



## CHAPTER I

### INTRODUCTION

#### *Michelia rajaniana* Craib

*Michelia* Linn., is a small genus of trees and shrubs of the family Magnoliaceae. Over forty-five species of *Michelia* are distributed widely in the tropical and subtropical Asia from India to China, Japan and Malaysia: four species are native to Thailand and more two other species are commonly cultivated. About 14 species are found in India (1, 2, 3).

According to the Index Kewensis, the 83 species of this genus are shown below :-

- Michelia aenea* Dandy
- M. alba* DC. (*M. longifolia* Blume)\*
- M. baillonii* Finet & Gagnep.
- M. balansae* Dandy
- M. baviensis* Finet & Gagnep.
- M. bodinieri* Finet & Gagnep.
- M. caerulea* DC.
- M. calcuttensis* Parmentier
- M. cathcartii* Hook & Thoms.
- M. cavaleriei* Finet & Gagnep. (*M. cavaleriei* Leveille,  
*M. leveilleana* Dandy)

- M. champaca* Linn. (*M. aurantiaca* Wall., *M. blumei* Steud.,  
*M. evonymoides* Burm., *M. pubinervia* Blume., *M. rheedii* Wight.,  
*M. champaca* Lour. ex Gomez)\*  
*M. chapensis* Dandy  
*M. chingii* Cheng  
*M. coerulea* Steud.  
*M. compressa* Sarg.  
*M. compressa* var. *formosana* Kanchira  
*M. compressa* var. *macrantha* Hatusima  
*M. constricta* Dandy  
*M. cris* Ruiz & Lopez  
*M. cumingii* Merrill & Rolfe  
*M. dandyi* Hu  
*M. doltsopa* Buch.-Ham. ex DC.  
*M. ecicatriscata* Miq.  
*M. excelsa* Blume  
*M. fallax* Dandy  
*M. figo* Spreng.  
*M. floribunda* Finet & Gagnep. (*M. kerii* Craib, *M. manipurensis*  
Craib)\*  
*M. farbesii* Baker  
*M. foveolata* Merrill ex Dandy  
*M. fulgens* Dandy  
*M. fuscata* Blume  
*M. glaba* Parmentier  
*M. gracilis* Kostel  
*M. gravis* Dandy ex Gagnep.

- M. griffithii* Finet & Gagnep.  
*M. gustavi* King  
*M. hypolampra* Dandy  
*M. kachirachirai* Kanchira & Yamamoto  
*M. kingii* Dandy  
*M. kisopa* Buch.-Ham. ex DC.  
*M. lacei* Smith  
*M. lanuginosa* Wall. (*M. velutina* DC.)  
*M. macclurei* Dandy  
*M. macrophylla* Don  
*M. magnifica* Hu  
*M. manipurensis* Watt ex Blandis  
*M. manni* King  
*M. martinii* Dandy (*M. martinii* Leveille)  
*M. masticata* Dandy  
*M. maudiae* Dunn.  
*M. mediocris* Dandy  
*M. microtricha* Hand.-Mazz.  
*M. mollis* (Dandy) McLaughl.  
*M. montana* Blume  
*M. nilagirica* Zenker (*M. glauca* Wight, *M. ovalifolia* Wight,  
*M. pulneyensis* Wight, *M. walkeri* Wight)  
*M. oblonga* Wall. (*M. lactea* Buch.-Ham. ex Wall.)  
*M. parviflora* Merrill (*M. parviflora* Rumph. ex DC.)  
*M. parvifolia* Blume (*M. parvifolia* DC.)  
*M. pealiana* Finet & Gagnep. (*M. pealiana* King)  
*M. phellocarpa* Finet & Gagnep.

- M. philippinensis* Dandy  
*M. pilifera* Bakh. (*M. velutina* Blume)  
*M. platyphylla* Merrill  
*M. platypetala* Hand.-Mazz.  
*M. punauana* Hook & Thoms.  
*M. rajaniana* Craib\*  
*M. scortechinii* Dandy  
*M. sinensis* Hemsl. & Wils.  
*M. skinneriana* Dunn.  
*M. subulifera* Dandy  
*M. sumatrae* Dandy  
*M. szechuanica* Dandy  
*M. tignifera* Dandy  
*M. tila* Buch.-Ham.  
*M. tonkinensis* Linn.  
*M. tsiampaca* Linn. (*M. velutina* Blume)  
*M. tsoi* Dandy  
*M. uniflora* Dandy  
*M. wardii* Dandy  
*M. wilsonii* Finet & Gagnep.  
*M. yulan* Kostel  
*M. yunnanensis* Franch ex Finet & Gagnep.

(The asterisked names are endemic species in Thailand)

Utilization of this genus has been reported in many countries. The wood is used excellently for boxes, furniture, building, decorative fittings, carving and carriage. The flowers, exceedingly fragrant are used for perfume (2, 3). The bitter substances in the plants make them medicinal such as the bark of *M. champaca* Linn. is used as stimulant,



diuretic and febrifuge; dried root and root bark are purgative and emmenagogue; the juice of the leaves is used in colic; flowers and fruits are stimulant, antispasmodic, stomachic and diuretic and are considered useful in dyspepsia, fever and in renal diseases; the flower oil is used as an application in cephalagia, ophthalmia, gout and rheumatism; fruits and seeds are considered useful for healing cracks in feet (2, 3, 5). The bark of *M. montana* Bl. is used as a bitter tonic in fevers (3). The bark and leaves of *M. nilagirica* Zenker are used as febrifuge. The bitter bark of *M. baillonii* (Pierre) Finet & Gagnep. is considered useful for stimulant and febrifuge (5). The flower buds of *M. alba* DC. are put into an infusion given to women for sapremia, following a miscarriage (5).

*Michelia rajaniana* Craib is known in various local names in Thailand as Champee luang จำปีหลวง (Chiang Mai), Cha-Kae ชะน (Karen-Mae Hong Son) (4).

*M. rajaniana* Craib is a medium-sized tree, to 25 m tall. Leaves elliptic to broadly ovate-oblong, 17-26 (-30) by 11-12 cm; apex obtuse; base rounded or truncate; lateral veins 15-22 pairs, almost parallel; glabrous above, densely greyish-tomentose beneath; petiole 3-3.5 cm long, tomentose, with stipular scars in lower  $\frac{1}{2}$ - $\frac{2}{3}$ . Flower-buds fusiform, 2.5-3 cm long; spathaceous bract densely sericeous; peduncle 1.2-1.5 cm long. Tepals 12 white to pale yellow, outer ones narrowly obvate, 3 by 1.4 cm; inner ones much narrower. Stamens 5-6 mm long, shortly appendaged. Gynoecium about 1 cm long; carpels 25-28, covered with golden hairs, the stigma black, beaked. Fruiting carpels 3-5 or more in a cluster; individual carpels globose or oblong-ovoid, about 1 cm long.

*M. rajaniana* Craib is found especially in the northern part of Thailand, in lower montane forest, or found at the edge of hill slope, at medium altitudes (1000-1300 m) (1).

In Thailand, there is no report about the medicinal uses of this plant..

Chemical studies of many other species of *Michelia* have been reported the presence of sesquiterpene lactones, the germacranolide group, for example micheliolide, compressanolide, parthenolide, costunolide, lanuginolide, santamarine and michelenolide from the root bark of *M. compressa* Sarg. (6); parthenolide, lanugilide, 11, 13-dehydrolanuginolide and dihydroparthenolide from the stem bark of *M. lanuginosa* Wall. (7) and parthenolide from the root of *M. champaca* Linn. (8). Some of the above mentioned sesquiterpene lactones such as micheldiolide, michelenolide, parthenolide, costunolide, santamarine, dehydrolanuginolide and epitulipinolide diepoxide are cytotoxic agents (9).

*M. rajaniana* Craib is found especially in the northern part of Thailand. Previously, there have been no reports on phytochemical studies of this plant. On phytochemical and biological screening, it was found that crude extract of the stem bark exhibits positive results with the mixture of 2 % resorcin in methanol and 2 % sulphuric acid (1:1) on TLC and the KB cytotoxicity assay. Hence it is indicated the presence of cytotoxic sesquiterpene lactones.

Accordingly, this present investigation deals with extraction, isolation and elucidation of sesquiterpene lactones in the stem bark, in order to contribute our knowledge of the constituents containing in this species and to search for compounds which might exert biological activities.



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Figure 1 *Michelia rajaniana* Craib :a, twig and flower

b, flower c, fruit (1)

Chemical Constituents of *Michelia* spp.

Members of the genus *Michelia* are found to contain a wide range of chemical constituents; sesquiterpene lactones, alkaloids, volatile oil, fixed oil, lignan and steroid.

A list of compounds found in various species of *Michelia* genus is shown in table 1 (page 9)



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Table 1 Chemical investigations of *Michelia* spp.

Botanical Origin	Plant Part	Chemical Substance	Category	Reference
<i>Michelia alba</i> DC.	-	Michelalbine	Alkaloid	10
	-	Oxoushinsunine	Alkaloid	10
	-	Salicifoline	Alkaloid	10,12
	-	Ushinsunine	Alkaloid	10
	-	Micheline	Alkaloid	11
	-	Normicheline	Alkaloid	11
	flowers	-	Essential oil	13
	leaves,	Lanuginoside	Sesquiterpene lactone	14
	trunk &	Liriiodenine	Alkaloid	14
	root bark	Sitosterol	Steroid	14
<i>M. cathcartii</i> Hook.f. & Thoms. Fl.	flowers,	-	Fixed oil	15
	oil	-	Volatile oil	15
<i>M. champaca</i> Linn.	bark	Michepressine	Alkaloid	16
	-	Oxyacanthine	Alkaloid	16

Table 1 (Continued)

Botanical Origin	Plant Part	Chemical Substance	Category	Reference
<i>M. compressa</i> Sarg.		Liriodenine	Alkaloid	17
		Oxoushinsunine	Alkaloid	17
		Ushinsunine	Alkaloid	17
		Magnoflorine	Alkaloid	18
	root	Liriodenine	Alkaloid	19
		Parthenolide	Sesquiterpene lactone	19
	bark	Magnoflorine	Alkaloid	20
		Oxyacanthine	Alkaloid	20
		Tetrahydroberberine	Alkaloid	20
		Tetrahydrojatrorrhizine	Alkaloid	20
	wood	Oxoushinsunine	Alkaloid	21
		Ushinsunine	Alkaloid	21
	root bark	Michelenolide	Sesquiterpene lactone	2
		Micheliolide	Sesquiterpene lactone	2

Table 1 (Continued)

Botanical Origin	Plant Part	Chemical Substance	Category	Reference
		Parthenolide	Sesquiterpene lactone	2
		Costunolide	Sesquiterpene lactone	2
		Santamarine	Sesquiterpene lactone	2
		Lanuginolide	Sesquiterpene lactone	2
		Dihydroparthenolide	Sesquiterpene lactone	2
		Compressenolide	Sesquiterpene lactone	2
		Liriodenine	Alkaloid	2
<i>M. compressa</i> Maxim.	bark	Ushinsunine	Alkaloid	21
var. <i>formosana</i> Kanchira		Liriodenine	Alkaloid	21
		Magnoflorine	Alkaloid	21
<i>M. doltsopa</i> Buch.-	fruit	Dihydroparthenolide	Sesquiterpene lactone	22
Ham. ex DC.		Parthenolide	Sesquiterpene lactone	22
		Lanuginolide	Sesquiterpene lactone	22

Table 1 (Continued)

Botanical Origin	Plant Part	Chemical Substance	Category	Reference
<i>M. excelisa</i> Blume	trunk & root bark	Sitosterol	Steroid	14
<i>M. figo</i> Spreng.	leaves	Magnolamine	Alkaloid	23
<i>M. fuscata</i> Flume	leaves	Magnolamine	Alkaloid	24,25
		Picrolanate	Alkaloid	24
		d-Laudanosine	Alkaloid	24
		d-Armejavine	Alkaloid	24
		Magnocurarine	Alkaloid	25
		Magnoflorine	Alkaloid	25
		Dehydrolanuginolide	Sesquiterpene lactone	25
	bark	Lipiferolide	Sesquiterpene lactone	26
		Deacetylanuginolide	Sesquiterpene lactone	26
		Michefuscalide	Sesquiterpene lactone	26
		Syringaresinol	Lignan	26



Table 1 (Continued)

Botanical Origin	Plant Part	Chemical Substance	Category	Reference
<i>M. hedyosperma</i> Law.	-	-	Essential oil	27
<i>M. lanuginosa</i> Wall.	trunk bark	-	Volatile oil	27
		Lanuginolide	Sesquiterpene lactone	28
		Dihydroparthenolide	Sesquiterpene lactone	28
		Michelanugine	Alkaloid	14, 29
		Liriodenine	Alkaloid	14, 29
		Parthenolide	Sesquiterpene lactone	7
		11, 13 Dehydroparthenolide	Sesquiterpene lactone	7
		Lanuginosine	Alkaloid	29
	Leaves	Sitosterol	Steroid	14
<i>M. paniculata</i> Linn.	flowers	-	Essential oil	13

Grangea maderaspatana Poir.

*Grangea* Adanson, a genus in the subtribe Grangeinae, the tribe Astereae, the family Compositae, is a genus of suberect or prostrate annual herbs. The occurrence of fourteen species of *Grangea* is found in tropical and subtropical Asia and Africa, all seasons (30, 31, 32, 33).

According to the Index Kewensis, the 14 species of this genus are shown below :-

- Grangea anthemoides* O. Hoffm.  
*G. chinensis* Lound. (*G. cuneifolia* Poir., *G. minima* Poir.,  
*G. minuta* Poir.)  
*G. cinera* Link.  
*G. dissecta* Boj. (*G. latifolia* Lam., *G. sonchifolia* Lound.)  
*G. domingensis* (Cass.) Gomez.  
*G. hispida* Humbert.  
*G. hippiodes* Merxm.  
*G. lanata* Humbert.  
*G. lanceolata* Poir.  
*G. madagacariensis* Batke.  
*G. maderaspatana* (Linn.) Poir. (*Artemisia maderaspatana* Roxb.,  
*Cotula maderaspatana* Willd., *C. sphaeranthus* Link.,  
*Grangea sphaeranthus* Koch. (33))  
*G. minima* Lipp.  
*G. mucronata* Buch.  
*G. strigosa* Gandoger

*Grangea maderaspatana* Poir. is known in various local names such as Phayaa mutti พญามุดดี (Suphan Buri); Yaa chaam luang พญาจามหลวง (Chiang Mai) (4, 33).

*G. maderaspatana* Poir. is prostrate or sometimes erect annual herb, stems spreading from the root prostrate, upto 25 cm long, whitish pubescent and glandular. Leaves alternate, lyrate-pinnatifid or almost bipinnatifid, upto 10 cm long, bearing 3-5 lobed or pinnatifid lateral segments 0.5-1.5 cm long, 2-10 mm broad, segments obtused or subacute at the apex, coarsely pubescent on both surfaces. Capitula (0.5) 0.75-1 cm diameter, phyllaries obvate, spathulate, 4.5 mm long, 2 mm broad, coarsely pubescent, margins scarious. Flowers yellow, glandular; female corollas 2 mm long, hermaphrodite corollas 2 mm long; anther-bases obtuses; styles-arms of disk florets flattened, cuneate, obtuse or with triangular points. Achenes greenish 1.25-1.5 mm long, minutely puberulent and glandular; stipes 0.5 mm long, pappus whitish, 0.5 mm long (31, 32, 34, 35).

Utilization of *Grangea maderaspatana* Poir. has been reported in many countries. The leaves are used as a stomachic, a sedative, a carminative, an antifatulence and an emmenagogue or to facilitate the return of the menses after parturition if the delay is accompanied by abdominal and kidney pain; further the leaves are used as a bechic and in antiseptic fomentations (5, 35, 36).

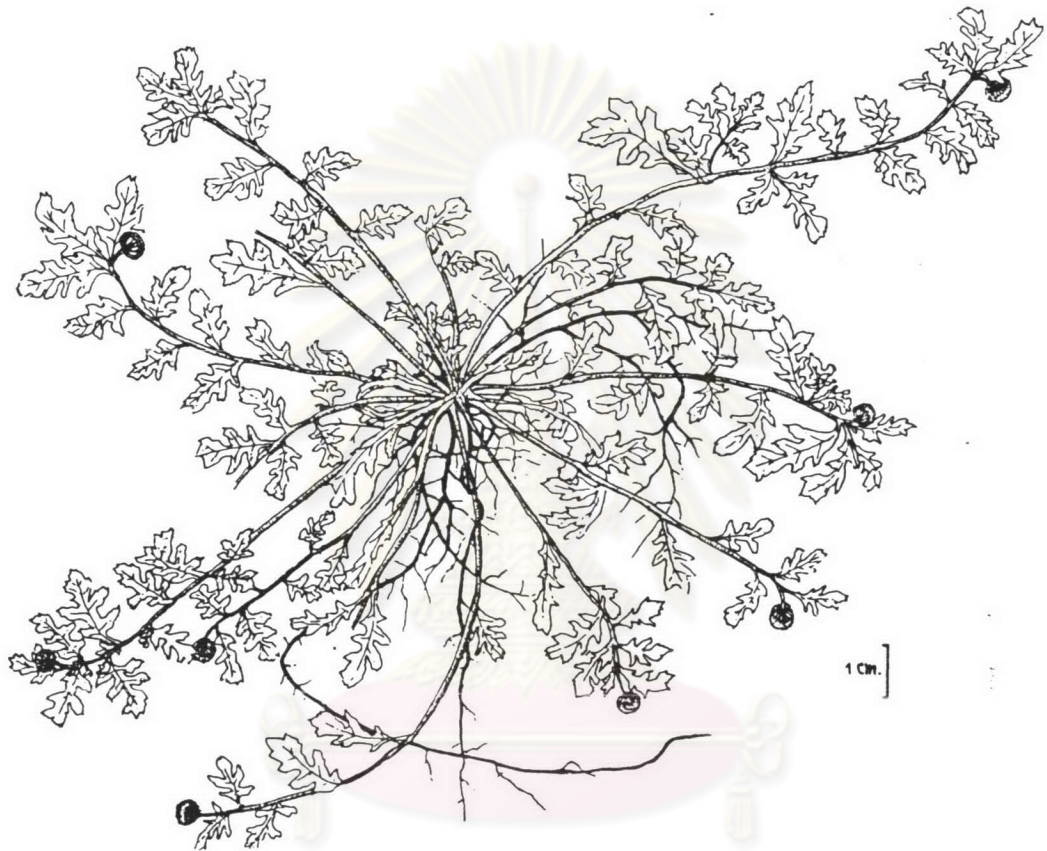
In Thailand, all parts of *G. maderaspatana* Poir. have been used in folk-loric medicine as bitter tonic, carminative, antifatulence and antidiarrhoea (37).

*Grangea maderaspatana* Poir. is only one species which is found on moist ground and paddy field in Thailand. Previously there have been three reports on phytochemical study of this plant, they found the presence of furanoditerpene, acetylene and steroid but no report on sesquiterpene lactones (38, 39, 40). On phytochemical and biological screening, it was found that the crude extract from the whole part of this plant exhibits positive results with the mixture of 2 % resorcin in methanol and 2 % sulphuric acid (1:1) on TLC and the KB cytotoxicity assay. Hence, it is indicated the presence of cytotoxic sesquiterpene lactone.

Accordingly, this present investigation deals with the extraction, isolation and elucidation of sesquiterpene lactones in the whole parts of this plant, in order to contribute our knowledge of the constituents containing in this species and to search for compounds which might exert biological activities.

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Figure 2 *Grangea maderaspatana* (Linn.) Poir. (35)

Chemical Constituents of *Grangea* sp.

Only one species, *Grangea maderaspatana* Poir., was studied on phytochemical studied and found to contain three groups of chemical constituents, furanoditerpene, acetylene and steroid.

A list of compounds found in *G. maderaspatana* Poir is shown in table 2 (page 18)

Table 2 Chemical constituents found in *Grangea* sp.

Botanical Origin	Plant Part	Compound	Reference
<i>Grangea maderaspatana</i> Poir	all parts	(-)-Hardwiekii acid	38
		ent-2 $\beta$ -Hydroxy-15, 16-epoxy-3, 13(16), 14-cleroclatrien-18- oic acid	38
		Strictic acid	38, 40
		3-Hydroxy-8- acetoxypentadeca-1, 9, 14-trien-4,6-diyne	38
		Chondrillasterol	39
		Chondrillasterone	39