

CHAPTER II

LITERATURE REVIEWS

Anthoxephalus chinensis Achille Richard is a tree in Subfamily Cinchonoideae, Family Rubiaceae (Burkill, 1870). Its synonyms are *A. cadamba* Miq.; *A. indicus* A. Rich.; *A. morindaefolius* Korth.; *Nauclea cadamba* Romb.; *Sarcoxephalus cadamba* Kurz. (Petelot, 1953. cited by Nijsiri Ruangrungsi, 1978).

This plant is known in Thai as "Kra-thum" (กระท่อม) "Ka-thum" (กะท่อม) and also known in various local names in Thailand as Ka-thum-bok "กะท่อมบก" (Bangkok), Ta-ku "ตะกู่" (Sukhothai), Tum-luang "ตุ่มหลวง", Tum-niang "ตุ่มเหนียง", Tum-kan-yao "ตุ่มก้านยาว", Tum-kan-suang "ตุ่มก้านซ่าง" (North), Ka-thum-phrai "กะท่อมพราย" (Khonkaen), Ko-som "โกส้อม" (Chaiyaphum), Khae-saeng "แคแสง", Ta-ko-som "ตะโกส้อม" (Cholburi), Ta-ko-yai "ตะโกใหญ่" (Trat), Ka-thum-khi-mu "กะท่อมชี่หมู" (Southern) (Royal Forest Department, 1948 cited by Nijsiri Ruangrungsi, 1978). Furthermore, this plant is also known as "Wind cinchona" in English and "Kadamb" in Hindi (Prasad and Bhattacharya, 1960. cited by Nijsiri Ruangrungsi, 1978).

It is a large deciduous tree of rapid growth, erect stem about 9 meters high and girds up to 1.5-2.1 meters. The trees are common in moist deciduous forests, grow rapidly in the first 6-8 years and attain their maximum size in about 20 years. At the age of at least five years, the tree sets flowers and fruits. The flowers are small, white or yellowish. An edible compound fruit is formed about the time of the periodic leaf-fall. The

young leaves have a slightly aromatic odor and an unpleasant taste, whereas, the older are without odour, and have a sour taste (Burkill, 1870). In figure 1. shows *A. chinensis* leaves.

In India, the bark of the tree is wildy used as a febrifuge and tonic, and in uterine complaints, blood disease, leprosy and dysentery. A decoction of the leaves serves as a gargle in case of aphthae and stomatitis. The compound fruit is used as astringent in case of diarrhoea (Burkill, 1870).

In 1978, Nijsiri Ruangrunsi could isolated and purified an indole glycosidic alkaloid from the leaves of *A. chinensis* by means of alumina column chromatography. From the physical, chemical properties and spectroscopic evidence have shown that it is 3α -dihydrocadambine. (Figure 2.)

Endo et al. (1983) shown that this agent extracted from the Oriental crude drug "chōtōkō", *Uncaria hookeri*, elicited a strong and long-lasting hypotension after injection into rats. In addition, Pongpan Aroonsang (1984) investigated pharmacological action of this alkaloid (ALK) in anaesthetized rats and isolated right and left rats atrial strips and reported that an intravenous infusion of ALK 0.4, 0.8, 1.6 and 3.2 mg/kg B.W. caused hypotensive effect in both systolic and diastolic blood pressure with accompanied by bi-phasic initial reduction followed by a small increased in heart rate (HR). Furthermore, it produced dose-dependent reduction in isolated rat atrial rate but slightly exhibited depression effect on left atrial isometric tension. However, the detail mechanism of this ALK on cardiovascular system was not yet clear.



Figure 1. *Anthocephalus chinensis* leaves.

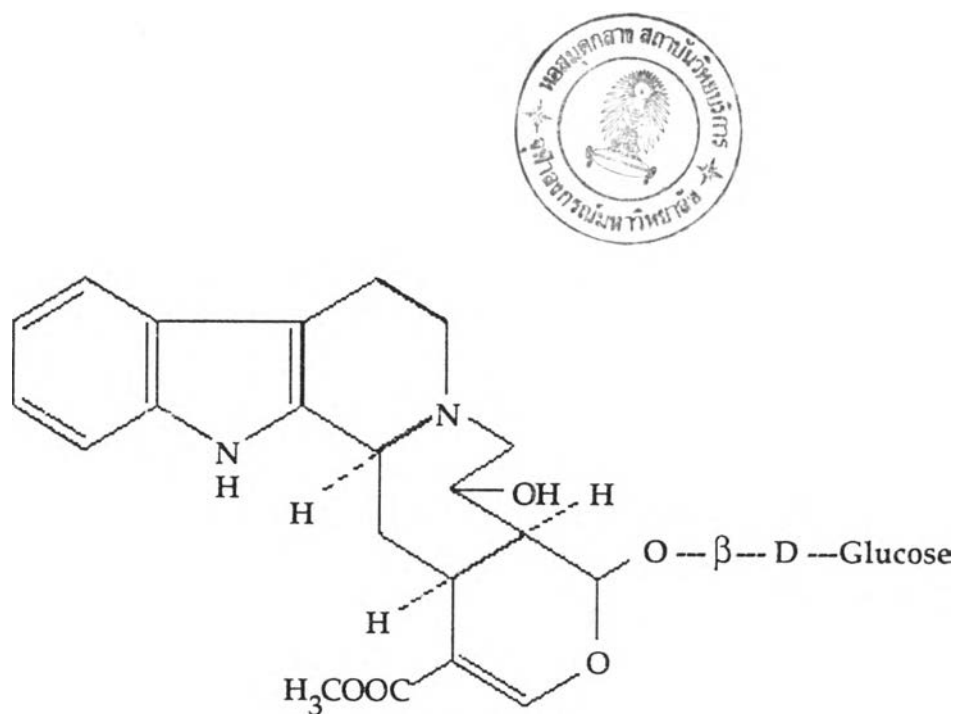


Figure 2. The structure of 3 α -dihydrocadambine (C₂₇ H₃₄ N₂ O₁₀)

Tupaia glis Diard (common tree shrew) is an animal in Order Insectivora , Suborder Menotyphla, Family Tupaiidae, Subfamily Tupaiinae. It's synonyms are *Sorex glis* Diard; *Cladobates belangeri* Wagner. Thailand has at least two species: *T. glis* found throughout the country, is much larger than *T. minor*, confined to the south.

Tree shrews are nervous and aggressive animals. They actually spend much of their time on the ground, foraging on the forest floor and eating anything they come across, including ants, termites, beetles, fruit, spiders, seeds, buds and even lizards and small rodents. There is no indication of a breeding season, pregnant females having been found in all seasons. Nests are built in holes in fallen trees, hollow bamboos, or similar sites; 1-3 (usually 2) young are born after a gestation period of 43-46 days. Their longevity is 2-3 years.

Historically, there has been wide difference of opinion as to which families belong in the order. Although, some authors have considered the tree shrews to be the primitive primates, the consensus now is to include them in a Suborder Menotyphla in the Order Insectivora. Some characteristics of tree shrews which have some bearing on this controversy :

- Hand and feet: There are 5 fully-formed digits on each hand and foot; thumb are capable of a wider range of movement. This may be considered the initial stage of the development of the grasping hand characteristic of the primates; in addition, like the primates, tree shrews generally use their hands in feeding ,and some species can grasp an insect one-handed.

- Vision: Although not as fully stereoscopic as in the primate, the tree shrew visual apparatus is differentiated to a high degree, and the retina includes an area without blood vessels in the central region (macula) as in lemurs. The orbits are completely encircled by bone, a condition not found in Lipotyphla (other Suborder in Order Insectivora) but found in all primates, this also seems to reflect an adaptation for arboreal living.

- Cranium: The cranium is rounder and more primate-like than in any Lipotyphla. However, from pyramidal tract in various prosimians concluded that tree shrews are unrelated to primates. Further, the morphology of the inner ear differs significantly from that of primates.

- Dentition: Unlike the rodents, which are specialized for gnawing, tree shrews have a complete set of teeth.

- Anatomy: Almost every detail its placenta represents a condition nearly ideally intermediate between generalized insectivores and the more generalized of the primates.

- Behavior: Tree shrews have changed from a totally insectivorous diet to include almost any small creature they come across as well as many fruits; they do not shovel through the forest litter with their muzzle as Lipotyphlans do.

Their more dextrous hands, better vision, and more complex brain enable them exploit quite a different niche than the Lipotyphla and this niche is moving toward a primate niche (Boonsong Lekagul and McNeely, 1988).

Even if they are not to be considered primates, tree shrews remain the most primate-like non-primates. And it seems very probable that the tree

shrews represent in their general structure a tolerably close approximation to the earliest phases in the evolution of the primates from generalized mammalian ancestors. (Clark,1965; Simon,1972 cited by Boonsong Lekagul and McNEELY,1988) In addition , from an evolutionary tree cited by Postlethwait J.H. and Hopson J.L.(1992) shows the prosimians and marmosets (as well as other New World monkeys) branched off quite early from the tree shrews that gave rise to the primates.

The fastigial nucleus (FN) of the cerebellum was interesting to those describing central autonomic pathways of the cardiovascular system because fastigiobulbar projections could elicited generalized sympathoexcitation (Del Bo, Sved and Reis, 1983; Dormer et al., 1986 ; Henry and Connor,1989). Electrical stimulation in rostral portions of FN (rFN) of the experimental animal in several species such as rat (Del Bo et al.,1983; Henry and Connor,1989), cat (Achari and Downman, 1970; Miura and Reis, 1970; Lutherer and Williams,1986), dog (Dormer et al., 1986), tree shrew (Chakkrit Luk-in , 1992) and monkey (Ratree Sudsuang et al., 1990) elevated HR and arterial pressure (AP), the so called fastigial pressor response (FPR) (Achari and Downman, 1970; Miura and Reis, 1970), correlated with increasing in respiratory rate (Lutherer and Williams , 1986; Lutherer, Williams and Everse , 1989), caused neurogenic cerebral vasodilatation (Mraovitch , Pinard and Seylaz , 1986) and increased the releasing of adrenal catecholamine (Del Bo et al.,1983), renal renin (Koyama, Ammons and Manning, 1980) and vasopressin (Del Bo, Sved and Reis , 1984). Similarly, stimulation in conscious animals also produced behavioral alteration that evoked alerting, licking, grooming, biting, eating and whining(Reis, Doba and Nathan,1973). Furthermore, bilateral lesions of FN attenuated vasopressin release in response to hemorrhage and

impaired the recovery of mean arterial pressure (MAP) after hemorrhage (Chen and Lutherer, 1985; Sved, Scott and Kole, 1985).

These cardiovascular responses were supported by anatomic evidence of connection between the FN and the areas involved in hemodynamic regulation. Afferent cardiovascular information may reach the FN from the parabrachial nucleus, the hypothalamus, the nucleus tractus solitarius and the locus coeruleus. In turn, the FN sent efferent projections to the nucleus tractus solitarius, reticular nuclei, parabrachial nucleus, as well as the septal region. However, the lesion studies disagreed as to the exact route of the fastigiobulbar pathway; some authors implicated the C1 "glycine sensitive" area, others proposed a role for the A5 "norepinephrine containing cells", and still others suggested that the medullary paramedian reticular nucleus served as the relay to spinal cord (Miura and Reis, 1970; Dormer et al., 1986; Henry and Connor, 1989).

Moreover, some studies suggested that the FPR may be due, at least in part, to stimulation of axon of passage while, the other clearly indicated the presence of neurons within rFN that responded to change in cardiovascular and respiratory function (Henry and Connor, 1989; Lutherer et al., 1989)

The above evidences confirmed that the FN, in some manner, involved in the integration of cardiovascular response. Including the previous observations about the detail mechanism of the ALK, 3α -dihydrocadambine, on the cardiovascular system was not clear. Thus, the aims of the present study was undertaken to reconfirm the effect of 3α -dihydrocadambine on blood pressure and HR in tree shrew (*Tupaia glis*). And to clarify the mechanism of action of ALK on central and peripheral

nervous system. Furthermore, to determine whether the powerful hypertensive response from stimulation of FN and hypotensive effect of ALK also be mediated from the same mechanism.