

Review Article

Chemical Constituents and Biological Properties of the Marine Soft Coral *Nephthea*: A Review (Part 2)

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Abstract

*This second part of the review dwells on *Nephthea chabrolii* and *Nephthea* Sp. which contain isoketochabrolic acid, ketochabrolic acid, sesquiterpenes, diterpenes and steroids. Corresponding biological activities such as anti-inflammatory and cytotoxic activities have also been observed for the isolated constituents. Most of the new compounds isolated from the genus *Nephthea* are from *N. chabrolii* and *N. Sp.*, among which steroids are the most abundant.*

Keywords: *Marine coral, Acyonaceae, Nephtheidae, Nephthea, Sesquiterpenes, Diterpenes, Steroids.*

Received: 16 May 2011

Revised accepted: 11 April 2012

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INTRODUCTION

Nephthea chabrolii and *Nephthea Sp.* have been broadly investigated and a large number of secondary metabolites such as: sesquiterpenes, diterpenes and steroids (Table 1a, 1b, 1c and 1d). Corresponding biological activities have also been reported for the extracts and the isolated constituents [1-6].

CHEMICAL CONSTITUENTS AND BIOLOGICAL PROPERTIES

Nephthea chabrolii

Initial investigations on *N. chabrolii*, reported two new sesquiterpenes germacrene C (**1**) and valerol (**2**) (Fig 1) and two new diterpenes, oxirane, 3-[2-(6,10-dimethyl-2-methylenebicyclo-undec-5-en-10-yl)ethyl]-2,2-dimethyl (**3**) and bicyclo-undec-5-ene-10-propanol, α -(1-chloro-1-methylethyl)-6,10-dimethyl-2-methylene (**4**) [7-8].

Anjaneyulu and Prakash reported a new steroid, 14 α ,24-dimethylcholestan-3 β ,25-diol (**5**) two new diterpenoids naphthol-A and B (**6-7**), and four new sesquiterpenoids, 1-acetoxygermacra-3,10(15)-diene (**8**), 1-acetoxygermacra-3,5,10(15)-triene (**9**), 1,4,5-gaia-6,9-dien-4-ol (**10**), and 1,5,6-gaia-3,10(15)-dien-7,11-epoxy-6 β -acetate (**11**) from the soft coral *N. chabrolii* [9-10].

Chemical examination of the soft coral *N. chabrolii* afforded two new sesquiterpenes (Fig 2), hydroxycolorenone (**12**) and methoxycolorenone (**13**) along with a known compound, (+)-cyclocolorenone, from the Indonesian soft coral *N. chabrolii*. Hydroxycolorenone (**12**) indicated potent insecticidal activity against neonate larvae of the polyphagous pest insect *Spodoptera littoralis* (EC₅₀ = 8.8 ppm and LC₅₀ = 453 ppm) [11].

Rao *et al* reported two new 19-oxygenated polyhydroxy steroids, 24-methylene cholest-

5-en-1 α ,3 β ,19-triol (**14**) and 24-methylene cholest-5-en-3 β ,7 β ,9 α ,19-tetrol (**15**), and four new sesquiterpenoids, 10 α -Methoxy-4 β -hydroxyguaian-6-ene (**16**), 6 β ,7 β -Epoxy-4 β -hydroxyguaian-10-ene (**17**), 4,15-Dihydroguaian-6,10-diene (**18**) and Guaian-4,6-dien-10 α -ol (**19**), along with the known compounds ergost-5,24(28)-dien-3 β ,19-diol, cholest-5-en-3 β ,7 β ,19-triol, and ergost-5,24(28)-dien-3 β ,7 β ,19-triol, were isolated from the soft coral *N. chabrolii* and characterized through interpretation of spectral data [12-13]. A new sterol, 4 α -methyl-24-methylene-5 α -cholestan-3 β ,8 β -diol (**20**), together with 4 α -methyl-24-methylenecholestan-3 β -ol, 4 α -methylcholestan-3 β -ol, and 24-methylenecholest-4-en-3-one was also reported [14].

Zhang *et al* reported three new norditerpenes (Fig 3a and 3b), chabrolols A-C (**21-23**), two new Polyhydroxylated steroids 24-methylcholesta-9(11), 24(28)-diene-3 β ,12 α ,19-triol (**24**) and 4 α -methyl-3 β ,14 β -dihydroxy-5 α -ergost-24(28)-en-23-one (**25**), together with the known compounds 24-methyl-7 β -acetoxycholesta-5,24(28)-diene-3 β ,19-diol, 24-methylcholest-24(28)-ene-3 β ,5 α ,6 β ,19-tetraol, 24-methyl-7-oxocholesta-5,24(28)-diene-3 β ,19-diol and 24-methylcholesta-5,24(28)-dien-3 β -ol.

Among the isolated compounds certain compounds indicated potent cytotoxic activities against prostate carcinoma LNCaP cell line [15-16]. Nine new diterpenoids, chabrolonaphthoquinone A (**26**), chabrolhydroxybenzoquinones A-D (**27-30**), and chabrolbenzoquinones A-D (**31-34**) were reported from the soft coral, *N. chabrolii* [17].

Su *et al* isolated eight new meroditerpenoid-related compounds (Fig 4a, 4b and 4c), chabrolonaphthoquinone B (**35**), chabrolbenzoquinones E-H (**36-39**), and chabrolhydroxybenzoquinones E-G (**40-42**), two new carboxylic acids, ketochabrollic acid

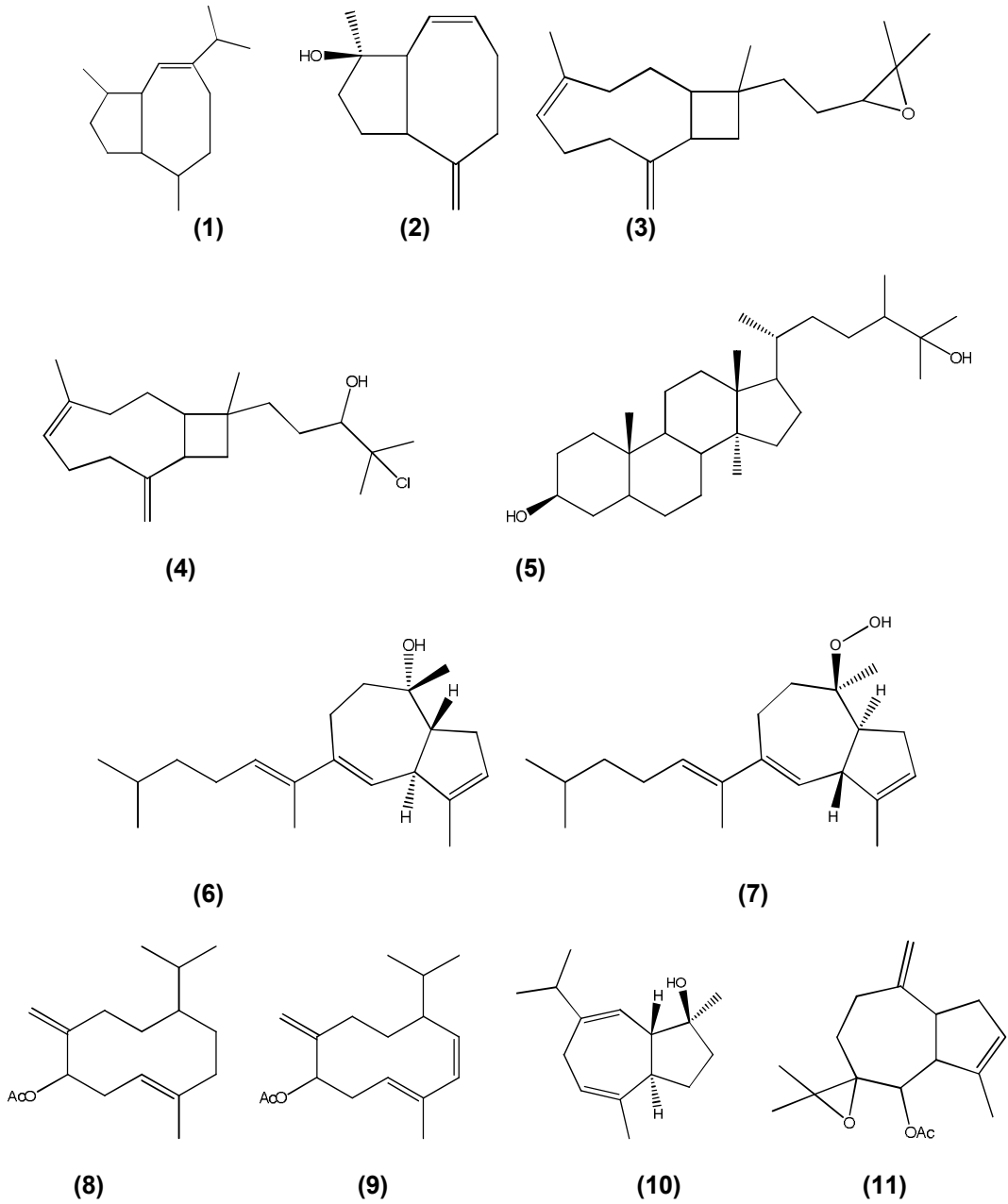
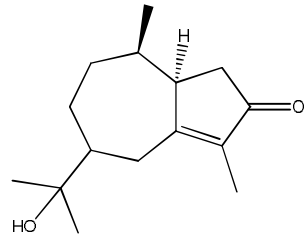
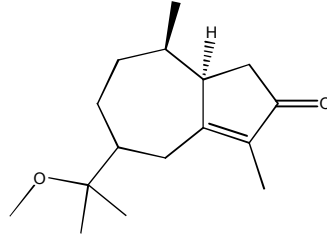


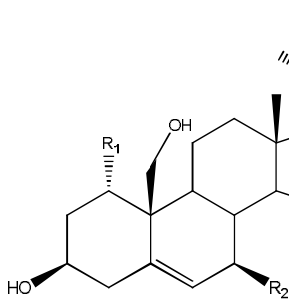
Fig 1: Compounds 1 – 11



(12)

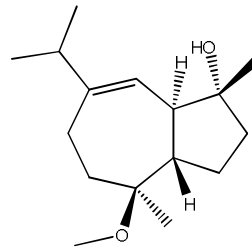


(13)

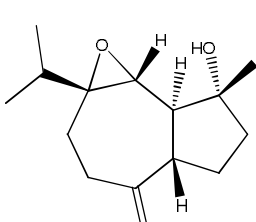


(14) $R_1 = OH, R_2 = H$

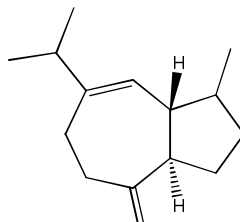
(15) $R_1 = H, R_2 = OH$



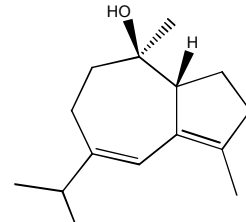
(16)



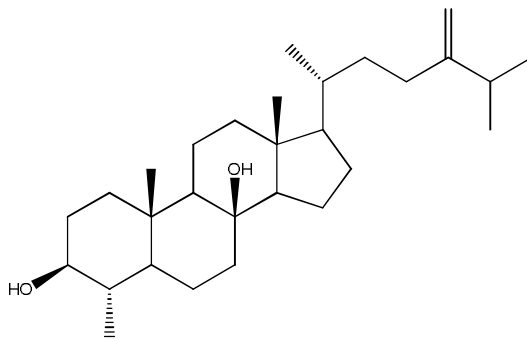
(17)



(18)



(19)



(20)

Fig 2: Compounds 12 – 20

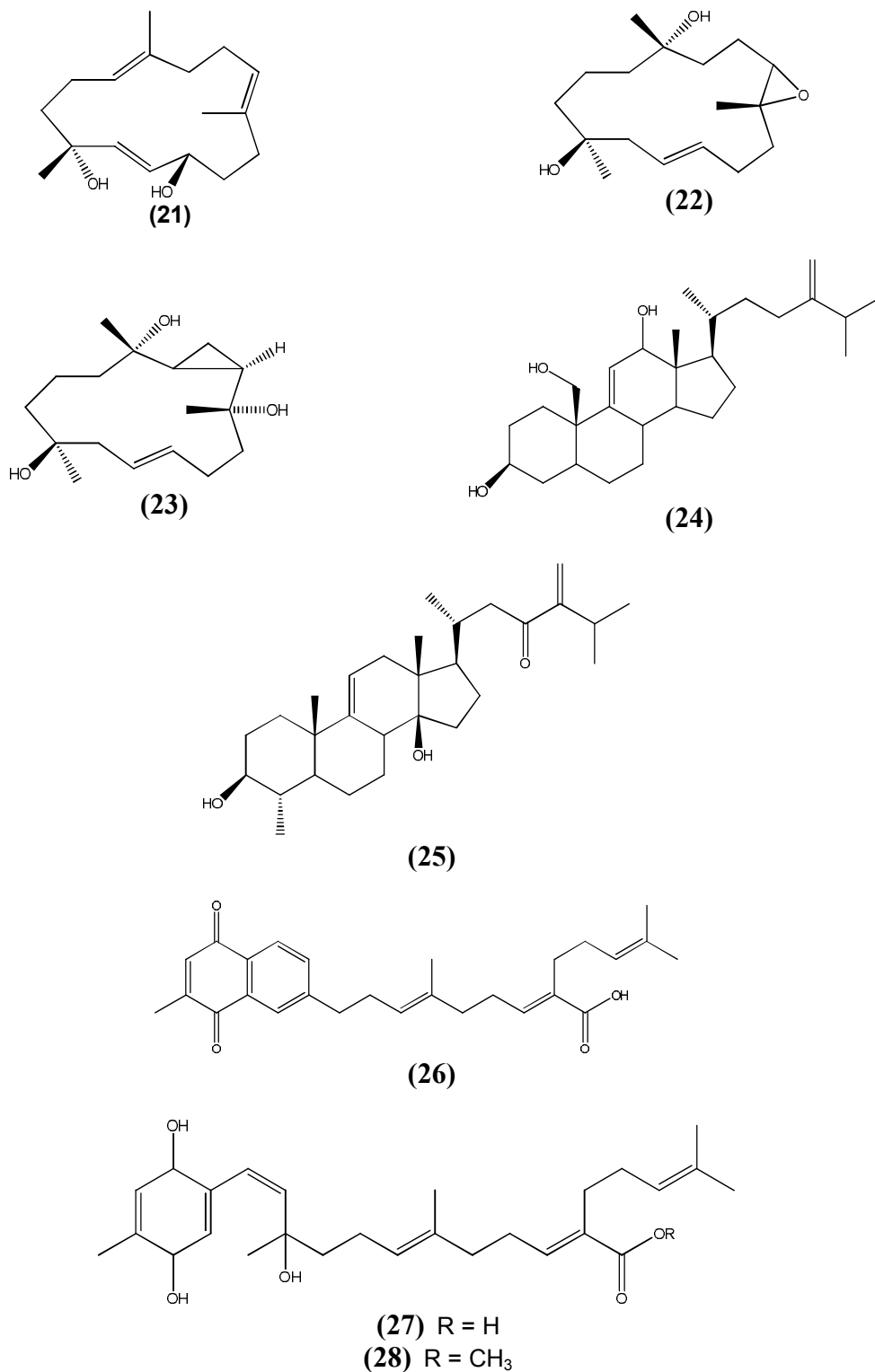


Fig 3a: Compound 21 - 28

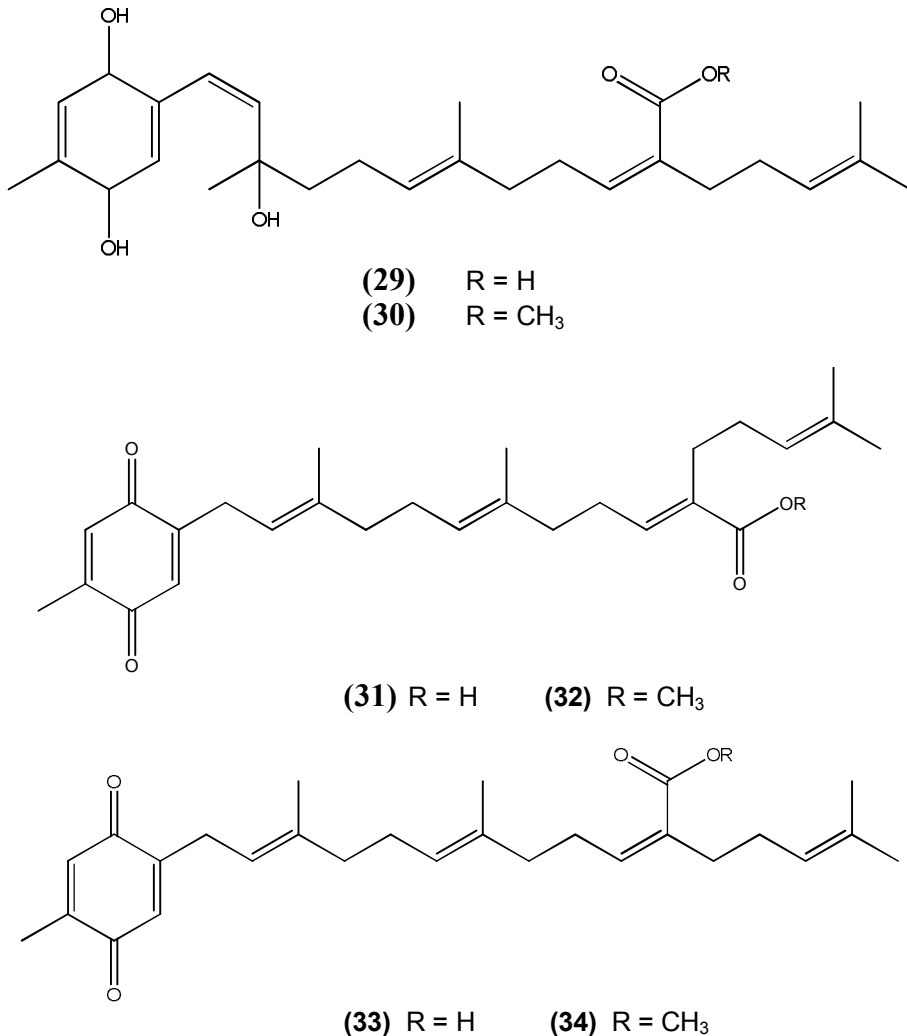
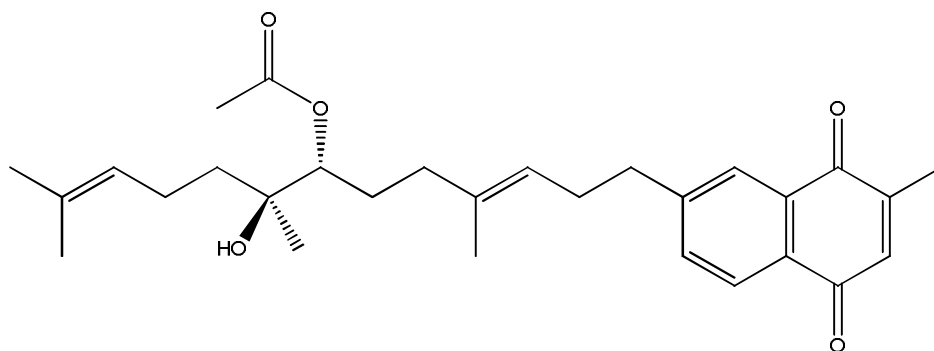


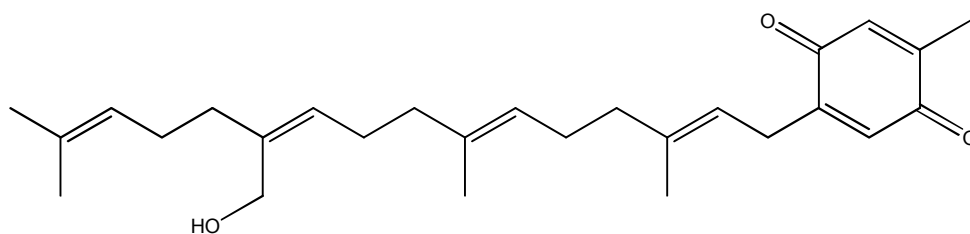
Fig 3b: Compounds 29 - 34

(43) and isoketochabrolic acid (44), one naphthoquinone derivative chabrolonaphthoquinone C (45), two new sesquiterpenoids, chabrolidiones A (46) and B (47), and nine new steroids, chabrolosteroids A-I (48-56), together with the known compounds (+)-aristolone and teuhetenone A, from the soft coral *N. chabrolii*. Compound (35) showed potent cytotoxic activity against MDA-MB-231 and Hep G2 cancer cell lines with IC₅₀ values of

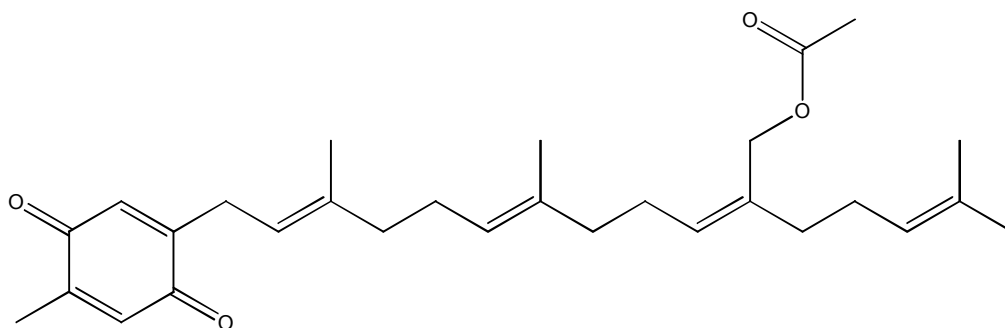
12.4 and 33.9 μM, respectively [18] while compound (45) showed moderate to weak cytotoxic activity against MDA-MB-231, MCF-7, Hep G2, and A-549 cancer cell lines with IC₅₀ values 8.4, 11.9 Hep G2 16.4, and 9.3 mg/ml, respectively [5]. Compound (49) showed weak cytotoxic activity against Hep 3B (IC₅₀, 19.9 mg/mL) [19]. While compound (56) exhibited moderate to weak cytotoxic activity against cancer cell lines Hep 3B and A-549 with IC₅₀ values of 15.6 and 17.8 mg/mL, respectively [6].



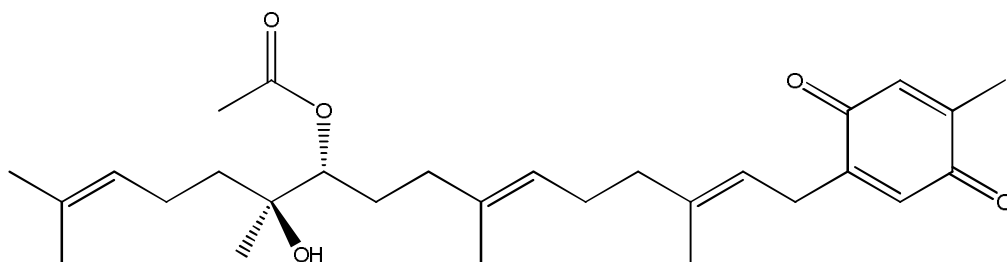
(35)



(36)



(37)



(38)

Fig 4a: Compounds 35 – 38

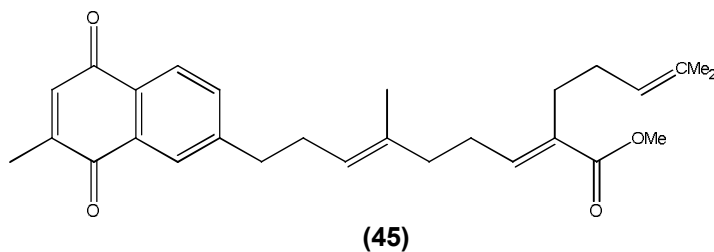
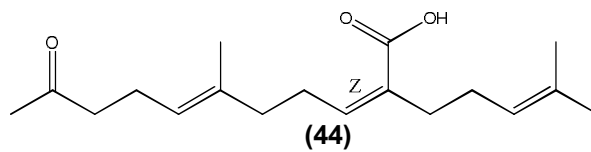
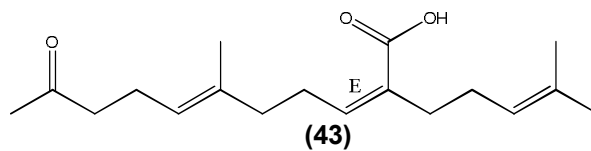
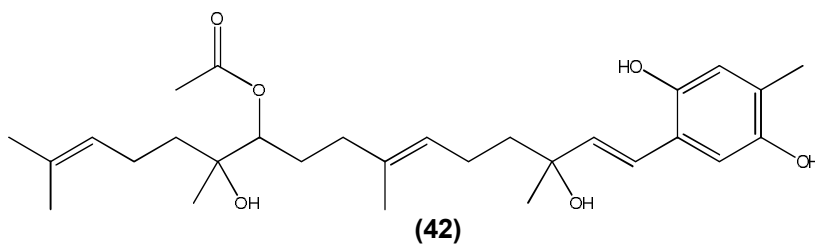
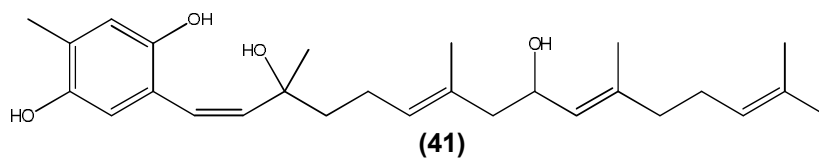
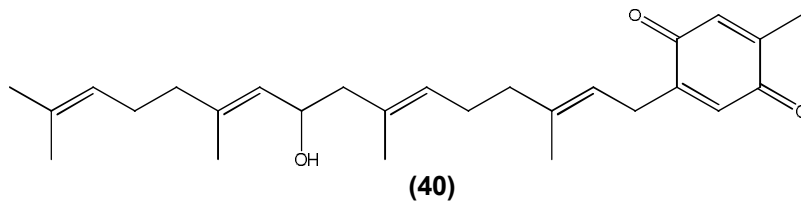
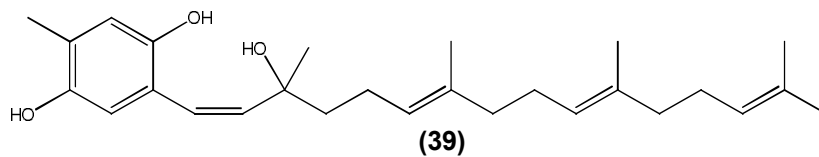


Fig 4b: Compounds 39 - 45

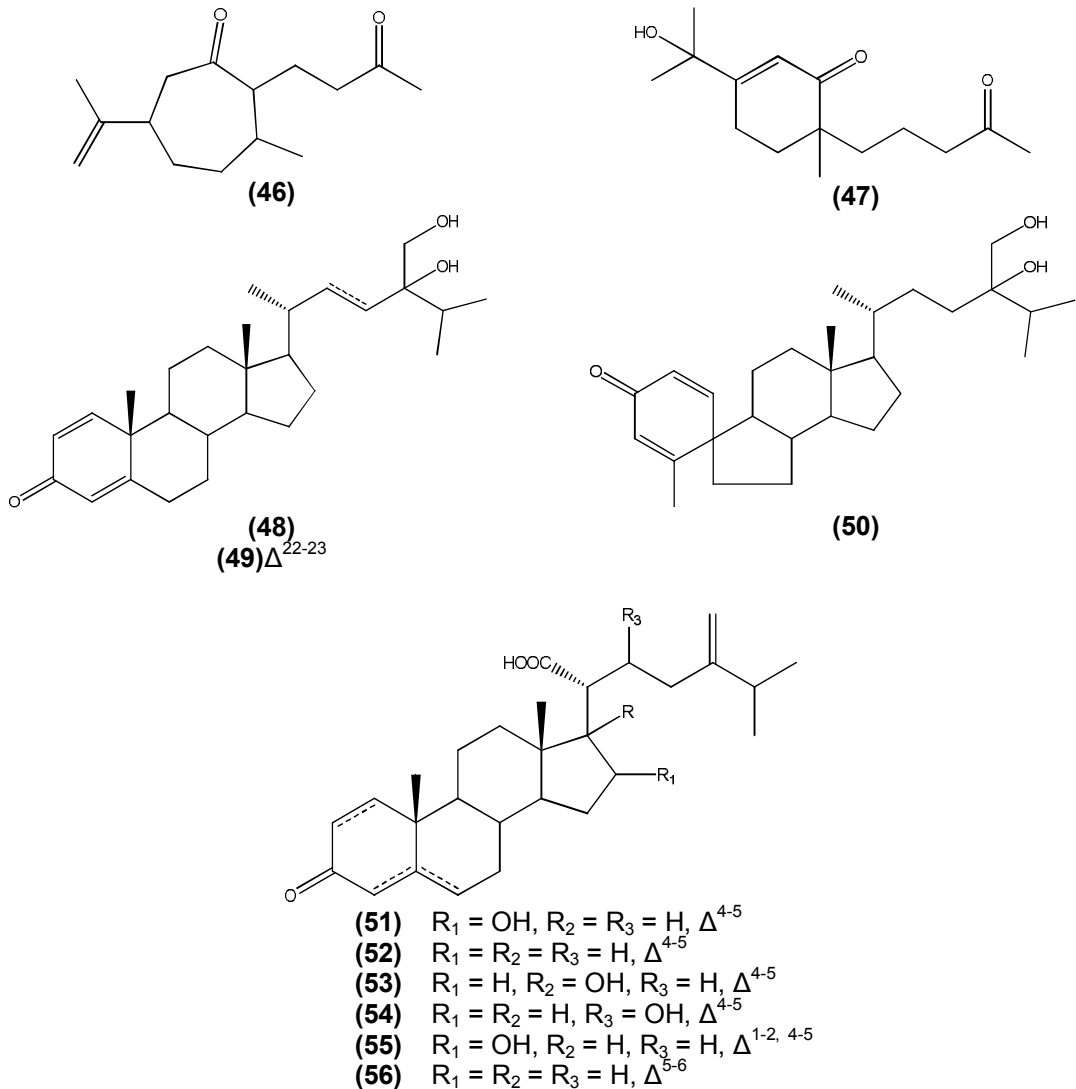


Fig 4c: Compounds 46 - 56

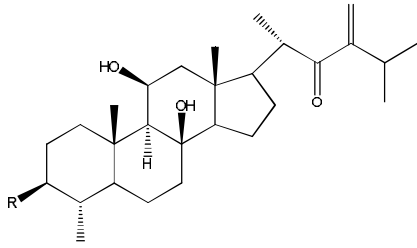
Examinations of the acetone extract of the soft coral *N. chabrolii* resulted in the isolation of eight new methylated steroids (Fig 5a and b), nebrosteroid A-H (**57-64**). The compounds exhibit anti-inflammatory activity while compounds (**57-59** and **64**), at a concentration of 10 μ M, reduced iNOS protein expression by 10.6 ± 0.5 , 9.6 ± 1.0 , 0 ± 0 and 32.8 ± 6.8 , respectively. Compounds (**60**, **61** and **63**) reduced iNOS levels to 0, 43.1 ± 7.9 , and 76.9 ± 9.4 %, respectively

and COX-2 to 63.9 ± 10.9 , 57.4 ± 5.1 , and 72.0 ± 10.5 %, respectively [20].

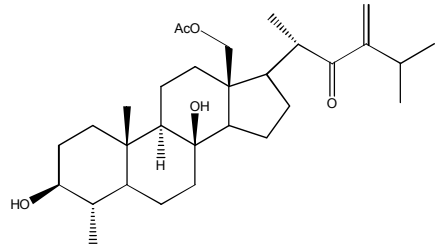
Cheng *et al* isolated five new steroids nebrosteroids I-M (**65-69**), and a new terpenoid chabranol (**70**). The steroids (**65-69**) indicated potent anti-inflammatory activity against RAW 264.7 macrophages and chabranol (**70**) indicated potent cytotoxic activity [1, 21-23]. The extracts of *N. chabrolii* have also been reported to possess cytotoxic

activity against human oral squamous cell

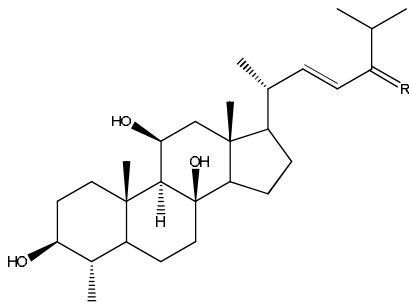
carcinoma SCC25 cells [24]



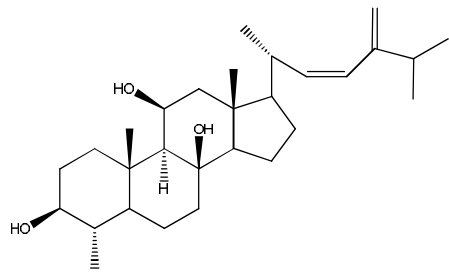
(57)R = OH
(58)R = OAc



(59)

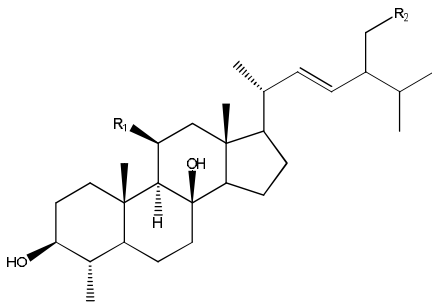


(60)R = CH₂
(61)R = O

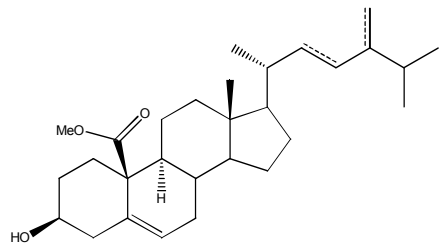


(62)

Fig 5a: Compounds 57 - 62



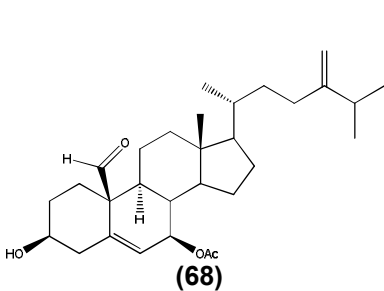
(63)R₁ = OH, R₂ = OAc
(64)R₁ = H, R₂ = OH



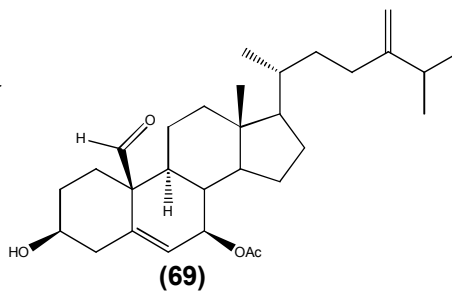
(65)Δ^{5-6, 24-28}

(66)Δ^{5-6, 22-23}

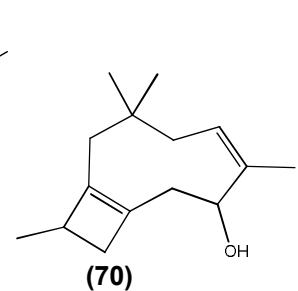
(67)Δ⁵⁻⁶



(68)



(69)



(70)

Fig 5b: Compounds 63 - 70
Nephthea Sp.

Earlier investigations led to the isolation of four new diterpenes nephthenol (**71**) and epoxynephthenol acetate (**72**), cembrene A (**73**) and cembrene C (**74**) from *N. sp.* [25-26]. A compound, 3-hydroxy-4-methoxyphenethylamine, was isolated and found to increase heart rate and blood pressure in rats [27].

Six new diterpenes 5-Methyl-2-tetraprenyl-p-benzoquinone (**75**) and its cyclized 2H-1- and 3,4-dihydro-2H-1-benzopyran derivatives 7-Methyltocotrienol (**76**) and 2H-1-Benzopyran-6-ol, 2,7-dimethyl-2-(4,8,12-trimethyl-3,7,11-tridecatrienyl) (**77**), (+)-(1S)-Isosarcophytol A (**78**), 2,6,10,12-Cyclotetradecatetraen-1-ol, 2,6,10-trimethyl-13-(1-methylethyl)-, acetate (**79**) and Oxirane, 2,2-dimethyl-3-[3-(1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-naphthalenyl)-3-buten-1-yl] (**80**) were identified from the soft coral *N. sp.*, [28-29]. Coll *et al.*, reported two known compounds Eudesma-4,7(11)-diene-8 β -ol and eudesma-4,7(11)-diene-8-one from the soft coral of *Nephthea* species [30].

Two new compound nephtheoxydiol (**81**) and nephthoside (**82**) along with ent-oplopanone, meso-1,3-Diphenyl-1,3-propanediol, nephthenol, nephthediol and nephthene were identified from the soft coral of *N. sp.*, [31-33]. Liu *et al* identified a cytotoxic compound, lemnabourside, from *N. sp.* Lemnabourside is a 5 α -reductase inhibitor; thus, it indicates the capacity to inhibit the conversion of testosterone into dihydrotestosterone and the incorporation of tritiated thymidine into human prostate androgen-dependent

carcinoma LNCaP cells, hence blocking cell proliferation (IC₅₀ = 37.5 μ M) [34].

Chemical screening of the soft coral *N. sp.*, afforded the identification of two new seco-cembranoid acetates (Figure 7a and 7b) (3E)-7-hydroxy-4,8,15,15-tetramethyl-1-[(E)-12-methyl-10-oxo-12-pentenyl]-3,8-decadienyl acetate (**83**) and (3E)-7-hydroxy-4,8,15,15-tetramethyl-1-[(Z)-12-methyl-10-oxo-12-pentenyl]-3,8-decadienyl acetate (**84**), and six new steroids 24-Methylenecholest-4-ene-3 β ,6 β -diol (**85**), 4 α -methyl-ergost-7,24(28)-diene-3 β -ol-23-one (**86**), 4 α -methyl-ergost-8(14),24(28)-diene-3 β -ol-23-one (**87**), 4 α -methyl-ergost-24(28)-en-3 β ,11 β -diol-23-one (**88**), ergost-5,25-diene-3 β ,24,28-triol (**89**) and ergost-5,24(28)-diene-3 β ,23-diol (**90**), together with a known steroid, 24-methylenecholesterol [35-37].

Rao *et al* reported a sphingosine derivative, 2-N-nonanoyl-4,5-dihydrosphingosine (**91**), a and a new sesquiterpene, 1 α -hydroxy-(+)-cyclocolorenone (**92**), along with a known compound (+)-cyclocolorenone from the soft coral of *Nephthea* species of the Indian Ocean [38-39].

Examination of the soft coral, *N. sp.*, afforded wax esters, cholesterol, 1-O-alkylglycerols, fatty acids and D(-)-2S,3R-2-amino-octadeca-4E,8E-diene-1,3-diol-N-palmitate. The extract was found to exhibit antiviral activity against Ranikhet disease virus and Vaccinia virus [2]. Bioassay-guided isolation of the soft coral *N. sp.*, led to the identification of two known sterols 24-methylcholest-5-ene-3 β ,8 β -diol and 24-methylenecholest-4-ene-3 β ,6 β -diol. The isolated sterols and exhibited appreciable cytotoxic activity [40].

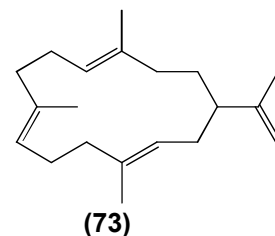
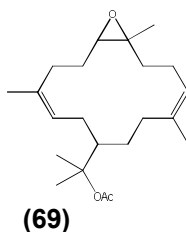
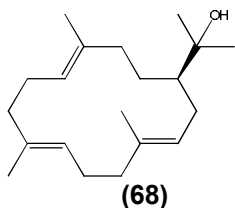


Fig 6a: Compounds 71 - 74

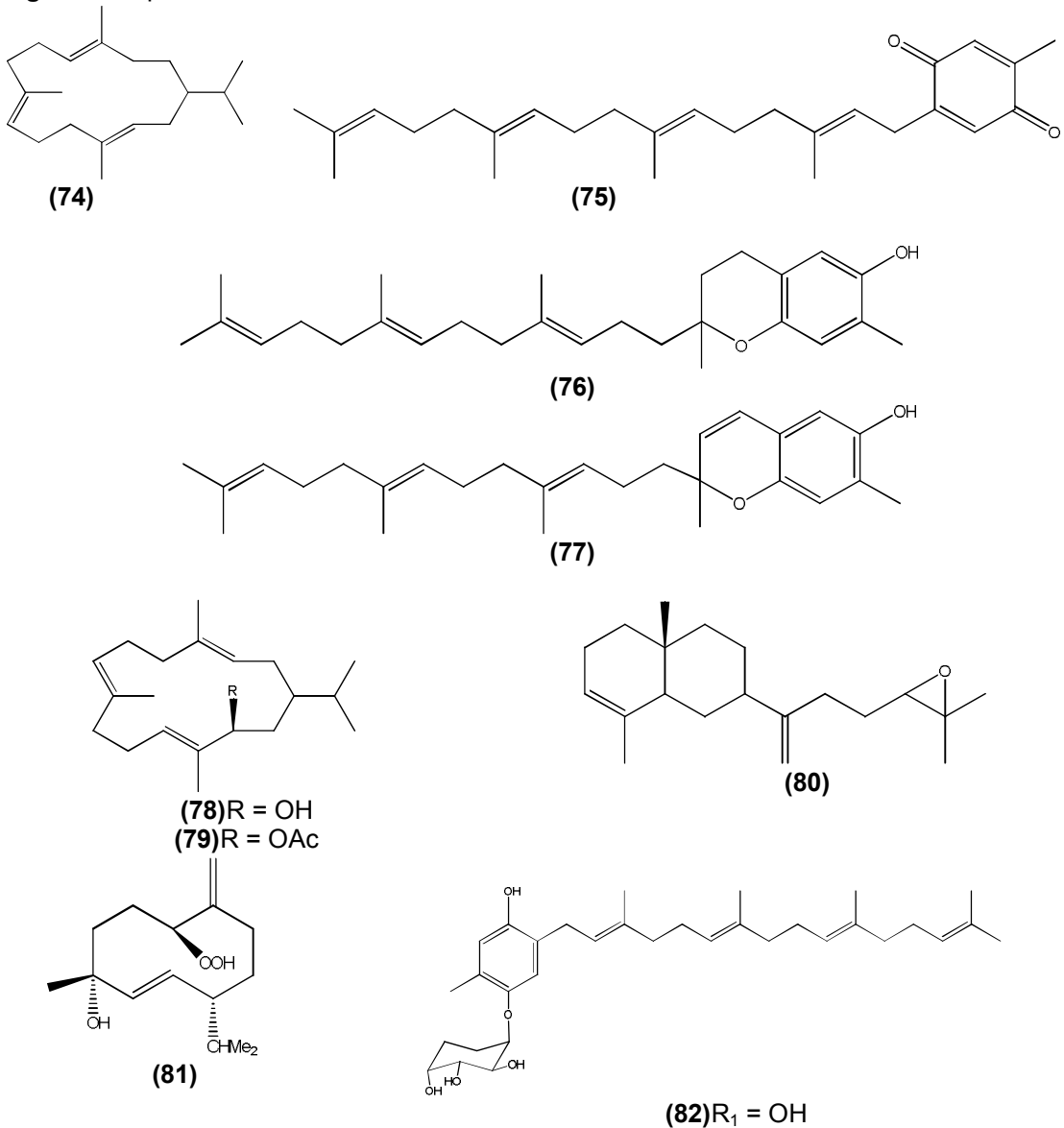
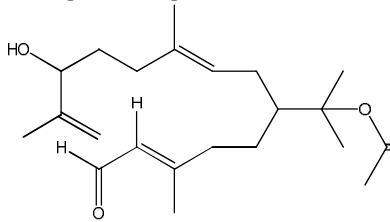


Fig 6b: Compounds 75 - 82

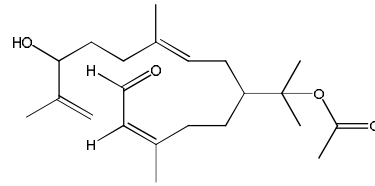
Five new sesquiterpenes, 2-deoxy-7-O-methyllemnacarnol (**93**), 2-deoxy-12 α -ethoxy-7-O-methyllemnacarnol (**94**), 2-deoxy-12 α -methoxy-7-O-methyllemnacarnol (**95**), nephthediol (**96**) and nephthetraol (**97**) were identified from the soft coral *N. sp.*, [41-42].

Chemical investigations of the soft coral *N. sp.* led to the identification of a new sterol (Fig 8), 4 α -methyl-ergosta-6,8(14),22 E -triene-3 β -ol (**98**), a new sesquiterpenoid 1-acetoxy-germacra-5,10(14)-diene-4-one (**99**) and a cembrane diterpene, 6-acetoxy-7,8-epoxynephthenol acetate (**100**) together with

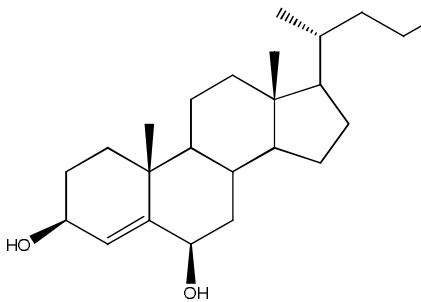
the known compound epoxynephenol acetate [4, 43-44].



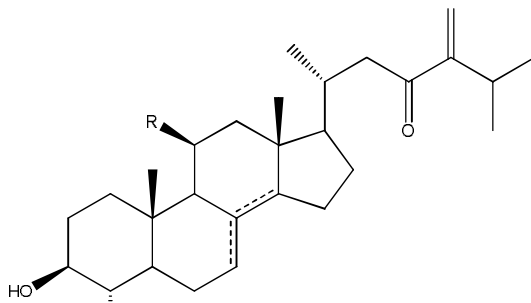
(83)



(84)



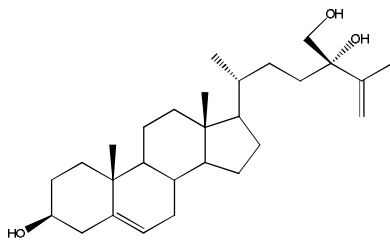
(85)



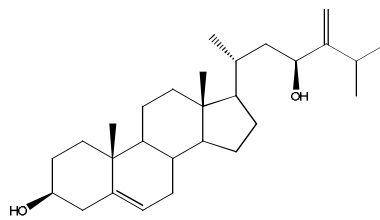
(86) $R_1 = H, \Delta^{7-8, 24-28}$

(87) $R_1 = H, \Delta^{8-14, 24-28}$

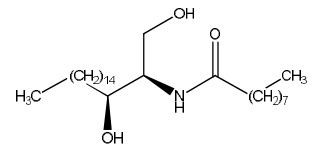
(88) $R_1 = OH, \Delta^{24-28}$



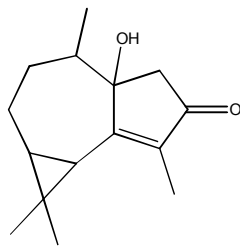
(89)



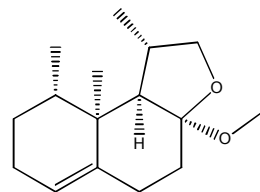
(90)



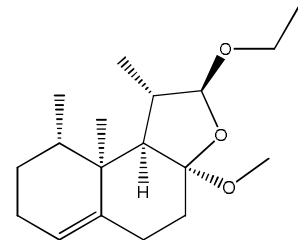
(91)



(92)



(93)



(94)

Fig 7a: Compounds 82 – 94

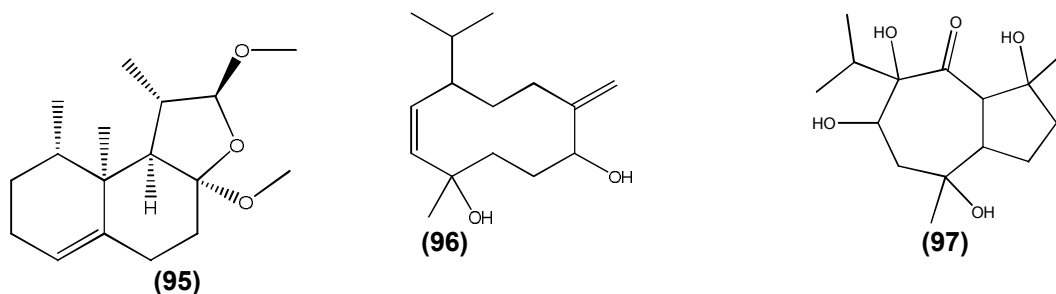


Fig 7b: Compounds 95 - 97

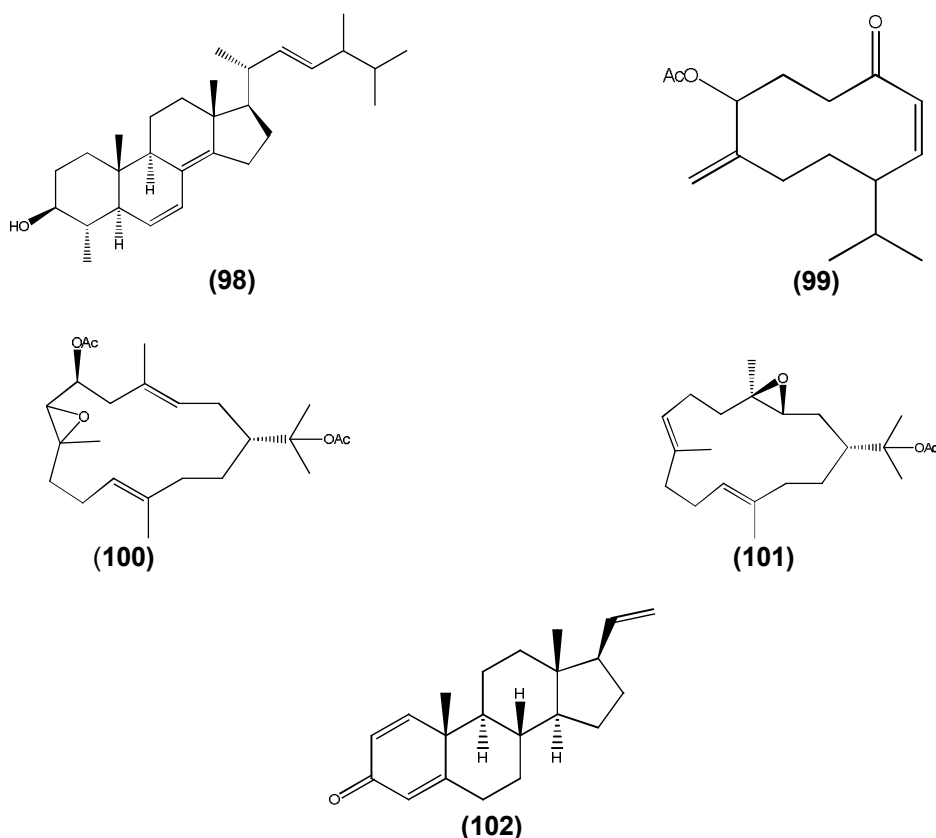


Fig 8: Compounds 95 - 102

Januar *et al* identified from the methanolic extract of soft coral *N. sp.* a new diterpene, 3,4-epoxy-nephtenol acetate (**101**) together with the known compounds decaryiol, 15-hydroxy-cembrenene, 2-hydroxy-nephtenol, nephtenol, and arachidonic acid [45]. A steroid, Pregna-1,4,20-trien-3-one (**102**), was

identified which was found to exhibit inhibitory activity against human colon adenocarcinoma SW480 cells ($IC_{50} = 2.5 \mu\text{g/ml}$) [46]. Furthermore two known alkaloids, nephoxaloid and caulerpin, have also been reported [47].

Table 1(a): New chemical constituents of *N. chabrolii* from the genus *Nephthea*

Isolated compound	No.	Class	Ref:
Germacrene C	1	Sesquiterpene	[7]
Valerol	2	Sesquiterpene	[7]
Oxirane, 3-[2-(6, 10-dimethyl-2-methylenebicyclo-undec-5-en-10-yl)ethyl]-2,2-dimethyl	3	Diterpene	[8]
Bicyclo-undec-5-ene-10-propanol, α -(1-chloro-1-methylethyl)-6,10-dimethyl-2-methylene	4	Diterpene	[8]
14 α ,24-Dimethylcholestan-3 β ,25-diol	5	Steroid	[9]
Naphthol-A	6	Diterpene	[10]
Naphthol-B	7	Diterpene	[10]
1-Acetoxygermacra-3,10(15)-diene	8	Sesquiterpene	[10]
1-Acetoxygermacra-3,5,10(15)-triene	9	Sesquiterpene	[10]
1,4,5-Guaia-6,9-dien-4-ol	10	Sesquiterpene	[10]
1,5,6-Gaia-3,10(15)-dien-7,11-epoxy-6 β -acetate	11	Sesquiterpene	[10]
Hydroxycolorenone	12	Sesquiterpene	[11]
Methoxycolorenone	13	Sesquiterpene	[11]
24-Methylene cholest-5-en-1 α ,3 β ,19-triol	14	Steroid	[12]
24-Methylene cholest-5-en-3 β ,7 β ,9 α ,19-tetrol	15	Steroid	[12]
10 α -Methoxy-4 β -hydroxyguaian-6-ene	16	Sesquiterpene	[13]
6 β ,7 β -Epoxy-4 β -hydroxyguaian-10-ene	17	Sesquiterpene	[13]
4,15-Dihydroguaian-6,10-diene	18	Sesquiterpene	[13]
Guaian-4,6-dien-10 α -ol	19	Sesquiterpene	[13]
4 α -Methyl-24-methylene-5 α -cholestan-3 β ,8 β -diol	20	Steroid	[14]
Chabrolol A	21	Diterpene	[15]
Chabrolol B	22	Diterpene	[15]
Chabrolol B	23	Diterpene	[15]
24-Methylcholesta-9(11), 24(28)-diene-3 β ,12 α ,19-triol	24	Steroid	[16]
4 α -Methyl-3 β ,14 β -dihydroxy-5 α -ergost-24(28)-en-23-one	25	Steroid	[16]
Chabrolonaphthoquinone A	26	Diterpene	[17]
Chabrolohydroxybenzoquinones A	27	Diterpene	[17]
Chabrolohydroxybenzoquinones A	28	Diterpene	[17]
Chabrolohydroxybenzoquinones A	29	Diterpene	[17]
Chabrolohydroxybenzoquinones A	30	Diterpene	[17]
Chabrolobenzoquinones A	31	Diterpene	[17]
Chabrolobenzoquinones A	32	Diterpene	[17]
Chabrolobenzoquinones A	33	Diterpene	[17]
Chabrolobenzoquinones A	34	Diterpene	[17]
Chabrolonaphthoquinone B	35	Diterpene	[18]
Chabrolobenzoquinones E	36	Diterpene	[18]
Chabrolobenzoquinones F	37	Diterpene	[18]
Chabrolobenzoquinones G	38	Diterpene	[18]
Chabrolobenzoquinones H	39	Diterpene	[18]
Chabrolohydroxybenzoquinones E	40	Diterpene	[18]
Chabrolohydroxybenzoquinones F	41	Diterpene	[18]
Chabrolohydroxybenzoquinones G	42	Diterpene	[18]
Ketochabrollic acid	43	Acid	[5]
Isoketochabrollic acid	44	Acid	[5]
Chabrolonaphthoquinone C	45	Quinone	[5]
Chabrolidiones A	46	Sesquiterpene	[5]
Chabrolidiones B	47	Sesquiterpene	[5]
Chabrolosteroid A	48	Steroid	[19]

Table 1(b): New chemical constituents of *N. chabrolii* from the genus *Nephtea* (*contd*)

Isolated compound	No.	Class	Ref
Chabrolosteroid B	49	Steroid	[19]
Chabrolosteroid C	50	Steroid	[19]
Chabrolosteroid D	51	Steroid	[6]
Chabrolosteroid E	52	Steroid	[6]
Chabrolosteroid F	53	Steroid	[6]
Chabrolosteroid G	54	Steroid	[6]
Chabrolosteroid H	55	Steroid	[6]
Chabrolosteroid I	56	Steroid	[6]
Nebrosteroid A	57	Steroid	[20]
Nebrosteroid B	58	Steroid	[20]
Nebrosteroid C	59	Steroid	[20]
Nebrosteroid D	60	Steroid	[20]
Nebrosteroid E	61	Steroid	[20]
Nebrosteroid F	62	Steroid	[20]
Nebrosteroid G	63	Steroid	[20]
Nebrosteroid H	64	Steroid	[20]
Nebrosteroid I	65	Steroid	[23]
Nebrosteroid J	66	Steroid	[23]
Nebrosteroid K	67	Steroid	[23]
Nebrosteroid L	68	Steroid	[23]
Nebrosteroid M	69	Steroid	[23]
Chabranol	70	Sesquiterpene	[1]
Nephtenol	71	Diterpene	[25]
Epoxynephtenol acetate	72	Diterpene	[25]
Cembrene A	73	Diterpene	[26]
Cembrene C	74	Diterpene	[26]
5-Methyl-2-tetraprenyl-p-benzoquinone	75	Diterpene	[28]
7-Methylcotrienol	76	Diterpene	[28]
2H-1-Benzopyran-6-ol, 2,7-dimethyl-2-(4,8,12-trimethyl-3,7,11-tridecatrienyl)	77	Diterpene	[28]
(+)-(1S)-Isosarcophytol A	78	Diterpene	[29]
2,6,10,12-Cyclotetradecatetraen-1-ol, 2,6,10-trimethyl-13-(1-methylethyl)-, acetate	79	Diterpene	[29]
Oxirane,2,2-dimethyl-3-[3-(1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-naphthalenyl)-3-buten-1-yl]	80	Diterpene	[29]
Nephteoxydiol	81	Sesquiterpene	[31]
Nephtoside	82	Tetraprenyltoluquinol	[32]
(3E)-7-hydroxy-4,8,15,15-tetramethyl-1-[(E)-12-methyl-10-oxo-12-pentenyl]-3,8-decadienyl acetate	83	Diterpene	[35]
(3E)-7-hydroxy-4,8,15,15-tetramethyl-1-[(Z)-12-methyl-10-oxo-12-pentenyl]-3,8-decadienyl acetate	84	Diterpene	[35]
Steroid 24-Methylenecholest-4-ene-3 β ,6 β -diol	85	Steroid	[36]
4 α -Methyl-ergost-7,24(28)-diene-3 β -ol-23-one	86	Steroid	[37]
4 α -Methyl-ergost-8(14),24(28)-diene-3 β -ol-23-one	87	Steroid	[37]

Table 1(c): New chemical constituents of *N. species* from the genus *Nephthea* (*contd*)

Isolated compound	No.	Class	Ref
4 α -Methyl-ergost-24(28)-en-3 β ,11 β -diol-23-one	88	Steroid	[37]
Ergost-5,25-diene-3 β ,24,28-triol	89	Steroid	[37]
Ergost-5,24(28)-diene-3 β ,23-diol	90	Steroid	[37]
2-N-nonanoyl-4,5-dihydrosphingosine	91	Sphingosine	[38]
1 α -Hydroxy-(+)-cyclocolorone	92	Sesquiterpene	[39]
2-Deoxy-7-O-methylmenacarnol	93	Sesquiterpene	[41]
2-Deoxy-12 α -ethoxy-7-O-methylmenacarnol	94	Sesquiterpene	[41]
2-Deoxy-12 α -methoxy-7-O-methylmenacarnol	95	Sesquiterpene	[41]
Nephtediol	96	Sesquiterpene	[42]
Nephtetraol	97	Sesquiterpene	[42]
4 α -Methyl-ergosta-6,8(14),22 <i>E</i> -triene-3 β -ol	98	Steroid	[43]
1-Acetoxy-germacra-5,10(14)-diene-4-one	99	Sesquiterpene	[44]
6-Acetoxy-7,8-epoxynephtenol acetate	100	Diterpene	[4]
3,4-Epoxy-nephtenol acetate	101	Diterpene	[45]
Pregna-1,4,20-trien-3-one	102	Steroid	[46]

CONCLUSION

A wide range of chemical and pharmacological investigations have been conducted on *N. chabrolii* and *N. Sp.*, over the years; however, the possibility of finding new secondary metabolites cannot be neglected. It would also be valuable to determine the structure - activity relationship of the isolated constituents and their corresponding biological activities. Furthermore, as indicated in first part of the review, it may be beneficial to investigate the other species of the genus *Nephthea*. This review provides support for the claim that marine natural products are an important source of secondary metabolites for drug discovery.

ACKNOWLEDGEMENT

The authors would like to acknowledge support for this work through a research grant (no. 1001/PKIMIA/811187); and the authors (F.A.) and (Y.C.K.) are also grateful to Universiti Sains Malaysia for the USM fellowship awards.

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