

CHAPTER II

LITERATURES REVIEWS

2.1 Previous study of diterpenoid compounds from *Croton oblongifolius* Roxb.

General Characteristic of *Croton oblongifolius* Roxb.

Croton oblongifolius Roxb. is a medium sized deciduous tree in the Euphorbiaceae family. There are about 700 species in this family. In Thailand, it is commonly called Plao Yai (central) or Plao Luang (Northern). It is distributed throughout forests or shrubs below 700 meters above sea level. Its calyx and ovary are clothed with minute orbicular silvery scales. Leaves are 5.6-12.0 by 13.0-24.0 cm in size and crowded toward the end of the branchlets. The shape of leaf blade is oblong-lanceolate. Its flowers are pale yellowish green and solitary in the axials of minute bracts on long erect racemes. The male flowers are located in the upper part of the length of pedicels of 4.0 mm. The calyx is more than 6.0 mm. Long and segments are ovate, obtuse and more than 2.5 mm long. The twelve stamens are inflexed in bud and the length of filaments is 3.0 mm. In female flowers, the pedicels are short and stout. Its sepals are more acute than in the male with densely ciliated margins. Petals are 2.0 mm long, with densely woolly margins. The three styles are 4.0 mm long. The diameter of the fruit is less than 1.3 cm., slightly 3-lobed and clothed with small orbicular and quite smooth on the back.²⁵⁻²⁸ In each fruit, the number of seeds are eight which are 6.0 mm long, rounded and quite smooth on the back. are shown in Fig.2.

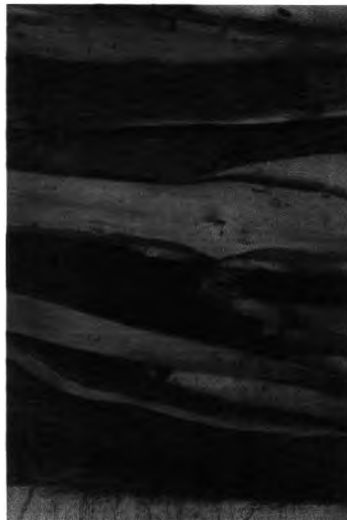


Figure 2. The stem-bark, leaf, flower and fruit of *Croton oblongifolius* Roxb.

From the literature surveys, *Croton oblongifolius* Roxb. has been widely studied and many diterpenoid compounds have been isolated and characterized. According to the observation of chemical constituents of *Croton oblongifolius* Roxb. from various locations in Thailand, it was found that the main components are differ in structure. The chemical constituents found in *C. oblongifolius*. could be categorized into seven groups including Cembrane diterpenoid, Clerodane, Labdane, Halimane, Pimarane, Isopimarane and Cleistanthane diterpenoid compounds, which are shown in Table 1.

Table 1. Chemical constituents of *Croton oblongifolius* Roxb.

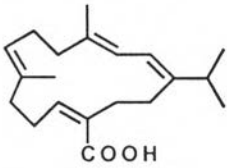
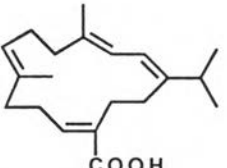
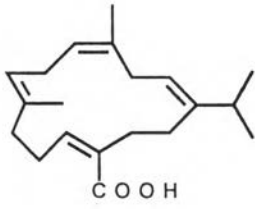
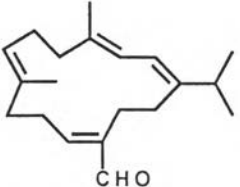
Plant parts	Substances	References
Bark	<p>Cembrane diterpenoid</p>  <p>Crotoncembraneic acid</p>	7,8
	 <p>Neocrotoncembraneic acid</p>	
	 <p>Poilaneic acid</p>	7,24
	 <p>Neocrotoncembranal</p>	

Table 1. Chemical constituents of *Croton oblongifolius* Roxb.

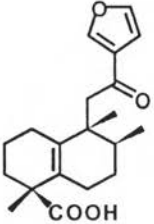
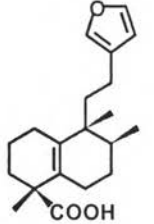
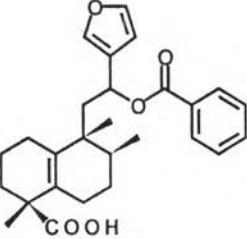
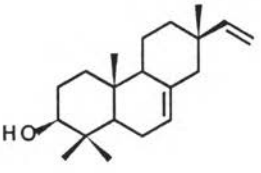
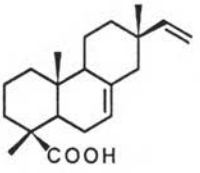
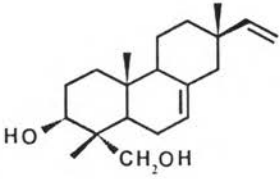
Plant parts	Substances	References
Bark	<p data-bbox="468 338 776 376">Halimane diterpenoid</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p data-bbox="489 701 751 734">Crotohalimoneic acid</p> </div> <div style="text-align: center;">  <p data-bbox="820 701 1074 734">Crotohalimaneic acid</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p data-bbox="648 1111 1002 1144">Benzoyl crotohalimoneic acid</p> </div>	7
Bark	<p data-bbox="468 1252 776 1290">Pimarane diterpenoid</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p data-bbox="494 1581 766 1615">19-Deoxyoblongifoliol</p> </div> <div style="text-align: center;">  <p data-bbox="879 1581 1064 1615">Oblongilic acid</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p data-bbox="748 1906 910 1939">Oblongifoliol</p> </div>	18,32 20

Table 1. Chemical constituents of *Croton oblongifolius* Roxb.

Plant parts	Substances	References
Bark	<p data-bbox="458 353 802 392">Isopimarane diterpenoid</p> <div data-bbox="668 472 883 645" style="text-align: center;"> </div> <p data-bbox="632 680 940 714">ent-Isopimara-7, 15-diene</p> <div data-bbox="668 745 883 918" style="text-align: center;"> </div> <p data-bbox="575 976 1037 1010">ent-Isopimara-7, 15-diene-19-aldehyde</p>	<p data-bbox="1210 546 1248 580">19</p> <p data-bbox="1210 817 1248 851">21</p>
Bark	<p data-bbox="458 1115 822 1153">Cleistanthane diterpenoid</p> <div data-bbox="625 1193 945 1366" style="text-align: center;"> </div> <p data-bbox="575 1442 1028 1476">Cleistantha-4, 13, 15-triene-3-oic acid</p>	<p data-bbox="1210 1249 1248 1283">33</p>

2.2 Biological activity review of diterpene compounds from *C. oblongifolius*

Diterpenoid compounds from *C. oblongifolius*. exhibit biological activity such as cAMP phosphodiesterase inhibition, antimicrobial, antiplatelet aggregation, cytotoxicity etc.

For example, the cemberane diterpene compound, neocrotoncembranal,²⁴ has activity against human tumor cell lines (P 388 cell line and 6 tumor cell lines; S-102 (hepatoma), Hep-G2 (hepatoma), SW 620 (colon), Chago (lung), Kato-3 (gastric), BT 474 (breast)). Crotocebraneic acid and Neocrotocebraneic acid⁷ have cAMP phosphodiesterase inhibitory activity.

The labdane diterpene compounds, from Prachub Kirikhun³¹ have activity against human tumor cell lines and also show the antiplatelet aggregation activity.

The clerodane diterpene compounds, for example hardwickiic acid,³⁴ show antimicrobial activity.

The cleistanthane diterpene, compounds from Loei,³³ have activity against human tumor cell lines.

Moreover, other diterpenoid compounds had been isolated from *C. oblongifolius*. such as, pimarane diterpene compounds. These compounds were isolated from the aerial part of *Momordica balsamian*, showing antiviral activity against HIV.³⁵

The isopimarane diterpene compounds isolated from leaves of *Orthosiphon aristatus*., show inhibitory activity on smooth muscle contractions caused by several stimulants.³⁶

Table 2 shows the cytotoxicity of some compounds isolated from the stem bark of *Croton oblongifolios* against 6 human cancer cell lines: Hs 27 (fibroblast), Hep-G2 (hepatoma), SW 620(colon), Chago(lung), KATO(gastric) and BT 474 (breast).

Table 2. Cytotoxicity against human cancer cell lines of some compounds isolated from *Croton oblongifolios*

Compound	% Survival (10 µg)					
	HS27 fibroblast	HepG2 hepatoma	SW620 colon	Chago lung	Kato gastric	BT474 breast
(-)-20-benzyloxyhardwickiic acid [37]	100	74	58	100	65	82
Labda-7,12-(E), 14triene-17al [6]	6	7	3	3	7	13
Labda-7,12-(E), 14triene-17-oic acid [6]	73	57	88	59	70	91
Labda-7,12-(E), 14diene [6]	100	61	73	72	47	75
Labda-7,12-(E), 14triene-17-ol [6]	64	7	3	82	6	11
Crotocebraneic acid [7]	82	71	6	3	6	7
Neorotocebraneic acid [7]	46	37	96	97	90	95
Neocrotocebranal [7]	82	71	6	3	6	7
Crotohalimaneic acid [7]	64	7	3	82	6	11
Crotohalimoneic acid [7]	91	86	0	0	70	0
Crovatin [7]	18	29	8	0	30	16
Isokolavenol [7]	36	93	97	18	94	89
Nidorellol [7]	9	21	12	27	30	16
(-)-Hardwickiic acid [38]	104	79	112	104	67	115
Kaur-16-en-19-oic acid [39]	108	77	42	52	73	80
(-)-Pimara-9(11),15-diene-19-ol [40]	89	14	62	66	16	43