CHAPTER I

INTRODUCTION

Aglaia odorata Lour. (family Meliaceae) [1] is a shrubby tree found in Thailand, Malaysia, China and The Philippines. In Thailand, it is commonly known as Prayong (Central) or Homglai (Peninsular) which is used as herbal medicine in the old days.[2] There are three kinds of this plant ; Prayong Baiyai (Aglaia chaudocensis Pierre.), Prayong (Aglaia odorata Lour.) and Prayong Paa (Aglaia odoratissima Bl. or Aglaia roxburghiana Hiern.).[1,2]

Prayong is a kind of shrub or small tree. It is 5-6 metres high with leaves as large as Kaeo leaves (Murraya paniculata Jack). There are five small leaves in oblong and tapering forms being sharp at the ends and gradually tapering at the thicker ends. The leave perimeter is smooth or a little wavy. Its flowers are in yellow bunches about 6-12 centimetres. There are a lot of small flowers with fragrant smell. They are usually grown as embellished plants for houses, temples or official places.

For medical uses [2,3], old-style doctors believe that roots of Prayong being boiled in water can be eaten as vomit medicine to extract poison and intoxicant. Its flowers can be boiled to relieve and fever use as remedy for hang-over. They can bleach lungs, quicken thirst and feeling oppressed.

They can be used to cure a stuffy feeling in the chest, coughing and feeling dizzy. Its roots and leaves can be used as heart nutriment remedy, they can also nurture blood and relieve fever.

1.1 The Chemical Constituents of Aglaia Species And Uses

From literature surveys, the chemical constituents of some Aglaia species have been summarized in the table 1.

Table 1 The Chemical Constituents of Some Aglaia (A.) Plants.

Scientific name	Plant parts	Isolated compounds	Reference
A. andamanica Hiern.	heart wood	β -sitosterol gedunin (1)	4
A. elliptifolia Merr.	roots,stems	rocaglamide (2)	5
A. pirifera Hance.	leaves	piriferine (3)	6
A. odoratissima Blume	seeds	essential oil (Priyangu) aromadendrene (4)	7

Table 1 (continued)

Scientific name	Plant parts	Isolated compounds	Reference
A. odoratissima Blume	seeds	cineole	7
		α -terpinene	
		citral	
		sesquiterpene	
		mixed fatty acids	8
		-linoleic	
		-oleic	
		-palmitic	
		-stearic	
		β -sitosterol	
		phytosterol	
		pigment	
		volatile oil	9
		essential oil	10
A. roxburghiana Miq.	leaves	roxburghiline (5)	11
		(roxburghilin)	12
	flowers	quercetin (6)	13
		myricetin (7)	
		rutin (8)	
		meratin (9)	

Table 1 (continued)

Scientific name	Plant parts	Isolated compounds	Reference
A. roxburghiana Miq.	flowers	(+)-odorinol (12)	14
	dried aerial parts	(+)-odorinol	15
		(+)-odorine (10)	
		cycloartenol (14)	
		29-nor-cycloartenol(15)	
		29-nor-cycloartan-24, 25-epoxy-3β-ol (16)	
		29-nor-cycloartan-23-ene-3β,25-diol (17)	
		28,29-bis-norcycloartan-24-methylene-3β,6α-diol (18)	
	leaves and fruits	roxburghiadiol A (19)	16,17
		roxburghiadiol B (20)	
A. odorata Lour.	leaves	Aglaiol (21)	18,19
		myricyl alcohol	20,21,22
		β-sitosterol	
		hydroxyketone	
		Aglaiondiol (22)	
		Aglaitriol (23,24)	

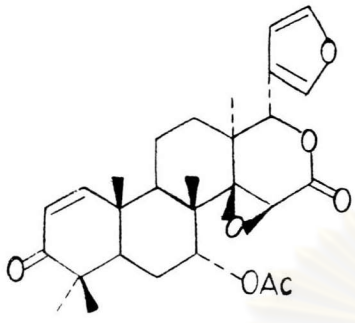
Table 1 (continued)

Scientific name	Plant parts	Isolated compounds	Reference
A. odorata Lour.	leaves	odorine (odoratine)(11)	23,24
		odorinol (odoratinol)(13)	
	leaves and twigs	(-)-odorinol (13)	25
	leaves	dammarane I (25), II (26) and III (27)	26,27
	stems	lupinifolin I (28) and II (29)	28
	flowers	tritriacontane ($C_{33}H_{68}$)	29
		ceryl alcohol ($C_{26}H_{54}O$)	
		β-sitosterol (31)	
		odoram (30)	
		(-)-α-humulene	31
		(-)-β-elemene	
		(-)-β-caryophyllene	
		(-)-copaene	
		Aglaiol A ($C_{15}H_{24}O$)	

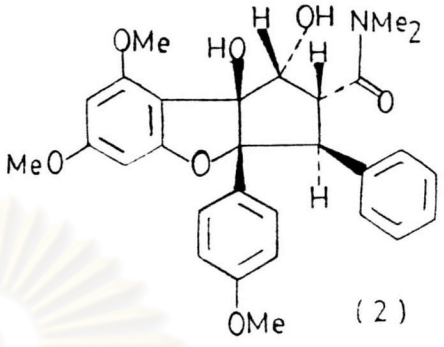
Table 1 (continued)

Scientific name	Plant parts	Isolated compounds	Reference
A. odorata Lour.	flowers	Aglaiol B ($C_{15}H_{26}O$) Aglaionol ($C_{17}H_{30}O_2$) linalool nonyl aldehyde juniper camphor palmitic acid aglaione aglaionolide ($C_{15}H_{26}O_3$)	31

Figure I The Chemical Constituents of Some Aglaia (A.) Plants.

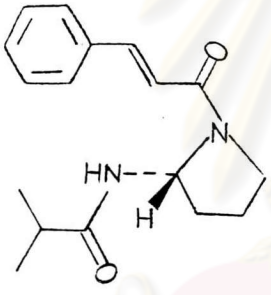


(1) Gedunin



(2)

(2) Rocaglamide

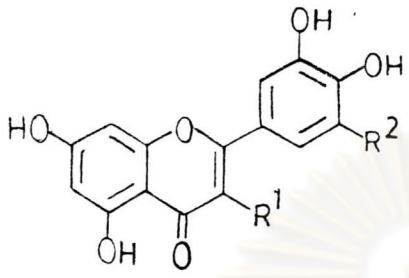


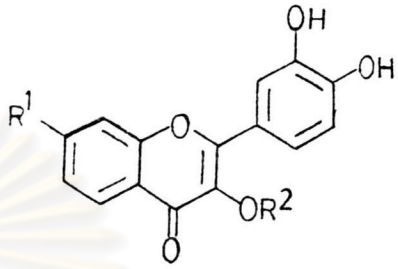
(3) Piriferine

(4) Aromadendrene

(5) Roxburghiline R = $-\overset{CH_3}{\underset{|}{C}}HEt$

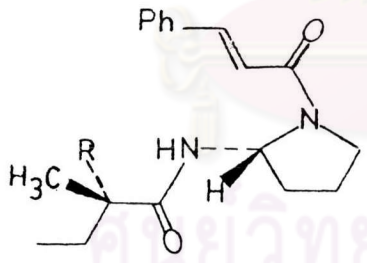
Figure I The Chemical Constituents of Some Aglaia (A.) Plants.

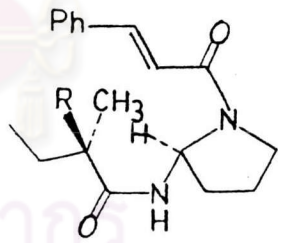




(6) Quercetin : R^1=OH , R^2=H (8) Rutin : R^1=OH , R^2=Rutinose

(7) Myricetin : R^1=OH , R^2=H (9) Meratin : R^1=H , R^2=Glu-Glu

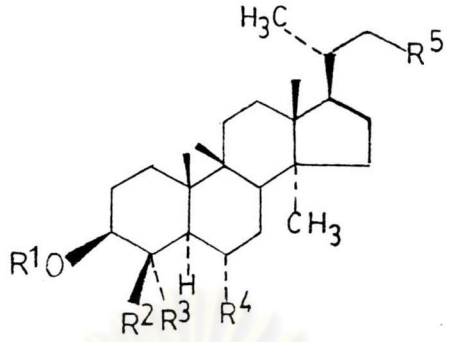




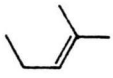
(10) (+)-Odorine : R=H (11) (-)-Odorine : R=H

(12) (+)-Odorinol : R=OH (13) (-)-Odorinol : R=OH

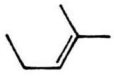
Figure I The Chemical Constituents of Some Aglaia (A.) Plants.



(14) Cycloartenol :

$R^1 = R^4 = H$, $R^2 = R^3 = CH_3$, $R^5 =$ 

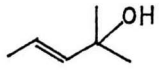
(15) 29-nor-Cycloartenol :

$R^1 = R^2 = R^4 = H$, $R^3 = CH_3$, $R^5 =$ 

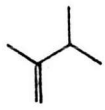
(16) 29-nor-Cycloartan-24,25-epoxy-3 β-ol :

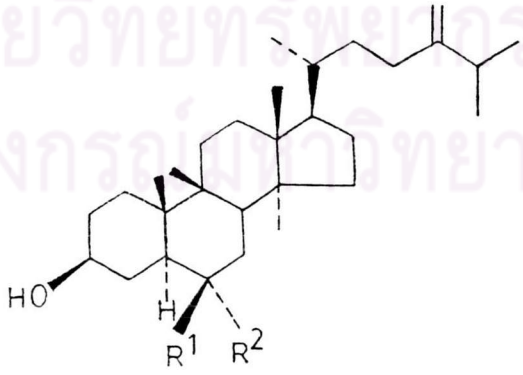
$R^1 = R^2 = R^4 = H$, $R^3 = CH_3$, $R^5 =$ 

(17) 29-nor-Cycloartan-23-ene-3 β,25-diol :

$R^1 = R^2 = R^4 = H$, $R^3 = CH_3$, $R^5 =$ 

(18) 28,29-bis-Norcycloartan-24-methylene-3 β,6 α-diol :

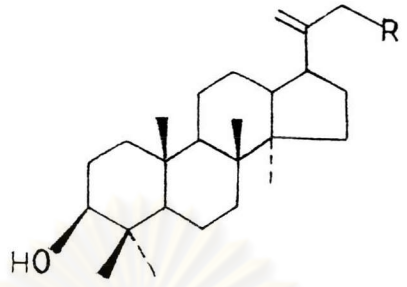
$R^1 = R^2 = R^4 = H$, $R^3 = CH_3$, $R^5 =$ 

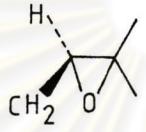


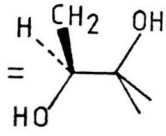
(19) Roxburghiadiol A : $R^1 = OH$, $R^2 = H$

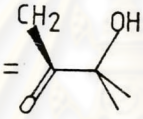
(20) Roxburghiadiol B : $R^1 = H$, $R^2 = OH$

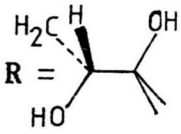
Figure I The Chemical Constituents of Some Aglaia (A.) Plants.

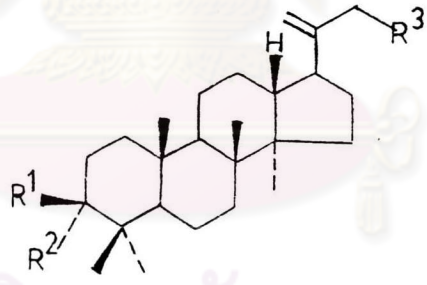


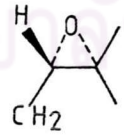
(21) Aglaiol : R = 

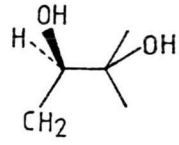
(23) Aglaitriol I : R = 

(22) Aglaiondiol : R = 

(24) Aglaitriol II : R = 



(25) Dammarane I : R^1R^2 = O , R^3 = 

(26) Dammarane II : R^1R^2 = O , R^3 = 

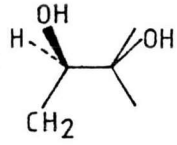
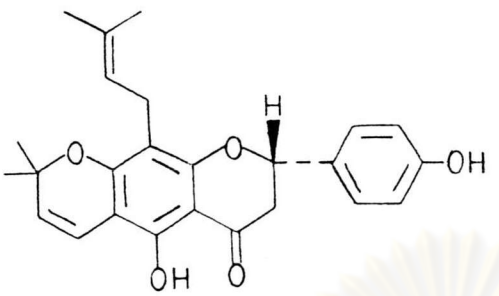
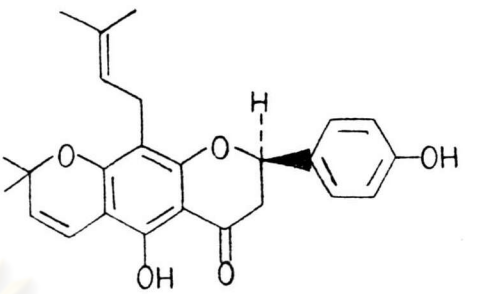
(27) Dammarane III : R^1 = OH, R^2 = H, R^3 = 

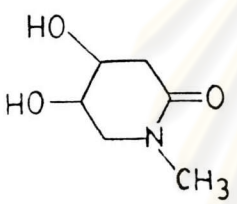
Figure I The Chemical Constituents of Some Aglaia (A.) Plants.



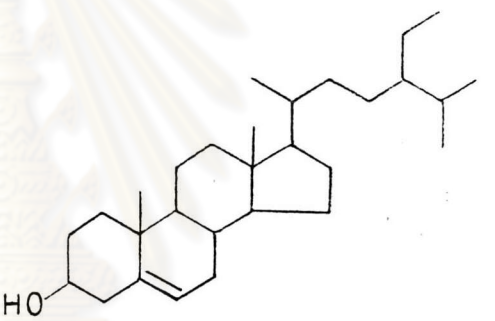
(28) Lupinifolin I



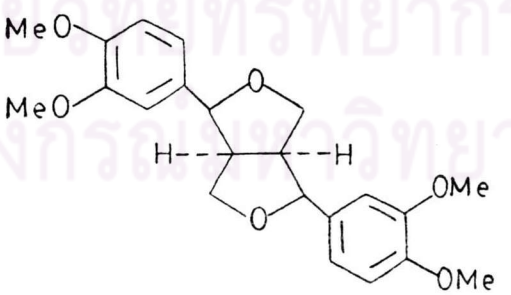
(29) Lupinifolin II



(30) Odoram
(was proposed in ref.29)



(31) β-sitosterol



(32) (-)-Eudesmin

Medical uses

Many compounds extracted from Aglaia plants have been used as medicines. For example, the volatile oil from the seeds of Aglaia odoratissima exhibits marked antibacterial and antifungal activity. The essential oil was effective against *Staphylococcus citreus* and *Rhizopus oryzae.* [9] The oil is comparatively more active against tape worms and hook worms than the standard anthemintics piperazine phosphate and hexylresorcinol but its lethal action against nodular worms is considerably less than that of hexylresorcinol. [10] Extract of Aglaia odorata has led to the characterization of (-)-odorinol (13) , a new diamide demonstrating significance *in vivo* antileukemic activity against P-388 lymphocytic leukemia growth in BDF_1 male mice.[37] Furthermore, the alcoholic extract of dried roots and stems of Aglaia elliptifolia lead to the isolation of a novel 1*H*-2,3,3a,8b-tetrahydrocyclopenta[*b*] benzofuran, rocaglamide (2), which was reported to exhibit significant antileukemic activity against P-388 lymphocytic leukemia in CDF_1 mice and inhibitory activity *in vitro* against cells derived from human epidermoid carcinoma of the nasopharynx (KB cell). [5] The isolation of Aglaia roxburghiana Miq. var. Beddomei yields (+)-odorinol which exhibits strong antiviral activity against Ranikhet disease virus (RVD) in chick embryo. [38]

1.2 Chemical Constituents of Aglaia odorata Lour.

The chemical constituents of Aglaia odorata Lour. have been studied since 1964. Many new compounds are isolated from the crude extracts of this plants.

In 1964, D. Shiengthong and A. Veerasarn [18,19] isolated a tetracyclic triterpene aglaiol (21) from the light petroleum ether and ether extracts of the dried leaves.

In 1969, U. Kokpol extracted the dried leaves with light petroleum ether and ether. He isolated myricyl alcohol, β-sitosterol and two new compounds ; aglaiondiol (22), two isomers of aglaitriol (23) [20,21].

In 1973, P. Karnthiang studied additionally the relative structure of aglaiol, aglaiondiol and aglaitriol. [22]

In the same year, R.B. Boar and K. Damps [26,27] determined the configuration of aglaiol which was (24S)-24, 25-epoxy-triterpene.

In 1974, A. Unphakorn isolated two new nitrogenous compounds from the leaves. Their structures were elucidated as odorine (11) and odorinol (13). The stereochemistry of odorine was established by synthesis of (-)-odorine and (+)-dihydro-odorine from L-proline [30]. [23,24]

In 1980, D. Shiengthong et al. isolated two crystalline compounds from the crude ether extracts of ground dried stems. The structure was identified as a flavanone compound, lupinifolin (28). It was believed that each of them should have been

consisted of enantiomers (I and II). [28]

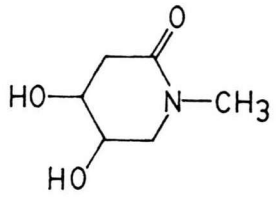
In 1979, some known compounds were also isolated and identified as a lignan: (-)-eudesmin (32) and a long chain alcohol: 1-triacontane. [32]

In 1981, L. Chutsin et al. [31] studied the floral essential oil of A. odorata , and found four sesquiterpene hydrocarbons constituting 75-80 % of the oil. They were isolated and identified as α-humulene, β-elemene , β-caryophyllene and copaene. The oxygenated components of the oil mainly consisted of aglaiol A ($C_{15}H_{24}O$), aglaiol B ($C_{15}H_{26}O$) , aglaionol ($C_{17}H_{30}O_2$). Among the minor oxygenated constituents were obtained linalool, nonyl aldehyde, juniper camphor, palmitic acid and two carbonylic compounds as aglaione (m.p. 55-56 ^{o}C) and aglaionolide ($C_{15}H_{26}O_3$) (m.p. 73-75 ^{o}C).

In 1986, W. Tiansong et al. [39] analyzed the volatile of dried flowers by using gas chromatography-mass spectroscopy (GC-MS) technique. Fifty-four compounds were obtained which included 21 sesquiterpenes, 8 aldehydes, 7 alkyl benzene 6 alkanes, 6 other oxygen-containing compounds and a nitrogen-containing compound. Twenty-nine of the compounds have not been reported previously in the study of the constituents of the essential oil from the flowers.

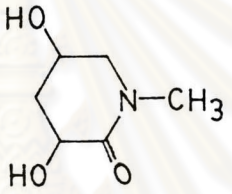
In 1981, P. Techasaowapark [29] studied the extracts from flowers of A. odorata. She isolated tritriacontane ($C_{33}H_{68}$), ceryl alcohol ($C_{26}H_{54}O$), β-sitosterol from the hexane extract and a nitrogenous compound named "odoram" from the

methanol extract. The possible structure was assigned as (-)-(4R,5R)-4,5-dihydroxy-1-methyl-2-piperidone (30) as shown.



4,5-dihydroxy-1-methyl-2-piperidone or odoram (30)

However, additional spectroscopic data [32] exhibited that odoram should be (-)-(3R,5R)-3,5-dihydroxy-1-methyl-2-piperidone (33) as shown .

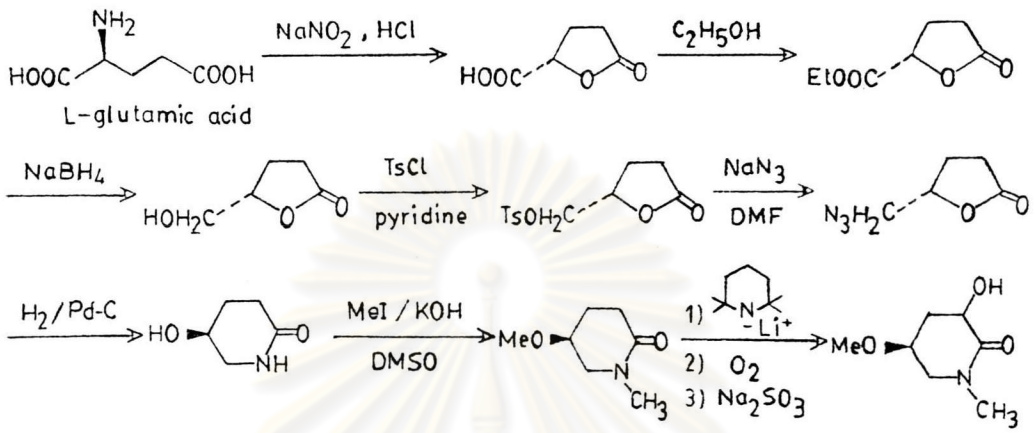


3,5-dihydroxy-1-methyl-2-piperidone (33)

To prove the structure of odoram, the synthesis of odoram or derivative of odoram was proposed.

In 1989, W. Rungruangkanokkul [32] had synthesized 3,5-dihydroxy-1-methyl-2-piperidone derivative which was named "3-hydroxy-5-methoxy-1-methyl-2-piperidone" (36). The starting material of synthetic pathway was L-glutamic acid [33] toward a compound that had structure similar to that of odoram namely (S)-5-hydroxy-2-piperidone (34) and then N-methylation [34] and α-hydroxylation [35] as shown in scheme I.

Scheme I The Synthetic Pathway of 3,5-Dihydroxy-1-methyl-2-piperidone Derivative : 3-Hydroxy-5-methoxy-1-methyl-2-piperidone.



From the above synthetic pathway, it could not accomplish to obtain odoram. So we would like to identify the structure of odoram by X-ray crystallographic method.