CHAPTER I

INTRODUCTION

Several kinds of plants have been reportedly used for therapeutic purposes. Variety of remidies are extracted from different parts of those medicinal plants. Various pure chemical substances had also been extracted from roots, leaves or bark of trees. As a result, there has been a wide variety of studies about their pharmacological and toxicological effects which are directed to investigation of possibilities of using of them for preventing or curring diseases.

Ancistrocladus tectorius (Lour.) Merr. the species used in this study is an example. The plant is widely distributed in several parts of Thailand such as Yala, Chon-Buri and Narathiwat. This plant is known in various local names in Thailand as Khon tee-maa (Yala) ; Khon maa khao ค้อนหมาขาว (Central) ; Khon maa-daeng (Nakhon Ratchasima) ; Khansong ค้นทรง, Thong khansong (Chon-Buri) ; Khon ma den (Suphan Buri) ; Sin-ta-ko-phlee ซิน ตะโกพลี (Lam-pang) ; Phan song (Trat) ; Yuulong ยูลง (Malaya-Nara-thiwat) ; Lin-kwaang ลิ่นกวาง, , Lin-Khwaai (Lampang) ; Haang kwaang หางกวาง (Nakhon Phanom) ; Huu kluuang (Prachin-Buri).

Ancistrocladus tectorius (Lour.) Merr. is a

woody climber grown in sandy lands in the immediate neighbourhood of the sea, found from the andamas, Burma and Indochina to Southern China and Hainan, Malay Penninsula, Anambas Island, West Dutch Borneo, Karimata and once collected in Southern Sumatra. In the youth and in open scrub it is often a shrub, later often trailing ; main shoots provided with scattered more or less erect small leaves, between and near which arise spreading non-foliate tendril-like shoots provided with 3-6 curved hooks, lower 2 rarely 3 hooks getting woody, hooks mostly unilateral, rarely 1-2 alternate these tendrils later woody, becomming branches, upper part vanishing. Leaves simple, alternate and crowded immediately above the second hook, variable in size and shape, mostly obovate-oblong, tapering towards the sessile petiole, apex obtuse, rounded, acute or even acuminate, blade 9-30 by 3-10 cm ; nerves 4-8 on either side, spreading, connected by a slightly looped intramarginal vein and a second feebler outer one, rather straight, numerous secondary veins often becomming as strong as the main nerves and parallel. The inflorescence lying between the crowded leaves, very rarely lateral in the place of a tendril on the main shoot, repeatedly dichotomous, branches divaricate, 8-15 cm. long. Flowers small, regular, crowded at their tips. Calyx 5 lobes unequal, oval, thin-margined, glabrous except the short ciliate rounded apex, some or all lobes provided with 1-3

conspicious crateriform prominent glands mostly shorter than the corolla 1.75-2.50 mm. long, soon enlarging. Petals 5, reddish color, oblique-oval, one margin often involute, acute, 3-3.5 by 1.75 mm. Styles erect, nearly as long as the nipple shaped ovay top, both 0.50 mm. high, stigma punctiform. Stamens 10, altemately unequal ; filament broadened at the base ; cells free, acute, more or less latrorse. Fruit dry, woody, indehiscent, surrounded by 5 spreading reddish, unequally enlarged calyxs. Seed large, obconical with flat-apex, mostly consisting of a ruminate endosperm. The young leaves are edible as vegetable. By the folk-lore medicine in the Easthern Thailand and Prachin-Buri, *Ancistrocladus tectorius* (Lour.) Merr. may posses antispasmodic activity.

From the extract of the stems many alkaloidal constituents were identified, namely, ancistrocladeine (Fourher et al., 1975), ancistrocladiene, hamatine and ancistrocline (Chen et al., 1981). In Malaya, alkaloids were also found in the leaves and stems of this plant. Some alkaloids which were isolated from plants and contained oxindole group were reported to have antispasmodic effect. They produced inhibition of spontaneous movement of isolated rabbit jejunum. Recently, Nijsiri Ruangrungsi and co-workers at the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University extracted ancistro-

tectorine, a new member of the naphthalene isoquinoline series of alkaloids, from *Ancistrocladus tectorius* (Lour.) Merr. Ancistrotectorine was extracted from powder of the leaves by organic solvent and purified by means of column and thin layer chromatography. Evidently, ancistrotectorine was pure. Its molecular structure is presented in Figure. 2. Considering its physio-chemical properties, it has been crystallized in acetone and the crystalls are yellow, the melting point ranges between 134-140 C. It is dissolved in chloroform, acetone, ether and ethanol. This compound has been identified as 7, 3'-linked naphthalene-isoquinoline and is the second compound in this category which has been found in nature (Ruangrungsi et al., 1985). There had been a promissing line of evidence that ancistrotectorine may posses some remarkable pharmacological actions.

Studies in experimental animals indicated that ancistrotectorine inhibited both spontaneous contraction in rabbit intestine and contraction stimutated by histamine, serotonin, barium chloride, calcium chloride and acetylcholine. Contraction of rat's vas deferens caused by serotonin, norepinephrine, calcium chloride, barium chloride and potassium chloride could also be inhibited by ancistrotectorine (Ketkosol, 1985). In addition, the spontaneous contraction and contraction induced by

oxytocin and serotonin in the uterus of rats and quinea-pig were markedly reduced by this compound. Ancistrotectorine also reduced the contraction of small intestine induced by carbachol in anesthetized rabbits, and reduced the movement of charcoal in small intestine of the experimental mice (Pasupat, 1985).

Smooth muscle contraction has been employed as pharmacological model for several years, a different type of approaches was used by many workers to investigate the mechanism of the contraction. Calcium ion is now generally considered to be the final activator of the contractile system under physiological conditions (Bolton, 1979). However, it is only recently that this idea has become widely accepted. The physiological role of calcium ion had been almost completely over looked in the biochemical approaches of the study of muscular contraction (Ruegg, J.C. 1976). In general, the activation of the contractile system of muscle is initiated by calcium ion released from a certain source(s) into the myoplasm. This contractile effect of calcium ion is exerted solely on the Ca-receptive protein, troponin, which together with tropomyosin, is located the thin filament. Although the detailed mechamism has not yet been clarified, it is certain that in the absence of calcium ion the troponin molecule inhibits the interaction of myosin and actin and that this

inhibition can be removed by calcium ion. Calcium ion may originate from extracellular medium or from some cellular storage sites (Heaslip J. and Rahwan. G. 1982). The situation in smooth muscle contraction is less clear although it was studied for a long time.

A large bulk of information suggests that the sources supplying activator calcium used for contraction may vary between different smooth muscle types and between contractions induced by different agents. Several studies have indicated that the entry of extracellular calcium for contraction in vascular smooth muscle may occur through two major pathways which have been designated as the potential dependent channel (PDC) and the receptor operated channel (ROC) (Platon, 1981). It has been suggested that activation of the PDC results from depolarization of the cell membrane, i.e., electrical stimulation or elevation of extracellular potassium, whereas, ROCs are coupled to membrane receptors (i.e., alpha-adrenoceptors) and are activated as a consequence of specific agonist-receptor interactions. The delineation of these two calcium entry mechanisms has not been demonstrated conclusively (Ebashi S. and Endo. M. 1968).

In this connection, experimental data will be accumulated systematically to point which concise pharmacological profile and therapeutic application can be justified.

On the ground of documentation of the effects of ancistrotectorine on spontaneous and induced contraction of smooth muscle, the main purpose of this study is to investigate the pharmacological effects of ancistrotectorine on smooth musele of another species, the rat also with special emphasis on vascular smooth muscle contractions. In addition, and attempt had been made to localize the possible site of action of ancistrotectorine in this system.

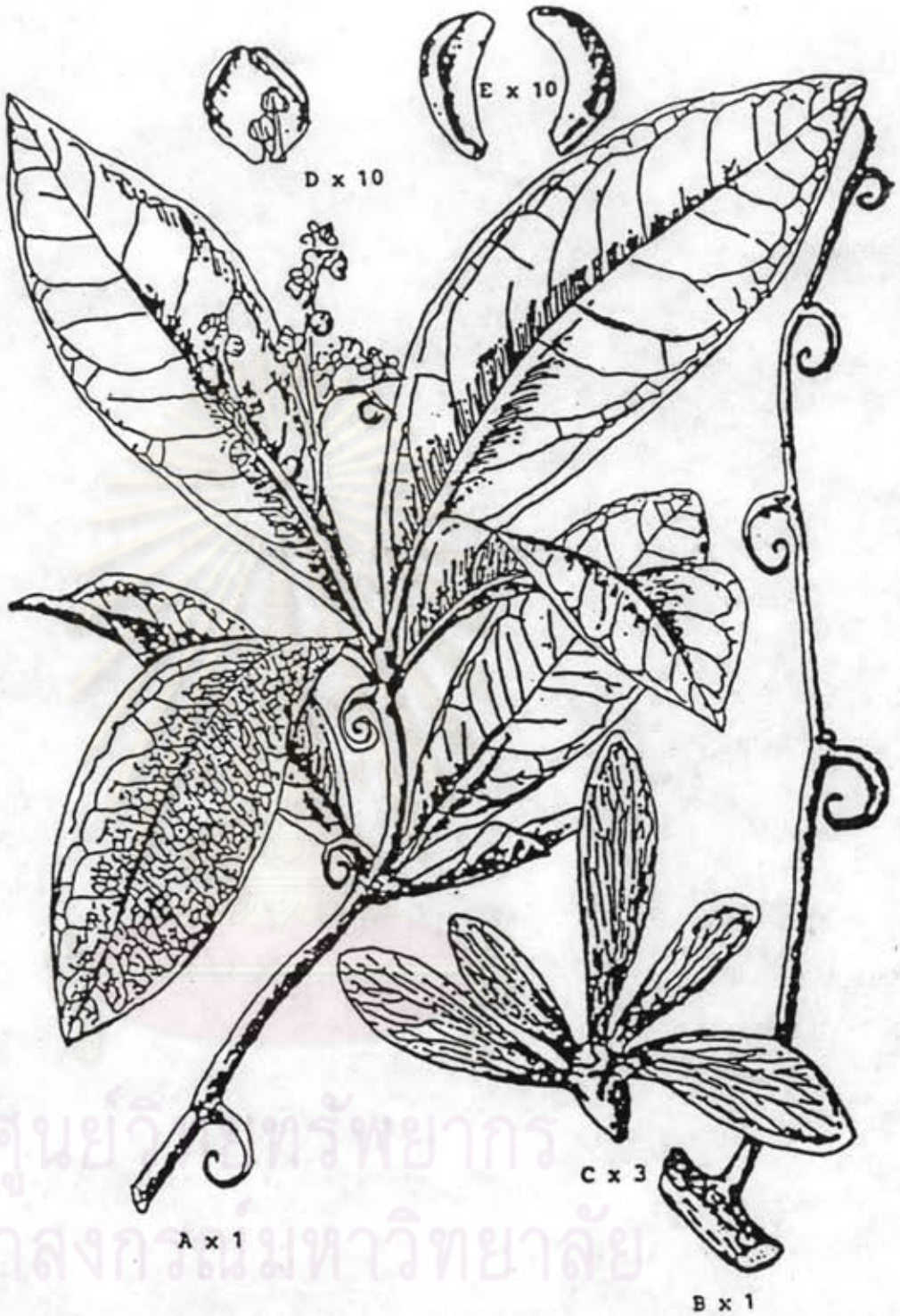
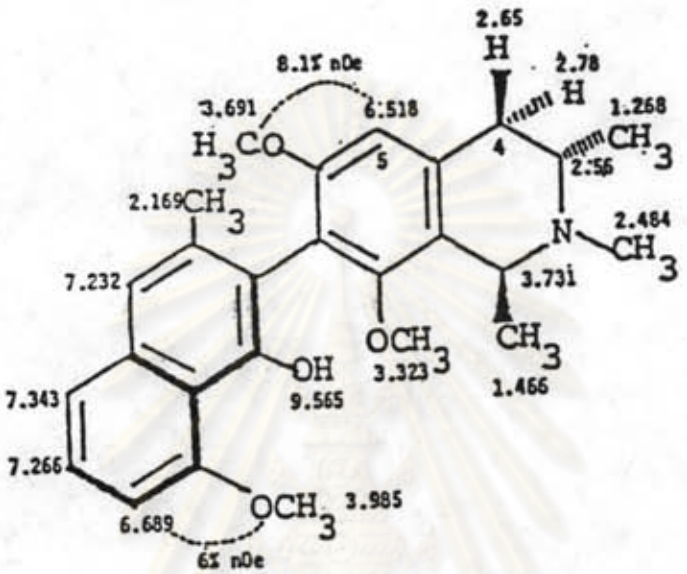


Figure . 1 *Ancistrocladus tectorius* (Lour.) Merr.

A. stem and flowering twig, B. hooked branch, C. fruit

D. petal and Stamens, E. sepals



Structure of Ancistrotectorine

(Stereochemistry omitted)

Figure. 2 The chemical structure of ancistrotectorine