CHATER II

HISTORICAL

1 Biology of sponges.

The biology of the sponges is less well known than that of other organisms. Sponges lack muscle, nerve and body organs. They have no digestive cavity or mouth. Biological interactions in the sponges take place at the cellular, rather than the level of organs.

Sponges are the sedentary filter feeders. Skeleton support in sponges is provided by a network of hard spicules, flexible fibers, foreign sand or a combination of the three. Spicules are small crystalline structures made of either calcium carbonate (in the mineral forms calcite or aragonite) or silicon dioxide (glass). In addition, collagen and spongin (protein) fibers produced the soft, classically "spongy" skeleton typical of many sponges. Sponges can be thought of as communal association of cell, loosely arrange to form a network of inhalent canals originate as small pores (ostia) on the outer surface of sponge and lead to spherical chambers. These chambers are lined with choanocytes, cell with whip- like flagella that beat rhythmic wave to pump water through the body in one direction. Water carried to sponges is filtered for food particle and oxygen and then expelled through one or several exhalent pores (oscutes). Complexity of the canal structure most often increase with sponges size.

Sponges vary greatly in growth form and size form thin encrusting sheets a fraction of an inch thick, to large barels or veses, with many grow to several feet in height and attain a volume of about two cubic yard (about a size or small cement mixer). Form a rather simple body plan, sponges have evolved myriad shapes, size and color. Three classes of sponges are recognized on the basis of their skeleton components, Demospongiae, Calcarea and Scleospongiae (Colin and Arneson, 1995).

1.1 Taxa and Description of a marine sponge, *Ircinia* sp.

Kingdom Animalia

Phylum Porifera

Class Demospongiae

Order Keratora

Family Spongiidea

Genus *Ircinia.*

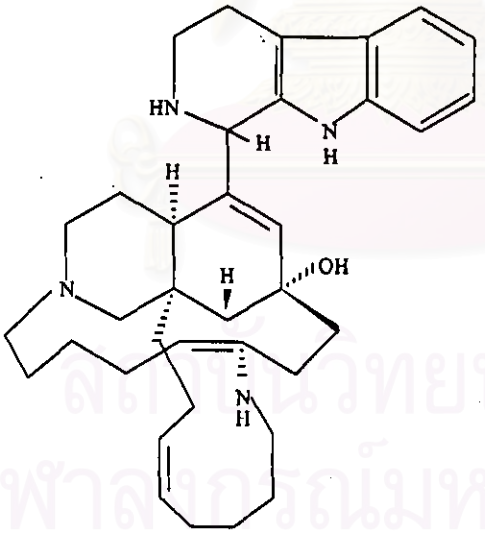
1.2 Biology of the genus *Ircinia.*

Ircinia with reticulum of primary (ascending) and secondary (interconnecting, thinner) spongin fiber. Fiber without pit, some cored by moderate quantities of foreign in clusion. Small, spherical choanocyte chambers (< 50 μm diameter). These genus contains filamentous spongin threads filling the choanosome, which the sponges extremey tough and difficult to tear. Typical form of *Ircinia,* with raised oscula, or massive and simple erect hollow branches and terminal oscula (Sterrer and Sterrer, 1986).

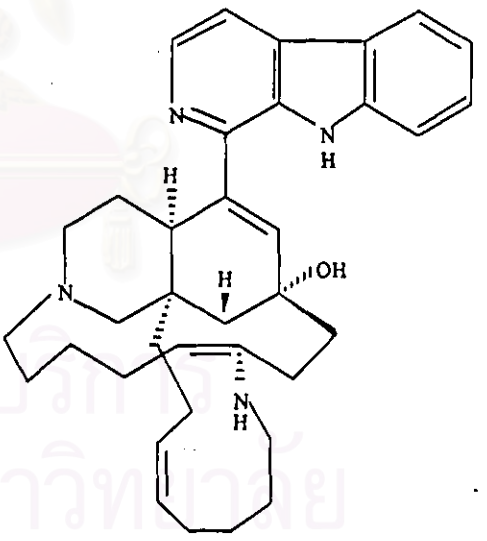
2 Chemical constituents of the genus *Ircinia*

Studies on the chemical constituents from the genus *Ircinia* began 25 years ago. There are 4 main groups of chemicals isolated from the genus *Ircinia*, including alkaloids, steroid derivatives, quinones and linear furanoterpenes which are the most abundant components in this genus. (Holler *et al.*, 1997).

The first group of compounds found in the *Ircinia* are the alkaloids which were isolated from Okinawa sponge, *Ircinia* sp., comprising of two new manzamine congeners, manzamines H (1) and J (2), and two known alkaloids, ircinals A (3) and B (4). These compounds exhibited cytotoxicity (Kondo *et al.*, 1992).



(1)



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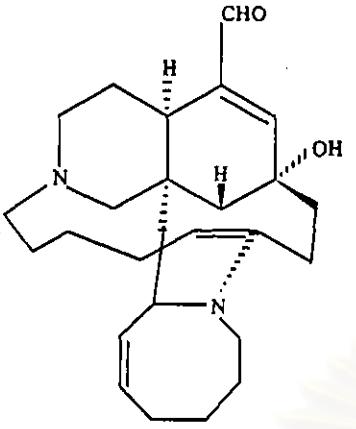

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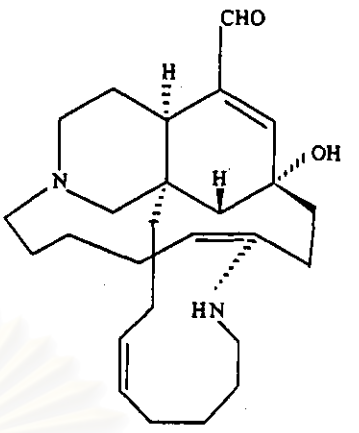
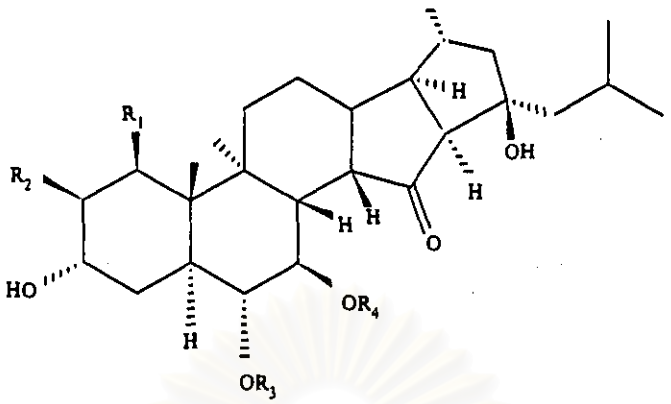
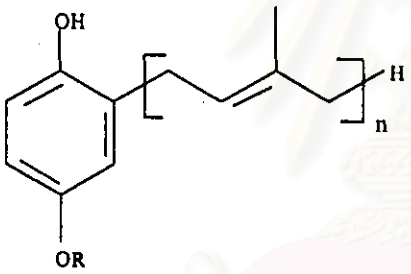


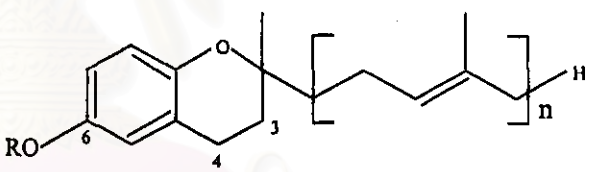
(4)

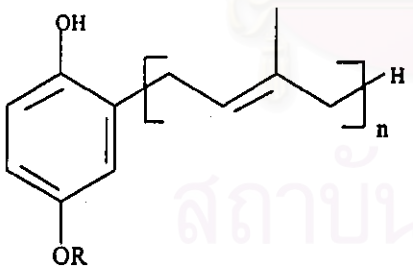
The second group is the pentacyclic steroid derivatives which were isolated from Okinawan marine sponge, *Ircinia* sp; xestobergsterols A (5), B (6) and C (7) (Kobayashi *et al.*, 1995). The third groups is the quinone compounds, containing the hepta prenyl hydroquinone 4-sulphate (8-10), prenylated benzopyran sulphates (11,12), prenylated hydroquinones (13-15) and hydroxylated 2-heptaprenyl hydroquinone (16), which showed activity in tyrosine proteine kinase (TPK) and HIV inhibitor (Bifuleo *et al.*, 1995). Other prenylated hydroduinone such as the hydroxylated-2-octaprenylhydroquinone (17) was isolated from *Ircinia spinosula* (Rosa *et al.*, 1995).



(5) $R_1 = R_2 = OH, R_3 = R_4 = H$
(6) $R_1 = R_3 = R_4 = H$
(7) $R_1 = R_3 = R_4 = H, R_2 = OH$







$R = SO^-_3Na^+$

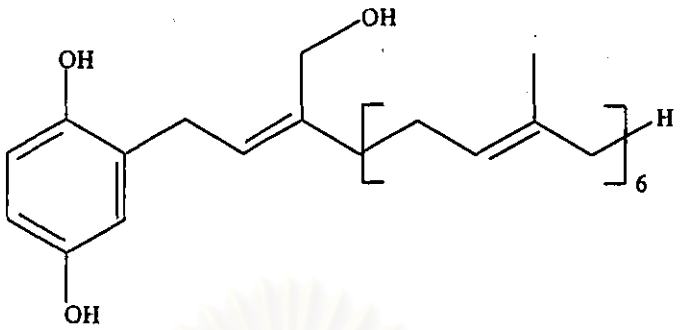
(8) n = 5, (9) n = 6, (10) n = 7

(11) n = 5

R = H

(12) n = 5, $\triangle^{3,4}$

(13)n = 4, (14) n = 5, (15) n = 6.



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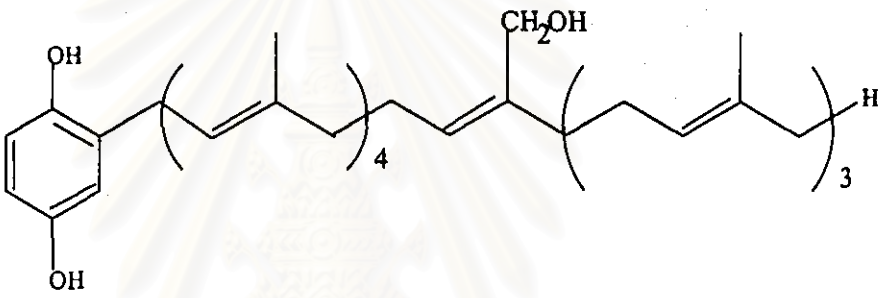


(17)

The linear furanoterpenes are the largest groups of constituents from in the genus *Ircinia*. Many kinds of linear furanoterpenes were isolated from the *Ircinia* for instance :

- Ircinin-1 (18) and Ircinin-2 (19) from *Ircinia oros* were found tobeisometric linear difuranoterpenes containing an unusual conjugated tetronic acid moiety (Faulker, 1973)

- Two new sesterterpene tetronic acids, (8Z, 13Z, 18S, 20Z)-strobilinin (20) and (7E, 12Z, 18S, 20Z)-variabilin (21), together with the known compounds (7E, 12E, 18S, 20Z)-variabilin (22), (7E, 13Z, 18S, 20Z)-variabilin (23) and (7Z, 12Z,

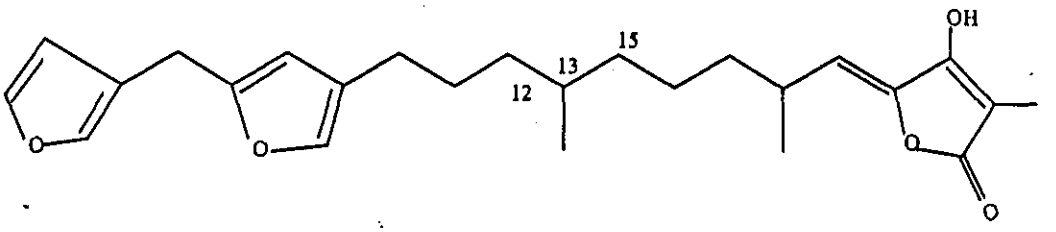
20Z)-variabilin (24), have been isolated from the sponge *Ircinia oros* as their 22-0 methyl derivative (25-29) (Holler *et al.*, 1997).

- Two new isomometric linear difurano-norsesterterpenes (30 and 31) have been isolated from the sponge *Ircinia oros* which are responsible for the biological activity on brine shrimp assay (Glulio *et al.*, 1990).

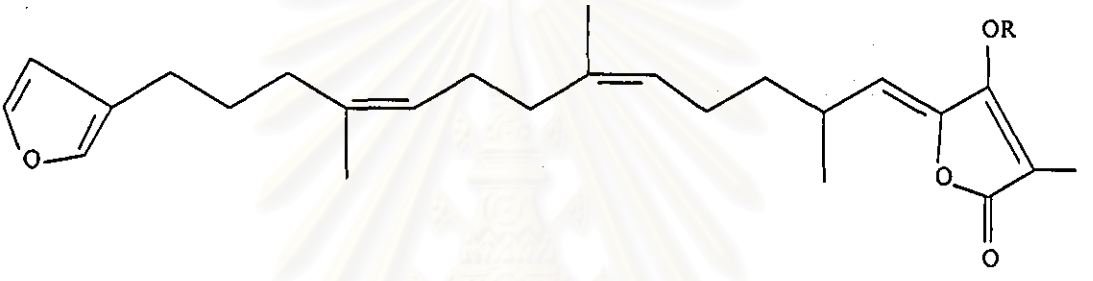
The other species of this genus is *Ircinia fasciculata*, produced compounds of fasciculatin (32) and variabilin (33) were shown to be a closely related monofurano-sesterterpene (Faulkner, 1973).

- Ketosesterterpenes (34-36) contain the lactone ring in the molecule which were isolated from *Ircinia* sp. (Barrow *et al.*, 1988).

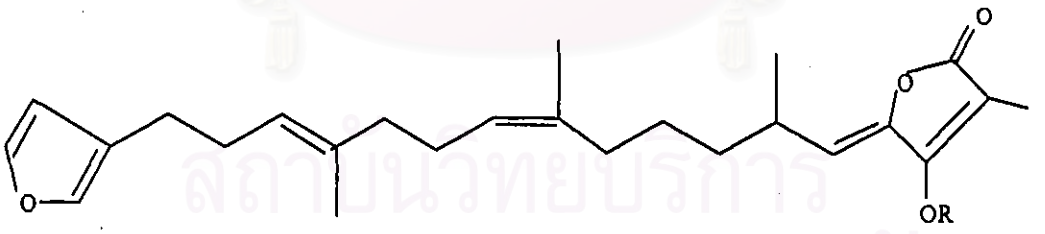
- A new sesterterpene tetronic acid [5-(13-(furan-3-yl)-2,6,10-trimethyltrideca-6,8-di-enyl]4-hydroxy-3-methylfuran-2(5H)-one] (37), extracted from *Ircinia* sp., exhibits antimicrobial activity (Capon and Macleod, 1987).



(18) $\triangle^{12,13}$ (19) $\triangle^{13,15}$

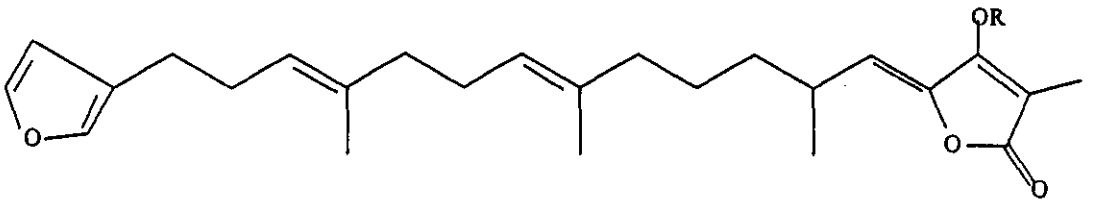


(20)R = H, (25) R = CH_3

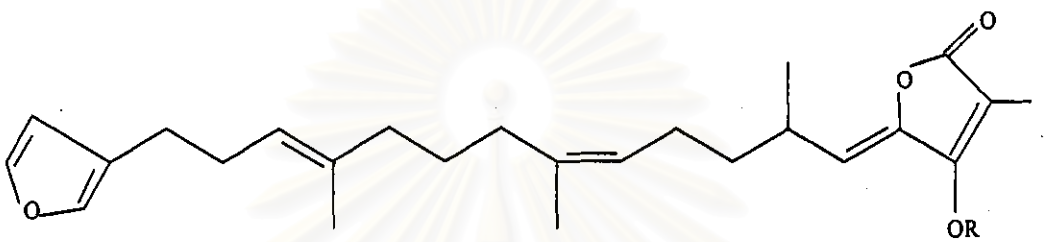


(21) R = H, (26) R = CH_3

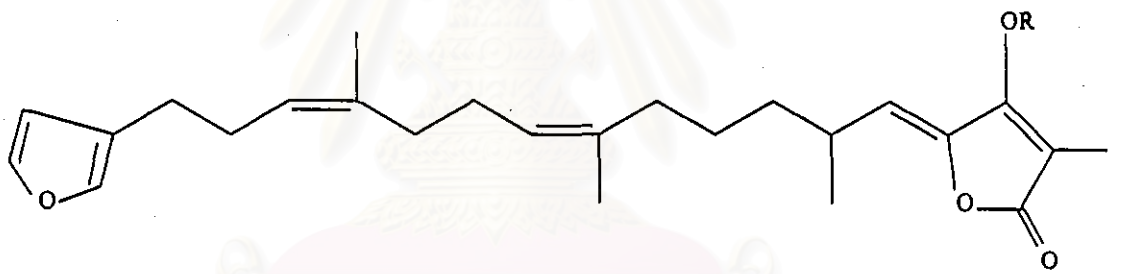
Figure 1. Chemical structures of the isolated compounds from genus *Ircinia*.



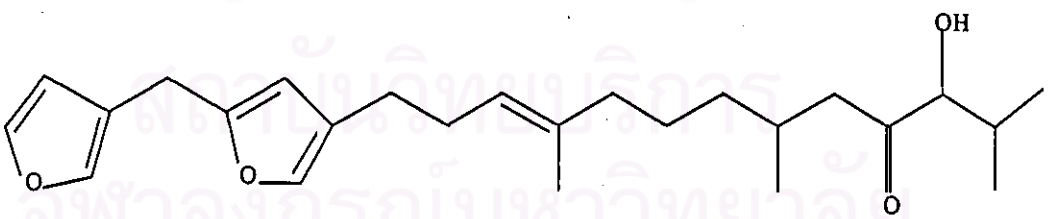
(22) R = H, (27) R = CH_3



(23) R = H, (28) R= CH_3

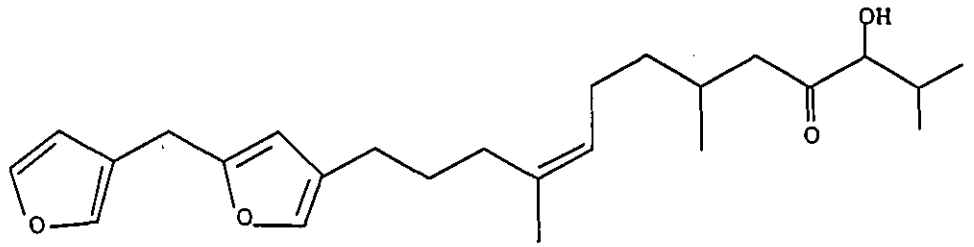


(24) R = H, (29) R = C



(30)

Figure 1. Continued



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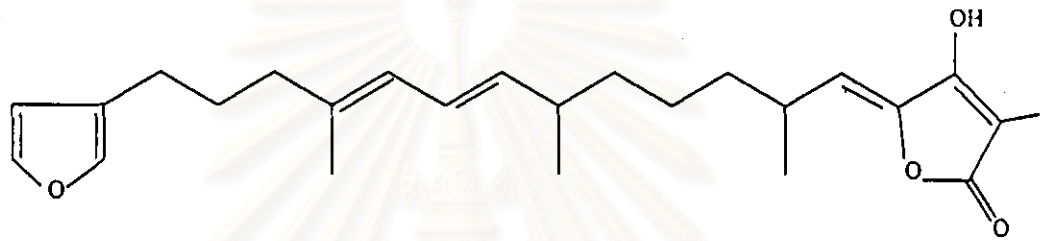

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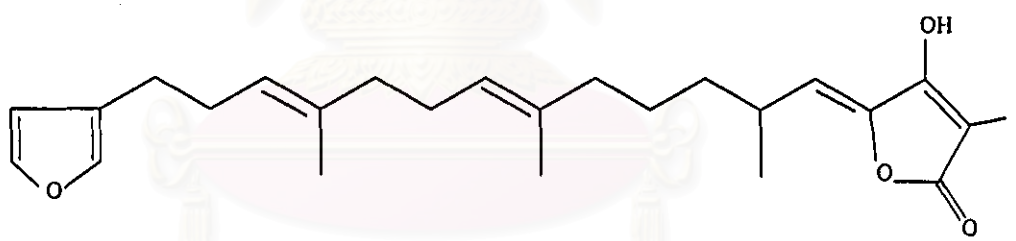

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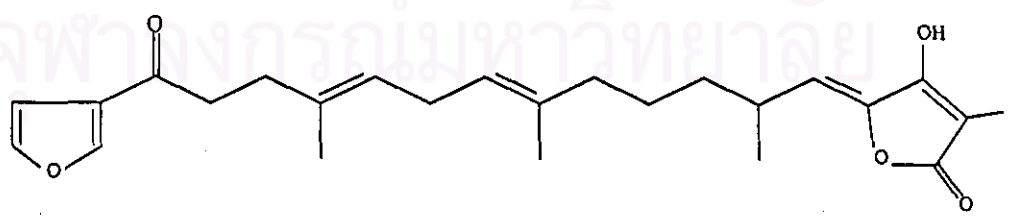
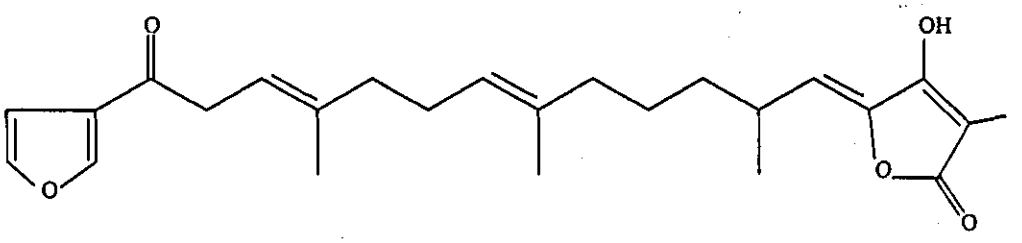


(34)

Figure 1. Continued.



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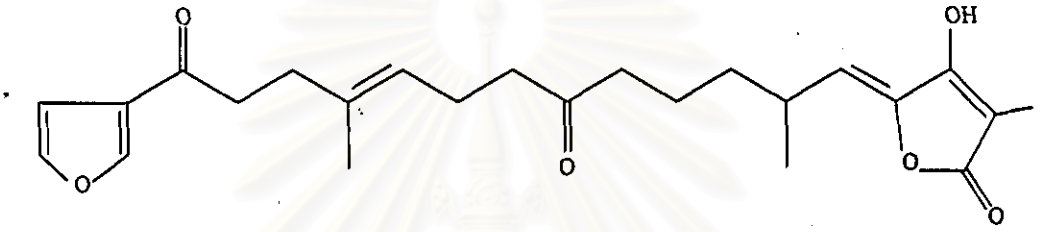
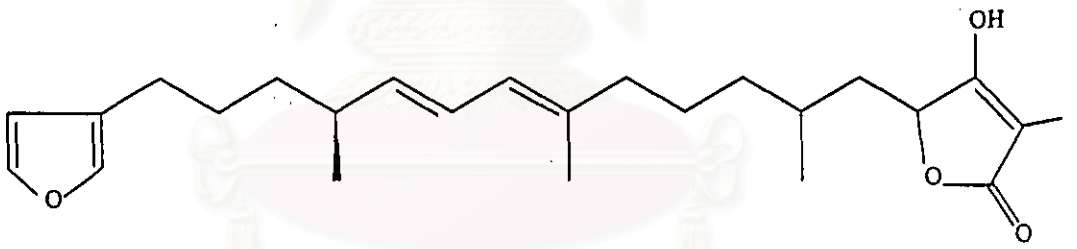


(36)



(37)

Figure 1. Continued.

3 The linear furanoterpenes.

3.1 Naturally occurring of a linear furanoterpenes.

Linear furanoterpenes are group of compounds which were found in nature. The main group of linear furanoterpenes found in marine sponges, is the linear C-21 furanoterpenes and related compounds. Furthermore, the sesterterpenes, C-25 compounds formed by successive head-to-tail additions of five isoprene units, are also relatively abundant in sponges, in contrast with their limited distribution elsewhere in insect protective waxes and fungi (Scheuer, 1983).

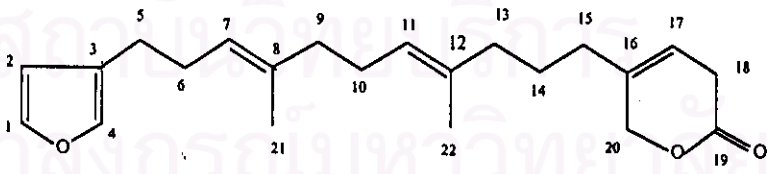
3.1.1 The C_{21} furanoterpenes.

Among the most unusual terpenes isolated from sponges are the linear furanoterpenes containing C-21 atoms, mainly occurring in the genus *Spongia*. The majority of them terminates in furan ring at both ends of the molecule and possess the same carbon skeleton. Oxidation in the central chain accounts for all their different. Lists of biological sources and chemical structures of C -21 furanoterpenes are shown in Table 1 and Figure 2, respectively.

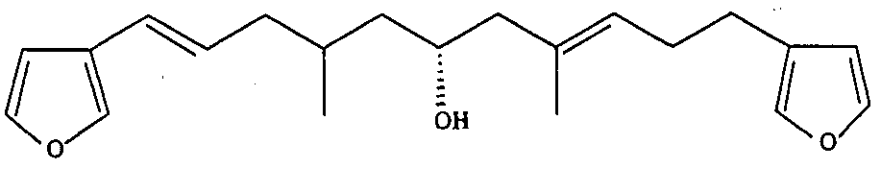
Table 1 List of C-21 furanoterpenes from marine sponges.

Compounds	Sources	References
Untenospogin B, (38)	*Hippospongia* sp.	Kobayashi *et al.*, 1993
Untenospogin C, (39)	*Hippospongia* sp.	Kobayashi *et al.*, 1993
Untenospongin A, (40)	*Hippospongia* sp.	Umeyama *et al.*, 1989
Kurospongin, (41)	*Spongia* sp.	Tanaka, and Higa, 1988
Furospongolide (43)	*Dysidea herbacea*	Kashman and Zviely, 1980
Furospongin-1, (42)	*Hippospongia communis*	Cimino, *et al.*, 1972
Furospongin-2, (44)	*Hippospongia communis*	Cimino, *et al.*, 1972
Dihydrofurospongin-2, (45)	*Hippospongia communis*	Cimino, *et al.*, 1972
Tetrahydrofurospongin-2, (46)	*Hippospongia communis*	Cimino, *et al.*, 1972

There are some linear furanoterpenes related to C-21 furanoterpene. It's furodendin a C-22 degraded terpene from the maine sponges *Phyllospongia dendyi* as shown below (Kazhlauskas and Zviely, 1979).



Furodendin.



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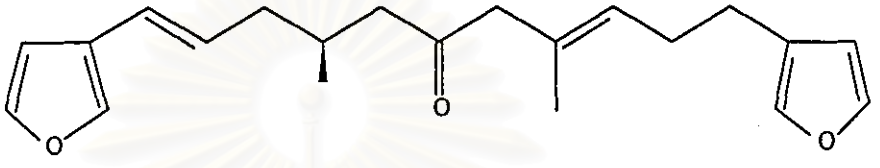

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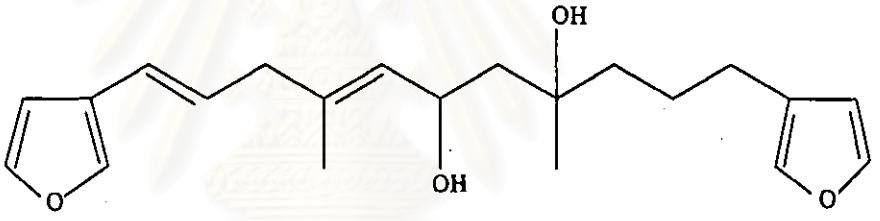

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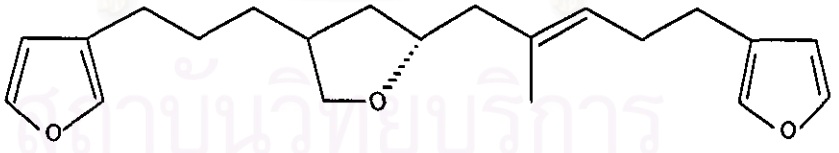
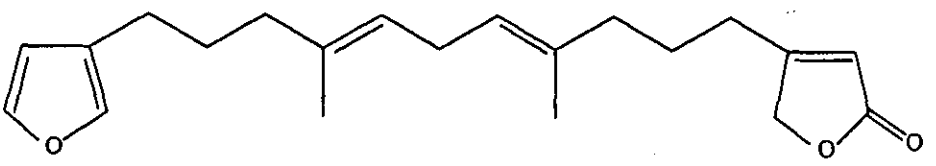


(41)

Figure 2. Structures of C-21 furanoterpenes isolated from marine sponges.



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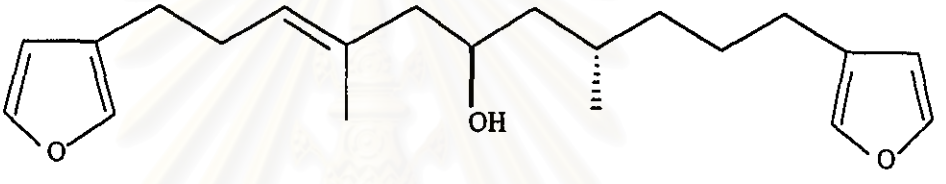

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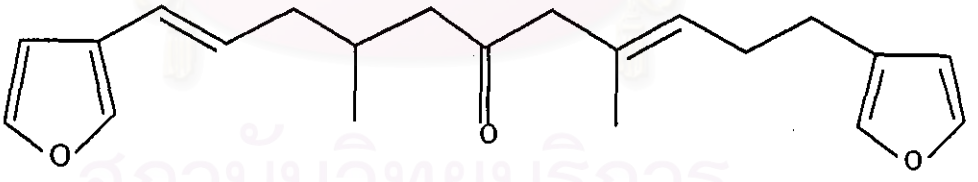
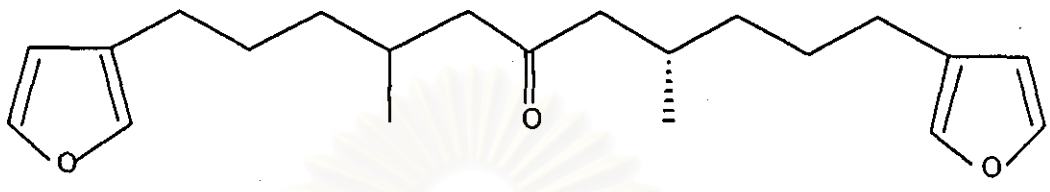


(44)

Figure 2 Continued



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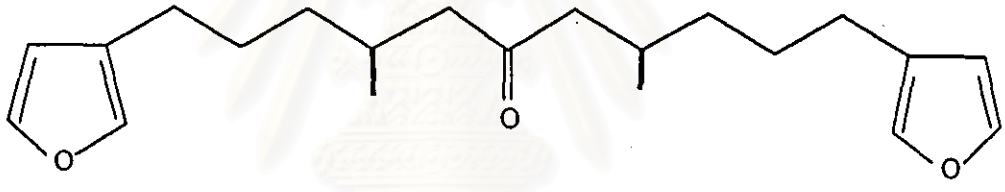


(46)

Figure 2 Continued.

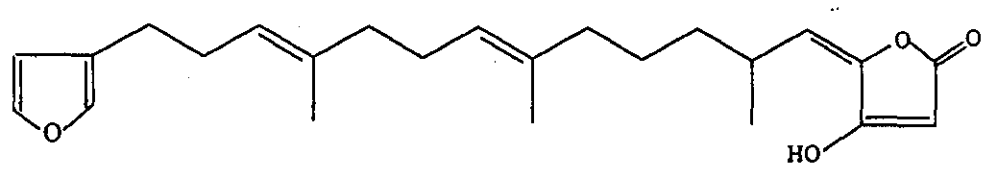
3.1.2 The furanosesterterpenes.

Sesterterpenoids are a small group of natural products that occur mainly in marine organisms. There are only about 200 natural sesterterpenoids known but a diverse array of about 25 carbon frameworks. Although they are C-25 compounds, there are a large number of nor and alkylated-sesterterpenoid. (Mann *et al.*, 1994). Marine sponges are rich in the rare C-25 terpenoids, especially, the linear series of sesterterpenes terminated by furan ring at one end and by tetronic acid moiety at the other end (Scheuer, 1978).

The distribution of the linear sesterterpenes in marine sponges is shown in Table 2 and Figure 3.

Table 2 List of furanosesterterpenes from marine sponges.

Compounds	Sources	References
Furospinulin, (48)	*Fasciospongia fovea*	Baker, 1996
Strobilin (49)	*Demospongia* sp.	Davis and Capon, 1994
Palominin (50)	*Demospongia* sp.	Davis and Capon, 1994
Isopalinurin, (51)	*Dysidea* sp.	Murray *et al.*, 1993
Furospinosulin-1, (52)	*Spongia* sp.	Urban *et al*, 1992
Cometin-A, (53)	*Spongia* sp.	Urban *et al*, 1992
Cometin-B, (54)	*Spongia* sp.	Urban *et al*, 1992
Cometin-C, (55)	*Spongia* sp.	Urban *et al*, 1992
Palinurin (56)	*Ircinia variabilis*	Loikas *et al*, 1989
Variabilin, (57)	*Ircinia variabilis*	Loikas *et al*, 1989
Furanosesterterpene, (58)	*Psammocinia rugosa*	Loikas *et al*, 1989
Furanosesterterpene methyl esters , (59) and (60)	*Psammocinia rugosa*	Loikas *et al.*, 1989
Ircinic acid, (61)	*Ircinia* sp.	Manes *et al.*, 1986
Hippospongin, (62)	*Hippospongia* sp.	Kobayashi *et al.*, 1986



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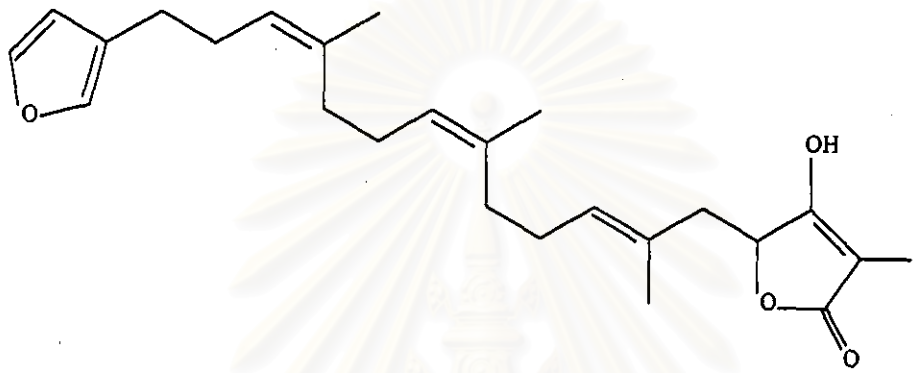
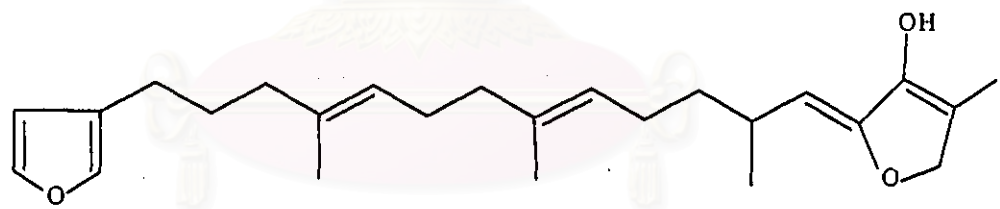


(49)



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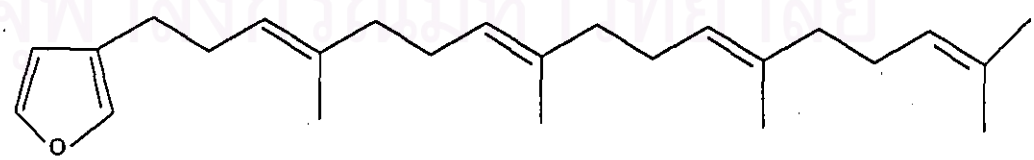
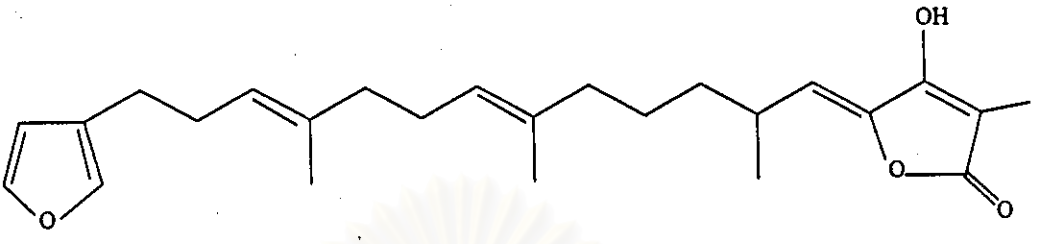
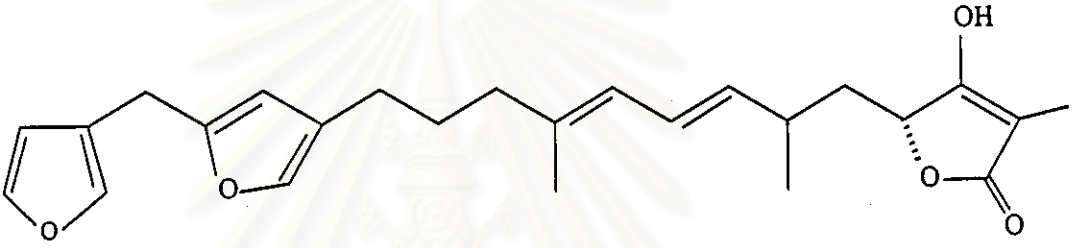


(51)

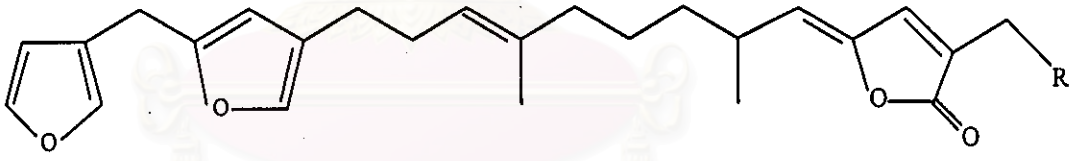
Figure 3. Structures of furanosesterterpenes isolated from marine sponges.



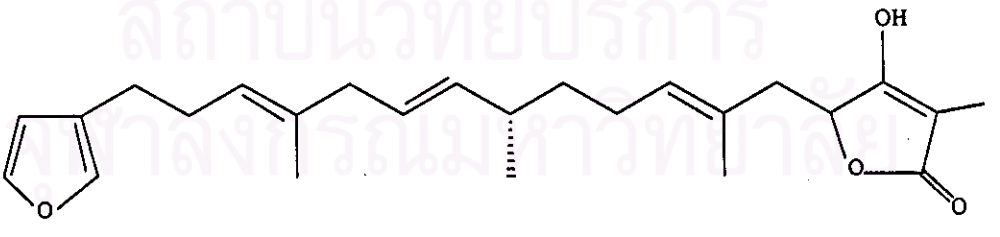
(52)



(53)

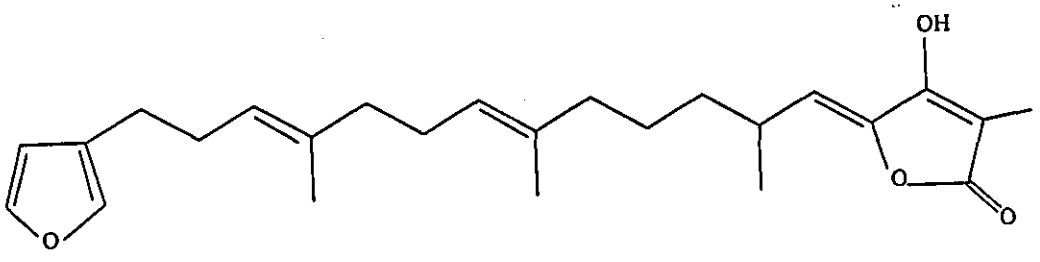


(54) R = OH, (55) R = H

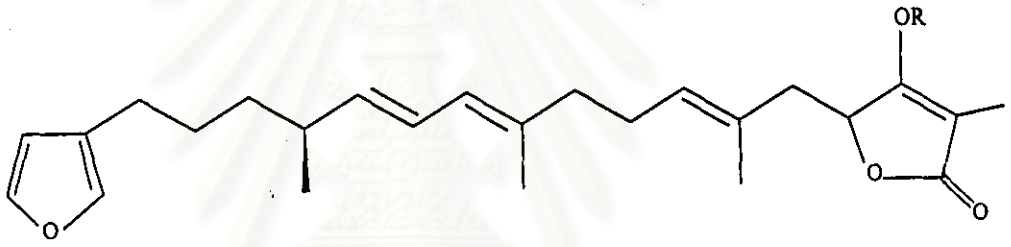


(56)

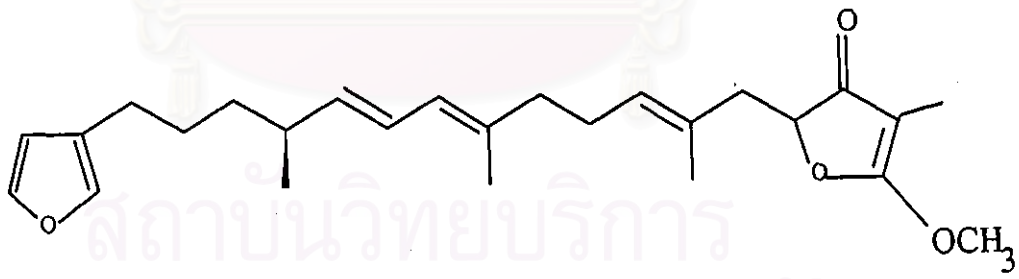
Figure 3. Continued.



(57)

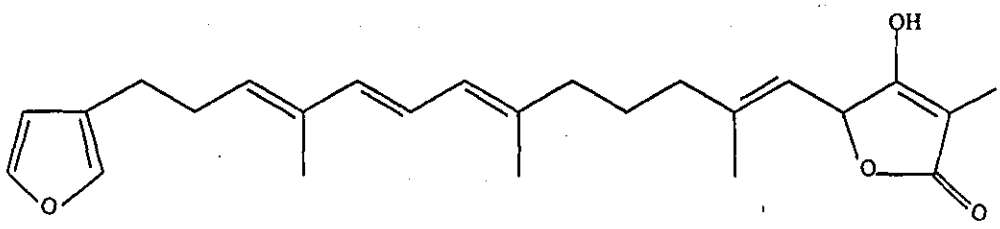


(58) R = H, (59) R = CH_3

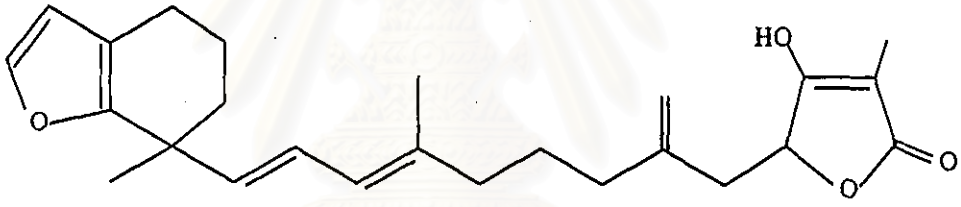


(60)

Figure 3. Continued.



(61)



(62)

Figure 3. Continued.

4 The Bioactivities of linear furanoterpenes

A large number of linear furanoterpenes exhibited cytotoxicity, antimicrobial and vasodilating activity. They are highly to moderately active to cytotoxic and antimicrobial activity, but, less active to vasodilating activity. There are also some reports described the activities.

4.1 Bioactivities of C-21 furanoterpenes

Marine sponges of the genus *Hippospongia* are rich source of bioactive compounds such as a C-21 furanoterpenes, untenospongin C (39) exhibited cytotoxicity against murine lymphoma L1210 cell in vitro with IC_{50} value of 3.8 μg/ml (Kobayashi, 1993).

Untenospongins A (40) and B (38) exhibited potent coronary vasodilating activity, markedly inhibiting KCl (40 mM) induced concentration of rabbit isolated coronary artery with IC_{50} value of 10^{-6} and $2x10^{-6}$ M, respectively (Umeyama *et al.*, 1989). In addition, kurospongin (46), a new C-21 furanoterpene had ichthyotoxin and feeding-deterrent properties (Tanaka and Higa, 1988).

4.2 Bioactivities of furanosesterterpenes

Linear furanosesterterpenes which were isolated from marine sponges are strongly active for antimicrobial activity, while slightly active to antiinflammatory acitivity and other biological activities. Some biological activities of compounds in this group are shown below.

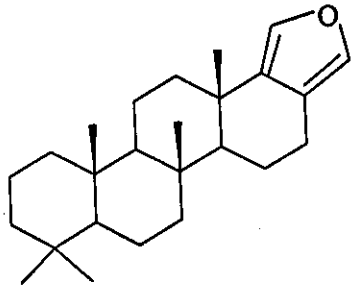
Variabilin (57) and stobilinin (48) and other related compounds which isolated from *Ircinia variabilis* are shown to possess antiviral and cytoxic activity and also exhibited antimicrobial agent (Holler *et al.*, 1997).

Difurano-norsesterterpenes (30, 31) isolated from *Ircinia oros* are responsible for the biological activity, with high activity (LD_{50} = 14 μg/ml) in brine shrimp assay (Giulio *et al.*, 1990).

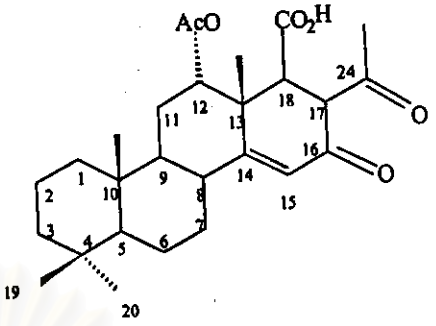
Three new furanosesterterpenes namely cometins A (65), B (66) and C (67), showed growth-inhibitory properties against the bacteria, *Staphylococcus aureus* and *Sarratia* sp. (Urban and Capon, 1992)

5 The scalarane sesterterpenes.

The scalaranes are among of the most common sesterterpenoids, particularly in the sponges. In many instances, scalaranes have been found in nudibranchs but probably they originated from sponges as a dietary source. The basic skeleton is exemplified by sacararin but many scalaranes bear one or two extra carbon atoms. The biogenetic introduction of the extra methyl groups at C-24 is interesting (Thomson, 1993)



Scararin



Scalarane

5.1 Naturally occurring of scalarane sesterterpenes

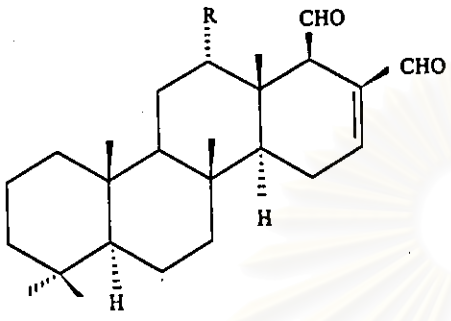
A large amount of sponges metabolites are alkylated scalarane sesterterpenes. Such compounds, often called homoscalaranes, can be further divided into four frameworks consisting of two monoalkylated (C-26) and two bis-alkylated (C-27) form. The 20 homosesterterpenes are abundant in the chemistry of both of sponges, *Lendenfeldia dendyi* and *Lendenfeldia frondosa*, while 20,22-bishomosesterterpenes have been repeatedly reported from *Phyllospongia, Carteriospongia* and *Strepsichordaria* (Jaspars *et al.*, 1997).

In recent years, quite a few scalarane-type C-25, C-26 and C-27 sesterterpenes have been isolated from various marine sponges, *Phyllospongia radiata, P. dendyi, P. foliascens, Dysidea herbacea, Spongia idia, S. nitens,* and *Cacospongia scalaris* (Kikuchi *et al.*, 1983).

List of biological sources and chemical structures of scalarane sesterterpenes in marine sponges are shown in Table 3 and Figure 4, respectively.

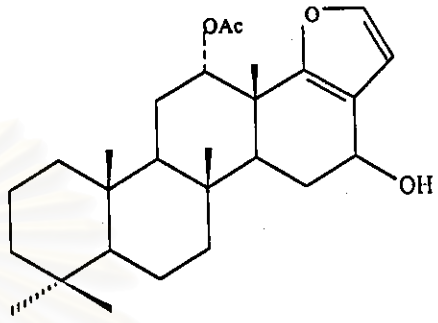
Table 3 List of scalarane sesterterpenes from marine sponges.

Compounds	Sources	References
12-Desacetoxyscalaradial, (63)	*Cacospongta mollior*	Rosa *et al.*, 1994
Scaladial, (64)	*Cacospongta mollior*	Rosa *et al.*, 1994
Furoscarol, (65)	*Cacospongta mollior*	Rosa *et al.*, 1994
12α-Acetoxy-16β-(3'R-hydroxybutanoyloxy)-20,24-dimethyl-24-oxoscalaran-25-al, (66)	*Strepsichordaia lendenfeldi*	Bowden *et al.*,1992
12α-Acetoxy-16β-(3'-hydroxypentanoyloxy)-20,24-dimethyl-24-oxoscalaran-25-al, (67)	*Strepsichordaia lendenfeldi*	Bowden *et al.*,1992
Phyllactone A, (68)	*Phyllospongia foliascens*	Fu *et al.*, 1992
Phyllactone E, (69)	*Phyllospongia foliascens*	Fu *et al.*, 1992
12α-Acetoxy-20,24β-dimethyl-17-eno-25-lactone, (70)		
16β, 22-dihydroxy-24-methyl-24-oxoscalaran-25, 12β-olactone, (73)	*Halichondria* sp.	Nagakawa *et al.*, 1987
12α-Acetoxy-24-methyl-24-oxoscalar-16-en-22, 25-dial, (71)	*Halichondria* sp.	Nagakawa *et al.*, 1987
Foliaspongin, (73)	*Phyllospongia foliascens*	Kikuchi *et al.*, 1983

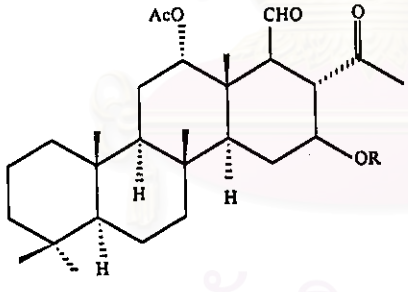


(63) R = H

(64) R = $OCOCH_3$

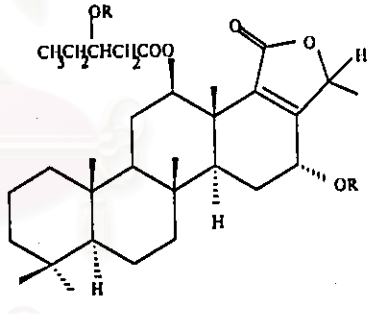


(65)



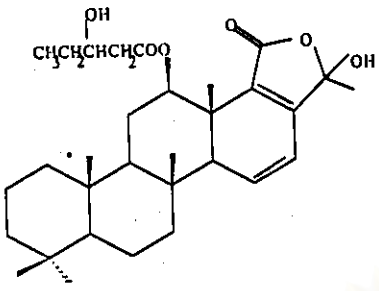
(66) R = $CH_3CHOHCH_2CO$

(67) R = $CH_3CH_2CHOHCH_2CO$

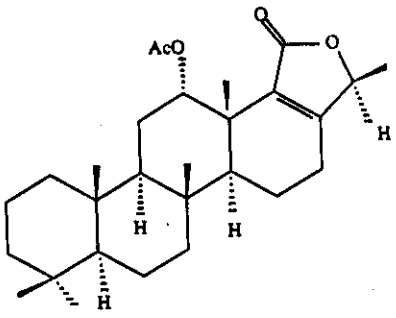


(68)

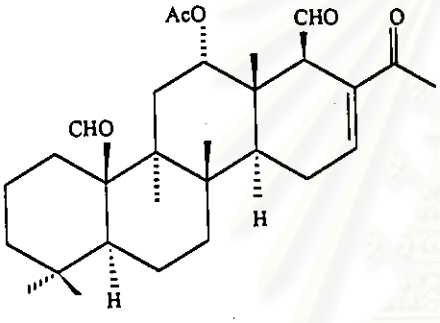
Figure 4. Structures of scalarane sesterterpenes islated from marine sponges.



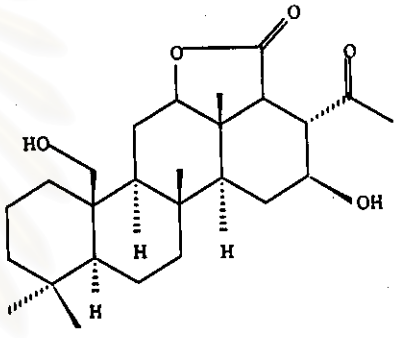
(69) Me - 26β



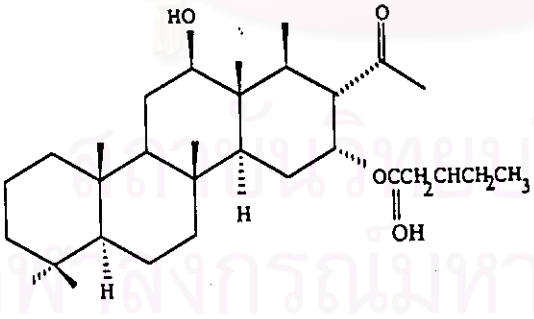
(70)



(71)



(72)



(73)

Figure 4 continued.

5.2 Bioactivities of scalarane sesterterpenes from marines sponges

They are few scalarane sesterterpenes showed some interesting biological activities, including, new sesterterpenes [12-descacetoxyscalaradial (63) and scalaradial (64)] which were isolated from marine sponge *Cacospongia mollior*. They exhibited highly cytoxic activity (Rosa *et al.*, 1994).

Bowden *et al.*, (1992) found that 12α-acetoxy-16β-(3′-R-hydroxybutanoyloxy)-20,24-dimethyl-24-oxoscalarane-25-al (66) and 12α-acetoxyl-16β-(3′-hydroxypentanoyloxy)-20,24-dimethyl-24-oxoscalarane-25-al (67) showed the incidence of anti-inflammatory and cytotoxic activity.

The foliaspongin (73) isolated from marine sponge, *Phyllospongia foliascens* (Pallas) showed anti-inflammatory activity (Kikuchi *et al.*, 1983).

16β, 22-dihydroxy-24-methyl-24-oxoscalaran-25, 12β-olactone (72) was shown to have the significant inhibitory activity (ID_{50} = 0.5μg/ml) on platelet aggregations caused by adenosine-5-diphosphate, collagen, or arachidonic acid (Nakagawa *et al.*, 1987).