Secondary metabolites from marine microorganisms and therapeutic efficacy: A mini review

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Marine ecosystem, covering over 70% of the Earth's area, is the place for a wide variety of animal and plant species whose number greatly exceeds that of terrestrial ones. Amongst those biodiversity, microbial world represents a potential research object to be explored as the recent investigations on marine microbes have given the impact to the entire world as a source of bioactive metabolites producers. Since years, there are signals of decreased interest in the search of new metabolites from traditional sources such as macro-algae and octo-corals, and the number of annual reports on marine sponges stabilized. Moreover, bioactive compounds from marine flora and fauna have been used extensively since years in the treatment of many severe diseases and serve as compounds of interest both in their natural form and as templates for synthetic modification. Marine sources are efficient producers of new secondary metabolites that show a range of biological activities including antibacterial, antifungal, anticancer, antitumor, cytotoxic, cytostatic, anti-inflammatory, anti-parasitic, anti-malaria, antiviral, antioxidant and anti-angiogenesis, etc. The present review gives an overview of the current research trends, chemistry of secondary metabolites from marine isolates and their possible roles in various efficient biological activities.

Keywords: Bioactive products, Secondary metabolites, Marine source

Introduction

The development of secondary metabolites from marine resources has been a subject of intense research due to their immense bioactive nature. There is an attractive demand and huge attention for developing new sources of bioactive natural products, able to control or suppress new illnesses. The marine ecosystem turned out to be an attractive field, focusing on the isolation of new secondary metabolites from marine organisms. The marine environment is rich source of both biological and chemical diversity which has become a major source of the production of secondary metabolites with their potential utilization in industrial products development. Several molecules isolated from various marine organisms (microorganisms, algae, fungi, invertebrates, and vertebrates) are currently under study at an advanced stage of clinical trials, some of them have already been marketed as drugs. Most of the marine sources produce extremely difficult compounds as toxins, appeared to be protein mixtures or highly polar compounds with very complex chemical structures. Thus, the interest moved rapidly from large toxin molecules to bioactive secondary metabolites that could be used as health supplements in daily human life.

The search for new bioactive agents from marine organisms has been resulted in the isolation of more than 10000 marine secondary metabolites. The reason behind this motivation could be the appearance of growing numbers of drug-resistant pathogens and serious infectious disease caused by them and more critical upcoming disorders. The terrestrial resources have been greatly explored; hence, researchers and industries are striving greatly to get lead molecules from marine resources. A broad range of biological and therapeutic efficacy has been detected for marine resources including antibiotics, antifungal, toxic, cytotoxic, neurotoxic, antimitotic, antiviral and antineoplastic activities. Nowadays, new targets have been added for the advance screening of marine resources and marine-based secondary metabolites such as AIDS, immunosuppression, anti-inflammation, Alzheimer disease, ageing processes and some tropical diseases.
Although marine resources have been limited to date, selected researches on biologically active compounds from marine flora and fauna have been published. This report summarizes the major sources for bioactive compounds of marine microorganisms. Finally, new approaches for the screening of metabolites from marine resources will be discussed. The goal of this article is to explore the overall information on bioactive secondary metabolites of marine sources and mechanisms of action of marine substances to bring new approach for handling the major public health problems.

**Features of marine ecosystem environment and their relevance to secondary metabolites**

Associations and interactions between micro- and macro-organisms are prominent features of marine ecosystem. However, the biological nature of these associations for specific organisms such as classified sponges has never been seriously investigated and defined which may involve symbiotic, specific and permanently associated organisms but not symbiotic or merely commensally presented microorganisms. With regard to secondary metabolism, these life forms are enormously productive and pose fascinating ecological questions and their investigation is being important due to the effective potential of marine natural products as drugs. A principally important hypothesis is that marine secondary metabolites are produced by invertebrate-associated bacteria and fungi. Whereas it seems most unlikely that fungi contribute directly to the biosynthesis of natural products found in marine animals and plants, few specific bacteria may also be involved.

Marine environment with its unique properties is considered significant for marine biotechnology due to following important reasons such as: i) a good adaptation of ecosystem that helps in development of novel genes and, ii) biotechnological production processes which are influenced by the special adaptations of organisms to their environment. Although some physical factors may influence the output of marine sources such as salinity, pH, low water potential, and high concentrations of sodium ions. While low temperature, oligotrophic nutrient conditions and high hydrostatic pressure are being unique parameters to the deep-sea environment. Literature survey shows that marine-derived fungi have been recognized as one of the tapped sources for the development of new biologically active secondary metabolites including anti-tumor, antibacterial, antiviral, antifungal, anti-inflammatory and anticancer activities and enzyme inhibitory compounds.

**History of marine natural products/secondary metabolites discovery**

Marine life forms are important sources of structurally diverse and biologically active secondary metabolites, several of which have inspired the development of new classes of therapeutic agents. These successful outputs have supported to overcome difficulties inherent to natural products-derived drugs, such as adequate sourcing of the agent and structural complexity related issues. Discovery on marine natural products during ancient days focused on the most conspicuous and easily collected organisms. In fact, before the exploration of the marine world, terrestrial world was the major source of secondary metabolite production due to access inability of marine life beyond the intertidal. Later on, marine natural products discovery had become an established sub-discipline of natural products chemistry and thousands of marine based compounds were described. Extensive work efforts provided by lead organizations or institutes on diverse classes of marine organisms resulted in their fairly well characterized major secondary metabolites, and more often known compounds or their closely relative sub-derivatives were being investigated.

Hence, attention was made onto smaller creatures that had previously escaped collection and examination, such as marine cyanobacteria, marine fungi, and diverse other groups of marine eubacteria. This emphasized a great reward on marine microorganisms with a wealth of new natural products chemistry, as well as the realization that many compounds previously isolated from marine macroorganisms such as sponges and tunicates, are actually metabolic products of associated microbes. This has resulted in the emergence of number of groups around the world who have sought to culture marine bacteria from various sources, including shallow and deep water sediments, animate as well as inanimate surfaces, and from within the tissues of other macroorganisms.

**Secondary metabolite production by marine microorganisms**

An essential aspect of marine originated microorganisms is their ability to produce secondary
metabolites. The Marine organisms are known as efficient producers of bioactive secondary metabolites or compounds\textsuperscript{13}. A large number of biologically active compounds have been isolated from marine environment, which have shown great ability to be used as cosmeceuticals as well as working as bioactive agents against skin diseases\textsuperscript{13, 14}. The natural products from marine secondary metabolism have also been well documented as a source of anticancer compounds, resulting from sponge-microbe symbiotic association\textsuperscript{15}, gorgonian\textsuperscript{16}, and actinomycetes\textsuperscript{17}.

In deep marine world, there are various types of bacteria, fungi, sponges, actinomycetes, cyanobacteria and algae those produce biologically active secondary metabolites\textsuperscript{17}. The discovery and development of marine bioactive compounds may be considered relatively a new platform when compared the discovery of bioactive compounds from terrestrial sources. A list of some important secondary metabolites produced by marine microbes has been summarized in Table 1.

**Secondary metabolites produced by bacteria:**

The marine microscopic communities play a major role for the changes in the distribution of certain chemical elements in ocean\textsuperscript{18}. The autonomous nature of the marine organisms to produce biologically active substances that possibly accumulate, modify, capture and use toxins of other organisms, is a confirmation of this phenomena\textsuperscript{19}. Recent researches conducted on bacteria associated with seaweed surface confirmed that some bacteria of *Firmicutes*, *Proteobacteria* and *Actinobacteria* species produce biological active compounds such as halobacillin and mixirin capable of inhibiting the growth of HCT-116 colorectal cancer cells\textsuperscript{20}. In addition, it has been also reported that the bacteria belonging to *Microbulbifer thermotolerans*, and *Pseudoalteromonas* sp, were capable of producing biofilms and produce chemical compounds, protect them from the other protozoa\textsuperscript{18}. Bacteria belonging to marine origin have always been found to produce antibacterial and anticancer compounds, resulting in the stability of ecology of diverse marine ecosystem\textsuperscript{18}. The interrelations between the ambiences epiphytic microorganism may result in the inhibition of pathogenic and competitor organisms\textsuperscript{18}. Some of the marine *Bacillus* species have been found to possess chemical compounds

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including lipopeptides, polypeptides, macrolactones, fatty acids, polyketides, lipoamides and isocoumarinis with anticancer activity. Although this type of bacteria can grow in almost any substrate, it is possible to suggest that this species seems to have ability to synthesize compounds capable of inhibiting HCT-116 colorectal cancer cells.

Marine Bacillus isolates produce structurally diverse classes of secondary metabolites, such as lipopeptides, polypeptides, macrolactones, fatty acids, polyketides, lipoamides, and isocoumarinis. Structures of important secondary metabolites isolated from marine bacteria such as 4-hydroxy-bensaldehyde and 2-n-pentyl-4-quinolinol are shown in Fig. 1. These structurally versatile compounds exhibit a wide range of biological activities, such as antimicrobial, anticaner, antialgal, and anti-peronosporomycetal. Marine based Bacillus strains might be useful as effective biocontrol agents against various phytopathogens as they rapidly grow in liquid media even under stressful conditions and readily form resistant spores. Hence, knowledge on diversity of marine microflora including actinobacteria, cyanobacteria and all other eubacteria may be detailed enough to allow some understanding of the patterns of natural products chemistry.

Secondary metabolites produced from actinomycetes/actinobacteria:

The best source of secondary metabolite producers of marine bacteria is the single genus of Streptomyces which provides vast majority of these compounds, distributed widely in the marine and terrestrial habitats. Actinobacteria which are the prolific producers of antibiotics and important suppliers to the pharmaceutical industry can produce a wide variety of secondary metabolites. The members of actinomycetaceae family are well known for their ability to produce secondary metabolites many of which are active against pathogenic microorganisms. Actinobacteria genus includes Streptomyces, Actinomyes, Arthrobacter, Corynebacterium, Frankia, Micrococcus, and Micromonospora etc. Secondary metabolites produced by the marine actinobacteria possess a wide range of biological efficacy and have been widely studied for antimicrobial activity. One of the marine bacterial strain Verruco sispora has been found to produce a novel polycyclic polyketide antibiotic abyssomicin C (Fig. 2). Abyssomicin C is considered to be a potent inhibitor of para-amino benzoic acid biosynthesis, resulting, therefore, in the inhibition of folic acid biosynthesis at an earlier stage as compared to chemical and synthetic sulfa drugs. In addition, essramycin is known to be a novel triazolo pyrimidine antibiotic which has been isolated from Streptomyces species. This molecule has been found to exert minimum inhibitory concentration value in the range of 2 to 8 µg/ml against both Gram-positive and Gram-negative bacteria. Another antibiotic called chinikomycin A has also been isolated from Streptomyces species which has been found to exhibit antitumor activity against different human cancer cell lines. However, chinikomycin A did not show the potent efficacy as antiviral, antimicrobial and phytotoxic agents.

Since the marine environmental conditions are extremely different from that of the terrestrial ones, marine microbes have more diversity in their characteristics which may lead in the production of entirely different and new bioactive compounds in their challenging living conditions. As reported previously, marine Streptomyces candidates have been found to produce well-known chemically diversified antibiotics which have also been isolated from terrestrial streptomycetes, as in the case of marine Micromonospora candidates. In this regards, newly identified marine members of a rare genus Verrucosispora seem to be a promising source for the production of novel bioactive secondary metabolites, as confirmed by the production of novel drug...
abyssomicin from a marine actinomycetes strain AB-18-032. These marine actinomycetes produce different types of new secondary metabolites with diverse range of biological activities, which can serve in future as potent therapeutic agents. The profile of marine actinomycetes is underexploited source for the discovery of novel types of secondary metabolites.

**Secondary metabolites produced from cyanobacteria:**

Marine cyanobacteria are the rich sources of complex bioactive secondary metabolites which derive from mixed biosynthetic pathways. Recently, natural products from several marine cyanobacteria have attracted huge attention due to their intriguing structures and exciting anti-proliferative or cancer cell toxic activities. Several important classes of marine cyanobacteria have been identified which showed toxicity against different cancer cell lines in the last few years, specifically belonging the genera *Lyngbya* or *Leptolyngbya*. A number of secondary metabolites from marine life have shown potent and mechanistically intriguing anti-inflammatory activity, and marine cyanobacteria have contributed to this recognition which includes potent anti-inflammatory bis-bromoindole agents from *Rivularia* species. Recently, a nitric oxide (NO) inhibition assay was used to screen marine cyanobacterial metabolites, and it was disclosed that several malyngamides were quite potent inhibitors in a mouse RAW macrophage cell line, especially those belonging to F series. Additionally, a few important secondary metabolites such as bisebromoamide and largazone have also been found to have potent anti-inflammatory activity (Fig. 3). Since cyanobacteria continue to be explored and their metabolites evaluated in an expanding number of biological measurements including neurosciences and inflammation, they are becoming exceptional sources for the development of lead compounds for drug discovery efforts.

![Fig. 2-Chemical structures of secondary metabolites from marine actinomycetes](image1)

![Fig. 3-Chemical structures of secondary metabolites from marine cyanobacteria](image2)

**Secondary metabolites produced from fungi:**

Marine fungi have been shown to be tremendous sources for new and biologically active secondary metabolites which are reflected by the increasing number of published literature dealing with compounds from variety of marine fungi. As a result of these consequences, number of secondary metabolites from marine-based fungi have been reported and described well. Although there is a huge diversity in the marine fungal species growing well aquatic environment, mainly these can be grouped into obligate and facultative marine fungi. A definition outlined by Kohlmeyer (1974), obligate marine fungi are those that grow and sporulate exclusively in a marine or estuarine habitat whereas facultative marine fungi belong to fresh water community or terrestrial areas and are also able to grow in the natural marine environment. Elessek et al. (2008) analyzed influence of polymeric 3-alkylpyridinium salts from the marine sponge *Reniera sarai* on the growth of algae and wood decay fungi. Furthermore, several marine-derived fungi produce organometallic compounds such as marine fungus *Fusarium* sp. produced a novel sesterterpene neomangicol. Lin et al. (2005) isolated a new compound diaporthelactone which showed cytotoxic activity against Raji cell lines. Fig. 4 shows the chemical structures of selected important biologically active secondary metabolites such as cladospolide E and 6-oxo-de-O-methyllasiodiplodin, isolated from marine algal resources.
Xiong et al. (2009) recently studied the bioactive potential of marine Cladosporium sp. in nutrient enriched cultivation media and reported number of compounds including methanephrine; cis-1-chloro-9-octadecene; 16-nitro bicyclo hexadecane-1-ol-13-one; 13-bromotetradecanoic acid; 2-phenazinol, 6-amino-; morphinan-2,4-diol-6-one, N-formyl-; and pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-3(phenylmethyl) with antibacterial activity against different bacterial species including Bacillus sp., Vibrio sp. and Micrococcus sp. in the presence of glucose or xylose. Another compound, cladospolide E, characterized as a nine-membered lactone, was isolated from the culture broth of the same fungus and was found to have weak antibacterial activity against E. coli, B. thuringiensis, B. subtilis, Mycobacterium smegmatis and S. aureus. Although plethora of studies on marine fungal metabolites have been done, here we discussed a brief on the bioactive compounds isolated from marine derived fungi and their possible roles in various efficient biological activities.

Secondary metabolites produced from sponges:
A successful marine discovery revealed a third marine anticancer agent, a polyether metabolite halichondrin A from the sponge Halichondria okadai. The halichondrin A was subsequently shown to possess exquisite cancer cell toxicity through an antitubulin mechanism, and more importantly, it has a new mechanism of action by binding near the vinca site on β-tubulin however showed different biochemical effects, including microtubule dynamics, as compared with other agents. Sponges have been considered as a gold mine for the chemists working on marine related secondary metabolite production. As per the literature survey, more than 12,000 compounds have been isolated from marine sources with hundreds of new compounds still being discovered every year. Due to vast diversity of marine organisms along with their diverse metabolisms, investigating efforts are being made in order to acquire compounds of interest synthetically. Marine sponges are rich sources of biologically active secondary metabolites with novel chemical structures, as confirmed by the evaluation of eighty four anti-inflammatory compounds isolated from marine sponges. Recently Serrati, et al. (2008) reported TGF betal antagonistic peptides isolated from marine sponge which inhibited TGF betal dependent angiogenesis. Previously, a number of researchers studied bioactive brominated metabolites from the red sea sponge Suberea mollis. Sponges produce a wide array of secondary metabolites ranging from derivatives of amino acids and nucleosides to macrolides, porphyrins, terpenoids, aliphatic cyclic peroxides and sterols. Pharmacologically important phytochemicals mainly originated from marine sponge have been reported to show inhibition of HIV by two bis-quinolizidine alkaloids petrosins isolated from the Indian marine sponge Petrosia similis. Bugni et al. (2004) and Lu, et al. (2007) investigated a series of kalihinols, diterpenes isolated from the Philippine marine sponge Acanthella cavernosa, as potential bacterial folate biosynthesis inhibitors. In addition, Han (2009) studied characterization of antifungal chitinase from Streptomycyes sp. DAI associated with South China Sea sponge Craniella australiensis. Marine sponges have been excellent sources for natural products that are biologically active which include the enzyme inhibitors, cell division-inhibitors, anti-viral, antifungal, antimicrobial, anti-inflammatory, anti-tumour, cytotoxic or cardiovascular properties. Several brominated natural products and other amino acid derivatives are present in complex structures such as cyclic peptides, polymere alkylpyridinium, sesquiterpene, quinones, onamides, mycalamides.
nucleotides to macrolides, porphyrins, terpenoids to aliphatic cyclic peroxides and sterols including some other important cytotoxic secondary metabolite.

Sladic and Gasic (2006) studied reactivity and biological activity of the marine sesquiterpene hydroquinone avarol and related compounds separated from the dictyoptera order of different sponges. Initially, so far, more than 3,700 new natural products have been separated from these groups. Nakao et al. (2004) reported the isolation of renieramycin-A was the new compound from the Japanese sponge Neopetrosia sp. which mainly inhibited recombinant Leishmania amazonensis proliferation in a dose-dependent manner, while showing cytotoxicity at ten-time higher concentration. Isolation of new anticancer agents derived from marine sources has been based on the collection of marine microorganisms of sponges with various types of extracts. Rashid et al. (2002) identified the pellynol-I, a new cytotoxic polyacetylene from the sponge Pellina species. Hirano et al. (2000) described pyrinodemins B-D, and potent cytotoxic bis-pyridine alkaloids from marine sponge Amphimedon sp. The occurrence of terpenes is not nearly as common and comprises well-known structural types, as well as rare structural skeletons. Chemical structures of some of the selected secondary metabolites from marine sponges Aplidium meridianum and Dragmacidin sp. are shown in Fig. 5.

Secondary metabolites produced from algae:
The marine environment, which contains a vast array of organisms with unique biological properties, is one of the most underutilized biological resources. To date, algae and micro-algae are referenced in the literature as sources of bioactive compounds for use as functional food ingredients. A number of algal species have been exploited, however others like the genus Sargassum and Codium have been considered to be invasive for their capacity of adaptation and their high growth rate. Due to the fact that marine algae are potential sources of new drugs, their studies have become a priority on the isolation of potentially effective marine secondary metabolites of therapeutic uses. The chemical screening of all marine seaweeds and their related organisms is necessary in order to establish which species can be exploited without consequences and those that must be protected. In addition, some of the algal species are well known reservoirs for carotenoids like compounds. For example, the micro-alga Dunaliella salina is able to accumulate large amount of b-carotene when cultivated under certain conditions. Chemical structures of some of the selected pholorotannins such as fucofuroeckol, dioxinodehydroeckol, phloroglucinol and 7-phloroeckol as secondary metabolites from marine algae are shown in Fig. 6. Several other carotenoids may present in more typical forms in these organisms such as fucoxanthin or
astaxanthin, however, fucoxanthin is the main pigment found in brown algae. In the year 2010, it was found in Mexico that marine algal species such as Codium fragile, Sargassum muticum, Endarachne binghamiae, Centroceras clavulatum and Laurencia pacifica possessed compounds such as palmitic acid that inhibited the growth of some selected Gram-negative bacteria including Proteus mirabilis, a major cause of infections. The red seaweed Laurencia (Ceramiales, Rhodomelaceae) is one of the most prolific algae in the production of secondary metabolites derived from the sea. Sesquiterpenes, diterpenes, triterpenes and acetogenins (characterized by the presence of halogens atoms in their chemical structures) have been found to present in red seaweed.

Conclusion
An increasing number of marine natural products are of interest as potential drugs. Apart from chemical and ecological reasons, it is thus of major importance for the evaluation of the pharmacological potential of marine natural products in order to confirm their efficacy as the best producers of beneficial compounds, possibly followed by cloning of the biosynthetic genes and biotechnological production. Despite of the fact that a wide range of antibacterial, antifungal and other biologically active agents have been found to be clinically significant, the development of marine microbes derived antibiotics is still in its juvenile stage. In conclusion, microbial symbionts or parasites of marine macro- and microorganisms remain a difficult area of study in the realm of marine natural products.

References
27 Berdy J, Bioactive microbial metabolites. J. Antibiot.,


