

Discovery of Novel and Biologically Active Compounds from Algae

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Abstract

The identification of new therapeutically active constituents from algae is generating growing attention due to the unique makeup of these organisms and the potential for widespread industrial use of these constituents. Recent study has concentrated on algae, which have a novel biochemical proclivity and a diverse variety of possible commercial uses, as a provider of novel biologically active constituents. The growing number of researchers are becoming interested in identifying novel physiologically active chemicals from algae, owing to its unique composition and the potential for vast commercial uses. It is very essential to identify the organisms of those species that produce bioactive secondary metabolites that could be a potential source for new drug development. A variety of constituents, such as carbohydrates, minerals, oil, proteins along with polyunsaturated fatty acids, are found in algae preparations. Additionally, biologically active constituents such as antioxidants (tocopherols or vitamin E), vitamin C and pigments (like phycobilins, carotenoids and chlorophylls) are found in algae preparations. These biologically active compounds possess different therapeutic properties, such as antimicrobial (antibacterial, antiviral, antifungal), antineoplastic, antioxidative and anti-inflammatory properties. They also have the potential to be used as food by humans. Algae have been discovered to be a significant source of physiologically active chemicals that may be used in a variety of goods for animals, plants, cosmetics, and medicines, among other things.

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1.1 Introduction

Water occupies almost 70% of Earth's surface. Therefore, it is a tremendous resource for the identification of novel/unique compounds with potential therapeutic uses. Over the last several decades, a vast variety of new chemicals obtained from marine creatures with pharmaceutically therapeutic benefits have been discovered. Because of this, marine resources are considered a promising source of new therapeutically active chemicals not only for the creation of active pharmaceutical ingredients but also for the development of food items [1].

The marine environment has a diverse range of fauna (sea hares, fishes, soft corals, sponges, nudibranchs, tunicates, sea slugs, bryozoans, echinoderms, shells, along with prawns) and flora (microorganisms such as micro/macroalgae, cyano- and actinobacteria, bacteria, fungi, halophytes). Among the most remarkable characteristics of marine life is the close connection that exists between different groups of creatures in order to enable them to adapt to the harsh and tough ocean circumstances that are significantly different than those that exist in a given ecosystem [2]. Phytoplankton (microalgae) have received tremendous interest nowadays because they are seen as a continuous raw material for producing a range of bioactive constituents. There are many different types of compounds that could be utilized in nutraceuticals, pharmaceuticals and as ingredients in some products like cosmetics. Some of these include terpenoids, amino acids, phycobiliproteins [3], fatty acids, chlorophylls, steroids, phenolic compounds, halogenated ketones, vitamins, and carotenes [4]. Photosynthetic microorganisms are known as cyanobacteria. They are Gram-negative and abundantly distributed throughout the environment. In various types of industries, including biofuel, nutrition, agriculture, and medicines, etc., they have a huge spectrum of biotechnological applications to offer [5].

Micro- and macroalgae (seaweeds), which make up the majority of marine algae, have possible potential use in different areas of biomedicine and marine pharmacology. Nowadays, tissue culture technologies are an up-and-coming area. As significant marine biological resources, algae are abundant on shallow, coastal, and backwater substrates and may be found in great quantities in shallow, coastal, and backwater habitats. It has also been discovered that algae may grow on a variety of solid objects such as rocks and stones as well as on dead corals, pebbles, and other small objects.

A surprising amount of agar is produced by algae in intertidal and shallow water, with a total production of about 6000 tonnes of total agar yield. Investigations have demonstrated that unrefined and refined compounds generated from marine algae showed significant antimicrobial action *in vitro* against a broad range of both Gram-negative as well as Gram-positive pathogenic microorganisms and also showed *in vivo* activity [6]. In addition to being interesting as research targets, because of their potential therapeutic qualities, the natural significant bioactive chemicals derived from microalgae are anticipated to be commercialized in the next several years [3].

In the aquatic environment, marine algae, including dinoflagellates (unicellular along with biflagellate organisms) and phytoplankton, are symbiotic in corals, seaweeds, and sea anemones, among other things. A wide variety of seaweeds are divided into four groups: Chlorophyta (means green algae), Rhodophyta (means Red algae), Phaeophyta (means Brown algae), and Cyanobacteria (certain filamentous Blue-green algae) [1]. Neoplasm (cancer, carcinoma or malignancy), diabetes, metabolic syndrome, obesity, chronic stress, stroke, immunological diseases and chronic respiratory sickness are all contributing to an increase in global morbidity and death. Dietary modification along with lifestyle modification are currently suggested as potential approaches to preventing or treating various ailments [3]. Furthermore, foods containing bioactive constituents may have the ability to behave as necessary nutrients. Antibiotics were formerly considered to be “magic bullets,” but by picking certain bacteria for treatment, they might end up becoming a contributing factor to the spread of illness [7].

1.2 Microalgae-Derived Natural Products

Microalgae are microorganisms of only one cell in size that flourish in salt water. It also thrives in freshwater environments. Their diameter or length ranges from 3 to 10 millimeters, and they are available in a variety of forms and sizes. Microalgae include both bacterial and eukaryotic species, and the term “microalgae” applies to both [8]. Cyanobacteria are structurally comparable to bacteria in terms of their composition. They are classified as microalgae, however, because of the presence of chlorophyll and other photosynthesis-related compounds in their composition. Known as green algae due to the fact that they have the same quantities of chlorophyll-a and chlorophyll-b as green plants [9, 10], they have been studied extensively.

Microalgae produce biocompounds by utilizing light energy along with inorganic nutrients (nitrogen, phosphorus, carbon dioxide, and other elements) and are classified as autotrophic microorganisms. They include nutrients of great nutritional value, such as proteins, lipids, carbohydrates, polymers, and pigments, as well as medicinal properties. In recent research, it has been shown that microalgae may create a vast variety of chemical constituents (compounds) with diversified biological functions, including phycobilins, polysaccharides, polyunsaturated fatty acids, proteins, sterols, carotenoids, and vitamins, among other substances [10].

Phaeophyta, i.e., brown algae, are a well-known commercialized alginate source due to their brown color. Alginates are straight, long chains of amino acids. They consist of residues of the amino acids. Alginates are usually observed in toothpastes and ice creams, where they are employed as thickening agents, foam stabilizers, and preservatives. When taken orally, a low-density agonic acid gel formed from alginate salts operate as a “raft” that floats over the stomach content, similar to corresponding gelatine. As a result, stomach acid is prevented from refluxing into the esophagus. Therefore, sodium/magnesium salts of agonic acid are included in variety of compound antacid formulations, such as Favicon (Reckitt & Coleman) or Alicen (Rorer), among others [11]. There are wide variety of applications of algae, from biofuel production, in particular bioethanol, macro- and microalgae fermentation, to enzyme extraction in the paper, textile, and detergent industries, and laboratory applications [12].

Bioactive constituents are substances that are physiologically active in the human body and have functional characteristics in the body. Many biologically active compounds that have the possibility of being used as useful components are being developed and manufactured, including polyphenols, phycocyanins, fatty acids, carotenoids, and other polyunsaturated compounds.

1.3 Bioprospecting for New Algae

Numerous new compounds were found in marine algae during the previous six decades, and a vast variety of these chemicals have been shown to have intriguing biological activities [13]. When it comes to the isolation of new species, there are numerous obstacles to overcome; the dearth of information regarding the metabolite demands of growth genus, pH, need for consumption of certain nutrients (e.g., sulphate, nitrogen sources, and phosphorus), and other growth parameters, like crop density and temperature, among others. It is critical to understand the chemical interactions

between strains that have not been thoroughly described or novel strains in order to maximize their production [3]. In 2009, Ou *et al.* [14] found that clinical studies are useful for concentrating efforts on extracting protective bioactive substances with specific therapeutic properties using various pharmacological models. The method of developing novel molecules as therapies, from preclinical validation through FDA clearance, is lengthy, laborious, and costly. A bioactive molecule with high therapeutic promise requires preclinical investigations, human clinical trials [14, 15], along with regulatory process permission from the FDA following post-trial for commercialization and marketing in the contemporary environment [15]. Keep in mind that not all of the medicines included in the database have been authorized by the Food and Drug Administration (FDA), but they are all recognized only after evaluation of biological action. In many other countries, medications are permitted for clinical use; however, in the United States, none of them have been approved. Animal and human clinical trials are conducted in order to evaluate the therapeutic property of the isolated constituents in various periods of development, using a variety of pharmacological models to do so [3]. Over 18,000 bioactive compounds have been identified to date. Despite this, only six drugs derived from marine sources have been clinically authorized and commercialized. Moreover, only a few algal isolates have been acknowledged clinically. Brentuximab vedotin, marketed under the trade name Adcetris, is, for instance, an antibody-drug combination made from bioactive molecules [16] derived from an algal source used to treat non-Hodgkin lymphoma [17]. Fucoidan extracts have anti-aging action on the human body in clinical double-blind trials [18]. Interestingly, the first antiviral algal component found from *Eucheuma/Chondrus*, a red edible alga, is iota-carrageenan (Carragelose). Numerous derivatives of dolastatin have been developed and are being clinically investigated in EMA tests and by the FDA [19]. These derivatives names are glembatumumab vedotin, depatuxizumab mafodotin, and pinatuzumab vedotin. It has been revealed in clinical studies that EPA, coupled with DHA, are essential amino acids from marine macroalgae that have clinical use [20]. As feed additives and immunological boosters, Ocean FeedTM from macroalgae and TascoTM from *A. nodosum* were already on the market [21].

There have been several well-publicized incidents in the UK of livestock and other animals being poisoned as a result of cyanobacteria contamination in their drinking water. *Anabaena flosaquae* is a plant that produces the alkaloid named anatoxin-a, which is a neurotoxin that depolarizes neuromuscular blocking and has both nicotinic and muscarinic action [5, 22].

1.4 Therapeutically Essential Natural Products

Marine organisms, which include both animals and plants, are the richest sources of bioactive constituents, which have a diverse variety of pharmacological actions, including free radical scavenging, anticancer, neuroprotective, analgesic, antimicrobial, and immunomodulatory properties, among other activities. Underwater drugs provide an alternate source for meeting the growing need for safe, effective, and low-cost medications, which is increasing in tandem with the world population's dramatic rise. In developed nations, the disease of neoplasm (cancer) is among the most prevalent causes of mortality, whereas communicable infections are the main cause of mortality in impoverished (developing) nations. Despite the significant advances in neoplasm or tumor therapy that have occurred over the past three decades, there is still a pressing need for novel medicines in the field of cancer biology, particularly in the relatively untapped field of marine anticancer chemicals, to combat cancer [2].

Chlorella and *Spirulina* are the most common microalgae species found on the market, and they dominate the whole market. The first is a green microalga that includes microalgae and also macroalgae, part of the broad phylum of Chlorophyta [12].

Polyketides, alkaloids, cyanopeptides, isoprenoids and other metabolites are among the cyanobacterial natural products classified according to their metabolic origins. While much of the research was focused on toxicity, many studies also have revealed that cyanobacteria create chemicals of considerable pharmaceutical and biotechnological importance. Forty percent (40%) of lipopeptides, others are less than 10% (e.g., fatty acids, amino acids, amides, and macrolides) make up cyanobacterial compounds. Therefore, Cyanobacteria activity is dominated by lip peptides such as cytotoxic (41%), antitumor (13%), antiviral (4%), and antibiotics (12%). The remaining 18% of cyanobacterial activity includes antimalarial, antimetabolic, and immunosuppressive agents, herbicides, antifeedant, and multi-drug resistance reversing agents, among others [23].

Various types of Blue-green algae are available in the market as organic algae nutraceuticals, as well as a source of pharmacologically important substances. Examples of such species are *Spirulina*, *Chlorella* and *Aphanizomenon flos-aquae*. *Spirulina* sp. is a kind of blue-green algae that is found in the ocean. Lipids, chlorophyll, protein, carotenoids, minerals, vitamins, and vibrant colors are all rich in this plant's composition. Moreover, they might contain helpful probiotic components [24]. As well as other carotenoids, minerals (including Ca and Fe) and B vitamins

(including B12), *Spirulina* sp. is a wonderful abundant source of potassium, calcium, magnesium, iron, selenium and zinc. As an added bonus, important component fatty acid is beneficial in potentiating hair and skin growth, regulating metabolism and maintaining bone health. It also ensures proper functioning of reproductive system. Numerous minerals and vitamins have powerful antioxidant activities that assist in the elimination of toxins from the environment and the prevention of diseases. Cyanobacteria have recently attracted the public's curiosity due to their high concentrations of bioactive chemicals and their potential as dietary supplements. They also serve as a model for organisms belonging to some very promising categories of organisms in terms of the production of bioactive chemicals. Scientific evidence demonstrating bioactive chemicals produced from blue-green algae may show therapeutic promise in the treatment of illness and health issues in both human clinical trials and animal clinical studies [1].

Agars as well as carrageenan are generated from species of red algae. Both the agents are utilized as gelling, thickening, and emulsifying agents, and are the most significant products obtained from red algal species. Agar is also utilized as a microbiological culture medium, and agarose, which is a component of nutrient agar used for microbial growth, is also utilized in electrophoresis, immunodiffusion, and gel chromatography, among other applications. It's also used as a hydrogel in the surgical dressing by Geistlich, which is another use. A carrageenan implant is a substance used in the pharmaceutical industry to induce inflammation in models for animal testing. It may be utilized to evaluate prospective anti-inflammatory and anti-arthritis medicines to produce edema. According to Blunden and Gordon [11], the gastrointestinal system of primates does not absorb high molecular weight carrageenans, and as a result, they are believed to be acceptable additions for human consumption, given that the molecular weight is tightly controlled.

1.5 Screening for Bioactive Constituents

Multidisciplinary approaches are needed for the determination of bioactive constituents. The advancement of analytical and molecular methods is a critical ongoing process that is required as a precondition for the targeting of novel products by means of high-throughput strategies. Public and private interest has been growing over the last few decades, along with their investments in marine biotechnology, which has further increased the possibility of generating information and collecting huge amounts

of data to elaborate a better understanding of different cellular processes and mechanism of biological actions. Furthermore, marine biotechnology tends to utilize genomics, transcriptomics, proteomics, metabolomics, metagenomics, and metatranscriptomics, etc. [25], in conjunction with heterologous expression or genetic engineering to identify potential bioactive species and increase the required constituents/substances production [26].

A “test first” approach or an “isolate first” method is used in the screening process of natural goods, respectively. Natural bioactive components have been discovered using both approaches, and a recent trend has been to advocate the use of a fusion method, in which extracted or fractioned extracts are evaluated for the presence of biologically active elements. Bioassays are only utilized when the extracts demonstrate a high level of biological activity [27]. In order to isolate or identify fractions of extracts for chemical characterization, a number of techniques might be utilized. One of these techniques is liquid chromatography–mass spectrometry (LC-MS) and another is nuclear magnetic resonance (NMR). If novel constituents are identified, they should be refined as well as evaluated utilizing biological tests. Ideally, those tests should be reliable, repeatable, quick, cost-effective, simple to run, and sensitive, and should also be reproducible [3].

Microorganisms play an increasingly significant role in modern life, since they have evolved into essential components of a number of human life functions, such as digestion and food assimilation, among others. They also focus on human well-being by providing diversified foods, chemicals, and medications. Many microbiological pathogens, including fungi, protozoa, viruses, and bacteria, are responsible for serious illnesses despite the fact that effective management strategies are available. Bacteria and fungi are responsible for the spoilage of food goods [6]. De Vera *et al.* carried out experiments on more than 30 marine microalgae strains (haptophytes, dinoflagellates, chlorophyta, and heterokontophytes) in order to obtain extracts for evaluation of biological activity. As part of their research, they chose a number of intriguing samples for additional investigation of marine bioactive compounds. The unialgal isolates were kindly provided by the Oceanographic Center of Vigo. The available strains were cultured in the lab environment to determine their viability. Cell-free culture medium extract and biomass extract (two types) were produced from each strain. In order to get knowledge about antibacterial, antiproliferative, and anti-cancer (apoptotic) characteristics, these two extracts were further analyzed in order to get information on these qualities [28].

As per the current scenario on the non-selective and unsystematic widespread use of antibiotics as antimicrobial agents, a new generation of antibiotic-resistant and genetically modified microorganisms has emerged, posing a serious threat to the treatment of infectious diseases. The negative consequences and side effects of frequently used antibiotics, as well as the increasing prevalence of infectious diseases, have fueled the pursuit of novel antimicrobial agents from diversified sources from the marine environment [6].

1.6 Extraction Methods

Various methods or techniques can be utilized to separate potential therapeutically or biologically active constituents from different varieties of algal biomass. Various extracting agents were utilized to extract soluble constituents derived from the microalgae matrix. The simplest approach is to separate algal powder using water or organic solvents for large-scale samples, with the latter being the preferred method. The extraction rates vary from 8 to 30% of the dry algal yield under these conditions [29].

New types of extraction methods, like enzymolysis and extraction aided by a microwave, have, however, recently emerged. The first has impressive impacts, with high catalytic effectiveness characteristics, high specificities, mild reactive and maximum efficiency [30]. Moreover, there were several advantages to using the latter technique, including shorter processing times, the use of less solvents, greater extraction rates, and the production of better low-cost products [31, 32]. Complementary to the investigation of soluble chemicals, cell-binding compounds (CBCs) that are attached to the cell wall and cannot be easily isolated by applying the conventional methods of isolation with aqueous solvents, are also being investigated.

This could also limit the study of marine-derived active components and their potential industrial applications. Of interest is the enzyme digestion of algae, which produces high biological yields compared to water and organic extracts [33], and which exhibits improved biological activity. Michalak and Chojnacka reviewed an examination on the use of enzyme assistants using seaweed as an alternate approach for increasing the recovery of industrially valuable chemicals from the sea [30].

Recent extraction methods extract biologically active constituents without causing any loss of that activity. These are supercritical fluid extraction (SFE), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE). Among others, enzyme-assisted extraction (EAE) and pressurized liquid extraction (PLE) also have the advantage of extracting

therapeutically active constituents. Moreover, this type of extraction method is distinguished by a larger yield of extraction, a shorter processing time, and, as a result, is more environmentally friendly as compared to previous extraction methods. The extraction of soxhlet, as well as liquid–liquid extraction along with solid–liquid extraction, are all examples of traditional extraction methods (SLE) [34]. Their primary disadvantage is the use of a huge quantity of solvents (many of which are hazardous) and the large amount of time needed for isolation [35].

Starting a decade ago, there seemed to be a substantial rise in the use of alternative techniques to replace traditional methods largely due to the numerous advantages of new extraction techniques. As per number of authors, new green technologies (e.g., higher yields) are superior to extraction by organic solvents, which incorporates the release of solvents. These solvents could be potentially hazardous for the environment and can also cause hydrothermal stress to extracts in terms of functional properties. The degradation of thermally labile compounds may also result from the high-temperature processing [36]. For instance, in the matter of the SFE utilization with carbon dioxide, the yield of the lipid removal was higher than in the case of Soxhlet solvent.

Because of the numerous advantages of new extraction techniques, it has been noticed that they have increasingly been used to replace old approaches in recent years. The superiority of new green technologies (e.g., better yield) over extraction techniques by organic solvent has been demonstrated by numerous authors. As a result of hydrothermal stress, organic solvent extraction entails the release of potentially toxic solvents into the surrounding environment. The functional characteristics of the extracts were severely harmed as a result of the release of potentially hazardous solvents. High-temperature processing can cause the deterioration of components that are thermally labile as well as the degradation of other constituents [36]. For example, when utilizing SFE with CO₂, the amount of lipid extracted from *Sargassum hemiphyllum* was greater than when using the Soxhlet solvent extraction technique with chloroform/methanol [37]. Tierney *et al.* discovered in their research that PLE was more efficient than standard SLE in the extraction of polyphenols using a water:acetone (20:80) mixture [38]. Denery *et al.* also had a parallel observation that compared to conventional solvent extraction techniques, PLE displayed more or equivalent carotenoids extraction abilities from *Haematococcus pluvialis* as well as *Dunaliella salina* [39]. Pasquet *et al.* examined extraction of pigment from two marine microalgae using two different approaches (one is cold and hot soaking and another is ultrasound-assisted extraction). Due to its high rate, uniform heating, reproducibility, and higher separation rates,

MAE has been selected as the most effective pigment extraction technique [40]. Authors investigated the emerging green technologies (such as MAE, SFE and PLE) being more capable of replacing traditional organic solvent extractions. Extraction with SFE is one of the most widely utilized methods of extraction on an analytic and preparatory scale nowadays [41]. Aim of this chapter is to show the unique qualities of biologically active constituents and their wide applications obtained from algal biomass. The utilization of extracts from various algae is widely described in different areas of food, nutraceuticals and fuel manufacturing. It also explains the application in agriculture (plants and animal products) and cosmetics of algal extracts.

New extraction techniques are widely used in several industries for obtaining algal extracts such as SFE, UAE, MAE, PLE, EAE, etc. These techniques protect against degradation of the bioactive constituents isolated from algae. Algae's unique properties allow for a wide range of applications to be developed. They contain a high concentration of kilo grains (such as eicosapentaenoic acid, docosahexaenoic acid, β -linoleic acid) and in components such as polyunsaturated fatty acids (PUFAs) protein, minerals, carbohydrates, fats, oil, (e.g., docosahexaenoic acid, eicosapentaenoic acid along with γ -linoleic acid), in addition to the amount of bioactive constituents. These bioactive constituents are polyphenols, carotenoids, terpenoids, and tocopherols, which have antiviral, antibacterial, antifungal, antioxidative, anti-inflammatory, and antitumor activities. For plants, animals and human beings, algal extracts generated in solvent-free conditions or algal extracts obtained from minimal use of solvents are safe. These all are used in modern agriculture for three different categories:

- Animals (feed additives),
- Plants (bioregulators, biostimulants, fertilizers), and
- Humans (food, cosmetics, pharmaceuticals) [31, 42].

1.7 Biosynthesis and Biological Activities

Due to the influence of time-course and cohabitation on biological substances, biochemical pathways have been developed to the point where many microalgal lines now assemble a large number of distinct compounds. Despite the fact that secondary plant metabolites are more comprehensive than algae-derived metabolites, the diversity of secondary algal-derived metabolites is orders of magnitude more than that of soil plants [5, 3]. Bioactive substances are additional nutritional components found in small

Table 1.1 Algae and cyanobacterial constituents with potential biological action.

Name of microalgae	Bioactive compounds	Biological action	Reference
<i>Arthrospira platensis</i> (also known as <i>Spirulina platensis</i>)	PUFAs (n-3) fatty acids, oleic acid, linolenic acid, (vitamin E), phytol, palmitoleic acid, sulfated polysaccharide	Antiviral action	[46–49]
<i>Botryococcus braunii</i>	Carotenoids, linear alkadienes	Antioxidant action	[50, 51]
<i>Caulerpa racemosa</i>	Polyphenols	Antioxidant action	[52]
<i>Chlorella ellipsoidea</i>	Zeaxanthin, violaxanthin	Anti-inflammatory action, anticancer action	[53, 54]
<i>Chlorella minutissima</i>	Eicosapentaenoic acid (EPA)	Antioxidant action, cholinesterases inhibitory action	[48]
<i>Chlorella protothecoides</i>	Zeaxanthin, canthaxanthin, lutein	Anti-inflammatory action, antifungal action	[55–57]
<i>Chlorella pyrenoidosa</i>	Sulfated polysaccharide, lutein	Antiproliferative action	[49]
<i>Chlorella</i> sp.	Carotenoids poly-unsaturated fatty acids, sulfated polysaccharides, sterols	Immunostimulant action, antitumor action, antioxidant action	[49, 53, 58, 59]
<i>Chlorella vulgaris</i>	Canthaxanthin, peptide, astaxanthin, oleic acid	Antioxidant action and antitumor action	[48, 53]
<i>Chlorella zofingiensis</i>	Lutein, astaxanthin	Anti-inflammatory action	[60, 61]

(Continued)

Table 1.1 Algae and cyanobacterial constituents with potential biological action.
(Continued)

Name of microalgae	Bioactive compounds	Biological action	Reference
<i>Cystoseira abies-marina</i> , <i>Halopitys incurvus</i>	Polyphenols, neo-antioxidants, and amino acids	Antimicrobial action and antioxidant action	[62]
<i>Dunaliella salina</i>	β -carotene (both trans and cis geometric isomers), oleic acid, palmitic acid, linolenic acid	Antioxidant action (restores the activity of hepatic enzymes)	[48–50, 63]
<i>Dunaliella tertiolecta</i>	7-Dehydroporiferasterol, ergosterol, Oxcholesterol acetate	Action on the nervous system	[64]
<i>Eucheuma spinosa</i>	Different types of galactose units	Antioxidant action	[65]
<i>Gelidium pusillum</i>	R-phycoyanin and R-phycoerythrin	Hypocholesterolemic action, antioxidant action, antineoplastic action, anti-inflammatory action, and hepatoprotective action	[66]
<i>Haematococcus pluvialis</i>	β -Carotene, oleic acid, astaxanthin, lutein, zeaxanthin, canthaxanthin	Antioxidant action	[46, 67, 68]
<i>Himanthalia elongata</i> <i>Hormosira banksii</i>	Polyphenols, polysaccharides	Antiviral action	[69, 70]

(Continued)

Table 1.1 Algae and cyanobacterial constituents with potential biological action.
(Continued)

Name of microalgae	Bioactive compounds	Biological action	Reference
<i>Isochrysis galbana</i>	Cholest-5-en-24-1,3-(acetyloxy)-, and 3 β -ol Ergost-5-en-3 β -ol, etc.	Antitubercular action	[71]
<i>Laurencia obtuse</i>	Phenolic constituents	Antioxidant action	[72]
<i>Lyngbya majuscula</i>	Lipopeptides	Antitumor action	[73, 74]
<i>Nostoc ellipsosporum</i>	Protein	Antiviral action	[75]
<i>Nostoc spongiaeforme</i> , <i>Nostoc linckia</i>	Borophycin and cryptophycin	Antibacterial action	[48, 76]
<i>Nostoc</i> sp. GSV 224	Cyclopeptide	Antineoplastic action	[77]
<i>Saccharina japonica</i>	Fucoxanthin, polyphenols, carotenoids, and phlorotannins	Antineoplastic action and antioxidant action	[78–80]
<i>Sargassum muticum</i> , <i>Sargassum vulgare</i>	Polyphenols, neo-antioxidants, amino acids	Antimicrobial action and antioxidant action	[62]
<i>Sargassum thunbergii</i>	Polysaccharides	Antioxidant action and antidiabetic action	[81]
<i>Scenedesmus bajacalifornicus</i>	Polyphenols, flavonoids and alkaloids	Antioxidant action, antidiabetic action, anti-inflammatory action	[82]
<i>Scytonema varium</i>	Polypeptide constituents	Antiviral action	[83]

(Continued)

Table 1.1 Algae and cyanobacterial constituents with potential biological action.
(Continued)

Name of microalgae	Bioactive compounds	Biological action	Reference
<i>Skeletonema marinoi</i>	Nucleoside inosine	Antiepileptic action	[84]
<i>Spirulina fusiformis</i>	Phycobiliproteins, diacylglycerols	Antibacterial action	[48, 85]
<i>Spirulina</i> sp.	Polysaccharides phycocyanin, C-phycocyanin, phenolic acids, tocopherols	Antiviral action	[53]
<i>Ulva prolifera</i>	Polysaccharides	Antioxidant activity, antihyperlipidemic action	[86]
<i>Undaria pinnatifida</i>	Neo-antioxidants, polyphenols, and amino acids	Antihyperlipidemic and antioxidative properties	[62]

amounts in foods. A variety of bioactive substances appear to provide health benefits. Microalgae and Cyanobacteria have been discovered to have a large number of physiologically active chemicals having antiviral, antibacterial, antifungal, and anticancer properties [43]. Phytoplankton (microalgae) are a diverse community of microscopic plants which also involve a diverse and wide range of physiological and biochemical characteristics, including up to 8–14% carotene, up to 50–70% protein (roughly equivalent to up to 50% protein in meat and 15–17% protein in wheat), over 40% glycerol, 30% lipids, and a notably higher concentration of water-soluble vitamins (B1, B2, B3, B6, B12) and fat-soluble vitamins (E, K, D) and others. A record of various bioactive constituents from algae along with cyanobacteria is presented in Table 1.1 [5, 22, 44, 45].

1.7.1 Antibacterial Action

In order to protect themselves from other invading organisms, algons produce an immense variety of chemically active constituents which include terpenoids, phlorotannins, amino acids, phenolic compounds, steroids,

alkenes, cyclic polysulfide and halogenated ketones [87]. Furthermore, organic extracts made from *Chaetoceros pseudocurvisetus* and the diatoms *Skeletonema costatum* were looked into and found to have antitubercular activity towards *Mycobacterium tuberculosis* and *Mycobacterium bovis* by Lauritano and his team, and according to various researchers, in standard human cell lines, they were found to be nontoxic [88]. Phlorotannins (derived from *Sargassum thunbergii*) have been shown to inhibit the growth of *Vibrio parahaemolyticus*, as a result of which membranes are destroyed and insignificant cytoplasmic leakage takes place [60]. Various bacteria, including *Candida albicans*, *Staphylococcus aureus*, *Aspergillus niger*, and *Escherichia coli*, have been shown to be susceptible to *Haematococcus pluvialis*. The susceptibility noticed is because of the presence of propanoic and butanoic acid molecules in the bacteria [89].

Spirulina fusiformis consisting of phycobiliproteins showed strong antibacterial action towards *Streptococcus pyogenes* and *Spirulina fusiformis* phycobiliproteins [84]. *Synechocystis* sp. extracts containing fatty acids reduced the development of the bacteria *Bacillus cereus* and *E. coli*, *C. coli*, as well as *C. albicans*. The C-phycocyanin generated by *Streptomyces platensis* seems to suppress the spread of *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *S. aureus*, *E. coli*, and *Klebsiella pneumoniae* in vitro [90].

Algal polysaccharides resembling fucoidan and laminarin are demonstrated to possess antibacterial action against *Staphylococcus aureus* and *E. coli* strains. According to some previous reports, it has been proven to impede the formation of *Helicobacter pylori* biofilms in the mucosa of stomach [91] as well as the proliferation of *H. pylori* [86]. Kubota *et al.* discovered that the bioactive constituent amphidinolide Q, which comes from the *Amphidinium* sp. (symbiotic dinoflagellate), was effective towards the bacteria *Bacillus subtilis*, *Staphylococcus aureus*, and *Escherichia coli*, as well as others [92].

Algal polysaccharides (fucoidan- and laminarin-like) showed efficient antimicrobial activity towards *E. coli* and *Staphylococcus aureus* strains. They have been shown to impede the production of *Helicobacter pylori* biofilms in the mucosa of stomach [93] and the growth of *H. pylori* [86]. The bioactive ingredient amphidinolide Q from the *Amphidinium* sp. was effective against the bacteria *B. subtilis*, *S. aureus*, and *E. coli* [92].

Pahayokolide A appeared to inhibit the formation of *Bacillus megaterium* and *Bacillus subtilis*, as well as exhibiting cytotoxic properties [94] derived from *Lyngbya* sp. [95]. Antibacterial activity against MRSA and vancomycin-resistant *Enterococcus faecium* (VRE) was demonstrated by the chemicals bromophycolide P and bromophycolide Q. These were separated from the Fijian red alga *Callophycus serratus* [96]. Neuraminidases A and B, two pyrone macrolides derived from the red alga *Neurymenia*

fraxinifolia [97], were found to have antimicrobial efficacy towards MRSA and VRE. A compound found in *Phaeodactylum tricornutum*, EPA, palmitoleic and hexadecatrienoic acids, among others, could reduce the growth of bacteria such as *B. cereus*, *S. aureus*, *S. epidermidis*, MRSA, and others [98]. *Bacillus subtilis*, *Micrococcus flavus*, and *Staphylococcus aureus* growth have been shown to be effected and inhibited by fatty acids derived from *Oscillatoria redekei* containing dimorphecolic, coriolic, and linoleic acids [99]. Antibacterial activity towards *E. coli*, *S. aureus* and *B. subtilis* was also observed in lipid fractions from *Chaetoceros muelleri*. They were also known to contain unsaturated fatty acids [triglycerides and docosapentaenoic acid (DPA)]. Mendiola *et al.* discovered DPA was present in unsaturated fatty acid from *Chaetoceros muelleri*. Many antimicrobial compounds discovered from the *Nostoc* sp., including noscomin, which was acquired from the terrestrial *Nostoc commune*. It was shown to possess antibacterial action towards bacteria such as *E. coli*, *B. cereus*, and *S. Epidermidis* [100]. It has been suggested that Muscoride A, an alkaloid derived from the plant *Nostoc muscorum*, may have antibacterial action towards *E. coli* and *B. subtilis* [101].

1.7.2 Antifungal Action

Antifungal activity of ethanolic fractions of *Laurencia paniculata* was investigated by Mickymaray and Alturaiki [102], which contained the sesquiterpene constituent aristolene in patients with bronchial asthma. The results revealed that the fractions had antifungal activity, particularly in patients with bronchial asthma. It was discovered that the compounds isolated from *Microcystis aeruginosa* demonstrated antifungal action, particularly towards the fungus *Aspergillus*. Hexadecanoic acid, methyl ester, and BHT were all found to be effective [102]. Shishido *et al.* and Marrez and Sultan identified scytophycin as a strong antifungal chemical from species of *Nostoc*, *Scytonema*, and *Anabaena* sp. [103, 104]. Researchers discovered other various types of antifungal chemicals called hassallidins from *Nostoc* sp. and *Anabaena* sp. The *Amphidinium* sp. as a symbiotic dinoflagellate [92], displayed antifungal efficacy towards *Candida albicans* due to derived chemical amphidinolide Q. Phycobiliproteins produced by *Porphyridium aerugineum* have the potential to provide resistance against *Clostridium difficile*. *C. albicans* is an acronym for *Candida albicans* [84]. *Chlorococcum humicola* growth was discovered to be inhibited by pigments and organic solvent extracts from *C. humicola*, such as chlorophyll a, carotene, and chlorophyll b, which were proven to be effective against the growth of the bacteria. There are many different types [4] such as *Aspergillus flavus*,

A. albicans, *Aspergillus niger* and others. When tested against *Aspergillus candidus*, nostofungicidine, which is produced from *N. commune*, showed significant antifungal effectiveness, according to the researchers [87]. The fatty acids having short chain produced from *H. phuvialis* were found to be effective against *C. albicans* in a laboratory setting [69]. Lipopeptides laxaphycin B along with laxaphycin C are obtained from species *Anabaena laxa*. These constituents displayed antifungal action towards *C. albicans*, *Saccharomyces cerevisiae*, *Aspergillus oryzae*, *Penicillium notatum*, and *Trichophyton mentagrophytes* [105]. Dahms *et al.* observed antifungal properties of fisherellin from *Fischerella muscicola* [106]. Ciguatoxin and okadaic acid are effective chemicals against fungi, synthesized by *Giardia toxics* and *Prorocentrum lima*, respectively [107]. In 2006, Washida *et al.* reported antimycotic activities. This action was shown by karatungiols. Its constituents were derived by the dinoflagellate *Amphidinium* [108]. Hassalldin A as well as Hassallidin B were obtained from *Hassallia* sp. displayed fungicidal properties [109] towards *Acremonium strictum*, *Fusarium* sp., *Aspergillus* sp., *Ustilago maydis*, *Penicillium* sp. and *Cryptococcus neoformans*. *Hapalosiphon welwitschii* as well as *Westiella* genus were also discovered to possess fungicidal agents such as N-methylwelwitindolinone C isocyanate and welwitindolinone A isonitrile [110].

1.7.3 Anti-Inflammatory Action

Whenever something affects, irritates, or damages our body, we experience inflammation as a quick reaction. As part of this response, the body recognizes the agents accountable for the attack and gets a chance to neutralize them as soon as feasible. Pain, redness, swelling, and warmth are all symptoms of inflammation that usually occur at the infection site. The anti-inflammatory chemicals absorption aids in the prevention of illness and the speeding up of the healing process. It regulates the immune response of body to the infection. Anti-inflammatory medicines derived from microalgae are widely used nowadays. When combined in food or applied topically in cosmetics and other pharmaceutical products, they are protective to the body's tissues. Researchers found that sulfurized polysaccharides as well as pigments [111] and PUFAs are the most important anti-inflammatory substances found in microalgae around the world [112]. The immunological response to many cyanobacterial polysaccharides can be improved by reacting through a variety of events, including reactive oxygen species, macroelectric phenomena, secreting chemokines and cytokines. As per J. K. Park *et al.*, these are signalling inflammatory and immune responses. The introduction of reactive oxygen into

various cyanobacterial polysaccharides is responsible for the activation of macrophage functions in the body. As a result of the chemical cytokines it secretes, cytokines can boost immune responses through a variety of mechanisms, including signaling immunological as well as inflammatory responses [113]. As a result, more types of cytokines were stimulated for further secretion [114]. Phycocyanine is one of the most essential cyanobacterial pigments and denotes a phycobiliprotein. It works as a photosynthetic antenna by the collection of light and energy. Phycocyanins recently became a highlight in medicine because they have various pharmaceuticals, like anti-inflammatory, antioxidant, and antineoplastic actions. The cytokines produced in greater quantities are responsible for anti-inflammatory action [115]. They inhibit the COX-2 enzyme which further inhibit the synthesis of prostaglandin E2 synthesis (PGE2). Based on its pharmacological action and distinctive properties, phycocyanin may be developed as a possible therapeutic agent against inflammation and neurodegenerative diseases. Different types of neurodegenerative diseases are Alzheimer's disease (memory loss), Parkinson's disease (personality disorder), Huntington's disease, etc. [116].

The pigment scytonemin was discovered in cyanobacteria as a secondary metabolite containing an aromatic alkaloid [117, 118]. According to the literature, its anti-inflammatory function on another normal cell has been shown to have no harmful effects. Scytonemin has also been proposed for use in the creation of an anticancer treatment that inhibits the advancement of the cell cycle [5].

1.7.4 Antiprotozoal Action

The antiprotozoal activity of several cyanobacterial compounds against the pathogenic parasite has been demonstrated in laboratory studies (e.g., malaria caused by *Plasmodium falciparum*, leishmaniosis caused by *Leishmania donovani* and sleeping sickness caused by *Trypanosoma brucei*). However, some cyanobacterial metabolites, particularly those that are effective against drug-resistant strains, also have antiprotozoal activity. The companeramides A and B are metabolites separated from the plant *Leptolyngbya* sp. which are cyclic depsipeptides. Now *Hyalidium* has been explored extensively by researchers [119]. These compounds, on the other hand, have antimalarial efficacy against three separate strains of *Plasmodium falciparum* which are chloroquine-resistant. Their therapeutic activity against a parasite is one hundred times lower than that of chloroquine, which limits their potential use as pharmaceutical agents in treating parasitic infections. Even so, some metabolites have shown a high

efficacy against the parasite, so they might replace antibiotic medications like dolastatins and hoshinolactam for protozoal infections. Dolastatins are indeed natural marine peptides and *Dolabella auricularia* (sea hare) was identified as the first members of this family [22].

Antiprotozoal activity [120] against the *Trichomonas vaginalis*, *Entamoeba histolytica*, *Leishmania mexicana*, *Trypanosoma cruzi*, *Giardia intestinalis*, etc., has been shown in *Lobophora variegata* extracts. Alkaloids of *Cladophora crispata* along with ethyl acetate constituents were found to possess antiprotozoal action towards protoscolices of *Echinococcus granulosus* hydatid cysts. The ethyl acetate constituents and alkaloids were isolated from the plant *Cladophora crispata* [121]. Inhibition of growth of *Leishmania braziliensis* was observed in algal extracts from the following species: *Canistrocarpus cervicornis*, *Caulerpa cupressoides*, *Ochtodes secundiramea*, *Anadyomene saldanhae*, *Dictyota* sp. and *Padina* sp. [122]. A polyanionic sulfated polysaccharide known as fucoidan [123], prevalent in numerous brown algae, was discovered. It has been shown to have an inhibitory effect on the intracellular amastigote part of *Leishmania donovani*. Dolabelladienetriol, derived from the *Dictyota paffii* plant, was tested for its leishmanicidal action against intracellular amastigotes. It was also found effective for antihuman immunodeficiency virus (HIV)-1 action. As HIV-1 has been shown to increase the amount of *Leishmania* parasites present in macrophages, dolabelladienetriol seems promising for chemotherapy of leishmaniasis. Elatol isolated from *Laurencia dendroidea* (the Brazilian red algae) [124], demonstrated antiprotozoal activity towards the amastigotes and trypomastigotes of *T. cruzi* species.

The *Sargassum hemiphyllum* has constituent sargaquinoic (meroterpenoid) [125], which was a powerful agent against *in-vitro Plasmodium falciparum* [126]. Fennel *et al.* discovered that, irrespective of its strong actions, dolastatins are not recognized as promising antiprotozoal drugs. Hoshinolactam is an aromatic metabolite of the lactam family produced by cyanobacteria. Separated from *Oscillatoria* sp., it demonstrated antiprotozoal action with IC_{50} equivalent (3.9 nM) to the commercial medicinal product pentamidine (4.7 nM) against *Trypanosoma brucei* [127]. Therefore, it has the potential to be utilized as effective alternate medication for trypanosomiasis caused by *Trypanosoma brucei*. Marine algae have various bioactive compounds with antimalarial/antiprotozoal activities which still need to be explored.

1.7.5 Antioxidant Action

The demand for algal foods is rising rapidly on the global platform, with excellent health benefits being used on the market as “functions or

nutraceuticals.” It is possible to prevent oxidative damage in cells caused by bioactive chemicals through a process of active oxygen and scavenging free radicals, which can help prevent cancer [128]. Serious health conditions like atherosclerosis, cardiac ailments, strokes, tumors, neurodegenerative disorders, muscular degeneration, infant retinopathy, renal disease and age-related diseases, are caused by oxidative stress [129]. Different algal constituents have antioxidant properties, in addition to anti-inflammatory, antibacterial and antiviral effects in reduction and/or disease prevention. These components are linolenic acid [130], cyanocyanine, oleic acid [46], B-12, vitamin E, palmitoleic acid [131], β -carotene, phycocyanin, zeaxanthin, etc. [55].

Inverted association with the consumption of fruit and vegetables was established in epidemiological studies. The antioxidant activity of these foods is attributed to this phenomenon [7]. Cyanobacterium phytochemicals along with pigments possess a active oxygen-free radical, or nitrogen scavenger, and therefore act as antioxidant. Often high oxygen levels and high irradiation are subjected to algae and cyanobacteria. These organisms tend to form an oxidative stress defense mechanism. The antioxidants found in microalgae (dimethyl sulfoniopropionate and mycosporic amino acids) have been identified and are extremely strong molecules that block ultraviolet light [132]. Skjånes *et al.* discovered that algae possess a variety of constituents that have antioxidant properties, including pigments, lipids, and polysaccharides [133].

1.7.6 Antineoplastic (Anticancer) Action

The photosynthetic microbes, including cyanobacteria and algae, developed to survive and flourish in a hostile atmosphere on the biochemical basis of bioactive compounds and secondary metabolites. Separated secondary metabolites have a high therapeutic value, which is further enhanced for antineoplastic properties by active pharmacological ingredients [2]. Cyanobacteria strains, such as *Oscillatoria*, *Nostoc*, and *Spirulina*, generate a mixture of acetyl Co-A synthesis and anabolic pathways to produce cytotoxic lipopeptides [23]. Recently, researchers discovered that somocystinamide, a marine lipopeptide derived from the seaweed *L. majuscula*, can activate the apoptosis pathway and restrict the growth of numerous cancer cell lines, including leukaemia. Others are carcinoma, melanoma, neuroblastoma and myeloma [73]. Didemnin [74, 134], lyngbyabellins [135], and hectochlorin are examples of lipopeptides that have been discovered [136].

Cyclopeptide cryptophycin produced by *Nostoc* also has demonstrated a great potential for anticancer to multidrug-resistant cells because of their effects on the cytoskeletal protein tubulin. Besides which, the effects against solid tumors have been highly effective. The cancer suppression mechanism has been connected to binding of tubulin [137, 138], which results in the depolymerization of microtubules [139] and the instability of microtubules, which results in cell cycle arrest and apoptosis, among other things [1]. Similarly, apratoxin A, a natural compound derived from marine cyanobacteria, inhibits the transcription factor STAT3 [140], which prevents G1 cells from becoming cancerous and induces apoptosis in different cell types [141, 142]. Based on their adaptation to exposed anthropogenic environment, cyanobiological flora in freshwater ponds generates an unpleasant smell. These blooms (blooms are accumulation of algal cells to any point where they discolor the water) of blue-green algae cultivate in vast numbers and are harmful to all creatures because of their cyanotoxin content. However, the promising properties of these toxins as anticancer drugs have been demonstrated. The clinical effectiveness of different carcinomas has been demonstrated by microcystins, cryptophicins, anatoxin A and numerous peptide toxins [143, 144]. Successful clinical trials of cyanobacterial depsipeptides like dolastatin 15, including tasidotin, soblidotin and cemadotin, were carried out [1]. A significant element in chemotherapy is the mechanism by which cyanobacterial metabolites act on tumor cells. Cells are programmed for apoptotic cell death to die from stimulus by changed homeostasis caused by infections, oncogenic transformations, oxidants, abnormal proliferation, and so on. There is therefore a high pharmacological value for anticancer treatment for metabolite-inducing apoptosis. A class of anticancer compounds known as cyanobacterial metabolites interconnect with molecular cell parts, such as DNA, protein kinases of the receiver and microtubules. Cell cycle controls protein synthesis. These interactions result in cell blockage [145], mitochondrial dysfunction, oxidative damage [146], and non-cascade activation [147]. Different pharmacoactive cyanobacterial constituents for powerful anticancer and apoptotic signalling have been tested. Calothrixin A revealed cell cycle G2 phase or M phase arrest in tumor cells of humans. Calothrixin A is a class of indolophenanthridine obtained from *Calothrix* [148]. So, phycobiliprotein (C-phycocyanin) was mentioned as scavenging peroxy and phormidium radicals from both *Lyngbya* and *Phormidium* [149].

Besides the abovementioned apoptotic markers, the sodium concentration in the cells is enhanced apart from a few metabolites, such as the antillatoxins as lipopeptides separated from the majuscula [150], and the hermitamides [151]. In marine environment, microalgae growing covers

nearly forty percent of worldwide economic output. Microalgal bloom natural products were already extensively investigated for bioactive antineoplastic compounds, polysaccharides, pigments, and secondary metabolites. Whereas C-phycocyanin and phycobiliprotein, from both *Phormidium* and *Lyngbya*, were discovered to neutralize, i.e., scavenging radicals of hydroxyl and peroxy [149]. When cultures are cultivated under specified conditions, such as in specialized medium, at specific temperatures, and under specific light, microalgal extracts have been proven to be effective in anticancer (antineoplastic) research [88].

In general, carotenoids, such as lutein, alpha-carotene, beta-carotene, xanthene, lycopene, and other terpenes found in algae and cyanobacteria, are abundant because they are photosynthetic byproducts. As a scavenger for singlet electron species, carotenoids and various terpenoids play a crucial role. All these scavengers are therefore used to avoid the proliferation of cancer cells as an antioxidant. In various cancers, there are few reports of carotenoid cancer activity. However, some cases had inversely affected the development of carotenoids, which subsequently was detected due to smoking effects in individuals affected by lung cancer [80]. However, the neoplasm proliferation risk was reduced by dietary carotenoids studied by numerous authors [152].

Algae water extracts mainly constitute chemical molecules like alkalis, polysaccharides, polyphenols, polyunsaturated fatty acids (PUFAs), fatty lipids, glycoproteins, terpenoids and vitamins. Many of these constituents were examined and discovered as efficient in producing anticancer activity. The anticancer properties of a few secondary metabolites, including hormothamnione A from *Chrysophaeum taylorii*, hormothamnion A in *Hormothamnion enteromorphoides*, and malyncamide D in *L. majuscula* [153], have been discovered after extracts of these plants were made and tested on numerous cell lines. In addition to studies involving active molecules, a number of experiments were carried out to establish antineoplastic efficacy utilizing crude extracts, for example, extract of carotenoid [154], crude organic solvent extracts [155], polyunsaturated aldehydes [156], and chrysolaminarin (polysaccharide) [157].

It could be expected that in the current scenario of several tumor ailments, microalgae-based nanoformulated delivery systems must be marketable presently. In the literature, however, the above aspects have not been explored up to now for marketing nanoformulation or sustainable, efficient formulations and proper use of microalgae medications in nanomedicine-based therapy. It might be good to test for the nanoformulation's marketing in cancer therapy with diatoms and other microalgal specimens without the danger of experiencing any adverse effects in

order to determine their effectiveness. Studies in this area will provide future opportunities to exploit or capitalize on the possibilities of marine natural microalgal-derived compounds with nanoformulated therapeutic activities [158].

1.7.7 Antiviral Action

Despite the fact that successfully reported vaccine inventions have provided acquired immunity, current efforts to develop medications such as antivirals have expanded dramatically as new or re-emerging infectious diseases have evolved or reappeared. Because viral pathogenic organisms can rapidly manipulate genetic make-up at a time when a treatment strategy is witnessed that results in drug resistance, it is possible that this is the case [159]. Algae are one source, which are well-known for their many medicinal properties.

Recently, researchers discovered that the *Phormidium tenue* and *Lyngbya lagerheimii* cyanobacteria have antiviral activity towards HIV, also known as the human immunodeficiency virus. In the following years, researchers discovered and identified a novel family of anti-HIV protein known as Cyanovirin-N [75], which restricts the virus from fusing with the cell and, as a result, renders the viral particles inactive [160]. Afterwards, calcium spirulan, a new SP, was discovered in *Spirulina platensis*. It was reported to suppress the reproduction of enveloped viruses of a large range, including the human cytomegalovirus [47], Herpes simplex virus type 1 (HSV-1), influenza A virus, mumps virus [161], HIV-1, and measles virus, among others [162]. The antiviral activity of spirulina-like compounds derived from *Arthrospira platensis* polysaccharide fractions was enhanced against human cytomegalovirus (HSV-1), which was previously reported [163].

In vitro antiviral activity against human cytomegalovirus, also known as HSV-1, was enhanced by a class of spirulina-like compounds derived from *Arthrospira platensis* polysaccharide fractions [163]. *Microcystis ichthyoblabe* produce depsipeptides A and B, which have been demonstrated to impede the replication of the influenza A virus [164]. According to an article written by Vijayakumar and Menakha, Nostoflan, a virucidal medicine for HSV-1, was produced by *Nostoc flagelliforme* [142]. Scytovirin, when used in nanomolar quantities, binds to the HIV glycoprotein and causes the virus' protein envelope to degrade [83].

For several decades, many polysaccharides identified in marine algae species were investigated and revealed to possess intriguing antiviral

properties [165]. As an example, carrageenan, a compound derived from the red algae *Gigartina skottsbergii*, has been discovered to be therapeutically active against viruses (both non-enveloped and enveloped). Polysaccharide samples, such as calcium spirulan, nostafan and naviculan from diatom *Navicula directa*, and galactan from red algae, have also been discovered to possess unexpected antiviral properties against HSV, DENV, HPV, HIV, and other viruses [165].

1.7.8 Anticoagulant Action

Marine algae are very important bioactive constituent possessing an anticoagulant property among all other marine sources. Phlorotannins produced from marine algae have shown tremendous promise in biomedical research as anticoagulant medicines [166]. Prothrombin time, activated partial thromboplastin time, as well as thrombin time are all measured to assess whether or not a medication has anticoagulant action. According to the findings of a study, substances containing anticoagulant proteins and antiplatelet as well as fibrinolytic enzymes, have the potential to regulate endothelial cell activities and trigger the fibrinolysis system [167].

Natural and healthy anticoagulant compounds that generate phenolic constituents or phlorotannins are derived from, for example, *Ecklonia stolonifera*, *Hizikia fusiformis*, *Ecklonia cava*, *Ecklonia kurome*, *Ishige okamurae*, *Eisenia bicyclis* and *S. thunbergii* [166]. Brown algae's fucoidan along with laminarans, red algae's carrageenan, and green algae's ulvan have all received a lot of interest in the sectors of food, cosmetics [168], and pharmaceuticals [169]. Due to their good health benefits, these oceanic algae are being explored as possible medicinal medication components.

1.7.9 Immunosuppressive Action

Immunosuppressive medicines, notably T and B cells, have the tendency to suppress the immune system in a variety of ways. They are essential in order to increase the probability of surviving allogeneic organ transplantation by lowering immunological responses of the host. An immunosuppressive effect of SQDG (sulfolipids) derived from blue-green algae was observed in a study to be significant in a human-mixed lymphocyte reaction while having no influence on overall immune competence [170]. The bioactive protein found in *Spirulina* (blue-green algae) boosts the intestinal immune system by a variety of ways [171]. *Spirulina* has been studied

for its potential to protect the kidney from heavy metals and pharmaceuticals by lowering glucose and lipid levels in the blood [172]. Chlorella's -1,3 glucan lowers blood cholesterol and free radicals [10]. Several immunosuppressive bioactive chemicals are found in blue-green algae.

Our goal in this chapter is to reveal the biological production of bioactive compounds by various green algal species. This review confirms that a variety of green algae possess biological active compounds. The phytochemicals in these algae show various beneficial effects, which was supported by variety of the literature.

1.8 Conclusion

Nature and its chemical equivalents are the principal sources of medicinal molecules used on a daily basis. Bioactive chemicals derived from algae have been widely studied for antibacterial, antioxidant, anti-inflammatory, anticoagulant, antiprotozoal, antitumor, and antiviral applications over the past several decades. In order to survive under severe environmental conditions, algae and cyanobacteria have developed natural defense mechanisms via the creation of bioactive compounds. Stress factors and oxidants were neutralized by bioactive molecules such as alkaloids and terpenoids. Extracted algal ingredients were examined for bioactivity against bacteria, fungus, viruses, and protozoa. In strict clinical tests, the proliferation of cancer was also inhibited.

In light of microalgae's shown ability to create bioactive compounds, these microorganisms have been thrust into the biotechnology limelight for potential uses in a wide range of fields of research, particularly the life sciences. Since the discovery of microalgal metabolites, which boost the body's defense mechanisms, researchers have been studying the use of microalgal biomass in a variety of meals, pharmaceutical products, and medicinal items. The found chemicals and their activity in the prevention as well as cure of numerous ailments, as well as the ongoing search for other, as of yet unreported metabolites, are clearly in need of further investigation.

Marine biotechnology in pharmaceuticals and food applications is an emerging sector that is globally encouraged by an increasing number of policy and financial instruments. Techniques for the optimization of culture conditions, harvesting and extraction methods, combined with recombinant techniques, have become essential to the majority of industrial models that may be put to achieving corporate use, especially in food and nutraceutical applications. The emergence of this sector has been

facilitated by the growing consumer demand for healthy foods that also have beneficial effects on health, combined with a less stringent legislation than that which applies to pharmaceutical substances [12].

Furthermore, in extreme temperatures worldwide, there are several algal and cyanobacterial bases and the pressure has yet to be identified. With vigilance, the identification and cultivation of these species could discover some new chemical compounds which can produce high therapeutic effectiveness. Such pharmaco-active moieties may, as observed for dolastatin 10, also be modified into analogues to improve clinical utilization. Besides, at the same time, a combination of two or more medicinal compounds can contribute in identifying and evaluating antagonistic, additive, or synergistic effects by *in-vitro* testing and clinical trials on animals to decrease toxicity problems. The challenge is still there to optimize our ability to access, identify as well as exploit them while remaining cost-effective. The task for researchers is also to establish the circumstances in which the large proportion of these microbes could be cultivated in order to provide a reliable source of supply in the future.

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