



Microalgae: An Untapped Resource for Natural Antimicrobials

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Abstract

Numerous biochemical compounds are synthesized by algae in a wide variety of ecosystems. To date, more than 18,000 new bioactive compounds have been isolated from marine algae; most are still uncharacterized. Therefore, the identification of novel prospective antimicrobials from microalgae presents a unique opportunity. A number of investigations have explored the therapeutic potential of algal extracts and extracellular compounds from a wide range of microalgae; they have confirmed antibacterial, antiprotozoal, antiviral, antifungal, and antiplasmodial activity. Chemical groups such as phenols, fatty acids, indoles, terpenes, acetogenins, and some volatile halogenated hydrocarbons derived from microalgae have shown antimicrobial activity. For example, supercritical extracts of the microalgal *Chaetoceros muelleri* have shown antimicrobial activity due to its lipid composition. Many algal species are also effective against a range of bacteria. For example, *Pithophora oedogonium* targets *Salmonella* and *Staphylococcus* spp. The algae *Rivularia bullata*, *Nostoc spongiaeforme*, *Codium fragile*, *Colpomenia peregrina* Sauvageau, *Cystoseira barbata*, and *Zanardinia typus* are active against many Gram-negative and Gram-positive bacteria.

Multidrug-resistant bacteria pose an increasing challenge to global health, with the future efficacy of antimicrobial drugs being uncertain. Most antimicrobial agents that are successfully used in clinical practice have drawbacks such as toxicity, lack of efficacy, and high costs; furthermore, their frequent use can

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result in the emergence of resistant strains of bacteria. Therefore, the development of alternative biodegradable compounds from natural sources with limited side effects is urgently needed. To date, the commercial applications of microalgae-derived compounds has not received as much attention as the fields of antibiotics production, pharmaceuticals, and supplementary biologically active compounds. However, microalgae are destined to become an important raw material for the efficient production of amino acids, vitamins, and other pharmaceuticals. The cultivation of microalgae may provide detailed insights on their practical applications and biotechnological characteristics, which may help researchers develop compounds of interest for their biomedical potential.

8.1 Introduction

The current healthcare system is experiencing a number of clinical problems related to organ transplantations, complicated surgeries, medical device implantation, and chemotherapy. Patients who have undergone these procedures are immunocompromised and thus more susceptible to infections. Furthermore, the global spread of multidrug-resistant bacteria and lack of new antibiotics under development limits the treatment options available to clinicians [81].

The discovery and development of antibiotics are among the most important advances in modern medicine for the life-saving treatment of infectious diseases. However, these “miracle drugs” have lost their efficacy with the appearance of multidrug resistance. Higher rates of morbidity and mortality occur when infectious diseases are caused by multidrug-resistant organisms. In addition, the treatment of these infections is very expensive and requires prolonged hospital stays. This situation is a global epidemiological and public health crisis [13] that is spreading through poor sanitation, person-to-person contact, international travel, and the food chain [91].

The World Health Organization considers multidrug-resistant bacteria to be a major public health concern [103]. Pathogenic bacteria that are resistant to various antimicrobial compounds have been increasing in evolution, prevalence, and distribution. The rapid dissemination of antibiotic-resistant genes through mobile genetic elements, such as plasmids and transposons, has resulted in the emergence of multidrug-resistant strains of many clinically important organisms. Obviously, this situation creates difficulties for clinicians with regard to therapeutic options [37, 62].

8.2 Alternative Sources for Antimicrobial Agents

Bacterial resistance to existing antibiotics, which are mostly derived from bacterial origins, has been increasing rapidly. Thus, there is a need to develop novel efficient compounds using different technologies, including synthetic and semi-synthetic

antibiotics [28]. However, the frequently increasing rate of resistance to these antimicrobial compounds, in addition to the paucity of newer drugs, means that continuous investigation is required to find novel molecules and metabolic targets. One promising avenue is the investigation of natural compounds, particularly those from unexploited sources [93]. These alternative antimicrobial agents from natural sources are expected to have minimal side effects, in addition to being environmentally friendly and biodegradable. Researchers are examining bioactive compounds from algae and microalgae as a potential source. A number of functional compounds have been isolated from microalgae. They have the ability to produce a broad range of biologically active compounds, including those with antibacterial, antifungal, enzyme-inhibiting, antiviral, cytotoxic, antiplasmodial, and immunostimulating activities [52].

Microalgae are a rich source of widely distributed bioactive compounds with commercial importance [106]. Microalgal bioactive compounds can be synthesized from secondary metabolism or directly from primary metabolism. These compounds include proteins, vitamins, fatty acids, and pigments with various antimicrobial properties, such as antibiotic, antifungal, antiviral, anticancer, antiprotozoan, antialgal, and antienzymatic activities [105]. Compounds such as B12, β -carotene, oleic acid, cyanovirin, palmitoleic acid, vitamin E, phycocyanin, linolenic acid, lutein, and zeaxanthin have antimicrobial, antioxidant, and anti-inflammatory properties for the reduction and prevention of diseases [36, 46, 64, 98]. In most microalgae, the bioactive compounds are accumulated in the biomass. In some cases, the metabolites are excreted into the medium; these are known as exometabolites. Bioactive metabolites of microalgal origin are of special interest in the development of new products for the medical, pharmaceutical, cosmetic, and food industries. Further research should be conducted with these bioactive compounds to verify their beneficial effects for humans, their degradability when released into the environment, and their effects when used in animals [106].

8.3 Algae

Algae are simple plants containing chlorophyll for photosynthesis. They may be single- or multi-cellular organisms; they may also exist in colonies, sometimes working together as simple tissues [10]. Algae range from unicellular organisms of 3–10 μm in size to 30-m-long giant kelp [43]. They are found ubiquitously on Earth, including in rivers, lakes, seas, and soils, as well as on walls, plants, and animals. Algae can be divided into two major groups: 1) macroalgae (seaweeds), including green algae, red algae, and brown algae; and 2) microalgae, which are described in the next section [31].

8.4 Microalgae

Microalgae are unicellular organisms consisting of both prokaryotes and eukaryotes. They grow in fresh or salt water and have varied shapes, with a diameter or length of approximately 3–10 μm . Cyanobacteria have very similar structural characteristics to bacteria, but they also contain the chlorophyll *a* required for photosynthesis. Microalgae are distributed all over the biosphere and are responsible for more than 40% of global photosynthesis [20].

Microalgae play a vital role in aquatic ecosystems as the basis of the food chain. They uptake H_2O and CO_2 . With the help of solar energy, they synthesize organic compounds, which are then accumulated or secreted as primary or secondary metabolites. Microalgae have the ability to survive under many environmental stress conditions, including salinity, drought, osmotic pressure, photo-oxidation, heat, cold, and ultraviolet exposure [101]. Due to this ability, they can be found in diverse environments, such as fresh water, extreme salinity, blackish water, desert sands, and moist soil. Microalgae have an extra advantage of significant metabolic plasticity, which is dependent on their physiological state (i.e., stressed vs. nonstressed conditions). Therefore, their secondary metabolism can be easily triggered by applying external stress [34].

Until the 1950s, microalgae were not studied for therapeutic purposes. More recently, extensive research efforts have been directed toward microalgae to find novel compounds that might lead to therapeutically useful agents [16, 66, 67]. Microalgae are being investigated as possible antiviral agents [11] to treat infectious diseases caused by previously unexposed viruses that have re-emerged in recent years. A number of algal extracts and extracellular products have proven antifungal, antibacterial, antiprotozoal, antiviral, and antiplasmodial activity [33, 41, 42, 55, 75], as described in the following sections.

8.5 Antimicrobial Activity of Microalgae

The antimicrobial activity of microalgae has been recognized in compounds belonging to several chemical classes, including terpenes, indoles, acetogenins, phenols, volatile halogenated hydrocarbons, and fatty acids [16, 66]. Numerous pressurized extracts from *Dunaliella salina* have shown antimicrobial activity, with the presence of several fatty acids and compounds such as β -cyclocitral, α - and β -ionone, phytol, and neophytadiene [41, 42].

Microalgae are a natural source of highly interesting biologically active compounds. These compounds have received much attention from researchers and manufacturers in recent years due to their potential applications in different life science fields, including as biomass for food/feed and as bioactive compounds for the medical and pharmaceutical industries [36]. Microalgae are promising sources for novel products because of their great biodiversity and recent developments in genetic engineering [46]. The extraction of bioactive compounds has been investigated in a variety of microalgae, including *Botryococcus braunii*, *Arthrospira* (*Spirulina*),

Dunaliella salina, *Chlorella vulgaris*, *Haematococcus pluvialis*, and *Nostoc* [68, 72, 76], as described in the following sections.

8.5.1 Spirulina

Spirulina (*Arthrospira*) is prokaryotic cyanobacteria that belongs to Cyanophyta. It arose more than 3 million years ago, forming the current oxygen atmosphere, and has been important in the regulation of the terrestrial biosphere [87]. *Spirulina* is the richest source of proteins, containing approximately 60–70% protein [48].

Calcium spirulan (Ca-SP), a novel sulfated polysaccharide extracted with hot water from *Spirulina platensis*, has shown antiviral activity against herpes simplex virus (HSV) type 1, measles virus, human immunodeficiency virus (HIV) 1, and influenza virus [38]. Both extracellular and intracellular spirulan-like molecules from the polysaccharide fractions of *S. platensis* displayed significant antiviral activities against wide range of viruses, including human cytomegalovirus and HIV-1 [1]. Methanolic and aqueous extracts from *S. platensis* reduced HIV-1 viral loads by approximately 50% and 23%, respectively [4]. *Spirulina platensis* and *Spirulina maxima* also demonstrated antiviral activity against HSV-1 and HSV-2, respectively [25, 40].

In an animal study, suspensions of *Escherichia coli* or *Staphylococcus aureus* were injected into 3-week-old chickens; *Spirulina* (0.1%) enhanced the chicken's bacterial clearance abilities by improving the activities of different phagocytotic cells, such as thrombocytes, macrophages, heterophils, and monocytes [85]. In another study, cultures of *S. platensis* displayed antibacterial activity against six *Vibrio* strains: *Vibrio anguillarum*, *Vibrio parahaemolyticus*, *Vibrio scophthalmi*, *Vibrio alginolyticus*, *Vibrio splendidus* and *Vibrio lentus* [57]. Phycobiliproteins extracted from *Spirulina fusiformis* showed significant antibacterial activity against *Streptococcus pyogenes* and *S. aureus* [70]. Furthermore, the antibacterial activities of purified C-phycocyanin from *S. platensis* clearly inhibited the growth of some multidrug-resistant bacteria, such as *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*, and *S. aureus* [89].

Spirulina has also exhibited antifungal activity [22]. A butanol extract of *Spirulina* sp. was reported to have activity of 13 mm against *Candida glabrata* [97]. Balb/C mice infected with candidiasis showed a stimulatory effect when *S. platensis* extract was tested [99]. In another study, the antifungal activity of the methanolic extract of *S. platensis* was tested against *Aspergillus flavus*; the reduction of glucosamine production was reported to be nearly 56% [69].

8.5.2 Nostoc

Microalgal biomasses of *Nostoc* have been used in the medical field and as dietary supplements because of their protein, vitamin, and fatty acid content. *Nostoc* contains a spectrum of polyunsaturated fatty acids that include essential fatty acids,

such as linoleic, α -linolenic, γ -linolenic, octadecatetraenoic, and eicosapentaenoic acids [108]. Essential fatty acids are precursors of prostaglandins, thus engendering significant interest from the pharmaceutical industry. The medical value of these microalgae has been demonstrated by their use in the treatment of fistulas and some forms of cancer [102].

Nostoc sp. is reported to have a number of secondary metabolites, including antimicrobial compounds. For example, tenuocyclamide a-d was found from *Nostoc spongiaeforme* [111], and noscomin and coniston a-e were found from *Nostoc commune* [50]. The diverse polysaccharides in *N. commune* have been shown to possess antibacterial activity along with antitumor, antiviral, and anti-inflammatory effects [92]. Nostocyclone A is another antimicrobial compound that has been isolated from *Nostoc* sp. [80]. Cyanovirin, a potential protein molecule produced by a *Nostoc* microalga, showed positive effects in the treatment of HIV and influenza A (H1N1) [98].

8.5.3 Chlorella

Chlorella was discovered by the Japanese, who are the traditional consumers of algae and use it as a food supplement. The microalga *Chlorella* is rich in chlorophyll, vitamins, proteins, minerals, polysaccharides, and essential amino acids. This microalga is 53% (w/w) protein, 23% (w/w) arbohydrate, 9% (w/w) lipids, and 5% (w/w) minerals and oligoelements [49].

Pratt et al. first isolated microalgal active compounds from *Chlorella*; in their study, a mixture of fatty acids (chlorellin) was isolated and demonstrated antibacterial activity against both Gram-negative and Gram-positive bacteria in vitro [82]. Interestingly, the authors also described a practical application during World War II derived from a previous experiment. *Chlorella* spp. were heavily inoculated in open sewage from military installations, rendering it bacteriologically safe for discharge into local streams. There was a reduction in the number of coliforms in the areas where *Chlorella* spp. were present compared with the areas where *Chlorella* spp. were absent [83].

8.5.4 Dunaliella

Dunaliella spp. are green, unicellular, halotolerant microalgae that belong to the Chlorophyceae group. These microalgae are extensively studied because of their diverse nature, including physiological aspects, tolerance of extreme habitats, and many biotechnological applications. *Dunaliella* spp. are a rich source of bioactive compounds, such as carotenoids, glycerol, lipids, enzymes, and vitamins [45, 84]. These microalgae are a major source of natural β -carotene; they are able to produce up to 14% of their dry weight under conditions of high salinity, light, and temperature as well as nutrient limitations [29].

Chang et al. reported that *Dunaliella* cells contained antibiotic substances. The crude extract of this microalga strongly inhibited the growth of *Bacillus cereus*, *S. aureus*, *Enterobacter aerogenes* and *Bacillus subtilis* [17]. In another study, *Dunaliella* microalga also showed antibacterial activity against various microorganisms of importance to the food industry, including *E. coli*, *S. aureus*, *Candida albicans*, and *Aspergillus niger* [41, 42, 45].

Minolenic acid extracted from *Dunaliella primolecta* Butcher (C-525) and *Chlorococcum* sp. (HS-101) [73] showed antibacterial activity against methicillin-resistant *S. aureus* (MRSA). Another study investigated extracts of *Dunaliella* spp. isolated from clean and polluted waters. The authors observed that a heat-labile non-proteinous substance produced by species from the polluted water had the ability to inhibit *E. coli*. It was therefore suggested that microalgae from highly competitive environments are more likely to produce compounds with antimicrobial activity [63] (Tables 8.1, 8.2, 8.3, and 8.4).

Table 8.1 Antibacterial activity of some algae species

Bioactive compound/Microalgae	Targeting bacteria	References
Ambiguine I isonitrile/ <i>Fischrella</i> sp.	<i>E. coli</i> ESS K-12, <i>Staphylococcus albus</i> , <i>Bacillus subtilis</i>	[86]
<i>Skeletonema costatum</i>	<i>Vibrio</i> spp.	[71]
Carbamidocyclophanes/ <i>Nostoc</i> sp.	<i>Staphylococcus aureus</i>	[12]
γ -lactone malyngolide 14/ <i>Lyngbya majuscula</i>	<i>Mycobacterium smegmatis</i> and <i>Streptococcus pyogenes</i>	[15]
Norbietane diterpenoid (20-nor-3a-acetoxyabieta-5,7,9,11,13-pentaene)/ <i>Microcoleus lacustris</i>	<i>S. aureus</i>	[35]
Noscomin/ <i>Nostoc commune</i>	<i>Bacillus cereus</i> , <i>Staphylococcus epidermidis</i> , <i>Escherichia coli</i>	[51]
Phenolic compound/ <i>Nostoc muscorum</i>	<i>B. subtilis</i> , <i>B. cereus</i> , <i>E. coli</i> , <i>Salmonella typhi</i> , <i>S. aureus</i>	[24]
Cycloedesmol/ <i>Chondria oppositoclada</i>	<i>S. aureus</i> , <i>Candida albicans</i>	[27]
Hapalindole T/ <i>Fischerella</i> sp.	<i>S. aureus</i> , <i>Pseudomonas P. aeruginosa</i> , <i>S. typhi</i> , <i>E. coli</i>	[3]
<i>Euglena viridis</i>	<i>Pseudomonas</i> , <i>Aeromonas</i> , <i>E. coli</i> , <i>Edwardsiella</i>	[18]
<i>Padina pavonica</i>	<i>Enterococcus faecalis</i> , <i>S. epidermidis</i>	[21]
<i>Ulva fasciata</i> , <i>Chaetomorpha aerea</i>	<i>Klebsiella pneumonia</i> , <i>P. aeruginosa</i> , <i>S. aureus</i>	[90]
<i>Ulva Lactuca</i>	<i>B. subtilis</i> , <i>B. pumilus</i>	[77]
<i>Cystoseira</i> sp., <i>Gelidium latifolium</i>		

Table 8.2 Antiprotozoan activity of some algae species

Bioactive compounds/Microalgae	Targeting protozoans	References
Ascosalpyrrolidinones/ <i>Ascochyta salicorniae</i>	<i>Plasmodium falciparum</i>	[74]
Viridamide A/ <i>Oscillatoria nigro Viridis</i>	<i>Trypanosoma cruzi</i> , <i>Leishmania exicana</i> , <i>Plasmodium falciparum</i>	[95]
Symplocamide A/ <i>Symploca</i> sp.	<i>T. cruzi</i> , <i>Leishmania donovani</i> , <i>P. falciparum</i>	[60]
Venturamides/ <i>Oscillatoria</i> sp.	<i>P. falciparum</i>	[61]
Snyderol sesquiterpene/ <i>Laurencia obtuse</i>	<i>Plasmodium falciparum</i>	[104]
Ambigol C/ <i>Fischerellambigua</i>	<i>T. rhodesiense</i> , <i>P. falciparum</i>	[112]
<i>Amphidinium</i> sp.	<i>Trichomonas foetus</i>	[109]
<i>Dinophysis fortii</i> , <i>Prorocentrum lima</i>	<i>T. foetus</i>	[9]
n-hexane, dichloromethane/ <i>Bostrychia tenella</i>	<i>T. cruzi</i> trypomastigotes, <i>Leishmania amazonensis</i> promastigotes	[19]

Table 8.3 Antiviral activity of some algae species

Bioactive compounds/Microalgae	Targeting protozoans	References
Spirulan/ <i>Spirulina</i> sp.	HIV-1 and HIV-2 (inhibits reverse transcriptase) HSV, influenza	[96]
Nostoflan/ <i>Nostoc flagilliforme</i>	HSV-1 (HF), HSV-2 (UW-268), human cytomegalovirus (Towne), influenza (NWS), adenovirus (type 2), Coxsackie (Conn-5)	[96]
Cyanovirin-N/ <i>Nostoc ellipsosporum</i>	HIV-1 (interacts with high mannose groups of envelope glycoproteins, gp120 and blocks its interaction with target cell receptors) HIV-2, HSV-6, Mesles virus Simian immunodeficiency virus, feline immunodeficiency virus	[96]
Tribromo 4,5-dihydroxybenzyl methyl ether/ <i>Symphyocladia latiuscula</i>	Wild-type HSV-1, APr HSV-1, and TK-HSV-1	[79, 78]
Sulfoquinovosyl diacylglycerol/ <i>Ishige okamurai</i>	HSV-2	[107]
Dollabelladiene 147, 10,18-diacetoxy – 8-hydroxy	HSV-1 and HIV-1	[6, 47]
2,6-dollabelladiene 148/ <i>Dictyota pfaffi</i>		
8,80-bieckol 151 and 8400-bieckol 152/	HIV-1 reverse transcriptase and protease	[30]
Venustatriol 302, thyrseferol 303 and thyrseferyl 23-acetate 304/ <i>Laurencia venusta</i>	Vesicular stomatitis Vesicular stomatitis Indiana virus, HSV-1	[88]

Table 8.4 Antifungal activity of some algae species

Bioactive compounds/Microalgae	Targeting fungus	References
<i>Ulva lactuca</i> , <i>Cystoseira</i> sp., <i>Gelidium latifolium</i>	<i>Candida albicans</i> , <i>Microsporium gypseum</i> , <i>Aspergillus niger</i>	[77]
<i>Padina pavonica</i>	<i>Candida</i> spp.	[21]
<i>Chlamydomonas reinhardtii</i>	<i>A. niger</i> , <i>Aspergillus fumigatus</i>	[32]
<i>Trentepohlia umbrina</i>	<i>A. niger</i> , <i>Trichoderma barsianum</i>	[94]
<i>Amphidinium</i> sp.	<i>A. niger</i>	[109]
<i>Dinophysis fortii</i> , <i>Prorocentrum</i> <i>lima</i>	<i>A. niger</i>	[9]

8.6 Natural Compounds

A number of chemical functional groups from algae have been reported to be bacterial inhibitors, including polysaccharides, phlorotannins, peptides, fatty acids, terpenes, and halogenated furanones, as described in the following sections.

8.6.1 Polysaccharides

Fucoidan- and laminarin-like algal polysaccharides have shown antibacterial activity against *E. coli* and *S. aureus* and have been used as oral drugs. They also prevent the adhesion of the biofilm forming *Helicobacter pylori* in gastric mucosa [8, 39, 53, 113]. In Ireland, ultrasound-assisted extraction was used to obtain laminarin from the brown seaweeds *Ascophyllum nodosum* and *Laminaria hyperborean*; the laminarin was shown to be a significant growth inhibitor of *E. coli*, *Listeria monocytogenes*, *S. aureus*, and *Salmonella typhimurium* [53]. Hot and cold water extraction was used to obtain polysaccharides from the brown seaweed *Dictyopteris membranacea* and red seaweed *Pterocladia capillacea*; these extracts showed antibacterial activity against Gram-negative *Pseudomonas fluorescens* and *E. coli* and Gram-positive bacteria *B. cereus* and *S. aureus* [2].

Spirulan and Ca-spirulan are the most important anticancer polysaccharides isolated from *Spirulina* spp.; they also showed effective and broad-spectrum activity against HIV-1, HIV-2, and influenza viruses. These sulfated polysaccharides inhibit the reverse transcriptase activity of HIV-1 (like azidothymidine) [26]. Another acidic polysaccharide, nostoflan from *Nostoc flagelliforme*, exhibits potent virucidal activity against HSV-1 [56].

8.6.2 Proteins and Peptides

Lectins are a diverse group of proteins that are found in algae, plants, animals, bacteria, and viruses [5]. They have various biological functions in humans, such as blood-protein regulation, carbohydrate binding, cell adhesion, and immune defense [65].

Lectins extracted from the red algae *Solieria filiformis* have demonstrated inhibitory effects against both Gram-negative and Gram-positive pathogenic bacteria [44]. The inhibition of bacterial growth is thought to occur by the binding of lectin with mannan, which is a linear polymer of the saccharide monomer mannose that arises on the cell surface of Gram-negative bacteria. Mannan acts as a hapten upon binding with a large lectin molecule, producing an immune response. However, it does not seem to inhibit the growth of Gram-positive *S. aureus* or *B. subtilis*, probably due to inappropriate lectin-polysaccharide binding sites on the cell surfaces of these species [100].

In another study, enzymatic hydrolysis was used with trypsin-extracted antibacterial peptides (>10 kDa mass) from *Saccharina longicuris*. Food spoilage from *S. aureus* was inhibited at concentrations of 0.31 to 2.5 mg/mL, indicating that the hydrolysate could be used as a potential agent for food preservation [7].

8.6.3 Fatty Acids

Antibacterial fatty acids, including 13-octadecadienoic acid and cyclopentaneacetic acid, have been obtained by ethanol extraction from *Sargassum vulgare* and by diethyl ether extraction from *Sargassum fusiforme*. Morphological variations were observed in *S. aureus* and *K. pneumonia* cells treated with these seaweed extracts. Transmission electron microscopy showed that the cell walls of both organisms were punctured, resulting in cell wall rupture, protoplasm shrinking, cytoplasmic vacuolation, cytoplasmic seepage, chromatin sprinkling, cell size reduction, and outer cell shape alteration [23]. In another study, long-chain fatty acids extracted from the green microalga *Planktochlorella nurekis* demonstrated antibacterial activity against *Campylobacter jejuni*, *E. coli*, *Salmonella enterica*, and *Lactobacillus johnsonii* [14].

8.6.4 Phlorotannins

The antibacterial activity of phlorotannins is reportedly due to the inhibition of oxidative phosphorylation. Phlorotannins could bind with bacterial proteins, such as cell membranes and enzymes, thus triggering bacterial cell lysis. Phloroglucinol compounds caused bacteriolysis of *Vibrio sp.* when tertiary structures, such as methyl- or acetyl-vinyl, were present [54]. Phlorotannins isolated from *Sargassum thunbergii* algae showed activity against *Vibrio parahaemolyticus* by destroying its cell wall and cell membrane, thus causing membrane permeability destruction and cytoplasm leakage [110].

Lee et al. extracted a wide range of solvents from brown seaweed, *Eisenia bicyclis* (Arame) and investigated them against antibiotic-resistant *Propionibacterium*-related acne. The phlorofucofuroeckol compound (phlorotannin with an alcohol substituent) showed the most potent antibacterial activity, including antimicrobial activity against MRSA [59].

8.6.5 Terpenes

A number of terpene compounds isolated from algae, such as diterpene-benzoate bromophycolides, have the ability to inhibit bacterial growth. Lane et al. extracted bromophycolides (diterpene-benzoate macrolides) from the Fijian red alga *Callophycus serratus* with methanol, dichloromethane, and water. The extracts significantly inhibited MRSA and vancomycin-resistant *Enterococcus faecium* [58].

8.7 Conclusion

Antimicrobial drug resistance is a serious concern, with limited or no treatment options for infections that are emerging globally. Antimicrobial agents may be derived from bacteria and fungi or chemically synthesized. However, resistance to these agents has led to the need for alternative natural sources. Algae are a potential alternative source for antimicrobial agents due to their diversity and ubiquitous nature, along with their ability to produce secondary metabolites that exhibit antimicrobial (i.e., antibacterial, antifungal, antiviral, antimalarial, and antiprotozoan) activities. Algae and their synthesized products have an ability to survive and adapt to a wide range of habitats, even when their environmental conditions are altered or stressed.

To date, there has been quite limited research into these microorganisms, and they predominantly remain an “untapped” resource. Thus, there is obviously a need for further study of the compounds described in this chapter for the treatment and prevention of various diseases, as well as an ongoing search for other undiscovered metabolites. Various technologies are available to assist in the systematic identification and purification of these natural products, which—when combined with in vivo experiments—could lead to novel antimicrobial agents.

References

1. Abdo SM, El-Senousy WM, Ali GH et al (2012) Antiviral activity of freshwater algae. *J Appl Pharm Sci* 2:21–25
2. Abou Zeid AH, Aboutabl EA, Sleem AA et al (2014) Water soluble polysaccharides extracted from *Pterocladia capillacea* and *Dictyopteris membranacea* and their biological activities. *Carbohydr Polym* 113:62–66
3. Asthana R, Srivastava A, Singh AP et al (2006) Identification of an antimicrobial entity from the cyanobacterium *Fischerella* sp. isolated from bark of *Azadirachta indica* (Neem) tree. *J Appl Phycol* 18:33–39
4. Ayeahunie S, Belay A, Baba TW, Ruprecht RM (1998) Inhibition of HIV-1 replication by an aqueous extract of *Spirulina platensis* (*Arthrospira platensis*). *J Acquir Immune Defic Syndr Hum Retrovirology* 18:7–12
5. Bahar AA, Ren D (2013) Antimicrobial peptides. *Pharmaceuticals* 6:1543–1575
6. Barbosa JP, Pereira RC, Abrantes JL et al (2004) In vitro antiviral diterpenes from the Brazilian brown alga *Dictyota pfaffii*. *Planta Med* 70:856–860

7. Beaulieu L, Bondu S, Doiron K et al (2015) Characterization of antibacterial activity from protein hydrolysates of the macroalga *Saccharina longicruris* and identification of peptides implied in bioactivity. *J Funct Foods* 17:685–697
8. Besednova NN, Zaporozhets TS, Somova LM et al (2015) Review: prospects for the use of extracts and polysaccharides from marine algae to prevent and treat the diseases caused by *Helicobacter pylori*. *Helicobacter* 20:89–97
9. Bhadury P, Wright PC (2004) Exploitation of marine algae: biogenic compounds for potential antifouling applications. *Planta* 219:561–578
10. Bold HC, Wynne MJ (1985) Introduction to the algae structure and reproduction, 2nd edn. Prentice-Hall Inc, Englewood Cliffs, pp 1–33
11. Borowitzka MA (1995) Microalgae as sources of pharmaceuticals and other biologically active compounds. *J Appl Phycol* 7:3–15. <https://doi.org/10.1007/BF00003544>
12. Bui HTN, Jansen R, Pham HTL, Mundt S (2007) Carbamidocyclophanes A-E, chlorinated paracyclophanes with cytotoxic and antibiotic activity from the Vietnamese cyanobacterium *Nostoc* sp. *J Nat Prod* 70:499–503. <https://doi.org/10.1021/mp060324m>
13. Bush K, Jacoby GA (2010) Updated functional classification of beta-lactamases. *Antimicrob Agents Chemother* 54:969–976. <https://doi.org/10.1128/AAC.01009-09>
14. Čermák L, Pražáková Š, Marounek M et al (2015) Effect of green alga *Planktochlorella nurekis* on selected bacteria revealed antibacterial activity in vitro. *Czech J Anim Sci* 60:427–435
15. Cardllina JH, Moore RE, Arnold EV, Clardy J (1979) Structure and absolute configuration of malyngolide, an antibiotic from the marine blue-green alga *Lyngbya majuscula* Gomont. *J Organomet Chem* 44:4039–4042. <https://doi.org/10.1021/jp001337a003>
16. Cardozo KHM, Guaratini T, Barros MP et al (2007) Metabolites from algae with economical impact. *Comp Biochem Physiol C Toxicol Pharmacol* 146:60–78. <https://doi.org/10.1016/j.cbpc.2006.05.007>
17. Chang T, Ohta S, Ikegami N et al (1993) Antibiotic substances produced by a marine green alga, *Dunaliella primolecta*. *Bioresour Technol* 44:149–153
18. Das BK, Pradhan J, Pattnaik PK et al (2005) Production of antibacterial from the fresh water alga *Euglena viridis* (Ehren). *World J Microbial Biotech* 21:45–50
19. De Felicio R, Dealbuquerque S, Young MCM et al (2010) Trypanocidal lei-shmanicidal and antifungal potential from marine red alga *Bostrychia tenella* J Agardh (Rhodomelaceae, Ceramiales). *J Pharm Biomed Anal* 52:763–769
20. De Morais MG, Vaz BDS, De Morais EG, Costa JAV (2015) Biologically active metabolites synthesized by microalgae. *Biomed Res Int* 2015:835761. <https://doi.org/10.1155/2015/835761>
21. Desbois AP, Lebl T, Yan LM et al (2008) Isolation and structural characterisation of two antibacterial free fatty acids from the marine diatom, *Phaeodactylum tricornutum*. *Appl Microbiol Biotechnol* 81:755–764
22. Duda-Chodak A (2013) Impact of water extracts of *spirulina* (WES) on bacteria, yeasts and molds. *Acta Sci Pol Technol Aliment* 12:33–39
23. El Shafay SM, Ali SS, El-Sheekh MM (2016) Antimicrobial activity of some seaweeds species from Red sea, against multidrug resistant bacteria. *Egypt J Aquat Res* 42:65–74
24. El-Sheekh MM, Osman MEH, Dyab MA, Amer MS (2006) Production and characterization of antimicrobial active substance from the cyanobacterium *Nostoc muscorum*. *Environ Toxicol Pharmacol* 21:42–50. <https://doi.org/10.1016/j.etap.2005.06.006>
25. Emad AS, Sanaa MMS, Vikramjit S (2010) Salt stress enhancement of antioxidant and antiviral efficiency of *Spirulina platensis*. *J Med Plant Res* 4:2622–2632. <https://doi.org/10.5897/JMPR09.300>
26. Feldmann SC, Reynaldi S, Stortz CA et al (1999) Antiviral properties of fucoidan fractions from *Leathesia difformis*. *Phytomedicine* 6:335–340
27. Fenical W, Sims JJ (1974) Cycloeuodesmol, an antibiotic cyclopropane containing sesquiterpene from the marine alga, *Chondria oppositoclada* Dawson. *Tetrahedron Lett* 15:1137–1140. [https://doi.org/10.1016/S0040-4039\(01\)82427-8](https://doi.org/10.1016/S0040-4039(01)82427-8)
28. Fernandes P (2006) Antibacterial discovery and development – the failure of success? *Nat Biotechnol* 24:1497–1503. <https://doi.org/10.1038/nbt1206-1497>

29. Francavilla M, Trotta P, Luque R (2010) Phytosterols from *Dunaliella tertiolecta* and *Dunaliella salina*: a potentially novel industrial application. *Bioresour Technol* 101:4144–4150. <https://doi.org/10.1016/j.biortech.2009.12.139>
30. Fukuyama Y, Kodaama M, Miura I et al (1989) Anti-plasmin inhibitor V. Structures of novel dimeric eckols isolated from the brown alga *Ecklonia kurome* Okamura. *Chem Pharm Bull* 37:2438–2440
31. Garson J (1989) Marine natural products. *Nat Prod Rep* 6:143–170
32. Ghasemi Y, Moradian A, Mohagheghzadeh A et al (2007) Antifungal and antibacterial activity of the microalgae collected from paddy fields of Iran: characterization of antimicrobial activity of *Chroococcus dispersus*. *J Biol Sci* 7:904–910. <https://doi.org/10.3923/jbs.2007.904.910>
33. Ghasemi Y, Yazdi MT, Shafiee A et al (2004) Parsiguine, a novel antimicrobial substance from *Fischerella ambigua*. *Pharm Biol* 42:318–322. <https://doi.org/10.1080/13880200490511918>
34. Guedes AC, Amaro HM, Malcata FX (2011) Microalgae as sources of high added-value compounds—a brief review of recent work. *Biotechnol Prog* 27:597–613. <https://doi.org/10.1002/btpr.575>
35. Gutierrez RMP, Flores AM, Solis RV et al (2008) Two new antibacterial norbietenol diterpenoids from cyanobacterium *Micrococcus lacustris*. *J Nat Med* 62:328–331
36. Harun R, Singh M, Forde GM, Danquah MK (2010) Bioprocess engineering of microalgae to produce a variety of consumer products. *Renew Sust Energ Rev* 14:1037–1047. <https://doi.org/10.1016/j.rser.2009.11.004>
37. Hawkey PM, Jones AM (2009) The changing epidemiology of resistance. *J Antimicrob Chemother* <https://doi.org/10.1093/jac/dkp256>
38. Hayashi T, Hayashi K, Maeda M, Kojima I (1996) Calcium spirulan, an inhibitor of enveloped virus replication, from a blue-green alga *Spirulina platensis*. *J Nat Prod* 59:83–87. <https://doi.org/10.1021/np960017o>
39. Hernández AJ, Romero A, Gonzalez-Stegmaier R et al (2016) The effects of supplemented diets with a phytopharmaceutical preparation from herbal and macroalgal origin on disease resistance in rainbow trout against *Piscirickettsia salmonis*. *Aquaculture* 454:109–117
40. Hernández-Corona A, Nieves I, Meckes M et al (2002) Antiviral activity of *Spirulina maxima* against herpes simplex virus type 2. *Antivir Res* 56:279–285. [https://doi.org/10.1016/S0166-3542\(02\)00132-8](https://doi.org/10.1016/S0166-3542(02)00132-8)
41. Herrero M, Ibáñez E, Cifuentes A et al (2006a) *Dunaliella salina* microalga pressurized liquid extracts as potential antimicrobials. *J Food Prot* 69:2471–2477
42. Herrero M, Jaime L, Martín-Álvarez PJ et al (2006b) Optimization of the extraction of antioxidants from *Dunaliella salina* microalga by pressurized liquids. *J Agric Food Chem* 54:5597–5603. <https://doi.org/10.1021/jf060546q>
43. Hillison CI (1977) *Seaweeds, a color-coded, illustrated guide to common marine 1977*. Plants of east coast of the United States, Keystone Books. The Pennsylvania State University Press, pp 1–5
44. Holanda ML, Melo VMM, Silva LCM (2005) Differential activity of a lectin from *Solieria filiformis* against human pathogenic bacteria. *Braz J Med Biol Res* 38:1769–1773
45. Hosseini Tafreshi A, Shariati M (2009) *Dunaliella* biotechnology: methods and applications. *J Appl Microbiol* 107:14–35. <https://doi.org/10.1111/j.1365-2672.2009.04153.x>
46. Ibáñez E, Cifuentes A (2013) Benefits of using algae as natural sources of functional ingredients. *J Sci Food Agric* 93:703–709. <https://doi.org/10.1002/jsfa.6023>
47. Ireland C, Faulkner DJ (1977) Diterpenes from *Dolabella californica*. *J Organomet Chem* 42:3157–3162
48. Ishimi Y, Sugiyama F, Ezaki J et al (2006) Effects of *Spirulina*, a blue-green alga, on bone metabolism in ovariectomized rats and hindlimb-unloaded mice. *Biosci Biotechnol Biochem* 70:363–368. <https://doi.org/10.1271/bbb.70.363>
49. Costa JAC, Morais MG (2013) Microalgae for food production. In: Soccol CR, Pandey A, Larroche C (eds) *Fermentation process engineering in the food industry*. Taylor & Francis, Boca Raton, p 486

50. Jaki B, Orjala J, Heilmann J et al (2000) Novel extracellular diterpenoids with biological activity from the cyanobacterium *Nostoc commune*. *J Nat Prod* 63:339–343
51. Jaki B, Orjala J, Sticher O (1999) A novel extracellular diterpenoid with antibacterial activity from the cyanobacterium *Nostoc commune*. *J Nat Prod* 62:502–503. <https://doi.org/10.1021/np980444x>
52. Jyotirmayee P, Sachidananda D, Das BK (2014) Antibacterial activity of freshwater microalgae: a review. *Afr J Pharm Pharmacol* 8:809–818. <https://doi.org/10.5897/AJPP2013.0002>
53. Kadam SU, O'Donnell CP, Rai DK et al (2015) Laminarin from Irish brown seaweeds *Ascophyllum nodosum* and *Laminaria hyperborea*: ultrasound assisted extraction, characterization and bioactivity. *Mar Drugs* 13:4270–4280
54. Kamei Y, Isnansetyo A (2003) Lysis of methicillin-resistant *Staphylococcus aureus* by 2, 4-diacetylphloroglucinol produced by *Pseudomonas* sp. AMSN isolated from a marine alga. *Int J Antimicrob Agents* 21:71–74
55. Kellam SJ, Walker JM (1989) Antibacterial activity from marine microalgae in laboratory culture. *Br Phycol J* 24:191–194
56. Kenji LK, Lee JB, Hayashi K et al (2005) Isolation of an antiviral polysaccharide, nostoflan, from a terrestrial cyanobacterium, *Nostoc flagilliforme*. *J Nat Prod* 68:1037–1041
57. Kokou F, Makridis P, Kentouri M, Divanach P (2012) Antibacterial activity in microalgae cultures. *Aquac Res* 43:1520–1527. <https://doi.org/10.1111/j.1365-2109.2011.02955.x>
58. Lane AL, Stout EP, Lin AS et al (2009) Antimalarial bromophycolides J-Q from the Fijian red alga *Callophycus serratus*. *J Organomet Chem* 74:2736–2742
59. Lee JH, Eom SH, Lee EH et al (2014) In vitro antibacterial and synergistic effect of phlorotannins isolated from edible brown seaweed *Eisenia bicyclis* against acne-related bacteria. *Algae* 29:47–55
60. Linnington RG, Edwards DJ, Shuman CF et al (2008) Symplocamide A, a potent cytotoxin and chymotrypsin inhibitor from marine cyanobacterium. *Symploca* sp. *J Nat Prod* 71:22–27
61. Linnington RG, Gonzalez J, Urena L et al (2007) Venturamides A and B: antimalarial constituents of the Panamanian marine cyanobacterium *Oscillatoria* sp. *J Nat Prod* 70:397–401
62. Livermore DM (2009) Has the era of untreatable infections arrived? *J Antimicrob Chemother* 64:29–36. <https://doi.org/10.1093/jac/dkp255>
63. Lustigman B (1988) Comparison of antibiotic production from four ecotypes of the marine alga, *Dunaliella*. *Bull Environ Contam Toxicol* 40:18–22
64. Markou G, Nerantzis E (2013) Microalgae for high-value compounds and biofuels production: a review with focus on cultivation under stress conditions. *Biotechnol Adv* 31:1532–1542. <https://doi.org/10.1016/j.biotechadv.2013.07.011>
65. Maverakis E, Kim K, Shimoda M (2015) Glycans in the immune system and the altered glycan theory of autoimmunity: a critical review. *J Autoimmun* 57:1–13
66. Mayer AMS, Hamann MT (2005) Marine pharmacology in 2001–2002: marine compounds with anthelmintic, antibacterial, anticoagulant, antidiabetic, antifungal, anti-inflammatory, antimalarial, antiplatelet, antiprotozoal, antituberculosis, and antiviral activities; affecting the cardiova. *Comp Biochem Physiol Toxicol Pharmacol* CBP 140:265–286. <https://doi.org/10.1016/j.cca.2005.04.004>
67. Mendes RL, Nobre BP, Cardoso MT et al (2003) Supercritical carbon dioxide extraction of compounds with pharmaceutical importance from microalgae. *Inorg Chim Acta* 356:328–334. [https://doi.org/10.1016/S0020-1693\(03\)00363-3](https://doi.org/10.1016/S0020-1693(03)00363-3)
68. Mendes RL, Reis AD, Palavra AF (2006) Supercritical CO₂ extraction of γ -linolenic acid and other lipids from *Arthrospira* (*Spirulina*) *maxima*: comparison with organic solvent extraction. *Food Chem* 99:57–63. <https://doi.org/10.1016/j.foodchem.2005.07.019>
69. Moraes de Souza M, Prietto L, Ribeiro AC et al (2011) Assessment of the antifungal activity of *Spirulina platensis* phenolic extract against *Aspergillus flavus*. *Ciencia e Agrotecnologia* 35:1050–1058
70. Najdenski HM, Gigova LG, Iliev II et al (2013) Antibacterial and antifungal activities of selected microalgae and cyanobacteria. *Int J Food Sci Technol* 48:1533–1540

71. Naviner M, Berge J-P, Durand P, Le Bris H et al (1999) Antibacterial activity of the marine diatom *Skeletonema costatum* against aquacultural pathogens. *Aquaculture* 174:15–24. [https://doi.org/10.1016/S0044-8486\(98\)00513-4](https://doi.org/10.1016/S0044-8486(98)00513-4)
72. Nobre B, Marcelo F, Passos R et al (2006) Supercritical carbon dioxide extraction of astaxanthin and other carotenoids from the microalga *Haematococcus pluvialis*. *Eur Food Res Technol* 223:787–790. <https://doi.org/10.1007/s00217-006-0270-8>
73. Ohta S, Shioimi Y, Kawashima A et al (1995) Antibiotic effect of linolenic acid from *Chlorococcum* strain HS-101 and *Dunaliella primolecta* on methicillin-resistant *Staphylococcus aureus*. *J Appl Phycol* 7:121–127. <https://doi.org/10.1007/BF00693057>
74. Osterhage C, Kaminsky R, Koeing GM et al (2000) Ascosalipyrrolidinone A, an antimicrobial alkaloid, from the obligate marine fungus *Ascochyta salicorniae*. *J Org Chem J Org Chem* 65:6412–6417
75. Ozemir G, Karabay NU, Dalay MC, Pazarbasi B (2004) Antibacterial activity of volatile components and various extracts of *Spirulina platensis*. *Phytother Res* 18:754–757
76. Palavra AMF, Coelho JP, Barroso JG et al (2011) Supercritical carbon dioxide extraction of bioactive compounds from microalgae and volatile oils from aromatic plants. *J Supercrit Fluids* 60:21–27. <https://doi.org/10.1016/j.supflu.2011.04.017>
77. Pandian P, Selvamuthukumar S, Manavalan R et al (2011) Screening of antibacterial and antifungal activities of red marine algae *Acanthaphora spicifera* (Rhodophyceae). *Biomed Sci Res* 3:444–448
78. Park H, Kurokawa M, Shiraki K et al (2005) Antiviral activity of the marine alga *Symphycloadia latiuscula*. Against herpes simplex virus (HSV-1) in vitro and its therapeutic efficacy against HSV-1 infection in mice. *Biol Pharm Bull* 28:2258–2262
79. Park HJ, Chung HY, Kim I et al (1999) Antioxidative activity of 2, 3, 6-tribromo-4, 5 dihydroxybenzyl methyl ether from *Symphycloadia latiuscula*. *J Fish Sci Technol* 2:1–7
80. Ploutno A, Carmeli S (2000) Nostocyclone A, a novel antimicrobial cyclophane from the cyanobacterium *Nostoc* sp. *J Nat Prod* 63:1524–1526. <https://doi.org/10.1021/np0002334>
81. Pop-Vicas A, Opal SM (2014) The clinical impact of multidrug-resistant gram-negative bacilli in the management of septic shock. *Virulence* 5:206–212. <https://doi.org/10.4161/viru.26210>
82. Pratt R, Daniels TC, Eiler JJ, Gunnison JB et al (1944) Chorellin, an antibacterial substance from *Chlorella*. *Science* 99:351–352
83. Pratt R, Mautner H, Gardner GM et al (1951) Report on antibiotic activity of seaweed extracts. *J Am Pharm Assoc Am Pharm Assoc (Baltim)* 40:575–579
84. Preetha K, John L, Subin C, Vijayan K (2012) Phenotypic and genetic characterization of *Dunaliella* (Chlorophyta) from Indian Salinas and their diversity. *Aquat Biosyst* 8:27. <https://doi.org/10.1186/2046-9063-8-27>
85. Quereshi MA, Ali RA, Hunter R (1995) Immuno-modulatory effects of *Spirulina platensis* supplementation in chickens. In: *Proceedings of the 44th Western poultry disease conference*. Sacramento, pp 117–121
86. Raveh A, Carmeli S (2007) Antimicrobial ambiguines from the cyanobacterium *Fischerella* sp. collected in Israel. *J Nat Prod* 70:196–201. <https://doi.org/10.1021/np060495r>
87. Romano I, Bellitti MR, Nicolaus B et al (2000) Lipid profile: a useful chemotaxonomic marker for classification of a new cyanobacterium in *Spirulina* genus. *Phytochemistry* 54:289–294
88. Sakemi S, Higa T, Jefford CW et al (1986) Venustatriol: a new antiviral triterpene tetracyclic ether from *Laurencia venusta*. *Tetrahedron Lett* 27:4287–4290
89. Sarada DVL, Kumar CS, Rengasamy R (2011) Purified C-phycoyanin from *Spirulina platensis* (Nordstedt) Geitler: a novel and potent agent against drug resistant bacteria. *World J Microbiol Biotechnol* 27:779–783. <https://doi.org/10.1007/s11274-010-0516-2>
90. Seenivasan R, Indu H, Archana G et al (2010) The antibacterial activity of some marine algae from South East Coast of India. *Am-Eur J Agric Environ Sci* 9:480–489
91. Sharma A (2011) Antimicrobial resistance: no action today, no cure tomorrow. *Indian J Med Microbiol* 29:91–92. <https://doi.org/10.4103/0255-0857.81774>

92. Sheng J, Zeng L, Sun H, Huang A (2001) Biological activities of protein-polysaccharides from *Nostoc commune*. *J Guang Acad Sci* 17:20–23
93. Sheridan C (2006) Antibiotics au naturel. *Nat Biotechnol* 24:1494–1496. <https://doi.org/10.1038/nbt1206-1494>
94. Simic S, Kosanic MM, Rankovic BR (2012) Evaluation of in vitro antioxidant and antimicrobial activities of green algae *Trentepohloa umbrina*. *Not Bot Horti Agro* 40:86–91
95. Simmons LT, Engene N, Urena LD et al (2008) Viridamides A and B, lipodepsipeptides with antiprotozoal activity from marine cyanobacterium. *Oscillatoria Nigro Viridis*. *J Nat Prod* 71:1544–1550
96. Singh RK, Tiwari SP, Rai AK et al (2011) Cyanobacteria: an emerging source for drug discovery. *J Antibio* 64:401–412
97. Sivakumar J, Santhanam P (2011) Antipathogenic activity of Spirulina powder. *Recent Res Sci Technol* 3:158–161
98. Smee DF, Bailey KW, Wong M-H et al (2008) Treatment of influenza A (H1N1) virus infections in mice and ferrets with cyanovirin-N. *Antivir Res* 80:266–271
99. Soltani M, Khosravi A-R, Asadi F, Shokri H (2012) Evaluation of protective efficacy of Spirulina platensis in Balb/C mice with candidiasis. *J Mycol Med* 22:329–234. <https://doi.org/10.1016/j.mycmed.2012.10.001>
100. Strathmann M, Wingender J, Flemming HC (2002) Application of fluorescently labelled lectins for the visualization and biochemical characterization of polysaccharides in biofilms of *Pseudomonas aeruginosa*. *J Microbiol Methods* 50:237–248
101. Tandeau de Marsac N, Houmard J (1993) Adaptation of cyanobacteria to environmental stimuli: new steps towards molecular mechanisms. *FEMS Microbiol Lett* 104:119–189. [https://doi.org/10.1016/0378-1097\(93\)90506-W](https://doi.org/10.1016/0378-1097(93)90506-W)
102. Temina M, Rezankova H, Rezanka T, Dembitsky VM (2007) Diversity of the fatty acids of the Nostoc species and their statistical analysis. *Microbiol Res* 162:308–321. <https://doi.org/10.1016/j.micres.2006.01.010>
103. Lancet T (2009) Urgently needed: new antibiotics. *Lancet* 374:1868. [https://doi.org/10.1016/S0140-6736\(09\)62076-6](https://doi.org/10.1016/S0140-6736(09)62076-6)
104. Topeu G, Aydogmus Z, Imre S et al (2003) Brominated sesquiterpenes from the red alga *Laurencia obtusa*. *J Nat Prod* 66:1505–1508
105. Volk RB (2008) A newly developed assay for the quantitative determination of antimicrobial (anticyanobacterial) activity of both hydrophilic and lipophilic test compounds without any restriction. *Microbiol Res* 163:161–167. <https://doi.org/10.1016/j.micres.2006.03.015>
106. Volk RB, Furkert FH (2006) Antialgal, antibacterial and antifungal activity of two metabolites produced and excreted by cyanobacteria during growth. *Microbiol Res* 161:180–186. <https://doi.org/10.1016/j.micres.2005.08.005>
107. Wang H, Li YL, Shen WZ et al (2007) Antiviral activity of a sulfoquinovosyldiacylglycerol (SQDG) compound isolated from the green alga *Caulerpa racemosa*. *Bot Mar* 50:185–190
108. Wang M, Xu YN, Jiang GZ et al (2000) Membrane lipids and their fatty acid composition in *Nostoc flagelliforme* cells. *Acta Bot Sin* 42:1263–1266
109. Washida K, Koyama T, Yamada K et al (2006) Karatungoils A and B, two novel antimicrobial polyol compounds, from the symbiotic marine dinoflagellate *Amphidinium* sp. *Tetrahedron Lett* 47:2521–2525. <https://doi.org/10.1016/j.tetlet.2006.02.045>
110. Wei Y, Liu Q, Xu C et al (2015) Damage to the membrane permeability and cell death of *Vibrio parahaemolyticus* caused by phlorotannins with low molecular weight from *Sargassum thunbergii*. *J Aquat Food Prod Technol* 25:323–333
111. Whitton BA (2008) Cyanobacterial diversity in relation to the environment. *NATO Secur through Sci Ser C Environ Secur* 17–43. https://doi.org/10.1007/978-1-4020-8480-5_2
112. Wright JLC, Boyd RK, de Freitas ASW et al (1989) Identification of domic acid, a neuroexcitatory amino acid in toxic mussels from Eastern Pince Edward Island. *Can J Chem* 67:481–490
113. Yu SH, Wu SJ, Wu JY et al (2015) Preparation of fucoidan-shelled and genipin-crosslinked chitosan beads for antibacterial application. *Carbohydr Polym* 126:97–107