Blue Economy

Volume 1 | Issue 2 Article 9

2023

Bioactive Molecules from Microalgae

Reham Gamal
National Institute of Oceanography and Fisheries, (NIOF), Cairo, Egypt, Reem_niof@yahoo.com

ISSN: 2805-2986 – e-ISSN: 2805-2994

REVIEW

Bioactive Molecules From Microalgae

Reham Gamal*

National Institute of Oceanography and Fisheries, (NIOF), Cairo, Egypt

Abstract

Over the past decade, microalgae screening, particularly Blue-green algae, which includes cyanobacteria, has been utilized for active pharmacological compounds and has been of increasing interest. Microalgae are capable of producing foodstuffs, feed additives, chemicals, and biofuels. Microalgae and marine cyanobacteria are abundant in a variety of chemical compounds, making them potential candidates for employment in biological processes that might be advantageous to human health. Microalgae are capable of producing a large number of essential bioactive molecules (functional components), and their traditional foods (breakfast cereals, spreads, baskets, cookies, brownies, energy bars, mayonnaise, desserts with gels, pastes, emulsions, ice cream, and drinks), which are consumed daily, improve health, lower the risk of illness, and lower medical expenses. The review introduces bioactive substances made by several microalgae that are used in a variety of industries, including petrochemical, textile, pharmaceutical, and food.

Keywords: Bioactive compounds, Bioactive molecules, Cyanobacteria, Microalgae

1. Introduction

Aquatic unicellular microorganisms known as microalgae, sometimes known as macrophytes, are described as being able to perform photosynthesis (Daneshvar et al., 2020) and can be found in both freshwater and marine environments. From three to ten micrometers, and in a variety of forms and sizes (Vu et al., 2021). Because of their physiological traits and the role that 'photo fermentation' plays, cyanobacteria, also known as blue-green algae, are frequently regarded as belonging to the same group (Hakobyan et al., 2019). They may grow as a single cell, a group of cells in a chain, or a tiny colony (Postma et al., 2023). They are vital to aquatic ecosystems because of their ability to photosynthesize (Malcata et al., 2018). As a potential source for the sustainable production of numerous bioactive chemicals, microalgae have garnered a lot of interest. These can be employed extensively in medications, cosmetics, food additives, and other natural chemicals, such as fatty acids, phycobiliproteins, chlorophyll, and carotenoids (Raposo et al., 2013). However, microalgae are thought to be an underutilized source of advantageous components that can be transformed into functionally useful components. Long-term effectiveness and several economic and health risk benefits are associated with this approach, which also lacks the drawbacks of conventional drug-based therapy approaches, which often have a short-term effect. In this review, we concentrate on microalgal components that may be beneficial to human health. To that purpose, this review first discusses typical processes used by various representative species of green algae to synthesize beneficial substances such as carotenoids and their derivatives. The biological actions of bioactive substances were then covered, with a focus on food and human health. We also went over these substances' chemical makeup, structural attributes, and dose-activity relationships. The following is a critical evaluation and conjecture for future possibilities, and we advise that more efforts should be put into algal research with an emphasis on the production of bioactive substances for human

Received 19 August 2023; revised 28 September 2023; accepted 1 October 2023.
Available online 12 January 2024

* National Institute of Oceanography and Fisheries Alexandria, Egypt.
E-mail address: Reham_niof@yahoo.com.

https://doi.org/10.57241/2805-2994.1007

health because microalgae are abundant in natural product reservoirs.

2. Bioactive molecules

Microalgae can biosynthesize, metabolize, collect, and exude a wide variety of primary and secondary metabolites, making them into veritable microbiological factories. Therefore, the food, pharmaceutical, and cosmetic industries could all benefit from using microalgae (Yamaguchi, 1997). Microalgae respond to changes in the external environment by altering their intracellular environment, just like any other creature. Therefore, altering the cultivation parameters such as the presence or absence of specific nutrients, temperature, light intensity, photoperiod, and the microalgae growth phase increases the biosynthesis of substances with high commercial value, such as drugs, enzymes, natural antioxidants, and many other substances (Palozza and Krinsky, 1992; Henriques et al., 1998). The most significant microalgal bioactive compounds with interest in the food, pharmaceutical, cosmetic, and commercial sectors are described in the sections that follow (Table 1).

3. Pigments

The wonderful spectrum of colors that may be seen by merely glancing about us is only produced by a small part of living stuff. However, the functioning of pigments goes beyond aesthetics; for example, some hues are engaged in activities like photosynthesis, defense, and reproduction which are crucial for life on Earth. A wide range of substances found in nature (such as chlorophyll, flavonoids, anthocyanins, carotenoids, betalains, and quinones) are needed to carry out this wide range of tasks. Color is among the most observable traits of microalgae. Microalgae produce a variety of accessory or secondary pigments, such as phycobiliproteins and a large variety of carotenoids (carotene and xanthophylls), in addition to chlorophyll, the principal photosynthetic pigment.

4. Chlorophylls

Chlorophyll a is the principal photosynthetic pigment in all algae (Fig. 1) and is the only kind of chlorophyll found in cyanobacteria (blue-green algae) and Rhodophyta. All algae contain one or more varieties of chlorophyll. Chlorophylls a and b are found in Chlorophyte and Euglenophyta algae, while chlorophylls c, d, and e are present in a number of marine algae and freshwater diatoms. Typically, there is between 0.5 and 1.5 % of dry weight in chlorophyll (Baker and Gunther, 2004; Gouveia et al., 2021). Chlorophylls have long been

Table 1. Useful bioactive compounds present in microalgae.

S. No	Name of the compound	Its different Types
1	Pigments/Carotenoids	Β-carotene, astaxanthin, lutein, zeaxanthin, canthaxanthin, chlorophyll, phycocyanin, phycoerythrin, fucoxanthin
2	Polyunsaturated fatty acids (PUFAs)	DHA(C22:6), EPA(C20:5), ARA(C20:4), GAL(C18:3)
3	Vitamins	A, B1, B6, B12, C, E, biotin, riboflavin, nicotinic acid, pantothenate, folic acid
4	Antioxidants	Catalases, polyphenols, superoxide dismutase, tocopherols
5	Other	Antimicrobial, antifungal, antiviral agents, toxins, amino acids, proteins, sterols, and MAAs for light protection.

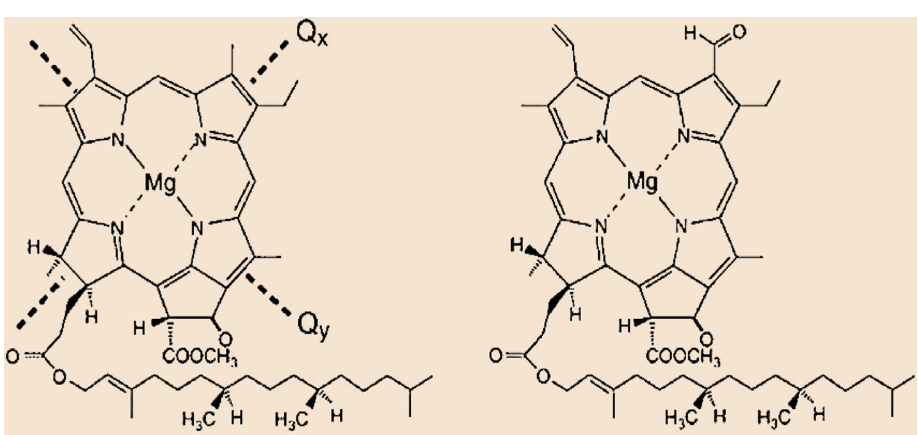

Fig. 1. The molecular structure of (A) chlorophyll a and (B) chlorophyll b.

utilized in medicine, and recent epidemiological studies have found a relationship between eating foods high in chlorophyll and a lower risk of colon cancer (Balder et al., 2006).

5. Carotenoid

Pigments called carotenoids may be responsible for the distinctive colors of fruits, vegetables, and other plants (Ben-Amotz and Fishler, 1998). Carotenoids are isoprenoid polyene pigments that are typically yellow to red in color and are generated from lycopene (Fig. 2). They are created from scratch by a few distinct types of microbes and photosynthetic organisms (Borowitzka, 1988). Microalgae are also thought to be a fantastic source of herbal meal colors and nutraceuticals (Dufosse´ et al., 2005). In response to various environmental and cultural stresses (such as light, temperature, salts, and nutrients), some microalgae can go through a process called carotenogenesis, in which the alga stops growing and drastically changes its carotenoid metabolism by accumulating secondary carotenoids in addition to harsh environments (Gouveia et al., 1996; Bhosale, 2004). Carotenoids appear to play a major role in algae as both light-harvesting pigments and photoprotective dealers, protecting the photosynthetic apparatus from solar radiation and its consequences (Ben-Amotz et al., 2021). They also participate in phototaxis and phototropism (Borowitzka, 1988).

6. Phycobiliproteins

In addition to chlorophyll and carotenoid lipophilic pigments, phycobiliproteins are the primary components of a complex assembly of photosynthetic light-harvesting antenna pigments called phycobilisomes, which are found in cyanobacteria (blue-green algae), Rhodophyta (purple algae), and cryptomonad algae (Glazer, 1994). This group of pigments has a wide range of uses, including labeling antibodies and being used as noticeably sensitive fluorescent markers in medical diagnosis; they are frequently used in multi-shade immunofluorescence or fluorescence-activated cell-sorter analysis (Becker, 1994; Sekar and Chandramohan, 2007). Additionally, these substances have demonstrated a wide range of pharmacological activities, such as antioxidant, anti-inflammatory, neuroprotective, and hepatoprotective actions (Bhat and Madyastha, 2000; Romay et al., 2003; Benedetti et al., 2004). A protein spine known as a phycobiliprotein is tetrapyrrole chromophoric prosthetic group-related (Fig. 3). The cyanobacterium Spirulina (Arthrospira), which produces phycocyanin (blue), and the *Rhodophyta Porphyridium*, which produces phycoerythrin (purple), are the two main herbal sources of phycobiliproteins. In Japan and China, phycocyanin is currently used as a brilliant blue natural color in food products like chewing gum, candies, dairy products, jellies, ice creams, soft drinks (like Pepsi1 blue), as well as in cosmetics like lipsticks, eyeliners, and eye shadows (Sekar and Chandramohan, 2007).

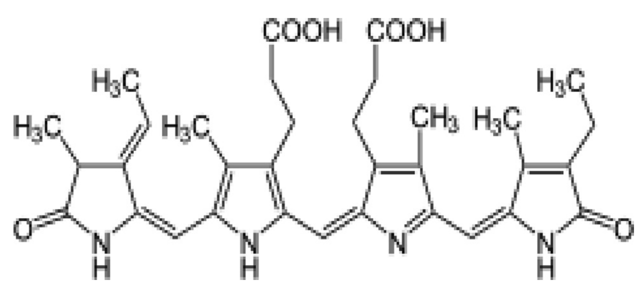

Fig. 3. Chemical structure of a phycocyanobilin.

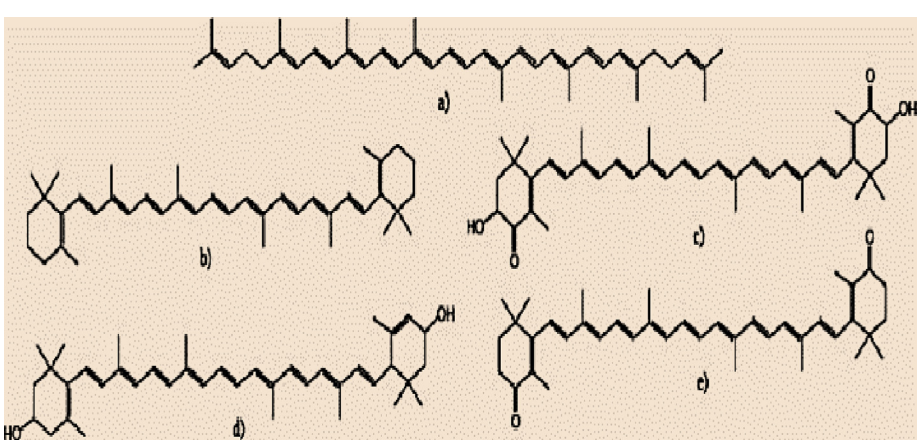

Fig. 2. Chemical structures of some carotenoids: (a) lycopene, (b) b-carotene, (c) astaxanthin, (d) lutein, and (e) canthaxanthin.

7. Polyphenols

Antioxidant substances called polyphenols have been linked to a variety of health advantages, including better cardiovascular health and defense against Alzheimer's disease and other malignancies (Ares et al., 2009). However, the inherent bitterness of these chemicals places restrictions on adding polyphenols to food, and food producers are keenly conscious of the need to make healthful products palatable. The bitterness, astringency, and distinctive flavor of polyphenol extracts can be diminished by using other substances such as sucrose, sucralose, polydextrose, and milk (Ares et al., 2009).

8. Polysaccharides

In the food industry, polysaccharides are frequently utilized as thickening and gelling agents. From macroalgae, such as Laminaria, Gracilaria, and Microcystis, many commonly used polysaccharides are extracted, along with agar, alginates, and carrageenan's (Borowitzka, 1988). Nevertheless, a lot of microalgae make polysaccharides, and some of them should have packages because of the opportunity to control the environmental factors affecting their bloom and the brief boom costs. The unicellular pink alga *Porphyridium cruentum* is the most promising microalga for commercial applications because it makes a sulfated galactan exopolysaccharide (EPS) that could replace carrageenan's in many products (Spolaore et al., 2006). Another example is *Chlamydomonas Mexicana*, which produces up to 25 % of its total natural production as extracellular polysaccharides, which have been approved for use in the US as soil conditioners (Borowitzka, 1988). The majority of microalgal carbohydrates are composed of polysaccharides, which are often separated into three groups: reserve glucans, extracellular polysaccharides, and mobile–wall polysaccharides (Granum, 2002). The most common forms of reserve glucans in microalgae are branched starches and b-1, 3-glucans. Red microalgae have been shown to provide distinct starch systems in addition to polyglucans of the glycogen, amylose, and amylopectin kinds (Shimonaga et al., 2007). A few unicellular pink algae, such as *Galdieria sulphuraria* and *Cyanidioschyzon merolae*, make up the Floridan starch, a particular type of starch that is more wonderfully branched than amylopectin (Barbier et al., 2005). These polysaccharides may typically be associated to the production of bioethanol through saccharification and subsequent or simultaneous fermentation because of the nature of the glycosidic connections in those polysaccharides (Ogaki et al., 2009). In diatoms, b-1, 3-glucans, also called *chrysolaminaran*, are frequently found. These are polymers of b-(13)-hyperlink glucopyranoside devices that can branch in the b-(16) and b-(12) positions and have a polymerization range of 20–60 (Granum, 2002; Barbier et al., 2005; Størseth et al., 2005; Shimonaga et al., 2007; Ogaki et al., 2009). *Chrysolaminaran* could form up to 20–30 % of the mobile dry weight and is a crucial component of the garage for continuously photosynthesizing carbon as well as a key substrate for marine diatom respiration (Sheehan et al., 1998). Dglucans b-(13)- exhibit immunostimulants, and it is thought that they are closely connected to the b-(16)-branches (Størseth et al., 2005). Microalgae have the ability to exude extracellular polymeric materials, which can either take the form of a capsular substance that tightly encloses the manufacturing microbial mobile or free slime matrices that are dispersed more widely into the surrounding environment. This polymeric fabric contains a significant amount (40–95 %) of EPS, which plays a crucial role in mobile attachment and adherence to surfaces, as well as in the production of a protective layer and the prevention of mobile desiccation (Nichols et al., 2009). The monosaccharides that makeup EPS are extremely diverse and can change depending on the boom phase (Allard and Tazi, 1993; Giroldo et al., 2005; Sua'rez et al., 2005; Mishra and Jha, 2009). The soluble mobile–wall polysaccharide complex, which covers *Porphyridium spp.* cells is one example of these EPS. It is made up of around ten different sugars, of which the essential ones are xylose, glucose, galactose, glucuronic acid, and half of ester sulfate groups (Arad et al., 1988; Geresh et al., 2009, 2022). It dissolves continuously in the medium. Considered to have useful organic properties, the sulfated heteropolymers made by *P. spp.* exhibit anti-retroviral, bio-lubricant, anti-inflammatory, hypercholesterolemic, and anti-mobile proliferative activity (Dvir et al., 2000; Talyshinsky et al., 2002). There are indicators that the *P. spp.* polysaccharide's sulfate structure is its chemically and physiologically active component (Keidan et al., 2006). The aqueous extract of Chlorella pyrenoidosa, which has immunostimulatory capabilities, is another intriguing example of microalgae polymeric materials (Sua'rez et al., 2005). Because of its polysaccharide content, it is available commercially under the name Respondin TM. It was discovered that it included precisely structured polysaccharides of the L-arabinofuranose and D-galactopyranose families (Sua'rez et al., 2005). Fig. 4 Cyclic b-(12)-D-glucans have also been isolated from the same extract (Sua'rez et al., 2008). These cyclic molecules

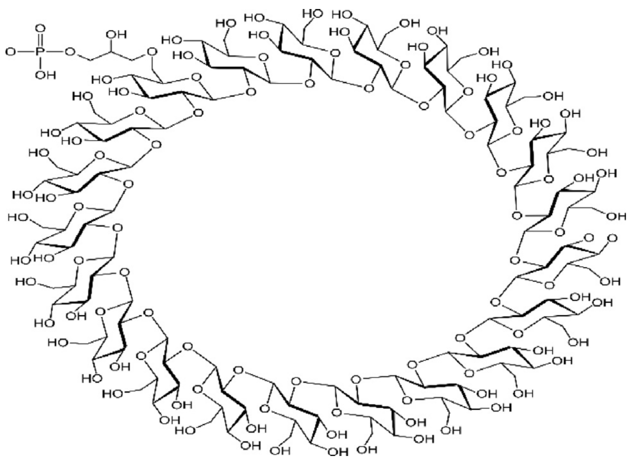

Fig. 4. Cyclic b-(1 → 2)-D-glucans isolated from Chlorella pyrenoidosa (Sua'rez et al., 2008).

are thought to play a role in osmoregulation in prokaryotes. Cyclic and linear b-(12)-D-glucans are both present in the portion of b-(12)-D-glucans that was removed from C. pyrenoidosa. Cyclic and linear b-(12)-D-glucans had rings that ranged in size from 18 to 35 and 20 glucose devices, respectively. These glucans with exceptionally low molecular weight also demonstrated a few immunostimulatory behaviors.

9. Protein

Due to the high protein content of many microalgae species, using microalgae as a sources of protein became a favorite pastime in the 1950s (Soletto et al., 2005). Additionally, virtually all algae's amino acid sample corresponds highly to that of other meal proteins. The ones that can be essential to people and animals can be provided by the cells because they can synthesize all amino acids (Guil-Guerrero et al., 2004). The amino acid composition of microalgae, which consists primarily of loose amino acids, varies significantly among species as well as during boom times and boom phases (Borowitzka, 1988; Ben-Amotz and Fishler, 1998; Balder et al., 2006; Gouveia et al., 2021). This is similar to how diverse bioactive chemicals are generated by microalgae.

10. Sterols

Microalgae incorporate specific styles of sterols which can be a feature of every species (Easa et al., 1994; Barret et al., 1995). Fig. 5. Moreover, research on bivalve manufacturing has counseled that the sort and amount of sterols found in nutritional microalgae had been without delay associated with the bivalve boom rate (Wikfors et al., 1991). Therefore, studying the sterol contents of hitherto unstudied microalgae, including novel and unusual species, can be extremely valuable. Low-density lipoprotein (LDL) cholesterol is present in substantial amounts and is often the top sterol in purple algae. The predominant sterols in purple algae are C-27 compounds. Desmosterol and 22E dehydrocholesterol, which may perhaps be the primary sterol in the Gigartinales class, are also present in excessive proportions (Bouzidi et al., 2008). On the other hand, fucosterol, along with Bifurcate, Cladostephus hirsitus, Dictyota dichotoma, and Cystoseira sides, is the predominant sterol in brown algae, and low-density lipoprotein cholesterol is a gift that is most beneficial in little amounts. There may not be a single dominant sterol in green algae, and the dominant sterol appears to vary throughout orders and families (Bouzidi et al., 2008). Additionally, sitosterol emerges as the main sterol found in young marine microalgae, along with *Isochrysis galbana* and *Diacronema planum* (Bandarra et al., 2003; Donato et al., 2003).

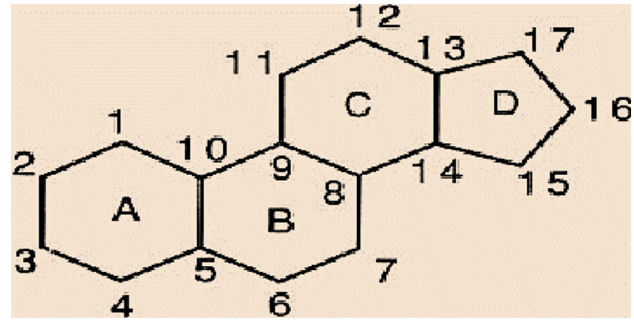

Fig. 5. Basic structure of sterols.

11. Vitamins and minerals

Microalgae biomass is a priceless source of nearly all essential vitamins, including A, B1, B2, B6, B12, C, E, nicotine, biotin, folic acid, and pantothenic acid, as well as a well-balanced mineral content. Some microalgae, like spirulina, include high levels of iron and vitamin B12, which makes them particularly suitable as nutritional supplements for vegetarians (Becker, 2004). An alga's nutritional value is influenced by its genotype, position in the bloom cycle, dietary repute, and light intensity (photosynthetic rate). As a result, the dietary content can be altered by a variety of lifestyle choices, even under pressure or through genetic engineering. However, environmental variables, harvesting procedures, and biomass drying techniques all affect nutritious molecular composition (Arad et al., 1988; Borowitzka, 1988; Allard and Tazi, 1993; Becker, 1994; Easa et al., 1994; Glazer, 1994; Barret et al., 1995; Gouveia et al., 1996; Sheehan et al., 1998; Brown et al., 1999; Bhat and Madyastha, 2000; Dvir et al., 2000; Granum, 2002; Talyshinsky et al., 2002; Bandarra et al., 2003; Donato et al., 2003; Romay et al., 2003; Becker, 2004; Benedetti et al., 2004; Bhosale, 2004; Guil-Guerrero et al., 2004; Barbier et al., 2005; Dufosse´et al., 2005; Giroldo et al., 2005; Soletto et al., 2005; Størseth et al., 2005; Sua'rez et al., 2005; Keidan et al., 2006; Spolaore et al., 2006; Sekar and Chandramohan, 2007; Shimonaga et al., 2007; Bouzidi et al., 2008; Durmaz et al., 2008; Ginzberg et al., 2008; Sua'rez et al., 2008; Ares et al., 2009; Geresh et al., 2009; Mishra and Jha, 2009; Nichols et al., 2009; Ogaki et al., 2009; Ben-Amotz et al., 2021; Geresh et al., 2022; Wikfors et al., 1991).

12. Lipids

Algae are valued raw materials for the production of exciting lipids since they are thought to contain these lipids. Microalgae are one of them and are important reasserts of commercially produced expensive compounds, including polyunsaturated fatty acids (Priyadarshani and Rath, 2012). Polyunsaturated fatty acids, such as the omega-3 fatty acids eicosatetraenoic acid and docosahexaenoic acid, the omega-6 fatty acid - linoleic acid, and arachidonic acid, typically make up the lipid fraction. It has been demonstrated that polyunsaturated fatty acids, because of their antibacterial, antifungal, and antioxidant activities, are essential for the proper functioning of the human body and its health (Ibãnez et al., 2012). They are widely employed as medications, functional foods, and dietary supplements (Coragliotti et al., 2012; Priyadarshani and Rath, 2012). Prior research has been done on the extraction of polyunsaturated fatty acids from algae and their precise makeup (Plaza et al., 2008). For the isolation of lipids (Michalak and Chojnacka, 2014). One of them, supercritical carbon dioxide extraction, is a promising one that most likely can be applied to the large-scale extraction of microalgae lipids. It creates solvent-loose lipids, is nontoxic, and selects acylglycerols excessively, and at an excessive rate. The high capital cost and the excessive strength needed for supercritical fluid compression are its primary hazards (Halim et al., 2012). Another group of intriguing lipids obtained from algal biomass are sterols. They were isolated from macro and microalgae, and Cardozo et al. (2007) and Volkman (2003) studied them inside the paintings. Phytosterols obtained from algae can be used in a variety of industries, including pharmaceuticals (for the production of therapeutic steroids), nutraceuticals, nutrition (for the inclusion of anticholesterol ingredients in everyday foods and for their anticancer characteristics), and cosmetics (Volkman, 2003; Francavilla et al., 2012).

13. Biofuel

Natural resources like sunlight, water, and O_2/CO_2 can be used to create sustainable energy sources like microalgae. The creation of biodiesel and bioethanol from microalgae has the potential to economically replace fossil fuels (Maschek and Baker, 2009; Gupta and Abu-Ghannam, 2011). Microalgae are regarded as an excellent prospect for producing biofuel, lipids through photosynthesis, and biomass (almost 77 % of dry cell mass) (Manzo et al., 2009; Abrantes et al., 2010).

14. Secondary metabolites with potential commercial value

Although the ecological function of secondary metabolites in microalgae or cyanobacteria is not fully understood, current research has suggested various potential roles. For instance, the marine dinoflagellates thought to play an ecological role as a feeding deterrent produce the brevetoxins that cause neurotoxic shellfish poisoning (NSP). It is believed that the chemical Lyngbyatoxin, which causes swimmer's itch, serves as an ecological defense against grazing (Pereira et al., 2004). Some secondary metabolites are alleged to function as symbiotic or sexual communication signals (Herrero et al., 2006). All types of molecules, including isoprenoids, polyketides, peptides, and macromolecules like nucleic acids, carbohydrates, proteins, and lipids, can contain secondary metabolites. Because algae and cyanobacteria may be found in so many different habitats, there is a high level of chemical variety. Secondary metabolites represent particular adaptations to these various environmental conditions. On a shallow tropical reef, filamentous cyanobacteria thrive and would anticipate the production of distinctive chemical structures with exclusive biological characteristics. Algae and cyanobacteria are becoming more valuable as commercial items as a result of their increased chemical and biological variety. For instance, algal species' distinctive structures are highly valuable as ingredients in human diet, cosmetics, and a variety of medications (Fig. 6).

15. Diterpenes

Along with diterpenes, the Dictyotaceae family of algae is capable of creating secondary metabolites.

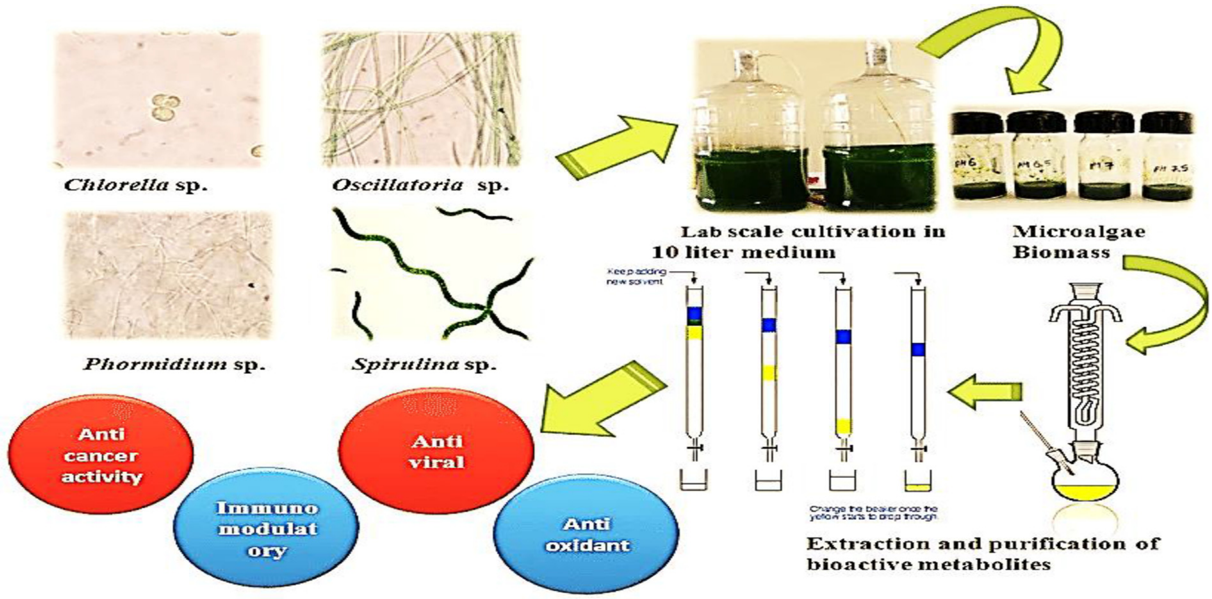

Fig. 6. Applications of Secondary metabolites from microalgae.

Dolabellanes, hydroazulenoids, xenicanes, and so-called extended sesquiterpenoids are a few types that can be separated (Vadlapudi, 2012). *Dictyota ciliolate,* a marine brown alga, has been used to extract diterpenes such as Dictyodial, Dictyol C, and Dicytol H (Yuan et al., 2020). It was claimed that they possessed cytotoxic, antiviral, and algicidal properties. For instance, diterpenes isolated from *Dictyota pfaff* and *Dictyota menstrual* prevented the infection of Vero cells with herpes simplex virus type 1 (Lee and Jeon, 2023). HIV-1 testing has been done on *Dictyota menstrualis diterpenes* (Ragan and Glombitza, 1986).

16. Antioxidants

Antioxidants are currently used in numerous products throughout the food (stuff) and pharmaceutical industries. Due to their crucial role in the development of fitness and improved diets, there is particular interest in their extraction (Yoshie et al., 2021). However, due to the threat they pose to human protection, the use of artificial antioxidants as food or medicine additives has been restricted. Their toxicity can cause a variety of fitness issues. Therefore, in order to eliminate side effects, it may be necessary to search for novel herbal oxidation inhibitors (Gupta and Abu-Ghannam, 2017). Tocopherol, carotenoids, polyphenols (such as phlorotannins, catechins, flavonoids, tannins, and lignans as well as mycosporine-like amino acids (MAA) are just a few examples of the wide range of secondary metabolites with antioxidant properties that algae are capable of creating. A particular group of these is the brown algal polyphenols, also referred to as phlorotannins. It has been reported that brown algae contain the most phlorotannins of all marine algae. These substances are oligomers of phloroglucinol (1, 3, 5-trihydroxy benzene), with a few exceptions (Nakayama et al., 1999). Antioxidants could be extracted from algal biomass using all available innovative approaches (Michalak and Chojnacka, 2020).

16.1. Conclusion

We've defined the importance of microalgae as numerous reasserts of bioactive compounds. The sizeable use of secondary metabolites as antibacterial and antifungal marketers has been recognized for over 60 years. Moreover, microalgae are supposed to be a critical uncooked cloth for amino acids, nutrients, and the production of different pharmaceuticals. Other extraordinarily successful packages of secondary metabolites are anticancer marketers, immune stimulants, and cholesterol-decreasing marketers, amongst others. Microalgae can offer a sizeable variety of critical bioactive molecules (useful ingredients), and their incorporation in conventional meals turns them into useful meals with healthful blessings without converting meal habits.

Conflicts of interest

We declare that we have no conflict of interest.

References

Abrantes, J.L., Barbosa, J., Cavalcanti, D., Pereira, R.C., et al., 2010. The effects of the diterpenes isolated from the Brazilian brown algae Dictyota pfaff and Dictyota menstrualis against the herpes simplex type-1 replicative cycle. Planta Med. 76, 339–344.

Allard, B., Tazi, A., 1993. Influence of growth status on composition of extracellular polysaccharides from 2 Chlamydomonas species. Phytochemistry 32, 41–47.

Arad, S., Friedman, O., Rotem, A., 1988. Effect of nitrogen on polysaccharide production in a Porphyridium sp. Appl. Environ. Microbiol. 54, 2411–2414.

Ares, G., Barreiro, G.C., Deliza, R., Gambaro, A., 2009. Alternatives to reduce the bitterness, astringency, and characteristic flavor of antioxidant extracts. Food Res. Int. 42, 871–878.

Baker, R., Gunther, C., 2004. The role of carotenoids in consumer choice and the likely benefits from their inclusion into products for human consumption. Trends Food Sci. Technol. 15, 484–488.

Balder, H.F., Vogel, J., Jansen, M.C., Weijenberg, M.P., van den Brandt, P.A., Westenbrink, S., et al., 2006. Heme and chlorophyll intake and risk of colorectal cancer in The Netherlands cohort study. Cancer Epidemiol. Biomarkers Prev. 15, 717–725.

Bandarra, N.M., Pereira, P.A., Batista, I., Vilela, M.H., 2003. Fatty acids, sterols, and a-tocopherol in Isochrysis galbana. J. Food Lipids 10, 25–34.

Barbier, G., Oesterhelt, C., Larson, M.D., Halgren, R.G., Wilkerson, C., Garavito, R.M., et al., 2005. Comparative genomics of two closely related unicellular thermo-acidophilic red algae, Galdieria sulphuraria, and Cyanidioschyzon merolae, reveals the molecular basis of the metabolic flexibility of Galdieria sulphuraria and significant differences in carbohydrate metabolism of both algae. Plant Physiol. 137, 460–474.

Barret, S.M., Volkman, J.K., Dunstan, G.A., Leroi, J.M., 1995. Sterols of 14 species of marine diatoms (Bacillariophyta). J. Phycol. 31, 360–369.

Becker, E.W., 1994. Microalgae: Biotechnology and Microbiology. Cambridge University Press, Cambridge, UK.

Becker, E.W., 2004. Microalgae in human and animal nutrition. In: Richmond, A. (Ed.), Handbook of Microalgal Culture: Biotechnology and Applied Phycology. Blackwell Science, London, UK, p. 566.

Ben-Amotz, A., Fishler, R., 1998. Analysis of carotenoids with emphasis on 9-cis-b-carotene in vegetables and fruits commonly consumed in Israel. Food Chem. 162, 515–520.

Ben-Amotz, A., Gressel, J., Avron, M., 2021. Massive accumulation of phytoene induced by norflurazon in Dunaliella bardawil (Chlorophyceae) prevents recovery from photoinhibition. J. Phycol. 23, 176–181.

Benedetti, S., Benvenuti, F., Pagliarani, S., Francogli, S., Scoglio, S., Canestrari, F., 2004. Antioxidant properties of a novel phycocyanin extract from the blue-green alga Aphanizomenon flos-aquae. Life Sci. 55, 2353–2362.

Bhat, V.B., Madyastha, K.M.C., 2000. Phycocyanin: a potent peroxyl radical scavenger in vivo and in vitro. Biochem. Biophys. Res. Commun. 275, 20–25.

Bhosale, P., 2004. Environmental and cultural stimulants in the production of carotenoids from microorganisms. Appl. Microbiol. Biotechnol. 63, 351–361.

Borowitzka, M.A., 1988. Vitamins and fine chemicals from microalgae. In: Borowitzka, M.A., Borowitzka, L.J. (Eds.), Micro-algal Biotechnology. Cambridge University Press, Cambridge, UK, pp. 153–196.

Bouzidi, N., Daghbouche, Y., El Hattab, M., Aliche, Z., Culioli, G., Piovetti, L., et al., 2008. Determination of total sterols in brown algae by Fourier transform infrared spectroscopy. Anal. Chim. Acta 61, 185–189, 2008.

Brown, M.R., Mular, M., Miller, I., Farmer, C., Trenerry, C., 1999. The vitamin content of microalgae used in aquaculture. J. Appl. Phycol. 11, 247–255.

Cardozo, K.H.M., Guaratini, T., Barros, M.P., Falcão, V.R., et al., 2007. Metabolites fromalgae with economical impact. Comp. Biochem. Physiol. C Toxicol. Pharmacol. 146, 60–78.

Coragliotti, A., Franklin, S., Day, A.G., Decker, S.M., 2012. Microalgal polysaccharide compositions. In: USA Patent Application 2012/0202768.

Daneshvar, E., Zarrinmehr, M.J., Hashtjin, A.M., Farhadian, O., Bhatnagar, A., 2020. Versatile applications of freshwater and marine water microalgae in dairy wastewater treatment, lipid extraction, and tetracycline biosorption. Bioresour. Technol. 268, 523–530.

Donato, M., Vilela, M.H., Bandarra, N.M., 2003. Fatty acids, sterols, a-tocopherol, and total carotenoids of Diacronema planum. J. Food Lipids 10, 267–276.

Dufossé, L.P., Calaup, A.Y., Arad Blanc SMP, Murthy, K.N.C., Ravishankar, G.A., 2005. Microorganisms and microalgae as a source of pigments for food use: a scientific oddity or an industrial reality? Trends Food Sci. Technol. 16, 389–406.

Durmaz, Y., Donato, M., Monteiro, M., Gouveia, L., Nunes, M.L., Pereira, T.G., et al., 2008. Effect of temperature on growth and biochemical composition (sterols, a-tocopherol, carotenoids, fatty acid profiles) of the microalga, Isochrysis galbana. Isr. J. Aquac. Bamidgeh 60, 188–195.

Dvir, I., Chayoth, R., Sod-Moriah, U., Shany, S., Nyska, A., Stark, A.H., et al., 2000. Soluble polysaccharides and biomass of red microalga Porphyridium sp. alter intestinal morphology and reduce serum cholesterol in rats. Br. J. Nutr. 84, 469–476.

Easa, H.S., Kornprobst, J.M., Rizk, A.M., 1994. Major sterol composition of some algae from Qatar. Phytochemistry 39, 373–374.

Francavilla, M., Colaianna, M., Zotti, M., Morgese, M.G., et al., 2012. Extraction, characterization and in vivo neuromodulatory activity of phytosterols from microalga Dunaliella tertiolecta. Curr. Med. Chem. 19, 3058–3067.

Geresh, S., Arad, S., Levy-Ontman, O., Zhang, W., Tekoah, Y., Glaser, R., 2009. Isolation and characterization of poly and oligosaccharides from the red microalga Porphyridium sp. Carbohydr. Res. 344, 343–349.

Geresh, S., Mamontov, A., Weinstein, J., 2022. Sulfation of extracellular polysaccharides of red microalgae: preparation, characterization and properties. J. Biochem. Biophys. Methods 50, 179–187.

Ginzberg, A., Korin, E., Arad, S., 2008. Effect of drying on the biological activities of a red microalgal polysaccharide. Biotechnol. Bioeng. 99, 411–420.

Giroldo, D., Vieira, A.A.H., Paulsen, B.S., 2005. Extracellular polysaccharides produced by a tropical cryptophyte as a carbon source for natural bacterial populations. Eur. J. Phycol. 40, 241–249.

Glazer, A.N., 1994. Phycobiliproteins: a family of valuable, widely used fluorophores. J. Appl. Phycol. 6, 105–112.

Gouveia, L., Veloso, V., Reis, A., Fernandes, H.L., Empis, J., Novais, J.M., 1996. Chlorella vulgaris used to color egg yolk. J. Sci. Food Agric. 70, 167–172.

Gouveia, L., Batista, A.P., Sousa, I., Raymundo, A., Bandarra, N.M., 2021. Microalgae in novel food products. In: Papadopoulos, K.N. (Ed.), Food Chemistry Research Developments: Chapter 2. Nova Science Publisher Inc, New York, USA.

Granum, E., 2002. Metabolism and Function of B-1,3-Glucan in Marine Diatoms PhD Thesis, Department of Biotechnology, Faculty of Natural Sciences and Technology. Trondheim, Norway: Norwegian University of Science and Technology (NTNU).

Guil-Guerrero, J.L., Navarro-Juaŕez, R., Loṕez-Martõnez, J.C., Campra-Madrid, P., Rebolloso-Fuentes, M.M., 2004. Functional properties of the biomass of the three microalgal species. J. Food Eng. 65, 511–517.

Gupta, S., Abu-Ghannam, N., 2011. Bioactive potential and possible health effects of edible brown seaweeds. Trends Food Sci. Technol. 22, 315–326.

Gupta, S., Abu-Ghannam, N., 2017. Recent developments in the application of seaweed or seaweed extracts as a means for enhancing the safety and quality attributes of foods. Innovat. Food Sci. Emerg. Technol. 12, 600–609.

Hakobyan, L., Gabrielyan, L., Trchounian, A., 2019. Biohydrogen by Rhodobacter sphaeroides during photo-fermentation: mixed vs. sole carbon sources enhance bacterial growth and H2 production. Int. J. Hydrogen Energy 44, 674–679.

Halim, R., Danquah, M.K., Webley, P.A., 2012. Extraction of oil from microalgae for biodiesel production: a review. Biotechnol. Adv. 30, 709–732.

Henriques, N.M., Navalho, J.C., Varela, J.C., Cancela, M.L., 1998. Dunaliella: Uma fonte natural de Beta-caroteno com potencialidades de Aproveitamento Biotecnolo'gico. Bolet. Biotecnol. 61, 12–17.

Herrero, M., Cifuentes, A., Ibãnez, E., 2006. Sub- and supercritical fluid extraction of functional ingredients from different natural sources: plants, food-by-products, algae, and microalgae—a review. Food Chem. 98, 136–148.

Ibãnez, E., Herrero, M., Mendiola, J.A., Castro-Puyana, M., 2012. Extraction and characterization of bioactive compounds with health benefits from marine resources: macro and microalgae, cyanobacteria, and invertebrates. In: Hayes, M. (Ed.), Marine Bioactive Compounds: Sources, Characterization and Applications. Springer Science+Business Media, LLC, New York, pp. 55–98.

Keidan, M., Broshy, H., van Moppes, D., Arad, S., 2006. Assimilation of sulfur into the cell-wall polysaccharide of the red microalga Porphyridium sp. (Rhodophyta). Phycologia 45, 505–511.

Lee, S.-H., Jeon, Y.-J., 2023. Anti-diabetic effects of brown algae-derived phlorotannins, and marine polyphenols through diverse mechanisms. Fitoterapia 86, 129–136.

Malcata, F.X., Pinto, I.S., Guedes, A.C., 2018. Marine Macro-And Microalgae: an Overview. CRC Press.

Manzo, E., CiavattaML, Bakkas S., Villani, G., et al., 2009. Diterpene content of the alga Dictyota ciliolata from a Moroccan lagoon. Phytochem. Lett. 2, 211–215.

Maschek, J.A., Baker, B.J., 2009. The chemistry of algal secondary metabolism. Algal Chem. Ecol. 1–24.

Michalak, I., Chojnacka, K., 2014. Review. Algal extracts: technology and advances. Eng. Life Sci. 14, 581–591.

Michalak, I., Chojnacka, K., 2020. Review. Algal extracts: technology and advances. Eng. Life Sci. 14, 581–591.

Mishra, A., Jha, B., 2009. Isolation and characterization of extracellular polymeric substances from micro-algae Dunaliella salina under salt stress. Bioresour. Technol. 100, 3382–3386.

Nakayama, R., Tamura, Y., Kikuzaki, H., Nakatani, N., 1999. Antioxidant effect of the constituents of Susabinori (Porphyra yezoensis). J. Am. Oil Chem. Soc. 76, 649–653.

Nichols, C.A.M., Nairn, K.M., Glattauer, V., Blackburn, S.I., Ramshaw, J.A.M., Graham, L.D., 2009. Screening microalgal cultures in search of microbial exopolysaccharides with potential as adhesives. J. Adhes. 85, 97–125.

Ogaki, M., Tanaka, S., Kawasaki, H., Ishii, T., 2009. Method of producing bio-ethanol. In: USPTO Patent Application 20090075353, Class: 435161 (USPTO).

Palozza, P., Krinsky, N.I., 1992. Antioxidant effects in vivo and in vitro: an overview. Methods Enzymol. 213, 403–420.

Pereira, H.S., Lẽao-Ferreira, L.R., Moussatcheˊ, N., Teixeira, V.L., et al., 2004. Antiviral activity of diterpenes isolated from the Brazilian marine algaDictyota menstrualis against human immunodeficiency virus type 1 (HIV-1). Antivir. Res. 64, 69–76.

Plaza, M., Cifuentes, A., Ibãnez, E., 2008. In the search of new functional food ingredients from algae. Trends Food Sci. Technol. 19, 31–39.

Postma, P.R., 't Lam, G.P., Barbosa, M.J., Wijffels, R.H., Eppink, M.H.M., Olivieri, G., 2023. Microalgal biorefinery for bulk and high-value products: product extraction within cell disintegration. In: Miklavcic, D. (Ed.), Handbook of Electroporation. Springer International Publishing, Cham, pp. 1–20.

Priyadarshani, I., Rath, B., 2012. Commercial and industrial applications of micro algae—a review. J. Algal. Biomass Util. 3, 89–100.

Ragan, M.A., Glombitza, K.-W., 1986. Phlorotannins, brown algal polyphenols. In: Round, F.E., Chapman, D.J. (Eds.), Progress in Phycological Research. Biopress, Bristol, pp. 129–241.

Raposo, M.F.D., de Morais, R.M.S.C., de Morais, A.M.M.B., 2013. Health applications of bioactive compounds from marine microalgae. Life Sci. 93, 479–486.

Romay, C.H., Gonzalez, R., Ledon, N., Remirez, D., Rimbau, V., 2003. Phycocyanin: a biliprotein with antioxidant, anti-inflammatory, and neuroprotective effects. Curr. Protein Pept. Sci. 4, 207–216.

Sekar, S., Chandramohan, M., 2007. Phycobiliproteins as a commodity: trends in applied research, patents, and commercialization. J. Appl. Phycol. 20, 113–116.

Sheehan, J., Dunahay, T., Benemann, J., Roessler, P.A., 1998. Look Back at the U.S. Department of Energy's Aquatic Species Program – Biodiesel from Algae. National Renewable Energy Laboratory Report Colorado, EUA.

Shimonaga, T., Fujiwara, S., Kaneko, M., Izumo, A., Nihei, S., Francisco, P.B., et al., 2007. Variation in storage a-polyglucans of red algae: amylose and semi-amylopectin types in Porphyridium and glycogen type in Cyanidium. Mar. Biotechnol. 9, 192–202.

Shuba Eyasu, S., Kifle, D., 2019. Microalgae to biofuels: 'Promising' alternative and renewable energy, review. Renewable Sustainable Energy Rev. 81, 743–755.

Spolaore, P., Joannis-Cassan, C., Duran, E., Isambert, A., 2006. Commercial applications of microalgae – review. J. Biosci. Bioeng. 101, 87–96.

Størseth, T.R., Hansen, K., Reitana, K.I., Skjermo, J., 2005. Structural characterization of b-D-(1→3)-glucans from different growth phases of the marine diatoms Chaetoceros mülleri and Thalassiosira weissflogii. Carbohydr. Res. 340, 1159–1164.

Suaŕez, E.R., Kralovec, J.A., Noseda, M.D., Ewart, H.S., Barrow, C.J., Lumsdena, M.D., Grindley, T.B., 2005. Isolation, characterization and structural determination of a unique type of arabinogalactan from an immunostimulatory extract of Chlorella pyrenoidosa. Carbohydr. Res. 340, 1489–1498.

Suaŕez, E.R., Bugden, S.M., Kai, F.B., Kralovec, J.A., Noseda, M.D., Barrow, C.J., Grindley, T.B., 2008. First isolation and structural determination of cyclic b-(1→2)-glucans from an alga, Chlorella pyrenoidosa. Carbohydr. Res. 343, 2623–2633.

Talyshinsky, M.M., Souprun, Y.Y., Huleihel, M.M., 2002. Antiviral activity of red microalgal polysaccharides against retroviruses. Cancer Cell Int. 2, 8.

Vadlapudi, V., 2012. Antioxidant activities of marine algae: a review. In: Capasso, A. (Ed.), Medicinal Plants as Antioxidant

Agents: Understanding Their Mechanism of Action and Therapeutic Efficacy. Research Signpost, Kerala, India, pp. 189−203.
Volkman, J.V., 2003. Sterols in microorganisms. Appl. Microbiol. Biotechnol. 60, 495−506.
Vu, C.H.T., Lee, H.-G., Chang, Y.K., Oh, H.-M., 2021. Axenic cultures for microalgal biotechnology: establishment, assessment, maintenance, and applications. Biotechnol. Adv. 36, 380−396.
Wikfors, G.H., Gladu, P.K., Patterson, G.W., 1991. In search of the ideal algal diet for oysters: recent progress, with emphasis on sterol. J. Shellfish Res. 10, 292, 191.
Yamaguchi, K., 1997. Recent advances in microalgal bioscience in Japan, with special reference to utilization of biomass and metabolites: a review. J. Appl. Phycol. 8, 487−502.
Yoshie, Y., Wang, W., Petillo, D., Suzuki, T., 2021. Distribution of catechins in Japanese seaweeds. Fish. Sci. 66, 998−1000.
Yuan, Y.V., Bone, D.E., Carrington, M.F., 2020. Antioxidant activity of dulse (Palmaria palmata) extract evaluated in vitro. Food Chem. 91, 485−494.