

CHAPTER I

INTRODUCTION



The plants in genus *Uncaria* have easily recognisable characters, all species are woody climbers, young branchlets are square, angular or rounded and the peduncles convert into recurved hooks. The form of the stipules are entire, shallowly to deeply bifid. The flowers are pentamerous subsessile or pedicellate, the interfloral bracteole is absent or present, if present the shape is filiform to spatulate. The calyx tube is short and the lobe is deltoid to narrow triangular or filiform, elliptic or suborbicular to ovate-oblong. All these are the main characters using in the classification of *Uncaria* species.

There are two species of this genus in Tropical America, three species in Africa and Madagascar, and 29 species in Asia, Malesia, Australia and Macronesia to New Hebrides (Ridsdale, 1978).

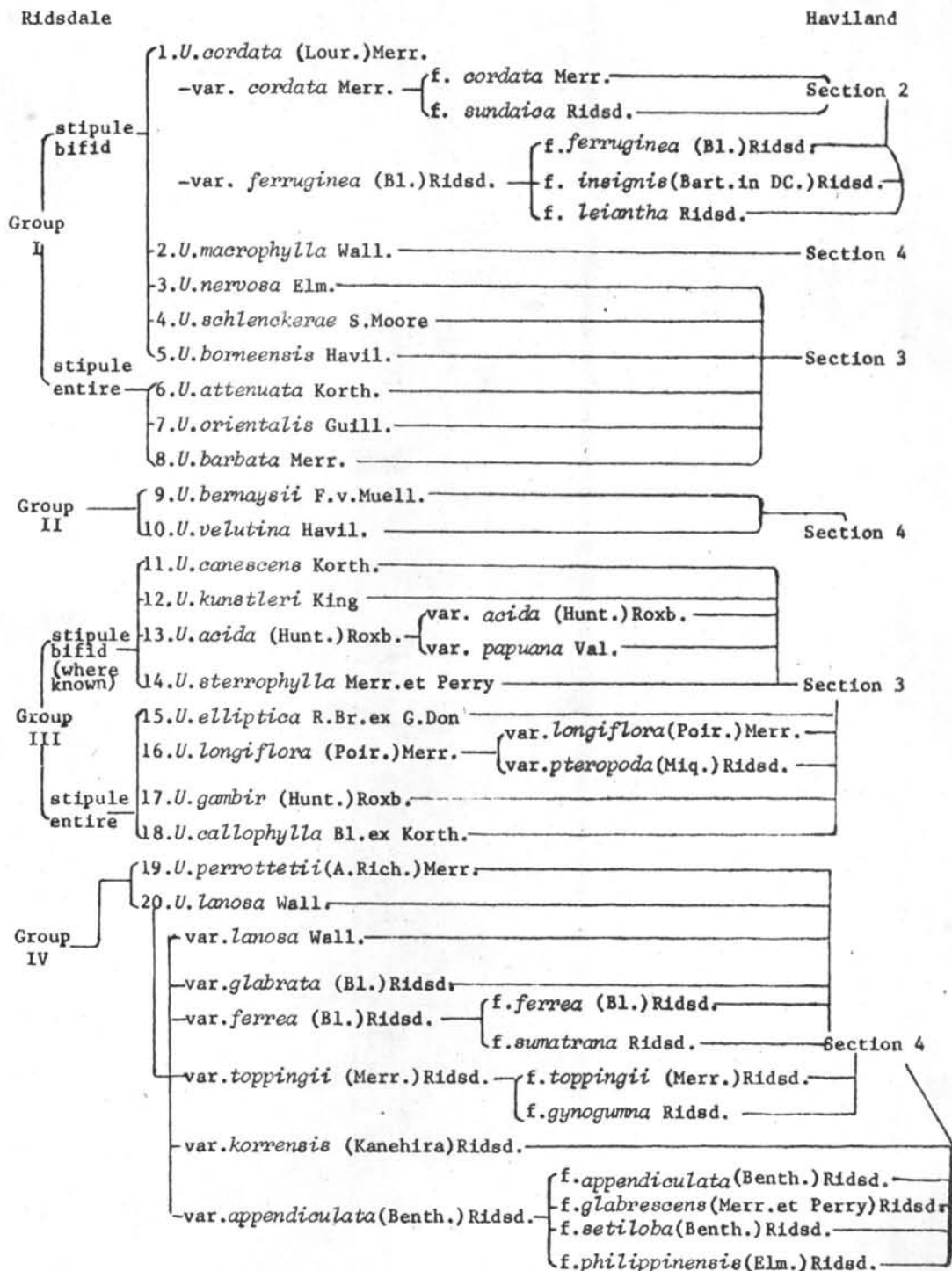
The description of *Uncaria macrophylla* Wall. follows those of the genus. The leaf is ovate to broadly elliptic (9-)12-15(-17)cm. x (5-)6-9(-12)cm., above glabrous, below sparsely to densely hairy. The stipule is ovate and bifid for $\frac{1}{2} - \frac{2}{3}$ of its length. The diameter of flowering head across the calyx is 15-20 mm. and across corolla about 50 mm. The interfloral bracteole is absent and the pedicel is 2-5 mm. long. The calyx shape is infundibular and the lobe is linear oblong. (Ridsdale, 1978).

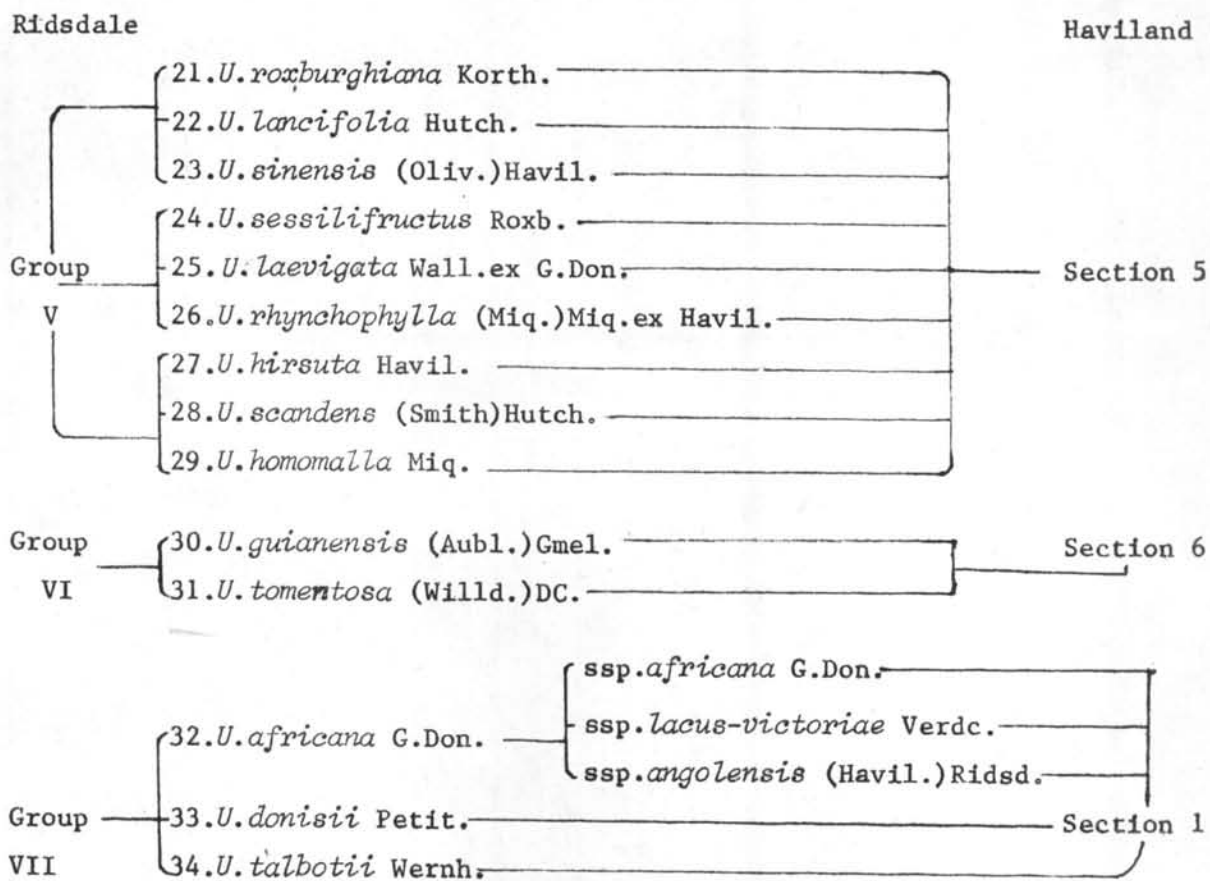
This species is distributed in India (Sikkim, Assam, Khasia, Manipur), Bhutan, Bangladesh, Burma (Upper and Lower), Thailand

(Northern:Chiang Mai), China (Yunnan, Kwangsi, Kwangtung, Hainan), Laos, North and South Vietnam (Ridsdale,1978).

The first species of *Uncaria* was described by Aublet in 1775 as *Ourouparia guianensis*. Schreber, in 1789, named this species *Uncaria guianensis* and the generic name *Uncaria* is now conserved over *Ourouparia*. Early botanists placed most of the Rubiaceae with globose flowering heads in the genus *Nauclea*. Later they were separated into genera of the tribe Naucleae of the sub-family Cinchonoideae. It has been noted that *Mitragyna* and *Uncaria* contain high yields of alkaloids and thus differ from other members of this tribe. Bremekamp has then proposed that these two genera are to be included in the sub-tribe Mitragynineae of the tribe Cinchoneae, sub-family Cinchonoideae, family Rubiaceae where it is now recognised.

The genus *Uncaria* has 120 specific names in the Index Kewensis which are now reduced to 34 species in Ridsdale's recent revision. Haviland, in 1897, divided the species of this genus into 6 informal sections, indicated in Figure 1 (pp. 3&4). Recently, Ridsdale has reinvestigated the species and divided into 7 groups which correspond well to the sections recognised by Haviland, with the exception of group II which now contains *U. bermaysii* and *U. velutina* from section 4 (see Figure 1). Otherwise the main difference is the species with entire stipules in group I had been placed in section 3 together with species of the revised revised group III (Ridsdale, 1978).





interfloral bracteoles : - absent in Groups I, II, III.
 - either absent or present in Group IV.
 - present in Groups V, VI, VII.

Figure I. Relationships within *Uncaria* arranged as a dendrogram.

In Thailand, most of *Uncaria* species are concentrated in the southern part. There were 25 specific names or 12 species according to Ridsdale's recent revision. An alphabetical list of *Uncaria* growing in Thailand as recognised by Ridsdale is presented as follows :-

(Craib, 1932; Ridsdale, 1978; Smitinand, 1980)

1. *Uncaria acida* (Hunt.) Roxb. var. *acida*

2. *U. attenuata* Korth.

Locality : Surat Thani, Chumpawn, Pattani

(*U. salaccensis* Bakh.f. nom provis)

Locality : Nakornrachasima

Local name : Khrua-See-Liam, "เครือสีเหลี่ยม"

3. *U. borneensis* Havil.

Locality : Peninsula

4. *U. canescens* Korth.

Locality : Peninsula, Phuket, Surat Thani

5.a) *U. cordata* (Lour.) Merr. var. *cordata* f. *cordata*

Locality : Peninsula, Surat Thani

(*U. pedicellata* King et Gamble)

Locality : Surat Thani, Pattani

Local name : Ai-Hom, "อ้ายโหม" (Surat Thani)

Leb-Rok, "เล็บรอก" (Pattani)

Kai-Kaa-Mae "ไก้กาแม" (malay-Narathiwat)

(*U. sclerophylla* King et Gamble)

Locality : Chantaburi, Surat Thani, Phuket, Ranong, Pattani,
Narathiwat

Local name : Ka-Phum, "กาพุ่ม" (Ranong)

Tao-Yan-Nam-Tao, "เกาย่านน้ำเต้า"(Surat Thani)

5.b) *Uncaria cordata* (Lour.) Merr. var. *ferruginea* (Bl.) Ridsd.

f. *ferruginea* (Bl.) Ridsd.

(*U. glaucescens* Craib)

Locality : Phuket, Ranong

Local name : Yan-Chieo-Chu, "ย่านเจียวจู้"

5.c) *U. cordata* (Lour.) Merr. var. *ferruginea* (Bl.) Ridsd. f.

leiantha Ridsd.

Locality : Southern; Chantaburi,

Peninsula; Surat Thani, Phuket, Nakorn Sritham-

marat, Pattani.

6. *U. elliptica* R.Br. ex G. Don.

Locality : Northern Peninsula

7. *U. homomalla* Miq.

Locality : Northern; Nan, Lampang.

Southeastern; Chantaburi, Prachinburi.

Southern; Rachaburi

Peninsula; Pattani

Local name : Ngop, "โงบ"; E-ngop, "อีโงบ" (Prachuap); Khao-Khwai-

-Mae-Lup, "เขาควายแมทลูป" (Lampang); Khao-Khwai-Mai-

-Wong, "เขาควายไม้อ่อง"

(*U. parvifolia* Ridl.)

Locality : Yala

(*U. quadrangularis* Geddes)

Locality : Southern

8. *Uncaria laevigata* Wall. ex G. Don.

Locality : Chiang Mai, Chantaburi

9. *U. lanosa* Wall.

Locality : Surat Thani, Phuket

U. lanosa Wall. var. *ferrea* f. *ferrea* (Bl.) Ridsd.

(*U. ferrea* DC.)

Locality : Ranong, Nakorn Srithammarat, Patalung-Trang Ridge

Local name : Ngop, "โง"; Nam-Chao-Chu, "ทามเจ้าชู้"

10. *U. longiflora* (Poir.) Merr. var. *longiflora*

Locality : Peninsula; Surat Thani, Pattani

(*U. longiflora* Merr.)

Locality : Chiang Mai

Local name : Kieo-Cho, "เกี้ยวชื้อ"

(*U. pteropoda* Miq.)

(*U. trinervis* Havil. var. *pteropoda*)

Locality : Surat Thani

11. *U. macrophylla* Wall.

Locality : Northern; Chiang Mai

Local name : Khao-Khwai-Mae-Lup, "เขากวายนแม่หลุบ"

12. *U. scandens* (Smith) Hutch.

Locality : Mae Hong Sorn, Udorn Thani

(*U. pilosa* Roxb.)

Locality : Udorn Thani, Nawng Kai

Several species of *Uncaria* were reported to be used as medicinal plants in many countries in Asia, the plants are listed below according to their uses (Burkill, 1870; Uphof, 1968; Phillipson *et al.*, 1978).

1. The astringent action.

1.1 local action.

- a) apply for skin disease, skin ulcer and burns.

Uncaria acida var. *acida* (Burkill, 1870)

U. gambir (Hunt.) Roxb. (Burkill, 1870)

U. sclerophylla (Hunt.) Roxb. (Phillipson *et al.*, 1978)

- b) gargle for sore throat and mouth ulcer.

U. gambir (Hunt.) Roxb. (Burkill, 1870)

- c) antibleeding and healing wound.

U. ferrea (Bl.) DC. (Burkill, 1870; Phillipson *et al.*, 1978)

U. gambir (Hunt.) Roxb. (Burkill, 1870)

U. guianensis (Aubl.) Gmel. (Phillipson *et al.*, 1978)

1.2 systemic action

antidiarrhea, antidysentery and anticholera.

U. gambir (Hunt.) Roxb. (Burkill, 1870)

U. guianensis (Aubl.) Gmel. (Phillipson *et al.*, 1978)

Gambier, which is the aqueous extracts from the partially fermented leaves and stems of *Uncaria gambir* (Hunt.) Roxb., was very well known as an astringent and tanning substance. Other species of *Uncaria* can also be the substituent sources of gambier such as :

Uncaria acida var. *acida*

U. bernaysii F.v. Muell.

U. callophylla Korth.

U. elliptica R. Br. ex G. Don.

Uncaria lanosa Wall.

U. ovalifolia Roxb.

2. Action on nervous system.

2.1 relief of nervous disease, convulsion

U. rhynchophylla Miq.

U. sinensis (Oliv.)Havil.

(Phillipson *et al.*, 1978)

2.2 relief of pain

U. acida var. *acida* (Burkill, 1870)

U. africana ssp. *africana* (stomach pain) (Phillipson
et al., 1978)

U. longiflora (Poir.)Merr. (Burkill, 1870)

2.3 sedative effect

U. rhynchophylla Miq.

U. sinensis (Oliv.)Havil.

(Phillipson *et al.*, 1978)

3. Treatment of fever and intermittent fever.

3.1 infantile fever and children's disease.

U. rhynchophylla Miq.

U. sinensis (Oliv.)Havil.

(Burkill, 1870; Phillipson *et al.*, 1978)

3.2 intermittent fever

U. gambir (Hunt.)Roxb. (Phillipson *et al.*, 1978)

4. Antiinflammation, Antirheumatism

4.1 antiinflammation

U. gambir (Hunt.)Roxb. (for stomatitis) (Phillipson
et al.,1978)

U. lanosa var. *ferrea* f. *ferrea* (for intestinal inflammation)
(Burkill,1870; Phillipson *et al.*,1978)

4.2 antirheumatism

U. longiflora (Poir.)Merr. (Burkill,1870)

5. Antihypertension

Gambier (Hsu *et al.*,1978)

U. rhynchophylla Miq. (crude alkaloids) (Chang *et al.*,1978)

6. Other action

6.1 relief of asthma

U. gambir (Hunt.)Roxb. (Phillipson *et al.*,1978)

6.2 slight antitumour activity

U. perrottetii (A.Rich)Merr. (Phillipson *et al.*,1978)

6.3 treatment of syphilis

U. africana ssp. *africana* (Phillipson *et al.*,1978)

U. gambir (Hunt.)Roxb. (for syphilitic sore) (Phillipson
et al.,1978)

6.4 antispasmodic action

U. rhynchophylla Miq. (Phillipson *et al.*,1978)

Pharmacological studies were made to examine the ganglion blocking effect on the rat superior cervical ganglion *in situ* by applying several indole alkaloids intraarterially. They showed only a ganglion blocking effect. Effect of uncarines C, E, F and isorhynchophylline was weak and short-acting but 2,3-*seco*-yohimbine displayed a prolong inhibitory effect. The effect of 1 mg hirsutine lasted longer than that of 500 µg hexamethonium (Harada *et al.*, 1974).

It is known that ganglion blocking agents, in large doses, exert a curare-like action on the neuromuscular junction. Hirsutine depressed elicited contractions both by direct stimulation of the muscle and of the sciatic nerve. Its depressive effect of about 50% lasted longer than one hour. Isorhynchophylline showed little effect which corresponds to its very weak ganglion blocking effect (Harada and Ozaki, 1976).

The effects of indole alkaloids on parasympathetic ganglionic transmission were studied on a guinea pig urinary bladder preparation *in situ*. Hirsutine most potently inhibited the contraction of urinary bladder induced by electrical stimulation of the pelvic nerves and intraarterial dimethylphenylpiperazinium, with no antagonising action to the acetylcholine-induced contraction. This alkaloid also showed a local anaesthetic action in frog sciatic nerve preparation. Hirsutine and isorhynchophylline elevated the tone of the spontaneous movement of the organ and augmented its amplitude. The stimulating action of hirsutine was not affected by pretreatment with tetrodotoxin, atropine, diphenhydramine or hexamethonium (Harada *et al.*, 1978).

Mitraphylline is a hypotensive and also exerts depressant effect on smooth muscle. Rhynchophylline exhibits a significant antipyretic and

hypotensive property (Saxton, 1965a; Chang *et al.*, 1978). This alkaloid has also been reported to paralyse parasympathetic nerve ending (Henry, 1949).

Since many *Uncaria* species were shown to be used as astringent and hypotensive agent, in fever and in the treatment of nervous disease, it is interesting to isolate more *Uncaria* alkaloids for further pharmacological studies. The present work is then undertaken to isolate alkaloids from the leaves of *Uncaria macrophylla* Wall.