

ฟลาโวนอยด์จากใบปานนั้นชี้แมวและแก่นหาดหนู

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สถาบันวิทยบริการ จุฬาลงกรณ์มหาวิทยาลัย

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FLAVONOIDS FROM *GONIOTHALAMUS TENUIFOLIUS* LEAVES AND
ARTOCARPUS GOMEZIANUS HEARTWOOD

Miss Saowalak Chaiwiriya

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย
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 AND ARTOCARPUS GOMEZIANUS HEARTWOOD

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渺瓦ลักษณ์ ชาญวิริยะ: ฟลาโวนอยด์จากใบปานหนันขี้แมวและแก่นหาดบุน (FLAVONOIDS FROM GONIOTHALAMUS TENUIFOLIUS LEAVES AND ARTOCARPUS GOMEZIANUS HEARTWOOD) อ. ที่ปรึกษา: รศ.ดร. กิตติศักดิ์ ลิขิตวิทยาภูมิ, อ. ที่ปรึกษา ร่วม: อ.ดร. บุญญา ศรีตุลารักษ์, 185 หน้า. ISBN 974-14-3487-1

การศึกษาทางพฤกษเคมีของใบปานหนันขี้แมว สามารถแยกสารบริสุทธิ์ในกลุ่มฟลาโวนอยด์ได้ 2 ชนิด คือ 3,5,7,3',4'-pentamethoxyflavone และ 5,3',4'-trihydroxy-3,7-dimethoxyflavone ส่วนการศึกษาทางพฤกษเคมีของแก่นหาดบุน สามารถแยกสารบริสุทธิ์จากสิ่งสกัดได้สาร 8 ชนิด ประกอบด้วยสารกลุ่มฟลาโวนอยด์ 6 ชนิด คือ cycloartocarpin, isocyclomorusin, norcycloartocarpin, artocarpin, norartocarpetin ซึ่งเป็นสารที่เคยมีรายงานมาก่อนและ artogomezianone ซึ่งเป็นสารที่พบครั้งแรกในธรรมชาติ. สารกลุ่ม stilbene 1 ชนิด คือ oxyresveratrol และสารกลุ่ม steroid ผสมกันคือ β -sitosterol และ stigmasterol การพิสูจน์โครงสร้างทางเคมีของสารที่แยกได้นี้อาศัยการวิเคราะห์スペkturm ของ UV, IR, MS, NMR ร่วมกับการเปรียบเทียบข้อมูลของสารที่ทราบโครงสร้างแล้ว และได้มีการทดสอบฤทธิ์ในการต้านเชื้อไวรัส herpes simplex ทั้ง type I และ II ของสารบริสุทธิ์แต่ละชนิดที่แยกได้ พบร่วมสาร 4 ชนิด ที่มีฤทธิ์ปานกลางในการต้านเชื้อไวรัส herpes simplex ทั้ง 2 ชนิด ได้แก่ สาร cycloartocarpin, isocyclomorusin, norartocarpetin และ oxyresveratrol



ภาควิชา.....เกศชเวท..... ลายมือชื่อนิสิต.....!สกุลล่า๒๘๔... นายวันรัช.....
สาขาวิชา.....เกศชเวท..... ลายมือชื่ออาจารย์ที่ปรึกษา.....
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SAOWALAK CHAIWIRIYA: FLAVONOIDS FROM GONIOTHALAMUS TENUIFOLIUS LEAVES AND ARTOCARPUS GOMEZIANUS HEARTWOOD.
THESIS ADVISOR: ASSOC. PROF. KITTISAK LIKHITWITAYAWUID, Ph.D., THESIS CO-ADVISOR: BOONCHOO SRITULARAK, Ph.D. 185 pp. ISBN 974-14-3487-1

Phytochemical study of the leaves of *Goniothalamus tenuifolius* King led to the isolation of two flavonoids including 3,5,7,3',4'-pentamethoxyflavone and 5,3',4'-trihydroxy-3,7-dimethoxyflavone. From the heartwood of *Artocarpus gomezianus* Wall. ex Tre'c, six flavonoids were isolated. They were identified as a new flavonoid named artogomezianone and five known flavonoids namely cycloartocarpin, isocyclomorusin, norcycloartocarpin, artocarpin and norartocarpentin. Furthermore, oxyresveratrol and a mixture of steroids consisting of β -sitosterol and stigmasterol were obtained. The identification and structure elucidation of the isolated compounds were achieved by analysis of their spectroscopic data (UV, IR, MS, NMR) in comparison with previously reported data. Evaluation of the anti-herpes simplex virus activity of the isolated compounds indicated moderate activity against both types of herpes simplex virus for cycloartocarpin, isocyclomorusin, norartocarpentin and oxyresveratrol.

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LIST OF ABBREVIATIONS AND SYMBOLS

α	=	alpha
Acetone- d_6	=	deuterated acetone
β	=	beta
br	=	broad (for NMR spectra)
C	=	concentration
$^{\circ}\text{C}$	=	degree Celsius
CDCl_3	=	deuterated chloroform
CHCl_3	=	chloroform
^{13}C NMR	=	carbon-13 nuclear magnetic resonance
COSY	=	correlation spectroscopy
1-D	=	one-dimensional
2-D	=	two-dimensional
d	=	doublet (for NMR spectra)
dd	=	doublet of doublets (for NMR spectra)
DEPT	=	distortionless enhancement by polarization transfer
DMSO- d_6	=	deuterated dimethylsulfoxide
EIMS	=	electron impact mass spectrum
ESIMS	=	electrospray ionization mass spectrometry
EtOAc	=	ethyl acetate
g	=	gram
μg	=	microgram
δ	=	chemical shift
^1H NMR	=	proton nuclear magnetic resonance
HMBC	=	^1H - detected heteronuclear multiple bond coherence
Hz	=	hertz
IC_{50}	=	median inhibitory concentration
IR	=	infrared spectrum
J	=	coupling constant
kg	=	kilogram

L	=	liter
μl	=	microliter
λ_{\max}	=	wavelength at maximal absorption
ϵ	=	molar absorptivity
ν_{\max}	=	wave number at maximal absorption
m	=	multiplet (for NMR spectra)
mg	=	milligram
ml	=	milliliter
<i>m/z</i>	=	mass to charge ratio
M^+	=	molecular ion
MeOH	=	methanol
MHz	=	megahertz
MS	=	mass spectrometry
MW	=	molecular weight
μM	=	micromolar
nm	=	nanometer
NMR	=	nuclear magnetic resonance
NOESY	=	nuclear overhauser effect correlation spectroscopy
PFU	=	plaque-forming units
ppm	=	part per million
s	=	singlet (for NMR spectra)
spp.	=	species
t	=	triplet (for NMR spectra)
TLC	=	thin layer chromatography
UV	=	ultraviolet

CHAPTER I

INTRODUCTION

Flavonoids are a large group of polyphenolic compounds that occur commonly in plants. This group of natural products contains more than 8000 known compounds, and this number is constantly growing because of the great structural diversity arising from the various hydroxylation, methoxylation, glycosylation and acylation patterns. Many flavonoids are endowed with biological activities, such as anti-inflammatory, antiallergic, antiischemic, antiplatelet, immunomodulatory, antitumoral (Pietta *et al.*, 2003), cytotoxic and antimicrobial activities (Liou *et al.*, 1993; Sato *et al.*, 1996). Flavonoids have also been shown to inhibit several enzymes, including lipoxygenases, cyclooxygenases, mono-oxygenases, xanthine oxidase, mitochondrial succinoxidase, reduced nicotinamide-adenine dinucleotide (NADH) oxidase, phospholipase A₂, topoisomerases and protein kinases. Several plants have been used as herbal remedies for their flavonoid contents (Pietta *et al.*, 2003). Therefore, it is interesting to investigate some flavonoids in plants.

The genus *Goniothalamus* belongs to the family Annonaceae of the order Magnoliales. This genus consists of 115 species which are distributed throughout the tropics and subtropics of the world especially Cambodia, Vietnam, Malaysia, China, Palau, Philippines, Thailand and Indonesia (Lan *et al.*, 2003). Plants in the genus *Goniothalamus* are small trees or shrubs. *Terminal buds* not enclosed by leaves. *Bark*: cream, gray, brown. *Leaves*: simple, two-ranked, not scale-like, stipules absent. *Flowers*: bisexual, stalked, about 0.5 cm long or across, solitary or in fascicles. *Petals and Sepals*: valvate, sepals membranaceous and generally persistent in fruit, inner petal whorl smaller than the outer. *Fruit*: berry-like, fleshy, not multiple. *Seeds*: 1-2 per fruit, less than 5 mm.

Goniothalamus tenuifolius King, locally known as 'Panan Kee Meaw', is a small tree or shrub growing in several parts of Thailand (ປີຍະ ເຂດມິກລິນ, 2544). It is a tree up to 2-7 m high. *Young twigs*: slender, pubescent, later glabrous and striate. *Leaves*: membranous, varying considerably in shape and size, lanceolate or oblong lanceolate, acuminate, base acute, rarely rounded, the margins sometimes slightly undulate glabrous or pubescent on the midrib and veins beneath, main nerves 8-11 pairs, fine, curving and interarching 5 mm from margin, reticulations faint and lax, length 8-18.5 cm, breadth 2-6 cm, petiole 5-8 mm long, glabrous or pubescent. *Flowers*: solitary, axillary, pendulous. *Pedicels*: 2-5 mm long, glabrous or pubescent with 2-3 minute bracts at base. *Sepals*: ovate, acute or acuminate, membranous, several-nerved and reticulate, persistent, varying much in size, 7 mm -2.7 cm long and 6 mm-2.2 cm broad. *Petals*: yellowish to pinkish, thinly coriaceous, pubescent, outer broadly lanceolate, acuminate, much contracted at the base, varying much in length with age, 2-3 cm long, inner ovate, acuminate, 1 cm long or less. *Stamens*: 2 mm long, numerous with flat-topped or convex connectives. *Ovaries*: about 3 mm long, narrow; style filiform, stigma funnel-shaped, split down the inner side. *Ripe carpels*: slight apiculate, pubescent or glabrescent, 1-1.2 cm long; stalks 4-5 mm long. *Seeds*: 1 rarely 2 (Sinclair, 1955).

The genus *Artocarpus* belongs to the tribe Artocarpeae, the family Moraceae of the order Urticales. The name '*Artocarpus*' is derived from the Greek words 'artos' (= bread) and 'karpos' (= fruit) (Morton and Miami, 1987). This genus consists of approximately 50 species, indigenous of the tropical and sub-tropical regions especially Burma, Thailand, Indo-China, South-China, Malaysia and Solomon Islands (Dassanayake and Fosberg, 1981). The plants in the genus *Artocarpus* are evergreen trees with latex. The twigs and the stem can produce a milky sap. *Leaves*: alternate, distichous, coriaceous, often very large, margin entire, lobe or pinnatifid, rarely pinnate leathery, penninerved. *Stipule*: free, intrapetiolar or lateral. *Flowers*: monoecious, densely crowded on globose or oblong 1-sexual solitary usually axillary receptacles, often mixed with scales which are often thickened or peltate at the apex. *Male flower*: *Perianth* 2-4 lobed or 2-4 partite, lobes obtus, valvate or slightly imbricate, calyx tubular. *Stamen* 1 erect, anthers globose to oblong. *Pistillode* 0. *Female flowers*: *Perianth* tubular, confluent below with the receptacle, mouth minute. *Ovary* straight, ovule

pendulous. Style central or lateral. *Stigma* 1-2 entire, equal or unequal. Flowers and bract fused laterally to form a syncarp, sometimes very large. Seed: pendulous, without endosperm, testa-membranous, albumen 0, embryo straight or incurved, cotyledons fleshy, equal or unequal (Forster and Forster, 1775; Kirtikar and Basu, 1980).

Several species in the genus bear edible fruit and are commonly cultivated: *Artocarpus communis* (Breadfruit), *A. integer* (Cempedak), *A. heterophyllus* (Jackfruit) and *A. odoratissimus* (Marang) (Morton and Miami, 1987).

The species of genus *Artocarpus* found in Thailand (Smitinand, 2001) are as follows.

<i>Artocarpus altilis</i> (Parkinson) Fosberg (<i>A. communis</i> J.R. & G. Forst., <i>A. incisa</i> Linn. f.)	ขันนสำปะລອ Khanun sampalo (Central); ສາເກ Sake (Central); Bread fruit tree; Bread nut tree.
<i>A. altissimus</i> J.J. Smith	ໄສນ Sanai (Surat Thani).
<i>A. chaplasha</i> Roxb.	ຫາດສ້ານ Haat san (Chiang Rai).
<i>A. dadah</i> Miq.	ທັງຄັນ Thang khan; ມ່ວງກວາງ Muang kwang (Yala); ຫາດຮຸມ Hat rum, ຫາດລູກໃຫຍ່ Hat luk yai (Trang); ຫາດຂອນ Hat khon (Narathiwat).
<i>A. elasticus</i> Reinw. ex Blume	ກະໂອກ Ka ok, ກະເຂາວ Ka-o (Peninsular); ຕື່ອກະ Tue-ka (Malay-Yala); ເຂາວ O (Trang, Ranong).
<i>A. gomezianus</i> Wall. ex Tre'c.	ຕະປັງ Ta pang, ທຳປັງ Tam-pang (Malay-Peninsular); ຫາດໜຸນ Hat nun (Northern); ອື່ນີ້ I po (Trang).
<i>A. heterophyllus</i> Lank. (<i>A. integrifolius</i> Linn. f.)	ຂັນນ Khanun (General); ຂະໜຸນ Kha-nu (Chanthaburi); ຂະເນອ Kha-noe (Khmer); ສີຂົ້ມ Si-khue, ປະໜ່ອຍໝາຍ Pa-noi (Karen-Mae Hong Son); ນະຍວຍຊະ Na-yuai-sa (Karen-Kanchanaburi); ນາກໂ ນາ-ko (Malay-Pattani); ເນນ Nen (Chaobon- Nakhon Ratchasima); ມະໜຸນ Manun (Northern,

	Peninsular); ձանգ, լայ Lang (Shan-Northern); մակմի Mak mi (Northeastern); մակլանg Mak lang (Shan-Mae Hong Son); Jack fruit tree.
A. <i>kemando</i> Miq.	խննիկ Khanun pa (Narathiwat); յադս Yatu (Malay-Narathiwat).
A. <i>integer</i> (Thunb.) Merr.	յայպաճա Champada (General); յայպաճա Champado (Peninsular); Champedak.
A. <i>lacucha</i> Roxb. (A. <i>lakoocha</i> Roxb.)	կայե Kaa-yae, տապէ Ta-pae, տապէնg Ta-paeng (Malay-Narathiwat); մահած Mahat (Peninsular); մահած բևի հողյ Mahat bai yai (Trang); հած Hat (General).
A. <i>lanceifolius</i> Roxb.	խննիկ Khanun pa (Peninsular); հնաց գապիտ Nang-ka-pi-to, հնաց գապիթ Nang-ka-pi-pit (Malay-Peninsular); նաց գապէնg Nang-ka-pi-pae (Malay-Narathiwat).
A. <i>nitidus</i> Tre'c. subsp. <i>lingnanensis</i> Jarrett (A. <i>parva</i> Gagnep.)	մահած չօյ Mahat khoi (Surat Thani).
A. <i>rigidus</i> Blume subsp. <i>rigidus</i>	խննիկ Khanun pa (Peninsular).
A. <i>rigidus</i> bl. subsp. <i>asperulus</i> Jarrett. (A. <i>calophyllus</i> Kurz)	խննիկ Khanun pan (Surat Thani).
<i>Artocarpus gomezianus</i> Wall. ex Tre'c., locally known in Thai as 'Hat nun', is a medium-sized to tall tree reaching 42 m and 210 cm girth. Bark: gray brown, cracking to scaly. Inner bark: pink, soft with creamy sap. Sapwood: pale yellow. Leaves: stalk 1.5-3 cm long, blade leathery, oblong to elliptic, 11-25 x 7-16 cm, apex shortly pointed, base more or less rounded, glabrous on both surfaces, upper surface shining, secondary nerves 10-15 pairs, nervation prominent on both surfaces; midrib and nerves drying black. Flower heads: solitary in leaf axils. Male head: obovoid to subglobose, 1-2.5 cm	

across on 0.7-1.7 cm long stalk. *Fruits*: subglobose, 8 cm across, yellow pink flesh, drying brown or black, with smooth velutinous surface, stalk 1.5-4.5 cm long. *Seeds*: ellipsoid, 1.2-1 cm (Kochummen, 1978).

A previous phytochemical study on the ethyl acetate extract of the leaves of *G. tenuifolius* showed the presence of several flavonoids, some of which possessed free radical scavenging activity with DPPH assay (Likhithwitayawuid *et al.*, 2006). This investigation is focused on the isolation of more polar compounds in the MeOH extract. As for *A. gomezianus*, tyrosinase inhibitors have been isolated from the roots including isocyclomorusin, norartocarpin, cudraflavone C, artocarpin, cycloartocarpin, albanin A and resveratrol. It is interesting to investigate the chemical compounds in other parts of this plant for more information on chemistry. In this study, preliminary anti-herpetic activity evaluation revealed that the MeOH extract of *G. tenuifolius* was devoid of activity whereas the *A. gomezianus* heartwood extract was active.

The main objectives in this investigation are as follows.

1. to isolate and purify compounds from the leaves of *G.tenuifolius* and from the heartwood of *A.gomezianus*.
2. to determine the chemical structure of each isolated compound.
3. to evaluate anti-herpetic potential of each isolated compound from the heartwood of *A.gomezianus*.

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Figure 1 *Goniothalamus tenuifolius* King.



Figure 2 *Artocarpus gomezianus* Wall. ex Tre'c.

CHAPTER II

HISTORICAL

1. Chemical constituents of *Goniothalamus* spp.

Several classes of chemical constituents have been isolated from the genus *Goniothalamus*. They can be classified as acetogenins, alkaloids, aza-anthraquinones, benzenoids, flavonoids, naphthoquinones, styrylpyrones, sterols, styrene derivatives, terpenoids and miscellaneous compounds (Tables 1-2 and Figure 3).

Table 1 Distribution of flavonoids in *Goniothalamus* spp.

Plant and Chemical compound	Plant part	Reference
<i>Goniothalamus borneensis</i> Pinocembrin [1]	Bark	Cao <i>et al.</i> , 1998
<i>Goniothalamus gardneri</i> 2',4'-Dihydroxy-4-6'-dimethoxy-chalcone [2]	Aerial part	Seidal, Bailleul and Waterman, 2000
2'-4'-Dihydroxy-4-6'-dimethoxy-dihydrochalcone [3]	Aerial part	Seidal <i>et al.</i> , 2000
2'-Hydroxy-4,4',6'-trimethoxy-chalcone [4]	Aerial part	Seidal <i>et al.</i> , 2000
2'-Hydroxy-4,4',6'-trimethoxy-dihydrochalcone [5]	Aerial part	Seidal <i>et al.</i> , 2000
Naringenin trimethyl ether [6]	Aerial part	Seidal <i>et al.</i> , 2000
rel-(1 β ,2 α) Di-(2,4-dihydroxy-6-methoxybenzoyl)-(3 β ,4 α) di-(4-methoxyphenyl)-cyclobutane [7]	Aerial part	Seidal <i>et al.</i> , 2000

Table 1 (continued)

Plant and Chemical compound	Plant part	Reference
2',4,4' –Trihydroxy-6'-methoxy-dihydrochalcone [8]	Aerial part	Seidal <i>et al.</i> , 2000
Tsugafolin [9]	Aerial part	Seidal <i>et al.</i> , 2000
<i>Goniothalamus tenuifolius</i>		
3',4'-Dihydroxy-3,5,7-trimethoxy-flavone [10]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
3'-Hydroxy-3,5,7,4'-tetramethoxy-flavone [11]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
4'-Hydroxy-3,5,7,3'-tetramethoxy-flavone [12]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
5-Hydroxy-3,7,3',4'-tetramethoxy-flavone [13]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
Kumatakenin [14]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
Pachypodol [15]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
3,5,7,3',4'-Pentamethoxyflavone [16]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
5,7,3',4'-Tetrahydroxy-3-methoxy-flavone [17]	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
<i>Goniothalamus thwaitesii</i>		
Annulatin [18]	Aerial part	Seidal <i>et al.</i> , 2000

Table 2 Distribution of miscellaneous constituents in *Goniothalamus* spp.

Plant and Chemical compound	Category	Plant part	Reference
<i>Goniothalamus amuyon</i>			
(-)-Anolobine [19]	Aporphine alkaloid	Wood	Lu, Wu and Leou, 1985
(-)-Anonaine [20]	Aporphine alkaloid	Wood	Lu et al., 1985
Goniodiol-7-monoacetate [21]	Styrylpyrone	Leaf	Wu, Duh and Chang, 1991
Goniodiol-8-monoacetate [22]	Styrylpyrone	Leaf	Wu et al., 1992
Goniotriol [23]	Styrylpyrone	Leaf	Wu et al., 1992
Liriodenine [24]	Oxoporphine alkaloid	Stem bark	Lu et al., 1985
Palmatine [25]	Protoberberine alkaloid	Stem bark	Lu et al., 1985
(-)-Tetrahydropalmatine [26]	Tetrahydro protoberberine alkaloid	Stem bark	Lu et al., 1985
<i>Goniothalamus andersonii</i>			
(+)-Goniothalamin [27]	Styrylpyrone	Leaf, Fruit, Root, Stem	Jewers et al., 1972
<i>Goniothalamus arvensis</i>			
5-Acetoxyisogoniothalamin oxide [28]	Styrylpyrone	Stem bark	Peris et al., 2000
3-Acetylalthalactone [29]	Styrylpyrone	Stem bark	Peris et al., 2000
Almuheptolide-A [30]	Benzenoid	Stem bark	Bermejo et al., 1998b
Almuheptolide-B [31]	Benzenoid	Stem bark	Bermejo et al., 1998b

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
Altholactone [32]	Styrylpyrone	Stem bark	Peris <i>et al.</i> , 2000
(+)-Etharvendiol [33]	Styrylpyrone	Stem bark	Bermejo <i>et al.</i> , 1998a
(-)-Etharvensis [34]	Styrylpyrone	Stem bark	Bermejo <i>et al.</i> , 1997
(+)-Garvensintriol [35]	Styrylpyrone	Stem bark	Bermejo <i>et al.</i> , 1998a
(+)-Goniofufurone [36]	Styrene derivative	Stem bark	Bermejo <i>et al.</i> , 1998a
<i>Goniothalamus borneensis</i>			
Altholactone [32]	Styrylpyrone	Bark	Cao <i>et al.</i> , 1998
Aristolactam-AIII [37]	Aristolactam alkaloid	Bark	Cao <i>et al.</i> , 1998
Cinnamyl cinnamate [38]	Miscellaneous	Bark	Cao <i>et al.</i> , 1998
Goniobutenolide A [39]	Styrene derivative	Bark	Cao <i>et al.</i> , 1998
Goniobutenolide B [40]	Styrene derivative	Bark	Cao <i>et al.</i> , 1998
Goniofufurone [36]	Styrene derivative	Bark	Cao <i>et al.</i> , 1998
Goniothalactam [41]	Aristolactam alkaloid	Bark	Cao <i>et al.</i> , 1998
Goniothalamin [27]	Styrylpyrone	Bark	Cao <i>et al.</i> , 1998
Goniothalesdiol [42]	Styrene derivative	Bark	Cao <i>et al.</i> , 1998
Goniotriol [23]	Styrylpyrone	Bark	Cao <i>et al.</i> , 1998
Stigmasterol [43]	Sterol	Bark	Cao <i>et al.</i> , 1998
<i>Goniothalamus cardiopetalus</i>			
Altholactone [32]	Styrylpyrone	Stem bark	Hisham <i>et al.</i> , 2000

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
Cardiobutanolide [44]	Styryllactone	Bark	Matsura, Takabe and Yoda, 2006
Cardiopetalolactone [45]	Styrylpyrone	Stem bark	Hisham et al., 2000
Etharvendiol [33]	Styryllactone	Bark	Matsura et al., 2006
Goniодiol [46]	Styryllactone	Bark	Hisham et al., 2003
Goniofufurone [36]	Styryllactone	Bark	Matsura et al., 2006
Goniofupyrone [47]	Styryllactone	Stem bark	Hisham et al., 2003
Goniopyprone [48]	Styryllactone	Stem bark	Hisham et al., 2003
Goniopyrone [49]	Styryllactone	Stem bark	Hisham et al., 2000
Goniothalamin [27]	Styryllactone	Stem bark	Hisham et al., 2003
Goniotriol [23]	Styryllactone	Bark	Matsura et al., 2006
Squamocin [50]	Styryllactone	Stem bark	Histam et al., 2000
<i>Goniothalamus cheliensis</i>			
Goniolactone A [51]	Bi-styrylpvrone	Root	Wang et al., 2002
Goniolactone B [52]	Flavanone-styrylpvrone	Root	Wang et al., 2002
Goniolactone C [53]	Flavanone-styrylpvrone	Root	Wang et al., 2002
Goniolactone D [54]	Flavanone-styrylpvrone	Root	Wang et al., 2002
Goniolactone E [55]	Flavanone-styrylpvrone	Root	Wang et al., 2002
Goniolactone F [56]	Flavanone-styrylpvrone	Root	Wang et al., 2002
<i>Goniothalamus dolichocarpus</i>			
(+)-Annonacin [57]	Acetogenin	Stem bark	Goh et al., 1995

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
(+)-5-Deoxygoniopyprone [58]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
(-)-Iso-5-deoxygoniopyprone [59]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
(-)-Iso-5-deoxygoniopyprone acetate [60]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
Isogoniothalamin epoxide [61]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
(+)-Goniodiol [46]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
(+)-Goniodiol diacetate [62]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
(+)-Goniothalamine [27]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
(+)-Goniothalamine epoxide [63]	Styrylpyrone	Stem bark	Goh <i>et al.</i> , 1995
<i>Goniothalamus donnaiensis</i>			
(+)-Annonacin [57]	Acetogenin	Root	Jiang and Yu, 1997
cis-Goniodonin [64] and 34- <i>epi</i> - <i>cis</i> -Goniodonin [65]	Acetogenin	Root	Jiang <i>et al.</i> , 1997
Donbutocin [66]	Acetogenin	Root	Jiang <i>et al.</i> , 1997
Donhepocin [67] and 34- <i>epi</i> -Donhepocin [68]	Acetogenin	Root	Jiang <i>et al.</i> , 1998a
Donnaienin [69]	Acetogenin	Root	Jiang <i>et al.</i> , 1998b
Donnaienin A [70] and 34- <i>epi</i> -Donnaienin A [71]	Acetogenin	Root	Jiang and Yu, 1997
Donnaienin B [72] and 34- <i>epi</i> -Donnaienin B [73]	Acetogenin	Root	Jiang and Yu, 1997
Donnaienin C [74] and 34- <i>epi</i> -Donnaienin C [75]	Acetogenin	Root	Jiang <i>et al.</i> , 1998c
Donnaienin D [76] and 34- <i>epi</i> -Donnaienin D [77]	Acetogenin	Root	Jiang <i>et al.</i> , 1998c
Donhexocin [78]	Acetogenin	Root	Jiang <i>et al.</i> , 1998a
Goniothalamicin [79]	Acetogenin	Root	Jiang and Yu, 1997
Isoannonacin [80]	Acetogenin	Root	Jiang and Yu, 1997
Murisolin [81]	Acetogenin	Root	Jiang and Yu, 1997

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
<i>Goniothalamus gardneri</i>			
Gardnerilins A [82]	Acetogenin	Root	Chen <i>et al.</i> , 1998a
Gardnerillins B [83]	Acetogenin	Root	Chen <i>et al.</i> , 1998a
Gardnerinin [84] and 34- <i>epi</i> -Gardnerinin [85]	Acetogenin	Root	Chen <i>et al.</i> , 1998b
Goniothalamusin [86]	Acetogenin	Aerial part	Seidal <i>et al.</i> , 1999
<i>Goniothalamus giganteus</i>			
8-Acetylgoniotriol [87]	Styrylpyrone	Stem bark	Fang <i>et al.</i> , 1990
Altholactone [32]	Styrylpyrone	Stem bark	El-Zayat <i>et al.</i> , 1985
Annomontacin [88]	Acetogenin	Stem bark	Fang <i>et al.</i> , 1992a
Annonacin [57]	Acetogenin	Stem bark	Alkofahi <i>et al.</i> , 1988
Asimilobin [89]	Acetogenin	Stem bark	Zhang <i>et al.</i> , 1995
2,4- <i>cis</i> and <i>trans</i> -Gigantecin [90]	Acetogenin	Stem bark	Alali <i>et al.</i> , 1997
2,4- <i>cis</i> and <i>trans</i> -Gonianeninone [91]	Acetogenin	Stem bark	Alali <i>et al.</i> , 1998
2,4- <i>cis</i> and <i>trans</i> -Xylomaricinone [92]	Acetogenin	Stem bark	Alali <i>et al.</i> , 1999
4-Deoxygigantecin [93]	Acetogenin	Stem bark	Alali <i>et al.</i> , 1997
9-Deoxygoniopyprone [94]	Styrylpyrone	Stem bark	Fang <i>et al.</i> , 1991a
Gigantecin [95]	Acetogenin	Stem bark	Alkofahi <i>et al.</i> , 1990
Gigantetrocin [96]	Acetogenin	Stem bark	Fang <i>et al.</i> , 1991c
Gigantetronenin [97]	Acetogenin	Stem bark	Fang <i>et al.</i> , 1992a
Gigantransenin A [98]	Acetogenin	Stem bark	Zeng, Zhang and McLaughlin, 1996
Gigantransenin B [99]	Acetogenin	Stem bark	Zeng <i>et al.</i> , 1996
Gigantransenin C [100]	Acetogenin	Stem bark	Zeng <i>et al.</i> , 1996

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
Gigantriocin [101]	Acetogenin	Stem bark	Fang et al., 1991c
Gigantrionenin [102]	Acetogenin	Stem bark	Fang et al., 1992a
Goniobutenolide A [39]	Styrene derivative	Stem bark	Fang et al., 1991b
Goniobutenolide B [40]	Styrene derivative	Stem bark	Fang et al., 1991b
Goniocin [103]	Acetogenin	Stem bark	Gu et al., 1994
Goniodenin [104]	Acetogenin	Acetogenin	Zhang et al., 1995
Goniodiol [46]	Styrylpyrone	Stem bark	Fang et al., 1991a
Goniofufurone [36]	Styrene derivative	Stem bark	Fang et al., 1990
7-epi-oniofufurone [105]	Styrene derivative	Stem bark	Fang et al., 1991b
Goniofupyrone [47]	Styrylpyrone	Stem bark	Fang et al., 1991b
Gonioheptolide A [106]	Benzenoid	Stem bark	Fang et al., 1993
Gonioheptolide B [107]	Benzenoid	Stem bark	Fang et al., 1993
Gonianenin [108]	Acetogenin	Stem bark	Gu et al., 1994
Goniopypprone [48]	Styrylpyrone	Stem bark	Fang et al., 1990
Goniotetracin [109]	Acetogenin	Stem bark	Alali et al., 1998
Goniothalamicin [79]	Acetogenin	Stem bark	Alkofahi et al., 1988; Fang et al., 1992b
Goniothalamin [27]	Styrylpyrone	Stem bark	El-Zayat et al., 1985
Goniotriocin [110]	Acetogenin	Stem bark	Alali et al., 1999
Goniotriol [23]	Styrylpyrone	Stem bark	Alkofahi et al., 1989
Goniotrionin [111]	Acetogenin	Stem bark	Alali et al., 1998
Pyragonicin [112]	Acetogenin	Stem bark	Alali et al., 1998
Pyranicin [113]	Acetogenin	Stem bark	Alali et al., 1998
<i>Goniothalamus griffithii</i>			
Altholactone [32]	Styryllactone	Stem Branch	Tien et al., 2006

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
Aristolactam A-II [114]	Aristolactam alkaloid	Root	Zhang <i>et al.</i> , 1999a
Goniodiol [46]	Styrylpyrone	Stem bark	Talapatra <i>et al.</i> , 1985
Goniodiol diacetate [62]	Styrylpyrone	Stem bark	Talapatra <i>et al.</i> , 1985
Goniodiol-7-monoacetate [21]	Styrylpyrone	Stem bark	Talapatra <i>et al.</i> , 1985
Goniothalamin [27]	Styrylpyrone	Stem Branch	Tien <i>et al.</i> , 2006
Griffithazanone A [115]	Aza-anthraquinone	Root	Zhang <i>et al.</i> , 1999a
Griffithdione [116]	4,5-Dioxo-aporphine alkaloid	Root	Zhang <i>et al.</i> , 1999a
Griffithinam [117]	Aristolactam alkaloid	Root	Zhang <i>et al.</i> , 1999a
4-Methyl-2,9,10-(2H)-1-azaanthracenetrione [118]	Aza-anthraquinone	Root	Zhang <i>et al.</i> , 1999a
Nor-cepharanone B [119]	Alkaloid	Root	Zhang <i>et al.</i> , 1999a
Taliscanine [120]	Aristolactam alkaloid	Root	Zhang <i>et al.</i> , 1999a
Velutinam [121]	Aristolactam alkaloid	Root	Zhang <i>et al.</i> , 1999a
<i>Goniothalamus leiocarpus</i>			
7- <i>epi</i> -Goniodiol [122]	Styrylpyrone	Stem bark	Mu <i>et al.</i> , 1999
Leiocarpin A [123]	Styrene derivative	Stem bark	Mu <i>et al.</i> , 1999
Leiocarpin B [124]	Flavanone-styrylpyrone	Stem bark	Mu <i>et al.</i> , 1999
Leiocarpin C [125]	Styrylpyrone	Stem bark	Mu <i>et al.</i> , 1999

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
<i>Goniothalamus macrophyllus</i>			
(+)-Goniothalamin [27]	Styrylpyrone	Stem bark,	Sam <i>et al.</i> , 1987
Goniothalamin oxide [63]	Styrylpyrone	Stem bark, Root	Sam <i>et al.</i> , 1987
<i>Goniothalamus malayanus</i>			
(+)-Isoaltholactone [126]	Styrene derivative	Stem bark	Colegate <i>et al.</i> , 1990
<i>Goniothalamus marcanii</i>			
Dielsiquinone [127]	Aza- anthraquinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
5-Hydroxy-3-amino-2-aceto-1,4-naphthoquinone [128]	Naphtho- quinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
Marcanine A [129]	Aza- anthraquinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
Marcanine B [130]	Aza- anthraquinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
Marcanine C [131]	Aza- anthraquinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
Marcanine D [132]	Aza- anthraquinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
Marcanine E [133]	Aza- anthraquinone	Stem bark	Soonthornchareonnon <i>et al.</i> , 1999
<i>Goniothalamus montanus</i>			
(+)-Isoaltholactone [126]	Styrene derivative	Stem bark	Colegate <i>et al.</i> , 1990

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
<i>Goniothalamus scortechinii</i>			
Scornazanone [134]	Aza-anthraquinone	Root	Din, Colegate and Razak, 1990
<i>Goniothalamus sesquipedalis</i>			
5-Acetoxyisogoniothalamin oxide [135]	Styrylpyrone	Stem bark	Hasan <i>et al.</i> , 1994
Aristolactam A-II [114]	Aristolactam alkaloid	Leaf, Twig	Talapatra <i>et al.</i> , 1988
Aurantiamid acetate [136]	Miscellaneous	Leaf, Twig	Talapatra <i>et al.</i> , 1988
(+)-Goniodiol [46]	Styrylpyrone	Leaf, Twig	Talapatra <i>et al.</i> , 1985
(+)-Goniodiol diacetate [62]	Styrylpyrone	Leaf, Twig	Talapatra <i>et al.</i> , 1985
Goniodiol-7-monoacetate [21]	Styrylpyrone	Leaf, Twig	Talapatra <i>et al.</i> , 1985
Goniopedaline [137]	Aristolactam alkaloid	Leaf, Twig	Talapatra <i>et al.</i> , 1988
Goniotriol [23]	Styrylpyrone	Leaf, Twig	Talapatra <i>et al.</i> , 1985
β -Sitosterol [138]	Steroid	Leaf, Twig	Talapatra <i>et al.</i> , 1988
Taliscanine [120]	Aristolactam alkaloid	Leaf, Twig	Talapatra <i>et al.</i> , 1988
<i>Goniothalamus tapis</i>			
Isoaltholactone [126]	Styrene derivative	Stem bark	Colegate <i>et al.</i> , 1990
<i>Goniothalamus tenuifolius</i>			
Aristolactam A-II [114]	Aristolactam alkaloid	Stem bark	Likhitwitayawuid <i>et al.</i> , 1997
Cepharanone B [139]	Aristolactam alkaloid	Stem bark	Likhitwitayawuid <i>et al.</i> , 1997

Table 2 (continued)

Plant and Chemical compound	Category	Plant part	Reference
Norcepharadione B [140]	4,5-Dioxo-aporpine alkaloid	Stem bark	Likhitwitayawuid <i>et al.</i> , 1997
Taliscanine [120]	Aristolactam alkaloid	Stem bark	Likhitwitayawuid <i>et al.</i> , 1997
<i>Trans</i> -cinnamic acid [141]	Miscellaneous	Leaf	Likhitwitayawuid <i>et al.</i> , 2006
Velutinam [121]	Aristolactam alkaloid	Stem bark	Likhitwitayawuid <i>et al.</i> , 1997
<i>Goniothalamus thwaitesii</i>			
Betulinic acid [142]	Triterpene	Aerial part	Seidal <i>et al.</i> , 2000
Friedelin [143]	Triterpene	Aerial part	Seidal <i>et al.</i> , 2000
Friedelinol [144]	Triterpene	Aerial part	Seidal <i>et al.</i> , 2000
<i>Goniothalamus umbrosus</i>			
Goniothalamin [27]	Styryllactone	Root	Rosli <i>et al.</i> , 2004
<i>Goniothalamus uvaroides</i>			
5-Acetylgoniothalamin [145]	Styrylpyrone	Root	Ahmad <i>et al.</i> , 1991
Goniothalamin [27]	Styrylpyrone	Root	Ahmad <i>et al.</i> , 1991
<i>Goniothalamus velutinus</i>			
Cepharanone B [139]	Aristolactam alkaloid	Stem bark	Omar <i>et al.</i> , 1992
Velutinam [121]	Aristolactam alkaloid	Stem bark	Omar <i>et al.</i> , 1992

2. Chemical constituents of *Artocarpus* spp.

According to previously reported phytochemical studies, the chemical constituents of plants in the genus *Artocarpus* can be classified into several groups as flavonoids, triterpenoids, steroids, stilbenes and miscellaneous compounds (Tables 3-5 and Figure 4).

Table 3 Distribution of flavonoids in *Artocarpus* spp.

Plant and chemical compound	Plant part	Reference
<i>Artocarpus altilis</i>		
Apigenin [146]	Heartwood	Shimizu <i>et al.</i> , 1998
Artobiloxanthone [147]	Bark	Aida <i>et al.</i> , 1993
Artocarpesin [148]	Heartwood	Shimizu <i>et al.</i> , 1998
Artocarpin [149]	Heartwood	Venkataraman, 1972
Artocarpus chalcone AC-3-1 [150]	Flower	Fujimoto <i>et al.</i> , 1987b
Artocarpus chalcone AC-3-2 [151]	Flower	Fujimoto <i>et al.</i> , 1987b
Artocarpus chalcone AC-5-1 [152]	Flower	Fujimoto <i>et al.</i> , 1987b
Artocarpus chalcone I [153]	Flower	Fujimoto, Agusutein and Made, 1987a
Artocarpus flavone AC-3-3 [154]	Flower	Fujimoto <i>et al.</i> , 1987b
Artocarpus flavone AC-5-2 [155]	Flower	Fujimoto <i>et al.</i> , 1987b
Artocarpus flavone KB-1 [156]	Bark	Fujimoto <i>et al.</i> , 1990
Artocarpus flavone KB-2 [157]	Bark	Fujimoto <i>et al.</i> , 1990
Artocarpus flavone KB-3 [158]	Bark	Fujimoto <i>et al.</i> , 1990
Artochamin B [159]	Cortex of the root	Lin <i>et al.</i> , 2006
Artochamin D [160]	Cortex of the root	Lin <i>et al.</i> , 2006
Artocommunol CC [161]	Cortex of the root	Lin <i>et al.</i> , 2006
Artomunoflavanone [162]	Cortex of the root	Lin <i>et al.</i> , 2006
Artomunoisoxanthone [163]	Cortex of the root	Lin <i>et al.</i> , 2006

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Artomunoxanthentrione [164]	Root bark	Shieh and Lin, 1992
Artomunoxanthone [165]	Root bark	Shieh and Lin, 1992
Artomunoxanthotrione epoxide [166]	Root bark	Lin, Shieh and Jong, 1992
Artonin E [158]	Bark	Hano <i>et al.</i> , 1990
Artonin F [167]	Bark	Hano <i>et al.</i> , 1990
Artonin K [168]	Bark	Aida <i>et al.</i> , 1993
Artonin V [169]	Root bark	Hano, Inami and Nomura, 1994
Artonol A [170]	Bark	Aida <i>et al.</i> , 1993
Artonol B [171]	Bark	Aida <i>et al.</i> , 1993
Artonol C [172]	Bark	Aida <i>et al.</i> , 1993
Artonol D [173]	Bark	Aida <i>et al.</i> , 1993
Artonol E [174]	Bark	Aida <i>et al.</i> , 1993
Cudraflavone A [175]	Root bark	Shieh and Lin, 1992
Cycloaltilisin [176]	Stem	Chen <i>et al.</i> , 1993
Cycloaltilisin 6 [177]	Bud cover	Patil <i>et al.</i> , 2002
Cycloaltilisin 7 [178]	Bud cover	Patil <i>et al.</i> , 2002
Cycloartobiloxanthone [179]	Bark	Hano <i>et al.</i> , 1990b
Cycloartocarpin [180]	Heartwood	Venkataraman, 1972
Cycloartomunin [181]	Root bark	Lin and Shieh, 1991
Cycloartomunoxanthone [182]	Root bark	Lin and Shieh, 1991
Cyclocommuin [183]	Root bark	Lin and Shieh, 1991
Cyclocommunol [184]	Root bark	Lin and Shieh, 1991
Cyclocommunomethonol [185]	Cortex of the root	Lin <i>et al.</i> , 2006
Cyclomorusin [186]	Stem	Chen <i>et al.</i> , 1993
	Root bark	Lin and Shieh, 1991

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Cyclomulberrin [187]	Stem Root bark	Chen <i>et al.</i> , 1993 Lin and Shieh, 1992a
Dihydroartomunoxyanthone [188]	Cortex of the root	Lin <i>et al.</i> , 2006
Dihydrocycloartomunin [189]	Root bark	Lin and Shieh, 1991
Dihydroisocycloartomunin [190]	Root bark	Lin and Shieh, 1992a
Dihydromorin [191]	Heartwood	Shimizu <i>et al.</i> , 1998
Engeletin [192]	Stem	Chen <i>et al.</i> , 1993
3'-Geranyl-2'-3,4,4'-tetrahydroxy – chalcone [193]	Leaf	Shimizu <i>et al.</i> , 2000
Isoartocarpentin [194]	Heartwood	Shimizu <i>et al.</i> , 1998
Isocyclomorusin (Cudraflavone A) [175]	Stem	Chen <i>et al.</i> , 1993
Isocyclomulberrin (Cyclocommuin) [183]	Stem	Chen <i>et al.</i> , 1993
Morin [195]	Heartwood	Venkataraman, 1972
Morusin [196]	Stem Bark	Fujimoto <i>et al.</i> , 1990
(+)-Norartocarpanone [197]	Heartwood	Shimizu <i>et al.</i> , 1998
Norartocarpentin [198]	Heartwood	Venkataraman, 1972
<i>Artocarpus champeden</i>		
Artoindonesianin A [199]	Root	Hakim <i>et al.</i> , 1999
Artoindonesianin B [200]	Root	Hakim <i>et al.</i> , 1999
Artoindonesianin M [201]	-	Syah <i>et al.</i> , 2002a
Artoindonesianin Q [202]	Heartwood	Syah <i>et al.</i> , 2002b
Artoindonesianin R [203]	Heartwood	Syah <i>et al.</i> , 2002b
Artoindonesianin S [204]	Heartwood	Syah <i>et al.</i> , 2002b
Artoindonesianin T [205]	Heartwood	Syah <i>et al.</i> , 2002b
Artoindonesianin U [206]	Heartwood	Syah <i>et al.</i> , 2004

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Artoindonesianin V [207]	Heartwood	Syah <i>et al.</i> , 2004
Artonin A [208]	Root	Hakim <i>et al.</i> , 1999
Artonin B [209]	Heartwood	Syah <i>et al.</i> , 2004
Cyclochampedol [210]	Stem bark	Achmad <i>et al.</i> , 1996; Paolo <i>et al.</i> , 1998
Cyclocommuin [183]	Heartwood	Syah <i>et al.</i> , 2004
5'-Hydroxycudraflavone A [211]	Heartwood	Syah <i>et al.</i> , 2004
<i>Artocarpus chaplacha</i>		
Artocarpesin [148]	Heartwood	Rao, Rathi and Venkataraman, 1972
Artocarpin [149]	Heartwood	Rao <i>et al.</i> , 1972
Chaplashin [212]	Heartwood	Rao <i>et al.</i> , 1972
Cycloartocarpesin [213]	Heartwood	Rao <i>et al.</i> , 1972
Cycloartocarpin [180]	Heartwood	Rao <i>et al.</i> , 1972
<i>Artocarpus dadah</i>		
Afelechin-3-O- α -L-rhamnopyra	Stem bark	Su <i>et al.</i> , 2002
Noside [214]	Twig	
(+)-Catechin [215]	Stem bark	Su <i>et al.</i> , 2002
Dihydromorin [191]	Twig	
Engeletin [192]	Stem bark	Su <i>et al.</i> , 2002
(+)-Epiafzelechin [216]	Twig	
(-)-Epiafzelechin-(4 β →8)-epicatechin [217]	Stem bark	Su <i>et al.</i> , 2002

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Gemichalcone B [218]	Twig	Su <i>et al.</i> , 2002
Isogemichalcone B [219]	Twig	Su <i>et al.</i> , 2002
Norartocarpentin [198]	Twig	Su <i>et al.</i> , 2002
Steppogenin [220]	Twig	Su <i>et al.</i> , 2002
<i>Artocarpus elasticus</i>		
Artelasticin [221]	Heartwood	Kijjoa <i>et al.</i> , 1996
Artelastin [222]	Heartwood	Kijjoa <i>et al.</i> , 1996
Artelastinin [223]	Heartwood	Kijjoa <i>et al.</i> , 1998
Artelastocarpin [224]	Heartwood	Cidade <i>et al.</i> , 2001
Artelastochromene [225]	Heartwood	Kijjoa <i>et al.</i> , 1996
Artelastofuran [226]	Heartwood	Kijjoa <i>et al.</i> , 1998
Artocarpesin [227]	Heartwood	Kijjoa <i>et al.</i> , 1996
Artocarpin [149]	Heartwood	Kijjoa <i>et al.</i> , 1996
Carpelastofuran [228]	Heartwood	Cidade <i>et al.</i> , 2001
Cycloartocarpesin [213]	Heartwood	Pendse <i>et al.</i> , 1976
Cycloartocarpin [180]	Heartwood	Pendse <i>et al.</i> , 1976
Integrin [229]	Heartwood	Pendse <i>et al.</i> , 1976
Norartocarpin [230]	Heartwood	Pendse <i>et al.</i> , 1976
<i>Artocarpus frettessi</i>		
Artoindonesianin X [231]	Root bark	Hakim <i>et al.</i> , 2003
Artoindonesianin Y [232]	Root bark	Hakim <i>et al.</i> , 2003

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
<i>Artocarpus gomezianus</i>	Root	Likhitwitayawuid, Sritularak and De-Eknamkul, 2000
	Heartwood	Venkataraman, 1972
	Heartwood	Venkataraman, 1972
	Root	Likhitwitayawuid <i>et al.</i> , 2000
	Root	Likhitwitayawuid <i>et al.</i> , 2000
	Heartwood	Venkataraman, 1972
	Root	Likhitwitayawuid <i>et al.</i> , 2000
	Root	Likhitwitayawuid <i>et al.</i> , 2000
	Heartwood	Venkataraman, 1972
	Root	Likhitwitayawuid <i>et al.</i> , 2000
<i>Artocarpus heterophyllus</i>	Leaf	An <i>et al.</i> , 1992
	Heartwood	Radhakrishnan, Rao and Venkataraman, 1965
	Root bark	Lin, Lu and Huang, 1995
	Heartwood	Radhakrishnan <i>et al.</i> , 1965
	Heartwood	Venkataraman, 1972
	Root bark	Lin <i>et al.</i> , 1995
	Root	Chung <i>et al.</i> , 1995
	Heartwood	Radhakrishnan <i>et al.</i> , 1965
	Root bark	Feng <i>et al.</i> , 1998
	Root	Dayal and Seshadri, 1974
Artonin A [208]	Root bark	Hano <i>et al.</i> , 1989

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Artonin B [209]	Root bark	Hano <i>et al.</i> , 1989
Artonin C [243]	Root bark	Hano, Aida and Nomura, 1990a
Artonin D [244]	Root bark	Hano <i>et al.</i> , 1990a
Artonin I [245]	Root bark	Hano <i>et al.</i> , 1989
Artonin J [246]	Root bark	Aida <i>et al.</i> , 1993
Artonin K [168]	Root bark	Aida <i>et al.</i> , 1993
Artonin L [247]	Root bark	Aida <i>et al.</i> , 1993
Artonin Q [248]	Bark	Aida <i>et al.</i> , 1994
Artonin R [249]	Bark	Aida <i>et al.</i> , 1994
Artonin S [250]	Bark	Aida <i>et al.</i> , 1994
Artonin T [251]	Bark	Aida <i>et al.</i> , 1994
Artonin U [252]	Bark	Aida <i>et al.</i> , 1994
Artonin X [253]	Bark	Shinomiya <i>et al.</i> , 1995
Catechin [215]	Leaf	Yamazaki <i>et al.</i> , 1987
Cudraflavone A [175]	Root bark	Lin <i>et al.</i> , 1995
Cyanomaclurin [254]	Heartwood	Radhakrishnan <i>et al.</i> , 1965
Cycloartocarpesin [213]	Heartwood	Pathasarathy <i>et al.</i> , 1969
Cycloartocarpin [180]	Heartwood	Venkataraman, 1972
Cycloartocarpin A [255]	Root bark	Lu and Lin, 1994
Cycloheterophyllin [256]	Bark	Rao <i>et al.</i> , 1971
Cycloheterophyllin diacetate [257]	Root bark	Hano <i>et al.</i> , 1989
Cycloheterophyllin peracetate [258]	Root bark	Feng <i>et al.</i> , 1998
Dihydromorin [191]	Heartwood	Venkataraman, 1972
Heteroartonin A [259]	Root bark	Chung <i>et al.</i> , 1995

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Heteroflavanone A [260]	Root bark	Lu and Lin, 1993
Heteroflavanone B [261]	Root bark	Lu and Lin, 1993
Heteroflavanone C [262]	Root bark	Lu and Lin, 1994
Heterophyllin [263]	Root bark	Hano <i>et al.</i> , 1989
Heterophyllol [264]	Root bark	Lu and Lin, 1993
Isocycloheterophyllin [265]	Bark	Rao, Varadan and Venkataraman, 1973
Kuwanon R [266]	Root bark	Shinomiya <i>et al.</i> , 1995
Kuwanon T [267]	Root bark	Shinomiya <i>et al.</i> , 1995
Morin [195]	Heartwood	Radhakrishnan <i>et al.</i> , 1965; Pathasarathy <i>et al.</i> , 1969; Mu and Li, 1982
Morin-calcium-chelate [195]	Heartwood	Mu and Li, 1982
Norartocarpentin [198]	Heartwood	Radhakrishnan <i>et al.</i> , 1965
Norartocarpin [230]	Heartwood	Venkataraman, 1972
Oxydihydroartocarpesin [268]	Heartwood	Pathasarathy <i>et al.</i> , 1969
Procyanidin B-3 [269]	Leaf	An <i>et al.</i> , 1992
Procyanidin C-1 [270]	Leaf	An <i>et al.</i> , 1992
<i>Artocarpus hirsuta</i>		
Artocarpanone [236]	Heartwood	Venkataraman, 1972
Artocarpesin [148]	Heartwood	Venkataraman, 1972
Artocarpentin [238]	Heartwood	Venkataraman, 1972
Artocarpin [149]	Heartwood	Venkataraman, 1972
Cyanomaclurin [254]	Heartwood	Venkataraman, 1972
Cycloartocarpesin [213]	Heartwood	Venkataraman, 1972

Table3 (continued)

Plant and chemical compound	Plant part	Reference
Cycloartocarpin [180]	Heartwood	Venkataraman, 1972
Dihydromorin [191]	Heartwood	Venkataraman, 1972
Morin [195]	Heartwood	Venkataraman, 1972
Norartocarpentin [198]	Heartwood	Venkataraman, 1972
Oxydihydroartocarpesin [268]	Heartwood	Venkataraman, 1972
<i>Artocarpus integer</i>		
Artocarpanone [236]	Heartwood	Pendse <i>et al.</i> , 1976
Artocarpesin [148]	Heartwood	Pendse <i>et al.</i> , 1976
Artocarpentin [238]	Heartwood	Pendse <i>et al.</i> , 1976
Catechin [215]	Leaf	Yamazaki <i>et al.</i> , 1987
Chaplashin [212]	Heartwood	Pendse <i>et al.</i> , 1976
Cycloartocarpesin [213]	Heartwood	Pendse <i>et al.</i> , 1976
Cycloartocarpin [180]	Heartwood	Pendse <i>et al.</i> , 1976
Cyclointegrin [271]	Heartwood	Pendse <i>et al.</i> , 1976
Cyanomaclurin [254]	Heartwood	Pendse <i>et al.</i> , 1976
Dihydromorin [191]	Heartwood	Pendse <i>et al.</i> , 1976
Integrin [229]	Heartwood	Pendse <i>et al.</i> , 1976
Morin [195]	Heartwood	Pendse <i>et al.</i> , 1976
Norartocarpentin [198]	Heartwood	Pendse <i>et al.</i> , 1976
Oxydihydroartocarpesin [268]	Heartwood	Pendse <i>et al.</i> , 1976
Oxyisocyclointegrin [272]	Heartwood	Pendse <i>et al.</i> , 1976
<i>Artocarpus lakoocha</i>		
Artocarpin [149]	Heartwood	Venkataraman, 1972

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Cycloartocarpin [180]	Heartwood	Venkataraman, 1972
5,7-Dihydroxyflavone-3-O- α -L-rhamnoside [273]	Root bark	Chauhan and Kumari, 1979a
5-Hydroxy-7,2'-4'-trimethoxyflavone [274]	Stemwood	Pavaro and Reutrakul, 1976
Galangin-3-O- α -L-(-)-rhamnopyranoside [275]	Root bark	Chauhan and Kumari, 1979a
Galangin-3-O- β -D-galactopyranosyl-(1→4)- α -L-rhamnopyranoside [276]	Root bark	Chauhan, Kumari and Saraswat, 1979b
Kaempferol-3-O- β -D-xylanopyranoside [277]	Root bark	Chauhan <i>et al.</i> , 1982
Norartocarpin [230]	Heartwood	Venkataraman, 1972
Norcycloartocarpin [278]	Heartwood	Venkataraman, 1972
Quercetin-3-O- α -L-rhamnopyranoside [279]	Root bark	Chauhan <i>et al.</i> , 1982
<i>Artocarpus lanceifolius</i>		
Artelasticin [221]	Heartwood	Syah <i>et al.</i> , 2001
Artelastofuran [226]	Heartwood	Syah <i>et al.</i> , 2001
Artobiloxanthone [147]	Bark	Hakim, 2002
Artoindonesianin G [280]	Heartwood	Syah <i>et al.</i> , 2001
Artoindonesianin H [281]	Heartwood	Syah <i>et al.</i> , 2001
Artoindonesianin I [282]	Heartwood	Syah <i>et al.</i> , 2001
Artoindonesianin P [283]	Bark	Hakim, 2002
Artonol B [171]	Bark	Hakim, 2002
Cycloartobiloxanthone [179]	Bark	Hakim, 2002
<i>Artocarpus nobilis</i>		
Artobilochromen [284]	Bark	Pavanarasivam, Sultanbawa and Mageswaran, 1974; Kumar <i>et al.</i> , 1977; Sultanbawa and Surendrakumar, 1989

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
Artobiloxanthone [147]	Bark	Sultambawa and Surendrakumar, 1989
Chromanoartobilochromen A [285]	Trunk bark	Kumar et al., 1977
Chromanoartobilochromen B [286]	Trunk bark	Pavanarasivam et al., 1974; Kumar et al., 1977
Chromanoartobilochromene [287]	Bark	Pavanarasivam et al., 1974
Cycloartobiloxanthone [179]	Bark	Pavanarasivam et al., 1974
(-)-Dihydrofuranoartobilochromen A [288]	Trunk bark	Kumar et al., 1977
(-)-Dihydrofuranoartobilochromen B-1 [289]	Trunk bark	Kumar et al., 1977
(-)-Dihydrofuranoartobilochromen B-2 [290]	Trunk bark	Kumar et al., 1977
Furanoartobilochromen A [291]	Bark	Pavanarasivam et al., 1974
Furanoartobilochromen B-1 [292]	Bark	Pavanarasivam et al., 1974
Furanoartobilochromen B-2 [293]	Bark	Pavanarasivam et al., 1974
2',4',4-Trihydroxy-3'-geranylchalcone [294]	Leaf	Fujimoto et al., 2004
2',4',4-Trihydroxy-3'-[6-hydroxy-3,7-dimethyl-2(E),7-octadiethyl] chalcone [295]	Leaf	Fujimoto et al., 2004
2',4',4-Trihydroxy-3'-[2-hydroxy-7-methyl-3-methylene-6-octaethyl] chalcone [296]	Leaf	Fujimoto et al., 2004
2',3,4,4'-Tetrahydroxy-3'-geranylchalcone [297]	Leaf	Fujimoto et al., 2004
2',3,4,4'-Tetrahydroxy-3'-[6-hydroxy-3,7-dimethyl-2(E),7-octadiethyl] chalcone [298]	Leaf	Fujimoto et al., 2004
Oxydihydromorusin [299]	Trunk bark	Kumar et al., 1977; Fukai and Nomura, 1993
<i>Artocarpus pithecogalla</i>		
Morin [195]	Heartwood	Mu and Li, 1982
Morin-calcium-chelate [195]	Heartwood	Mu and Li, 1982

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
<i>Artocarpus rigida</i>		
Artobiloxanthone [147]	Stem Bark	Hano, Inami and Nomura, 1990
Artonin E [158]	Stem Bark	Hano <i>et al.</i> , 1990
Artonin G [300]	Stem Bark	Hano <i>et al.</i> , 1990
Artonin H [301]	Stem Bark	Hano <i>et al.</i> , 1990
Artonin M [302]	Stem Bark	Hano <i>et al.</i> , 1990
Artonin N [303]	Stem Bark	Hano <i>et al.</i> , 1990
Artonin O [304]	Stem Bark	Hano <i>et al.</i> , 1990
Artonin P [305]	Stem Bark	Hano <i>et al.</i> , 1990
Cycloartobiloxanthone [179]	Stem bark	Hano <i>et al.</i> , 1990
<i>Artocarpus rotundo</i>		
Artoindonesianin L [306]	Root bark	Suhartati <i>et al.</i> , 2001
Artonin E [158]	Root bark	Suhartati <i>et al.</i> , 2001
Artonin M [302]	Root bark	Suhartati <i>et al.</i> , 2001
Artonin O [304]	Root bark	Suhartati <i>et al.</i> , 2001
Cycloartobiloxanthone [179]	Root bark	Suhartati <i>et al.</i> , 2001
<i>Artocarpus teysmanii</i>		
Artoindonesianin C [307]	Root bark	Makmur <i>et al.</i> , 2000
Artonin J [246]	Root bark	Makmur <i>et al.</i> , 2000
Cycloartobiloxanthone [179]	Root bark	Makmur <i>et al.</i> , 2000
<i>Artocarpus tonkinensis</i>		
Artotonkin [308]	Stem bark	Lien <i>et al.</i> , 1988

Table 3 (continued)

Plant and chemical compound	Plant part	Reference
<i>Artocarpus venenosa</i>		
Paratocarin A [309]	Stem bark	Nomura, Hano and Aida, 1998
Paratocarin B [310]	Stem bark	Nomura et al., 1998
Paratocarin C [311]	Stem bark	Nomura et al., 1998
Paratocarin D [312]	Stem bark	Nomura et al., 1998
Paratocarin E [313]	Stem bark	Nomura et al., 1998
Paratocarin F [314]	Stem bark	Nomura et al., 1998
Paratocarin G [315]	Stem bark	Nomura et al., 1998
Paratocarin H [316]	Stem bark	Nomura et al., 1998
Paratocarin I [317]	Stem bark	Nomura et al., 1998
Paratocarin J [318]	Stem bark	Nomura et al., 1998
Paratocarin K [319]	Stem bark	Nomura et al., 1998
Paratocarin L [320]	Stem bark	Nomura et al., 1998

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Table 4 Distribution of triterpenoids in *Artocarpus* spp.

Plant and chemical compound	Plant part	Reference
<i>Artocarpus altilis</i>		
α -Amyrin [321]	Latex	Ultee, 1949
α -Amyrin acetate [322]	Fruit	Altman and Zito, 1976
β -Amyrin acetate [323]	Latex	Ultee, 1949
Cycloart-23-ene-3 β -25-diol [324]	Fruit	Altman and Zito, 1976
Cycloart-24-ene-3 β -ol [325]	Fruit	Altman and Zito, 1976
Cycloart-25-ene-3 β -24-diol [326]	Fruit	Altman and Zito, 1976
Cycloartenol [325] (Cycloart-24-ene-3 β -ol)	Stem Bark	Pavanatasivum and Sultanbawa, 1973
Cycloartenone [327]	Stem Bark	Pavanatasivum and Sultanbawa, 1973
Cycloartenyl acetate [328]	Stem Bark	Pavanatasivum and Sultanbawa, 1973
Lupeol acetate [329]	Root bark	Shieh and Lin, 1992
<i>Artocarpus champeden</i>		
Cycloartenone [327]	Stem bark	Achmad <i>et al.</i> , 1996
Cycloeucalenol [330]	Stem bark	Achmad <i>et al.</i> , 1996
Glutinol [331]	Stem bark	Achmad <i>et al.</i> , 1996
24-Methylenecycloartenone [332]	Stem bark	Achmad <i>et al.</i> , 1996
<i>Artocarpus chaplasha</i>		
Cycloartenyl acetate [328]	Stem bark	Mahato, Banerjee and Chakravarti, 1971
Isocycloartenol acetate [333]	Stem bark	Mahato <i>et al.</i> , 1971
Lupeol acetate [329]	Stem bark	Mahato <i>et al.</i> , 1971
<i>Artocarpus elasticus</i>		
β -Amyrin acetate [323]	Latex	Ultee, 1949

Table 4 (continued)

Plant and chemical compound	Plant part	Reference
Lupeol acetate [329]	Latex	Ultee, 1949
<i>Artocarpus gomezianus</i>		
Lupeol acetate [329]	Leaf	Kingroungpet, 1994
Simiarenonol [334]	Leaf	Kingroungpet, 1994
<i>Artocarpus heterophyllus</i>		
Cycloartenone [327]	Fruit	Nath and Mukherjee, 1939; Barton, 1951
	Stem bark	Pavanatasivum and Sultanbawa, 1973
	Root	Dayal and Seshadri, 1974
	Latex	Barik et al., 1994
Betulin [335]	Root bark	Lu and Lin, 1994
Betulinic acid [336]	Root	Dayal and Seshadri, 1974
	Root bark	Lu and Lin, 1994
Butyrospermol [337]	Fruit	Barton, 1951
Cycloartenol [325]	Fruit	Barton, 1951
	Wood	Nogueira and Correia, 1958
	Stem Bark	Pavanatasivum and Sultanbawa, 1973
	Latex	Barik et al., 1994
Cycloartenyl acetate [328]	Stem bark	Pavanatasivum and Sultanbawa, 1973
9,19-Cyclolanost-23-ene-3 β ,25-diol (Cycloart-23-ene-3,25-diol) [324]	Fruit	Kielland and Malterud, 1994
9,19-Cyclolanost-25-ene-3 β ,24-diol [326]	Fruit	Kielland and Malterud, 1994
9,19-Cyclolanost-3-one-24,25-diol [338]	Latex	Barik et al., 1994
Ursolic acid [339]	Root	Dayal and Seshadri, 1974
	Root bark	Lu and Lin, 1994

Table 4 (continued)

Plant and chemical compound	Plant part	Reference
<i>Artocarpus integer</i> Cycloartenone [327]	Latex	Pant and Chaturvedi, 1989
<i>Artocarpus lakoocha</i> β-Amyrin acetate [323] Cycloartenol [325] Cycloartenone [327] Cycloartenyl acetate [328] Lupeol [329] Lupeol acetate [329]	Stem Bark	Kapil and Joshi, 1960
	Stem Bark	Pavanasaivum and Sultanbawa, 1973
	Stem Bark	Pavanasaivum and Sultanbawa, 1973
	Stem Bark	Pavanasaivum and Sultanbawa, 1973
	Root bark	Chauhan and Kumari, 1979
	Stem Bark	Kapil and Joshi, 1960
<i>Artocarpus nobilis</i> Cycloartenol [325] Cycloartenone [327] Cycloartenyl acetate [328]	Stem Bark	Pavanasaivum and Sultanbawa, 1973
	Heartwood	Pavanasaivum and Sultanbawa, 1973
	Stem Bark	Pavanasaivum and Sultanbawa, 1973
	Heartwood	Pavanasaivum and Sultanbawa, 1973
	Stem Bark Heartwood	Pavanasaivum and Sultanbawa, 1973

Table 5 Distribution of miscellaneous constituents in *Artocarpus* spp.

Plant and chemical compound	Category	Plant part	Reference
<i>Artocarpus altilis</i>			
γ -Aminobutyric acid [340]	Amino acid	Leaf	Durand <i>et al.</i> , 1962
Artocarbene [341]	Stilbene	Heartwood	Shimizu <i>et al.</i> , 1997
4-Prenyloxyresveratrol [342]	Stilbene	Heartwood	Shimizu <i>et al.</i> , 1997
β -sitosterol [138]	Steroid	Root bark	Shieh and Lin, 1992
<i>Artocarpus chaplasha</i>			
Oxyresveratrol [343]	Stilbene	Heartwood	Rao <i>et al.</i> , 1972
Resorcinol [344]	Benzenoid	Heartwood	Rao <i>et al.</i> , 1972
β -Resorcylaldehyde [345]	Benzenoid	Heartwood	Rao <i>et al.</i> , 1972
Resveratrol [346]	Stilbene	Heartwood	Rao <i>et al.</i> , 1972
β -sitosterol [138]	Steroid	Stem bark	Mahato <i>et al.</i> , 1971
<i>Artocarpus dadah</i>			
Dadahol A [347]	Neolignan	Twig	Su <i>et al.</i> , 2002
Dadahol B [348]	Neolignan	Twig	Su <i>et al.</i> , 2002
3-(2,3-Dihydroxy-3-methylbutyl)-resveratrol [349]	Stilbene	Stem bark	Su <i>et al.</i> , 2002
3-(γ,γ -Dimethylallyl) oxyresveratrol [350]	Stilbene	Stem bark	Su <i>et al.</i> , 2002
3-(γ,γ -Dimethylallyl) resveratrol [351]	Stilbene	Stem bark	Su <i>et al.</i> , 2002
3-(γ,γ -Dimethylpropenyl) moracin M [352]	Stilbene	Stem bark	Su <i>et al.</i> , 2002
Moracin M [353]	Stilbene	Twig	Su <i>et al.</i> , 2002
Oxyresveratrol [343]	Stilbene	Stem bark	Su <i>et al.</i> , 2002
Resveratrol [346]	Stilbene	Twig	Su <i>et al.</i> , 2002

Table 5 (continued)

Plant and chemical compound	Category	Plant part	Reference
<i>Artocarpus elasticus</i> β-sitosterol [138]	Steroid	Heartwood	Pendse <i>et al.</i> , 1976
<i>Artocarpus gomezianus</i>	Stilbene	Root	Likhitwitayawuid and Sritularak, 2001
	Phenolic glycoside	Leaf	Kingroungpet, 1994
	Stilbene	Root	Likhitwitayawuid and Sritularak, 2001
	Stilbene	Bark	Hakim <i>et al.</i> , 2002
	Stilbene	Bark	Hakim <i>et al.</i> , 2002
	Alcohol	Leaf	Kingroungpet, 1994
	Phenolic compound	Heartwood	Venkataraman, 1972
	Naphthalene	Root	Likhitwitayawuid <i>et al.</i> , 2000
	Benzenoid	Root	Sritularak, 1998
	Stilbene	Root	Likhitwitayawuid <i>et al.</i> , 2000
β-sitosterol [138]	Steroid	Leaf	Kingroungpet, 1994
Stigmasterol [43]	Steroid	Root	Sritularak, 1998
<i>Artocarpus heterophyllus</i> Acetylcholine [362]	Amine	Seed	Pereira, Medina and Bustos, 1962

Table 5 (continued)

Plant and chemical compound	Category	Plant part	Reference
Artocarpus integra α -D-Galactose specific lectin [363]	Lectin	Seed	Suresh, Appukuttan and Basu, 1982
Artocarpus integrifolia lectin [364]	Lectin	Seed	Chatterjee, Sarkar and Rao, 1982; Namjuntra and Culavatnatol, 1984
Artocarpus lectin CE-A-I [365]	Lectin	Seed	Ferreira <i>et al.</i> , 1992
Aurantiamide acetate [366]	Protein	Seed	Chakraborty and Mandal, 1981
9-Hydroxytridecyl docosanoate [367]	Lipid	Root bark	Lu and Lin, 1994
4-Hydroxyundecyl docosanoate [368]	Lipid	Latex	Pant and Chaturvedi, 1989
Jacalin [369]	Lectin	Seed	Hagiwara <i>et al.</i> , 1988 Ferreira <i>et al.</i> , 1992
Lymphoagglutinin [370]	Lectin	Seed	Arora <i>et al.</i> , 1987
Recinoleic acid [371]	Lipid	Seed oil	Daulatabad and Mirajkar, 1989
β -sitosterol [138]	Steroid	Heartwood Root Root bark	Pathasarathy <i>et al.</i> , 1969 Dayal and Seshadri, 1974 Lu and Lin, 1994
<i>Artocarpus hirsuta</i>			
Lymphoagglutinin [370]	Lectin	Seed	Arora <i>et al.</i> , 1987
<i>Artocarpus integer</i>			
Artocarbene [341]	Stilbene	Aerial part	Boonlaksiri <i>et al.</i> , 2000

Table 5 (continued)

Plant and chemical compound	Category	Plant part	Reference
Artocarpus lectin C [372]	Lectin	Seed	Hashim, Gendeh and Jaafar, 1992
4-Hydroxyundecyl docosanoate [368]	Lipid	Latex	Pant and Chaturvedi, 1989
4-Methoxy-2,2-dimethyl-6-(2-(2,4-dihydroxy) phenyl-trans-ethenyl) chromene [373]	Stilbene	Aerial part	Boonlaksiri <i>et al.</i> , 2000
4-Prenyloxyresveratrol [374]	Stilbene	Aerial part	Boonlaksiri <i>et al.</i> , 2000
β -sitosterol [138]	Steroid	Heartwood	Pendse <i>et al.</i> , 1976
<i>trans</i> -4-Isopentenyl-3,5,2',4'-tetrahydroxystilbene [374]	Stilbene	Aerial part	Boonlaksiri <i>et al.</i> , 2000
<i>trans</i> -4-(3-Methyl- <i>E</i> -but-1-enyl)-3,5,2',4'-tetrahydroxystilbene [375]	Stilbene	Aerial part	Boonlaksiri <i>et al.</i> , 2000
<i>Artocarpus lakoocha</i>			
ALA-I [376]	Isolectin	Seed	Wongkham <i>et al.</i> , 1995
ALA-II [377]	Isolectin	Seed	Wongkham <i>et al.</i> , 1995
Artocarpus lakoocha lectin [378]	Lectin	Seed	Chatterjee <i>et al.</i> , 1982
Lakoochins A [379]	Stilbene	Root	Puntumchai <i>et al.</i> , 2004
Lakoochins B [380]	Stilbene	Root	Puntumchai <i>et al.</i> , 2004
Lymphoagglutinin [370]	Lectin	Seed	Arora <i>et al.</i> , 1987
Oxyresveratrol [343]	Stilbene	Heartwood	Venkataraman, 1972; Likhitwitayawuid and Sritularak, 2001
Resorcinol [344]	Benzoid	Heartwood	Venkataraman, 1972
Resveratrol [346]	Stilbene	Heartwood	Venkataraman, 1972
β -sitosterol [138]	Steroid	Root bark	Chauhan and Kumari, 1979

Table 5 (continued)

Plant and chemical compound	Category	Plant part	Reference
<i>Artocarpus lignanensis</i> Artocarpus lectin [381]	Lectin	Seed	Zhang <i>et al.</i> , 1999
<i>Artocarpus masticatus</i> Artocarpus lectin AM [382]	Lectin	Seed	Blasco <i>et al.</i> , 1996
<i>Artocarpus melinoxylus</i> Artocarpus lectin AME [383]	Lectin	Seed	Blasco <i>et al.</i> , 1996
<i>Artocarpus rigida</i> Artocarpol A [384] Artocarpol C [385] Artocarpol D [386] Artocarpol E [387] Artocarpol F [388]	Phenolics	Root bark	Ko, Lin, and Yang, 2001
	Phenolics	Root bark	Ko <i>et al.</i> , 2001
	Phenolics	Root bark	Ko <i>et al.</i> , 2001
	Phenolics	Root bark	Ko <i>et al.</i> , 2001
	Phenolics	Root bark	Ko <i>et al.</i> , 2001

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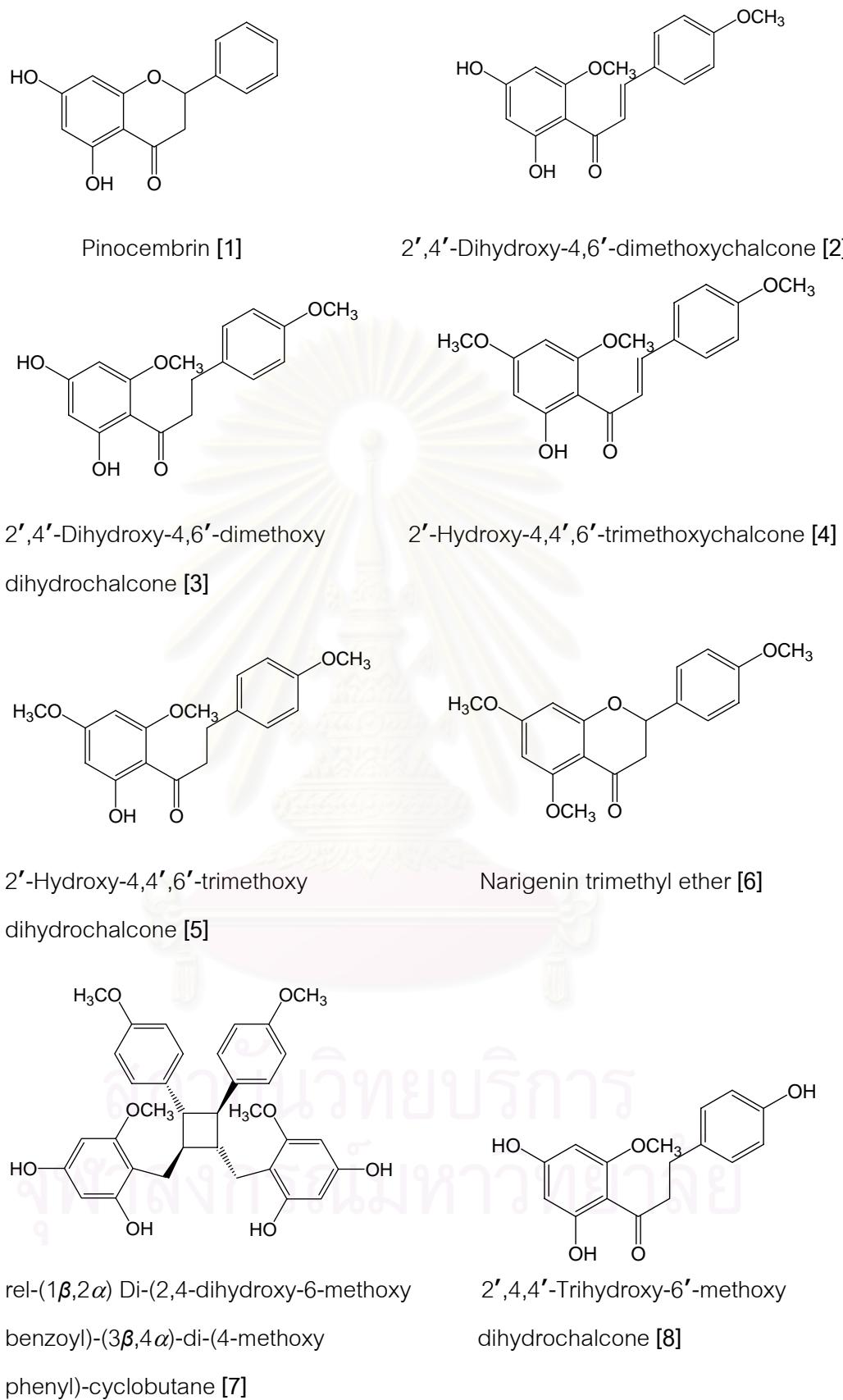


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp.

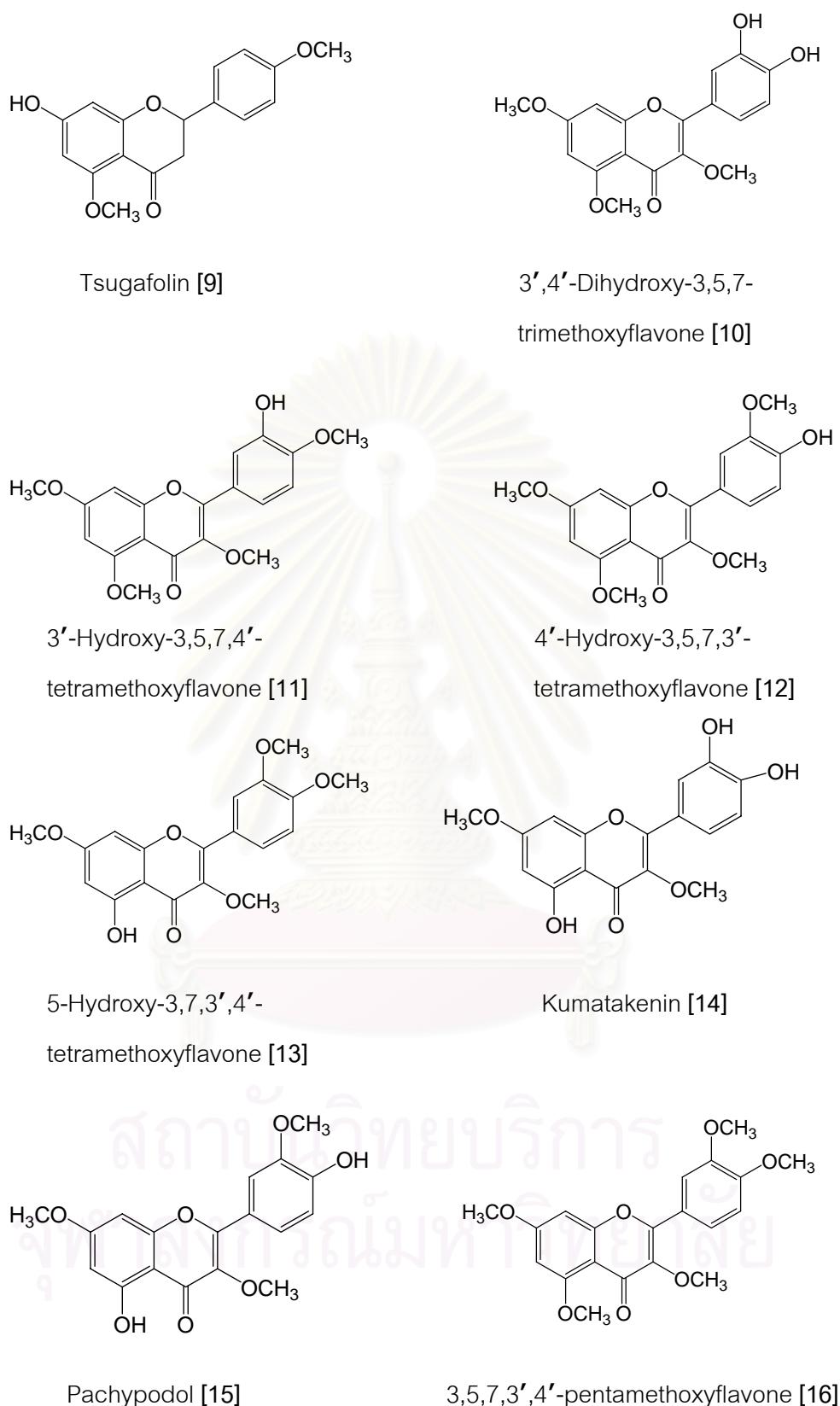


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

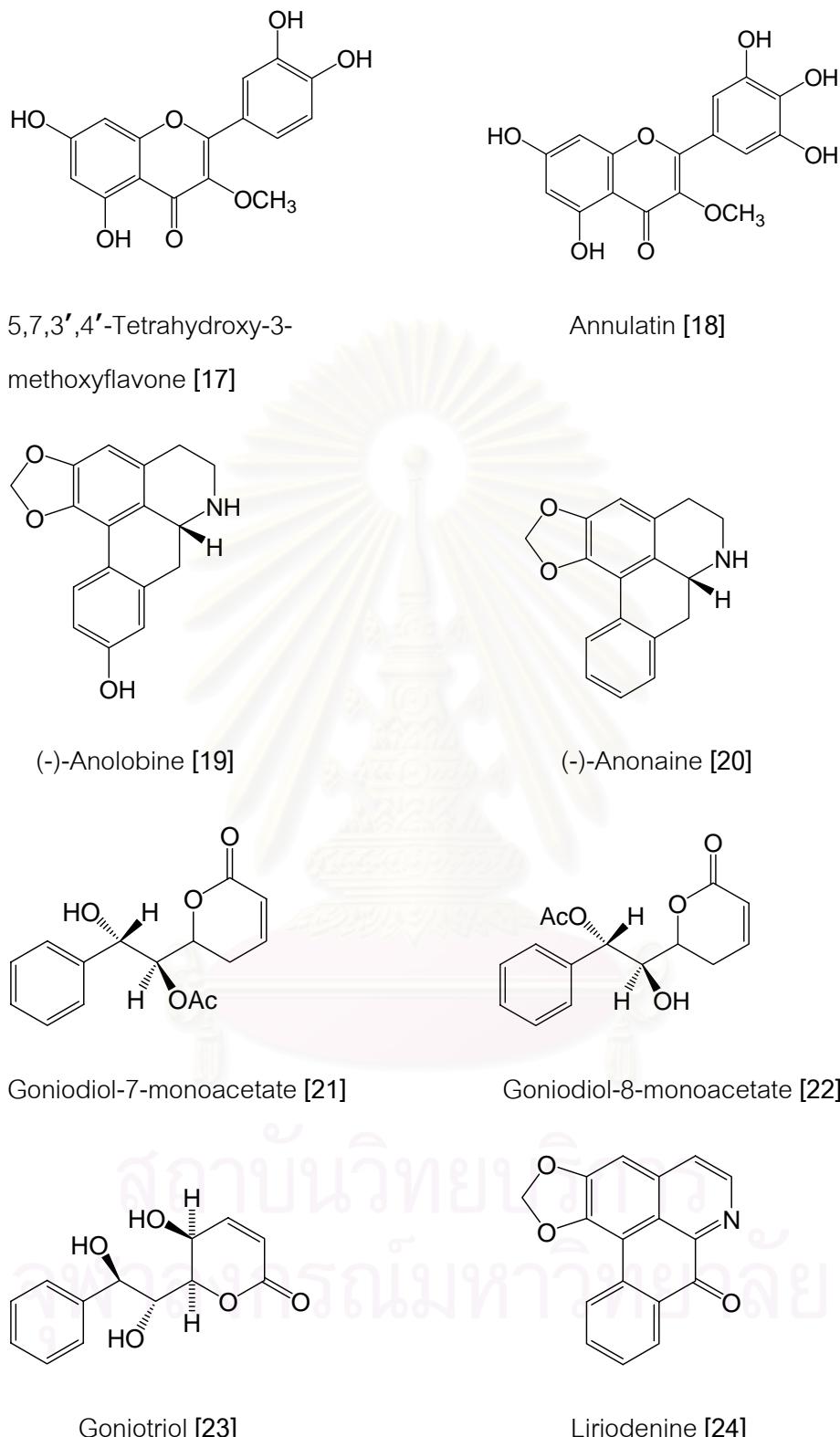


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

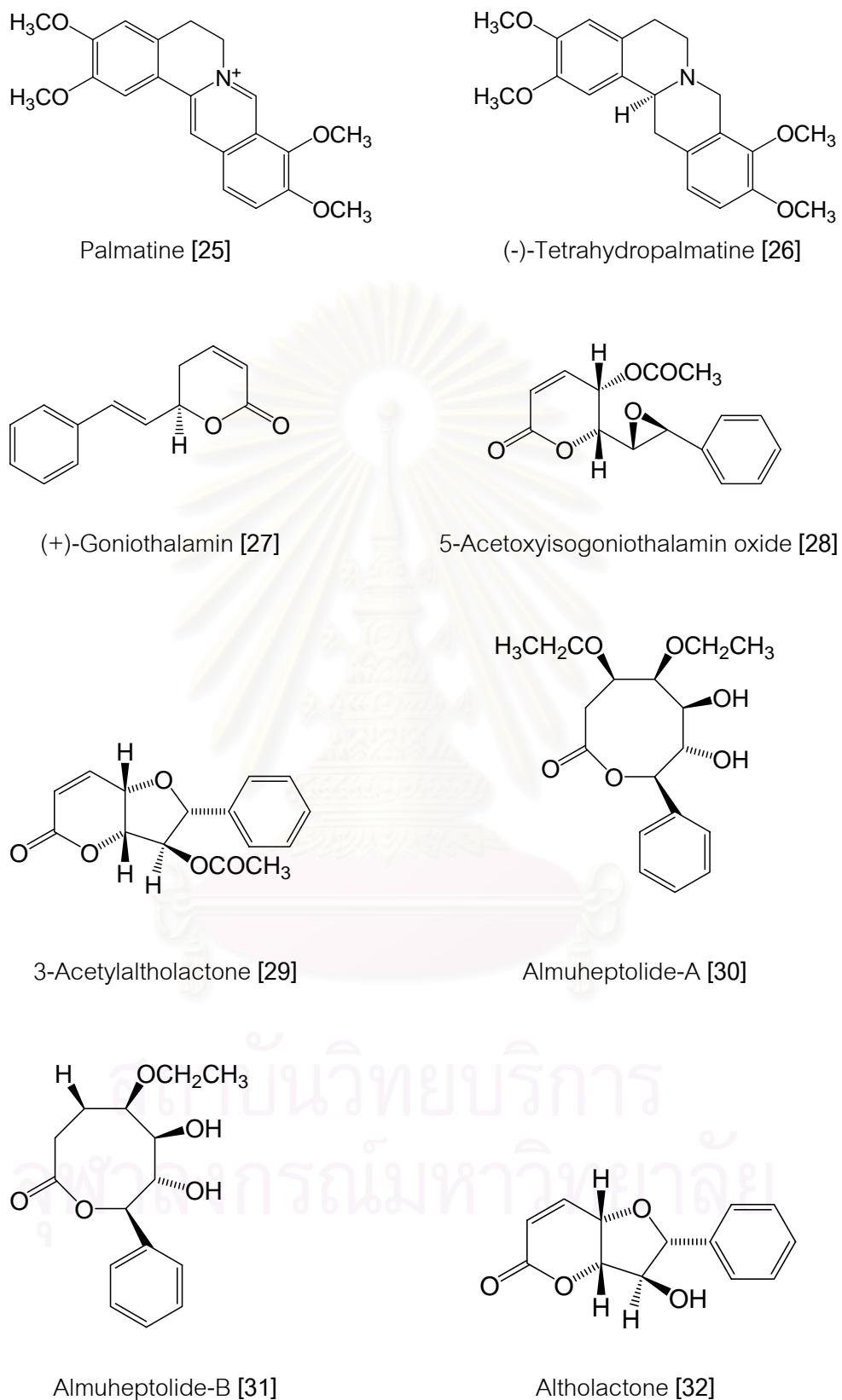


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

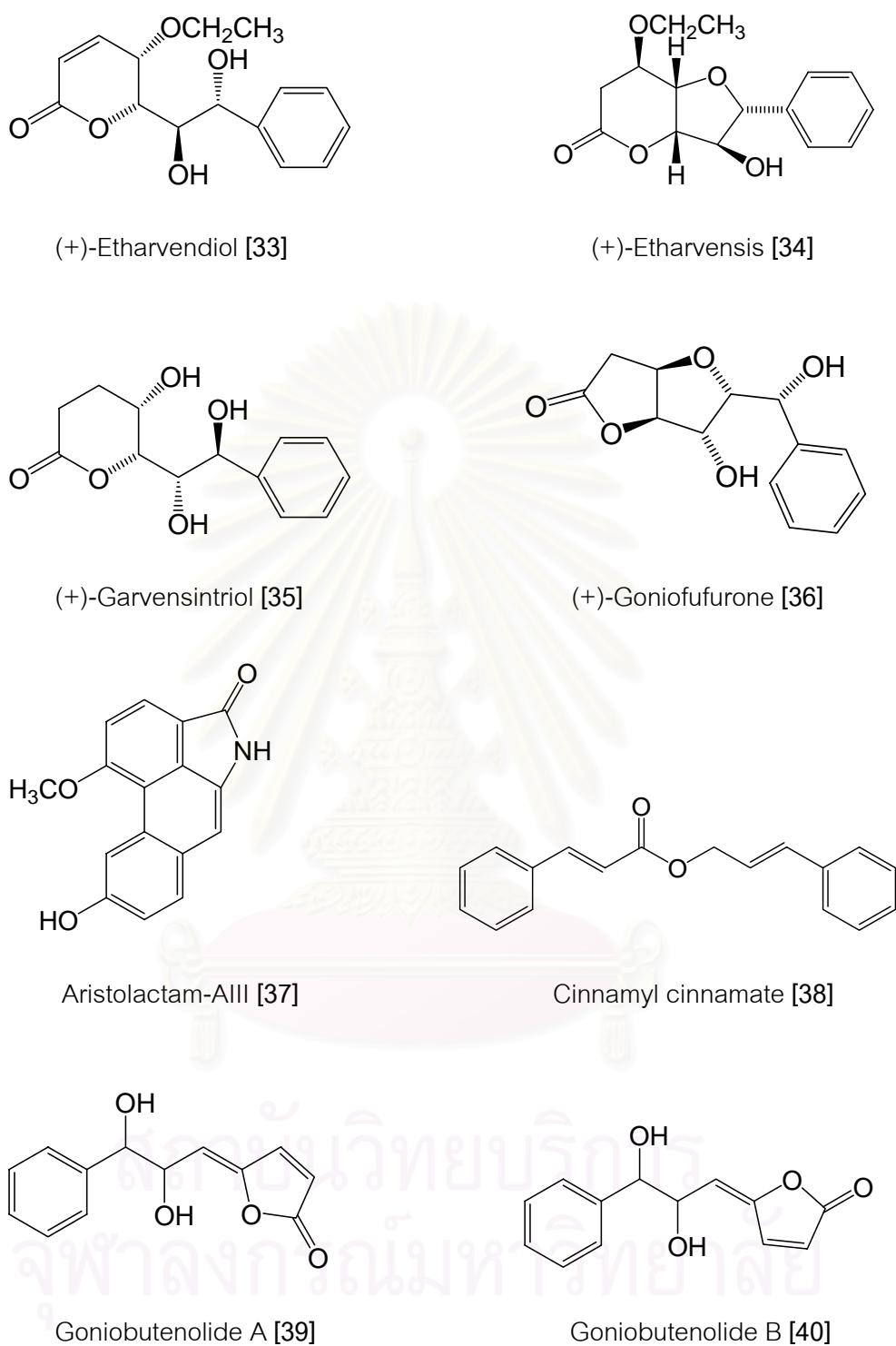


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

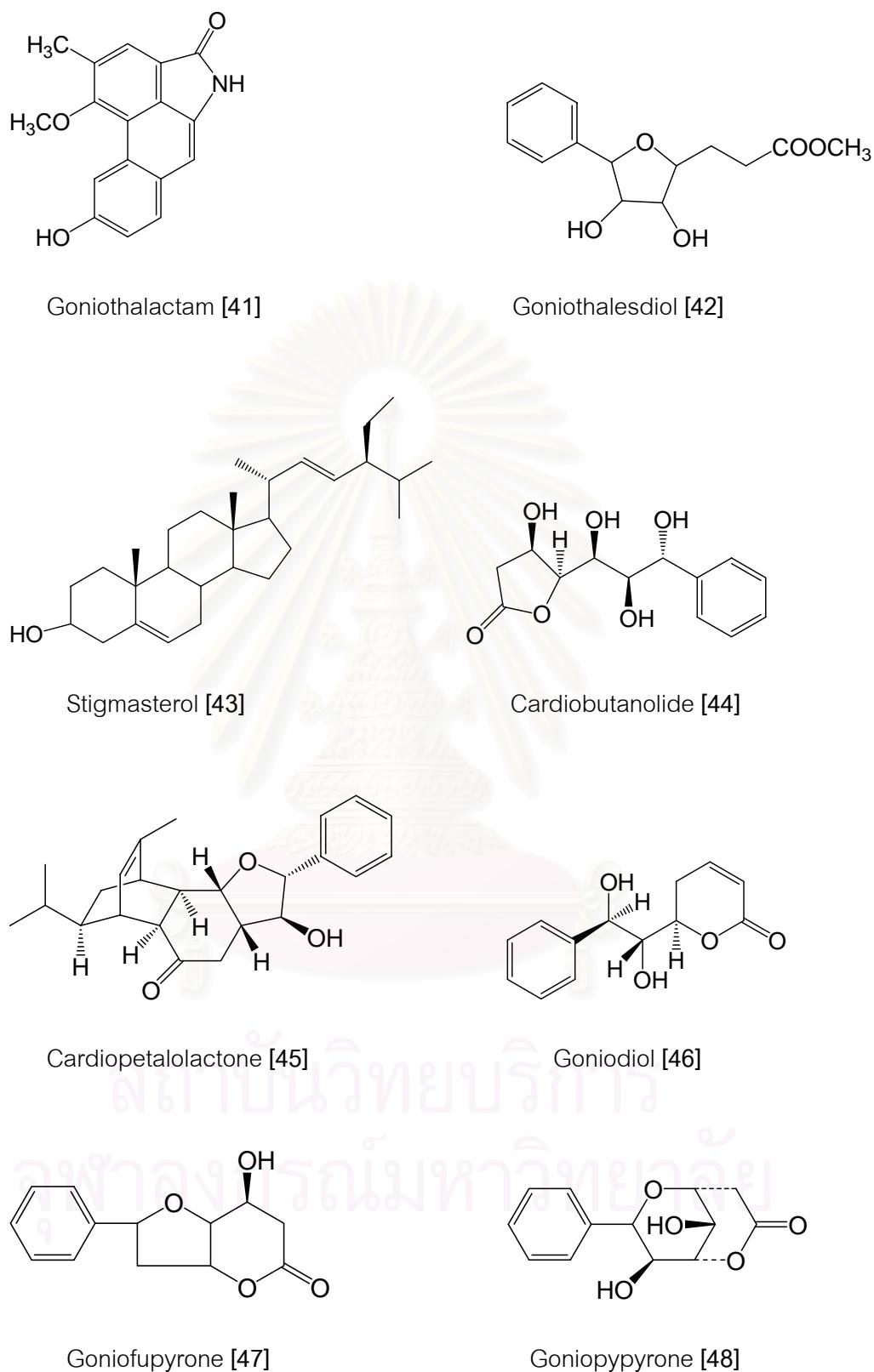


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

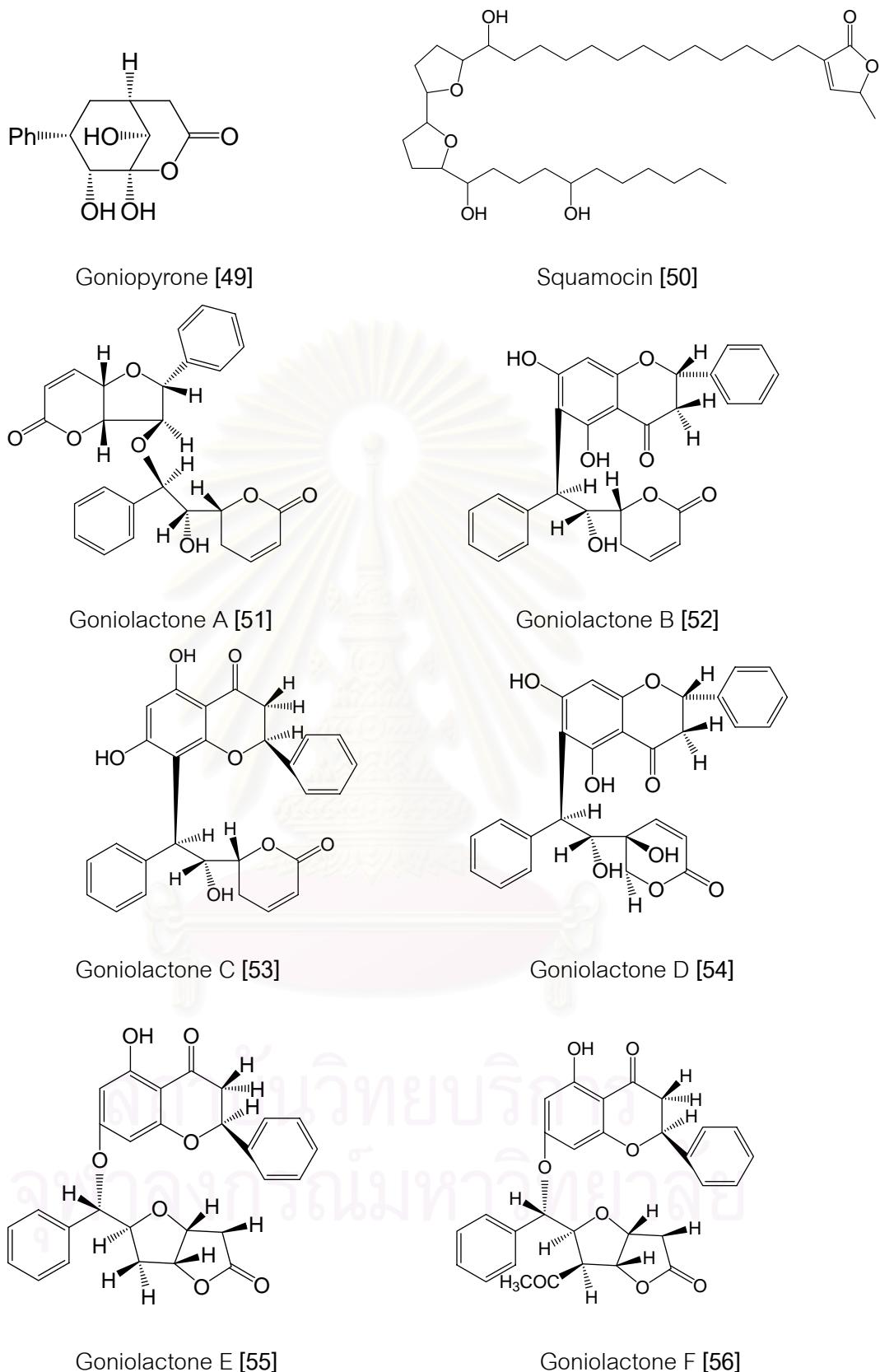


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

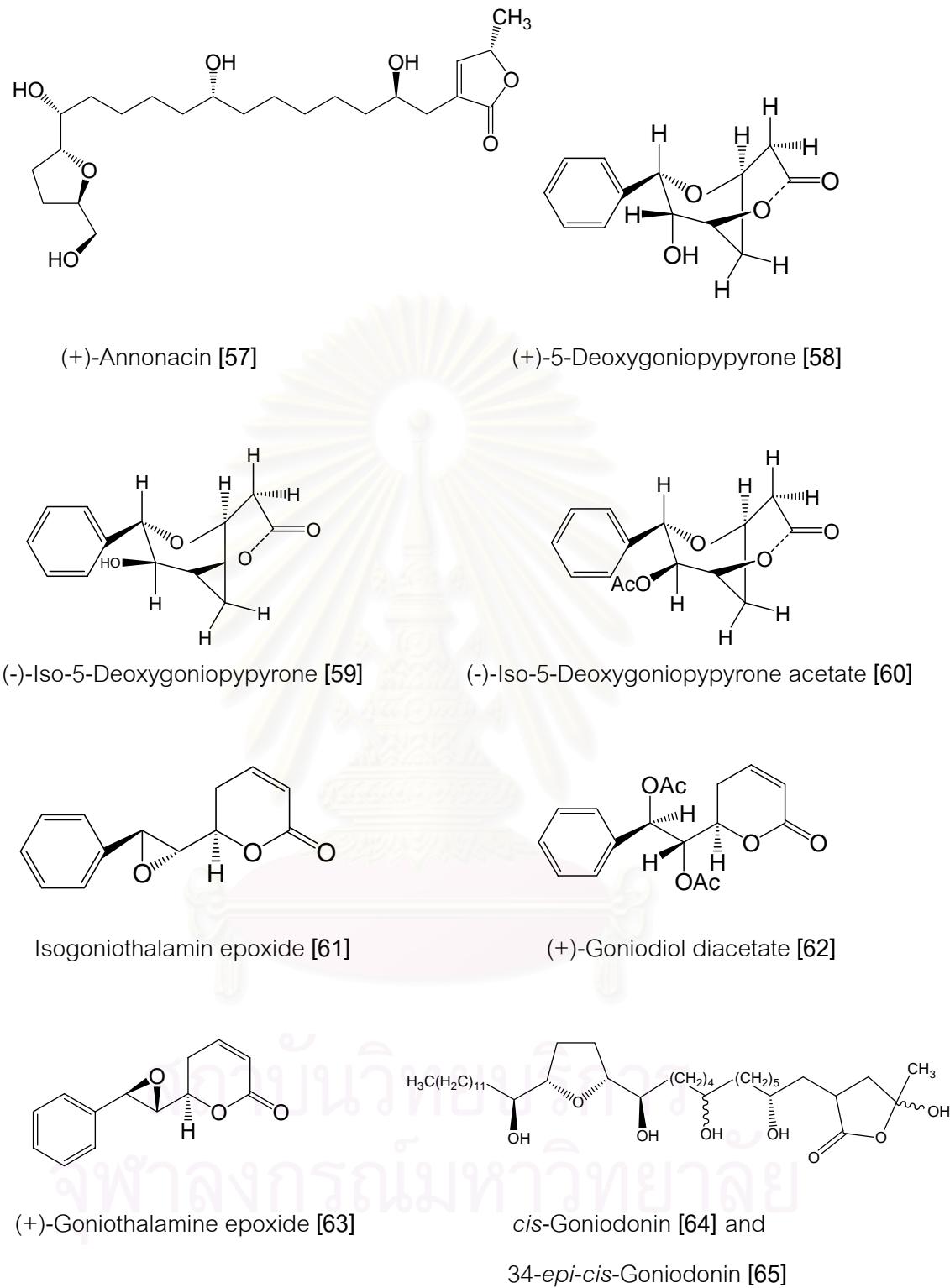
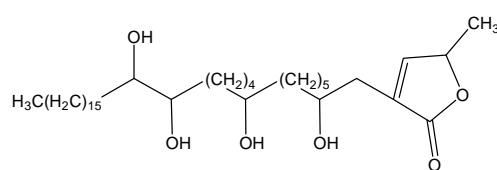
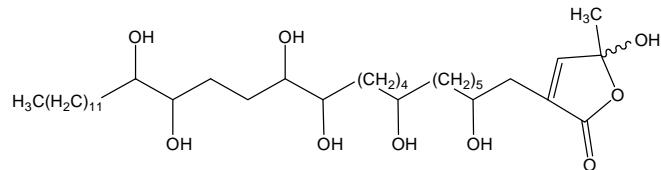


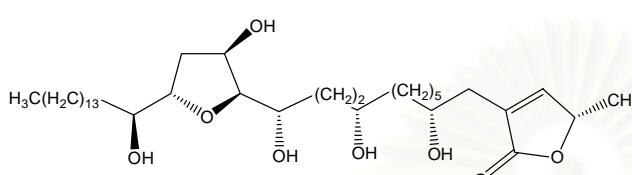
Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)



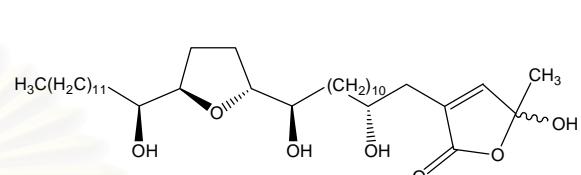
Donbutocin [66]



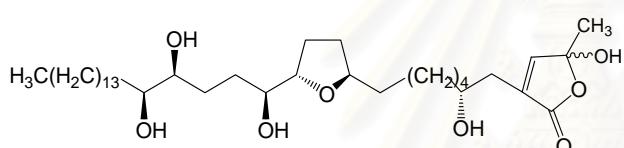
Donhepocin [67] and



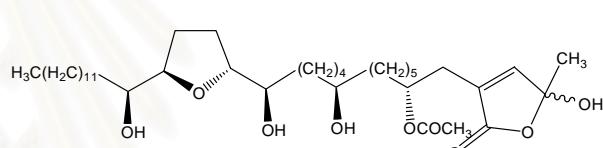
Donnaienin [69]



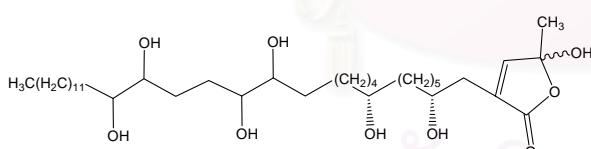
Donnaienin A [70] and



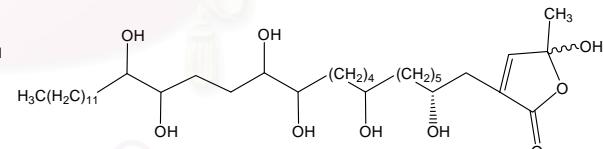
Donnajenin B [72] and



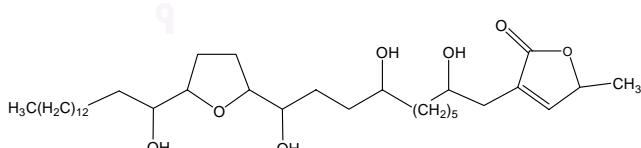
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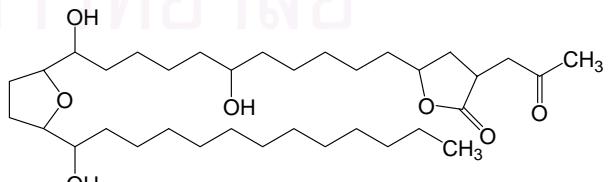
Donnaienin D [76] and



Donhexocin [78]

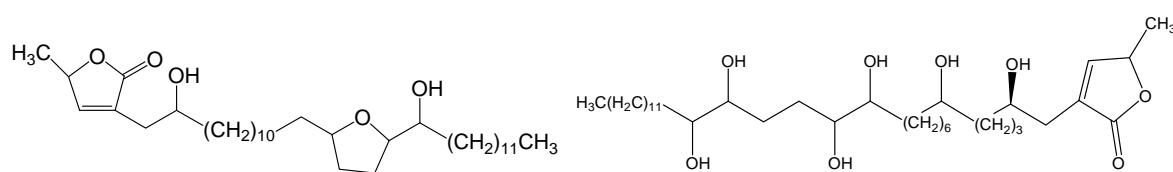


Goniothalamicin [79]



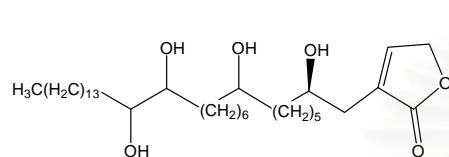
Isoannonacin [80]

Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

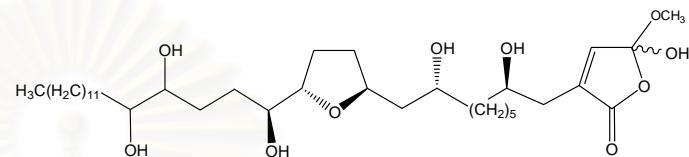


Murisolin [81]

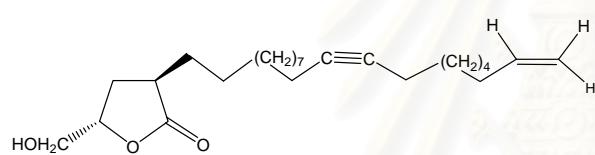
Gardnerilins A [82]



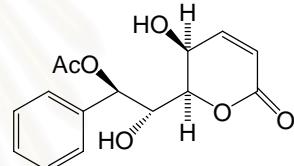
Gardnerilin B [83]



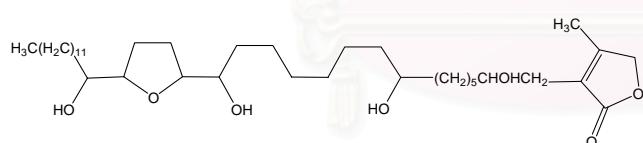
Gardnerinin [84] and 34-epi-gardnerinin [85]



Goniothalamusin [86]

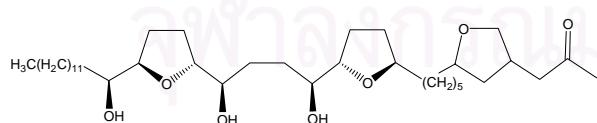


8-Acetylgoniotriol [87]



Annomontacin [88]

Asimilobin [89]



2,4-cis and trans-Gigantecin [90]

Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

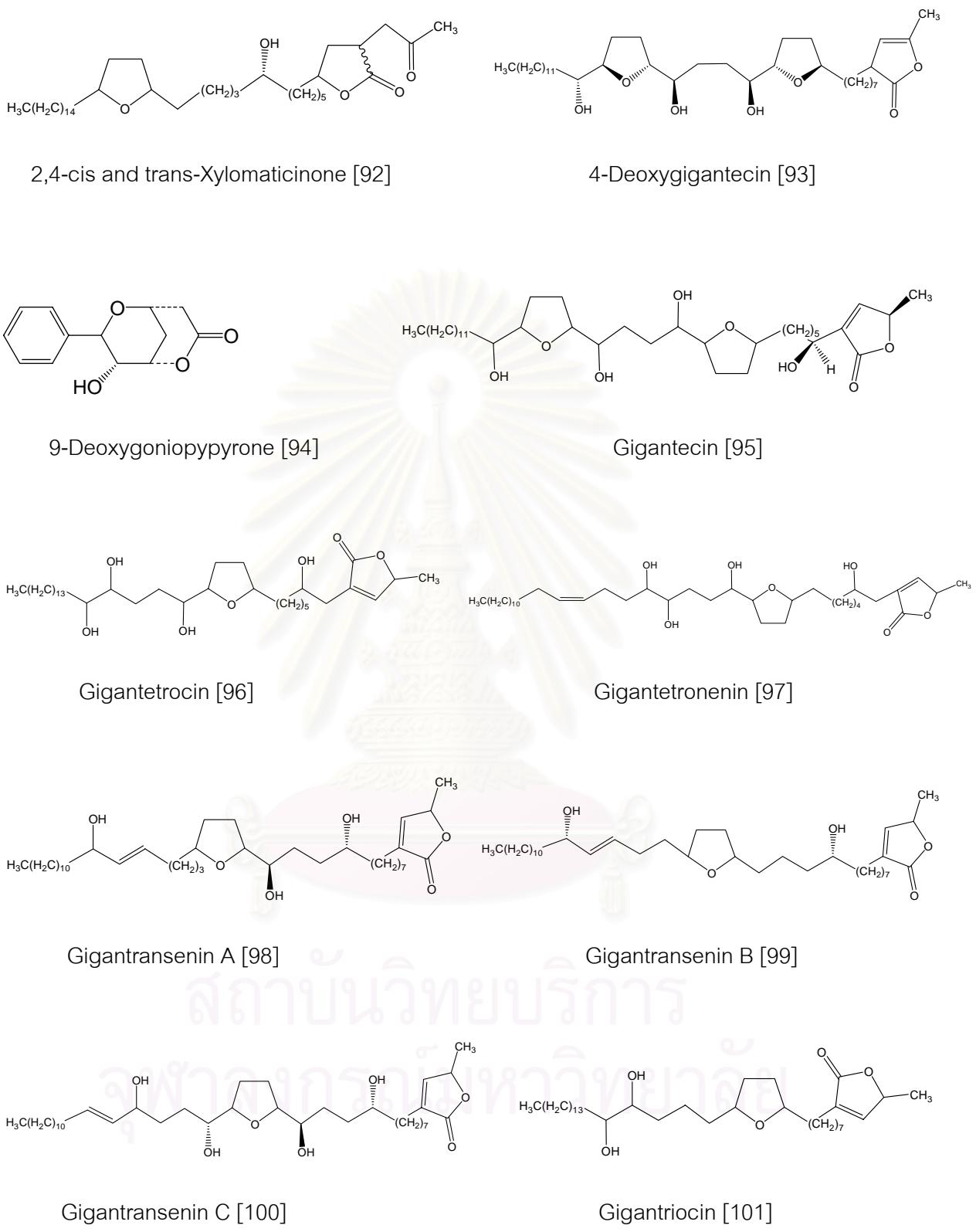


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

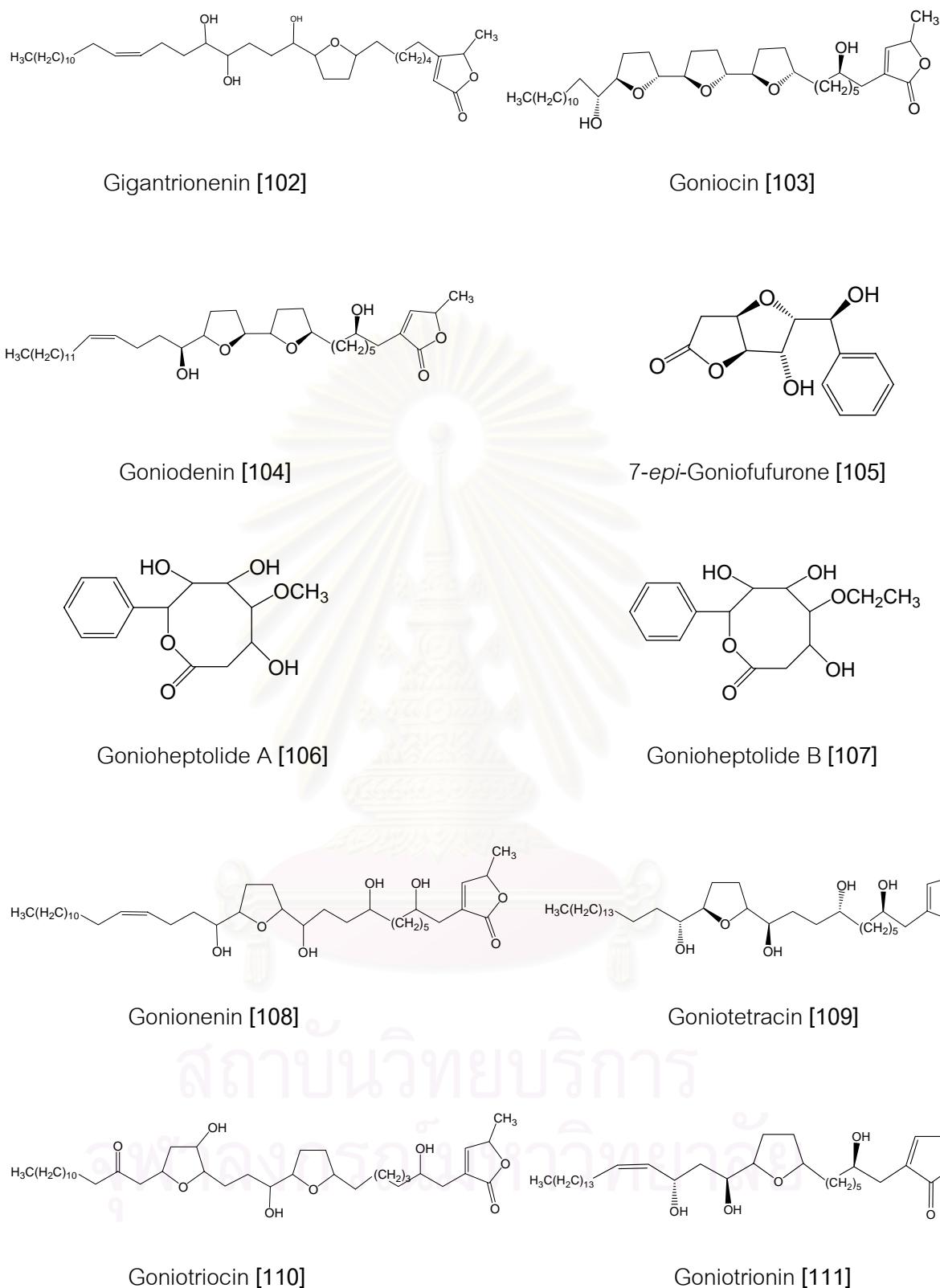


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

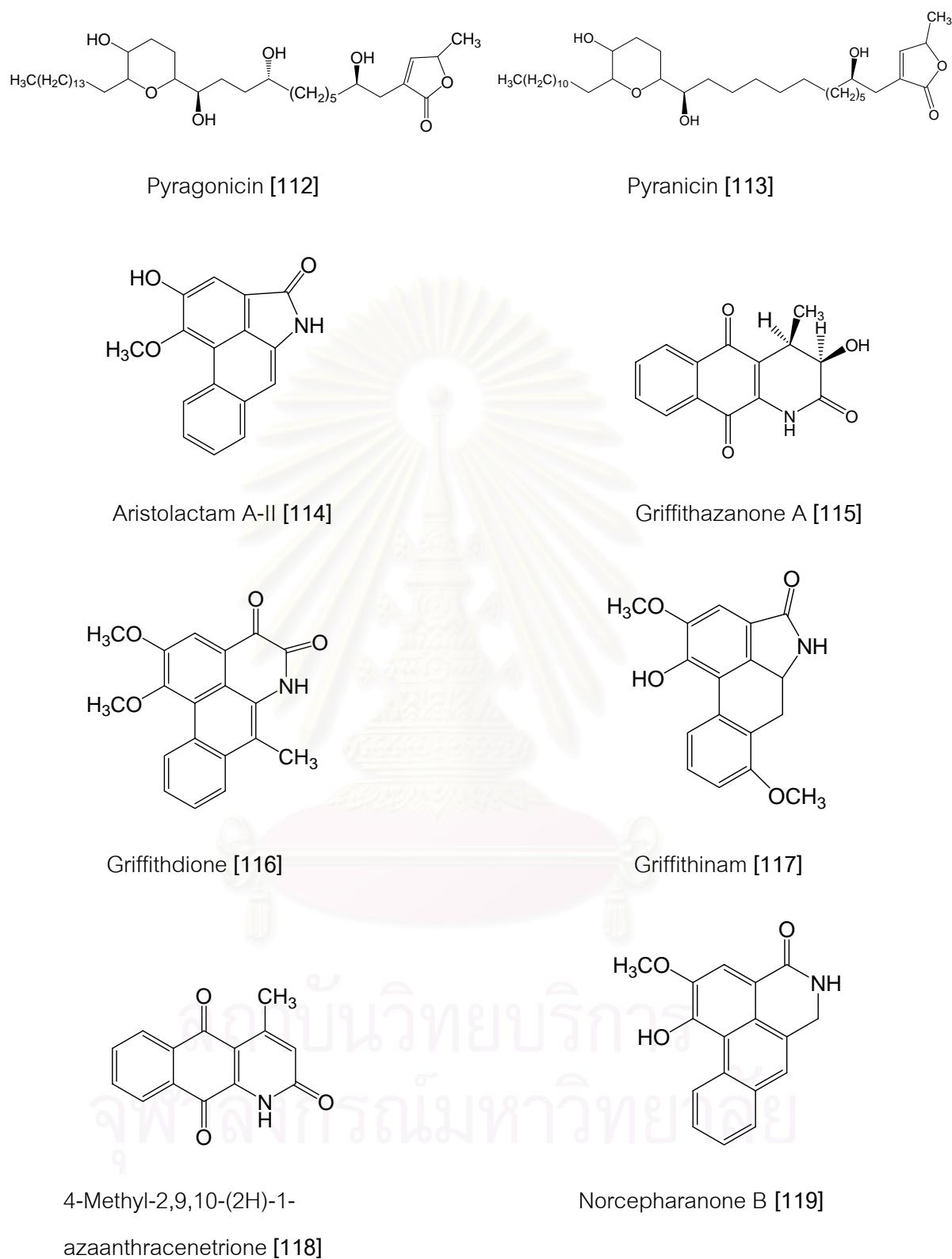


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

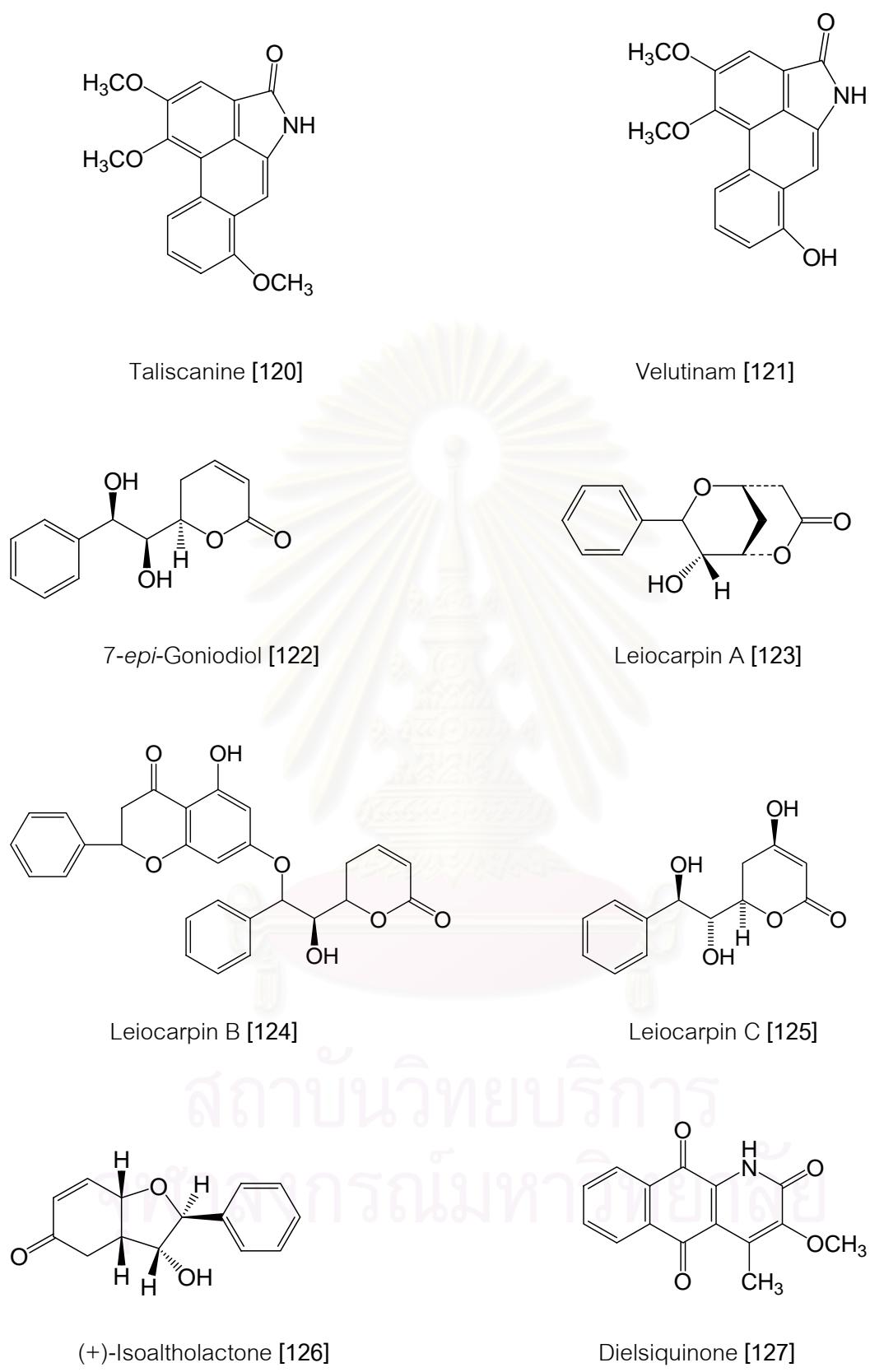
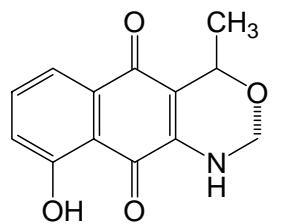
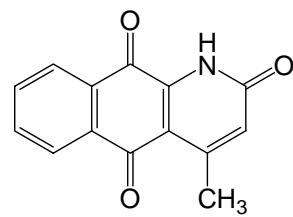


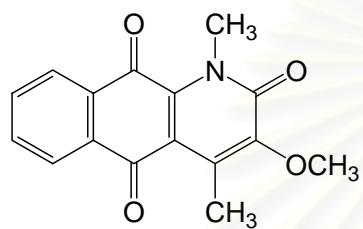
Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)



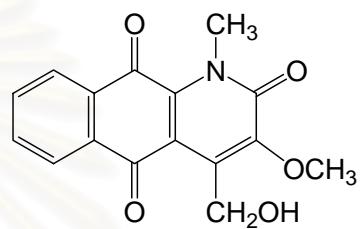
5-Hydroxy-3-amino-2-aceto-
1,4-naphthoquinone [128]



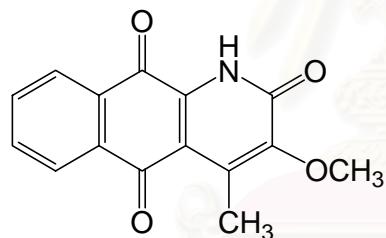
Marcanine A [129]



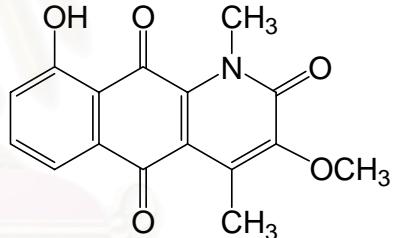
Marcanine B [130]



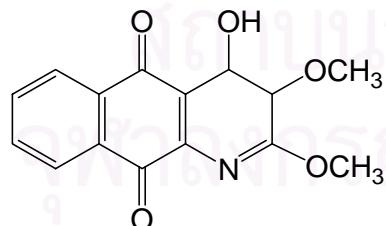
Marcanine C [131]



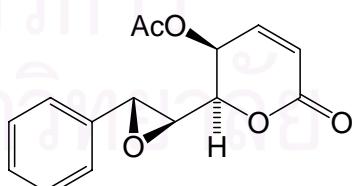
Marcanine D [132]



Marcanine E [133]



Scornazanone [134]



5-Acetoxyisogoniothalamin oxide [135]

Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

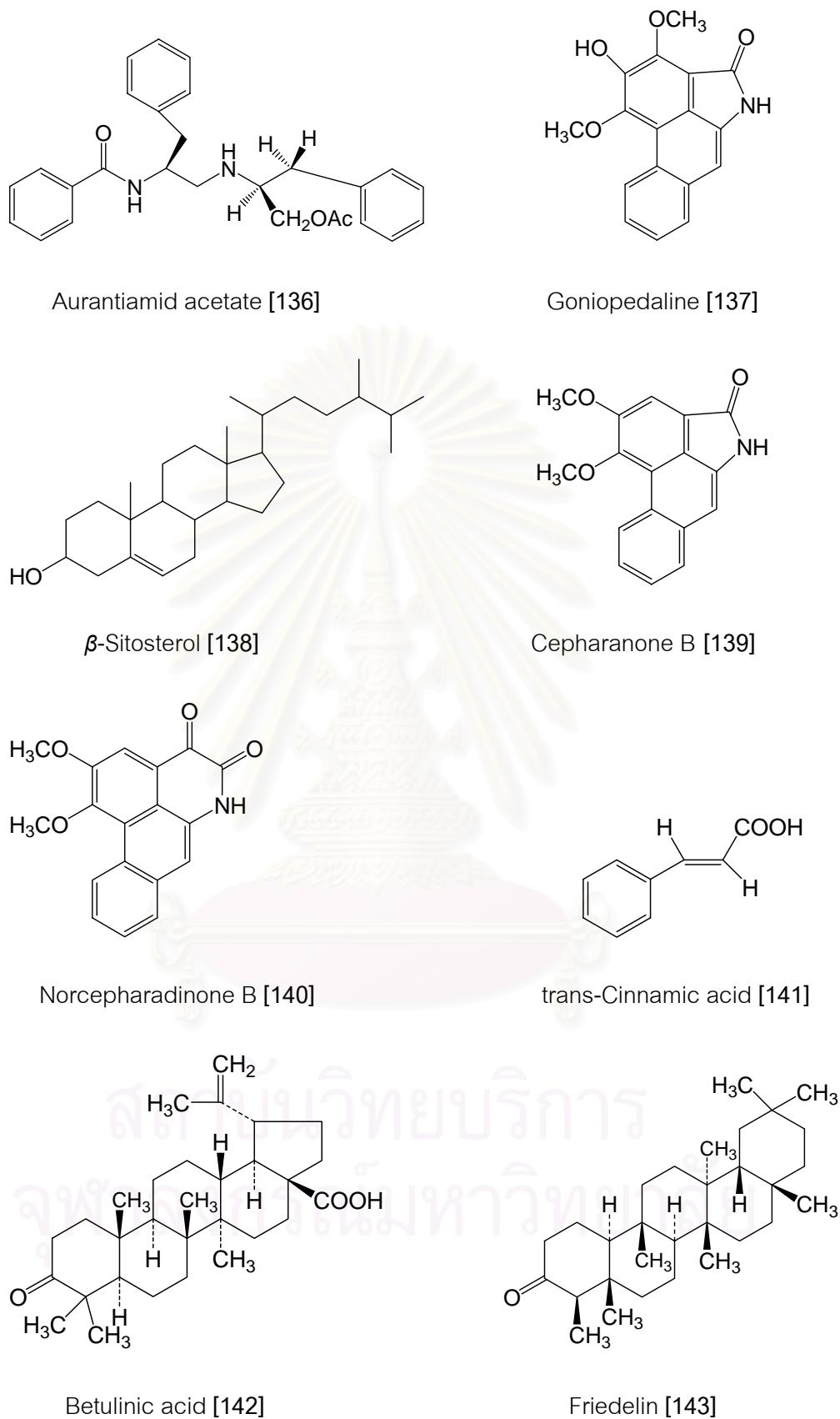
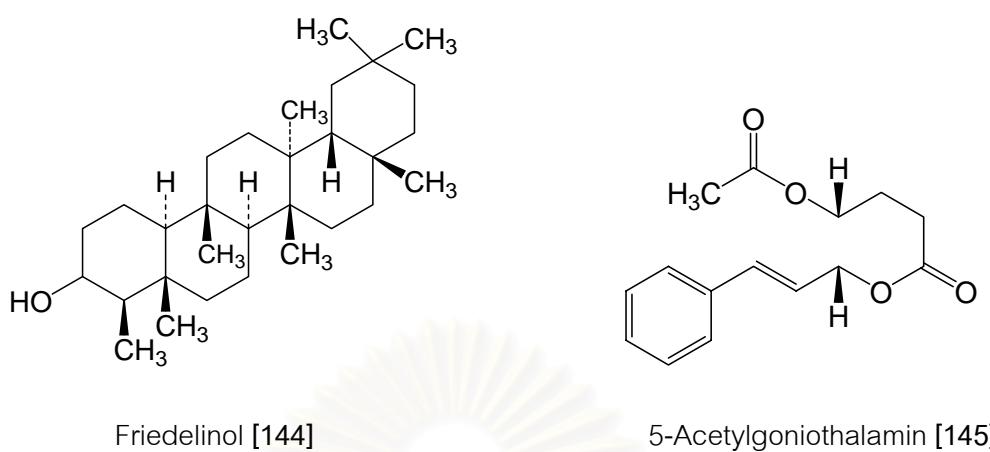


Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)



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Figure 3 Structures of compounds previously isolated from *Goniothalamus* spp. (continued)

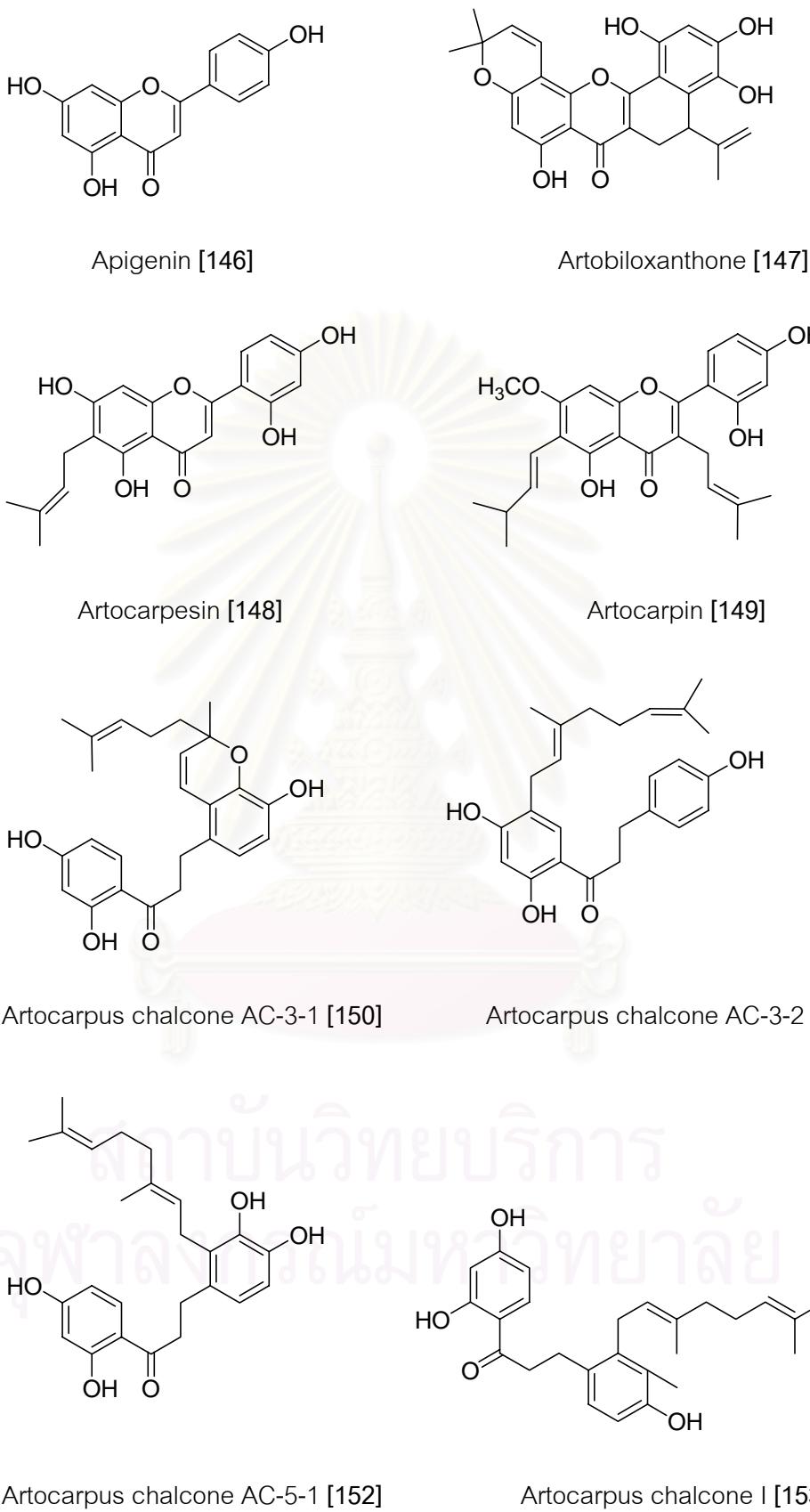
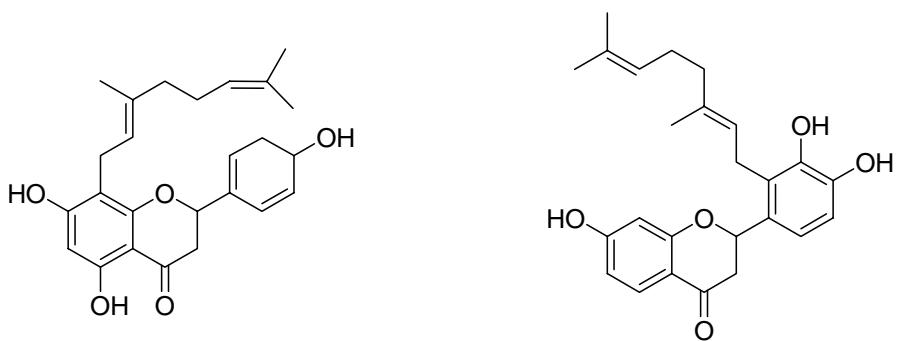
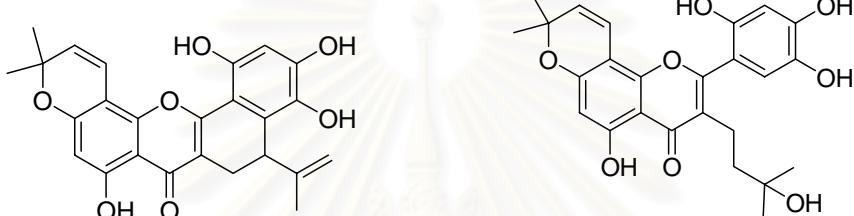


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp.



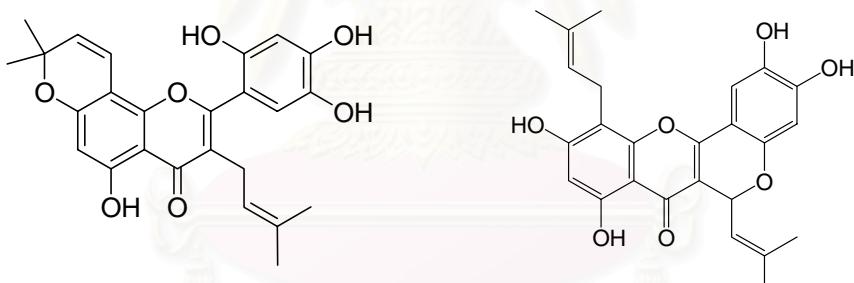
Artocarpus flavone AC-3-3 [154]

Artocarpus flavone AC-5-2 [155]



Artocarpus flavone KB-1 [156]

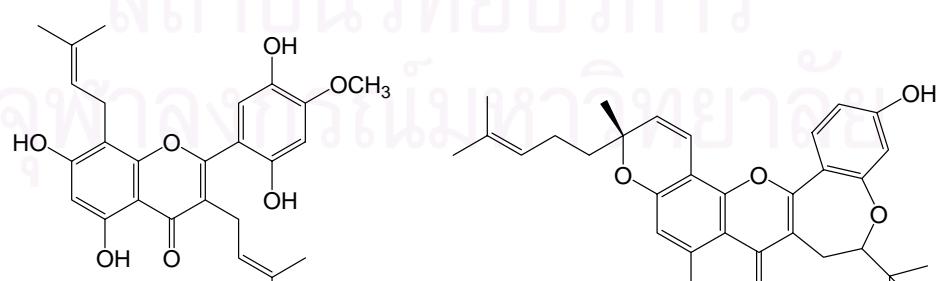
Artocarpus flavone KB-2 [157]



Artocarpus flavone KB-3 [158]

Artochamin B [159]

(Artonin E)



Artochamin D [160]

Artocommunol CC [161]

Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

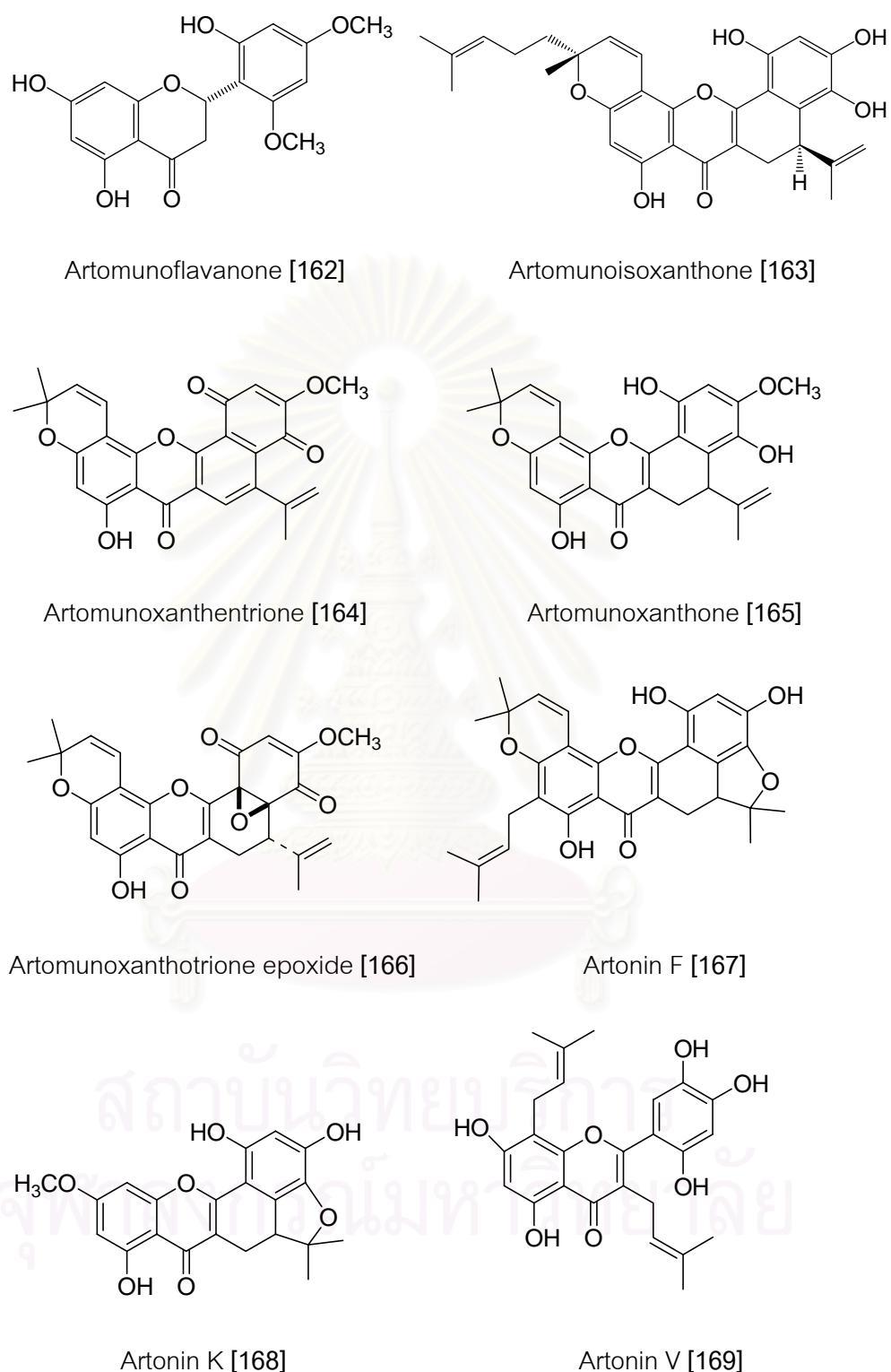


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

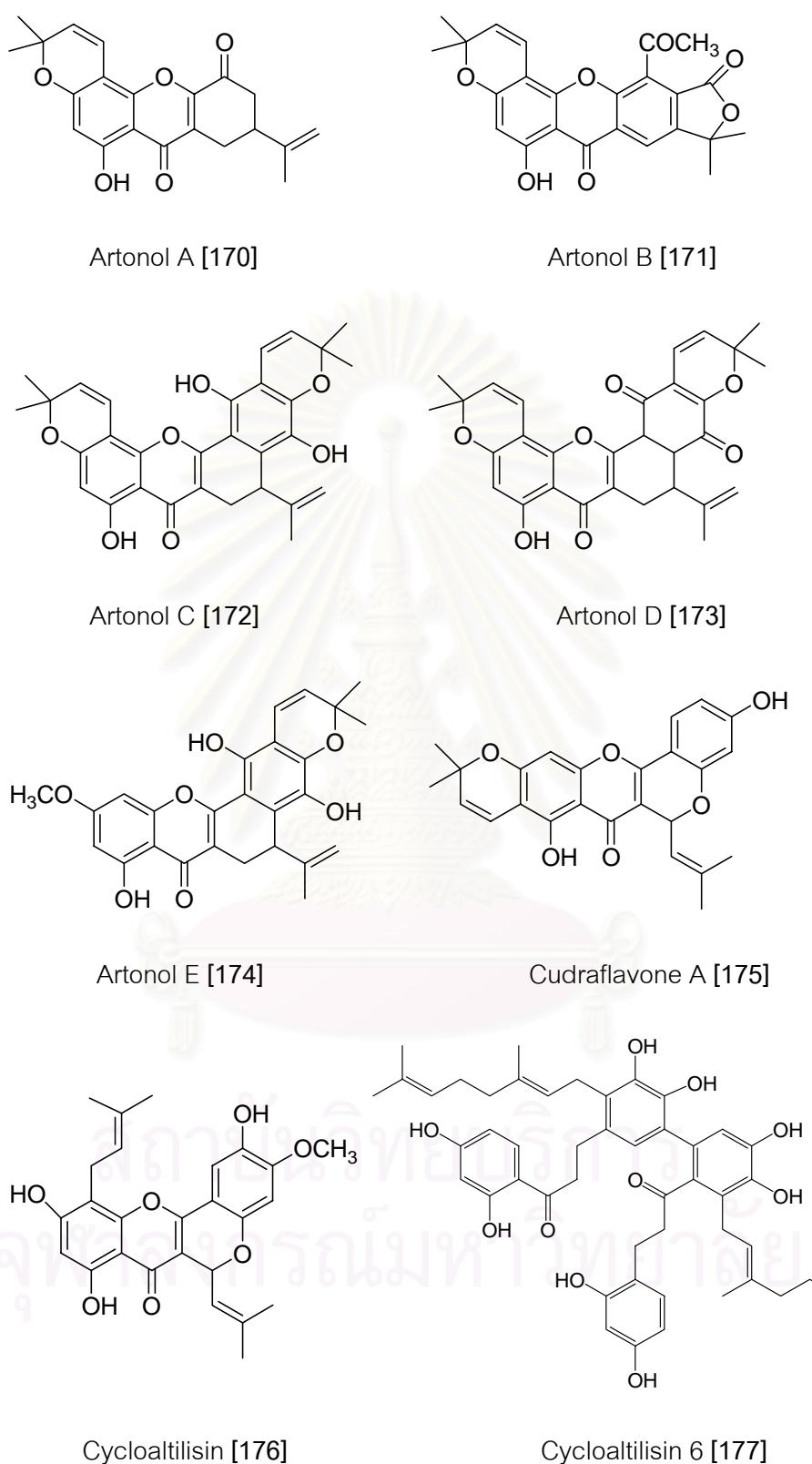


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

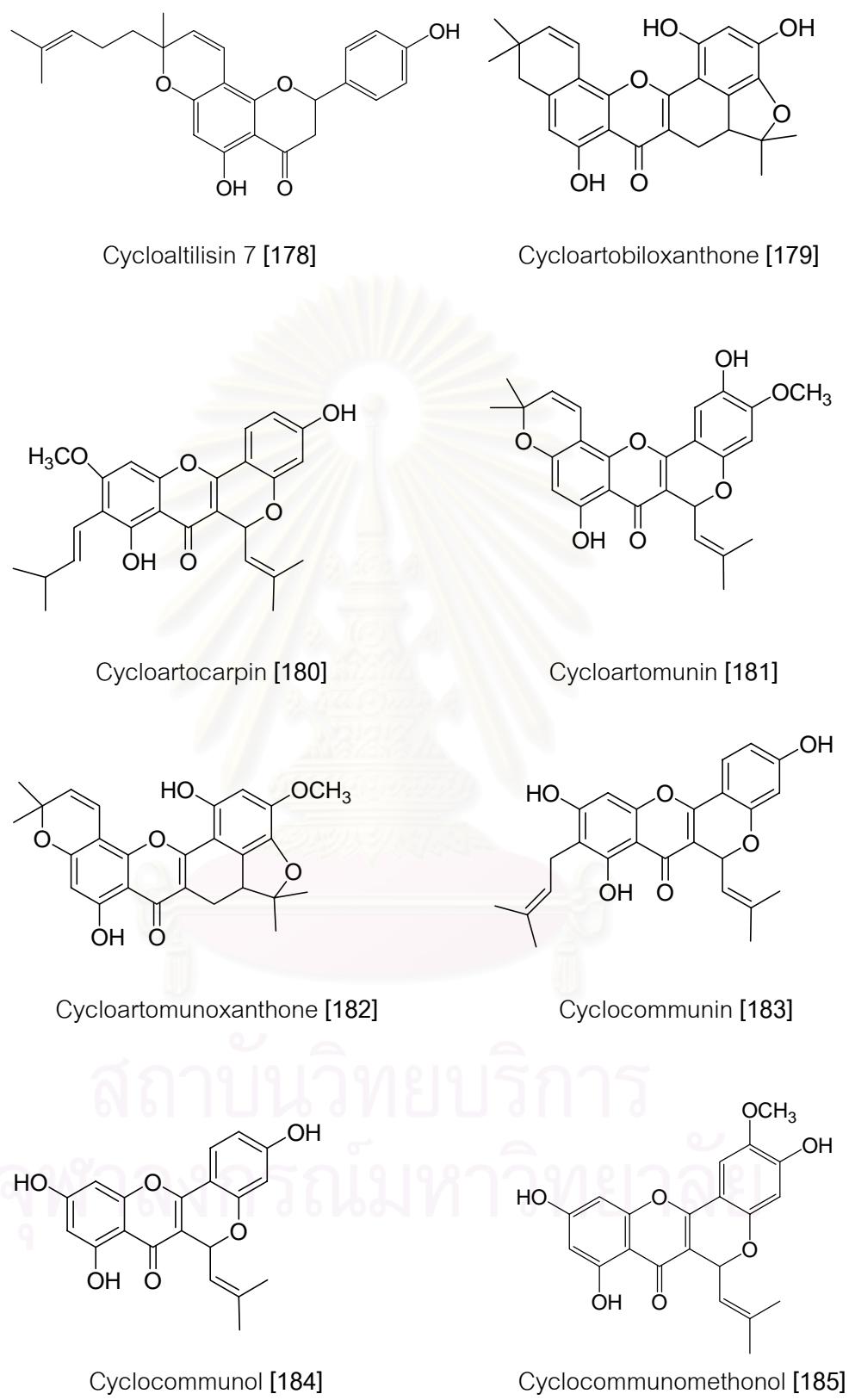


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

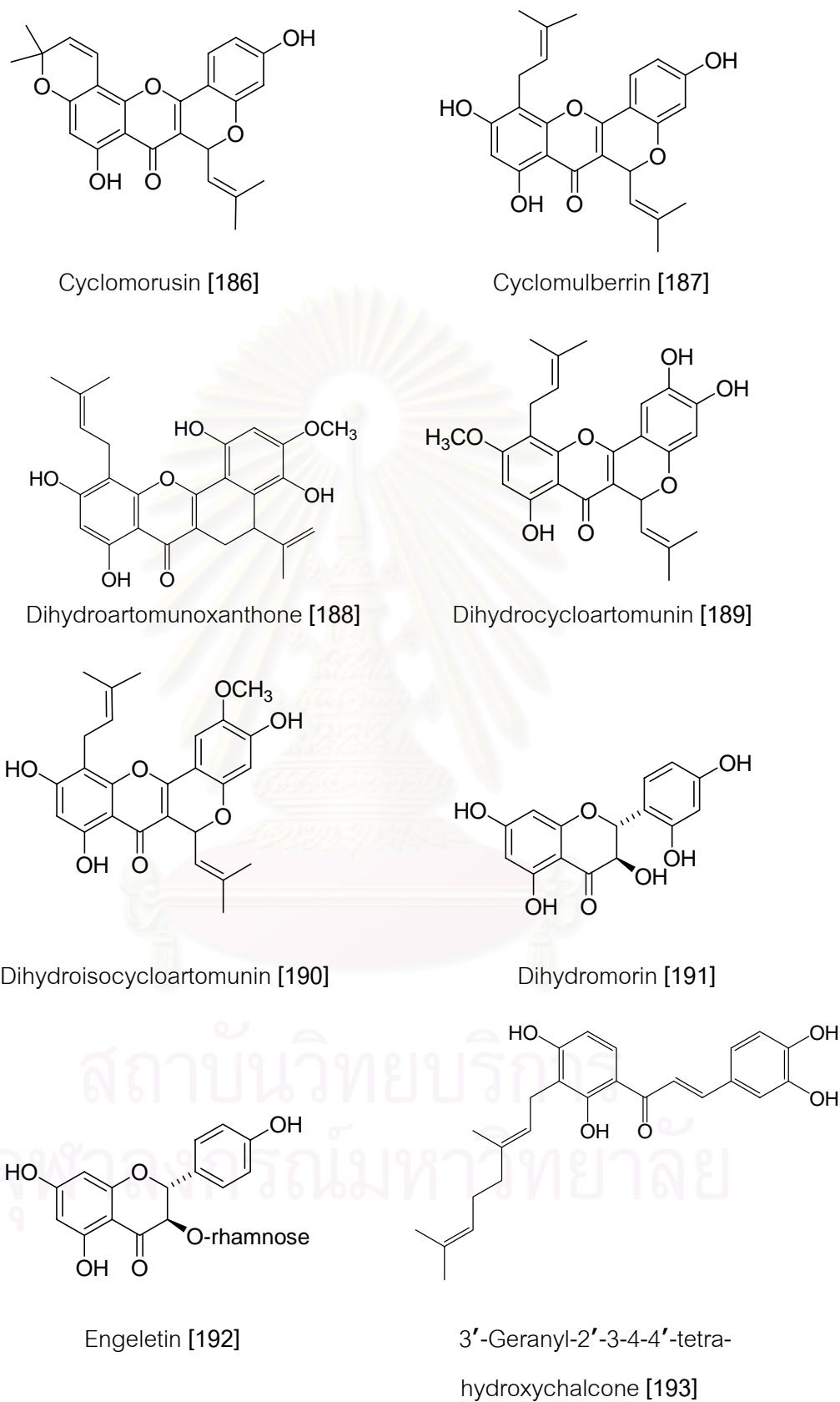


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

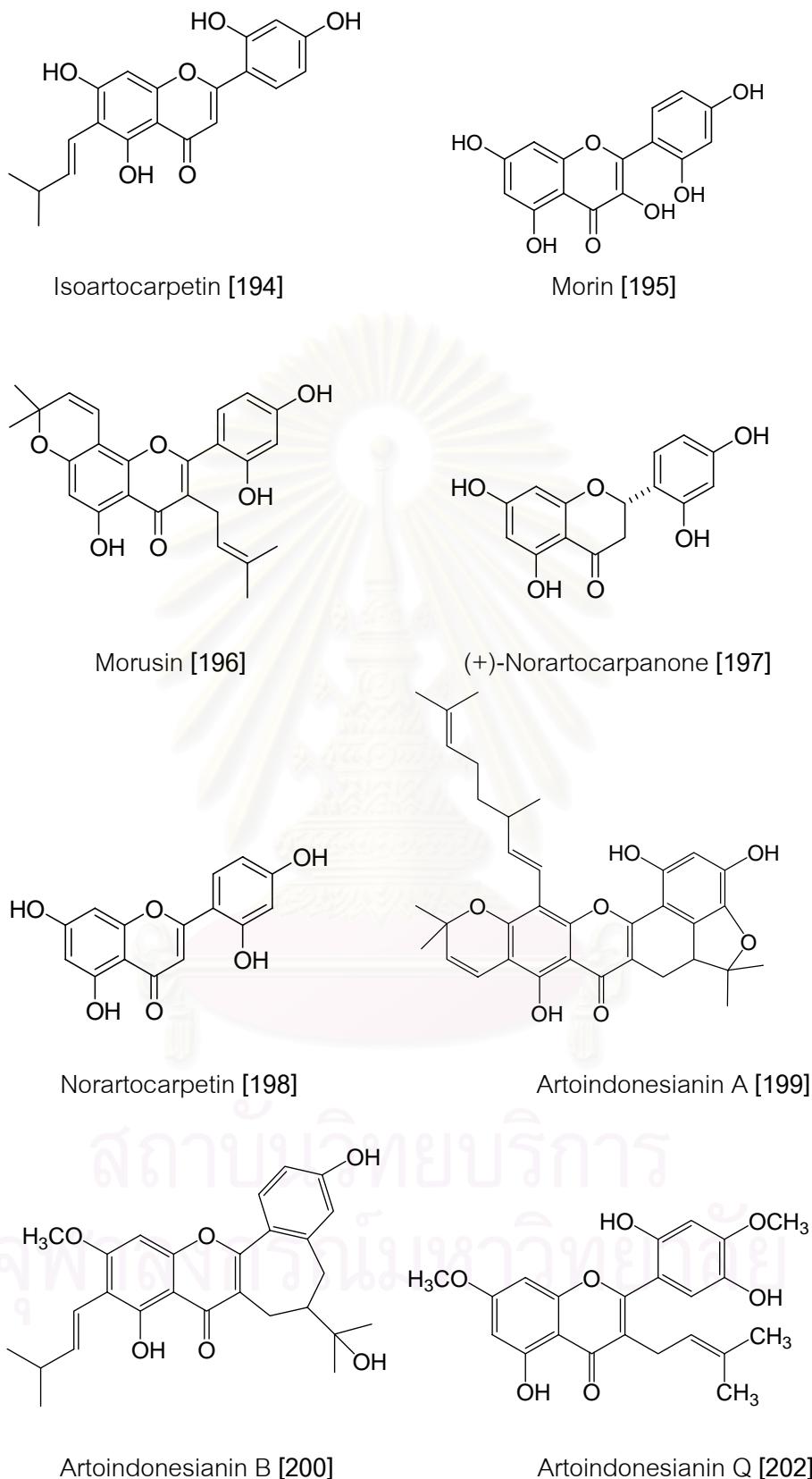


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

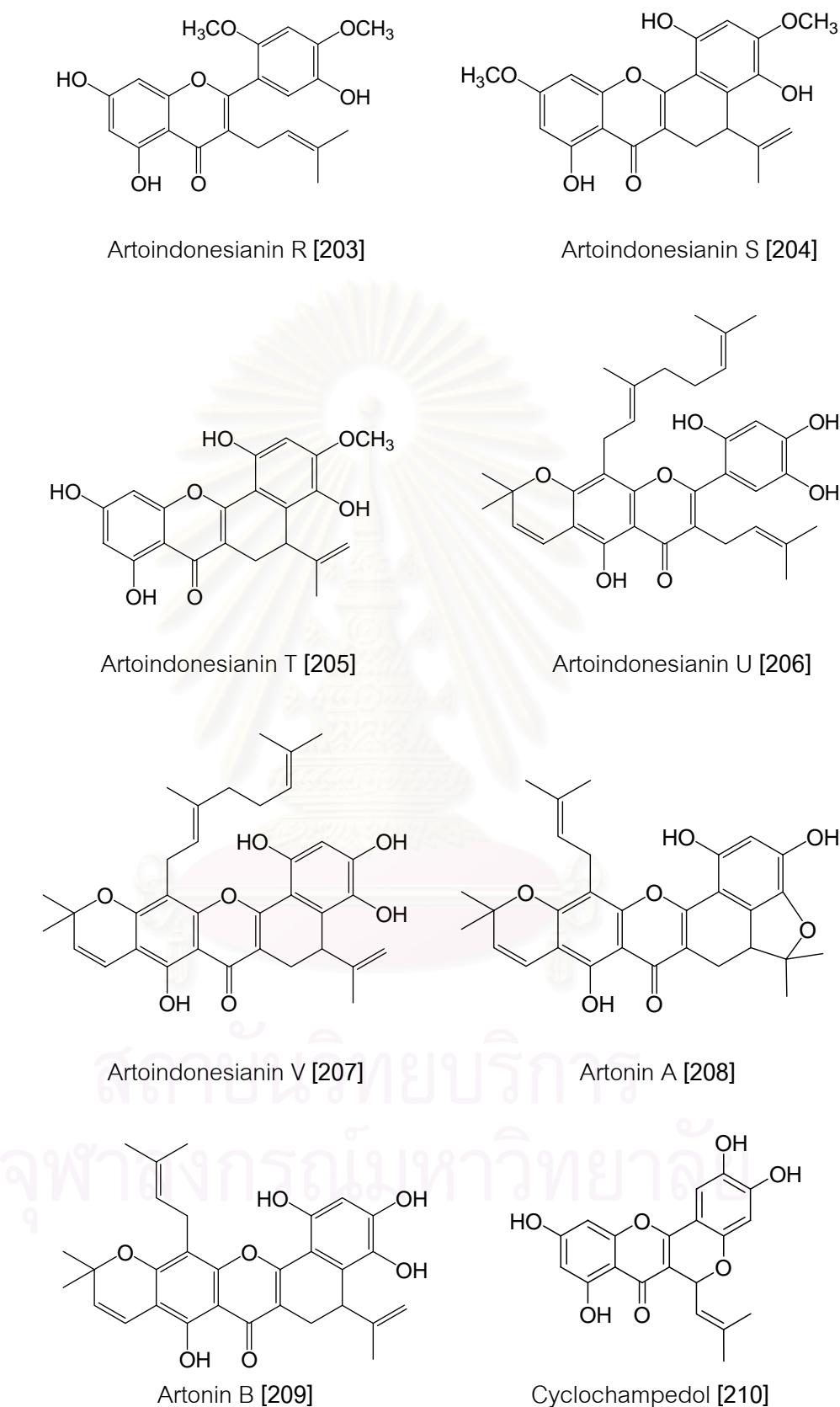


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

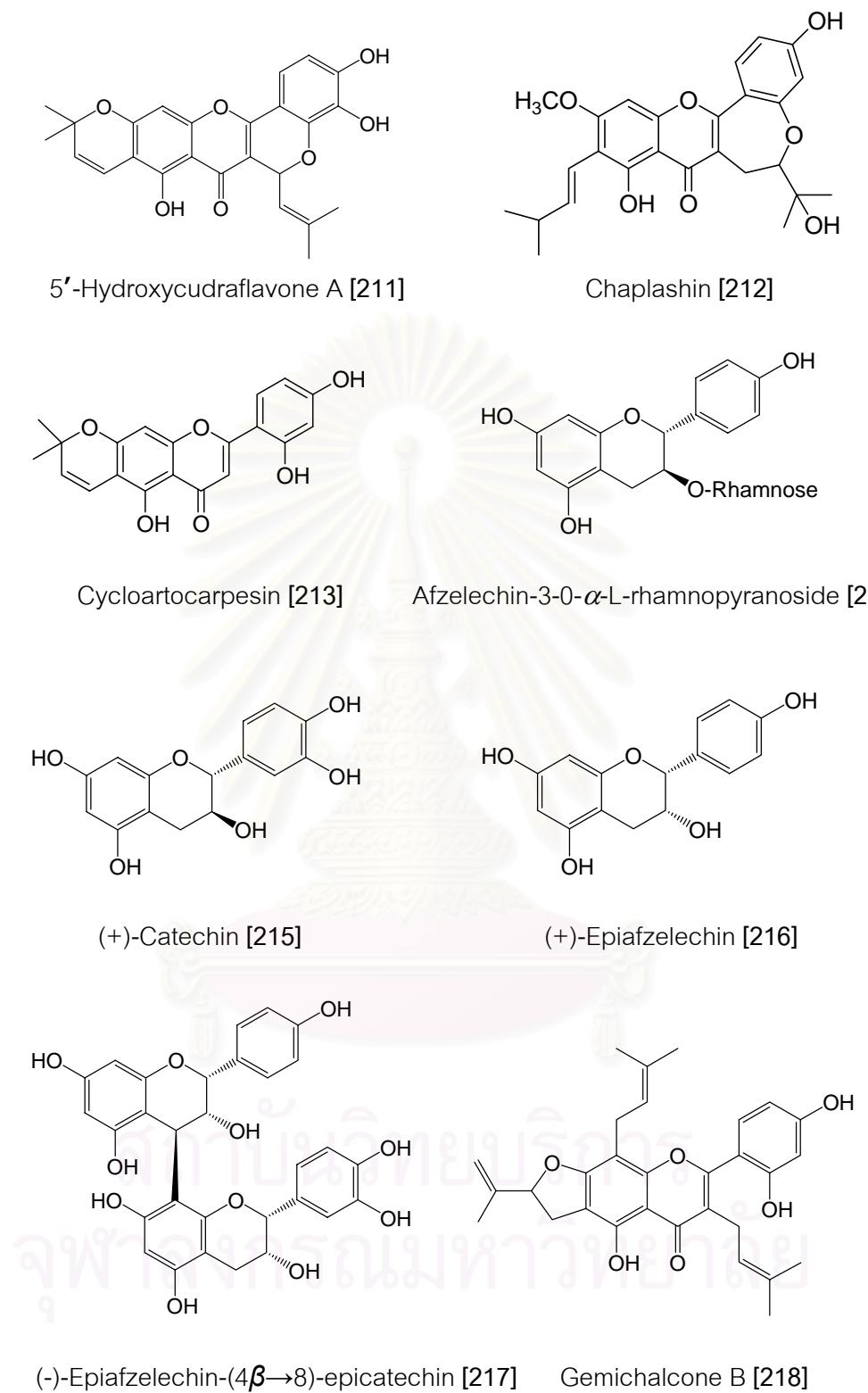


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

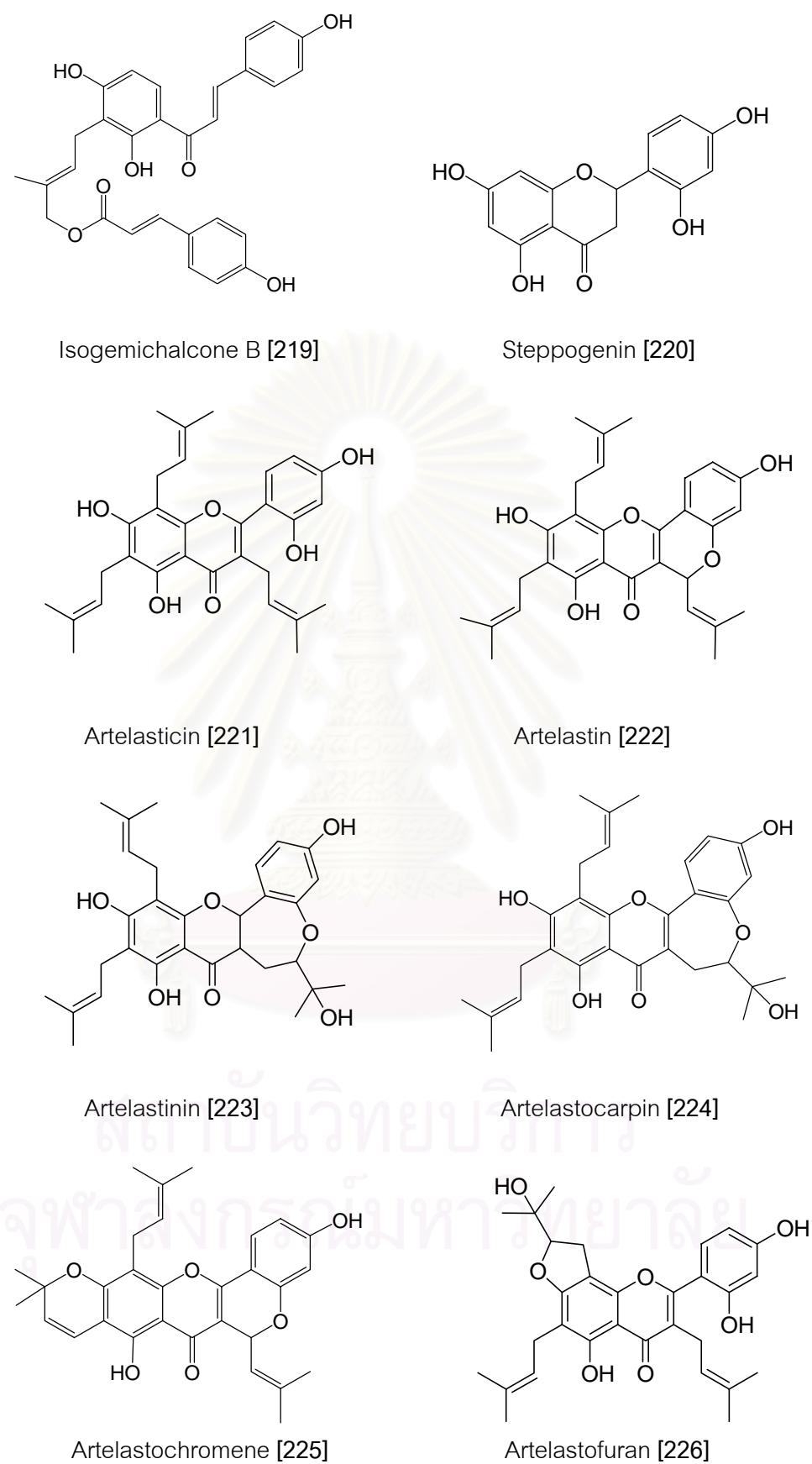


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

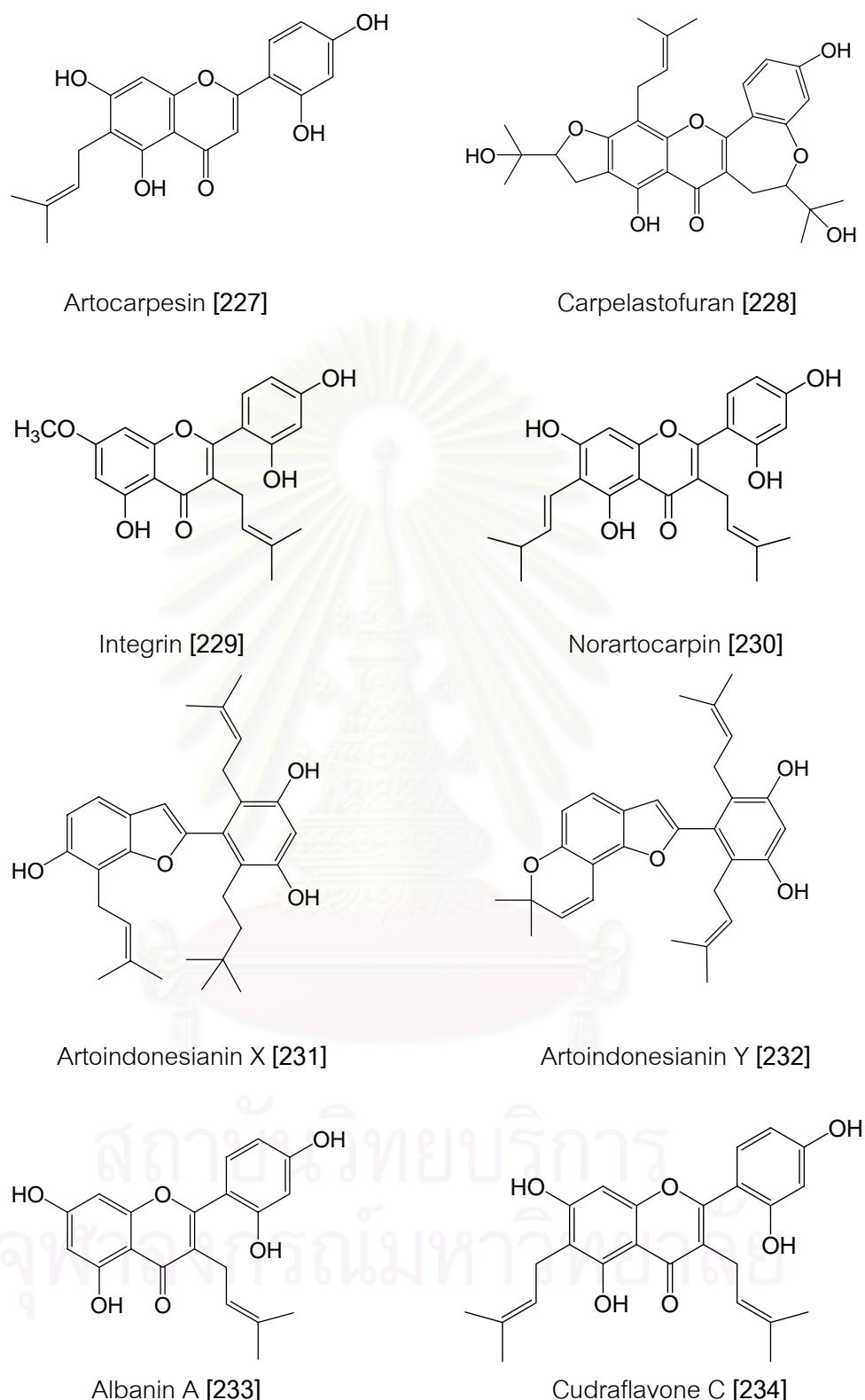


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

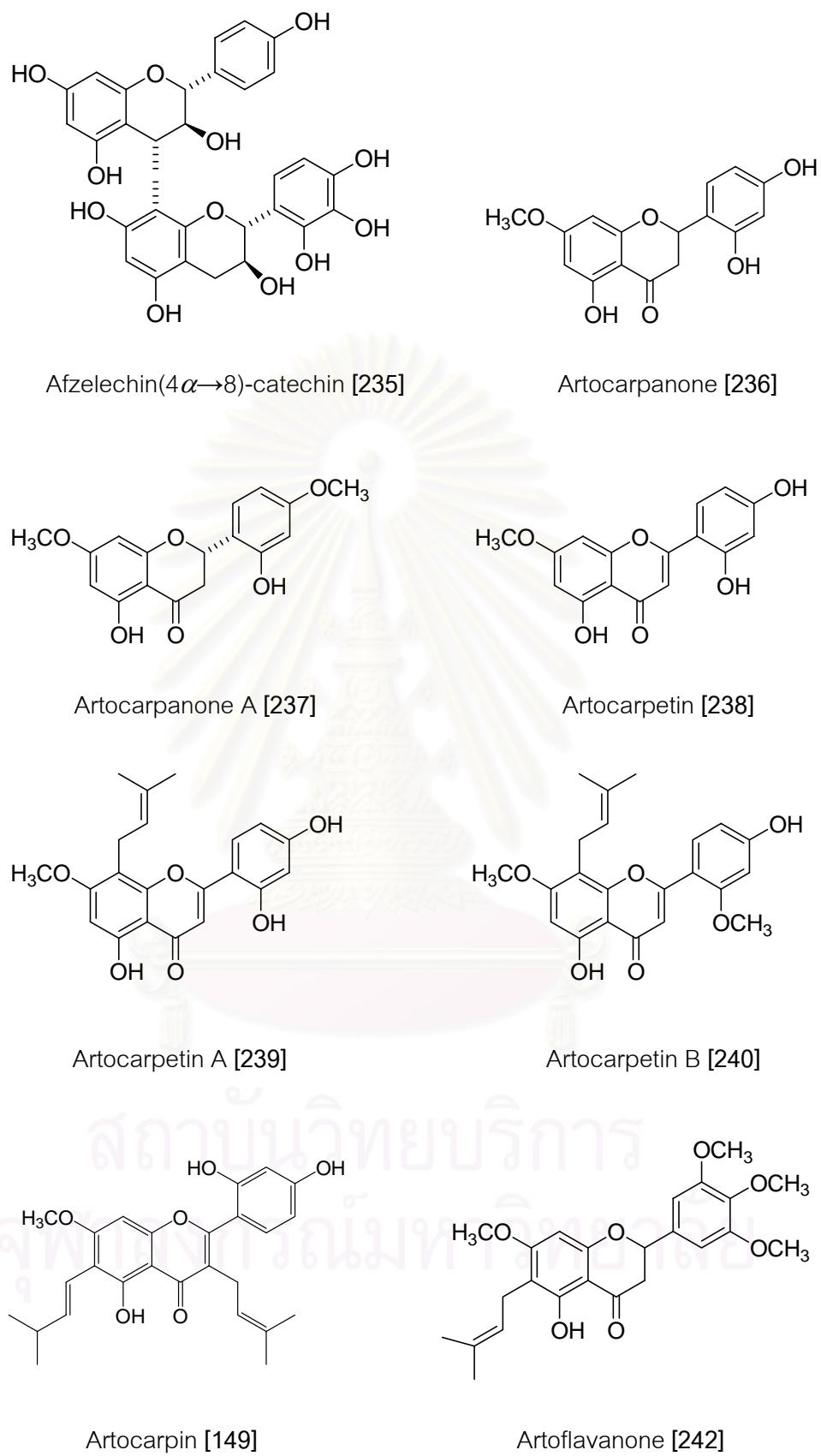


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

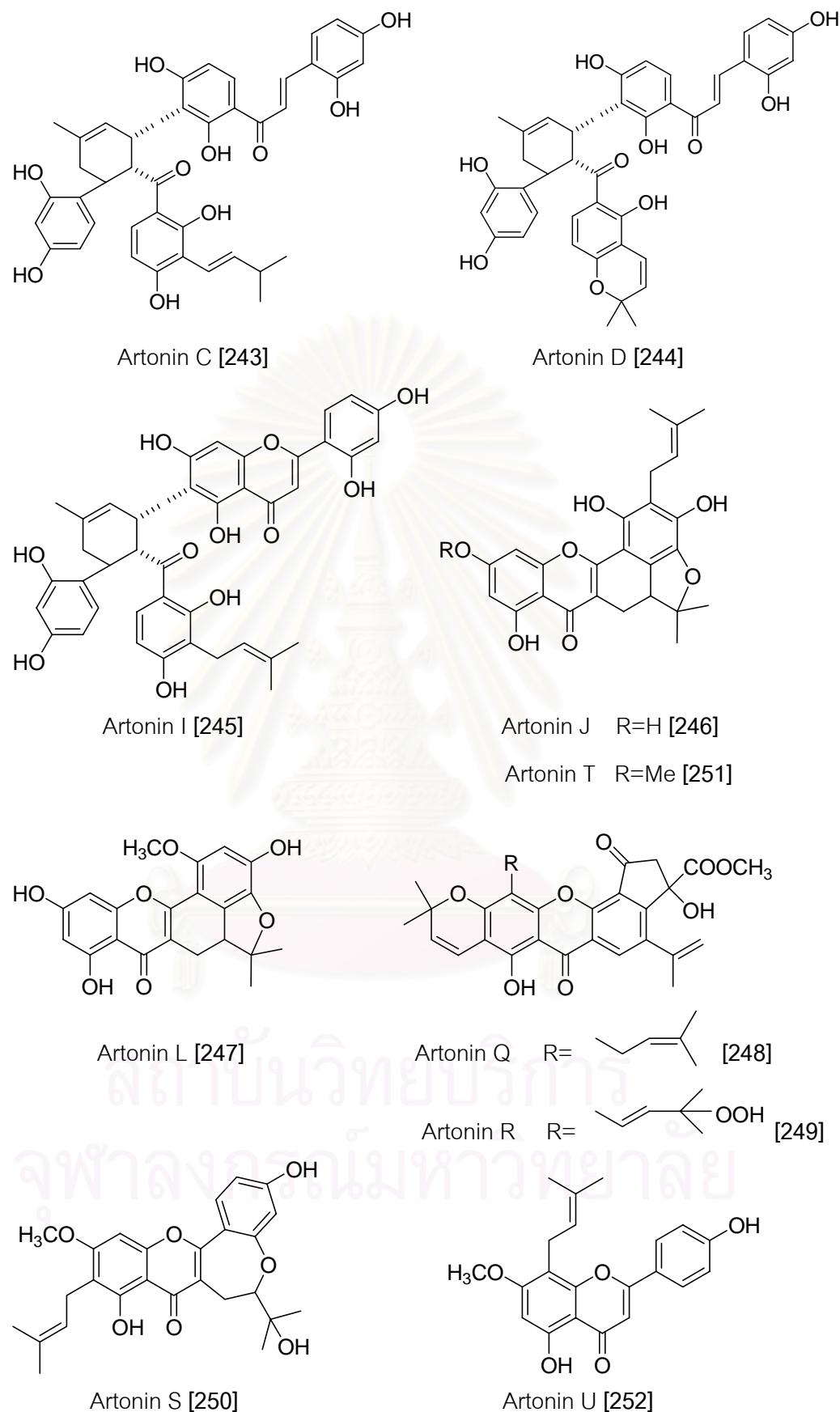


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

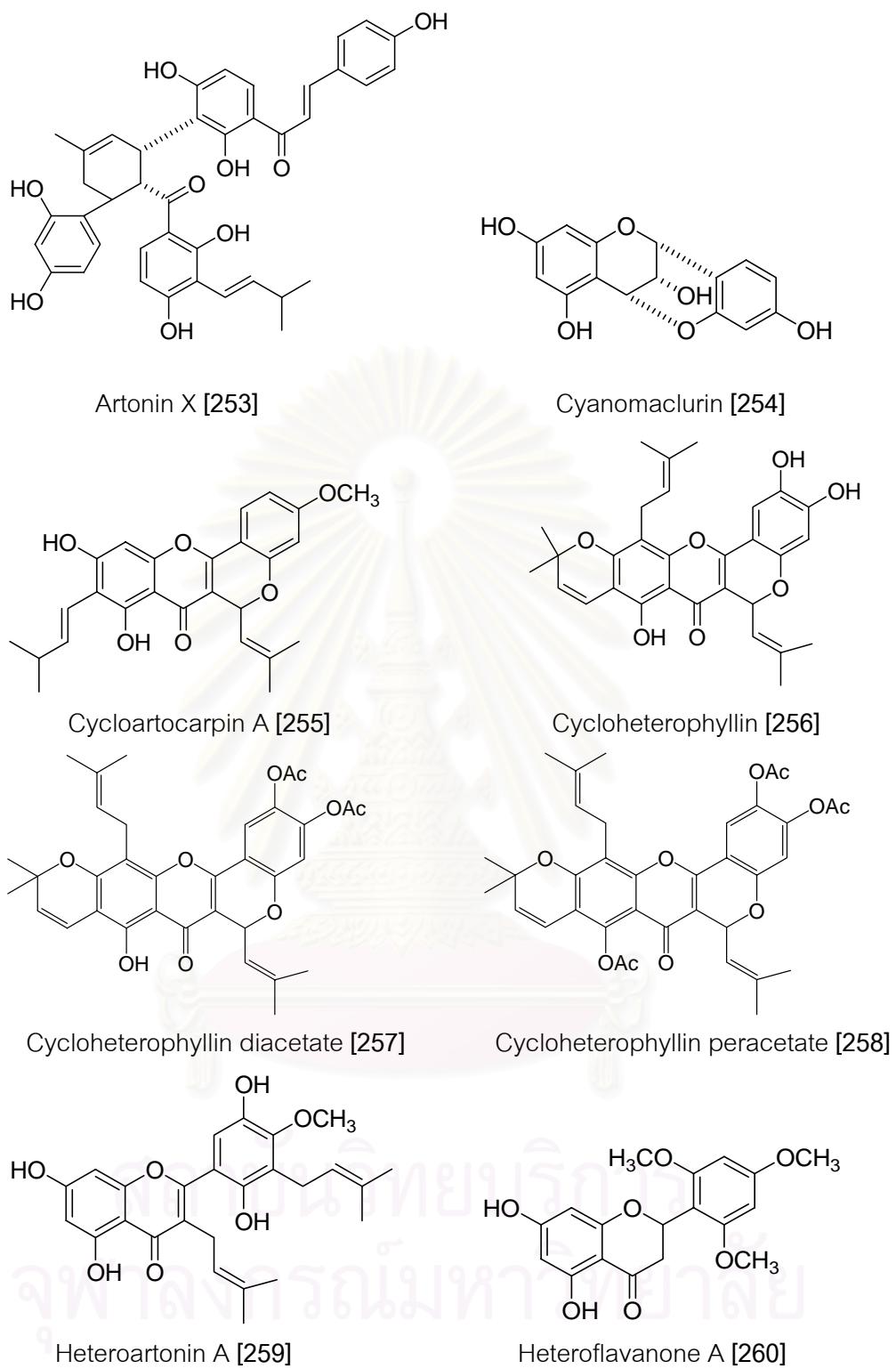


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

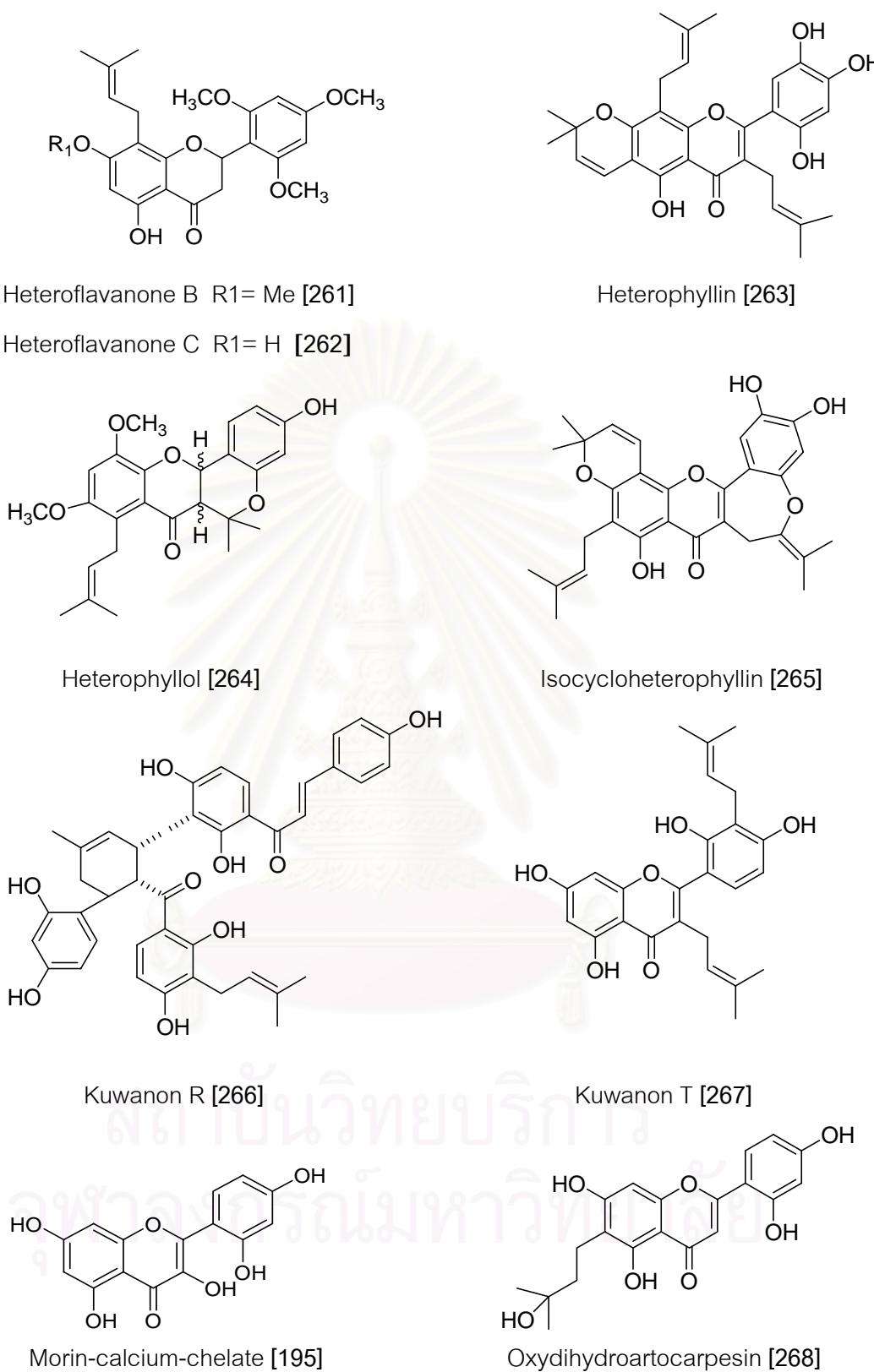


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

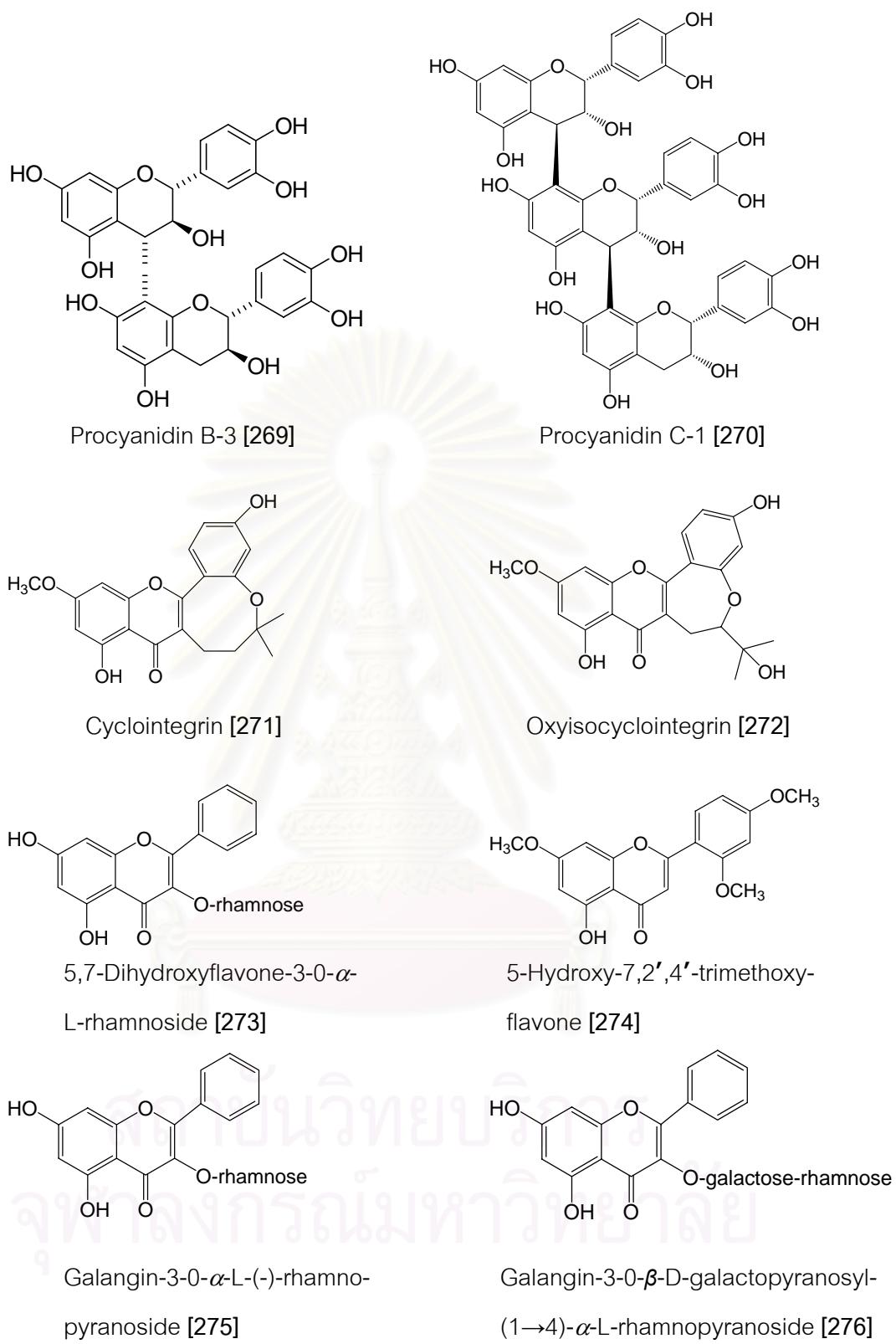


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

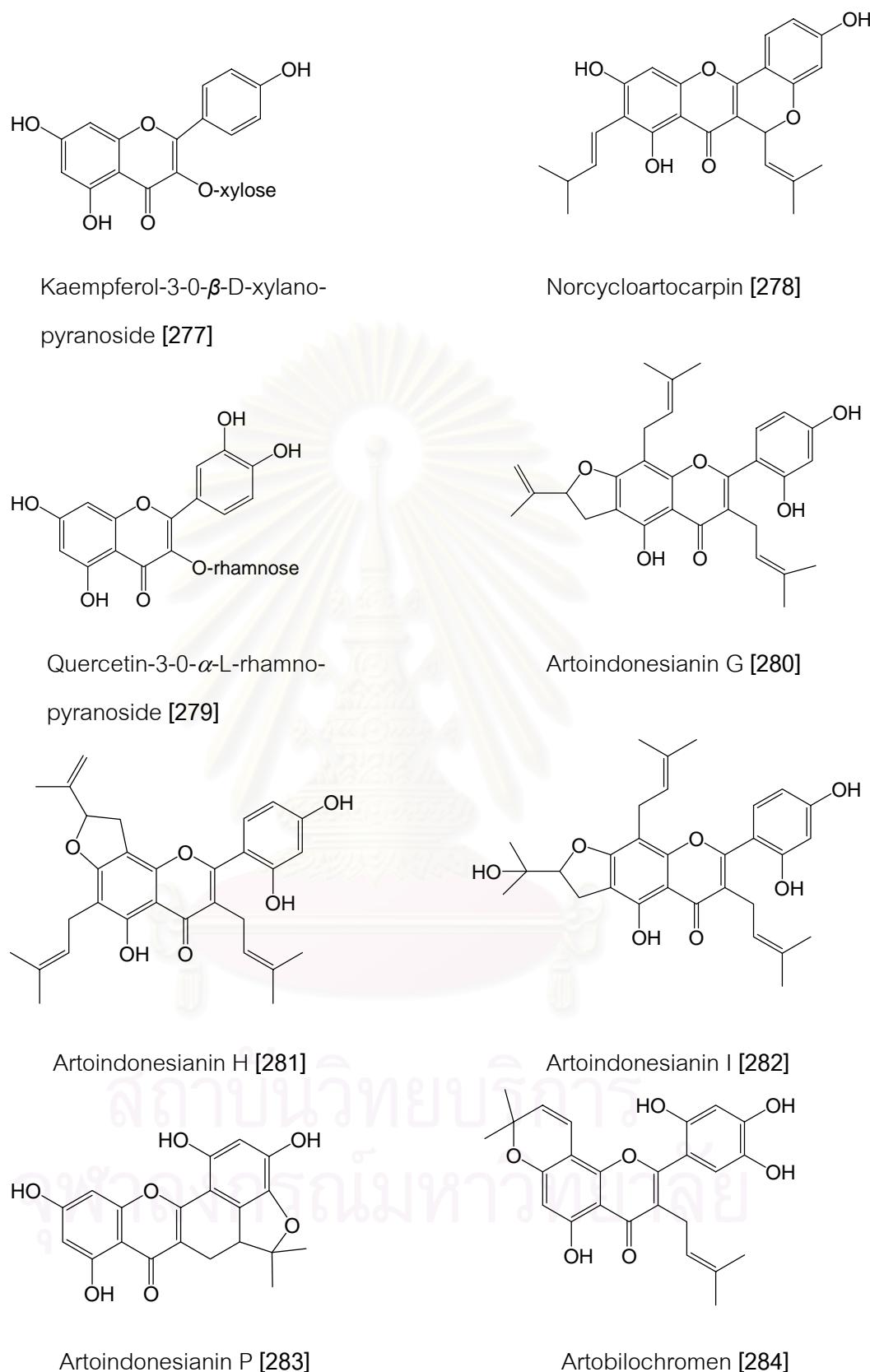


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

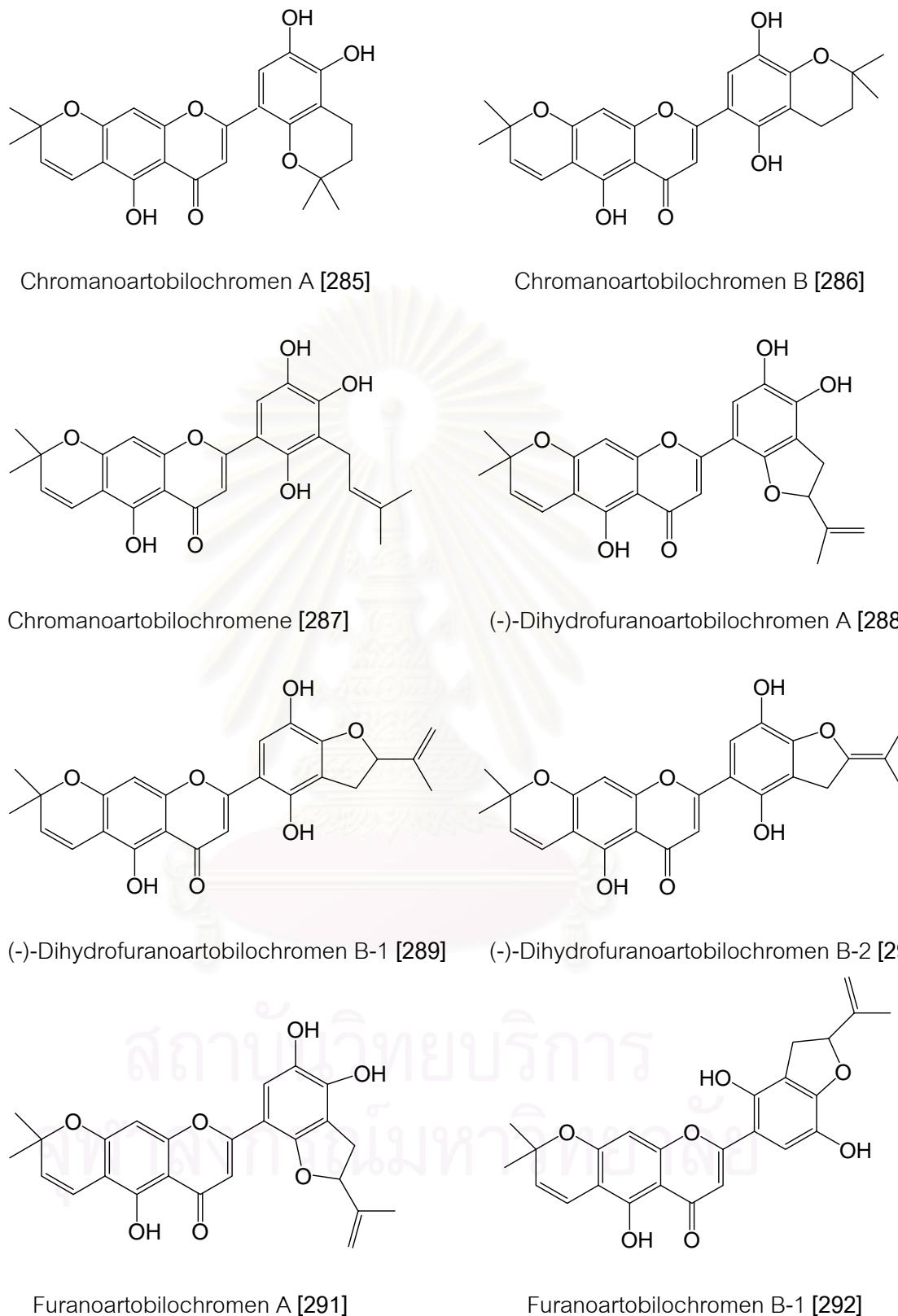


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

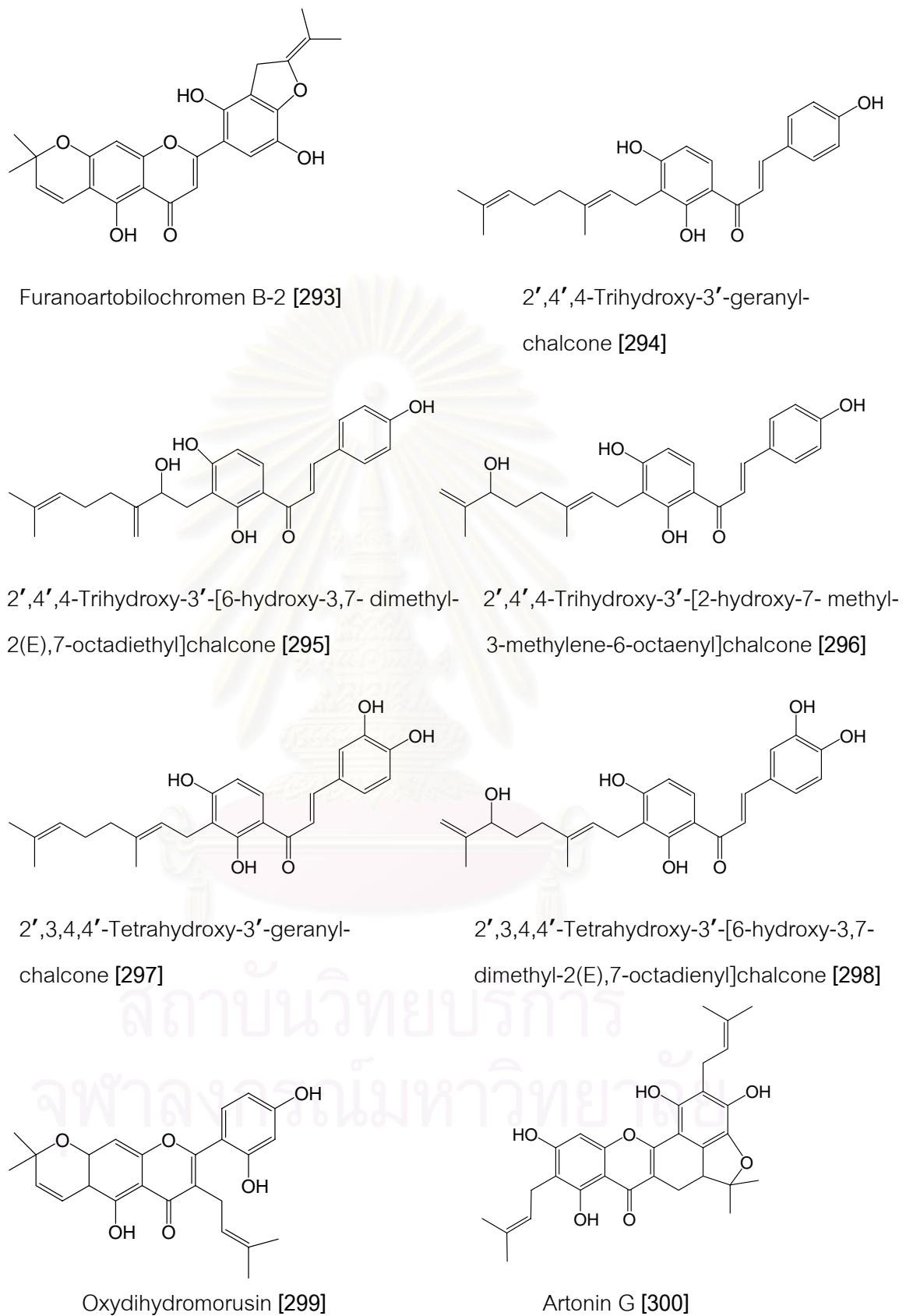


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

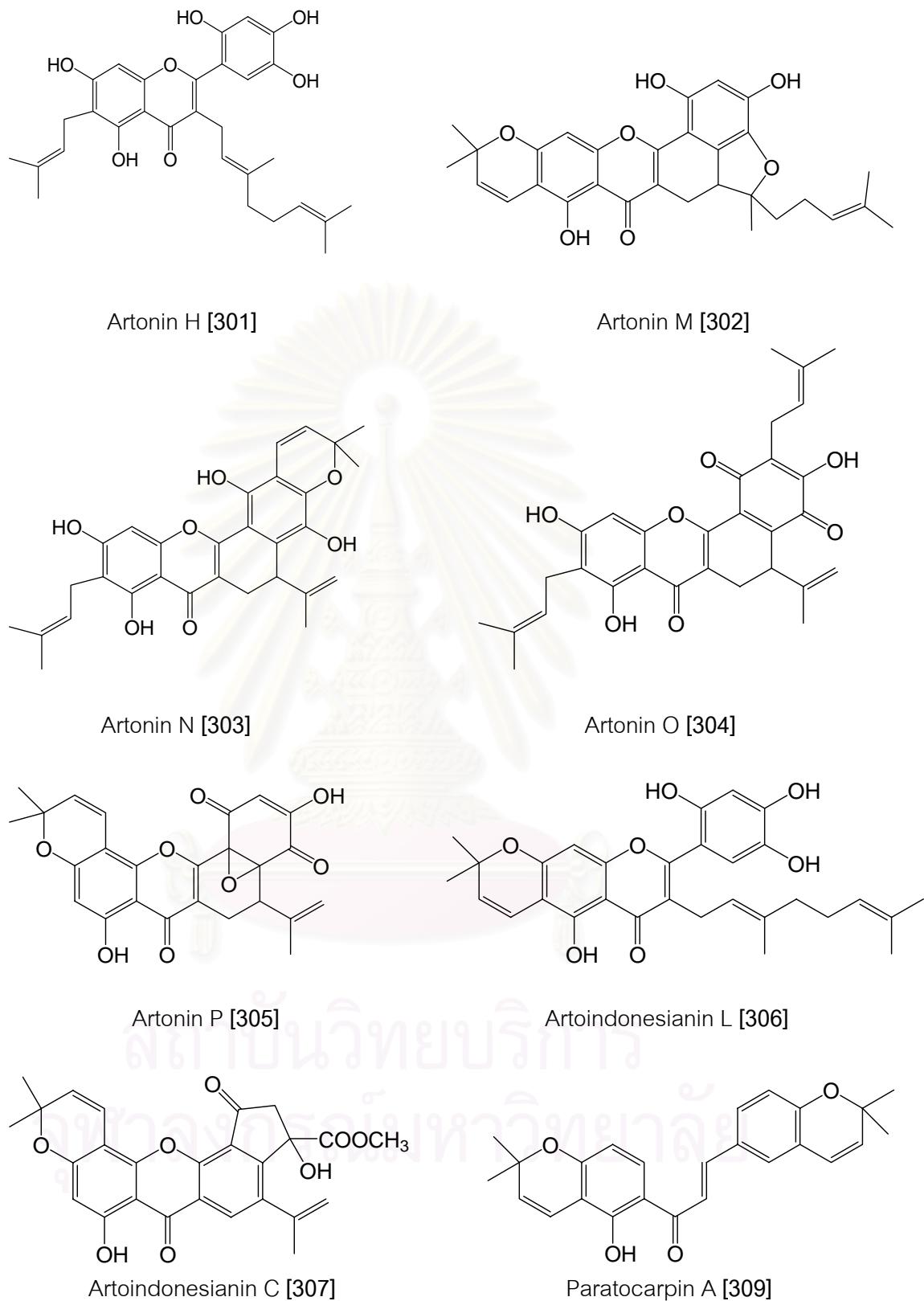


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

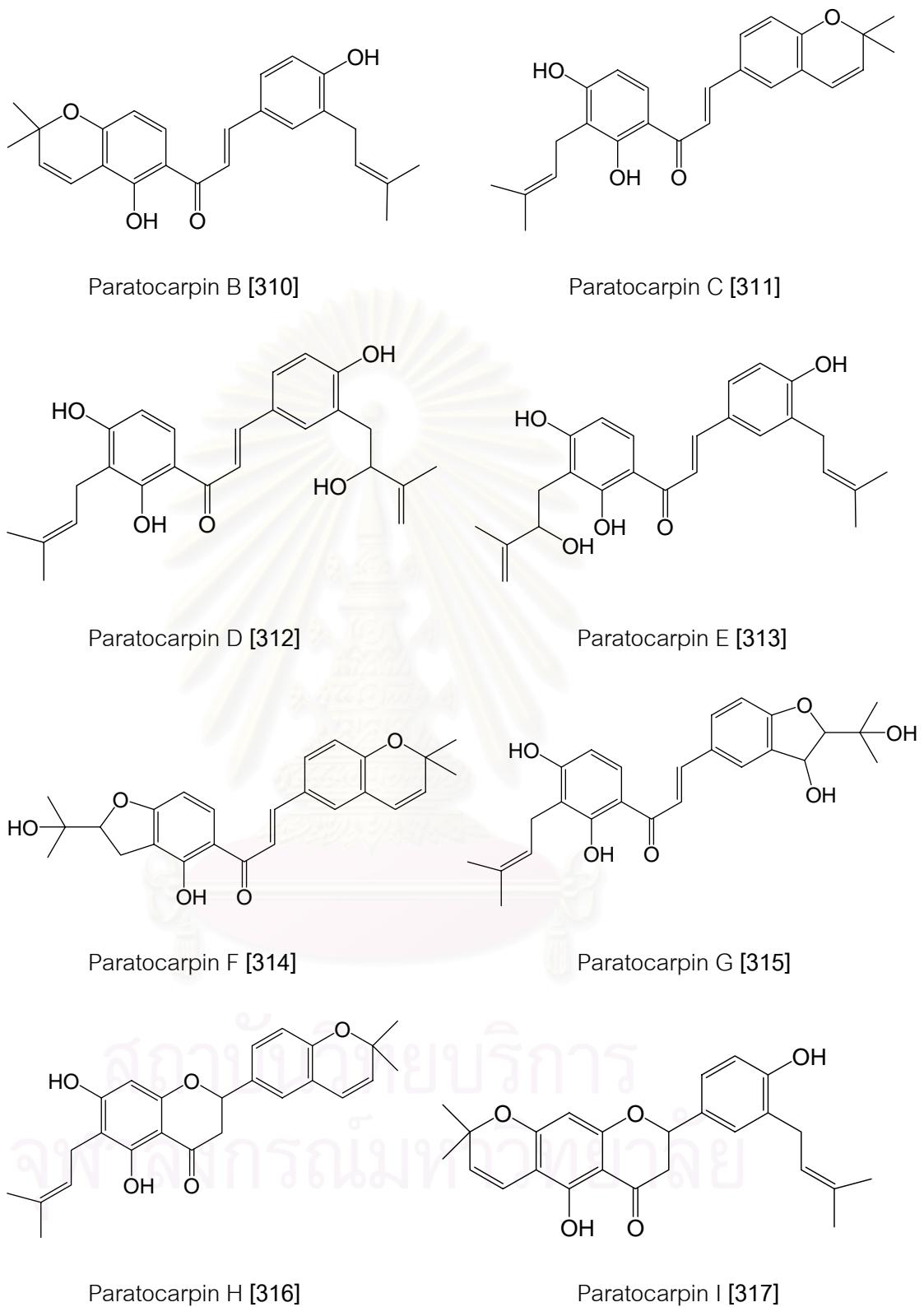


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

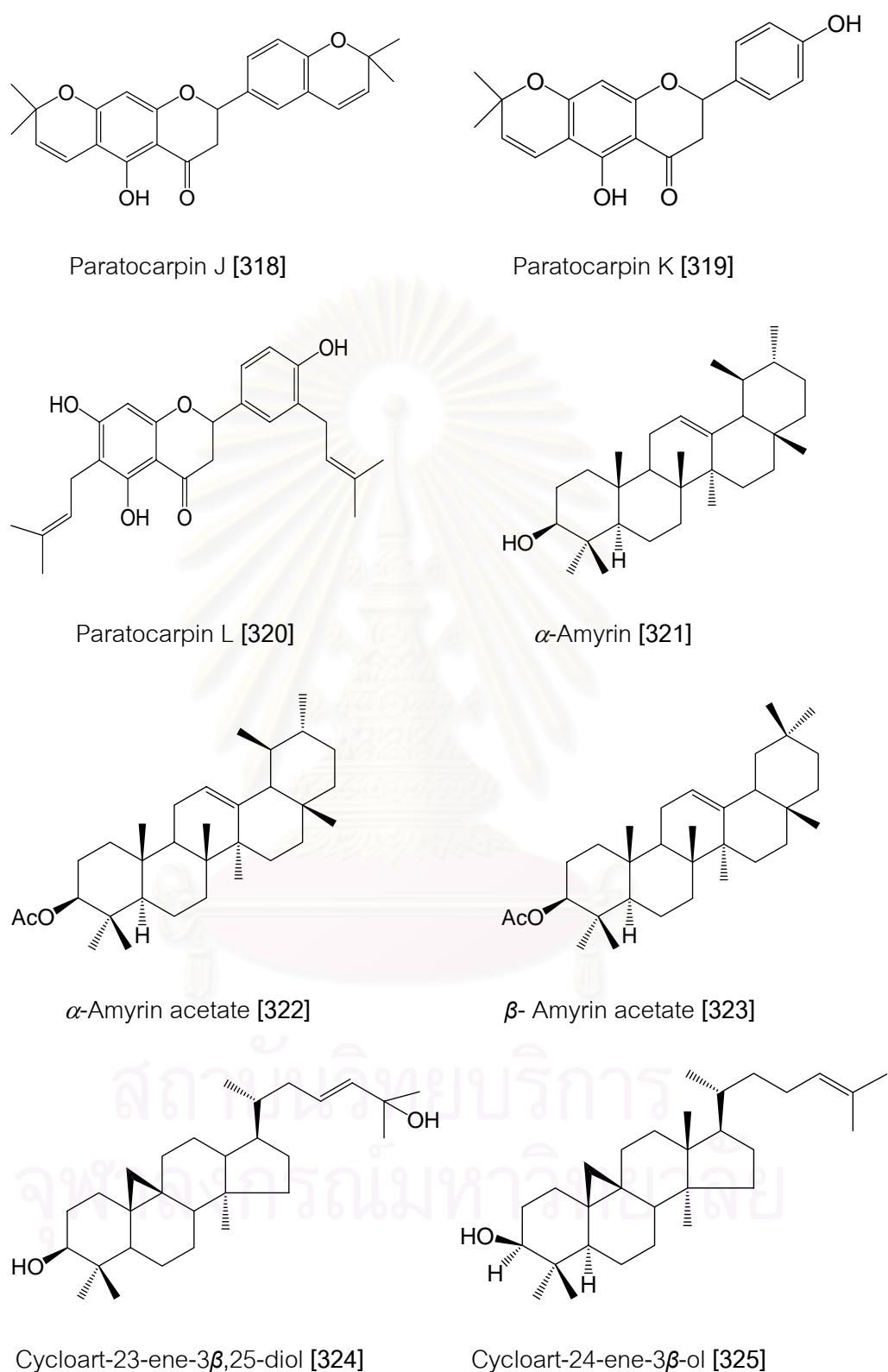


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

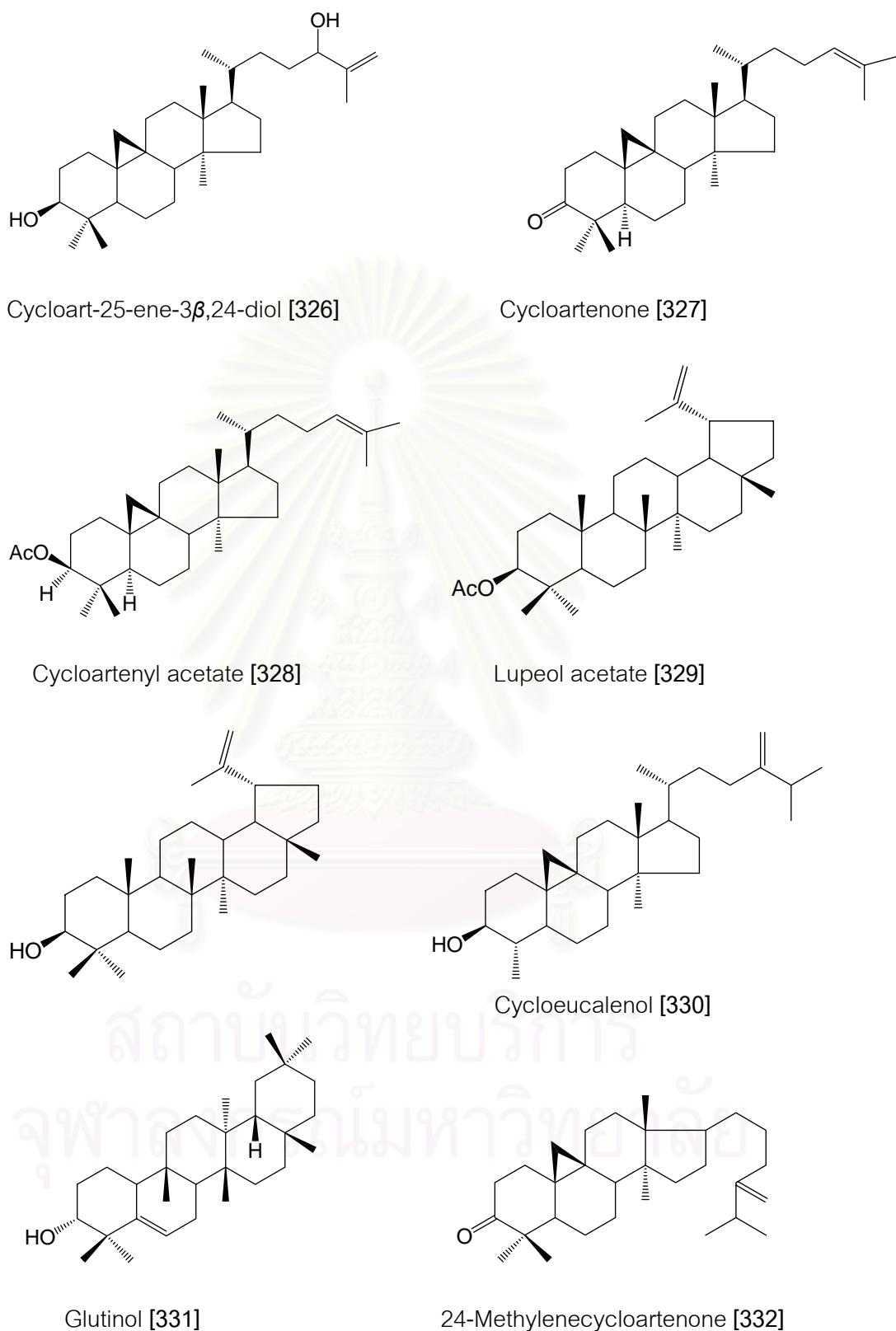


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

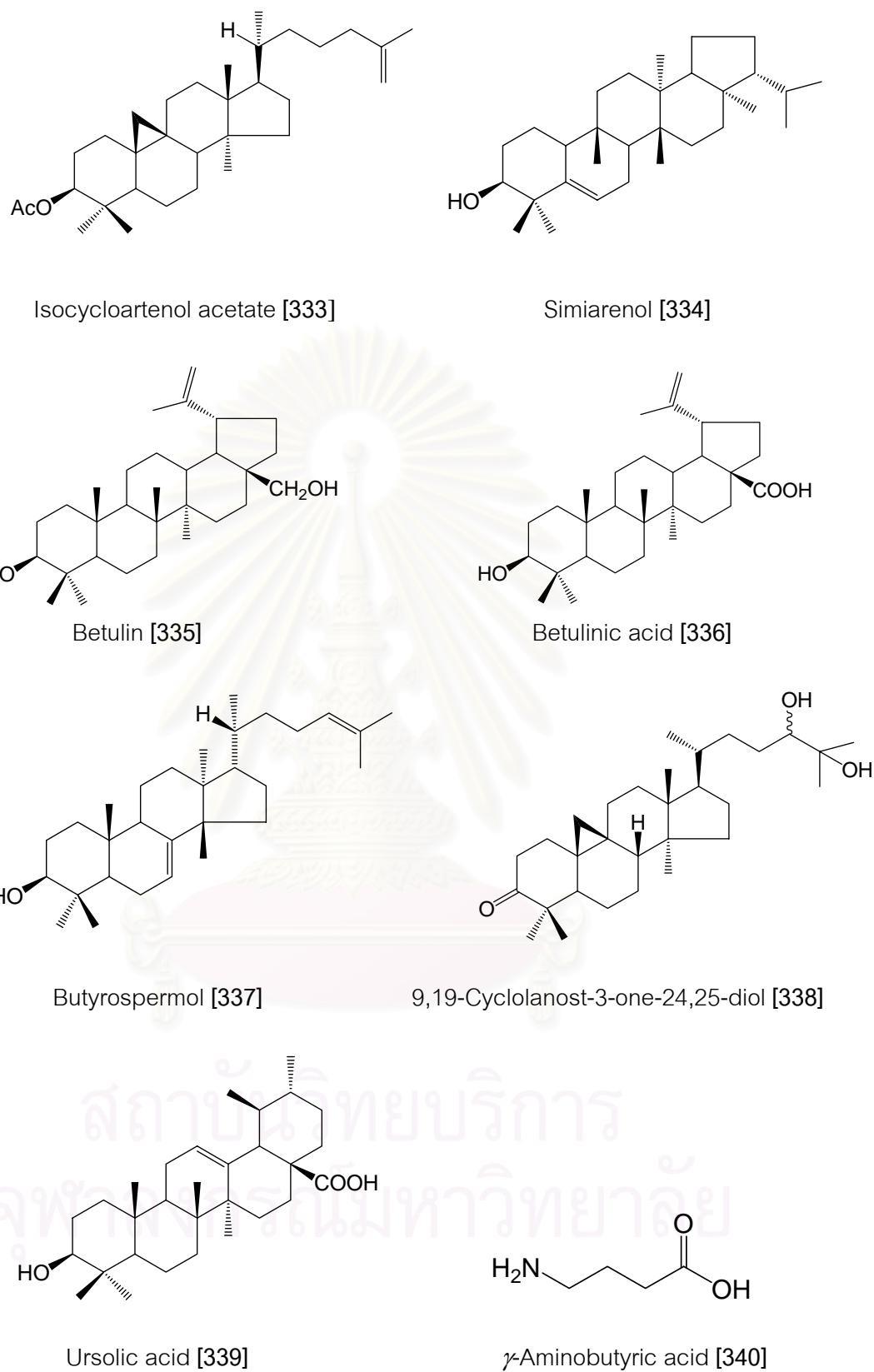


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

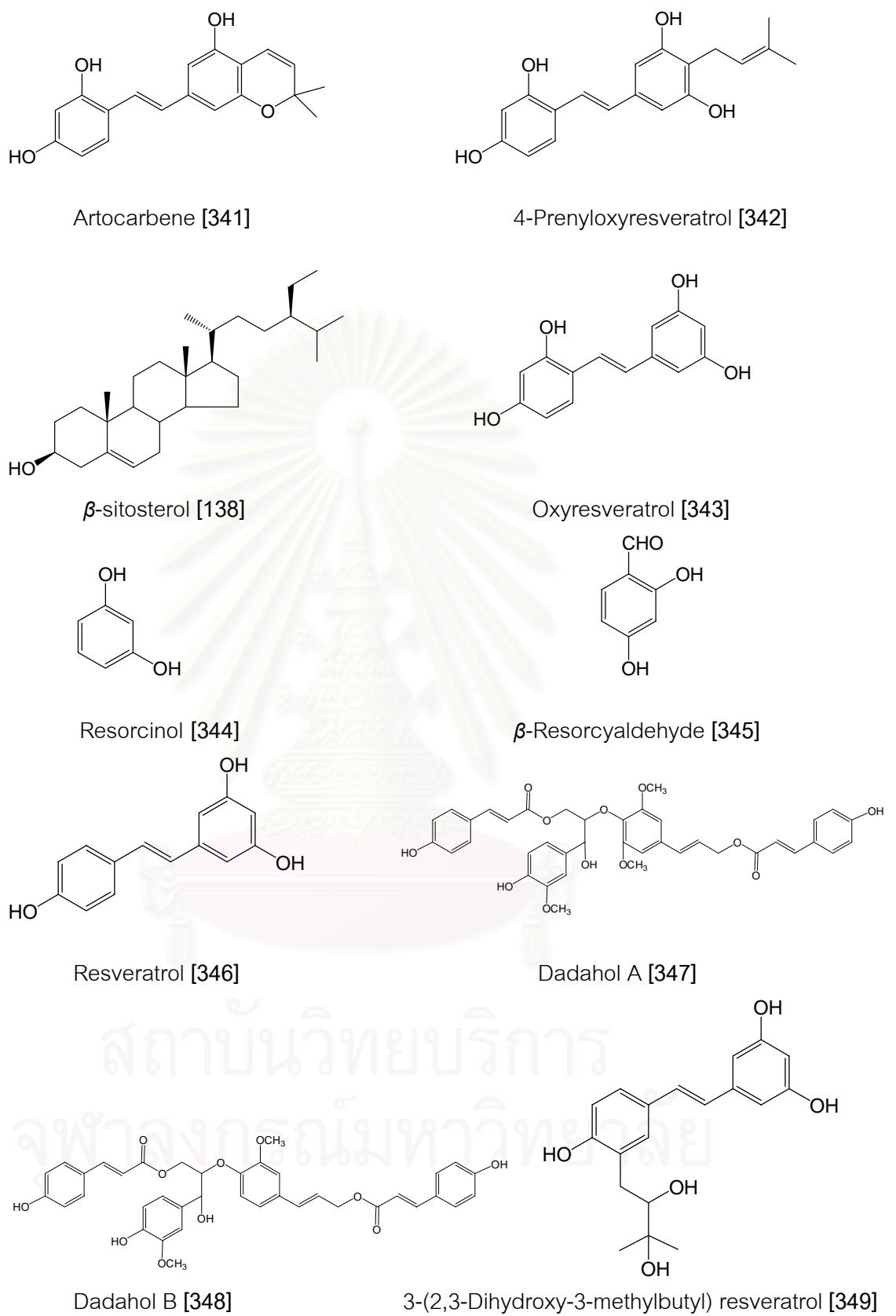


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

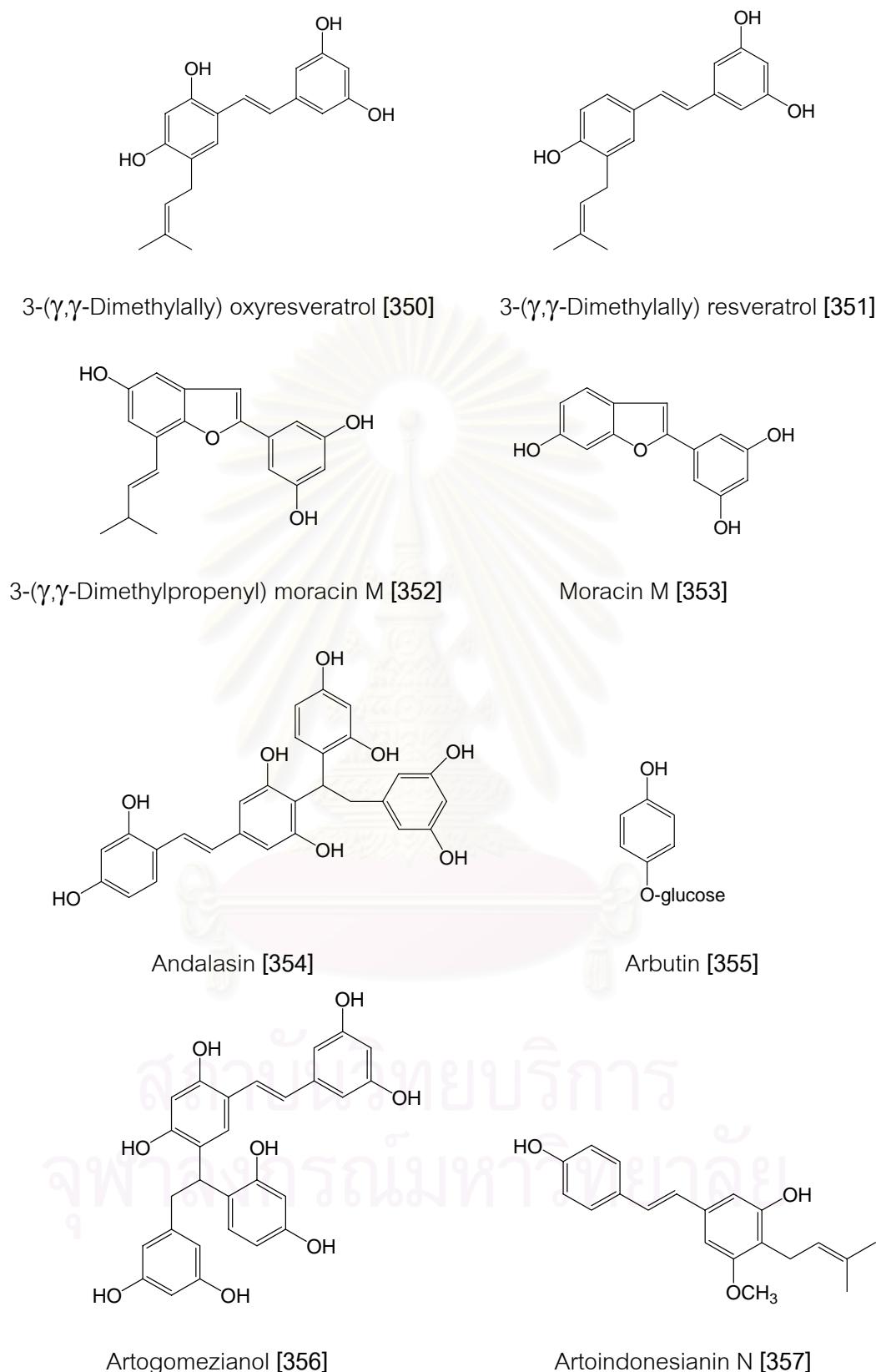
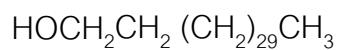
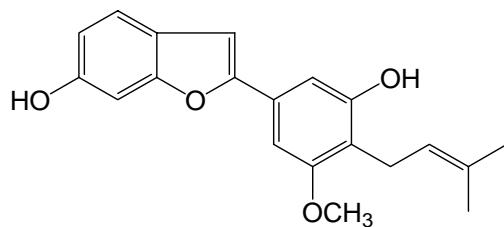
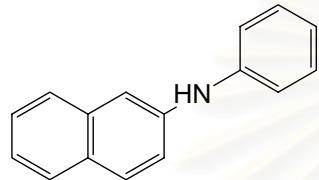
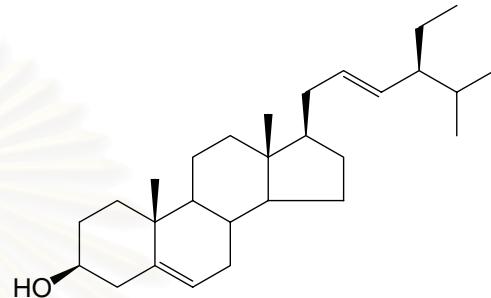


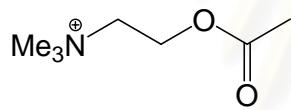
Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)



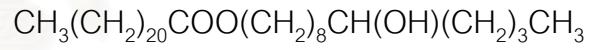
1-Dotriacontanol [359]

Phenyl- β -naphthylamine [361]

Stigmasterol [43]



Acetylcholine [362]



9-Hydroxytridecyl docosanoate [367]



4-Hydroxyundecyl docosanoate [368]

Recinoleic acid [371]

Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

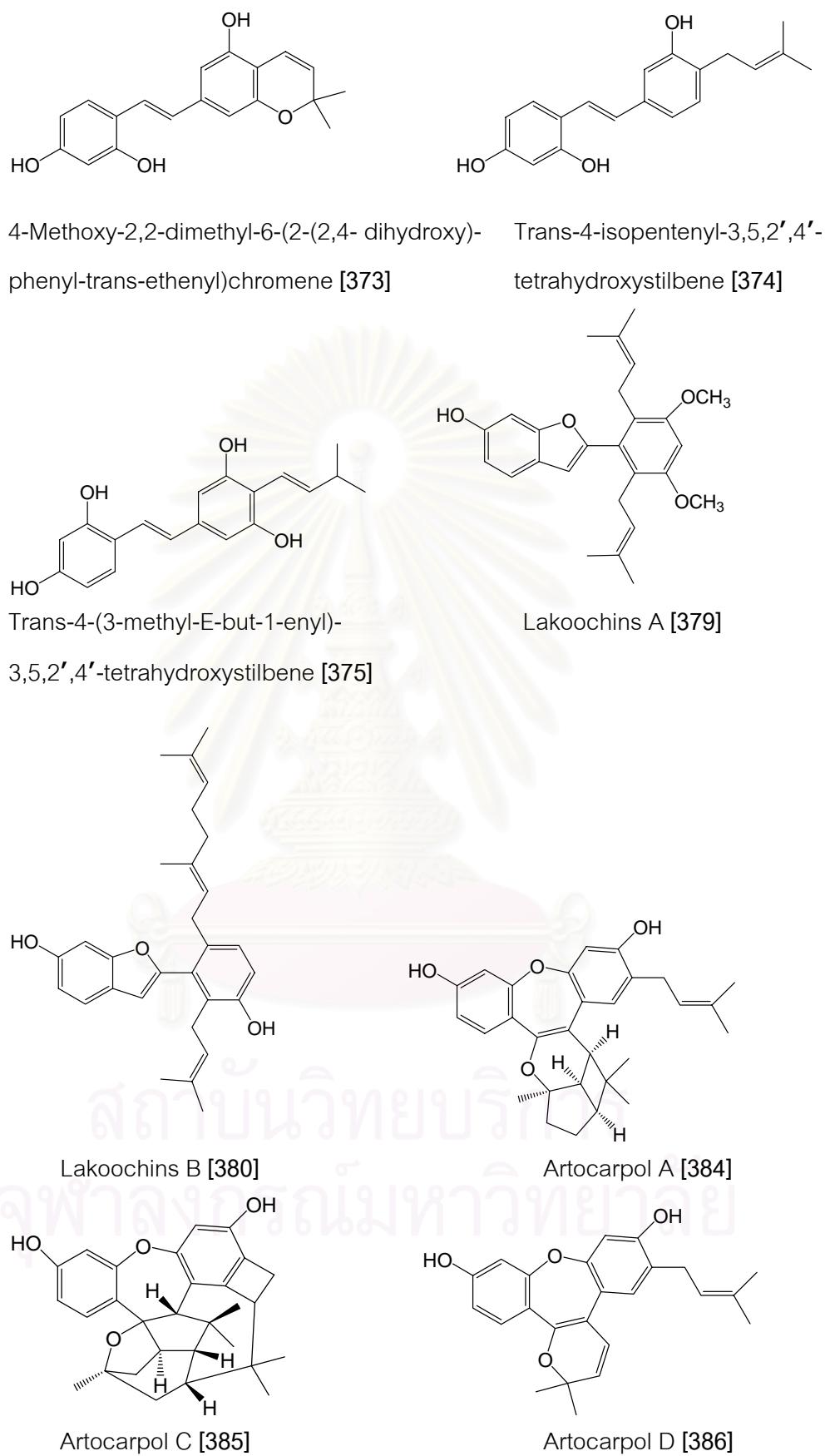
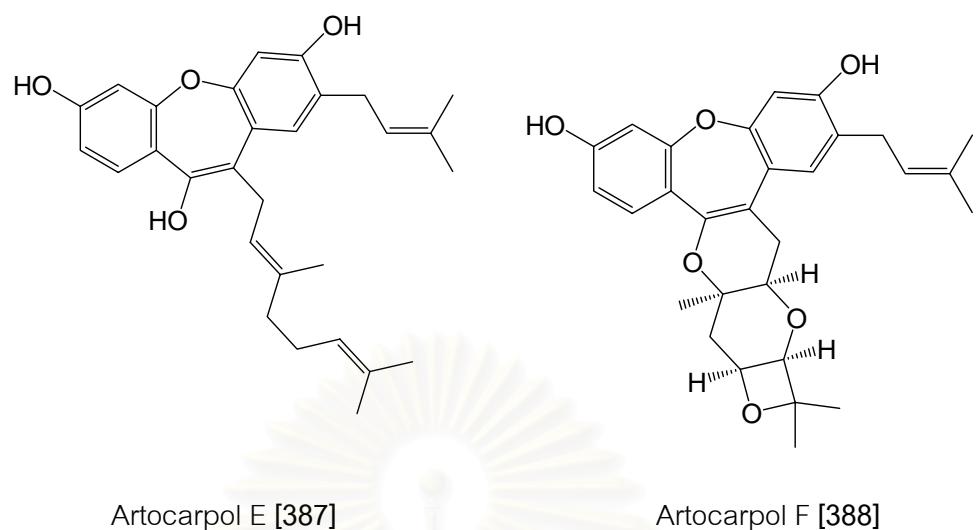


Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)



Artocarpol E [387]

Artocarpol F [388]

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Figure 4 Structures of compounds previously isolated from *Artocarpus* spp. (continued)

3. Traditional uses and biological activities of *Goniothalamus* spp.

Ethnobotanical uses of several species of the genus *Goniothalamus* are well known in many countries. In folk medicine of Malaysia, *G. macrophyllus* has been used to treat hypertension, swelling and to invigorate women after childbirth (Goh et al., 1999). Other reported uses of *G. macrophyllus* are antimalarial, antipyretic and abortifacient property (Nijila et al., 2002). *G. scorchedinii* is used for antipyretic and antimalarial properties (Kamel et al., 2002). The seeds of *G. amuyon* are reported to be useful for the treatment of edema and rheumatism (Lan et al., 2003). *G. borneensis* and *G. andersonii* have been used as a mosquito repellent by the natives in Sabah, East Malaysia (Cao et al., 1998). *G. umbrosus* has abortifacient and anti-cancer property. In China, the stem bark of *G. griffithii* is applied as pesticidal agents (Chen and Yu, 1999). In Thailand, the *G. tenuifolius* stem bark is tonic (Likhitwitayawuid et al., 2006). In Borneo, *Goniothalamus* spp. are widely used in the practice of traditional medicine especially in treating diarrhea, fever, skin diseases, antidotes and most commonly used as postparturition aid and abortifacient. Some of the species are also used as natural insecticide (Fassihuddin, 2004).

Many plants of the genus *Goniothalamus* have provided bioactive acetogenins, alkaloids, styryllactones and flavonoids. Styryllactones or their derivatives, which have been reported in almost all of the *Goniothalamus* species studied, are characteristic compounds of this genus (Cao et al., 1998). The alkaloids produced by many *Goniothalamus* species, being part of the Annonaceae family, are notably aporphines, some of which are known to be biologically active (Mix et al., 1982).

Many bioactive styryllactones that have been isolated from *Goniothalamus* spp. exhibited antitumor activity (Zhang et al., 1999b). Among them, goniopypyrone and altholactone are the most cytotoxic styryllactones (Mereyala and Joe, 2001). Some styryllactone derivatives exhibited strong anti-proliferative activity in MCF-7 and MDA-MB-231 cell lines (Hawariah and Stanslas, 1998). Tetrahydroxy-mono-tetrahydrofuran fatty acid-lactone (acetogenin) has been isolated from ethanolic extracts of the stem bark of *G. giganteus*. This compound was found to be cytotoxic,

insecticidal and inhibited the formation of crown gall tumors on potato disc (Alkofahi *et al.*, 1988).

According to Fassihuddin in 2004, some of the alkaloids isolated from *Goniothalamus* species including goniopedaline, aristolactam AII, aristolactam BII and velutinam showed cytotoxicity on various human tumor cell lines.

In 2006, there has been a report describing the presence of flavonoids in the leaves of *G. tenuifolius*, which showed free radical scavenging activity on the DPPH decoloration test (Likhitwitayawuid *et al.*, 2006).

4. Traditional uses and biological activities of *Artocarpus* spp.

Plants of the genus *Artocarpus* have been widely used in traditional medicine in many countries. In Trinidad and Bahamas, *Artocarpus altilis*, a decoction of the breadfruit leaf is used to lower blood pressure and relieve asthma. Crushed leaves are applied on the tongue as a treatment for thrush. The leaf juice is employed as ear-drops. Ashes of burned leaves are used on skin infection. A powder of roasted leaves is employed as a remedy for enlarged spleen. The crushed fruit is poulticed on tumors to ripen them. Toasted flowers are rubbed on the gum around an aching tooth. The latex is used on skin diseases and is bandaged on the spine to relieve sciatica. Diluted latex is taken internally to overcome diarrhea. In Indonesia, the flower of *A. altilis* or breadfruit is used against parulis (Fukai *et al.*, 2003). The ashes of the leaves with coconut oil and curcuma are used on skin disease with creeps like herpes. The fruit meat is used for cough, the root bark for diarrhea and dysentery, the seeds for aphrodisiac. In the Philippines, a decoction of the bark is used to treat stomachache and vulnery. In New Guinea, the latex is taken to treat dysentery (Perry, 1980).

A. heterophyllus (*A. integrifolia* Linn.), or Jackfruit plant, has edible fruit. Its seeds are nutritious and widely used as a food source. Antitryptic and antichymotryptic activities of the crude extract of jackfruit seeds have been reported (Kundu *et al.*, 1989). The pulp and seeds are tonic, cooling and pectorial. Its roots are used for treating diarrhea and fever. Leaf ash is applied to ulcers and wounds (Khan *et al.*, 2003). In Burma, China and Philippines, the sap is used to treat ulcers

and abscess. In Malaysia and Peninsular, the bark is employed as poultices. In Indo-China, the wood is used as a sedative in convulsions. The boiled leaves are used to activate the secretion of milk in women and animals, as antisyphilitic and vermifuge (Perry, 1980).

In Indonesia, the sap from the wounded bark of *A. dadah* is used to clean foul leg-wounds. The strip of *A. elasticus* is applied as a bandage to treat lumbago. The leaves of *A. elasticus* with rice are applied to treat tuberculosis and the latex for the treatment of dysentery. In Indo-China, the latex of *A. rigidus* is used to treat the wound of domestic animals. The boiled bark of *A. ovatus* is applied to treat stomachache. The fresh leaves of *A. rubroveniosus* are taken to lower fevers. In Burma, the juice and seeds of *A. lakoocha* are purgative and the bark is astringent. Its heartwood is applied as the eradication of tapeworms. The crude extract of roots is used for antimycobacterial activity (Perry, 1980).

Prenylated flavones from *Artocarpus* species were shown to be a source of interesting biological activities including cytotoxic (Liou et al., 1993), anticomplementary (Nascimento et al., 1997), anti-platelet (Lin et al., 1993) and antimicrobial (Sato et al., 1996) activities. They have also been described as inhibitors of arachidonate 5-lipoxygenase (Reddy et al., 1991) and TNF- α releasing (Nomura et al., 1998). The natural prenylated flavones isolated from *A. elasticus* were found to have antiproliferative activity. Artelastin has been found to exhibit the highest antiproliferative activity of prenylated flavones from *A. elasticus* (Cerqueira et al., 2003). Flavones from the heartwood of *A. heterophyllus* showed intensive antibacterial, antiplatelet and antidiabetic activities (Khan et al., 2003). Flavonoid derivatives isolated from *A. gomezianus* possessed potent tyrosinase inhibitory activity (Likhithwitayawuid, Sritularak and De-EKnamkul, 2000).

CHAPTER III

EXPERIMENTAL

1. Sources of Plant Materials

The leaves of *Goniothalamus tenuifolius* King were collected from Kaengkrachan, Phetchaburi province, Thailand. The heartwood of *Artocarpus gomezianus* Wall. ex Tre'c. was collected from Trang province, Thailand. The plant was identified by comparison with herbarium specimens in the Botany Section, Technical Division, Department of Agriculture, Ministry of Agriculture and Co-operatives, Bangkok, Thailand.

2. General Techniques

2.1 Analytical Thin-Layer Chromatography (TLC)

Technique	:	One dimension, ascending
Adsorbent	:	Silica gel 60 F ₂₅₄ (E. Merck) precoated plate
Layer thickness	:	0.2 mm
Distance	:	6 cm
Temperature	:	Laboratory temperature (30-35°C)
Detection	:	1. Ultraviolet light at wavelengths of 254 and 365 nm 2. Anisaldehyde and heating at 105°C for 10 min

2.2 Preparative Thin-Layer Chromatography (PLC)

Technique	:	One dimension, ascending
Adsorbent	:	Silica gel 60 F ₂₅₄ (E. Merck) precoated plate
Layer thickness	:	0.2 mm
Distance	:	15 cm
Temperature	:	Laboratory temperature (30-35°C)
Detection	:	Ultraviolet light at wavelengths of 254 and 365 nm

2.3 Column Chromatography

2.3.1 Vacuum liquid column chromatography

Adsorbent	:	Silica gel 60 (No. 7734) particle size 0.063-0.200 mm (70-230 mesh ASTM) (E. Merck)
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Packing method	:	Dry packing
Sample loading	:	The sample was dissolved in a small amount of organic solvent, mixed with the adsorbent, triturated, dried and then placed gently on top of the column.
Detection	:	Fractions were examined by TLC observing under UV light at the wavelengths of 254 and 365 nm

2.3.2 Flash Column Chromatography

Adsorbent	:	Silica gel 60 (No. 9385) particle size 0.040-0.063 mm (230-400 mesh ASTM) (E. Merck)
Packing method	:	Wet packing
Sample loading	:	The sample was dissolved in a small amount of organic solvent and then applied gently on top of the column.
Detection	:	Fractions were examined by TLC observing under UV light at the wavelengths of 254 and 365 nm

2.3.3 Gel filtration Chromatography

Gel filter	:	Sephadex LH 20 (Pharmacia)
Packing method	:	Gel filter was suspended in the eluant and left standing to swell for 24 hours prior to use. It was then poured into the column and allowed to set tightly.
Sample loading	:	The sample was dissolved in a small amount of organic solvent and then applied gently on top of the column.
Detection	:	Fractions were examined by TLC observing under UV light at the wavelengths of 254 and 365 nm

2.4 Spectroscopy

2.4.1 Ultraviolet (UV) Absorption Spectra

UV (in methanol) spectra were obtained on a MiltonRoy spectronic 3000 Array Spectrophotometer (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.4.2 Infrared (IR) Absorption Spectra

IR spectra were recorded on a Perkin Elmer spectrum one FT-IR 1760 Spectrophotometer with UATR technique (Chulabhorn Research Institute)

2.4.3 Mass Spectra

Electron impact mass spectra (EIMS) were measured on a Finnigan Mat GCQ-Mass Spectrometer (Chulabhorn Research Institute). High Resolution mass spectra were obtained in the Time-of-flight technique (TOF) manner with a Bruker Daltonics mass spectrometer (Chulabhorn Research Institute).

2.4.4 Proton and Carbon-13 Nuclear Magnetic Resonance (^1H and $^{13}\text{C-NMR}$) Spectra

$^1\text{H-NMR}$ (300 MHz), $^{13}\text{C-NMR}$ (75 MHz), NOESY, COSY, HMQC spectra were obtained with a Bruker Avance DPX-300 FT-NMR spectrometer (Faculty of Pharmaceutical Sciences, Chulalongkorn University). HMBC spectra was obtained with a JEOL JMN-A 500 NMR spectrometer (Scientific and Technological Research Equipment Center, Chulalongkorn University).

Solvents for NMR spectra were deuterated acetone (acetone- d_6), deuterated dimethylsulfoxide (DMSO- d_6) and deuterated chloroform (CDCl_3). Chemical shifts were reported in ppm scale using the chemical shift of the solvent as the reference signal.

2.5 Physical Properties

2.5.1 Optical Rotation

Optical rotations were measured on a Perkin Elmer 341 polarimeter (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.5.2 Circular Dichroism (CD) Spectra

CD Spectra were recorded on a JASCO J-715 spectropolarimeter (Pharmaceutical Research Instrument Center, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2.6 Solvents

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

3. Extraction and Isolation

3.1 Extraction and Isolation of Compounds from *Goniothalamus tenuifolius*

3.1.1 Extraction

The dried leaves of *Goniothalamus tenuifolius* (1.3 kg) were extracted four times with hexane (10 L, 3 days each) and then filtered. The filtrates were pooled and evaporated under reduced pressure at temperature not exceeding 40°C to yield a hexane extract (syrupy mass 29.4 g, 2.26% based on dried weight of leaves).

The marc was then extracted four times with ethyl acetate (10 L, 3 days each) and then filtered. The filtrates were pooled and evaporated under reduced pressure at temperature not exceeding 40°C to yield an ethyl acetate extract (syrupy mass 97.7 g, 7.51% based on dried weight of leaves).

Finally, the marc was extracted four times with methanol (10 L, 3 days each). Removal of the organic solvent gave a methanol extract (syrupy mass 114.7 g, 8.82% based on dried weight of leaves).

3.1.2 Isolation

The methanol extract was separated by vacuum liquid column chromatography using a sintered glass filter column of silica gel (No. 7734). The methanol extract (50 g) was dissolved in a small amount of methanol, triturated with silica gel (No. 7734) and dried under vacuum. Elution was performed in a polarity gradient manner with mixtures of methanol and dichloromethane (0.2:9.8 to 1:9) as the solvents. The eluants were collected 500 ml per fraction and examined by TLC (SiO_2) using 5% methanol in dichloromethane as developing solvent. Fractions with similar chromatographic patterns were combined to yield 8 fractions: fraction A (0.5 g), fraction B (3.0 g), fraction C (1.6 g), fraction D (2.0 g), fraction E (3.3 g), fraction F (6.6 g), Fraction G (9.1 g), Fraction H (22.8 g).

3.1.2.1 Isolation of Compound GT1

Fraction B (3.0 g) was separated by column chromatography using silica gel (No. 9385, 115 g) as the adsorbent. Gradient elution was performed using mixtures of ethyl acetate and hexane. Sixty fractions (50 ml, each) were collected and combined based on their chromatographic patterns (silica gel, ethyl acetate: hexane = 6:4) to yield 10 fractions (Fraction B1 to Fraction B10).

Fraction B9 (328 mg) was further separated on a column using silica gel (No. 9385, 65 g) as the adsorbent. Elution was performed in a polarity gradient manner with dichloromethane and methanol (9.8:0.2 to 9:1). Eluates with similar TLC behavior (silica gel, MeOH: CH_2Cl_2 = 1:19) were combined to give 6 fractions (fraction B9-1 to fraction B9-6). Fraction B9-1 gave compound GT1 as pale yellow needles [3.4 mg, $2.61 \times 10^{-4}\%$ based on dried weight of the leaves, R_f values= 0.14, silica gel, ethyl acetate: hexane (6:4)]. This compound was identified as 3,5,7,3',4'-pentamethoxyflavone [16].

3.1.2.2 Isolation of Compound GT2

Fraction C (1.6 g) was fractionated by column chromatography using silica gel (No. 9385, 65 g) as the adsorbent. Gradient elution was performed using mixtures of ethyl acetate and hexane (2:8 to 8:2). The eluates were collected and combined according to their TLC chromatographic patterns (silica gel, ethyl acetate: hexane= 6:4) to give 8 fractions (fraction C1 to fraction C8). Fraction C4 gave compound GT2 as pale yellow needles [4.9 mg, $3.77 \times 10^{-4}\%$ based on dried weight of the leaves, R_f values= 0.38, silica gel, ethyl acetate: hexane (6:4)]. This compound was identified as kumatakenin [14].

3.2 Extraction and Isolation of Compounds from *Artocarpus gomezianus*

3.2.1 Extraction

The dried and powdered heartwood of *Artocarpus gomezianus* (3.8 kg) was extracted with methanol four times (30 L, 3 days each) and then filtered. The filtrates were pooled and evaporated under reduced pressure at temperature not exceeding 40°C to yield a methanol extract (syrupy mass 160.4 g, 4.22 % based on dried weight of heartwood).

3.2.2 Isolation

The methanol extract was divided into two portions: A (80 g) and B (80.4 g). Each was dissolved in a small amount of methanol, triturated with silica gel (No. 7734) and dried under vacuum. It was then fractionated by vacuum liquid column chromatography using a sintered glass filter column of silica gel (No. 7734). Elution was performed in a polarity gradient manner with mixtures of ethyl acetate and hexane (2:8 to 8:2) as the solvents. The eluants were collected 500 ml per fraction and examined by TLC (SiO_2) using ethyl acetate: hexane (1:1) as developing solvent. Fractions with similar

chromatographic pattern were combined to yield 12 fractions (fraction A to fraction L).

3.2.2.1 Isolation of Isolate AG1

AG1 was obtained as colorless needles from fraction I through recrystallization from methanol [6.3 mg, $1.65 \times 10^{-4}\%$ based on dried weight of the heartwood, silica gel, Rf values= 0.38, ethyl acetate: hexane (4:6)]. This isolate was identified as a mixture of β -sitosterol and stigmasterol [138, 43].

3.2.2.2 Isolation of Compound AG2

Compound AG2 was obtained as a yellow powder from fractions A-H through recrystallization from ethyl acetate [108.7 mg, $2.86 \times 10^{-3}\%$ based on dried weight of the heartwood, silica gel, Rf values= 0.44, ethyl acetate : hexane (4:6)]. This compound was identified as cycloartocarpin [180].

3.2.2.3 Isolation of Compound AG3

After recrystallization of compound AG2, the mother liquors from fractions A to H were combined, dried and then separated by column chromatography using silica gel (No. 9385) as the adsorbent. Elution was performed in a polarity gradient manner with ethyl acetate and hexane (2:8 to 5:5). Twenty-six fractions (30 ml each) were collected. The eluates were examined by TLC (SiO_2) using ethyl acetate: hexane (3:7) as the developing solvent. Fractions showing similar chromatographic patterns were combined to yield 5 major fractions: fractions 1-5, fractions 6-13, fractions 14-16, fractions 17-21, fractions 22-26.

The TLC chromatogram of fractions 1-5 showing only one spot under UV light at 254 nm [Rf values= 0.61, silica gel, ethyl acetate: hexane (4:6)]. These fractions were combined and dried under reduced pressure to give compound AG3 as a yellow powder (7.8 mg, $2.05 \times 10^{-4}\%$ based on dried weight of the heartwood). This compound was identified as isocyclomorusin [175].

3.2.2.4 Isolation of Compounds AG4, AG5 and AG6

Fraction J (1.3 g) was fractionated by column chromatography using silica gel (No.9385) as the adsorbent. Elution was performed in a polarity gradient manner with ethyl acetate and hexane (3:7 to 7:3). Sixty-seven fractions (50 ml each) were collected and examined by TLC (SiO_2) using ethyl acetate: hexane (4:6) as the developing solvent. Fractions with similar chromatographic patterns were combined to

give 8 fractions: fraction J1 to fraction J8.

Fraction J4 (71.5 mg) was further separated by gel filtration chromatography using a column of Sephadex LH 20 with methanol as the eluant. Sixteen fractions were collected (25 ml per fraction) and combined according to their TLC chromatographic patterns (silica gel, ethyl acetate: hexane= 4:6) to yield 5 fractions: fraction J4-1 to fraction J4-5.

Fraction J5 (512 mg) was divided into four portions. Each portion was separated by gel filtration chromatography using a column of Sephadex LH 20 with methanol as the eluant. The eluates were collected 25 ml per fraction and examined by TLC (SiO_2) using ethyl acetate: hexane (4:6) as the developing system. Fractions with similar chromatographic pattern were combined to give 6 fractions: fraction J5-1 to fraction J5-6.

Fraction J4-4 and fraction J5-5 were combined and showed only one spot on TLC under UV light at 254 nm [Rf values= 0.34, silica gel, ethyl acetate: hexane (4:6)]. Evaporation of the combined fractions under reduced pressure gave compound AG4 as a yellow powder (55.6 mg, $1.46 \times 10^{-3}\%$ based on dried weight of the heartwood). This compound was identified as norcycloartocarpin [278].

Fraction J4-2 and fraction J5-3 were combined. The TLC chromatogram of the combined fractions showed only one spot under UV light at 254 nm [Rf values= 0.34, silica gel, ethyl acetate: hexane (4:6)]. Evaporation of this combined fraction under reduced pressure gave compound AG5 as a yellow powder (114.8 mg, $3.02 \times 10^{-3}\%$ based on dried weight of the heartwood). This compound was identified as artocarpin [149].

The TLC chromatogram of fraction J5-1 showed only one spot under UV light at 254 nm [Rf values= 0.2, silica gel, ethyl acetate: hexane (4:6)]. Evaporation of this fraction under reduced pressure gave compound AG6 as a yellow powder (12.2 mg, $3.21 \times 10^{-4}\%$ based on dried weight of the heartwood). This isolate is a new compound, and its structure is elucidated as artogomezianone [389].

3.2.2.5 Isolation of Compound AG7

Fraction K (2.8 g) was separated by vacuum liquid column chromatography using a sintered glass filter column of silica gel (No. 7734). Elution was

performed in a polarity gradient manner with mixtures of methanol and dichloromethane (0.2:9.8 to 1:9) as the solvents. Forty fractions (200 ml, each) were collected and combined based on their TLC chromatographic patterns (silica gel, MeOH: CH₂Cl₂ =0.5:9.5) to give 10 fractions: fraction K1 to fraction K10.

Fraction K8 (457.5 mg) was further separated by column chromatography using silica gel (No.9385) as the adsorbent. Elution was performed in a polarity gradient manner with acetone and hexane (3:7 to 6:4). The eluates were collected and examined by TLC (SiO₂) using acetone: hexane (1:1) as the developing system. Fractions showing similar chromatographic pattern were combined to yield 11 fractions: fraction K8-1 to fraction K8-11.

Fraction K8-4 (21.8 mg) was separated by gel filtration chromatographic technique (Sephadex LH 20) with methanol as the eluant. The eluates were examined by TLC (silica gel, acetone: hexane= 1:1). Fractions giving the same chromatographic patterns were combined to yield 7 fractions: fraction K8-4-1 to fraction K8-4-7.

The TLC chromatogram of fraction K8-4-4 showed only one spot under UV light at 254 nm [Rf values= 0.33, silica gel, acetone: hexane (1:1)]. Evaporation of this fraction under reduced pressure gave compound AG7 as yellow prisms (4.3 mg, 1.13x10⁻⁴% based on dried weight of the heartwood). It was identified as norartocarpetin [198].

3.2.2.6 Isolation of Compound AG8

Fraction K9 (558.4 mg) was fractionated by column chromatography using silica gel (No. 9385) as the adsorbent. Elution was performed in a polarity gradient manner with acetone and hexane (3:7 to 6:4). Twenty-six fractions (50 ml each) were collected. The eluates were examined by TLC using acetone: hexane (1:1) and combined according to their TLC chromatographic patterns to give 5 fractions: fraction K9-1 to fraction K9-5.

Fraction K9-2 was further separated by gel filtration chromatography using a column of Sephadex LH 20 with acetone as the eluant. The eluates were collected and combined according to their TLC chromatographic patterns (silica gel, acetone: hexane= 1:1) to yield 4 fractions (fraction K9-2-1 to fraction K9-2-4).

Fraction K9-2-1 gave compound AG8 as white powder [17.9 mg, $4.71 \times 10^{-4}\%$ based on dried weight of the heartwood, Rf values= 0.25, silica gel, acetone: hexane (1:1)]. This compound was identified as oxyresveratrol [343].

4. Physical and spectral data of isolated compounds

4.1 Compound GT1 (3,5,7,3',4'-Pentamethoxyflavone)

Compound GT1 was obtained as pale yellow needles, soluble in chloroform (3.4 mg, $2.61 \times 10^{-4}\%$ based on dried weight of leaves).

UV : λ_{\max} nm (log ε), in methanol; Figure 6

246 (2.36), 340 (2.03)

$^1\text{H-NMR}$: δ ppm, 300 MHz, in CDCl_3 ; Figure 7, Table 6

$^{13}\text{C-NMR}$: δ ppm, 75 MHz, in CDCl_3 ; Figure 8, Table 6

4.2 Compound GT2 (Kumatakenin)

Compound GT2 was obtained as pale yellow needles, soluble in acetone (4.9 mg, $3.77 \times 10^{-4}\%$ based on dried weight of leaves).

UV : λ_{\max} nm (log ε), in methanol; Figure 9

256 (1.18), 354 (0.92)

$^1\text{H-NMR}$: δ ppm, 300 MHz, in acetone- d_6 ; Figure 10, Table 7

$^{13}\text{C-NMR}$: δ ppm, 75 MHz, in acetone- d_6 ; Figure 11, Table 7

4.3 Isolate AG1 (β -Sitosterol and Stigmasterol)

Isolate AG1 was obtained as colorless needles, soluble in chloroform (6.3 mg, $1.65 \times 10^{-4}\%$ based on dried weight of heartwood).

$^1\text{H-NMR}$: δ ppm, 300 MHz, in CDCl_3 ; Figure 12, Table 8

$^{13}\text{C-NMR}$: δ ppm, 75 MHz, in CDCl_3 ; Figure 13, Table 8

4.4 Compound AG2 (Cycloartocarpin)

Compound AG2 was obtained as a yellow powder, soluble in acetone (108.7 mg, $2.86 \times 10^{-3}\%$ based on dried weight of heartwood).

$[\alpha]_{\text{D}}^{20}$: +148.7° (c 0.096 g/100ml)

EIMS : m/z (% relative intensity); Figure 16

434 (M^+ , 64), 391 (53), 379 (35), 378 (32), 335 (100), 321 (30),

189 (7), 147 (9), 137 (9), 41 (16)

UV	: λ_{\max} nm (log ϵ), in methanol; Figure 14 258 (2.15), 291 (2.59), 370 (2.16)
IR	: ν_{\max} cm ⁻¹ , KBr disc; Figure 15 3387 (br), 2961, 2866, 2167, 1650, 1618, 1584, 1479, 1450, 1208, 1081, 977
¹ H-NMR	: δ ppm, 300 MHz, in DMSO- <i>d</i> ₆ ; Figure 17, Table 9
¹³ C-NMR	: δ ppm, 75 MHz, in DMSO- <i>d</i> ₆ ; Figure 18, Table 9

4.5 Compound AG3 (Isocyclomorusin)

Compound AG3 was obtained as a yellow powder, soluble in acetone (7.8 mg, 2.05x10⁻⁴% based on dried weight of heartwood).

[α] _D ²⁰	: +61.2° (c 0.1045 g/100ml)
EIMS	: <i>m/z</i> (% relative intensity); Figure 23 418 (M^+ , 39), 404 (24), 403 (100), 385 (12), 363 (33), 348 (13), 347 (47), 203 (7), 194 (8)
UV	: λ_{\max} nm (log ϵ), in methanol; Figure 21 293 (3.45), 370 (2.82)
IR	: ν_{\max} cm ⁻¹ , KBr disc; Figure 22 3277 (br), 2921, 2851, 1653, 1617, 1590, 1553, 1464, 1186, 1137, 1082, 987, 817
¹ H-NMR	: δ ppm, 300 MHz, in acetone- <i>d</i> ₆ ; Figure 24, Table 10
¹³ C-NMR	: δ ppm, 75 MHz, in acetone- <i>d</i> ₆ ; Figure 25, Table 10

4.6 Compound AG4 (Norcloartocarpin)

Compound AG4 was obtained as a yellow powder, soluble in acetone (55.65 mg, 1.46x10⁻³% based on dried weight of heartwood).

[α] _D ²⁰	: +153.0° (c 0.1035 g/100ml)
EIMS	: <i>m/z</i> (% relative intensity); Figure 28 420 (M^+ , 48), 403 (16), 377 (22), 365 (38), 364 (34), 349 (15), 321 (100), 309 (25), 207 (9)
UV	: λ_{\max} nm (log ϵ), in methanol; Figure 26 257 (2.96), 292 (3.18), 367 (2.82)
IR	: ν_{\max} cm ⁻¹ , KBr disc; Figure 27

3228 (br), 2959, 1615, 1563, 1455, 1354, 1212, 1081, 985, 812

¹H-NMR : δ ppm, 300 MHz, in acetone-*d*₆; Figure 29, Table 11

¹³C-NMR : δ ppm, 75 MHz, in acetone-*d*₆; Figure 30, Table 11

4.7 Compound AG5 (Artocarpin)

Compound AG5 was obtained as a yellow powder, soluble in acetone (114.75 mg, 3.02x10⁻³% based on dried weight of heartwood).

EIMS : *m/z* (% relative intensity); Figure 33

436 (M^+ , 100), 419 (13), 405 (14), 394 (21), 393 (51), 381 (25),
379 (20), 363 (25), 337 (72), 323 (12), 319 (15), 253 (9), 179 (12),
123 (9), 55 (10), 43 (17), 41 (31)

UV : λ_{max} nm (log ϵ), in methanol; Figure 31

214 (3.09), 278 (3.02)

IR : ν_{max} cm⁻¹, KBr disc; Figure 32

3325 (br), 2959, 2920, 1643, 1615, 1476, 1449, 1350, 1204, 977

¹H-NMR : δ ppm, 300 MHz, in acetone- *d*₆; Figure 34, Table 12

¹³C-NMR : δ ppm, 75 MHz, in acetone- *d*₆; Figure 35, Table 12

4.8 Compound AG6 (Artogomezianone)

Compound AG6 was obtained as a yellow powder, soluble in acetone (12.2 mg, 3.21x10⁻⁴% based on dried weight of heartwood).

$[\alpha]_D^{20}$: +28.4° (c 0.1020 g/100ml)

EIMS : *m/z* (% relative intensity); Figure 39

452 (M^+ , 100), 417 (31), 409 (47), 401 (32), 391 (100), 381 (43),
373 (17), 335 (19), 325 (64), 309 (14), 295 (15), 227 (10), 191 (9),
179 (11)

UV : λ_{max} nm (log ϵ), in methanol; Figure 36

278 (4.57), 322 (3.10)

IR : ν_{max} cm⁻¹, KBr disc; Figure 37

3249 (br), 2958, 1643, 1619, 1480, 1452, 1353, 1206, 1160,
978, 810

¹H-NMR : δ ppm, 300 MHz, in acetone- *d*₆; Figure 40, Table 13

¹³C-NMR : δ ppm, 75 MHz, in acetone- *d*₆; Figure 41, Table 13

4.9 Compound AG7 (Norartocarpetin)

Compound AG7 was obtained as yellow prisms, soluble in acetone (4.3 mg , $1.13 \times 10^{-4}\%$ based on dried weight of heartwood).

EIMS	: m/z (% relative intensity); Figure 52
	286 (M^+ , 100), 269 (10), 258 (13), 244 (6), 229 (6), 153 (43), 134 (14), 95 (5), 69 (7)
UV	: λ_{\max} nm ($\log \epsilon$), in methanol; Figure 50
	250 (1.69), 263 (1.72), 348 (2.22)
IR	: ν_{\max} cm^{-1} , KBr disc; Figure 51
	3273 (br), 1661, 1612, 1508, 1455, 1358, 1170, 1029, 853, 829
$^1\text{H-NMR}$: δ ppm, 300 MHz, in acetone- d_6 ; Figure 53, Table 14
$^{13}\text{C-NMR}$: δ ppm, 75 MHz, in acetone- d_6 ; Figure 54, Table 14

4.10 Compound AG8 (Oxyresveratrol)

Compound AG8 was obtained as a white powder, soluble in acetone (17.9 mg , $4.71 \times 10^{-4}\%$ based on dried weight of heartwood).

EIMS	: m/z (% relative intensity); Figure 57
	244 (M^+ , 100), 227 (24), 226 (74), 198 (38), 197 (30), 181 (17), 173 (9), 170 (14), 169 (17), 147 (11), 141 (14), 115 (18), 77 (7), 69 (8)
UV	: λ_{\max} nm ($\log \epsilon$), in methanol; Figure 55
	327 (2.44)
IR	: ν_{\max} cm^{-1} , KBr disc; Figure 56
	3263 (br), 1687, 1589, 1456, 1280, 1150, 969, 822
$^1\text{H-NMR}$: δ ppm, 300 MHz, in acetone- d_6 ; Figure 58, Table 15
$^{13}\text{C-NMR}$: δ ppm, 75 MHz, in acetone- d_6 ; Figure 59, Table 15

5. Determination of Anti-Herpes Simplex Virus (HSV) Activity

In this study, plaque reduction assay (PRA) was performed against HSV-1 and HSV-2 for all isolated compounds.

5.1 Inactivation

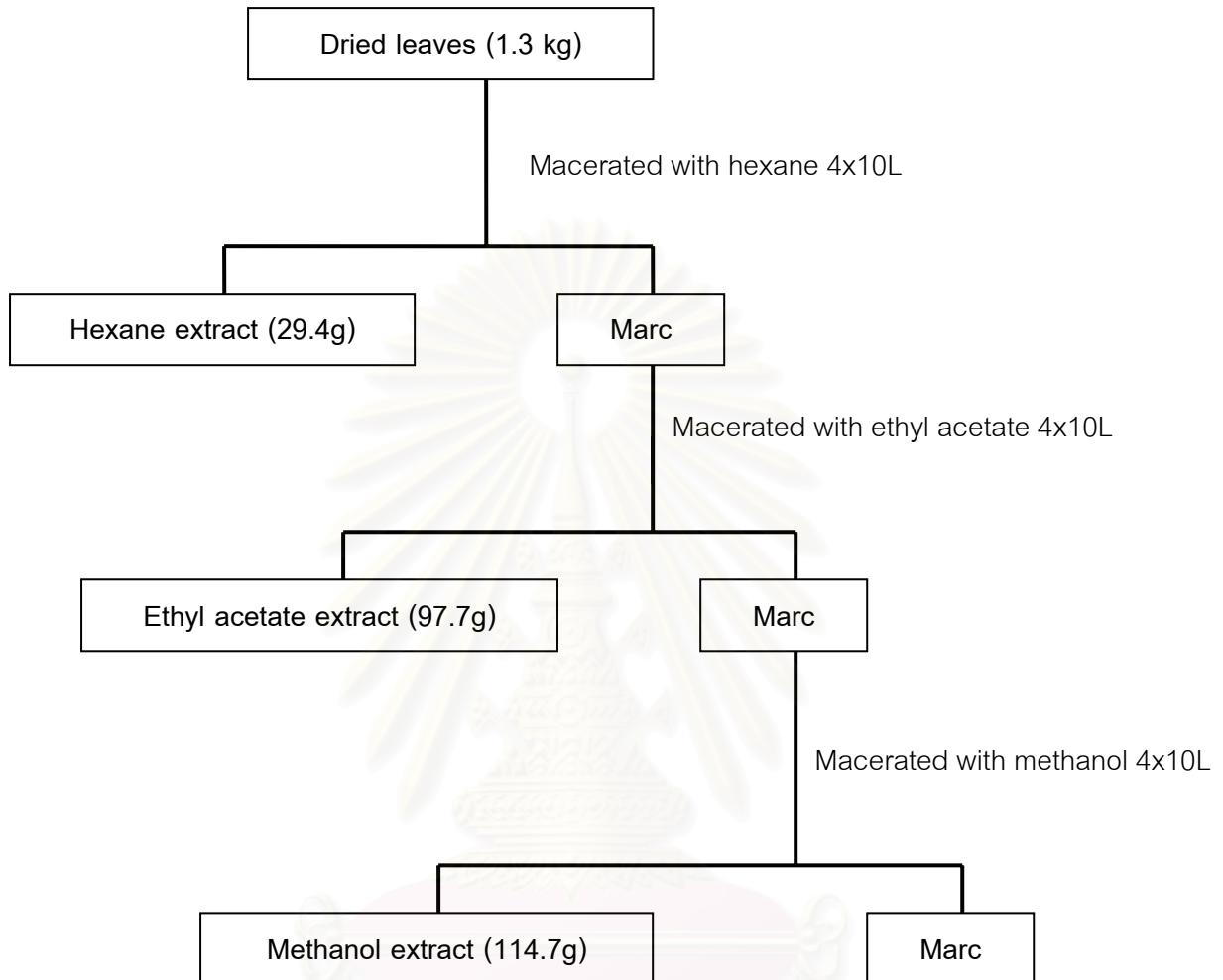
Virus (30 PFU/ 25 μL) was mixed with 25 μL of test compound in a

5% CO₂ incubator at 37°C for an hour. The mixture was then added onto Vero cells (6x10⁵ cells/ml, 50µl/well) in a 96-well microtiter plate and incubated at 37°C for 1 hour. The overlay medium containing various concentration of test compound (100µl/well) was added to the Vero cells and incubated at 37°C in humidified CO₂ incubator for 2 days. After incubation, the cells were fixed in 10% formalin and stained with 1% crystal violet for an hour. The number of plaques was counted under an inverted microscope. The percent plaque inhibition was determined. The graph plotted between values of various concentrations and percent plaque inhibition was used for IC₅₀ (inhibitor concentration at 50% of virus growth) determination.

5.2 Post- treatment

Virus (30 PFU/ 25 µL) was added into Vero cells (6x10⁵ cells/ml, 50µl/well) in a 96-well microtiter plate and incubated at 37°C for 1 hour. Fifty µl of each test compound dilution and overlay medium (100µl/well) were added to the 96-well microtiter plate and incubated at 37°C in humidified CO₂ incubator for 2 days. The cells were fixed in 10% formalin and stained with 1% crystal violet for an hour. The plaques were counted under an inverted microscope. The percent plaque inhibition was determined. The graph plotted between values of various concentrations and percent plaque inhibition was used for IC₅₀ determination.

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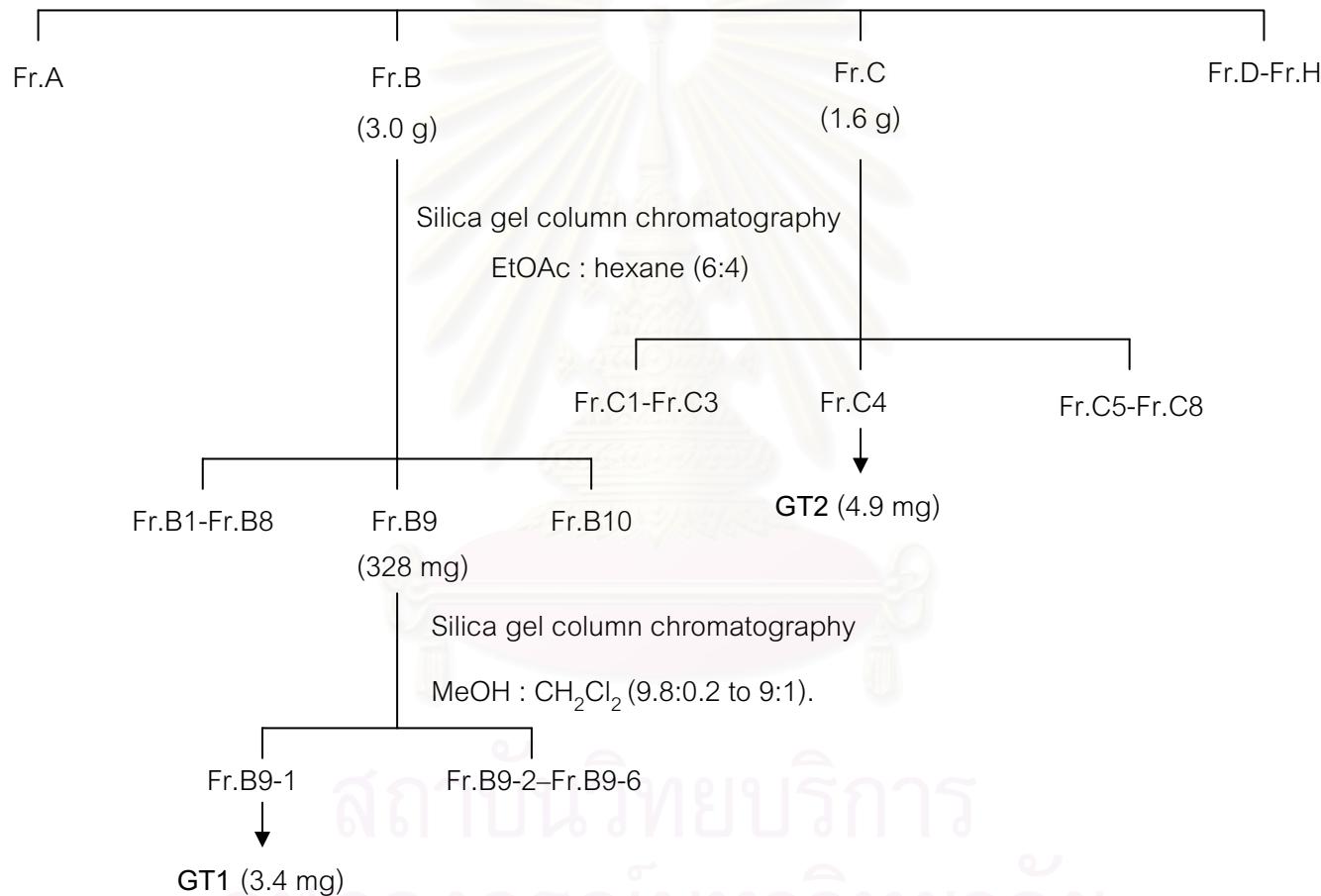


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Schemes 1: Extraction of *Goniothalamus tenuifolius* Leaves

Methanol extract (114.7 g) from leaves of *Goniothalamus tenuifolius* King

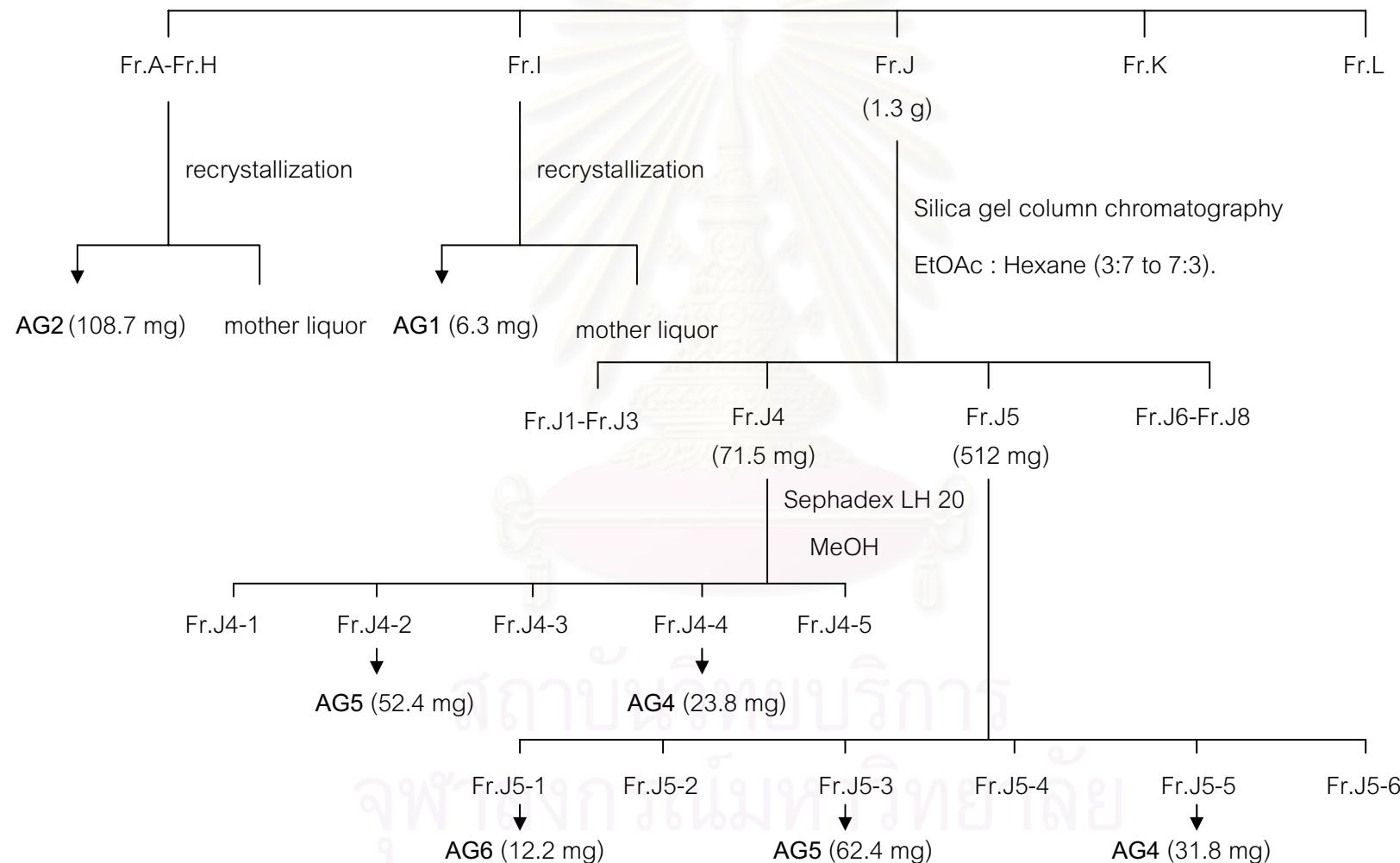
Vacuum liquid column chromatography, Silica gel No.7734, Methanol: Dichloromethane (0.2:9.8 to 1:9)



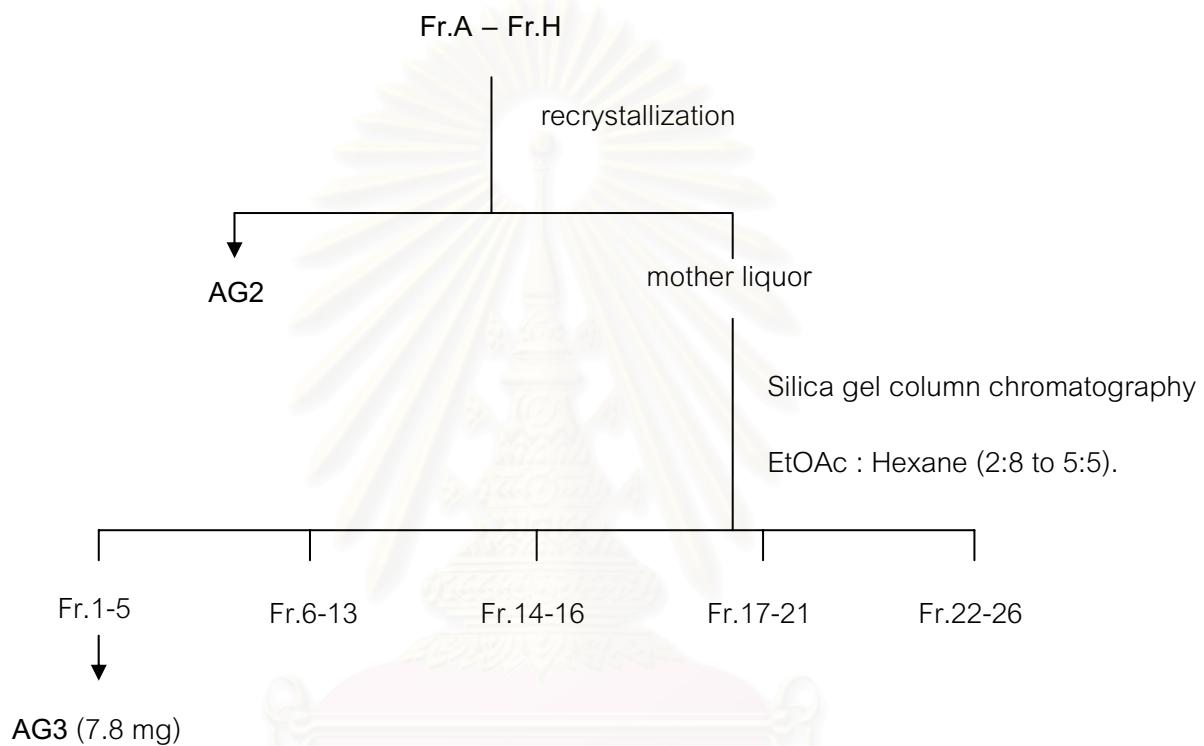
Schemes 2: Isolation of compounds GT1 and GT2

Methanol extract (160.4 g) from heartwood of *Artocarpus gomezianus* Wall. ex Tre'c.

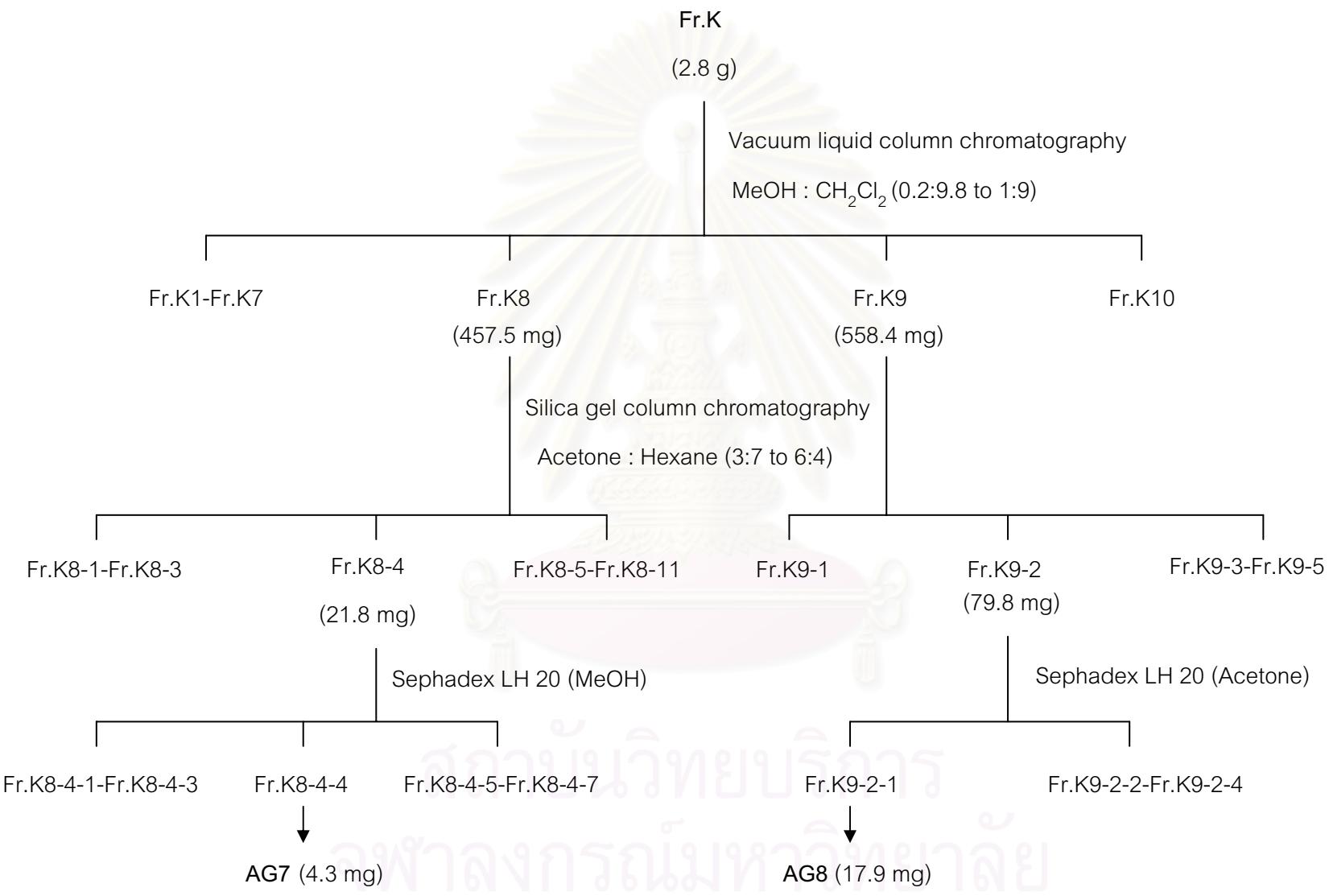
Vacuum liquid column chromatography, Silica gel No.7734, Ethyl acetate : Hexane (2:8 to 8:2)



Schemes 3: Isolation of compounds AG1, AG2, AG4, AG5, AG6



Schemes 4: Isolation of compound AG3



Schemes 5: Isolation of compounds AG7 and AG8

CHAPTER IV

RESULTS AND DISCUSSION

A methanol extract (114.7g) obtained from the dried leaves of *Goniothalamus tenuifolius* King was separated using several chromatographic techniques to afford two pure compounds (GT1 and GT2).

The dried heartwood of *Artocarpus gomezianus* Wall. ex Tre'c. (3.8 kg) was extracted with methanol to give a methanol extract (160.4 g). The methanol extract was then separated using several chromatographic techniques to yield eight pure compounds (AG1 to AG8).

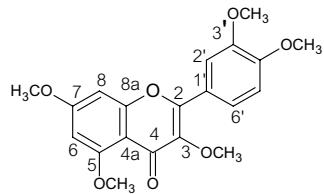
The structure determinations of all isolates were performed by interpretation of their UV, IR, NMR and MS data and then confirmed by comparison with previously reported values.

1. Structure Determination of Isolated Compounds

1.1 Structure Determination of Compound GT1

Compound GT1 was obtained as pale yellow needles. It was identified as 3,5,7,3',4'-pentamethoxyflavone [16] by comparison of its UV absorptions, ¹H and ¹³C NMR data with reported values (Likhitwitayawuid *et al.*, 2006). This methylated flavone was previously isolated from the fruits of *Amomum koenigii* (Dong, 1999). The UV spectrum (Figure 6) showed absorptions at 246, 340 nm.

The ¹H NMR spectrum (Figure 7 and Table 6) exhibited the presence of five methoxyl groups at δ 3.85, 3.88, 3.94, 3.94, 3.94 (3H each, s). In the aromatic region, signals for the A ring protons appeared at δ 6.32 (br s, H-6) and 6.48 (br s, H-8). The B ring protons displayed signals at δ 6.95 (d, $J=8.7$ Hz, H-5'), 7.67 (br s, H-6') and 7.69 (br s, H-2'). The ¹³C NMR, DEPT90, DEPT135 spectra (Figure 8 and Table 6) showed twenty signals, corresponding to five methoxyls, five methines and ten quarternary carbons.



3,5,7,3',4'-pentamethoxyflavone [16]

Table 6 NMR Spectral data of compound GT1 (CDCl_3) and 3,5,7,3',4'-pentamethoxy flavone (CDCl_3)

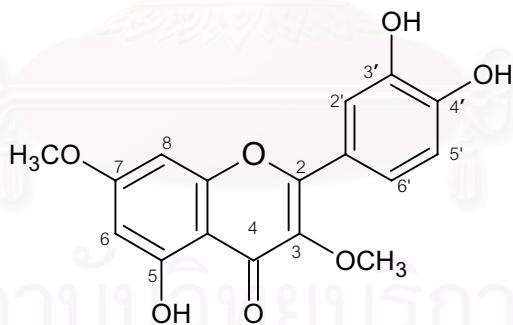
position	compound GT1		3,5,7,3',4'-Pentamethoxyflavone	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
2	-	152.5 (s)	-	152.5 (s)
3	-	141.0 (s)	-	141.1 (s)
4	-	173.9 (s)	-	174.0 (s)
5	-	161.1 (s)	-	161.0 (s)
6	6.32 (br s)	95.7 (d)	6.33 (d, 1.8)	95.7 (d)
7	-	163.9 (s)	-	163.8 (s)
8	6.48 (br s)	92.9 (d)	6.48 (d, 1.8)	92.8 (d)
8a	-	158.6 (s)	-	158.7 (s)
4a	-	109.5 (s)	-	109.5 (s)
1'	-	123.4 (s)	-	123.4 (s)
2'	7.69 (br s)	111.3 (d)	7.69 (br s)	111.3 (d)
3'	-	148.7 (s)	-	148.7 (s)
4'	-	150.7 (s)	-	150.8 (s)
5'	6.95 (d, 8.7)	110.7 (d)	6.95 (d, 8.4)	110.8 (d)
6'	7.67 (br s)	121.5 (d)	7.66 (br s)	121.6 (d)
3-OCH ₃	3.94 (s)	59.8 (q)	3.93 (s)	59.9 (q)
5-OCH ₃	3.94 (s)	55.6 (q)	3.93 (s)	55.7 (q)
7-OCH ₃	3.88 (s)	55.8 (q)	3.88 (s)	55.9 (q)
3'-OCH ₃	3.85 (s)	55.9 (q)	3.86 (s)	56.0 (q)
4'-OCH ₃	3.94 (s)	56.3 (q)	3.93 (s)	56.3 (q)

1.2 Structure Determination of Compound GT2

Compound GT2 was isolated as yellow needles. It was determined as 5,3',4'-trihydroxy-3,7-dimethoxyflavone [14] by comparison of its UV absorptions, ¹H and ¹³C NMR data with previously published values (Likhitwitayawuid *et al.*, 2006). This compound has been previously isolated from the leaves of *Combretum quadrangulare* (Ganzera *et al.*, 1998) and *Larrea cuneifolia* (Valesi *et al.*, 1972). The UV spectrum (Figure 9) exhibited absorptions at 256, 354 nm, characteristic of a flavone skeleton.

The ¹H NMR spectrum (Figure 10) showed a H-bonded phenolic proton at δ 12.87 ppm, indicating a 5-hydroxyflavone structure. It also revealed the presence of a methoxy group at δ 4.08, 4.11 (3H each, s). The A ring displayed signals for protons with meta-coupling at δ 6.46 (d, $J=1.8$ Hz, H-6) and 6.80 (d, $J=1.8$ Hz, H-8). The B ring showed a splitting pattern at δ 7.13 (d, $J=8.4$ Hz, H-5'), 7.74 (br d, $J=8.4$ Hz, H-6') and 7.86 (br s, H-2').

The ¹³C NMR (Figure 11) exhibited seventeen carbon signals. The ¹H NMR and ¹³C NMR data were shown in Table 7.



5,3',4'-trihydroxy-3,7-dimethoxyflavone [14]

Table 7 NMR Spectral data of compound GT2 (acetone- d_6) and kumatakenin

position	compound GT2		kumatakenin		
	^1H (mult, J in Hz)	^{13}C (mult)	^1H (mult, J in Hz)	^{13}C (mult)	
	acetone- d_6	acetone- d_6	benzene- d_6	acetone- d_6	acetone- d_6
2	-	157.5 (s)	-	-	157.6 (s)
3	-	139.9 (s)	-	-	140.0 (s)
4	-	179.3 (s)	-	-	179.5 (s)
5	-	162.7 (s)	-	-	162.7 (s)
6	6.46 (d, 1.8)	98.4 (d)	6.22 (d, 2.5)	6.29 (d, 1.8)	98.4 (d)
7	-	166.4 (s)	-	-	166.5 (s)
8	6.80 (d, 1.8)	92.5 (d)	6.32 (d, 2.5)	6.62 (d, 1.8)	92.7 (d)
8a	-	156.1 (s)	-	-	156.9 (s)
4a	-	106.4 (s)	-	-	106.5 (s)
1'	-	122.8 (s)	-	-	122.8 (s)
2'	7.86 (br s)	116.2 (d)	7.61 (d, 2.5)	7.70 (d, 1.8)	116.3 (d)
3'	-	145.5 (s)	-	-	145.9 (s)
4'	-	149.0 (s)	-	-	149.2 (s)
5'	7.13 (d, 8.4)	116.0 (d)	6.85 (d, 9.0)	6.97 (d, 8.4)	116.3 (d)
6'	7.74 (br d, 8.4)	122.0 (d)	7.53 (dd, 9.0, 2.5)	7.57 (dd, 8.4, 1.8)	122.1 (d)
3-OCH ₃	4.08 (s)	59.8 (q)	3.80	3.82 (s)	60.1 (q)
7-OCH ₃	4.11 (s)	56.2 (q)	3.21	3.95 (s)	56.3 (q)
OH	12.87 (br s)	-	-	12.64 (br s)	-

1.3 Structure Determination of Isolate AG1

Compound AG1 was isolated as colorless needles. Anisaldehyde TS test gave a purple color, indicative of a steroid skeleton. Through comparison of its ^1H and ^{13}C NMR spectral data with reported values (Wright *et al.*, 1978; Iribarren and Pomilio, 1985), it was identified as a mixture of β -sitosterol [138] and stigmasterol [43].

The ^1H NMR spectrum (Figure 12) of compound AG1 showed the signals at δ 5.00 (0.2H, dd, $J= 15.0, 8.4$ Hz), 5.14 (0.2H, dd, $J= 15.0, 8.4$ Hz) which were due to H-22 and H-23 of stigmasterol, and at 5.32 (1H, d, $J= 4.5$ Hz) which was H-6 of β -sitosterol and stigmasterol. The integration of H-6, H-22 and H-23 were approximately in the ratio of 1:0.2:0.2. Therefore, it could be calculated that AG1 was a mixture of β -sitosterol and stigmasterol in the ratio of 4:1.

The ^{13}C NMR spectrum (Figure 13) exhibited forty-six signals. Comparison of these data with reported ^{13}C NMR data of β -sitosterol and stigmasterol (Wright *et al.*, 1978) was demonstrated in Table 8.

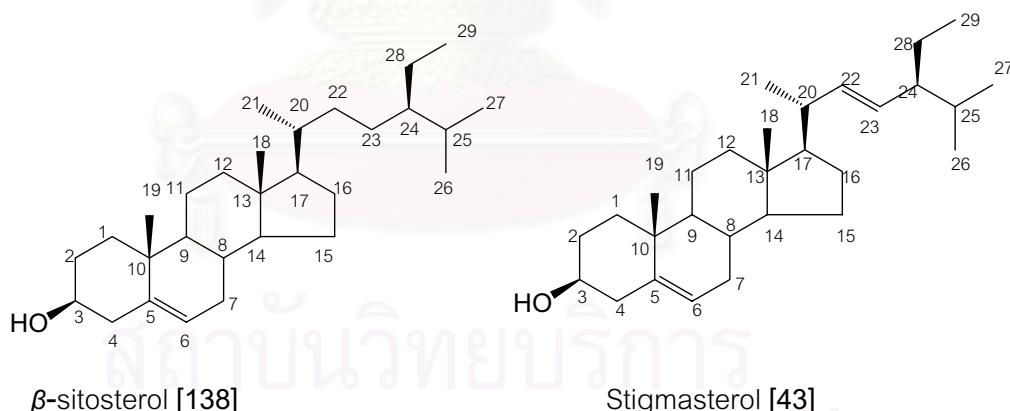


Table 8 ^{13}C NMR Spectral data of isolate AG1 (CDCl_3) and β -sitosterol, stigmasterol (CDCl_3)

Carbon position	Chemical shift (ppm)		
	β -sitosterol	Stigmasterol	Isolate AG1
1	37.31	37.31	36.83
2	31.57	31.67	31.24
3	71.69	71.81	71.41
4	42.45	42.35	41.79, 41.88
5	140.76	140.80	140.52
6	121.59	121.69	120.38
7	31.92	31.94	31.48
8	31.92	31.94	31.48
9	50.17	50.20	49.71
10	36.51	36.56	36.08
11	21.11	21.11	20.65
12	39.81	39.74	39.35
13	42.33	42.35	41.88
14	56.79	56.91	56.34, 56.45
15	24.32	24.39	23.87
16	28.26	28.96	27.81, 28.47
17	56.11	56.06	55.64, 55.69
18	11.87	12.07	11.42, 11.55
19	19.40	19.42	18.96
20	36.17	40.54	35.71, 39.92
21	18.82	21.11	18.35
22	33.95	138.37	33.53, 138.07
23	26.13	129.32	25.67, 128.94
24	45.85	51.29	45.42, 50.81
25	29.18	31.94	28.74, 31.48

Table 8 (continued)

Carbon position	Chemical shift (ppm)		
	β -sitosterol	Stigmasterol	Isolate AG1
26	19.84	21.26	19.37, 20.77
27	19.04	19.02	18.60
28	23.09	25.44	22.65, 24.95
29	12.32	12.27	11.55, 11.95

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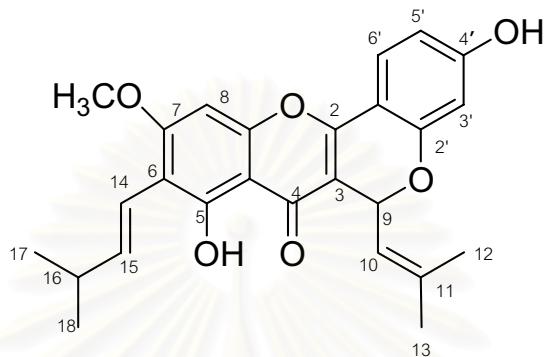
1.4 Structure Determination of Compound AG2

Compound AG2 was obtained as a yellow powder. The EI mass spectrum (Figure 16) displayed a molecular ion peak at m/z 434, consistent with the molecular formula $C_{26}H_{26}O_6$. It also showed other major peaks at m/z 391 [$M-CH_3-CO$]⁺ or [$M-C_3H_7$]⁺, 379 [$M-C_4H_7$]⁺ and the base peak at m/z 335 [$M-C_3H_7-C_4H_8$]⁺ indicating the presence of pyrano- γ,γ -dimethylallyl and $^1\Delta$ -isopentenyl moieties in this structure. The UV absorptions (Figure 14) at 258, 291 and 370 nm were characteristics of a flavone skeleton (Markham, 1982). The IR spectrum (Figure 15) showed absorption bands at 3387 (hydroxyl group), 2961 (C-H stretching of alkane), 1450-1618 (aromatic ring) and 1650 (carbonyl group) cm^{-1} .

The ^1H NMR spectrum (Figure 17 and Table 9) showed a $^1\Delta$ -isopentenyl group at C-6 of ring A at δ 1.03 (6H, d, $J=6.6$ Hz, H₃-17 and H₃-18), 2.41 (1H, m, H-16), 6.45 (1H, d, $J=16.2$ Hz, H-14) and 6.63 (1H, dd, $J=16.2, 6.6$ Hz, H-15). The methoxyl group of C-7 appeared at δ 3.92 (3H, br s), while the chelated hydroxyl group of C-5 appeared at δ 13.54. The presence of ring D, resulting from oxidative cyclization of 2'-hydroxyl group with the allylic methylene of a prenyl group at C-3 (Chen, Huang and Ou, 1993), was indicated by ^1H -NMR signals at δ 1.64 (3H, br s, H₃-13) and 1.88 (3H, br s, H₃-12) for two vinyl methyl protons, a doublet at δ 6.13 (1H, d, $J=9.3$ Hz, H-9) and 5.41 (1H, d, $J=9.3$ Hz, H-10). The ABX-type aromatic proton signals appeared at δ 6.35 (1H, br s, H-3'), 6.56 (1H, d, $J=8.7$ Hz, H-5') and 7.68 (1H, d, $J=8.7$ Hz, H-6'). The ^1H NMR spectrum also showed a singlet of an aromatic proton at δ 6.80. Their relationships were confirmed by the ^1H - ^1H COSY correlations (Figure 19). From the NOESY spectrum (Figure 20), H-9 (δ 6.13) showed NOE interaction with H₃-12 (δ 1.88), H-10 (δ 5.41) showed NOE interaction with H₃-13 (δ 1.64), whereas H-8 (δ 6.80) showed NOE interaction with 7-OCH₃ (δ 3.92).

The ^{13}C NMR, DEPT 90 and DEPT 135 spectrum (Figure 18 and Table 9) exhibited twenty-six carbon signals, corresponding to five methyls, nine methines and twelve quarternary carbons.

From all of the above spectral data and comparison with reported values (Lu and Lin, 1994; Likhitwitayawuid *et al.*, 1999), this compound was identified as cycloartocarpin [180].



Cycloartocarpin [180]

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Table 9 NMR Spectral data of compound AG2 ($\text{DMSO}-d_6$) and cycloartocarpin ($\text{DMSO}-d_6$)

position	compound AG2		cycloartocarpin	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
2	-	155.5 (s)	-	156.1 (s)
3	-	108.6 (s)	-	109.3 (s)
4	-	177.8 (s)	-	178.4 (s)
4a	-	104.6 (s)	-	105.4 (s)
5	-	158.0 (s)	-	158.4 (s)
6	-	108.8 (s)	-	109.6 (s)
7	-	162.3 (s)	-	162.9 (s)
8	6.80 (s)	90.7 (d)	6.75 (s)	91.5 (d)
8a	-	154.8 (s)	-	155.4 (s)
9	6.13 (d, 9.3)	68.9 (d)	6.12 (d, 9.3)	69.8 (d)
10	5.41 (br d, 9.3)	121.1 (d)	5.41 (br d, 9.0)	121.9 (d)
11	-	138.3 (s)	-	138.9 (s)
12	1.88 (3H, br s)	18.4 (q)	1.89 (3H, br s)	19.4 (q)
13	1.64 (3H, br s)	25.4 (q)	1.66 (3H, br s)	26.4 (q)
14	6.45 (d, 16.2)	115.7 (d)	6.44 (d, 16.5)	116.5 (d)
15	6.63 (dd, 16.2, 6.6)	141.5 (d)	6.62 (dd, 16.5, 5.7)	142.2 (d)
16	2.41 (m)	32.5 (d)	2.42 (m)	33.5 (d)
17	1.03 (3H, d, 6.6)	22.6 (q)	1.04 (3H, d, 6.6)	23.6 (q)
18	1.03 (3H, d, 6.6)	22.6 (q)	1.04 (3H, d, 6.6)	23.6 (q)
1'	-	106.4 (s)	-	107.2 (s)
2'	-	157.6 (s)	-	158.3 (s)
3'	6.35 (br s)	103.8 (d)	6.36 (br s)	104.6 (d)
4'	-	163.5 (s)	-	164.2 (s)
5'	6.56 (d, 8.7)	110.2 (d)	6.56 (d, 8.1)	111.0 (d)
6'	7.68 (d, 8.7)	125.4 (d)	7.66 (d, 8.4)	126.2 (d)
5-OH	13.54 (br s)	-	13.54 (br s)	-
7-OCH ₃	3.92 (s)	56.4 (q)	3.91 (br s)	57.3 (q)

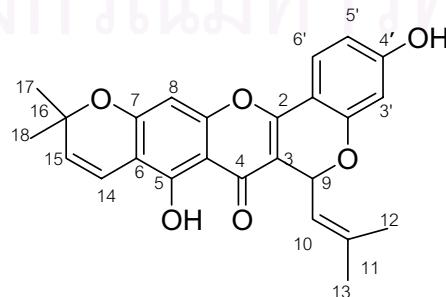
1.5 Structure Determination of Compound AG3

Compound AG3 was obtained as a yellow powder. The UV spectrum (Figure 21) showed characteristics of a flavone chromophore with absorption maxima at 293 and 370 nm. The IR spectrum (Figure 22) exhibited absorptions at 3277 (hydroxyl group), 1464-1617 (aromatic ring), 1653 (carbonyl group), 1186 (ether linkage) cm^{-1} . The EI mass spectrum (Figure 23) revealed a molecular ion peak at m/z 418, suggesting the molecular formula $\text{C}_{25}\text{H}_{22}\text{O}_6$. It also showed intense peaks at m/z 403 [M-Me]⁺, 363 [$\text{M-C}_4\text{H}_7$]⁺ and 347 [$\text{M-C}_5\text{H}_{11}$]⁺.

The ^1H NMR spectrum (Figure 24 and Table 10) showed the presence of two methyl groups at δ 1.22 (6H, s, H₃-17 and H₃-18) and *cis*-olefinic protons at δ 5.51 and 6.41, characteristics of a 2,2-dimethyl chromene (Sultana and Surendrakuma, 1989). It also exhibited signals for a γ,γ -dimethylallyl moiety, with H-9 and H-10 resonating at δ 5.96 (d, $J=9.6$ Hz) and 5.23 (d, $J=9.6$ Hz) and vinyl methyl protons at δ 1.71 and 1.45. The chelated hydroxyl proton of C-5 position appeared as a sharp singlet signal at δ 13.20, while H-8 showed at δ 6.21. The three aromatic proton signals appearing at δ 6.19 (d, $J=1.8$ Hz), 6.38 (dd, $J=8.7, 1.8$ Hz), 7.46 (d, $J=8.7$ Hz) were due to H-3', H-5' and H-6', respectively.

The ^{13}C NMR, DEPT 90 and DEPT 135 spectra (Figure 25 and Table 10) suggested the presence of four methyl carbons, eight methine carbons and thirteen quaternary carbons. The most downfield signal at δ 177.8 was assigned to C-4

By comparison of these data with reported values, compound AG3 was identified as isocyclomorusin [175] (Chen *et al.*, 1993; Likhitwitayawuid *et al.*, 1999). This compound was first reported from the stem of *Artocarpus altilis* (Chen *et al.*, 1993).



Isocyclomorusin [175]

Table 10 NMR Spectral data of compound AG3 (acetone- d_6) and isocyclomorusin (DMSO- d_6)

position	compound AG3		isocyclomorusin	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
2	-	156.2 (s)	-	156.4 (s)
3	-	109.3(s)	-	109.2 (s)
4	-	178.6 (s)	-	178.5 (s)
4a	-	105.3 (s)	-	105.7 (s)
5	-	156.2 (s)	-	156.4 (s)
6	-	105.3 (s)	-	105.6 (s)
7	-	162.2 (s)	-	159.2 (s)
8	6.21 (s)	95.5 (d)	6.50 (s)	95.5 (d)
8a	-	156.4 (s)	-	156.5 (s)
9	5.96 (d, 9.6)	69.7 (d)	6.10 (d, 9.3)	69.7 (d)
10	5.23 (br d, 9.6)	121.4 (d)	5.40 (br d, 8.7)	121.9 (d)
11	-	139.1 (s)	-	139.1 (s)
12	1.71 (3H, br s)	18.3 (q)	1.83 (3H, br s)	19.2 (q)
13	1.45 (3H, br s)	25.4 (q)	1.62 (3H, br s)	26.3 (q)
14	6.41 (d, 9.9)	115.3 (d)	6.57 (d, 9.9)	115.4 (d)
15	5.51 (d, 9.9)	129.0 (d)	5.77 (d, 9.9)	129.8 (d)
16	-	78.0 (s)	-	78.8 (s)
17	1.22 (br s)	27.9 (q)	1.40 (br s)	28.7 (q)
18	1.22 (br s)	27.9 (q)	1.40 (br s)	28.6 (q)
1'	-	107.2 (s)	-	107.2 (s)
2'	-	158.3 (s)	-	158.4 (s)
3'	6.19 (d, 1.8)	104.3 (d)	6.35 (d, 2.1)	104.6 (d)
4'	-	163.9 (s)	-	164.5 (s)
5'	6.38 (dd, 8.7, 1.8)	110.6 (s)	6.55 (dd, 8.1, 2.1)	111.1 (s)
6'	7.46 (d, 8.7)	126.1 (d)	7.62 (d, 8.1)	126.3 (d)
5-OH	13.20 (s)	-	13.16 (br s)	-

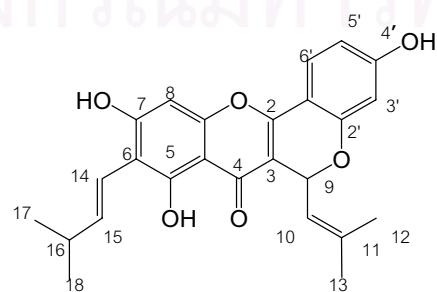
1.6 Structure Determination of Compound AG4

Compound AG4 was obtained as a yellow powder. Its UV spectrum (Figure 26) in methanol showed characteristics of a flavone chromophore with maxima at 257, 292, 367 nm. The IR spectrum (Figure 27) exhibited absorptions at 3228 (hydroxyl group), 1455-1615 (aromatic ring), 1699 (carbonyl group) cm^{-1} . The EI mass spectrum (Figure 28) afforded a molecular ion peak at m/z 420, corresponding to the molecular formula $\text{C}_{25}\text{H}_{24}\text{O}_6$. Other significant peaks appeared at m/z 377 [$\text{M}-\text{C}_3\text{H}_7]^+$, 365 [$\text{M}-\text{C}_4\text{H}_7]^+$.

The structure of compound AG4 was similar to that of compound AG2, except for the absence of methoxyl group. The ^1H NMR spectrum (Figure 29 and Table 11) showed signals for a $^1\Delta$ -isopentenyl group at C-6 of ring A at δ 1.05 (6H, d, $J=6.9$ Hz, H₃-17 and H₃-18), 2.44 (1H, m, H-16), 6.59 (1H, d, $J=16.2$ Hz, H-14), and 6.75 (1H, d, $J=16.2$, 6.9 Hz, H-15). It also possessed a γ,γ -dimethylallyl, as indicated by the two methine protons at δ 5.45 (d, $J=9.3$ Hz, H-10) and 6.19 (d, $J=9.3$ Hz, H-9), two methyl singlets at δ 1.69 (H₃-13) and 1.92 (H₃-12). The chelated hydroxyl group of C-5 showed at δ 13.74, while H-8 appeared at δ 6.60. The aromatic proton signals of ring B appearing at δ 6.41 (1H, d, $J=2.1$ Hz), 6.61 (1H, br d, $J=8.7$ Hz), 7.67 (1H, d, $J=8.7$ Hz) could be assigned to H-3', H-5' and H-6', respectively.

The ^{13}C NMR, DEPT 90 and DEPT 135 spectra (Figure 30 and Table 11) indicated the presence of four methyl carbons, nine methine carbons and twelve quarternary carbons.

These spectral analyses led to the identification of compound AG4 as norcycloartocarpin [278]. It has been previously isolated from the heartwood of *Artocarpus lakoocha* (Venkataraman, 1972).



Norcycloartocarpin [278]

Table 11 NMR Spectral data of compound AG4 (acetone- d_6) and cycloartocarpin (DMSO- d_6)

position	compound AG4		cycloartocarpin	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
2	-	155.9 (s)	-	156.1 (s)
3	-	109.3 (s)	-	109.3 (s)
4	-	178.9 (s)	-	178.4 (s)
4a	-	105.1 (s)	-	105.4 (s)
5	-	160.1 (s)	-	158.4 (s)
6	-	109.3 (s)	-	109.6 (s)
7	-	161.9 (s)	-	162.9 (s)
8	6.60 (s)	94.1 (d)	6.75 (s)	91.5 (d)
8a	-	155.3 (s)	-	155.4 (s)
9	6.19 (d, 9.3)	70.0 (d)	6.12 (d, 9.3)	69.8 (d)
10	5.45 (d, 9.3)	121.9 (d)	5.41 (br d, 9.0)	121.9 (d)
11	-	138.6 (s)	-	138.9 (s)
12	1.92 (3H, br s)	18.4 (q)	1.89 (3H, br s)	19.4 (q)
13	1.69 (3H, br s)	25.6 (q)	1.66 (3H, br s)	26.4 (q)
14	6.59 (d, 16.2)	116.9 (d)	6.44 (d, 16.5)	116.5 (d)
15	6.75 (dd, 16.2, 6.9)	142.1 (d)	6.62 (dd, 16.5, 5.7)	142.2 (d)
16	2.44 (m)	33.2 (d)	2.42 (m)	33.5 (d)
17	1.05 (3H, d, 6.9)	22.6 (q)	1.04 (3H, d, 6.6)	23.6 (q)
18	1.05 (3H, d, 6.9)	22.6 (q)	1.04 (3H, d, 6.6)	23.6 (q)
1'	-	108.1 (s)	-	107.2 (s)
2'	-	158.4 (s)	-	158.3 (s)
3'	6.41 (d, 2.1)	104.3 (d)	6.36 (br s)	104.6 (d)
4'	-	163.6 (s)	-	164.2 (s)
5'	6.61 (br d, 8.7)	110.4 (d)	6.56 (d, 8.1)	111.0 (d)
6'	7.67 (d, 8.7)	126.1 (d)	7.66 (d, 8.4)	126.2 (d)
5-OH	13.74 (br s)	-	13.54 (br s)	-

1.7 Structure Determination of Compound AG5

Compound AG5 was obtained as a yellow powder. The UV maxima (Figure 31) at 214, 278 nm and the IR absorptions (Figure 32) at 3325 (hydroxyl group), 1449-1643 (aromatic ring), 1701 (conjugated carbonyl) cm^{-1} were suggestive of a flavone skeleton. The EIMS spectrum (Figure 33) showed a $[\text{M}]^+$ ion peak at m/z 436, analyzed for $\text{C}_{26}\text{H}_{28}\text{O}_6$.

The ^1H NMR spectrum (Figure 34 and Table 12) displayed one methoxyl group at δ 3.95. Signals for aromatic protons appeared at δ 6.55 (1H, d, $J=2.4$ Hz, H-3'), 6.51 (1H, dd, $J=8.4$, 2.4 Hz, H-5') and 7.19 (1H, d, $J=8.4$ Hz, H-6'). The chelated hydroxyl group at C-5 appeared at δ 13.95, and H-8 showed at δ 6.54. It also revealed the presence of signals for ${}^1\Delta$ -isopentenyl group at δ 1.07 (6H, d, $J=6.9$ Hz, H₃-17 and H₃-18), 2.42 (1H, m, H-16), 6.58 (1H, d, $J=16.2$ Hz, H-14) and 6.71 (1H, dd, $J=16.2$, 6.9 Hz, H-15). Furthermore, it possessed prenyl group at C-3, as indicated by the methylene protons at δ 3.11 (2H, d, $J=6.9$ Hz, H-9) and 5.11 (1H, br t, $J=6.9$ Hz, H-10) and two methyl protons at δ 1.42 (H₃-12) and 1.55 (H₃-13).

The ^{13}C NMR, DEPT 90 and DEPT 135 spectra (Figure 35 and Table 12) showed twenty-six carbon signals, corresponding to five methyls, one methylene, eight methines and twelve quaternary carbons.

By comparison of these data with previously published data, compound AG5 was identified as artocarpin [149] (Likhithwitayawuid *et al.*, 2000). Artocarpin was previously found in several species of the genus *Artocarpus* (Venkataraman, 1972).

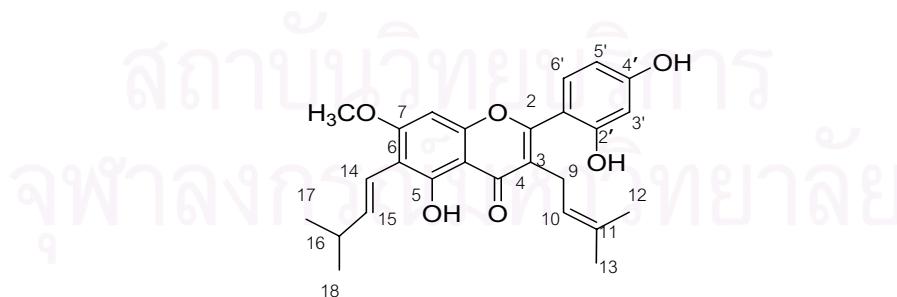


Table 12 NMR Spectral data of compound AG5 (acetone- d_6) and artocarpin (DMSO- d_6)

position	compound AG5		artocarpin	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
2	-	161.1 (s)	-	162.9 (s)
3	-	120.6 (s)	-	121.1 (s)
4	-	182.0 (s)	-	182.7 (s)
4a	-	104.2 (s)	-	105.0 (s)
5	-	158.5 (s)	-	158.9 (s)
6	-	108.4 (s)	-	109.1 (s)
7	-	162.5 (s)	-	163.4 (s)
8	6.54 (s)	89.1 (d)	6.65 (s)	91.0 (d)
8a	-	155.9 (s)	-	158.6 (s)
9	3.11 (d, 6.9)	23.3 (t)	3.02 (d, 6.7)	24.5 (t)
10	5.11 (br t, 6.9)	121.2 (d)	5.05 (br t, 7.0)	122.3 (d)
11	-	131.4 (s)	-	132.1 (s)
12	1.42 (br s)	17.9 (q)	1.38 (br s)	18.2 (q)
13	1.55 (br s)	25.1 (q)	1.55 (br s)	26.3 (q)
14	6.58 (d, 16.2)	115.6 (d)	6.50 (d, 16.5)	116.7 (d)
15	6.71 (dd, 16.2, 6.9)	141.2 (d)	6.64 (dd, 16.5, 6.9)	142.0 (d)
16	2.42 (m)	32.6 (d)	2.44 (m)	33.4 (d)
17	1.07 (d, 6.9)	22.3 (q)	1.06 (d, 6.6)	23.5 (q)
18	1.07 (d, 6.9)	22.3 (q)	1.04 (d, 6.6)	23.5 (q)
1'	-	111.5 (s)	-	111.7 (s)
2'	-	156.1 (s)	-	157.3 (s)
3'	6.55 (d, 2.4)	102.5 (d)	6.45 (d, 1.8)	103.5 (d)
4'	-	160.1 (s)	-	161.3 (s)
5'	6.51 (dd, 8.4, 2.4)	106.8 (d)	6.36 (dd, 8.1, 2.1)	107.6 (d)
6'	7.19 (d, 8.4)	131.3 (d)	7.12 (d, 8.4)	131.9 (d)
5-OH	13.95 (br s)	-	13.89 (br s)	-
7-OCH ₃	3.95 (br s)	-	3.89 (br s)	-

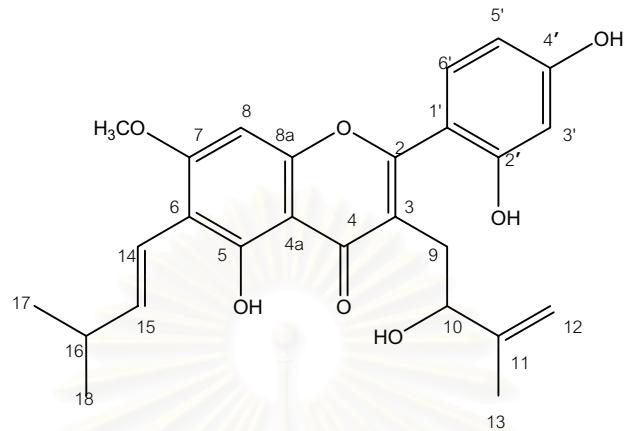
1.8 Structure Determination of Compound AG6

Compound AG6 was isolated as a yellow powder. It showed an $[M]^+$ ion peak at m/z 452 in the EIMS (Figure 39) and an $[M+H]^+$ ion at m/z 453.1908 in the high resolution positive ESIMS (Figure 38), corresponding to the molecular formula $C_{26}H_{28}O_7$. The IR spectrum (Figure 37) showed absorption bands of hydroxyl (3249 cm^{-1}), carbonyl group (1700 cm^{-1}), aromatic ring ($1452\text{-}1643\text{ cm}^{-1}$). The UV spectrum (Figure 36) exhibited absorption at 278, 322 nm, suggestive of a flavone chromophore.

The structure of compound AG6 resembled that of compound AG5 (artocarpin), having a $^1\Delta$ -isopentenyl group at C-6 of ring A. The 1H NMR spectrum (Figure 40 and Table 13) showed signals for this moiety at δ 1.10 (6H, d, $J=6.9\text{ Hz}$, $H_3\text{-}17$ and $H_3\text{-}18$), 2.45 (1H, m, H-16), 6.60 (d, $J=16.2\text{ Hz}$, H-14) and 6.73 (dd, $J=16.2, 6.9\text{ Hz}$, H-15). A sharp singlet at δ 13.83 indicated a chelated OH group. It also showed a methoxy proton signal at δ 3.98, and the position of the methoxy at C-7 was confirmed by NOESY data (Figure 44). The aromatic protons of ring B showed an ABX pattern at δ 6.54 (d, $J=2.1\text{ Hz}$, H-3'), 6.54 (d, $J=9.0, 2.1\text{ Hz}$, H-5') and 7.33 (d, $J=9.0\text{ Hz}$, H-6'). Coupling between these protons were confirmed by a $^1H\text{-}^1H$ COSY experiment (Figure 43). The singlet at δ 6.59 was assigned to H-8. Furthermore, this compound possessed two pairs of methylene protons at δ 2.60 (1H, dd, $J=13.8, 8.7\text{ Hz}$, H-9), 2.80 (1H, dd, $J=13.8, 5.1\text{ Hz}$, H-9), and at δ 4.68, 4.83 (1H each, s, H-12), a methine doublet at δ 4.44 (br s, H-10) and one methyl singlet at 1.59 ($H_3\text{-}13$).

The ^{13}C NMR, DEPT 90 and DEPT 135 spectra (Figure 41 and Table 13) indicated the presence of four methyls, two methylenes, eight methines and twelve quaternary carbons. The HMBC spectrum (Figure 45-49) showed correlation of the long-range coupled 1H and ^{13}C nuclei. The intramolecular H-bonded hydroxyl group showed long range correlations with C-5, C-6 and C-4a. The methylene protons at position 9 showed long range correlations with C-2, C-3 and C-4. Other HMBC correlations are summarized in Table 13.

From the above data, compound AG6 was identified as a new flavone and named artogomezianone [389].



Artogomezianone [389]

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Table 13 NMR Spectral data of compound AG6 (acetone- d_6)

position	compound AG6		HMBC (correlation with ^1H)
	^1H (mult., J in Hz)	^{13}C (mult)	
2	-	163.3 (s)	H-9 and H-6'
3	-	119.8 (s)	H-9
4	-	183.8 (s)	H-9
4a	-	105.4 (s)	5-OH and H-8
5	-	159.7 (s)	5-OH and H-14
6	-	109.9 (s)	5-OH and H-15
7	-	163.9 (s)	H-14 and 7-OCH ₃
8	6.59 (s)	90.5 (d)	-
8a	-	156.9 (s)	-
9	2.60 (dd, 13.8, 8.7) 2.80 (dd, 13.8, 5.1)	32.9 (t)	-
10	4.44 (br s)	73.9 (d)	H-9, H-12 and H-13
11	-	148.7 (s)	H-9 and H-13
12	4.68, 4.83 (br s)	110.4 (t)	H-13
13	1.59 (br s)	17.6 (q)	H-12
14	6.60 (d, 16.2)	116.9 (d)	H-15, H-16
15	6.73 (dd, 16.2, 6.9)	142.3 (d)	H-14, H-16, H-17 and H-18
16	2.45 (m)	33.9 (d)	H-14, H-15, H-17 and H-18
17	1.10 (d, 6.9)	23.0 (q)	H-15 and H-16
18	1.10 (d, 6.9)	23.0 (q)	H-15 and H-16
1'	-	112.9 (s)	H-3' and H-5'
2'	-	157.4 (s)	H-3' and H-6'
3'	6.54 (d, 2.1)	104.1 (d)	H-5'
4'	-	161.5 (s)	H-5' and H-6'
5'	6.54 (dd, 9.0, 2.1)	108.2 (d)	H-3'
6'	7.33 (d, 9.0)	132.8 (d)	-
5-OH	13.83 (br s)	-	-
7-OCH ₃	3.98 (s)	56.6 (q)	-

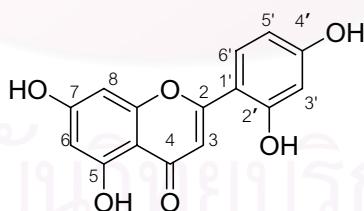
1.9 Structure Determination of Compound AG7

Compound AG7, a yellow prism, was analyzed for $C_{15}H_{10}O_6$ from its $[M]^+$ ion peak at m/z 286 in the EIMS (Figure 53). Other significant peaks showed at 269 $[M-OH]^+$, 258 $[M-CO]^+$, 153 $[M-C_8H_5O_2]^+$ and 134 $[M-C_7H_4O_4]^+$. The UV absorptions (Figure 51) at 250, 263, 348 nm and the IR bands (Figure 52) at 3273 (hydroxyl group), 1455-1612 (aromatic ring), 1661 (carbonyl group) cm^{-1} were suggestive of a flavone skeleton.

The ^1H NMR spectrum (Figure 54 and Table 14) displayed six aromatic and olefenic protons at δ 6.2-7.9, together with chelated hydroxyl protons at δ 13.11. The meta-coupled signals at δ 6.22 and 6.48 could be assigned to H-6 and H-8. The ABM-type aromatic proton signals exhibited at δ 6.59 (br s), 6.55 (br d, $J=8.7$ Hz) and 7.82 (d, $J=8.7$ Hz) were due to H-3', H-5' and H-6', respectively.

The ^{13}C NMR, DEPT 90 and DEPT 135 spectra (Figure 55 and Table 14) showed fifteen carbon signals, indicating six methine carbons and nine quaternary carbons.

Based on the above spectral evidence, compound AG7 was identified as norartocarpin [198] (Likhitwitayawuid *et al.*, 1999). It was first found in *Artocarpus heterophyllus* (Venkataraman, 1965).



Norartocarpin [198]

Table 14 NMR Spectral data of compound AG7 (acetone- d_6) and norartocarpentin (DMSO- d_6)

position	compound AG7		norartocarpentin	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
2	-	162.0 (s)	-	162.4 (s)
3	7.06 (s)	107.2 (d)	7.00 (s)	107.2 (d)
4	-	182.1 (s)	-	182.5 (s)
4a	-	103.9 (s)	-	104.3 (s)
5	-	161.1 (s)	-	162.1 (s)
6	6.22 (br s)	98.1 (d)	6.18 (d, 1.8)	99.4 (d)
7	-	163.3 (s)	-	164.6 (s)
8	6.48 (br s)	93.2 (d)	6.44 (d, 1.8)	94.6 (d)
8a	-	157.5 (s)	-	158.0 (s)
1'	-	109.4 (s)	-	109.4 (s)
2'	-	157.9 (s)	-	159.5 (s)
3'	6.59 (br s)	103.0 (d)	6.50 (br s)	104.0 (d)
4'	-	161.5 (s)	-	162.4 (s)
5'	6.55 (br d, 8.7)	107.8 (d)	6.44 (m)	108.9 (d)
6'	7.82 (d, 8.7)	129.6 (d)	7.76 (d, 8.7)	130.5 (d)
5-OH	13.11 (br s)	-	13.06 (br s)	-

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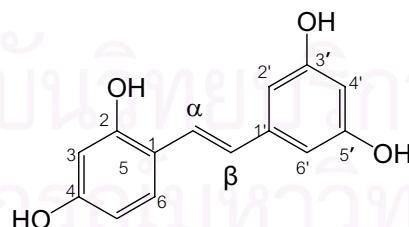
1.10 Structure Determination of Compound AG8

Compound AG8 was obtained as a white powder. The molecular weight should be 244 ($C_{14}H_{12}O_4$) as shown by an $[M]^+$ ion peak at m/z 244 in the EIMS (Figure 58). The IR spectrum (Figure 57) exhibited absorption bands at 3263 (hydroxyl group), 1687 (C=C), 1456-1589 (aromatic ring), 969 (*trans* -CH=CH-)cm⁻¹. The UV spectrum (Figure 56) showed a maximal absorption at 327 nm, suggestive of a stilbene skeleton.

The ¹H NMR spectrum (Figure 59 and Table 15) revealed six aromatic protons at δ 6.23 (1H, br s), 6.38 (1H, dd, J =8.4, 2.4 Hz), 6.43 (1H, br s), 6.51 (2H, br s) and 7.40 (1H, d, J =8.4 Hz), typical for H-4', H-5, H-3, H-2', H-6' and H-6, respectively. *Trans* olefinic protons at δ 6.88 and 7.33 (1H each, d, J =16.5 Hz) could be assigned to H- β and H- α .

The ¹³C NMR, DEPT 90 and DEPT 135 spectra (Figure 60 and Table 15) showed fourteen carbon signals, suggesting the presence of eight methine carbons and six quaternary carbons.

This compound was identified as oxyresveratrol [343] by analysis of the above spectral data and comparison with earlier reported ¹H and ¹³C NMR data (Likhithwitayawuid *et al.*, 2001). It has been previously isolated from Osage orange wood (*Toxylon pomiferum, Maclura pomifera*) (Gerber, 1986).



Oxyresveratrol [343]

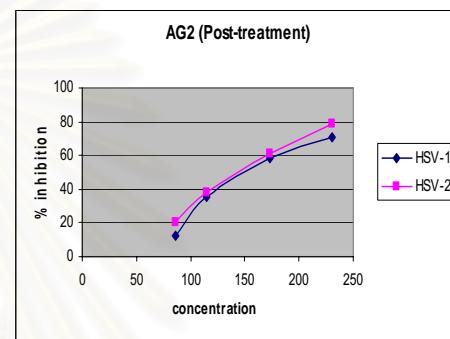
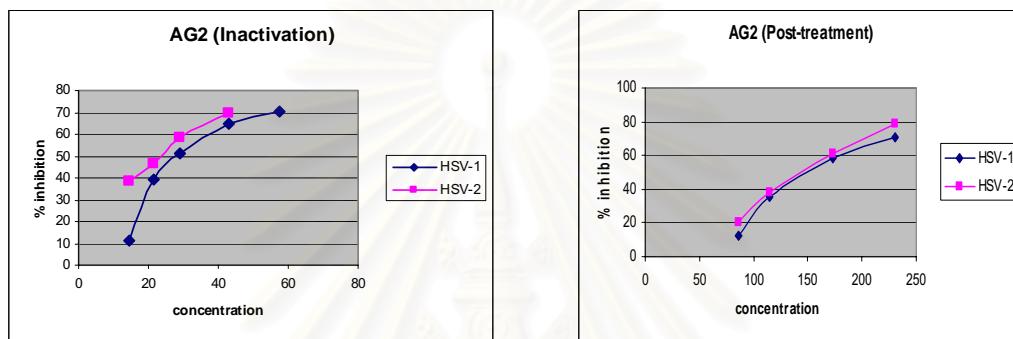
Table 15 NMR Spectral data of compound AG8 (acetone- d_6) and oxyresveratrol (DMSO- d_6)

position	compound AG8		oxyresveratrol	
	^1H (mult., J in Hz)	^{13}C (mult)	^1H (mult., J in Hz)	^{13}C (mult)
1	-	115.9 (s)	-	115.4 (s)
2	-	155.6 (s)	-	156.1 (s)
3	6.43 (br s)	102.2 (d)	6.33 (d, 2.4)	102.7 (d)
4	-	157.8 (s)	-	158.2 (s)
5	6.38 (dd, 8.4, 2.4)	107.1 (d)	6.25 (dd, 8.4, 2.4)	107.4 (d)
6	7.40 (d, 8.4)	126.9 (d)	7.34 (d, 8.4)	127.3 (d)
1'	-	140.3 (s)	-	140.1 (s)
2'	6.51 (br s)	104.1 (d)	6.35 (d, 1.8)	104.2 (d)
3'	-	158.2 (s)	-	158.5 (s)
4'	6.23 (br s)	100.9 (d)	6.08 (s)	101.5 (d)
5'	-	158.2 (s)	-	158.5 (s)
6'	6.51 (br s)	104.1 (d)	6.35 (d, 1.8)	104.2 (d)
α	7.33 (d, 16.5)	123.0 (d)	7.15 (d, 16.5)	123.3 (d)
β	6.88 (d, 16.5)	124.9 (d)	6.77 (d, 16.5)	124.7 (d)

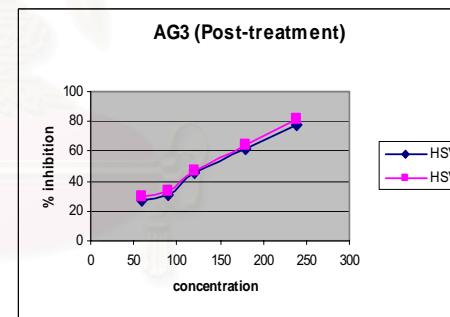
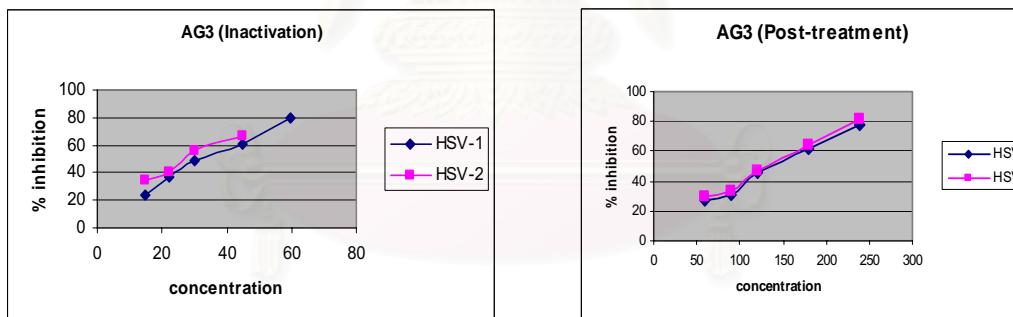
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2. Anti- Herpes Simplex Activity

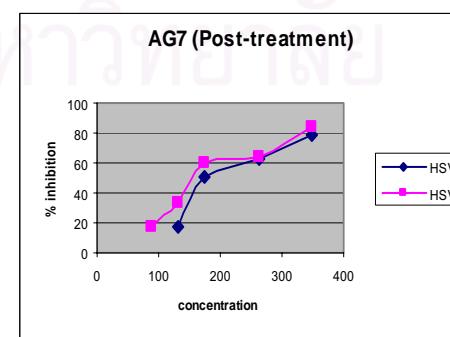
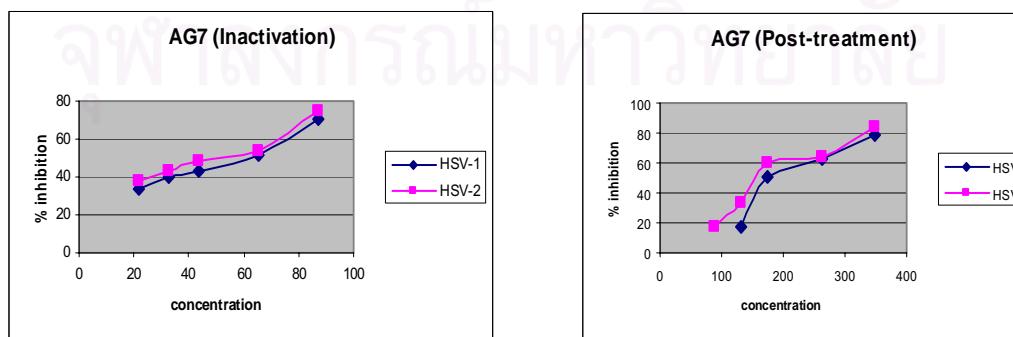
Evaluation of anti herpes simplex activity of pure compounds from the heartwood of *Artocarpus gomezianus* was performed by the plaque reduction assay (Inactivation and Post- treatment). Compounds exhibiting more than 50% inhibition without cytotoxicity at 25 µg/ml were further evaluated for IC₅₀ (inhibition concentration at 50% of virus growth). Acyclovir was employed as positive control. The result are summarized in Table 16



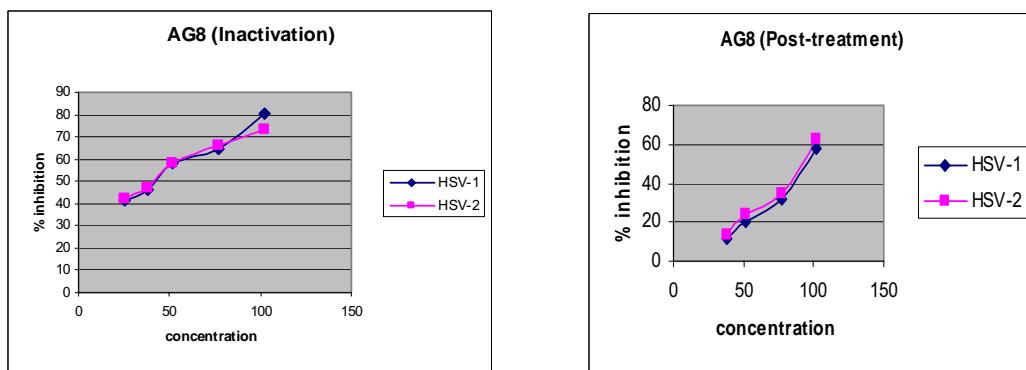
A. AG2



B. AG3



C. AG7



D. AG8

Figure 5 Anti-herpes simplex virus activity of compound AG2, AG3, AG7 and AG8 on plaque reduction assay

Table 16 Percentage of HSV inhibition by pure compounds isolated from *A. gomezianus*

compounds	IC ₅₀ (μM)		IC ₅₀ (μM)	
	Inactivation		Post- treatment	
	HSV-1	HSV-2	HSV-1	HSV-2
AG2	28.2	23.5	150.4	148.5
AG3	30.4	27.2	130.5	126.6
AG4	-	-	-	-
AG5	-	-	-	-
AG6	-	-	-	-
AG7	63.0	52.2	174.0	155.5
AG8	42.8	42.5	95.2	91.5
Acyclovir	1.45	2.85	6.25	7.15

(-) Cytotoxicity at 25 $\mu\text{g}/\text{ml}$

From Table 16, seven pure compounds were determined for anti-herpes simplex activity. It was found that cycloartocarpin [180], isocyclomorusin [175], norartocarpentin [198], oxyresveratrol [343] showed moderate activity against both types of virus in Inactivation assay but weak anti-HSV activity in Post-treatment assay.

CHAPTER V

CONCLUSION

In this study, two known 3-methoxyflavone compounds were isolated from the leaves of *Goniothalamus tenuifolius* King (Annonaceae). They were identified as 3,5,7,3',4'-pentamethoxyflavone [16] and 5,3',4'-trihydroxy-3,7-dimethoxyflavone [14]. Chemical investigation of the heartwood of *Artocarpus gomezianus* Wall. ex Tre'c. (Moraceae) led to the isolation of a new compound, named artogomezianone [389] and six known compounds including cycloartocarpin [180], isocyclomorusin [175], norcycloartocarpin [278], artocarpin [149], norartocarpentin [198], oxyresveratrol [343] and mixture of β -sitosterol [138] and stigmasterol [43]. The isolated compounds were evaluated for anti-herpes simplex virus activity. Cycloartocarpin [180], isocyclomorusin [175], norartocarpentin [198] and oxyresveratrol [343] showed moderate activity against both types of herpes simplex virus in the Inactivation assay and weak activity in the Post-treatment method.

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APPENDIX

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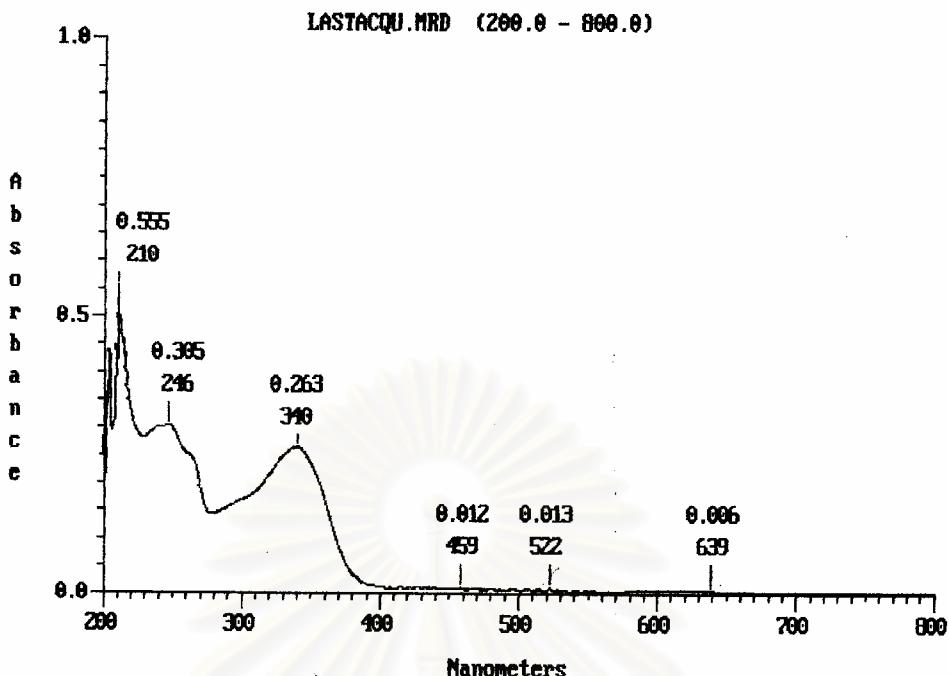


Figure 6 UV Spectrum of compound GT1 (Methanol)

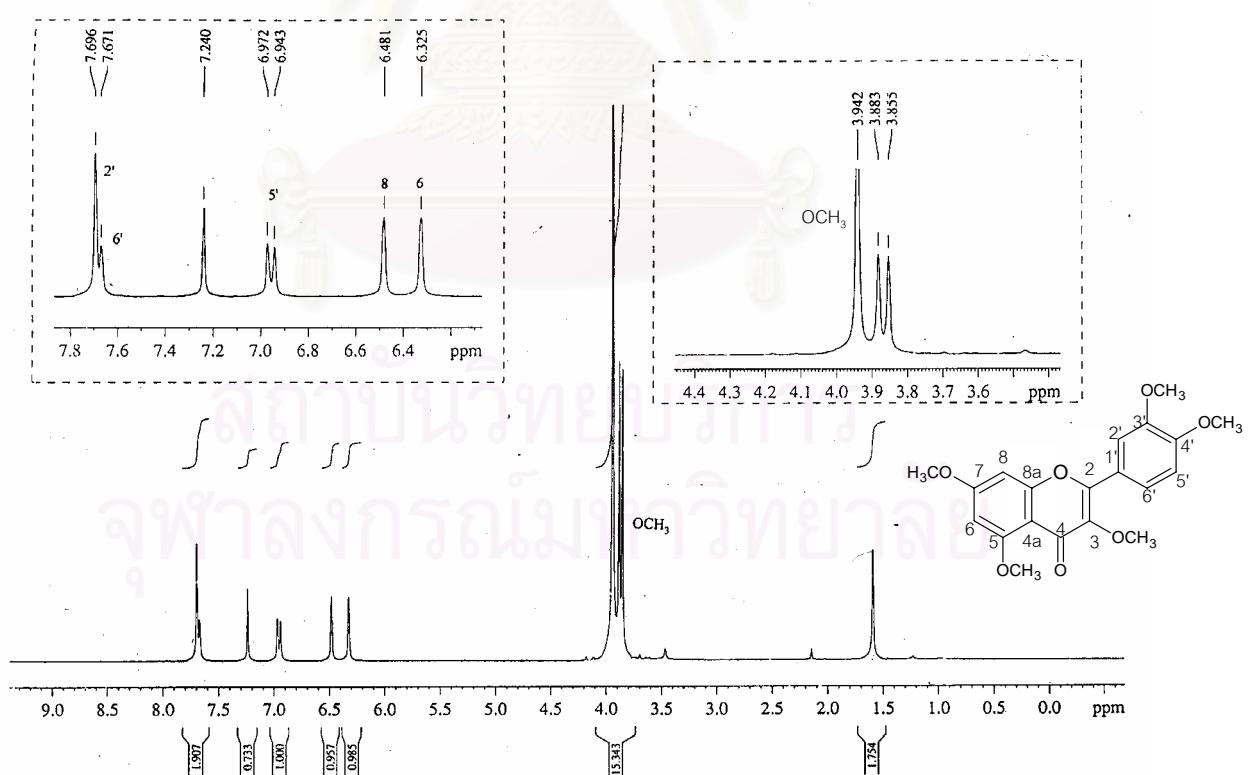


Figure 7 ^1H -NMR (300 MHz) Spectrum of compound GT1 (CDCl_3)

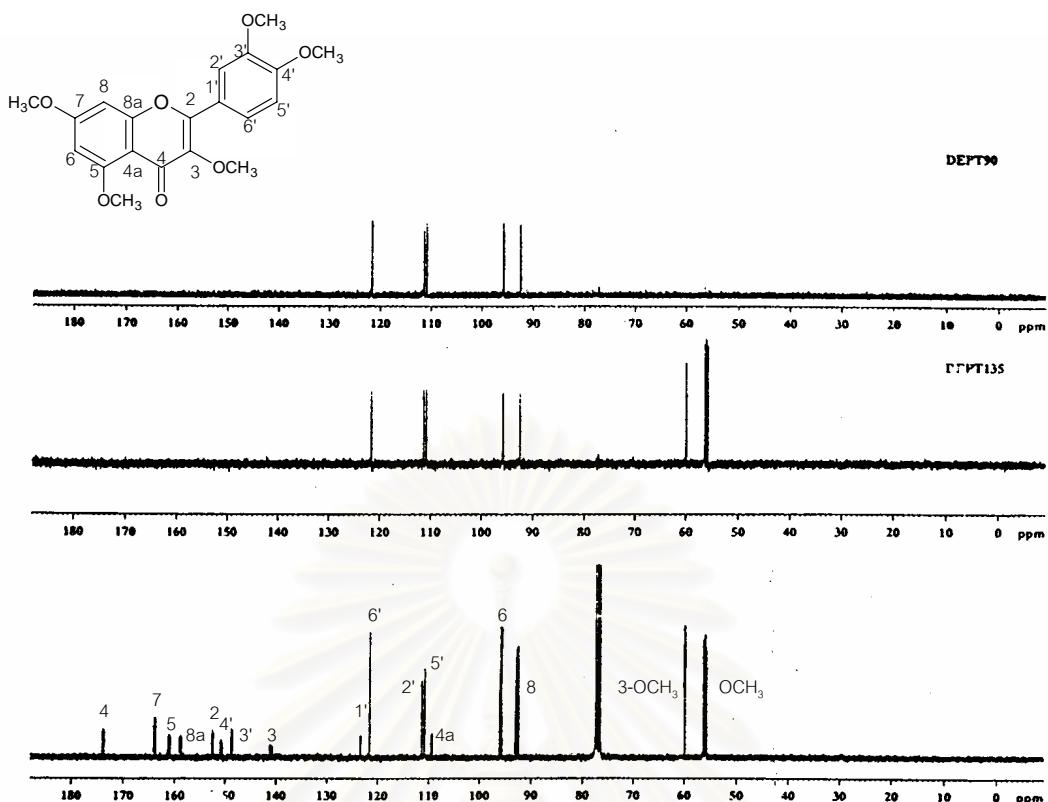


Figure 8 ^{13}C -NMR (75 MHz) Spectrum of compound GT1 (CDCl_3)

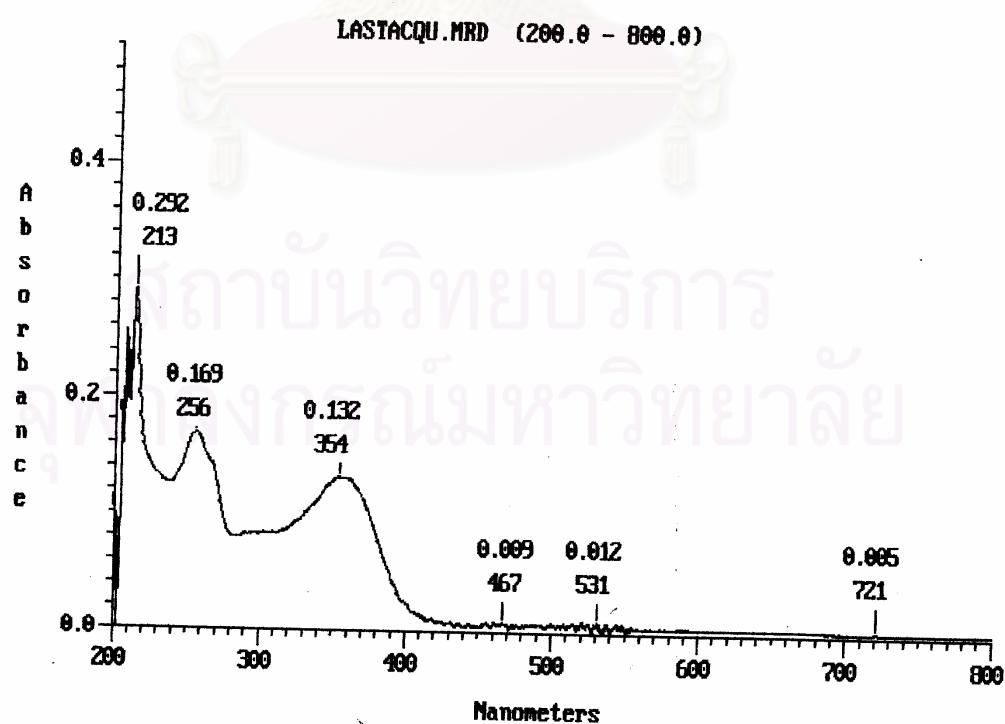


Figure 9 UV Spectrum of compound GT2 (Methanol)

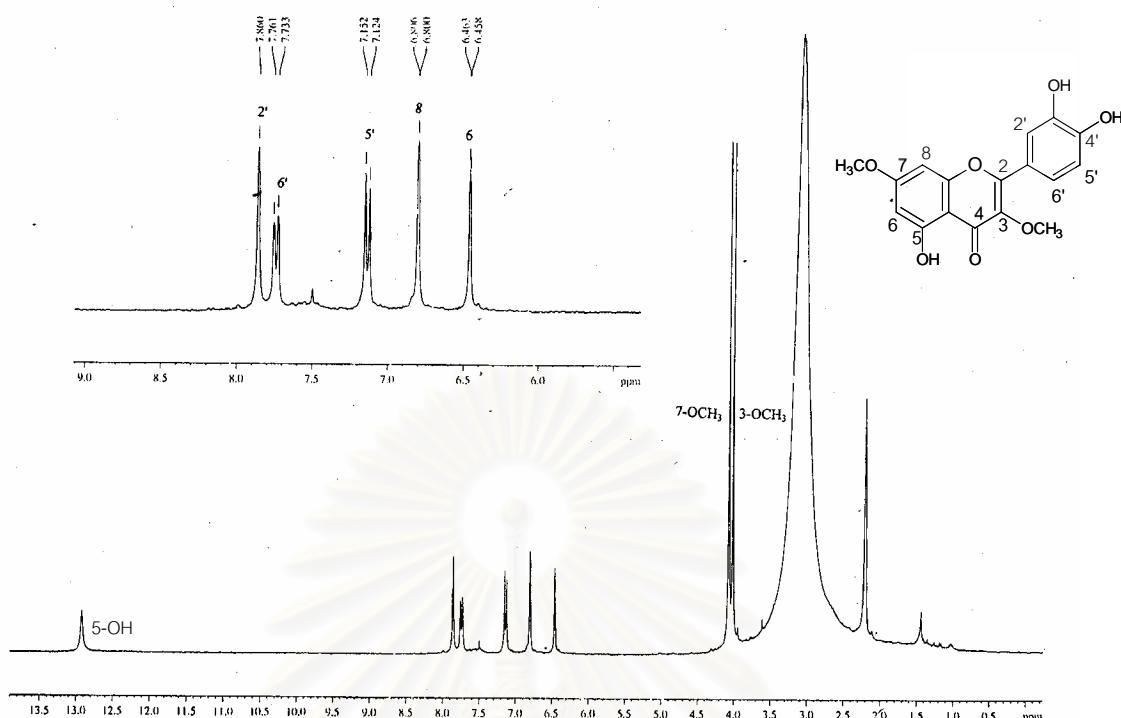


Figure 10 ^1H -NMR (300 MHz) Spectrum of compound GT2 (DMSO- d_6)

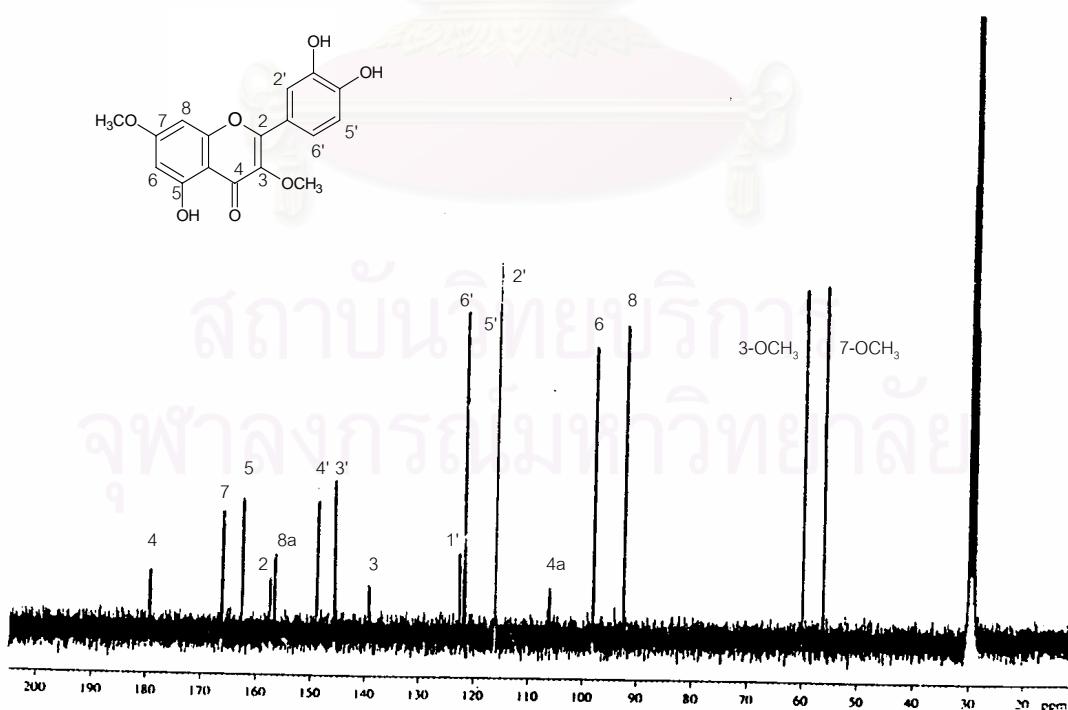
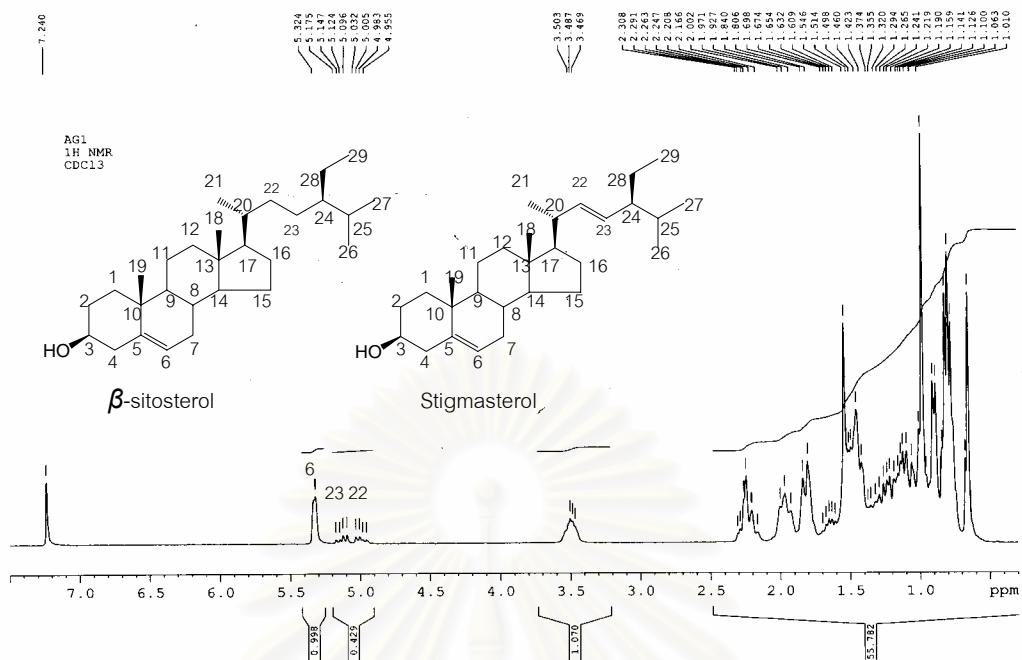
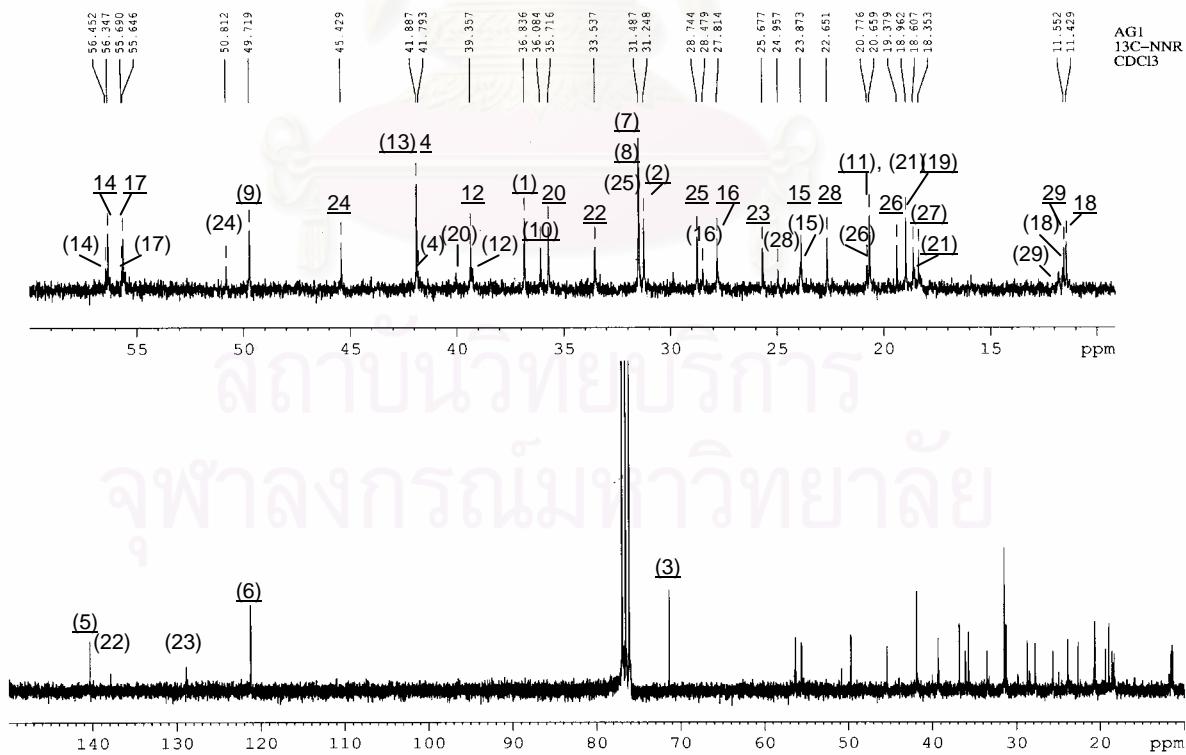


Figure 11 ^{13}C -NMR (75 MHz) Spectrum of compound GT2 (DMSO- d_6)

Figure 12 ^1H -NMR (300 MHz) Spectrum of compound AG1 (CDCl₃)Figure 13 ^{13}C -NMR (75 MHz) Spectrum of compound AG1 (CDCl₃)

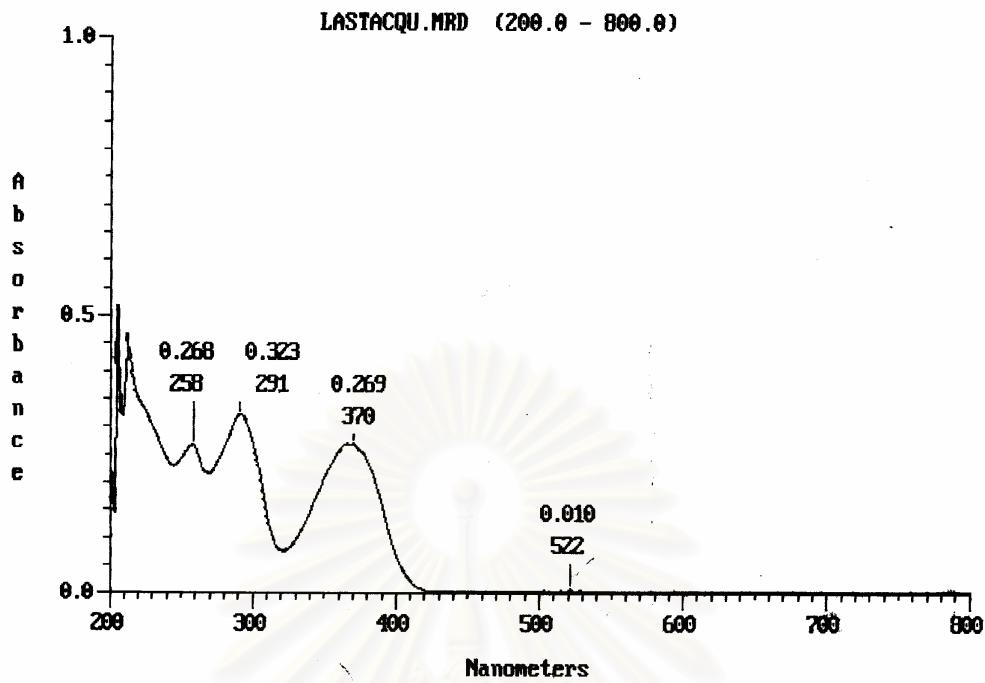


Figure 14 UV Spectrum of compound AG2 (Methanol)

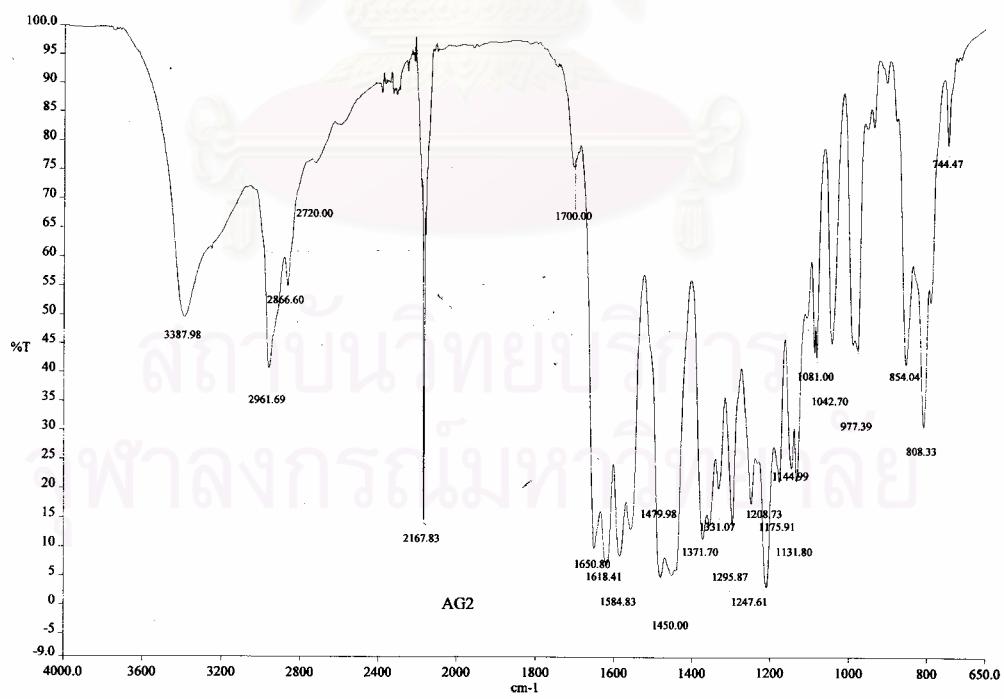


Figure 15 IR Spectrum of compound AG2

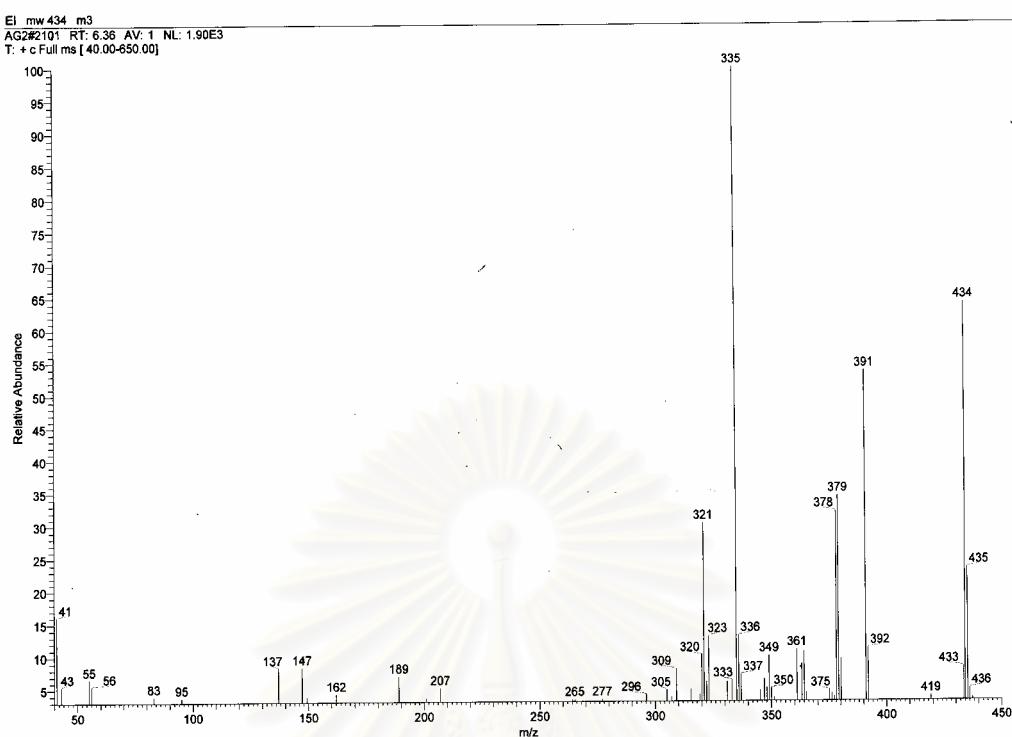


Figure 16 Mass Spectrum of compound AG2

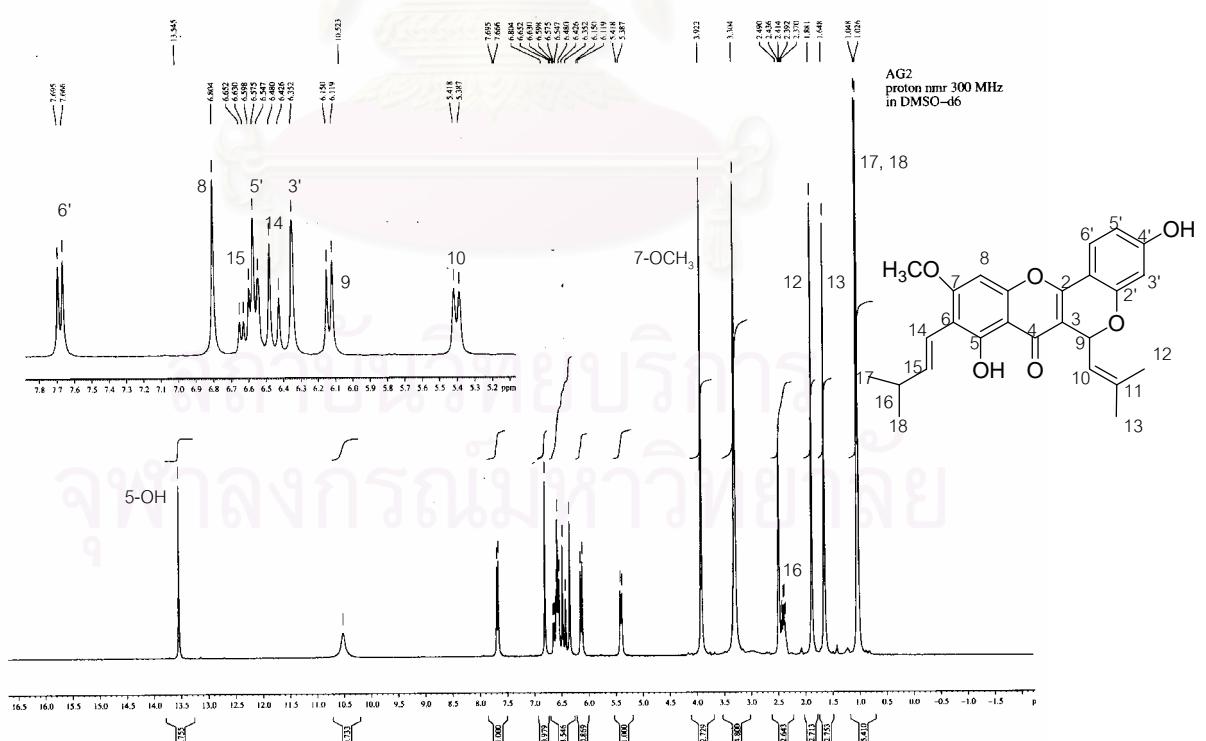


Figure 17 ^1H -NMR (300 MHz) Spectrum of compound AG2 (DMSO- d_6)

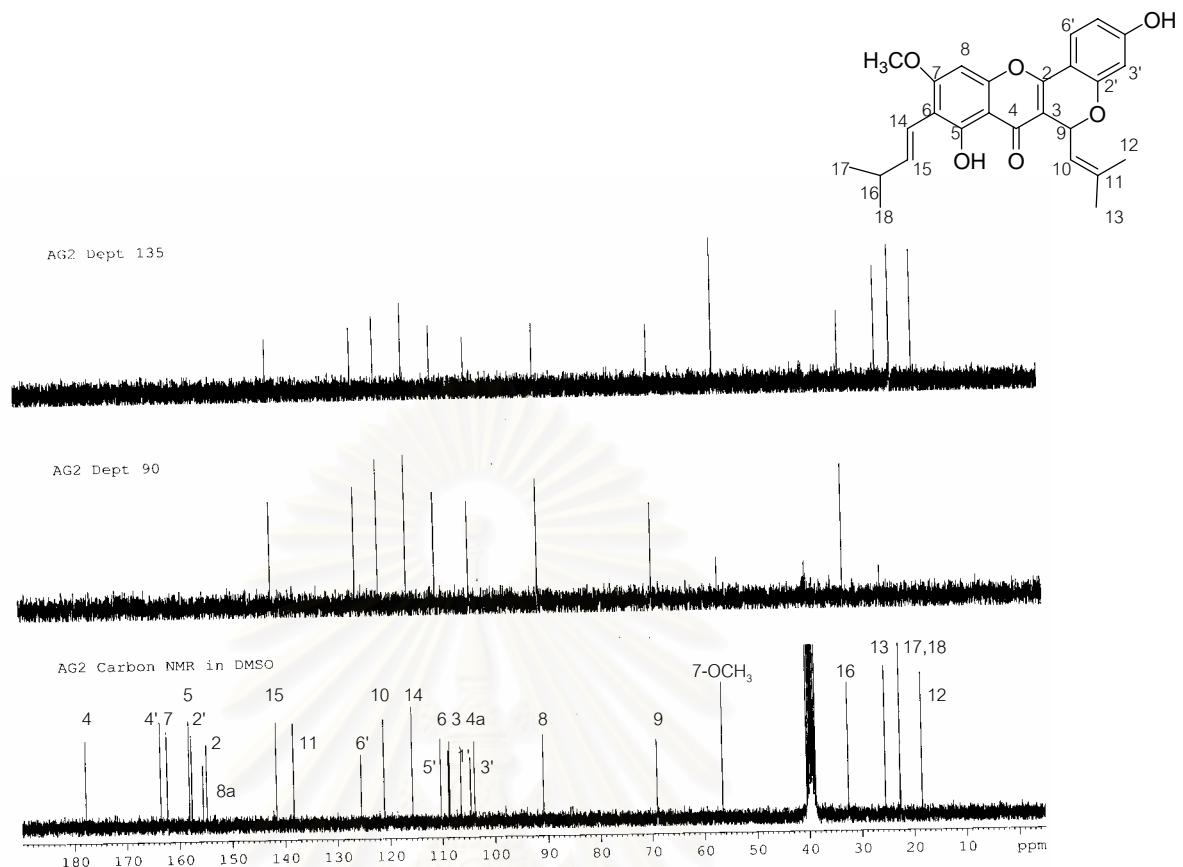


Figure 18 ^{13}C -NMR (75 MHz) Spectrum of compound AG2 ($\text{DMSO}-d_3$)

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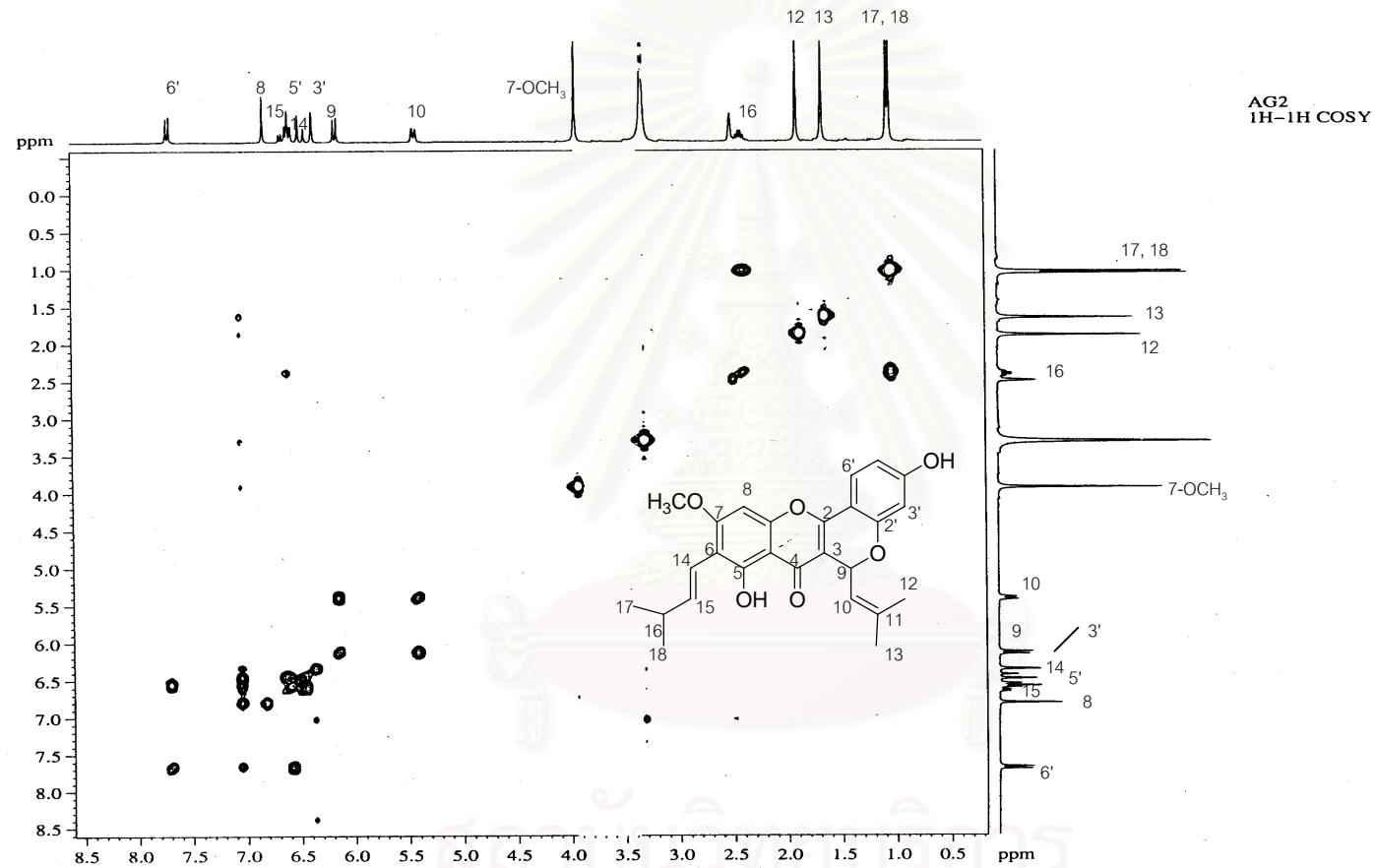


Figure 19 ^1H - ^1H COSY Spectrum of compound AG2 (DMSO- d_6)

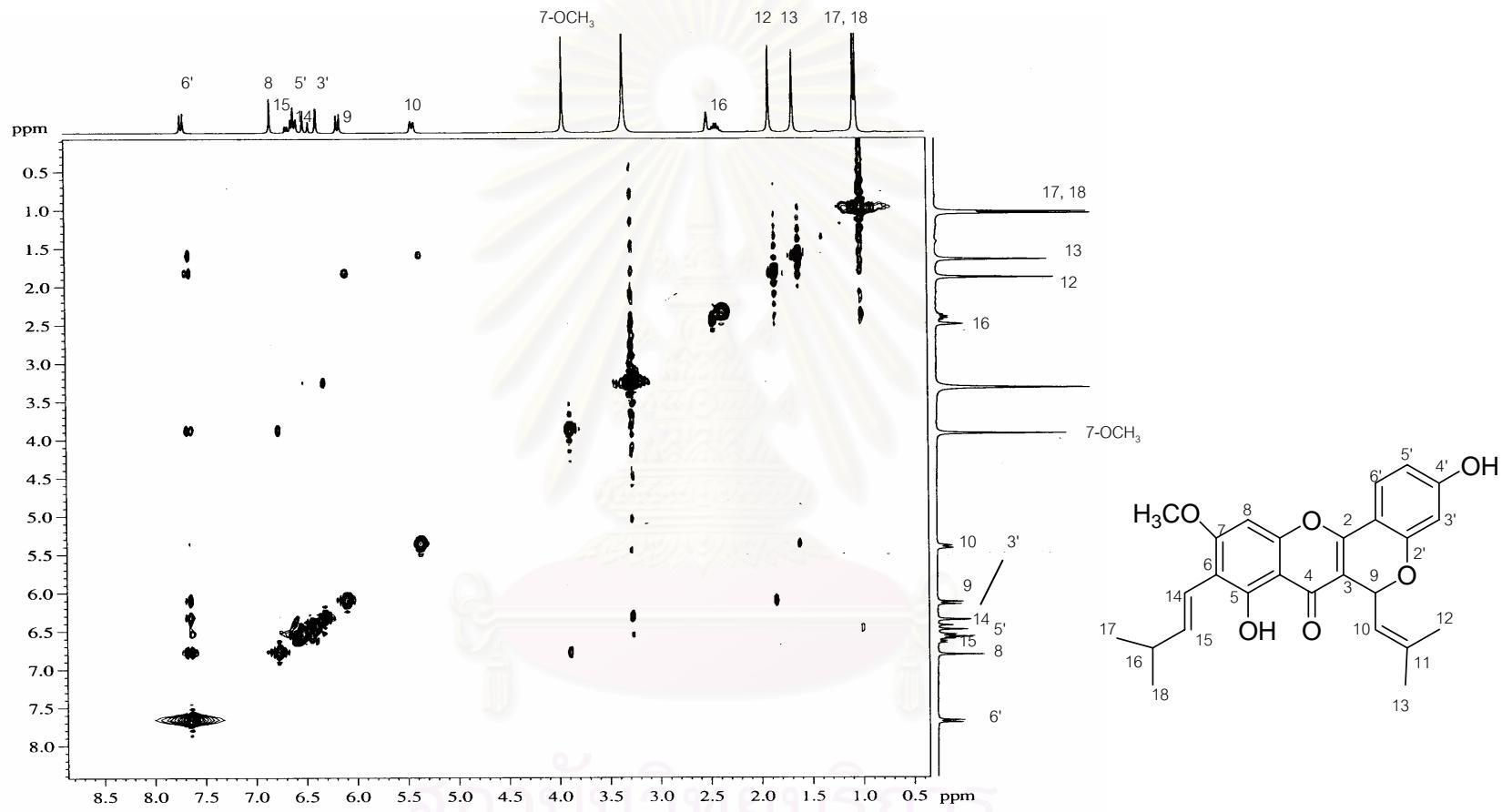


Figure 20 NOESY Spectrum of compound AG2 ($\text{DMSO}-d_6$)

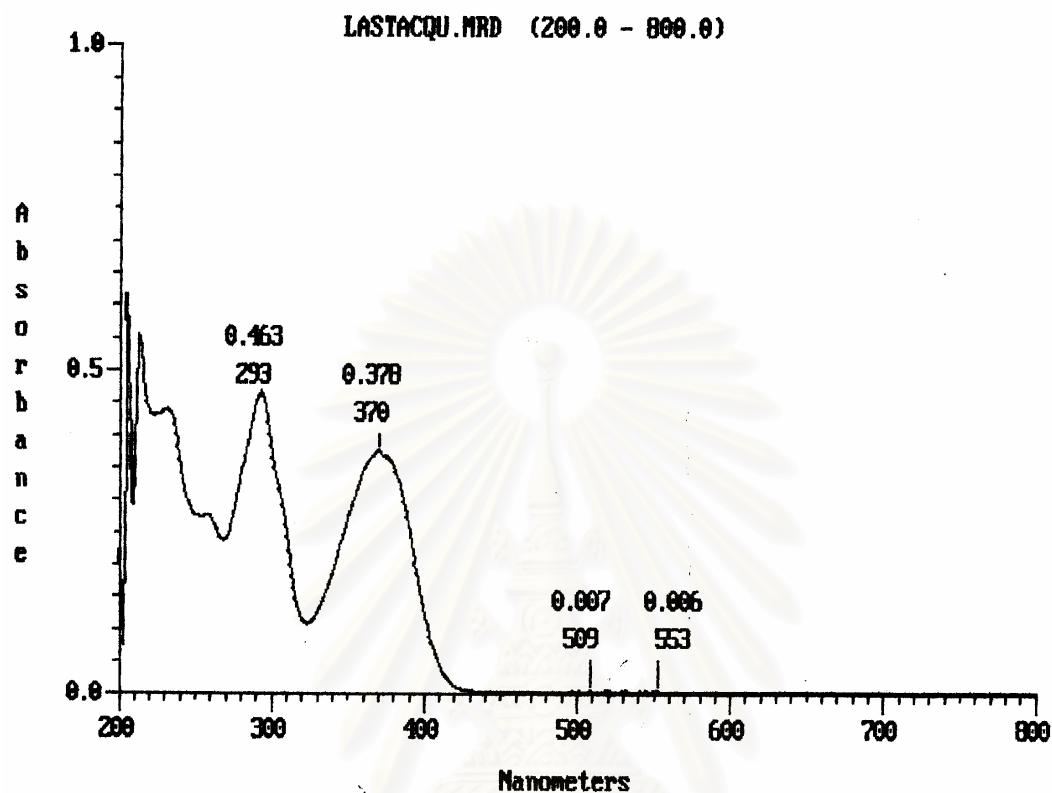


Figure 21 UV Spectrum of compound AG3 (Methanol)

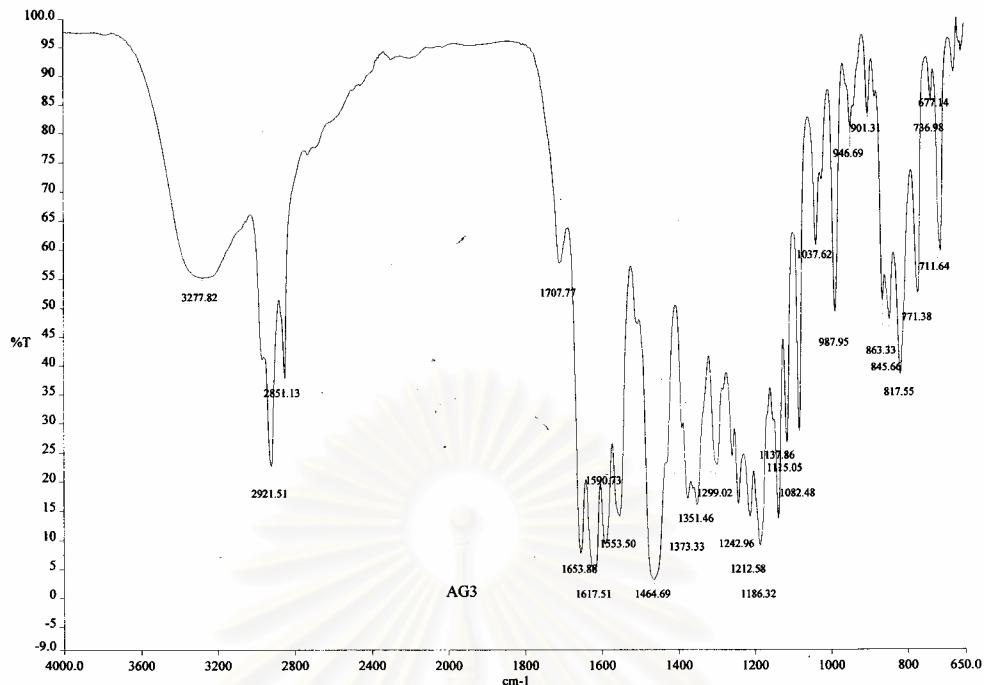


Figure 22 IR Spectrum of compound AG3

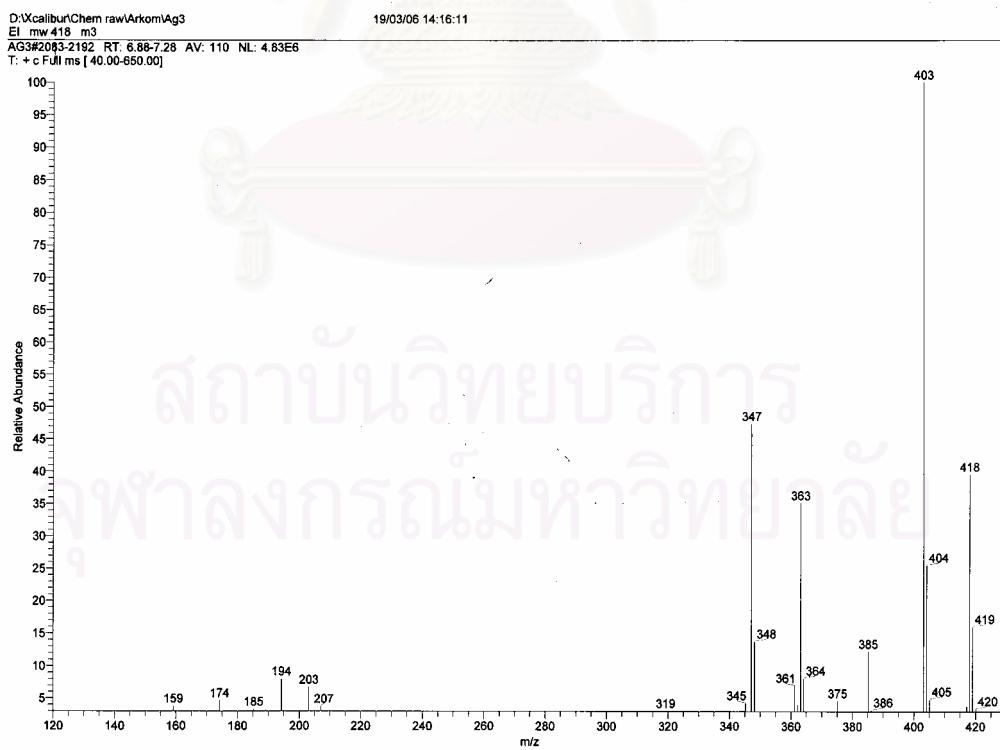
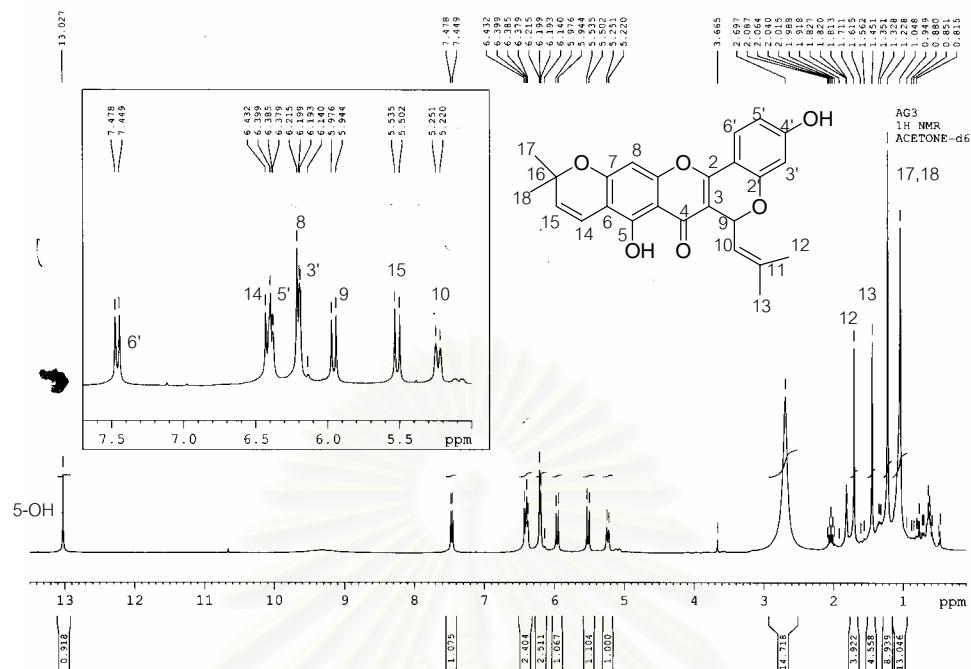


Figure 23 Mass Spectrum of compound AG3



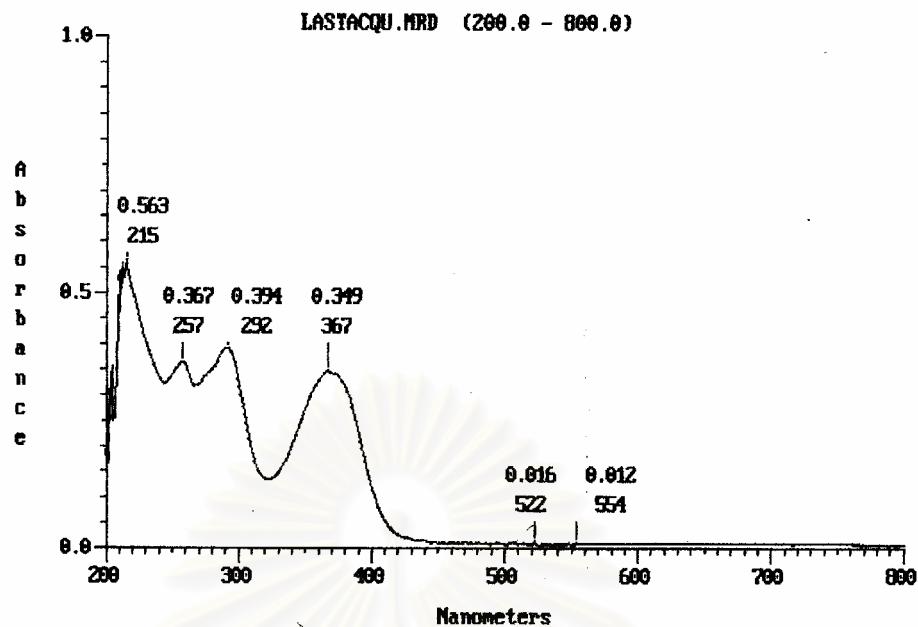


Figure 26 UV Spectrum of compound AG4 (Methanol)

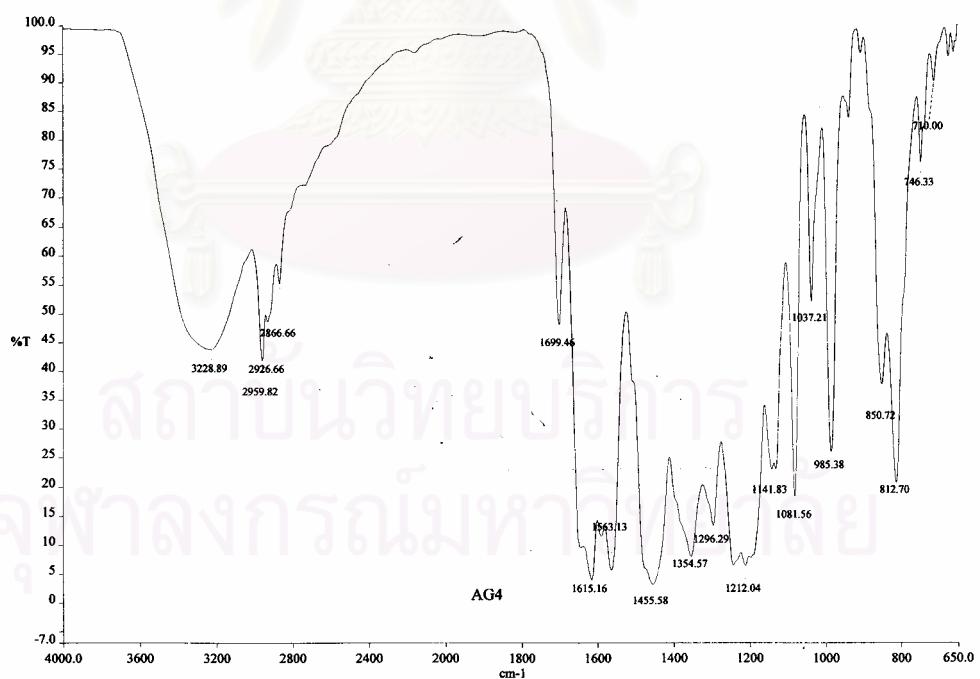


Figure 27 IR Spectrum of compound AG4

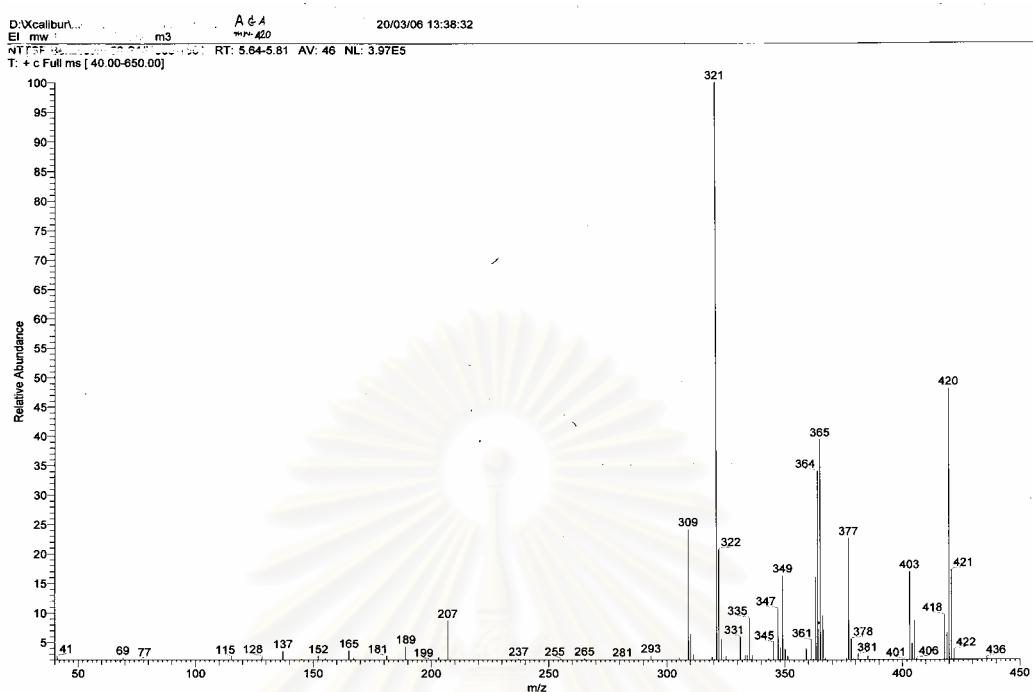
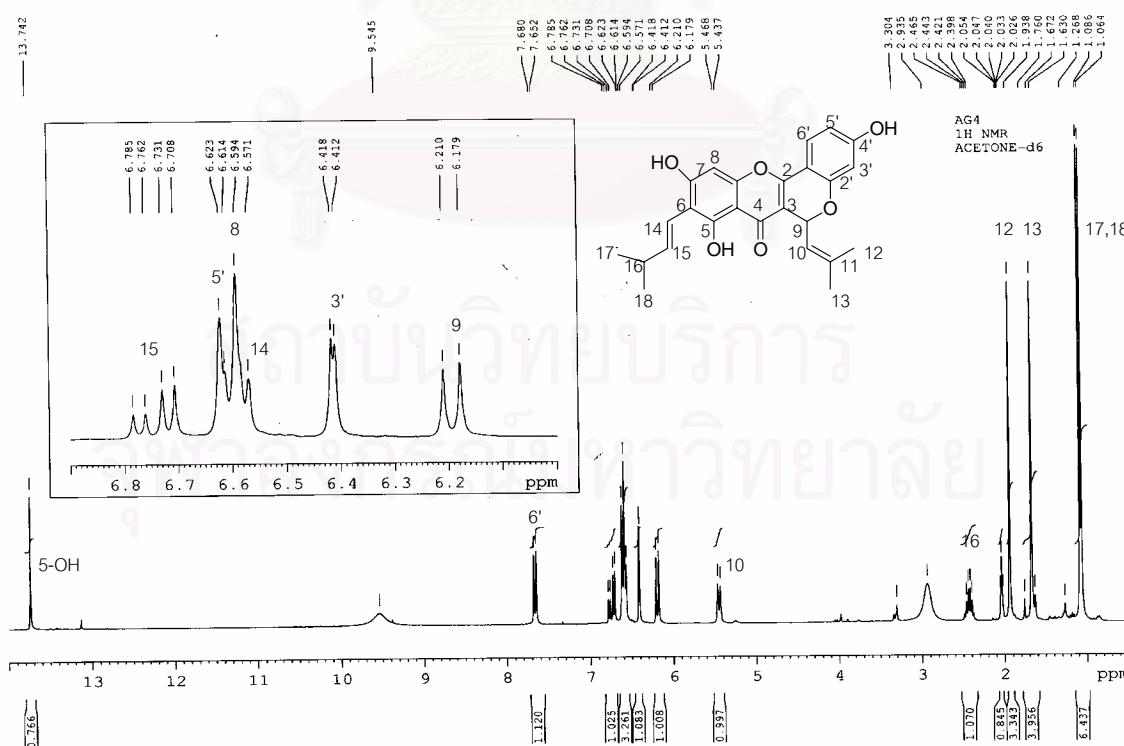


Figure 28 Mass Spectrum of compound AG4

Figure 29 ^1H -NMR (300 MHz) Spectrum of compound AG4 (Acetone- d_6)

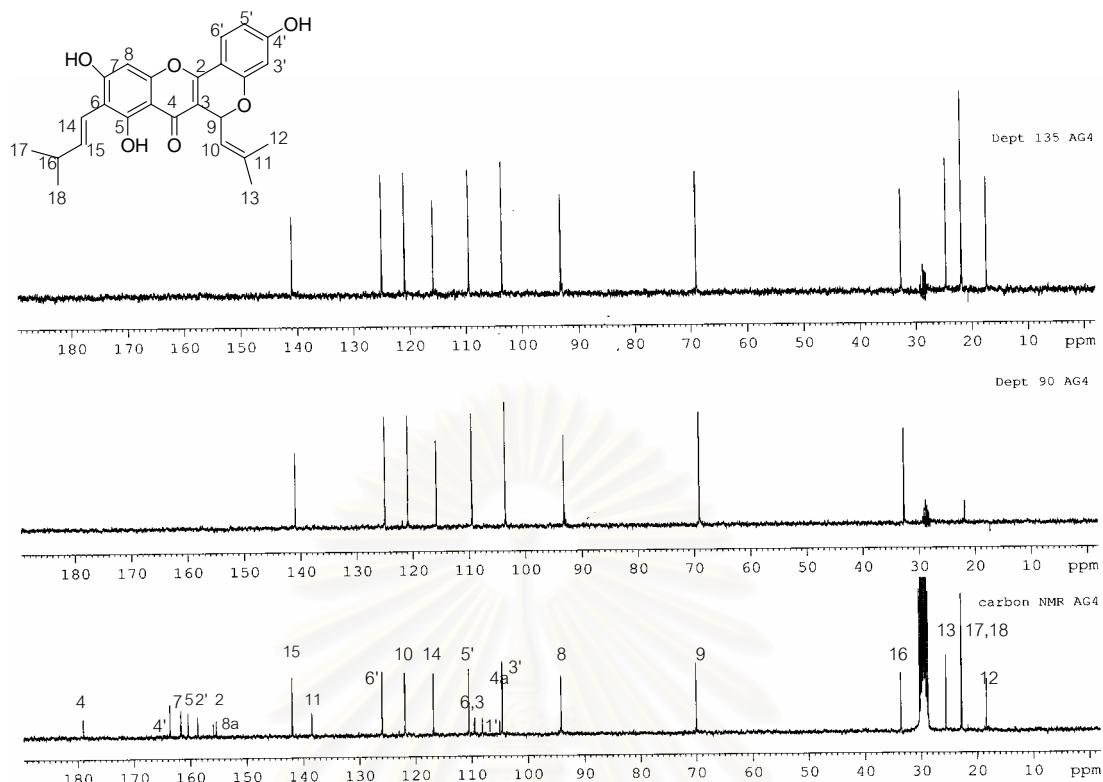


Figure 30 ¹³C-NMR (75 MHz) Spectrum of compound AG4 (Acetone-*d*₆)

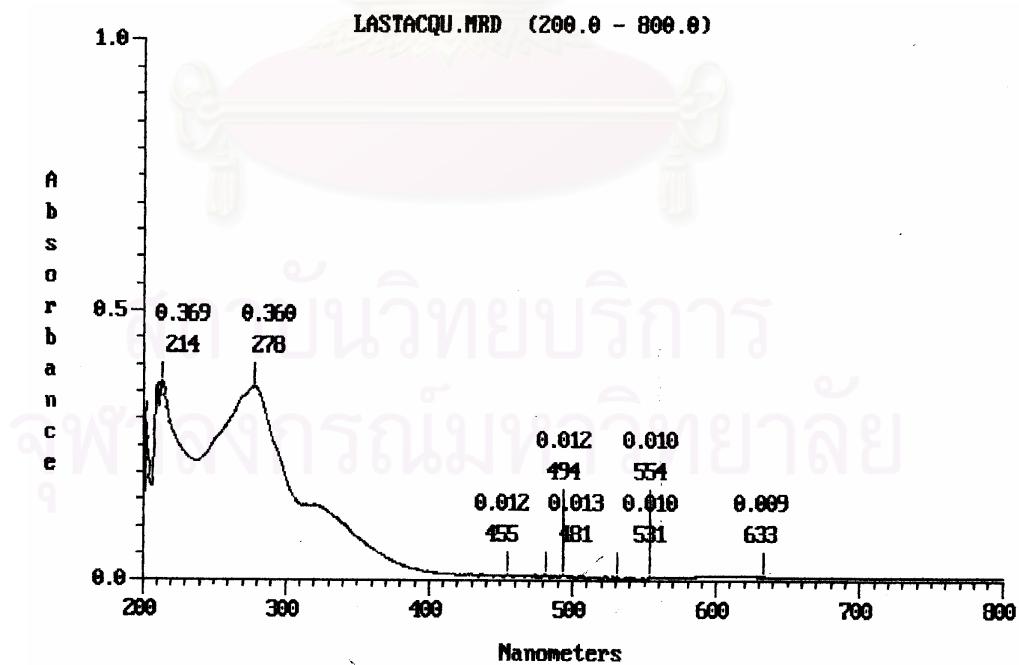


Figure 31 UV Spectrum of compound AG5 (Methanol)

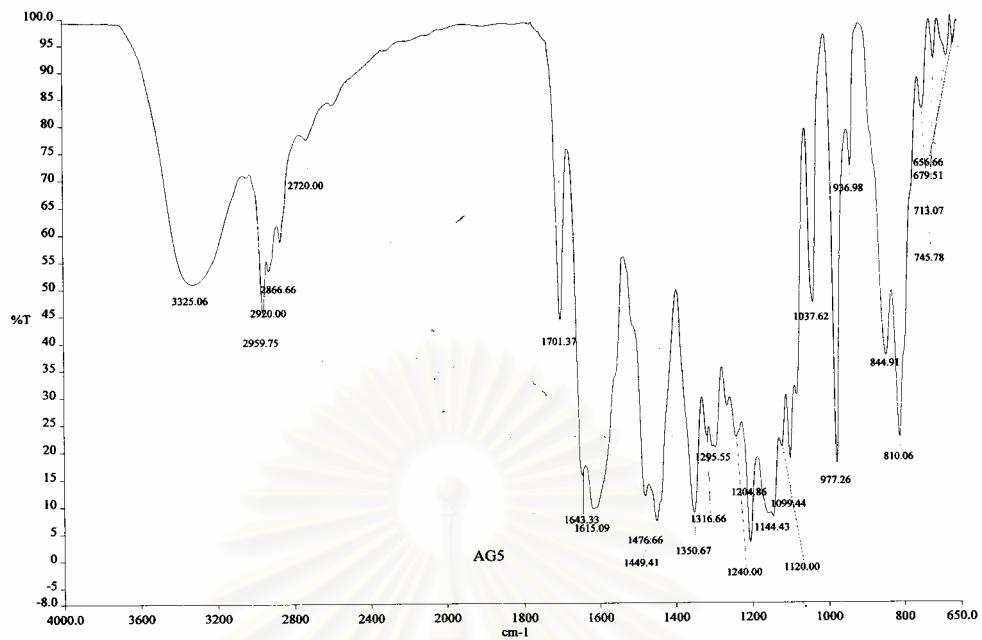


Figure 32 IR Spectrum of compound AG5

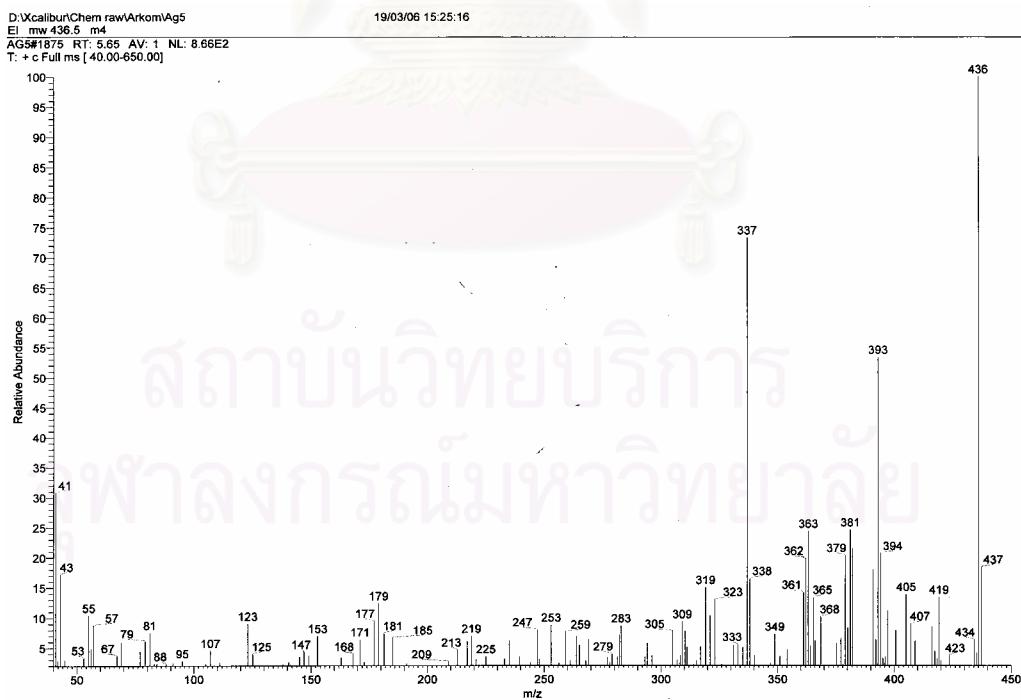


Figure 33 Mass Spectrum of compound AG5

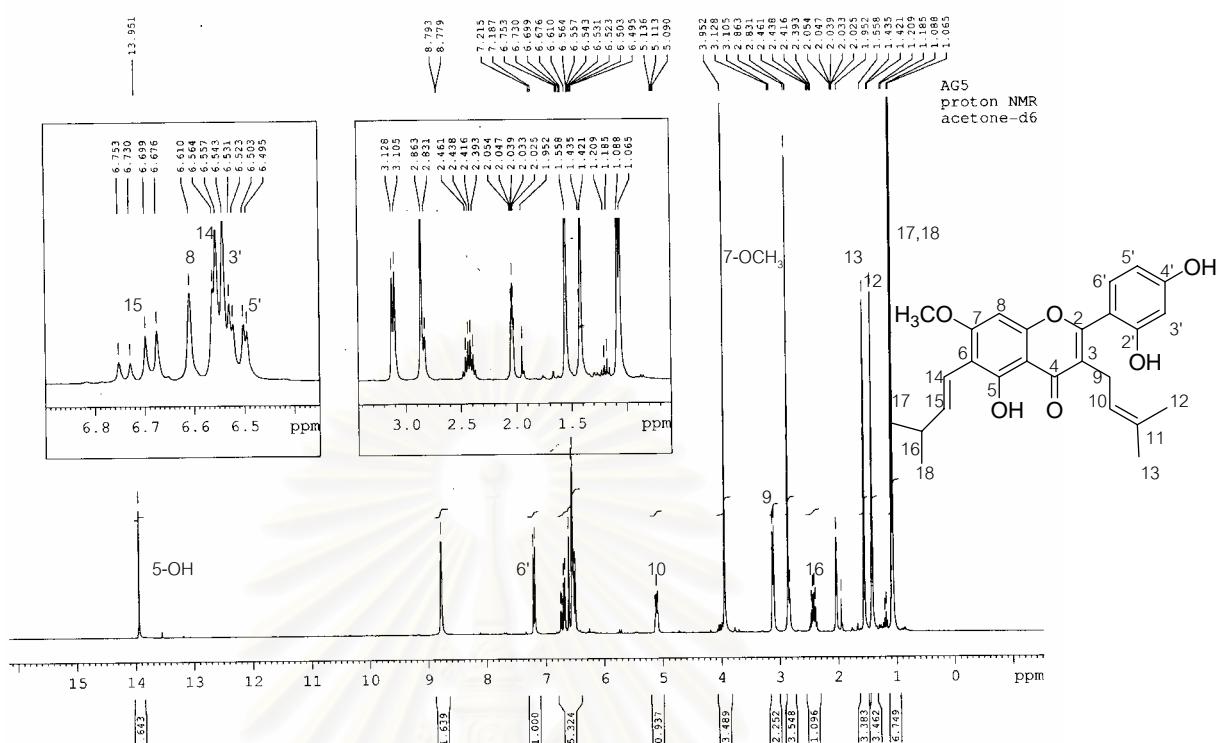


Figure 34 ^1H -NMR (300 MHz) Spectrum of compound AG5 (Acetone- d_6)

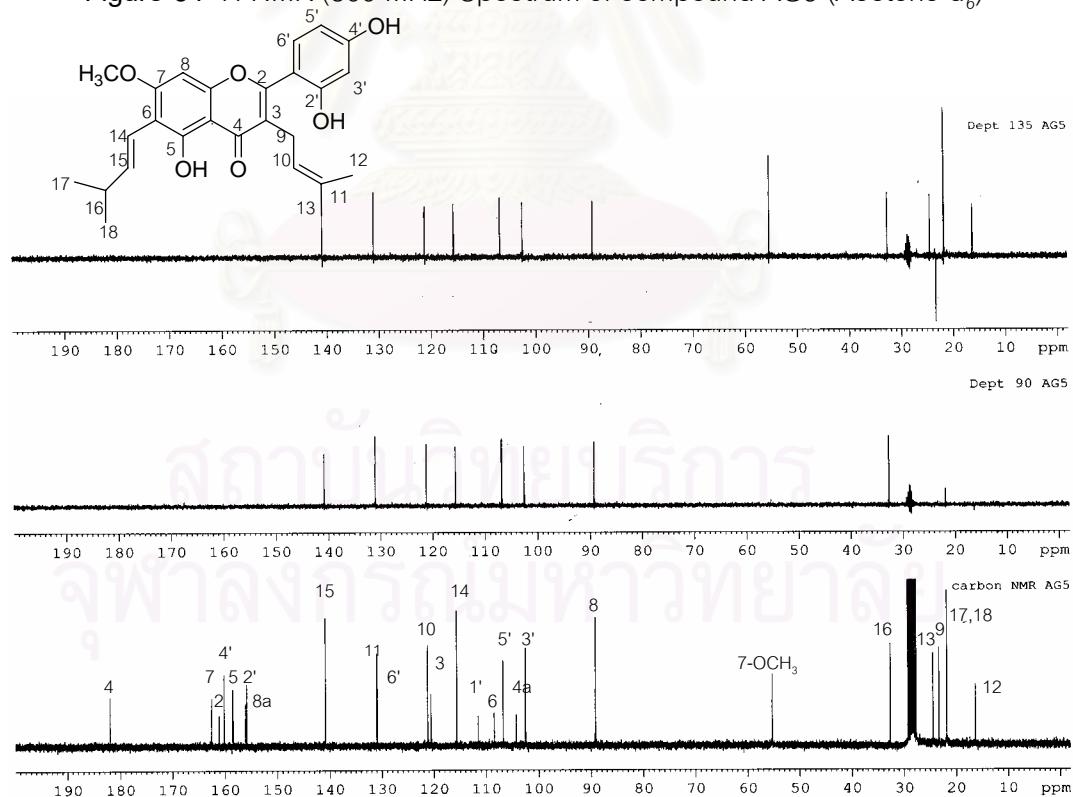


Figure 35 ^{13}C -NMR (75 MHz) Spectrum of compound AG5 (Acetone- d_6)

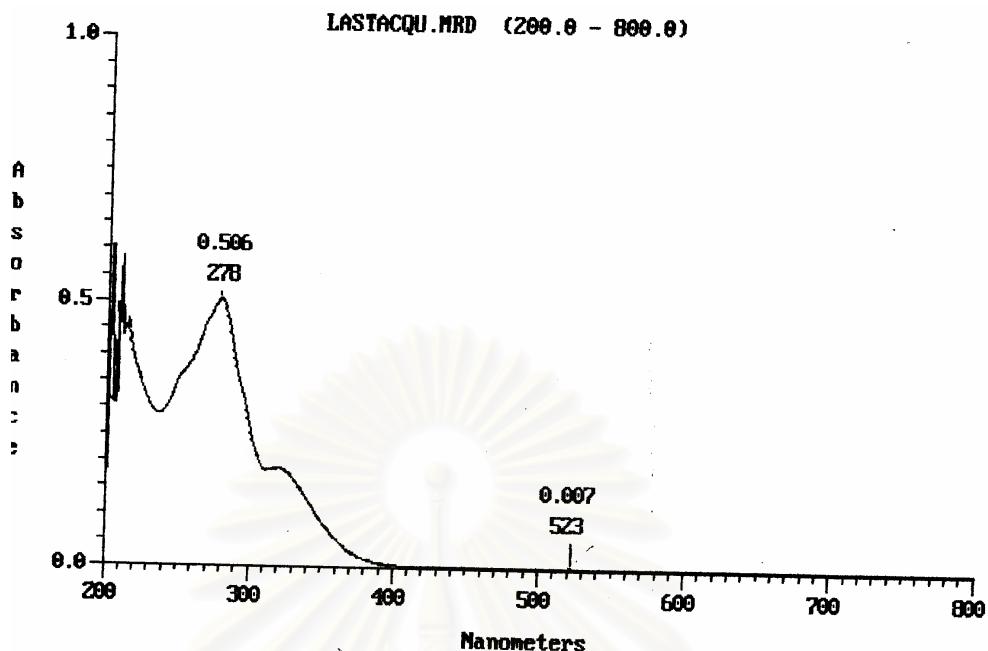


Figure 36 UV Spectrum of compound AG6 (Methanol)

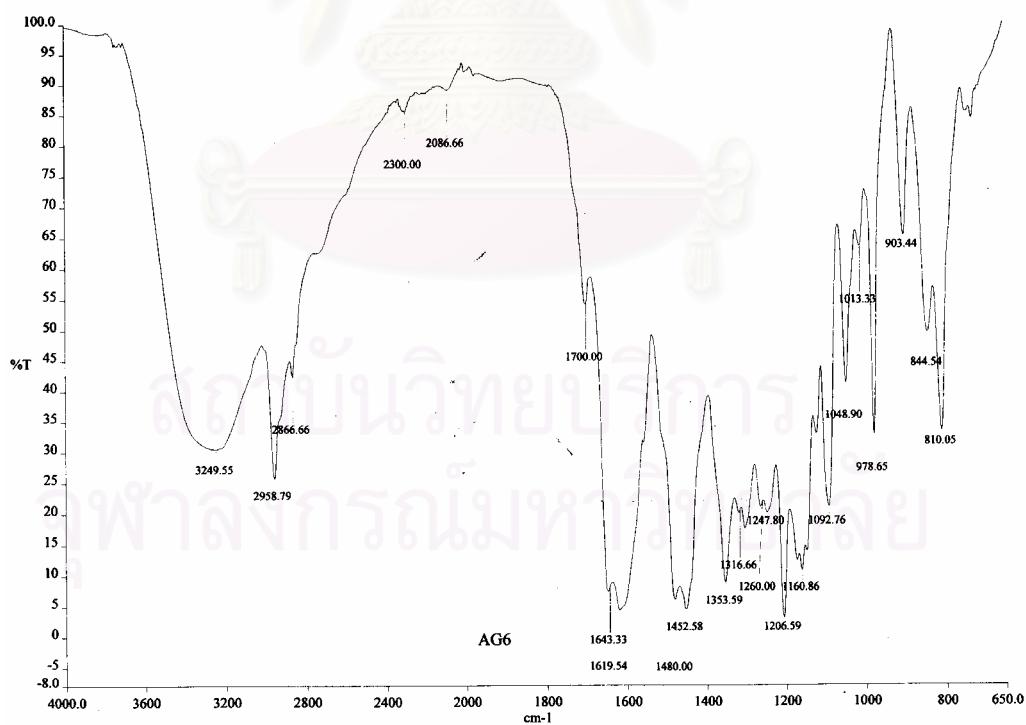


Figure 37 IR Spectrum of compound AG6

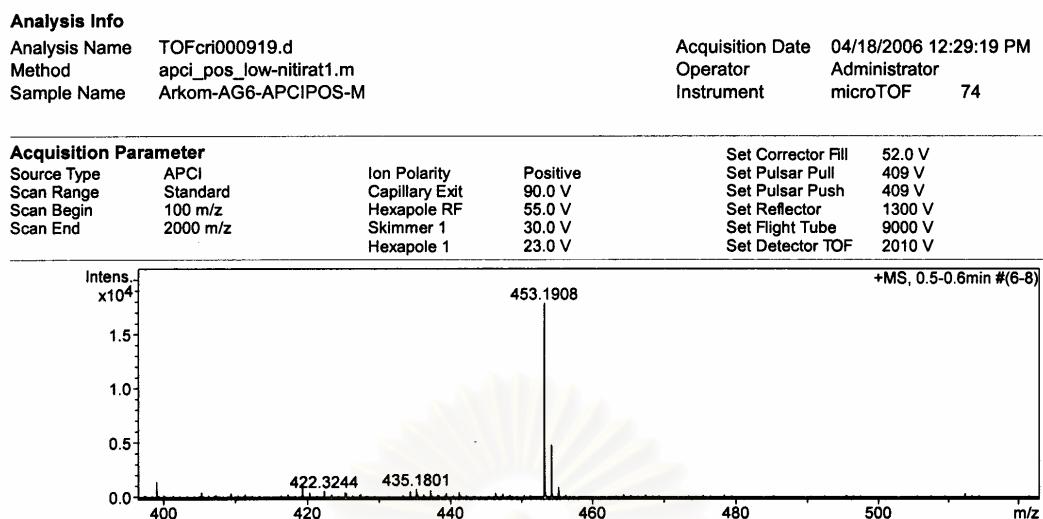
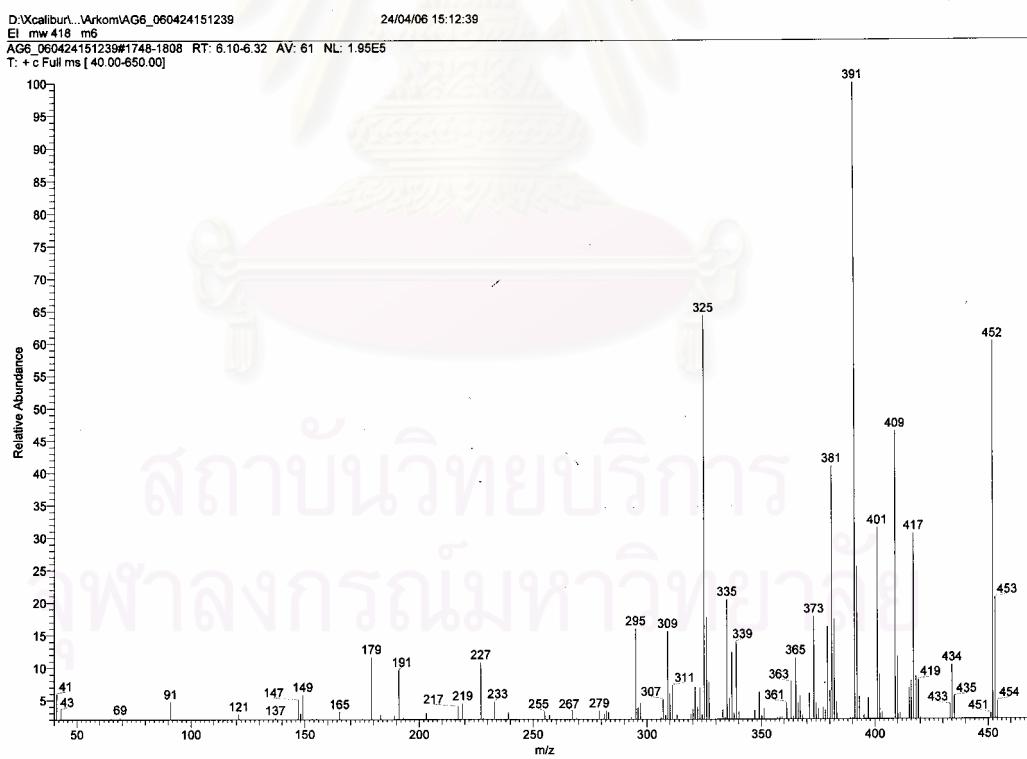


Figure 38 HRESI Mass Spectrum of compound AG6



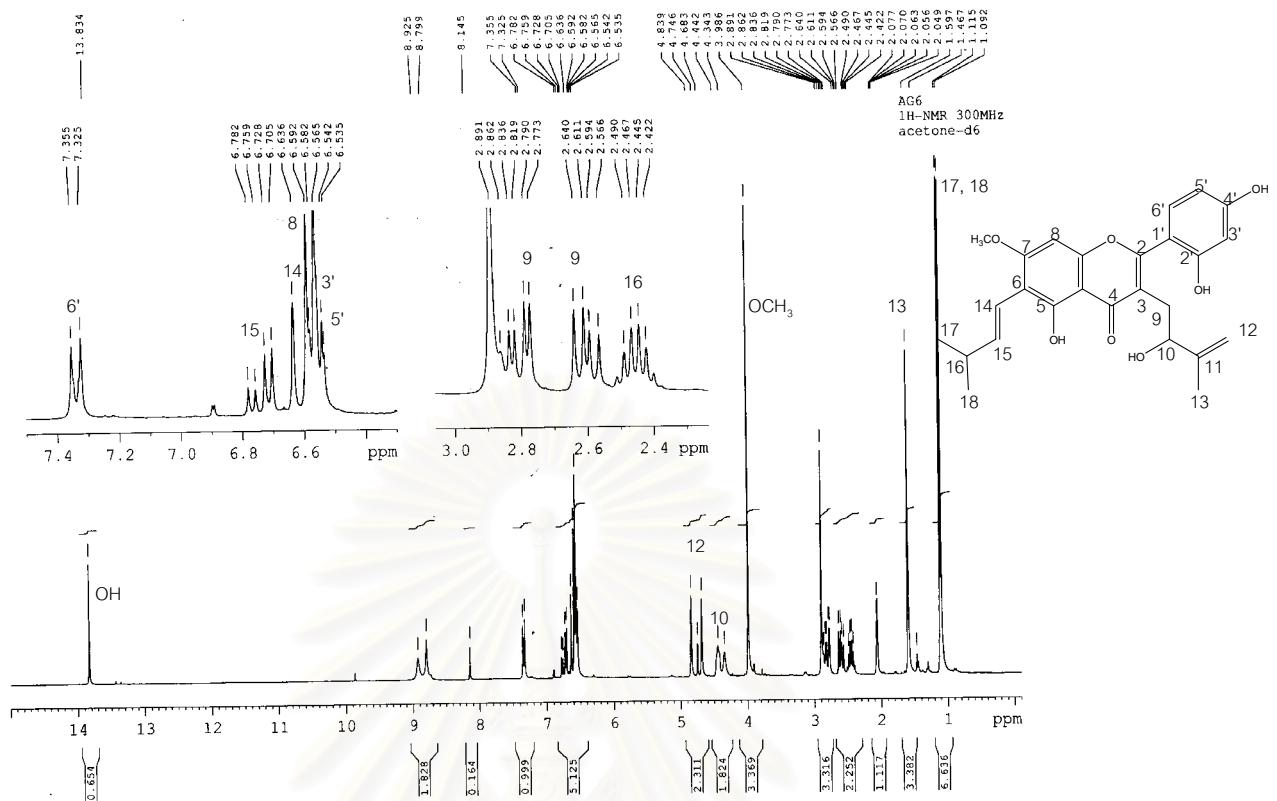


Figure 40 ^1H -NMR (300 MHz) Spectrum of compound AG6 (Acetone- d_6)

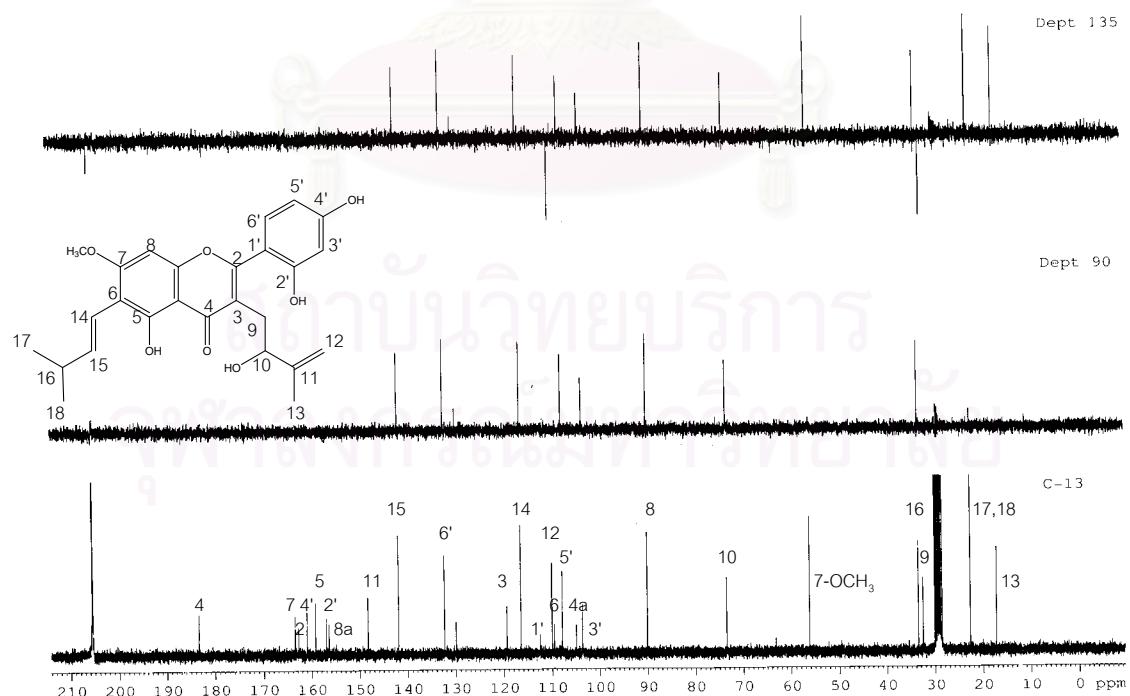


Figure 41 ^{13}C -NMR (75 MHz) Spectrum of compound AG6 (Acetone- d_6)

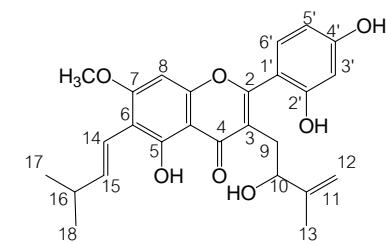
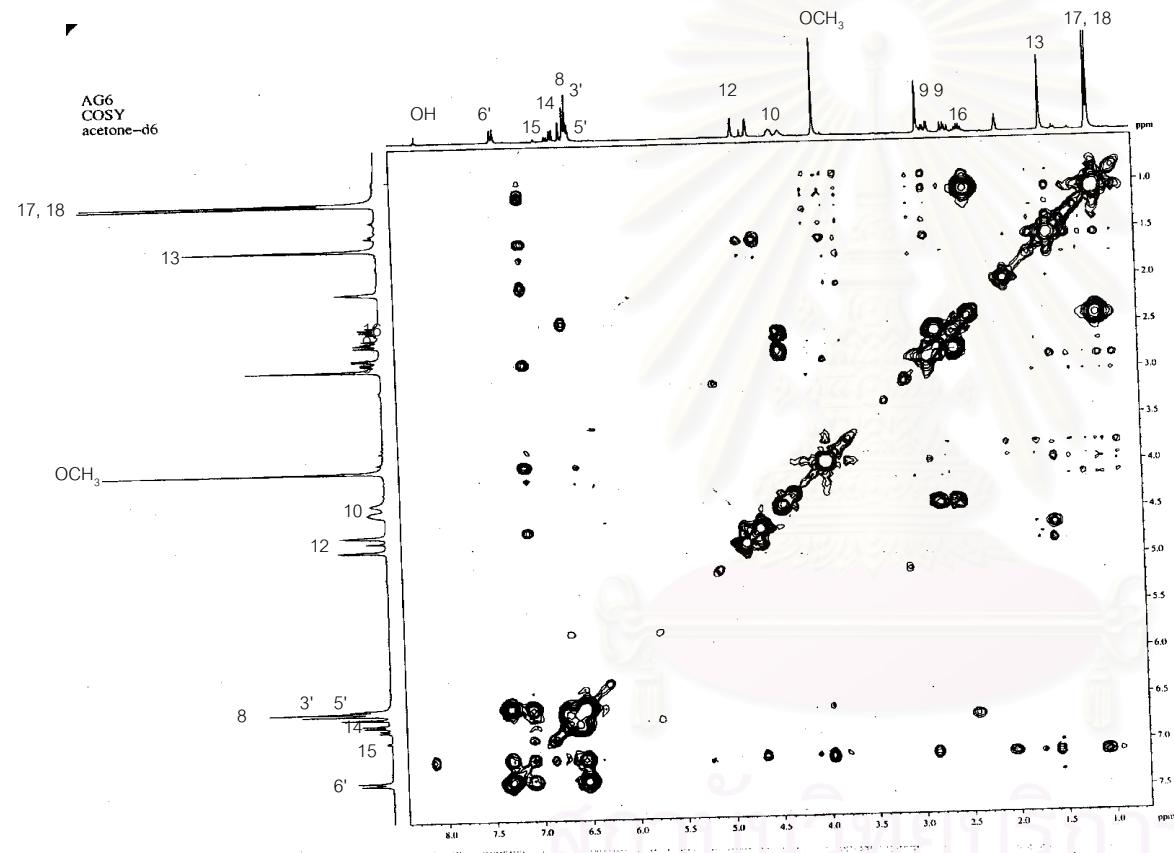


Figure 42 ^1H - ^1H COSY Spectrum of compound AG6 (Acetone- d_6)

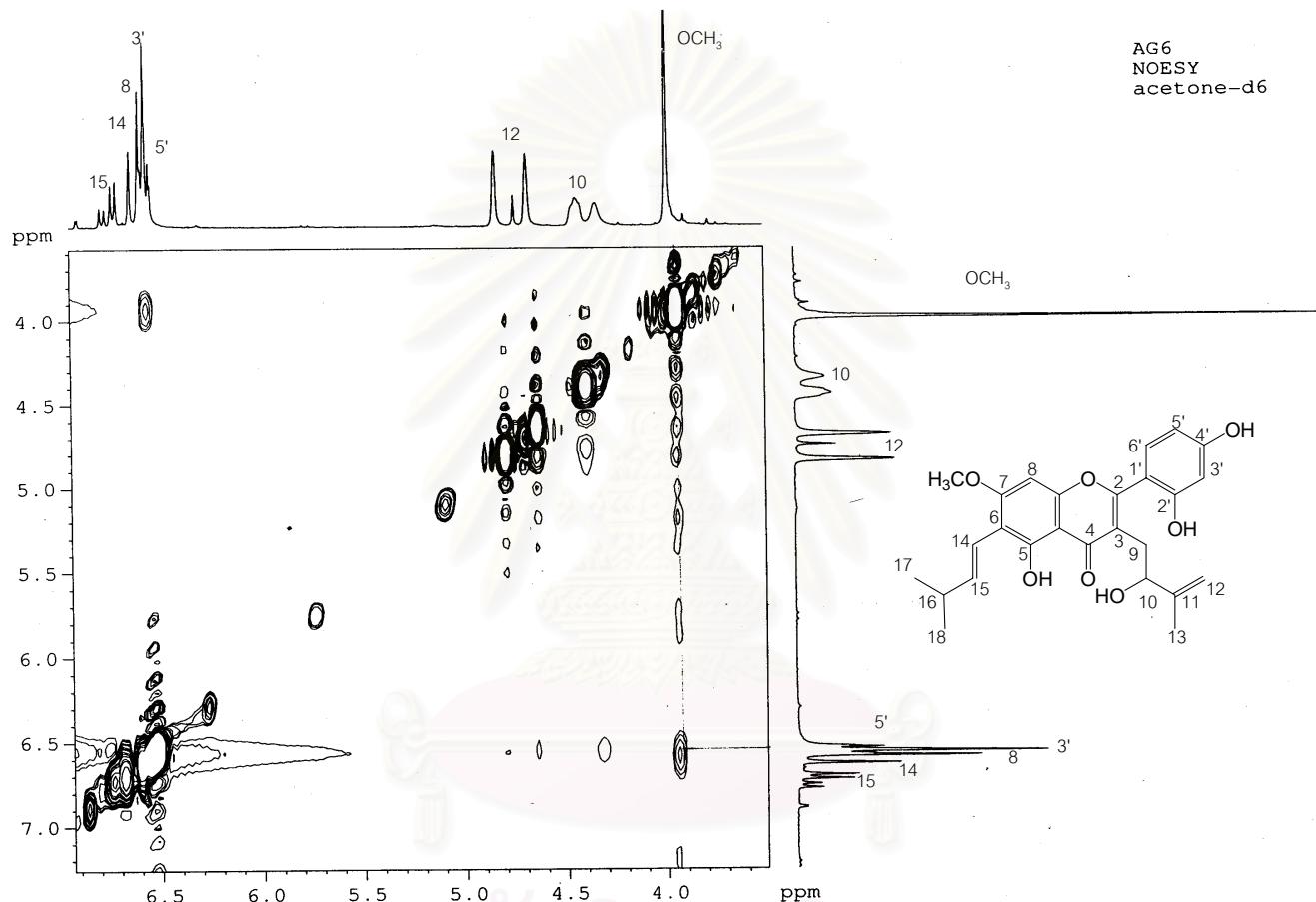


Figure 43 NOESY Spectrum of compound AG6 (Acetone - d_6)

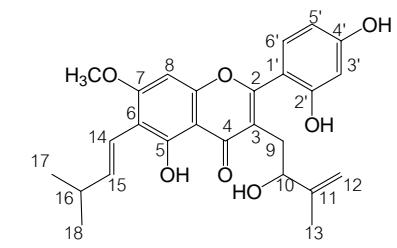
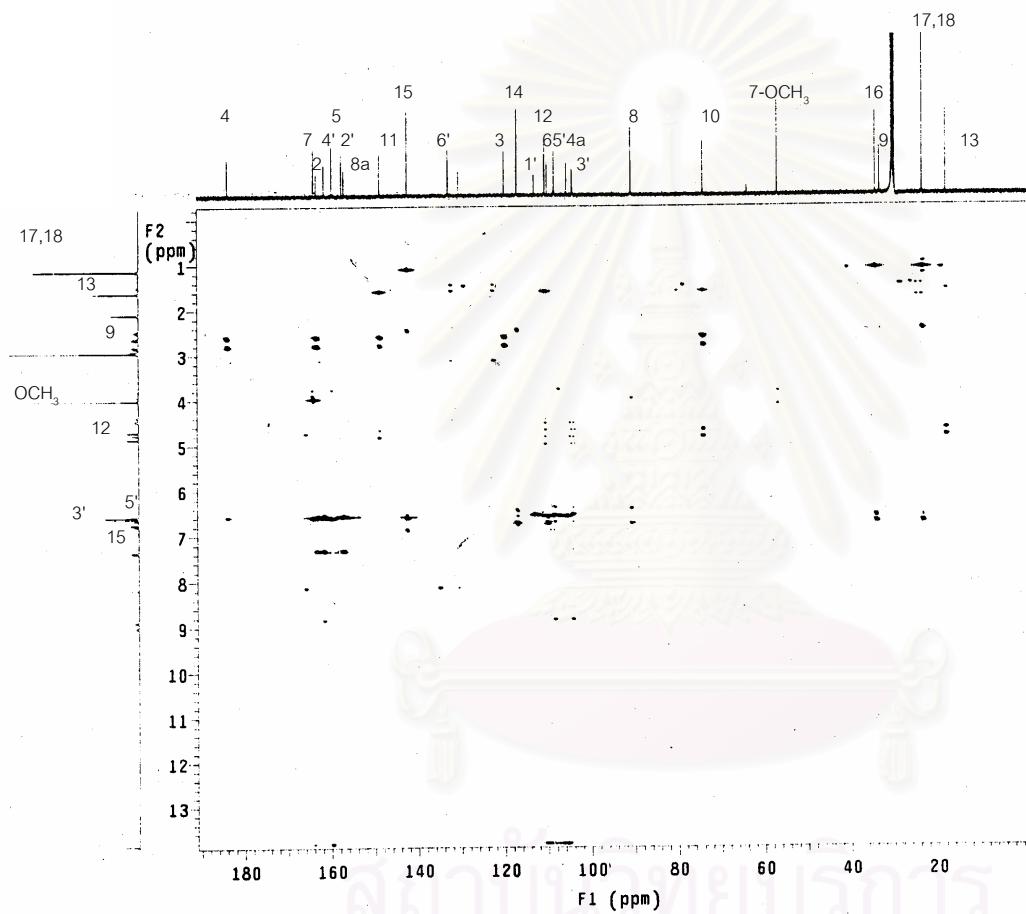


Figure 44 HMBC Spectrum of compound AG6 (Acetone - d_6)

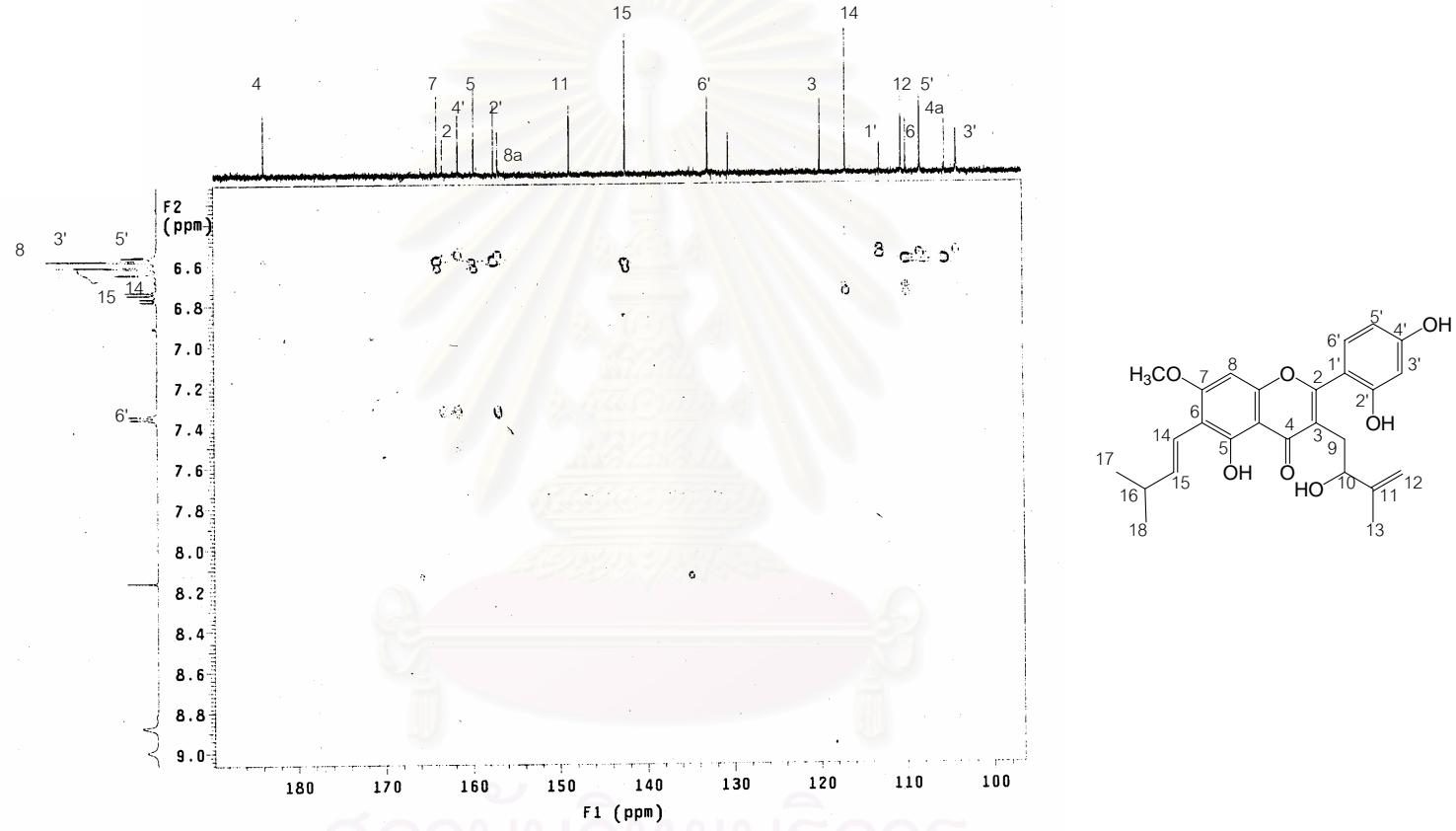


Figure 45 HMBC Spectrum of compound AG6 (Acetone -*d*₆)

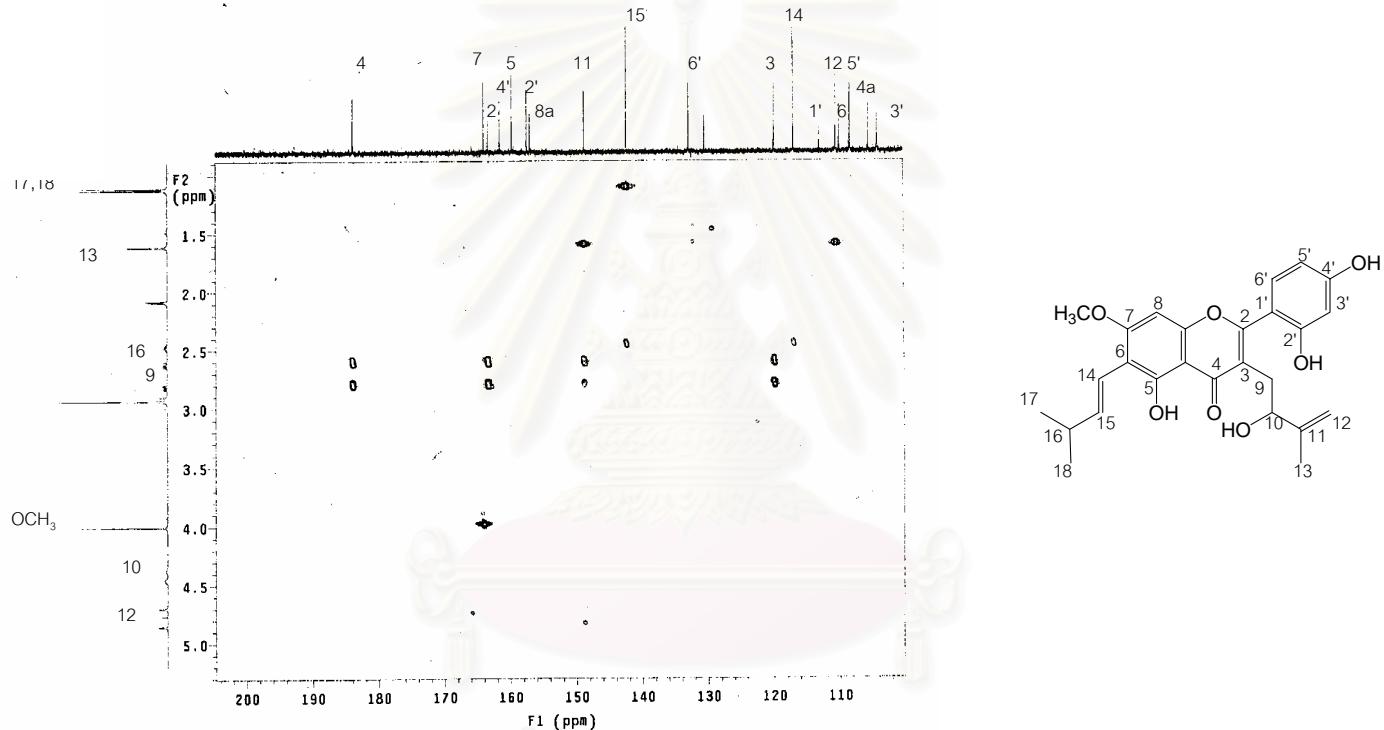


Figure 46 HMBC Spectrum of compound AG6 (Acetone-*d*₆)

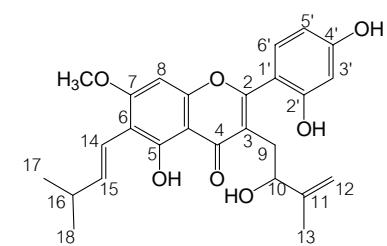
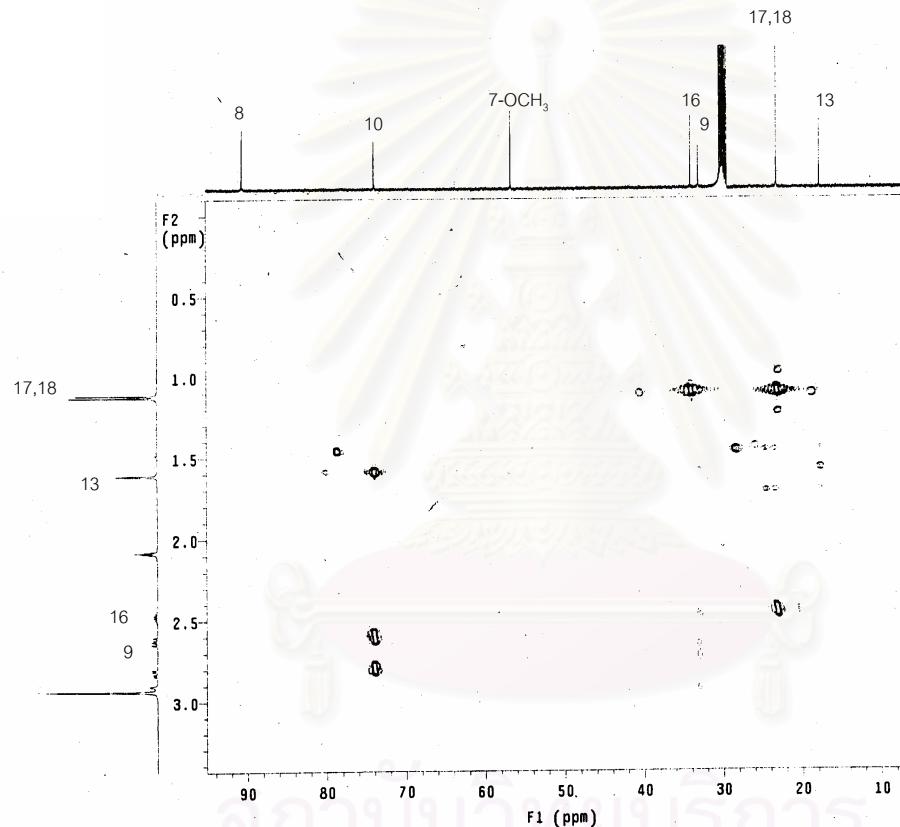


Figure 47 HMBC Spectrum of compound AG6 (Acetone- d_6)

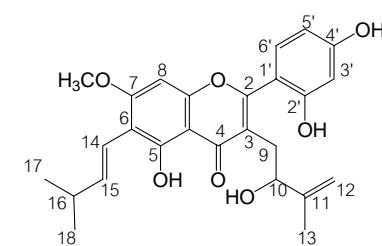
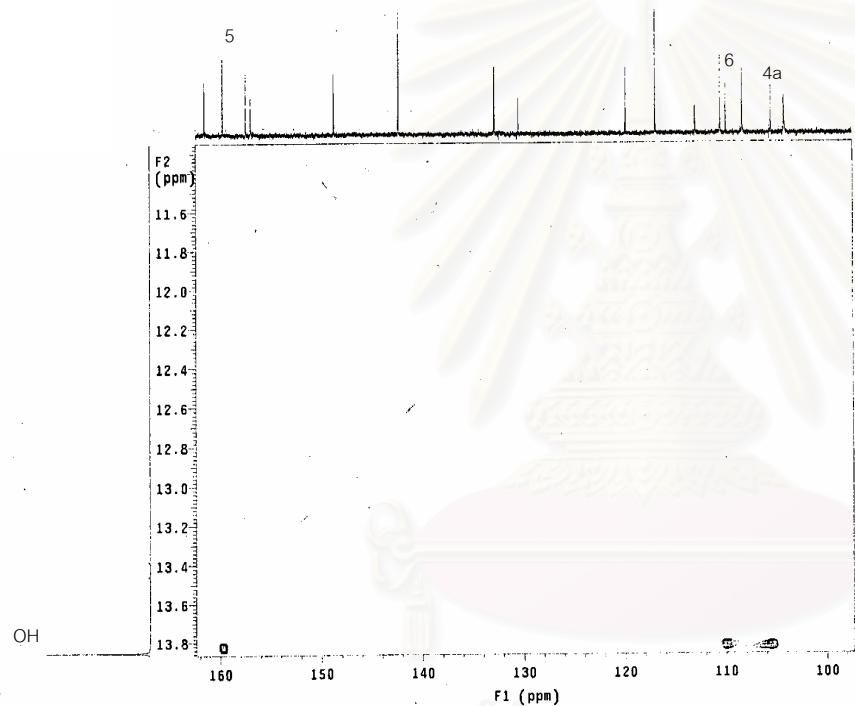


Figure 48 HMBC Spectrum of compound AG6 (Acetone - d_6)

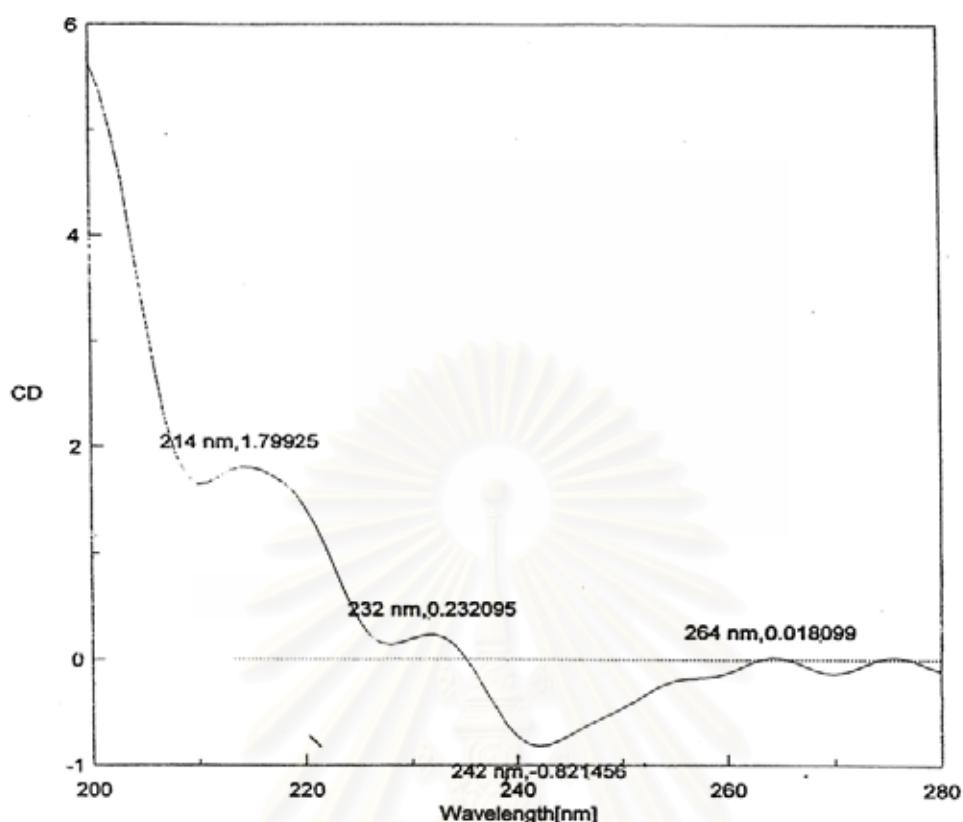


Figure 49 CD Spectrum of compound AG6 (MeOH)

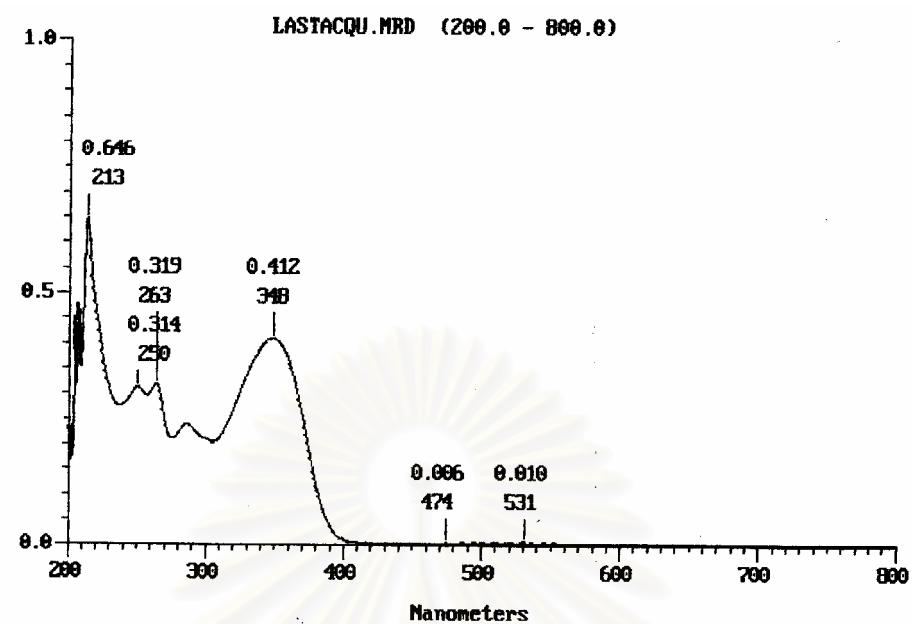


Figure 50 UV Spectrum of compound AG7 (Methanol)

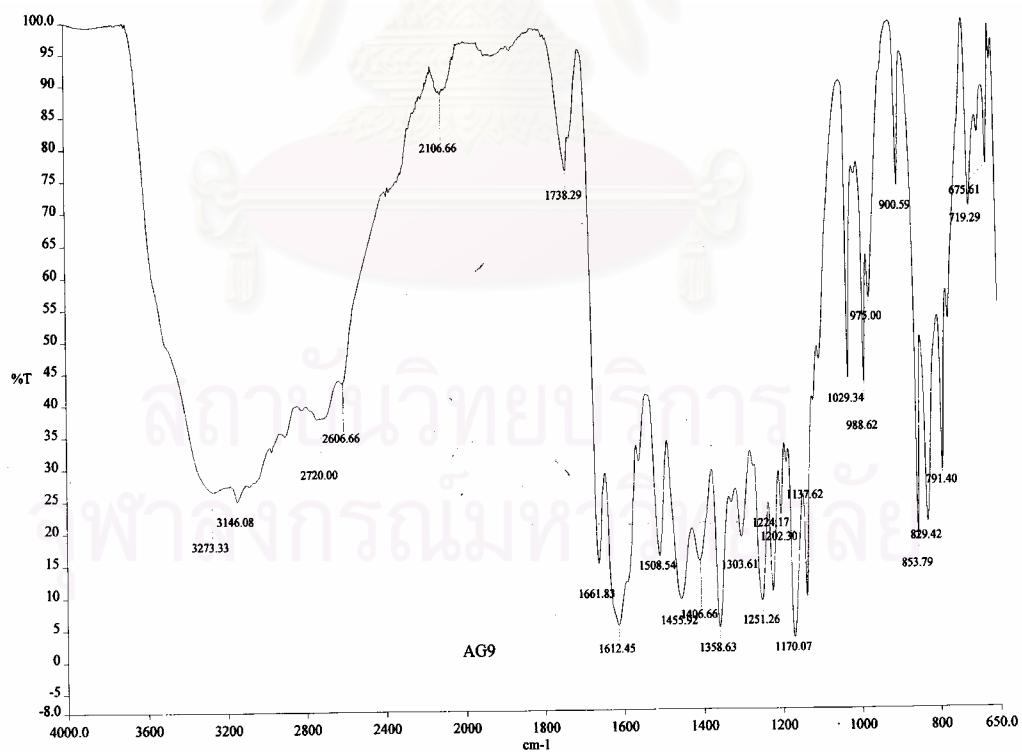


Figure 51 IR Spectrum of compound AG7

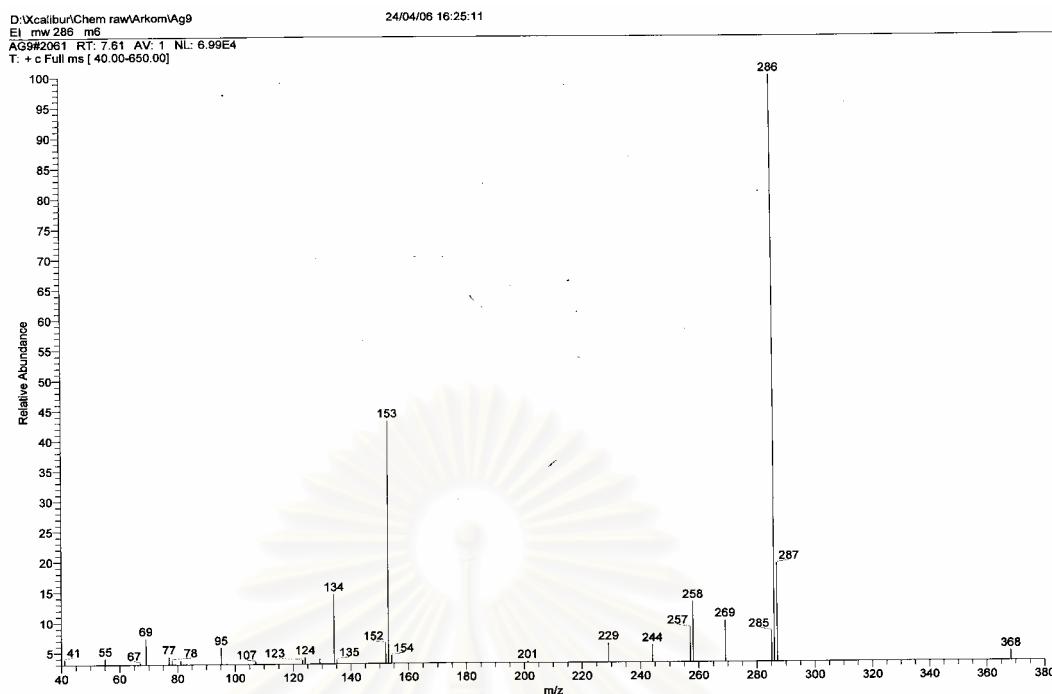


Figure 52 Mass Spectrum of compound AG7

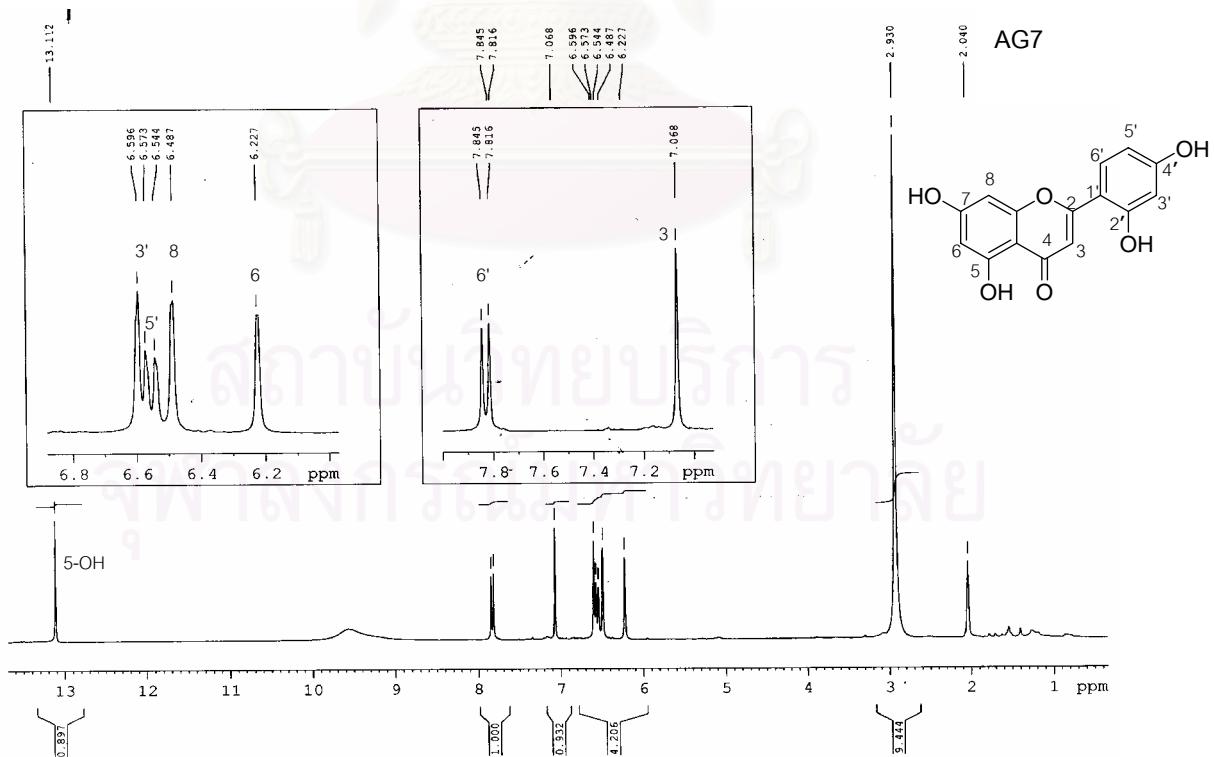


Figure 53 ^1H -NMR (300 MHz) Spectrum of compound AG7 (Acetone- d_6)

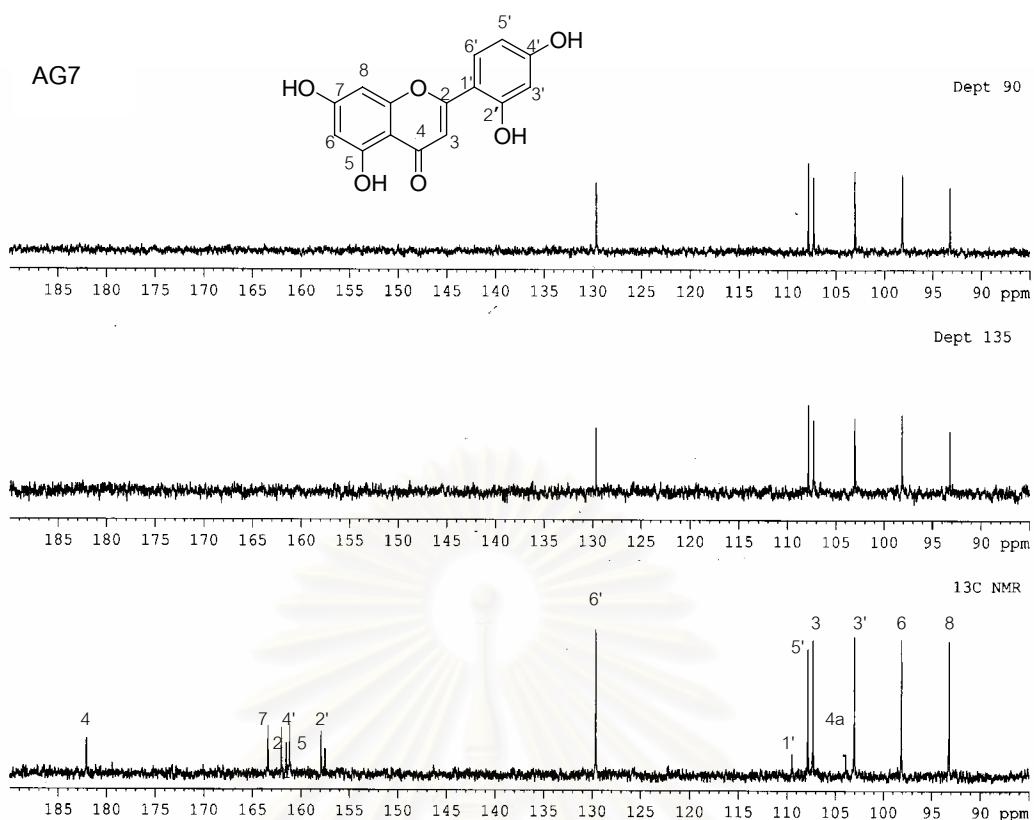


Figure 54 ^{13}C -NMR (75 MHz) Spectrum of compound AG7 (Acetone- d_6)

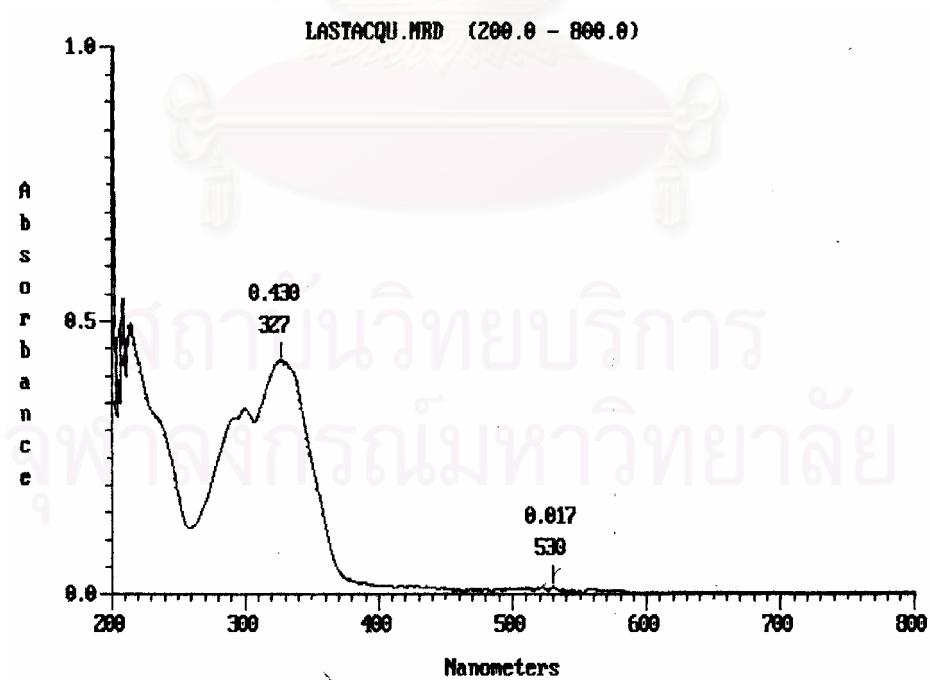


Figure 55 UV Spectrum of compound AG8 (Methanol)

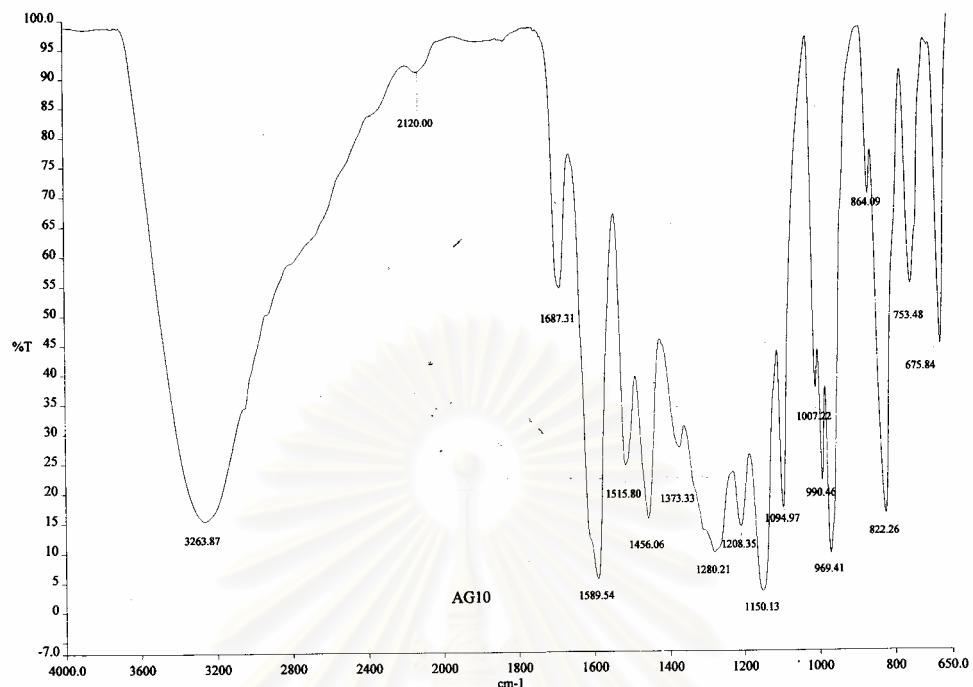


Figure 56 IR Spectrum of compound AG8

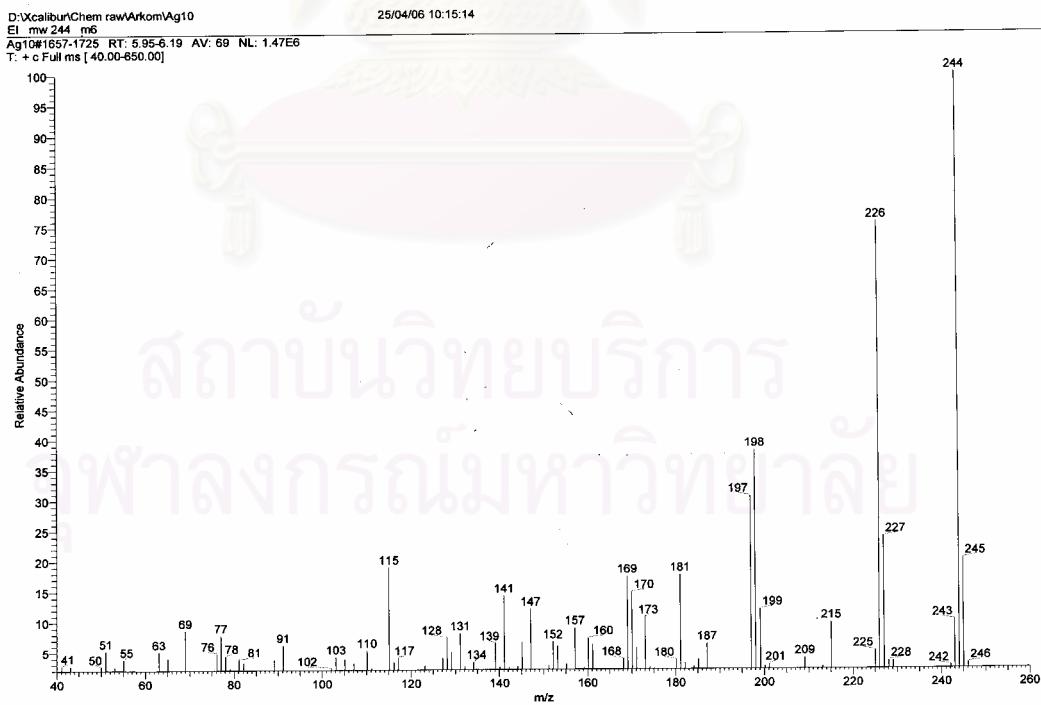


Figure 57 Mass Spectrum of compound AG8

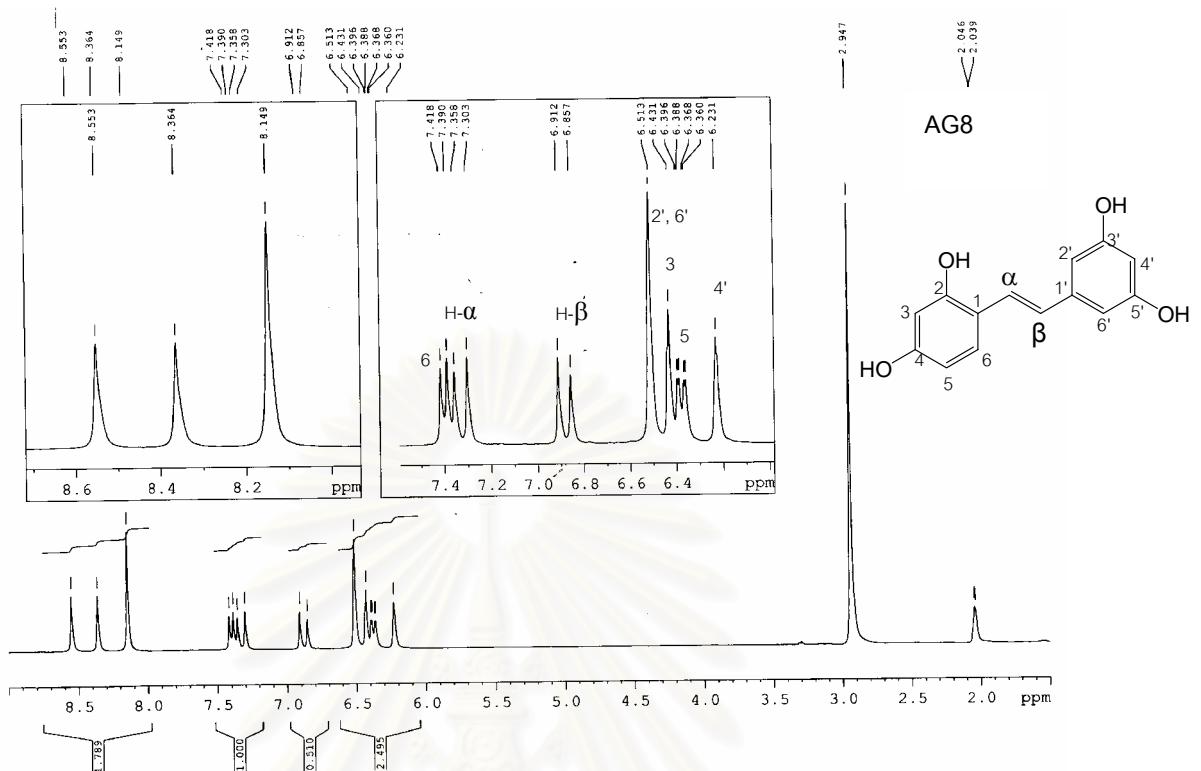


Figure 58 ^1H -NMR (300 MHz) Spectrum of compound AG8 (Acetone- d_6)

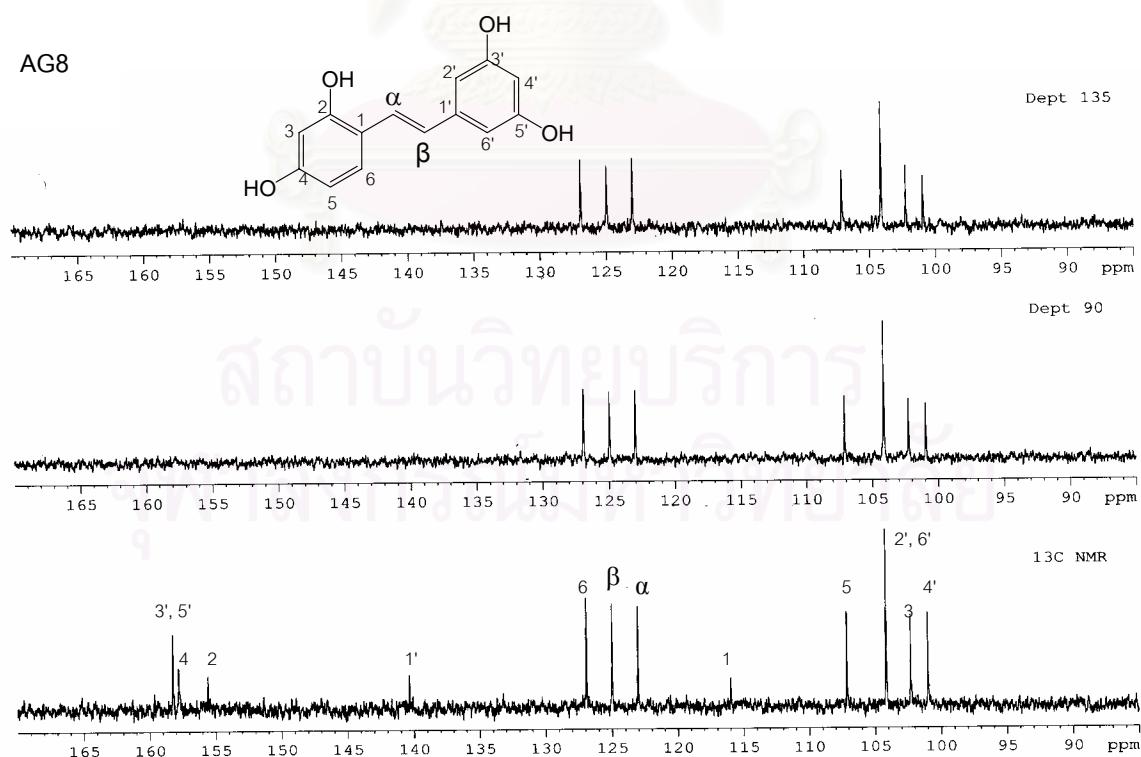


Figure 59 ^{13}C -NMR (75 MHz) Spectrum of compound AG8 (Acetone- d_6)

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Poster Presentation

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