CHAPTER I

HISTORICAL INTRODUCTION

Plants in the genus *Dysoxylum* belong to the family Meliaceae (Hooker and Jackson, 1885). According to Mabberley and Pannell (1989), there are about 70 species of tropical Eastern Asia and Western Pacific, 17 species of which are found in Malaya as follows :

Dysoxylum acutangulum Miq.

D. alliaceum (Blume) Blume.

D. angustifolium King.

D. arborescens (Blume) Miq.

D. cauliflorum Hiern

D. cyrtobotryum Miq.

D. densiflorum (Blume) Miq.

D. dumosum King.

D. excelsum Blume.

D. flavescens Hiern

D. grande Hiern

D. macrocarpum Blume.

D. mollissimum Blume.

D. papillosum King.

D. rigidum (Ridley) Mabb.

D. rugulosum King.

D. sp. 1

The plant used in this investigation was found in Uthai Thani province, Thailand. The herbarium specimen of this plant was submitted to the Botany Section, Technical Division, Department of Royal Forest, Ministry of Agriculture and co-operative, Thailand, where it was identified as *Dysoxylum grande* Hiern. A preliminary study of this plant was done in 1992 by the auther and it was found that the leaf extract give a positive test for alkaloids. The result was confirmed by thin-layer chromatographic data.

The medicinal uses of the Meliaceous plants are well documented. The following pages contain literature survey about the medicinal uses and poisonous properties of plants in the family Meliaceae.

Several species of *Dysoxylum* were reported to be used as medicinal plants in many Asian countries. In Indo-China, the essential oil of *D. loureiroi* Pierre (*Epicharis loureiroi*) was used in native medicine. In Malay Peninsula, a poultice of the fruits of *D. cauliflorum* Hiern was used to treat rheumatism, and a plaster of the boiled roots was applied to treat abdominal pain. In Indonesia, the nauseous juice of the bark of *D. gaudichaudianum* (A Juss.) Miq. was used internally as emetic and externally as astringent (Perry, 1980).

Volkonsky (1937) studied the leaves of *Melia azedarach* L. for insecticidal effect, it was noticed that some types of the insects have never touched the leaves of ihis plant. Other plants sprinkled with extract of *Melia* leaves were equally protected against locust.

Carratala (1939) reported the death of a 3 year-old child some days after eating the fruits of *Melia azedarach* Linn. An aqueous extract of the fruits when injected into the rabbit (1 ml sc.) produced dyspnea, tremor, convulsion and death on the following day. When given by mouth, the extract also produced gastrointestinal symptoms.

Guevara(1940) performed the pharmacodynamic study of the fruits of *Lansium domesticum* Corr. and found that the peel of fruit contains a resin which checks diarrhoea and relieves intestinal spasm. A dilute aqueous suspension of the resin inhibits the contraction of rabbit intestine *in vitro*.

Sinha and Gulati (1963) studied the seed cake of *Azadirachta indica* Juss. and found that the alcoholic extract of seed cake left after the oil expression shown repellant action against migratory locusts, the marc was inactive.

Berndt (1965) reported the use of margosa oil from *Azadirachta indica* A Juss. in dermatological preparations in Indian pharmacy.

During 1968-1972, Dhar *et al.* performed the experiments on the biological activity screening of Indian plants including plants in family Meliaceae. The results were summarized in Table 1.

Table 1. The biological activity screening of some Meliaceous plants.

Plant	Part	Activity observed	Reference
Aglaia odoratissima Bl.	px	anticancer	Dhar(1973)
Amoora wallichii King.	st	anthelmintic	Dhar(1968)
		antiviral	"
		anticancer	"
Aphanamixis polystachya	st	anticancer	Dhar(1968)
(Wall.) Parker.		blood pressure	"
Cedrela microcarpa C.DC.	px	CNS effect	Dhar(1973)
Cedrela toona Roxb.	sb	spasmogenic	Dhar(1968)
		anticancer	"
C. toona Roxb.	lf	antiprotozoa	Dhar(1968)
		hypoglycaemic	"
		spasmogenic	"
		CNS effect	"
Cipadessa fruticosa Bl.	px	spasmogenic	Bhakuni(1969)
Dysoxylum binectariferum	px	CNS effect	Dhar(1973)
Hook.f.			
D. procerum Hiern.	px	-	Dhar(1973)
Melia azedarach L.	sb	antiviral	Bhakuni(1969)
		spasmogenic	"
		anticancer	"

(px = plant excluding, st = stem, sb = stem bark, lf = leaves)

Martinez Nadal *et al.* (1973) investigated the toxicological effects of the active principles of *Swietenia mahogani* Jacq. and found that the precipitates obtained from the bark by diethyl ether extraction, petroleum ether extraction and an oil obtained from the seeds were sufficiently toxic to *Drosophila melanogaster* to warrant their use as pesticides. The active principles were apparently non-toxic to human.

Qadri and Rao (1977) studied the effect of combining some indegenous plant seed extracts against household insects and found that neem (*Azadirachta indica* Juss.) extract showed synergistic action in combination with custard apple (*Annona recticulata* L.) seed extract against pulse beetle, lesser grain borer and housefly. This combination was half as toxic against lesser grain borer and equitoxic to DDT against housefly.

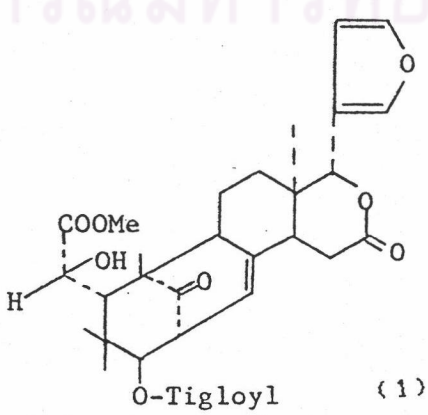
Hu and co-workers (1983) performed the experiment on chinaberry seed oil (*Melia azedarach* Linn.) effect on rice insects. It was found that the oil acted as antifeedant to yellow rice borers, White-backed planthoppers and brown planthoppers and showed some systemic effects. However it had insignificant antifeedant effects on striped rice borers and pink rice borers but showed no effect on leaf-hoppers and rice thrips.

Chiu (1984) performed bioassay studies on the active principles of Meliaceous plants including neem (*Azadirachta indica* Juss.) and chinaberry (*Melia toosendan* Sieb & Zucc.). It was found that, both azadirachtin (39) and toosendanin showed potential as strong antifeedants as demonstrated by the bioassays results with the larvae of *Spodoptera litura*.

Further phytochemical studies of Meliaceous plants were reported as follows :

Volkonsky (1937) studied the leaves of *Melia azedarach* L. and reported the presence of the alkaloid paraisine.

Guha-Sircar and Chakravarty (1951) studied the seeds of *Swietenia macrophylla* King. From this study, two crystalline substances were isolated one of which non-bitter named swietenine (1), the other bitter named swietenolide (2). The structure and steriochemistry of 1 and 2 were determined later in 1965 by Connolly *et al.* (1965,1965).



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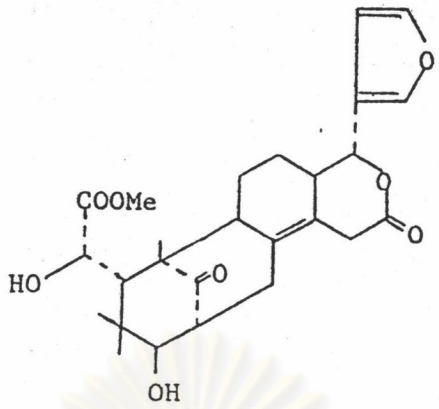
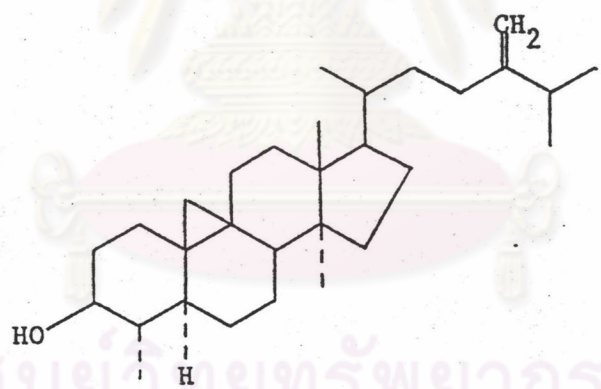


(2)

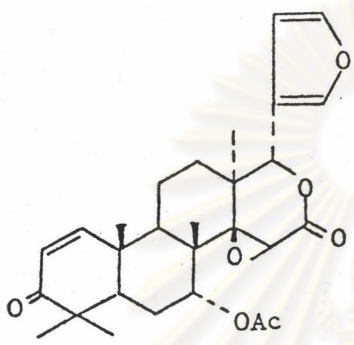
Amoros-Marin *et al.* (1959) reported the isolation of cycloeuclalenol (3) from the unsoponifiable fraction of the oil from the wood of *Swietenia mahogani* Jacq.



(3)

Akisanya and co-workers (1960) investigated some species of the genus *Entandrophragma* and the following results were reported. From the timber of *Entandrophragma angolense* (Welw.) C.DC., two triterpenes, gedunin (4), the structure subsequently characterized by Akisanya *et al.* (1961), and methyl

angolensate (5) were reported. Another triterpene, entandrophragmin (6) was isolated from *Entandrophragma cylindricum* Sprague. of which structure was characterized by Taylor and Wragg (1967).



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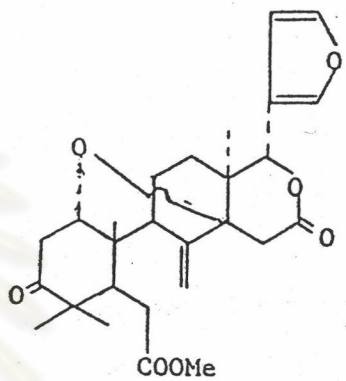

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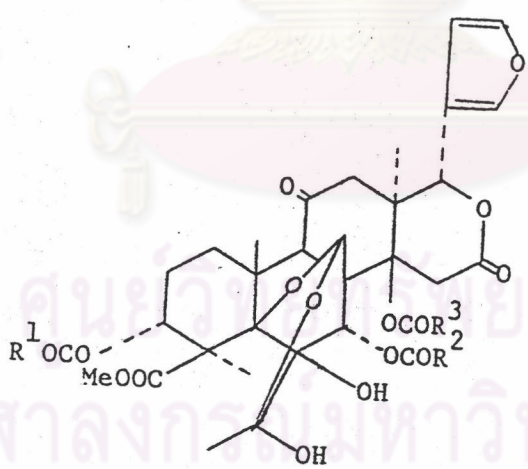
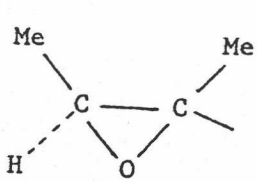


R^1 = Me_2CH-

R^2 = MeEtCH —

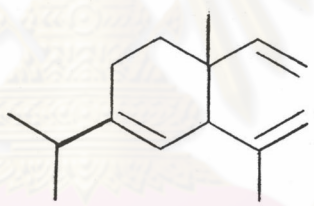
R^3 =



(6)

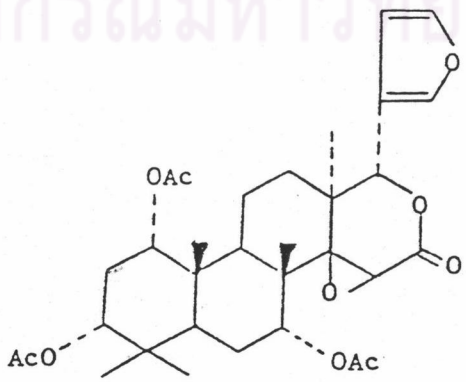
In addition, gedunin (4) was also obtained from *Entandrophragma delevoyi* De Wild. and *Xylocarpus granatum* Koen. as well (Taylor, 1965). Besides these, there were some reports on the isolation of methyl angolensate (5) from the heartwood of *Cedrela odorata* L. (Chan, Magnus and Mooto (1967)) and the seeds of *Swietenia mahogani* Jacq. (Taylor, 1969).

Gough and Powell (1961) isolated the sesquiterpene from the wood oil of *Dysoxylum frazenarum* Benth. and three years later Gough and Sutherland (1964) described this structure as δ-elemene (7).



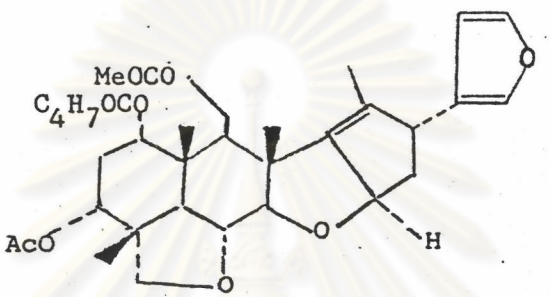
(7)

Bevan *et al.* (1962) isolated a new furanoid lactone called khivorin (8), from the heartwood of *Khaya ivorensis* A. Chevalier.



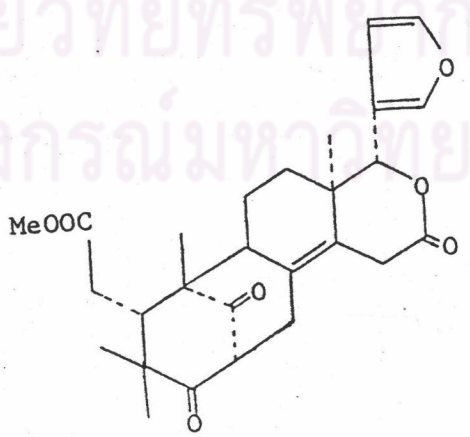
(8)

Henderson *et al.* (1964) investigated the seed oil of *Melia azedirachta* Linn. and found the presence of triterpenoid, salannin (9). Five years later, this compound was also found in the mature fruits of *Melia dubia* Cav. by Silva *et al.* (1969).



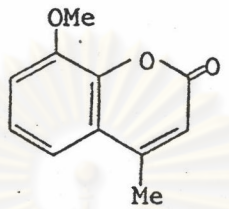
(9)

Connolly *et al.* (1965) isolated and characterized a crystallinelactone, mexicanolide (10) from *Cedrela mexicana* M. Roem.



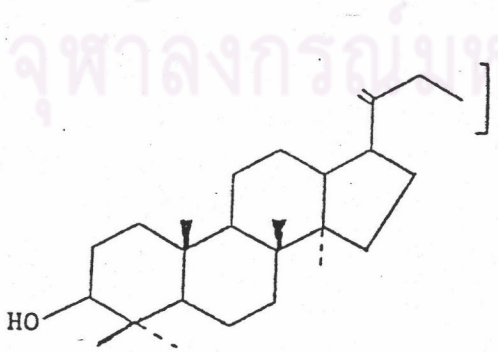
(10)

In the same years, Bevan and Ekong (1965) extracted two specimens of *Ekebergia senegalensis* A. Juss. from the Plateau province of Northern Nigeria and noted that the major crystalline product was 8-methoxy-4-methyl coumarin (11).



(11)

In addition, Shiengthong *et al.* (1965) studied the leaves of *Aglaia odorata* Lour. and reported the presence of tetracyclic triterpene, aglaiol (12). The configuration of this compound was further determined by Boar *et al.* (1977,1973). The leaves of the same plants were further investigated by Shiengthong *et al.* (1974) and the presence of two more tetracyclic triterpenes, aglaiondiol (13) and aglaitriol (14) were reported



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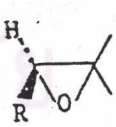

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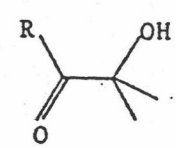

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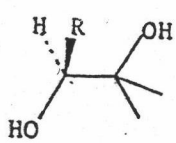
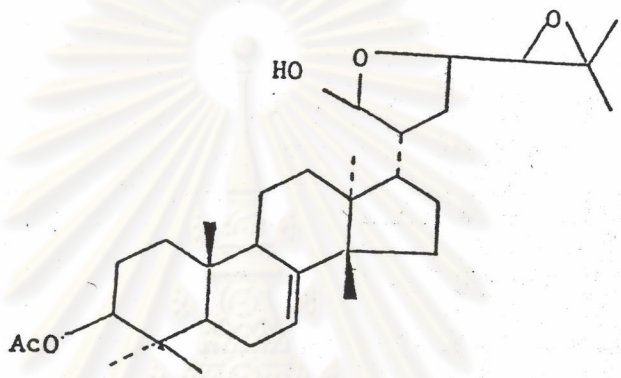


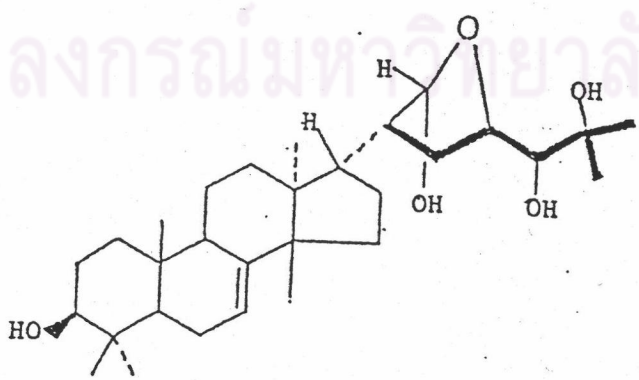
In 1967, serveral phytochemical studied of Meliaceous plants were reported as follows :

Chatterjee and Kundu (1967) isolated a new triterpene, aphanamixin (15), from the petroleum extract of the fruits of *Aphanamixis polystachya* (Wall.) Parker.



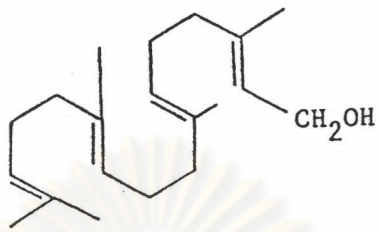
(15)

Lavie and co-worker (1967) reported the identification of crystalline substance with antifeedant activity from the fruits of *Azadirachta indica* Juss. as meliantriol (16).



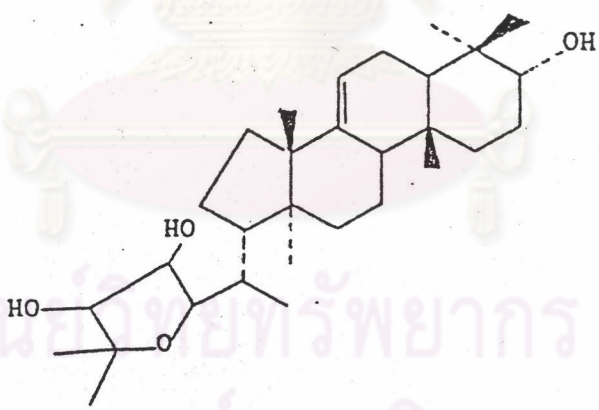
(16)

Nagasampagi *et al.* (1967) isolated geranylgeraniol (17) from the wood of *Cedrela toona* Roxb.



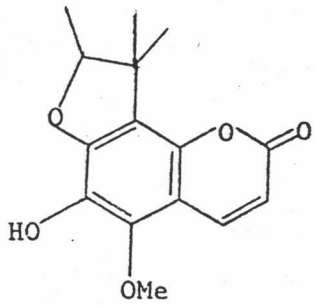
(17)

Connolly and co-workers (1967) isolated a new triterpenoid, mexicanol (18) from the heartwoods of *Cedrela glaziovii* C.DC. and *C. mexicana* M. Roem.



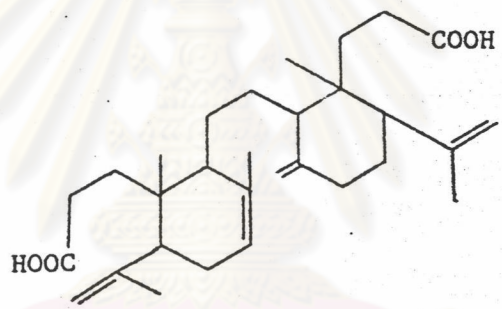
(18)

McCabe *et al.* (1967) obtained nieshoutol (19) from the heartwood of *Ptaeroxylon obliquum* Radlk. and the stucture was confirmed by Murray and Ballantyne (1969).



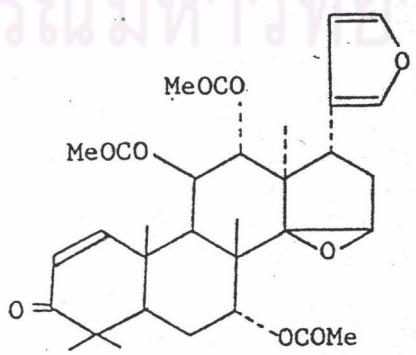
(19)

Kiang *et al.* (1967) examined the peel of the fruits of *Lansium domesticum* Corr. and reported the isolation of, a new triterpenoid acid, named lansic acid (20)



(20)

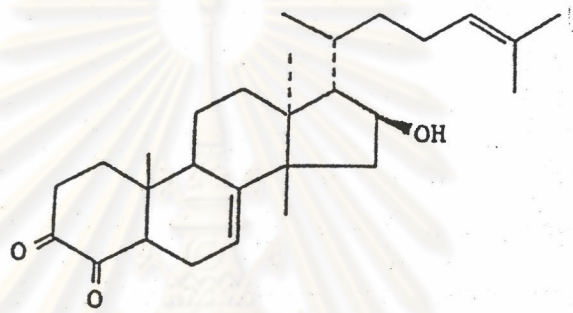
Okarie and Taylor (1967) extracted the timber of *Trichillia heudelottii* Planch. ex Oliv. and reported the presence of heudelottin (21).



(21)

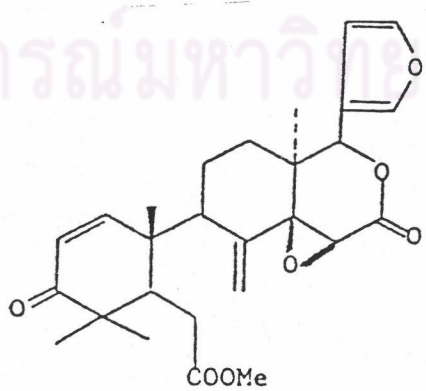
In 1968, there are four phytochemical studies of Meliaceous plants reported as follows :

Chang and Chiang (1968) performed phytochemical studied on the bark of *Melia azedarach* and reported the isolation of a new triterpenoid of the euphane (20 β-H) series, named kulinone (22).



(22)

Okarie and Taylor (1968) examined the seed of *Cedrela odorata* L. and reported the presence of limonoid, mexicanolide (10), andirobin (23) and 6-deoxy swietenolide (24), together with a new compound which had been identified as 6-hydroxy mexicanolide (25).



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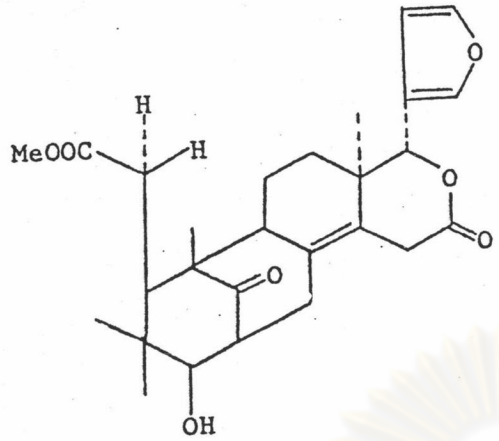

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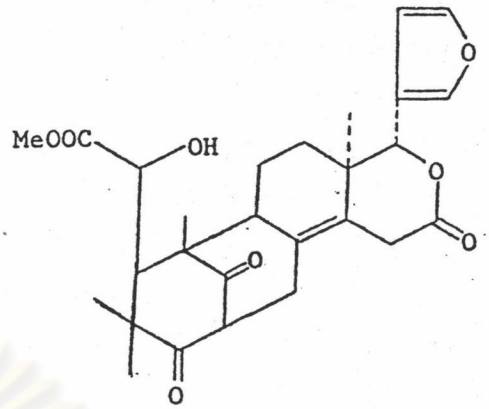
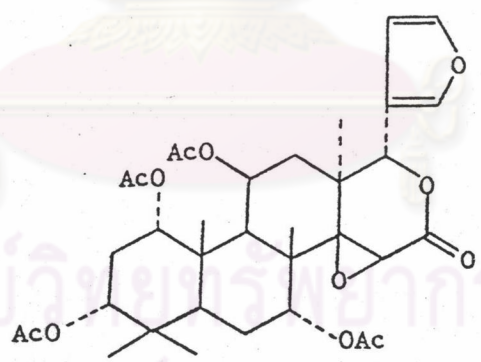


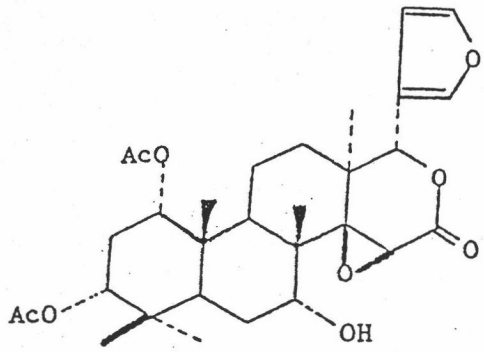
(25)

Taylor (1968) extracted the timbers of *Khaya madagascariensis* Jumella et Perrier and found that the main constituent of this extract was 11β-acetoxykhivorin (26).



(26)

Connolly *et al.*(1968) obtained grandifolione (27) from the trunk wood of *Khaya grandifoliola* C.DC.. Three years laters, the precence of grandifoliolenone (28), from the same plant, was reported by Connolly and McCrindle (1971).



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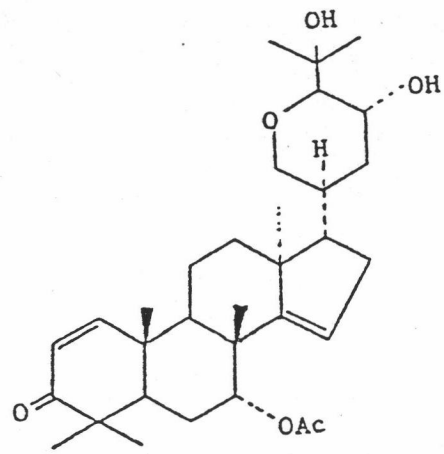
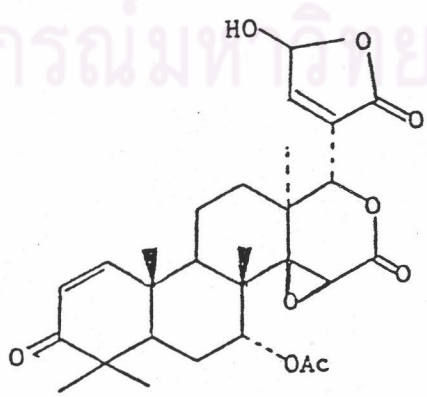


(28)

In 1969, Johns and Lamberton (1969) performed phytochmical screening of some New Guinea plants for alkaloid and found positive result in serveral species of *Aglaia*. The leaves of one species were then further investigated but the result showed the presence of tiglamide as a major constituent in the crude alkaloid fraction.

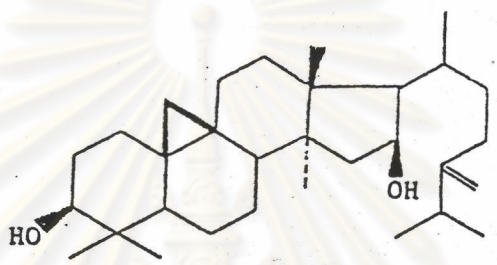
In the same year, Burke and co-workers (1969) examined the benzene extract of *Cedrela odorata* L. and reported the isolation of gedunin (4) together with a new non-furanoid tetranortriterpenoid, photogedunin (29).



(29)

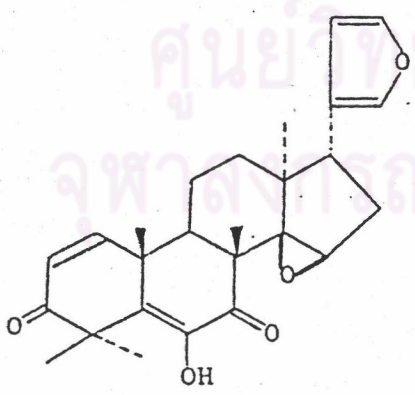
In 1971, Two phytochemical studies of Meliaceous plants were carried out and the results were reported as follows :

Chakraborty and Basak (1971) isolated a new tetracyclictriterpene, cyclomahogenol (30) from the leaves of *Swietenia mahogani* Jacq.



(30)

Chatterjee and co-workers (1971) reported the presence of cedrelone (31), 1,2-dihydrocedrelone (32) from the seeds of *Cedrela toona* Roxb.



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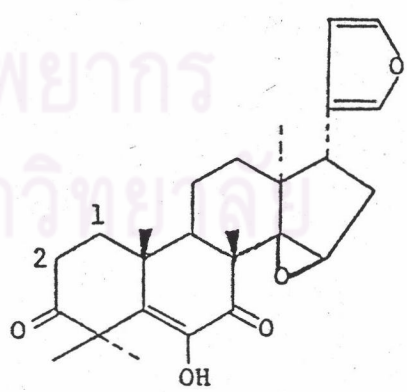
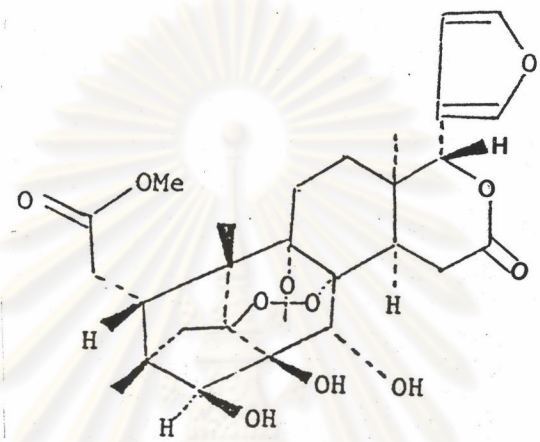


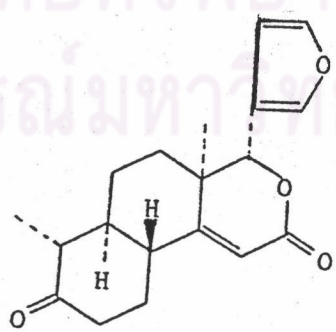
(32)

In 1972, Arndt and Baarschers (1972) extracted the bark of *Entandrophragma caudatum* Sprague. by the conventional alkaloid extraction method and obtained a meliacin named phragmalin (33).



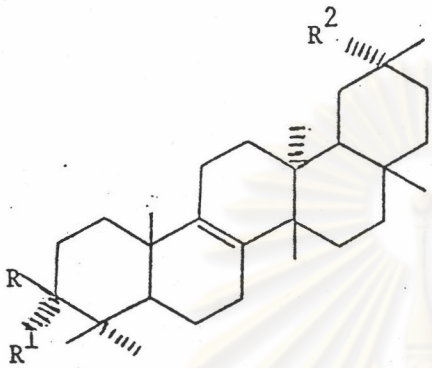
(33)

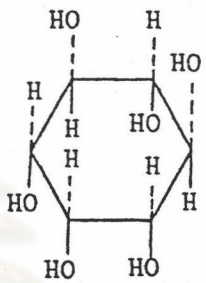
Chan *et al.* (1972) investigated the specimen of *Cedrela odorata* obtained from St Elizabeth, Jamaica and reported the precence of a new compound odoratin (34)



(34)

In the same years, Sim and Lee (1972) isolated bryonolic acid (35), bryononic acid (36), mesoinositol (37) and mucic acid (38) from the fruits hulls of *Sandoricum indicum* Cav.

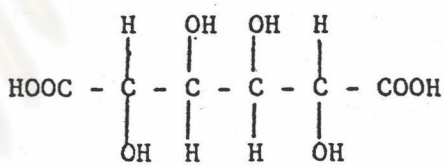




(37)

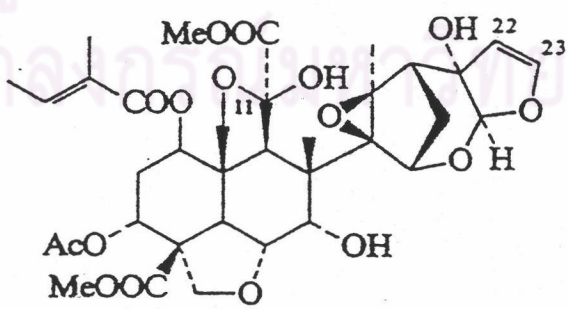
(35) R = OH, R^1 = H, R^2 = COOH

(36) R = R^1 = O, R^2 = COOH



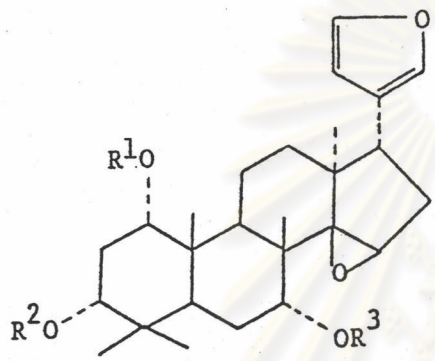
(38)

In 1973, Morgan and Thornton (1973) isolated an insecticidal active compound, azadirachtin (39) from the fruits of *Melia azedarach* Linn.



(39)

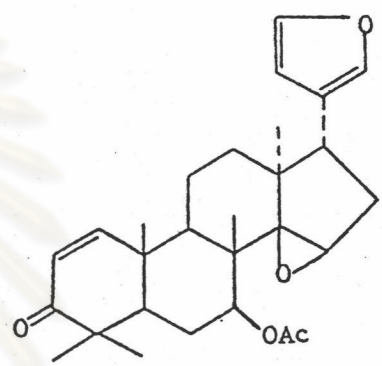
In the same years, Chan *et al.* (1973) investigated the ripe fruits of *Trichilia havanensis* Jacq. and reported the presence of four new tetranortriterpenes called havanensin triacetate (40), havanensin-3,7-diacetate (41), havanensin-1,7-diacetate (42) and trichilenone acetate (43).



(40) $R^1 = R^2 = R^3 = Ac$

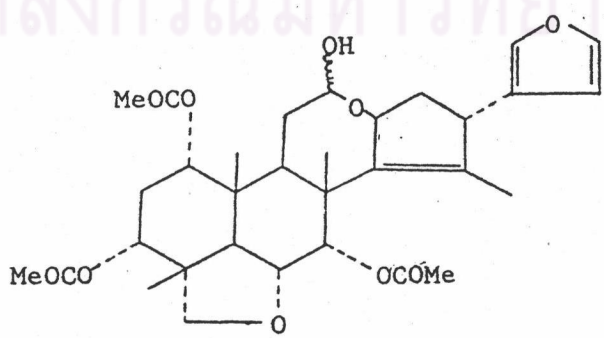
(41) $R^1 = H$, $R^2 = R^3 = Ac$

(42) $R^2 = H$, $R^1 = R^3 = Ac$



(43)

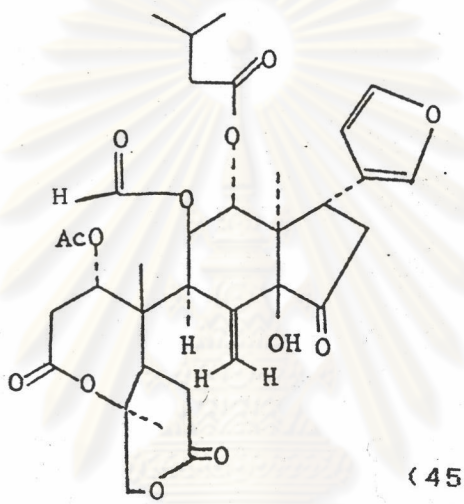
Adesida and Okorie (1973) isolated a new limonoids, heudebolin (44) from the bark of *Trichilia heudelotii* Planchex Oliv.



(44)

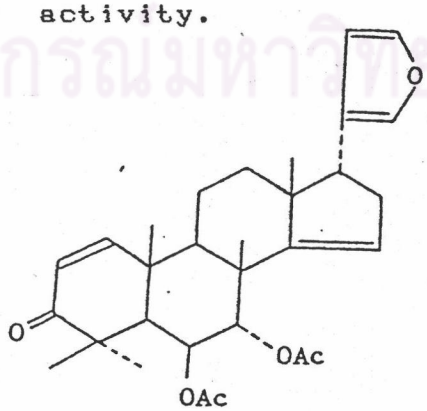
In 1976, there are three phytochemical studies of some Meliaceous plants were performed and reported as follows :

Connolly (1976) investigated the seeds of *Aphanamixis polystacha* (Wall) Parker and reported the presence of limonoid compound called rohitukin (45).



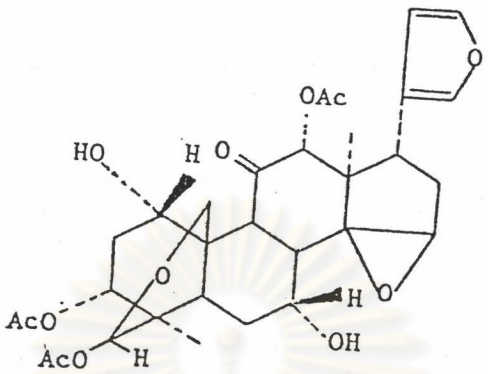
(45)

Singh *et al.* (1976) extracted the fruits of *Dysoxylum binectariferum* Hook.f. and obtained dysobinin (46), a new tetranortriterpene of the meliacin group showing general CNS-depressant action and mild anti-inflammatory activity.



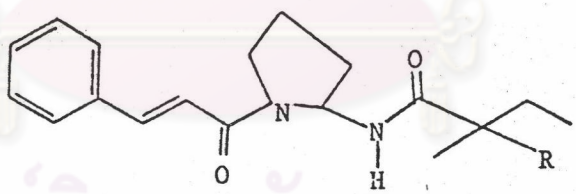
(46)

Ochi and Kotsuki (1976) isolated a new limonoids, sendanin (47) from the bark of *Melia azedarach* Linn. var *japonica* Makino.



(47)

The alkaloid chemistry of Meliaceous plants became more interesting in 1979 when Shiengthong *et al.* (1979) isolated 2 new alkaloids, odorine (48) and odorinol (49) from the leaves of *Aglaia odorata* Lour.

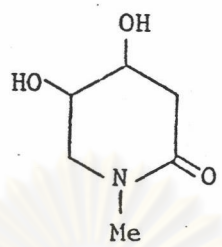


(48) = H

(49) = OH

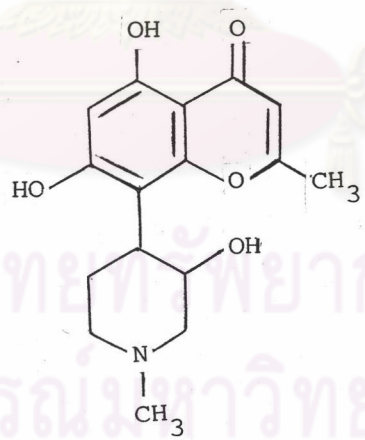
This result was supported by the work of Purushothaman *et al.* (1979) on the isolation of roxburghiline (48) which found to be identical with odorine (48) from the close related species *Aglaia roxburghiana* Hiern. Two years later, Techasauwapak (1981)

worked on the flower specimen of *A. odorata* Lour. and reported the isolation of a new alkaloid call odoram (50).



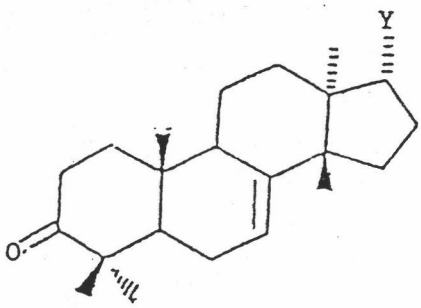
(50)

Harmon and co-workers (1979) reported the isolation and structure determination of a novel alkaloid, rohitukine (51), from the dried leaves and stems of *Amoora rohituka* Wight & Arn. (*Aphanamixis polystachya* (Wall) Parker).



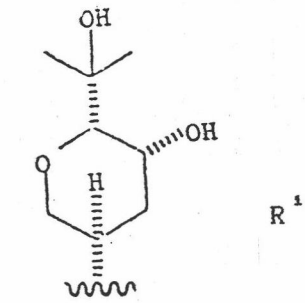
(51)

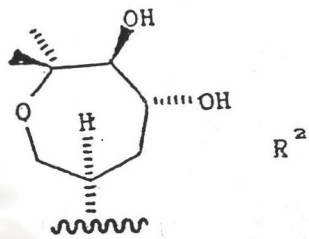
Jolad *et al.* (1980) reported the isolation of a new triterpenoid, hispidone (52) and known triterpenoid bourjotinolone A (53) from dried leaves *Trichilia hispida* Penning.



(52) Y = R^2

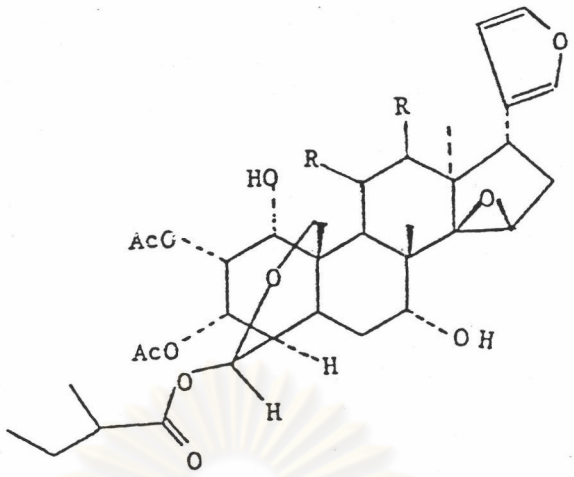
(53) Y = R^1





Pillai and Santhakumari (1981) reported the pharmacological study of nimbidin a compound isolated from the oil of *Azadirachta indica* Juss. seeds, in comparison with two standard anti-inflammatory agents, phenylbutazone, a non-steroid and prednisolone, a steroid, against various experimental models of inflammation. The results showed that nimbidin effective in both acute and chronic phases of inflammation and it can be considered as a general anti-inflammatory agent.

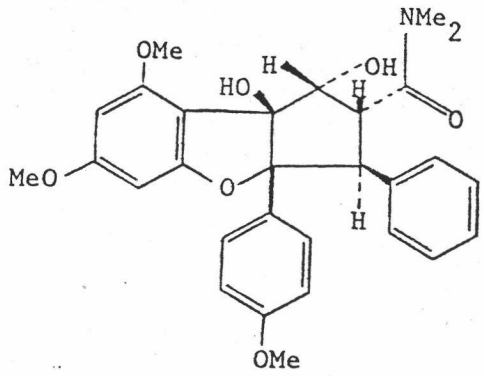
In the same year, Nakatani *et al.* (1981) studied the root bark of *Trichilia roka* P.Br. and isolated a new limonoids, Trichilins (54) which were antifeedants against the Southern army worm, *Spodoptera eridania* and the Mexican bean beetle, *Epilachna varivestis*.



(54)

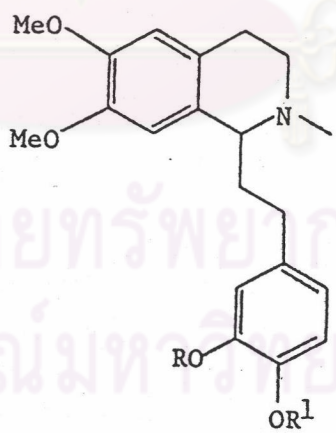
Kubo and Klocke (1982) studied the fresh fruit of *Trichilia roka* P.Br. and reported the presence of a limonoid, sendanin (47), bearing an insect growth inhibitory activity against the important North American cotton insect pests, pink bollworm, *Pectinophora gossypiella*, fall armyworm, *Spodoptera frugiperda*, tobacco budworm, *Heliothis virescens* and cotton budworm, *Heliothis zea*.

In the same year, King *et al.* (1982) worked on the specimen of *Aglaia elliptifolia* Merr. and obtained a novel 1 *H*,-2,3,3a,8b-tetrahydrocyclopenta [*b*] benzofuran, rocaglamide (55), with significant antileukemic activity against P 388 lymphocytic leukemia in CDF_1 mice.



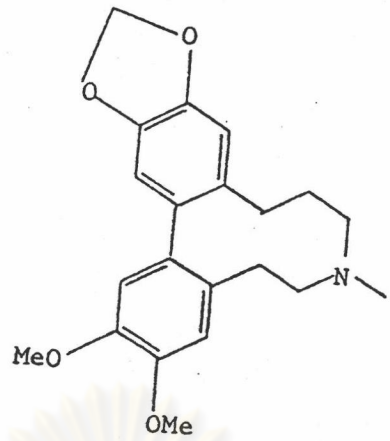
(55)

Aladesanmi *et al.* (1983) studied the leaves of a Fiji plant *Dysoxylum lenticellare* Gillespie, and obtained three new alkaloids dysoxyline (56), S-(+)-homolaudanosine (57) and dysazecine (58) and two known alkaloids, 3-epischelhammeicine (59) and 2,7-dihydrohomoerysotrine (60).

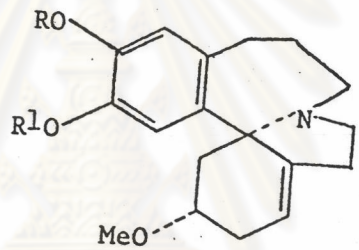


(56) R, R^1 = $-CH_2-$

(57) R = R^1 = -Me



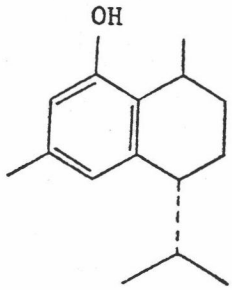
(58)



(59) R, R^1 = $-CH_2-$

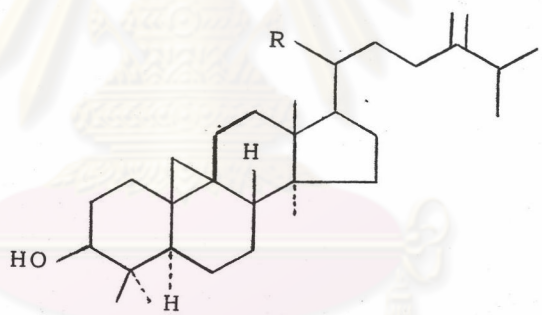
(60) R = R^1 = -Me

Nishizawa et *al.* (1983) extracted the seeds of *Dysoxylum acutangulum* Miq. and *Dysoxylum alliaceum* Bl. and obtained a fish poison principle, (+)-8-hydroxycalamenene (61), a new natural sesquiterpene phenol. This compound showed not only significant toxicity against fish but also antibacterial activity.



(61)

In the same year, Purushothaman and co-workers (1983) isolated a new tetracyclic triterpene acid, heynic acid (62) and 24-methylenecycloartane-3β-21-diol (63) from the leaves and fruits of *Heynea trijuga* Roxb.

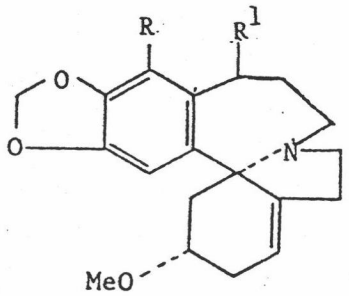


(62) R = -COOH

(63) R = $-CH_2OH$

In 1984, there were six reports on phytochemical studies of Meliaceous plants summarized as follows :

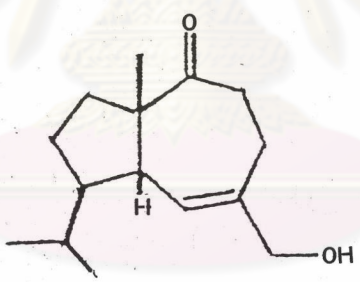
Aladesami *et al.* (1984) isolated two new homoerythrina alkaloids, deshomerythrine (64) and 3-epi-12-hydroxyschelhammericine (65) from the leaves of *Dysoxylum lenticellare* Gillespie.



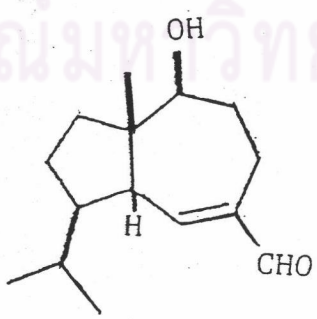
(64) R = -OMe, R^1 = H

(65) R = H, R^1 = OH

Nishizawa *et al.* (1984) isolated and identified, a unique sesquiterpenoids, name aphanamol I (66) and II (67) from dried peel of *Aphanamixis grandifolia*, as minor toxic principles.

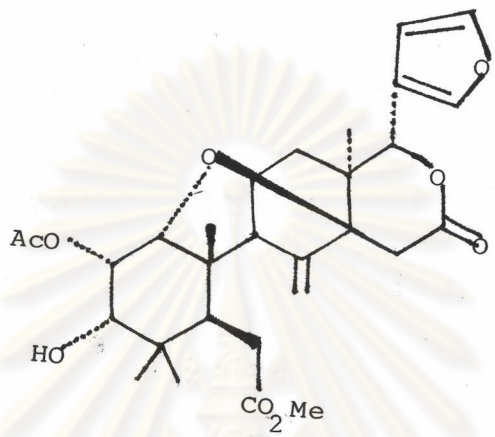


(66)

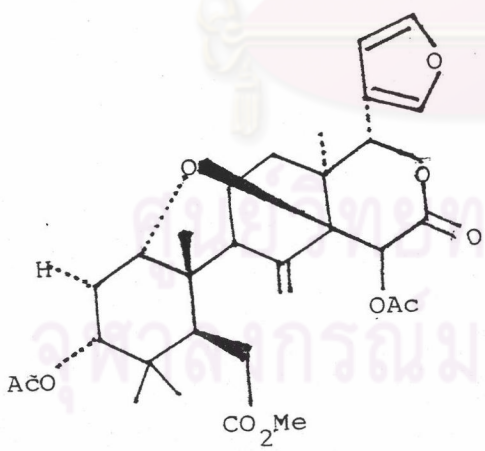


(67)

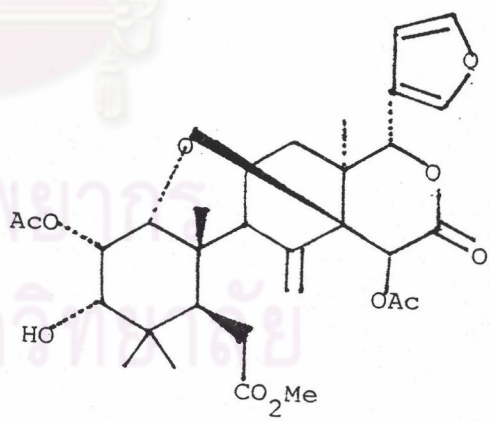
Taylor and Taylor (1984) isolated three limonoid, E.P. I (68), E.P. 2 (69), E.P. 3 (70) from seeds of *Ekebergia pterophylla* (C.DC.) Holm.



(68)

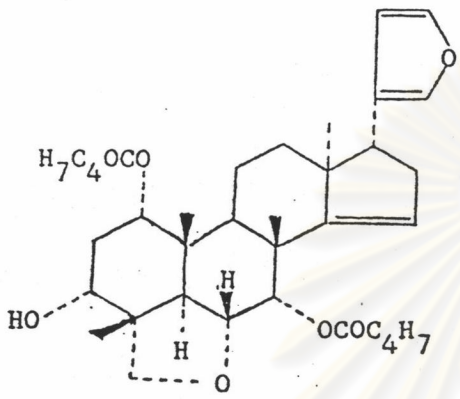


(69)

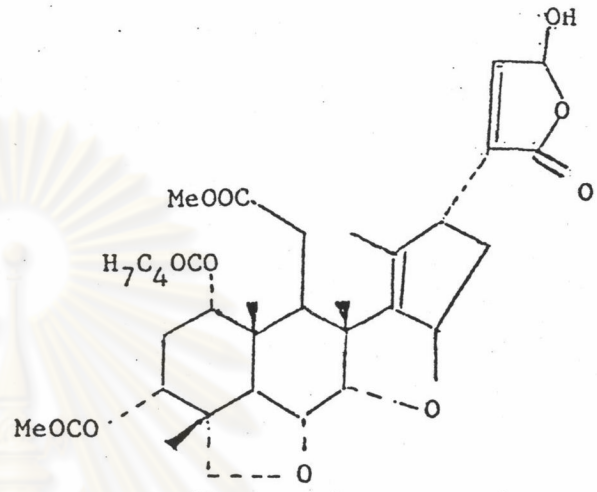


(70)

Purushothaman *et al.* (1984) reported the isolation of two new tetranortriterpenoids, compositin (71) and compositolide (72) from the leaves and seeds of *Melia dubia* Cav.

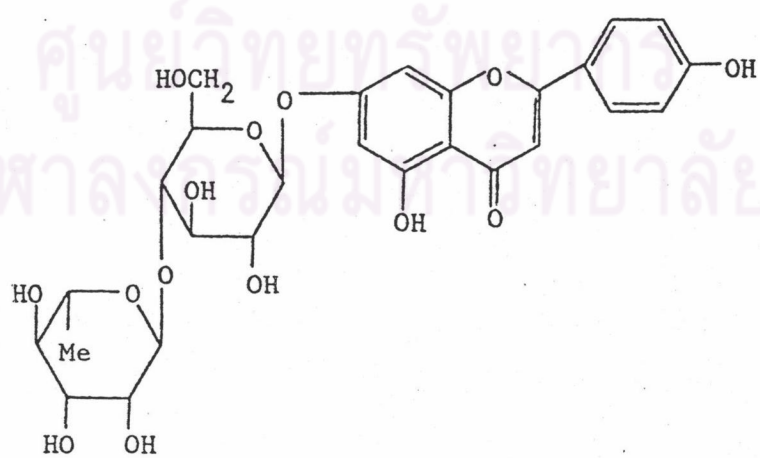


(71)



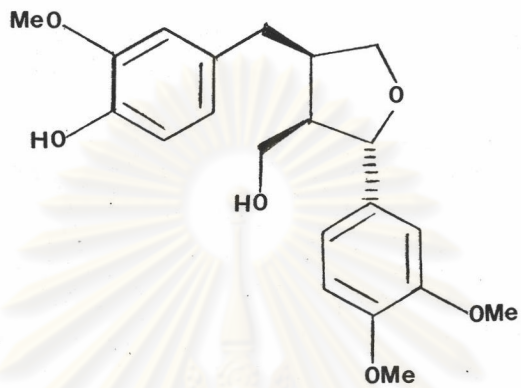
(72)

Mishra and Srivastava (1984) isolated a new flavone glycoside, 4,5-dihydroxyflavone-7-*O*-α-L-rhamnopyranosyl-(1-4)-β-D-glucopyranoside (73) from the stem barks of *Melia azedarach* Linn.



(73)

Ayoub and Kingstone (1984) reported the isolation of a compound with anticancer activity from the seed of *Turrea nilotica* Kotschy and Peyr. as laricіresinol-4-mono-methyl ether (74).

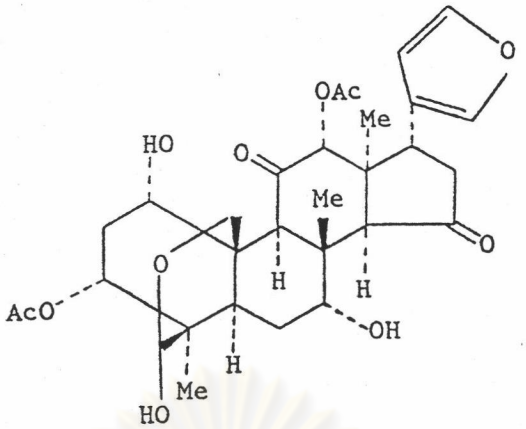


(74)

In 1985, several phytochemical studied of Meliaceous plants were reported as follows :

King *et al.* (1985) studied the stem and root bark of *Aglaia elliptifolia* Merr. and isolated rocaglamide (55). This compound showed antileukemic activity against P-388 lymphocytic leukemia in mice and inhibitory activity *in vitro* against cell derived from human epidermoid carcinoma of the nasopharynx (KB) cell.

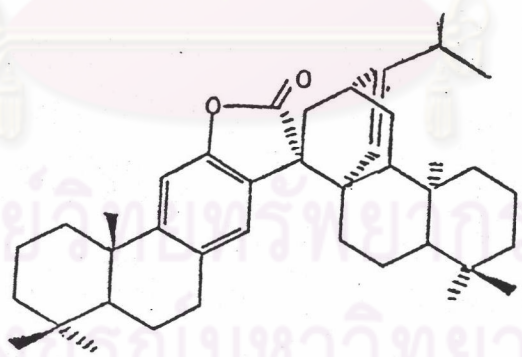
Jingxi and Axing (1985) isolated a new compound, isochuanliansu (75) from the bark of traditional Chinese medicine, *Melia toosendan* Sieb. et Zucc. and *Melia azedarach* Linn.



(75)

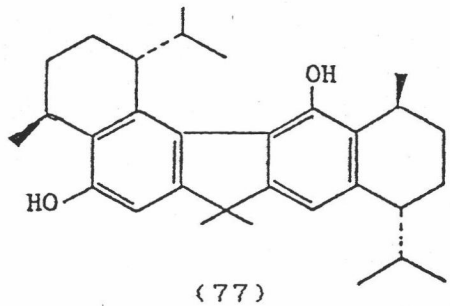
Kraus *et al.* (1985) isolated azadirachtin (39) from *Azadirachta indica* Juss. and the structure was revised based on extended reinvestigation of NMR data.

Onan *et al.* (1985) isolated a new bis-diterpene ferrubietolide (76) from *Dysoxylum lenticellare* Gillespie



(76)

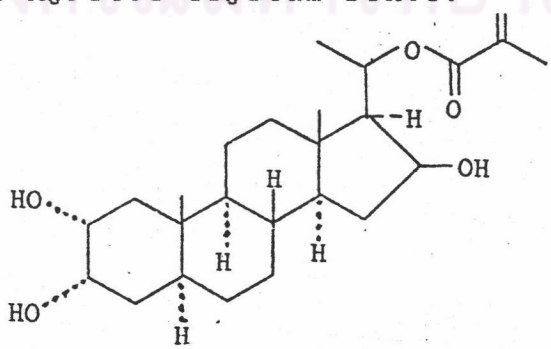
Nishizawa and co-workers (1985) isolated an unsymmetricaldimeric sesquiterpene name bicalamenene (77) from the hexane extract of the dried peel of *Dysoxylum alliaceum* Bl.



(77)

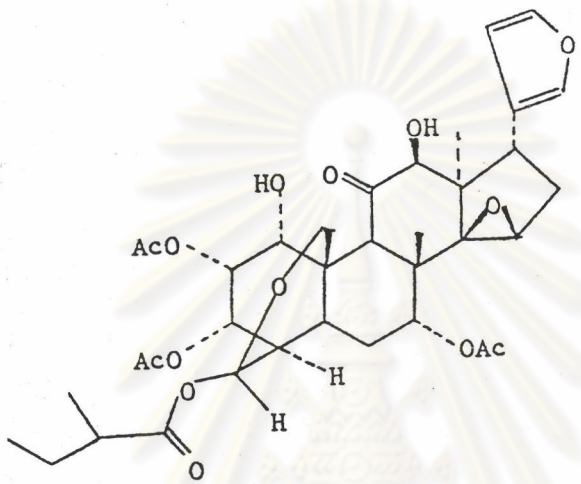
Vasudev *et al.* (1985) extracted the trunk, root bark, leaves and other parts of *Dysoxylum binectariferum* Hook.f. and reported the isolation of a chromone alkaloid identified as 5,7-dihydroxy-8-(3-hydroxy-1-methyl-4-piperidinyl)-2-methyl-4H-1-benzopyran-4-one, the structure of which was identical to that of rohitukine (51) previously isolated from *Amoora rohituka* Wight & Arn (*Aphanamixis polystachya* (Wall) Parker). The alkaloid andits salt showed excellent analgesic and immunomodulating activity *in vivo* and *in vitro*.

Nakatani *et al.* (1985) investigated the root bark of *Melia azedarach* Linn. var *japonica* Makino. and reported the presence of a new steroid, azedarachol (78) which showed antifeedant activity against the larvae of the insect pest *Ajrotis sejetum* Denis.



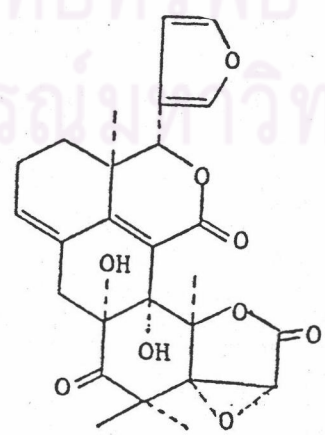
(78)

Nakatani and co-workers (1985) reported the isolation of a new limonoids called 7-acetyltrichilin A (79) from the root bark of *Trichilia roka* P.Br. This substance showed antifeedant activity against North American and Japanese pest insects.

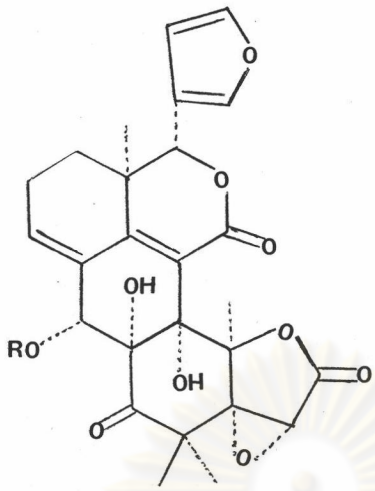


79)

Nishizawa *et al.* (1985,1988) isolated six tetranortriterpenes of novel skeleton, dukunalides A (80) B (81), C (82), D (83), E (84), F (85), as a bitter principle of the seeds of *Lansium domesticum* Corr.



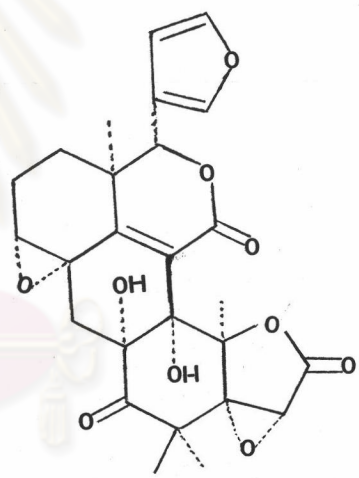
(80)



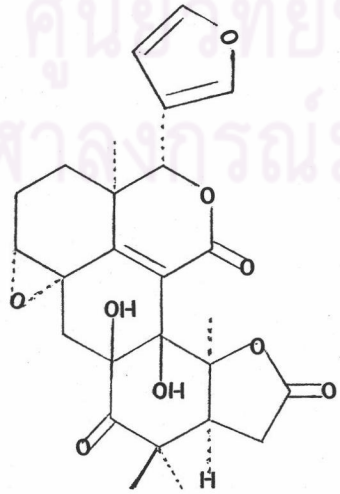
(81) R = CH_3CO

(82) R = H

(83) R = $-BrC_6H_4CO$

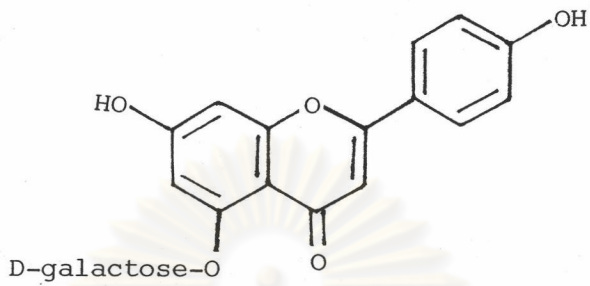


(84)



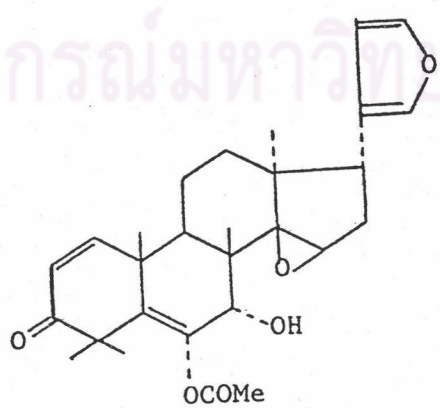
(85)

Gutpa and Srivastava (1985) isolated apigenin-5-O-β-D-galactopyranoside (86) from the ethanol extract of the roots of *Melia azedarach* Linn.

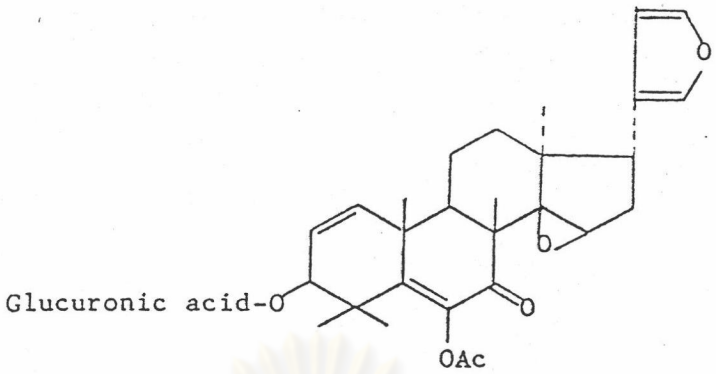


(86)

Srivastava and Gupta (1985) isolated two new limonoids besides salannin (9) from the roots of *Melia azedarach* Linn. the structures of the new limonoids have been established as 6-acetoxy-7α-hydroxy-3-oxo-14β, 15β-epoxymeliac-1,5-diene (87) and 6-acetoxy-3β-hydroxy-7-oxo-14β,15β-epoxymeliac-1,5-diene-3-O-β-D-glucoronopyranoside (88) on the basis of chemical and spectroscopic studies. Both compounds were found to exhibit antimicrobial activity.

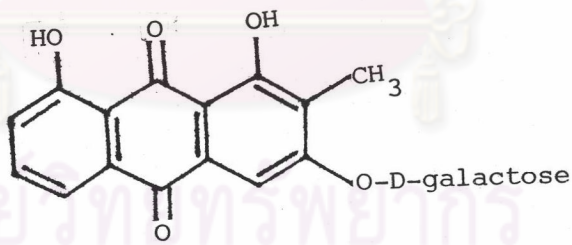


(87)

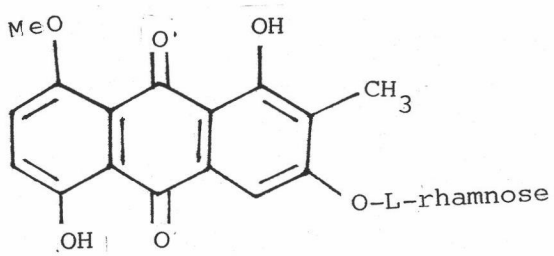


(88)

Srivastava and Mishra (1985) isolated two new anthraquinone glycosides from the stem bark of *Melia azedarach* Linn. and characterized as 1,8-dihydroxy-2-methylanthraquinone-3-O-β-D-galactopyranoside (89) and 1,5-dihydroxy-8-methoxy-2-methylanthraquinone-3-O-L-rhamnopyranoside (90) on the basic of chemical and spectral evidences.

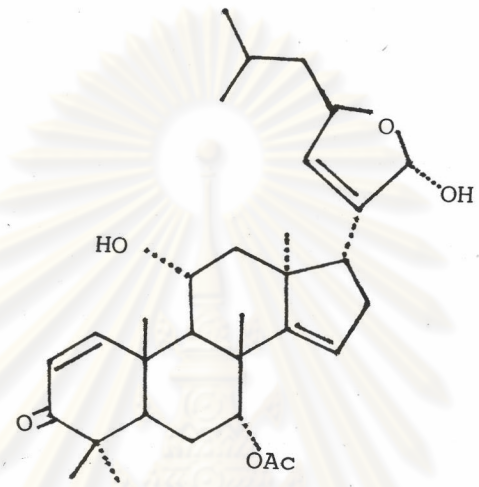


(89)



(90)

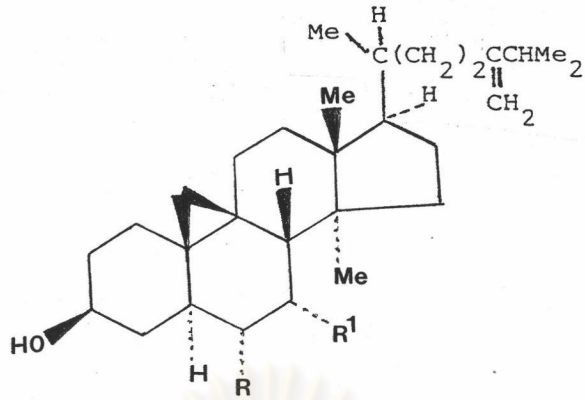
Siddiqui *et al.* (1985) isolated a new triterpenoid, named azadirachtol (91) from the fruits of *Azadirachta indica* Juss. of which the structure was reported on the basis of chemical and spectral data.



(91)

In 1986, there were five reports on phytochemical studies of the plants in the family Meliaceae as follows :

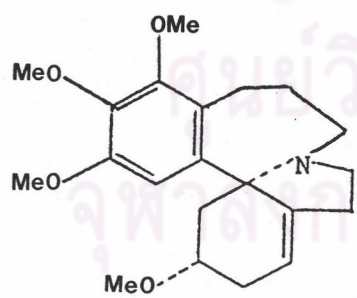
Purushothaman *et al.* (1986) isolated two new triterpenes, roxburghiadiol A (92) and B (93) from the leaves and fruits of *Aglaia roxburghiana* Hiern. Their structures were established on the basis of chemical and spectroscopic evidences.



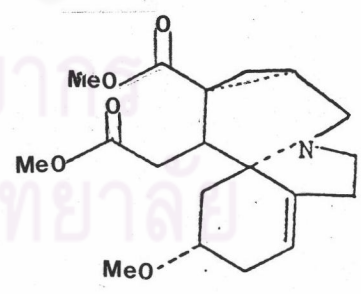
(92) R = H, R^1 = OH

(93) R = OH, R^1 = H

Aladesanmi *et al.*(1986) reported three alkaloids, 2,7-dihydrohomoerysotrine (60), 18-metthoxy-2,7-dihydroho moerysotrine (94) and lenticellarine (95) from the methanol extracted of the leaves of *Dysoxylum lenticellare* Gillespie, of these lenticellarine was found to be a novel natural product with unusal carbon skeletal.

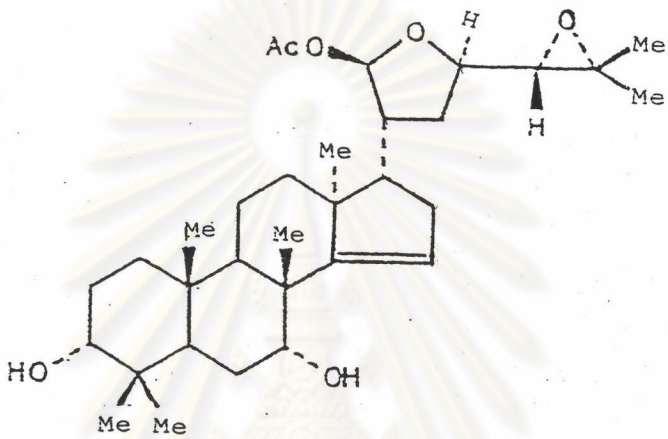


(94)

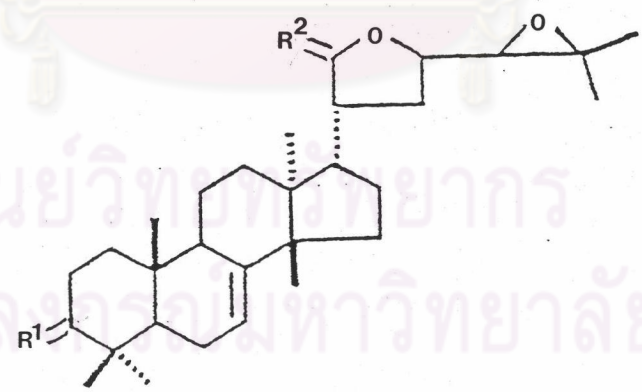


(95)

Nakanishi and Inada (1986a,1986b) isolated a new apotirucallane-type triterpene, 21-*O*-acetyltoosendantriol (96) and a new tirucallane-type triterpenoid derivative, lipomelianol (97) together with a known triterpenoid, melianone (98) from the fruits of *Melia toosendan* Sieb et Zucc.



(96)

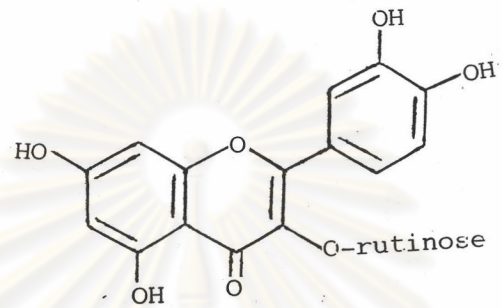


(97) R^1 = α-H,β-OCO(CH_2)nCH_3, n = 10,12,14,16

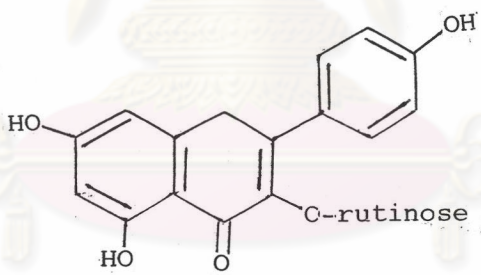
R^2 = H,OH; C_{21} epimeric mixture

(98) R^1 = O, R_2 = H,OH; C_{21} epimeric mixture

Marco *et al.* (1986) reported the isolation and characterization of two flavonol glycosides, rutin (99) and kaempferol-3-O-β-rutinoside (100) from the leaves of *Melia azedarach* Linn.

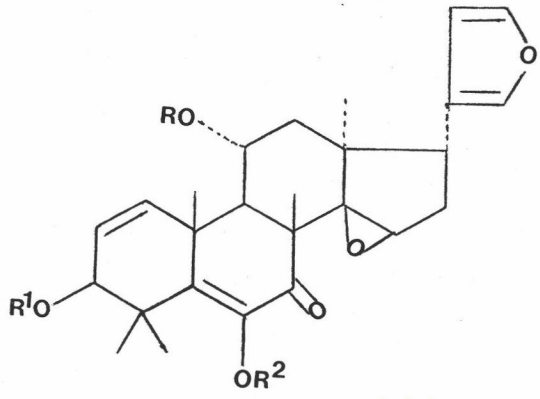


(99)

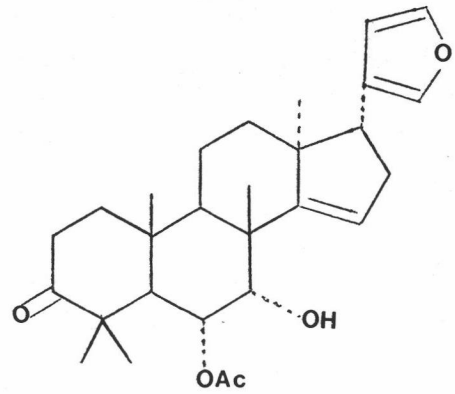


(100)

Srivastava (1986) reported the structure of a new limonoid glycoside, 6-acetoxy-11α-hydroxy-7-oxo-14β,15β-epoxymeliacin-1,5-diene-3-O-α-L- rhamnopyranoside (101) which occurred together with salannin (9) and meldenin (102) in the seeds of *Melia azedarach* Linn. The glycoside showed antibacterial activity.



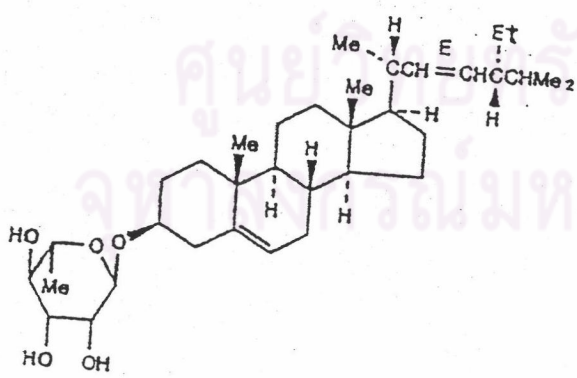
(101) R = H, R^1 = L-Rhamnose, R^2 = Ac



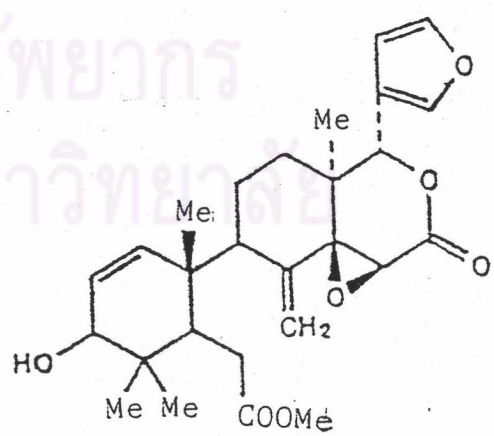
(102)

In 1987, there were five phytochemical reports on Meliaceous plants listed as follows :

Agnihotri (1987) and Agnihotri *et al.* (1987) isolated a new saponin, poriferasterol 3-O-α-L-rhamnopyranoside (103) and a new limonoid, amoorinin (104) from the stem bark of *Amoora rohituka* Wall.

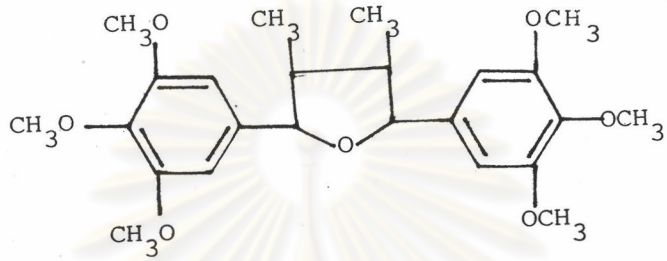


(103)



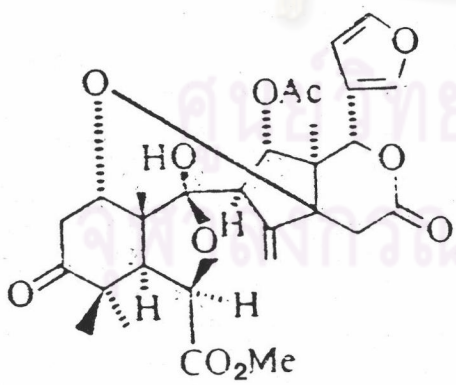
(104)

Ngowgarmratana and Saifah (1987) isolated and characterized a lignan compound called grandisin (105) from the pentane extract of the stem bark of *Aglaia pirifera* Hance.

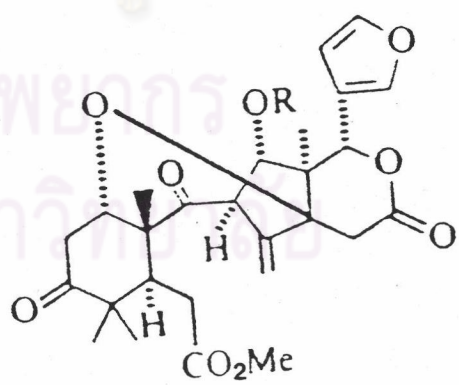


(105)

Purushothaman *et al.* (1987) isolated two new tetranortriterpenoids, trijugins A (106) and B (107) from the leaves of *Heynea trijuga* Roxb.

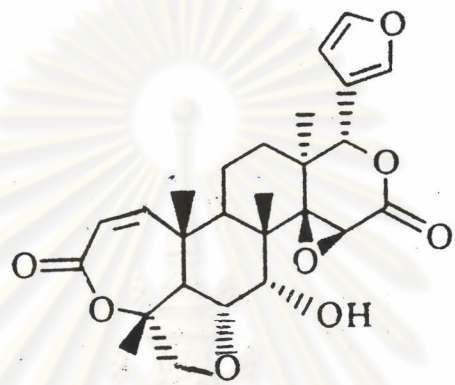


(106)



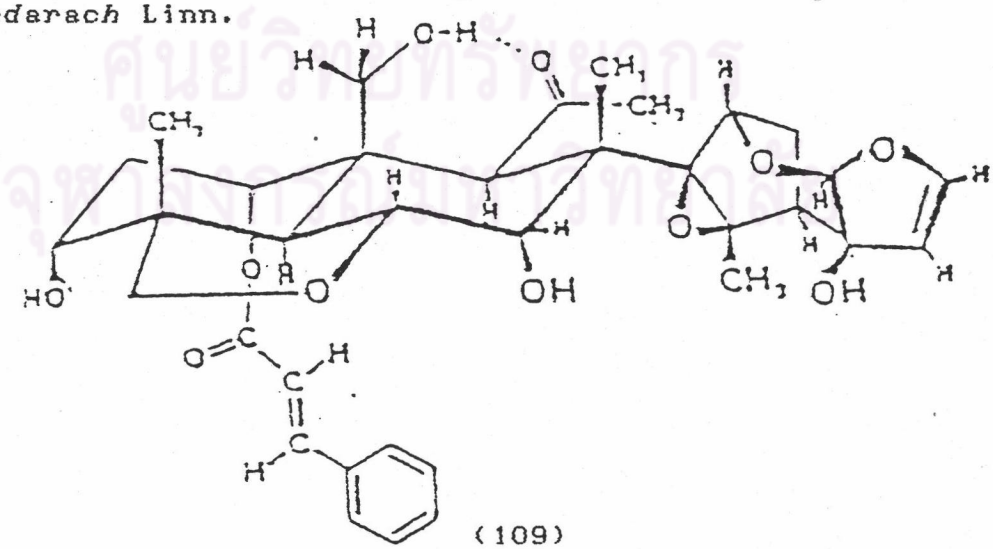
(107) R = H

Jogia and Andersen (1987) isolated a new limonoid, dysoxylin (108) from the fresh leaves of *Dysoxylum richii* (Gray) C.DC. The proposed structure was based on spectral assignments and chemical interconversions.



(108)

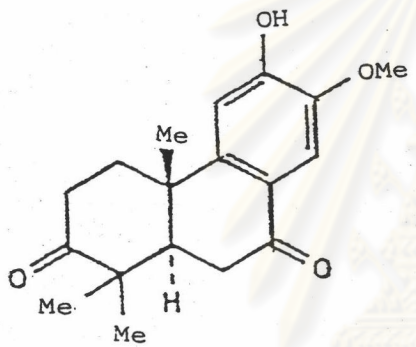
Lee *et al.* (1987) isolated a new insecticidal tetranortriterpenoid, 1-cinnamoylmelianolone (109) from methanolic extracts of the fruit of *Melia azedarach* Linn.



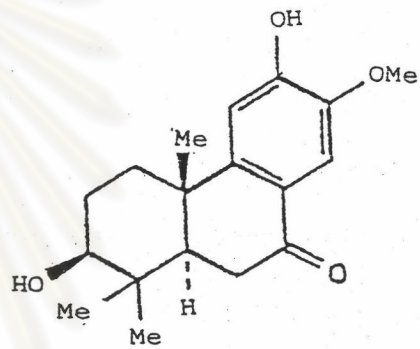
(109)

In 1988, there were thirteen phytochemical reports on the plants in family Meliaceae listed as follows :

Siddiqui and co-workers (1988) isolated two new diterpenoids, nimbionone (110) and nimbionol (111), from the acidic fraction of the bark of *Azadirachta indica* Juss. and the two compounds showed significant antibacterial activity.

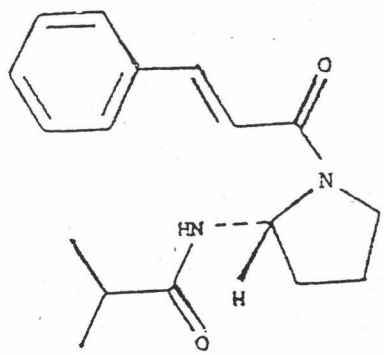


(110)



(111)

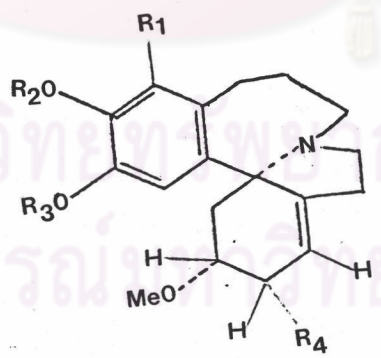
Saifah *et al.* (1988) isolated and characterized a new pyrrolidine alkaloid, piriferine (112) from the leaves of *Aglaia pirifera* Hance. The new alkaloid was identified as *N*-cinnamoyl-2(2-methylpropanoylamino)-pyrrolidine by analysis of spectral data.



(112)

Aladesanmi *et al.* (1988) isolated a new homoerythrina-derived alkaloid with molluscicidal activity, lenticellarine (95), from the leaves of *Dysoxylum lenticellare* Gillespie. The structure was determined by spectroscopic methods.

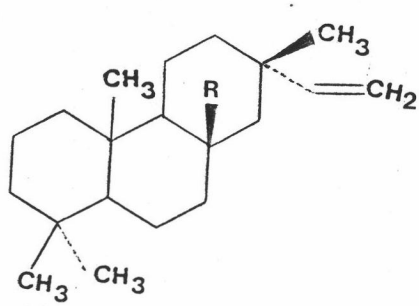
Aladesanmi (1988) reported the isolation and structure elucidation of nine constituents from the stem of *Dysoxylum lenticellare* Gillespie. Two new alkaloids, lenticellarine (95) and 3-epi-2,18-dimethoxyschelhammericine (113). One new diterpene, 8β-methoxysandaracopimarene (114), and six known compounds, 8β-hydroxysandaracopiamarene (115), phyllocladene (116), 3-epi-schelhammericine (117), 2,7-dihydrohomoerysothrine (60), p-hydroxyacetophenone (118), and 3-epi-18-methoxy-schelhammericine (119).



(113) $R_1 = R_4 = OCH_3$, $R_2, R_3 = CH_2$

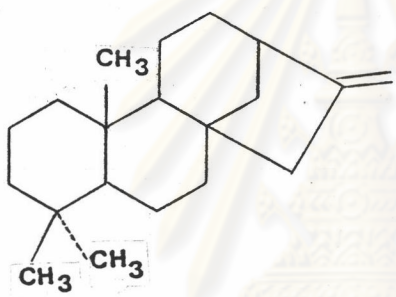
(117) $R_1 = R_4 = H$, $R_2, R_3 = CH_2$

(119) $R_1 = OCH_3$, $R_2, R_3 = CH_2$, $R_4 = H$

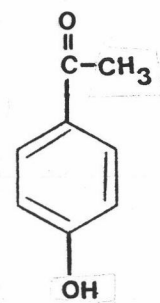


(114) R = OCH_3

(115) R = OH



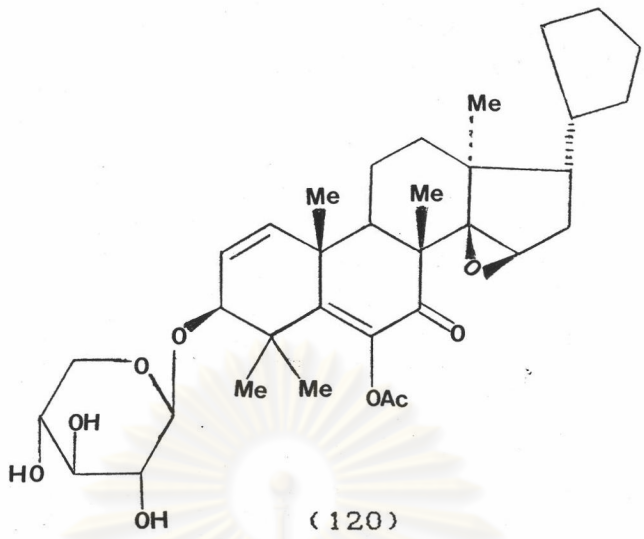
(116)



(118)

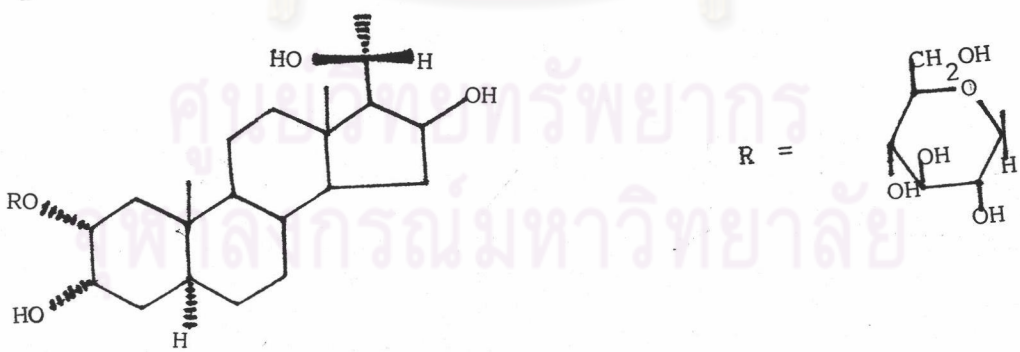
Naik and Kattige (1988) isolated piperidinylbenzopyranone, (+)-cis-5,7-dihydroxy-2-methyl-8-[4-(3-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyrane-4-one (51) from the stem bark of *Dysoxylum binectariferum*. Hook.f. This compound was found to be the anti-inflammatory and immunomodulatory principle.

Rusia and Srivastava (1988) isolated a new limonoid glycoside, 6-acetoxy-3β-hydroxy-7-oxo-14β-epoxymeliac-1,5-diene-3-O-β-D-xylopyranoside (120) from the seed of *Melia azedarach* Linn.



(120)

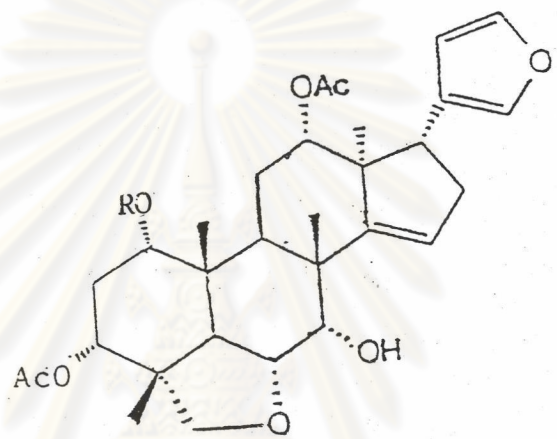
Nakanishi *et al.* (1988) isolated a new pregnane glycoside, toosendanoside (121) from the leaves of *Melia toosendan* Sieb et Zucc. Its structure has been assigned as (20R)-5-α-pregnane-2α,3α,16β,20-tetrol-2-O-β-D-glucopyranoside, based on lines of chemical and spectral evidences.

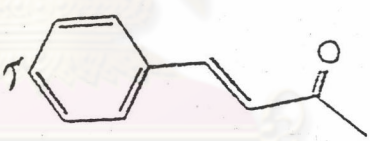


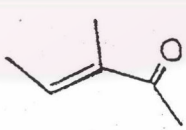
(121)

Rajab and Bentley (1988a,1988b) published two papers on phytochemical studied of the fruits of *Melia volkensii* Giirke and reported the isolation and

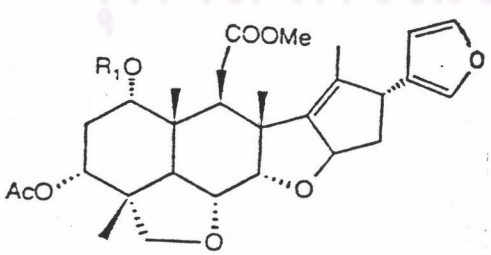
characterization of three new tetranortriterpenes, 1-cinnamoyltrichilinin (122), 1-tigloyltrichilinin (123), and 1-acetyltrichilinin (124), together with ohchinin-3-acetate (125) and a new limonoid, volkensin (126) together with a known limonoid, salannin (9). A new limonoid showed its high activity as an antifeedant against larvae of the fall army-worm, *Spodoptera frugiperda*.

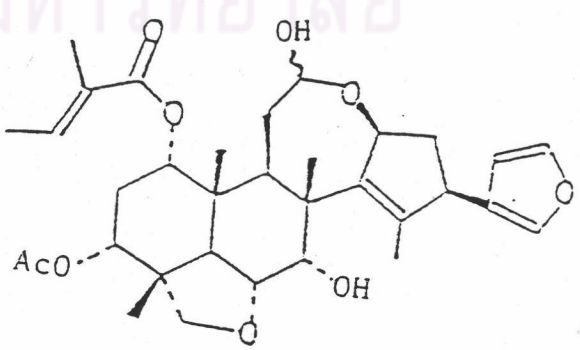


(122) R = 

(123) R = 

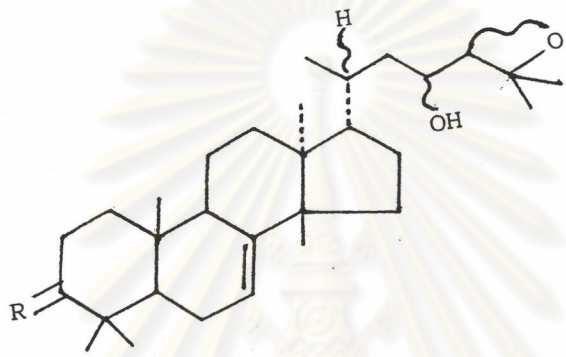
(124) R = Ac





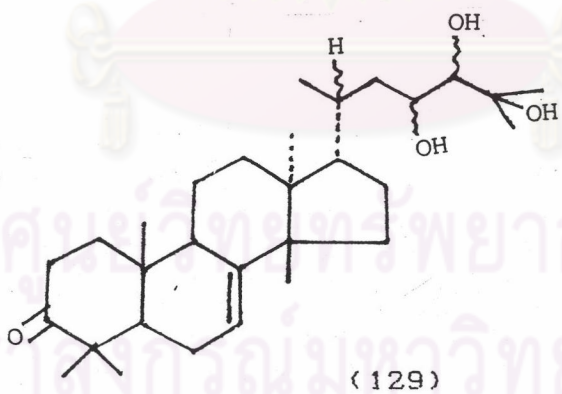
(125) R = cinnamate (126)

Mulholland and Taylor (1988) studied wood and bark of *Turraea nilotica* and reported the presence of a new protolimonoid, 24,25 epoxy-23-hydroxy-7-tirucallen-3-one, name niloticin (127), together with two closely related compounds, dihydroniloticin (128) and the triol derivative of niloticin (129)



(127) R = OH

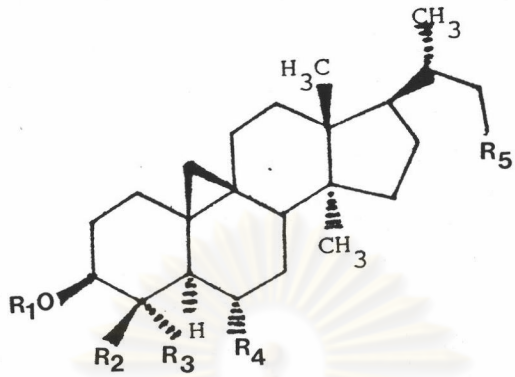
(128) R = H, OH



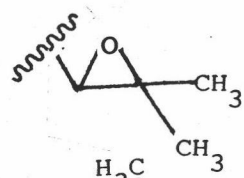
(129)

Vishnoi and Shoeb (1988) reported the isolation and characterization of two new triterpenoids, 29-nor-cycloartan-24,25-epoxy-3β-ol (130) and 29-nor-cycloartan-23-ene-3β-25-diol (131) together with 29-nor-cycloartenol (132) and 28,29-bis-nor-cycloartane-24-methylene-3β-6α-

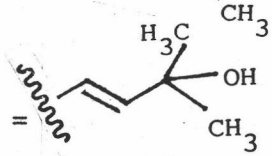
diol (133) from the aerial parts of *Aglaia roxburghiana* Hiern.



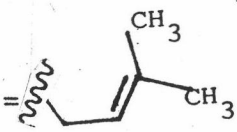
(130) R^1, R^2, R^4 = H, R^3 = CH_3, R^5 =



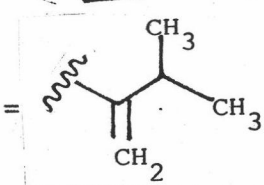
(131) R^1, R^2, R^4 = H, R^3 = CH_3, R^5 =



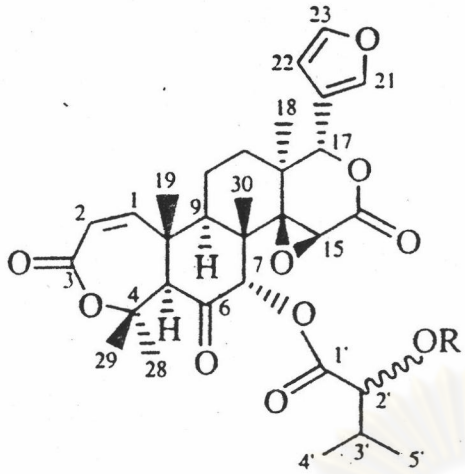
(132) R^1, R^2, R^4 = H, R^3 = CH_3, R^5 =



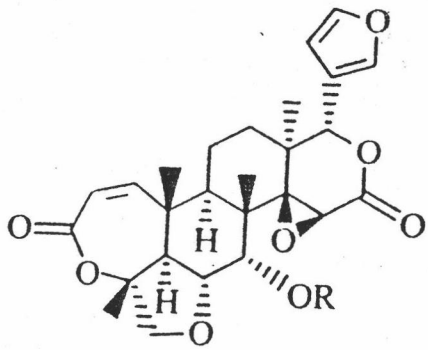
(133) R^1, R^2, R^3 = H, R^4 = OH, R^5 =



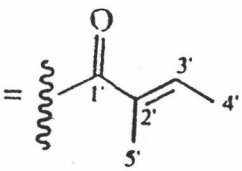
Jogia and Andersen (1989a,1989b) published two papers on phytochemical studied of the leaves of *Dysoxylum richii* (Gray) C.DC. and reported the isolation and charecterization of a new limonoids, dysoxylone (134) as well as two new metabolites, tigloyldysoxylin (135) and 6α-acetoxyobacunol acetate (136) together with a known limonoid dysoxyline (56) and a sulfur rich antibiotic, dysoxysulfone (137). The structure of dysoxysulfone had been determined by a single crystal x-ray diffraction analysis.

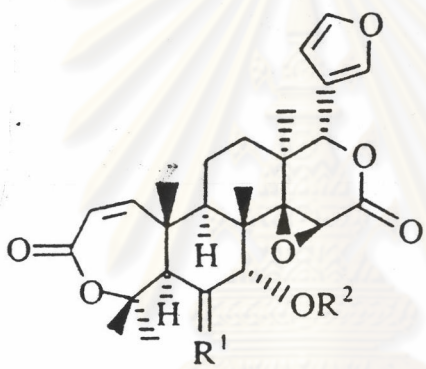


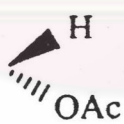
(134) R = H

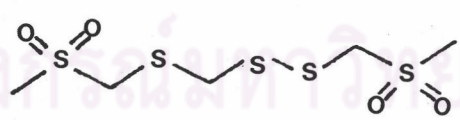


(135) R =



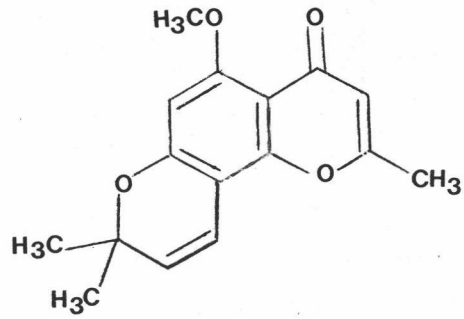


(136) R^1 =  , R^2 = Ac



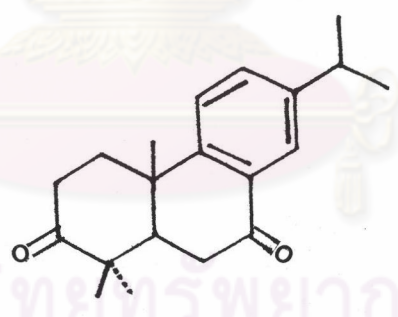
(137)

Langenhoven et *al.* (1989) investigated the leaves and twigs of *Ptaeroxylon obliquum* (Thumb.) Radlk. and obtained an antihypertensive chromone, methylalloptaeroxylin (138) from benzene fraction.

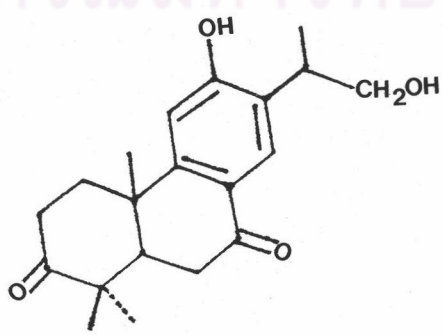


(138)

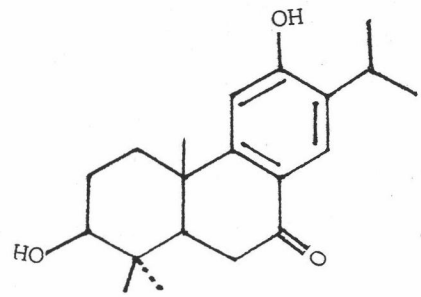
Ara and Siddiqui (1990) isolated three new tricyclic abietane type diterpenoids, margocin (139), margocinin (140) and margocilin (141) from the root bark of *Azadirachta indica* Juss., the structure of which have been elucidated as 8,11,13-abietatrien-3,7-dione, 8,11,13-abietatrien-12,16-dihydroxy-3,7-dioneand, and 8, 11,13-abietatrine-3β,12-dihydroxy-7-one , respectively.



(139)

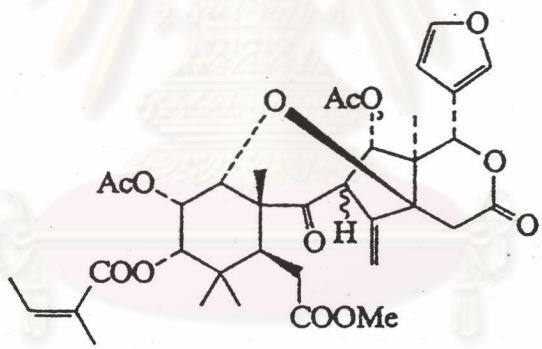


(140)

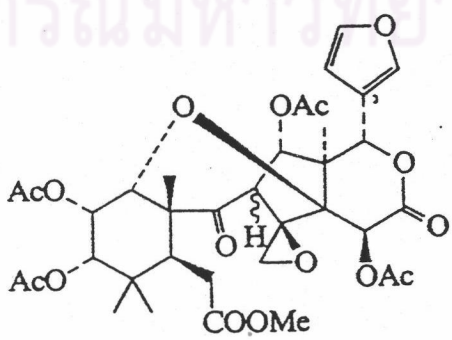


(141)

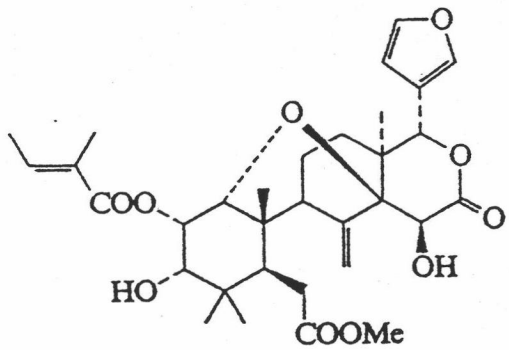
Kehrli et *al.* (1990) investigated the seed of *Ekebergia pterophylla* (C.DC.) Holm. and reported the isolation of five limonoids, E.P. 1 (68), E.P. 3 (70), E.P. 4 (142), E.P. 5 (143) and E.P. 6 (144).



(142)

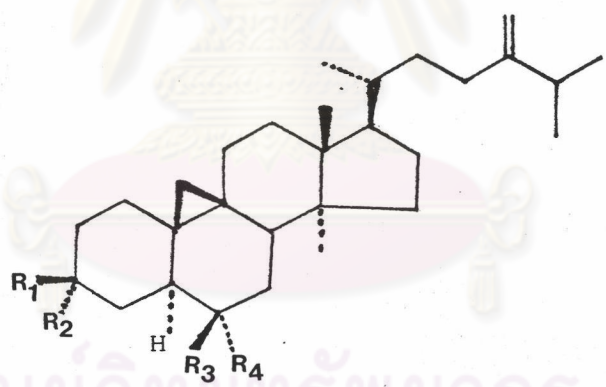


(143)



(144)

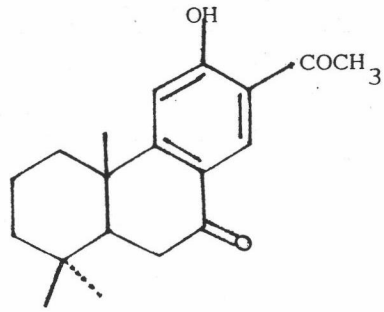
Balakrishna and Kundu (1990) isolated two 14α-methylsterols, roxburghiadiol A (145) and roxburghiadiol B (146) from the leaves and fruits of *Aglaia roxburghiana* Hiern.



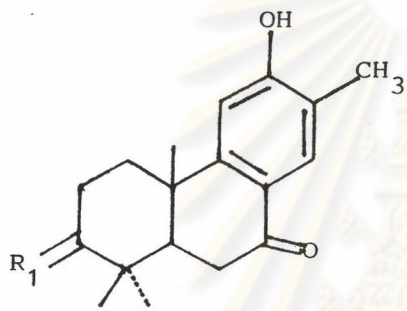
(145) R_1, R_3 = OH, R_2, R_4 = H

(146) R_1, R_4 = OH, R_2, R_3 = H

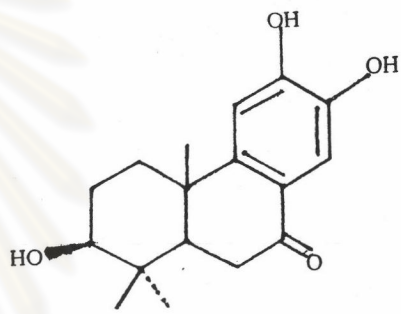
Ara and Siddiqui (1990) isolated three new tricyclic diterpinoids, nimbosodione (147), nimbisonol (148) and demethylnimbionol (149) from the stem bark of *Azadirachta indica* Juss.



(147)

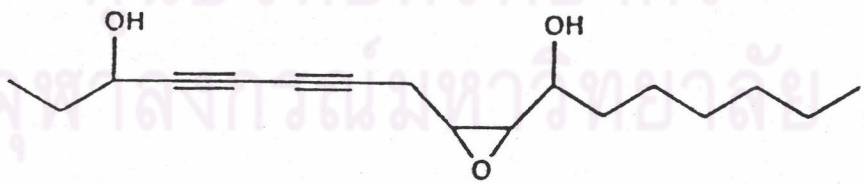


(148) R_1 = β-OH,H



(149)

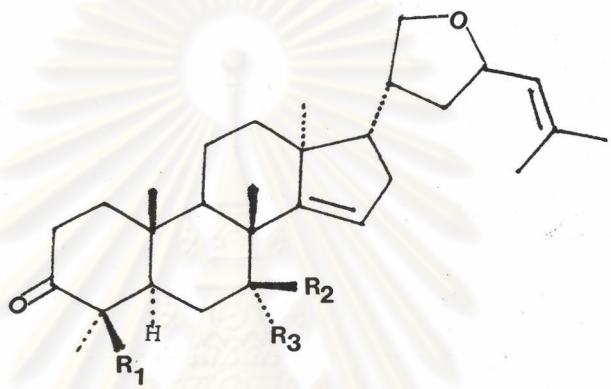
Wakabayashi *et al.* (1991) isolateda polyacetylene,α-hexyl-3-(6-hydroxy-2,4-octadiynyl)oxiranemerthanol (150) from the wood of *Swietenia mahogani* Jacq.



(150)

Adesanya *et al.* (1991) reported the isolation and characterization of five new apotirucallane-derived

triterpenes, dysorones A (151), B (152), C (153), D (154) and E (155), and β-sitosterol from the leaves of *Dysoxylum roseum* C.DC., the major compound, dysorone E (155), exhibits moderate cytotoxic activity *in vitro* against the growth of KB human buccal carcinoma cells.



(151) $R_1 = CH_2OH$, $R_2, R_3 = O$

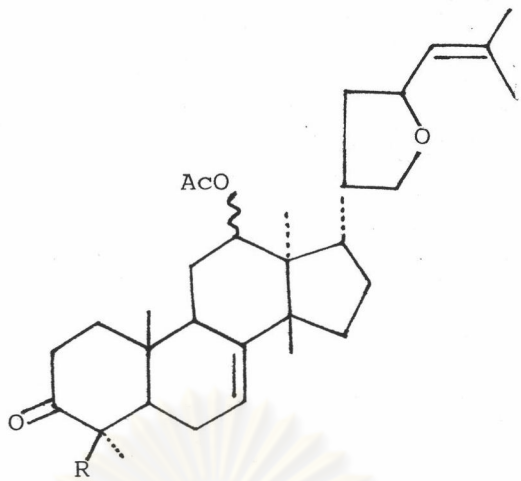
(152) $R_1 = CH_2OH$, $R_2 = H$, $R_3 = OH$

(153) $R_1 = Me$, $R_2, R_3 = O$, Δ^1

(154) $R_1 = Me$, $R_2 = H$, $R_3 = OH$, Δ^1

(155) $R_1 = CH_2OH$, $R_2, R_3 = O$, Δ^1

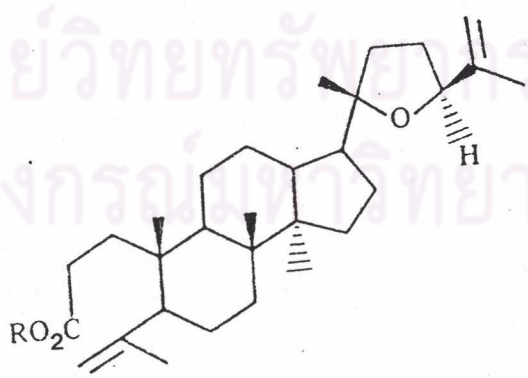
Olugbade (1991) isolated two new triterpenoids, prieurone (156) and 29-hydroxy-prieurone (157) from the leaves of *Trichilia prieuriana* A.Juss.



(156) R = Me

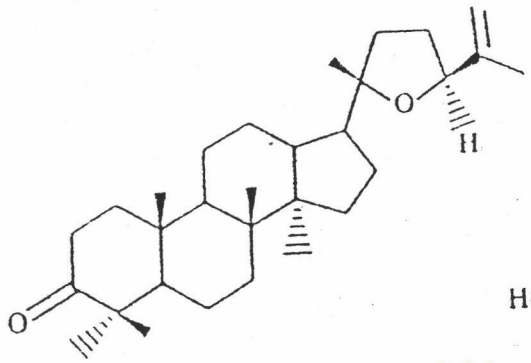
(157) R = CH_2OH

Aalbersberg *et al.* (1991) investigated the fruits of *Dysoxylum richii* (Gray) C.DC. and reported the isolation of four new dammarane-type triterpenoids, name methyl richenoate (158), richenone (159), richenol (160), and richenoic acid (161) together with four known triterpenoids, ocotillone (162), cabraleone (163), shoreic acid (164) and eichlerianic acid (165).

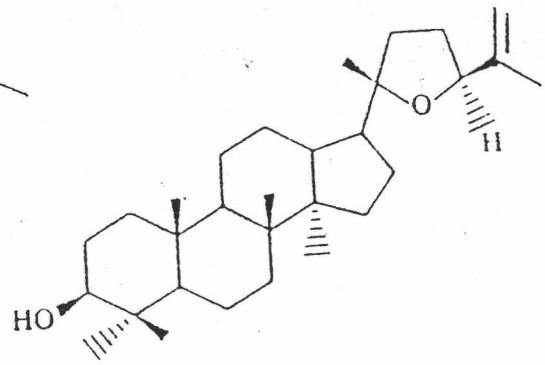


(158) R = Me

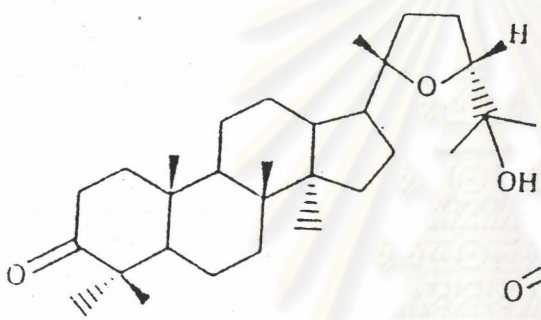
(161) R = H



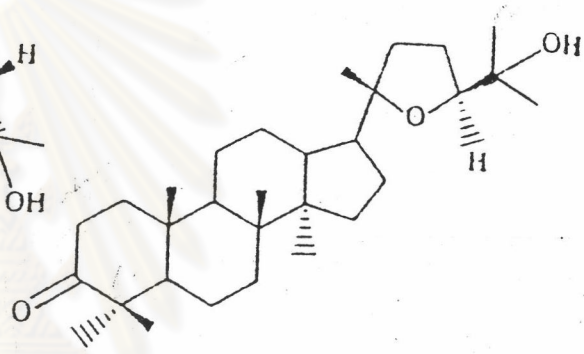
(159)



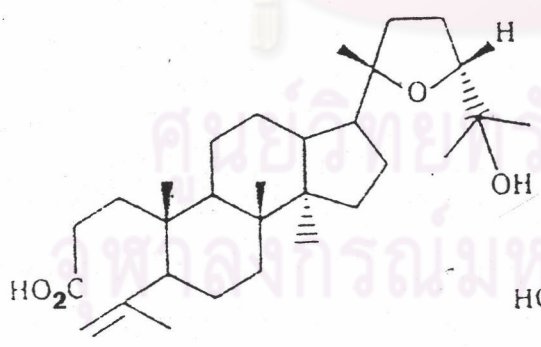
(160)



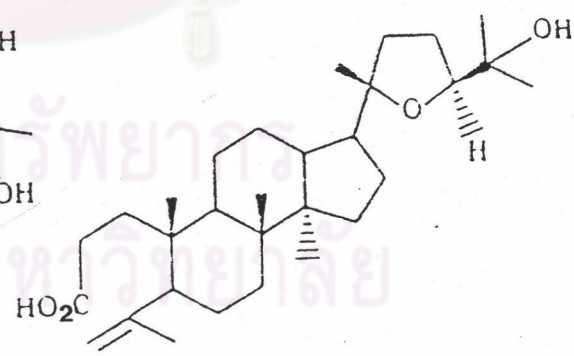
(162)



(163)



(164)



(165)

The pharmacological activities of the Meliaceous plants were listed in the following table according to the literature survey.

Table 2 : Pharmacological activities of the Meliaceous plants.

Plant Name	Chemical Constituent	Pharmacological activity	Reference
Aglaia elliptifolia Merrill.	rocaglamide (55)	anti-leukemic	King *et al.* (1982)
Aglaia roxburghiana	ethanolic extract	antivirus	Vishnoi *et al.* (1988)
Aphanamixis grandifolia	aphanamol I (66)	toxic principle	Nishisawa *et al.* (1984)
	aphanamol II (67)	toxic principle	
Azadirachta indica	meliantriol (16)	antifeedant	Lavie and co-workers (1967)
	azadirachtin (39)	antifeedant	
	nimbionone (109)	antibacterial	Siddiqui *et al.* (1988)
	nimbionol (111)	antibacterial	
	nimbidin (54)	anti-ulcer	Pillai and Santha (1984)
		anti-arthritic	
		anti-inflammatory	
		antipyretic	

Table 2 (cont.)

Plant Name	Chemical Constituent	Pharmacological activity	Reference
Dysoxylum alliaceum	(+)-8-hydroxycalamenene (61)	antibacterial	Nishizawa *et al.* (1983)
Dysoxylum binectariferum Hook.f.	dysobinin(46)	CNS-depressant	Singh *et al.* (1976)
	rohitukine (51)	analgesic	Vasudev *et al.* (1985)
		immunomodulatory activity	
		anti-inflammatory	Naik *et al.* (1988)
Dysoxylum lenticellarare Gillespie	dysoxyline (56)	cardiac effect	Aladesanmi and Ilesanmi (1987)
	homolaudanosine	cardiac effect	
	3-epi-12-hydroxy-schelhammericine (65)	cardiac effect	
	lenticellarine (95)	molluscidal activity	Adesanmi (1988)
	methanolic extract	cardio depressant	Adesanmi and Aladesanmi (1988)
Dysoxylum richii	dysoxysulfone (137)	antibacterial	Jogia *et al.* (1989)

Table 2 (cont.)

Plant Name	Chemical Constituent	Pharmacological activity	Reference
Dysoxylum roseum C.DC.	dysorone E (155)	exhibits moderate cytotoxic activity	Adesanya *et al.* (1991)
Melia azedarach Linn.	N9GI	anti-tumor	Termo (1985)
	limonoid glycoside (101)	antibacterial	Srivastava (1986)
	sendanin (47)	anti-murine P-388 lymphocyticleukemia	Pettit *et al.* (1983)
	meliatoxin	acute nervous symthom	Oelriches *et al.* (1984)
Melia volkeinsii Gurke	volkensin (126)	antifeedant	Rajab and Bentley (1988)
Swierenia mahagani	swietemahonin A	inhibition against PAF-induced aggregation (PAF antagonists)	Ekimoto *et al.* (1991)
	" D		
	" E		
	" G		
Turrea nilotica	lericiresinol 4 mono methyl ether (74)	anti-cancer	Ayoub and kingston (1984)

From the above information, chemical characterization of plants in the family Meliaceae is very interesting, especially in those of plant genus *Dysoxylum*. It is the purpose of this investigation to investigate the chemical constituents of the leaves of *Dysoxylum grande* Hiern. to prove the chemical nature of alkaloids and some other compounds that occur in the leaves. The results may serve as piece of support to disclose the nature of alkaloids in Meliaceae family. Moreover, some isolated compounds would provide information to carify their structures which lead to the valuable information in the field of chemotaxonomy.