Review on Biomedical Applications of Marine Algae-Derived Biomaterials

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Abstract

Marine algae have gained substantial attention from various scientific and commercial fields. The reason behind its importance is due to the rich source of bioactive compounds like proteins, carbohydrates, lipids, and other pigments. Marine algae-derived carrageenans polysaccharides are used in food, medicine, cosmetic items, gelling, emulsifying, and stabilizing agents. The carrageenan has also photoprotective activity as it protects against the UVB-induced apoptosis in HaCaT cells and inhibits skin aging and cancers. Marine algae-derived macromolecules including polysaccharides and proteins have anticoagulant and photoprotective activities. The marine algae used in health sector is not limited to a food supplement only, rather, the derivatives from it are increasingly used in the biomedical application too. Different biological activities of marine algae as immunomodulatory, anti-tumor, anti-viral, anti-cancer, anti-aging, anti-oxidant, and anti-diabetic are discussed in this review. This mini-review is comprehensively based on the bioactivities materials from brown, red, green, and blue-green algae used in various biomedical fields.

Keywords
Marine Algae, Anti-Cancer, Anti-Inflammatory, Biomaterials, Biomedical, Polysaccharides, Photoprotective

1. Introduction

Marine algae are virtuous bases of nutrient food sources and bioactive secondary metabolites used in the pharmaceutical industry, biomedical field and also have valuable outcomes on human health. Commonly marine algae are grown in salty or brackish water, sunlight and rocky places rather than sand shingle shores or in a littoral zone. Among all marine flora and fauna, algae are the fastest-growing organisms on Earth and can grow in tropical, cold-temperate, and Polar Regions. In general, marine algae are divided into two categories; the 1st one is microalgae, which consist of dinoflagellates, blue-green algae, bacillariophyte, diatoms and the other is macroalgae (seaweeds), which contains green, brown, and red algae. Microalgae have potency to produced extremely high quantity of biomaterials that are used in biomedical fields. Nonetheless, red algae and their derived compounds have stronger biologically activity than other algae while seaweeds are the source of human food and gums. The Phycocolloides as like agar-agar, alginic acid and carrageenan are major components of red and brown algae cell walls which are mostly used in pharmaceutical field [1]. The algae are available in both microscopic and macroscopic forms. The green microalgae are the largest group among all marine algae, distributed under Phylum Chlorophyta. The green microalgae like Spirulina, Arthospira Platensis, Chlorella pyrenoidosa,
**2. Methodology**

A basic and thorough overview of the literature surveyed to identify the biomedical applications of Marine algae-derived biomaterial was conducted till 2021. Many offline and online databases were taken into consideration. The review articles and research papers published by various reputed publishers such as Elsevier, Springer, and Taylor & Francis imprints, Hindawi were considered as the data collection primary resource for this review article. Some online databases including NCBI, PubMed, Google Scholar, ProQuest, Scopus, and EBSCO were also accessed using keywords relating to the topic for data mining. The paid articles were accessed through the Centre Library facility of Siksha O Anusandhan University. The conference proceedings, magazines, WebPages, and book chapters were also reviewed and accessed as the other sources of literature to maximize the information about the current bottlenecks, the extent of research carried out, and the potential utility of the topic. In this review, we discussed about various bioactive materials of different marine algae. The current updates of marine algae-derived biomaterial are the main highlight of this review which will create a deep insight among the researchers about the updates and future research about the field of Marine Biotechnology.

**3. Nutritional Activity**

The Chlorella Vulgarisare (Chlorella) green algae from the phylum Chlorophyta contain protein approximately 50%-60% of its body weight. It is popular as a food supplement and widely used in the food industry due to its richness in protein and other essential amino acid. It also contains nutrients like β-1,3-glucan, β-carotene, vitamins B-complex and useful minerals like K⁺, Na⁺, Mg²⁺, Fe, and Ca²⁺. Most importantly a nucleoprotein found in Chlorella Vulgaris is used as a growth factor and tissue repairing. Similarly, various other bioactive molecules found in marine algae are alginate in Eisenia Bicycles and Macrocystis Pyrifera; Agar in Gelidiella Acrorosa; Retinol, Thiamine, Riboflavin, pyridoxine, B8, Folic Acid, Cobalamin, C, E in Spirulina Platensis; Vitamin C in Undaria Pinnatifida and Porphyra umbilicalis; Vitamin E in Nannochloropsis Oculata; Vitamin A, B1, B2, B12 and C in Scedesmus Quadriracuda; and Vitamin A, B1, B2, B6, B8 in Chlorella Pyrenoidosa [7]. Other side seen that, microalgae can produce polysaturated fatty acids with multiple double bonds (PUFAs) as Phaeodactylum, Monodus, Nitzchia, and Isochrysis have been used to produce PUFAs while Cryptococnidium, Nannochloropsis, and other algae species used in the food manufacturing industry[8].

Marine algae are commonly used in food industries to improve the quality of food products. In addition, algae are used in different meat products as pasty, steaks, frankfurters, sausages, and also used in fish foodstuffs, and oils for long-term storage. The algae are also used in cereal
or crops, as pasta, flour, and bread. Although, algae are used for the fermentation of foods as cheese, cream, milk desserts, yogurt, cottage cheese, and processed cheese. The algae such as Enteromorpha Himanthalia elongata, Undaria pinnatifida, and porphyra umbilicalis have potency to maintain the anti-oxidant activity of meat and cereal products. Meat and its derived products are rich in proteins and vitamins but sometimes seen that lack of dietary fiber and an excess amount of sodium in meat, which can cause serious health hazards for humans [9]. The addition of algae Sea Spaghetti (Halomonas elongata), Wakame (Undaria pinnatifida), and Nori (Porphyra umbilicalis) in meat can increase K, Ca, Mg, Mn and decrease salt content including fat and water binding properties. In addition, bread is a cereal-based product, to improve its quality green algae Ulva lactuca, and 2.5% of powdered Laminaria algae were added. Pasta is also a cereal-based product that has low protein and essential amino acids so high-protein additives are required to improve the quality of pasta. Studied that algae Undaria pinnatifida, rich in fucoxanthin was used 10% in pasta. In Indian brown algae, Sargassum marginatum was used in pasta for improved bio-functionality and quality. In Chinese, egg noodles were made by the addition of green algae Monostroma nitidum for better taste [10].

4. Biological Activities of Marine Alga

4.1. Anti-Microbial Activity

Marine algae have strong antibacterial, anti-fungal, and germicidal properties. The methanol extract of Sargassum Polycystum has strong antimicrobial activity. The methanol extract algae contained phenolic and alkaloid compounds which show antimicrobial activity [11]. The extract from Sargassum Polycystum has potentially inhibited the growth of bacteria like Escherichia coli, Proteus vulgaris, Erwinia caratovora, and Klebsiella pneumonia. Similarly, the extracts from Sargassum Polycystum can prohibit the growth of fungi like Aspergillus niger, Rhizopus Stolonifer. The chloroform and ethanol extract of Sargassum tenerrimum has the highest antibacterial activity against Staphylococcus aureus. The c-lactone malyngolide 14 was identified from the dichloromethane extract of the blue-green alga Lyngbya majuscula which inhibits Mycobacterium smegmatis & Streptococcus pyogenes. The Lyngaroside A 60 was identified from the green alga Codium iyengarii shows antibacterial activity. The main antimicrobial agent, which acts against the microbes of the blue-green algae is Lyngbya majuscula [12].

4.2. Anti-Oxidant and Anti-Inflammatory Activity

The carotenoids found in marine algae have antioxidant property which works as an immunity booster, wound healing, and other medical practices. The carotenoids from various marine algae have specialized health benefits as follows. The carotene isolated from Dunaliella shows both antioxidant and anti-inflammatory effects. Haematococcus pluvialis, Chlorella zofingiensis, and Chlorella vulgaris all have anti-oxidant, anti-inflammatory, and anti-tumor properties [13]. The antioxidant and anti-inflammatory activity are seen in zeaxanthin carotenoids that are produced from Dunaliella salina and Porphyridium cruentum as well as Chlorella protothecoids. Lutein has a specialized therapeutic role in age-related muscular degeneration (AMD), Atherosclerosis, retinal and neural damages. Although, Dunaliella salina, and Chlorella protothecoids derived carotenoids have anti-Oxidant and anti-Inflammatory activity. The lopophorins A 142 and B 143 were identified from the Caribbean brown alga Lobophora variegata (Dictyotales) which has anti-inflammatory activities and also potency inhibitors of tropical PMA-induced edema in the mouse ear. However, the microalgae Nannochloropsis Gaditana and Chlamydomonas debaryana produce oxylipins, which help to reduce inflammation [14].

4.3. Anti-Cancer Activity

The Violaanthin that has anti-inflammatory and anti-cancer potency is extracted from Dunaliella tertiolecta and Chlorella ellipsoidea. Fucocanthin which is found in Phaeodactylum tricornutum has antioxidant, anti-inflammatory as well as anti-cancerous properties. Curacin A 4 was identified from marine Cyanobacterium Lyngbya majuscle that is a new type of anticancer drug. The astaxanthin found in green microalgae Haematococcus Pluvialis, Chlorella zofingiensis, and Chlamydomonas nivalis has both anticancer & antioxidant properties. Most importantly the b-carotene found in Dunaliella salina has can specifically identify and destroy only neuroblastoma cells while unreflecting normal healthy cells, due to this ability, the Dunaliella has great importance in cancer therapy. The fucocanthin molecules from diatom are also very effective against inflammation, obesity, diabetes, malaria, and treatment of cancer cells by pro-apoptotic process [15].

4.4. Anti-Diabetic Activity

The Dieckol molecules isolated from a brown alga called Ecklonia cava are anti-diabetic due to their hepatoprotective role and anticoagulant activities. The report found from in vivo testing that the fucosterol was identified from the brown alga Pelvetia siliquosa shows anti-diabetic activity [16]. It was recommended to consume as a dietary supplement for the diabetic patient. Similarly, phlorotannins found in Asosophyllum nodosum can act against α-glucosidase and α-amylase that are helpful to digestion of starch and regulating blood sugar levels. The Ecklonia stolonifera species is used for anti-hypolipidemic activities due to the presence of molecules like
3.5. Anti-Ageing Activity

In contrast, marine algae exposed to solar radiation can produce anti-aging and photoprotective molecules. All the molecules have the potential to reabsorb ultraviolet rays like UVA and UVB and can prevent the production of free radicals. Some algae are the major source of phenolic compounds with photoprotective Shinorine, Porphyra-334, polythene, eckstolonol, eckol, sargachromenol, tetraprenyltoluquinol chromane meroterpenoid, setonemin, and sargaquinonic acid are examples of active compounds in this category. Edible brown algae including Ecklonia cava, Eisenia bicyclis, and Ecklonia stolonifera have another phenolic ingredient called eckstolonol that helps protect skin's HaCat cells from damage caused by sunlight. The Eckstolonol (200M) in table 1 can repair UV-B-induced damage by activating the enzymes catalase and superoxide dismutase, which aids in the removal of excessive ROS.

3.6. Anti-Viral Activity

Marine algae-derived Phenolic compounds like phlorotannin and dieckol. These molecules can help in the reduction of LDL cholesterol level and triglyceride while the increase in HDL cholesterol.

3.7. Anti-Fungal Activity

Cyanobacteria are known as blue-green algae because it contains chlorophyll a and its related compounds. The cyanobacteria can produce secondary metabolism as Biologically active nitrogenous chemicals and cyclic polyethers. An inhibitor of fungal plant diseases, Majuscuiamide C 16, was discovered in the blue-green algae Lyngby majuscula. The antifungal properties of dinoflagellates have been demonstrated by the discovery of Goniodomin A 23 from Goniodoma (Alexandrium) sp. and gambier acid from Gambierdiscus toxicus culture medium, respectively. The Capisterones A 67 and B 68 are identified from green alga Panicillus capitatus shows antifungal activity against the marine algal pathogen Lindra thallasiae. The meroditerpenoid was identified from the brown alga Cystoseira tamariscifolia and characterized as methoxybifurcarenone 138. It has antifungal activity against 3 tomato pathogenic fungi and antibacterial activity against Agrobacterium tumefaciens and Escherichia coli.

3.8. Immunosuppressive and Cytotoxicity Activity

According to several investigations found that Lyngbya majuscula, a type of blue-green algae native to Venezuela, contains immunosuppressive lipoproteins known as microcolins A 17 and B 18. Murine mixed lymphocytes and murine P388 leukemia are both suppressed in vitro by microcolins. Isorawsonol 30 is a phytochemical derived from the green alga Arrainvillia rawsonii. It has antifungal, photoprotective, and immunosuppressive properties. In addition, the marine alga provided Communesins A 34, B 35, and Penostatins A 36, B 37, C 38, D 39, and E 40 which shows Immunosuppressive and cytotoxicity activity. The aplysin-9-ene 291, epiaplysinol 292 and debromoepiaplysinol 293, were identified from red alga Laurencia tristicha. Debromo-epiaplysinol 293 shows cytotoxicity to the HeLa cell line.

3.9. Phytoprotective Activity of Marine Algae

Different species of marine algae have various chemical compositions. As red and brown algae are rich in sulfated polysaccharides such as carrageenan and fucoidan. The Carrageenans are thickening agents often used in food, medicine, cosmetic items, gelling, emulsifying, and stabilizing properties. Reported that, carrageenan bases skin products are antioxidant, detoxifying, cleansing, hydrating, and revitalizing activities. The carrageenan has also photoprotective activity as it protects against the UVB-induced apoptosis in HaCaT cells and inhibits the production of H2(ROS) because excess amounts of ROS can cause skin aging and cancers. The chemical structure of carrageenan is in Figure-1.

Brown algae have sulfated polysaccharide called fucoidan, the biological activity of fucoidan is in Table-1 and the chemical structure is in Figure-1. Fucoidan, an antioxidant found in brown algae such as Ecklonia cava, Undaria pinnatifida, Costariacrostata, and Fucus evanesce, has photoprotective properties. Fucoidan's photoprotective properties were discovered in UVB-irradiated human skin fibroblasts. As the MMP-1 activity is suppressed by fucoidan's photoprotective properties. UV-irradiated human skin has collagen degradation and photaging caused by MMP-1. Sulfated polysaccharides diminish NF-B expression by inhibiting NF-B, which in turn lowers MMP-1 levels. The photoprotective action of low-molecular-weight fucoidan is greater than that of UV filtering effects. Aside from that, carotenoids protect photosynthetic organisms like algae and cyanobacteria from the sun's ultraviolet radiation.
The carotenoid content in brown algae increased UVB exposure. The canaliculate plant *Pelvetia Canaliculata* and the fucoxanthin of brown algae have photoprotective activity against UVB-induced photoaging. Photoprotective activities on Human dermal fibroblasts and hairless mice exposed to ionizing radiation have both shown the effect *in vitro* and *in vivo*. Fucoxanthin's photoprotective activity is based on ROS scavenging as a mode of action. There's a UV-sensitive gene called Filagrin to inhibit wrinkle formation. Fucoxanthin can increase filagrin promoter activity in UV-induced sunburns [28].

Different species of red algae and their biological activities are discussed below; As Solieria chordates have the absorption of UVB light and free radical scavengers. This plant, *Porphyra umbilicalis*, can prevent UV-ray damaged skin from erythema [29]. This plant, *Porphyra yezoensis*, can modify the viability of UVB-exposed HaCaT [30]. *Solieria chordalis* can protect synthetic chlorophyll solution from UVB, while *Polysiphonia morrowii* can shield HaCaT from UVB-induced cell damage. The HACT can be protected from UVB-induced cell damage using *Chondracanthus tenellius*, and can prevent HaCaT from UVB-induced cell damage are *Bonnemaisonia hamifera*, *Lomentaria hakodatensis*, *Macrocystis pyrifera*, and *Porphyra columbina* [31]. The following section discusses various brown algae species and their biological activity. When used as a UVB irradiated human keratinocyte model, *Sargassum muticum* inhibits wrinkle formation on UVB-induced mice *in vivo* and as a human skin cell model *in vitro*. HaCaT can be protected by *Undaria crenata* against UVB-induced cell damage. Several plants can shield the developing zebrafish embryo from UVB damage, including *Lessonia vadose*, *Lessonia black*, *Ascophyllum nodosum*, *Saccharina latitissima*, *Fucus veneiculosus*, *Ecklonia maximum*, and *Durvillaea Antarctica* [32].
Figure 1. The Algae derived chemical compounds with their 3D structures.
### Table 1. List of marine algae and their derived biological active compounds.

| Sl.no | Algae species | Compounds | Biological activity | References |
|-------|---------------|-----------|---------------------|------------|
| 1     | Ecklonia stolonifera | Phlorofucofuroeckol A & B | Anti-inflammatory | 34 |
| 2     | Ecklonia. cava | Dieckol | Antitumor activity. | 35 |
| 3     | Ishige foliacea | Octaphlorethol A | Anti-inflammatory. | 36 |
| 4     | Cystoseira mediterranea, Pierocladia capillacea | Flavonoids & tannin | Antimicrobial. | 37 |
| 5     | Cymopolia barbata | 3,7-hydroxycymopolone | Antimitogenous. | 38 |
| 6     | Caulerpa racemosa | Racemosin A | Neuroprotective. | 39 |
| 7     | Caulerpa racemosa | Caulerprenylols A | Antifungal. | 39 |
| 8     | Ulva prolifera | pyrrolopipera-zine-2,5-dione | Antialgal. | 40 |
| 9     | Cymopolia barbata | 7-Hydroxycymopolone (PBQ2) | Chemotherapeutic, Anticancer. | 40 |
| 10    | Caulerpa racemosa and Caulerpa genus | Caulerpin | Anti-microbial. | 41 |
| 11    | Brown algae | Alginate | Antitumour, Antifungal. | 42 |
| 12    | Red algae | Carrageenan | Antioxidant, drug delivery. | 43 |
| 13    | Green algae | Ulvan | Anti-microbial. | 43 |
| 14    | Adenocystis, Utricularis, Grateloupia, longifolia, Laminaria, guryanovae, Codium, atlanticum, Monostroma nitidum | Sulfated polysaccharides | Anti-HIV, Anti-tumor, Anti-coagulant. | 44 |
| 15    | Arthospira platensi | Spirulan | Anti-coagulant, anti-thrombic activity. | 45 |
| 16    | Isochrysis galbana; chaetoceros, Skeletonema; Pavlova lutheri | Brassica sterol, Stigmasterol | Anti-bacterial, Hypocholesterolemic. | 46 |
| 17    | Ecklonia stolonifera, Ascophyllum nodosum, Ulva lactuca, palmaria palmate, Alaria esculenta. | Phlorotannin | Anti-hypertension, Anti-cancer, Anti-radio-protective, Anti-photocarcinogenic, Anti-diabetic, Anti-allergy, Anti-proliferative, Anti-antiaging, Anti-Matrix metalloproteinase. | 47 |
| 18    | Myagropsis, myagroides, Brown algae | Fucoxanthins | Anti-inflammatory, Anti -diabetic, Anti-angiogenic. | 44 |
| 19    | Pelvetica siliquosa, Sargassum Vulgare, Undaria, Pinnatifida, Himanthalia, elongate, Chondrus, Crispus, Porphyra, Ulva, and Porphyra species. | Fecosterols | Anti-cancer, Anti-diabetic, Anti-fungicidal. | 49 |
| 20    | Spirulina maxima | Eugenol, Hydroxy-cinnamic acids, Hydroxy benzoic acids, kaempferol, chrysin, galangin, Pinostrobin | Antioxidant, Anti-hepatoprotective. | 50 |

### 3.10. Anti-Coagulant Activity

The marine algae have anticoagulants properties because those contain sulphated glycosaminoglycans and include sulfated polysaccharides like heparin and heparan sulfate. In the algae group, the Phaeophyta (brown algae), Chlorophyta (green algae) and Rhodophyta (red algae) are the most abundant, among them anticoagulant polysaccharides have been isolated from red and brown algae are carrageenans and fucoidans, respectively. The homogenous polysaccharides of galactose or fucose are commonly found in red and brown algae. However, there was no report on green algae containing anticoagulant polysaccharides. But reported that Codium fragile ssp. tomentose, of green algae, has excellent anticoagulant polysaccharides. Recently reported that green algae are heterogeneous polysaccharides and homogenous galactan. Algal anticoagulant polysaccharides are used for antithrombin III (AT III) and heparin cofactor II (HC II) that are endogenous inhibitors, called SERPIN. In contrast, some algal anticoagulant polysaccharides are used directly to inhibit fibrin polymerization or thrombin activity without potentiating AT III and HC II. Algal anticoagulant polysaccharides can activate the fibrinolysis system and modulate endothelial cell functions. The bioactive compounds of marine algae show anti-platelet and
and tested by people. The accurate results to be known when it is sold in market so needs to long term research to achieve major compounds acts as photoprotection. From the past few decades, the healthy” with nontoxic materials. Different species of marine algae have several properties without any toxicity and a good safety profile. Marine algae are produced a wide variety of biological active compounds with significant effects. The marine algae-derived molecules are better than synthetic compounds used in various food and medicinal production. It is used in skincare products also as photoprotection. From the past few decades, the studies on the potential use of marine algae in human health benefits have been increased the importance in various sectors. Microalgae-derived compounds have high demand in pharmaceutical, nutraceutical, cosmetic, animal feed, biological waste treatment, and other multifunctional activities due to the richness in bioactive molecules. Microalgae have the potential activity to treat cancer, inflammation, Alzheimer’s, CVDs, malaria, leishmaniasis, TB, HIV etc through major sources of natural bioactive compounds like carotenoids, PUFAs, proteins, polysaccharides, glycolipids. It was also found that different biologically active compounds from marine algae-like aflatoxins, dolestatins, majusculamides, carotenes have an excellent health benefit. So that researchers should be exploring the potential use of bioactive compounds from marine algae in advanced biomedical applications and field of biotechnology. Algae-based biomaterials show a prominent future in pharmaceutical and cosmeceutic fields. But still there is no clear evidence found about bioactive compounds in algae so needs to long term research to achieve major compounds of algae and that can be used in biomedical applications, the accurate results to be known when it is sold in market and tested by people.

5. Conclusions

Marine algae have potential source of bioactive substances in the medical and cosmetic fields. Marine algae-derived compounds have unique chemical structures with excellent biological activities and are also “natural and healthy” with nontoxic materials. Different species of marine algae have several properties without any toxicity and a good safety profile. Marine algae are produced a variety of biological active compounds with significant effects. The marine algae-derived molecules are better than synthetic compounds used in various food and medicinal production. It is used in skincare products also as photoprotection. From the past few decades, the studies on the potential use of marine algae in human health benefits have been increased the importance in various sectors. Microalgae-derived compounds have high demand in pharmaceutical, nutraceutical, cosmetic, animal feed, biological waste treatment, and other multifunctional activities due to the richness in bioactive molecules. Microalgae have the potential activity to treat cancer, inflammation, Alzheimer’s, CVDs, malaria, leishmaniasis, TB, HIV etc through major sources of natural bioactive compounds like carotenoids, PUFAs, proteins, polysaccharides, glycolipids. It was also found that different biologically active compounds from marine algae-like aflatoxins, dolestatins, majusculamides, carotenes have an excellent health benefit. So that researchers should be exploring the potential use of bioactive compounds from marine algae in advanced biomedical applications and field of biotechnology. Algae-based biomaterials show a prominent future in pharmaceutical and cosmeceutic fields. But still there is no clear evidence found about bioactive compounds in algae so needs to long term research to achieve major compounds of algae and that can be used in biomedical applications, the accurate results to be known when it is sold in market and tested by people.

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