

CHAPTER I

INTRODUCTION

Family Meliaceae belongs to the order Sapindales. According to Styles and Pennington in their *A Generic monograph of the Meliaceae* (Pennington and Styles, 1975), the family can be divided into four subfamilies (see **Table 1**). Meliaceae comprises of 51 genera and about 550 species. Almost all of the species are woody plants growing in the tropics and subtropics. They are mostly trees, ranging from forest giants down to small treelets. The bark configuration does not appear to vary significantly at the subfamily, tribe, or generic levels. Smooth, scaly, and diphloic type barks are present in most of the larger genera. The leaves are almost always spirally inserted and very often clustered near the branch tips, but the arrangement is usually inconstant and varies from opposite to spiral. The indumentums are sometimes diagnostic of a genus, e.g. *Aglaia* is characterized by stellate hairs or peltate scales. The inflorescence is very variable but generally in some form of panicle or thyrse. In *Chisocheton* and *Guarea* the panicle branches are often greatly reduced in length and the main axes are elongated. The resulting thyrseoid inflorescence may be up to a meter long, as in *Chisocheton penduliflorus*. A single whorl of three or five free petals greatly exceeding the calyx in length is a unique rule for the family. The stamens are usually partially or completely united by a tube with or without lobes. The fruits are present in the forms of capsule, berry or drupe. The seeds have fleshy aril or sarcotesta, or are covered by corky outer layers (Pennington and Styles, 1975).

Table 1. Subfamilies of Meliaceae

Subfamily	Tribe	Genus
1. Melioideae	1. Turraeeae	<i>Munronia, Naregamia, Turraea, Humbertioturraea, Caloddecaryia, Nymania</i>
	2. Melieae	<i>Melia, Azadirachta</i>
	3. Vavaeeae	<i>Vavaeeae</i>
	4. Trichilieae	<i>Trichilia, Pseudobersama,</i>

Table 1. Subfamilies of Meliaceae (continued)

Subfamily	Tribe	Genus
1. Melioideae		<i>Pterorhachis</i> , <i>Walsura</i> , <i>Lepidotrichilia</i> , <i>Malleastrum</i> , <i>Ekebergia</i> , <i>Astrotrichilia</i> , <i>Owenia</i> , <i>Cipadessa</i>
	5. Aglaieae	<i>Aglaia</i> , <i>Lansium</i> , <i>Aphanamixis</i> , <i>Reinwardtiodendron</i> , <i>Sphaerosacme</i>
	6. Guareeae	<i>Heckeldora</i> , <i>Cabralea</i> , <i>Ruagea</i> , <i>Turraeanthus</i> , <i>Guarea</i> , <i>Chisocheton</i> , <i>Megaphyllaea</i> , <i>Synoum</i> , <i>Anthocarapa</i> , <i>Pseudocarapa</i> , <i>Dysoxylum</i>
	7. Sandoriceae	<i>Sandoricum</i>
2. Quivisianthoideae	Quivisianthoideae	<i>Quivisianthe</i>
3. Capuronianthoideae	Capuronianthoideae	<i>Capuronianthus</i>
4. Swietenioideae	1. Cedreleae	<i>Cedrela</i> , <i>Toona</i>
	2. Swietenieae	<i>Khaya</i> , <i>Neobeguea</i> , <i>Soymida</i> , <i>Entandrophragma</i> , <i>Chukrasia</i> , <i>Pseudocedrela</i> , <i>Schmardaea</i> , <i>Swietenia</i> , <i>Lovoa</i>
	3. Xylocarpeae	<i>Carapa</i> , <i>Xylocarpus</i>

The genus *Chisocheton* belongs to the subfamily Melioideae. There are 51 species belonging to this genus, which can be arranged in four sections based on their fruit, flower and indumentums (Mabberley, 1979).

According to Smittinand (2001) *Chisocheton* species found in Thailand are :

Chisocheton ceramicus (Miq.) C.DC. หน้ทจ

C. cumingianus (C.D.C.) Harms subsp. *balansae* (C.DC.) Mabb. หน้ททท syn.

C. siamensis Craib

C. macrophyllus King subsp. *fulvescens* Mabb. ททสี่อ (Ta suea)

C. patens Blume ส้จเครีชด

C. penduliflorus Planch. ex Hiern หน้ทข้ซ้จ

C. pentandrus (Blanco) Merr. subsp. *paucijugus* (Miq.) Mabb. ๕๗๓๓

C. tomentosus (Roxb.) Mabb. ๓๕๓๓ syn. *C. rubiginosus* King

Both *C. penduliflorus* and *C. tomentosus* belong to the same section, section Clemensia.

***Chisocheton penduliflorus* Planch. ex Hiern** (พญาไม้ช้าง) is a pachycaul treelet or tree with blackish bark up to 10 m height and 10 cm diameter found growing in the rain forest of Malaysia and the south of Thailand. Leafy twigs are 6-7m in diameter. Leaves are imparipinnate, with up to 8 pairs of leaflets and petiole is up to 22 cm long. Inflorescence grows up to 7 m long, supra-axillary, pendulous, unbranched, or with branches up to 7cm long, usually with flowers congested in subsessile cymes at distal end like a bell-rope. Infructescence contains 10-15 recurved dehiscent fruits, silky pubescent with hairs, rostrate when young, recurved, up to 5 cm long, splitting into 3 valves. Each fruit has 3 seeds, arillate, with black testa, covered on inner surface by red-orange aril (Mabberley, 1979).

Genus *Aglaia* also belongs to the subfamily Melioideae of family Meliaceae, the largest genus of the subtropical and tropical angiosperm. *Aglaia* consists of about 130 species, which are distributed mainly in the Indo-Malayan region, southern China, and the Pacific Islands (Prokch *et al.*, 2001). The genus can be classified into 2 sections, *Amoora* and *Aglaia*, according to fruit dehiscence (Pannell, 1992). Section *Amoora* is fruit dehiscence.

For example, two species, *Aglaia lawii* and *A. teysmanniana*, have intermediate flower characteristic, but were placed in section *Amoora* because of their dehiscent fruits (Muellner *et al.*, 2005). Within each section, the species can be differentiated mainly on the structure, density and distribution of the indumentum.

All *Aglaia* species are woody, ranging from treelets of a few meters height to large trees up to 40 m height. An axillary bud grows to form a new apical meristem if the shoot apex is damaged. There is almost always some sticky white exudate, known as latex, which flows out from the cut trunk of *Aglaia*. The indumentums of peltate scales or stellate hairs are a characteristic of genus *Aglaia*. The inflorescence is a panicle which varies greatly. In the dehiscent fruit, there is a tough, bright orange, red,

yellow or white outer skin and the flesh beneath are either solid or milky with a high percentage of lipid (Pannell, 1992).

Aglaiia species found in Thailand are as follows (Pannell, 1992; Smittinand, 2001):

A. aspera Teijsm. & Binn.

A. argentea Blume ส้มเขียวคล่อง

A. chittagonga Miq. ประตงศ์

A. crassinervia Kurz ex Hiern

A. cucullata (Roxb.) Pellegr. แสมแดง

A. edulis (Roxb.) Wall. ค้างคาว *syn. A. pirifera* Hance

A. elaeagnoidea (A. Juss.) Benth. กระตูดเขียว *syn. A. hoanensis* Pierre,

A. roxburghiana (Wight & Arn.) Miq.

A. elliptica Blume

A. erythrosperma C.M. Pannell

A. eximia Miq.

A. exstipulata (Griff.) Theob. ส้มเขียวคล่อง

A. domestica (Correa) Pellegr. ลางสาด *syn. Lansium domesticum* Correa

A. forbesii King

A. gigantea (Pierre) Pellegr. คางคอก

A. grandis Korth. ex Miq.

A. korthalsii Miq. (Gee Ya)

A. lawii (Wight) C.J.Saldanha ex Ramamoorthy ส้มกะโหล่ง *syn.*

A. andamanica Hiern

A. leptantha Miq.

A. leucophylla King

- A. meliosmoides* Craib กระตุกลิง *syn. A. simplicifolia* (Bedd.) Harms
- A. odorata* Lour. ประยงค์
- A. odoratissima* Blume ประยงค์ป่า
- A. oligophylla* Miq. ประยงค์ใบใหญ่
- A. pachyphylla* Miq.
- A. palembanica* Miq. สังเคียดหยามผีเสื้อ
- A. perviridis* Hiern
- A. pyramidata* Hance จันทร์ระมัด *syn. A. silvestris* (M.Roem) Merr.
- A. rubiginosa* (Hiern) Pannell ชมพูเสมีด
- A. rufinervis* (Blume) Benth. สังเคียดลาช *syn. A. trichomstemon* C. DC.
- A. spectabilis* (Miq.) Jain & Bennet
- A. tenuicaulis* Hiern สังเคียดใบใหญ่
- A. teysmaniana* (Miq.) Miq.
- A. tomentosa* Teijsm. & Binn. สังเคียดสังสาต *syn. A. cordata* Hiern

cf. *Aglaia erythrosperma* C.M. Pannell is a tree up to 35 m high, with a rounded crown, growing in the evergreen forest of Thailand, Malaysia, and Indonesia. The bole is up to 23 m in height, up to 150 cm in circumference, with small L-shaped buttresses outwards up to 70 cm. The outer bark is pinkish-brown with reddish-brown and grey patches, lenticellate and with longitudinal cracks, flaking off in irregular scales up to 15 cm in diameter. Leaves imparipinnate up to 60 cm long and 40 cm wide, obovate in outline. The upper surface of the leaflets is shiny dark green. Inflorescence is up to 20 cm long; the peduncle, branches and pedicels are densely covered with stellate scales. Flowers are 4.5 mm long and 3.5 mm wide, obovoid; pedicels are 1 mm long. Infructescence is up to 25 cm long with few fruits. Fruits are up to 10 cm in diameter, bright orange-red, densely covered with reddish-brown stellate hair on the outside. This plant resembles *A. erythrosperma* C.M. Pannell and *A. spectabilis* (Miq.) Jain & Bennet, but its leaf margin is not as recurved as in *A. erythrosperma*. However, its characteristic shiny dark green leaflets hint at its being

A. erythrosperma. *A. erythrosperma* and *A. spectabilis* are sometimes difficult to distinguish and they may represent a single variable species.

The chemical constituents of several *Chisocheton* species have been investigated e.g. spermidine alkaloids (Tzouros *et al.*, 2004) and triterpenoids (Padilla *et al.*, 1933; Saikia *et al.*, 1978; Connolly *et al.*, 1979; Chatterjee *et al.*, 1989; Bordoloi *et al.*, 1993; Inada *et al.*, 1993; Gunning *et al.*, 1994; Patra *et al.*, 1998; Yadav *et al.*, 1999a, 1999b, 1999c; Bhattacharyya *et al.*, 2003, 2004; Sarmah *et al.*, 2003a, 2003b). Some compounds from *Chisocheton* species exhibited antifungal activity (Bordoloi *et al.*, 1993; Sarmah *et al.*, 2003a, 2003b), insecticidal activities (Gunning *et al.*, 1994) and inhibitory effect on Epstein – Barr virus activation (Inada *et al.*, 1993).

Aglaia species are more widely studied than *Chisocheton* and the presence of various types of compounds have been reported, flavaglines which displayed biological activities such as antifungal (Engelmeier *et al.*, 2000), anticancer (King *et al.*, 1982; Dumontet *et al.*, 1996; Cui *et al.*, 1997; Lee *et al.*, 1998; Mohamad *et al.*, 1999; Proksch *et al.*, 2001; Baumann *et al.*, 2002; Hwang, *et al.*, 2004; Hausott *et al.*, 2004; Rivero-Cruz, *et al.*, 2004; Chumkaew *et al.*, 2006; Kim, Kinghorn and Swanson, 2006; Su, *et al.*, 2006; Salim, *et al.*, 2007), insecticidal activities (Ishibashi *et al.*, 1993; Janprasert *et al.*, 1993; Nugroho *et al.*, 1997a, 1997b; Brader *et al.*, 1998; Bacher *et al.*, 1999; Chaidir *et al.*, 1999; Nugroho *et al.*, 1999; Hiort *et al.*, 1999; Schneider *et al.*, 2000; Dreyer *et al.*, 2001; Greger *et al.*, 2001; Bringmann *et al.*, 2003) and PAF antagonism (Ko *et al.*, 1992).

A preliminary bioactivity screening has revealed that the 95% ethanol extract of the leaves of *C. penduliflorus* exhibited cytotoxic activity against human small cell lung cancer (NCI-H-187) and breast cancer (BC) cell lines with IC₅₀ of 8.80 and 8.87 µg/ml, respectively, as well as antimycobacterial activity against *Mycobacterium tuberculosis* with MIC of 50 µg/ml. The 95% ethanol extract of the leaves of cf. *A. erythrosperma* exhibited cytotoxic activity against small cell lung cancer (NCI-H187), oral human epidermoid carcinoma (KB) and breast cancer (BC) cell lines with IC₅₀ of 2.35, 7.60 and 4.88 µg/ml, respectively, as well as antimycobacterial activity with MIC of 3.125 µg/ml, and antimalarial activity against *Plasmodium falciparum* (K1 strain) with IC₅₀ of 2.50 µg/ml. The 95% ethanol extract of the seeds of cf. *A. erythrosperma* exhibited cytotoxic activity against NCI-H187, KB and BC cell lines

with IC_{50} of 0.08, 0.87 and 0.38 $\mu\text{g/ml}$, respectively, as well as antimycobacterial activity (MIC 200 $\mu\text{g/ml}$) and antimalarial activity (IC_{50} of 1.50 $\mu\text{g/ml}$). Therefore, these plants were selected for further investigation of their bioactive chemical constituents. The purposes of this research are as follows:

1. Isolation and purification of compounds from selected parts of *Chisocheton penduliflorus* and cf. *Aglaia erythrosperma*.
2. Determination of the chemical structures of the isolated compounds.
3. Evaluation of biological activities of the isolated compounds.



A

Figure 1. *Chisocheton penduliflorus* Planch. ex Hiern

A) Fruits

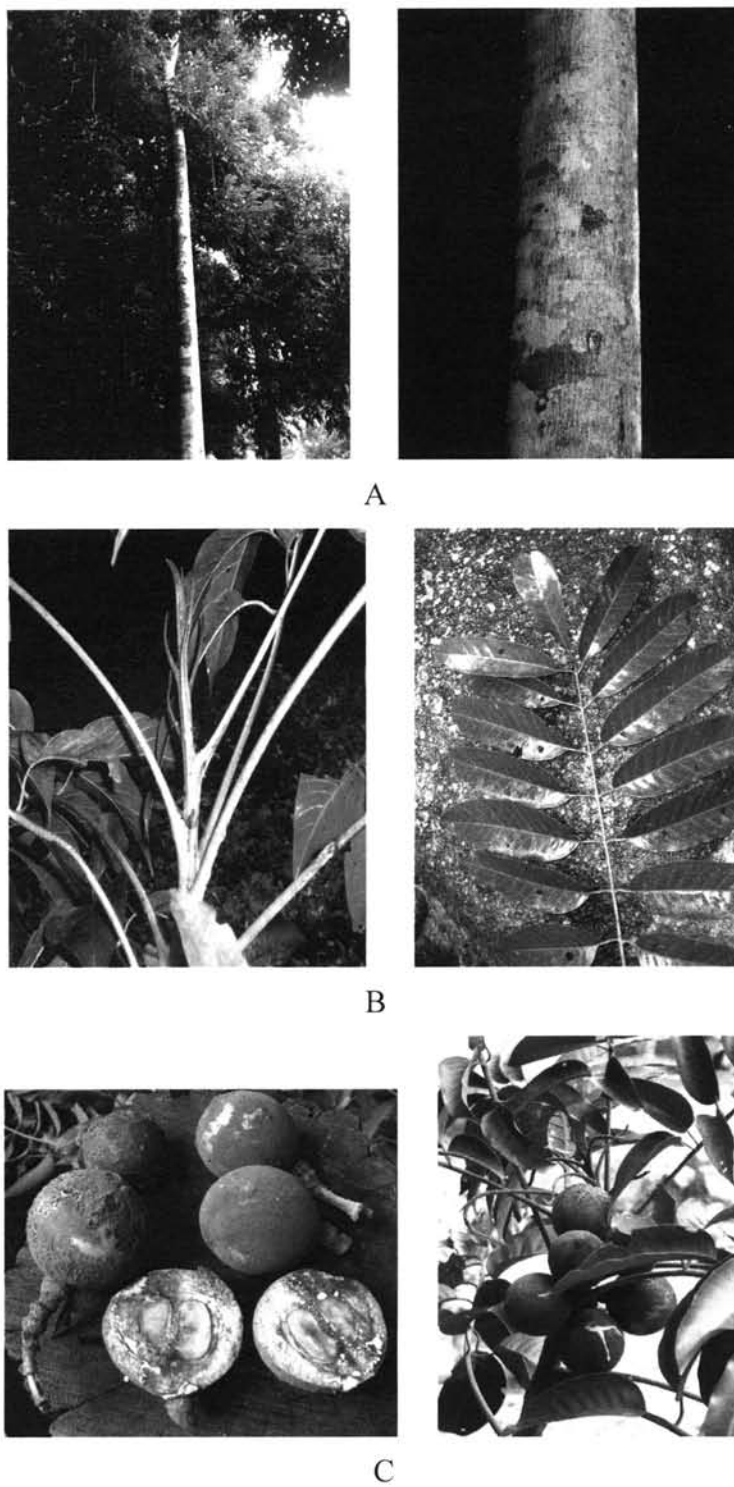


Figure 2. *cf. Aglaia erythrosperma* C.M. Pannell
A) Stem and bark, B) Leaves, C) Fruits with milky latex