CHAPTER 1
INTRODUCTION

Various Thai medicinal plants have been gradually reaccepted for treatment in primary health care system. Especially during the economic crisis of Thailand, if Thai medicinal plants are widely used among people, a demand of modern drugs mostly imported from aboard will be reduced. Certain medicinal plants can be applied to treat diseases as well as modern drugs. There are several attempts to integrate the traditional and modern system of medicine in order to implement them properly. The study of chemical constituents from medicinal plants together with their pharmacological activities including clinical trials is important to confirm some of these claims.

Among plants in family Sapindaceae, ***Arfeuillea arborescens*** **Pierre** is one of interesting plant. It has been claimed having several activities[1,2] such the heartwood, used internally as anthelmintic. Boiling water extract of stem bark is used orally to stimulate appetite, relief thirsty and used as antipyretic. For external use, the extract is taken a bath in order to relief itchness. It is also claimed as an anticancer medicinal plant[3] like *Vinca roseus*, a source of material for producing vinblastine and vincristine[4]. The most popular common name of *A. arborescens* in Thai is "Kongkhaaduead", which might come from the mode of drug preparation, decoction. Other common ones are "Talai", "Talaikongkhaa" and "Samui kui", ect.

Primary brine shrimp cytoxicity screening of ethanolic extract of *A. arborescens* stems exhibited attractive result. Chemical constituents in the stems were further coarsely separated with various solvents into crude extracts. Some of them gave higher activity than previous testing. Anticell lines inhibition screening of certain extracts also showed satisfactory result.

As for the study of chemical constituents, only one study has been reported.[5] The interesting biological activities and unextended study of chemical constituents from this plant were attractive reasons for further investigation.

1.1 Botanical Aspect and Distribution[6,7]

Arfeuillea arborescens is a medium size tree, 15-30 meters high, mostly distributes in deciduous forests north of Isthmus of Kra. Leaves are paripinate: leaflets arrange like feather, no terminal leaflet, but short rachis end. Flowers are reddish green, in hairy panicles. Fruits are in flated, bladder-like, 3-4 cm long, 3-winged, papery capsule with not lobed.

The plant family Sapindaceae is found in all tropical zones of the world. In Southeast Asia, the Nephelieae is noticeable since it contains a number of famous fruit trees like the Longan, Lychee and Rambutan. A recent botanical survey of Sapindaceae in Thailand by Welzen found 23 genera[6], nearly half of them including genus *Arfeuillea* are monotypic, only one specie is presence in the genus.

List of genera* :

1. *Allophylus cobbe*
2. *Amesiodendron chinense*
3. *Arfeuillea arborescens*
4. *Arytera litoralis*
5. Cardiospermum
6. Dimocarpus
7. Dodonea (viscosa)
8. *Filicium decipiens*
9. *Ganophyllum falcatum*
10. *Glenniea philippinensis*
11. Guioa
12. Harpullia
13. Lepisanthes
14. *Litchi chinensis*
15. Mischocarpus
16. Nephelium
17. Paranephelium
18. Pometia
19. Sapindus (rarak)
20. *Schleichera oleosa*
21. *Sisyrolepis muricata*
22. Xerospermum
23. *Zollingeria dongnaiensis*

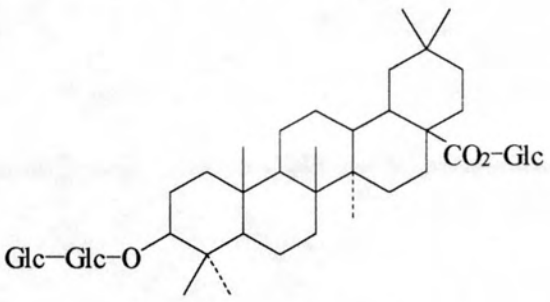
* If certain genera are monotypic, the species name (italic) will be provided. When the species name is between brackets, the specimen might be another introduced species; consequently, one mentioned in the list and key to species of that genus should be checked to be certain.

Figure 1.1 (a) flowers, (b) fruits, (c) leaves and (d) stems of *A. arborescens*

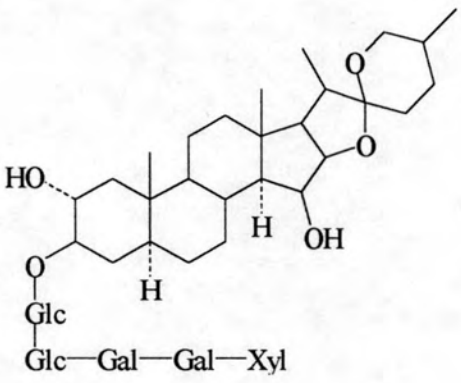
1.2 Chemotaxonomy of Sapindaceae

As already mentioned earlier for chemical constituents study of *A. arborescens*, isolation of long chain ketone and a mixture of stigmasterol and *β*-sitosterol from the barks was reported[5]. Literature surveys of chemical constituents from plenty of plants in other genus frequently reported the isolation of saponins. They have been well-known for a long time as common components in several Sapindaceae. Consequently, it is not surprising that the family receives its name from saponins. Other than Sapindaceae, they also found in certain families such Leguminose, Araliaceae, Caryophyllaceae, Primulaceae and Asteraceae. Most saponins have detergent properties, a bitter taste, haemolytic activity, give stable foam in water, are toxic to fish (piscicidal) and also form molecular complex with cholesterol. They have divers biological and pharmacological activities, some of them such fungicidal and piscicidal effects have been known for many years. Particularly, piscicidal activity is prominent in the plants from Sapindaceae. Their chemical structure consist of a sugar moiety linked to aglycone or sapogenin. They can be categorized into three classes depend on aglycon structure: triterpenoid, steroid and steroid alkaloid. In terms of Sapindaceae, the two latter were hardly found.

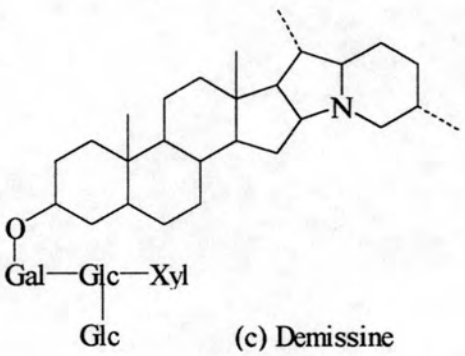
Oleanane saponins containing unsaturation at C-12 or olean-12-en, one type of triterpenoid saponins, are most common in Sapindaceae. They may be monodesmosides which have a single chain, normally attached at C-3. Another kind is bidesmosides which have two sugar moieties, often with one attached through an ether linkage at C-3 and one attached through an ester linkage (acyl glycoside) at C-28. The number of monosaccharide units in each sugar chain range from two and six. L-rhamnose, D-xylose, D-glucose and L-arabinose are typically found, and the last one is most frequently attached directly to the aglycone [see Sapindoside A **(1)** - *β*-Hederin **(14)**]. Saponins in some genera[8] are listed in Figure 1.4-1.7



(a) Ginsenoside R_0

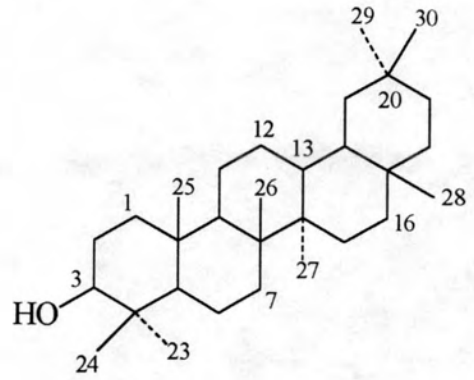


(b) Digitonin

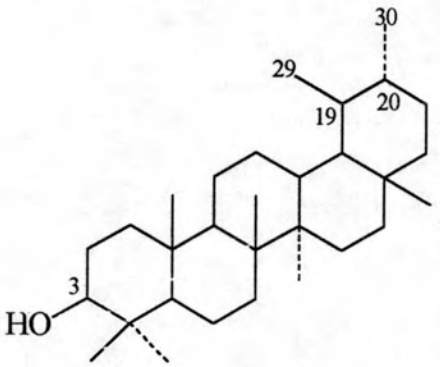


(c) Demissine

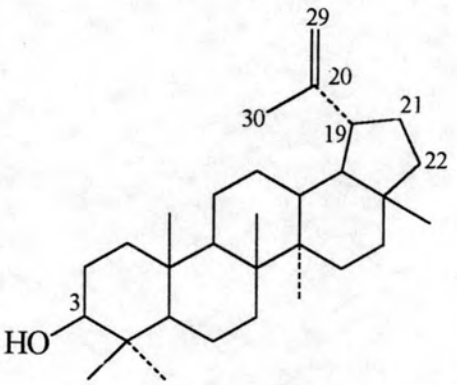
Figure 1.2 Examples of (a) triterpenoid, (b) steroid, (c) steroid alkaloid saponins



Oleananes type

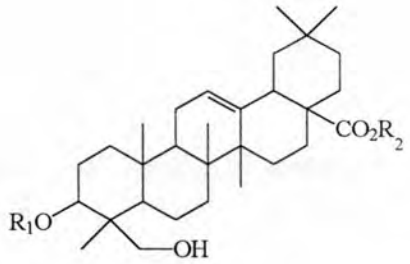


Ursanes type



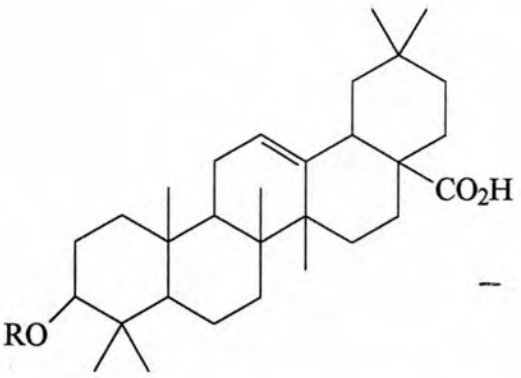
Lupanes type

Figure 1.3 The main types of triterpene aglycone



	R_1	R_2
Sapindoside A **(1)**	Ara^{2}—Rha	H
Sapindoside B **(2)**	Ara^{2}—Rha^{3}—Xyl	H
Sapindoside C **(3)**	Ara^{2}—Rha^{3}—Xyl^{4}—Glc	H
Sapindoside D **(4)**	Ara^{2}—Rha^{3}—Xyl^{4}—Glc^{6}(Glc^{2})—Rha	H
Sapindoside E **(5)**	Ara^{2}—Rha^{3}—Xyl	Ara^{2}—Rha^{3}—Xyl^{4}—Glc^{6}(Glc^{2})—Rha
Mukurozi saponin E_1 **(6)**	Ara^{2}—Rha^{3}—Xyl^{4}—Ac	H
Mukurozi saponin G **(7)**	Ara^{2}—Rha^{3}—Xyl^{4,3}Ac	H
Mukurozi saponin X **(8)**	Ara^{2}—Rha	Glc^{2}—Glc
Mukurozi saponin Y_1 **(9)**	Ara^{2}—Rha^{3}—Xyl	Glc^{2}—Glc
Mukurozi saponin Y_2 **(10)**	Ara^{2}—Rha^{3}—Ara	Glc^{2}—Glc

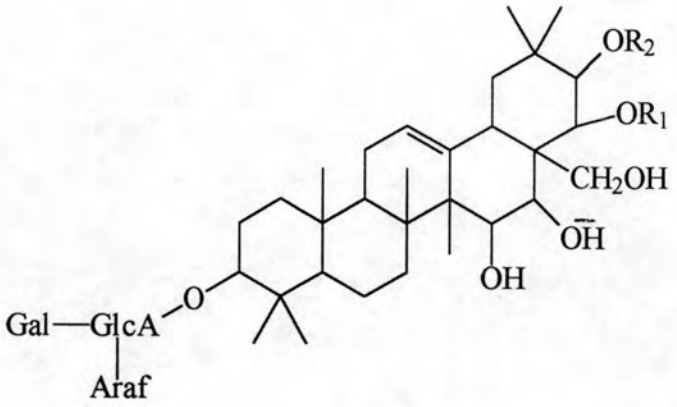
Figure 1.4 Hederin type saponins isolated from *Sapindus spp*



	R
Fatsiaside A_1 **(11)**	Ara
Scabioside B **(12)**	Ara^{4}—Glc
β-Hederin **(13)**	Ara^{2}—Rha

Figure 1.5 Saponins from *Thinouia coriacea*

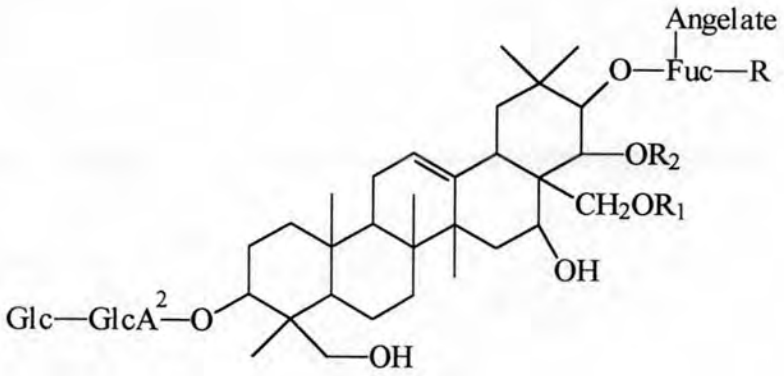
Unlike other families, certain saponins isolated from family *Dodonaea* [Dodonoside A **(14)** - B **(15)]** and *Xanthoceras* [Bunkankasaponin A **(16)** - D **(19)]** also contain rare monosaccharide units such β-D-glucuronic acid, β-D-fucose and furanoarabinose



	R_1	R_2
Dodonoside A* **(14)**	C(O)CHCH$_2$CH$_3$ with CH$_3$	O, C(O)C—CHCH$_3$ with CH$_3$
Dodonoside B* **(15)**	Angelate	O, C(O)C—CHCH$_3$ with CH$_3$

Figure 1.6 R_1-barrigenol type saponins from *Dodonae viscosa*

*R_1 and R_2 in dodonoside A and B may be interchangable.

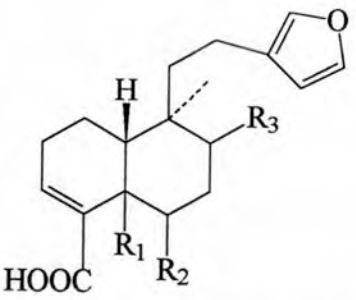


	R_1	R_2	R_3
Bunkankasaponin A **(16)**	H	Ac	Ac
Bunkankasaponin B **(17)**	H	Ac	Angelate
Bunkankasaponin C **(18)**	Ac	H	Ac
Bunkankasaponin D **(19)**	Ac	H	Angelate

Figure 1.7 Protoaescin type saponins from *Xanthoceras sorbifolia* Bunge

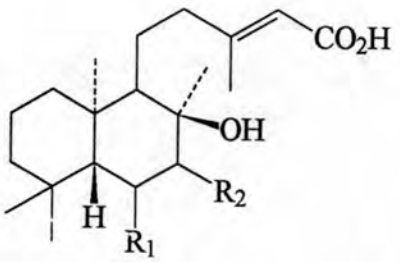
Although saponins were asserted as representative metabolites in this family, but many chemical investigations even in polar fraction of some particular plants did not report the isolation of any saponins. For examples, several phytochemical studies of certain plants in the Nephelieae always reported the presence of fatty acid, amino acid, protein[9-12] and non-saponin bitter principles[13]. Remarkably, some genera were grouped in this family though they had various characters quite unlike most Sapindaceae plants. This might be a reason why saponins were not found in certain genera.

In non-polar fractions, labdane diterpenes **[(20)-(24)]** were frequently isolated from *Dodonae spp.* whereas certain flavonoids **[(25)-(27)]** and coūmarins **[(28)-(30)]** were occasionally found. Furthermore, olean-12-en sapogenins **[(31)-(33)]** distributed in several genera, especially in *Harpullia spp.* Many small molecules were also likely to be dominant in this family such benzeneacetamide in the leaves of *Litchi chinensis*, which was latter synthesized as a starting material for making antacids, nylon, synthetic rubber, plastic and shampoo.



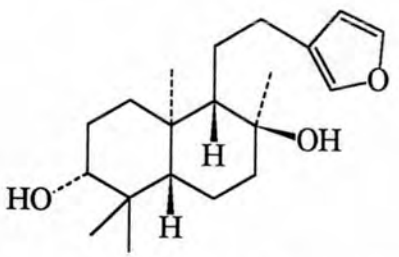
Dodonic acid **(20)** : $R_1 = CH_3$, $R_2 = OH$, $R_3 = CH_3$

Hautriwaic acid **(21)** : $R_1 = CH_2OH$, $R_2 = H$, $R_3 = CH_3$



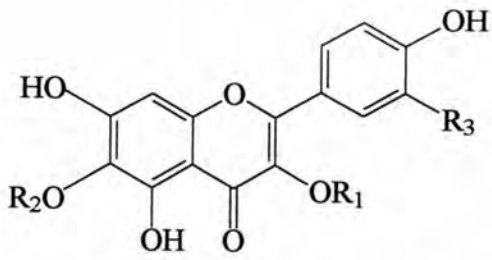
ent-7β,8α-dihydroxy-13*E*-labden-15-oic acid **(22)** : $R_1 = H$, $R_2 = \beta$-OH

ent-6α,8α-dihydroxy-13*E*-labden-15-oic acid **(23)** : $R_1 = \alpha$-OH, $R_2 = H$



ent-15,16-epoxy-13(16),14-labdadiene-3β,8α-diol **(24)**

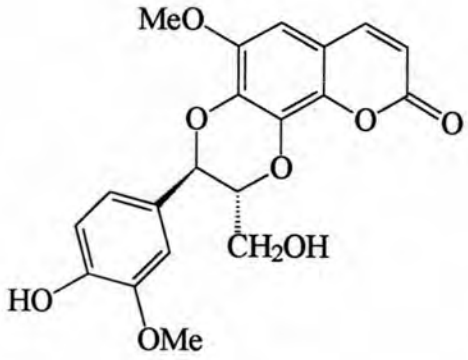
Figure 1.8 Some labdane diterpenes isolated from *Dodonae spp.*



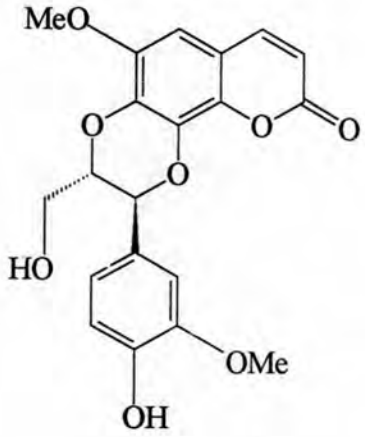
Aliarin **(25)** : $R_1 = R_2 = CH_3$, R_3 = Prenyl

Viscosol **(26)** : $R_1 = R_2 = H$, R_3 = 4-Hydroxydihydroprenyl

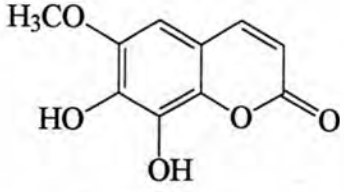
Isorhamnetin **(27)** : $R_1 = R_2 = H$, $R_3 = OCH_3$



Cleomiscosin A **(28)**

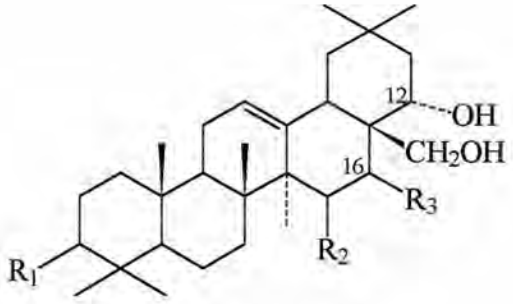


Cleomiscosin B **(29)**



Fraxetin **(30)**

Figure 1.9 An example of flavonoids and coumarins found in *Dodonae spp.*



Harpullone **(31)** : R_1 = 3-ketone, $R_2 = R_3$ = α-OH

16-O-Angeloylcamelliagenin A **(32)** : R_1 = β-OH, R_2 = H, R_3 = Angeloyl

16-O-Tigloylcamelliagenin A **(33)** : R_1 = β-OH, R_2 = H, R_3 = Tigloyl

Figure 1.10 Some oleane-12-en saponins distributed in *Harpullia spp.*

In this research, *A. arborescens* extracts, especially non-polar extracts, will be first separated by mean of chromatography techniques and then purified by proper methods such recrystalization to afford chemical constituents. Next, structure elucidation of them will be carried out by spectroscopy techniques. Finally, biological activity of the isolated pure compounds will be studied.