

CHAPTER I



INTRODUCTION

Human has used plants in various ways for long time including medicinal plants. Because of their biological diversity, human can obtain numerously valuable benefits from these natural resources. Fortunately, Thailand is located in the tropical region of the world and has abundant kinds of plant, especially herbs which are used as medicinal plants. In addition, the main sources for the development of new therapeutic agents are plants and microorganism. The popularity of utilizing chemicals from plants might be due to their low side effects, reasonable cost and greater availability. Especially during the economic crisis of Thailand, using local medicinal plants can reduce the import of modern drugs from foreign countries. For example, an anti-peptic ulcer drug was developed from Plao noi (*Croton sublyratus* Kurz.) and some chemical constituents from Portai tree (*Thespesia populnea*) posses anti-tumor and antifungal properties. Both of them are Thai medicinal plants. These trends have generated the worldwide interest in herb medicines and medicinal plants.

In terms of natural product chemistry research, this thesis is focused on searching for compounds from the tropical Thai plant, *Croton oblongifolius* Roxb.

The genus *Croton* belongs to the family Euphorbiaceae [1] and has 700 species. They are distributed over all warm countries and are reported to possess important medicinal uses. *Croton oblongifolius* Roxb is a small deciduous tree and available throughout evergreen forests, deciduous forests and in the groves of brushwood in Thailand.

The various common names of *C. oblongifolius* Roxb. has been called in each part of Thailand: Plao Yai (in Central part), Plao Luang (in Northern part),

Poh (in Kamphaeng Phet province), Khwa-wuu (in Karen, Kanchanaburi province), Saa-kuu-wa (in Karen, Mae Hong Son province) and as Haa-yoeng (in Shan, Mae Hong Son province).

1.1 Botanical Characteristics of *Croton oblongifolius* Roxb.

C. oblongifolius Roxb. is a medium sized medicinal plant. The leaves fall between 5.6-12.0 cm by 13.0-24.0 cm in size. The leaf blade is oblong-lanceolate shaped. The flowers are solitary and pale yellowish-green. The female flowers are located in the lower part of the raceme, while the male flowers are located in the upper part of the raceme. The male flowers are narrowly shaped with pedicels 4.0 mm long. The male calyx are more than 6.0 mm and have segments that are ovate, obtuse and more than 2.5 mm long. The six male petals have a wooly texture and are 3.0 mm long and elliptic-lanceolate. The twelve stamens are inflexed in the bud and have filaments 3.0 mm long. The female flowers, the pedicels are short and stout. Its sepals are more acute than the sepals in the male flower and have densely ciliated margins. The fruit of the plant has a diameter of less than 1.3 cm and is slightly 3-lobed and is clothed with small orbicular scales. In addition, within each fruit there are eight seeds, each seed approximately 6.0 mm long, rounded and quite smooth on the back [2].

1.2 *C. oblongifolius* Roxb. as herbal medicines.

C. oblongifolius has been used as a medicinal plant in Thailand. The bark can be used to inhibit chronic enlargements of the liver, the leaves can cure scabies, the fruits and seeds can be used as laxatives and the flowers can be used to kill parasites. In addition, the heartwood can be used in remedying faint and the roots (when not taken in large doses, which can be poisonous and harmful) can also be used to treat dysentery or chronic rheumatism.

The previous studies of chemical constituents from *C. oblongifolius* revealed many diterpenoid compounds. For example, labda-7,12(*E*),14-triene and its derivatives were isolated from Prachupkhirikhan province [2], neocrotocembraneic acid and neocrotocembranal were obtained from Vicheinburi, Petchaboon province [3], crotohalimaneic acid, crotohalimoneic acid and benzoyl crotohalimanolic acid were obtained from Pakchong, Nakornrachsima province [3], 3-acetoxy-labda-8(17),12(*E*),14-triene-2-ol, 2-acetoxy-labda-8(17),12(*E*),14-triene-3-ol and labda-8(17),12(*E*),14-triene-2,3-diol were obtained from Wang Sa Phung, Loei province [4], (-)-hardwickiic acid, labda-7,13(*Z*)-diene-17,12-olide, labda-7,13(*Z*)-diene-17,12-olide-15-ol and (-)-20-benzoyloxyhardwickiic acid from Udon Thani province [5], (2*E*,7*E*,11*E*)-1-isopropyl-1,4-dihydroxy-4,8-dimethylcyclotetradeca-2,7,11-triene-12-carboxylic acid and methyl-15,16-epoxy-12-oxo-3,13(16),14,clerodatriene-20,19-olide-17-oate were obtained from Uttaradit province [6].

Further more, some diterpenoid compounds showed effective cytotoxic activity against 5 tumor cell lines, Hep-G2 (hepatoma), SW 620 (colon), Kato-3 (gastric), BT 474 (breast) and Chago (lung). For instance, labda-7,12(*E*),14-triene-17-al showed strong activity against Hep-G2, SW 620, Chago, Kato-3 and BT 474 [2]. Neocrotocembranal showed strong activity against SW 620 and Kato-3 [3]. Labda-8(17),12(*E*),14-triene-2,3-diol was active with Hep-G2, SW 620, Chago, Kato-3 and BT 474, 2-acetoxy-labda-8(17),12(*E*),14-triene-3-ol was active with Kato-3 and SW 620, 3-acetoxy-labda-8(17),12(*E*),14-triene-2-ol was active with Kato-3 and BT 474 [4]. Labda-7,13(*Z*)-diene-12,17-olide was active with SW 620, Chago and Kato-3, labda-7,13(*Z*)-diene-12,17-olide-15-ol was active with Hep-G2, Chago, SW 620 and Kato-3 [5].



Figure 1 *Croton oblongifolius* Roxb.

Although the study of chemical constituents from *C. oblongifolius* have been investigated for long time, new compounds are still discovered and some of them give effective bioactivity. Therefore it was decided to investigate diterpenoid compounds of the stem bark of *C. oblongifolius* Roxb from Chachoengsao province.

This research deals with the diterpenoid compounds isolated from *C. oblongifolius*, Chachoengsao province. The hexane crude extract was separated by mean of column chromatography and purified by proper methods such as recrystallization. The structure elucidation was carried out by spectroscopic techniques. Finally, cytotoxic activity against human cancer cell lines of the isolated compounds was studied.

1.3 The purposes of research

1. To investigate the chemical constituents from stem bark of *C. oblongifolius* Roxb. from Chachoengsao province.
2. To elucidate the structures of isolated compounds.
3. To examine the cytotoxic activity against human tumor cell lines of isolated compounds.