

CHAPTER 1

INTRODUCTION

Amomum is a plant in the family *Zingiberaceae* containing about 150 to 180 species found in Southeast Asia.^[1] There are 16 species grown in Thailand. Several *Amomum* species have been used in traditional herbal medicine in Southeast Asia. For example, the seed of *A. villosum* and *A. testaceum* are often used in medicine against coughs and colds. The sap of *A. aculeatum* is used to treat fever and influenza. In India, *A. fenzlii* is also used to treat malaria. In Thailand, the rhizome of *Amomum* species is used for stomach ache. Most interesting is that a diterpene peroxide isolated from *A. testaceum* fruit in Thailand showed promising results in the treatment of *Plasmodium falciparum*, the most resistant type of malaria.^[2]

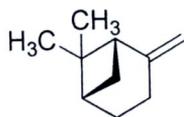
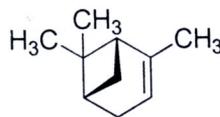
Amomum uliginosum belongs to the ginger group. The stems are tall and slender like the common lalang. It can be found in Thailand, Peninsular Malaysia and Borneo. It is such a common ginger that with a little searching, one can easily find the plant growing at forest edges, the road, stream or riverbanks. These stems can attain a height of 2 to 3 m, with about 16-20 pairs of leaves on the upper half of the stem. Leaves are large but narrow, about 50 cm long and 5-11 cm wide. The characteristics of the leaves are the short petioles and long narrow tips in a drooping position. Like the leafy stems, the inflorescences of *A. uliginosum* also emerge from the running rhizome, usually a short distance from the stem. However, the inflorescence stalk is short and buried in the soil and only the inflorescence head can be seen above the ground.

Flowers are arranged close together, opening about 2-4 each time. The most distinct part of the flower is the concave white lip, which has a bright yellow band at the centre and two red line rambutans. The rhizome has essential oil with ginger aroma (Figure 1).^[3]



Figure 1 Morphological illustration of *Amomum uliginosum*

There have not been many previous phytochemical and bioactivity studies on *A. uliginosum*, except for the report on the investigation of rhizome essential oil by GC and GC/MS. Forty-seven compounds were identified which β -pinene and α -pinene being the major constituents of the oil. [3]

 β -pinene α -pinene.

However, a previous study on other *Amomum* species described the isolation of the monoterpenoids, sesquiterpenoids, diterpenoids, flavonoids, ketones, phenolics and miscellaneous as show in Table 1, 2, 3, 4, 5, 6 and 7 respectively.

From our preliminary investigations on the bioactivities of the rhizome of *A. uliginosum*, we found that the crude hexane, CH_2Cl_2 and MeOH extracts showed cytotoxicity against KB (oral cavity cancer), BC (human breast cancer cell line) and NCI-H187 (small cell lung cancer) cell lines with IC_{50} values ranging from 17.26-44.49 $\mu\text{g}/\text{mL}$. As a part of our interest in chemical constituents and biological activities from natural sources, the rhizomes of *A. uliginosum* were collected for further study. The present studies are therefore aimed to investigate chemical constituents from the rhizome of *A. uliginosum*. The isolated compounds will be tested for their biological activities.

Table 1 Monoterpenoids from *Amomum* species

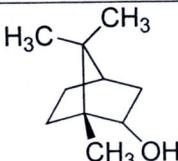
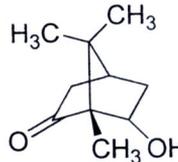
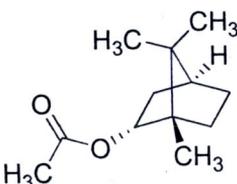
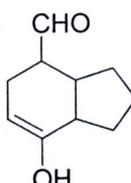
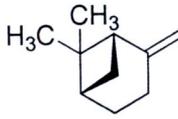
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 (-)-Borneol (1)	<i>A.xanthioides</i> MeOH [seeds]		2009[4]
 (+)-5-Endohydroxy champhor (2)	<i>A.xanthioides</i> MeOH [seeds]		2009[4]
 Bornyl acetate (3)	<i>A.xanthioides</i> MeOH [seeds]		2009[4]
 Bicyclic[4,3,0]-non-4-en (4)	<i>A.tsao-ko</i> MeOH [fruits]	human nonsmall cell lung cancer A549 and human melanoma SK- Mel-2	2005[14]
 β -Pinene (5)	<i>A.hypoleucum</i> ^a <i>thwaites</i> <i>A.cannicarpum</i> ^b <i>A.testaceum</i> ^c Essential oils [rhizomes] ^a [fruits] ^b [leaves] ^c	antibacterial activity ^{a,b}	2007[15] ^a 2006[28] ^b 2001[18] ^c

Table 1 Monoterpenoids from *Amomum* species (continued)

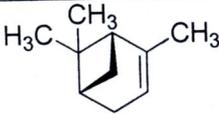
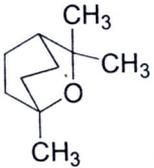
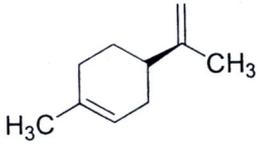
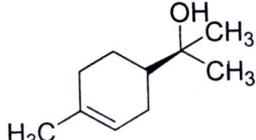
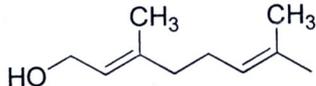
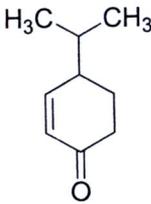
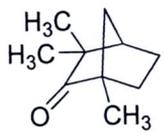
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 α -Pinene (6)	<i>A. subulatum</i> Essential oils [fruits]	antibacterial activity	2008[22]
 1-8-Cineole (7)	<i>A. tsao-ko</i> ^a <i>A. testaceum</i> ^b <i>A. tsao-ko</i> ^c Essential oils [fruits] ^{a,b,c}	antibacterial activity ^c	2004[16] ^a 2001[18] ^b 2011[20] ^c
 Limonene (8)	<i>A. tsao-ko</i> Essential oils [fruits]		2004[16]
 α -Terpineol (9)	<i>A. tsao-ko</i> Essential oils [fruits]		2004[16]
 Geraniol (10)	<i>A. tsao-ko</i> Essential oils [fruits]		2004[16]
 Cryptone (11)	<i>A. hypoleucum thwaites</i> Essential oils [rhizomes]	antibacterial activity	2007[25]
 Fenchone (12)	<i>A. testaceum</i> Essential oils [fruits]	antibacterial activity	2001[18]

Table 1 Monoterpenoids from *Amomum* species (continued)

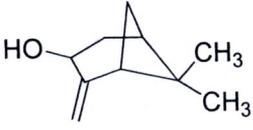
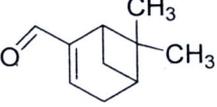
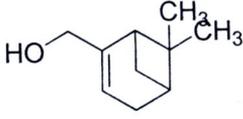
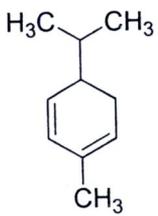
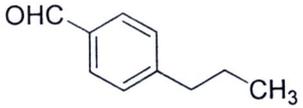
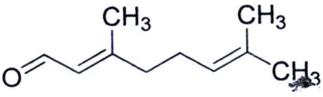
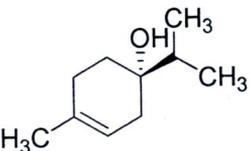
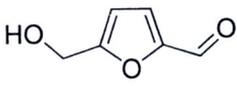
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 Trans-pinocarveol (13)	<i>A. testaceum</i> Essential oils [fruits]	antibacterial activity	2001[18]
 Mytenal (14)	<i>A. testaceum</i> Essential oils [fruits]	antibacterial activity	2001[18]
 Myrtenol (15)	<i>A. testaceum</i> Essential oils [fruits]	antibacterial activity	2001[18]
 α -Phellandrene (16)	<i>A. tsao-ko</i> Essential oils [fruits]	antibacterial activity	2004[16] 2011[20]
 4-Propyl-benzaldehyde (17)	<i>A. tsao-ko</i> Essential oils [fruits]	antibacterial activity	2011[20]
 (E)-Citral (18)	<i>A. tsao-ko</i> Essential oils [fruits]	antibacterial activity	2011[20]
 Terpinene-4-ol (19)	<i>A. subulatum</i> Essential oils [fruits]	antibacterial activity	2008[22]
 5-(Hydroxyl)-2-furaldehyde (20)	<i>A. subulatum</i> Essential oils [fruits]	antibacterial activity	2008[22]

Table 2 Sesquiterpenoids from *Amomum* species

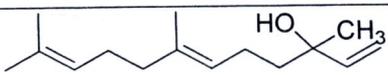
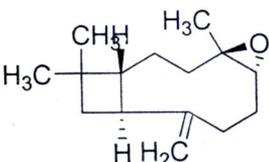
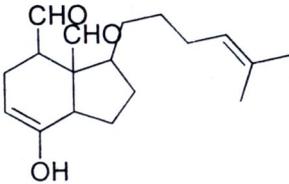
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 Nerolidol (21)	<i>A.xanthioides</i> ^a <i>A.tsao-ko</i> ^b MeOH [seeds] ^a Essential oil [fruits] ^b	antibacterial activity	2009[4] ^a 2011[20] ^b
 Carophylene oxide (22)	<i>A.xanthioides</i> ^a <i>A.hypoleucum</i> ^b <i>A.cannicarpum</i> ^c MeOH [seeds] ^a Essential oil [rhizomes] ^b [leaves] ^c	humam cancer cell line ^b antibacterial activity ^c	2009[4] ^a 2007[15] ^b 2006[17] ^c
 7-Hydroxy-2,6-cycloenica-9, 13-diene-18,19-dial (23)	<i>A.tsao-ko</i> MeOH [fruits]	human nonsmall cell lung cancer A549 and human melanoma SK-Mel-2	2005[14]

Table 3 Diterpenoids from *Amomum* species

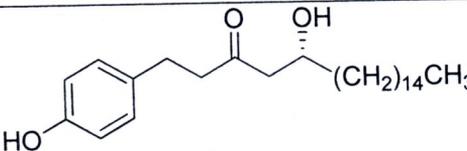
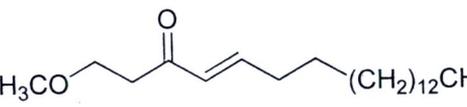
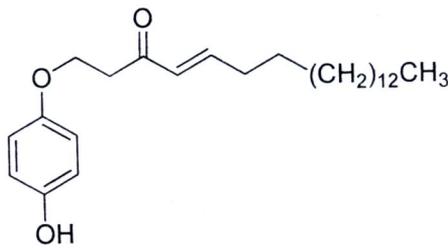
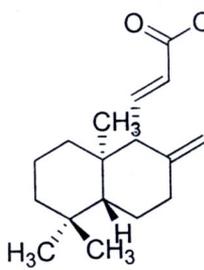
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 <p>(<i>R</i>)-5-Hydroxy-1-(4-hydroxyphenyl) icosan-3-one (24)</p>	<i>A. aculeatum</i> Hexane [leaves]	humam cancer cell line	2007[5]
 <p>1-Methoxy-<i>E</i>-4-eicosen-3-one (25)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>1-(4'-Hydroxy-phenoxy)-<i>E</i>- 4-eicosen-3-one (26)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>Amoxantin A (<i>E</i>)-15,16-Bisnorlabda-8(17), 11-diene-13-one) (27)</p>	<i>A. xanthioides</i> MeOH [seeds]	human nonsmall cell lung cancer A549 and human melanoma SK- Mel-2	2010[24]

Table 4 Flavopenoids from *Amomum* species

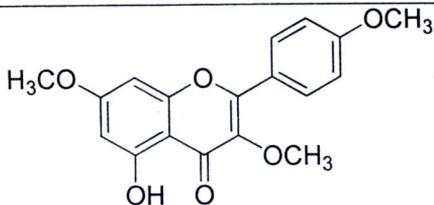
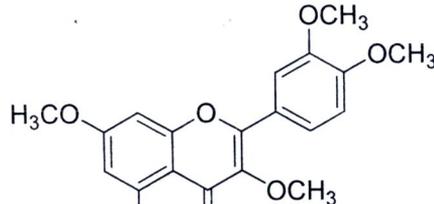
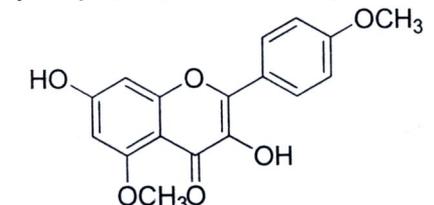
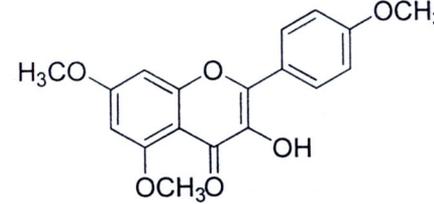
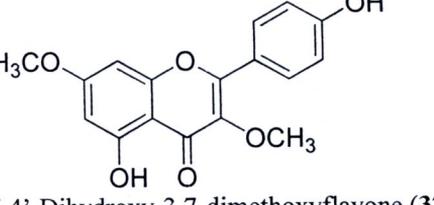
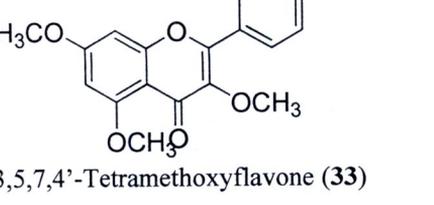
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 <p>5-Hydroxy-3,7,4'-trimethoxyflavone (28)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>5-Hydroxy-3,7,3',4'-tetramethoxyflavone (29)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>3,7-Dihydroxy-5,4'-dimethoxyflavone (30)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>3-Hydroxy-5,7,4'-trimethoxyflavone (31)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>5,4'-Dihydroxy-3,7-dimethoxyflavone (32)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>3,5,7,4'-Tetramethoxyflavone (33)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]

Table 4 Flavopenoids from *Amomum* species (continued)

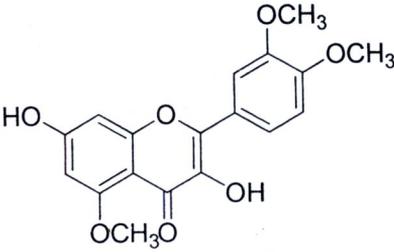
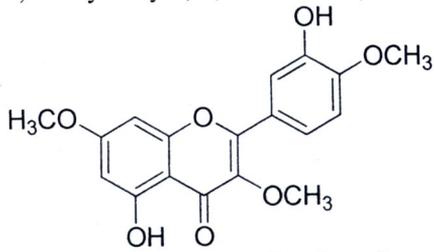
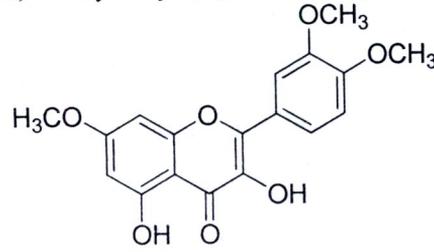
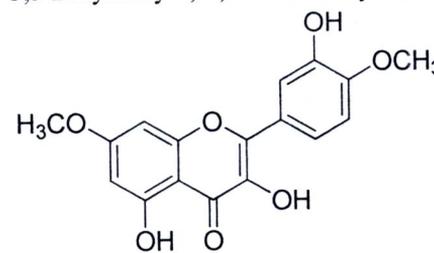
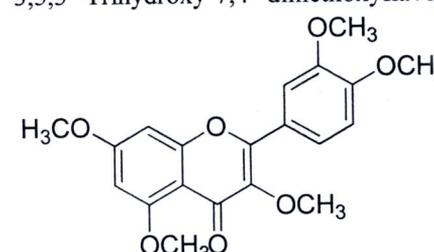
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 <p>3,7-Dihydroxy-5,3',4'-trimethoxyflavone (34)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>5,3'-Dihydroxy-3,7,4'-dimethoxyflavone(35)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>3,5-Dihydroxy-7,3',4'-dimethoxyflavone (36)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>3,5,3'-Trihydroxy-7,4'-dimethoxyflavone (37)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]
 <p>3,5,7,3',4'-Pentamethoxyflavone (38)</p>	<i>A. koenigii</i> MeOH [fruits]		1999[9]

Table 4 Flavopenoids from *Amomum* species (continued)

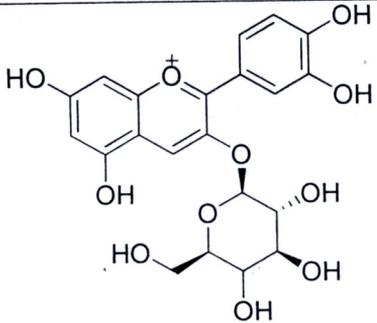
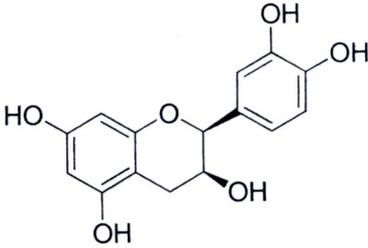
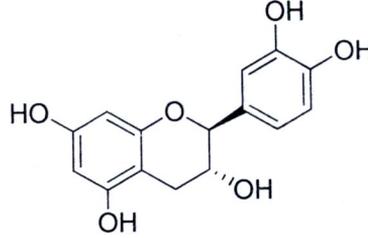
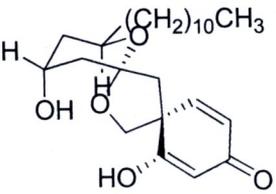
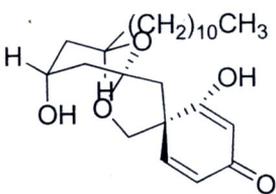
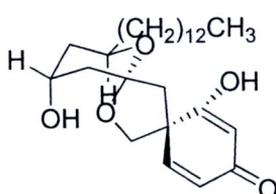
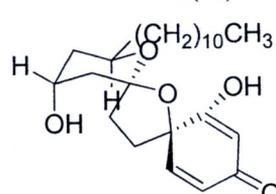
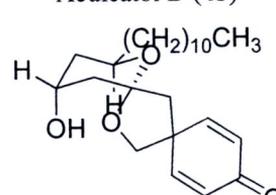
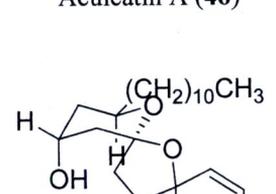
Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 <p>Cyanidin-3-glucoside (39)</p>	<i>A.subulatum</i> MeOH [seeds]		1999[9]
 <p>Epichtechin (40)</p>	<i>A.tsao-ko</i> EtOAc [fruit]	antioxidant activity	2000[11]
 <p>(2<i>S</i>,3<i>R</i>)-Ent-catechin (41)</p>	<i>A.tsao-ko</i> EtOAc [fruit]	antioxidant activity	2000[11]

Table 5 Ketone from *Amomum* species

Compound	Plant [Extract, part]	Biological activity	Year [ref.]
 <p>Aculeatol A (42)</p>	<i>A. aculeatum</i> [leaves]	several human cancer cell lines	2007[5]
 <p>Aculeatol B (43)</p>	<i>A. aculeatum</i> Hexane [leaves]	several human cancer cell lines	2007[5]
 <p>Aculeatol C (44)</p>	<i>A. aculeatum</i> Hexane [leaves]	several human cancer cell lines	2007[5]
 <p>Aculeatol D (45)</p>	<i>A. aculeatum</i> Hexane [leaves]	several human cancer cell lines	2007[5]
 <p>Aculeatin A (46)</p>	<i>A. aculeatum</i> Hexane [leaves]	several human cancer cell lines	2007[5]
 <p>Aculeatin B (47)</p>	<i>A. aculeatum</i> Hexane [leaves]	several human cancer cell lines	2007[5]

**Table 6** Phenolic from *Amomum* species

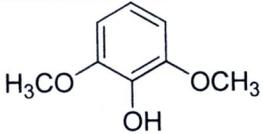
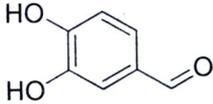
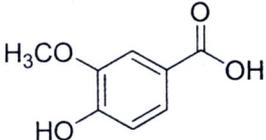
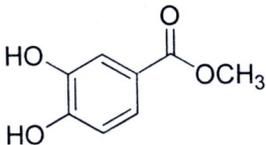
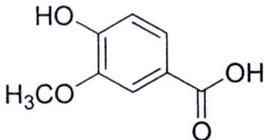
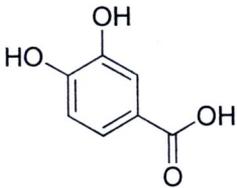
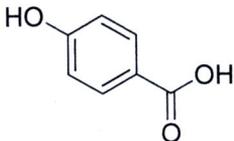
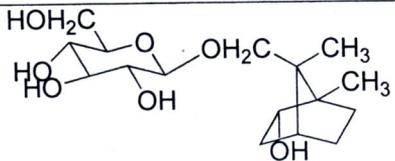
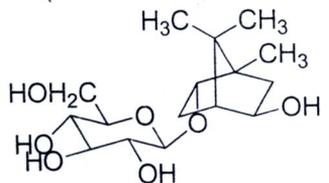
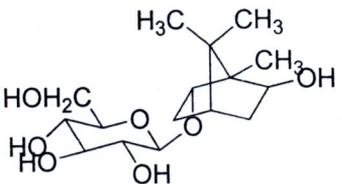
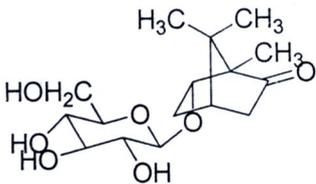
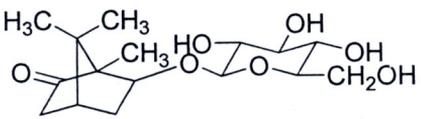
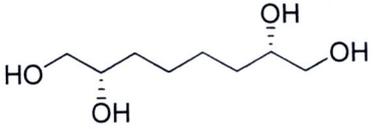
Compound	Plant [Extract,part]	Biological activity	Year [ref.]
 2,6-Dimethyl phenol (48)	<i>A.tsao-ko</i> EtOAc [fruit]		2000[11]
 3,4-Dihydroxy benzaldehyde (49)	<i>A.tsao-ko</i> EtOAc [fruit]		2000[11]
 Vanillic acid (50)	<i>A.xanthioides</i> MeOH [seeds]		2009[4]
 Protocatechuic acid methyl ester (51)	<i>A.xanthioides</i> MeOH [seeds]		2009[4]
 4-Hydroxy-3-methoxy benzoic acid (52)	<i>A.tsao-ko</i> EtOAc [fruit]		2000[11]
 3,4-Dihydroxy benzoic acid (53)	<i>A.tsao-ko</i> EtOAc [fruit]		2000[11]
 4-Hydroxy benzoic acid (54)	<i>A.tsao-ko</i> EtOAc [fruit]		2000[11]


Table 7 Miscellaneous from *Amomum* species

Compound	Plant [Extract,part]	Biological activity	Year [ref.]
 <p>(1<i>R</i>,2<i>S</i>,4<i>R</i>,7<i>S</i>)-Vicodiol-9-<i>O</i>-β-D-glucopyranoside (55)</p>	<i>A.xanthiodes</i> Wall.		2003[7]
	MeoH [seeds]		
 <p>(1<i>R</i>,2<i>S</i>,4<i>S</i>,5<i>R</i>)-Angelicoidenol-2-<i>O</i>-β-D-glucopyranoside (56)</p>	<i>A.xanthiodes</i> Wall.		2003[7]
	MeoH [seeds]		
 <p>(1<i>S</i>,2<i>S</i>,4<i>R</i>,6<i>S</i>)-Bornane-2,6-diol 2-<i>O</i>-β-D-glucopyranoside (57)</p>	<i>A.xanthiodes</i> Wall.		2003[7]
	MeoH [seeds]		
 <p>(1<i>R</i>,4<i>S</i>,6<i>S</i>)-6-Hydroxybornan-2-one 6-<i>O</i>-β-D-glucopyranoside (58)</p>	<i>A.xanthiodes</i> Wall.		2003[7]
	MeoH [seeds]		
 <p>(1<i>S</i>,4<i>R</i>,6<i>S</i>)-6-Hydroxybornan-2-one 6-<i>O</i>-β-D-glucopyranoside (59)</p>	<i>A.xanthiodes</i> Wall.		2003[7]
	MeoH [seeds]		
 <p>(2<i>S</i>,7<i>S</i>)-(-)-Octane-1,2,7,8-tetrol (60)</p>	<i>A.xanthiodes</i> Wall.		2003[7]
	MeoH [seeds]		