CHAPTER I

INTRODUCTION

1.1 Botanical Aspects of the Harrisonia

Harrisonia perforata Merr. belongs to the family of "Simaroubaceae"[1], a mainly tropical family centered in the New World. Plants in this family usually contain very bitter substances. Their leaves are spirally arranged and stipules present in few genera. They usually have compound, axillary, but rarely terminal inflorescence and uni- or bisexual flowers. Sepals, 3 to 5 number, are almost always connate, varied from valvate to slightly imbricate. Their petals, also 3 to 5 in number, are free and imbricate or valvate. Stamens inserted at the base of an intrastaminal and hypogynous disk are either isomerous or dimerous, but mostly obdiplostemonous (not rarely with a scale at the inner base). Plants in this family have separate carpels, 4 to 5 celled ovaries, and indehescent (often drupaceous or a samara) fruits.

Plants in this genus "Harrisonia" are both perennial and shrubber trees with thorns, erect or sprawling shrubs with height up to 12 m. and pithy branches [2]. The older branches are glabrous and lenticellate. The stipular thorns are accrescent, conical, slightly recurved up to 7 mm. and finally caducous. Annual shoots have small persistant budscales and sometimes spines at the base [3].

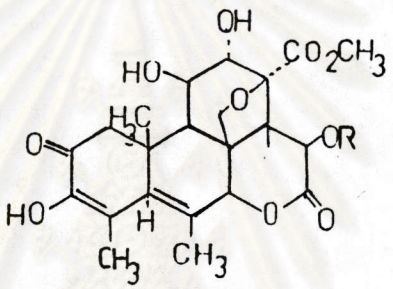
Harrisonia perforata Merr. is a shrubber tree with thorns and 1 to 15 jugates (up to ca. 20 cm. in length) of odd-pinnate leaves. Rhachis is narrowly winged, usually with a rib above, and pubescent, especially on top. Leaflets are 10 to 20 by 5 to 15 in dimension, with petiole length of 0.5 to 3 cm. Branches of cymes and thyrses for some length adnate to the peduncel which has pedicels of up to 2 mm. in length. Calyx is ca. 1.5 high, having 0.75 cm. lobes. Petals are lanceolate, rarely oblong, and 6 to 9 by 11 to 15 mm. in dimension. Stamens have the following aspects : anthers (ca. 1.5 to 4.5 mm.); filaments (7 to 10 mm.); and densely woolly ligule at the margin (ca. 2 mm.). Cup-shaped disk is 1 to 2 mm. high and the ovary are slightly lobed with height of 0.5 to 1 mm. Style is pubescent with length of 5 to 8 mm. The fruit of this plant has the dimension of 4 to 9 by 11 to 15 mm. with at least 1 mm. thick coriaceous exocarp and hard endocarp without a suture [4].

This plant has been found in all parts of Thailand, Hainan, Cambodia, Cochina, Malaysia and some other countries in Asia. It is often on limestone, in deciduous forest, in thickets and along roadside, mostly in open/exposed places.

1.2 Chemical Constituents of Simaroubaceae Studies

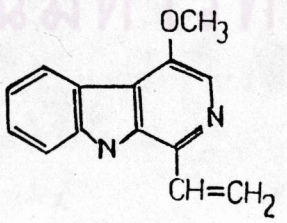
The plants in Simaroubaceae has been studies and many compounds were identified as summarized as follows :

In 1967 Judith Polonsky, Zoia Baskevith and A. Gandemer [5] found a new quassinoid compound called "bruceins" (I) which was a new compound from seed of *Brucea amarissima* Desv.



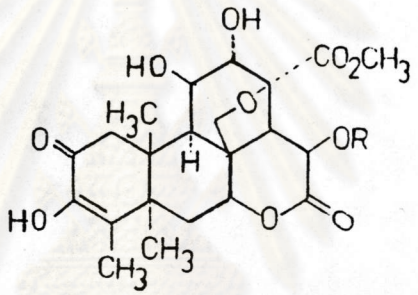
(I)

In 1970 John S.R. and A.A. Sioumis [6] found a new alkaloid, 4-methoxy-1-vinyl-β-carboline (II) and its dihydro derivatives from bark of *Picrasma javanica* Bl.



(II)

In 1975 Ronald W. Britton and Morris S. Kupchan [7] found new potent antileukemic principles, bruceantin (III), bruceantinol (IV) and a new companion quassinoid bruceantarin (V) from alcoholic extract of stem bark of *Brucea antidysenterica*. These compounds showed significant inhibitory activity in vitro against cells derived from human carcinoma of the nasopharynx, intramuscular carcinosarcoma in rats and lymphocytic leukemia in mice.

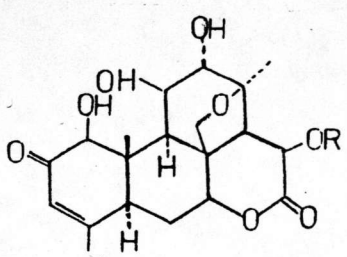


III R = $CO{=}CMeCHMe_2$

IV R = $COCH{=}CMeCMe_2OH$

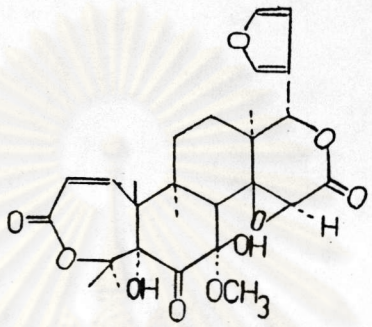
V R = COC_6H_5

One year later, Merris S. Kucphan and David R. Streelman [8] investigated the ethyl acetate extract of the dried sap of *Quassinoid amara* and found new quassinoid compound called "quassimarin"(VI) which showed antileukemic activities.



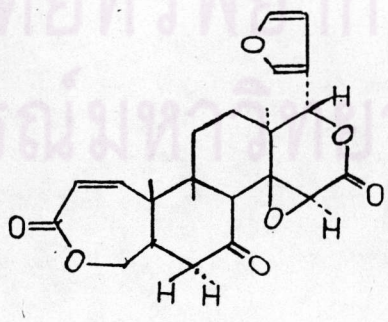
(VI)

In the same year, Kobu.I.et,al. [9] isolated harrisonin (VII) from the root bark of an East African shrub, *Harrisonia abyssinica* Oliv. Harrisonin was a new compound with insect antifeeding, cytotoxic and antibacterial properties.



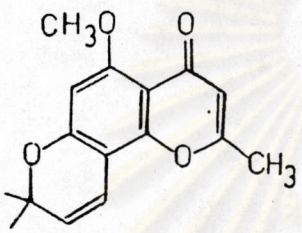
VII

Although *Harrisonia perforata* Merr. has been investigated in various aspects, mostly in herbs, for a long time, its chemical studies started only ten years ago. In 1982 Sombat Ruangkrit [10] isolated obacunone (VIII) from the chloroform extract of its root bark.

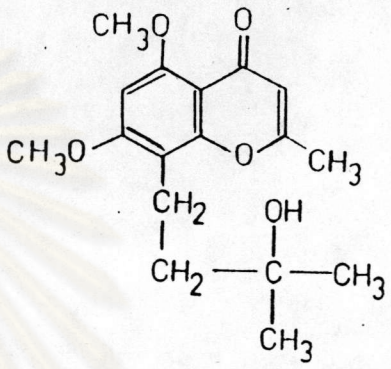


VIII

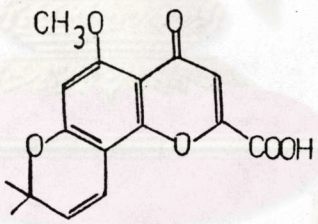
In 1983 Wang Mei-Xin, Zhang Min-Sheng and Zhu Yuan-Long [11,12] found three new compounds from the root bark, perforatin A (IX), perforatin B (X) and perforatic acid (XI). The last compound showed anticancer in mouse.



IX

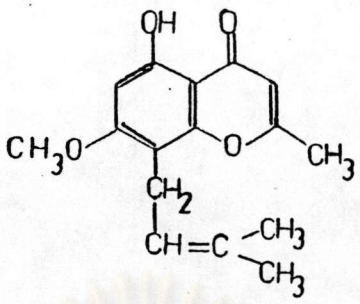


X

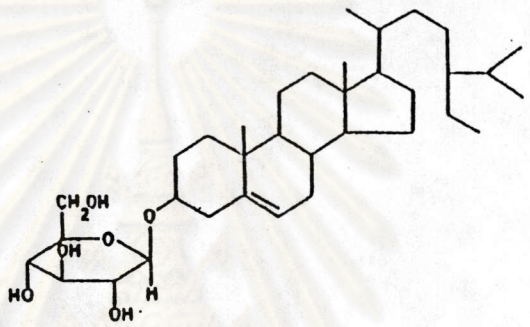


XI

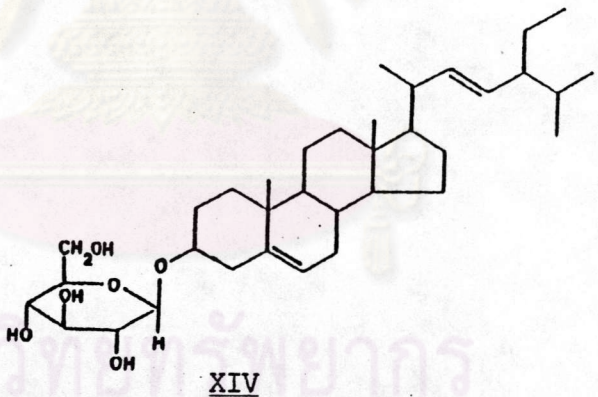
In 1990 Pakamas Lauethongsan [13] studied the root of *Harrisonia perforata* Merr. and isolated 4 compound, the mixture of steroids, perforatic acid (XI), heteropeucenin-7-methyl ether (XII) and steroid glycosides which consist of β-sitosteryl-3-O-glucopyranoside (XIII), stigmasteryl-3-O-glucopyranoside (XIV) and chloresteryl-3-O-glucopyranoside (XV).



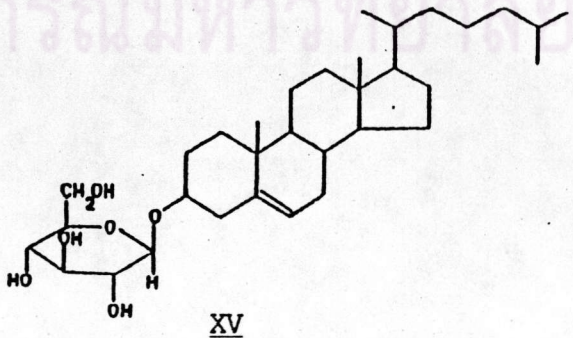
XII



XIII



XIV



XV

Finally, in 1991 Lindsay T. Bryne et.al. [14] found perforatin A, B and harrisonin from leaves of *Harrisonia perforata* Merr. The compounds from Simaroubaceae that have been studied are shown in Table 1.1

Table 1.1 Some compounds isolated from plants in Simaroubaceae family

Scientific name	Plant parts	Organic compounds	Ref.
1. *Aeschrion*			
A. crenata	bark	1-carbomethoxy-β-carboline	15
		crenatin	
		parain, 12-norquassin	5
2. *Ailanthus*			
A. altissima	leaf	amino acid composition	5
A. excelsa	leaf	vitexin	5
	root bark	canthin-6-one	16
A. giraldii	root	dimethylallyl-2-(1H)-	17
		quinoline	
A. malarbarica	bark	malanthin	5
		malabaricol	18
		carboline alkaloid	19
	stem	triterpenoids	20

(continued)

Table 1.1 (continued)

Scientific name	Plant parts	Organic compounds	Ref.
3. *Brucea*			
B. amarissima	seed	bruceines, oleic acid	5
		triolein, bruceolides	
		bruceoside A, bruceosin	21
		brusatol	
B.antidysenterica	root	bruceantin, bruceantinol	7
B. sumatrana	seed	brusatol, bruceine, terpene	22
4. *Castela*			
C. texana	root	simaroubolidanes	5
C. tweediei	root bark	quassinoids	5
5. *Eurycoma*			
E. longifolia	root	eurycomalactone	23
		saponins, steroids	24
6. *Hannoa*			
H. undulata	root bark	quassinoids	25
7. *Harrisonin*			
H. abyssinica	root bark	harrisonin, obacunone	9
		5-dehydrooriciopain	26
	root	alloptaeriexylin, peucenin	27

(continued)

Table 1.1 (continued)

Scientific name	Plant parts	Organic compounds	Ref.
H. perforata	root bark	β-sitosterol, obacunone	10
	root	heteropeucenin	11
		5-methoxy-heteropeucenin	
		perforatin A and B	
		perforatic acid	12
	leaf	harrisonin, perforatin A	14
		perforatin B	
8. *Perriera*			
P.madagascariensis	seed	glaucarubinone	28
		glaucarubin	
9. *Picralima*			
P. nitida	root bark	alkaloids, picraline	5
		picracine, akuammicine	
10. *Picrasma*			
P. ailanthoides	leaf	nigaki alcohol	29
	stem	nigakilactone	30
		1-hydroxymethyl-β-carboline	31
		diterpene	29
P. crenata	bark	1-carbomethoxy-β-carboline	32
		crenatine, crenatidine	

(continued)

Table 1.1 (continued)

Scientific name	Plant parts	Organic compounds	Ref.
	wood	quassin	5
P. excelsa	wood	N-methoxy-1-vinyl-β-carbo-	33
		line, canthin-6-one	
		5-methoxycanthin-6-one	
		4-methoxy-5-hydroxycanthin-	
		6-one	
P. quassinoids	leaf	anthocyanins	5
	wood	picrasins	
11. *Quassia*			
Q. africana	root bark	simalikalactone	5
		simalikahemiacetal	
		quassin	
Q. amara	stem	18-hydroxyquassine	8
12. *Samadera*			
S.indica	wood	indacanthinone	34
13. *Simaruba*			
S.amara	root bark	triterpenes, melianone	5
S.glauca	seed	glaucarubinone	

1.3 Pharmacological Activities

In the past, local medical used plants in Simaroubaceae family as herbs which are tabulated in Table 1.2.

The works that involve the pharmacological activities of *Harrisonia perforata* Merr. Mongkhon Morkhasamit [35] studied on the ethanolic crude extract that exhibited antihistamine property and has effected on the smooth muscle from mice's small intestine. The other utilities parts of *Harrisonia perforata* Merr. were summarized in Table 1.3.

Table 1.2 The utilities as herbs from Simaroubaceae family [3]

Scientific Names	Plant parts	Utilities
Brucea javanica	fruit	antidysentery
		antidiarrhoea
		febrifuge
Eurycoma longifolia	root	febrifuge
	root bark	febrifuge
Harrisonia perforata	wood	antidiarrhoea
	root bark	antidysentery
Picrasma javanica	bark	febrifuge

Table 1.3 The utilities of *Harrisonia perforata* Merr.

Plant parts	Utilities
root	febrifuge, antihistamine
bark	antiseptic
branch	toothbrush
wood	febrifuge
	antidysentery
root bark	antidiarrhoea

1.4 The Goal of This Research

The goal of this research can be summarized as follow :

1. To extract and isolate the organic constituents from the root of *Harrisonia perforata* Merr.

2. To elucidate the structural formulas of the isolated substances from the root of *Harrisonia perforata* Merr.

3. To increase the plant taxonomy of Simaroubaceae.