

Chapter II

Historical

Botanical aspect of Annonaceae

Annonaceae are confined mostly to moist tropical lowland forests (Sinclair, 1955) comprised of about 120 genera and 2,000 species (Leboeuf *et al.*, 1982). The centre of distribution of this family are Asia and Australasia. Backer and Bakhuizen Van Den Brink (1963) described the family Annonaceae as below :-

The family Annonaceae is mostly trees, erect shrubs or climbers, with striated stems; not latiferous, neither resiniferous. Leaves distichous, extipulate, simple, pinnately nerved, entire, mostly with sunk midrib above. Flowers in 1 to many flowered inflorescences, bisexual or rarely monoecious; sepals 3, rare 2 or 4, free or connate, mostly valvate, rarely imbricate; petals mostly 6, rarely 3 or 4, in 2 whorls of 3, or by absence of one the whorls in a single series, valvate, imbricate or rarely valvate at the base but imbricate at the tips, free, cohering by their edges or connate into a mitreform cap, often scented; torus broad, convex, conical or flattened, rarely subconcave, glabrous or hairy; stamen 1 to 3 or many, spirally arranged on the torus, fertile or in female flowers reduced or staminodial; filament very short or absent; anthers adnate; anther-cells 2, dorsal or lateral, linear, longitudinally dehiscing;

gynoecium apocarpous, or syncarpous and 1-celled; ovules parietal, 1 to many, superior ovary; ripe carpels sessile or stalked, mostly free, usually dry and 2-valved; seeds 1 to many; embryo minute; aril often present.

The genus *Fissistigma* is usually climbers. Leaves with maray stout, parallel lateral nerves, brown-hairy beneath. Flowers in terminal, leaf-opposed or axillary, leafy, solitary, racemose-cymes or panicles, bisexual; sepals 3, valvate, united at the very base; petals in 2 whorls of 3, much longer than calyx, valvate, coriaceous with thickened edges; outer set at last patent or obliquely downwardly directed; inner set smaller, triquetrous, erect with recurved apex and strongly concave base, acuminate, free, sessile; torus raised, with a flat apex, glabrous between the stamens, densly pubescent between the ovaries; stamens ∞ , connective slightly produced, concealing the cells; ovaries ∞ , 4- ∞ -ovuled; style pilose; stigma (in gava) hardly widened; ripe carpels stalked, \pm globose, thick-walled; seeds 1-8, shining brown (Backer and Bakhuizen Van Den Brink, 1963; Sinclair, 1955).

According to the Index Kewensis, the 82 species of the genus *Fissistigma* are shown as follow :-

Fissistigma acuminatissimum Merrill

F. africanum Merrill

F. balansae Merrill

F. beccarii Merrill

F. bicolor Merrill

- F. borneense* Merrill
- F. bracteolatum* Chatterjee
- F. capitatum* Merrill ex Li
- F. cavleriei* Rehder
- F. chloroneuron* (Hand. - Mazz.) Chun
- F. chrysosericeum* Merrill
- F. cinerascens* Merrill
- F. clementis* Merrill
- F. cupreonitens* Merrill Chun
- F. cylindricum* Merrill
- F. elegans* Merrill
- F. elmeri* Merrill
- F. fagifolium* Merrill
- F. fulgens* Merrill
- F. fuscum* (Craib) R.E. Fries
- F. globosum* C.Y. Wu ex P.T. Li
- F. guinanense* Y. Wan
- F. hainanense* Merrill
- F. hypoglaucum* Merrill
- F. kentii* Merrill
- F. kinabaluense* Merrill
- F. kingii* (Boerb.) Burkill
- F. korthalsii* Merrill

- F. kwangsiense* Tsiang P.T. Li
F. lanuginosum Merrill
F. latifolium Merrill
F. leichhardtii Merrill
F. litseaefolium Merrill
F. longipes Merrill
F. longipetalum Merrill
F. mabiforme Merrill
F. maccraei Merrill
F. maclurei Merrill
F. macranthum Merrill
F. maingayi Merrill
F. manubriatum Merrill
F. minuticalyx (Mc Gregor W.W. Smith) Chatterjee
F. oblongum Merrill
F. obtusifolium Merrill
F. oldhamii Merrill
F. olicarpum W.T. Wang
F. ovalifolium Merrill
F. ovoideum Merrill
F. pallens Merrill
F. paniculatum Merrill
F. parviflorum Merrill

- F. petelotii* Merrill
- F. poilanei* (Ast) Tsiang P.T. Li
- F. polyanthoides* (D.C.) Merrill
- F. polyanthum* Merrill
- F. prismaticum* Merrill
- F. puntulatum* Merrill
- F. retusum* Rehder
- F. rigidum* Merrill
- F. rubiginosum* Merrill
- F. rufinerve* Merrill
- F. rufen* Merrill
- F. rugosum* F. Since
- F. santapaui* D. Das
- F. schefferi* Merrill
- F. schlechteri* Merrill
- F. sericeum* A.C. Smith
- F. shangtzeense* Tsiang P.T. Li
- F. sphaerocarpum* (Miq.) Backer
- F. stenopetalum* (F. Muell.) R.E. Fries
- F. tientangense* Tsiang P.T. Li
- F. thorelii* Merrill
- F. tonkinense* Merrill
- F. tungfangense* Tsiang P.T. Li

F. uhrii Merrill

F. uonicum Merrill

F. verrucosum Merrill

F. villosissimum Merrill

F. villosum (Ast) Merrill

F. wallichii Merrill

F. xylopetalum Tsiang P.T. Li

F. zippelii Merrill

According to the Thai Plant Names of the Royal Forest Department, there are four species of *Fissistigma* in Thailand (Smitinand, 1980). They are as follow :-

Fissistigma bicolor Merr., ก้วยมะสัง Kluai ma sang (Nakhon Si Thammarat).

F. latifolium Merr. var. *ovoidea* J. Sincl., นมวัว Nom wua (Nakhon Si Thammarat).

F. minuticalyx Chatterijee, นมควาย Nom khwaai (Chiang Rai).

F. rubiginosum Merr., ไคหลง Khlong (Malay-Pattani); นมวัว Nom wua (Songkhla);

ย่านเลือด yaan lueat (Surat Thani).

Besides these species, there are also three species of *Fissistigma* kept as herbarium specimen at the Royal Forest Department. They are as follow :-

Fissistigma glaucescens (Hance) Merr.

F. polyanthoides (DC.) Merr.

F. thorelii Merr.

Fissistigma polyanthoides is a little scandant; undulating branch in pubescent then darkish smooth. Leaves ellipse, round at base and apex, 11-13 cm. long, 6 cm. wide, lateral nerve 15 pairs. Flowers ; sepal hairy outside, inside hairless; petal 6, the outer about 4 times longer than sepal, outside hairy, inside smooth except margin, involucre oval-triangular; stamen lodge parallel and adjoining; stigma (and style) cylindrical, hairy up to apex; ovules 4; carpels spherical, silky, pulp little abundance, big like plum. Flowering from March to October (Whitmore, 1972).

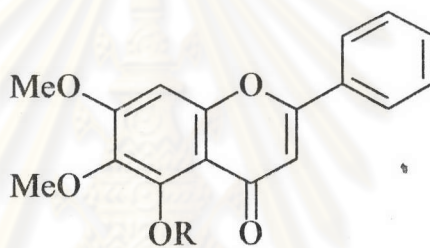
The Annonaceous plants are used in folk medicine and as a source of edible fruits, edible oils, soap and raw material for perfumery. The Annonaceous plants produce not only alkaloidal compounds but also non alkaloidal compounds belonging to various phytochemical groups (Leboeuf *et al.*, 1982).

The non-alkaloidal constituents of Annonaceae are carbohydrates, lipids, amino acids and proteins, polyphenols, essential oils, terpenes and aromatic compounds.

Because of the nutritional and economic importance of the species of *Annona*, a large number of studies have been done on the sugars, lipids and proteins contained in their fruits and seeds. The sugar found in the Annonaceous plants are sucrose, glucose and fructose whereas the amino acids are citrulline, γ butyric acid and proline.

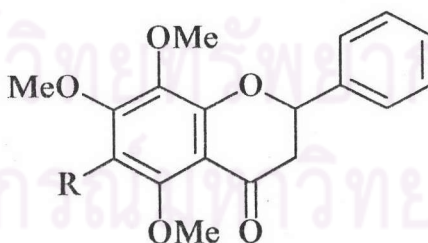
Polyphenols reported in the Annonaceous plants are caffeic acid, p-hydroxybenzoic acid, catechin procyanidin and tannin.

The major group of polyphenols are flavonoids. There were a lot of records of flavonoids in *Uvaria*, *Annona*, *Cananga*, *Pachypodanthium* and *Popowia*. From the whole stem and the ripe fruit of *Popowia cauliflora*, seven flavonoids were isolated (Waterman and Pootakahm, 1979). The structure of these flavonoids were shown below.



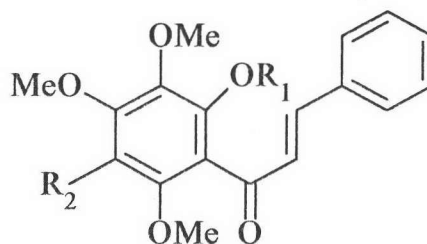
5,6,7-trimethoxyflavone, $R = \text{Me}$

5-hydroxy-6,7-dimethoxyflavone, $R = \text{H}$



5,7,8-trimethoxyflavanone, $R = \text{H}$

5,6,7,8-tetramethoxyflavanone, $R = \text{OMe}$



2'-hydroxy-3',4',6'-trimethoxychalcone,

$R_1 = R_2 = H$

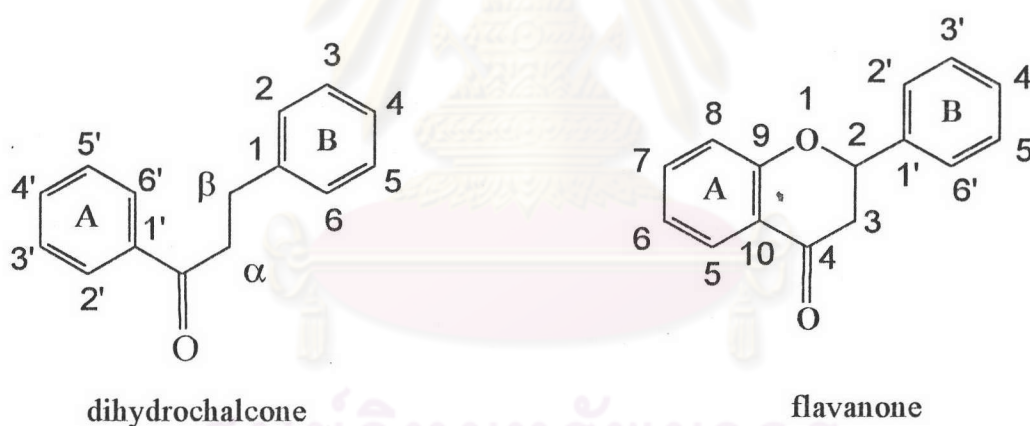
2',3',4',6'-tetramethoxychalcone,

$R_1 = CH_3, R_2 = H$

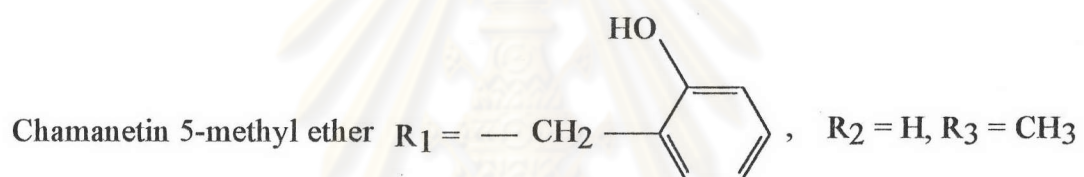
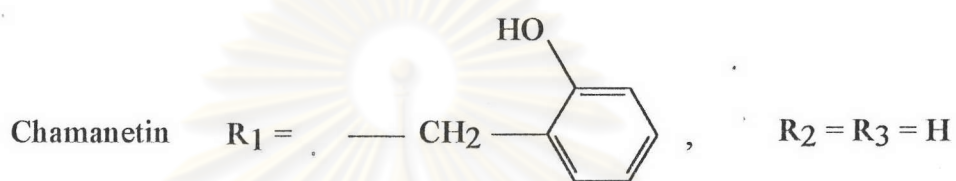
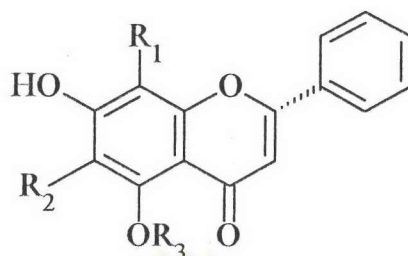
2'-hydroxy-3',4',5',6'-tetramethoxychalcone,

$R_1 = H, R_2 = OCH_3$

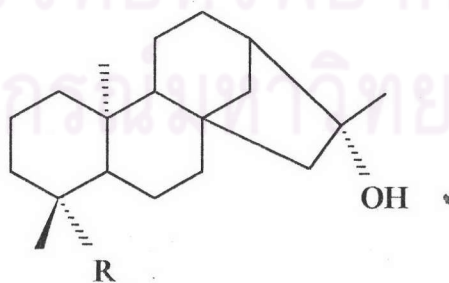
A common feature among the flavonoids isolated in the Annonaceae plants is the absence of B-ring substitution. (Leboeuf *et al*, 1982)



Since 1976, C-benzylated flavanones and C-benzylated dihydrochalcones have been obtained from several species of *Uvaria*. Some of these showed cytotoxic, antitumor and antimicrobial properties. For example, Chamanetin and chamanetin 5-methyl ether isolated from *Uvaria chamae* showed antimicrobial activity. (El-Sohly *et al*, 1979; Hufford and Lasswell, 1978a, 1978b, Lasswell and Hufford, 1976).



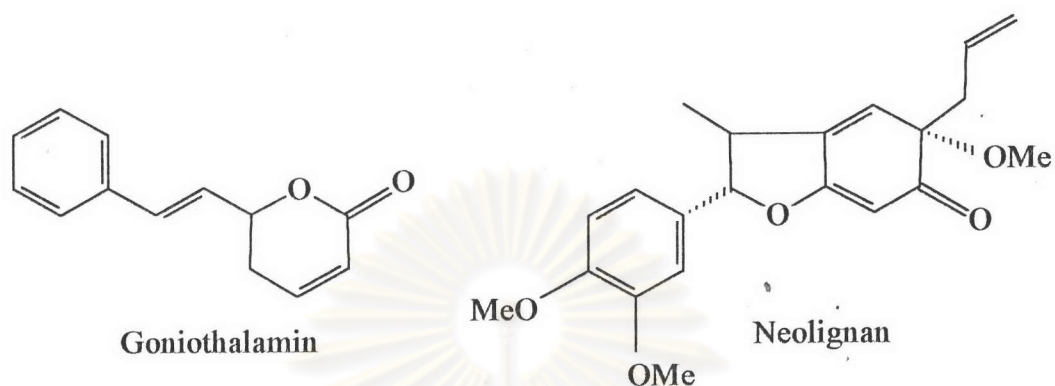
As for the terpene, the kaurane diterpene have been reported in several *Ammonia* species and *Xylopiya aethiopica*. (Adesogan and Durodola, 1976; Eshiet *et al*, 1971).



(-) kauran - 16 α - ol, $R = \text{Me}$

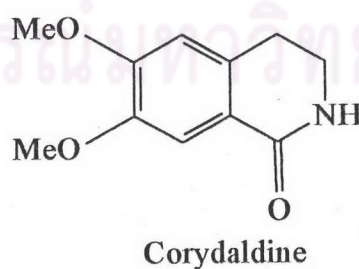
(-) kauran - 16 α , 19 - diol, $R = \text{MeOH}$

Aromatic compounds were isolated from Annonaceous plants are such as the lactone goniotalamin and the lignan type compound, neolignan (Leboeuf, 1982)..



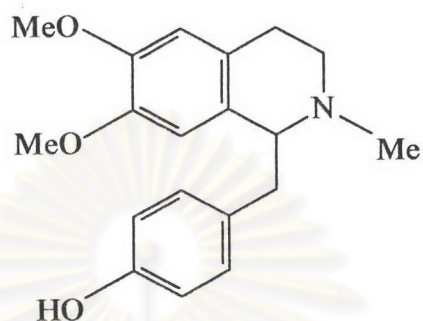
The alkaloidal compounds isolated from Annonaceous plants are mainly in isoquinoline type and its derivatives such as benzyltetrahydroisoquinolines, bisbenzylisoquinolines, bisbenzyltetrahydroprotoberberines, protoberberines tetrahydroprotoberberines, aporphines, etc.

Corydaldine is a example of isoquinolone isolated from the stem bark of *Enantia polycarpa* (Jossang, Leboeuf, and Cave', 1977).



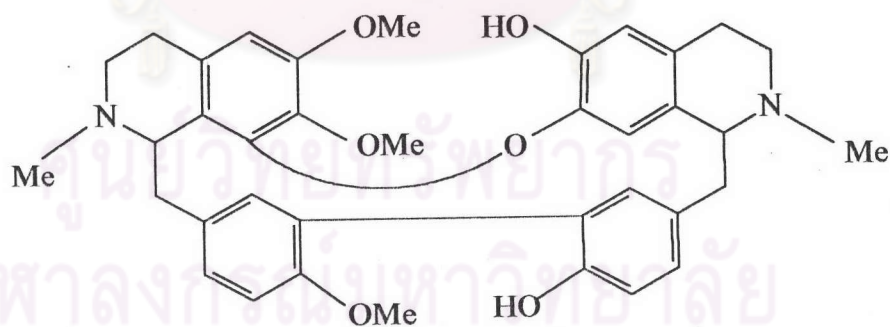
Most Benzyltetrahydroisoquinolines were isolated from *Ammona* and *Xylopiä*.

The most frequently occurent of this group is reticuline (Leboeuf, 1982).



Reticuline

Bisbenzylisoquinolines and bisbenzyltetrahydroisoquinolines were isolated from *Crematosperma*, *Guatteria*, *Isolona*, *Phaeanthus*, *Popowia* and *Uvaria*. Phlebicine, a bisbenzyltetrahydroisoquinoline, were isolated from *Crematosperma polyphlebium*. (Leboeuf, 1982).



Phlebicine

The chemical constituents that found in *Fissistigma* was summarized in table 1.

The major group of these compounds were isoquinoline alkaloids.

Table 1 Occurrence of chemical compounds in *Fissistigma* spp.

Plant species	Chemical constituent	Group	Part use	Reference
<i>Fissistigma glaucescens</i> (Hance) Merr.	(-)-Norannuradhapurine (1)	aporphines	entire plant stem wood stem bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	(-)-Anolobine (2)	aporphines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Anonaine (3)	aporphines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Asimilobine(4)	aporphines	entire plant stem bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	Atherosperminine (5)	phenanthrenes	entire plant stem wood root bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985 Wu <i>et al.</i> , 1990
	<i>N</i> -noratherosperminine (6)	phenanthrenes	entire plant stem wood	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	<i>N</i> -methylatherosperminine (7)	phenanthrenes	entire plant stem wood stem bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	(-)-Calycinine (Fissistigine A, Fissoldine) (8)	aporphines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Crebanine (9)	aporphines	entire plant stem wood stem bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	(-)-Discretamine (10)	tetrahydroprotoberberines	entire plant stem wood stem bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	Fissicesine (11)	phenanthrenes	root bark	Wu <i>et al.</i> , 1990
	Fissicesine - <i>N</i> -oxide (12)	phenanthrenes	root bark	Wu <i>et al.</i> , 1990
	(+)- <i>O</i> -methylflavinantine (13)	morphinandienones	entire plant	Lu <i>et al.</i> , 1985

Table 1 Occurrence of chemical compounds in *Fissistigma* spp. (cont.)

Plant species	Chemical constituent	Group	Part use	Reference
<i>Fissistigma oldhamii</i> (Hemsl.) Merr.	Kaufumine (14)	oxoaporphines		Wu <i>et al.</i> , 1987
	Liriodenine (15)	oxoaporphines	entire plant stem wood	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	Oxocrebanine (16)	oxoaporphines	entire plant stem wood	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	Palmatine (17)	protoberberines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Tetrahydro-palmatine (18)	tetrahydroprotoberberines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Xylophine (19)	aporphines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Norannuradhapurine (1)	aporphines	entire plant stem wood	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	(-)-Anolobine (2)	aporphines	entire plant stem wood	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	Anonaine (3)	aporphines	entire plant	Xu <i>et al.</i> , 1982 Lu <i>et al.</i> , 1985
	(-)-Asimilobine (4)	aporphines	entire plant	Lu <i>et al.</i> , 1985
	Atherosperminine (5)	phenanthrenes	entire plant	Lu <i>et al.</i> , 1985
	<i>N</i> -noratherosperminine (6)	phenanthrenes	entire plant	Lu <i>et al.</i> , 1985
	<i>N</i> -methylatherosperminium (7)	phenanthrenes	entire plant	Lu <i>et al.</i> , 1985

Table 1 Occurrence of chemical compounds in *Fissistigma* spp. (cont.)

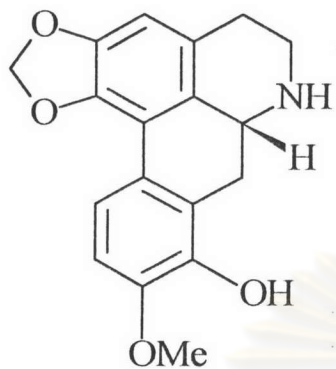
Plant species	Chemical constituent	Group	Part use	Reference
	(-)-Calycinine (Fissistigine A Fissoldine) (8)	aporphines	stem bark	Xu <i>et al.</i> , 1982 Lu and Wu, 1983 Xu <i>et al.</i> , 1983 Lu, Wu <i>et al.</i> , 1985
	(-)-Crebanine (9)	aporphines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Discretamine (10)	tetrahydropro- toberberines	entire plant	Lu <i>et al.</i> , 1985
	Fissistigine B (20)			Xu <i>et al.</i> , 1982
	Fissistigine C (21)			Xu <i>et al.</i> , 1982
	(+)- <i>O</i> -methylfla- vinantine (13)	morphinandie- nones	entire plant stem bark	Lu <i>et al.</i> , 1985 Lu, Wu <i>et al.</i> , 1985
	Liriodenine (15)	oxoaporphines	entire plant	Lu <i>et al.</i> , 1985
	Oxocrebanine (16)	oxoaporphines	entire plant	Lu <i>et al.</i> , 1985
	Palmatine (17)	protoberberines	entire plant	Lu <i>et al.</i> , 1985
	(-)-Tetrahydro- palmatine (18)	tetrahydropro- toberberines	entire plant	Lu <i>et al.</i> , 1985
	Xylopine (19)	aporphines	stem bark	Xu <i>et al.</i> , 1983 Lu, Wu <i>et al.</i> , 1985
	<i>N</i> -norxylopine (22)	aporphines	entire plant	Lu and Wu, 1983

Table 1 Occurrence of chemical compounds in *Fissistigma* spp. (cont.)

Plant species	Chemical constituent	Group	Part use	Reference
	<i>N</i> -methyl-2,3,6-trimethoxy morphinandien-7-one (23)	morphinandienone		Wu <i>et al.</i> , 1993
	<i>N</i> -nor-2,3,6-trimethoxy morphinandien-7-one (24)	morphinandienone		Wu <i>et al.</i> , 1993
<i>Fissistigma kwangsiense</i> Tsiang P.T. Li	8-hydroxy-5,6,7-trimethoxy-flavanone (25)	flavonoid (flavanone)		Shang <i>et al.</i> , 1994
<i>Fissistigma lanuginosum</i> Merrill	6,7-Dimethoxy-5,8-dihydroxy-flavone (26)	flavonoid (flavone)		Alias, Y. <i>et al.</i> , 1995
	Isofissistin (27)	flavonoid (chalcone)		Alias, Y. <i>et al.</i> , 1995

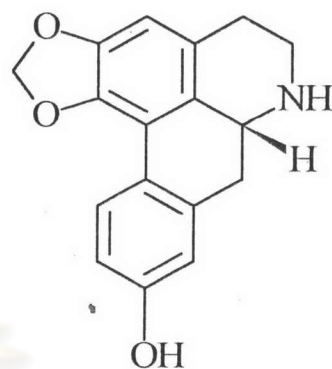
The structure formular of the chemical constituents were shown in page 19 - 24.

ศูนย์วิทยทรัพยากร
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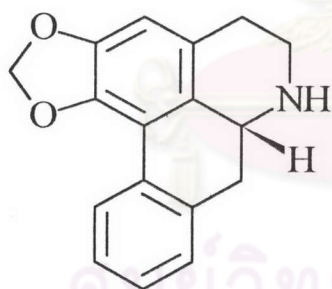
(1)

(-)-Norannuradhapurine



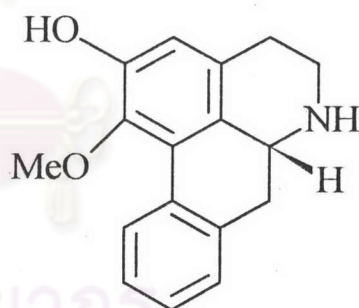
(2)

(-)-Anolobine



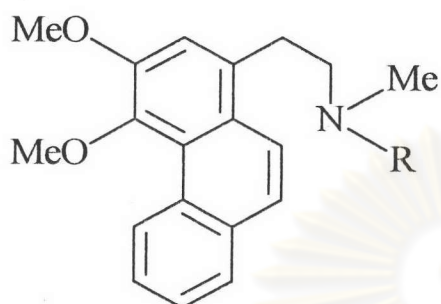
(3)

(-)-Anonaine

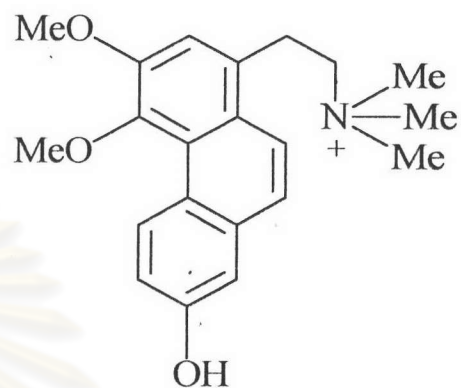


(4)

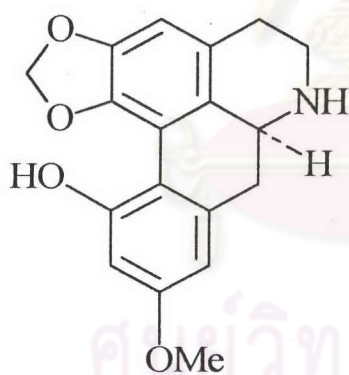
(-)-Asimilobine



(5) Atherosperminine R = Me

(6) *N*-noratherosperminine R = H

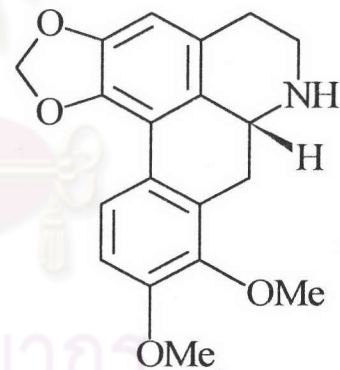
(7)

N-methylatherosperminine

(8)

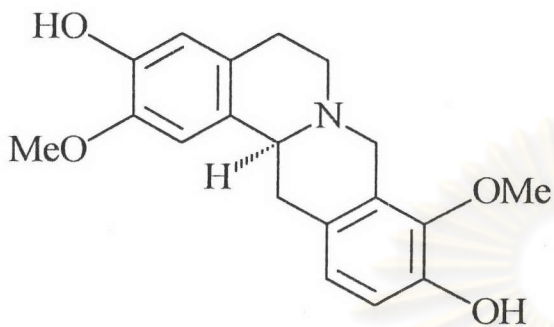
(-)-Calycinne

(Fissistigine A, Fissoldine)

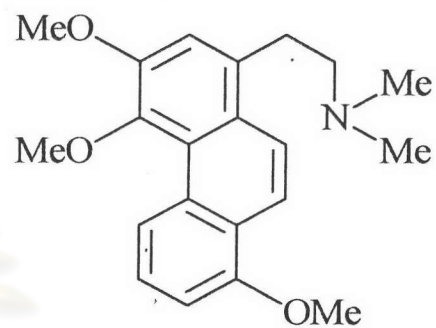


(9)

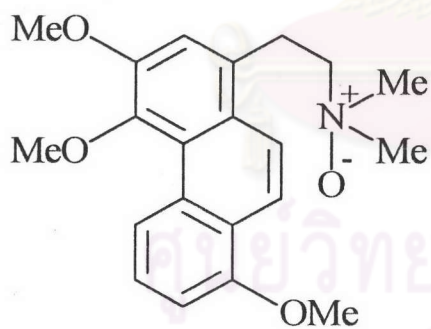
(-)-Crebanine



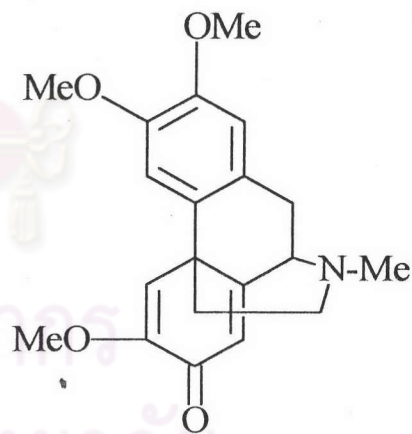
(10)
(-)-Discretamine



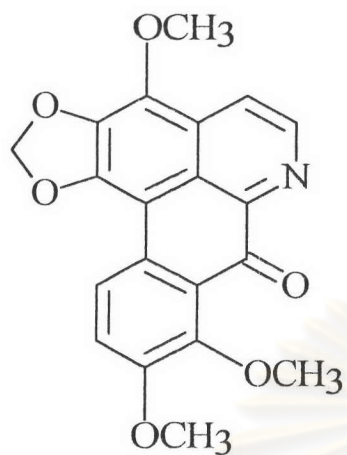
(11)
Fissicesine



(12)
Fissicesine -N-oxide

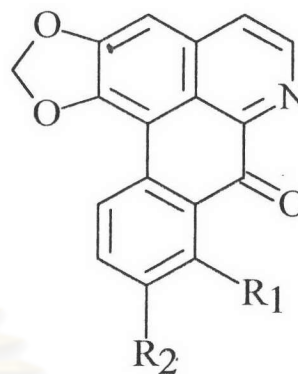
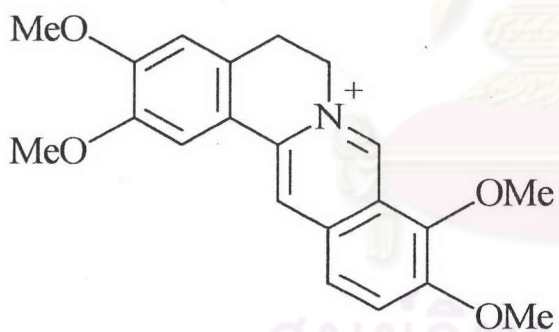


(13)
(+)-O-methylflavinantine



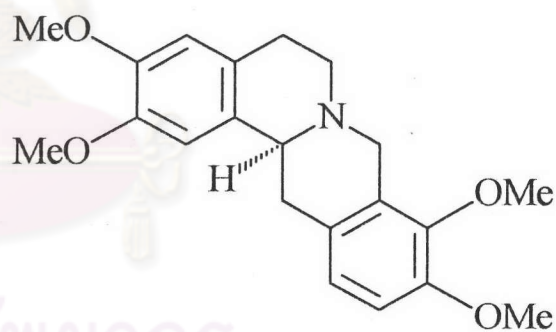
(14)

Kaufumine

(15) Liriodenine $R_1 = R_2 = H$ (16) Oxocrebanine $R_1 = R_2 = OMe$ 

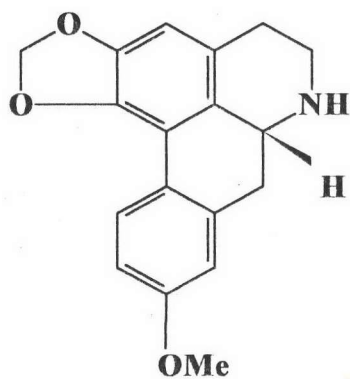
(17)

Palmatine

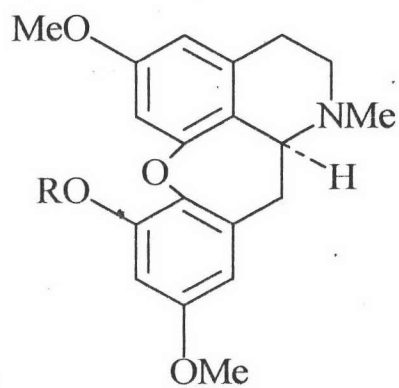


(18)

(-)-Tetrahydropalmatine

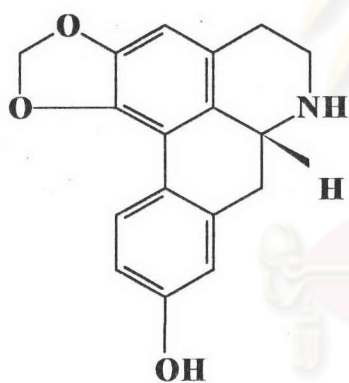


(19)
(-)-Xylopinine



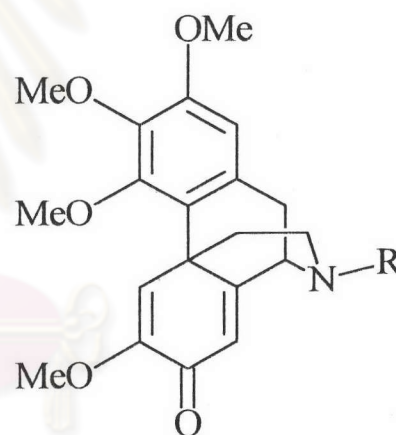
(20) Fissistigine B R = H

(21) Fissistigine C R = Me



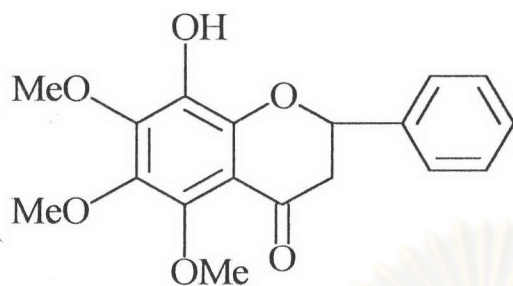
(20)

N-norxylopinine



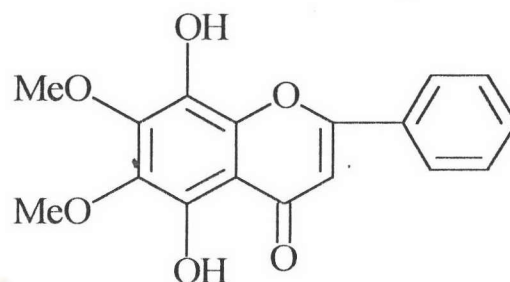
(23) *N*-methyl-2,3,6-trimethoxymorphinandien-7-one R = Me

(24) *N*-nor-2,3,6-trimethoxymorphinandien-7-one R = H



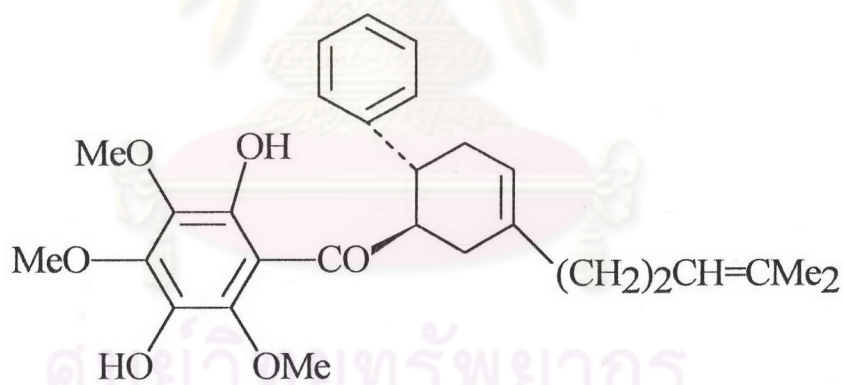
(25)

8-hydroxy-5,6,7-trimethoxyflavanone



(26)

6,7-dimethoxy-5,8-dihydroxyflavone



(27)

Isofissistin