CHAPTER II

HISTORICAL

Croton oblongifolius Roxb. is an indigenous plant known in Thailand as เปล้าใหญ่ Plao yai (Central), เปล้าหลวง Plao luang (Northern), คาะวู Khwa-wuu (Karen-Kanchanaburi), เซ่งเค่คั้ง Seng-khe-khang, สะกาวา Sa-kaa-waa, ส่าคุวะ Saa-kuu-wa (Karen-Mae-Hong Son), เปาะ Poh (Kamphaeng Phet), ห้าเยิ่ง Haa-yoeng (Shan-Mae-Hong Son) (Smitinand, 1980).

1. Characteristics of the genus *Croton*

The genus *Croton* belongs to the family Euphorbiaceae. In this family, there are 800 genera and 5000 species. The *Croton* comprises 700 species of trees or shrubs (rarely herbs). Leaves usually alternate, usually 2-glandular at the base. Flowers monoecious, solitary or clustered on the rachis of a terminal raceme; bracts small. Male flowers: Calyx 5- (rarely 4-6-) partite; segments imbricate or subvalvate. Petals 5 (rarely 4-6-), never exceeding but sometimes shorter than the calyx. Disk of 4-6 glands opposite the sepals. Stamens many, inserted on a hairy receptacle; filaments free, inflexed in bud, at length straight; anthers adnate, with parallel cells. Pistillode 0. Female flowers : sepals usually more ovate than in the male, rarely accressent in fruit. Petals smaller than the sepals or obsolete. Disk annular, or of 4-6 glands opposite the sepals. Ovary 3-(rarely 2-4-) celled; ovule solitary in each cell; Style usually long and slender, 2-4-cleft. Capsule subequally 6-valved, or of 3 separating 2-valved cocci. Seeds smooth; caruncle small; testa crastaceous; albumen copious; cotyledons broad. Tropics and subtropics (Blatter, Caius and Mhaskar, 1975).

According to Tem Smithinand (1980), the species of the genus *Croton* found in Thailand are as follows.

Croton argyratus Bl.	เปล้า Plao (Prachuap Khiri Khan)
Croton birmanicus Muell Arg.	บะกัง Ba kang (Phrae)

Croton budopensis Gagnep.	= *Croton argyratus* Bl.
Croton cascarilloides Raeusch	เปล้าเงิน Plao ngoen (Songkhla); เปล้าน้ำเงิน Plao nam ngoen (Prachuap Khiri Khan)
Croton caudatus Geisel	กระดอหดใบขน Krado hot bai khon (Chanthaburi)
Croton columnaris Airy Shaw.	เปล้าคำ Plao Kham (Sukhothai)
Croton crassifolius Geisel.	ปังคี Pang Khee, พังคี Pang Khee (Chiang Mai)
Croton cumingii Muell.Arg.	= *Croton cascarilloides* Raeusch
Croton hutchinsonianus Hoss.	เปล้าแพะ Plao phae (Northern)
Croton longissimus Airy Shaw.	เปล้าน้อย Plao noi (Lampang)
Croton oblongifolius Roxb.	เปล้าใหญ่ Plao yai (Central), เปล้าหลวง Plao luang (Northern), ควะวู Khwa-wuu (Karen-Kanchanaburi), เซ่งเค่คัง Seng-khe-khang, สะกาวา Sa-kaa-waa, ส่ากูวะ Saa-kuu-wa (Karen-Mae-Hong Son), เปาะ Poh (Kamphaeng Phet), ห้าเยิ่ง Haa-yoeng (Shan-Mae Hong Son)
Croton pierrei Gagnep.	= *Croton cascarilloides* Raeusch.
Croton robustus Kurz.	เปล้าเลือด Plao lueat (Lampang)
Croton rottleri Geisel.	= *Chrozophora rottleri* Juss.ex Spreng.
Croton siamensis Craib.	= *Croton robustus* Kurz.
Croton tiglium Linn.	มะข่าง Ma khaang, มะคัง Ma Khang, มะตอด Ma tot, หมากทาง Maak thaang, หัสคืน Has Khuen (Northern); ลูกผลาญศัตรู Luuk Phlaan Sattruu, สลอด Salot, สลอดต้น Salot ton,

หมากหลอด Maak lot (Central); หมาก ของ Maak-yong (Shan-Mae Hong Son); Croton oil plant

Croton tomentosus Muell. Arg. = *Croton crassifolius* Geisel.

Croton trachycaulis Airy Shaw. ขี้อ้น Khee on (Prachuap Khiri-Khan)

2. **Characteristics of *Croton oblongifolius* Roxb.**

Croton oblongifolius Roxb. is medium sized tree; young shoots, branchlets, inflorescence, calyx and ovary clothed with minute orbicular silvery scales. Leaves 12.5- 25 by 5.7-11.5 cm., crowded towards the ends of the branchlets, oblong-lanceolate, subacute, glabrous when fully grown, more or less crenate or serrate, penninerved, base usually acute with no apparent glands above the petioles; main nerves numerous, slender; petioles 2-3.2 cm. long. Flowers pale yellowish green, solitary or fascicled in the axils of minute bracts on long erect often fascicled racemes, the males in the upper part of the raceme, the females in the lower part. Male flowers: pedicels variable in length, reaching 4 mm. long, slender. Calyx more than 6 mm. across when flattened out, divided about ¾ the way down; segments more than 2.5 mm. long, ovate, obtuse. Petals 3 mm. long, elliptic-lanceolate, obtuse, woolly. Stamens 12, inflexed in bud; filaments 3 mm. long, the lower half hairy. Female flowers : Pedicels short, stout. Sepals more acute than in the male with densely ciliate margins. Petals 2 mm. long, obovate, with densely woolly margins. Styles 3, nearly 4 mm. long, each again subdivided into 2 long slender curled branches 3 mm. long. Capsules less than 1.3 cm. diam, subglobose, a little depressed, slightly 3-lobed, clothed with small orbicular scales. Seeds 8 by 6 mm., ellipsoid, rounded and quite smooth on the back (Blatter, Caius and Mhaskar, 1995).

3. Chemical constituents of the genus *Croton*

From previous phytochemical studies, the abundant metabolites from plants of this genus are terpenoids. The major type of terpenoids found from the *Croton* is diterpenes, a class of compounds with a wide range of structure types.

The distribution of di- and higher terpene compounds is summarized in the table below.

Table 1 Distribution of di- and higher terpenoids in the genus *Croton*

Plant and chemical compound	Category	Plant part	Reference
Croton argyrophylloides Muell. Arg..			
ent-kaur-16-en-15-oxo-18-oic acid [1]	kaurane diterpene	bark	Monte, Dantas and Braz, 1988.
3,12-dioxo-15,16-epoxy-4-hydroxy-cleroda-13(16),14-diene [2]	clerodane diterpene	bark	Monte *et al.*, 1988.
Aa1CM [3]	kaurane diterpene	trunk wood	Monte, Andrade and Craveiro, 1984.
Aa7CM [4]	kaurane diterpene	trunk wood	Monte *et al.*, 1984.
C. aromaticus L.			
(-)-hardwickiic acid [5]	clerodane diterpene	root	Bandara *et al.*, 1990.
C. cajucara Benth.			
trans-dehydrocrotonin [6]	clerodane diterpene	bark	Tavares *et al.*, 1996.
cis-dehydrocrotonin [7]	clerodane diterpene	bark	Kubo, Asaka and Shibata, 1991.
cajucarins A [8]	clerodane diterpene	cortex	Itokawa *et al.*, 1990.

Plant and chemical compound	Category	Plant part	Reference
C. cajucara Benth. (cont.)			
cajucarins B [9]	clerodane diterpene	cortex	Itokawa *et al.*, 1990.
t- crotonin [10]	clerodane diterpene	cortex	Itokawa *et al.*, 1989.
C. californicus Muell. Arg.			
12-deoxyphorbol-13,20-diester [11]	tigliane diterpene	entire plant	Chavez *et al.*, 1982.
(-)-hardwickiic acid [5]	clerodane diterpene	entire plant	Luzbetak *et al.*, 1979.
barbascoic acid [12]	clerodane diterpene	leaf	Wilson, Neubert and Huffman, 1976.
(-)-Me barbascoate [13]	clerodane diterpene	leaf	Wilson *et al.*, 1976.
C. caudatus Geisel.			
stigmastan-3,6-dione, 5α [14]	steroid	stem bark	Banerji, Nandi and Kundu, 1988.
taraxerone [15]	triterpene	stem bark	Banerji *et al.*, 1988.
taraxerol [16]	triterpene	stem bark	Banerji *et al.*, 1988.
taraxeryl acetate [17]	triterpene	stem bark	Banerji *et al.*, 1988.

Plant and chemical compound	Category	Plant part	Reference
C. caudatus Geisel. (cont.)			
β-sitosterol [18]	steroid	stem bark	Banerji *et al.*, 1988.
isocrotocaudin [19]	clerodane diterpene	stem bark	Chatterjee, Banerjee and Bohlmann, 1978.
crotocaudin [20]	labdane diterpene	stem bark	Chatterjee, Banerjee and Bohlmann, 1977.
teucvidin [21]	labdane diterpene	stem bark	Chatterjee *et al.*, 1977.
C. celtidifolius Baill.			
β-sitosterol [18]	steroid	leaf, twig	Amaral and Barnes, 1997.
C. chilensis Muell. Arg.			
crotonic acid [22]	clerodane diterpene	entire plant	Borques *et al.*, 1995.
C. corylifolius Lam.			
crotofolin A [23]	crotofolane diterpene	entire plant	Burke *et al.*, 1976.
crotofolin E [24]	crotofolane diterpene	entire plant	Burke *et al.*, 1979.
corylifuran [25]	clerodane diterpene	leaf, twig	Burke *et al.*, 1976.

Plant and chemical compound	Category	Plant part	Reference
C. crassifolius Geisel.			
acetyl aleuritolic acid [26]	triterpene	root	Boonyarathanakorn -kit *et al.*, 1988.
chettaphanin - I [27]	halimane diterpene	root	Boonyarathanakorn -kit *et al.*, 1988.
β-amyrin [28]	triterpene	root	Boonyarathanakorn -kit *et al.*, 1988.
C. cumingii Muell. Arg.			
β-sitosterol [18]	steroid	stem	Tomita, Lee and Nakano, 1965.
C. diasii			
diasin [29]	halimane diterpene	trunk wood	De Alvarenga *et al.*, 1978.
β-s tosterol [18]	steroid	trunk wood	De Alvarenga *et al.*, 1978.
C. dichogamus Pax.			
cro oxides A [30]	crotofolane diterpene	leaf	Jogia *et al.*, 1989.
cro oxides B [31]	crotofolane diterpene	leaf	Jogia *et al.*, 1989.

Plant and chemical compound	Category	Plant part	Reference
C. draco Schlecht.			
draconin [32]	clerodane diterpene	bark	Rodriguez-Hahn, Rodriguez and Romo, 1975.
β-sitosterol [18]	steroid	bark	Rodriguez-Hahn *et al.*, 1975.
stigmasterol [33]	steroid	bark	Rodriguez-Hahn *et al.*, 1975.
C. eleuteria Benn.			
cascarillin [34]	clerodane diterpene	stem bark	Birtwistle *et al.*, 1962.
cascarillin A [35]	clerodane diterpene	stem bark	Birtwistle *et al.*, 1962.
C. haumanianus J. Leonard.			
crotocorylifuran [36]	clerodane diterpene	stem bark	Tchissamhou *et al.*, 1990.
crotohaumanoxide [37]	crotofolane diterpene	stem bark	Tchissamhou *et al.*, 1990.
lupeol [38]	triterpene	stem bark	Tchissamhou *et al.*, 1990.
C. hovarum Leandri.			
3,12-dioxo-15,16-epoxy-cleroda-13(16),14-dien-9-al [39]	clerodane diterpene	leaf	Krebs and Ramiarantsoa, 1997.

Plant and chemical compound	Category	Plant part	Reference
C. hovarum Leandri. (cont.)			
3α,4β-dihydroxy-15,16-epoxy-19-nor-12-oxo-cleroda-5(10),13(16),14-triene [40]	clerodane diterpene	leaf	Krebs *et al.*, 1997.
3α,4β-dihydroxy-15,16-epoxy-12-oxo-cleroda-13(16),14-diene-19-al [41]	clerodane diterpene	stem bark	Krebs *et al.*, 1996.
β-amyrin [28]	triterpene	stem bark	Krebs *et al.*, 1996.
C. hutchinsonianus Hoss.			
ent-kaur-16β,17-diole [42]	kaurane diterpene	stem bark	Li *et al.*, 1990.
ent-kaur-16β,17,19-triole [43]	kaurane diterpene	stem bark	Li *et al.*, 1990.
β-sitosterol [18]	steroid	stem bark	Li *et al.*, 1990.
β-sitosterol-D-glucoside [44]	steroid	stem bark	Li *et al.*, 1990.
C. jatrophoides Pax.			
dumsin [45]	triterpene	root bark	Kubo *et al.*, 1990.
C. joufra Roxb.			
swassin [46]	clerodane diterpene	stem	Roengsumran *et al.*, 1982.

Plant and chemical compound	Category	Plant part	Reference
C. kerrii Airy Shaw			
(*E,E,Z*)-11-hydroxymethyl-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-ol [47]	acyclic diterpene	leaf	Sato, Ogiso and Kuwano, 1980.
(*E,E,E*)-11-formyl-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-ol [48]	acyclic diterpene	leaf	Sato *et al.*, 1980.
C. lacciferus Blanco.			
ent-kaur-15-en-17-hydroxy-3β-yl-acetate [49]	kaurane diterpene	root	Bandara and Wimalasiri, 1988.
ent-kaur-15-en-17-ol [50]	kaurane diterpene	root	Bandara *et al.*, 1988.
ent-kaur-3α,16β,17-triol [51]	kaurane diterpene	root	Bandara *et al.*, 1988.
ent-kaur-16β,17-diol [52]	kaurane diterpene	root	Bandara *et al.*, 1988.
16αH-*ent*-kaur-17-oic acid [53]	kaurane diterpene	root	Bandara, Wimalasiri and Macleod, 1988.
ent-15β,16-epoxykauran-17-ol [54]	kaurane diterpene	root	Bandara *et al.*, 1988.
ent-kaur-15-en-3β,17-diol [55]	kaurane diterpene	root	Bandara *et al.*, 1988.
3β-acetoxy-D-friedoolean-14-en-28-oic acid [56]	triterpene	root	Bandara *et al.*, 1988.
oleanolic acid [57]	triterpene	root	Bandara *et al.*, 1988.

Plant and chemical compound	Category	Plant part	Reference
C. lechleri Muell. Arg.			
korberin A [58]	clerodane diterpene	stem bark	Cai, Chen and Phillipson, 1993.
korberin B [59]	clerodane diterpene	stem bark	Cai *et al.*, 1993.
crolechinol [60]	clerodane diterpene	bark	Cai *et al.*, 1993.
crolechinic acid [61]	clerodane diterpene	bark	Cai *et al.*, 1993.
β-sitosterol [18]	steroid	sap	Cai *et al.*, 1993.
β-sitosterol-D-gluco pyranoside [62]	steroid	sap	Cai *et al.*, 1993.
C. levatii Guillaumin.			
crovatin [63]	clerodane diterpene	stem bark	Moulis *et al.*, 1992.
C. linearis Jacq.			
insecticidal diterpene [64]	acyclic diterpene	leaf, twig	Alexander *et al.*, 1991.
C. macrostachy(u)s Hochst.			
lupeol [38]	triterpene	stem bark, twig	Addae-Mensah *et al.*, 1992.
betulin [65]	triterpene	stem bark, twig	Addae-Mensah *et al.*, 1992.

Plant and chemical compound	Category	Plant part	Reference
C. matourensis Aubl.			
maravuic acid [66]	labdane diterpene	bark	Schneider *et al.*, 1995.
C. megalocarpus Hutch.			
epoxychiromodine [67]	clerodane diterpene	bark	Addae-Mansah *et al.*, 1992.
O-acetyl aleuritolic acid [26]	triterpene	bark	Addae-Mansah *et al.*, 1992.
chiromodine [68]	clerodane diterpene	bark	Addae-Mansah *et al.*, 1989.
lupeol [38]	triterpene	bark	Addae-Mansah *et al.*, 1989.
betulin [65]	triterpene	bark	Addae-Mensah *et al.*, 1989.
β-sitosterol [18]	steroid	bark	Addae-Mansah *et al.*, 1989.
C. nepetaefolius Baill.			
croton casbane diterpene [69]	casbane diterpene	stem	Moura *et al.*, 1990.
C. nitens Sw.			
crotonitenone [70]	casbane diterpene	leaf, twig	Burke *et al.*, 1981.

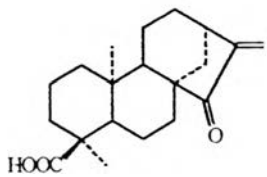
Plant and chemical compound	Category	Plant part	Reference
C. niveus Jacq.			
nivenolide [71]	labdane diterpene	leaf	Rojaz and Rodriguez-Hahn, 1978.
C. oblongifolius Roxb.			
oblongifoliol [72]	pimarane diterpene	stem bark	Rao *et al.*, 1968.
19-deoxyoblongifoliol [73]	pimarane diterpene	stem bark	Aiyar and Seshadri, 1972.
3-deoxyoblongifoliol [74]	pimarane diterpene	stem bark	Aiyar *et al.*, 1972.
oblongifolic acid [75]	pimarane diterpene	stem bark	Aiyar and Seshadri, 1970.
ent-isopimara-7,15-diene [76]	pimarane diterpene	stem bark	Aiyar and Seshadri, 1971
ent-isopimara-7,15-diene-19-aldehyde [77]	pimarane diterpene	stem bark	Aiyar *et al.*, 1971.
19-hydroxy-*ent*-isopimara-7,15-diene [78]	pimarane diterpene	stem bark	Aiyar *et al.*, 1971.
(-)-hardwickiic acid [5]	clerodane diterpene	stem bark	Aiyar and Seshadri, 1972.
11-dehydro-(-)-hardwickiic acid [79]	clerodane diterpene	stem bark	Aiyar *et al.*, 1972.
crotocembraneic acid [80]	cembrane diterpene	stem bark	Roengsumran *et al.*, 1998a.
neocrotocembraneic acid [81]	cembrane diterpene	stem bark	Roengsumran *et al.*, 1998a.

Plant and chemical compound	Category	Plant part	Reference
C. oblongifolius Roxb. (cont.)			
labda-7,12(*E*),14-triene [82]	labdane diterpene	stem bark	Roengsumran *et al.*, 1998b.
labda-7,12(*E*),14-triene-17-al [83]	labdane diterpene	stem bark	Roengsumran *et al.*, 1998b.
labda-7,12(*E*),14-triene-17-ol [84]	labdane diterpene	stem bark	Roengsumran *et al.*, 1998b.
labda-7,12(*E*),14-triene-17-oic acid [85]	labdane diterpene	stem bark	Roengsumran *et al.*, 1998b.
acetyl aleuritolic acid [26]	triterpene	stem bark	Aiyar and Seshadri, 1971.
β-sitosterol [18]	triterpene	stem bark	Rao *et al.*, 1968.
stigmasterol [33]	steroid	stem bark	Surachetpan, 1996.
campesterol [86]	steroid	stem bark	Surachetpan, 1996.
C. poilanei Gagnep.			
poilaneic acid [87]	cembrane diterpene	leaf	Aiyar *et al.*, 1981.
C. penduliflorus Hutch.			
penduliflaworosin [88]	halimane diterpene	root bark	Adesogan, 1981.
C. pyramidalis Donn.Sm.			
[89] furolactone diterpene	labdane diterpene	leaf, stem	Rodriguez-Hanh *et al.*, 1981.

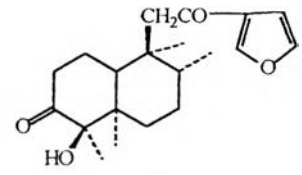
Plant and chemical compound	Category	Plant part	Reference
C. sonderianus Muell.Arg.			
6α-hydroxyannenone [90]	clerodane diterpene	root	Silveira and McChesney, 1994.
6α,7β-dihydroxyannenone [91]	clerodane diterpene	root	Silveira *et al.*, 1994.
6α,7β-diacetoxyannenone [92]	clerodane diterpene	root	Silveira *et al.*, 1994.
(-)-hardwickiic acid [5]	clerodane diterpene	root	McChesney and Silveira,1990.
trans-annonene [93]	clerodane diterpene	root	McChesney *et al.*, 1990.
trans-cascarillone [94]	clerodane diterpene	root	McChesney *et al.*, 1990.
12-hydroxyhardwickiic acid [95]	clerodane diterpene	root	McChesney and Silveira,1989.
sonderianial [96]	clerodane diterpene	root	McChesney *et al.*,1989.
sonderianin [97]	clerodane diterpene	root	Craveiro *et al.*, 1981.
sonderianol [98]	cleistanthane diterpene	heartwood	Craveiro and Silveiro, 1982.
3,4-secosonderianol [99]	cleistanthane diterpene	heartwood	Craveiro *et al.*, 1982.
C. sparsiflorus Morong.			
12-O-dodecanoyl-13-O-acetylphorbol-20-linolenate [100]	tigliane diterpene	seed	Upadhyay and Hecker, 1976.

Plant and chemical compound	Category	Plant part	Reference
C. sparsiflorus Morong. (cont.)			
ursolic acid [101]	triterpene	leaf, stem	Satish *et al.*, 1972.
β-sitosterol [18]	steroid	leaf, stem	Satish *et al.*, 1972.
C. sublyratus Kurz.			
plaunotol [102]	acyclic diterpene	stem	Ogiso *et al.*, 1978.
geranylgeraniol ester A [103]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
geranylgeraniol ester B [104]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
geranylgeraniol ester C [105]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
geranylgeraniol ester D [106]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
geranylgeraniol ester E [107]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
geranylgeraniol ester F [108]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
geranylgeraniol ester G [109]	acyclic diterpene	stem	Kitazawa *et al.*, 1982.
ent-3α-hydroxy-13-epimanool [110]	labdane diterpene	stem	Kitazawa and Ogiso, 1981.
plaunol A [111]	clerodane diterpene	stem	Kitazawa *et al.*, 1979.

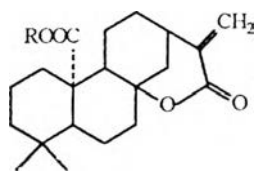
Plant and chemical compound	Category	Plant part	Reference
C. sublyratus Kurz. (cont.)			
plaunol B [112]	clerodane diterpene	stem	Kitazawa *et al.*, 1979.
plaunol C [113]	clerodane diterpene	stem	Kitazawa *et al.*, 1980.
plaunol D [114]	clerodane diterpene	stem	Kitazawa *et al.*, 1980.
plaunol E [115]	clerodane diterpene	stem	Kitazawa *et al.*, 1980.
plaunolide [116]	clerodane diterpene	stem	Takahashi *et al.*, 1983.
ent-16β,17-dihydroxy kaurane [117]	kaurane diterpene	stem	Kitazawa and Ogiso, 1981.
C. tiglium L.			
β-sitosterol [18]	steroid	seed	Mukherjee, 1969.
crotofolin A [23]	crotofolane diterpene	seed	Burke *et al.*, 197[illegible].
phorbol [118]	tigliane diterpene	seed	Kim *et al.*, 1994.
croton factor A [119]	tigliane diterpene	seed	Kim *et al.*, 1994.



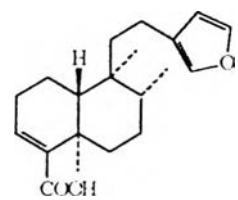
[1] *ent*-kaur-16-en-15-oxo-18-oic acid



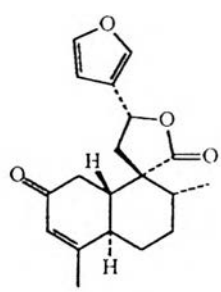
[2] 3,12-dioxo-15,16-epoxy-4-hydroxy-cleroda-13(16),14-diene



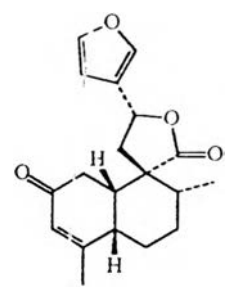
R = H [3] Aa1CM
R = Me [4] Aa7CM



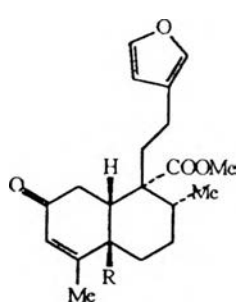
[5] (-)-hardwickiic acid



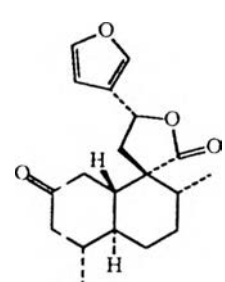
[6] *trans*-dehydrocrotonin



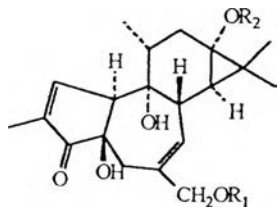
[7] *cis*-dehydrocrotonin



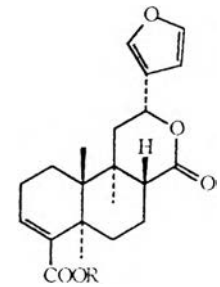
R = CHO [8] cajucarins A
R = H [9] cajucarins B



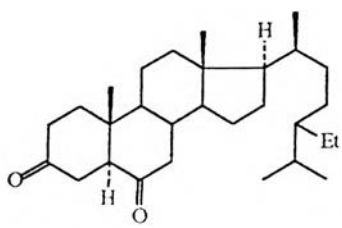
[10] *t*-crotonin



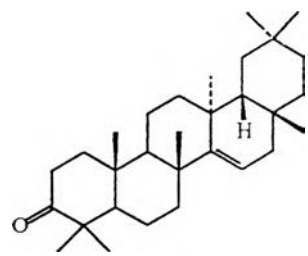
[11] 12-deoxyphorbol-13,20-diester
$R_2 = CO(CH_2)_8Me$
$R_1 = CO(CH_2)_8Me$
$= CO(CH_2)_{10}Me$
$= CO(CH_2)_{12}Me$
$= CO(CH_2)_{14}Me$



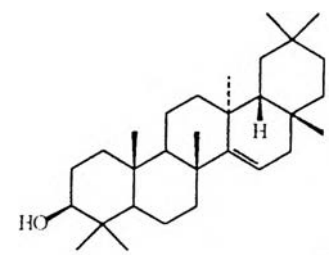
R = H [12] barbascoic acid
R = Me [13] (-)-Me barbascoic acid



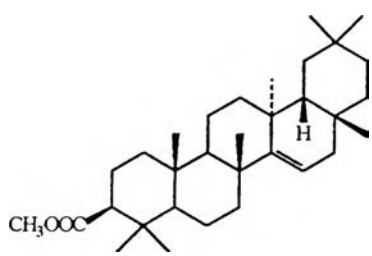
[14] stigmastan-3,6-dione,5α



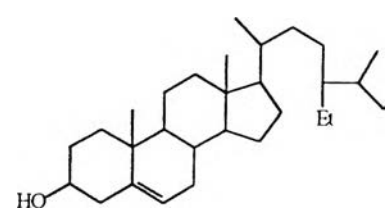
[15] taraxerone



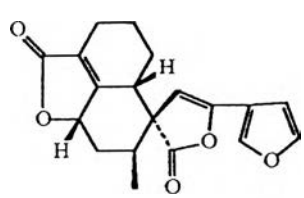
[16] taraxerol



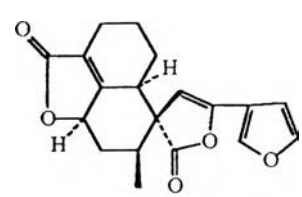
[17] taraxeryl acetate



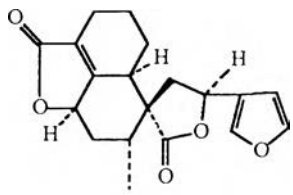
[18] β-sitosterol



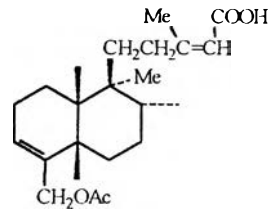
[19] isocrotocaudin



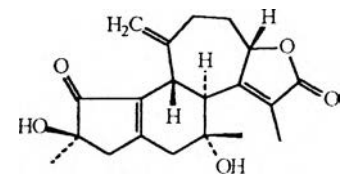
[20] crotocaudin



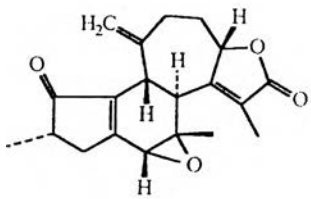
[21] teucvidin



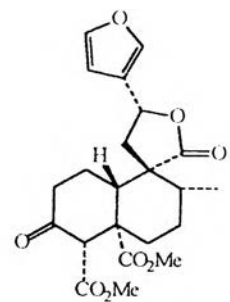
[22] crotonic acid



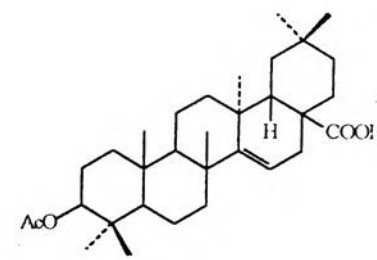
[23] crotofolin A



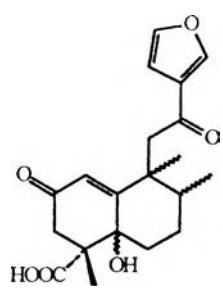
[24] crotofolin E



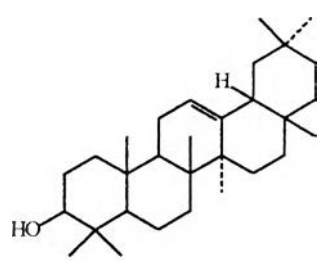
[25] corylifuran



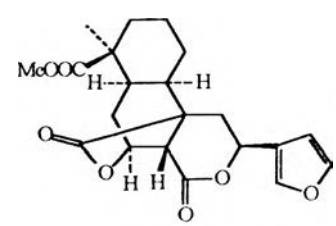
[26] Acetyl aleuritolic acid



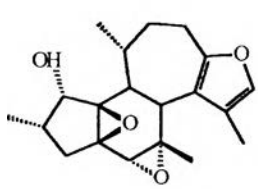
[27] chettaphanin - I



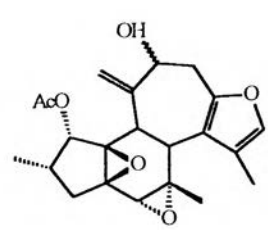
[28] β-amyrin



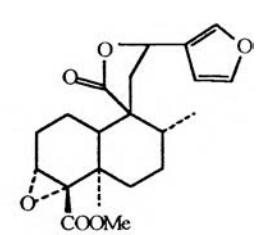
[29] diasin



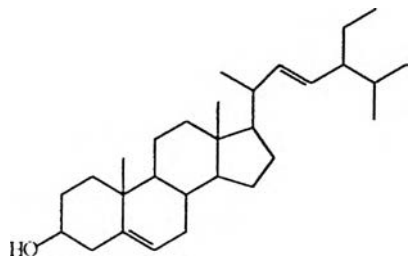
[30] crotoxides A



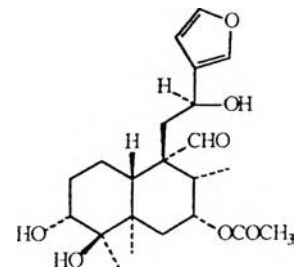
[31] crotoxides B



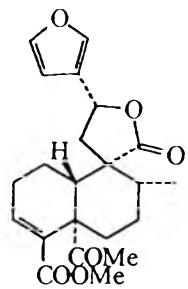
[32] draconin



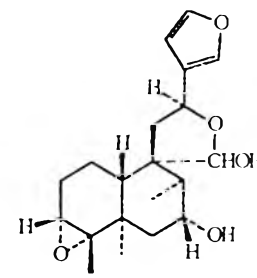
[33] stigmasterol



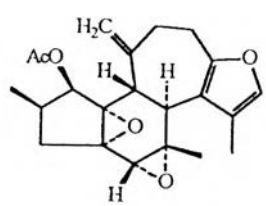
[34] cascarillin



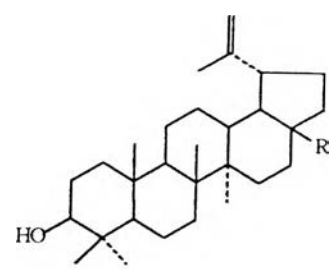
[36] crotocorylifuran



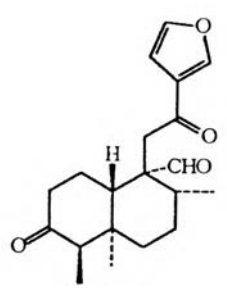
[35] cascarillin A



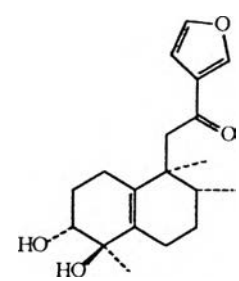
[37] crotohaumanoxide



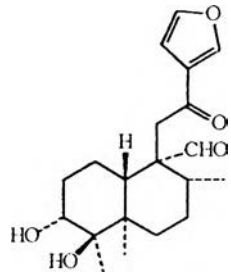
R = CH_3 [38] lupeol



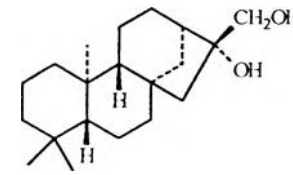
[39] 3,12-dioxo-15,16-epoxy-cleroda-13(16),14-dien-9-al



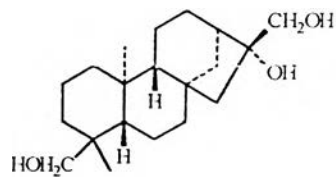
[40] 3α,4β-dihydroxy-15,16-epoxy-19-nor-12-oxo-cleroda-5(10),13(16),14-triene



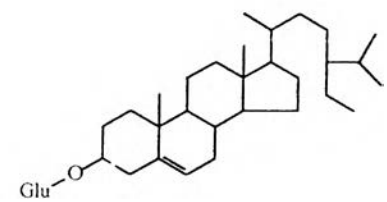
[41] 3α,4β-dihydroxy-15,16-epoxy-12-oxo-cleroda-13(16),14-diene-9-al



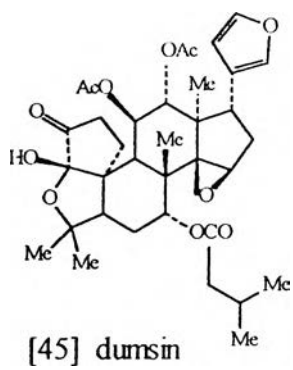
[42] *ent*-kaur-16β,17-diol



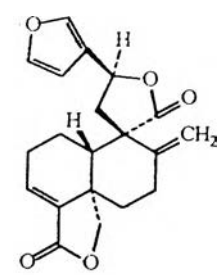
[43] *ent*-kaur-16β,17,19-triol



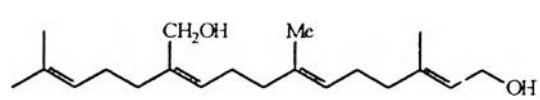
[44] β sitosterol-D-glucoside



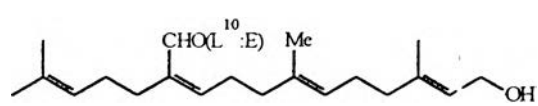
[45] dumsin



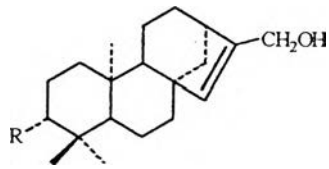
[46] swassin



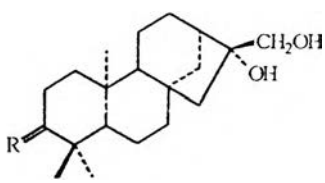
[47] (*E,E,Z*)-11-hydroxymethyl-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-ol



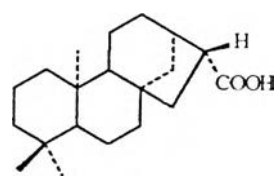
[48] (*E,E,E*)-11-formyl-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-ol



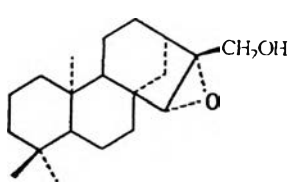
R = OAc [49] *ent*-kaur-15-en-17-hydroxy-3β-yl-acetate
R = H [50] *ent*-kaur-15-en-17-ol



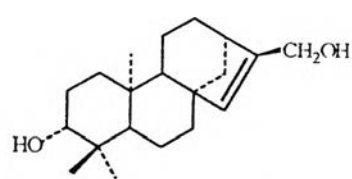
R = αOH, H [51] *ent*-kaur-3α,16β,17-triol
R = H_2 [52] *ent*-kaur-16β, 17-diol



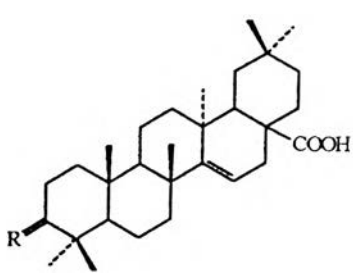
[53] 16αH-*ent*-kaur-17-oic acid



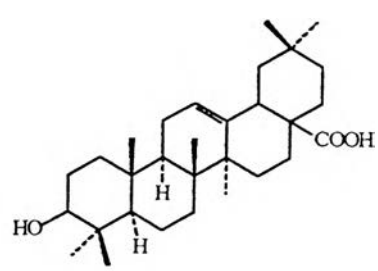
[54] *ent*-15β,16-epoxykauran-17-ol



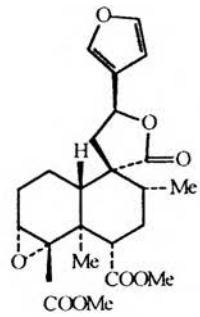
[55] *ent*-kaur-15-en-3β,17-diol



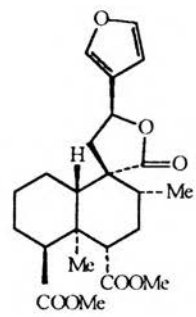
[56] 3β-acetoxy-D-friedolean-14-en-28-oic acid
R = H, β-OAc



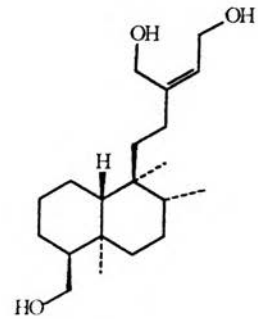
[57] oleanolic acid



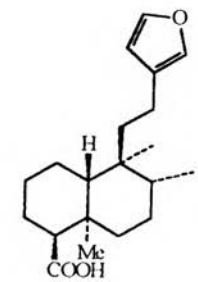
[58] korberin A



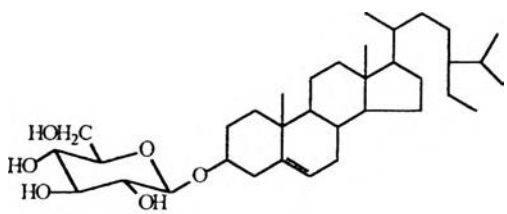
[59] korberin B



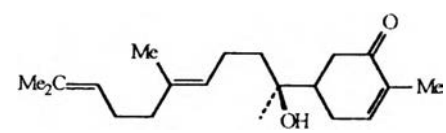
[60] crolechinol



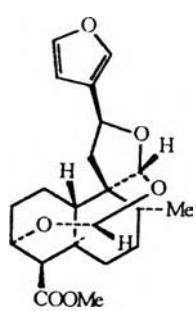
[61] crolechinic acid



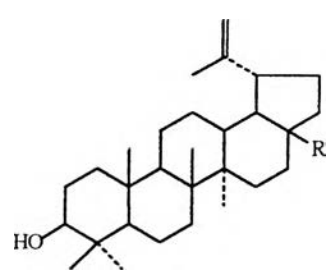
[62] β-sitosterol-D-glucopyranoside



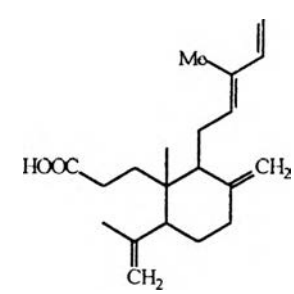
[64] insecticidal diterpene



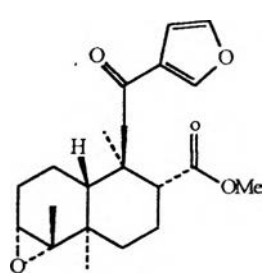
[63] crovatin



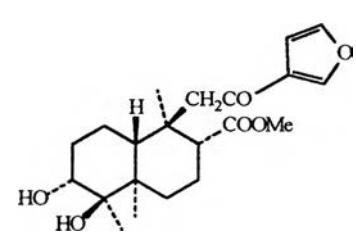
R = CH_3 [38] lupeol
R = OH [65] betulin



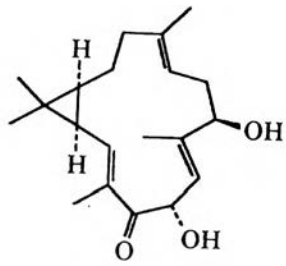
[66] maravuic acid



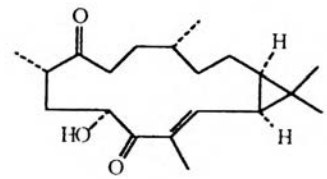
[67] epoxychiromodine



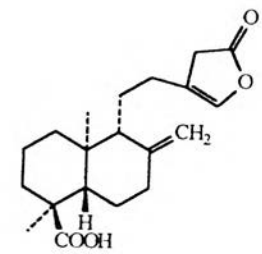
[68] chiromodine



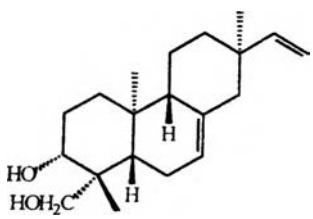
[69] croton casbane diterpene



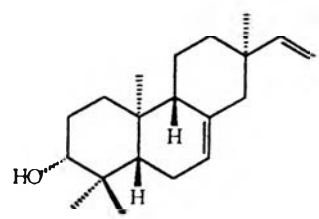
[70] crotonitenone



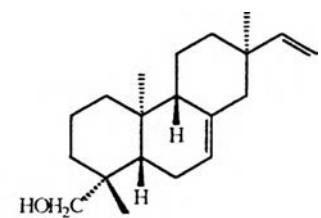
[71] nivenolide



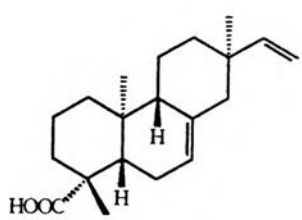
[72] oblongifoliol



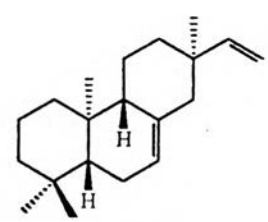
[73] 19-deoxyoblongifoliol



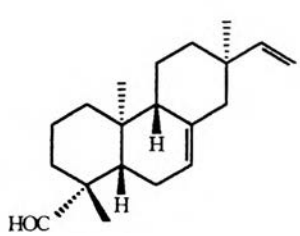
[74] 3-deoxyoblongifoliol



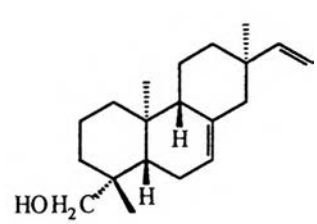
[75] oblongifolic acid



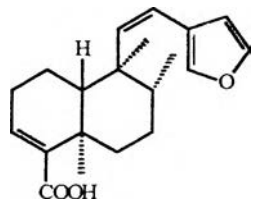
[76] *ent*-isopimara-7,15-diene



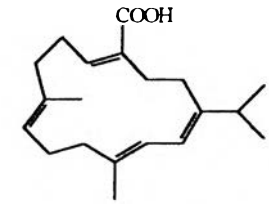
[77] *ent*-isopimara-7,15-diene-19-aldehyde



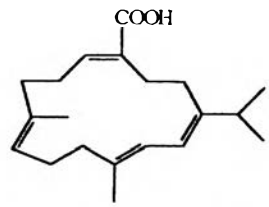
[78] 19-hydroxy-*ent*-isopimara-7,15-diene



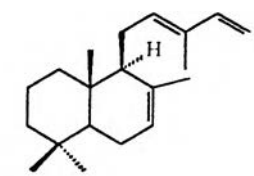
[79] 11-dehydro-(-)-hardwickiic acid



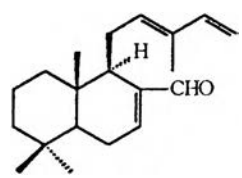
[80] crotocembraneic acid



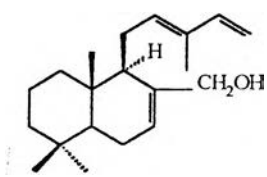
[81] neocrotocembraneic acid



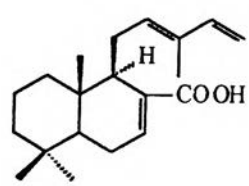
[82] labda-7,12(*E*),14-triene



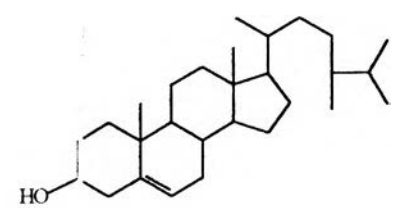
[83] labda-7,12(*E*),14-triene-17-al



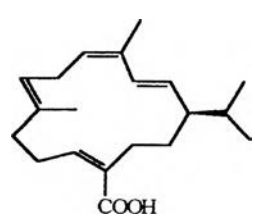
[84] labda-7,12(*E*),14-triene-17-ol



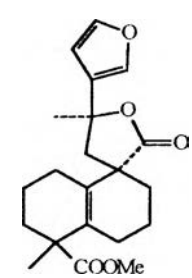
[85] labda-7,12(*E*),14-triene-17-oic acid



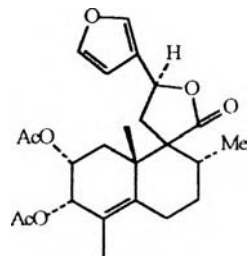
[86] campesterol



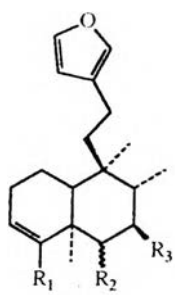
[87] poilaneic acid



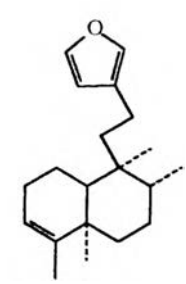
[88] penduliflaworosin



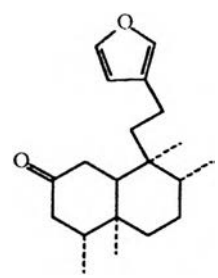
[89] furolactone diterpene



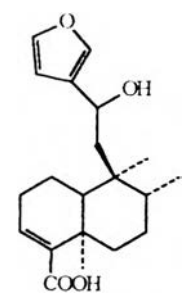
	R_1	R_2	R_3
[90] 6α-hydroxyannonene	Me	αOH	H
[91] 6α,7β-dihydroxyannonene	Me	αOH	OH
[92] 6α,7β-diacetoxyannonene	Me	αOAc	OAc



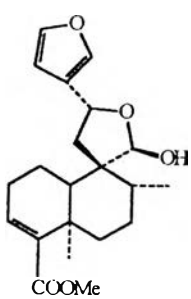
[93] *trans*-annonene



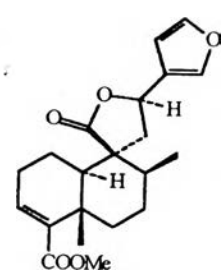
[94] *trans*-cascarillone



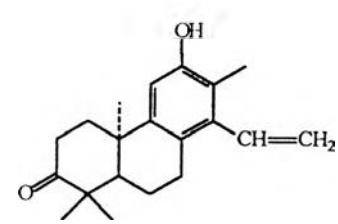
[95] 12-hydroxyhardwickiic acid



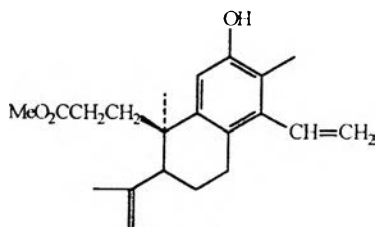
[96] sonderianial



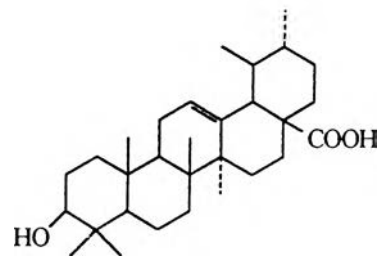
[97] sonderianin



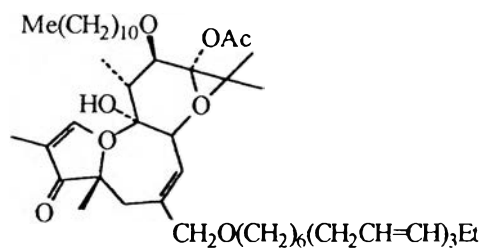
[98] sonderianol



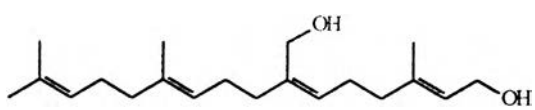
[99] 3,4-secosonderianol



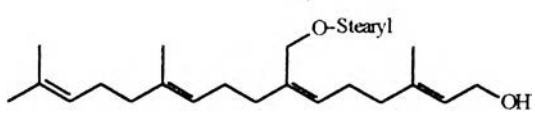
[101] ursolic acid



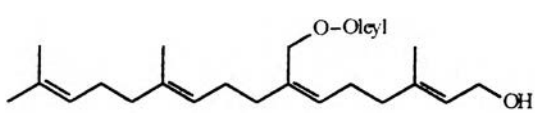
[100] 12-O-dodecanoyl-13-O-acetylphorbol-20-linolenate



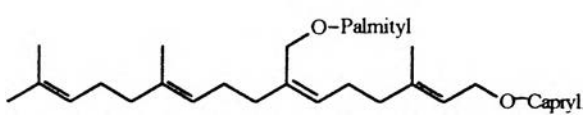
[102] plaunotol



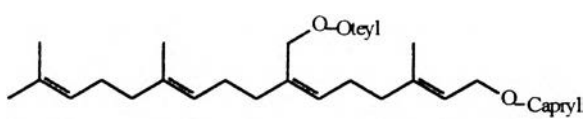
[103] geranylgeraniol ester A



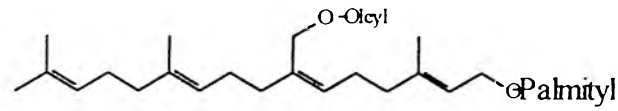
[104] geranylgeraniol ester B



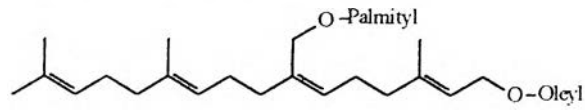
[105] geranylgeraniol ester C



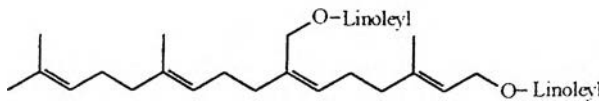
[106] geranylgeraniol ester D



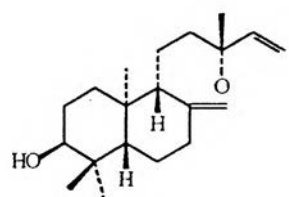
[107] geranylgeraniol ester E



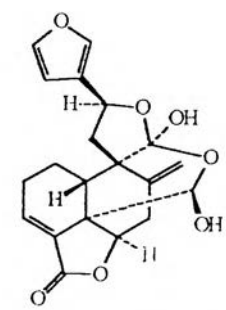
[108] geranylgeraniol ester F



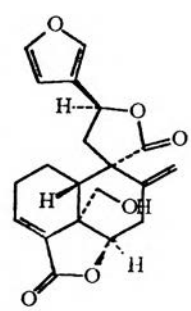
[109] geranylgeraniol ester G



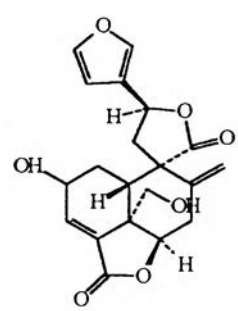
[110] *ent*-3α-hydroxy-13-epimanool



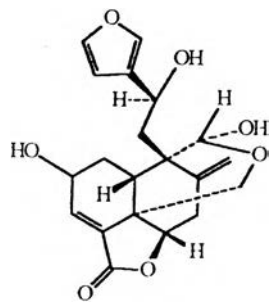
[111] plaunol A



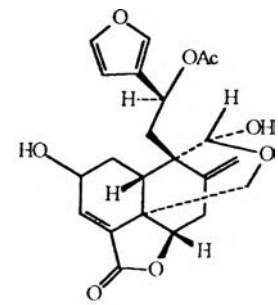
[112] plaunol B



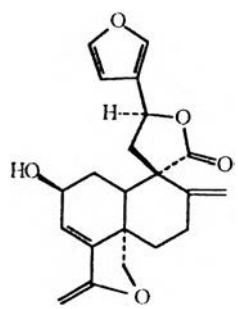
[113] plaunol C



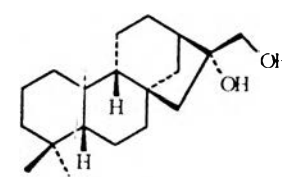
[114] plaunol D



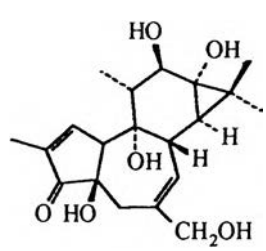
[115] plaunol E



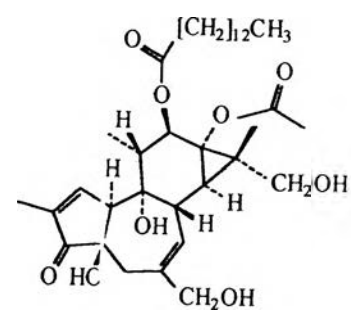
[116] plaunolide



[117] *ent*-16β,17-dihydroxykaurane



[118] phorbol



[119] croton factor A1

4. Biogenesis of labdane and kaurane diterpenes

The key precursor in the formation of most diterpenes is geranylgeranyl diphosphate. Important reactions in its transformation are hydrolysis of diphosphate group, reduction of double bonds and cyclization to form different types of diterpenes (Luckner, 1990).

Labdanes, bicyclic diterpenes, are one of the largest classes of diterpenes. In gymnospermae, they are found in Pinaceae (Hanson, 1994). In the monocotyledons, they are present in Zingiberaceae (Hanson, 1988). Labdanes widely distribute among the dicotyledons are in the families Compositae, Rosaceae, Acanthaceae, Labiatae, Cistaceae, Nolanaceae, Scrophulariaceae, Lythraceae, Verbenaceae, Caprifoliaceae, Meliaceae, Gesneriaceae, Annonaceae and Euphorbiaceae (Hanson, 1984-1998). They are also found in Mollusca of the animal kingdom (Hanson, 1997).

Kauranes, tetracyclic diterpenes, were found in the lower plants, liverwort (Hanson, 1986). The families Compositae, Labiatae, Annonaceae, Araucariaceae, Aristolochiaceae, Rosaceae, Leguminosae, Umbelliferae and Euphorbiaceae are found to be the sources of this type of diterpenes (Hanson, 1984-1998).

5. Pharmacology of diterpenes

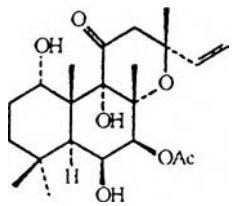
5.1 Labdane diterpenes

The discovery of new labdanes increased the number of pharmacological activities. For example :Forskolin [120], an epoxy labdane derivative isolated from the roots of the Indian herb *Coleus forskohii* (Labiatae), provided the major pharmacological effects including vasodilation, lowering of blood pressure, positive inotropy in cardiac muscle and bronchodilation (Hanson, 1991). The hexane extract of *Sideritis javalambrensis* (Labiatae) showed anti-inflammatory activity and *ent*-16-hydroxy-*ent*-13-epimanoyl oxide [121] was isolated (Alcarez *et al.*, 1989). This effect has also been described for andrographolide [122], neoandrographolide [123], deoxyandrographolide [124] and deoxydehydro-andrographolide [125] from the well known medicinal herb *Andrographis*

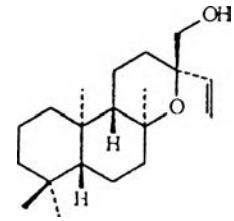
paniculata (Acanthaceae) (Manez *et al.*,1990). More interesting, andrographolide [122] was found to show significant cytotoxicity against KB and P388 cell (Siripong *et al.*, 1992). The cytotoxic lactone accuminolide [126] from *Neouvaria acuminatissima* (Annonaceae) showed significant activity against a number of human cancer cell lines (Hanson, 1997). Galanals A [127] from *Alpinia galanga* (Zingiberaceae) showed antifungal activity (Morita and Itokawa, 1988). The seeds of *Alpinia zerumbet* (Zingiberaceae) which are used in Chinese medicine for stomach problems, have been shown to contain zerumin A [128] (Hanson, 1998). Leonotinin [129] was obtained from *Leonotis nepetaefolia* (Labiatae), a plant used for treating skin infection (Hanson, 1998). For hepatoprotective effect, andrographolide [122] showed a significant dose dependent protective activity against paracetamol-induced toxicity on isolated rat hepatocyte (Visen *et al.*, 1993).

5.2 Kaurane diterpenes

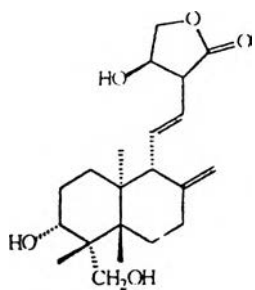
Stevioside, from *Stevia rebaudiana* (Compositae), is not only a sweetener but also a hypotensive agent. It induces diuretic, natriuresis and a fall in the renal reabsorption of glucose (Hanson, 1994). The hydroxylactone tripterifordin [130], obtained from *Tripterygium willfordii* roots, has been shown to possess anti-HIV activity (Hanson, 1994). The termite antifeedant activity of extract of *Xylopia aethiopica* (Annonaceae) has been attributed to the presence of *ent*-kaur-16-en-19-oic acid [131] (Hanson, 1997). 17-O-β-D-glucopyranosyl-16β-H-*ent*-kaur-19-oic acid [132] has been isolated from *Inula britannica* (Compositae), a Chinese medicinal plant used in treatment of inflammation (Hanson, 1998). *Siegesbeckia pubescens* (Compositae) is a Chinese medicinal plant used for the treatment of rheumatic arthritis, from which a number of hydroxylated kaurenes, including [133], have been isolated (Hanson, 1994).



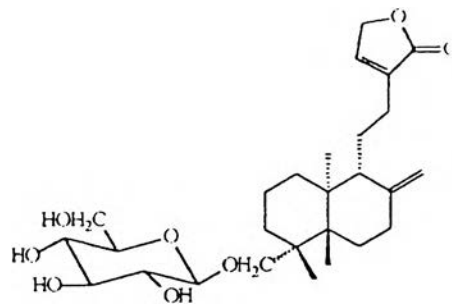
[120] forskolin



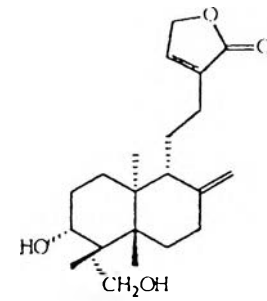
[121] *ent*-16OH-*ent*-13-epimanoyl oxide



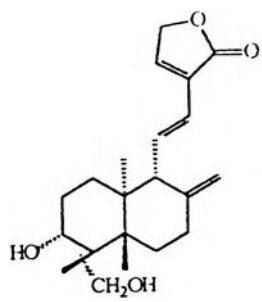
[122] andrographolide



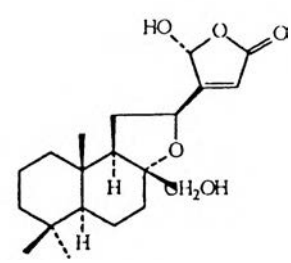
[123] neoandrographolide



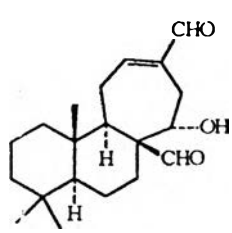
[124] deoxyandrographolide



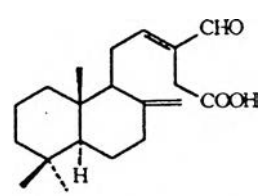
[125] deoxydehydroandrographolide



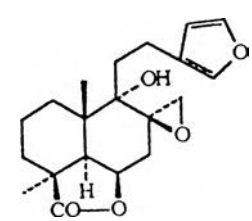
[126] accuminolide



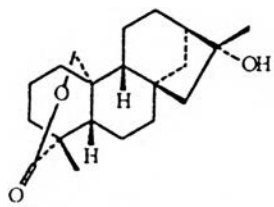
[127] galanals A



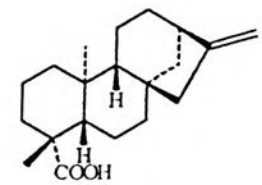
[128] zerumin A



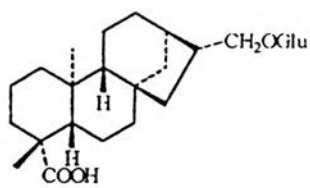
[129] leonotinin



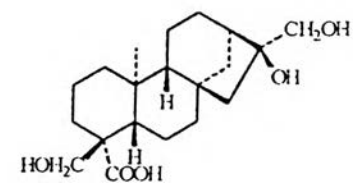
[130] tripterifordin



[131] *ent*-kaur-16-en-19-oic acid



[132] 17-O-β-D-glucopyranosyl-16β-H-*ent*-kaur-19-oic acid



[133]