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Review Article

The Ocean's Treasure Trove: Bioactive Compounds from Sea Sponges

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ABSTRACT

Sea sponges are among the oldest living creatures on Earth that have evolved complex chemical defenses to thrive in the ocean's competitive environment. These marine animals have developed an impressive array of bioactive compounds with therapeutic applications. This article explores bioactive compounds derived from sea sponges, showcasing their remarkable therapeutic potential. The article begins by introducing the fascinating world of sea sponges, highlighting their unique biology and ecology. We then delve into the various bioactive compounds isolated from sea sponges. The review highlights the anticancer properties of sea sponge-derived compounds demonstrating their potential in cancer treatment. We also explore their antimicrobial and anti-inflammatory activities, showcasing their potential in combating infectious diseases and inflammatory disorders. The article further discusses the challenges and opportunities in harnessing the bioactive potential of sea sponges. This review serves as a comprehensive resource for researchers, scientists, and students interested in marine biomedicine and natural product drug discovery.

Keywords: Sea sponges, Bioactive compounds, Therapeutic potential, Anticancer, Anti-inflammatory, Marine biomedicine, Drug discovery.

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INTRODUCTION

The Earth's surface is predominantly covered by oceans, which encompass a vast array of ecosystems that support an incredible 87% of the planet's biodiversity.[1] Research on marine-based substances has led to the discovery of many biologically active compounds with possible medical uses.[2] Scientists have discovered around 30,000 bioactive substances from the ocean. The ocean's unique ecosystem is a rich source of diverse bioactive compounds, with numerous examples already demonstrating therapeutic potential across a range of diseases.[3] The marine-derived compounds are being explored for their potential to create functional foods and dietary supplements. Marine-derived natural products have demonstrated impressive therapeutic potential, exhibiting anti-inflammatory, antimicrobial, and anticancer activities, among others.[4] Marine microorganisms are source of novel pharmaceuticals, aligning with traditional drug discovery models that rely on natural products. Additionally, the scalability of microbial fermentation processes offers a viable solution for meeting the demand for large-scale production of bioactive compounds derived from marine microorganisms.[4] Recent advances in marine biotechnology have revealed that microorganisms from marine environments are a rich source of novel natural products.[1] Microbiomes associated with deep-sea sponges display a distinctive profile, characterized by lower complexity and higher diversity compared to their shallow-water counterparts.[5] Sea sponges are a treasure trove of bioactive compounds, offering promising leads for therapeutic applications. For instance, certain species like *Axinella donnani* and *Clathria compressa* have been found to harbor antibacterial compounds. Others, such as *Aaptos aaptos* and *Dactylospongia metachromia*, contain antiviral compounds.[6,7]

OVERVIEW OF DIFFERENT TYPES OF SEA SPONGE AND BIOACTIVE COMPOUND PRESENT IN THEM

Aplysina aerophoba

The Mediterranean sponge *Aplysina aerophoba* thrives in sunlit environments and attaches itself to stable surfaces like rocks. Its vibrant yellow hue is attributed to the unstable pigment uranidine, which transforms when exposed to air. Interestingly, this sponge harbors a vast array of bacteria and contains high levels of brominated alkaloids, particularly isoxazoline alkaloids. These compounds can be broken down into smaller

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3,5 dibromotyrosin structures, which exhibit antibacterial properties. Research has shown that the isolated brominated metabolites from *Aplysina aerophoba* display moderate to potent cytostatic and antimicrobial activities.[8] Researchers examined the osteogenic potential of a crude acetonic extract derived from the Mediterranean sponge *Aplysina aerophoba*, with a particular emphasis on its prominent bromotyrosine-derived compounds. The research utilized zebrafish larvae as a model to assess mineralization and bone development. The findings identified aerophobin-1 as a promising pro-osteogenic agent, presenting potential applications in regenerative medicine.[9] A thorough examination of the sponge's chemical composition led to the identification of four prominent brominated alkaloids, which were characterized as distinct compounds.[10] It yielded a unique Gram-positive bacterium, which was classified within the Rubrobacter genus following an in-depth examination of its genetic characteristics.[11] Aeroplysinin-1, a natural compound derived from marine sources, has shown exceptional anti-inflammatory and anti-angiogenic effects. Moreover, Aeroplysinin-1 has demonstrated broad-spectrum antimicrobial activity, inhibiting the growth of diverse microorganisms, including fungi, protozoa, and viruses. Additionally, research has indicated that this compound can suppress tumor growth or induce apoptosis in various cell lines, including those of endothelial, monocytic, and cancerous origin.[12] Aeroplysinin-1 exhibits anti-inflammatory properties by modulating endothelial cell responses. Its mechanism involves inhibiting key signaling molecules, ultimately hindering the activation of pro-inflammatory pathways. This discovery opens possibilities for Aeroplysinin-1's potential use in managing cardiovascular diseases. Additionally, Aeroplysinin-1 has been found to exhibit anti-angiogenic properties.[13,14] A team of scientists discovered two new compounds, Microsphaerones A and B, in a fungus that lives inside *Aplysina aerophoba*. The discovery of Microsphaerones A and B is significant, as they represent the first gamma-pyrone derivatives isolated from this fungal genus.[15] Researchers discovered beneficial bacteria in *Aplysina aerophoba*, that produce antimicrobial compounds.[16] A comprehensive study examined how controlled growth conditions influence the bacterial communities associated with *Aplysina aerophoba* sponges. Over six months, sponges were cultivated under varying temperatures, light exposure, and nutrient levels. Using denaturing gradient gel electrophoresis and sequencing, researchers identified a diverse bacterial community spanning five phyla. Despite reduced biomass and compromised morphology, the sponges maintained distinct microbial associations. Notably, a Cyanobacteria strain exhibited adaptive responses to changing light conditions. Moreover, the cultivation period saw an increase in characteristic brominated compounds.[17]

Axinella corrugate

Axinella corrugate species are typically found in exposed deep reef environments. They are native to the Indian and Pacific Oceans. Characteristically, these sponges are relatively small, usually under 20 cm in size, and display vibrant yellow or orange hues. Researchers isolated novel compounds from the marine sponge *Axinella corrugata*, including ester derivatives of a coumarin-based carboxylic acid. Notably, these compounds demonstrated potent inhibitory activity against the SARS-coronavirus.[18,19] A symbiotic fungus associated with it has been found to produce a compound with antibacterial properties.[20] It contains two unique proteins with distinct abilities to bind to red blood cells. One protein strongly binds to cells from various animals, but this binding is blocked by specific sugars. The other protein targets rabbit red blood cells and is inhibited by certain sugars and compounds.[21]

Hyrtios erectus

Hyrtios erectus, a marine sponge, is classified within the phylum Porifera. Specifically, it falls under the class Demospongiae, order Dictyoceratida, and family Thorectidae. This sponge is characterized by its distinctive blackish hue.[22,23] Researchers examined the impact of a *Hyrtios erectus* marine sponge extract on the proliferation and survival of MCF-7 breast cancer cells.[22] Scientists extracted a total of 20 sesterterpenes, 12 of which were novel, from *Hyrtios erectus* found near Chuuk Island. Tests showed that some of these compounds slowed the growth of various cancer cells.[24] Scientists discovered two new scalarane-type sesterterpenes, Hyrtioscalaranes A and B. These compounds showed promising anti-inflammatory and antioxidant properties. After purifying the extract, researchers found that Hyrtioscalaranes A and B targeted a specific enzyme involved in inflammation more selectively than a commonly used anti-inflammatory drug.[25] Scientists analyzed extracts from the marine sponge *Hyrtios erectus* and identified two notable compounds. One was a previously discovered oxysterol, while the other was a new alkyl benzoate derivative. The two key compounds exhibited significant toxicity against human breast cancer cells.[26] Researchers investigated compounds from *Hyrtios erectus* for their ability to combat malaria, specifically targeting a strain of *Plasmodium falciparum* that is resistant to chloroquine. Following extraction with 85% methanol, three compounds - smenotronic acid, ilimaquinone, and pelorol - were isolated and structurally elucidated using advanced spectroscopic methods. *In vitro* evaluations of these compounds against *P. falciparum* revealed promising results, with pelorol demonstrating notable antimalarial activity.[27] Scientists investigated the chemical composition of *Hyrtios erectus*, uncovering a range of distinctive compounds, including 5-hydroxy-1H-indole-3-carboxylic acid methyl ester, hyrtiosulawesine, and the hyrtiosin A and B analogs.[28] Research has shown that hyrtiosal, a compound extracted from the marine sponge *Hyrtios erectus*, possesses anti-HIV properties by blocking the interaction between

HIV-1 integrase and viral DNA.[29] Researchers discovered that a compound extracted from *Hyrtios erectus* effectively blocks a key enzyme involved in insulin signaling. Therefore, is a potential target for treating obesity and type 2 diabetes.[30]

Spongia officinalis

Spongia officinalis, is a widespread species found in the Mediterranean Sea, northeastern Atlantic Ocean, and beyond. It is a member of the Dictyoceratida order.[31] Bioactive terpenes were extracted from *Spongia officinalis*, revealing a diverse range of compounds. The extract contained sesterterpenes and C_{21} furanoterpenes, including four newly discovered oxidized metabolites. Additionally, six known furospongin-series compounds and three scalarane sesterterpenes were isolated. Researchers made a significant discovery, finding that two key compounds, tetrahydrofurospongin-2 and dihydrofurospongin -2, triggered the formation of biofilms in *Escherichia coli*. Additionally, the isolated compounds were tested for their ability to combat bacterial and fungal growth.[32] Researchers isolated a series of bioactive diterpenes like 3-Nor-spongiolide A, Spongiolides A, and Spongiolides B, whose chemical frameworks were elucidated using cutting-edge spectroscopic methods.[33] Scientists have extracted a variety of bioactive substances from a marine sponge, *Spongia officinalis*, which was cultivated through aquaculture. The extracted compounds included several known substances, such as Jellynolide A and sponalisolides, as well as new metabolites. Jellynolide A, was obtained as a colorless oil.[34] Researchers discovered two new compounds in a marine sponge species. The extracted compounds included a unique acetoxy diterpenoid and an unusual 18-nor-spongian derivative. Additionally, six known metabolites were identified.[35] Scientists isolated anti-inflammatory steroids from *Spongia officinalis*, including a novel, highly degraded steroid featuring a unique 5/6/5-tricyclic structure.[36] Researchers examined a unique compound produced by a *Bacillus* bacterium living in association with the *Spongia officinalis*. The compound, (3S, 6S)-3,6-diisobutylpiperazine-2,5-dione, was analyzed using advanced spectroscopic techniques. Tests showed that the compound had antibacterial properties.[37] Researchers evaluated the anticonvulsant and pain-relieving properties of extracts and fractions derived from *Spongia officinalis*. The results showed promising anticonvulsant and analgesic effects, indicating potential uses in therapy.[38] Researchers discovered anticancer compounds in a fungus called *Penicillium* sp., which lives inside a marine sponge. The extracted compounds demonstrated impressive anticancer activity.[39] Researchers investigated the potential of *Spongia officinalis*, to yield anti-inflammatory and anticancer compounds. They tested the sponge's methanol extract and fractions in rats with induced inflammation and in human cancer cells grown in the lab. The results showed that the extract and fractions had significant anti-inflammatory and anticancer effects, with the effects increasing as the dose increased.[40]

Petrosia ficiformis

Petrosia ficiformis, a massive, wine-colored sponge is widely distributed throughout the Mediterranean Sea and Macaronesia, including the Azores, Madeira, and Canary Islands.[41] A recent study yielded five newly discovered polyacetylenes from *Petrosia ficiformis*.[42] Scientists identified 12 unusual stanols with a distinctive 5 beta-dihydro nucleus in the marine sponge *Petrosia ficiformis*. Interestingly, these compounds were absent in earlier samples of the same sponge, leading researchers to speculate that they might be formed through bacterial processing of the sponge's natural sterols.[43] Scientists discovered a new sterol, (24R)-24,26-Dimethylcholesta-5,26-dien-3 beta-ol, in the marine sponge *Petrosia ficiformis*. A thorough examination revealed a diverse range of monohydroxy sterols, including common and rare types. Using advanced spectroscopy and comparison with a synthetic version, researchers confirmed the structure of a newly identified minor sterol, (24R)-24,26-dimethylcholesta-5,26-dien-3β-ol, also known as 26(29)-dehydroaplysterol.[44] Researchers investigated the antimicrobial properties of bacteria living on the marine sponge *Petrosia ficiformis*. The study aimed to explore the potential link between the sponge's natural products and those produced by its associated microorganisms. Using a combination of traditional and molecular techniques, the researchers identified 57 bacterial strains with distinct characteristics.[45]

Niphates erecta

The Lavender rope sponge, scientifically known as *Niphates erecta*, is a highly variable species. The surface texture varies from smooth and porous to spiky. The color of *Niphates erecta* ranges from pale purple, pink, bluish, or grey on the exterior to a lighter shade internally. The sponge is compressible, tough, yet easy to cut. The marine sponge *Niphates erecta* has a widespread distribution, occurring in areas of Bermuda. Scientists discovered a novel glycoprotein, niphatevirin, from the marine sponge *Niphates erecta*, demonstrating potent anti-HIV properties. Niphatevirin exhibited significant anti-HIV activity, protecting human lymphoblastoid cells from HIV-1-induced damage.[46] An exploration of marine organisms in the Colombian Caribbean Sea uncovered promising antiherpes properties. Specifically, three species of marine sponges - Aka *cachacrouense, Niphates erecta*, and *Dragmacidon reticulatum* - showed notable potential, justifying further research to isolate and identify the bioactive compounds driving this activity.[47]

Halichondria panicea

Halichondria panicea exhibits highly variable morphology. Typically found on open coastlines, it can form a low-lying crust with distinctive "volcano-like" exhalant openings. It typically exhibits a cream-yellow hue. A distinctive seaweed-like odor is also characteristic of *Halichondria panicea*. Geographically, this species is distributed across the North Atlantic region, ranging

from the Barents Sea to the Mediterranean.[48] Scientists found that certain types of sea sponges are home to bacteria that produce antibiotics. These antibiotics can effectively combat strains of bacteria that are resistant to multiple drugs. The discovery of these bacteria and their antibacterial compounds could lead to the development of new medicines.[49] Scientists have identified new complex lipids in a type of marine sponge. One of these lipids has a unique fatty acid component and was found to have a specific structure. Researchers used advanced techniques to determine the lipid's composition. Additionally, a second complex lipid was discovered in the same sponge species, notable for its unusually long fatty acid chain.[50] Researchers discovered four novel gamma-pyrones, designated as nocapyrones A-D, in an organic extract of the Nocardiopsis strain HB383.[51] Scientists discovered a new compound mayamycin, derived from a type of bacteria *Streptomyces* sp., that shows promise in fighting cancer and antibiotic-resistant bacteria.[52]

Cliona celata

Studies on the ethyl acetate fraction of *Cliona celata* revealed its potential anti-inflammatory properties. Mechanistic investigations showed that this fraction impeded the nuclear migration of NF-κB p65 subunits, accompanied by decreased phosphorylation and degradation of IκB-α. Additionally, ECC strongly suppressed NF-κB-mediated gene expression and DNA-binding activity, accompanied by decreased nuclear p65 protein levels. Mechanistic investigations revealed that ECC inhibits NF-κB activation by preventing IκB degradation, thereby modulating the inflammatory response.[53] Researchers assessed the efficacy of *Cliona celata* marine sponge extracts as larvicides, ovicides, and repellents against Anopheles stephensi, a key malaria vector. The study examined the effectiveness of various solvent extracts of *C. celata* in controlling *Anopheles stephensi* populations. The findings revealed that the methanol extract demonstrated the highest larvicidal activity, significantly impacting fourth-instar larvae at a concentration of 500 ppm. Conversely, the hexane extract proved to be the most potent repellent against *Anopheles stephensi*.[54] Researchers investigated the multifaceted inhibitory effects of *Cliona celata* on TNF-α-mediated MMP-9 production, exploring its influence on NF-κB and AP-1 signaling pathways, enzymatic activity, and cellular migration. MMP-9 plays a pivotal role in extracellular matrix degradation, contributing to the pathological proliferation and migration of vascular smooth muscle cells in atherosclerotic lesions.[55] A novel aminosteroid, Clionamine B, derived from the marine sponge *Cliona celata*, has been shown to induce autophagy. Researchers developed an efficient synthesis of Clionamine B, utilizing tigogenin, a plant-derived sapogenin, as the starting material. A key step in the synthesis involved the stereoselective introduction of the α-hydroxyl group at C-20, accomplished through the oxidation of a γ-lactone enolate with molecular oxygen. The resulting synthetic Clionamine B exhibited robust autophagy-inducing activity in MCF-7 human breast cancer cells.[56] Scientists found that *Cliona celata*, possesses notable antioxidant and anti-inflammatory activities.[57]

Corticium candelabrum

Corticium candelabrum, a Homosclerophorida-order sponge, is native to the eastern Atlantic Ocean and Mediterranean Sea. Typical habitats include coralline algae communities in shady positions, such as vertical walls, under overhangs, and in caves, at depths of up to 20 meters.[58] *Corticium candelabrum* typically inhabits rocky areas beneath the littoral zone in the Mediterranean region. *Corticium candelabrum* is a prolific source of bioactive compounds, featuring a diverse array of terpenoids, alkaloids, and peptides. The therapeutic potential of these secondary metabolites has sparked significant interest in biomedical research. Investigations have revealed that compounds isolated from *Corticium candelabrum* exhibit a broad spectrum of biological activities, including antimicrobial, antiviral, and anticancer properties.[59]

Crella spinulata

Crella spinulata is a demosponge species within the Crella genus and Crellidae family. Notably, research has demonstrated that *Crella spinulata* exhibits anti-proliferative effects and induces cell cycle arrest in colon cancer cells under *in vitro* conditions. A recent study investigated the anticancer properties of *Crella spinulata's* mesohyl against the Caco-2 colon cancer cell line. Using MTT assays and flow cytometry, the results showed that *Crella spinulata* significantly inhibited Caco-2 cell proliferation.[60] *Crella spinulata* has shown significant antimicrobial and cytotoxic properties.[61] Studies have found that extracts and mesohyls from marine sponges, including *Crella spinulata*, can inhibit the growth and migration of liver cancer cells. A novel 3D cell culture system, known as primmorph, provides a sustainable method for producing bioactive compounds from marine sponges for potential use in cancer therapies. The anticancer effects of primmorph extracts and mesohyls from *Crella spinulata* were assessed through various assays, including cell viability, colony formation, cell cycle analysis, and apoptosis. Treatment with these extracts significantly reduced the migration and proliferation of liver cancer cells (HepG2). Notably, the primmorph extract of *Crella spinulata* exhibited the most promising anticancer activity, demonstrating both antiproliferative and antimigratory effects.[62] Researchers have discovered a novel class of compounds, designated as shishicrellastatins, derived from the marine sponge *Crella spinulata*.[63]

Cribrochalina vasculum

Cribrochalina vasculum, a marine sponge belonging to the Niphatidae family and Haplosclerida order, exhibits a unique morphology. Its shape is variable, often resembling a funnel or bowl, but can also be irregular.[64] Research has identified

compounds from the marine sponge *Cribrochalina vasculum* as potential anticancer agents. Notably, two acetylene alcohols derived from the sponge disrupted tumor cell signaling mediated by IGF-1R, offering a promising avenue for cancer treatment.[65] Scientists have identified a range of bioactive compounds in the Caribbean sponge *Cribrochalina vasculum*, including a distinct class of hydroxyalkynyl lipids with significant biological activity. Detailed analysis revealed three prominent compounds: 3-hydroxydocosa-(4E, 15E)-dien-1-yne, 3-hydroxy-16-methyleicos-(4E)-en-1-yne, and 3-hydroxy-19-methyleicos-(4E)-en-1-yne. Further examination of the sponge's lipophilic extract led to the discovery of four novel acetylene metabolites, each displaying unique structural characteristics.[66] A novel compound, 23-methyl-5,9-pentacosadienoic acid, was isolated and characterized from the marine sponge *Cribelochalina vasculum* through a comprehensive extraction and analysis process.[67] Scientists have detected a small quantity of the sterol 23-Epidihydrocalysterol in the marine sponge *Cribrochalina vasculum*. A novel sterol featuring a cyclopropane ring was isolated from *C. vasculum* and characterized using advanced analytical techniques.[68]

Fasciospongia cavernosa

Fasciospongia cavernosa, a species of sea sponge, is distinguished by its robust, fleshy walls and expansive, cavernous interior. Its unique appearance is marked by prominent, longitudinal ridges, or fascioles, that run along its surface. The marine sponge *Fasciospongia cavernosa* inhabits tropical waters, typically in shallow coral reefs and rocky crevices, and is widespread across the Indo-Pacific region, including nations such as Australia, Indonesia, and the Philippines. Researchers have isolated a novel cacospongionolide derivative from this sponge, designated as cacospongionolide F. Spectroscopic analysis and chemical transformations revealed its unique structure, identifying it as a bioactive sesterterpene. The absolute configuration of cacospongionolide F was elucidated employing a variant of the Mosher esterification approach. The antimicrobial properties and toxicity of cacospongionolide F to brine shrimp and fish have been investigated.[69] Scientists have isolated a unique lectin from the marine sponge *Fasciospongia cavernosa*, which exhibits specificity for D-galactose and N-acetyl-D-galactosamine.[70] Scientists have discovered a novel compound, Cacospongionolide E, in *Fasciospongia cavernosa*. This compound demonstrated potent inhibition of human secretory phospholipase A2 (PLA2), surpassing the efficacy of the well-established compound manoalide. Notably, Cacospongionolide E exhibited no toxicity towards human neutrophils. Biological assessments revealed pronounced activity in the Artemia salina bioassay and moderate toxicity in the Gambusia affinis fish lethality test.[71] Scientists have discovered a new sesterterpene, cacospongionolide B, in the marine sponge *Fasciospongia cavernosa*, native to the Adriatic region.[91] Scientists have discovered that two sesterterpenoids, cacospongionolide and scalaradial, derived from marine sources, exhibit potent pro-apoptotic effects, inducing programmed cell death in human carcinoma cell lines.[72] Furthermore, Cacospongionolide B, a sesterterpene has shown strong anti-inflammatory properties.[73] Scientists have identified Cacospongionolide B, a distinctive compound found in the *Fasciospongia cavernosa*, as a potent suppressor of human synovial phospholipase A2 (sPLA2) activity. This suppression has been demonstrated to modulate inflammatory responses over both acute and chronic timeframes.[74] Researchers investigated the anti-inflammatory properties of cavernolide, a unique C_{21} terpene lactone isolated from the marine sponge *Fasciospongia cavernosa*.[75]

Halichodrian bowerbanki

Halichondria bowerbankii, a marine species known by several common names, thrives in bays and harbors. Originating in the North Atlantic, its native range extends from Iceland and Norway to the Mediterranean, Azores, and eastern North America.[76] The marine sponge *Halichondria bowerbanki* has been found to contain a bioactive compound known as Halichondamide A. Research has shown that Halichondamide A exhibits notable anticancer properties, with moderate inhibitory effects observed in certain cancer cell lines, particularly those linked to hepatic and mammary tumors.[77]

Hyattella intestinalis

Hyattella intestinalis, a demosponge, boasts a distinctive body composition featuring pebble needles and spongine fibers, allowing for substantial water absorption. This species is classified within the genus Hyattella and family Spongiidae. Researchers have isolated spongian diterpenes from *Hyattella intestinalis*, revealing moderate antiviral activity against adenovirus. Advanced chromatographic and spectroscopic techniques facilitated the identification of three previously unknown compounds. Notably, one of these compounds exhibited significant antiviral properties.[78] Scientists have identified a distinct group of norsesterterpenes, termed mooloolabenes A-E, in the Australian marine sponge *Hyattella intestinalis*. Furthermore, a previously unknown sesterterpene, mooloolaldehyde, displaying structural similarities to scalarane compounds, was also isolated from this species. Biological evaluation of the extracted compounds revealed significant anticancer potential, characterized by pronounced cytotoxic effects against the P388 cancer cell line.[79] Scientists have found that certain bacteria living in the marine sponge *Hyattella intestinalis* show strong potential in combating malaria. Laboratory tests revealed that these bacteria effectively inhibit the growth of *Plasmodium falciparum*, the parasite responsible for the disease.[80]

Iotrochota baculifera

Iotrochota baculifera, a demosponge species, boasts a distinctive skeletal structure composed of elongated, slender spicules. Characterized by its porous body and intricate network of canals and chambers, this sea sponge belongs to the Iotrochotidae family. Chemical analysis of specimens collected from the Indian Ocean revealed a range of sphingolipids, including the novel glycosphingolipid iotroridoside-B and a mixture of four sphingolipid components, featuring two newly discovered compounds.[81] A chemical study of the marine sponge *Iotrochota birotulata*, sampled from the waters off Port Royal, Jamaica, aimed to identify its primary constituents and assess the bioactivity of its crude extracts. The analysis revealed a range of compounds, notably renierapurpurin, a carotenoid derivative previously unreported in this species. Additional isolated compounds included a tyrosine derivative and the ubiquitous steroid β-sitosterol.[82]

Ircinia strobilina

Ircinia strobilina, a marine sponge belonging to the Irciniidae family, is recognizable by its grey or glossy black hue and unique conular spiny surface features. This species is predominantly found in the Caribbean Sea, with documented occurrences near Florida, the Virgin Islands, Cuba, and Venezuela. Researchers have isolated and characterized a lectin from *Ircinia strobilina*, discovering its potential to combat biofilm formation. Specifically, this lectin demonstrated significant inhibitory effects on biofilm formation in certain bacterial strains, including *Staphylococcus aureus* and *Staphylococcus epidermidis*.[83] The sponge's fatty acid composition was characterized by elevated levels of demospongic acids, a distinct group of fatty acids typical of certain sponge species.[84]

Jaspis johnstoni

Jaspis johnstoni, a sea sponge belonging to the Ancorinidae family, exhibits a distinctive astrophorid morphology. Characterized by its robust, globular body and siliceous spicule-based skeleton, this species thrives in tropical and subtropical waters, including coral reef environments and rocky crevices. A chemical examination of Fijian *Jaspis johnstoni* specimens revealed two cytotoxic compounds, toyocamycin and 5-(methoxycarbonyl)tubercidin, which are part of the pyrrolo[2,3-d]pyrimidine nucleoside family.[85] Jasplakinolide possesses antifungal and antiproliferative properties.[86]

Lendenfeldia chondrodes

Lendenfeldia chondrodes, a vibrant blue sea sponge, is a popular aquarium species. Belonging to the Thorectidae family, this sponge boasts a distinctive appearance.[87] Scientists have identified polybrominated diphenyl ethers (PBDEs) in the marine sponge *Lendenfeldia chondrodes*. These compounds have shown potential therapeutic value due to their ability to inhibit specific protein kinases, CDK7 and FynB, which play critical roles in cellular processes.[88] Researchers have identified novel compounds in *Lendenfeldia chondrodes*. Two previously unknown 1-deoxynojirimycin derivatives were discovered through analysis of the sponge's aqueous extract.[89] Researchers have identified a novel epidioxy sterol with antifouling properties in the marine sponge *Lendenfeldia chondrodes*.[90]

Luffariella variabilis

Scientists have identified a range of cytotoxic manoalide-type sesterterpenes in *Luffariella variabilis*. An in-depth examination of the sponge's chemical constituents led to the isolation of 13 previously unknown linear terpenes, featuring 11 distinctive manoalide derivatives characterized by their acyclic frameworks. Additionally, a polyprenylphenol derivative and a polyprenylbenzaldehyde derivative were identified.[91] Researchers identified two novel furanosesterterpenoids in the marine sponge *Luffariella variabilis*. One of these compounds exhibited considerable cytotoxic effects against NBT-T2 cells, suggesting its potential as a valuable candidate for future studies.[92] An investigation into the chemical composition of *Luffariella variabilis* led to the discovery of acetylated sesterterpenes.[93] Scientists discovered a novel manoalide-related sesterterpene, (4E,6E) -dehydro-25-O-methylmanoalide, in extracts of the marine sponge *Luffariella variabilis*. This finding was complemented by the identification of the established compound (4E,6E)-dehydromanoalide.[94] A subsequent examination of a variant of this sponge species resulted in the isolation of an additional new manoalide-related sesterterpene, 24-O-ethylmanoalide.[95] Researchers have discovered two novel β-carboline alkaloids, variabines A and B, in t *Luffariella variabilis*. Spectroscopic analysis revealed the structural composition of these compounds, with variabine A featuring a sulfonated group distinct from variabine B. Notably, variabine A's sulfate group is a unique characteristic among previously identified β-carboline alkaloids. Assessment of variabine B's biological activity revealed potent inhibition of proteasome function and disruption of a key protein-protein interaction. Conversely, variabine A exhibited negligible impact on these biological pathways.[96] The marine sponge *Luffariella variabilis* yields a compound called manoalide, which boasts a dual pharmacological profile. Notably, manoalide has been found to block calcium channels and exhibit antimicrobial properties.[97] Researchers have discovered a new class of anti-inflammatory sesterterpenes, known as luffariellins, which provide significant contributions to the field of chemotaxonomy.[98]

Pachychalina alcaloidifera

The tropical sea sponge *Pachychalina alcaloidifera*, a member of the Niphatidae family, is native to the Indo-Pacific region. It typically thrives in shallow coral reef environments within this geographic range. Investigations into ingenamine G, a marine alkaloid isolated from the *Pachychalina alcaloidifera*,

uncovered its dual capacity for inducing cytotoxic and genotoxic effects. Notably, ingenamine G displayed moderate toxicity towards human lymphocytes. Additional analyses suggested that this compound may also possess genotoxic potential, leading to chromosomal instability and genetic alterations. Human lymphocytes were exposed to varying concentrations of ingenamine G, and the results indicated that all concentrations tested exhibited cytotoxicity, reduced mitotic activity, and induced chromosomal damage. DNA strand breaks increased at higher concentrations, and high concentrations of ingenamine G disrupted mitotic spindle formation, inducing chromosomal instability.[99] A thorough examination of the sponge's chemical constituents revealed a subset of four bis-piperidine alkaloids, including madangamine F, haliclonacyclamine F, arenosclerin D, and arenosclerin E. Employing spectroscopic techniques enabled the characterization of these compounds, which exhibited pronounced cytotoxic effects against a range of cancer cell lines.[100]

Pandaros acanthifolium

Pandaros acanthifolium belongs to Pandaros genus, part of the Microcionidae family. A detailed chemical examination of this species uncovered a diverse array of steroidal glycosides, including four novel compounds, designated as acanthifoliosides G-J. Characteristic structural features of these compounds include a highly oxygenated D ring and unique sugar moieties. Interestingly, acanthifolioside G demonstrated remarkable antioxidant and cytoprotective activities.[101] Researchers have identified novel antiprotozoal compounds in the *Pandaros acanthifolium* sponge. A thorough chemical analysis yielded 12 new steroidal glycosides with potential therapeutic benefits. Laboratory tests revealed that several of these compounds demonstrated significant efficacy against various parasitic protozoa. Notably, two compounds showed potent growth-inhibiting effects against specific parasites.[102] A comprehensive chemical examination of *Pandaros acanthifolium* led to the identification of seven previously unknown steroidal glycosides. This investigation uncovered a subset of four novel compounds, termed pandarosides A-D, alongside three methyl ester analogs corresponding to pandarosides A, C, and D.[103] A detailed re-examination of the chemical constituents of the Caribbean sponge *Pandaros acanthifolium* uncovered six novels steroidal saponins. Spectroscopic analysis and comparative studies enabled the identification of these compounds, comprising Pandarosides K-M and their corresponding methyl esters. Biological evaluations revealed that these new compounds exhibited moderate to weak antiprotozoal activity. Additionally, their cytotoxic properties against human cancer cell lines, as well as their capacity to induce hemolysis and liposome permeabilization, were assessed in conjunction with previously characterized pandarosides and acanthifoliosides. The findings indicated that select pandarosides displayed notable cytotoxic effects, whereas certain acanthifoliosides exhibited pronounced hemolytic activity.[104]

CONCLUSION

The ocean's depths hold a treasure trove of bioactive compounds, with sea sponges emerging as a rich source of novel and diverse molecules. These compounds have shown immense potential in addressing various human health challenges, including cancer, inflammation, and infectious diseases. The unique structural and functional properties of these compounds make them attractive candidates for pharmaceutical development. As research continues to unravel the secrets of sea sponge-derived bioactives, it is essential to adopt sustainable and eco-friendly approaches to harness these treasures. By doing so, we can unlock the full potential of the ocean's treasure trove, leading to the discovery of new life-saving medicines and a deeper appreciation for the importance of marine conservation.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

NF-κB: Nuclear factor kappa **B; IκB:** inhibitor of nuclear factor kappa B; **MMP-9:** Matrix metalloproteinase-9; **MTT:** 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide; **NSCLC:** Non-small-cell lung cancer; **SCLC:** Small-cell lung cancer; **PARP:** Poly (ADP-ribose) polymerase; **IL-1β:** Interleukin-1 beta; **IL-6:** Interleukin 6; **IL-8:** Interleukin 8; **PPAR-α:** Peroxisome proliferator-activated receptor alpha; **PPAR-γ:** Peroxisome proliferator-activated receptor gamma.

SUMMARY

Sea sponges are a rich source of bioactive compounds with potential therapeutic benefits. This review provides an overview of the various bioactive compounds isolated from sea sponges, including their structural diversity and pharmacological properties. The potential applications of these compounds in treating diseases are discussed, along with the challenges and opportunities in developing sea sponge-derived therapeutics. The importance of sustainable approaches in harnessing the medicinal potential of sea sponges is also highlighted.

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