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RECENT DEVELOPMENTS ON MARINE ALGAE AND SPONGES AS MARINE NUTRACEUTICALS

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ABSTRACT

Nutraceutical is a hybrid term coined from 'nutrition' and 'pharmaceutical' that refers to the food or dietary supplements. They are important food components that have both nutritional and therapeutic properties. Human health and wellness are mostly controlled by the consumption of nutritious foods, which are provided through nutraceuticals. This review discusses the pharmacological activities of the marine algae and sponges. Marine algae and sponges are a novel diet with potential nutritional value that can be employed in industry and medicine for a variety of applications. They show pharmacological activities due to the presence of wide variety of bioactive compounds like polysaccharides, lipids, proteins, fatty acids, vitamins, minerals and secondary metabolites like alkaloids, terpenoids, steroids, isoprenoids, quinones etc. Several studies shown that they exhibit antibacterial, antioxidant, anticancer, antifouling, antiviral, antiinflammatory and immunosuppressive activities. Daily intake of these biologically active ingredients through marine supplements can help to combat several diseases such as cancer, gastrointestinal diseases, viral diseases, bacterial diseases etc.

Keywords: Anticancer, Antifouling, Antiinflammatory, Marine algae, Nutraceuticals, Sponges

INTRODUCTION

The demand for sustainable food supplements, such as nutraceuticals, is growing as the world's population is increasing **[1]**. Nutraceutical, a dietary supplement which is a hybrid term of 'nutrition' and 'pharmaceutical' has a potential to deliver a concentrated form of a bioactive ingredient from a food, placed in a non-food matrix, and utilized to improve health in levels greater than those available from typical foods **[2]**. Bioactive substances found in everyday foods or botanical sources are referred to as nutraceuticals that supplies beneficial effects in addition to the nutritional essential components **[3]**. Certain polysaccharides, fatty acids, vitamins, peptides and minerals are some of the bioactive molecules that can be extracted or synthesized chemically or biotechnologically **[4]**.

In contrast to terrestrial ecosystems, the marine ecosystem has a greater diversity of living organisms, which provides several benefits for human health and nutrition **[5]**. The marine ecosystem's tremendous diversity and dynamics make it a suitable reservoir for finding novel compounds and developing marine nutraceuticals. Although more than 20,000 marine bioactive chemicals have been identified, only a small percentage of them have been properly investigated and used to some extent. Marine habitats have been termed as the "Natural Medicine Chest of the New Millennium" and are rapidly growing as a global industry. Fish, algae, crustaceans, sponges, mollusks, actinomycetes, fungi, tunicates, and a variety of other microorganisms have all been used as potential natural product sources. Health issues arises due to potential harmful effects of allopathic drugs due to misuse, overuse and uncontrolled applications of these pharmaceuticals **[6].** Nutraceuticals from natural sources can help to prevent or treat a variety of ailments without any side effects and also enhances one's standard of living. Because of their safe nature, marine-based nutraceuticals are a viable alternative to allopathic medications **[7]**. Among them algae and sponges are widely used as nutraceutical supplements due to their lot of availability in the marine environment. Algae extracts were employed as supplements in a variety of industries, including food, dairy, and pharmaceuticals. Because of their antioxidant, anticancer, and antibacterial characteristics, they are employed as one of the most important therapeutic sources **[8]**.

Marine sponges (Porifera), which are multicellular invertebrates, are considered as the largest suppliers of new marine natural products (NMNP) among all the marine animals studied. With this myriad of NMNP available, numerous studies have revealed a broad spectrum of biological activities for these compounds, including anticancer, antiviral, antibacterial, antifungal, antiinflammatory, antifouling and a range of other bioactivities. Furthermore, as infectious microbes change and develop resistance to existing drugs, marine sponges provide new therapeutic options for bacterial, fungal, and viral infections **[9]**.

In this review we have focused on the nutraceutical benefits of marine algae and sponges and their bioactive compounds that have been shown to have pharmacological activities

MARINE NUTRACEUTICALS AND THEIR BIOACTIVE COMPOUNDS

Marine algae

Algae are classified into two types: microalgae and macroalgae, both of which are employed as nutraceuticals

Microalgae

Microalgae are a diverse group of autotrophic organisms which produce more biomass per surface than any other natural source because of their ability to grow rapidly, efficiently use light energy, fix atmospheric carbon dioxide. Bioactive substances such as vitamins B1, B2, B6, B12, A, C, E, H, astaxanthin, polysaccharides, and polyunsaturated fatty acids are abundant in microalgae which support human and animal health. This ability of microalgae to synthesize a variety of compounds confers nutraceutical properties with an elevated potential for industrial exploitation **[10]**.

Microalgae have been used as a human food source or nutritional supplements for hundreds of years. *Spirulina, Chlorella, Dunaliella, Nostoc, Botryococcus, Anabaena, Chlamydomonas, Scenedesmus* and other major microalgae genus are more commonly found in dietary supplements **[8]**. A dry cake was prepared from blue-green masses which was known as 'tecuitlatl' is used as a food supplement. For centuries, *Spirulina* (known as 'dihé') has been using as a food on a daily basis. *Nostoc,* filamentous cyanobacteria, has been also widely used as food. Nowadays, *Chlorella* and *Spirulina* have been widely commercialized as nutritional supplement worldwide **[11]**.

Spirulina usually called as "The Original Blue Nutraceutical" is the best example of microalgae as a food. *Spirulina* is used as a supplement and is high in nutrients such B vitamins, phycocyanin, chlorophyll, vitamin E, omega-6 fatty acids, and minerals **[12]**. Elements such as potassium, calcium, chromium, copper, iron, magnesium, manganese, phosphorus, selenium, sodium, and zinc are all abundant in *spirulina*. Weight loss, diabetes, high blood pressure, and hypertension are some of the health benefits of commercial *Spirulina* brands **[13]**.

Chlorella usually called as "The Green Nutraceutical is readily available as a health food, food supplement and nutraceutical **[10]**. *Chlorella* is regarded as a valuable functional food and nutraceutical due to its nutrient content and favourable health effects. Regarding to its composition, *Chlorella* is made up of protein, chlorophyll, dietary fibre and a variety of minerals and vitamins **[14]**. *Chlorella* is also high in lutein, which is used to prevent and treat macular degeneration **[15]**. *Chlorella* ingestion has resulted in a considerable reduction in low density lipoprotein (LDL) and cholesterol levels **[10]**.

Dunaliella is best known for the pigment beta-carotene, which amounts approximately to 14% of its dry weight. *Dunaliella* sp. can produce up to 400 mg betacarotene m^{-2} under perfect growing conditions. Alpha-carotene, lutein, and lycopene are the other important pigments. Carotenoids from *Dunaliella* have strong antioxidant capabilities that help to prevent lipid peroxidation and enzyme inactivation. Studies have demonstrated that beta-carotene of *Dunaliella* can prevent cancer of different organs like lungs, stomach, colon, rectum, breast, prostate and ovary by means of its antioxidant activity **[8]**.

Haematococcus sp. is a green alga with numerous uses in the nutraceutical, pharmaceutical, cosmetics and aquaculture industries. *Haematococcus* sp. produces a red pigment called astaxanthin, which causes *Haematococcus* cells to appear red. In the United States, the Food and Drug Administration (FDA) has approved the sale of *Haematococcus pluvialis* as a novel dietary supplement **[8]**.

Macroalgae

Macroalgae, usually called as seaweed, is the most widely used in the nutraceutical sector since it offers wide range of foods and food additives **[4].** Agarose, a source of metabolites and bioactive molecules with specific nutritional and medicinal qualities, is one of the most important macroalgae products. Proteins, phenotics, pigments, furanone, polyunsaturated fatty acids, L-kainic acid, phlorotannins, phycocolloids (carrageenan and agar), and minerals are among these metabolites and bioactive molecules **[16]**. Macroalgae also provide vital nutrients as well as novel bioactive compounds for human nutrition **[17]**. Red and brown seaweeds, for example, are good providers of important fatty acids **[18]** and alternative resources of minerals, vitamins and proteins **[19]**. They have been utilized to make bioactive peptides which help to increase protein digestion. Angiotensin-converting enzyme (ACE) inhibitors have recently been identified as antihypertensive bioactive peptides. Macroalgae are similarly high in insoluble and soluble dietary fibre because they are mostly made up of indigestible sulfated polysaccharides and are not digested by stomach enzymes **[20]**. Fucan, laminaran, carrageenan, agar and alginate are examples of functional and storage polysaccharides observed in red and brown seaweeds. Based on biological activity, brown seaweed alginates are used as hydrocolloids and brown seaweed fucans are used in the food and cosmetics sectors **[4]**.

Marine sponges

A sponge is a sessile invertebrate that can be found in tropical, temperate, and polar environments **[21]**. There are around 8000 species of sponges in the phylum porifera, which includes marine sponges. They are comprised of a jelly-like layer sandwiched between two thin layers of cells, and they may have a spicule skeleton made of silica, calcium carbonate, and a protein called Spongin **[22]**. In terms of product diversity, marine sponges are considered as champion producers **[23]**. Sponges are responsible for approximately 5300 distinct products, and hundreds of new compounds are found every year, according to the report **[32]**. Nucleosides, terpenes, sterols, cyclic peptides and alkaloids are some of the chemically diversified bioactive substances produced by sponges **[24]**. These substances found to posses most common antiinflammatory, antitumor, antibiotic, antifouling, antiviral, antimalarial, activities. Sponge products and chemical diversity are remarkable **[25]**. Sponge products include unique alkaloids, fatty acids, peroxides, nucleosides, sterols, bioactive terpenes, cyclic peptides and amino acid derivatives (often halogenated). Marine sponges offer the potential to develop new medications to treat diseases such as malaria, cancer and a variety of viral diseases **[26]**.

PHARMACOLOGICAL APPLICATIONS

Marine Algae

Antioxidant Activity

Antioxidant activity has been discovered in a variety of algae, particularly those with a marine origin, such as red algae, green algae, and brown algae. Many researchers have used anti-oxidant tests such as superoxide anion (O_2), 1,1-diphenyl-2-picrylhydrazyl (DPPH), peroxyl radical (ROO•) and hydroxyl radical (OH•) to prove the antioxidant activity of various algae species. Some of the algae which possess anti-oxidant properties are listed in the **Table 1**.

Table 1: Antioxidant activity of marine algae [27, 28, 29, 30,8]

Species name	Major compound / Extract	Mode of action
Sargassum micracanthum	Plastoquinones	At IC_{50} = 0.95–44.3 µg/ml show Anti-oxidative activity and lipid peroxidation.
Hijikia fusiformis	Fucoxanthin	DPPH radical scavenging, anti-oxidative activity.
Chondracanthus acicularis	Lambda-carrageenan	At IC_{50} = 0.046, 0.357 and 2.267 mg/ml inhibits superoxide radicals, hydroxyl radicals, and lipid peroxidation respectively.
Eucheuma denticulatum	Iota-carrageenan	At IC_{50} = 0.332, 0.281 and 0.830 mg/ml inhibits superoxide radicals, hydroxyl radicals and lipid peroxidation respectively.
Gelidiella acerosa	Phytol	At IC_{50} = 25–125 µg/ml show antioxidant activity
Kappaphycus alvarezii	Kappa-carrageenan	At IC_{50} = 0.112, 0.335 and 0.323 mg/ml inhibits superoxide radicals, hydroxyl radicals and lipid peroxidation

		respectively
Porphyra/Pyropia sp.	Phycoerythrobilin	At IC_{50} = 0.048 mmol/g show antioxidant activity
Rhodomela confervoides	Bromophenols	At IC_{50} = 5.22–23.60 µM show antioxidant activity
Ulva pertusa	Sulfated polysaccharides	Superoxide radicals scavenging activity
Ulva prolifera	Pheophorbide A	At IC_{50} = 71.9 µM show antioxidant activity
Ulva lactuca	Aqueous and methanolic extracts	Radical scavenging activity
Ulva lactuca	Flavanoids	Potent antioxidant activity
Gracilaria caudate	Sulfated polysaccharides	Increased Catalase and Superoxide dismutase activity
Sargassum polycystum	Fucoidan	At IC_{50} = 712.2-759.6 µg/ml show antioxidant activity DPPH (IC_{50} = 4640 and 4500 µg/ml)
Anabaena	methanol extract	Radical scavenging activity using DPPH
Callophyllis japonica	Ethanolic extract	Inhibit cellular apoptosis mediated by H_2O_2
Gracilaria tenusistipitata	Aqueous extract	Protect against H_2O_2 induced DNA damage, growth inhibition and cell cycle
Eisenia bicyclis, Ecklonia cava, and Eckloniakurome	Phlorotannins.	DPPH radical scavenging Activities
Ulva fasciata Delile	Sesqueterpenoids	Radical scavenging activity
Ulva reticulate	hot water extract	Reduce hepatic oxidative stress

Anticancer Activity

Algal species include a wide range of anti-cancer intracellular substances. Polysaccharides are the essential components that have anti-cancer actions, according to various studies on algae. Some of the species which possess anticancer activities are listed in the **Table 2**.

Table 2: Anticancer activity of marine algae [28,29,30,8]

Species name	Major compound / Extract	Mode of action /Type of cell lines
Ulva lactuca	Methanolic extract	Antiproliferative effect on the MCF-7 breast cancer cell line. Significant cytotoxic effect on the colon cancer cell line (CACO-2).
Ulva lactuca	Sulfated polysaccharide	Induce cell reactivity to *Ulex europaeus*-1 lectins to inhibit cancer cell proliferation. Inhibit proliferation of human epithelial colorectal adenocarcinoma cells (CACO-2)
Ulva lactuca	Extracts of *n*-hexane, ethyl acetate, chloroform and ethanolic	Anticancer activity against breast MCF-7 and colorectal HCT-116 cancer cells
Ulva lactuca	Ethanolic extract	The blood cancer (MOLT-3) cell line has been shown to have strong selective cell proliferation inhibition.
Sargassum polycystum	Fucoidan	Anticancer activity against the MCF-7 breast cancer cell line at IC_{50} = 50 µg/mL
Sargassum hornery, *Ecklonia cava*, and *Costaria costata*	Fucoidans	Anticancer activity on human colon cancer cells.
Sargassum filipendula	Hetero fucans	Antiproliferative activity on prostate, cervical, and liver cancer cells
Plocamium telfairiae	Methanolic extract	HT-29 colon cancer cells undergo caspase-dependent apoptosis.
Gracilaria tenuistipitata	Ethanol and methanol extracts	On Ca9-22 oral cancer cells, it has antiproliferative action and is also responsible for cellular death, oxidative stress, and DNA damage.
Gracilaria corticata	Aqueous extract	Inhibition of human leukemia cell lines proliferation
Sargassum oligocystum	Aqueous extract	Inhibition of human leukemia cell lines proliferation
Laminaria japonica	Glycoproteins	Anticancer activity on human colon cancer cells
Spirulina platensis	Extracts	Chemo preventive activity against carcinogenesis induced by dibutyl nitrosamine
Spirulina maxima	Extracts	Inhibit viability of human cancer cells and also Suppress the expression of Bcl2 in A549 cells
Red microalgal species	polysaccharides	Anticancer activity in two human cancer cell lines MCF-7 and

		HeLa.
Undaria pinnatifida	Aqueous extract	Anticancer avtivity against Mammary tumour cells
Undaria pinnatifida	Aqueous extract	Activity against Breast cancer
Porphyridium cruentum	polysaccharides	Cancer preventive action
Caulerpa prolifera	Sulphated polysaccharides	Inhibited HeLa cell growth by 58 percent

Antibacterial Activity

The majority of investigations on algae species revealed that they create a variety of physiologically active secondary metabolites with antibacterial properties. Among the diverse group of algae, seaweeds are the source of antibacterial compounds. Some of them are listed in the **Table 3**.

Table 3: Antibacterial activity of marine algae [30, 28, 29, 8]

Species name	Major compound / Extract	Target species
Cladophora fascicularis	2-(20,40-dibromophenoxy)-4,6-dibromoanisol	*Bacillus subtilis, Staphytococcus aureus* and *Escherichia coli*,
Ulva lactuca	Ethyl acetate and methanolic extracts	*Pseudomonas fluorescens, Staphytococcus aureus, Aeromonas hydrophila, Vibio anguillarum, Pseudomonas aeruginosa*, and *Salmonella typhimurium*
Ulva lactuca	Ethanolic extract	Gram positive bacteria such as *Streptococcus mutans*, *Bacillus subtilis*, *Staphytococcus aureus, Staphylococcus saprophyticus*, *Streptococcus pyogenes, Staphylococcus epidermidis* and *Bacillus cereus*. Gram negative bacteria such as *Escherichia coli*, *Salmonella typhimurium*, *Serratia marcescens* and *Neisseria meningitides.*
Ulva lactuca	Ethanolic extract	*Escherichia coli*, *Serratia marcescens*, *Salmonella typhi*, *Acinetobacter calcoaceticus*, *Enterobacter cloacae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Enterococcus faecalis*, *Streptococcus pyogenes* and *Bacillus cereus*
Ulva lactuca	Ethanolic extract	food spoilage bacteria such as *Escherichia coli*, *Micrococcus luteus*, and *Brochothrix thermosphact*
Kappaphycus alvarezii	Bis-(2,3,6-tribromo-4,5-dihydroxybenzyl) ether (3) 3-bromo-5-(hydroxymethyl) benzene-1,2-diol	*Porphyromonas gingivalis*
Ulva fasciata, Gracilaria corticata, Sargassum wightii and *Padina tetrastromatica*	Aqueous extract	*Gracilaria corticata* against *Proteus mirabilis* and *Padina tetrastromatica* against *Vibrio harveyi* and *Staphylococcus aureus*
Cladophora fascicularis	Extracts	*Staphylococcus aureus*, *Escherichia coli* and *Bacillus subtilis*
Dictyota dichotoma and *Padina gymnosora*	Aqueous extract	*Bacillus megatherium* and *Staphylococcus aureus*
Gracilaria dendroides	Extracts	*Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa* and *Stapylococcus aureus*
Mastocarpus stellatus, Laminaria digitata and *Ceramium rubrum*	methanolic and hexane extract	fish pathogens

Antiinflammatory Activity

Oxidative stress has a significant impact in the growth of cancer, endothelial dysfunction, pulmonary illnesses, gastrointestinal diseases and atherosclerosis. Inflammatory responses are present in all of these diseases. Bowel inflammation is produced by a variety of factors, one of which is an increase in acetic acid production, particularly while fasting. Some of the antiinflammatory activities of marine algae are listed in the **Table 4**.

Table 4: Antiinflammatory activity of marine algae [28, 29, 8]

Species name	Major compound / Extract	Mode of action
Ulva lactuca	sulfated polysaccharides	Show anti-inflammatory effect by inhibition of edema
Ulva lactuca	Monounsaturated fatty acids (MUFA)	Activators of the antiinflammatory Nrf2-ARE pathway responses
Ulva lactuca	Se nanoparticles coated with *Ulva lactuca* polysaccharide (ULP-SeNPs)	Antiinflammatory effects by NF-κB hyper activation in colonic tissues and macrophages is inhibited, reducing the symptoms of acute colitis
Chlorella marina	Lycopene	The activity of cyclooxygenase in monocytes is reduced by Supplementation with algal lycopene and also protect against the inflammation induced by high-cholesterol diet (HCD)
Dunaliella bardawil	beta-carotene	Reduce acetic acid induced inflammation
Spirulina platensis	C-phycocyanin	Suppression of iNOS and COX-2 activation inhibits NO and PGE_2 overproduction.
Sargassum wightii	Alginic acid	Reduction of enzymes such as cyclooxygenase, lipoxygenase and myeloperoxidase.
Neorhodomela aculeata	Methanol extract	Reduce inducible nitric oxide synthase resulting in decrease in nitric oxide levels.
Lobophora variegate	Fucans	Inhibits nitric oxide synthase and cyclooxygenase activity
Bryothamnion triquetrum	Methanol extract	Inhibits L-arginine-nitric oxide pathway
Gracilaria caudate	Sulphated polysaccharide fraction	Inhibits myeloperoxidase (MPO) activity

Antiviral Activity

Marine algal polysaccharides have drawn a lot of attention as antiviral compounds due to their ability to inhibit influenza and mumps virus. The antiviral activities of some of the marine algal species are listed in the **Table 5**.

Table 5: Antiviral activity of marine algae [28, 30]

Species name	Major compound / Extract	Target Species
Ulva lactuca	2-((1*E*,3*E*)-4-chloro-2-mercaptobuta-1,3-dienyl) 1,2,3,4,4b,5,6,8a,9,10-decahydrophenanthrene3,5,10-triol,	Coxsackie B4 virus, Hepatitis A virus (HAV-H10) and Herpes simplex virus type-1 (HSV-1) and type-2 (HSV-2)
Ulva lactuca	Polysaccharides	Anti-H1N1 activity is low against influenza A/PR/8/34 virus
Ulva lactuca	Sulfated polysaccharide	Inhibit Japanese encephalitis virus (JEV) infection in Vero cells
Lobophora		Inhibit the activity of HIV reverse transcriptase

variegata*, *Dictyota mertensii*, *Spatoglossum schroederi*, and *Fucus vesiculosus	**Fucans**	
Many species of marine algae	**Sulphated polysaccharides**	**Inhibition of replication of *Orthopoxvirus*, *flavivirus*, *herpesvirus*, *togavirus*, *rhabdovirus*, and *Arenavirus***
Gelidium cartilagineum	**Polysaccharides**	**Defends the embryonic eggs against influenza B or mump virus.**

Marine sponges

Antimicrobial Activity

Antibiotic-resistant bacteria, such as *Staphylococcus aureus*, pose a significant threat and are involved in the spread of serious diseases. Many antibiotics are now resistant to a wide range of bacteria, prompting the development of new antibiotic classes. Marine sponge crude extracts have varied antibacterial efficacy against marine and terrestrial bacteria. Sponge crude extracts have antibacterial action against both Gram positive and Gram negative microorganisms. Marine sponges were found to have around 800 antibacterial compounds. The antibiotic manolide was discovered to be one of the first sesterterpenoids isolated from the marine sponge *Luffariella variabilis*. Antimicrobial activity was tested on several species of sea sponges, which are given in the **Table 6**.

Table 6: Antimicrobial activity of marine sponges [22, 31, 32]

Species name	Major compound / Extract	Target species
Clathria compressa	**Clathric acid**	**Inhibit the growth of methicillin resistant *Staphylococcus aureus* ATCC 33,591(MRSA), *Staphylococcus aureus* ATCC 6538P and vancomycin-resistant *Staphylococcus aureus* (VRSA).**
Siliquariaspongia sp.	**Motualevic acid A Motualevic acid B Motualevic acid E Motualevic acid F**	**At a concentration of 10µg, the Compounds motualevic acid A and B exhibit strong activity against *Staphylococcus aureus*. At a concentration of 10µg, Motualevic acid A exhibit antibacterial activity against MRSA. At a concentration of 50 µg, Motualevic acid E exhibit weak antibacterial activity against *Staphylococcus aureus*. At concentrations of 2µg and 5µg, Motualevic acid F exhibit potent antibacterial activity against *Staphylococcus aureus* and MRSA respectively.**
Aplysia aerophoba*, *Verongia thiona	**Aerothionin**	***Mycobacterium tuberculosis***
***Plakina* sp.**	**Plakinamine A Plakinamine B (Steroidal alkaloid)**	***Staphylococcus aureus*, *Candida albicans*.**
Aplysina cavernicola	**Aeroplysinin and aerthionin and other dibromo and dichlorotyrosine derivatives**	***Bacillus subtilis* and *Proteus vulgaris***
Discodermia kiiensis/Lithistida	**Discodermins B, C and D (Cyclic peptide)**	***Bacillus subtilis***
Arenosclera brasiliensis	**Arenosclerins A-C (Alkyl pepridine alkaloid)**	***Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis***
Arenosclera	**Haliclona cyclamine E**	***Staphylococcus aureus*, *Pseudomonas aeruginosa***

brasiliensis	**(Alkylpiperidine alkaloids)**	
Axinella sp./Halichondrida	**Axinellamines B-D (Imidazo-azolo-imidazole alkaloid)**	***Helicobacter Pylori, Micrococcus Luteus***
Caminus sphaeroconia	**Caminosides A-D (Glycolipids)**	***Escherichia coli, Staphylococcus aureus***
Acanthostrongylophora sp	**6-hydroxymanzamine E (Alkaloid)**	***Mycobacterium tuberculosis***
Cribrochalina sp	**Cribrostatin 3 (Alkaloid)**	***Neisseria gonorrheae* (antibiotic resistant strain)**
Cribrochalina sp	**Cribrostatin 6 (Alkaloid)**	***Streptococcus pneumoniae* (antibiotic resistant strain)**
Aaaptos aaptos	**Isoaaptamine (Alkaloid)**	***Staphylococcus aureus***
Fasciospongia sp	**(–)-Microcionin-1 (Terpenoid)**	***Micrococcus Luteus***

Antiviral Activity

Because sponges are a rich source of antiviral property compounds, certain innovative ways are being used to introduce new antiviral medicines from marine sources, as well as numerous promising treatment possibilities. Bioactive substances with antiviral activity can be found in a variety of sponges. The researchers became interested in discovering novel compounds after screening and testing anti-HIV drugs from sponges. Many studies recently found that different sponges produce HIV-inhibiting chemicals. Avarol, for example, is a chemical that delays the development of HIV infection to a level. Despite the fact that many compounds have been proven to be anti-HIV agents, the mechanism of action remains unknown. Even with the introduction of HIV-inhibiting chemicals from sponges, they do not have a higher potential for combating AIDS than other viral infections. The antiviral activities of some of the marine sponge species are listed in the **Table 7**.

Table 7: Antiviral activity of marine sponges [22, 30, 31]

Species name	Major compound / Extract	Target species
Dactylospongia metachromia	**Metachromin A**	**At an EC_{50} of 0.8 µM Inhibit the Hepatitis B viral production**
Stachybotri sp.	**Stachybogrisephenone B Grisephenone A 3,6,8-trihydroxy-1-methylxanthone**	**Enterovirus 71 (EV71).**
Jaspis sp	**Jaspamide (Macrocyclic Depsipeptide)**	***Candida albicans***
Euryspongia sp.	**Eurysterols A-B (Sterols)**	***Candida albicans, Amphoterician B- resistant***
Monanchora unguifera	**Mirabilin B (Tricyclic guanidine Alkaloid)**	***Candida neoformans***
Spongosorities sp	**Hamacanthin A (Indole alkaloid)**	***Candida albicans***
Spongosorities sp	**Macanthins A-B (Indole alkaloid)**	***Candida albicans, Candida neoformans***
Agelas sp	**Agelasines and Agelasimines (Purine derivative)**	***Candida krusei***
Aaptos aaptos	**4-Methylaaptamine (Alkaloid)**	**HSV-1**
Theonella sp.	**Papuamides A–D (Cyclic**	**HIV-1**

	depsipeptides)	
Cryptotethya crypta	**Ara-A (Nucleoside)**	**HSV-1, HSV-2, VZV**
Dysidea avara	**Avarol (Sesquiterpene Hydroquinone)**	**HIV-1**
Xestospongia sp. Haplosclerida	**Haplosamates A and B (Sulfamated steroid)**	**HIV-1**
Halicortex sp	**Dragmacidin F (Alkaloid)**	**HIV-1**
Hamigera tarangaensis	**Hamigeran B (Phenolic Macrolide)**	**Herpes and polio virus**
Mycale sp	**Mycalamide A-B (Nucleosides)**	**A59 coronavirus, HSV-1**
Siliquariaspongia mirabilis	**Mirabamides A, C and D (Peptide)**	**HIV-1**
Stylissa carteri	**Oroidin (Alkaloid)**	**HIV-1**

Antimalarial Activity

Malaria is caused mostly by Plasmodium strains. Many antibiotics, including chloroquinone, pyrimethamine and sulfadoxine are resistant to multi-drug resistant plasmodium strains, making treatment extremely difficult. To combat multidrug-resistant plasmodium strains, new antimalarial medicines must be developed. Invitro antimalarial activity of terpenoid isocyanates, isothiocyanates, and isonitriles derived from sponges was found to be selective against *Plasmodium falciparum*. The antimalarial activity of some marine sponges are listed in the **Table 8**.

Table 8: Antimalarial activity of marine sponges [30, 31]

Species name	Major compound	Target species
Phakellia Ventilabrum	**Alkaloids**	**Antimalarial activity against *Plasmodium falciparum***
***Zyzzya* sp.**	**Bispyrroloiminoquinone alkaloid, tsitsikammamine C**	**Inhibit ring and trophozoite stages of the malaria parasite life Cycle**
***Zyzzya* sp.**	**Makaluvamines and damirones A**	**Potent growth inhibitory activity against both *Plasmodium falciparum* lines**
***Iotrochota* sp**	**N-cinnamoyl-amino acids, iotrochamides A and B**	**Antimalarial activity by Inhibiting *Trypanosoma brucei***
***Acanthella* sp./ Halichondrida**	**Kalihinol A (Isonitril-containing kalihinane diterpenoid)**	**Antimalarial activity against *Plasmodium falciparum***
***Hymeniacidon* sp**	**Diterpenoid β-lactam (alkaloid), Monamphilectine-A**	**Antimalarial activity against *Plasmodium falciparum***
Cymbastela hooperi	**Diisocyanoadociane (Tetracyclic diterpene)**	**Antimalarial activity against *Plasmodium falciparum***
Diacarnus erythraeanus	**Sigmosceptrellin-B (Norsesterterpene acid)**	**Antimalarial activity against *Trypanosoma gondii, Plasmodium falciparum***
Agelas oroides	**(E)-Oroidin (Alkaloids)**	**Antimalarial activity against *Plasmodium falciparum***
Plakortis simplex	**Plakortin andDihydroplakortin Cycloperoxidase**	**Antimalarial activity against *Plasmodium falciparum***
Haliclona sp./ Haplosclerida Cymbastela hooperi/ Halichondrida Diacarnus levii/ Poecilosclerida	**Manzamine A (Alkaloids)**	**Antimalarial activity against *Trypanosoma gondii, Plasmodium berghei, Plasmodium falciparum***

Antifouling Activity

Antifouling properties of natural sponge-derived chemicals were recently investigated for their less harmful effects. Sponge-derived compounds promote barnacle larvae settlement, prevent macroalgal fouling, and repel the blue mussel *Mytilus edulis galloprovincialis.* Chemicals with antifouling properties are noted in the **Table 9**.

Table 9: Antifouling activity of marine sponges [22, 30]

Species name	Major compound	Mode of action
Agelas sp.	Agelasine D	Prevent the settlement of larvae *Balanus improvises.*
Cymbastela hooperi	Diterpene isonitrile	At concentration 10 µg/mL, inhibit the settlement of the diatom *Nitzschia Closterium*
Haliclona sp.	Poly 3-alkylpyridinium salt Saraine-1 Haminol-2 Haminol-4	At EC_{50} = 0.19 µg/mL, poly-3 alkylpyridinium salt was potent to inhibit the settlement of the *Amphibalanus (Balanus) amphitrite*. with an EC_{50} of 0.53 and 0.28 µg/mL, Saraine-1 and haminol-2 equally inhibit the settlement of the larvae of *Amphibalanus* amphitrite respectively. At concentration of 10µg/mL. Haminol-2 and haminol-4 completely inhibit the settlement of *Amphibalanus amphitrite*
Haliclona sp. and *Reniera sarai*	poly 3-alkylpyridinium salts, saraine, and haminols	poly 3-alkylpyridinium salts inhibit the settlement of *Balanus amphitrite*. Cypris larvae, by reversible, nontoxic antifouling mechanism
Acanthella cavernosa/Halichondrida	Kalihinene X (Isocyanoterpenoid)	Inhibit larval settlement and metamorphosis of the barnacle larvae of *Balanus Amphitrite* at EC_{50}= 0.49 µg/ml
Acanthella cavernosa/Halichondrida	Kalihipyran B (Isocyanoterpenoid)	At IC_{50}= 0.85 µg/ml inhibit larval settlement of *Balanus Amphitrite*
Acanthella cavernosa/Halichondrida	10β Formarnidokalihinol (Isocyanoterpenoid)	Antifouling effect at EC_{50}= 0.095 µg/ml
Pseudoceratina purpurea/Verongida	Ceratinamide A and B (Bromotyrosine derivative)	Ceratinamide A and B show Antifouling effect against barnacle *Balanus Amphitrite* at EC_{50}= 0.10 µg/ml and 2.4 µg/ml respectively
Axinyssa sp./Halichondrida	Axinyssimides(Sesquiterpene) carbonimide dichlorides	Axinyssimides A show antifouling effect against barnacle *Balanus Amphitrite* at EC_{50}= 1.2 µg/ml. Axinyssimides B show 70% inhibitionat the concentration of 0.5 µg/ml. Axinyssimides C show more than 90% inhibition at the concentration of 0.5 µg/ml.

Antitumour Activity

Protein Kinase C inhibitors include several sponge-derived chemicals. Because of the regulation of phospholipase A2 activity, massive amounts of PKC enzyme are associated with the pathophysiology of arthritis and psoriasis, as well as tumour growth. PKC is the receptor protein for tumor-promoting phorbol esters, and PKC inhibitors prevent carcinosarcoma cells from attaching to the endothelium. Glycosylation of receptors, particularly fucose-containing residues, is important for carcinosarcoma cells and leukocytes to bind to endothelium receptors. Non-specific inhibitors are useful for treating cancer, but the main disadvantage is that they also harm healthy cells. Chemicals with antitumour properties are noted in the **Table 10**.

Table 10: Antitumour activity of marine sponges [22, 31, 32]

Species name	Major compound	Mode of action
Dactylspongia elegans T3	19-methoxydictyoceratin-A (Sesquiterpene quinines)	Anticancer activity against the human cancer cell lines DU145, SW1990, Huh7, and PANC-1.
Haliclona gracilis	Gracilosulfates A, B, C, D, E, F and G (Steroid)	Antitumor activity against human prostate cancer.
Pachypellina species	8-hydroxymanzamine A	Anti-tumor activity
Xestospongia sp	Renieramycin M (tetrahydroisoquinoline)	Inhibit progression and metastasis of lung cancer cells
Monanchora Pulchra	Monanchocidin (polycyclic guanidine alkaloid)	Induce cell death in THP-1 human monocytic leukemia cells, HeLa human cervical cancer cells.
Spongia sp.	Spongistatin-I (macrocyclic lactone polyether)	Inhibition of mitosis, Microtubule assembly and the vinblastine binding to tubulin result in cytotoxic cell death in various cancer cell lines.
Aaptos aaptos/Hadromerida	Isoaaptamine (Benzonaphthyridine alkaloid)	Anti tumour activity by Protein kinase C inhibition.
Hymeniacidonaldis/Halichondrida	Debromohymenialdisine (Pyrrole-guanidine alkaloid, prenylhydroquinone derivative)	Anti tumour activity by Protein kinase C inhibition.
Discodermia dissolute/ Lithistida	Discodermolide (Linear tetraene lactone)	Antitumour activity by Stabilization of microtubules.
Mycdle hentschett/ Poecilosclerida	Peloruside A (Macrocyclic lactone)	Antitumour activity by Stabilization of microtubules.
Plakinastrella sp./ Homosclerophorida	Elenic acid (Alkylphenol)	Antitumour activity by Topoisomerase II inhibition.
Leucetta cf. chagosensis	Naamine D Imidazole alkaloid	Antitumour activity by Nitric oxide synthetase inhibition.

Antiinflammatory Activity

Sponges have shown to be a good source of anti-inflammatory properties. Manolide is the first anti-inflammatory substance discovered in a marine sponge, and it has been demonstrated to be beneficial. The mode of action is based on the irreversible suppression of arachidonic acid release from membrane phospholipids by blocking phospholipase A2 from attaching to membranes. Lipooxygenase, another enzyme implicated in inflammation, was discovered to be inhibited by a few sponge derived chemicals. The Antiinflammatory activity of some of the marine sponges are listed in the **Table 11**.

Table11: Antiinflammatory activity of marine sponges [31]

Species name	Major compound	Mode of action
Luffariella variabilis/ Dictyoceratida	Manoalide (Cyclohexane sesterterpenoid)	Phospholipase A2 inhibitor
Dysidea sp./ Dendroceratida	Dysidotronic acid (Drimane sesquiterpenoid)	Phospholipase A2 inhibitor
Ircinia oros/ Dictyoceratida	Ircinin-1 and -2 (Acyclic sesterterpenoid)	Phospholipase A2 inhibitor
Spongia sp./ Dictyoceratida	Spongidines A-D (Pyridinium alkaloid)	Phospholipase A2 inhibitor
Petrosaspongia nigra/ Dictyoceratida	Petrosaspongiolides M-R (Cheilantane sesterterpenoid)	Phospholipase A2 inhibitor
Cacospongia scalaris/ Dictyoceratida	Scalaradial (Scalarane sesterterpene)	Phospholipase A2 inhibitor
Topsentia genitrix/ Halichondrida	Topsentin (Bis-indole alkaloid)	Phospholipase A2 inhibitor
Suberea sp./Verongida	Subersic acid (Diterpene benzenoid)	Lipoxygenase inhibitor
Jaspis splendens/ Astrophorida	Jaspaquinol (Diterpene benzenoid)	Lipoxygenase inhibitor

Antiparasite Activity

Antiparasitic and antimalarial activities have been discovered in marine sponge compounds against the parasites *Leishmania* and *T. cruzi,* which cause Leishmaniasis and Chagas disease, respectively. The Antiparasitic activities of some of the marine sponges are listed in the **Table 13**.

Table 13: Antiparasitic activity of marine sponges [22, 33]

Species name	Major compound /Extracts	Target species
Verongula rigida	**Alisiaquinone A Alisiaquinone B Alisiaquinone C Alisiaquinol 11-hydroxyaerothionin Purealidin B Aeroplysinin-A**	**11-hydroxyaerothionin Exhibit leishmanicidal activity against *Leishmania.* Compound purealidin B show anti-malarial activity against *Plasmodium falciparum* strain. Compound aeroplysinin-A inhibit the growth of the parasite *Trypanosoma cruzi.***
Latrunculia sp.	**discorhabdins A discorhabdins C dihydrodiscorhabdin C (Pyrroloiminoquinone Alkaloids)**	**Antiparasitic activity against D6 *Plasmodium falciparum***
Hyattella sp.	**Psammaplysin F (Bromotyrosine alkaloid)**	**Antiparasitic activity against Dd2 *Plasmodium falciparum* 3D7 *Plasmodium falciparum***
Sarcotragus sp.	**Aqueous extract ethyl acetate extract dichloromethane extract**	**Antiparasitic activity by targeting *Leishmania* major Promastigotes Stages**
Mycale laxissima Clathria echinata Agelas cerebrum	**Organic extract**	**Antiparasitic against *Plasmodium berghei***
Amphimedon	**organic extracts**	**Antiparasitic against *Trypanosoma cruzi* trypomastigotes**
Tethya ignis Tethya rubra Dysidea avara Mycale angulosa Condrosia reniformes	**acetone extracts**	**Antiparasitic activity against *Trypanosoma cruzi* epimastigote**
Pandaros acanthifolium	**acanthifolioside A acanthifolioside D acanthifolioside E acanthifolioside F (steroid glycosides)**	**Antiparasitic activity against *Leishmania donovani***
Axinyssa djiferi	**Glycosphingolipids: axidjiferoside-A, -B and -C glycosphingolipids**	**Antiparasitic activity against FCB1 *Plasmodium* falciparum**
Plakinastrella mamillaris	**Plakortide U Plakortides R Plakortides T (Endoperoxide polyketides)**	**Antiparasitic activity against FcM29 *Plasmodium* falciparum**
Plakortis halichondrioides	**plakortide E Endoperoxide Plakortis halichondrioides**	***Trypanosoma* bruci**

CONCLUSION

The demand for nutritious food has been increasing with increase in human population. Marine nutraceuticals are the innovative health benefit products which provide healthy living. Marine algae and sponges are one of the best natural sources to meet nutritive demands due to their good health benefits. They have wide range of bioactive compounds and metabolites which are responsible for the healthy living of the humans, because of which they are used as daily food supplements. The findings proved that the bioactive compounds and metabolites have many pharmaceutical applications such as antimicrobial, antiviral, antiinflammatory, antioxidant, anticancer, antifouling, anti-parasite agents which are used to treat many life threatening diseases.

Conflict of interest:

The authors declare that there are no conflicts of interest.

Author contributions:

All authors contributed to the preparation of the manuscript. Professor G. Rajitha contributed equally to the editing.

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