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Review on Marine Sponge: Derived Natural Products and formulations

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ABSTRACT

Sponges are the rich sources of bioactive natural products from marine habitats. Since many sponges harbor diverse bacterial communities, it has long been suspected that many sponge-derived compounds are of microbial origin. The present review gives a comprehensive overview of the source, taxonomy, country of origin or geographical position, chemical class, and biological activity of sponge-derived new natural products. Also this review aims at describing some of the most highly cited reviews of the last decade on sponge-derived bioactive compounds and the most promising substances extracted and isolated from marine sponges for pharmaceutical applications. Preset study gives new developments in the field of marine sponge metabolite research and important findings for bioactive compounds from in vitro, in vivo and clinical studies for therapeutic drug applications.

Keywords: Marine drug, Sponges**,** phylum Porifera**.**

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INTRODUCTION

Sponges are the ancient, efficient designed multicellular parazoan organisms and show relatively little differentiation and tissue coordination. A sponge is a sessile, sedentary, filter-feeding primitive aquatic invertebrate animal which attaches itself to solid surfaces from intertidal zone to depths of 29,000 ft (85000m) or more, where they can get sufficient food to grow.[1] Marine sponges represent a significant component of benthic communities throughout the world, in terms of both biomass and their potential to influence benthic or pelagic processes. Sponges (phylum Porifera) are among the oldest of the multicellular animals (Metazoa) and possess relatively little in the way of differentiation and coordination of tissues.[2] Sponges are among the richest sources of bioactive natural products from marine habitats.[3]

Sponges have been the focus of much recent interest due to the following two main (and often interrelated) factors: (i) they form close associations with a wide variety of microorganisms and (ii) they are a rich source of biologically active secondary metabolites. This increasing research interest has greatly improved our knowledge of sponge-microbe interactions, and yet, as apparent throughout this article, many gaps remain in our knowledge of these enigmatic associations. For example, we still lack a clear picture of microbial diversity and the factors which influence it in these hosts. Similarly, the physiology of most sponge associated microorganisms remains unclear, as do many fundamental aspects of sponge symbiont ecology. (Throughout this article, the terms "symbiont" and "symbiosis" are used in their loosest possible definitions, to refer simply to two [or more] different organisms that live together over a long period.[2]

Sponges feed on microscopic organisms (protozoa, bacteria and other small organisms in water) and organic particles. There are about 10,000 known species inhabit a wide variety of marine and fresh water habitats and are found throughout deep ocean depths to rock pools, warm tropical seas to frozen arctic seas, rivers and streams. They are very diverse and occur in various colors, sizes and shapes such as tubular (tube-like), globular (ball-shaped), caliculate (cup-shaped), arbores cent (plant-shaped), flabellate (fan-shaped) and amorphous (shapeless). The scientific term for sponges is Porifera meaning "pore-bearing" and has bodies full of pores and channels allowing water to circulate through them, consisting of jelly-like mesohyl sandwiched between two layers of cells.[1] despite a simple body plan, are remarkably efficient at obtaining food from the surrounding water.[2] The more than 6,000 described species of sponges inhabit a wide variety of marine and freshwater (somewhat more restricted) systems and are found throughout tropical, temperate, and Polar Regions. [2] The shapes of their bodies are adapted for maximal efficiency of water flow through the

central cavity, where it deposits the nutrients, and leaves through a hole called the osculum. Several sponges have spicules of silicon dioxide or calcium carbonate and a mesh of proteins called spongin as an internal skeleton.[1]

One of the remarkable properties of sponges is their ability to suffer damage and regenerative capacity. Marine sponges have attracted growing attention as a source of overwhelming structurally diverse secondary metabolites with potential biological activities and were placed at the top with respect to discovery of biologically active chemical constituents. [1] Marine invertebrate produce a plethora of bioactive compounds, which serve as inspiration for marine biotechnology, particularly in drug discovery programs and biomaterials development.[8] Although thousands of chemical compounds have been reported in the literature from these sponges, only few of them are clinically described. Many studies revealed that sponge-derived metabolites are used directly in therapy or as a prototype of bioactive leads to develop more active and less toxic analogs. Sponges are most primitive type of aquatic animals in existence which are dominating many benthic habitats, featuring a cell-based organization where different cells conduct all forms of bodily function, but do not form tissues. They consume food and excrete waste products within cells without a body cavity .[1]

Many research groups are working to find new possible anti-inflammatory molecules, and marine sponges represent a rich source of biologically active compounds with pharmacological applications Several ecological studies reported that high quantity of bioactive constituents.[9] Produced by sponges often serve defensive against environmental threats such as predation, microbial infection, competition for space or overgrowth by fouling organisms. For this reason, marine sponges are the subject of attraction for chemists due to the sheer number of metabolites produced, the novelty of structure encountered, and the therapeutic potential of these compounds in the treatment of human diseases. Scientists working in the field of natural product chemistry and research suggest that these sponges have promising potential to provide future drugs which can serve various diseases. In this chapter, we describe main isolated chemical entities from sponges and their pharmacological application.[1]

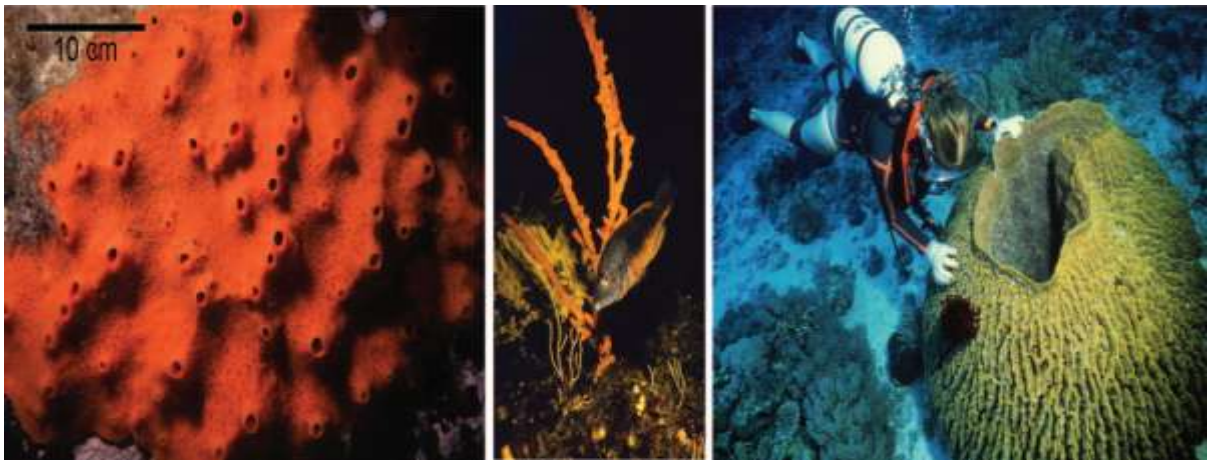

Figure 1: Different species of Sponge

1] Jorn Piel et.al : In this literature since many sponges harbor diverse bacterial communities, it has long been suspected that many sponge-derived compounds are of microbial origin. For a diverse range of complex polyketides, ribosomally modified peptides, and nonribosomal peptides from the sponge *Theonella swinhoei*, "Entotheonella" bacteria were identified as source using metagenomic and single-bacterial analysis. "Entotheonella" belong to a new, uncultivated candidate phylum termed "Tectomicrobia" and exhibit a rich and variable specialized metabolism involving unusual biosynthetic steps. Functional characterization of enzymes suggests that "Entotheonella" spp. offer interesting biotechnological opportunities in addition to their high drug discovery potential. The talk presents methods to study "Entotheonella" and provides insights into the function of these bacteria in various sponges. In addition, biosynthetic studies on selected sponge natural products are discussed, as well as practical implications for the generation of sustainable production systems.[4]

2) **Johan Garderes et.al:** An overview on the diversity of 39 lectins from the phylum Porifera is presented, including 38 lectins, which were identified from the class of demosponges, and one lectin from the class of hexactinellida. Their purification from crude extracts was mainly performed by using affinity chromatography and gel filtration techniques. Other protocols were also developed in order to collect and study sponge lectins, including screening of sponge genomes and expression in heterologous bacterial systems. The characterization of the lectins was performed by Edman degradation or mass spectrometry. Regarding their physiological roles, sponge lectins showed to be involved in morphogenesis and cell interaction, biomineralization and spiculogenesis, as well as host defense mechanisms and potentially in the association between the sponge and its microorganisms. In addition, these lectins exhibited a broad range of bioactivities, including modulation of inflammatory response, antimicrobial and cytotoxic activities, as well as

anticancer and neuromodulatory activity. In view of their potential pharmacological applications, sponge lectins constitute promising molecules of biotechnological interest.[5]

3) **Cinzia Calcabrini et al:** Despite the huge investment into research and the significant effort and advances made in the search for new anticancer drugs in recent decades, cancer cure and treatment continue to be a formidable challenge. Many sources, including plants, animals, and minerals, have been explored in the oncological field because of the possibility of identifying novel molecular therapeutics. Marine sponges are a prolific source of secondary metabolites, a number of which showed intriguing tumor chemopreventive and chemotherapeutic properties. Recently, Food and Drug Administration-approved drugs derived from marine sponges have been shown to reduce metastatic breast cancer, malignant lymphoma, and Hodgkin's disease. The chemopreventive and potential anticancer activity of marine sponge-derived compounds could be explained by multiple cellular and molecular mechanisms, including DNA protection, cell-cycle modulation, apoptosis, and anti-inflammatory activities as well as their ability to chemosensitize cancer cells to traditional antiblastic chemotherapy. The present article aims to depict the multiple mechanisms involved in the chemopreventive and therapeutic effects of marine sponges and critically explore the limitations and challenges associated with the development of marine sponge-based anticancer strategy.[6]

4) **Ana Zovko et al :** In this work two acetylene alcohols, compound 1 and compound 2, which were isolated and identified from the sponge *Cribrochalina vasculum*, and which showed antitumor effects were further studied with respect to targets and action mechanisms. Gene expression analyses suggested insulin like growth factor receptor (IGF-1R) signaling to be instrumental in controlling anti-tumor efficacy of these compounds in non-small cell lung cancer (NSCLC). Indeed compounds 1 and 2 inhibited phosphorylation of IGF-1Rβ as well as reduced its target signaling molecules IRS-1 and PDK1 allowing inhibition of pro-survival signaling. *In silico* docking indicated that compound 1 binds to the kinase domain of IGF-1R at the same binding site as the well known tyrosine kinase inhibitor AG1024. Indeed, cellular thermal shift assay (CETSA) confirmed that *C. vasculum* compound 1 binds to IGF-1R but not to the membrane localized tyrosine kinase receptor EGFR. Importantly, we demonstrate that compound 1 causes IGF-1Rβ but not Insulin Receptor degradation specifically in tumor cells with no effects seen in normal diploid fibroblasts. Thus, these compounds hold potential as novel therapeutic agents targeting IGF-1R signaling for anti-tumor treatment.[7]

5) Wei Wang et al: Recently, the studies on the antiviral activities of marine natural products, especially marine polysaccharides. Marine-derived polysaccharides and their lower molecular

weight oligosaccharide derivatives have been shown to possess a variety of antiviral activities. This paper will review the recent progress in research on the antiviral activities and the mechanisms of these polysaccharides obtained from marine organisms. In particular, it will provide an update on the antiviral actions of the sulfated polysaccharides derived from marine algae including carrageenans, alginates, and fucans, relating to their structure features and the structure–activity relationships. In addition, the recent findings on the different mechanisms of antiviral actions of marine polysaccharides and their potential for therapeutic application will also be summarized.[8]

6) **Clara Grosso et al:** This review aims to summarize the potential of drugs derived from marine invertebrates in the field of neuroscience. Their role in neuroscience research and development of new therapies targeting the central nervous system will be addressed, with particular focus on neuroinflammation and neurodegeneration. In addition, the neuronal growth promoted by marine drugs, as well as the recent advances in neural tissue engineering, will be highlighted.[9]

7) **Susan Costantini et al**: In the present study, we tested different concentrations of the methanol extract from the marine sponge, *Geodia cydonium*, on normal human breast epithelial cells (MCF-10A) and human breast cancer cells (MCF-7). Their results show that this extract has no cytotoxic effects on both cell lines whereas it induces a decrease in levels of VEGF and five proinflammatory cytokines (CCL2, CXCL8, CXCL10, IFN-γ, and TNF-α) only in MCF-7 cells in a dosedependent manner, thereby indicating an anti-inflammatory effect. Moreover, interactomic analysis suggests that all six cytokines are involved in a network and are connected with someHUB nodes such asNF-kB subunits and ESR1 (estrogen receptor 1). They also report a decrease in the expression of two NFKB1 and c-Rel subunits by RT-qPCR experiments only in MCF-7 cells after extract treatment, confirming NF-kB inactivation. These data highlight the potential of *G. cydonium* for future drug discovery against major diseases, such as breast cancer.[10]

8) **Tatiana da Rosa Guimarães et al:** The *n*-butanol fraction (BF) obtained from the crude extract of the marine sponge *Petromica citrina*, the halistanol-enriched fraction (TSH fraction), and the isolated compounds halistanol sulfate (**1**) and halistanol sulfate C (**2**), were evaluated for their inhibitory effects on the replication of the Herpes Simplex Virus type 1 (HSV-1, KOSstrain) by the viral plaque number reduction assay. The TSH fraction was the most effective against HSV-1 replication (SI = 15.33), whereas compounds **1** (SI = 2.46) and **2** (SI = 1.95) were less active. The most active fraction and these compounds were also assayed to determine the viral multiplication step(s) upon which they act as well as their potential synergistic effects. The anti-HSV-1 activity detected was mediated by the inhibition of virus attachment and by the penetration into Vero cells,

the virucidal effect on virus particles, and by the impairment in levels of ICP27 and gD proteins of HSV-1. In summary, these results suggest that the anti-HSV-1 activity of TSH fraction detected is possibly related to the synergic effects of compounds **1** and **2**.[11]

9) Cherie A. Motti: Eight naturally occurring marine-sponge derived sesquiterpenoid quinones were evaluated as potential inhibitors of pyruvate phosphate dikinase (PPDK), a C4 plant regulatory enzyme. Of these, the hydroxyquinones ilimaquinone, ethylsmenoquinone and smenoquinone inhibited PPDK activity with IC50's (reported with 95% confidence intervals) of 285.4 (256.4 – 317.7), 316.2 (279.2 – 358.1) and 556.0 (505.9 – 611.0) μM, respectively, as well as being phytotoxic to the C4 plant *Digitaria ciliaris*. The potential anti-inflammatory activity of these compounds, using bee venom phospholipase A2 (PLA2), was also evaluated. Ethylsmenoquinone, smenospongiarine, smenospongidine and ilimaquinone inhibited PLA2 activity (% inhibition of 73.2 + 4.8 at 269 μM, 61.5 + 6.1 at 242 μM, 41.0 + 0.6 at 224 μM and 36.4 + 8.2 at 279 μM, respectively). SAR analyses indicate that a hydroxyquinone functionality and a short, hydroxide/alkoxide side-chain at C-20 is preferred for inhibition of PPDK activity, and that a larger amine side-chain at C- 20 is tolerated for PLA2 inhibitory activity.[12]

10) **Edwin L. Cooper:** According to Wallace, despite recent developments in combinatorial chemistry that can rapidly generate thousands of new chemicals, the pharmaceutical industry still relies heavily on a staggering array of undiscovered possibilities from the natural environment. These could lead to the discovery of novel compounds that will surely extend the boundaries of their chemical research efforts. The terrestrial environment has been mined for compounds for many years. 13

11) **Muhammad Saleem et al:** In this review, seven compounds of unusual structures are reported. Among them, myrothenone A (**102**) showed enzyme tyrosinase inhibiting properties, and was found to be more potent than kojic acid. Some metabolites exhibit cytotoxic activity aswell. In some cases, it is extremely difficult to provide sufficient amounts of active substances from fungi due to their limited levels of biosynthesis. The limited quantity might be due to the rare occurrence of the such organisms themselves, or geographic, seasonal or sexual variations may affect the amount and nature of produced secondary metabolites. On the other hand, the structural complexity in most of the interesting bioactive substances precluded the development of commercially viable syntheses. Cases of direct isolation of target compounds from bacterial or fungal symbionts of invertebrates are rare. Although fermentation of microorganisms is a possible way, it does not apply to metabolites produced strictly by macro organisms. Research on marine

fungi and use of biotransformation and biotechnological methods may help to obtain potent candidates for the treatment of diseases.[14]

12) **Ana Martins at el:** The aim of this review is to outline the paths of marine natural products discovery and development, with a special focus on the compounds that successfully reached the market and particularly looking at the approaches tackled by the pharmaceutical and cosmetic companies that succeeded in marketing those products. The main challenges faced during marine bioactives discovery and development programs were analyzed and grouped in three categories: biodiversity (accessibility to marine resources and efficient screening), supply and technical (sustainable production of the bioactives and knowledge of the mechanism of action) and market (processes, costs, partnerships and marketing). Tips to surpass these challenges are given in order to improve the market entry success rates of highly promising marine bioactives in the current pipelines, highlighting what can be learned from the successful and unsuccessful stories.[15]

13) **O. Kayser et al:** Natural products are not only the basis for traditional or ethnic medicine. Only recently, they have provided highly successful new drugs such as Artemisinin. Furthermore, screening natural products found in all sorts of environments such as the deep sea, rain forests and hot springs, and produced by all sorts of organisms ranging from bacteria, fungi and plants to protozoa, sponges and invertebrates, is a highly competitive field where all of the major pharmaceutical companies are encountered. Already, many new natural product groups have revealed antiparasitic properties of surprising efficacy and selectivity, as will be shown in this review for plant-derived alkaloids, terpenes and phenolics. Many novel lead structures, however, have severe chemico-physical drawbacks such as poor solubility. Here, innovative drug formulations and carrier systems might help, as discussed by the authors in another article of this series.[16]

14) Stamatios Perdicaris et.al : This review aims at describing some of the most highly cited reviews of the last decade on sponge-derived bioactive compounds and the most promising substances extracted and isolated from marine sponges for pharmaceutical applications. The review is covering mainly new developments of the last five years in the field of marine sponge metabolite research and important findings for bioactive compounds from in vitro, in vivo and clinical studies for therapeutic drug applications.[54]

CONCLUSION

Marine sponge (Porifera) is one of the major groups of biological organisms which provide huge number of natural products and secondary metabolites with interesting pharmacological properties

and led in the formation of novel drugs. These natural products possesses vast range of therapeutic application, including antimicrobial, antihypertensive, antioxidant, anticancer, anticoagulant, anti-inflammatory, immune modulator, and wound healing and other medicinal effects. In this chapter we included the most important and biologically active marine sponge-derived compounds and presented selected studies of most important bioactive and promising natural products and secondary metabolites from marine sponges.

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