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Review article

A Review about A Significant Source of Bioactive Compounds: Microalgae

Hilal Soyocak [a,*], Dilara Kızılkaya [a] & Nebahat Şule Üstün [a]

[a] Department of Food Engineering, Faculty of Engineering, University of Ondokuz Mayıs, Samsun Türkiye

Abstract

Microalgae are single-celled microorganisms with different morphological, physiological, and genetic characteristics. They have an essential place in the aquatic ecosystem due to their photosynthetic feature. Microalgae produce various bioactive compounds as products of primary or secondary metabolism. The bioactive compounds they have; bioactive peptides, polyunsaturated fatty acids, bioactive polysaccharides, vitamins, phenolic compounds, and pigments. These components they produce can accumulate in the biomass and be released into the development environment. Thanks to the bioactive components they produce, microalgae have functional properties such as antioxidant, antimicrobial, antidiabetic, anticarcinogenic, and antihypertensive. Thanks to these features, it is reported that it has many uses and can acquire new areas of use day by day. Today, four microalgae species draw attention from the microalgae, which has a field of use in industries such as food, cosmetics, pharmaceutics, and aquaculture. These are Spiruna, Chlorella, Dunaliella and Haematococcus. Chlorella contains beta-1,3-glucan, which has antioxidant properties and acts as a free radical scavenger. Spirulina, on the other hand, can be used as a food supplement with its high amino acid content (62%). It is also a rich source of vitamins A, B1, B2, B12, and xanthophylls. Microags meet the essential fatty acids needs of fish with the polyunsaturated fatty acids they contain. Microalgae are the primary source of polyunsaturated fatty acids known as fish oil, such as eicosapentaenoic acid and docosahexaenoic acid. It has been reported that microalgae are an under-researched source in terms of both supplementary food and functional ingredient addition in the food industry for a healthy diet. The scope of this review, it is aimed to explain the bioactive compounds possessed by microalgae and the functional properties of these compounds.

Keywords: Microalgae, Bioactive Component, Antioxidant Activity, Phenolic Compound.

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* **Corresponding author:**

Soyocak H. is a research assitant in the Department of Food Engineering at Ondokuz Mayıs University in Samsun, Turkey. Her research interests include the Food and Biothecnology. He has lived, worked, and studied in Samsun, Türkiye.
Email: hilal.tombuloglu@omu.edu.tr

INTRODUCTION

Algae are autotrophic and photosynthetic organisms that can live in aquatic and semi-aquatic environments such as oceans, seas, lakes, rivers, streams, watercourses, and waste waters, they have a widespread area and can grow easily (Akyıl et al., 2016; Sasa et al., 2020). In terms of external appearance, they are observed in different structures ranging from unicellular and filamentous structures to plant morphology. Algae that do not show true root, stem, and leaf structures are eukaryotic creatures with a cellulose wall (Sasa et al., 2020). Their ability to perform photosynthesis produces two-thirds of the world's photosynthetic carbon requirement and increases the aquatic environment's nutritional value and oxygen ratio. Algae are macro and micro according to their size; According to the pigments they contain, they are classified as brown, green, red algae, and cyanobacteria. Macroalgae are large-sized, visible, and plant-like organisms that comprise a distinct Protista group. These form the feeding, sheltering, and breeding environment of living creatures in aquatic environments (Deniz Şirinyıldız and Yorulmaz, 2022; Sasa et al., 2020).

Microalgae can be found both in prokaryotic (cyanobacteria) and eukaryotic (green algae). Microalgae are important organisms that contain bioactive compounds with high nutritional value and important functional properties such as lipids, proteins, carbohydrates, pigments, and polymers. General composition of miroalgae has been studied by several researchers and it has been determined that it generally contains: (ı) protein between 7.4% and 63%, (ıı) lipid between 4.3-13.8%, and (ııı) carbohydrates between 15-38%. In addition, when their other bioactive components are examined, they contain 0.1-0.2% carotene, 0.5-1.5% chlorophyll, and 2-3% astaxanthin in dry matter (Uzuner and Haznedar, 2020). They have important functional properties such as antioxidant, antimicrobial, anticarcinogen, antidiabetic, with the α-tocopherol, β-carotene, glutathione, ascorbic acid, flavonoids, hydroquinones, phycocyanins, proline, and phenolic compounds they contain (Deniz Şirinyıldız and Yorulmaz, 2022; Sasa et al., 2020). Microalgae contain polyunsaturated fatty acids and omega fatty acids essential for humans. Fish is thought to be the primary source of these fatty acids. However, fish consume essential fatty acids by consuming microalgae (Deniz Şirinyıldız and Yorulmaz, 2022). Microalgae are divided into three classes in the literature -; diatoms (*Bacillariophyceae*), green algae (*Chlorophyceae*), and golden algae (*Chrysophyceae*).

Biomass increase and bioactive compound production efficiency of microalgae are highly dependent on environmental conditions (light, temperature, pH). Although the theoretical biomass yield was determined as 100-200 g dry weight $m^{-2}day^{-1}$ according to the studies, it was realized as 15-30 g dry weight $m^{-2}day^{-1}$ in practice (Sun et al., 2018). Microalgae contain glucose, sucrose, starch, and glycogen as carbohydrates. Microalgae, which have a significant essential oil content, contain eicosapentaenoic acid (EPA), α-linolenic acid, docosapentaenoic acid (DPA) and doxahexaenoic acid (DHA). What makes microalgae really important is its high protein and bioactive component content.

As micronutrients, they contain vitamins A, C, E, and B group and folic acid. With these features, microalgae can be used both as a direct food and as a food supplement. *Arthrospira*, *Chlorella*, *Dunaliella*, *Haaematococcus*, *Schizochytrium* spp. and *Porphyridium cruentum*, and *Crypthecodinium cohnii* spp. are evaluated as GRAS (generally considered safe) by the United States Food and Drug Administration (FDA) (Sevencan, 2019; Tsvetanova and Yankov, 2022).

Microalgae have significant biodiversity, and with the recent developments in genetic engineering, this group of microorganisms is considered an essential source for new products and applications (de Morois et al., 2015). Within the scope of this review, it is aimed to explain the bioactive compounds contained in microalgae. The bioactive compounds of microalgae and their functional properties will be examined, and their effects on human health will be described. Finally, the status of these compounds in the food industry and their potential for use will be presented.

Microalgae and Bioactive Compounds

Bioactive compounds originating from microalgae can be synthesized directly as a result of secondary metabolism as well as primary metabolism products. It has been determined that these bioactive compounds formed due to microalgae metabolism have antifungal, antiviral, antialgal, anti-enzymatic, antibiotic, anti-inflammatory, anticancer, antioxidant, and antibacterial properties. Many bioactive compounds accumulate in the microalgae biomass, but these metabolites are sometimes released into the breeding medium. Recent studies have shown that microalgae can produce carotenoids, phycobilins, polyunsaturated fatty acids, proteins, polysaccharides, vitamins, and sterols as bioactive compounds (de Morois et al., 2015; Zhou et al., 2022). There is a great interest in microalgae, which is a source of many important compounds in the food, nutraceutical, biofuel, and cosmetic industries (Zhou et al., 2022). The biochemical compounds produced by microalgae are shown in Figure 1.

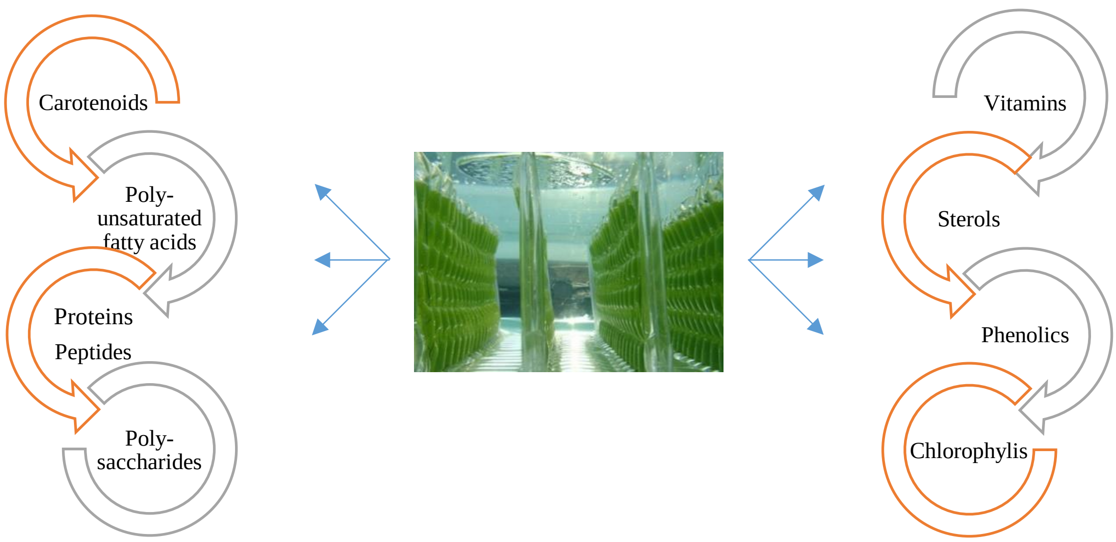
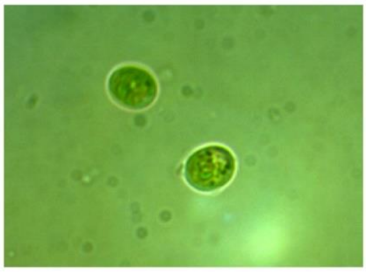


Figure 1. Biochemical compounds produced by microalgae (Zhou et al., 2022)

Protein

Proteins, major compounds for the human body, play an essential role in cell growth and development. Microalgae are considered a new source of the high protein they contain. For example, Spirulina has 70% of its dry-weight protein, which is higher than that of meat (17%), fish (19%), and eggs (47%). Thus, it is thought that microalgae will play an important role in vegetarian and vegan diets. Proteins contained in microalgae are a source of bioactive peptides. With enzymatic hydrolysis, the bioactive peptides they have become usable. Today, these compounds are generally obtained from vegetable and animal proteins. Studies on bioactive peptides from microalgae need to increase (Zhou et al., 2022). The microalgae *Spirulina* and *Chlorella* (Figure 2) are recommended by FAO/WHO as high-quality proteins when evaluated regarding balanced amino acid content and digestibility. These are the most popular species in the microalgae industry with their high protein content (50-70%). The Japanese company Tavelmout produces protein from Spirulina and reports that their protein yield is 20 times higher than soybeans. *Spirulina*, *Chlorella*, or extracted proteins can be used in various food products. Protein-enriched functional food can be obtained by adding dairy products, bread, biscuits, noodles, and pasta (Balasubramaniam et al., 2021).

Spirulina sp. LEB 18



Chlorella fusca LEB 111

Figure 2. *Spirulina* sp LEB 18 and *Chlorella fusca* LEB 111 in the LEB/FURG strain bank (de Morais et al., 2015)

Enzymatic hydrolysis (gastrointestinal protease), microbial enzymatic hydrolysis, exothermic enzymes, and proteolytic processes are used to obtain bioactive peptides from microalgae. It has been determined that the obtained peptides have antioxidative and antihypertensive properties on human health. Studies have shown that microalgae-derived bioactive peptides reduce oxidative stress and related diseases (Ejike et al., 2017). Lee et al. (2009) conducted a study using proteases to obtain water-soluble antioxidants from *Chlorella ellipsoidea* and *Tetraselmis suecica* (*T. suecica*). At the end of the study, it was reported that the enzymatic production of water-soluble antioxidants obtained from *T. suecica* successfully resulted. The compounds obtained by studies in African green monkey liver cells have been determined to prevent oxidative damage and have good hydrogen peroxide scavenging activity. A study was conducted on bioactive peptides obtained from *Chlorella ellipsoidea* against oxidative stress caused by free radicals. In the study, bioactive peptides were obtained by enzymatic hydrolysis (papain, trypsin, pepsin, and α-chymotrypsin). Pepsin hydrolyzed peptides showed a higher antioxidant effect than the others. Using chromatographic methods, the structure of the bioactive peptide was determined to be leucine-asparagine-glycine-aspartic acid-valine-tryptophan. As a result of antioxidant activity analysis, the DPPH value was determined as 0.92 mM, and the IC50 value was determined as 1.42 mM (Ko et al., 2012).

Polysaccharides, which have a complex structure, have various properties such as antioxidant, antimicrobial, and antiviral activity thanks to these structures. Microalgae produce bioactive polysaccharides, divided into storage polysaccharides (SP) and cell wall polysaccharides. While SPs are used as an energy source to realize vital events for the cell, cell wall polysaccharides are responsible for maintaining cell integrity. Extracellular polysaccharides (EPS) are the most studied microalgae polysaccharides in the cell wall polysaccharides group (Zhou et al., 2022). It has been determined that sulfated microalgae polysaccharides in this group have antiviral effects. *Cochlodinium polykrikoides* produce a sulfated polysaccharide together with mannose, galactose, glucose, and uronic acid, and these EPS inhibited the cytopathic effects of influenza A and B viruses (Türkmen and Akyurt, 2021).

Fatty acids

Among the fatty acids, polyunsaturated fatty acids (PUFAs) containing 18 carbons and above cannot be synthesized by animals and higher plants because no enzymes are used to synthesize these fatty acids. For these reasons, polyunsaturated fatty acids, which are considered essential by animals and humans, should be taken with foods. Although fish are generally thought to be the source of essential fatty acids, the primary producers are microalgae living in the oceans. Polyunsaturated fatty acids are found between 20-60% among the microalgae lipids. The w-3 and w-6 fatty acids in the PUFAs group play an important role in human metabolism. W-3 fatty acids, considered essential fatty acids, are a group of great importance among brain lipids. EPA and DHA fatty acids treat diseases such as cancer, Alzheimer's, rheumatoid arthritis, heart diseases, psoriasis, and atherosclerosis. Among microalgae, *Spirulina* and *Chlorella* are preferred for algal oil production. It is thought that microalgae will be an alternative source for PUFAs in the future and will be selected in terms of vegan and vegetarian nutrition (Asgharpour et al., 2015; Bule et al., 2018; Zhou et al., 2022).

Vitamins

Microalgae are an important source of almost all vitamins. It has been reported that Spirulina is a rich source of B1, B2, and B12 (Balasubramaniam et al., 2021). Microalgae produce especially antioxidant vitamins provitamin A (β-carotene), vitamins B, C, and E, and folic acid, inositol, and biotin (Zhou et al., 2022). Microalgae synthesize vitamin A as a provitamin. Synthesized β-carotene is the precursor of several carotenoids and is more active against reactive oxygen species than vitamins E and C. Vitamin E has antioxidant properties and a protective effect against photo oxidants. Tocopherols produced by microalgae are generally associated with polyphenol production and protect against abiotic stresses such as light, metals, and nutrient deficiency. Vitamins K1 and K2 are redox cofactors and act as secondary electron acceptors in photooxidation reactions. Thus, they prevent oxidation reactions from continuing. Vitamin C is used in various functions in the cell. These tasks can be listed as hormone synthesis, cofactor of many enzymes, and antioxidant production. Ascorbic acid (vitamin C) protects microalgae against light-induced radicals. Vitamin B1, essential in acetyl-CoA synthesis, tricarboxylic acid cycle, and pentose phosphate pathway, protects microalgae against abiotic and biotic stresses. In addition, the hypothesis that this vitamin has an antioxidant effect has been thrown, but its action mechanism has not yet been determined. Niacin (vitamin B3) in the structure of NAD and NADP contributes to the antioxidant cell mechanism. NAD and NADP react with H+ in the environment. Vitamin B6 is a cofactor of many metabolic enzymes. Compared with ascorbic acid and α-tocopherol, it is an essential antioxidant against reactive oxygen species. The vitamins they contain and their amounts are summarized in Tables 1 and 2 (Balasubramaniam et al., 2021; Del Mondo et al., 2020).

Table 1. Vitamins and amounts of various microalgae (Del Mondo et al., 2020)

Microalgea class	Microalgea species	Vitamin A	Vitamin C	Vitamin E	Vitamin D	Vitamin K
Cyanobacteria	*Anabaena*	0.28	2	4	-	200.25
	Synechococcus	0.18	-	1.40	-	-
	Arthrospira	0.65	-	0.11-2.5	0.004	12.7
Chlorophyta	*Chlorella*	0.01-0.13	0.10-15	0.01-2	0.004	0.73
	Dunaliella	0.01-0.63	0.16-2.2	0.12-1.9	-	0.1
	Tetraselmis	0.05-4.28	0.19-3	0.04-6.32	14	28
Haptophyta	*Isochrysis*	0.01-0.27	0.12-4.45	0.06-0.12	5	8
	Pavlova	0.10-0.26	0.84-1.3	0.14-0.35	0.35-39	6.5
Bacillariophyceae	*Chaetoceros*	0.52-0.97	0.1-18.79	0.89-1.63	-	-
	Skeletonema	0.14	0.06-6.7	0.11	11	5.5
Eustigmatophyceae	*Nannochloropsis*	0.05-0.08	2.5-6.04	0.02-4.72	0.35-0.48	0.17

Vitamin D and K are stated as µg/g DW, others as mg/g DW.

Table 2. B group vitamins and their amounts in various microalgae (Del Mondo et al., 2020)

Microalgea class	Microalgae species	Vitamin B_1	Vitamin B_2	Vitamin B_3	Vitamin B_5	Vitamin B_6	Vitamin B_7	Vitamin B_9	Vitamin B_{12}
Cyanobacteria	*Anabaena*	5.8	55	78	88	7	0.18	15	1.5
	Aphanizomenon	40	6	130	8	13	-	1	6
	Arthrospira	10-23.8	33-45	0.13-149	13	9.6	-	0.27-4.8	0.5-6.6
Chlorophyta	*Chlorella*	18-23	20-68	0.15-250	21.4-190	1.9-25	0.45-1.1	3.1-34	0.08-2.5
	Dunaliella	9-29	9-31.2	10	5-13.2	2.2-4	0.9	0.4-53.7	0.04-0.7
	Haematococcus	4.7	17	66	14	3.6	-	2.9	1.2
	Tetraselmis	32.3-627	19.1-42	1410	37.7	2.8-155	0.8-1.3	3-20	1.95-9
Haptophyta	*Isochrysis*	14-462	14-30	2690	9.1	1.8-183	1	3	0.6-89
	Pavlova	36-290	6-50	955	-	4-8.4	1.9	23	1.7-1162
Eustigmatophyceae	*Nannochloropsis*	70	22-25	0.12	-	3.6	1.1	17-22	0.3-1.7

B7 and B12 are given as ng/g DW, while others are given as µg/g DW.

Other Bioactive Compounds

Phenolic Compounds: Phenolic compounds, which are secondary metabolites of microalgae, have a complex structure and contain various groups such as flavonoids, phenolic acids, stilbenes, and phlorotannins. They have different functional properties such as antioxidant, anti-allergic, anti-aging, and anti-inflammatory. These functional properties are related to the chemical structure of the compounds. For example, antioxidant capacity depends on the number of hydroxyl groups in their structure and their position in the structure. Flavonoids can chelate with metals, thus preventing the onset of oxidation. They are also very effective against reactive oxygen species. It has been reported that gallic, ferulic, caffeic, synaptic, and coumaric acids are phenolic acids in microalgae. Ferulic and caffeic acid are the two main precursors of lignins. Salicylic acid was determined in two groups of cyanobacteria (Scenedesmus and Phaeodactylum). Naringenin, the precursor compound of flavanols, has been detected in Haptophyta diacronema and Haematococcus, green microalgae. Among the flavonoids detected in different microalgae groups, rutin, quercetin, and kaempferol have an essential place (Del Mondo et al., 2021; Zhou et al., 2022). Li et al. (2007) examined the total phenolic compound content of 23 microalgae species and the relationship between phenolic compounds and antioxidant capacity. In the study, phenolic compounds were extracted using different chemicals (hexane, ethyl acetate, and water), and the amount was determined. As a result of the antioxidant capacity analysis of microalgae extracts, the highest values were found for Synechococcus sp. FACHB 283 has been identified in Chlamydomonas nivalis and Nostoc ellipsosporum CCAP 1453/17 species, and it has been reported that these microalgae can be used as natural antioxidants. The calculations to determine the correlation between phenolic compounds and antioxidant capacity determined that the correlation was very low (Table 3). The correlation between various plants' antioxidant capacity and phenolic compounds was higher than in microalgae. For this reason, it has been explained that microalgae may contain different compounds and phenolic compounds with antioxidant properties.

Table 3. Antioxidant capacity, phenolic compound and the relationship between them obtained as a result of hexane extraction of different microalgae (Li et al., 2007)

Algea species	Phenolic contents (mg GAE/g)	Antioxidant capacity (µmol Trolox/g)	Correlation
Anabaena flos-aquae FACHB 245	5.48	9.27	
Chlamydomonas nivalis	4.55	11.41	
Chlorella protothecoides	14.35	3.49	
Chlorella pyrenoidosa	4.0-13.90	2.14-8.48	
Chlorella vulgaris	3.12-11.57	1.43-5.53	
Chlorella zofingiensis	3.47	1.83	
Crypthecodinium cohnii	2.70-12.68	0.01-0.41	$R^2 = 0.0075$
Nitzschia laevis	2.37	2.21	
Nostoc ellipsosporum	2.68-39.87	0.08-3.84	
Schizochytrium sp.	13.61	0.12	
Schizochytrium mangrovei	2.22	0.01	
Synechococcus sp FACHB 283	2.12	7.17	
Thraustochytrium sp. 26185	4.0	0.01	

GAE: gallic acid equivalent

In a study to determine the bioactive compounds of *Nannochloropsis ocu*lata and *Chlorella vulgaris* species, phenolic compounds, which are secondary metabolites of microalgae, were studied. Microalgae extracted with methanol were tested by chromatographic analysis. As a result of the analyzes performed by HPLC, nine phenolic compounds were determined in *Chlorella vulgaris* and six in *Nannochloropsis oculata*. Quercetin pentosidehexoside, lutein 7-0-glucooside and chicoric acid were determined in both species (Bhuvana et al., 2019).

Pigments: Pigments have essential functions on microalgae's colors and photosynthetic abilities and are classified as water and oil-soluble molecules. While chlorophyll and carotenoids are soluble in oil, phycocyanins are soluble in water (İlter et al., 2017; Zhou et al., 2022).

Carotenoids are present in plants and microorganisms as light-harvesting and protective pigments. According to their mechanism of action, they are divided into two groups primary and secondary carotenoids. Primary carotenoids are involved in photosynthesis, while secondary carotenoids protect microalgae from environmental stress conditions. The primary carotenoids β-carotene, α-carotene, and lutein have been determined in many microalgae species. Microalgae carotenoids are diverse and available in different colors (yellow, orange, red). *Dunaliella*, *Spirulina maxim* and *Spirulina hem*atococcus are important β-carotene producers in microalgae. β-carotene is used as a food coloring in various foods and beverages. It is also used in animal nutrition as a precursor of vitamin A. Astaxanthin, which is in the carotenoids group, has eight times higher antioxidant activity than vitamin E and β-carotene. Thus, it is defined as the most potent antioxidant among carotenoids. The main source of zeaxanthin and lutein is microalgae. These sources can be said as *Dunaliella salina* and *Chlorella protothecosis*. Lutein-3 is a pigment in animal tissues, foods, cosmetics, and drugs (Bule et al., 2018;

Guedes et al., 2011; Zhou et al., 2022). The carotenoids determined in microalgae and the synthesizing microalgae species are given in Table 4.

Chlorophylls, which are responsible for photosynthesis and the green color of microalgae, are involved in the absorption and transport of light energy. So far, five different chlorophyll pigments have been identified and they are named; a, b, c, d, e, and f. Chlorophyll a is the most abundant pigment in all photosynthetic organisms, while chlorophyll b ranks second and is found in plants and microalgae. Chlorophyll f is defined in the cyanobacteria group. Chlorophylls are extracted from plants and microalgae for use in biotechnological applications. Chlorophyll synthesis from microalgae occurs more efficiently than plants. Environmental factors affecting chlorophyll accumulation in microalgae; light, temperature, nitrogen, carbon source, phosphorus, and micronutrients (iron, zinc, manganese). Microalgae grown under high light have low chlorophyll content, while chlorophyll increases at low light intensity. For example, *Chlorella* sp. It has been determined that the amount of chlorophyll increases as the light intensity decreases during development (da Silva Ferreira and Sant'Anna, 2017; Zhou et al., 2022).

Phycocyanins, mainly found in cyanobacteria and having a blue color, are defined as secondary light-harvesting pigments. With their light absorption properties, they can be used in various fields, such as immunology laboratories, biology, and the production of fluorescent dyes (Zhou et al., 2022).

Table 4. Carotenoids synthesized by microalgae and their amounts

Carotenoids	Mikroalgae	Content	Reference
α-carotene	*Chlorella sorokiniana* *Chlorococcum spp.* *Chlamydocapsa spp.*	420 μg/g DW 36-87 μg/g FD 12-56 μg/g FD	Matsukawa et al. 2000 Leya et al. 2009
β-carotene	*Coelastrella striolata* *Chlorella sorokiniana* *Chlamydomonas nivalis* *Chlorococcum spp.* *Chlamydocapsa spp.*	5.2-7.0 mg/g DW 600 μg/g DW 0.03-0.07 μg/ μg chlorophyll a 42-752 μg/g FD 117-638 μg/g FD	Abe et al. 2007 Matsukawa et al. 2000 Remias et al. 2005 Leya et al. 2009
Astaxanthin	*Chlamydomonas nivalis* *Neochloris wimmeri* *Scotiellopsis oocystiformis* *Chorella zofingiensis*	7.78-25.24 μg/ μg chlorophyll a 19.2 mg/g 10.9 mg/g 6.8 mg/g	Remias et al. 2005 Orosa et al. 2001
Canthaxanthin	*Coelastrella striolata* *Asterarcys quadricellulare*	1.5 mg/g DW 14 μg/md DW	Abe et al. 2007 Singh et al. 2019
Fucoxanthin	*Mallomonas sp.* *Cyclotella meneghiniana* *Paralina longispina*	26.6 mg/g DW 2-2.3 mg/g DW 1.4 mg/g DW	Petrushkina et al. 2017
Lutein	*Chlorella sorokiniana* *Chlamydomonas nivalis* *Chlorococcum spp.* *Chlamydocapsa spp.*	4300 μg/g DW 0.11-0.23 μg/ μg chlorophyll a 1610-4348 μg/g FD 3546-3890 μg/g FD	Matsukawa et al. 2000 Remias et al. 2005 Leya et al. 2009
Violaxanthin	*Chlorococcum spp.* *Chlamydocapsa spp.*	350-1205 μg/g FD 998-1042 μg/g FD	Leya et al. 2009
Zeaxanthin	*Chlorella sorokiniana* *Chlorococcum spp.* *Chlamydocapsa spp.*	140 μg/g DW 46-109 μg/g FD 173 μg/g FD	Matsukawa et al. 2000 Leya et al. 2009

DW: dry weight, FD: frezee dry

Functional Properties of Bioactive Compounds Synthesized from Microalgae

Antioxidant Activity

Various methods are used to reduce oxidative damage in the food, pharmaceutical, and cosmetic industries. Oxidative reactions caused by radicals such as hydrogen peroxide, hydroxyl radical, and free oxygen species cause various damages. For example, in the food industry, it significantly impacts the product's shelf life. Chemicals with antioxidant properties are used to stop or slow down oxidative reactions. Due to the health effects of synthetic antioxidants such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), and propyl gallate (PG), which are synthesized in the laboratory, the tendency to use natural products is increasing. Components with antioxidant properties obtained from microalgae; carotenoids, phenolic compounds, fatty acids, tocopherol, flavonoids, and alkaloids. These components play a significant role in the control of oxidative processes (Bule et al., 2018). Batista et al. (2017) added four different microalgae biomass (*Arthrospira platensis, Chlorella vulgaris, Tetraselmis* *suecica*, and *Phaeodactylum tricornutum*) to cookies. They examined the total phenolic compounds and their in vitro antioxidant activities. 2% and 6% biomass was added to the cookie dough, and the cookies prepared during eight weeks of storage were compared with the control sample. Regarding digestibility during storage, no difference was determined between the control and sample groups. Regarding total phenolic compounds and in vitro antioxidant activity, the samples with microalgae added had higher values than the control sample. The phenolic compound content (0.9 mg GAE g-1) of *Arthrospira platensis* added cookies was higher than the other samples. The antioxidant activity values are respectively determined as *Phaeodactylum tricornutum* (248 mmol TEAC kg-1), *Chlorella vulgaris* (193 mmol kg-1), *Arthrospira platensis* (~160 mmol TEAC kg-1) and *Tetraselmis suecica* (~160 mmol TEAC kg-1). Rodriguez-Garcia and Guil-Guerrero (2008) investigated the antioxidant activities of three microalgae species (*Porphyridium crue*ntum, *Phaeodactylum tricornutum*, and *Chlorella vulgaris*). As a result of the analysis, *Chlorella vulgaris* extract had a higher antioxidant activity value than other microalgae extracts and synthetic antioxidants (BHA, BHT). As a result of the study, it was stated that microalgae extracts could be used instead of herbal extracts or synthetic antioxidants in various fields.

Antimicrobial Activity

Various antimicrobial compounds synthesized by microalgae are used in the pharmaceutical industry, food industry (functional food ingredient), animal health (antibiotic), biopesticides in agriculture, and wastewater cleaning. Antimicrobial properties of microalgae depend on the microalgae variety, the type of solvent used in the extraction, and the extract concentration obtained. For example, Brown algae are more effective against foodborne microorganisms than other species. The components synthesized by microalgae, proteins, polysaccharides, polyunsaturated fatty acids (especially EPA and DHA), polyphenols, flavonoids, and carotenoids have antimicrobial activity potential. Studies have shown that microalgae have antimicrobial activity against *Staphylococcus aureus* (*Staph. aureus*), *Escherichia coli* (*E.coli*), *Salmonella* spp., *Bacillus cereus* and *Listeria monocytogenes* bacteria (Table 5) (Pina-Pérez et al., 2017; Stirk et al. van Staden, 2022).

E. coli is one of the important microorganisms for the food industry, Staph. aureus, *Candida albicans*, and *Aspergillus niger*, the antimicrobial effect of the extract obtained from *Dunaliella salina* was investigated. The study tested different extraction solvents (hexane, petroleum ether, water) and times (40, 100, and 160°C). In the extractions performed with different parameters, the highest antimicrobial activity for each solvent was determined at 160°C. The lowest extraction efficiency (1.8-9.2%) was obtained when water was used as a solvent. The lowest growth occurred when the extract prepared with petroleum ether was used for each microorganism. For example, when petroleum ether extract was used against *E. coli*, 9 mg bacteria were determined per milliliter. In comparison, 30 mg bacteria were detected per mL in aqueous extract (extraction temperature 40°C) (Herrero et al., 2006).

Table 5. Antimicrobial effect of various microalgae extracts against foodborne bacteria (Pina-Pérez et al., 2017; Stirk and van Staden, 2022)

Microorganism	Microalgae
Gram (+) Bacteria	
Staphylococcus aureus	*Chlorella vulgaris, Nostoc sp., Turbinaria conoides, Scenedesmus oedogonium*
Bacillus cereus	*Spirulina naxima, Dictyopteris undulata, Laurencia okamurae*
Listeria monocytogenes	*Dunaliella salina, Himanthalia elongata*
Gram (-) Bacteria	
Escherichia coli O157:H7	*Ascophyllum nodosum, Ulva rigida, Dunaliella salina, Padina gymnospora*
Salmonella spp	*Dictyota dichotoma, Turbinaria conoides, Dunaliella salina, Pithophora oedogonium*

Anticancer Activity

Treatments such as ionized radiation, alkylating agents, and DNA topoisomerase inhibitors used in cancer treatment damage normal and cancer cells. Components with anticancer properties obtained from microalgae protect normal cells from genetic damage. For this reason, the obtained components have a field of use in preventing cancer. Studies on components with anticancer properties originating from microalgae have been increasing in recent years. Examples of these components are phycocyanins in the phycobiliprotein group. Phycocyanins are a compound produced by *Spirulina platensis*. Apart from this, it is also synthesized by *Limnothrix* sp. (Balasubramaniam et al., 2021; Bule et al., 2018). Samarakoon et al. (2013) investigated the anticancer properties of compounds synthesized by four different marine microalgae species (*Chlorella ovalis*, *Nannchloropsis oculata*, *Amphidinium carterae*, and *Phaeoductylum tricornutum*). *Chlorella ovalis* ethyl acetate fraction and *Amphidinium carterae* chloroform fraction were determined to have the highest anticancer activity among other microalgae species compared. The components synthesized by microalgae in the literature and their effects are briefly summarized in Table 6.

Table 6. Anticancer compounds synthesized by microalgae

Component	Microalgae	Effect	Reference
Lutein	*Chlorella vulgaris*	Colon cancer cells	Cha et al., 2008
Violaksantin	*Dunaliella tertiolecta*	Human breast and prostate cancer cells	Pasquet et al., 2011
Fukoksantin	*Phaeodactylum tricornutum*	Human liver and colon cancer cells	Neumann et al., 2019
Fikosiyanin	*Spirulina platensis*	liver cancer cell, human lung cancer cell	Prabakaran et al., 2020; Deniz et al., 2016
	Limnothrix sp.	Prostate cell, human lung cancer cell	Gantar et al., 2012; Safaei et al., 2019

Conclusion

Microalgae with the ability to reproduce in different habitats, have started to attract a lot of attention today because it is both easy to produce and economical. Thanks to their properties, biomass and microalgae extracts can be used in food, livestock, pharmacy, and cosmetics. It is also essential in vegetarian nutrition with its high protein content, adding functional properties to food formulations. The primary source of polyunsaturated fatty acids, such as EPA and DHA, which are abundant in fish, are microalgae living in the seas. Microalgae, a rich source of bioactive components, has various functional properties: antioxidant, antimicrobial, anticancer, and antidiabetes. Thanks to the bioactive peptides, polyunsaturated fatty acids, phenolic compounds, carotenoids, and flavonoids they contain, they have these properties. For example, fucoidan that a sulfated polysaccharide, prevents the proliferation of human lymphoma cells thanks to its kinase activity. The extraction technique has a high effect on the bioactive compounds obtained from microalgae, like thermally sensitive carotenoids, it is more appropriate to use non-thermal extraction techniques. Also, the cell structures of algae affect the efficiency of extraction. It is necessary to determine the appropriate extraction method for the bioactive compound planned to be extracted. Specific studies are needed for this. Microalgae is a vital resource to be studied. This review briefly explains the bioactive components synthesized by microalgae and their functional properties.

REFERENCES

Abe, K., Hattori, H., & Hirano, M. (2007). Accumulation and antioxidant activity of secondary carotenoids in the aerial microalga Coelastrella striolata var. multistriata. *Food chemistry*, *100*(2), 656-661.

Akyıl, S., İlter, I., Mehmet, K. O. Ç., & Kaymak-Ertekin, F. (2016). Alglerden elde edilen yüksek değerlikli bileşiklerin biyoaktif/biyolojik uygulama alanları. *Akademik Gıda*, *14*(4), 418-423.

Asgharpour, M., Rodgers, B., & Hestekin, J. A. (2015). Eicosapentaenoic acid from Porphyridium cruentum: Increasing growth and productivity of microalgae for pharmaceutical products. *Energies*, *8*(9), 10487-10503.

Batista, A. P., Niccolai, A., Fradinho, P., Fragoso, S., Bursic, I., Rodolfi, L., ... & Raymundo, A. (2017). Microalgae biomass as an alternative ingredient in cookies: Sensory, physical and chemical properties, antioxidant activity and in vitro digestibility. *Algal research*, *26*, 161-171.

Balasubramaniam, V., Gunasegavan, R. D. N., Mustar, S., Lee, J. C., & Mohd Noh, M. F. (2021). Isolation of industrial important bioactive compounds from microalgae. *Molecules*, *26*(4), 943.

Bhuvana, P., Sangeetha, P., Anuradha, V., & Ali, M. S. (2019). Spectral characterization of bioactive compounds from microalgae: N. oculata and C. vulgaris. *Biocatalysis and Agricultural Biotechnology*, *19*, 101094.

Bule, M. H., Ahmed, I., Maqbool, F., Bilal, M., & Iqbal, H. M. (2018). Microalgae as a source of high-value bioactive compounds. *Front. Biosci*, *10*(2), 197-216.

Cha, K. H., Koo, S. Y., & Lee, D. U. (2008). Antiproliferative effects of carotenoids extracted from Chlorella ellipsoidea and Chlorella vulgaris on human colon cancer cells. *Journal of agricultural and food chemistry*, *56*(22), 10521-10526.

da Silva Ferreira, V., & Sant'Anna, C. (2017). Impact of culture conditions on the chlorophyll content of microalgae for biotechnological applications. *World Journal of Microbiology and Biotechnology*, *33*(1), 20.

de Morais, M. G., Vaz, B. D. S., de Morais, E. G., & Costa, J. A. V. (2015). Biologically active metabolites synthesized by microalgae. *BioMed research international*, *2015*.

Del Mondo, A., Smerilli, A., Sané, E., Sansone, C., & Brunet, C. (2020). Challenging microalgal vitamins for human health. *Microbial Cell Factories*, *19*(1), 1-23.

Del Mondo, A., Smerilli, A., Ambrosino, L., Albini, A., Noonan, D. M., Sansone, C., & Brunet, C. (2021). Insights into phenolic compounds from microalgae: Structural variety and complex beneficial activities from health to nutraceutics. *Critical Reviews in Biotechnology*, *41*(2), 155-171.

Deniz, I., Ozen, M. O., & Yesil-Celiktas, O. (2016). Supercritical fluid extraction of phycocyanin and investigation of cytotoxicity on human lung cancer cells. *The Journal of Supercritical Fluids*, *108*, 13-18.

Deniz Şirinyıldız, D., & Yorulmaz, A. (2022). Alternatif ve sürdürülebilir bir gıda kaynağı olarak algler. *Toros University Journal of Food Nutrition and Gastronomy*, *1*(1), 101-117.

Ejike, C. E., Collins, S. A., Balasuriya, N., Swanson, A. K., Mason, B., & Udenigwe, C. C. (2017). Prospects of microalgae proteins in producing peptide-based functional foods for promoting cardiovascular health. *Trends in Food Science & Technology*, *59*, 30-36.

Gantar, M., Dhandayuthapani, S., & Rathinavelu, A. (2012). Phycocyanin induces apoptosis and enhances the effect of topotecan on prostate cell line LNCaP. *Journal of medicinal food*, *15*(12), 1091-1095.

Guedes, A. C., Amaro, H. M., & Malcata, F. X. (2011). Microalgae as sources of carotenoids. *Marine drugs*, *9*(4), 625-644.

Herrero, M., Ibáñez, E., Cifuentes, A., Reglero, G., & Santoyo, S. (2006). Dunaliella salina microalga pressurized liquid extracts as potential antimicrobials. *Journal of food protection*, *69*(10), 2471-2477.

İlter, I., Akyıl, S., Koç, M., & Kaymak-Ertekin, F. (2017). Alglerden elde edilen ve gıdalarda doğal renklendirici olarak kullanılan pigmentler ve fonksiyonel özellikleri. *Turkish Journal of Agriculture-Food Science and Technology*, *5*(12), 1508-1515.

Ko, S. C., Kim, D., & Jeon, Y. J. (2012). Protective effect of a novel antioxidative peptide purified from a marine Chlorella ellipsoidea protein against free radical-induced oxidative stress. *Food and chemical toxicology*, *50*(7), 2294-2302.

Lee, S. H., Chang, D. U., Lee, B. J., & Jeon, Y. J. (2009). Antioxidant activity of solubilized Tetraselmis suecica and Chlorella ellipsoidea by enzymatic digests. *Journal of Food Science and Nutrition*, *14*(1), 21-28.

Leya, T., Rahn, A., Lütz, C., & Remias, D. (2009). Response of arctic snow and permafrost algae to high light and nitrogen stress by changes in pigment composition and applied aspects for biotechnology. *FEMS microbiology ecology*, *67*(3), 432-443.

Li, H. B., Cheng, K. W., Wong, C. C., Fan, K. W., Chen, F., & Jiang, Y. (2007). Evaluation of antioxidant capacity and total phenolic content of different fractions of selected microalgae. *Food chemistry*, *102*(3), 771-776.

Matsukawa, R., Hotta, M., Masuda, Y., Chihara, M., & Karube, I. (2000). Antioxidants from carbon dioxide fixing Chlorella sorokiniana. *Journal of applied phycology*, *12*, 263-267.

Neumann, U., Derwenskus, F., Flaiz Flister, V., Schmid-Staiger, U., Hirth, T., & Bischoff, S. C. (2019). Fucoxanthin, a carotenoid derived from Phaeodactylum tricornutum exerts antiproliferative and antioxidant activities in vitro. *Antioxidants*, *8*(6), 183.

Orosa, M., Valero, J. F., Herrero, C., & Abalde, J. (2001). Comparison of the accumulation of astaxanthin in Haematococcus pluvialis and other green microalgae under N-starvation and high light conditions. *Biotechnology Letters*, *23*, 1079-1085.

Pasquet, V., Morisset, P., Ihammouine, S., Chepied, A., Aumailley, L., Berard, J. B., ... & Picot, L. (2011). Antiproliferative activity of violaxanthin isolated from bioguided fractionation of Dunaliella tertiolecta extracts. *Marine drugs*, *9*(5), 819-831.

Prabakaran, G., Sampathkumar, P., Kavisri, M., & Moovendhan, M. (2020). Extraction and characterization of phycocyanin from Spirulina platensis and evaluation of its anticancer, antidiabetic and antiinflammatory effect. *International Journal of Biological Macromolecules*, *153*, 256-263.

Petrushkina, M., Gusev, E., Sorokin, B., Zotko, N., Mamaeva, A., Filimonova, A., ... & Kuzmin, D. (2017). Fucoxanthin production by heterokont microalgae. *Algal Research*, *24*, 387-393.

Pina-Pérez, M. C., Rivas, A., Martínez, A., & Rodrigo, D. (2017). Antimicrobial potential of macro and microalgae against pathogenic and spoilage microorganisms in food. *Food chemistry*, *235*, 34-44.

Remias, D., Lütz-Meindl, U., & Lütz, C. (2005). Photosynthesis, pigments and ultrastructure of the alpine snow alga Chlamydomonas nivalis. *European Journal of Phycology*, *40*(3), 259-268.

Rodriguez-Garcia, I., & Guil-Guerrero, J. L. (2008). Evaluation of the antioxidant activity of three microalgal species for use as dietary supplements and in the preservation of foods. *Food chemistry*, *108*(3), 1023-1026.

Safaei, M., Maleki, H., Soleimanpour, H., Norouzy, A., Zahiri, H. S., Vali, H., & Noghabi, K. A. (2019). Development of a novel method for the purification of C-phycocyanin pigment from a local cyanobacterial strain Limnothrix sp. NS01 and evaluation of its anticancer properties. *Scientific reports*, *9*(1), 9474.

Samarakoon, K. W., Ko, J. Y., Rahman, S. M. M., Lee, J. H., Kang, M. C., Kwon, O. N., ... & Jeon, Y. J. (2013). In vitro studies of anti-inflammatory and anticancer activities of organic solvent extracts from cultured marine microalgae. *Algae*, *28*(1), 111-119.

Sasa, A., Şentürk, F., Üstündağ, Y., & Erem, F., (2020). Alglerin gıda veya gıda bileşeni olarak kullanımı ve sağlık üzerine etkileri. *Uluslararası Mühendislik Tasarım ve Teknoloji Dergisi*, *2*(2), 97-110.

Sevencan, A. (2019). Mikroalg Nedir? Biyoaktif Bileşenleri Nelerdir? Nasıl Yetiştirilir? Güncel Konular. URL: https://www.birbes.com/?p=19005. Date of Access: August 17 2023.

Singh, D. P., Khattar, J. S., Rajput, A., Chaudhary, R., & Singh, R. (2019). High production of carotenoids by the green microalga Asterarcys quadricellulare PUMCC 5.1. 1 under optimized culture conditions. *PloS one*, *14*(9), e0221930.

Stirk, W. A., & van Staden, J. (2022). Bioprospecting for bioactive compounds in microalgae: Antimicrobial compounds. *Biotechnology Advances, 59*, 107977.

Sun, H., Zhao, W., Mao, X., Li, Y., Wu, T., & Chen, F. (2018). High-value biomass from microalgae production platforms: strategies and progress based on carbon metabolism and energy conversion. *Biotechnology for biofuels*, *11*, 1-23.

Türkmen, A., & Akyurt, İ. (2021). Antiviral Effects of Microalgae. *Turkish JAF Sci. Tech*, 412-419.

Tsvetanova, F., & Yankov, D. (2022). Bioactive compounds from red microalgae with therapeutic and nutritional value. *Microorganisms, 10*(11), 2290.

Uzuner, S., & Haznedar, A. (2020). Fonksiyonel Gıda İçin Sağlıklı Takviye: Mikroalgler. *Sinop Üniversitesi Fen Bilimleri Dergisi*, *5*(2), 212-226.

Zhou, L., Li, K., Duan, X., Hill, D., Barrow, C., Dunshea, F., ... & Suleria, H. (2022). Bioactive compounds in microalgae and their potential health benefits. *Food Bioscience*, 101932.Algae