CHAPTER II

LITERATURE REVIEW

There are 700 species of trees or shrubs in genus Croton. *C. oblongifolius* is a medium-sized tree. Branches have brown scales. Leaves are a kind of simple leaf and alternated as shown in Fig 1. The general characteristi c of *C. oblongifolius* was assigned by Department of Phamaceutical Botany, Faculty of Phamacy, Mahidol University. [7]

2.1 General Characterization of the plants in the Genus Croton.

The genus of Croton is composed of 700 species of trees or shrubs. Leaves are usually alternate with 2-glandular stipule at the base. Their flowers are either single or cluster on the rhachis of a terminal raceme and bracts are small. There are 5 calyxes, 5-petals and 4-6 glands' disk opposite the sepals in Male flowers. There are many stamens inserted on a hairy receptacle and anthers are donated with pararellel cells. In female flowers, sepals are usually more oval than males, petals are smaller than sepals or sometimes missing and disk annular of 4-6 glands are opposite the sepals. In each cell, there are three ovaries with single ovule, styles are usually long and slender. Seeds are smooth, albumen copious and broad cotyledons.

2.2 General Characterization of *Croton oblongifolius* Roxb.

Croton oblongifolius Roxb. is a medium sized tree. Its calyx and ovary are covered with minute orbicular silvery scales. Leaves are 5.7-11.5 by 12.5-25.2 cm. in size, and crowded toward the end of branches. Leaf blade's shape is oblong-lanceolate and the base is normally acute with no apparent glands above the petioles which are 1.3-6.0 cm. long. Flowers are pale yellowish green and single in the axials of minute bracts on long erect racemes. The male flowers are locate on the upper part of the raceme while the females are in the lower part. Male flowers are slender and have the length of pedicels of 4.0 mm. Calyx is more than 6.0 mm. long andsegments are ovate, obtuse and more than 2.5 mm. long. Petals are 3.0 mm. long, elliptic- lanceolate and woolly. The twelve staments are inflexed in bud and the length of filaments are 3.0 mm. In female flowers, the pedicels are short and stout. Theirs sepals are more acute than male's with densely ciliated margins. Petals are 2.0 mm long, with densely woolly margins. The tree styles are 4.0 mm long. Diameter of fruit is less than 1.3 cm, slightly 3-lobed and clothed with small orbicular scales. In each fruit, the number of seeds are eight which are 6.0 mm. long, rounded and quite smooth on the back.

2.3 The previous study of chemical constituents of *Croton oblongifolius* Roxb.

The chemical constituents of *C. oblongifolius* have been studied since 1968 by the Indian scientists [9-13].In Thailand, Roengsumran, S., and co-workers have investigated the chemical constituents of *C. oblongifolius* from various locations

in Thailand. They found many new diterpenoid compounds. The chemical constituents that were found in *C. oblongifolius* were assigned below.

In 1968, Seshadri, T. R., Rao, P.S., Sachdev, G.P., and Singh, H. B. studied chemical constituents from the bark of *Croton oblongifolius* Roxb. They found a new diterpene alcohol, oblongifoliol together with β-sitosterol. [9]

In 1969, Seshadri, T. R., Aiyar, V. N., Rao, P. S., and Sachdev, G. P., found deoxyoblongifoliol from the stem bark of *Croton oblongifolius* Roxb. [10]

In 1970, Seshadri, T. R., and Aiyar, V. N. studied the structure of oblongifolic acid, the major diterpene acid component of the bark, it was assigned as isopimara-7(8),15-diene-19-oic acid. [11]

In 1971, Seshadri, T. R., and Aiyar, V. N. determined the structures of oblongifoliol and deoxyoblongifoliol again. Two components have been assigned their structures as *ent*-isopimara-7,15-diene-3β,19-diol and *ent*-isopimara-7,15-diene-3β-ol, respectively. In the same year, three minor components were found from the bark. The first one was *ent*-isopimara-7,15-diene, the second was 19-hydroxy-*ent*-isopimara-7,15-diene and the last one was *ent*-isopimara-7,15-diene-19-aldehyde. Moreover, Acetyl aleuritolic acid, 3b-acetoxy-olean-14(15)-ene-28-oic acid, has been obtained from the bark also. [12]

In 1972, Seshadri, T. R., and Aiyar, V. N. found two closly related furanoid diterpenes from the bark. One was *ent*-15,16-epoxy-3,11,13(16),14-clerodatetraen-19-oic acid or 11-dehydro(-)-hardwickiic acid and the second was (-)-hardwikiic acid. They studied other parts of *Croton oblongifolius* Roxb. including the root-

bark, wood, and leaves. Most reported isolated compounds from the stem-bark were in poor yields, while the leaves gave only waxy materials. [13]

In 1998, Roengsumran, S., Achayindee, S., Petsom, A., Phudhom, K., Singtothong, P., Surachetapan, C., and Vilaivan, T., found two new cembranoids, crotocembraneic acid and neocrotocembraneic acid, isolated from the stem bark of *Croton oblongifolius*. Their structures were established on the basis of spectroscopic analysis. [14]

In the same year, Roengsumran, S., Petsom, A., Sommit, D., and Vilaivan, T., found four new labdane diterpene compounds, labda-7,12(*E*), 14-triene, labda-7,12(*E*), 14-triene-17-ol, labda-7,12(*E*), 14-triene-17-al, and labda-7,12(*E*), 14-triene-17-oic acid. These compounds gave effective cytotoxicity against cancer cell lines especially the aldehyde compound, labda-7,12(*E*), 14-triene-17-al. [16]

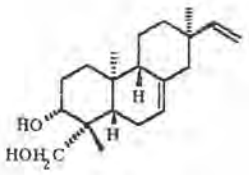
In 1999, Roengsumran, S., Singtothong, P., Phudhom, K., Ngamrochanavanich, N., Petsom, A., and Chaichantipyuth, C., found a new cembranoid diterpene, neocrotocembranal, isolated from the stembark of *Croton oblongifolius*. This compound inhibited platelet aggregation induced by thrombin, and exhibited cytotoxicity against P-388 cells in vitro. [15]

There were many diterpenoid compounds isolated and characterized from *Croton oblongifolius* and they are tabulated in Table **1**.

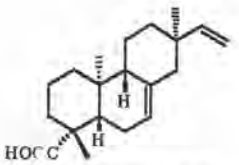
Table 1: **The previous studied of chemical constituent in hexane crude extract from stem barks of *Croton oblongifolius* Roxb.**

Organic Compounds	Area	References
Poilaneic acid	Petchaboon	[4]
Crovatin	Kanchanaburi	[4]
Isokolavenol	Kanchanaburi	[4]
Crotohalimaniec acid	Nakornrachsima	[4]
Benzoyl crotohalimanolic acid	Nakornrachsima	[4]
Crotohalimoneic acid	Nakornrachsima	[4]
Nidorellol	Chonburi	[4]
Labda-7, 13(Z)-diene-17,12-olide-15-ol	Udonthani	[5]
Oblongifoliol	India	[9]
19-Deoxyoblongifoliol	India	[10]
Oblongifolic acid	India	[11]
ent-Isopimara-7,15-diene	India	[12]
ent-Isopimara-7,15-diene-19-aldehyde	India	[12]
11-Dehydro(-)-hardwickiic acid	India	[13]
(-)-Hardwickiic acid	India	[13]
Crotocembraneic acid	Petchaboon	[14]
Neocrotocembraneic acid	Petchaboon	[14]
Neocrotocembranal	Petchaboon	[15]
Labda-7,12(*E*),14-triene	Prachuab Kirikhan	[16]
Labda-7,12(*E*),14-triene-17-ol	Prachuab Kirikhan	[16]
Labda-7,12(*E*),14-triene-17-al	Prachuab Kirikhan	[16]
Labda-7,12(*E*),14-triene-17-oic acid	Prachuab Kirikhan	[16]

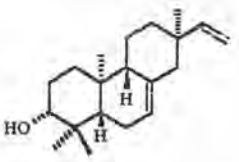
Isopimarane Group



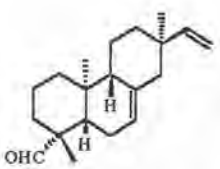
Oblongifoliol



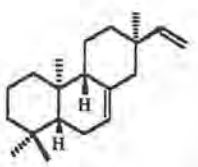
Oblongifolic acid



19-Deoxyoblongifoliol

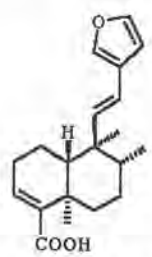


ent-Isopimara-7,15-diene-19-aldehyde

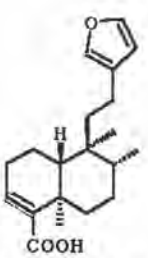


ent-Isopimara-7,15-diene

Clerodane Group

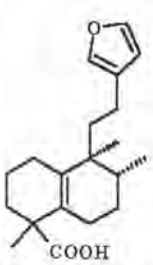


11-Dehydro-(-)-hardwickiic acid

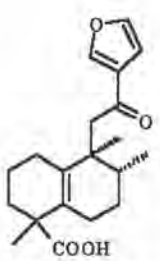


(-)-Hardwickiic acid

Halimane Group

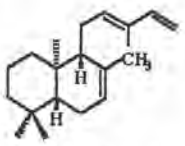


Crotohalimaneic acid

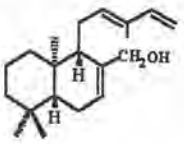


Crotohalimoneic acid

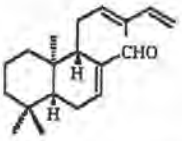
Labdane Group



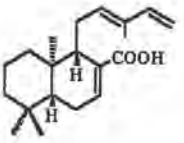
Labda-7,12(*E*),14-triene



Labda-7,12(*E*),14-triene-17-ol

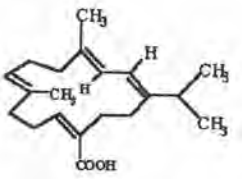


Labda-7,12(*E*),14-triene-17-al

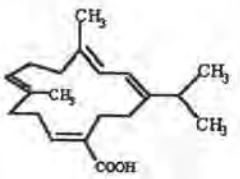


Labda-7,12(*E*),14-triene-17-oic acid

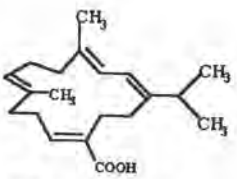
Cembrane Group



Crotocembraneic acid



Neocrotocembraneic acid



Neocrotocembranal

Figure 2: The structure of the chemical constituents of *Croton oblongifolius* Roxb.

2.4 Biological activity of diterpenoid compounds isolated from *C. oblongifolius* Roxb.

Diterpenoid compounds isolated from *C. oblongifolius* Roxb. have many biological activities such as cytotoxicity, cAMP phosphodiesterase inhibition, antimicrobial and antiplatelet aggregation etc. For example, hardwickiic acid has antimicrobial activity [5], labdane from Prachuab Kirikhan were active to against human tumor cell lines [2], neocrotocembranal, neocrotocembraneic acid and poilaneic acid have cAMP phosphodiesterase inhibition activity [4].