

Chemical diversity and bioactivity of marine sponges of the genus *Oceanapia*: A review

Keisham S. Singh*, Supriya Tilvi

Bioorganic Chemistry Laboratory, CSIR-National Institute of Oceanography,
Dona Paula-403004, Goa, India

*For correspondence: keisham@nio.org or keisham.sarjit@gmail.com

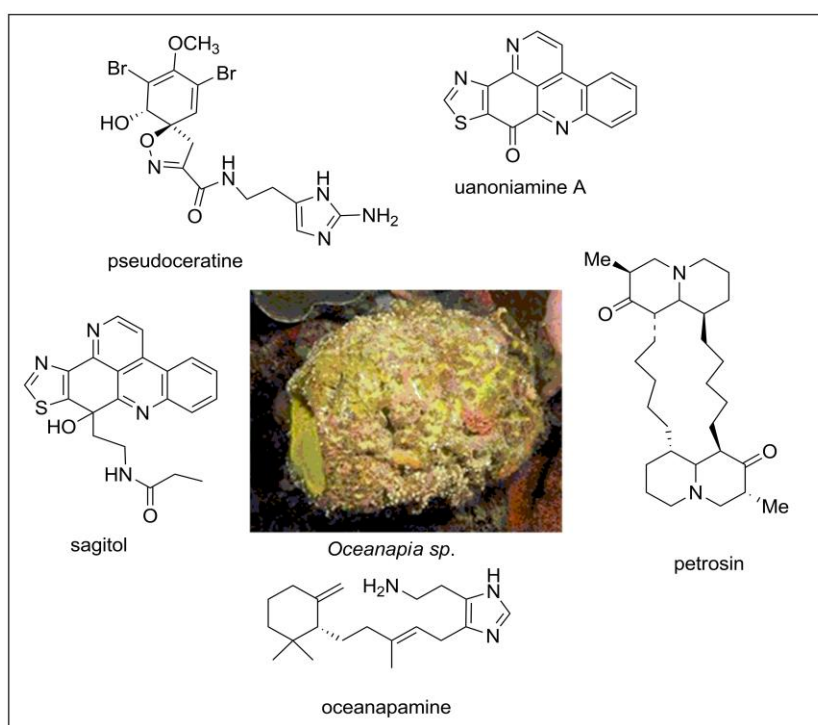
Tel: +91-0832-2450392; fax: +91-0832-2450607.

Abstract:

The marine sponges of the genus *Oceanapia* sp. is comprised of more than 50 species and are distributed in the seas around the tropical and subtropical regions. They are mainly found in the northern Indian oceans, Japan, and the south pacific coast. They are highly colored and known to be a rich source of various secondary metabolites, particularly, alkaloids. Several other secondary metabolites were also reported from this genus which include terpenes, sphingolipids, ceramides, cerebrosides, acetylenic acids, and thiocyanatins etc. Many of these compounds isolated from this genus exhibited various biological properties including anticancer, antimicrobial, anti-HIV, ichthyotoxicity and nematocidal activities. Although several secondary metabolites have been reported from this genus, a dedicated review of the chemicals and biological activities of this genus is so far lacking. Keeping this in mind this review describes the various chemical entities isolated from the sponges of the genus *Oceanapia* detailing their chemical structures along with their reported biological properties.

Keywords: Marine sponges, alkaloids, *Oceanapia* sp., biological activity, ceramides, sphingolipids, acetylenic acids.

Graphical abstract



Metabolites of Marine sponge *Oceanapia* sp.

Contents

1. *Introduction*
2. *Alkaloids*
 - 2.1. *Pyridoacridine alkaloids*
 - 2.2. *Quinolizidine alkaloids*
 - 2.3. *Phloeodictyne alkaloids*
 - 2.4. *Sequiterpene and Brominated alkaloids*
3. *Ceramides, sphingolipids and their derivatives*
4. *Thiocyanatins, halogenated and acetylenic acids*
5. *Miscellaneous*
6. *Conclusion*

1. Introduction

Marine sponges are rich sources of several secondary metabolites and constitute nearly half of the compounds discovered from marine invertebrates. More than 5000 species of marine sponges are known, many of them have been investigated for their chemical and biological properties [1, 2]. Marine sponges, belonging to the genus *Oceanapia* is comprised of more than 50 species distributed in tropic and subtropical region and are abundant of various secondary metabolites. These include alkaloids [3], sterols [4], ceramides [5], cerobroside [6], bromotyrosine [7] and acetylenic acids [8] possessing several bioactivities including anti-anticancer [9], antimicrobial [8], nematocidal [10] and cytotoxicity [11], etc. Over the past years, numerous reviews on the bioactive potential of marine sponges such as anticancer [12], cytotoxicity [13], antimicrobial [14], antiviral [15] and anti-malarial [16] have been appeared. Although a few recent reports were available for marine sponges of the genus *Suberea* [17], *Stelletta* [18], and genera belonging to *Mycale*, *Biemna* and *Clathria* [19].

However, review detailing on the chemicals and bioactivities of marine sponge species is scarce. It is noteworthy that, several interesting secondary metabolites have been isolated from *Oceanapia sp.* [3, 5, 6]. Therefore, a comprehensive review on this important and prolific sponge species seems to be timely and necessary. This review describes various secondary metabolites isolated from the sponges of the genus *Oceanapia* along with their bioactivities. In order to simplify the contents, this manuscript is divided into five headings *viz.* alkaloids, ceramides and cerobrosides; sphingolipids and glycosides, and finally miscellaneous which covers all the other remaining compounds isolated from this species.

2. Alkaloids:

Alkaloids are the prominent secondary metabolites isolated from the sponges of genus the *Oceanapia*. These include pyridoacridine, petrosamine, quinolizidine, pyrimidinium, bromotyrosine and sesquiterpene alkaloids. In the subsequent sections, chemicals and reported bioactivities of these alkaloids are discussed under the respective sub-headings.

2.1. Pyridoacridine alkaloids:

The marine sponges of the genus *Oceanapia* are the rich source of several pyridoacridine alkaloids. Pyridoacridine alkaloids represent a group of highly colored marine derived alkaloids based on 11-*H*-pyrido[4,3,2-*mn*]acridine skeleton [20]. They are the largest group of marine alkaloids mostly isolated from sponges and tunicates. Pyridoacridine alkaloids exhibited a wide range of biological activities including cytotoxicity, anti-HIV activity, topoisomerase-II inhibition, production of reactive oxygen species and Ca²⁺ release, the intercalation of DNA, anti-bacterial and anti-fungal activity [21]. In 1998, Proksch and co-workers isolated three pyridoacridine alkaloids, kuanoniamine-C (**1**), kuanoniamine-D (**2**) and *N*-deacyl derivative of kuanoniamine (**3**) from an *Oceanapia sp.* (Figure 1) [3]. Kuanoniamine-C (**1**) and kuanoniamine-D (**2**) showed insecticidal activity when tested against *Spodoptera littoralis* with LC₅₀ values of 156 ppm [(0.46 (SE))] and 59 ppm [(0.30 (SE))], respectively. However, *N*-deacyl derivative (**3**) did not show any significant activity. In 2007, Kijjoa *et al.* reported pyridacridine alkaloids, kuanoniamineA (**4**) along with the known kuanoniamine C (**1**) from the marine sponge *O. sagittaria* (Sollas), collected from the Gulf of Thailand [9]. The *in vitro* screening of kuanoniamine A (**4**) and kuanoniamine C (**1**) against the five human tumor cell lines MCF-7 (ER+), MDA-MB-231 (ER-), SF-268, NCI-H460, UACC-62 and non-tumor cell line MRC-5 showed a potent inhibition of the growth for all the five tumor cells by kuanoniamine A (**4**) with GI₅₀ values ≤ 5 μM. Kuanoniamine A (**4**) also exhibited potent inhibition in the growth of non-tumor cell line, MRC-5. Similarly, kuanoniamine C (**1**) exhibited inhibition in the growth of all the five tumor cell lines but with much lower effective at least ten time less potent than that for kuanoniamine A (**4**) (Figure 1).

In 1996, Faulkner and co-workers isolated pyridoacridine alkaloid, sagitol (**5**) from the sponge *O. sagittaria* [22]. In later years, Ibrahim *et al.* isolated a related alkaloid, sagitol C (**6**) from an unidentified *Oceanapia species* collected from the Indonesian water (Figure 1) [11]. The cytotoxic effect of sagitol C (**6**) against L5178Y (mouse lymphoma cell), PC12 (brain tumor cells of rats), and HeLa (human cervix carcinoma) cell lines displayed 93%, 88%, and 76% growth suppression at a concentration of 24.6 μM. Further, at a concentration 12.3 μM the effect was observed at 81%, 74% and 37% with ED₅₀ (s) values of 0.7 and 0.9, respectively [11].

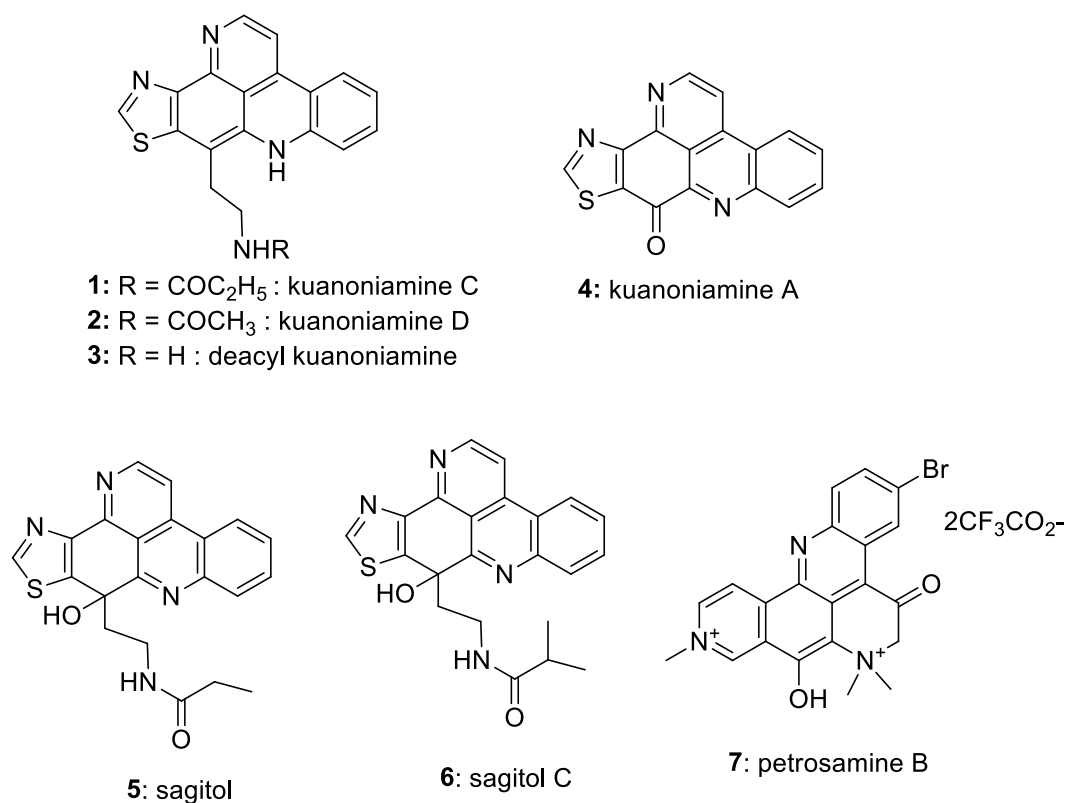


Figure 1. Chemical structures of kuanoniamines (**1-4**), sagitols (**5** and **6**) and petrosamin B (**7**) alkaloids.

A novel alkaloid petrosamine B (**7**) was isolated by Hooper and coworkers from the Australian *Oceanapia* sp. [23]. Petrosamine-B (**7**) exhibited inhibitor on *Helicobacter pylori* enzyme aspartyl semialdehyde dehydrogenase [23].

2.2. Quinolizidine and 1-Oxoquinolizidine alkaloids:

Quinolizidine/1-oxoquinolizidine alkaloids represent a group of the alkaloids family, which contained a quinolizidine or a 1-oxaquinolizidine ring. Several these alkaloids viz., petrosin, xestospongins and araguspongines have been isolated from numerous marine sponges such as *Petrosia seriata* [24], *P. similis* [25], *Xestospongia* sp. [26, 27], *Haliclonaexigua* [28], *Niphates* sp. [29]. They possessed diverse biological properties such as anti-tuberculosis, antimalarial, antifouling and vasodilative activity. In 2011, Our group reported, petrosin (**8**) along with several other quinolizidine and related alkaloids; xestospongins C-J (**9-16**) from the ethyl acetate extract of the marine sponge *Oceanapia* sp. collected from Mandapam, Tamil Nadu, India (Figure 2) [30]. The isolated compounds **8**, **9** and **10** exhibited antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus*. Further, xestospongins-C (**9**) and xestospongins-D (**10**) were found to be active against the pathogens *Rhodotorula*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Candida albicans* and *Aspergillus*

niger. Previously, these alkaloids **8-13** and **15** were reported from other marine sponges and found to be exhibiting vasodilative and anti-HIV properties [25-29].

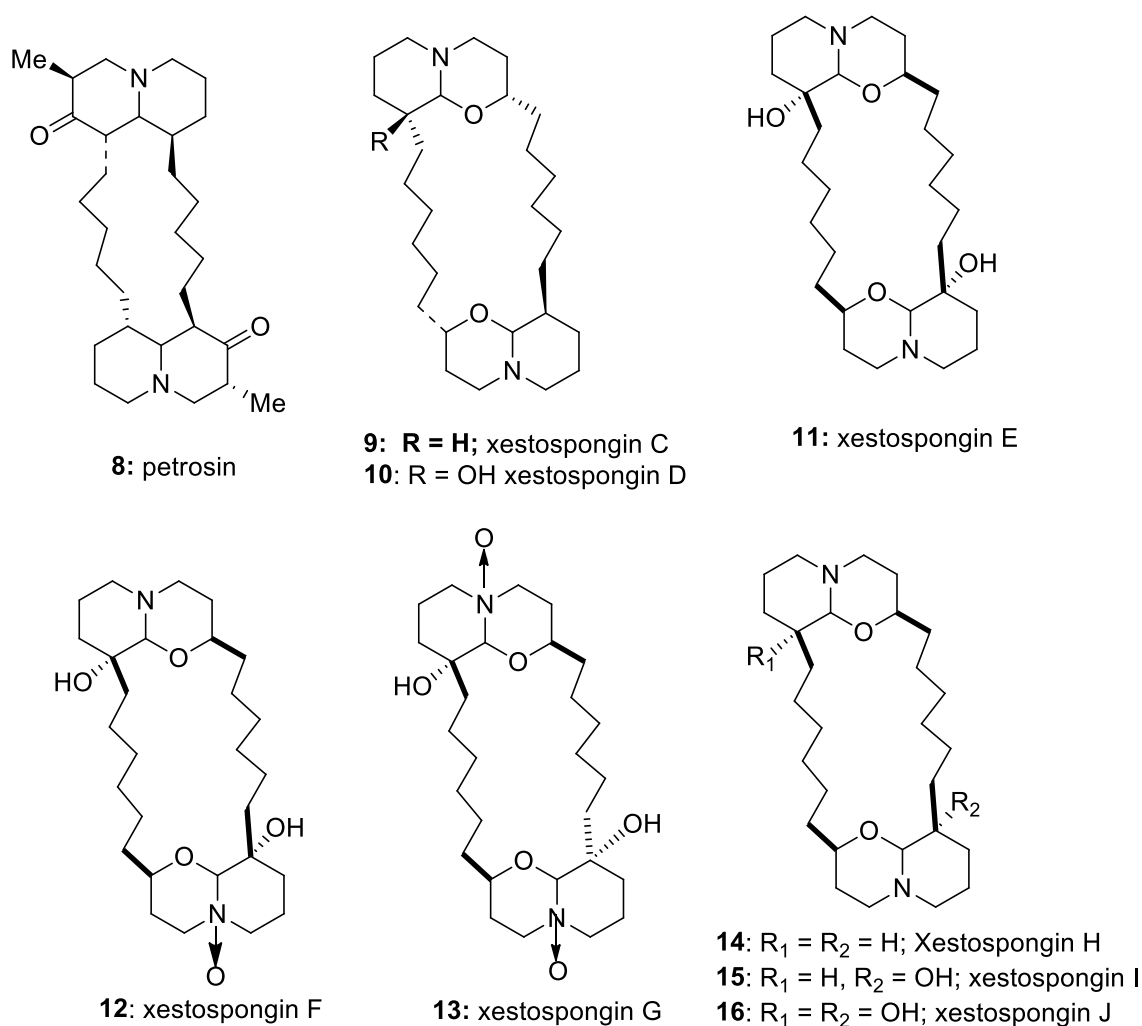


Figure 2. Chemical structures of petrosin and xestospongins alkaloids.

2.3. Phloeodictynealkaloids:

Phloeodictyenes are a group of alkaloids containing the novel 1, 2, 3, 4-tetrahydropyrrolo[1,2-a]pyrimidinium skeleton. In 1992, Kourany-Lefoll *et al.* isolated novel perimidinium alkaloids known as phloeodictyenes A & B (**17** & **18**) that possessed antibacterial and cytotoxicity activity towards human cancer lines from the sponge *Phloeodictyon* (Figure 3) [31] which is now included to the genus, *Oceanapia* [32]. The phloeodictyenes A & B (**17** & **18**) represent the first natural products having bicyclic 1, 2, 3, 4-tetrahydro-6H-pyrrolo[1,2-a]pyrimidinium ring system. The compounds **17** and **18** exhibited cytotoxicity against KE3 human nasopharyngeal carcinoma cells with IC₅₀ values of 1.5 and 11.2 µg/mL, respectively. In the subsequent years, they isolated several other phloeodictyene alkaloids

A1-A7 (**19-25**) and C1-C2 (**26-27**) from the same sponge *Phloeodictyon* [= *Oceanapia*] sp. (Figure 3) [33]. The compounds exhibited *in vitro* antibacterial activities against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Clostridium perfringens* and *Bacteroides fragilis* as well as moderate cytotoxicity against the KB human oropharyngeal carcinoma cells.

A few years later, Mancini *et al.* [16] reported more alkaloids related to phloeodictyne family (**28-32**) from the marine sponge *Oceanapia fistulosa* (Figure 3). Due to the complex nature of the mixture, they were unable to isolate the compounds in pure form. However, they could obtain enriched mixtures of the compounds adequate for bioassay and succeeded characterization of the individual compounds by Tandem mass spectrometry. The compounds were tested for *in vitro* antiplasmodial activity and were found to be active against chloroquine-resistant *Plasmodium falciparum*, with IC₅₀ values ranging from 0.6 to 6 μ M, while cytotoxicity against human A-549 cell line was low thus, making them as a potential candidate for anti-malarial agents.

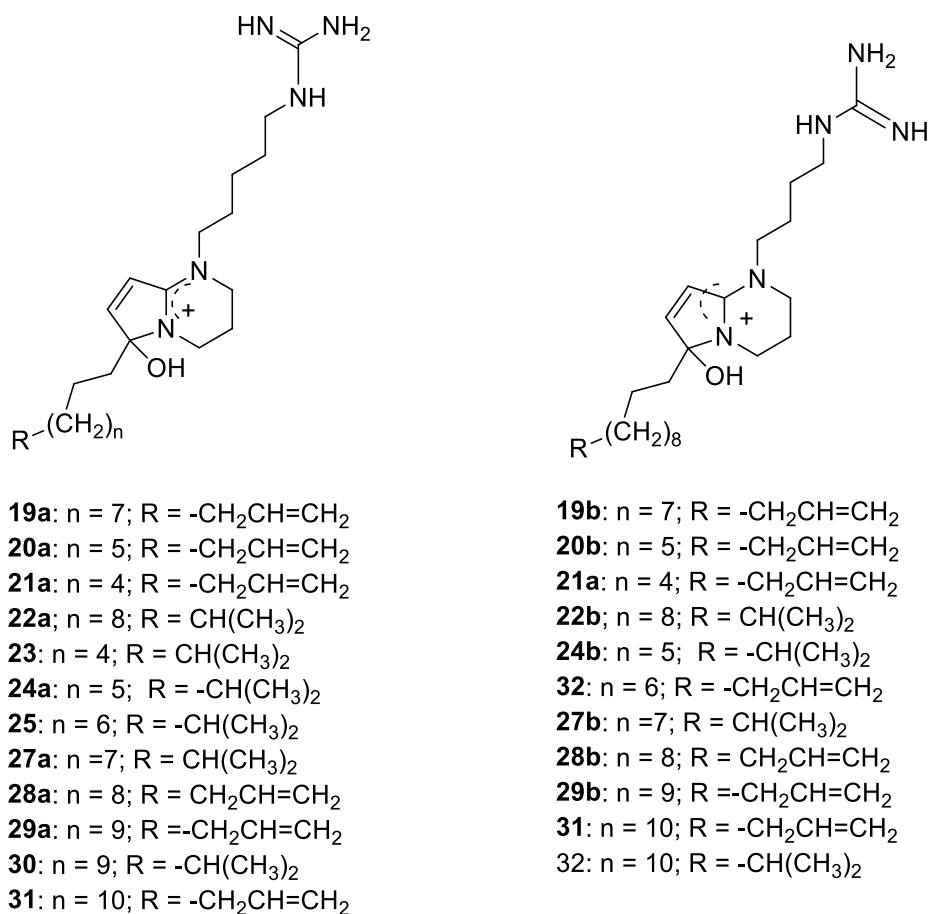
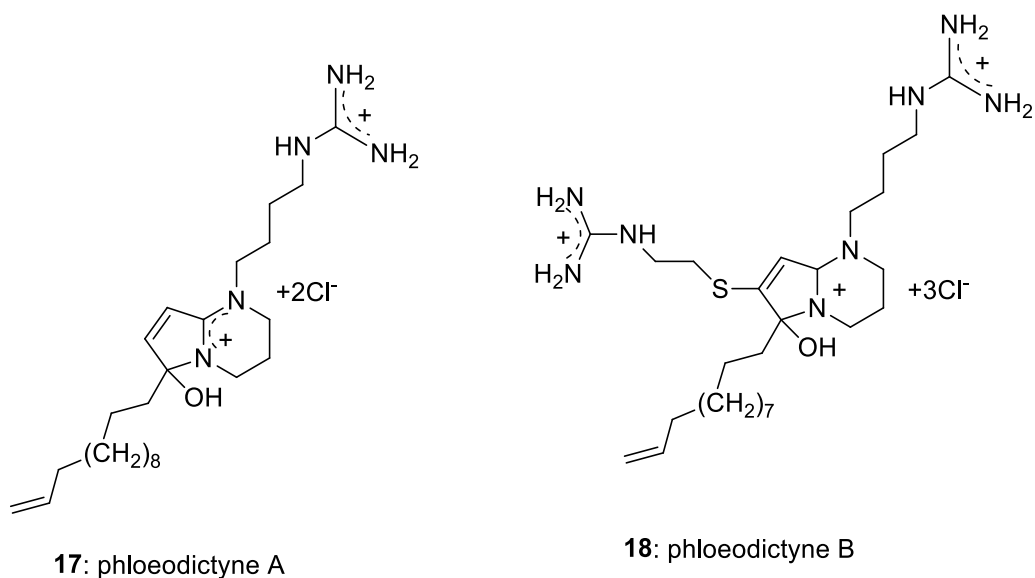


Figure 3. Structures of phloeodictyne alkaloids isolated from *Oceanapia* sp.

2.4. Sesquiterpene and Brominated alkaloids:

Balwey and co-workers isolated nobel bromotyrosine alkaloids (**33**) along with pseudoceratine (**34**) and the compounds (**35**) and (**36**) from the extract of an *Oceanapia* sp. obtained from NIH (Figure 4) [7]. Compound (**33**) contained a rare amino-imidazole ring coupled to aromatic substituent. Notably,

with the exception of compound (**33**) all of bromotyrosine derived alkaloids isolated are exclusively limited to the sponges of the order Verongida. Compound (**33**) exhibited very strong inhibition against mycobacterial enzyme, mycothiol S-conjugate amidase (MCA).

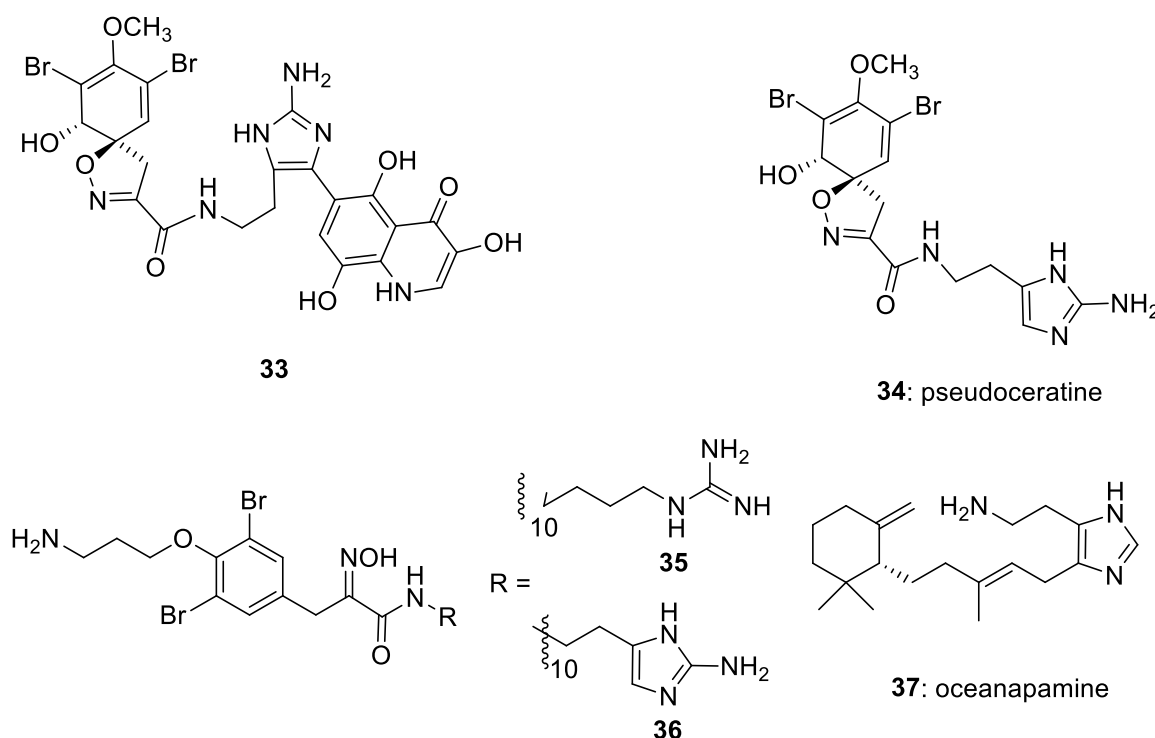


Figure 4. Structures of bromotyrosine and sesquiterpene alkaloids isolated from *Oceanapia sp.*

It is noteworthy that alkaloids are the main secondary metabolites obtained from marine sponges [2]. However, alkaloids derived from terpene are relatively rare and only a few reports are available in the literature [34]. In 1995, Faulkner and co-workers isolated a sesquiterpene alkaloid, Oceanapamine (**37**) from *Oceanapia sp.* collected from Philippine waters (Figure 4) [35]. The absolute configuration of Oceanapamine (**37**) was assigned to be R which showed $[\alpha]_D, -6.4$ (c = 3.1, MeOH). The assignment was further confirmed by the oxidation of oceanapamine (**37**) with osmium tetra oxide and sodium periodate to obtain a known diketone compound whose absolute configuration was established. Oceanapamine (**37**) exhibited antimicrobial property against *B. subtilis* and *E. coli* at 25 $\mu\text{g}/\text{disk}$, while against *S. aureus* and *C. albicans* at 50 $\mu\text{g}/\text{disk}$ and *P. aeruginosa* at 100 $\mu\text{g}/\text{disk}$.

3. Ceramides, sphingolipids and their derivatives

Ceramides are long chain fatty acid of sphingosine amides while their glycosyl derivatives are known as cerobrosides. Sphingosine was first known from brain tissue and later its derivatives were isolated from several organisms including seaweeds [36, 37], Symbiotic dinoflagellates [38], and sea anemones [39]. In general, most of the sphingosine derivatives occur as mixtures of homologous or

isomeric compounds, and therefore, separation of pure sphingosine remains a challenge and hardly achieved though eagerly desired. In 1994, Mancini *et al.* succeeded in the isolation of a series ceramides, oceanapins A-F (**38-43**) from the Haplosclerid sponge *Oceanapia cf. tenuis* (Figure 5) [40]. Oceanapins A-F (**38-43**) are unique in that they possess branched on both sphingosine and fatty acid chains. A few years later in 2006, Makarieva and coworkers isolated new ceramides (**44**) containing non-branched and iso-branched along with the known bifunctional sphingolipid, rhizochalin (**45**) from *Oceanapia sp.* [41]. They established that the isolated compounds contained mixture of ceramides having both normal and *iso*-termini in the sphingosine bases. In the same year, they isolated two other new cerebroside (**46 & 47**) from *Oceanapia sp.* (Figure 6) [6]. NMR spectra of cerebroside **46** coincide with the spectra of previously reported cerebroside, chalicylindroside, A(1)-A(4) obtained from *H. cylindrata* [23], while **47** was similar to that of chalicylindrosides B1-B6. It is notable that rhizochalin, (**45**) was first isolated from the sponge *Rhizochalinain crusteta* [42], which is now considered as synonyms to the genus *Oceanapia*. Rhizochalin and its derivatives possesses several biological properties such as cytotoxic and antimicrobial properties [43].

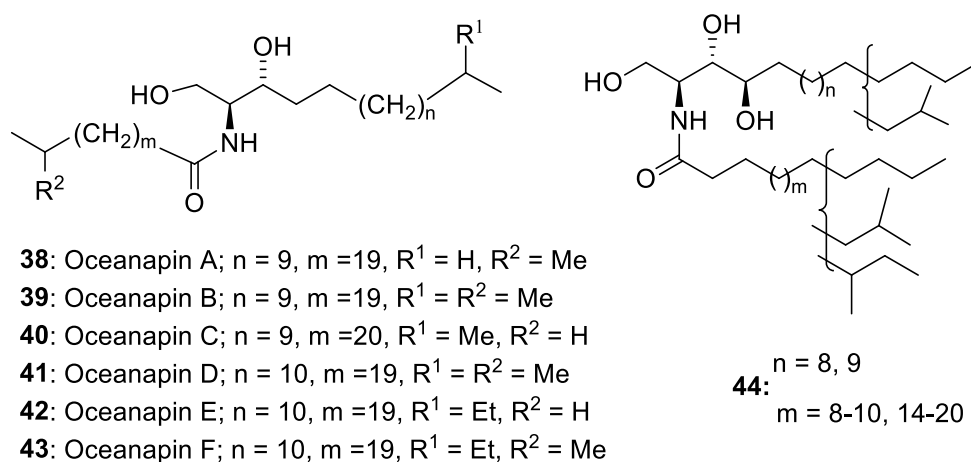
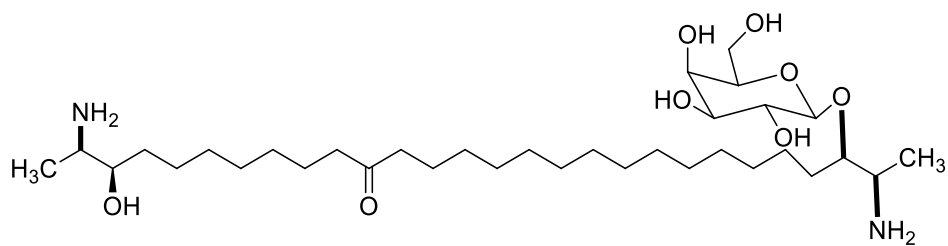
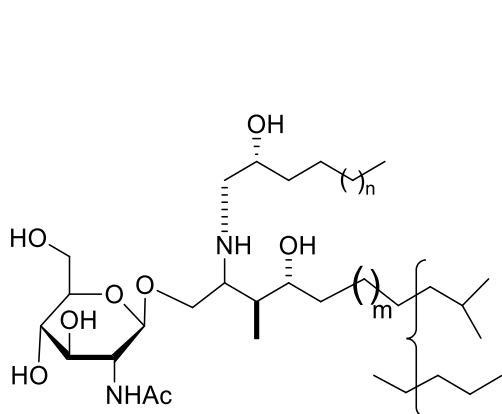


Figure 5. Chemical structures of Oceanapins (**38-43**) and new ceramides, **44** isolated from *Oceanapia sp.*

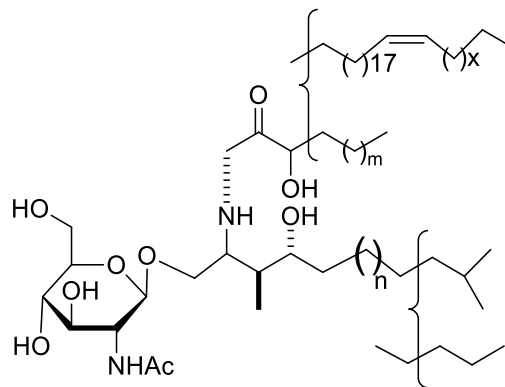
It is noteworthy that marine organisms are the rich source of various sphingolipids [44] and glycosides [45]. Interestingly, rhizochalin and its derivatives are found in several species of the genus *Oceanapia*. In 2006, Guzii *et al.* isolated two new headed-sphingolipid like compounds, rhizochalin B (**48a**) and rhizochalinin B (**49a**) as their peracetates **48b** and **49b** from an unidentified *Oceanapia sp.* collected from the north-west of Australia (Figure 6) [46]. Subsequently, Gaydou and coworkers isolated sphingolipids, rhizochalin and aglycone as their per-acetates *viz.*, rhizochalin per-acetate (**50**) and peracetyl aglycone (**51**) from the *Oceanapia ramsayi* [47].



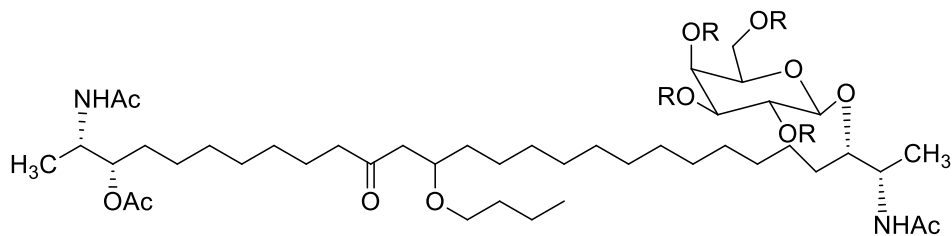
45: rhizochalin



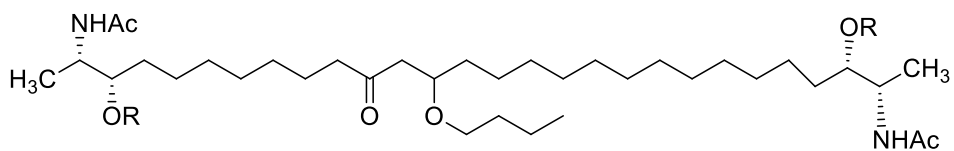
46: $m = 12, 13$; $n = 8, 9$



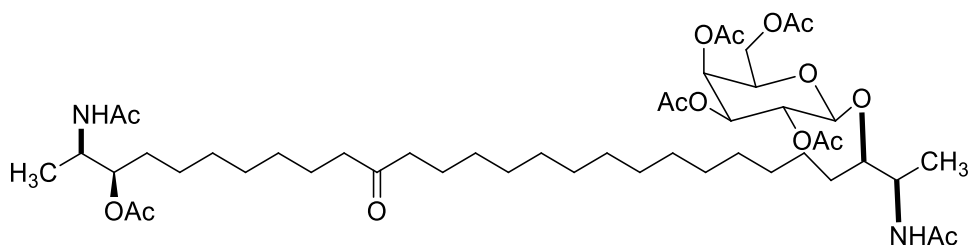
47: $x = 2, 4$; $m = 20, 21, 22$; $n = 6, 7, 8$



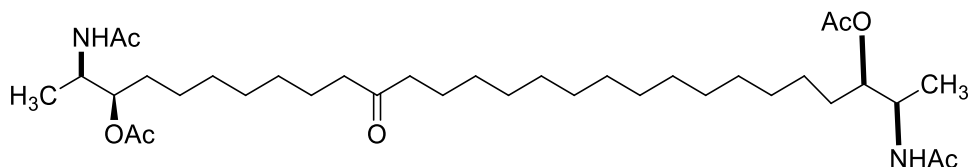
48a: $R = H$
48b: $R = Ac$



49a: $R = H$
49b: $R = Ac$



50: rhizochalin per acetate



51: aglycone of rhizochaline per acetate

Figure 6. Chemical structures of rhizochalin, cerebrosides and their derivatives.

In 1999, Nicholas *et al.* isolated a novel bis- α,ω -amino alcohol glycoside, oceanapiside (**52**) from the *Oceanapia phillipensis* collected off the coast of southern Australia (Figure 7) [48]. Oceanapiside (**52**) is a naturally occurring amphiphilic lipids having polar functionality at both the termini and exhibits significant antifungal activity against the pathogen, Fluconazole-resistant yeast, *Candida glabrata* with a MIC value of 10 $\mu\text{g/mL}$. They have also isolated its aglycone **53** from the remaining fraction when eluted with $\text{NH}_3\text{-MeOH-CHCl}_3$ which had shown indeed higher antifungal activity against *C. glabrata* than oceanapiside (**52**) with the MIC value of 3 $\mu\text{g/mL}$. In subsequent years, Nicholas and Molinski established the absolute configuration of oceanapiside (**52**) as 2S, 3R-26R, 27R using circular dichroism (CD) and revealed that it contains erythro and threo relative configurations at C1, 2 and C-26, 27, respectively [49].

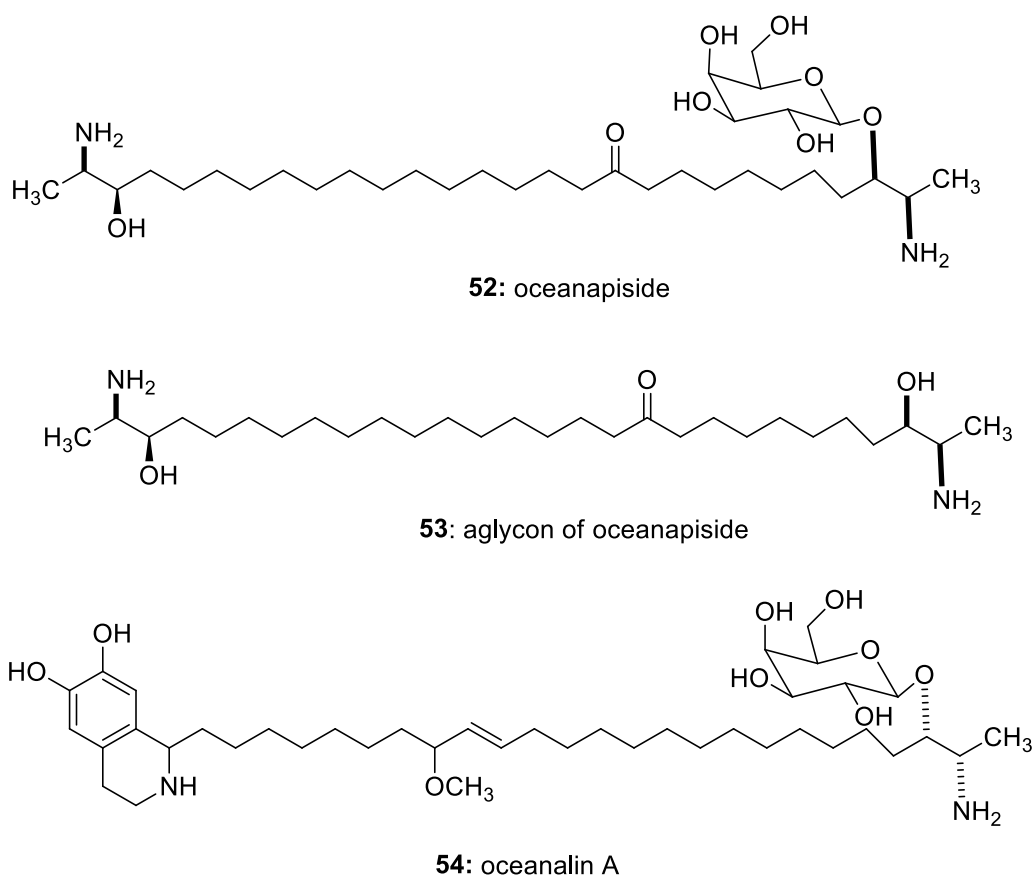


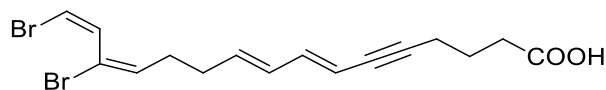
Figure 7. Structures of oceanapiside (**52**), aglyco of oceanapiside (**53**) and oceanalin A (**54**).

In 2005, Molinski and coworkers isolated a novel hybrid α,ω -bifunctionalized sphingoidtetrahydroisoquinoline β -glycoside, oceanalin A (**54**) from a marine sponge *Oceanapia sp.* (Figure 7) [50]. Oceanalin A exhibited *in vitro* antifungal activity against the human pathogen *Candida glabrata* with the MIC 30 $\mu\text{g/mL}$. Oceanalin A (**54**) is also a bifunctionalized sphingolipids, like rhizochalin (**45**) and oceanapiside (**52**) which differ from the mammalian long chain bases, D-sphingosines and they exhibited antifungal against *C. glabrata*.

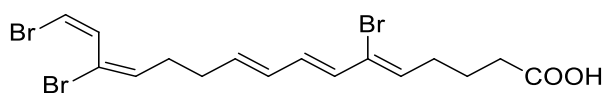
4. Thiocyanatins, halogenated and acetylenic acids

Oceanapia sp. contained numerous less common class of compounds such as halogenated acid, acetylenic acids, dithiocyanates and thiocyanatins, In 1993, Ichiba et al. reported two new brominated fatty acids, (**55** & **56**) from *Oceanapia sp.* (Figure 8) [51].The compounds are unstable in pure state and therefore, bioactivity was tested for the mixture of compounds which displayed weak cytotoxicity against KB cells and mild antimicrobial activity against gram positive bacteria. In the subsequent years, Matsunaga *et al.* isolated a novel C14-acetylenic acid (**57**) from *Oceanapia sp.* [8]. The isolated acetylenic acid exhibited selectivity in the antimicrobial activity assay. It showed moderate activity against *S. cerevisiae* and *Candida albicans*, but no activity against *Penicillium chrysogenum* and *Mortierellara manniana*. In 2001, Capon and coworkers isolated three dithiocyanates namely,

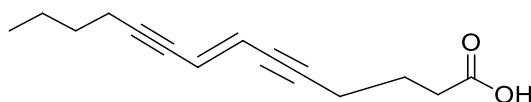
thiocyanatins A (**58**), B (**59**) and C (**60**) from *Oceanapia sp.* collected off the coast Australia [52]. Compound (**58**) exhibited *in vitro* nematocidal activities, but no significant activity was observed for the compounds **59** & **60**. A few years later his group reported the related compounds, thiocyanatins D1 (**61**), D2 (**62**), thiocarbamate thiocyanates, thiocyanatins E1 (**63**) and E2 (**64**) from *Oceanapia sp.* [10]. The inseparable compounds D1 and D2 (**61** & **62**) as well as E1 and E2 (**63** & **64**) were obtained along with the previously isolated thiocyanates A-C (**58-60**) (Figure 8).



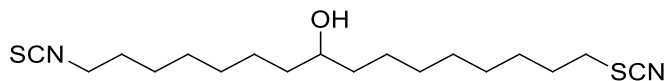
55: (7E,9E,13E,15E)-14,16-dibromohexadeca-7,9,13,15-tetraen-5-ynoic acid



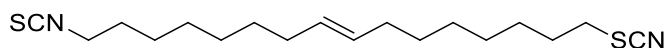
56: 6,14,16-tribromohexadeca-pentaenoic acid



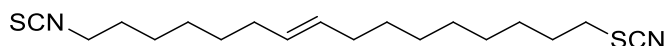
57: acetylenic acid



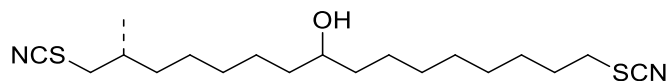
58: thiocyanatin A



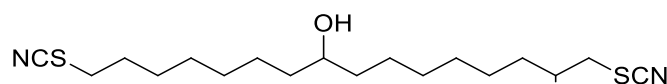
59: thiocyanatin B



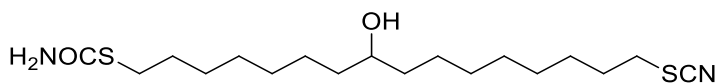
60: thiocyanatin C



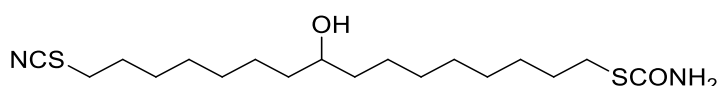
61: thiocyanatin D1



62: thiocyanatin D2



63: thiocyanatin E1



64: thiocyanatin E2

Figure 8. Structures of halogenated, acetylenic acid and thiocyanatins from *Oceanapia sp.*

5. Miscellenous

Marine sponges of the genus *Oceanapia* sp. contained other common secondary metabolites as well, such as sterols, furanoditerone and some common organic compounds. Sterols are the end products of metabolic transformation and available in diverse chemical structures. Very few steroidal compounds have been isolated from *Oceanapia* species although they are one of the most abundant metabolites in plant and animals in both marine and terrestrial organisms. In 1999, Fu et al. isolated C-14 epimeric pair of polyhydroxy sterols, tamasterone sulfates (**65** & **66**) as the new metabolites from an unidentified species of *Oceanapia* (Figure 9) [53]. In subsequent years, Stonik and coworkers isolated a unique 24R-24, 25-methylene-5 α -cholestan-3 β -ol (**67**) from a marine sponge *Oceanapia* sp. collected from the North-Western Australia [4]. Literature survey revealed that terpene isolated from this genus is also very scarce. Cafieri et al. isolated furanoditerpene (**68**) along with halogenated indole-derivatives viz., 3-bromoindole (**69**), 6-bromo-3-indolecarboxyaldehyde (**70**), and 6-bromo-5-hydroxy-3-indolecarboxyaldehyde (**71**) from Caribbean sponge *O. bartschi* [54]. Furanoditerpene (**68**) was previously isolated from *Dysidea* sponges and found to exhibit antibiotic property [55]. A 6-methoxy-2(3H)-benzoxazolinone commonly known as coixol was reported from an *Oceanapia* sp. collected from Indian Ocean [56]. Coixol (**72**) was isolated by column chromatography and it is cytotoxic to shrimp with the LC₅₀ value of 52.93 \pm 6.48 ppm.

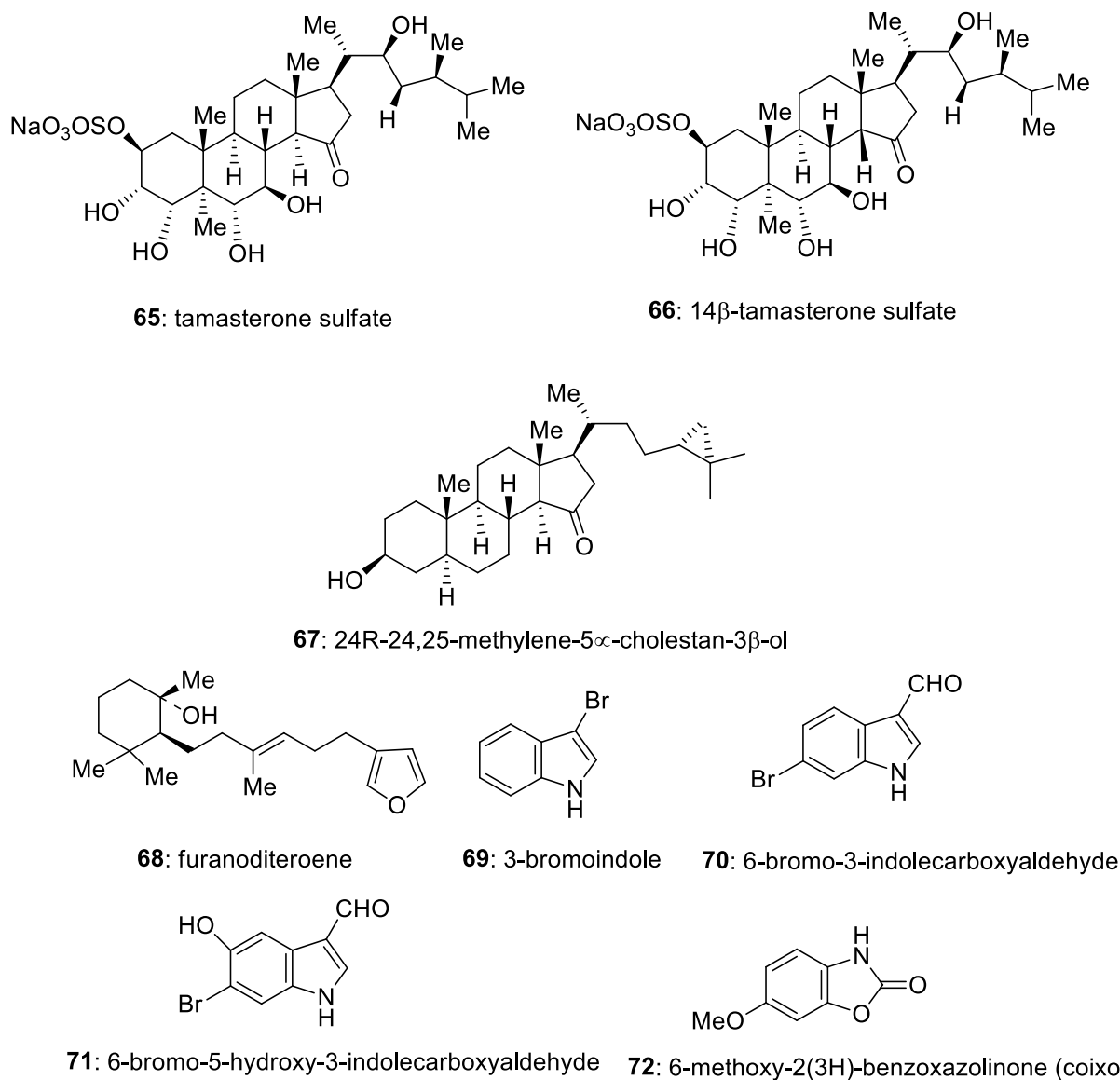


Figure 9. Chemical structures of sterols (**65-67**), furan (**68**), indole derivatives (**69-71**) and coixol (**72**).

6. Conclusion:

This review describes the various secondary metabolites isolated from the marine sponges of the genus, *Oceanapia*. The secondary metabolites reported from this genus have been discussed under the headings: alkaloids, ceramides, sphingolipids and their derivatives; thiocyanatins, halogenated acids and acetylenic acids, and finally miscellaneous covering all the other remaining compounds isolated from this genus detailing their chemical structures and reported bioactivities. The majority of the metabolites reported from this genus are alkaloids and this section has been deliberated under the subheadings; pyridoacridines, quinolizidines, phloeodictynes, sesquiterpene and brominated alkaloids. We believed that the review will help in the ready reference to numerous compounds and their biological potential derived from this genus. In addition the chemicals and bioactivities details

presented in this manuscript may find interest to synthetic organic chemists' particularly, medicinal research communities for targeted synthesis of bioactive compounds.

Conflict of interest: The authors have no conflict of interest.

Acknowledgement: We thank CSIR for financial support (OLP2006) and Director, CSIR-NIO for encouragement.

References

- [1] Ancheeva, E.; El-Neketi, M.; Song, W.; Lin, W.; Daletos, G.; Ebrahim, W.; Proksch, P. Structurally Unprecedented Metabolites from Marine Sponges. *Curr. Org. Chem.*, **2017**, *21*(5), 426-449.
- [2] Singh, K. S.; Majik, M. S. Bioactive alkaloids from marine sponges in *Marine Sponges: Chemicobiological and biomedical applications* (Editors: Ramjee Pallela and Ehrlich Hermann), Springer, **2016**, 257-286.
- [3] Eder, C.; Schupp, P.; Proksch, P.; Wray, V.; Steube, K.; Müller, C. E.; Frobenius, W.; Herderich, M.; van Soest, R. W. M. Bioactive pyridoacridine alkaloids from the Micronesian sponge *Oceanapia sp.* *J. Nat. Prod.*, **1998**, *61*(2), 301-305.
- [4] Santalova, E. A.; Makarieva, T. N.; Ponomarenko, L. P.; Denisenko, V. A.; Krasokhin, V. B.; Mollo, E.; Cimino, G.; Stonik, V. A. Sterols and related metabolites from five species of sponges. *Biochem System Ecol.*, **2007**, *35*(7), 439-446.
- [5] Mancini, I.; Guella, G.; Debitush, C.; Pietra, F. Oceanapins A–F, Unique Branched Ceramides Isolated from the Haplosclerid Sponge *Oceanapia cf. tenuis* of the Coral Sea. *Helv. Chim. Acta*, **1994**, *77*(1), 51-58.
- [6] Guzii, A. G.; Makarieva, T. N.; Svetashev, V. I.; Denisenko, V. A.; Dmitrenok, P. S.; Pokanevich, E. V.; Santalova, E. A.; Krasokhin, V. B.; Stonik, V. A. New cerebrosides from the marine sponge *Oceanapia sp.* *Russ. Chem. Bull.* **2006**, *55*(5), 928-933.
- [7] Nicholas, G. M.; Newton, G. L.; Fahey, R. C.; Bewley, C. A. Novel bromotyrosine alkaloids: Inhibitors of mycothiol S-conjugate amidase. *Org Lett.*, **2001**, *3*(10), 1543-1545.
- [8] Matsunaga, S.; Okada, Y.; Fusetani, N.; van Soest, R. W. M. An antimicrobial C14 acetylenic acid from a marine sponge *Oceanapia Species.* *J. Nat. Prod.*, **2000**, *63*(5), 690-691.
- [9] Kijjoa, A.; Wattanadilok, R.; Campos, N.; Nascimento, M. S. J.; Pinto, M.; Herz, W. Anticancer activity evaluation of Kuanoniamines A and C isolated from the marine sponge *Oceanapia sagittaria*, collected from the Gulf of Thailand. *Mar. Drugs*, **2007**, *5*(2), 6-22.
- [10] Capon, R. J.; Skene, C.; Liu, E. H.; Lacey, E.; Gill, J. H.; Heiland, K.; Friedel, T. Nematocidal thiocyanatins from a southern Australian marine sponge *Oceanapia sp.* *J. Nat. Prod.*, **2004**, *67*(8), 1277-1282.
- [11] Ibrahim, S. R. M.; Mohamed, G. A.; Elkhayat, E. S.; Fouad, M. A.; Proksch, P. Sagitol C, a new cytotoxic pyridoacridine alkaloid from the sponge *Oceanapia sp.* *Bull. Fac. Pharm. Cairo*, **2013**, *51*(2), 229-232.

- [12] Calcabrini, C.; Catanzaro, E.; Bishayee, A.; Turrini, E.; Fimognari, C. Marine sponge natural products with anticancer potential: An updated review. *Mar. Drugs*, **2017**, *15*(10), 310.
- [13] Mioso, R.; Marante, F. J. T.; Bezerra, R. S.; Borges, F. V. P.; Santos, B. V. O.; Laguna, I. H. B. Cytotoxic compounds derived from marine sponges. A review (2010–2012). *Molecules*, **2017**, *22*(2), 208.
- [14] Vitali, A. Antimicrobial peptides derived from marine sponges. *Am. J. Clin. Microbiol. Antimicrob.*, **2018**, *1*(1), 1006.
- [15] Sagar, S.; Kaur, M.; Minneman, K. P. Antiviral lead compounds from marine sponges. *Mar. Drugs*, **2010**, *8*(10), 2619-2638.
- [16] Mancini, I.; Guella, G.; Sauvain, M.; Debitus, C.; Duigou, A. G.; Ausseil, F.; Menou, J. L.; Pietra, F. New 1, 2, 3, 4-tetrahydropyrrolo[1,2-a]pyrimidinium alkaloids (phloeodictynes) from the New Caledonian shallow-water haplosclerid sponge *Oceanapia fistulosa*. Structural elucidation from mainly LC-tandem-MS-soft-ionization techniques and discovery of antiplasmodial activity. *Org. Biomol. Chem.*, **2004**, *2*(5), 783-787.
- [17] El-Demerdash, A.; Atanasov, A. G.; Horbanczuk, O. K.; Tammam, M. A.; Abdel-Mogib, M.; Hooper, J. N. A.; Sekeroglu, N.; Al-Mourabit, A.; Kijjoa, A. Chemical diversity and biological activities of marine sponges of the genus *Suberea*: A systematic review. *Mar Drugs*, **2019**, *17*(2), 115.
- [18] Wu, Q.; Nay, B.; Yang, M.; Ni, Y.; Wang, H.; Yao, L.; Li, X. Marine sponges of the genus *Stelletta* as promising drug sources: chemical and biological aspects. *Acta Pharm. Sinica B*, **2019**, *9*(2), 237–257.
- [19] El-Demerdash, A.; Tammam, M. A.; Atanasov, A. G.; Hooper, J. N. A.; Al-Mourabit, A.; Kijjoa, A. Chemistry and biological activities of the marine sponges of the genera *Mycale* (*Arenochalina*), *Biemna* and *Clathria*. *Mar. Drugs*, **2018**, *16*(6), 214.
- [20] Patterson, A. M.; Capell, L. T.; Walker, D. F. The ring index, 2nd ed.; *American Chemical Society*: Washington, DC, **1960**.
- [21] Marshall, K. M.; Barrows, L. R. Biological activities of pyridoacridines. *Nat. Prod. Rep.* **2004**, *21*(6), 731-751.
- [22] Salmond, C. E.; Faulkner, D. J. Sagitol, a pyridoacridine alkaloid from the sponge *Oceanapia sagittaria*. *Tetrahedron Lett.* **1996**, *37*(51), 9147-9148.
- [23] Carroll, A. R.; Ngo, A.; Quinn, R. J.; Redburn, J.; Hooper, J. N. A. Petrosamine B, an Inhibitor of the *Helicobacter pylori* enzyme aspartyl semialdehyde dehydrogenase from the Australian Sponge *Oceanapia* sp. *J. Nat. Prod.*, **2005**, *68*(5), 804-806.
- [24] Braekman, J. C.; Daloze, D.; de Abreu, P. M.; Piccinni-Leopardi, C.; Germain, G.; Van, M. M. A novel type of bis-quinolizidine alkaloid from the sponge: *Petrosia seriata*. *Tetrahedron Lett.*, **1982**, *23*(41):4277-4280.
- [25] Goud, T. V.; Reddy, N. S.; Swamy, N. R.; Ram, T. S.; Venkateswarlu, Y. Anti-HIV active petrosins from the marine sponge *Petrosia similis*. *Biol. Pharm. Bull.*, **2003**, *26*(10) 1498-1501.

- [26] Orabi, K. Y.; El Sayed, K. A.; Hamann, M. T.; Dunbar, D. C.; Al-Said, M. S.; Higa, T.; Kelly, M. Araguspongines K and L, New bioactive bis-1-oxaquinolizidine *N*-Oxide alkaloids from Red sea specimens of *Xestospongia exigua*. *J. Nat. Prod.*, **2002**, 65(2), 1782-1785.
- [27] Kobayashi, M.; Kawzoe, K.; Kitagawa, I. Araguspongines B, C, D, E, F, G, H, and J, new vasodilative bis-1-oxaquinolizidine alkaloids from an Okinawan marine sponge, *Xestospongia sp.* *Chem. Pharm. Bull.*, **1989**, 37(6), 1676-1678.
- [28] Venkateswarlu, Y.; Reddy, V. R. Bis-1-oxaquinolizidines from the sponge *Haliclona exigua*. *J. Nat. Prod.* **1994**, 57(9), 1283-1285.
- [29] Pettit, G. R.; Orr, B.; Herrald, D. L.; Doubek, D. L.; Tackett, L.; Schmidt, J. M.; Boyd, M. R.; Pettit, R. K.; Hooper, J. N. A. Isolation and X-ray crystal structure of racemic Xestospongine D from the Singapore marine sponge *Niphates sp.* *Bioorg. Med. Chem. Lett.*, **1996**, 6(12), 1313-1318.
- [30] Singh, K. S.; Das, B.; Naik, C. G. Quinolizidines alkaloids: Petrosin and xestospongins from the sponge *Oceanapia sp.* *J. Chem. Sci.* **2011**, 123(5), 601-607.
- [31] Kourany-Lefoll, E.; País, M.; Sevenet, T.; Guittet, E.; Montagnac, A.; Fontaine, C.; Guenard, D.; Adeline, M. T.; Debitus, C. Phloeodictines A and B: new antibacterial and cytotoxic bicyclic amidinium salts from the new caledonian sponge, *Phloeodictyon sp.* *J. Org. Chem.* **1992**, 57(14), 3832-3835.
- [32] Desqueyroux-Faundez, R.; Valentine, C.; Family Phloeodictyidae carter, 1882: In systema porifera: A guide to the classification of sponges; Hooper, J. N. A.; van Soest, R.W. M. (eds.); Kluwer academic, Plenum publishers: New York, **2002**, pp. 893-905.
- [33] Kourany-Lefoll, E.; Laprèvote, O.; Sevenet, T.; Montagnac, A.; País, M.; Debitus, C. Phloeodictines A1-A7 and C1-C2, antibiotic and cytotoxic guanidine alkaloids from the new caledonian sponge, *Phloeodictyon sp.* *Tetrahedron*, **1994**, 50(11), 3415-3426.
- [34] Killday, K. B.; Longley, R.; McCarthy, P. J.; Pomponi, S. A.; Wright, A. E.; Neale, R. F.; Matthew, A. Sesquiterpene-derived metabolites from the deep water marine sponge *Poecillastra sollasi*. *J. Nat. Prod.* **1993**, 56(4), 500-507.
- [35] Boyd, K. G.; Harper, M. K.; Faulkner, D. J. Oceanapamine, a sesquiterpene alkaloid from the Philippine sponge *Oceanapia sp.* *J. Nat. Prod.* **1995**, 58(2), 302-305.
- [36] Garg, H. S.; Sharma, M.; Bhakuni, D. S.; Pramanik, B. N.; Bose, A. K. An antiviral sphingosine derivative from the green alga *Ulva fasciata*. *Tetrahedron Lett.* **1992**, 33(12), 1641-1644.
- [37] Nielsen, P. G.; Carlé, J. S.; Christophersen, C. Final structure of caulerpicin, a toxin mixture from the green alga *Caulerpa racemosa*. *Phytochemistry*, **1982**, 21(7), 1643-1645.
- [38] Kobayashi, J.; Ishibashi, M.; Nakamura, H.; Hirata, Y.; Yamasu, T.; Sasaki, T.; Ohizumi, Y. Symbioramide, a novel Ca²⁺-ATPase activator from the cultured dinoflagellate *Symbiodinium sp.* *Experientia*, **1988**, 44(9), 800-802.
- [39] Chebaane, K.; Guyot, M. Occurrence of erythro-docosasphinga-4, 8-dienine, as an ester, in *Anemonia sulcata*. *Tetrahedron Lett.*, **1986**, 27(13), 1495-1496.

- [40] Mancini, L.; Guella, G.; Debitush, C.; Pietra, F. Oceanapins A-F, unique branched ceramides isolated from the Haploscerid sponge, *Oceanapia cf. tenuis* of the Coral Sea. *Helv. Chim. Acta*, **1994**, 77(1), 52-58.
- [41] Guzii, A. G.; Makarieva, T. N.; Svetashev, V. I.; Denisenko, V. A.; Dmitrenok, P. S.; Pokanevich, E. V.; Santalova, E. A.; Krasokhin, V. B.; Stonik, V. A. New ceramides from sea sponge *Oceanapia sp.* *Russ. J. Bioorg. Chem.* **2006**, 32(3), 288-294.
- [42] Makarieva, T. N.; Denisenko, V. A.; Stonik, V. A.; Milgrom, Y. M.; Rashkes Y. W. Rhizochalin, a novel secondary metabolite of mixed biosynthesis from the sponge *Rhizochalin aincrustata*. *Tetrahedron Lett.* **1989**, 30(47), 6581-6584.
- [43] Khana, P.; Kang, B. S.; Yun, H. J.; Cho, H. G.; Makarieva, T.; Choi, H. S. Aglycon of Rhizochalin from the *Rhizochalinaincristata* induces apoptosis via activation of AMP-activated protein kinase in HT-29 colon cancer cells. *Bio. Pharm. Bull.* **2011**, 34(10), 1553-1558.
- [44] Muralidhar, P.; Radhika, P.; Krishna, N.; Rao, D. V.; Rao, C. B. Sphingolipids from marine organisms: A review. *Nat Prod. Sci.* **2003**, 9(3), 117-142.
- [45] Kalinin, V. I.; Ivanchina, N. V.; Krasokhin, V. B.; Makarieva, T. N.; Stonik, V. A. Glycosides from marine sponges (Porifera, Demospongiae): Structures, taxonomical distribution, biological activities and biological roles. *Mar. Drugs* **2012**, 10(8), 1671-1710.
- [46] Makarieva, T. N.; Guzii, A. G., Denisenko, V. A.; Dmitrenok, P. S.; Stonik, V. A.; New two-headed sphingolipids-like compounds from the marine sponge *Oceanapia sp.* *Russ. Chem. Bull. Int. Ed.* **2008**, 57(3), 669-673.
- [47] Bensemhoun, J.; Bombarda, I.; Aknin, M.; Faure, R.; Vacelet, J.; Gaydou, E. M. Marine bifunctional sphingolipids from the sponge *Oceanapia ramsayi*. *Molecules*, **2008**, 13(4), 772-778.
- [48] Nicholas, G. M.; Hong, T. W.; Molinski, T. F.; Lerch, M. L.; Cancilla, M. T.; Lebrilla, C. B. Oceanapiside, an antifungal Bis- α,ω -amino alcohol glycoside from the marine sponge *Oceanapia phillipensis*. *J. Nat. Prod.* **1999**, 62(12), 1678-1681.
- [49] Nicholas, G. M.; Molinski, T. F. Enantiodivergent biosynthesis of the dimeric sphingolipid Oceanapiside from the marine sponge *Oceanapia phillipensis*. Determination of remote stereochemistry. *J. Am. Chem. Soc.* **2000**, 122(17), 4011-4019.
- [50] Makarieva, T. N.; Denisenko, V. A.; Dmitrenok, P. S.; Guzii, A. G.; Santalova, E. A.; Stonik, V. A.; MacMillan, J. B.; Molinski, T. F. Oceanalin A, a hybrid α,ω -bifunctionalized sphingoid tetrahydroisoquinoline β -glycoside from the marine sponge *Oceanapia sp.* *Org. Lett.*, **2005**, 7(14), 2897-2900.
- [51] Ichiba, T.; Scheuer, P. J. Michelle, K. B. Sponge-derived polyunsaturated C16 di- and tribromocarboxylic acids. *Helv. Chim. Acta*, **1993**, 76(8), 2814-2816.
- [52] Capon, R. J.; Skene, C.; Liu, E. H.; Lacey, E.; Gill, J. H.; Heiland, K.; Friedel, T. The Isolation and synthesis of novel nematocidal dithiocyanates from an Australian marine sponge, *Oceanapia sp.* *J. Org. Chem.*, **2001**, 66(23), 7765-7769.

- [53] Fu, X.; Ferreira, M. L. G.; Schmitz, F. J.; Kelly, M. Tamosterone sulfates: A C-14 epimeric pair of polyhydroxylated sterols from a new Oceanapiid sponge genus. *J. Org. Chem.*, **1999**, *64*(18), 6706-6709.
- [54] Cafieri, F.; Fattorusso, E.; Mahajnah, Y.; Mangoni, A. 6-Bromo-5-hydroxy-3-indolecarbaldehyde from the Caribbean sponge *Oceanapia bartshi*. *Z. Naturforsch.*, **1993**, *48*(10), 1408-1410.
- [55] Walker, R. P.; Faulkner, D. J. Diterpenes from the sponge *Dysidea amblia*. *J. Org. Chem.*, **1981**, *46*(6), 1098-1102.
- [56] Venkateswarlu, Y.; Reddy, N. S.; Ramesh, P.; Rao, J. V. Coixol: a bioactive principle from a marine sponge *Oceanapia sp.* *Biochem. Syst. Ecol.*, **1999**, *27*(5), 519-520.