Chapter 6

Cyanobacteria and Microalgae in the Production of Valuable Bioactive Compounds

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Additional information is available at the end of the chapter

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Abstract

In the last decades, an increasing attention has been directed toward the possibilities of growing algae commercially. This interest has been partially due to the fact that some strains of microalgae and cyanobacteria have demonstrated the ability to produce a variety of bioactive products. Both, primary and secondary metabolism of these microorganisms has been demonstrated to play a key role in the production of special chemicals. Antioxidants, for instance, can be produced by some algal strains to protect photosynthetic cells from oxidative stress. Microalgae can produce a variety of polyunsaturated and monounsaturated fatty acids with clear health benefits for human nutrition. Potential products obtained from cyanobacteria and microalgae exhibiting interesting medical properties include polysaccharides, glycerol, glycoproteins, and antibiotics. From the aforementioned products, especially relevant has become the search of new antibiotics. The potential spread of bacterial resistance and the foreseen decrease on efficiency on antibiotics, has largely stimulated the research on novel antibiotics sources. Among these sources, cyanobacteria and microalgae have demonstrated a vast and just barely explored potential.

Keywords: bioactive products, pharmaceuticals, primary and secondary metabolism, microalgae, cyanobacteria, antibiotics

1. Introduction

Cyanobacteria (prokaryotic green-blue algae) and microalgae (eukaryotic microalgae) are regularly found in water bodies, desert crusts, or even in symbiosis with other animals. They can live in large varieties of environmental conditions, including low or high temperatures, high-light intensities, pH and salinity [1]. In the last decades, increasing attention has been paid to

the potential of growing these kinds of organisms with commercial purposes. Part of the added value of this type of biomass is based on the fact that it can be used in human and animal nutrition (i.e. fish feed in aquaculture facilities). Moreover, some extracts from microalgae can be used to produce cosmetics and a variety of different bioactive products, such as pharmaceutical compounds [2–4]. The diversity of cyanobacteria and microalgae is immense, with species, genera, or even classes being discovered every year. On the estimated millions of exiting species, about 30,000 have been described; but nowadays, not more than a dozen is regularly cultivated and exploited in large scale for commercial biotechnological purposes. On top of that, research on how the culture conditions affect the production of important bioactive substances remains nowadays very scarce. Some authors, such as Spoehr and Milner [5], proved that manipulating microalgae or cyanobacteria growth conditions, for instance, by applying different forms of stress to the cells, could promote the production of biomass with valuable secondary metabolites, some of which presents pharmaceutical and/or industrial values. In most of the cases, the production of valuable metabolic products by cyanobacteria and microalgae is a two-step process. In the first step, the microorganisms are grown under optimal conditions to maximize the production of biomass. This process is followed by a second step where stress factors, such as high light intensity or nutrients deprivation, are applied to the culture to induce the production of valuable secondary metabolites with the pursued pharmaceutical [6, 7] or antioxidant properties. In this chapter, the production of a variety of bioactive compounds by cyanobacteria and microalgae has been reviewed.

2. Valuable bioactive products from cyanobacteria and microalgae

Variations in temperature, light, pH, salinity and nutrient availability have been extensively investigated to study their impact on microalgae growth and their primary and secondary metabolic products. Primary metabolites are those directly involved in normal growth development, reproduction, cell division, or metabolism. They include for instance the production of lipid, such as polyunsaturated fatty acids (PUFA) [8–11], antioxidants such as carotenoids, and some types of proteins (**Figure 1**). Secondary metabolites are those compounds that are not used by organisms for their primary needs and include compounds that act as hormones, antibiotics, or toxins, among others [12]. The production of secondary metabolites appears to be specie and strain specific [13], and is possibly associated to the exposure of the microorganism to specific environmental conditions [6, 14] caused, for instance, by stress factors. In a study carried out by Lustigaman in 1988, the production of antibiotic activity by *Dunaliella* spp. was investigated. The study was based on isolating extracts of these microalgae from two different environmental scenarios; one clean and one polluted water system. The study demonstrated that nonproteinous substances inhibiting the activity of the bacteria *Escherichia coli* were only produced by the microalgae *Dunaliella* spp. under exposure to the polluted water. It was, therefore, suggested that microalgae growing in adverse conditions are more likely to produce secondary metabolites with antibacterial activity [15].

Nowadays, the major products obtained from microalgae with industrial use are carotenoids and algal biomass, which are mainly used for human and animal feed and for aquaculture.

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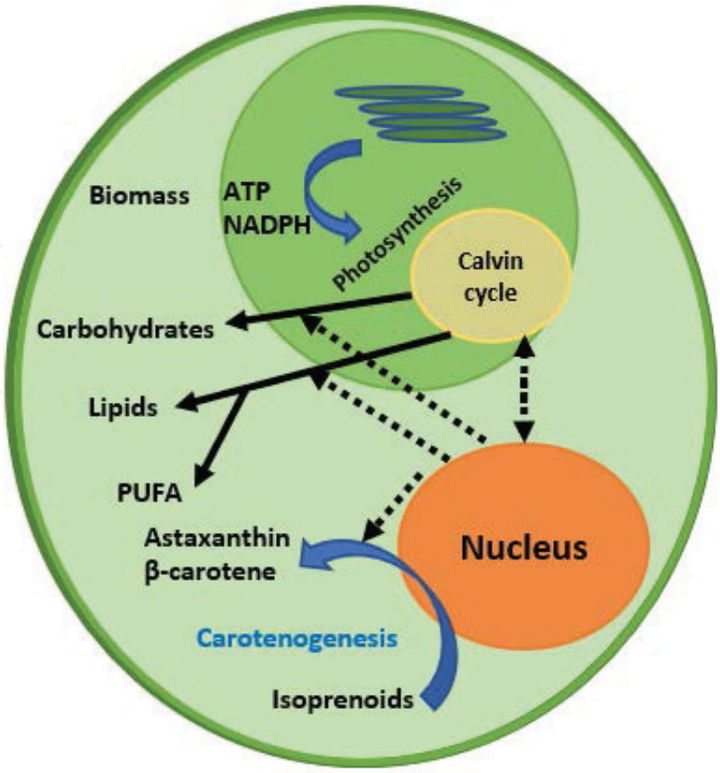


Figure 1. Example of some primary metabolic routes and their products in microalgae. Adapted from Rosenberg et al. [16].

Microalgae can also produce other antioxidants, such as vitamins C and E, and even butylated hydroxytoluene (BHT). Fatty acids are also produced as primary metabolic products, playing an important role protecting the cells against oxidative stress. Other metabolic products obtained from microalgae and exhibiting medical properties are special polysaccharides, glycerol and myscosporine-like amino acids (MAA). In addition to the aforementioned compound families, glycoproteins, antifreeze proteins and antibiotics can also be produced by these microorganisms. Some of these substances have demonstrated a set of interesting bioactivities [11]. An overview of the potential bioactive metabolites is presented in **Figure 2**.

2.1. Antioxidants

Eukaryotic microalgae and cyanobacteria are often exposed to high oxygen levels and high irradiance conditions. As a response to this potential oxidative stress, these organisms have developed defense systems based on the production of different antioxidants. The main goal of these substances is to preserve cells from oxidative stress, which may otherwise cause damage to essential biological structures, such as DNA, proteins and lipids. Oxidative stress in humans and animals can also lead to severe health problems, such as atherogenesis, cancer, neurodegenerative diseases, infant retinopathy, muscular degeneration and renal failure, along with other problems [17–19]. Dietary intake of antioxidants from these organisms has shown the ability to limit or prevent certain health issues. For instance, many substances found in algae,

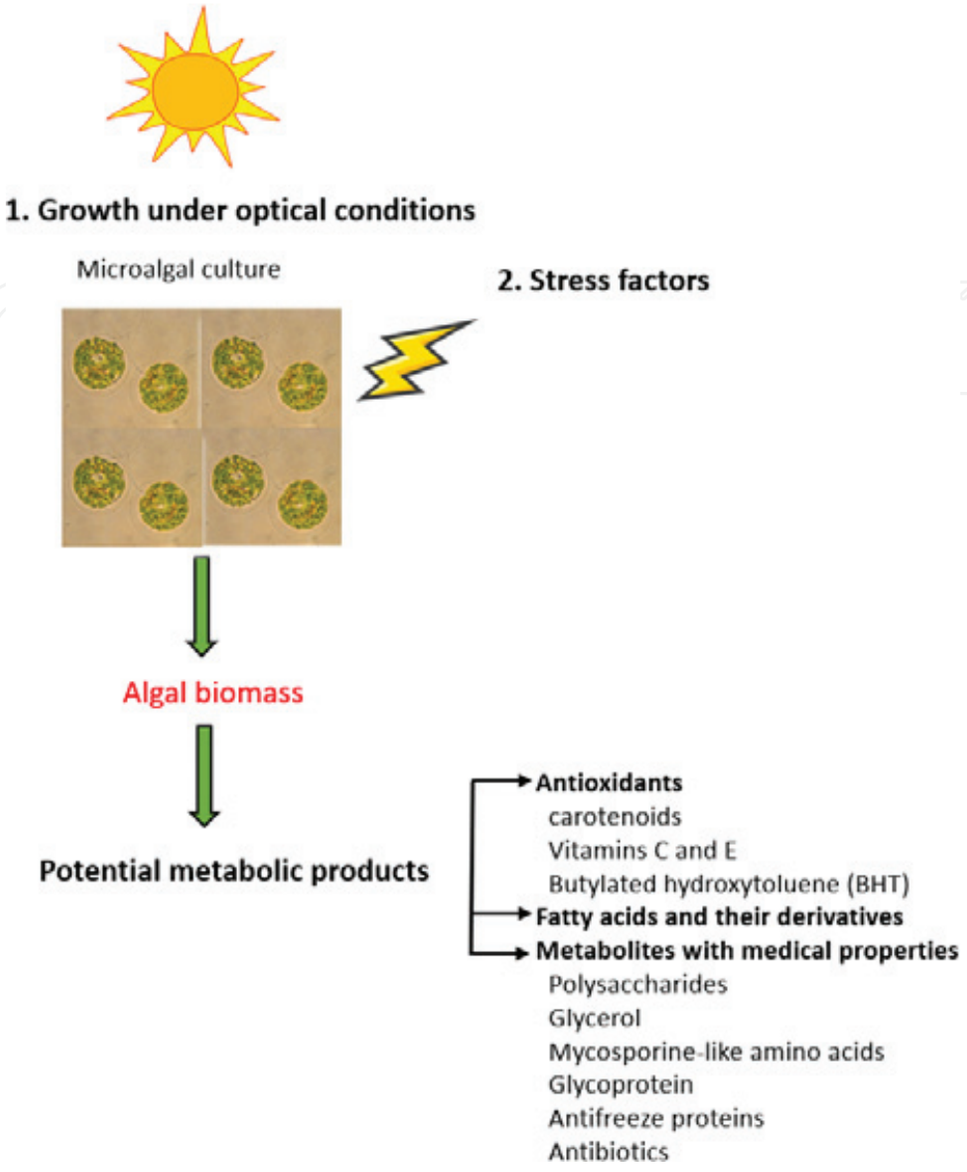


Figure 2. Overview of the potential bioactive metabolites produced by microalgae and cyanobacteria. Adapted from Skjånes et al. [11].

such as carotenoids, vitamins C and E or butylated hydroxytoluene (BHT) have such antioxidant effects [11]. Carotenoids have been largely used as supplement in human nutrition as well as in food and animal feed, poultry and fish. Vitamin C may be found in tablets for human consumption as well as in meat, where it has been largely used to prevent oxidation processes and the discoloration of the product during storage. Vitamin E can be commonly found in supplements for human health and has been largely used in food industry. Another largely used antioxidant is astaxanthine. This substance has become very popular recently as supplement for human nutrition and is commonly found in, i.e., salmon food formulations to intensify the pigmentation of the fish growth in aquaculture facilities. **Table 1** gathers some examples of microalgae and the type of antioxidant substance that they produce.

Specie of microalgae	Type of antioxidant substance	Ref.
Botryococcus braunii	β-Carotene BHT	[20, 21]
Chlamydocapsa nivalis	Phenolic antioxidants	[22]
Chlorella pyrenoidosa	Vitamins E	[23]
Chlorella spp.	Vitamin C	[24]
Chlorella vulgaris	Vitamins C and E Lutein (carotenoid)	[20] [25]
Scenedesmus obliquus	Vitamins C and E	[20]
Scenedesmus quadricauda	Vitamins C and E	[23]
Chlamydocapsa spp.	Lutein, canthaxanthin and astaxanthin (carotenoids)	[26]

Table 1. Antioxidant substances produced by microalgae.

2.2. Fatty acids and their derivatives

Fatty acids are essential components of the diet. They can occur in the cells as glycolipids and phospholipids forming the cellular membranes, or as storage products for energy and carbon in the form of triglycerides [27]. In some cases, triglycerides may also have a role protecting against oxidative stress, and the lack of these nutrients can cause severe damage to the organism. Fatty acids can be produced by eukaryotic microalgae and cyanobacteria, and in some cases they can produce them in large amounts [28]. The truly essential fatty acids are omega-3 fatty acids, such as linoleic acid and α-linoleic acid. Both humans and animals are dependent on obtaining them from the diet, because they are used as starting points for building longer chains of fatty acids. Food supplements of omega-3 are known to have beneficial health effects in the prevention of coronary heart disease, hypertension, type 2 diabetes, renal disease and chronic obstructive pulmonary disease, among others [29]. A summary including the production of fatty acids produced by microalgae is presented in **Table 2**. Some of the industrial applications of fatty acids include cosmetic formulations, food, personal care, and pharmaceutical products.

2.3. Polysaccharides

Certain polysaccharides from microalgae have been shown to have remarkable biomedical properties. Several studies have demonstrated that microalgae, such as *Chlorella vulgaris* and *Scenedesmus quadricauda* are able to presumably produce sulfated polysaccharides that function as protection against microcystin oxidative stress [35]. Crude polysaccharide extracts obtained from *Chlorella stigmatophora* and *Phaeodactylum tricornutum* showed anti-inflammatory activity in the carrageenan-induced paw edema test [36]. Moreover, other crude polysaccharide extracts from *Chlorella pyrenoidosa* presented antitumoral activity against A549 (cell human lung carcinoma) *in vitro* [37]. Furthermore, polysaccharides can also present other

Specie of microalgae	Type of fatty acid	Ref.
Ankistrodesmus sp.	α-linolenic acid	[30]
Botryococcus braunii	Linoleic acid	[31]
Botryococcus spp.	α-linolenic acid	[31]
Chamydomonas spp.	α-linolenic acid	[32]
Chlorella minutissima	Eicosapentaenoic acid	[33]
Scenedesmus obliquus	α-linoleic acid Linoleic acid	[23]
Scenedesmus quadricauda	α-linoleic acid	[34]

Table 2. Fatty acids produced by microalgae.

health-promoting effects on, for instance, gastric ulcers, wounds and constipations [38, 39]. However, their exact function in the algae cells remains still unknown.

2.4. Glycerol

Glycerol can function as osmoregulator and osmoprotector of enzymes. This substance has been accumulated in substantial amounts in halotolerant species during salt stress conditions. The production of glycerol in algae is regulated by external water activity, but high light intensities may inhibit its production [40]. In some cases, the algae can also excrete glycerol as a response to high concentrations of CO_2 rather than salt stress condition [41]. Glycerol is widely used in cosmetics, pharmaceuticals, paint, food, tobacco, pulp and paper, or in the production of a large variety of chemicals [42]. Some examples of microalgae producing glycerol are *Brachiomonas submarina* [43], *Chlamydomonas* spp. [41] and *Dumaliella salina* [44]. Glycerol can be found in a large variety of commercial products and applications, such as cosmetics and food products, drugs and pharmaceuticals.

2.5. Lectins

Lectins are carbohydrate-binding proteins that are located within protein bodies in the cell. Lectins from algae have high specificity for complex oligosaccharides, glycoproteins, or glycolipids. They are useful in medical science, for instance, for the detection of disease-related alterations of glycan synthesis, and for cell markers for diagnosis purposes including infectious agents, i.e., viruses, bacteria, fungi and/or parasites. Different strains of *Chlorella*, such as *Chlorella minutissima* [45], *Chlorella pyrenoidosa* [46, 47] and *Chlorella* spp. [45] produce metabolites with antimicrobial activity and this activity has been preliminary hypothesized to be due to lectins [47]. Studies conducted with other algae strains, such as *Desmococcus olivaceus* [45], *Scenedesmus quadricauda* [46] and *Scenedesmus* sp. [45, 48], have reported that the production of

these lectins can be induced by growth-limiting conditions like nutrient deprivation and/or light stress conditions [49].

Some companies, for instance, Lectin Labs Ltd., have developed lectin formulations, and claim that these lectins interfere or destroy the development of the disease-causing processes, even in cases where antibiotics are ineffective.

2.6. Mycosporine-like amino acids

Mycosporine-like amino acids (MAA) are a group of molecules consisting of an amino acid bound to a chromophore molecule that absorbs light. These amino acids are involved in protecting the organism against UV radiation and are produced in significant amounts by, for example, the high UV-tolerant snow algae *Chlamydomonas nivalis* and other green algae species. The production of MAA is induced by exposing the microalgae to UV-light and the resulting irradiance stress reactions. Nevertheless, there are indicators pointing out that a decrease in nitrogen levels leads to a decrease in the production of MAA [50, 51]. MAAs from algae have been explored for commercial purposes which have resulted, for instance, in commercial skin-care products for UV protection [52]. Some examples of microalgae that produce MAA are *Ankistrodesmus spiralis*, *Chlorella minutissima*, *Scenedesmus* sp. and *Scotiella nivalis* [51].

2.7. Glycoproteins

Glycoproteins are relevant biological structures formed by a protein covalently linked to one or more carbohydrate units. These structures have a large set of biological functionalities and some microalgae have demonstrated to be a potential source of them. For instance, a glycoprotein obtained from *Chlorella vulgaris* was found to exhibit anticancer activity through antimetastatic immunopotentiation [53, 54]. Other microalgae presenting anticancer activity are *Desmococcus olivaceus* [45], *Scenedesmus* sp. [45, 48], *Dunaliella bardawil* [55] and *Dunaliella salina* [44], among others. However, little has been done to identify similar compounds with activity from other algal species, nor to consider possibilities for optimization of the production of these glycoproteins by manipulating growth conditions [11].

2.8. Antifreeze proteins

Cold adapted strains of green algae, such as those living in polar environments, are often producers of antifreeze proteins (AFPs), also designated as ice structuring proteins (ISPs). These proteins are key elements for the survival of some organisms, since they prevent damages occurring as a result of very low temperatures. They exhibit unique properties because they are able to bind to ice crystals, prevent recrystallization and protect other proteins from damage. AFPs extracted from algae or other microorganisms can be used for cryopreservation, frozen food preservation, transgenic crops and even weather modification [56–58]. There are some microalgae such as *Chlorella pyrenoidosa* that can produce AFPs that additionally exhibit

antifungal properties [46, 47]. AFPs are currently being explored in some formulations to reduce cold-induced damage in medical, food and cosmetic products with the target of lengthening shelf life of the frozen gods. The extraordinary properties of AFPs allow hypothesizing a growing number of businesses including AFPs in their future formulation of products.

2.9. Antibiotic activity

Some strains of microalgae can produce metabolites with antibiotic activity aimed at killing or inhibiting bacterial growth. In some cases, this activity has only been identified in general extracts from the algal culture, without properly determining the chemical identity of the active compound/s [45, 47]. There are indications that antibiotics are more likely to occur in strains isolated from environments polluted by bacteria than in strains isolated from cleaner environments [59]. For instance, the methanolic extracts of *Tetraspora cylindrica* present antibacterial activity against *Corynebacterium diphtheria*, *Klebsiella pneumoniae* and *Shigella boydii*, among others. These extracts also present antifungal activity against: *Curvularia lunata*, *Fusarium sporotrichoids*, *Macrophomina phaseolina*, *Rhizoctonis solani*, *Sclerotium rolfsii* and *Trichoderma harzianum* [60].

In the last decade, the screening and bioprospecting of microalgae and cyanobacteria for antibiotics and pharmacologically active compounds has received a lot of attention. This is because a large number of antibiotic compounds, many of them with unusual and novel structures, have been isolated and characterized from extracts of microalgae [15]. Similarly, many cyanobacteria have been shown to produce antiviral and antineoplastic compounds. A range of pharmacological activities have also been observed in some extracts of microalgae which active principles, in most of the cases, are still unknown. Several of these bioactive compounds found in microalgae extracts may find application in human or veterinary medicine and agriculture. Others could be used, for instance, as research tools or as structural models for the development of new drugs [15]. Microalgae are particularly attractive as natural sources of bioactive molecules because they have the potential to produce these compounds in culture. This enables the production of structurally complex molecules which are difficult or impossible to produce by chemical synthesis [61].

Many of the antibiotics and pharmaceuticals in current use have their origins in nature and are the product of systematic screening of terrestrial organisms, such as higher plants and soil microbes. For instance, of approximately 13500 known naturally occurring antibiotics, 5500 are produced by actinomycetes, while approximately 3300 are produced by higher plants and, of these, about 90 are in current medical use [62]. Much of the work concerned with the isolation, screening, and physiology of antibiotic-producing microorganisms has been focused on heterotrophs. However, very little attention has been paid to other groups, such as microalgae which are able to grow under diverse nutritional conditions: photo-autotrophically or chemoheterotrophically [63].

Moreover, many marine algae produce antibiotics substances that are capable of inhibiting bacteria, viruses, fungi and other epibionts. It also appears that the antibiotic characteristic is dependent on many factors, i.e., the algae strain, the microorganisms, the season and the growth condition [64–67]. Several extractable compounds, for instance, cyclic polysulfides and halogenated compounds, are toxic to microorganisms and, therefore, responsible for the antibiotic activity of some marine algae [68–70].

2.9.1. Antibacterial activity of cyanobacteria

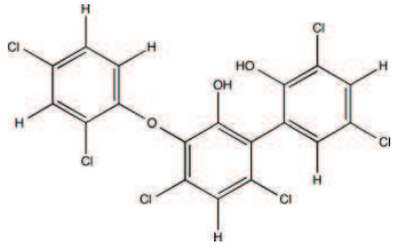
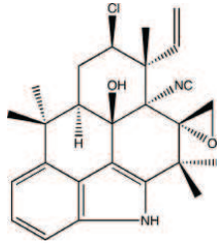
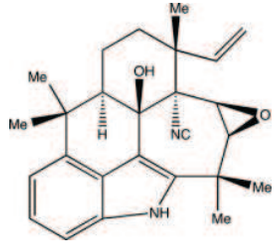
Cyanobacteria are phototrophic organisms with a classic prokaryotic cell organization, but similar to eukaryotes they conduct photosynthesis and respiration in their active membrane system [71]. Microalgae grow ubiquitously and produce, in addition to toxins, a wide range of bioactive metabolites with potential application in biotechnology [72]. These characteristics have made them the focus of intense examination in the last decade [73, 74].

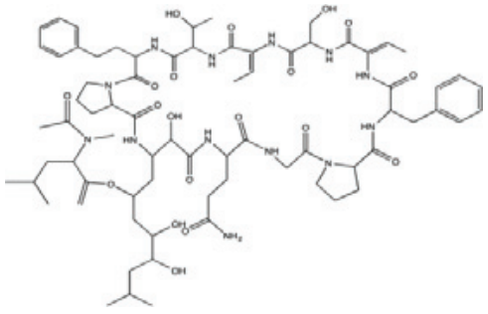
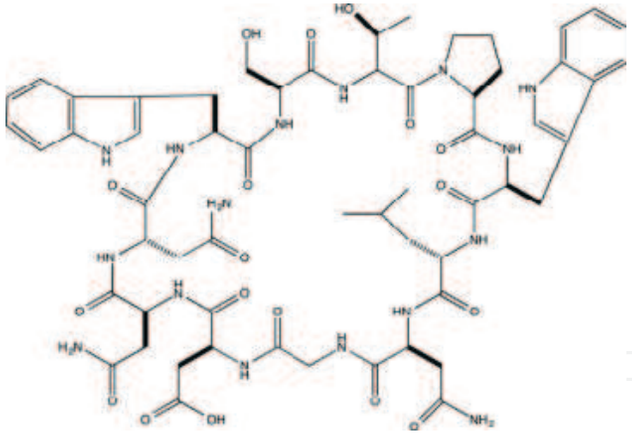
To date, only a few compounds have been extracted and commercialized, including nutraceuticals, cosmetic products and other high-value molecules [39, 75]. Some purified compounds have promising commercial applications as bioplastics, biofertilizers, antiviral, antifungal, anticancer and antibacterial drugs [76–78]. **Table 3** illustrates some examples of antibacterial, antifungal and antimycobacterial compounds extracted from cyanobacteria.

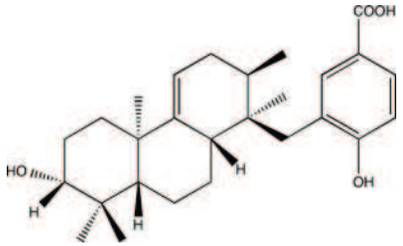
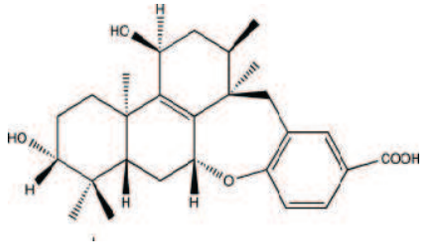
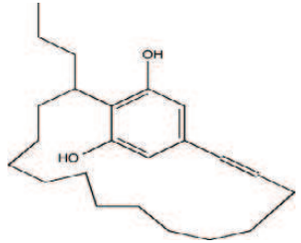
2.9.2. Antibacterial activity of microalgae

The production of bioactive compounds from cyanobacteria has received more attention than from eukaryotic microalgae. The reason may be probably based on the simpler culture methods available for cyanobacteria growth, and also to their greater resistance to bacterial contamination [89]. Nevertheless, more and more studies have recently focused on the synthesis of bioactive compounds, such as isoprenoids, polyketides, no ribosomal peptides, polyunsaturated fatty acids and alkaloids, by eukaryotic microalgae [90], used to inhibit bacterial activity [6, 91, 92]. In addition, further studies have identified fatty acids, terpenes, carbohydrates, glycolipids, lipoproteins, bromophenols and tannins, among other, as compounds that exhibit antibacterial activity against human pathogens [93, 94].

Microalgae accumulate cell-associated antibacterial substances [95, 96], and some studies have shown different levels of antibacterial activity in different microalgae cultures [95, 97–99]. Moreover, crude extracts from different species of eukaryotic microalgae have shown effectiveness against both Gram positive (Gram+) and Gram negative (Gram−) bacteria, as well as *Mycobacterium tuberculosis* [100–104]. This could suggest, therefore, the potential of microalgae for the production of compounds with a broad-spectrum activity, which is highly desired for the production of new antibiotics. However, many compounds extracted from these organisms are likely to be impractical as antibiotics for medical uses as a result of, for instance, its toxicity or inactivity *in vivo* [61]. **Table 4** presents a summary of the eukaryotic microalgae with the highest antibacterial activity or the widest spectrum of activity of large screening programs to date.

Compound	Species	Chemical structure	Molecular formula	Activity [79]
Ambigol A [80]	*Fischerella ambigua* [80]	 [80]	$C_{18}H_8Cl_6O_3$	Antibacterial Antifungal
Fischambiguine B [81]	*Fischerella ambigua* [81]	 [81]	$C_{26}H_{29}ClN_2O_2$	Antimycobacterial
Ambiguine I isonitrile [82, 83]	*Fischerella* sp. and *ambigua* [82, 83]	 [82, 83]	$C_{26}H_{30}N_2O_2$	Antibacterial Antimycobacterial
Pahayokolide A [84]	*Lyngbya* sp. [84]		$C_{72}H_{1\ 05}N_{13}O_{20}$	Antibacterial

Compound	Species	Chemical structure	Molecular formula	Activity [79]
		 [84]		
Kawaguchi peptin B [85]	*Microcystis aeruginosa* [85]	 [85]	$C_{58}H_{76}N_{16}O_{18}$	Antibacterial
Noscomin [86]	*Nostoc commune* [86]		$C_{27}H_{38}O_4$	Antibacterial Antifungal

Compound	Species	Chemical structure	Molecular formula	Activity [79]
		 [86]		
Diterpenoid [87]	*Nostoc commune* [87]	 [87]	$C_{22}H_7O_5$	Antibacterial
Nostocycline A [88]	*Nostoc* sp. [88]	 [88]	$C_{23}H_{34}O_2$	Antibacterial

Adapted from Senhorinho et al. [15].

Table 3. Antibacterial compounds extracted from microalgae.

Microalgae specie	Antibacterial compound/Fraction	Gram+ inhibition	Gram− inhibition	Ref.
Green algae				
Chlamydomonas reinhardtii	Aqueous or methanolic and hexanolic extracts	*Bacillus subtilis* *Staphylococcus aureus* *Staphylococcus epidermidis*	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella typhi*	[106]
Chlorella minutissima	Ethanolic extracts	*S. aureus*	*E. coli* *P. aeruginosa*	[45]
Chlorella pyrenoidosa	Various organic solvent extracts: ethanol, acetone, diethyl ether, and methanol	*B. subtilis* *S. aureus*	*E. coli* *P. aeruginosa*	[46]
Chlorella vulgaris	Chlorellin	*B. subtilis* *S. aureus* *Streptococcus pyogenes*	*E. coli* *P. aeruginosa*	[97]
Chlorella vulgaris	Aqueous or methanolic and hexanolic extracts	*B. subtilis* *S. aureus* *S. epidermidis*	*E. coli* *P. aeruginosa* *S. typhi*	[106]
Chlorococcum HS-101	α-linolenic acid	*B. subtilis* *Bacillus cereus* *S. aureus* *MRSA*	*Enterobacter aerogenes*	[107–109]
Chlorococcum humicola	Various organic solvent extracts: acetone, benzene, chloroform, diethyl ether, ethyl acetate, ethanol, hexane, and methanol Purified pigments: carotenoid and chlorophyll	*B. subtilis* *S. aureus*	*E. coli* *P. aeruginosa* *Salmonella typhimurium* *Klebsiella pnemoniae* *Vibrio cholerae*	[110]
Desmococcus olivaceus	Ethanolic extracts	*S. aureus*	*E. coli* *P. aeruginosa*	[45]
Dunaliella primolecta	Polyunsaturated fatty acids: α-linolenic acid	*B. cereus* *B. subtilis* *S. aureus* *MRSA*	*E. aerogenes*	[107, 109]
Dunaliella salina	Indolic derivative Polyunsaturated fatty acids β-ionone and neophytadiene	*S. aureus*	*E. coli* *P. aeruginosa*	[111–113]
Dunaliella sp.	Lysed cells	*S. epidermidis* *Micrococcus luteus*	*Proteus vulgaris*	[59]
Haemotococcus pluvialis	Short-chain fatty acids	*S. aureus*	*E. coli*	[114, 115]
Klebsormidium sp.	Pellet	*B. Subtilis*	No effect	[116]
Pseudokirchneriella subcapitata	Methanolic extracts	*S. aureus*	*P. aeruginosa*	[111]
Scenedesmus obliquus	Long-chain fatty acid	*S. aureus*	*E. coli* *P. aeruginosa* *Salmonella* sp.	[117]
Scenedesmus quadricauda	Various organic solvent extracts: ethanol, acetone, diethyl ether, and methanol	*B. subtilis* *S. aureus*	*E. coli* *P. aeruginosa*	[46]

Microalgae specie	Antibacterial compound/Fraction	Gram+ inhibition	Gram− inhibition	Ref.
Scenedesmus sp.	Ethanolic extracts	*S. aureus*	*E. coli* *P. aeruginosa*	[45]
Red algae				
Porphyridium aerugineum	Phycobiliproteins	*S. aureus* *S. pyogenes*	Not tested	[118]
Porphyridium sordidum	Pellet	*B. subtilis*	*E. coli* *Pseudomonas fluorescens*	[116]
Porphyridium purpureum	Methanolic extracts	*B. subtilis*	*E. coli* *Pseudomonas fluorescens*	[116]
Rhodella reticulate	Exopolysaccharides	*S. aureus* *B. cereus* *S. pyogenes*	No effect	[118]
Diatoms				
Asterionella glacialis	Whole cell	*S. aureus* *S. epidermidis* *M. luteus* *Sarcina* sp.	*E. coli*	[119]
Attheya longicornis	Methanolic extracts	*S. aureus* *MRSA*	No effect	[120]
Chaetoceros mulleri	Unsaturated fatty acid-containing lepidic fractions (triglycerides and docosa-pentaenoic acid (DPA))	*B. subtilis* *S. aureus*	*E. coli*	[121, 122]
Navicula delognei	Transphytol ester Hexadecatetraenoic and octadecatetraenoic acids	*S. aureus* *S. epidermidis*	*S. typhimurium* *P. vulgaris*	[123]
Phaeodactylum tricornutum	Eicosapentaenoic acid [124] Palmitoleic and hexadecatrienoic acids (HTA)	*B. cereus* *Bacillus Weihenstephanensis* *S. aureus* *S. epidermidis* *MRSA*	No effect	[125]
Rhizosolenia alata	Various organic solvent extracts: acetone, chloroform, chloroform: methanol (1:1), methanol: distilled water (4:1) and distilled water.	*B. subtilis*, *S. aureus*	*E. coli* *P. aeruginosa* *P. vulgaris* *S. typhi* *V. cholerae*	[126]
Skeletonema costatum	Aqueous and organic extracts: chloroform: methanol (2:1).	*B. subtilis* *S. aureus*	*P. aeruginosa*	[95]
Hapotophytes				
Isochrysis galbana	Chlorophyll a derivative: Pheophytin a and chlorophyllide a	*S. aureus* *Streptococcus faecalis* *S. pyogenes* *Micrococcus* sp.	Not tested	[127, 128]

Adapted from Falaise et al. [105].

Table 4. Antibacterial activity observed in different extracts from microalgae against human pathogens.

3. Conclusions

Cyanobacteria and microalgae have demonstrated a large potential as innovative sources of a large variety of bioactive compounds, such as fatty acids, antioxidants, antifreeze proteins and even antibiotics. While the characterization of substances as fatty acids is relatively well-established and straightforward, an information gap still remains in the elucidation of structures of antibiotics. Despite the fact that a variety of extracts obtained from microalgae biomass have demonstrated a clear antibiotic capacity, the structure of the molecules involved in the observed activity still remains unclear. There is a clear and almost unrevealed potential in the development of innovative nutraceutical and pharmaceutical industries based on cultivation of microalgae and cyanobacteria and their exploitation in the production of bioactive substances. Cyanobacteria and microalgae adapted to extreme environments for sure have an enormous potential that thorough bioprospecting approaches can help to unveil.

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Conflict of Interest

The authors certify that they have no conflict of interest.

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