 plaque forming units of HSV-1 (KOS) or HSV-2 (Baylor186). After 1 hr incubation at room temperature for virus adsorption, the cells were added with overlay media containing various concentrations of the compound. The infected cultures were incubated at 37 °C for 2 days. The infected cells were fixed and stained, and then the number of plaques was counted. The 50% effective concentration (EC_{50}) was determined from the curve relating the plaque number to the concentration of the compound. Acyclovir was used as a positive control. In the inactivation assay, each of 30 plaque forming units of HSV-1 or HSV-2 was mixed with various concentrations of compound and incubated for 1 hour, and then the mixture was added to Vero cells in 96-well tissue culture plate. After 1 hour incubation for virus adsorption, the overlay media were added. The infected cultures were incubated at 37 °C for 2 days. The infected cells were fixed, stained, and the plaques were counted. The 50% effective concentration (EC_{50}) was determined.

7. Determination of cytotoxicity

The cytotoxicity assay against two cancerous human-cell lines, including KB (oral human epidermal carcinoma) and MCF-7 (breast cancer) cells, was done by the Bioassay Laboratory, National Center for Genetic Engineering and Biotechnology (BIOTEC). The test was performed using resazurin microplate assay method (REMA) (O' Brien *et al.*, 2000), with ellipticine, doxorubicin and tamoxifen as positive controls. The protocols according to bioassay laboratory guideline (Bioassay laboratory protocol 01, 2009) are as follows:

Assay	Cancer cell growth inhibition
Method	Resazurin microplate assay (REMA)
Positive control	Doxorubicin, ellipticine, and tamoxifen
Negative control	0.5% DMSO
Maximum final test concentration	50 μg/mL

Description

Two cancerous human-cell lines are available for this assay:

1. KB cell line (epidermoid carcinoma of oral cavity, ATCC CCL-17)
2. MCF-7 cell line (breast adrenocarcinoma, ATCC HTB-22)

This assay was performed as follows:

1. Cells at a logarithmic growth phase were harvested and diluted to 7×10^4 cells/ml for KB and 9×10^4 cells/ml for MCF-7 in fresh medium.
2. Consecutively, 5 μL of test sample diluted in 5% DMSO, and 45 μL of cell suspension were added to 384-well plates then incubated at 37°C in 5% CO_2 incubator.
3. After incubation period (3 days for KB and MCF-7), 12.5 μL of 62.5 μg/mL resazurin solution was added to each well, then incubated at 37°C for 4 hours.
4. SpectraMax M5 multi-detection microplate reader (Molecular Devices, USA) measured the fluorescence signal at the excitation and emission wavelengths of 530 nm and 590 nm, respectively. Calculated the percent inhibition of cell growth by using the following equation:

$$\% \text{ Inhibition} = [1-(FU_T/FU_C)] \times 100$$

whereas, FU_T and FU_C are the mean fluorescent unit from treated and untreated conditions, respectively.

Dose response curves were plotted from 6 concentrations of 2-fold serially diluted test compounds and the sample concentrations that inhibit cell growth by 50% (IC_{50}) can be acquired by using the SOFTMax Pro software (Molecular Devices, USA).

CHAPTER IV

RESULTS AND DISCUSSION

In this study, the dried and powdered whole plants of *Dendrobium williamsonii* (1 kg) were macerated with methanol. The methanol extract was concentrated under reduced pressure to give 165.9 g of a crude extract. This methanol crude extract was evaluated for DPPH free radical scavenging activity and showed approximately 90% inhibition at a concentration of 200 µg/ml. It was then separated by vacuum liquid chromatography to yield six fractions. Fractions D was further separated by silica gel column chromatography, and then by Sephadex LH-20 gel filtration to give six pure compounds [**DW1**-**DW6**] including, 2 phenylpropanoids, 2 bibenzyls, a flavone and a benzoic acid derivative. The structures of these compounds were determined by spectroscopic analysis, including UV, IR, MS and NMR. They were evaluated for DPPH free radical scavenging activity. In addition, they were assayed for anti-*herpes simplex* activity (HSV-1, and HSV-2), and cytotoxicity against two types of cancer cells.

1. Structure characterization of isolated compounds

1.1 Structure determination of compound DW1

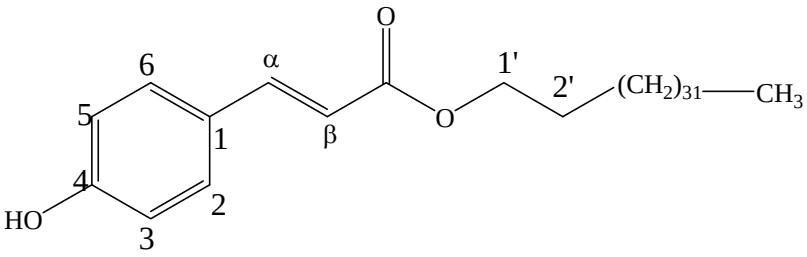
Compound DW1 was obtained as a white powder. The ESI mass spectrum (Figure 3) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 663, suggesting the molecular formula $C_{43}H_{76}O_3$**.** The UV spectrum (Figure 4) of this compound exhibited maximal absorptions at 312 and 226 nm. The IR spectrum (Figure 5) showed absorption peaks at 3390 cm^{-1} for hydroxyl group, at 1603, 1585, 1515, 1469, 1170 cm^{-1} for aromatic ring and at 1710 cm^{-1} for carbonyl group.

The ^1H NMR spectrum (Figure 6 and Table 2) exhibited a signal for a methyl group at δ_H 0.85 (3H, t, J = 7.0 Hz, CH_3) which could be correlated to the carbon at δ_C 14.1. In addition, the ^1H NMR spectrum showed two signals (4H) in the aromatic region at δ_H 6.82 (2H, d, J = 8.5 Hz, H-3, H-5), 7.40 (2H, d, J = 8.5 Hz, H-2, H-6) and *trans*- olefinic protons at 6.27 (1H, d, J = 16.0 Hz, H-β) and 7.60 (1H, d, J = 16.0 Hz,

H-α). Moreover, there were three signals in the aliphatic region at δ_H 1.23 (62H, brs, CH_2-n), 1.67 (2H, m, CH_2-2′), 4.16 (2H, t, J = 7.0 Hz, CH_2O-1′).

The ^{13}C NMR spectrum (Figure 7 and Table 2) exhibited four signals for six aromatic carbons, two signals of two olefinic carbons, signals at δ_C 22.6-31.9 for long chain CH_2 (32 carbons), a signal at δ_C 64.7 ($\underline{C}H_2O$-1′) and a signal at δ_C 167.7 for a carbonyl group.

By comparing the ^1H, ^{13}C NMR properties and MS data of this compound with previously published data (Mahmood *et al*., 2003), compound DW1 was identified as tetratriacontanyl-*trans*-*p*-coumarate [**289**] (Pei *et al*., 1989).



Tetratriacontanyl-*trans*-*p*-coumarate [**289**]

Table 2 NMR spectral data of compound DW1 (in $CDCl_3$) and eicosanyl-*trans-p*-coumarate (in $CDCl_3$)

Position	**Compound DW1**		**Eicosanyl-*trans-p*-coumarate** [a]	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
1	-	127.1	-	125.8
2,6	7.40 (d, 8.5)	130.0	7.42 (d, 8.2)	130.7
3,5	6.82 (d, 8.5)	115.8	6.83 (d, 8.2)	115.7
4	-	157.8	-	157.7
α	7.60 (d, 16.0)	144.4	7.62 (d, 17.0)	144.2
β	6.27 (d, 16.0)	115.5	6.30 (d, 17.0)	114.8
1′OCH_2	4.16 (t, 7.0)	64.7	4.18 (t, 6.5)	64.7
2′ CH_2	1.67 (m)	31.9	1.68 (m)	31.9
$(CH_2)_{31}$	1.23 br s	22.6-31.9	1.25 br s	22.6-31
CH_3	0.85 (t, 7.0)	14.1	0.87 (t, 6.5)	14.1
C=O	-	167.7	-	167.4

[a] ^1H NMR and ^{13}C NMR data from: Mahmood *et al*., 2003.

DW1 was compared with eicosanyl-*trans-p*-coumarate with focus on the phenylpropane partial structure.

1.2 Structure determination of compound DW2

Compound DW2 was obtained as a white powder. The ESI mass spectrum (Figure 8) showed a sodium adduct molecular ion $[M+Na]^+$ at *m/z* 525, suggesting the molecular formula $C_{32}H_{54}O_4$**.**

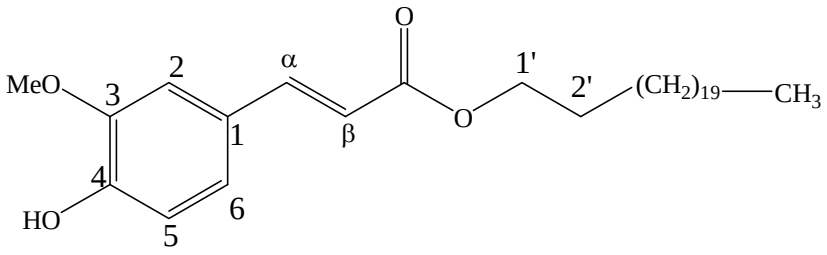
The UV spectrum (Figure 9) of this compound exhibited maximal absorptions at 325, 235 and 220 nm. The IR spectrum (Figure 10) showed absorption bands at 3425 cm^{-1} for hydroxyl group, at 1633, 1604, 1594, 1517 and 1467 cm^{-1} for aromatic ring , at 1712 cm^{-1} for carbonyl group and at 1271 cm^{-1} for COO stretching of ester group.

The ^1H NMR spectrum (Figure 11 and Table 3) exhibited signals for an ABM aromatic proton spin system at δ_H 7.05 (1H, dd, *J* = 8.0 Hz, 1.5 Hz, H-6), 7.01 (1H, d, *J* = 1.5 Hz, H-2), and 6.89 (1H, d, *J* = 8.0 Hz, H-5), *trans*- olefinic proton signals at 7.58 (1H, d, *J* = 16.0 Hz, H-α), 6.26 (1H, d, *J* = 16.0 Hz, H-β) and a methoxyl at δ_H 3.90. In addition, this spectrum of DW2 exhibited signals in the aliphatic region at δ_H 1.23 (38H, brs, CH_2-n), 1.69 (2H,q, *J* = 7.0 Hz, 2′-CH_2) and 4.16 (2H, t, *J* = 7.0 Hz, CH_2O-1′).

The ^{13}C NMR spectrum (Figure 12 and Table 3) exhibited signals for thirty-two carbons including six signals for six aromatic carbons, two signals for two olefinic carbons, signals at δ_C 22.7-31.9 for long chain CH_2 (20 carbons), a signal at δ_C 64.6 ($\underline{C}H_2$O-1′) a methoxyl group at δ_C 55.9 and a signal at δ_C 167.4 for a carbonyl group.

From the above data and through comparison with previously reported data (Ulubelen *et a*l ., 1994), Compound DW2 was identified as *trans* -docosanoylferulate [**124**]. TLC analysis with an authentic sample confirmed its identity.

trans –Docosanoylferulate was earlier isolated from *D. falconeri* (Sritularak and Likhitwitayawuid, 2009).



Trans -Docosanoylferulate [**124**]

Table 3 NMR spectral data of compound DW2 (in $CDCl_3$) and *trans* -docosanoylferulate (in $CDCl_3$)

Position	**Compound DW2**		***Trans*-Docosanoylferulate**[a]	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
1	-	127.0	-	127.0
2	7.01 (d, 1.5)	109.3	7.03 (d, 2.0)	109.2
3	-	147.9	-	147.8
4	-	146.7	-	146.7
5	6.89 (d, 8.0)	114.7	6.92 (d, 8.0)	114.6
6	7.05 (dd, 8.0,1.5)	115.6	7.08 (dd, 8.0, 2.0)	115.6
α	7.58 (d, 16.0)	142.0	7.61 (d, 16.0)	142.1
β	6.26 (d, 16.0)	123.0	6.39 (d, 16.0)	123.0
3-OMe	3.90 (s)	55.9	3.92 (s)	55.9
1′OCH_2	4.16 (t, 7.0)	64.6	4.19 (t, 7.0)	64.6
2′ CH_2	1.69 (q, 7.0)	31.9	1.70 (q, 7.0)	31.9
OC=O	-	167.4	-	167.4
$(CH_2)_{20}$	1.23 (br s)	22.7-31.9	1.25 (br s)	22.6-31.9
CH_3	0.85 (t, 7.0)	14.1	0.87 (t,7.0)	14.1

[a] From: Ulubelen *et a*l ., 1994.

1.3 Structure determination of compound DW3

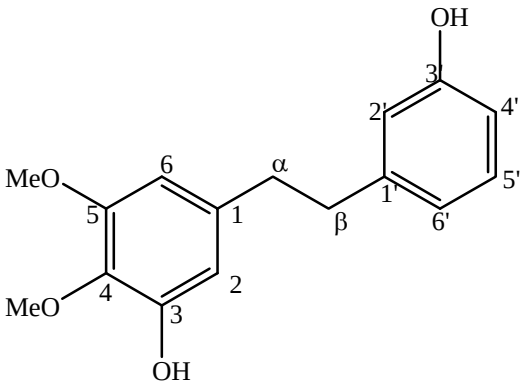
Compound DW3 was obtained as a brown amorphous solid. The ESI mass spectrum **(**Figure 13**)** showed a pseudomolecular ion $[M+H]^+$ at *m/z* 275, suggesting the molecular formula $C_{16}H_{18}O_4$**.**

The UV (Figure 14) absorptions at 210 and 281 nm were suggestive of a bibenzyl skeleton (Zhang *et al*., 2008a). The IR spectrum (Figure 15) showed absorption bands for hydroxyl (3400 cm^{-1}) and aromatic (1593, 1512, 1455 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 16 and Table 4) showed characteristic methylene protons for a bibenzyl at δ_H 2.83 (4H, brs, H_2-α, H_2- β), which could be related to two methylene carbons at δ_C 37.6 and 37.5 ppm in the ^{13}C NMR spectrum. In addition, the ^1H NMR data exhibited signals for six aromatic protons at δ_H 7.16 (1H, dd, *J* = 7.6 ,7.5 Hz, H-5′), 6.78 (1H, br d, *J* = 7.5 Hz, H-4′), 6.76 (1H, br d, *J* = 7.6 Hz H-6′), 6.68 (1H, br s, H-2′), 6.49 (1H, br s, H-2), and 6.28 (1H, br s, H-6). Moreover, the ^1H NMR spectrum revealed the presence of two methoxyl groups at δ_H 3.87 (3H) and 3.81 (3H).

The ^{13}C NMR spectrum (Figure 17 and Table 4) showed sixteen carbon signals, including six aromatic quaternary carbons, two methoxyls, six aromatic methines and two methylenes. Furthermore, the NOESY spectrum (Figures 18 and 19) exhibited a cross peak between H-6 and the methoxyl at δ_H 3.87, placing this methoxyl at C-5.

Through comparison of its ^1H NMR, ^{13}C NMR, UV and MS data with those reported in the literature (Giner e*t al*., 1993), DW3 was identified as 3,3′-dihydroxy-4,5-dimethoxybibenzyl. This is the first reported of this compound from the genus *Dendrobium*.



3,3′-Dihydroxy-4,5-dimethoxybibenzyl [**290**]

Table 4 NMR spectral data of compound DW3 (in $CDCl_3$) and 3,3′-Dihydroxy-4,5-dimethoxybibenzyl (in $CDCl_3$)

Position	**Compound DW3**		**3,3′-Dihydroxy-4,5-dimethoxybibenzyl** [a]	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
1	-	143.5	-	143.3
2	6.49 (br s)	108.0	6.47 (d, 1.9)	108.0
3	-	148.9	-	148.6
4	-	138.1	-	138.0
5	-	152.1	-	152.0
6	6.28 (br s)	104.6	6.25 (d, 1.9)	104.3
α	2.83	37.5	2.81 (m)	37.4
β	2.83	37.6	2.81 (m)	37.5
1′	-	133.0	-	133.5
2′	6.68 (br s)	115.4	6.67 (m)	115.3
3′	-	155.7	-	155.8
4′	6.78 (br d, 7.5)	112.9	6.78 (dd, 8.7, 7.5)	112.8
5′	7.16 (dd, 7.6, 7.5)	129.4	7.15 (dd, 8.7, 7.5)	129.2
6′	6.76 (br d, 7.6)	120.7	6.76 (dt, 7.5, 1.1)	120.3
OMe	3.87 (s), 3.81 (s)	60.9,55.8	3.87 (s), 3.81 (s)	60.8,55.6

[a] from: Giner e*t al* . 1993.

1.4 Structure determination of compound DW4

Compound DW4 was obtained as a brown amorphous solid. The ESI mass spectrum (Figure 20) showed a pseudomolecular ion $[M+H]^+$ at *m/z* 305, suggesting the molecular formula $C_{17}H_{20}O_5$.

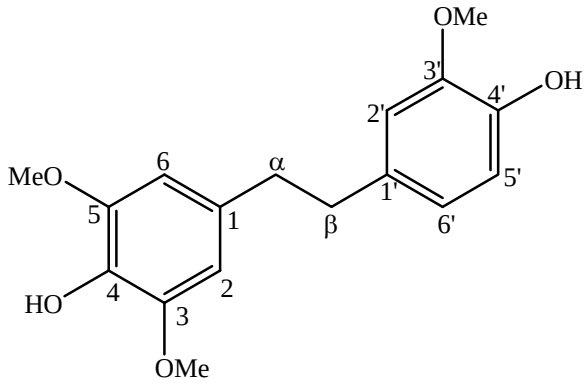
The UV spectrum (Figure 21) showed characteristic absorptions for a bibenzyl skeleton at λ_{max} 219 and 280 nm (Zhang *et al*., 2008a). Its IR spectrum (Figure 22) exhibited absorption bands at 3410 (hydroxyl), at 1609, 1517, 1463 (aromatic) and at 1227, 1115 (C-O) cm^{-1}.

The ^1H NMR spectrum (Figure 23 and Table 5) displayed characteristic signals for a bibenzyl at δ_H 2.84 (4H, brs, H_2–α, H_2-β) and ^{13}C NMR data (Figure 24 and Table 5) showed signals for methylene carbons at δ_C 37.8 and 38.3. Moreover, the ^1H NMR spectrum exhibited a nine proton singlet at δ_H 3.86 representing three aromatic methoxyl groups, five aromatic protons at δ_H 6.38 (2H, s, H-2, H-6), 6.63 (1H, br s, H-2′), 6.86 (1H, d, *J* = 8.1 Hz, H-5′) and 6.69 (1H, br d, *J* = 8.1 Hz, H-6′).

The ^{13}C NMR spectrum (Figure 24 and Table 5) exhibited seventeen carbon signals, including three methoxyls, two methylenes, five methines and seven quaternary carbons.

From the above data and through comparison with previously reported data (Majumder and Zen 1987). Compound DW4 was identified as moscatilin [**8**]. In addition, it was confirmed by comparison with an authentic sample by TLC.

Moscatilin was a bibenzyl derivative firstly isolated from *D. moscatum*. Besides, this compound was also found in *D.* amoenum, *D.* aurantiacum var. *denneanum*, *D. chrysanthum*, *D. densiflorum*, *D. gratiotissimum*, *D. loddigesii*, *D. longicornu* and *D. secundum* (Majumder and Sen 1987; Majumder *et al*., 1999; Fan *et al*., 2001; Yang *et al*., 2006a; Yang *et al*., 2006b; Hu *et al*., 2008a; Zhang *et al*., 2008a; Ito *et al*., 2010).



moscatilin [**8**]

Table 5 NMR spectral data of compound DW4 (in $CDCl_3$) and Moscatilin (in $CDCl_3$)

Position	Compound DW4		Moscatilin[a]	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
1	-	132.8	-	132.8
2,6	6.38 (s)	105.2	6.30 (s)	105.2
3,5	-	146.8	-	146.8
4	-	133.6	-	133.5
α	2.84 (s)	37.8*	2.79 (s)	37.8*
β	2.84 (s)	38.4*	2.79 (s)	38.8*
1′	-	132.9	-	132.8
2′	6.63 (br s)	111.2	6.60 (d, 2.0)	111.2
3′	-	146.2	-	146.1
4′	-	143.7	-	143.7
5′	6.86 (d, 7.8)	114.1	6.77 (d, 8.0)	114.1
6′	6.69 (brd, 8.1)	121.0	6.74 (dd, 8.0,2.0)	121.0
3,5-OMe	3.86 (s)	55.8	3.81 (s)	56.2
3′-OMe	3.87 (s)	55.2	3.81 (s)	55.8

* Value in the same column are interchangeable.

[a] From: Majumder and Zen 1987.

1.5 Structure determination of compound DW5

Compound DW5 was obtained as a yellow powder. The ESI mass spectrum (Figure 25) showed a pseudomolecular ion $[M+H]^+$ at *m/z* 271, suggesting the molecular formula $C_{15}H_{10}O_5$.

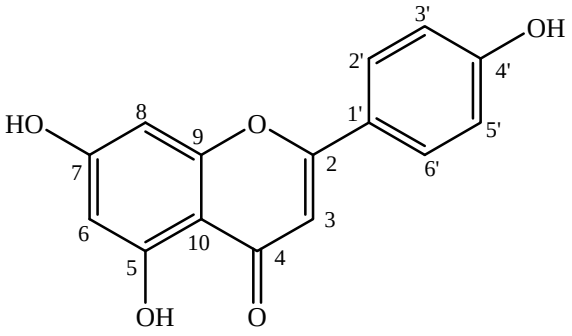
The UV spectrum (Figure 26) exhibited absorptions at λ_{max} 220 and 269 nm. Its IR spectrum (Figure 27) showed absorption bands at 3390 (hydroxyl), at 1655, 1608, 1508, 1453 (aromatic) and at 1156 (C-O) cm^{-1}.

The ^1H NMR spectrum (Figure 28 and Table 6) showed signals for seven aromatic protons, including δ_H 7.93 (2H, d, *J* = 8.7 Hz, H-2′, H-6′), 7.02 (2H, d, *J* = 8.7 Hz, H-3′, H-5′), 6.63 (1H, s, H-3), 6.53 (1H, d, *J* = 1.7 Hz, H-8), and 6.25 (1H, d, *J* = 1.7 Hz, H-6).

The ^{13}C NMR spectrum (Figure 29 and Table 6) exhibited fifteen carbon signals, including seven quaternary carbons, seven methines and a signal at δ_C 183.1 for a carbonyl group.

Through comparison of its ^1H NMR, ^{13}C NMR UV and MS data with those reported in the literature (Han *et al*., 2007), DW5 was identified as apigenin [**95**].

Apigenin was a flavonoid previously isolated from *Cayratia japonica* and *D. crystallium.* The compound showed potent inhibitory effects against the MAO both MAO-A and MAO-B with IC_{50} values of 1.7 and 12.8 µM, respectively (Han *et al*., 2007; Wang *et al*., 2009).



Apigenin [**95**]

Table 6 NMR spectral data of compound DW5 (in acetone-d_6) and apigenin (in DMSO- d_6)

Position	Compound DW5		Apigenin[a]	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
2	-	165.1	-	164.1
3	6.63	104.1	6.82	102.3
4	-	183.1	-	181.7
5	-	161.9	-	161.4
6	6.25 (d,1.7)	99.7	6.23 (d)	98.8
7	-	163.4	-	163.7
8	6.53 (d, 1.7)	94.7	6.52 (d)	93.9
9	-	158.8	-	157.3
10	-	105.3	-	103.7
1′	-	123.3	-	121.1
2′, 6′	7.93 (d, 8.7)	129.2	7.96 (d)	128.4
3', 5′	7.02 (d, 8.7)	116.9	6.96	115.9
4′	-	161.9	-	161.1
5-OH	13.01 (s)	-	13.0 (s)	-

[a] From: Han *et al*., 2007.

1.6 Structure determination of compound DW6

Compound DW6 was obtained as a colorless powder. The ESI mass spectrum (Figure 30) showed a pseudomolecular ion $[M+H]^+$ at *m/z* 169, suggesting the molecular formula $C_8H_8O_4$.

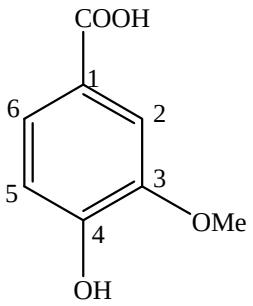
The UV spectrum (Figure 31) showed absorptions at λ_{max} 220, 260 and 287 nm. Its IR spectrum (Figure 32) exhibited absorption bands at 3485 (hydroxyl), at 1680, 1597, 1434 (aromatic) and at 3485 (COOH) cm^{-1}.

The ^1H NMR spectrum (Figure 33 and Table 7) exhibited signals for three aromatic protons, including δ_H 7.58 (1H, dd, *J* = 8.5 , 2.0 Hz, H-6), 7.55 (1H, d, *J* = 2.0 Hz, H-2), and 6.89 (1H, d, *J* = 8.5 Hz, H-5). These spectral data suggested the presence of three substituents on the aromatic ring. The ^1H NMR spectrum also showed a methoxyl signal at δ_H 3.89 (s).

The ^{13}C NMR spectrum (Figure 34 and Table 7) showed eight carbon signals, including six aromatic carbons, carbonyl carbon of carboxylic acid at δ_C 167.4, and a methoxyl at δ_C 56.3.

From the above data and through comparison with previously reported data (Yaguchi *et al*., 1988), Compound DW6 was identified as vanillic acid [**88**].

Vanillic acid was a benzoic acid derivative previously isolated from *D. chrysotoxum* (Li *et al*., 2009c).



Vanillic acid [**88**]

Table 7 NMR spectral data of compound DW6 (in acetone-d_6) and vanillic acid (in $CDCl_3$)

Position	Compound DW6		Vanillic acid[a]	
	δ_H (mult., *J* in Hz)	**δ_C**	**δ_H (mult., *J* in Hz)**	**δ_C**
1	-	122.9	-	123.4
2	7.55 (d, 2.0)	113.4	8.00 (d, 2.0)	113.7
3	-	152.0	-	152.4
4	-	148.0	-	148.0
5	6.89 (d, 8.5)	115.5	7.24 (d, 8.1)	115.9
6	7.58 (dd, 8.5, 2.0)	124.8	8.09 (dd, 8.1, 2.0)	124.7
COOH	-	167.4	-	169.0
3-OMe	3.89 (s)	56.3	3.78 (s)	55.6

[a] From: Yaguchi ., 1988.

All of the isolated compounds were evaluated for DPPH free radical scavenging activity and anti-herpes simplex virus activity. Since some bibenzyls and flavonoids are known to have cytotoxic activity (Chen *et al*., 2008), the polyphenolic compounds obtained in this study were also subjected to assays for cytotoxicity.

2. DPPH Free Radical Scavenging Activity

Free radicals are molecules containing at least an unpaired electron in the outer orbital. They are highly reactive due to the presence of the unpaired electron. The most important free radical are reactive oxygen species (ROS), which include superoxide ($O_2^{\bullet -}$), peroxyl ($RO_2^{\bullet}$), alkoxyl ($RO^{\bullet}$), hydroxyl ($OH^{\bullet}$), hydroperoxyl ($H_2O_2^{\bullet}$), and nitric oxide ($NO^{\bullet}$) radicals (Pietta, 2000). Free radicals are generated in cells by metabolism, environmental pollutants, exposure to radiation, and grilled food. The excess of ROS may be very harmful, since they can attack proteins in tissues, lipids in cell membranes, and DNA. This oxidative damage is the cause of aging and several degenerative diseases, such as cancer, cardiovascular disease, and neurodegenerative diseases (Valko, 2007).

Defense mechanisms against free radical-induced oxidative stress involve (i) preventive mechanisms, (ii) repair mechanisms, (iii) physical defenses, and (iv) antioxidant defenses (Valko, 2007). Enzymatic antioxidant defenses consist of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Non-enzymatic antioxidants are composed of ascorbic acid (Vitamin C), carotenoids, glutathione (GSH), α-tocopherol (Vitamin E), and plant polyphenols such as phenol, phenolic acids, flavonoids, tannins, and lignans (Pietta, 2000). Consequently, antioxidants with free radical scavenging activities may have an influence in the prevention of free radical relevant diseases.

The methanolic extract from the whole plant of *Dendrobium williamsonii* exhibited a positive result for DPPH radical scavenging assay. Its free radical scavenging activity was approximately 90 % inhibition at a concentration of 200 µg/ml. The DPPH assay measures the capability of a substance to decolorize a methanolic solution of 1,1-diphenyl-2-picrylhydrazyl radical (Arabshahi and Urooj, 2007; Amarowicz *et al*., 2010). Pure compounds isolated from this extract were initially tested at 100 µg/ml. Compounds showing more than 50% inhibition were further evaluated for IC_{50} values. Vitamin C and quercetin were used as positive controls. The results were summarized in Table 8.

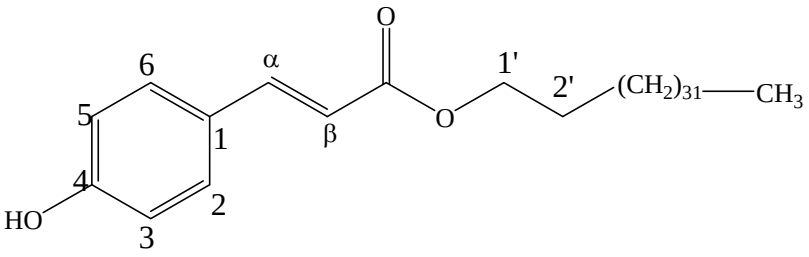
Table 8 Percentage of DPPH reduction of compounds isolated from *Dendrobium williamsonii*

Compound	**% DPPH reduction at 100 µg/ml**	**IC $_{50}$ (µg/ml) (Mean ±SD)**	**IC $_{50}$ (µM) (Mean ±SD)**
Tetratriacontanyl-*p*-coumarate **DW1** [**289**]	23.03	-	-
Trans-Docosanoylferulate **DW2** [**124**]	33.75	-	-
3,3'-dihydroxy-4,5-dimethoxybibenzyl **DW3** [**290]**	80.87	5.36 ± 0.36	19.56 ± 1.30
Moscatilin **DW4** [**8**]	88.52	2.60 ± 0.38	8.56 ± 1.24
Apigenin **DW5** [**95**]	87.98	5.22 ± 0.32	19.34 ± 1.19
Vanillic acid **DW6** [**88**]	44.90	-	-
Vitamin C	72.42	7.47 ± 0.41	42.46 ± 2.31
Quercetin	92.89	2.52 ±0.14	8.34 ± 0.47

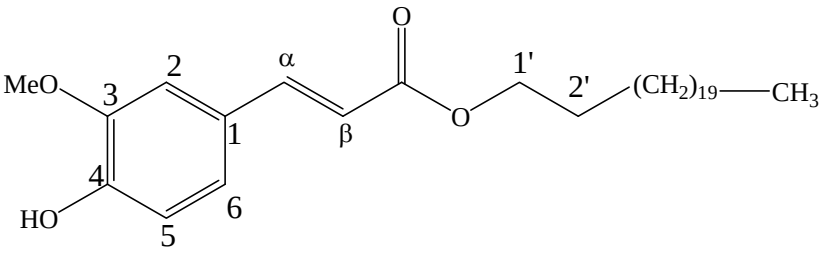
From Table 8, it could be seen that compounds DW3-DW5 exhibited moderate DPPH free radical scavenging activity with IC_{50} values of 19.56 ± 1.30, 8.56 ± 1.24 and 19.34 ± 1.19 µM, respectively. Vitamin C (IC_{50} = 42.46 ± 2.31 µM) and quercetin (IC_{50} = 8.34 ± 0.47 µM) were used as positive controls. In addition, the DW1, DW2 and DW 6 showed weak activity against DPPH free radical scavenging at concentration 100 µg/ml.

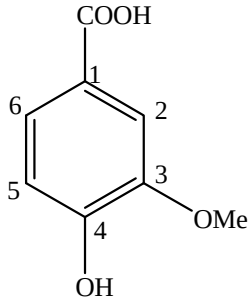
Moreover, moscatilin isolated from *D. nobile* exhibited DPPH free radical scavenging activity with IC_{50} values of 14.5 µM (Zhang *et al*., 2007a).

It appeard that both the number and position of hydroxyl groups on the aromatic rings showed a significant role on the free radical scavenging activity of bibenzyls. It seemed that the substitution of hydroxyl groups at *ortho* or *para* position might be enhance for the activity more than *meta* substitution (Yang *et al* ., 2009).



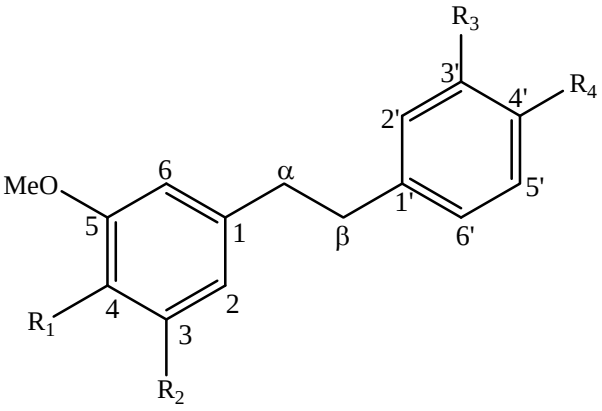
DW 1 [**289**]

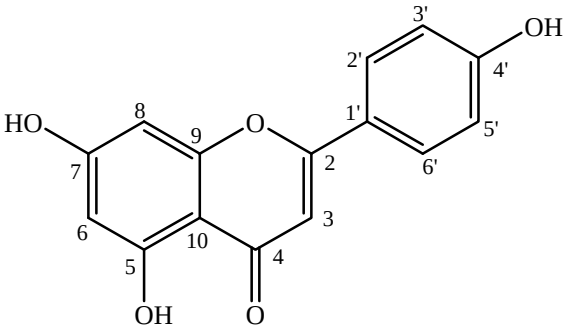




DW 2 [**124**]

DW6 [**88**]





DW 5 [**95**]

	R_1	R_2	R_3	R_4
DW 3 [**290**] :	OMe	OH	OH	H
DW 4 [**8**] :	OH	OMe	OMe	OH

3. Cytotoxic Activity

All of the compounds isolated from the methanolic extract of *Dendrobium williamsonii* were submitted on cytotoxicity evaluation to the bioassay laboratory of National Center for Genetic Engineering and Biotechnology (BIOTEC). This cytotoxicity assays were carried out on two human cancer cell lines including KB (oral human epidermal carcinoma cells) and MCF-7 (breast cancer cells). The results were summarized in Table 9.

Table 9 IC_{50} Values (μM) for cytotoxicity of isolated compounds and positive controls.

Compound	**IC_{50} (μM)**	
	KB	**MCF-7**
Tetatriacontanyl-*p*-coumarate [**DW1**]	inactive	inactive
trans-Docosanoylferulate [**DW2**]	inactive	inactive
3,3′-Dihydroxy-4,5-dimethoxybibenzyl [**DW3**]	195.0	inactive
Moscatilin [**DW4**]	43.5	inactive
Apigenin [**DW5**]	inactive	inactive
Vanillic acid [**DW6**]	inactive	inactive
Ellipticine	1.8	-
Doxorubicin	0.99	15.1
Tamoxifen	-	24.9

Inactive = Less than 50% inhibition at concentration of 50 μg/ml.

3,3′-dihydroxy-4,5-dimethoxybibenzyl exhibited weak cytotoxicity and moscatilin exhibited moderate cytotoxicity against KB cells. However, these compounds were not active against MCF-7 cells. In addition, tetratriacontanyl-*trans*-*p*-coumarate, *trans*- docosanoylferulate, apigenin and vanillic acid did not show cytotoxic activity.

Moscatilin was shown to induce apoptosis in colorectal cancer cell lines by tubulin depolymerization and DNA damage (Chen *et al*., 2008). Moreover, moscatilin exhibited anti-angiogenic effect both *in vitro* and *in vivo* by inhibiting signaling pathways of angiogenic factor (Tsai *et al*., 2010). In addition, moscatilin from *D. gratiosissimum* was showed moderate cytotoxicity against HL-60 cell with IC_{50} 0.082 µM (Zhang *et al*., 2008a).

4. Anti-Herpes Simplex Virus Activity

Herpes simplex virus (HSV) causes an infective disease that influences approximately 70% to 95% of adults in the world. Ther are two types of HSV: HSV-1 and HSV-2. HSV-1 is associated with oral, pharyngeal, facial, ocular, and central nervous system infections and largely transmitted by oral secretions and nongenital contact. HSV-2 is frequently involved with anal and genital infections and is mainly transmitted sexually by genital secretions. (Fatahzadeh and Schwartz, 2007). The clinical symptoms of the disease exhibit different severity such as blisters or ulcers on the mouth, lips and gums, or genitals. In addition, many patients unfortunately face repeated attacks. In immuno-compromised patients and neonates, HSV infections can cause serious systemic illnesses. At present, drug-resistant strains of HSV frequently increase following therapeutic treatment. Resistance to acyclovir and related nucleoside analogues can occur following mutation in either HSV thymidine kinase (TK) or DNA polymerase. Viral strains connected with clinical resistance are almost always defective in TK production. Therefore, new antiviral agents exhibiting different mechanisms of action are urgently needed (Khan *et al*., 2005).

The chemical components obtained from the whole plant of *Dendrobium williamsonii* were evaluated for anti-herpes simplex activity (HSV-1 and HSV-2) by plaque reduction assay (Lipipun *et al*., 2003; Chansriniyom *et al*., 2009). First, each pure compound was tested for anti-HSV activity at a concentration of 100 µg/mL. Compounds exhibiting more than 50% inhibition were further evaluated for IC_{50} values. Acyclovir was used as a positive control. The results were summarized in Table 10.

Table 10 Anti-herpes simplex virus activity of isolated compounds by plaque reduction assay.

Compound	**Post treatment (IC_{50}) µM**		**Inactivation (IC_{50}) µM**	
	HSV-1	**HSV-2**	**HSV-1**	**HSV-2**
Tetatriacontanyl-*p*-coumarate [**DW1**]	inactive	inactive	inactive	inactive
trans-Docosanoylferulate [**DW2**]	inactive	inactive	inactive	inactive
3,3′-Dihydroxy-4,5-dimethoxybibenzyl [**DW3**]	273.7± 45.6	304.1± 52.6	304.1± 52.5	334.5± 52.5
Moscatilin [**DW4**]	inactive	inactive	inactive	inactive
Apigenin [**DW5**]	inactive	inactive	inactive	inactive
Vanillic acid [**DW6**]	inactive	inactive	inactive	inactive
Acyclovir	1.3 ± 0.08	2.6 ± 0.17	0.9 ± 0.17	1.8 ± 0.02

Inactive = Less than 50% inhibition at concentration of 100 µg/ml.

As shown in Table 10, only 3,3′-dihydroxy-4,5-dimethoxybibenzyl exhibited anti-herpes simplex virus acitivity. It showed weak anti-HSV activity against HSV-1 and HSV-2. In the post-treatment assay the IC_{50} values were 273.7 ± 45.6 µM (HSV-1), 304.1 ± 52.6 µM (HSV-2) and in the inactivation assay the IC_{50} values were 304.1 ± 52.5 µM (HSV-1), 334.5 ± 52.5 µM (HSV-2).

CHAPTER V

CONCLUSION

In this study, six compounds were isolated from the methanol extract of *Dendrobium williamsonii* Rchb.f. They were characterized as tetratriacontanyl-*p*-coumarate [**289**], *trans*–docosanoylferulate [**124**], 3,3′-dihydroxy-4,5-dimethoxybibenzyl [**290**], moscatilin [**8**], apigenin [**95**] and vanillic acid [**88**]. These isolated compounds were evaluated for DPPH free radical scavenging activity, anti-herpes simplex virus effects, and cytotoxicity. 3,3′-Dihydroxy-4,5-dimethoxybibenzyl [**290**], moscatilin [**8**], and apigenin [**95**] exhibited moderate DPPH free radical scavenging activity. Only 3,3′-dihydroxy-4,5-dimethoxybibenzyl [**290**] showed weak anti-HSV activity against HSV-1 and HSV-2. The bibenzyls 3,3′-dihydroxy-4,5-dimethoxybibenzyl [**290**] exhibited weak cytotoxicity and moscatilin [**8**] exhibited moderate cytotoxicity against KB cells. In addition, tetratriacontanyl-*p*-coumarate [**289**] and 3,3′-dihydroxy-4,5-dimethoxybibenzyl [**290**] were firstly isolated from *D. williamsonii*. Finally, the chemical data obtained in this study might be useful for chemotaxonomic syudy of plants in the genus *Dendrobium*.

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APPENDIX

BIORESOURCES RESEARCH UNIT

Low resolution report

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Sample Name	DW30	Instrument	micrOTOF Bruker

Acquisition Parameter

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Scan End	1500 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Source

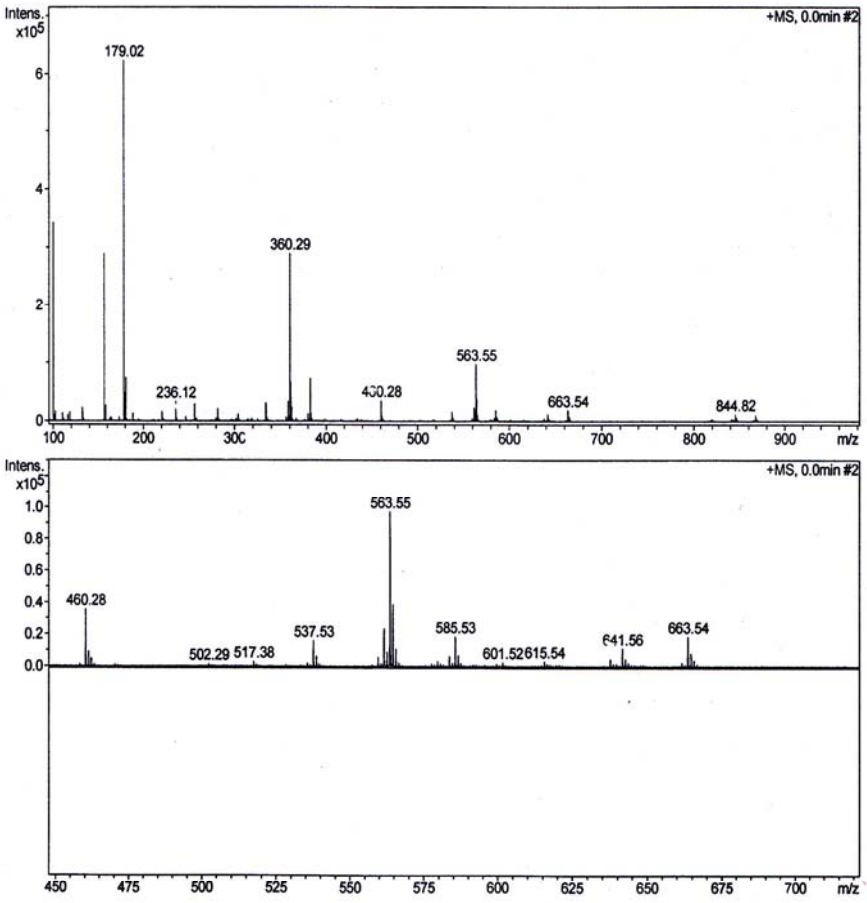

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Figure 3 Mass spectrum of compound DW1

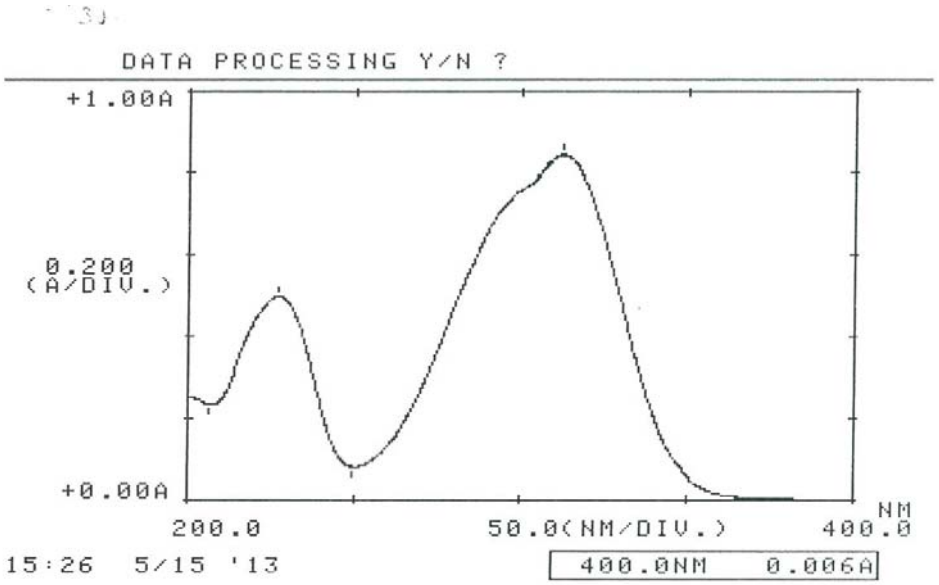

Figure 4 UV spectrum of compound DW1 (MeOH)

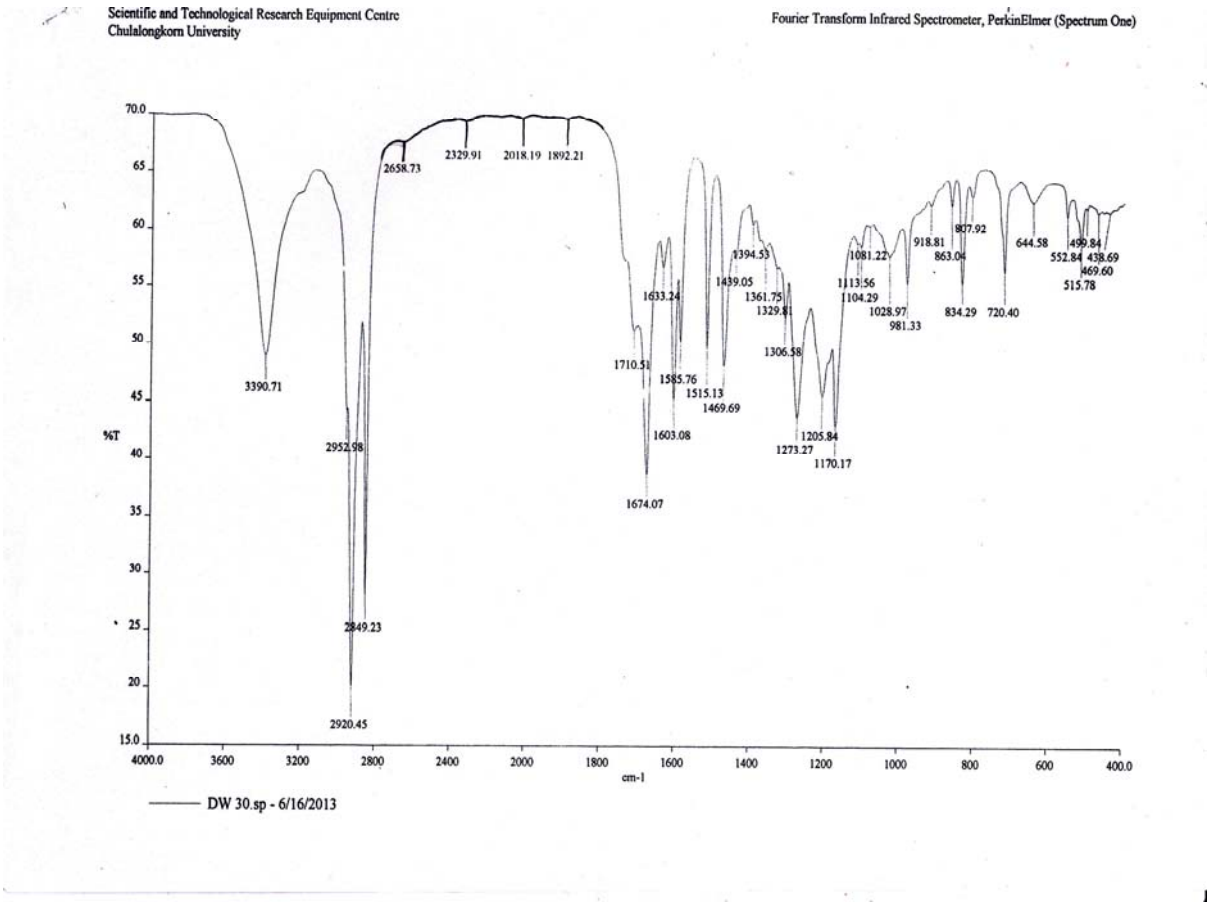

Figure 5 IR spectrum of compound DW1

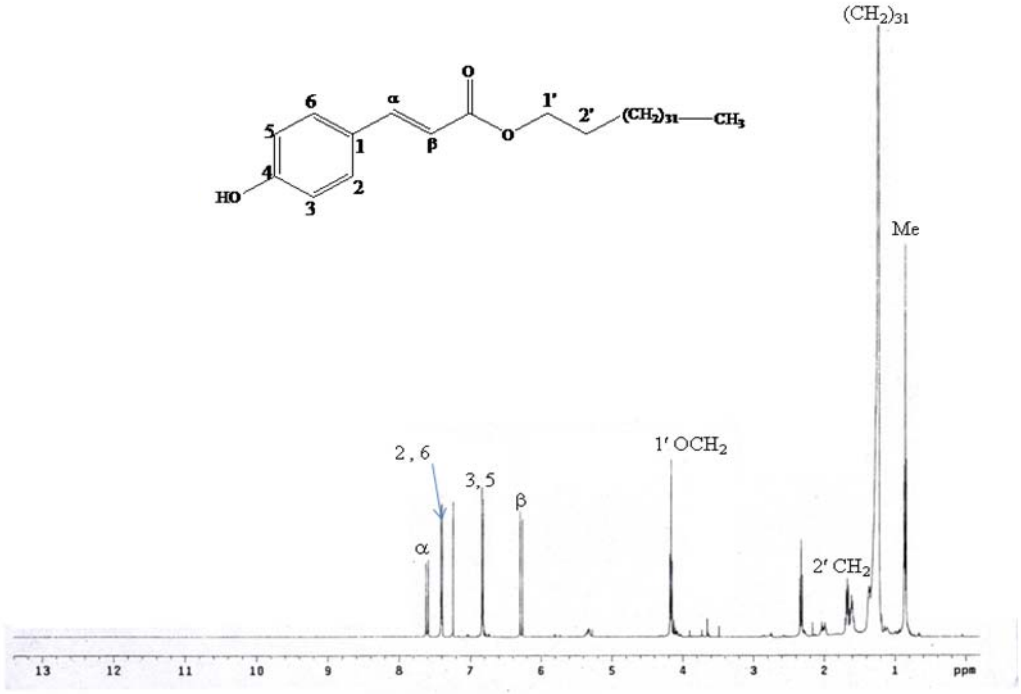

Figure 6 ^{1}H-NMR (500 MHz) spectrum of compound DW1 ($CDCl_3$)

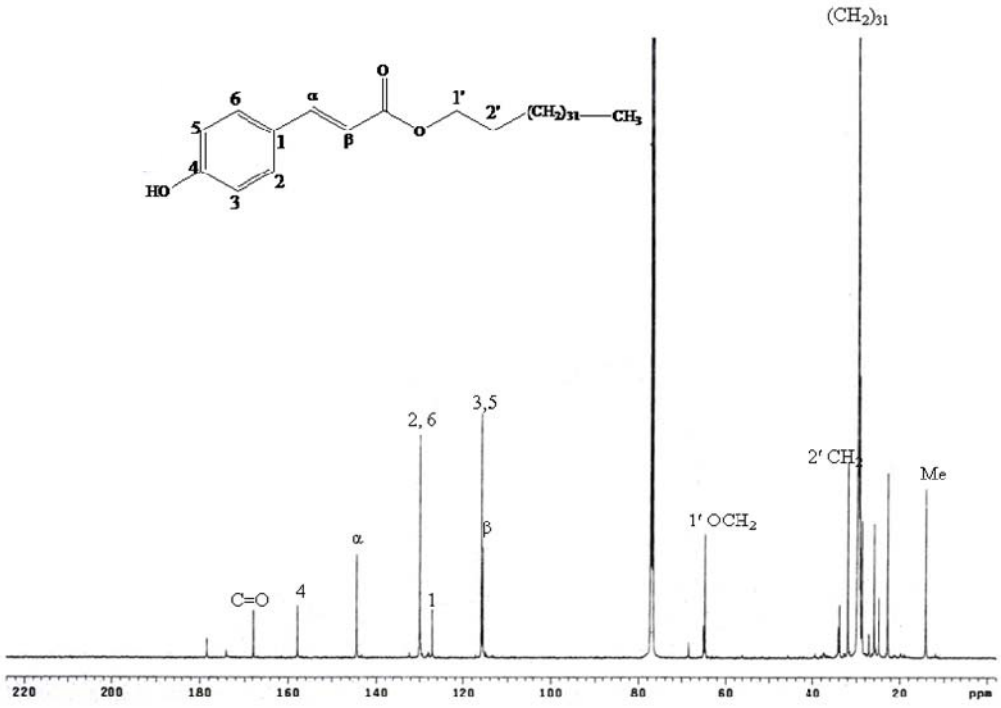

Figure 7 ^{13}C-NMR (125 MHz) spectrum of compound DW1 ($CDCl_3$)

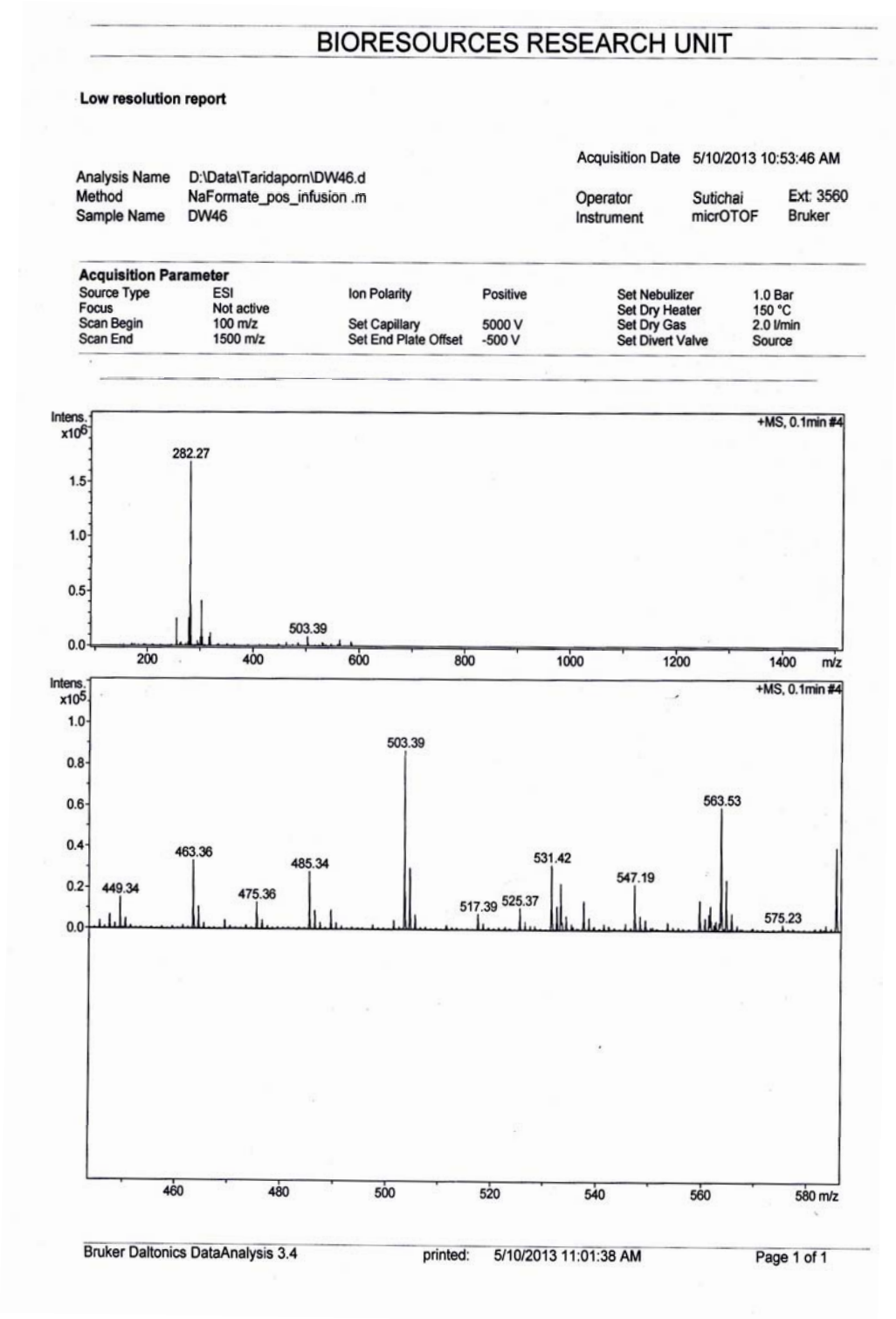

Figure 8 Mass spectrum of compound DW2

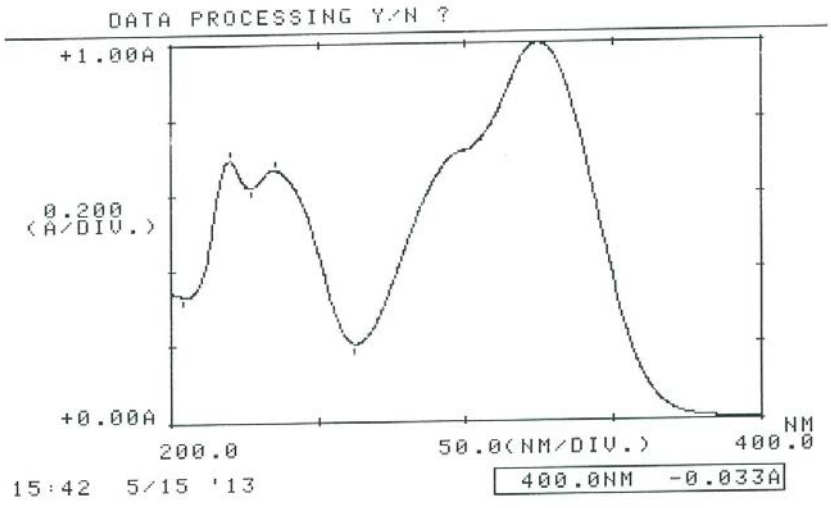

Figure 9 UV spectrum of compound DW2 (MeOH)

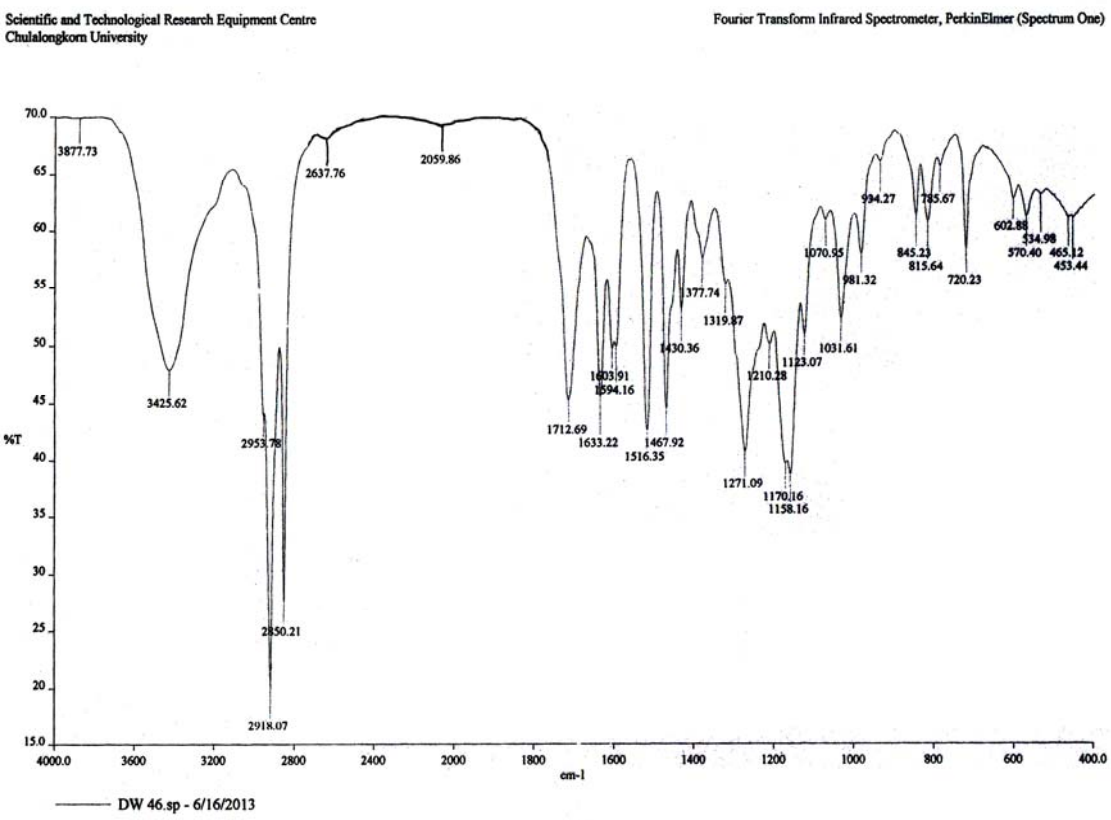

Figure 10 IR spectrum of compound DW2

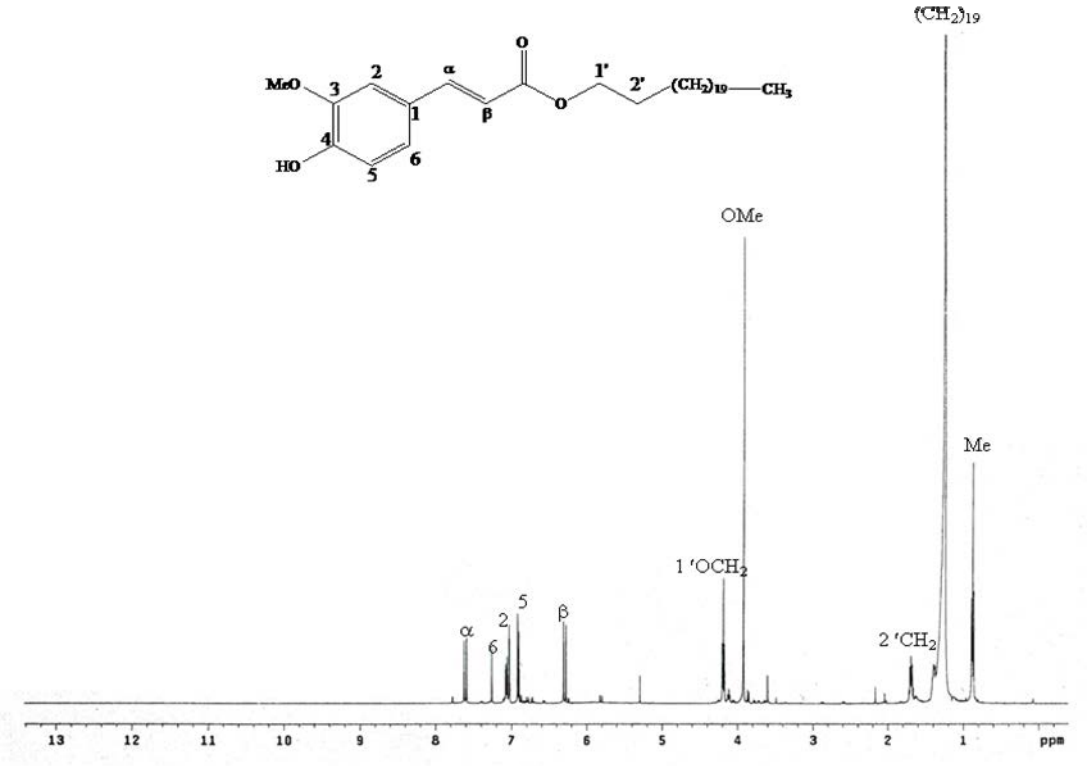

Figure 11 ^{1}H-NMR (500 MHz) spectrum of compound DW2 ($CDCl_3$)

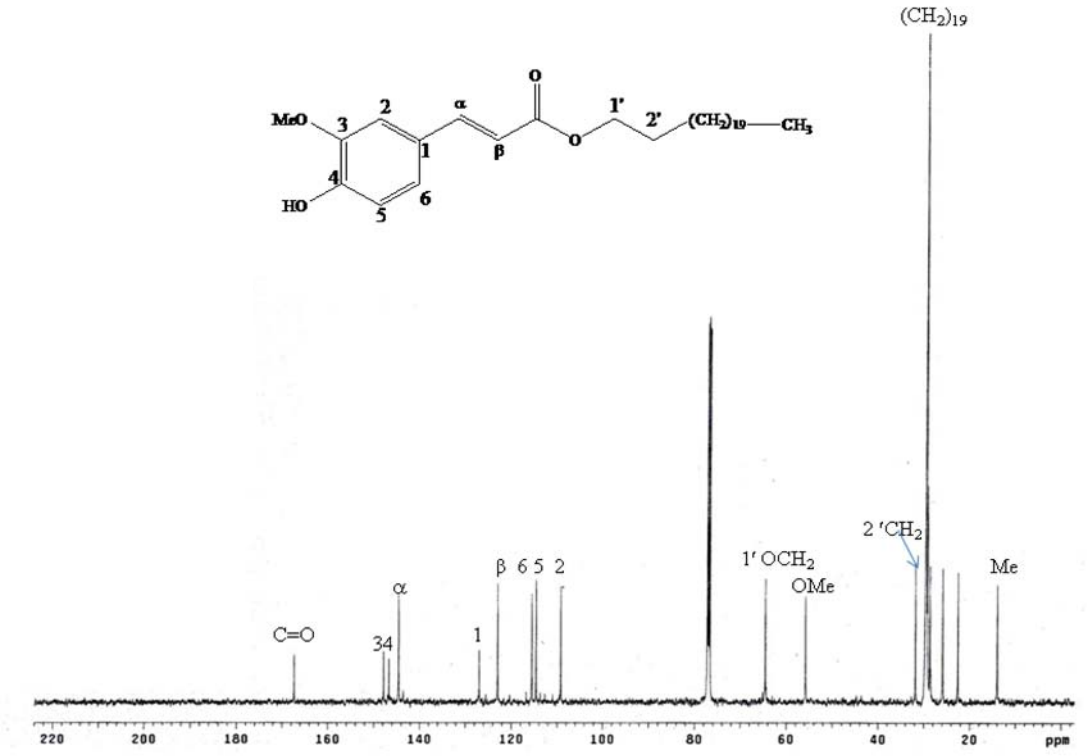

Figure 12 ^{13}C-NMR (125 MHz) spectrum of compound DW2 ($CDCl_3$)

BIORESOURCES RESEARCH UNIT

Low resolution report

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Sample Name	DW1	Instrument	micrOTOF Bruker

Acquisition Parameter

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Scan Begin	100 m/z	Set Capillary	5000 V	Set Dry Gas	2.0 l/min
Scan End	1500 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Source

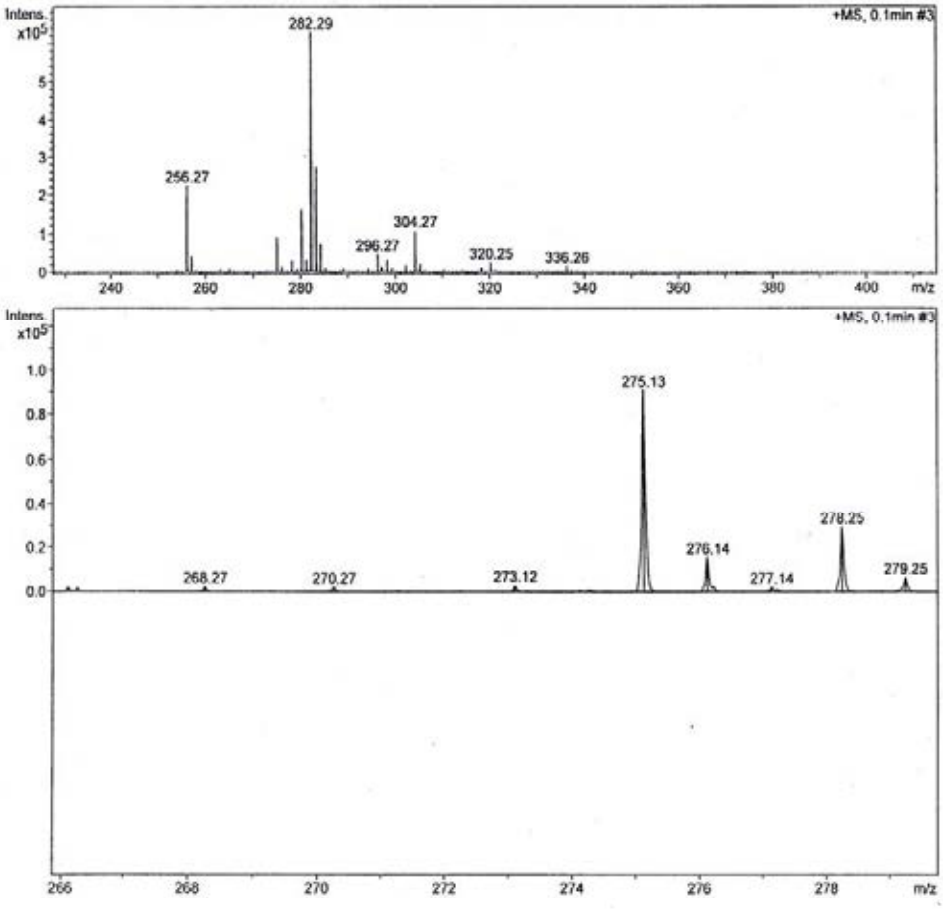

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Figure 13 Mass spectrum of compound DW3

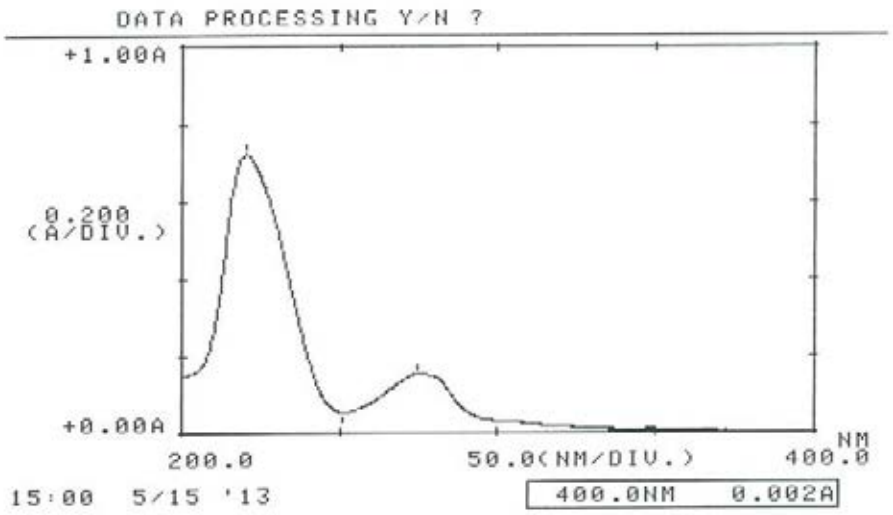

Figure 14 UV spectrum of compound DW3 (MeOH)

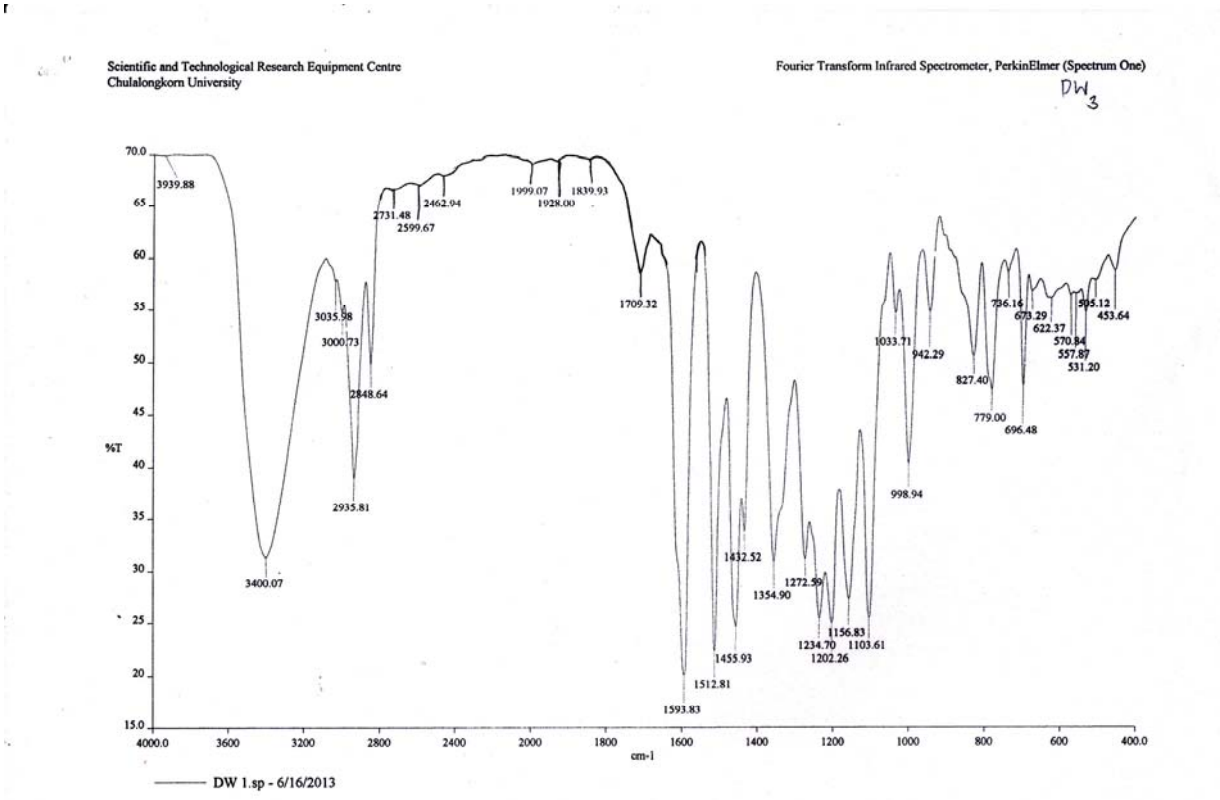

Figure 15 IR spectrum of compound DW3

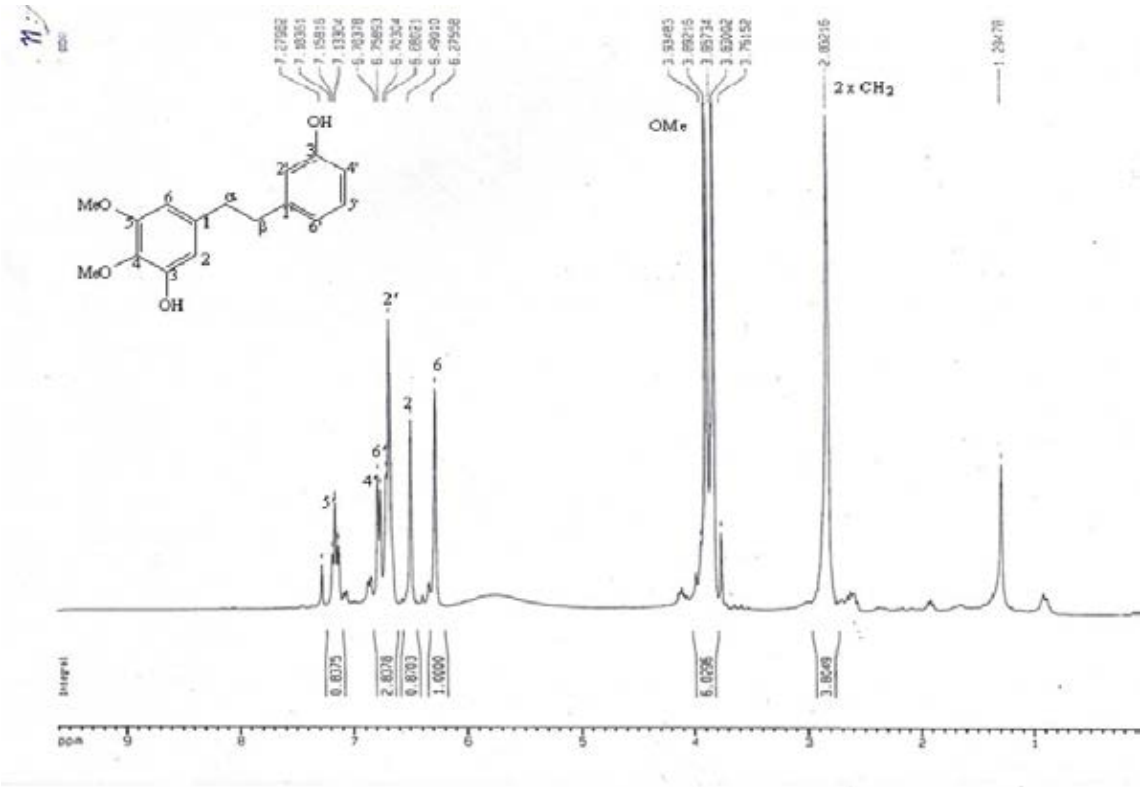

Figure 16 ^{1}H-NMR (300 MHz) spectrum of compound DW3 ($CDCl_3$)

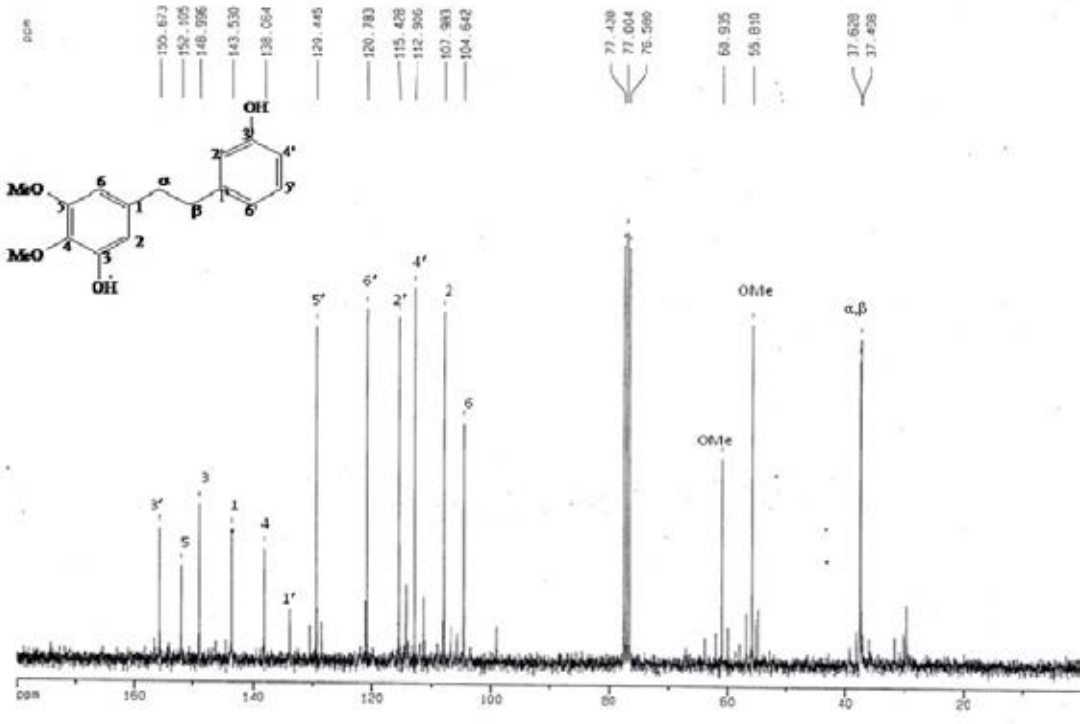

Figure 17 ^{13}C-NMR (75 MHz) spectrum of compound DW3 ($CDCl_3$)

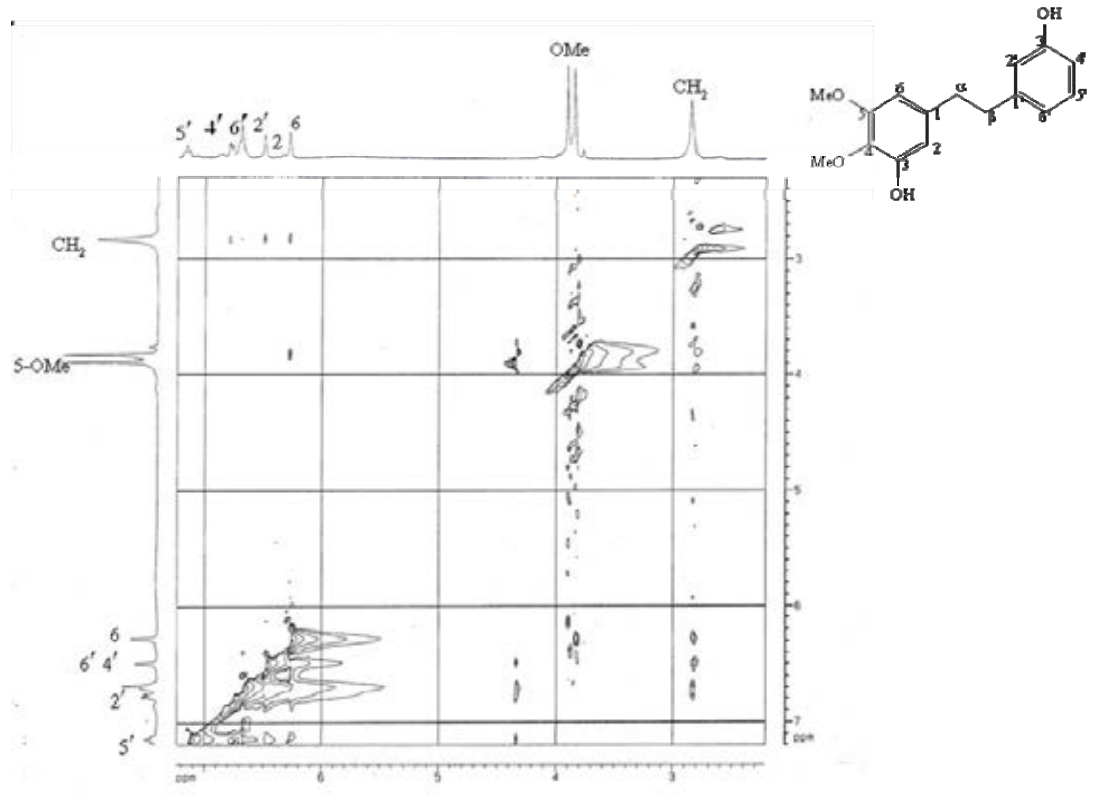

Figure 18 NOESY spectrum of compound DW3 ($CDCl_3$)

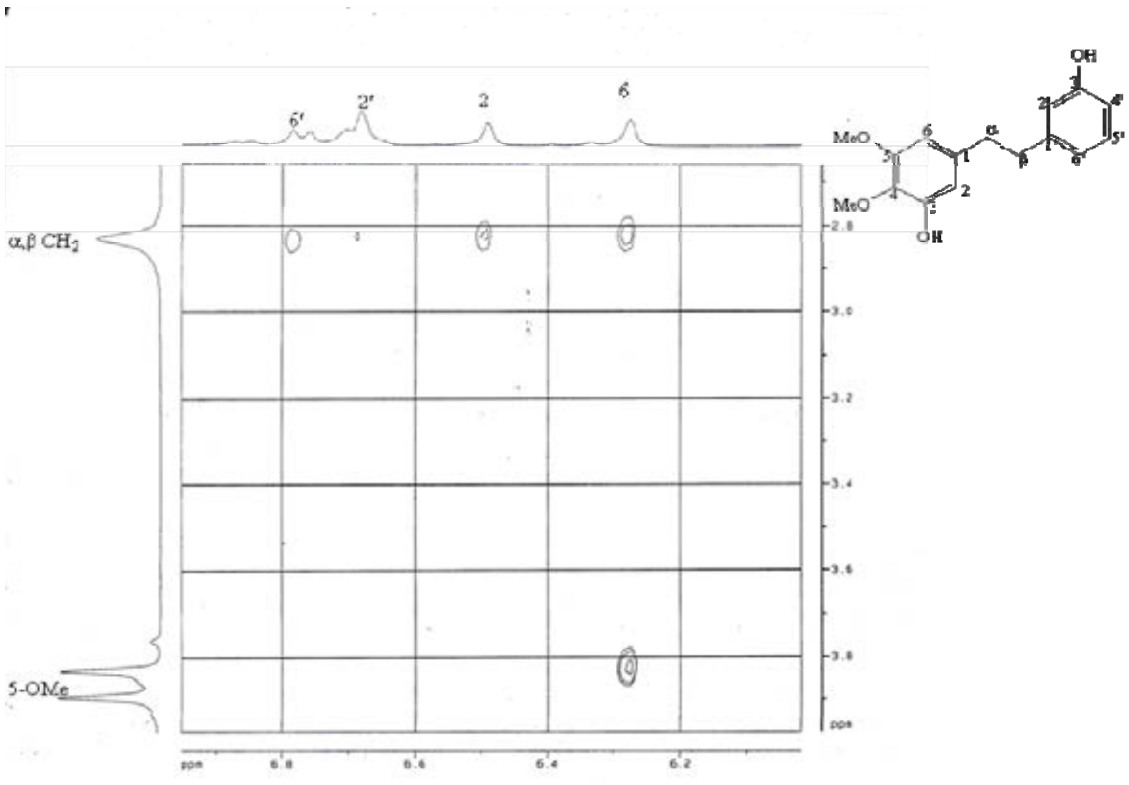

Figure 19 NOESY spectrum of compound DW3 ($CDCl_3$)

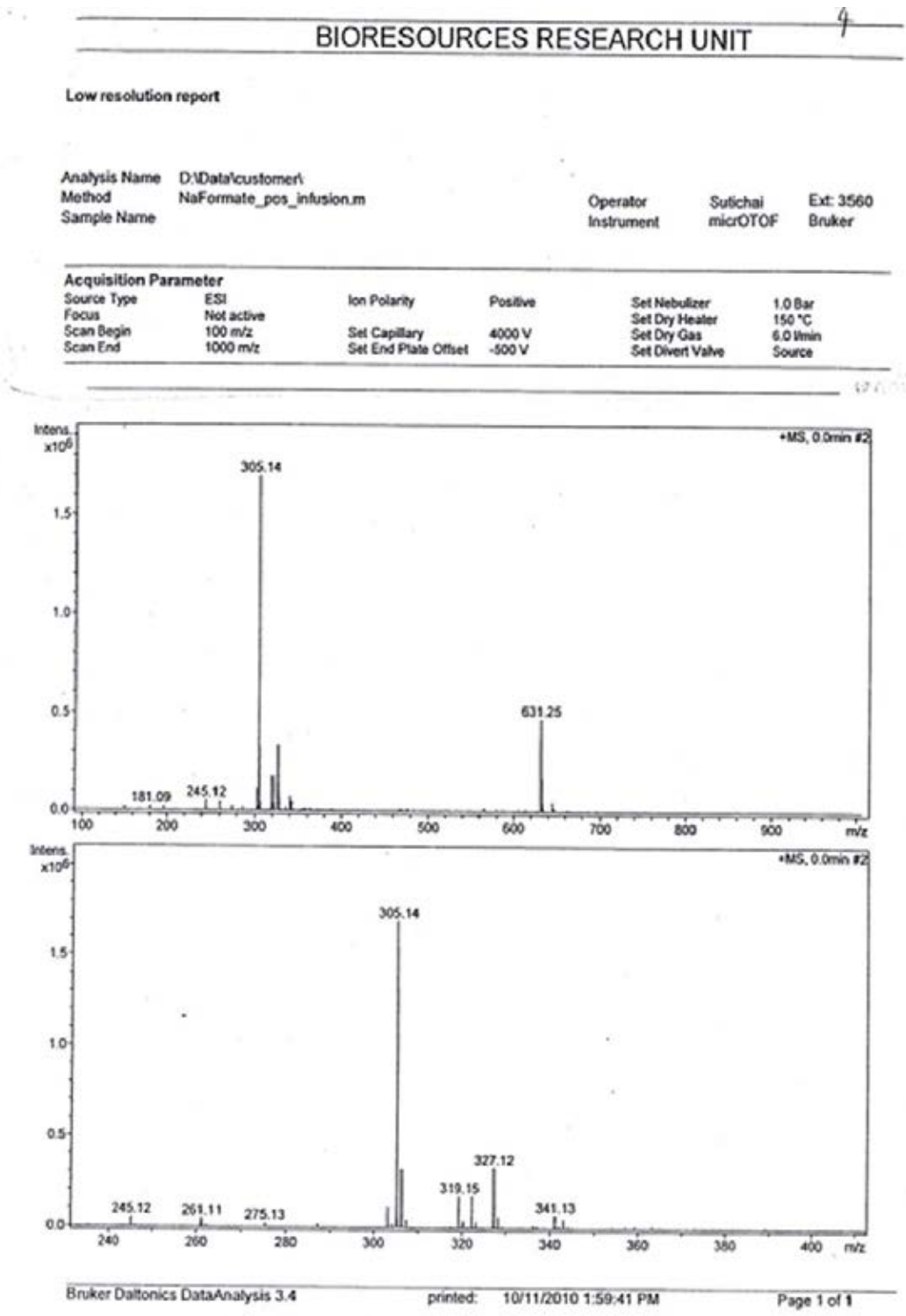

Figure 20 Mass spectrum of compound DW4

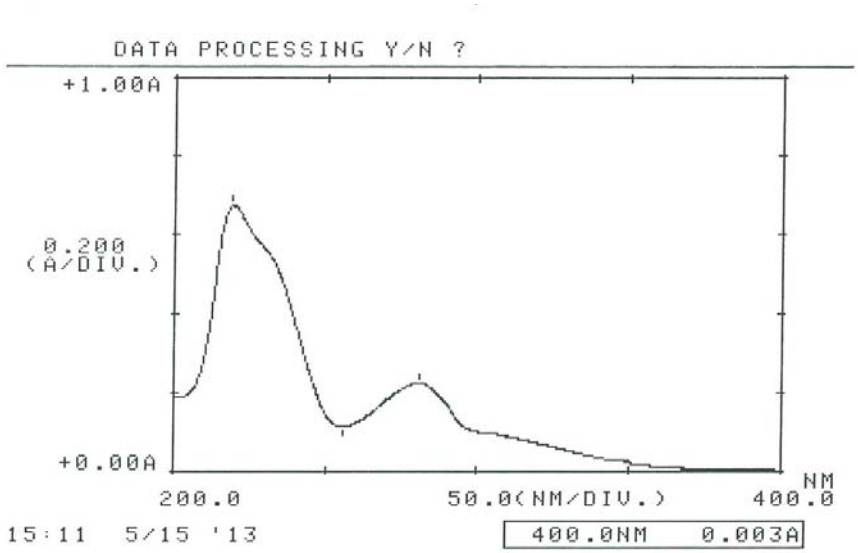

Figure 21 UV spectrum of compound DW4 (MeOH)

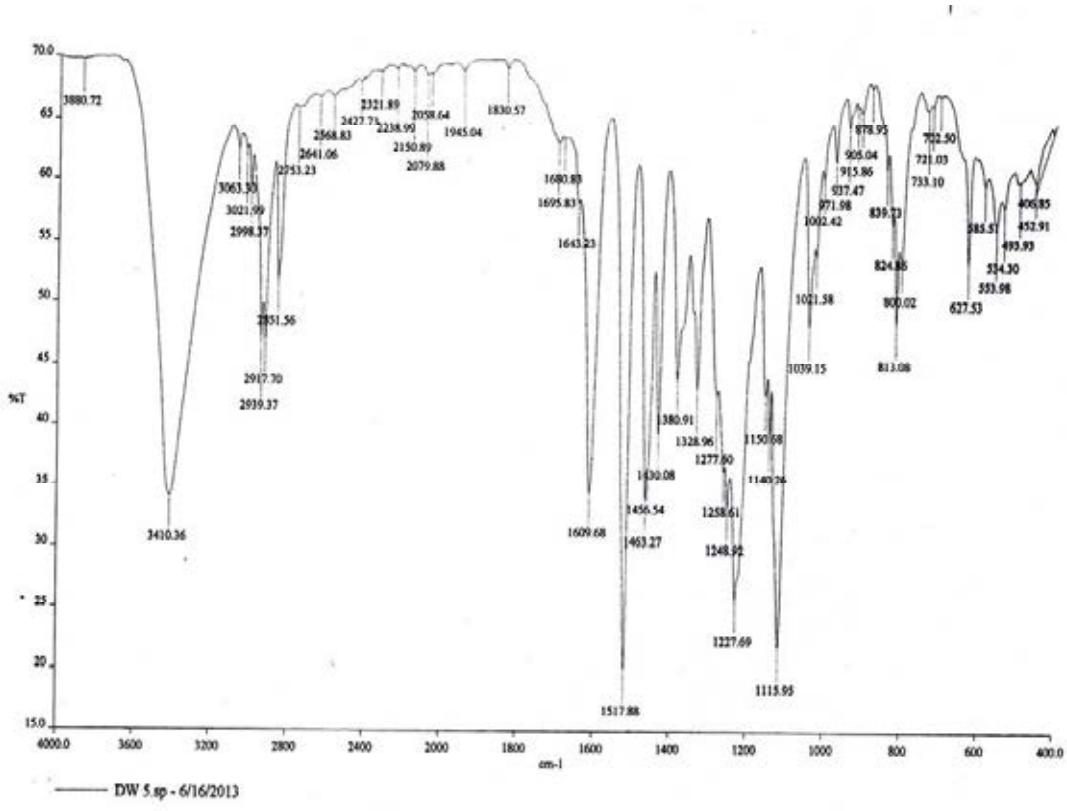

Figure 22 IR spectrum of compound DW4

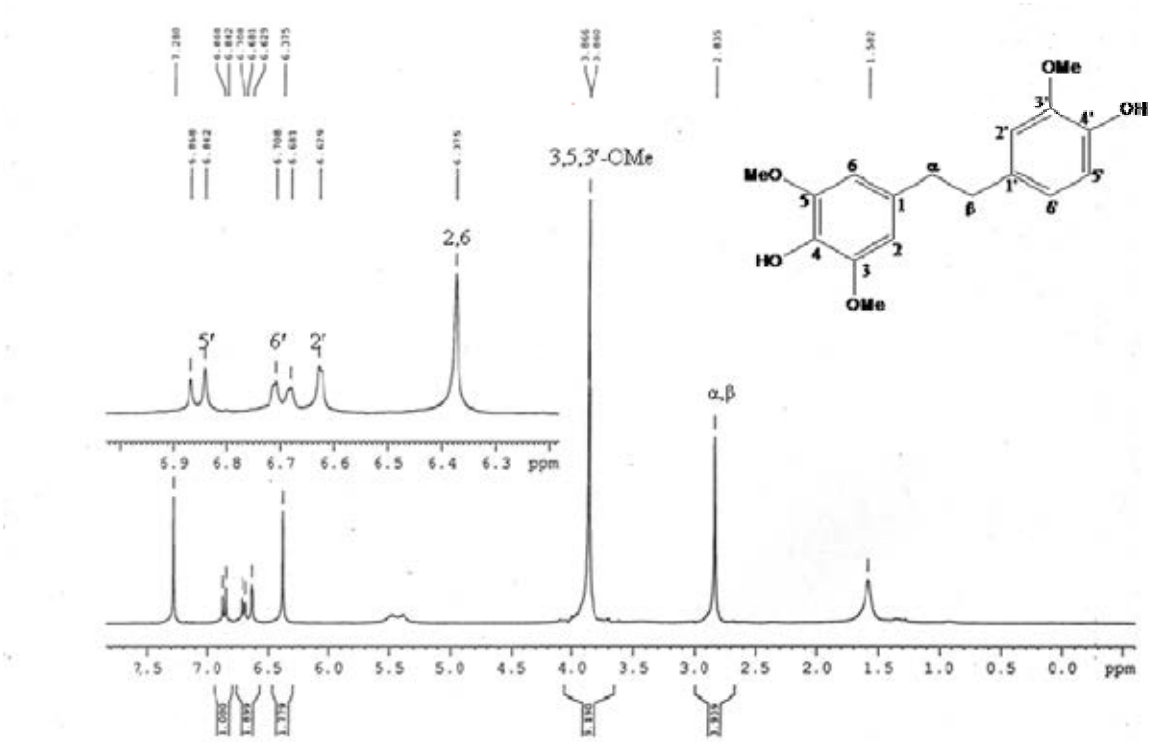

Figure 23 ^{1}H-NMR (300 MHz) spectrum of compound DW4 ($CDCl_3$)

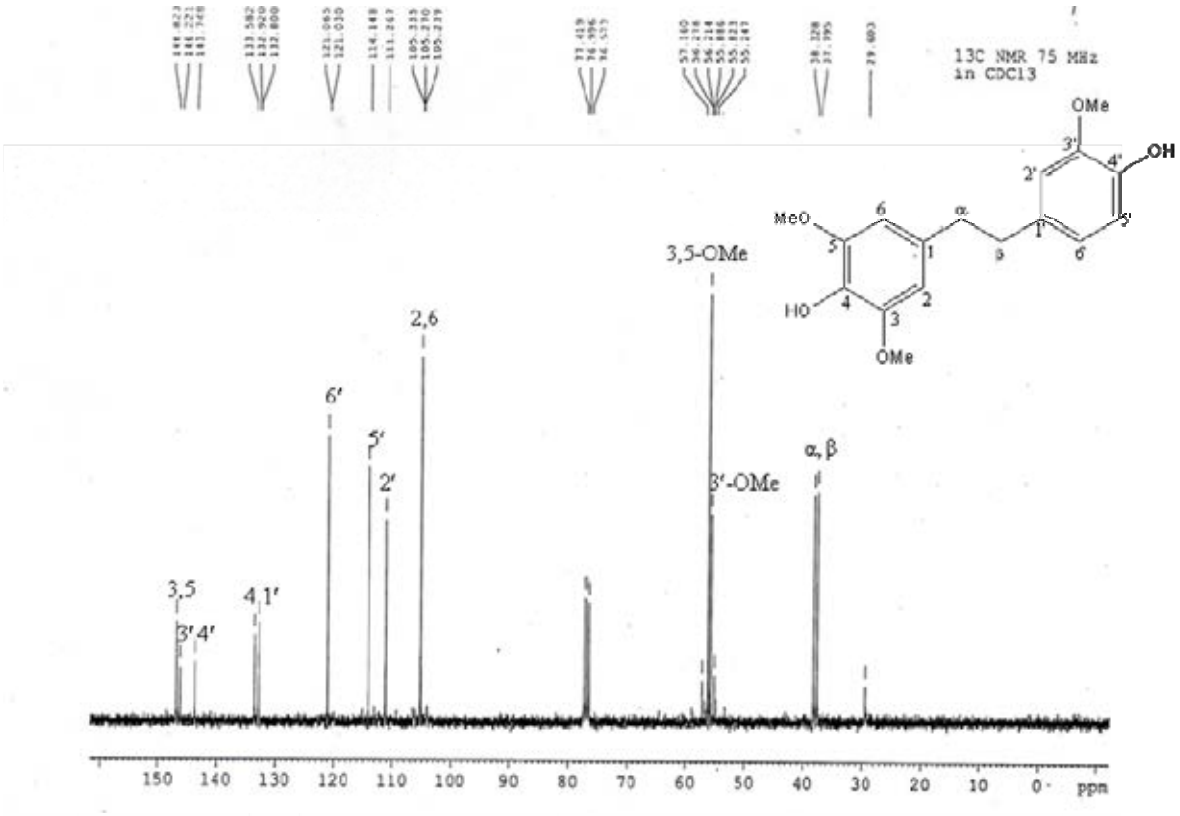

Figure 24 ^{13}C-NMR (75 MHz) spectrum of compound DW4 ($CDCl_3$)

BIORESOURCES RESEARCH UNIT

Low resolution report

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Sample Name	DW11	Instrument	micrOTOF Bruker

Acquisition Parameter

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Scan End	1500 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Source

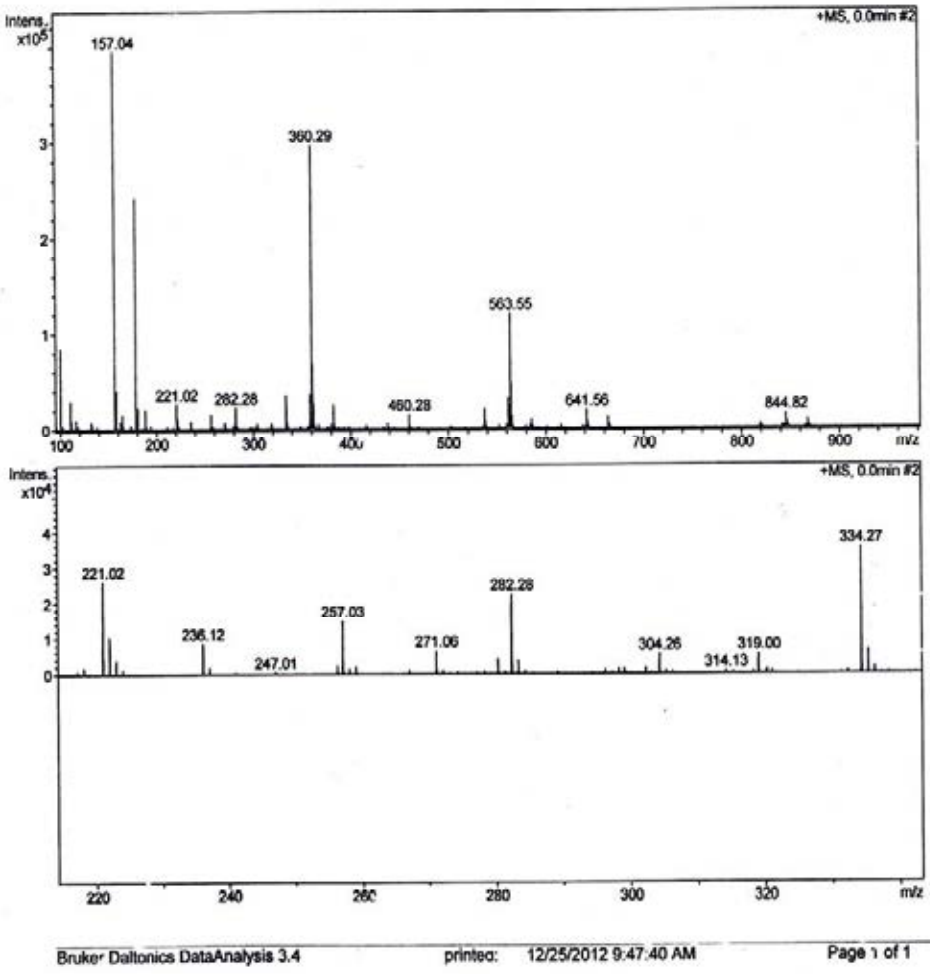

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Figure 25 Mass spectrum of compound DW5

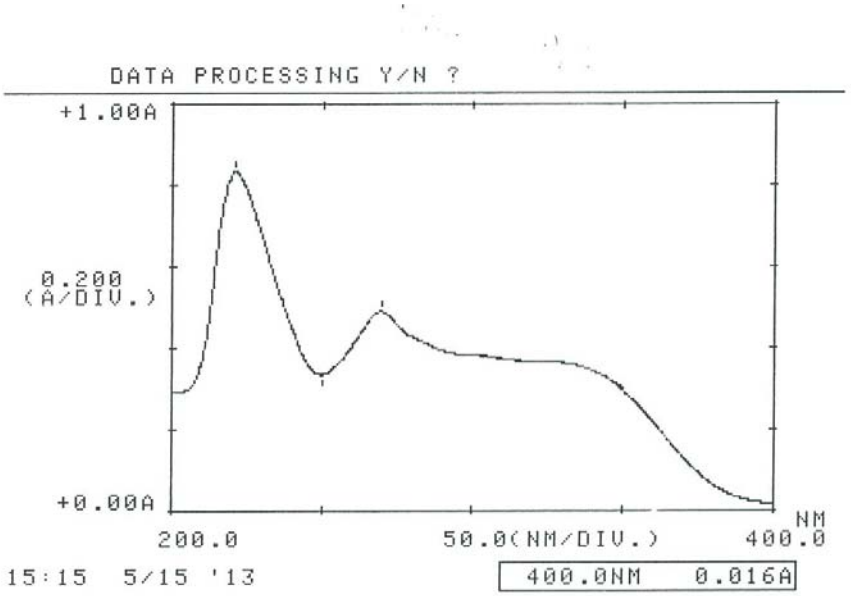

Figure 26 UV spectrum of compound DW5 (MeOH)

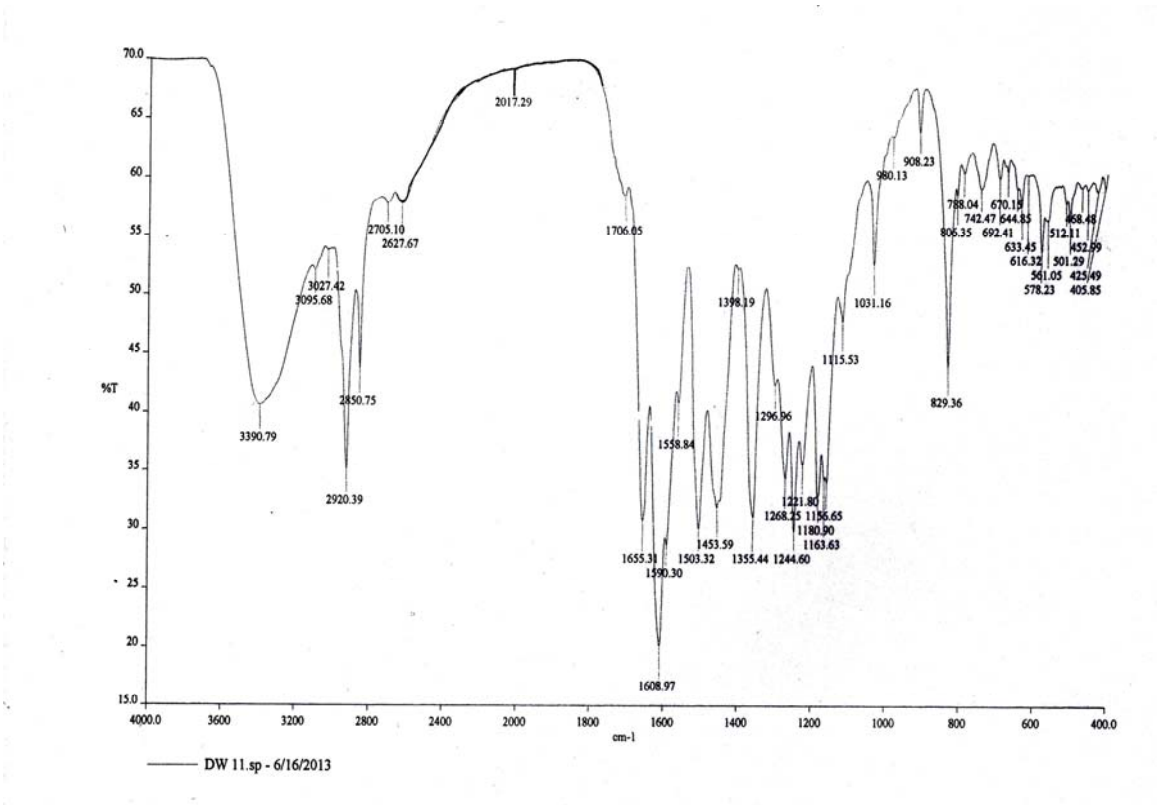

Figure 27 IR spectrum of compound DW5

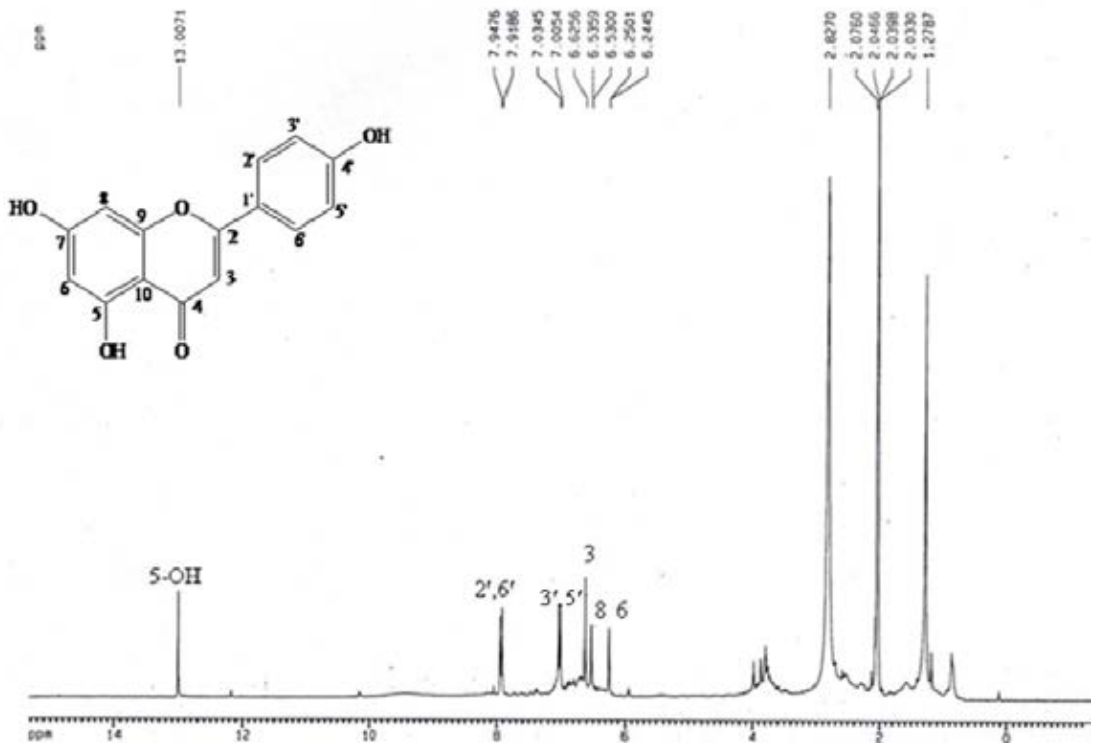

Figure 28 ^{1}H-NMR (300 MHz) spectrum of compound DW5 (Acetone-d_6)

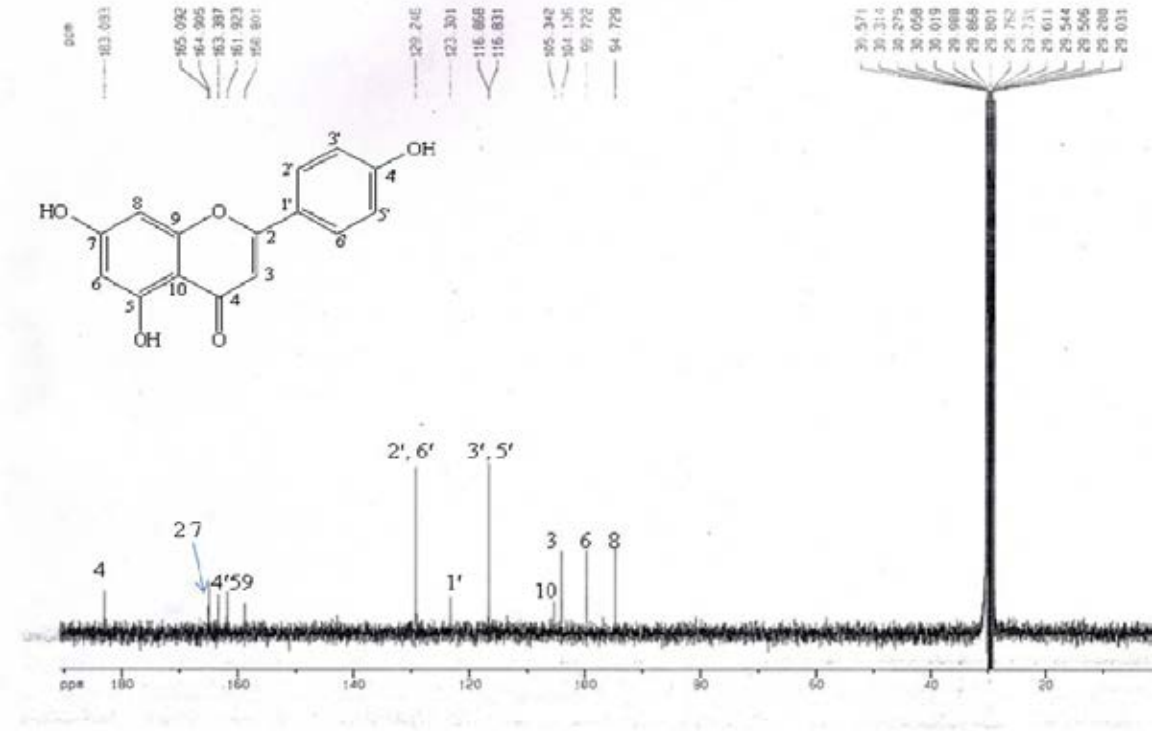

Figure 29 ^{13}C-NMR (75 MHz) spectrum of compound DW5 (Acetone-d_6)

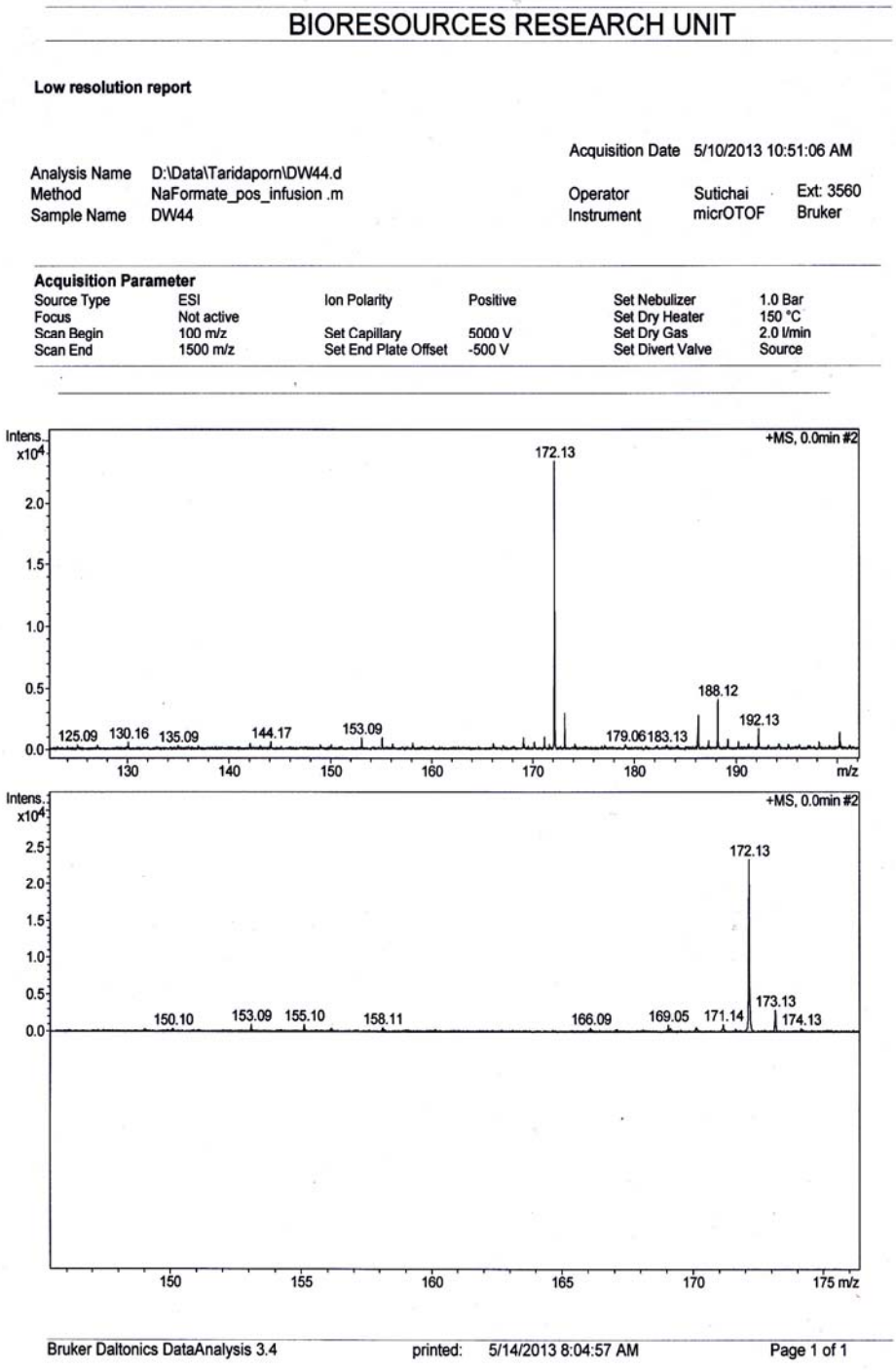

Figure 30 Mass spectrum of compound DW6

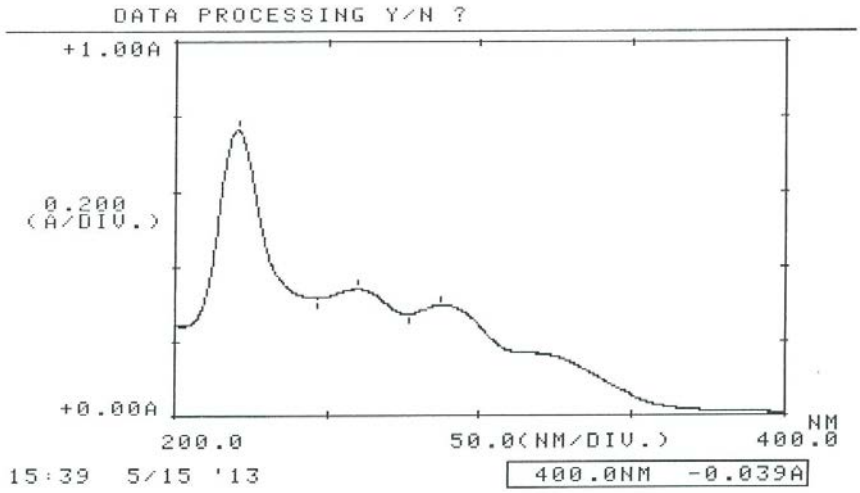

Figure 31 UV spectrum of compound DW6 (MeOH)

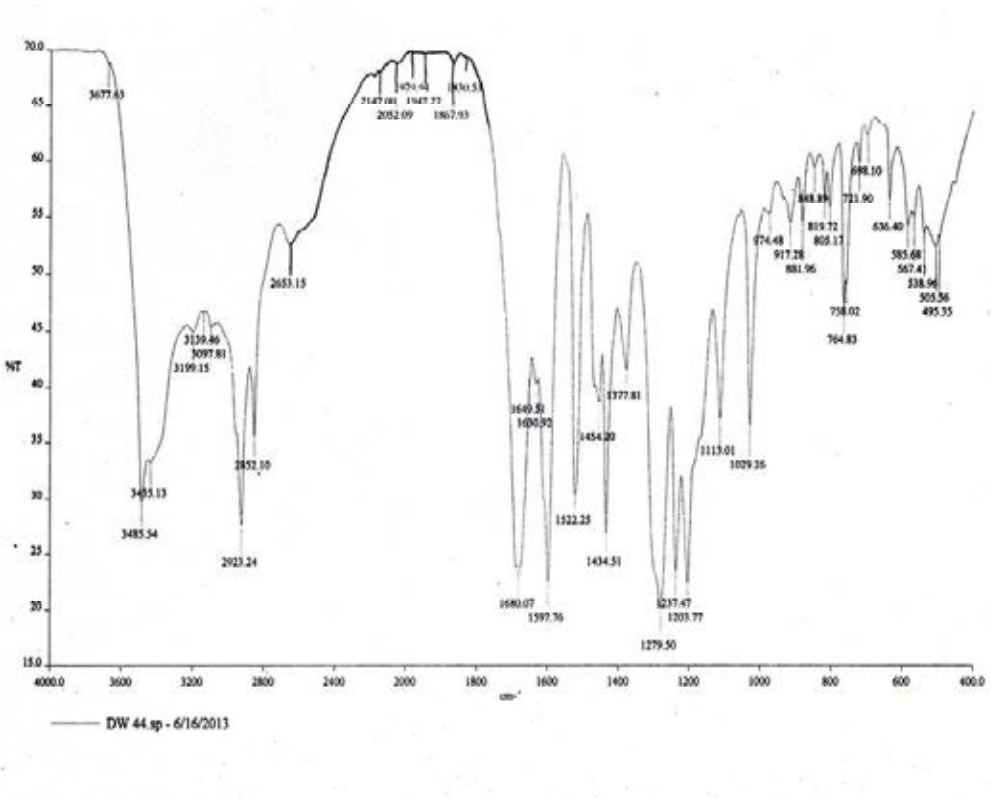

Figure 32 IR spectrum of compound DW6

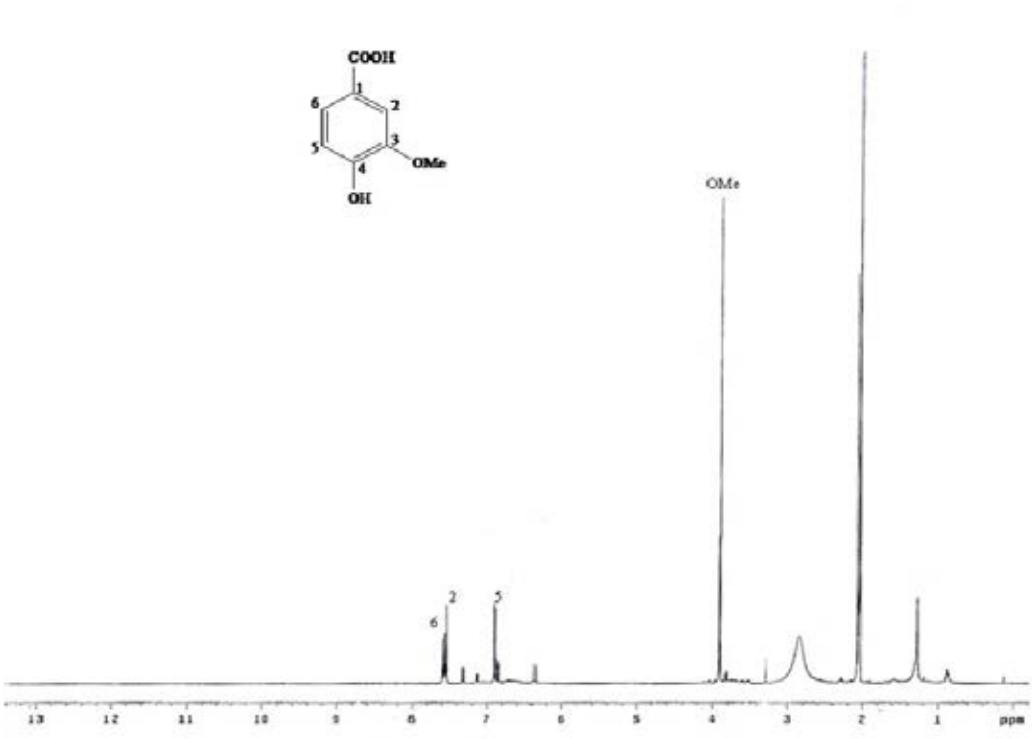

Figure 33 ^{1}H-NMR (500 MHz) spectrum of compound DW6 (Acetone-d_6)

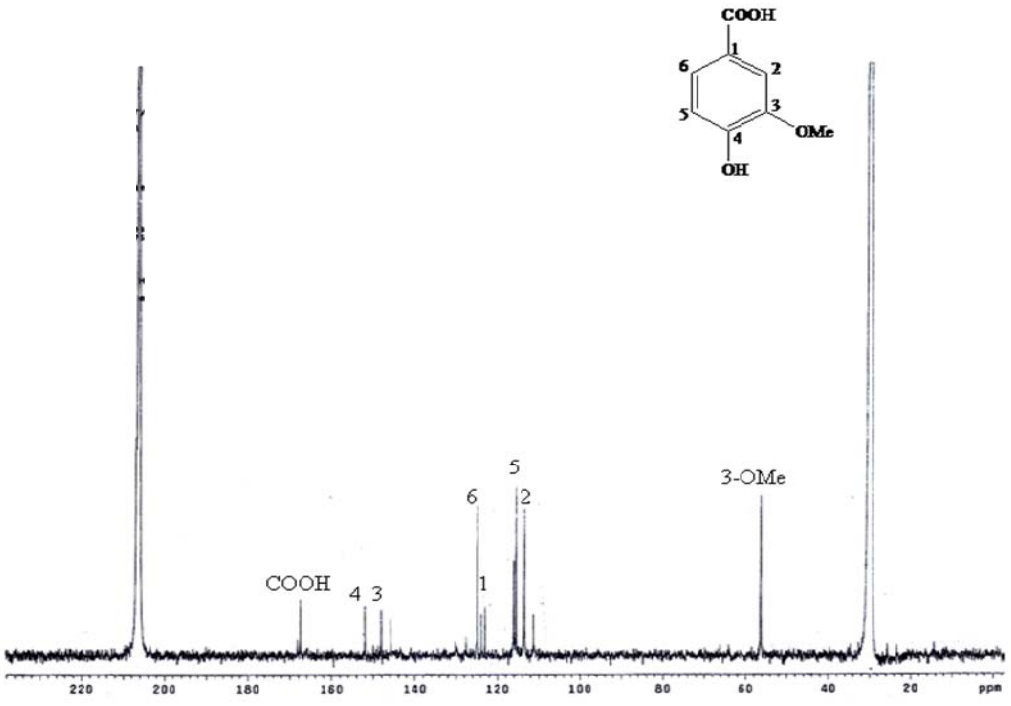

Figure 34 ^{13}C-NMR (125 MHz) spectrum of compound DW6 (Acetone-d_6)

VITA

Miss Pathrapa Rungwichaniwat was born on January 6, 1987 in Bangkok, Thailand. In 2009, she received her bachelor's degree from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Thailand.

Oral presentation

Pathrapa Rungwichaniwat, Boonchoo Sritularak and Kittisak Likhitwitayawuid.

Chemical constituents and DPPH free radical scavenging activity of *Dendrobium williamsonii*. Proceedings of the 7th Srinakharinwirot Academic Conference on "East-West Higher Education Experience",1-2 April 2013 in Srinakharinwirot University, Bangkok, Thailand. p32.