

## CHAPTER I

### INTRODUCTION



The Annonaceae is a large family of aromatic trees, shrubs, or climbers which occur in tropical and subtropical regions. The leaves of these plants are alternate, entire and exstipulate. The fragrant flowers are located at terminal, leaf-opposed or at axillary. They are solitary or crowded, regular and mostly trimerous. The perianth is usually in the whorls of three. The stamens are usually numerous, hypogynous and spirally arranged. The carpels are generally numerous and free. The fruit is usually an aggregate of berries but in a few genera, specially *Annona*, the berries coalesce with an edible fleshy receptacle and are edible. The seeds have a copious, ruminant endosperm (Leboeuf *et al.*, 1982).

The Annonaceae comprises of about 130 genera and 2,300 species. In Thailand, about 41 genera and 195 species of this plant family can be found (ปิยะ เฉลิมกลิ่น, 2544). The genera and approximate number of species of the Annonaceae in Thailand are as follows.

<i>Alphonsea</i> (6)	<i>Meiogyne</i> (2)
<i>Anaxagorea</i> (2)	<i>Melodorum</i> (2)
<i>Annona</i> (4)	<i>Mezzettia</i> (1)
<i>Anomianthus</i> (1)	<i>Miliusa</i> (11)
<i>Artabotrys</i> (11)	<i>Mitrella</i> (1)
<i>Cananga</i> (3)	<i>Mitrephora</i> (6)
<i>Cleistopetalum</i> (1)	<i>Monocarpia</i> (2)
<i>Cythocalyx</i> (3)	<i>Neouvaria</i> (1)
<i>Cyathostemma</i> (6)	<i>Orophea</i> (7)
<i>Dasoclema</i> (1)	<i>Phaeanthus</i> (1)
<i>Dasymaschalon</i> (8)	<i>Platymitra</i> (1)
<i>Dendrokingstonia</i> (1)	<i>Polyalthia</i> (30)
<i>Desmos</i> (3)	<i>Popowia</i> (1)
<i>Disepalum</i> (1)	<i>Pseuduvaria</i> (6)
<i>Ellipeia</i> (1)	<i>Pyramidanthe</i> (1)
<i>Ellipeiopsis</i> (1)	<i>Sageraea</i> (2)
<i>Enicosanthum</i> (4)	<i>Stelechocarpus</i> (1)

<i>Fissistigma</i> (10)	<i>Trivalvaria</i> (1)
<i>Friesodielsia</i> (5)	<i>Uvaria</i> (18)
<i>Goniothalamus</i> (23)	<i>Xylophia</i> (5)
<i>Marsypopetalum</i> (1)	

A few examples of major annonaceous genera native to Thailand are:- *Polyalthia*, which is the genus possessing the largest number of species e.g. *P. cauliflora* (จำปาหอม), *P. longifolia* (อโศกอินเดีย) and *P. jucunda* (ยางเหลือง); *Goniothalamus*, which contains species such as *G. giganteus* (ปาดินช้าง), *G. griffithii* (สะบันงาป่า) and *G. macarnii* (ข้าวหลาม); and *Uvaria* e.g. *U. grandiflora* (กล้วยหนุสัง), *U. hamiltonii* (กล้วยพวงพอน), and *U. microcarpa* (ก้นช้าง). The plants of this family are famous for their fragrant and uniquely beautiful flowers, therefore they were used for decoration and flowers were used in aromatherapy i.e. Ilang Ilang oil from *Cananga odorata*. Many fruits of this family are edible e.g. those of *Annona squamosa* and *A. muricata*. In addition, a number of these plants are used medicinally, for examples, the leaves of *A. squamosa* and *A. reticulata* have been used as anthelmintic (นันทวัน บุญยะประกฤษร์ และ อรณข โขดชัยเจริญพร, 2541), whereas the leaves of *Cananga latifolia* can be used to cure bacterial infection of the wound (นันทวัน บุญยะประกฤษร์ และ อรณข โขดชัยเจริญพร, 2543). The root and stem of *Artabotrys harmandii* have been used as treatment for fever and skin diseases, whereas the stem of *Polyalthia stenopetala* is used as appetite stimulant (นันทวัน บุญยะประกฤษร์ และ อรณข โขดชัยเจริญพร, 2541).

*Ellipeiopsis cherrevensis* R. E. Fr. (synonym: *Ellipeiopsis ferruginea*) is one of the only two species of its genus. Its distribution is limited to Thailand and Cambodia (มูลนิธิมหาวิทยาลัยมหิดล, 2544; Kijjoa *et al.*, 2002). The genus *Ellipeiopsis* belongs to the tribe Uvarieae of subfamily Annonoidae, therefore it is very closely related to genus *Uvaria* and it is highly possible that a previously investigated species, *Uvaria ferruginea* (Schulte *et al.*, 1982; Kodpinid *et al.*, 1983; Kodpinid, Thebtaranonth and Thebtaranonth, 1985), is in fact an identical species to *Ellipeiopsis cherrevensis*.

*Ellipeiopsis cherrevensis* or “Nom-maew-paa” is a small shrub (1-1.50 m height) growing in deciduous forest in the northern, north-eastern, eastern and middle parts of Thailand. Its branches and leaves are covered with condensed brown hair. The leaves are simple, alternate, ovate, 5-9 cm by 10-14 cm with obvious convex veins at the lower surface and the groove of midrib at the upper surface. The petiole is 0.5 - 0.7 cm long. The flower is yellow, regular, 2-2.5 cm in diameter, located at

the terminal or axillary. The sepals are in two whorls, trimerous each. The fruits are aggregated with 8-12 berry fruitlets having green color turning to red when ripe.

Another annonaceous plant investigated in this study, *Stelechocarpus cauliflorus* R. E. Fr. or “Ngum-Ngo”, is an erect tree, 8-15 m in height, with branches generated from the stem parallel to the ground. The leaves are elliptic-ovate-oblong-lanceolate, 4-8 cm by 15-25 cm, coriaceous, shining with midrib raised on upper surface. The petiole is 0.5-0.9 cm in length. Its monoecious flowers are yellow to brown color, fascicled on tubercles on the trunk and older branches. The pedicels are 2-6.5 cm. The small sepals are 3, whereas the petals are in 2 whorls of 3, oval or oval-oblong and are much larger than the calyx. The brown to black fruits are aggregate, broadly rounded, 4-5 cm in diameter, with 4-6 seeds. This plant can be found growing in evergreen forest in the south of Thailand.

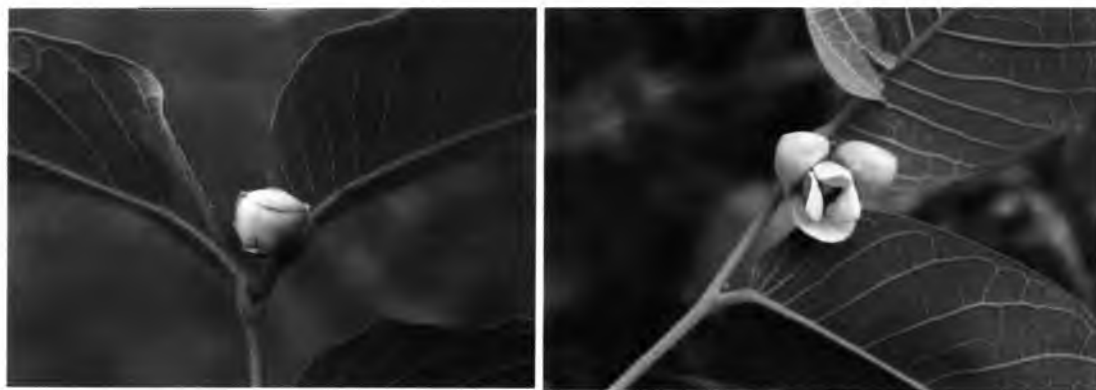
Numerous studies on the Annonaceae have reported the presence of various kinds of compounds which display biological activities such as anticancer, antimalarial and antituberculosis activities. However, there has been no previous report on *S. cauliflorus* and only one phytochemical study of *E. cherrevensis*, although there have been a number of earlier studies on the chemical constituents of *Uvaria ferruginea*.

Our preliminary bioactivity screening has revealed that the 95% ethanol extract of the aerial parts of *E. cherrevensis* exhibited cytotoxic activity against human small cell lung cancer (NCI-H187), oral human epidermoid carcinoma (KB) and breast cancer (BC) cell lines at IC<sub>50</sub> values of 0.01, 0.15 and 3.54 µg/ml, respectively, as well as antimycobacterial activity against *Mycobacterium tuberculosis* at MIC value of 100 µg/ml. The 95% ethanol extract of the leaves and stems of *S. cauliflorus* exhibited antimycobacterial activity at MIC values 50 and 200 µg/ml, respectively. It also stimulated lymphocyte proliferation with stimulation index (SI) of 1.20 and 1.32, respectively. 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 the aerial parts of *Ellipeiopsis cherrevensis* and *Stelechocarpus cauliflorus*.
2. Determination of chemical structures of the isolated compounds.
3. Evaluation of biological activities of the isolated compounds.



A



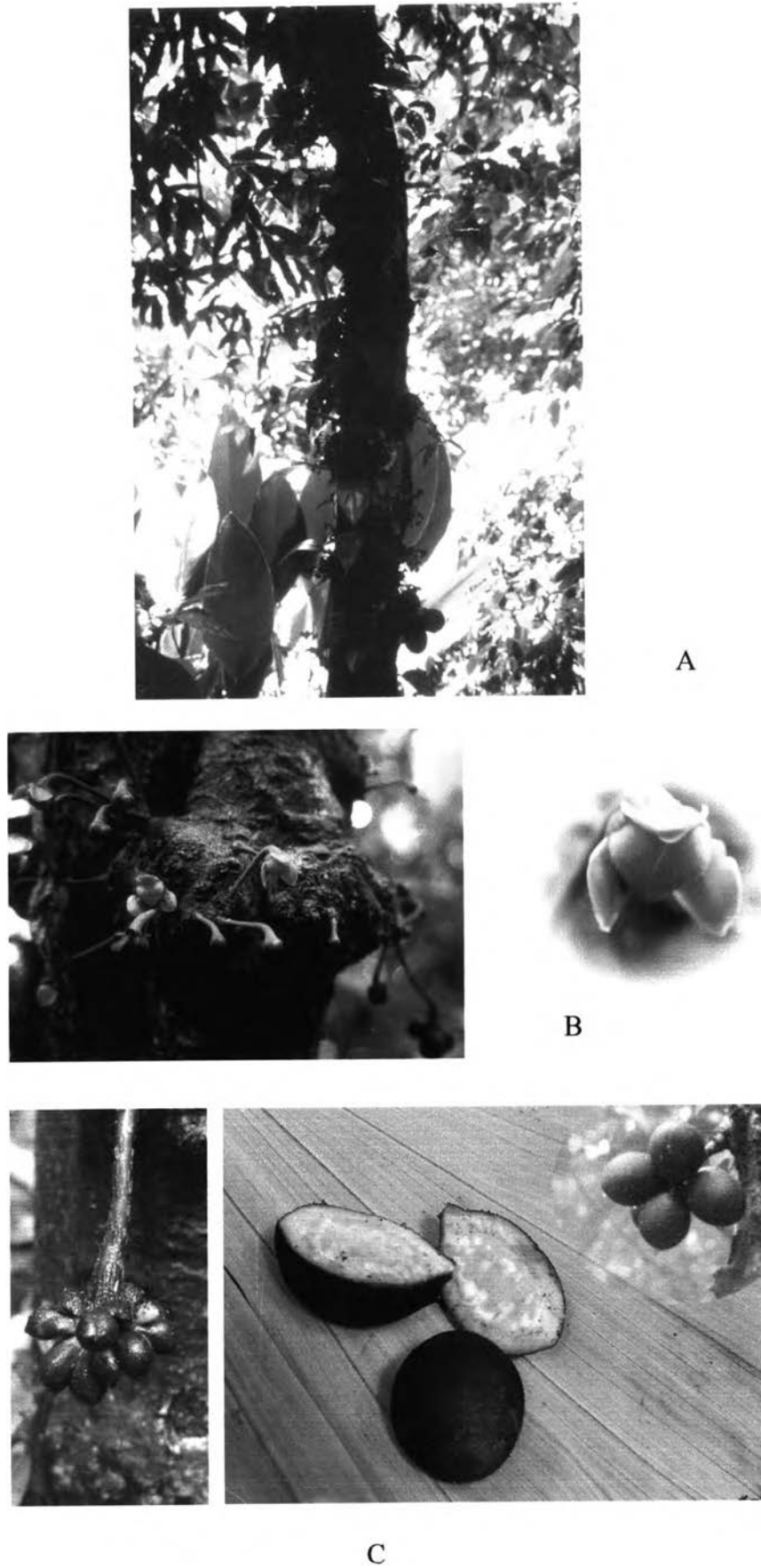
B



C

D

**Figure 1.** *Ellipeiopsis cherrevensis* R. E. Fr.  
A) Whole plant, B) Flower, C) Fruits, D) Leaves



**Figure 2.** *Stelechocarpus cauliflorus* R. E. Fr. A) Stem, B) Flowers, C) Fruits