# CHAPTER II
# SURVEY OF LITERATURE

## 2.1 Taxo and Classification of *Diospyros ehretioides*

Kingdom : Plantae (Plants)

Division : Magnoliophyta (Flowering plants)

Class : Magnoliopsida (Dicotyledons)

Order : Ericales

Family : Ebenaceae

Genus : *Diospyros*

Species : *Diospyros ehretioides* Wall.ex G. Don

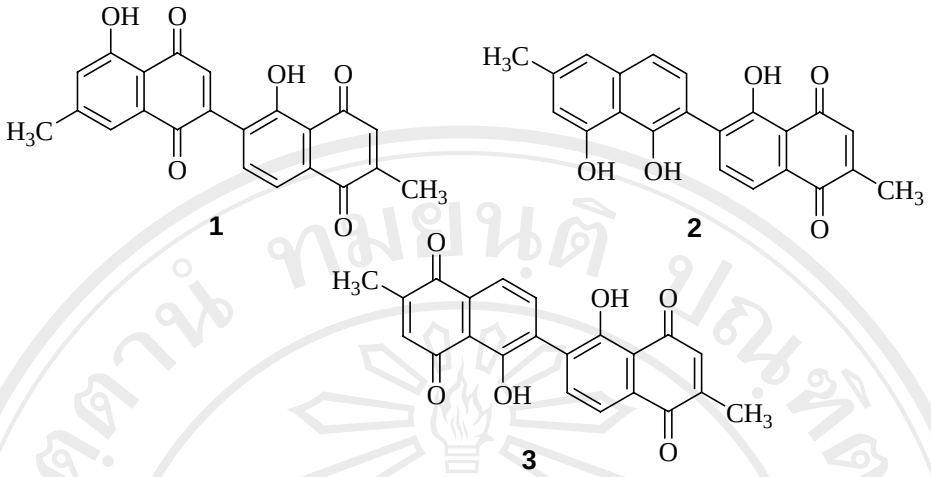
Plant synonyms: *Diospyros harmandii* Lec.

*Diospyros putii* Fletcher

## 2.2 Chemistry of compounds from *Diospyros* species

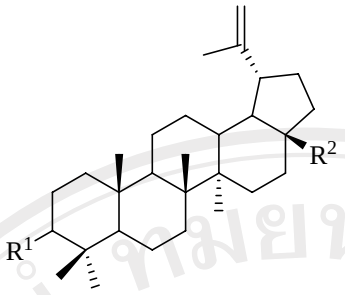
### 2.2.1 *Diospyros ehretioides* Wall. Ex G. Don

Phytochemical studies of the wood of *Diospyros ehretioides* revealed the presence of a dimeric naphthoquinones, namely, ehretione **[1]** ebenone **[2]** and elliptinone **[3]** which were also found in the stem bark of *Diospyros ebenum.* Moreover, elliptinone **[3]** was found in the roots, barks and fruits of several *Diospyros* species, but there have been no reports on biological activities of any substance from this plant.

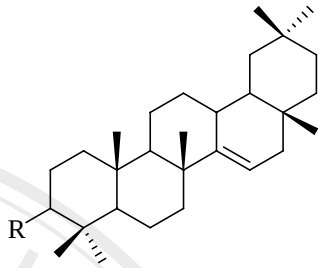



2.2.2 *Diospyros rhodocalyx*

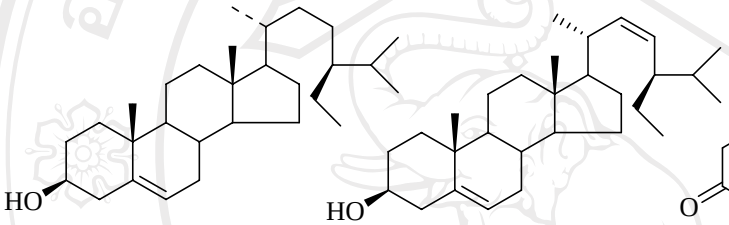
Sutthivaiyakit *et al*.[8] isolated lupenone **[4]**, lupeol **[5]**, betulin **[6]**, betulinic acid **[7]**, taraxenone **[8]**, taraxerol **[9]**, teraxeryl acetate **[10]**, β-sitosterol **[11]**, stigmasterol **[12]**, stigmasta-4-en-3-one **[13]** and 1-O-ethyl-β-D-glucopyranoside tetraacetate **[14]** from the barks of *Diospyros rhodocalyx*. These compounds have never been biologically explored.



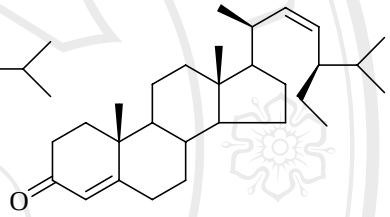

**4** $R^1$ = =O $R^2$ = $CH_3$
**5** $R^1$ = OH $R^2$ = $CH_3$
**6** $R^1$ = OH $R^2$ = $CH_2OH$
**7** $R^1$ = OH $R^2$ = COOH




**8** R = =O
**9** R = OH
**10** R = $OCOCH_3$




**11** **12**

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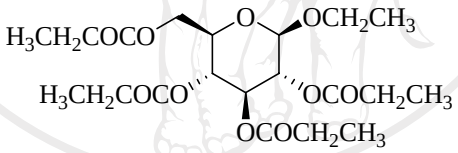


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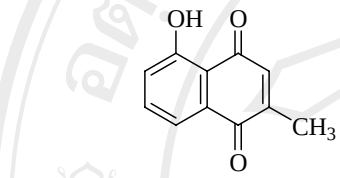
2.2.3 Other species of *Diospyros*

According to the literature, several types of compounds were isolated from the genus *Diospyros*. Plumbagin **[15]** and 7-methyljuglone **[16]** are the most widely-distributed monomeric naphthoquinones and were found to accumulate in significant quantities in a number of *Diospyros* species. The orange-red pigment plumbagin **[15]** was the first naphthoquinone which was isolated along with a colourless β-hydro product of 7-methyljuglone from *Diospyros hebecarpa*[9]. It is interesting to note that plumbagin **[15]** was found mostly in the leaves and heartwood,

while 7-methyljuglone **[16]** was in the barks and wood. Moreover, the root barks of *Diospyros chamaethamnus*[10] contained seven quinone compounds, i.e., 2-methylnaphthazarin **[17],** biramentaceone **[18]**, mamegakinone **[19]**, xylospyrin **[20]**, diospyrin **[21]** and diosquinone **[22]**, isodiospyrin **[23].** Moreover, 3-methyl-naphthalene-1,8-diol **[24]** and diospyrol **[25]** were isolated from the berries of *Diospyros mollis*.



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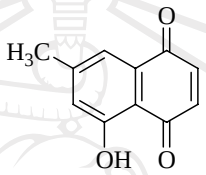

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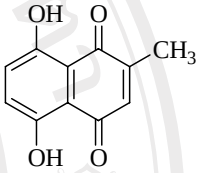

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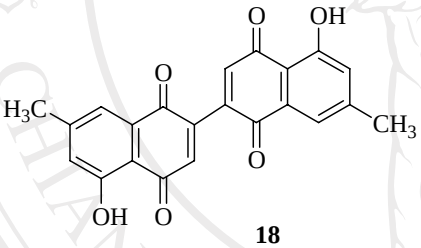

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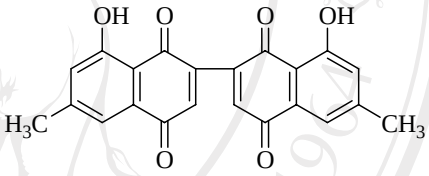

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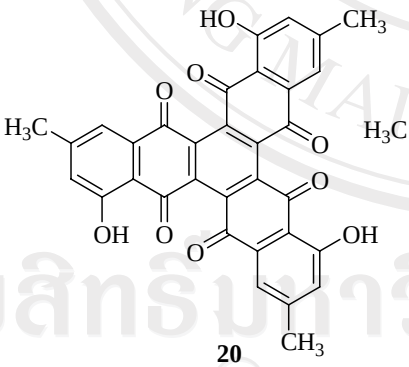

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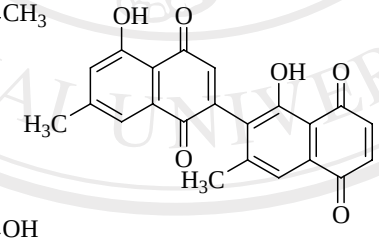

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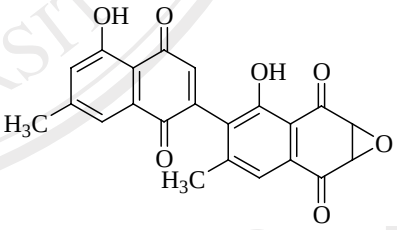

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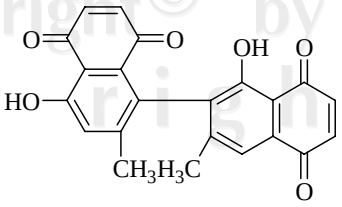

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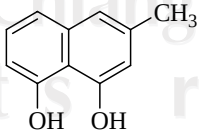

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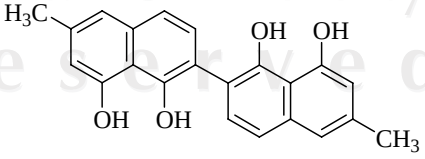
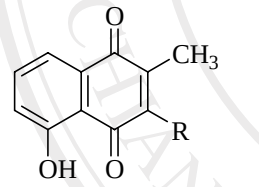
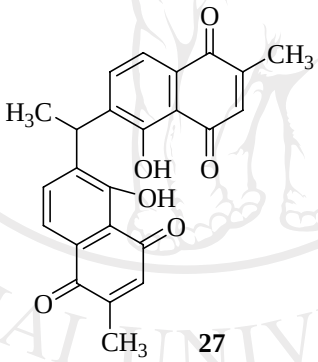


**25**

Higa *et al.*[11] isolated three quinones from the fresh fruits of *Diospyros maritima*, i.e., 3-bromoplumbagin **[26]**, ethylidene-6,6′-biplumbagin **[27]** and 3-(2-hydroxyethyl) plumbagin **[28]**. They also found six known naphthoquinones, i.e., 3-chloroplumbagin **[29]**, 3-methylplumbagin **[30]**, plumbagin **[15]**, droserone **[31],** elliptinone **[3]** and maritinone **[32]** together with eight known terpenes, abbeokutone **[33]**, 3α,16α,17-trihydroxy kaurane **[34]**, lupenone **[4**], lupeol **[5]**, betulin **[6]**, betulinic acid **[7]**, friedelin **[35]** and oleanolic acid **[36]** and a coumarin, namely, scopoletin **[37]**. Among these isolated compounds, plumbagin **[15]** showed strong ichthyotoxic, germination inhibitory and antifungal activities.



**26 R = Br**
**28 R = $CH_2CH_2OH$**
**29 R = Cl**
**30 R = $CH_3$**
**31 R = OH**



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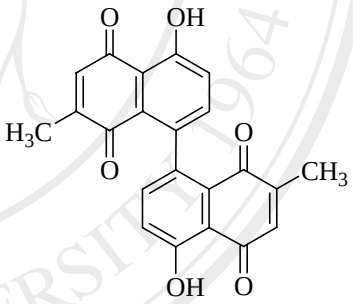

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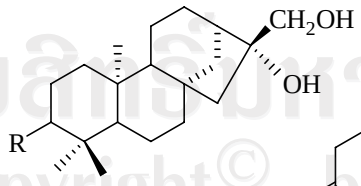
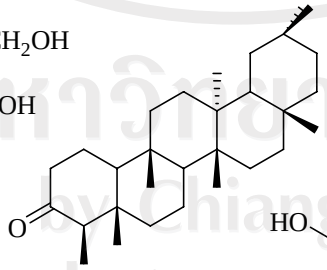


**33 R = =O**
**34 R = OH**



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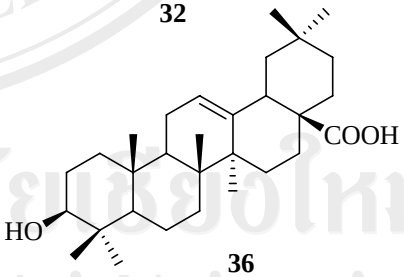

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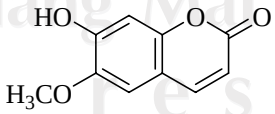
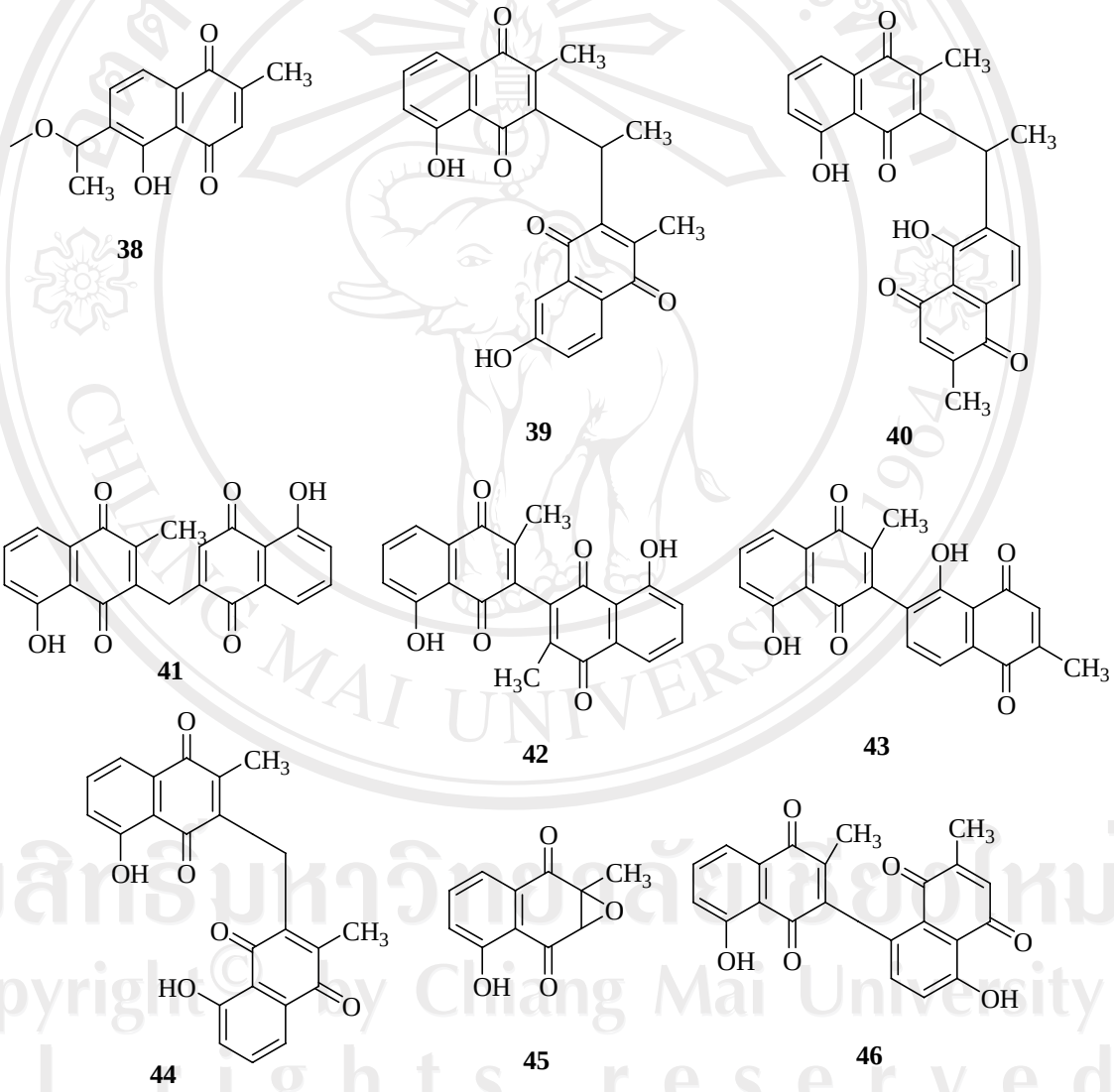


**37**



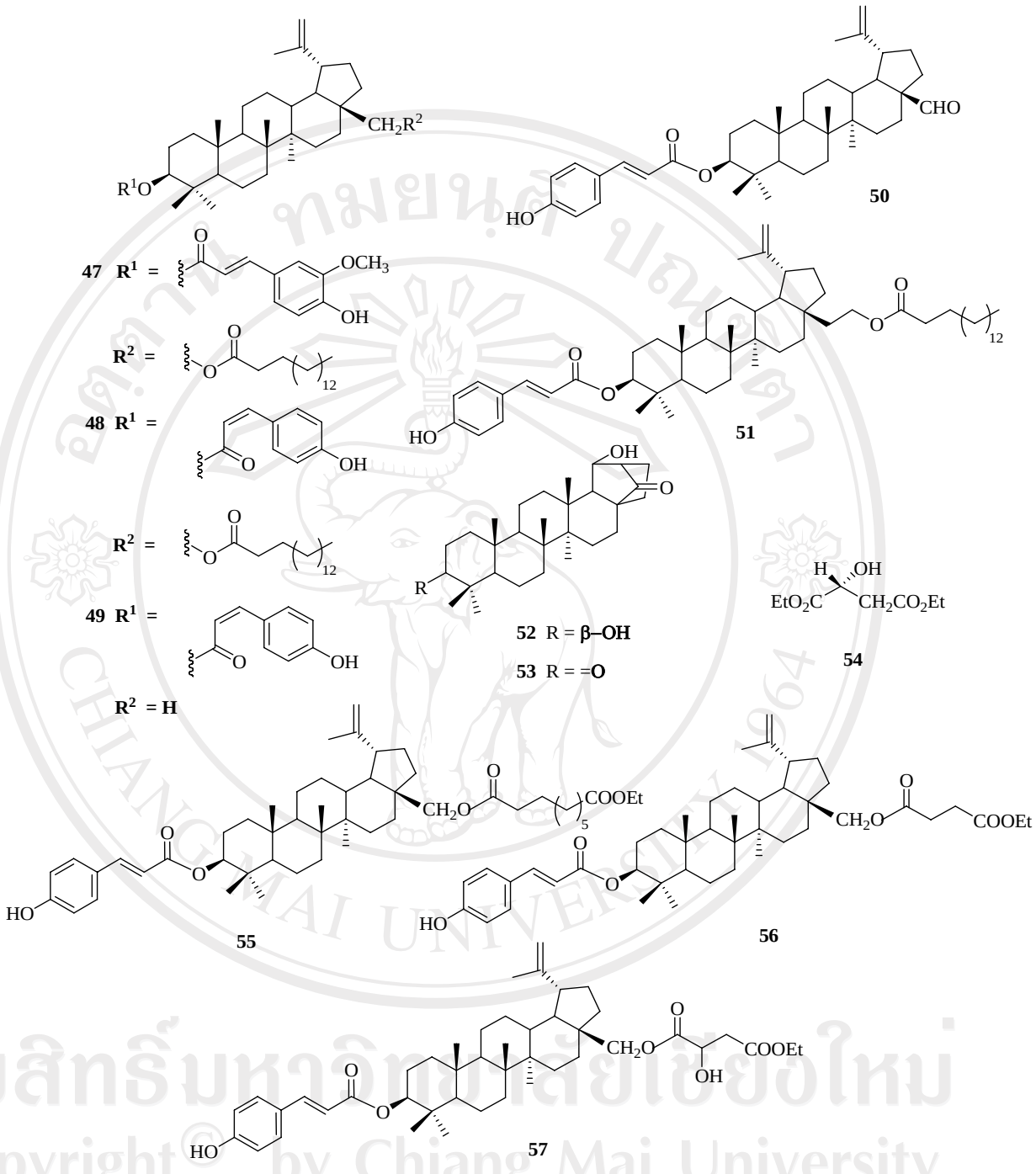
Later, they[12] isolated three new naphthoquinones, i.e., 6-(1-ethoxyethyl)plumba-gin **[38]**, ethylidene-3,3′-biplumbagin **[39]** and ethylidene-3,6′-

biplumbagin **[40]** and other six known naphthoquinones, namely, isozeylanone **[41]**, 3,3′-biplumbagin **[42]**, chitranone **[43]**, methylene-3,3′-biplumbagin **[44]**, 2,3-epoxyplumbagin **[45]** and 3,8′-biplumbagin **[46].** Compounds **[42], [43], [45]** and **[46]** also showed strong ichthyotoxic activity as found earlier in compound **[15].** In addition, compound **[45]** presented mild germination inhibitory activity.




Kuo *et al.* studied chemical constituents of the stems of the same plant as did Higa *et al.*, and led to the isolation of three lupane-type triterpenes[13], 3-(*E*)-feruloyl-

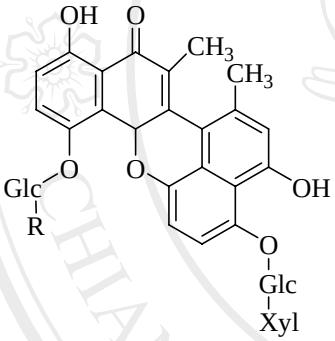
28-palmitoylbetulin **[47]**, 3-(*Z*)-coumaroyl-28-palmitoylbetulin **[48]** and 3-(*Z*)-coumaroyllu -peol **[49]** and subsequently two lupane derivatives[14], 3-(*E*)-coumaroylbetulinaldehyde **[50]** and 3-(*E*)-coumaroyl-28-palmitoylbetulin **[51]**. Moreover, six compounds were isolated from the heartwood of the same plant by Kuo *et al.*[15] namely, diospyrolide **[52]**, diospyrolidone **[53]**, diethyl(2*R*)–malate **[54]**, 3-(*E*)-coumaroylbetulin-28-yl ethyl nonanedioate **[55],** 3-(*E*)-coumaroylbetulin-28-yl-ethyl succinate **[56]**, and 3-(*E*)-couma -roylbetulin-28-yl ethyl(2*R*)-2-hydroxysuccinate **[57]**. However, there have been no reports on biological activities of any substance from this plant.



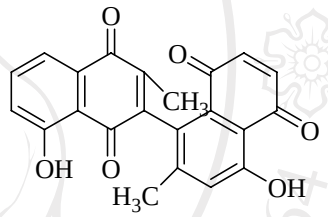



Wu and colleagues[16] isolated binaphthalene glycosides, 1′,2-binaphthalen-4-one-2′,3-dimethyl-1,8′-epoxy-1,4′,5,5′,8,8′-hexahydroxy-8-O-β-glucopyranosyl-5′-O-β-xylo -pyranosyl(1→6)-β-glucopyranoside **[58]** and 1′,2-binaphthalen-4-one-2′,3-

dimethyl-1,8′-epoxy-1,4′,5,5′,8,8′-hexahydroxy-,5′,8-di-O-β-xylopyranosyl(1→6)-β-glucopyrano –side **[59]** from the twigs of *Diospyros lycioides* which exhibited antimicrobial activity. Moreover, Khan and Rwekika[17] isolated another binaphthoquinone **[60]** from the leaves of *Diospyros greeniway* and an unusual novel tetrameric naphthoquinone **[61]** from the root barks of *Diospyros mafiensis*. Ishimaru *et al.*[18] isolated a naphthalene glycoside **[62]** from callus cultures of *Diospyros kaki*, but no biological activity test was performed.




**58** R = H , Glc = glucose, Xyl = xylose
**59** R = Xyl, Glc = glucose, Xyl = xylose

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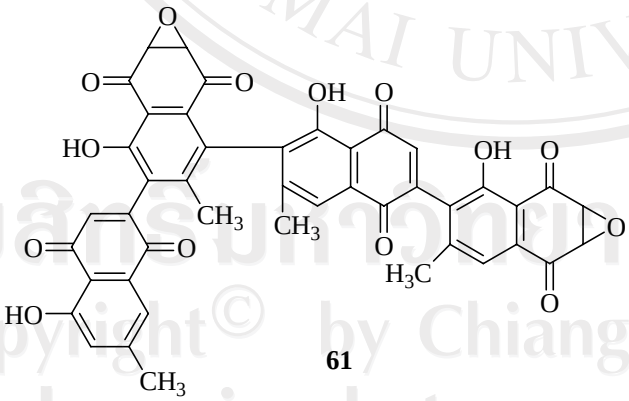


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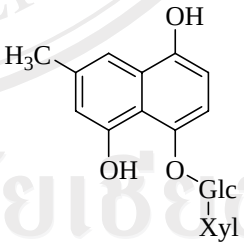
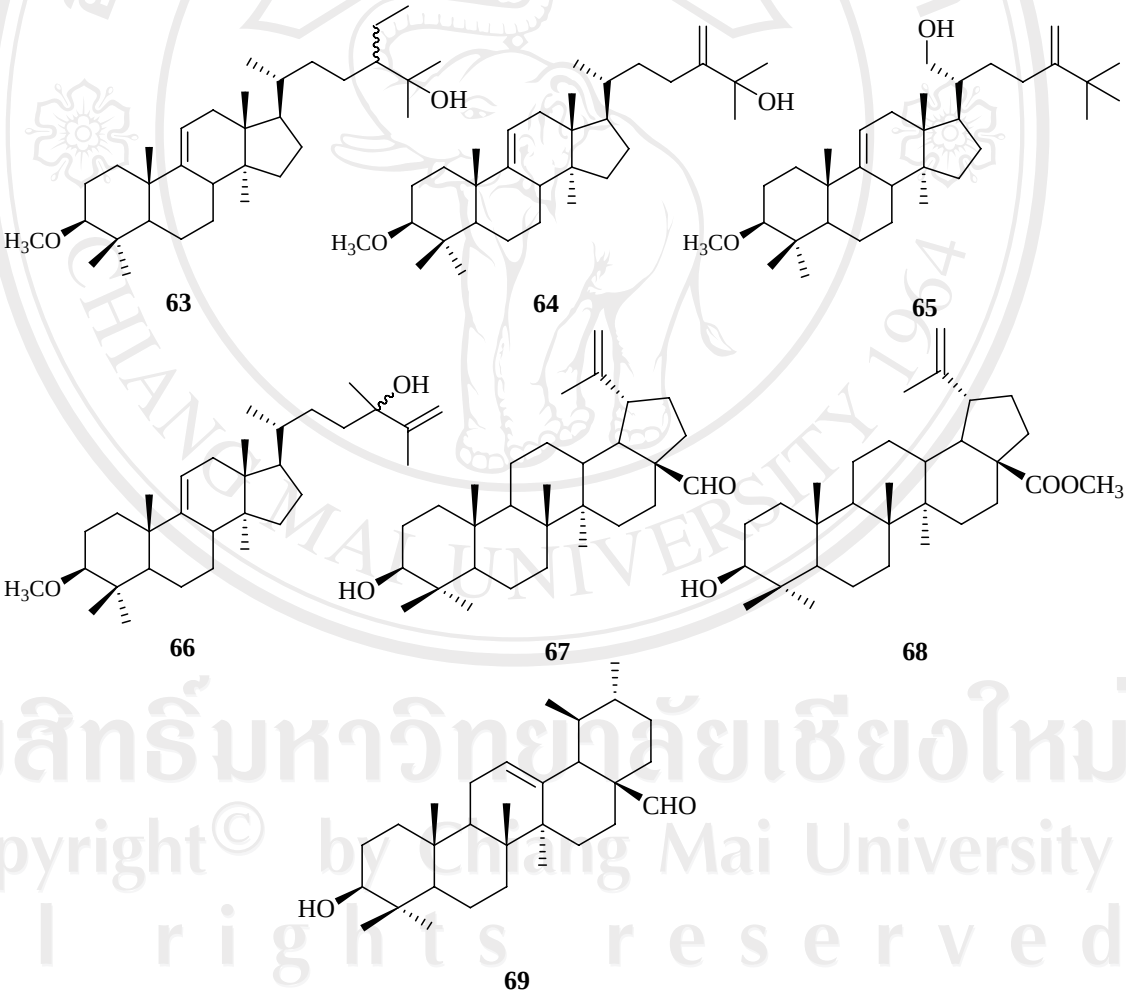



**62**

Chen *et al*.[19] isolated four lanostane-type triterpenes, 24-ethyl-3β-methoxyla-nost-9(11)-en-25-ol **[63],** 3β-methoxy-24-methylenelanost-9(11)-en-25-ol **[64],** 3β-me- thoxy-25-methyl-24-methylenelanost-9(11)-en-21-ol **[65]** and 3β-methoxy-24-methyl -lanosta-9(11),25-dien-24-ol **[66]** together with three known triterpenes, namely, betulinaldehyde **[67],** betulinic acid methyl ester **[68]** and ursaldehyde **[69]** from the methanol extract of the twigs of *Diospyros discolor*. The biological activity of this plant has however not been investigated.



The extract of the stem and heartwood of *Diospyros maritima* Blume has usually been used to treat rheumatic disease in Taiwan[13,15]. Moreover, a methanol extract from the twigs of *Diospyros lycioides* demonstrated antimicrobial activity against common oral pathogens, including *Streptococcus mutans* and *Porphyromonas gingivalis* (MIC 2.5 and 0.156 mg/mL, respectively)[16].

Preliminary screening revealed that the dichloromethane ($CH_2Cl_2$) extract of *Diospyros ehretioides* fruits showed moderate antitubercular activity with the minimum inhibitoryconcentration (MIC) value of 25 µg/mL and also demonstrated strong cytotoxicity towards nasopharyngeal carcinoma (KB) and breast cancer (BC-1) cell lines with $IC_{50}$ values of 2.88 and 1.94 µg/mL, respectively. Therefore, it was decided to investigate these fractions in order to isolate bioactive compounds and to further investigate the chemical constituents in the dichloromethane extract.