A review of bioactive compounds from marine organisms with special mention on the potential of marine sponges in pharmacological applications

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Abstract
A variety of biologically active compounds with unique structures and pharmacological properties have been reported to occur in marine organisms. Demospongiae, an important class of marine sponge is known for producing the largest number and diversity of secondary metabolites isolated till recent times. The review covers the diverse class of bioactive compounds isolated for therapeutic drug applications from different marine organisms. It is an attempt to update the marine research community with results of our ongoing search for bioactive secondary metabolites from marine sponge Spongosorites halichondriodes which has exhibited antibacterial, antifungal, cytotoxic, anti-inflammatory and immunomodulatory activity in our studies.

Spongosorites halichondriodes (order Halichondrida, family Halichondriidae) is a predominant marine sponge collected from west coast of Mumbai, India. The sponge S. halichondriodes has shown presence of Octadecadienoic acid (Linoleic acid), ergostan tetraen-ol, dihydroxy cholanoic- methyl esters, C₆ saturated and unsaturated esters like 3β, 4β, 7α, 12α-tetrahydroxy-5β-cholan-24-oic acid methyl ester, 7α, 12β- dihydroxy-5β-cholan-24-oic acid methyl ester, novel isocoumarin citrinolactone A, a triterpenoid glycyrrhetinic acid as well as other unknown compounds such as nucleoside inosine.

Keywords: Marine sponges, Spongosorites, bioactive compounds, glycosylated sterol derivatives.

Introduction
Chemical substances derived from animals, plants and microorganisms have been used to treat human diseases since the dawn of medicine. The investigation of these chemical substances from natural products as source of human therapeutics reached its peak in the period 1970–1980, which resulted in strong influence of non-synthetic molecules to pharmaceutical industries (Koehn and Carter, 2005). Later, between 1981 and 2002, natural products or natural product-derived drugs comprised 28% of all new chemical entities (NCEs) (Newman et al., 2003). In addition, 24% of these NCEs were synthetic or natural mimic compounds, based on the study of pharmacophores related to natural products (Newman et al., 2000). This combined percentage (52% of all NCEs) proved that natural products are important sources for new drugs and are also good leads for further modification during drug development.

Over 20 new drugs were launched in the market between 2000 and 2005, originating from microorganisms, marine organisms, terrestrial plants, vertebrates and invertebrates. These drugs, together with several other natural products or their analogs undergoing clinical trials, continue to demonstrate the importance of compounds from natural sources in modern drug discovery.
efforts (Chin et al., 2006). Currently, over a 100 new products are in clinical development, particularly as anti-cancer agents and anti-infective. More interestingly, application of molecular biology techniques is increasing the availability of novel compounds that can be conveniently produced in bacteria or yeasts. Combinatorial chemistry approaches based on natural product scaffolds to create are also helpful in screening libraries that closely resemble drug-like compounds. Various screening approaches were being developed to improve the ease with which natural products can be used in drug discovery campaigns and data mining. Virtual screening techniques were also applied to databases of natural products (Harvey, 2008).

Marine organisms have a shorter history of utilization in the treatment and prevention of human disease. Among the first bioactive compounds from marine sources, an anticancer drug (cytosine arabinoside, Ara-C) and an antiviral drug (adenine arabinoside, Ara-A) were approved in 1965. Their discovery led scientists to study marine organisms extensively over the past 30 years. Then, drug discovery research from marine organisms is accelerating and now involves interdisciplinary research including biochemistry, biology, ecology, organic chemistry and pharmacology (Capon, 2001; Haefner, 2003). Thousands of new marine natural products have been reported, belonging to chemical classes of steroids, terpenoids, isoprenoids, nonisoprenoids, quinones, brominated compounds, nitrogen heterocyclics, and nitrogen sulphur heterocyclics. Many new developments of the last five years in this field of research and important findings for bioactive compounds from in vitro, in vivo and clinical studies for therapeutic drug applications have been covered by Perdicaris et al., 2013.

In the last five years, we have found huge potential in marine sponges of Mumbai coastal region. Herein, we are elaborating on the results of their compounds and pharmacological activity. Along with it, we have classified different pharmacological classes of compounds reported from marine organisms, and have tried to contribute in terms of the research findings from the marine sponge, *Spongosorites halichondriodes*. There are few reports about this species having cytotoxic property due to the presence of mono and bis indole alkaloids (Bao et al., 2007a, b), but we contribute adding more detailed biological activity of *S. halichondriodes*.

**Bioactive compounds from marine organisms**

**a. Antibacterial compounds**

The antimicrobials derived from the sea organism belong to the class of phenol, lactone, sterol, terpenoid, phthalate, fatty acid, cyclic polysulphide, steroidal glycoside, polysaccharide, sulphated glycoside, protein, acetylene, terpene, indole derivative, glycerol derivative, glycoproteins etc. Anti-microbial peptides are a “new” class of antimicrobial compounds with pharmaceutical potential, because of their broad spectrum activity for bacteria, fungi and virus. Their molecular targets are bacterial membranes and intracellular molecules like DNA, RNA and proteins (Sperstad et al., 2011). Donia and Hamann (2003) have extensively reviewed potential anti-infective agents from marine flora. Squalamine, the first aminosterol isolated from the dogfish shark *Squalus acanthias* (Squalidae) showed potent antimicrobial activity, with an MIC of 1·0 µg/mL. It inhibited *Staphylococcus aureus*, and also exhibited antiangiogenic and anti-tumour properties. It is currently in clinical trials for the treatment of advanced non-small-cell lung cancer. Cribrostatins, another compound from a blue sponge *Cribrochalina* sp. showed potent antineoplastic and antimicrobial activities. Cribrostatin 3 showed potent inhibitory activity against *Neisseria gonorrhoeae*, with an MIC of 0·09 µg/mL (Pettit et al., 2000). A potent antibacterial diterpene, bromosphaerone was isolated from *Sphaerococcus coronopifolius*, which showed antibacterial activity against *S. aureus*, with an MIC of 0·047 µg/mL (Etahiri et al., 2001) (Fig. 1). Pestalone, product of marine fungus was isolated from the surface of the brown alga *Rosenvingea* sp. of the genus *Pestalotia* had potent antibiotic activity against methicillin-resistant *S. aureus*, with an MIC of 0·037 µg/mL, and Vancomycin-resistant *Enterococcus faecium*, with an MIC of 0·078 µg/mL (Cueto et al., 2001). Jorumycin, a dimeric isoquinoline alkaloid was isolated from the mantle and mucus of the Pacific nudibranch *Jorunna funebris*. It inhibited the growth of various Gram positive bacteria eg. *Bacillus subtilis*, *Staphylococcus aureus* at a concentration of 0·050 µg/mL, with an inhibition zone of 16 mm. Despite its high potency, its cytotoxic effects at IC50 of 0·012 µg/mL and the difficulty in
obtaining a pure stable preparation hindered its development as a drug (Fontana et al., 2000). Seven monoindole derivatives have been isolated from Spongosorites sp. among which, five compounds were unique indole pyruvic acid derivatives (Bao et al., 2007a). Bis (indole) alkaloids (topsentin and hamaconthin class) were also isolated from this species. Hamaconthin class exhibited more potent antibacterial activity than those of the topsentin class (Oh et al., 2005) (Fig. 2). Symbiotic microorganisms are also being explored in recent past as an alternative source for production of host bioactive metabolites. In one of the findings, a marine Gram-positive Bacillus licheniformis SAB1 bacterium identified by 16S rDNA, was isolated from sponge Halichondria sp. and showed significant antimicrobial activity (Devi et al., 2010). In our own work, we have isolated a symbiont gram negative bacterium from marine sponge Halichondria glabrata which has shown promising antimicrobial activity with GenBank submission no. KF488586 (Jogani and Kumar, 2014).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure type</th>
<th>Source</th>
<th>Activity MIC</th>
<th>Cytotoxicity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aurantoside</td>
<td>Polyketide</td>
<td>Silquariaspongia japonica, sponge</td>
<td>0.16µg/ml 0.63µg/ml (A. fumigates)</td>
<td>&gt;5 µg/ml (murine leukaemia cells)</td>
<td>Donia and Hamam, 2003</td>
</tr>
<tr>
<td>Halichon dramide</td>
<td>Macrolide</td>
<td>Halichondria sp. sponge</td>
<td>C albicans 0.2 µg/mL</td>
<td>Highly toxic to mice at 1.4mg/kg</td>
<td>Mc Innes,2008</td>
</tr>
<tr>
<td>Fascaplysin</td>
<td>Bis (indole) alkaloid</td>
<td>Fascaplysinopsis sp. sponge</td>
<td>S cerevisiae 0·1 µg/disk (20 mm zone) C albicans at 1 µg/ disk (11 mm zone)</td>
<td>L1210 IC50 0·2 µg/mL</td>
<td>Dalisay et al., 2011</td>
</tr>
<tr>
<td>Ptilomycalin A</td>
<td>Polycyclic guanidine alkaloid</td>
<td>Ptilocaulis spiculifer sponge</td>
<td>C albicans 0·8 µg/mL HSV 0·2 µg/mL</td>
<td>P388 IC50 0·1 µg/mL</td>
<td>Dalisay et al., 2011</td>
</tr>
<tr>
<td>Halichona diamine</td>
<td>Alkaloid</td>
<td>Halichona sp.</td>
<td>C albicans 1 µg/disk</td>
<td>Not measured</td>
<td>Wattanadilok et al., 2007</td>
</tr>
<tr>
<td>Halishigamide A</td>
<td>Macrolide</td>
<td>Halichondria sp. sponge</td>
<td>Trichophyton mentagrophytes 0·1 µg/mL</td>
<td>L1210 IC50 0·0036 µg/mL KB IC50 0·012 µg/mL</td>
<td>Kobayashi et al., 1997</td>
</tr>
</tbody>
</table>

b. Anti-fungal compounds

Antifungal compounds from marine organism cover marine macrolides, aminoalcohols and related heterocyclic structures, including oxazoles and other alkaloids, peptides as well as a few representative terpenoids and polyketides. Jasplakinolide is the first example of a cyclodepsipeptide which was isolated from a sponge (Fig. 3) and was identified from a Jaspis sp. Also named jaspamide, is a 19-membered macrocyclic depsipeptide with selective in-vitro antimicrobial activity and a MIC of 25 µg/mL against Candida albicans. The in-vivo topical activity of a 2% solution of Jasplakinolide against a Candida vaginal infection in mice was similar to that of Miconazole nitrate (Crevis et al., 1986). Most antifungal compounds from marine origin are found to be cytotoxic. Consequently, they have not been considered promising for clinical applications. Table 1 enlists marine
natural products that show potent antifungal activity, but the evidence of their cytotoxicity is not available (Donia and Hamam, 2003). Structures for these compounds are shown in Fig. 3. D-Phtosphingosine is the corresponding 4-hydroxy analog of D-sphinganine and the major sphinganoid base found in the sphingolipids of higher plants and many invertebrates. The chain length of sphingoid bases is important for antifungal activity. In a comparative study, the antifungal activity of sphingolipids against Candida glabrata was found to be negligible for short-chain 2-amino-3-alkanol homologs, but increased with chain-length (C18) (Nicholas et al., 2002). Kabiramide C and ulapualides A and B were the first described members of a unique family of trisoxazole macrolides in antifungal class of compounds. Two very potent antifungal macrolides, phorboxazoles A and B with novel parent ring structures were isolated in a sponge of the genus Phorbas from Western Australia (Molinski, 2004). Three new antifungal peroxides were isolated from two sponges, Plakortis halichondriodes from Jamaica and Plakinastrella onkodes collected in Florida, in addition to known plakortides E, F and H (Pomponi and Wright, 2002). The compounds like cyclic peptide Aciculitin B from Aciculites ciliate, tetramic acid glycoside aurantoside E from Plakinolopha mirabilis, 4α-isocyanogorgon-11-ene from Axinyssa terpinis, and the biphenyl ether 3, 5-dibromo-2-(3, 5-dibromo-2-methoxyphenoxy) phenol from an unidentified sponge might be used as molecular probe to uncover novel antifungal drug targets or as lead for new compound with improved antifungal properties (Li et al., 2012). Bioassay guided isolation and identification of marine red-sea sponge Negombata magnifica resulted in latrunculin B, a lead molecule for designing new antifungal for managing common fungal diseases in aquaculture (Devi et al., 2013).

c. Anti-tumor compounds

Sponges have been a rich source of cytotoxic compounds like bryostatins. Other such compounds reported from sponges are the antineoplastic alkaloid Niphatesine D, which was extracted from a Niphates species (Kitagawa and Kobayashi, 1990); the Epinardins, isolated from an unidentified species (Ambrosion et al., 1996); and the globostellatic acids A to D, which are isomalabaracane triterpene constituents of Stelleta globostellata (Ryu et al., 1996). Probably the best known of the compounds with potential as anticancer drugs are the macrolides known as bryostatins, isolated primarily from the bryozoan, Clavelina picta, although some have been extracted from sponges and tunicates. Examples of active compounds from tunicates are the cytotoxic alkaloids clavepictine-A and -B, reported for Clavelina picta (Raub et al., 1991) and the cytotoxic dimeric disulphide alkaloid polycarpine (Fig. 4), isolated from Polycarpa clavata (Kang and Fenical, 1996). Anticancer agents (e.g., bryostatins, discodermolide, eleutherobin and sarcodictyin) have been isolated from bacteria of marine flora (Blunden, 2001). Arenicolides is a 26-membered polyunsaturated macrolactone, produced by the obligate marine actinomycyte Salinispora arenicola strain CNR-005 isolated from marine sediment (Carlos et al., 2009). Sponge derived compounds for treating cancer and inflammation in preclinical/clinical trials are listed in Table 2. There is a large number of triterpenoid those exhibits cytotoxicity against a variety of tumor cells, as well as anticancer efficacy in preclinical animal models and has been reviewed (Li et al., 2013).

![Antitumor compounds from marine organisms](image-url)

**Table 2:** Sponge derived compounds for treating cancer and inflammation in preclinical/clinical trials

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Disease</th>
<th>Marine sponge source</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halichondrin B</td>
<td>Cancer</td>
<td>Halichondria okadai</td>
<td>Hirata and Uemura 1986</td>
</tr>
<tr>
<td>KRN 7000</td>
<td>Cancer</td>
<td>Agelas mauritianus</td>
<td>Nakagawa et al., 2000</td>
</tr>
<tr>
<td>LAF 389</td>
<td>Cancer</td>
<td>Jaspiis digonoxea</td>
<td>Salomon et al., 2004</td>
</tr>
<tr>
<td>Laulimalide</td>
<td>Cancer</td>
<td>Cacospongia mycofijiensis</td>
<td>Mooberry et al., 2004</td>
</tr>
<tr>
<td>IPL 512.602</td>
<td>Inflammation</td>
<td>Petrosia contignata</td>
<td>Hedner, 2007</td>
</tr>
<tr>
<td>Manoalide</td>
<td>Inflammation</td>
<td>Luffariella valiablis</td>
<td>Newman and Cragg, 2004</td>
</tr>
<tr>
<td>Salycylhalimide A and B</td>
<td>Cancer</td>
<td>Haliclona sp.</td>
<td></td>
</tr>
</tbody>
</table>
d. Immunosuppressive compounds

There are very few marine natural products which have been described having immunosuppressive activity. The first time two immunosuppressive compounds, 4 alpha-methyl-5 alpha-cholest-8-en-3 beta-ol and 4, 5-dibromo-2-pyrrolic acid were isolated from a deep water marine sponge, *Agelas flabelliformis*. Both compounds were highly active in suppression of the response of murine splenocytes in the two-way mixed lymphocyte reaction (MLR) with little to no demonstrable cytotoxicity at lower doses (Gunasekera et al., 1989). Till date, the most promising candidates for immunosuppressive therapy among marine natural products are discodermolide isolated from *Discodermia* species and microcolin A (Fig. 5). The isolated pure natural product discodermolide exhibited potent suppressive activity in the murine two-way MLR and concanavalin A stimulation of splenocyte cultures. In another study, FW635I1 (Daidzein) and FW635I2 (Genistein) were found to possess immunosuppressive and antitumor activities without any antimicrobial activities produced from *Micromonospora carbonacea* FIM 02-635 (Hong and Rong, 2006). In another attempt, components extracted from marine sponge *Aurora globostellata* and a total of 10 marine bacterial strains from *Callyspongia difusa* were evaluated. The bacterial strains showed potential to fight infections as well as production of immunomodulators (Chairman et al., 2013; Kalirajan et al., 2013).

e. Anti-inflammatory compounds

A number of potential anti-inflammatory compounds have been isolated from marine invertebrates that exhibit phospholipase A2 (PLA2) inhibitory activity. A wide range of marine compounds have been investigated for their anti-inflammatory properties. Cacospongionolide B and petrosaspongiolide M are representative examples of anti-inflammatory compounds in experimental models of acute or chronic inflammation. The mechanisms of action of these compounds include phospholipase A, inhibition as well as the control of nuclear factor-B activation and inflammatory gene expression (Alcaraz and Paya, 2006). Other PLA2 inhibitors are the sesterterpenes variabilin from *Ircinia variabilis*, cacospongionolide B from *Fasciospongiaca vernosa* and petrosaspongiolide M from *Petrospongia nigra*, as well as the sesquiterpene bolinaquinone from *Dysidea* sp. Variabilin inhibits human synovial PLA2 (IC$_{50}$ 6.9 µM) but not 5-lipoxygenase or cyclooxygenases 1 and 2 in vitro (Escrig et al., 1997). These sesquiterpenes were found to inhibit human neutrophil degranulation, superoxide generation, leukotriene B4 (LTB4) production (variabilin), TPA-induced ear oedema (variabilin and bolinaquinone topically) as well as carrageenan induced paw oedema (variabilin, petrosaspongiolide M and bolinaquinone, p.o.) in mice (Giannini et al., 2001; Haefner, 2003). By far, Manoalide, a non-steroidal sesterterpenoid isolated from a marine sponge, has proven to be a potent analgesic and anti-inflammatory compound. It inhibited phospholipase A2 from extracellular sources (snake venoms, bee, etc.), the release of arachidonic acid from rabbit polymorphonuclear leukocytes as well as calcium mobilization (Mayer 1989). The findings on IPL-576092, inhibiting the release of histamine from rat mast cells and also from the lung tissue of guinea pigs led its introduction into clinical trials (Fig. 6). Pseudopterosins are a constituent of the cosmetic “anti-wrinkle cream” sold by Estee Lauder under the brand name “Resilience” from the Caribbean gorgonian *Pseudopterogorgia elisabethae* (Newman and Cragg, 2004). In one of the recent studies, screening of marine sponge extracts led to anti-inflammatory agents Girolline as an inhibitor of protein synthesis targeting TLR signaling pathways (Fung et al., 2014).
Taxonomy status of *Spongosorites halichondriodes* (Dendy, 1905)

Kingdom: Animalia  
Phylum: Porifera  
Class: Demospongiae  
Order: Halichondrida  
Family: Halichondriidae  
Genus: *Spongosorites*

**Metabolites from the sponge, *Spongosorites* sp. from earlier work**

Marine sponges are the most primitive multicellular animals and contain many metabolites, including lipids, in particular glycolipids especially unusual long-chain Δ5, 9 FA with no counterpart in the terrestrial world. They sometimes contain a third double bond or a bromine atom in the long chain structure (Litchfield and Morales, 1976). Sponges also contain special structural features in their cell membranes, in particular phospholipid FA and sterols, since sterol–phospholipid interactions are assumed to play a major role in cell membranes (Barnathan and Kornprobst, 1998). Phospholipids like methylene-interrupted PUFA, very long chain acids known as demospongic acids. Marine invertebrates, e.g. sponges, are filter feeders and consequently they can be associated with microorganisms. Thus, particular fatty acid appears as biomarkers for such organisms. Seven monoindole derivatives were isolated from the methanol extract of a marine sponge *Spongosorites* sp. by bioactivity-guided fractionation. Five compounds were unique indole pyruvic acid derivatives (Bao *et al.*, 2007a). Bis (indole) alkaloids, of the topsentin class and hamacanthin class, from the same sponge were investigated using several biological assays. In the evaluation of antimicrobial activity against various strains of bacteria and fungi, compounds of the hamacanthin class exhibited more potent antibacterial activity than those of the topsentin class (Oh *et al.*, 2006; Bao *et al.*, 2007b). These bis indole alkaloids showed the fibronectin-binding activity which highlighted the potential of these compounds for the treatment of *S. aureus* infections via inhibition of sortase activity (Oh *et al.*, 2005).

**Bioactivities of metabolites from *Spongosorites halichondriodes***

We review here the various biological activities studied in different marine sponges worldwide. Along with we update with the recent research findings with all the studies done on the extracts of *S. halichondriodes*.

**Antimicrobial and antifungal activity**

Various metabolites from marine sponges and tunicates have been shown to possess antimicrobial, cytotoxic or antiparasitic properties, in agreement with the need for soft-bodied organisms to develop the art of chemicals against their predators. The interesting species of marine sponges reported in terms of different activities are *Ircinia felix, Topsentia ophiraphidites* and *Pandaros acanthifolium*. The active components from these species may yield useful candidates in the search for new pharmaceutical leads (Lutta *et al.*, 2008). A new bis (indole) alkaloid of the hamacanthin class along with topsentin class, from *Spongosorites* sp. has been studied for Sortase A inhibiting activity. The fibronectin-binding activity data highlighted the potential of these compounds for the treatment of *S. aureus* infections via inhibition of sortase activity (Nondo *et al.*, 2011). In the evaluation of antimicrobial activity against various strains of bacteria and fungi, compounds of the hamacanthin class exhibited more potent antibacterial activity than those of the topsentin class. Deoxytopsentin and hamacanthin A also exhibited significant antibacterial activity against methicillin resistant *Staphylococcus aureus*, with MIC values of less than 12.5 µg/mL. In the antifungal activity test, hamacanthins, especially...
Murray et al. (1995) reported the isolation of dragmacidin from Agelas oroides and Axinella damicornis were quite promising in inhibiting the growth of Pseudomonas aeruginosa and gentamycin resistant strains of Listeria monocytogenes and Enterococcus faecalis as well as broad spectrum activity against all the other bacteria. In another study by Ines et al., 2007, extracts of the sponges Agelas oroides and Axinella damicornis were quite promising in inhibiting the growth of Pseudomonas aeruginosa and gentamycin resistant strains of Listeria monocytogenes and Enterococcus faecalis as well as broad spectrum activity against all the other bacteria. In a report by Ines et al. (2007) comparatively only three among 9 sponge extracts show moderate capacity of growth inhibition against fungi strains. However, the antifungal activity of most of the sponge extracts was not so promising, which is not in agreement with our results from S. halichondriodes extracts (Kumar and Pal, 2012a). It showed moderate activity against both bacteria and fungi strains. The non-polar and polar extracts from S. halichondriodes have shown promising antimicrobial activity against both Gram negative and Gram positive bacteria. It also showed brine shrimp toxicity. The methanol and ethyl acetate extract showed presence of compounds like 5-α-Cholane- 3 β- ol, Dihydrocholesterol, cholesterol, 3-β, 6-α Dihydroxy-5-α-cholan-24- oic acid methyl ester. The hexane extract indicated presence of terpenoids like citronellyl acetate and butyrate along with pregnanediol. All these compounds have sufficient literature support of possessing antibacterial and anti-inflammatory activity (Kumar et al., 2012c; Kumar and Pal, 2013).

Cytotoxic activity

Murray et al. (1995) reported the isolation of dragmacidin D from a deep water marine sponge Spongosorites sp. collected from the southern Australian coast. Dragmacidin D was found to be active against human lung tumor cell lines and inhibited in vitro growth of the P-388 murine and A-549 with IC50 values of 1.4 and 4.5µg/mL, respectively. Four new bisindole alkaloids, nortopsentins A-D were isolated from the Caribbean deep sea sponge Spongosorites ruetzleri belonging to the same genus (Sakemi and Sun, 1991). The structures of nortopsentins A-D were established mainly on the basis of NMR spectroscopic data and were found to contain an imidazole ring between two indole units. Compounds exhibited cytotoxic activity against P-388 cells with IC50 values of 7.6, 7.8, 1.7 and 0.9 µg/mL, respectively. There are reports on subclasses of pyrrole alkaloids and their anticancer nature from marine sponges. A dipyroloquinone, Zyzzyanone A was isolated from the Australian marine sponge Zyzzya fuliginosa which showed mild cytotoxic activity against mouse Ehrlich carcinoma cells with IC50 value of 25 µg/mL (Utkina et al., 2004). Seven other novel pyrroloiminoquinones, the makaluvamines A-F were isolated from the Fijian sponge Zyzzya cf. marsailis. They exhibited potent in vitro cytotoxicity against the human colon tumor cell line HCT-116, topoisomerase II sensitive CHO cell line XRS-6, and also inhibited the catalytic activity of topoisomerase II (Radisky et al., 1993). Pyrinodemin A, a pyridine alkaloid from Okinawan marine sponge Amphimedon sp. demonstrated potent cytotoxicity in vitro against murine leukemia L-1210 and KB epidermoid carcinoma cells with IC50 values of 0.058 and 0.5 µg/mL, respectively (Tsuda and Kobayashi, 1997). Spongosorites halichondriodes sponge extracts have also showed strong toxicity with LC50 dose ranging from 5.24-1000 µg/mL speculating the toxic characteristic of the sponge. Guided by the brine shrimp test considered to be a preliminary cytotoxicity assay the extracts were tested in human cell lines. The ethyl acetate extract showed inhibition of % control growth at GI50 of 19.7 µg/mL where for extracts, GI50 value ≤ 20µg/mL is considered to be active (Kumar and Pal, 2012a). The active extract has shown presence of inosine and 2, 2, 6, 6-Tetramethyl-4-piperidone in its GC-MS results. The earlier results of similar types of alkaloids have shown positive cytotoxicity activity in various cell lines. These alkaloids might be responsible for the positive cytotoxic activity in S. halichondriodes extracts which can be confirmed by further studies. In a recent review by Senthilkumar et al. (2013), antiangiogenic compounds and angiogenic regulators from marine sponge derived for cancer were explained for their role in inhibiting cancer cell proliferation and tumor angiogenesis.

Anti-inflammatory activity

In one of the studies, investigation of the in-vitro metabolism of glycyrrhetinic acid by liver microsomes and to examine possible metabolic interactions that glycyrrhetinic acid may have with other cytochrome P450 (CYP) substrates, it was incubated with rat and human liver microsomes. The results suggested that glycyrrhetinic acid has the potential to interact with a wide range of xenobiotics or endogenous chemicals that are CYP2C9, CYP2C19 and CYP3A4 substrates (Zhao et al., 2012). It potently inhibits the activity of mammalian pols including pol λ and also reduces TNF-α production and NF-κB activation and suppresses mouse ear inflammation stimulated by TPA. Thus, glycyrrhetinic acid could be an anti-inflammatory agent based on pol λ inhibition (Ishida et al., 2012).
The GC-MS has shown presence of moderate amounts of glycyrrhetinic acid in marine sponge *S. halichondriodes*, which is a pentacyclic triterpenoid derivative of the beta-amyrin type obtained from the hydrolysis of glycyrrhizic acid, obtained from herb liquorice. This is the first report showing presence of glycyrrhetinic acid in any marine sponge. In the study of anti-inflammatory activity in rats, the ethyl acetate extract of sponge has shown strong anti-inflammatory activity. The glycyrrhetinic acid along with presence of compounds like 5-α-Cholestan-3-β-ol, Dihydrocholesterol, cholesterol, 3-β, 6-α Dihydroxy -5-α-cholan-24-oic acid methyl ester might be responsible for the activity which can be further confirmed by bioassay guided fractionation in vitro assay (Kumar et al., 2014).

**Immunosuppressive activity**

In one of the studies by Purushottama et al. (2009) three crude extracts of *Halichondria panicea* had shown immunostimulative effects at lower concentrations. However, at higher concentrations, they exhibited immunosuppressive effects. The investigation of *S. halichondriodes* suggested that methanolic extract derived from the sponge may suppress both humoral and cellular immune responses. The extract not only suppressed nonspecific immune response, but also decreased humoral as well as cell-mediated immunity effectively. In the study, the nature of the compounds causing immunosuppressive activity was not known. However the presences of alkaloids, steroids, terpenoids and flavonoids were detected by preliminary pharmacognosy chemical tests. Later confirming presence of sterol compounds in the extract by LC-MS-MS they were understood to be responsible for the bioactivity (Kumar et al., 2012c; Kumar et al., 2012d).

*Spongiosorites halichondriodes*

A variety of biologically active compounds with unique structures and pharmacological properties have been reported to occur in marine sponges. This review is an attempt to update the marine sponge researchers about bioactive compounds of *Spongiosorites halichondriodes* a predominant marine sponge collected from western coast in Mumbai. This work investigated the antibacterial, antifungal, cytotoxicity anti-inflammatory and immunological properties of *S. halichondriodes*. Antimicrobial studies used Proteus vulgaris, Bacillus subtilis, Staphylococcus aureus, Salmonella typhi, Klebsiella pneumonia, Escherichia coli, Psuedomonas aeruginosa and three pathogenic fungi, Aspergillus flavus, Aspergillus niger and Metarhizium anisopliae for the test. Artemia salina assay was used for checking cytotoxic properties of the extracts before testing it on cell lines. All the extracts showed positive activity in all the three assays. Ethyl acetate extracts demonstrated activity on MDA-MB-435 human breast cell line (Kumar et al., 2012a). The antioxidant and anti-inflammatory effects were also investigated. The anti-inflammatory effect was evaluated by carrageenan induced hind paw edema in rats. Hexane, ethyl acetate and butanol extract from *S. halichondriodes* (100, 200 and 500 mg/kg) and Diclofenac as positive control were studied and ethyl acetate extract reduced hind paw swelling significantly with increasing dose at 200 and 500 mg/kg (Kumar et al., 2014). The present study also mentioned immunomodulatory activity of methanolic extract of marine sponge *S. halichondriodes*. The extract was studied for haemagglutinating antibody titre, delayed-type hypersensitivity response and cyclophosphamide-induced myelo suppression for their immunomodulatory potential. The evaluation of immunomodulatory potential by oral administration of methanolic extract of marine sponge (200 mg/kg) evoked a significant decrease in total WBC count as compared to control, in antibody titre values, and also in delayed type hypersensitivity reaction induced by sheep red blood cells. It also prevented myelo suppression in cyclophosphamide drug treated rats. The extract possessed immunosuppressant activity (Kumar et al., 2012d). Further GC-MS and the fragmentation pattern of active extracts, showed presence of cholesterol and stigma-diene-ol which were the most abundant of 5 compounds identified in the butanol fraction. Octadecadienoic acid (Linoleic acid) and ergostan tetraen-ol and Dihydroxy cholan-24-oic esters prevailed in the same fraction. C29 unsaturated stanols containing a 5α-cholesterol nucleus were found to be present. Identification was based on NIST library search and mass bank, for matching the fragmentation pattern of the unknown compounds (Kumar et al., 2012c). The composition of ethyl acetate and butanol extracts were also subjected to LC-MS/MS identifying C29-C38 saturated and unsaturated esters like 3β, 4β, 7α, 12α-tetrahydroxy-5β-cholan-24-oic acid methyl ester, 7α, 12α-dihydroxy-5β-cholan24-oic acid methyl ester, novel Isocoumarin citrinolactone A, a triterpenid glycyrrhetinic acid as well as other unknown compounds in this species such as nucleoside inosine was identified. Other compound identified was 3β, 6β, 7α-trihydroxy-5β-cholan-24-oic acid methyl ester (Kumar et al., 2013). All the sterol ester derivatives are reported here for the first time in *S. halichondriodes*, family Halichondriidae supported by literature reports for the occurrence of 3β-hydroxy sterols considered as a biomarker for this family.

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**References**


Bioactive compounds from marine sponges


