ISSN: 2347-467X, Vol. 09, No. (3) 2021, Pg. 917-927

Current Research in Nutrition and Food Science

www.foodandnutritionjournal.org

Microalgae as a Potential Source of Bioactive Food Compounds

MANISHAA SRI MAHENDRAN[1], ANTO CORDELIA TANISLAUS ANTONY DHANAPAL[1], LING SHING WONG[2], GOVINDARAJU KASIVELU[3], SINOUVASSANE DJEARAMANE*[4]

[1]Department of Chemical Science, Faculty of Science, Universiti Tunku Abdul Rahman, Kampar, 31900 Malaysia.
[2]Life Science Division, Faculty of Health and Life Sciences, INTI International University, Nilai, 71800 Malaysia.
[3]MoES - Earth Science & Technology Cell (Marine Biotechnological Studies), Sathyabama Institute of Science and Technology (Deemed to be University) Chennai, India.
[4]Department of Biomedical Science, Faculty of Science, Universiti Tunku Abdul Rahman, Kampar, 31900 Malaysia.

Abstract

Microalgae are unicellular, photosynthethic organisms that can grow on diverse aquatic habitats like ponds, lakes, rivers, oceans, wastewater and humid soils. Recently, microalgae are gaining importance as renewable sources of biologically active food compounds such as polysaccharides, proteins, essential fatty acids, biopigments such as chlorophylls, carotenoids, astaxanthin, as well as vitamins and minerals.The bioactive food compounds of microalgae enable them to be part of multitude of applications in numerous industrial products for healthy life and ecosystem. This review article summarizes the applications of biologically active food compounds derived from microalgae as nutraceuticals, healthy dietary supplements, pharmaceuticals and cosmetics. Further, this review article highlights the importance of research focus on the identification and extraction of bioactive food compounds from the huge numbers of microlage that exist in nature for sustainable global food security and economy.

Article History

Received: 25 September 2020

Accepted: 01 November 2021

Keywords

Therapeutic applications;
Bioactive food Compounds;
Microalgae;
Nutraceuticals;
Pigments.

Introduction

Increasing awareness on the positive effect of diet on human wellbeing has brought novel natural ingredients and functional food products into a new extraordinary age.[1] The functional food is commonly defined as a diet comprising more than one useful

CONTACT Sinouvassane Djearamane sinouvassane@utar.edu.my Department of Biomedical Science, Faculty of Science, Universiti Tunku Abdul Rahman, Kampar, 31900 Malaysia.

Doi: http://dx.doi.org/10.12944/CRNFSJ.9.3.18

constituents that proffer supplementary health benefits in addition to the rudimentary, alimentary and energetic importance that each food offers.[2] Functional foods have been linked with improved health and quality of life, good health promotion, and decreased threat of ailment.[1] Public awareness on healthy diet is increasing in recent times as it is important for the prevention of chronic diseases including cancer, cardiovascular problems, and osteoporosis.[3] Besides, the societal necessity to minimize the prescription of pharmaceutical products due to their adverse side effects and minimize the cost of healthcare, has encouraged the government agencies and the industries towards the wide usage of functional foods.[4]

The utilization of microalga *Nostoc* to survive hunger among Chinese people has inferred that human beings had used microalgae as a food supplement over thousands of years.[5] Certain blue-green microalgae such as, *Aphanizomenon* and *Spirulina* have been utilized for thousands of years by humans as food.[6]

Microalgae comprise a vast diversity of micro organisms from prokaryotic cyanobacteria to eukaryotic microalgae that can synthesize bioactive substances by using carbon dioxide, nutrients (nitrogen, phosporus, potassium) and solar energy proficiently.[7] The carotenoids, long-chain fatty acids, sugars, both essential and non-essential amino acids, minerals, enzymes and vitamins are the most sought after bioactive compounds produced by the microalgae that are essential for human nutrition and wellbeing. Thus, microalgae are perceived as ideal candidates for modern "nutraceutical" or "pharma food".[8]

Arthospira plantesis, *Haematococcus pluvialis, Dunaliella salina*, and *Chlorella vulgaris* are the most commonly used microalgae as food supplements in human and feed additives for animals as they are the most biotechnologically relevant microalgae.[9] In addition, microlgae products are used in cosmetic industries as skin cream pigments and in pharmaceutical applications owing to their superior therapeutic values.[10] Furthermore, microalgae function as probiotic agents and are incorporated in traditional food products such as pasta, biscuits, salad dressings and mayonnaise to enhance the intake of nutritionally diverse foods that promotes human health outcomes.[3] Interestingly, microlagae are also used as a natural food colorant or as a dietary substitute in snack foods, pasta, gums, candy bars, snacks and drink mixes.[11]

Due to the abundance of accessible microalgae bestowed in nature, selecting the most appropriate microalgae for specific applications in food technology is extremely important for successful production of novel foods.[3] Conversely, biomass manufacturing systems that are currently in use have to be modifiedusing more advanced technologies, in operational as well as technological levels, to enrich the bioactive compounds produced by the microalgae.[1, 12]

To highlight the importance of usage of the products synthesized and extracted from microalgae as an alternative source for naturally produced healthy food supplements, this review article summarizes the nutritional values and the therapeutic applications of the bioactive compounds derived from microalgae.

Bioactive Food Compounds of Microalgae

Microalgae are the fascinating life forms, whose evolution is not only to survive but also to flourish in the harshest surroundings of the planet. They do this by naturally generating an outstanding collection of defensive and nourishing compounds like flavonoids, phospholipids, special carotenoids, antioxidants, oils rich in nutrients, non-digestible oligosaccharides and fatty acids.[12] The biosynthesis of the bioactive compounds including natural antioxidants and drugs from microalgae are stimulated and enhanced by manipulating the cultivation procedures like increasing or decreasing the temperature , nutrients, growth phase, photoperiod and light intensity for optimal growth and high yield.[12]

Lipids

The oils derived from microalgae can be a good substitute for the currently used vegetable oils as the microlagal oils are rich in essential fatty acids. For an example, the concentrations of linoleic and alpha-linolenic acids in microalgal oils are greater than the oils obtained from rape seed (canola), soy or sunflower oils.[13]

The developement of high concentrations of nutritionally important polyunsaturated long-chain fatty acids (PUFAs), such as docosahexaenoic acid (DHA, 22:6, ω−3) and eicosapentaenoic acid (EPA, 20:5, ω−3) can be made possible through microalgal oils. The EPA and DHA supplements are well known for thier beneficial effects to enhance brain function, especially to improve children's cognitive performance and also prevent cardiovascular diseases and inflammation.[14] Interestingly, microalgal oils can be considered as a natural gift to vegetarians since the oils derived from microalgae can be a best substitute for fish oils. Also the chemical pollutants, like mercury, present in the fish supplies can contaminate the fish oils that in turn might cause health hazards to the consumers. Hence, microalgal oils can be a better alternative for fish oils available in the market[15]

Initially, the primary objective of the research development on algal lipids was targeted towards the synthesis of biodiesel. However, the wider usage of microlagal omega fatty acids in infant formulations and also as nutraceutical agents have attracted the current market considerably.[16] Numerous microalgae strains have been analyzed for fatty acid content and great accumulations of DHA and EPA have been found in the strains of the genera *Nannochloropsis, Phaeodactylum,* and *Koliella.* Not ably, the arachidonic acid of *Porphyridium cruentum* helps to improve normal growth, improve visual and functional development in infants. Similarly, the eicosapentaenoic acid present in *Nannochloropsis* sp. has beneficial effects on cardiovascular system as it offers protection against atherosclerosis and nervous sytem towards mental development and support.[16]

Proteins

In the 1950s itself, microalgae were proposed as a novel protein source[17] due to their high protein content and rich amino acid profile.[18] The hydrolysates or peptides of microlagal proteins can be produced by various enzymatic processes and fermentation.[19] The protein constituents of microlage provide numerous health benefits such as antihypertensive, antioxidant, anticancer, immune-modulatory, anticoagulant, and hepato-protective.[20] The microalgae commonly used in the formulation of protein products are *Spirulina* (65% protein), *Dunaliella* (57% protein) and *Chlorella* (55% protein).[21] Special attention has been given to *Spirulina* among all the studied microalgae species due to its supreme quality and protein quantity (60–70 percent of dry weight) with easy digestability.[22] Phycobiliproteins are a curious category of microalgae proteins,which are the accessory photosynthetic pigments, including phycocyanin, phycoerythrin, phycoerythrocyanin, and allophycocyanin. The *Synechococcus sp*.and *Arthrospira sp*. are the most important algae currently used to extract phycobiliproteins. The phycobiliproteins are used in dairy products, chewing gums, sweets and ice creams as natural colorants and also find application in several nutraceutical products including tablets and, capsules.[23] Numerous beneficial health effects of phycobiliproteins including neuroprotective, antioxidant, hepatoprotective, anti-inflammatory, anticancer and hypocholesterolemic have been reported.[24]

Solvent extraction, enzyme hydrolysis and microbial fermentation techniques are utilized to produce bioactive microalgae peptides. Enzymatic hydrolysis are preferred in food and pharmaceutical industries due to the absence of residual organic solvents or potentially harmful compounds in food.[25] Advanced high throughput analysis and molecular studies of algal peptides are required to fully benefit the superior novel proteins from the microalgae.

Carbohydrates

A relatively low photo conversion efficiency of algae enables them to build up large carbon concentrations (greater than 50% by dry weight) with substantial biofuels in microalgae, which in particular act as protective, storage and structural molecules.[26] The use of microalgae as a sustainable source of carbohydrates is a potential area that should be explored further.[27] The glycogen (α1,4-based glucan), hybrid starch and amylopectin-like polysaccharides (starch) that are closely related to the plant are present in cyanobacteria, red algae and green algae respectively.[28] Microalgae contain both prominent sugars like mannose, galactose, xylose, arabinose and glucose, and also less frequent sugars, including rhamnoses, fucose and uronic acids.[29] Cultivation and environmental factors can modulate nearly 33-64% on the content of microalgae carbohydrates as they relate to the carbon source and metabolism (e.g. autotrophy, heterotrophy and mixotrophy).[30]

Some microalgae polysaccharides can be used in industries commercially, taking into account of the rapid growth by crop control.[31] Isolated polysaccharides from microalgae, such as *P.cruentum*, *S.platensis*, *D. Salina*, *Rhodella reticulate* and *Schizochytrium* sp., displayed useful antioxidant properties and efficient scavenging capabilities on superoxide radicals, hydroxyl radicals and hydroxyl peroxide.[32] Recent research disclosed the occurance of high content polysaccharides in *Isochrysis galbana* (up to 25% dry cell weight).[33] The rich carbohydrate content of microalgae can serve as an alternative source of sustainable energy that can be supplemented to alleviate hunger and poverty.

Phytochemicals

Phytochemicals are group of bioactive compounds available in microalgae with diverse biological features including antioxidant, anti-inflammatory and antimicrobial activities. Phenolics are the most abundant phytochemicals that exist in microalgae and are well known for their antioxidant properties.[34] The phenolic compounds are generally divided into 10 categories, namely phenolic acid, hydroxycinnamic acid, basic phenol, xanthone, flavonoid, stilbene acid, anthraquinone, coumarins, naphthoquinones and lignins.[35] Flavonoids are the active scavengers for various forms of reactive oxygen species (ROS) and lipid peroxyl radicals to prevent lipid peroxidation and oxidative stress.[34]

Arthrospira extracts exhibited antioxidant activities by preventing the peroxidation of LDL cholesterol which leads to constraining atherosclerotic plaques and strokes.[35] Antioxidant effects evaluated by testing oxidation stability demonstrated that chlorogenic and caffeic acids found in this microalgae have greater antioxidant activity than other phenolic acids.[36] The combined effects of these phenolics and 13-cis-retinoic acid have been documented to not only prevent lipid peroxidation but also protective against various cancer.[36] Numerous earlier findings have confirmed the antioxidant potential of phenolic compounds obtained from *Chlorella* and *Dunaliella*.[37] The presence of these phytonutrients and bioactive substances make the microalgae a potent source of nutritional ingredients, nutraceuticals and dietary supplements.

Vitamins and Minerals

Microalgae also produce large amount of essential micronutrients such as vitamins and minerals.[38] Microalgal biomass have been reported to constitute important vitamins (e.g., Thiamin (B1), Riboflavin (B2), Pyridoxine (B6), Cyanocobalamine (B12), vit C and vit E) and sufficient mineral content (e.g., sodium, potassium, copper, magnesium, iron and zinc). The cobalamin (vitamin B12) is commonly present in the green and red algae at high concentrations[34] that makes microalgae as an alternative source of B12 especially for vegans and vegetarians.

Fabregas and Herrero performed a research in 1990 to find out the vitamin content of different strains of microalgae. They observed that, relative to traditional food sources, microalgae consist of a greater concentration of four vitamins; provitamin A, vitamin B1, vitamin E and folic acid. *Dunaliella tertiolecta* has been confirmed to have the capacity to synthesize vitamin B12 (cobalamin), vitamin B2 (riboflavin), vitamin E (tocopherol) and provitamin a (β-carotene). *Tetraselmis suecica* has also been an outstanding source of vitamin B1 (thiamin), vitamin B3 (nicotinic acid), vitamin B5 (pantothenic acid), vitamin B6 (pyridoxine) and vitamin C (ascorbic acid), and *Chlorella* sp contains a high concentration of vitamin B7 (biotin). A research by Shim et al. found that about 9-18% of *Chlorella* species are a plentiful source of vitamin B12.[39]

There are several bioactive food compounds derived from microalgae that can be employed in therapeutic applications. For instance, γ-Linolenic acid (GLA) and vitamins from *S. platensis* are utilized as immunity boosters.[40, 41] Proteins from *S.platensis* and *D.salina*, short chain fatty acids from *H.pluvialis*, proteins and dietary fibers from *Chlorella* and phenylethylamine from *Aphanizomenon* are used as health food supplements.[41,42.43,44,45] Besides, Eicosapentaenoic acid (EPA), Arachidonic acid (ARA) and vitamins derived from *P.cruentum* are consumed as nutraceuticals to enhance the blood clotting and immune system.[46,47] Table 1 outlines the therapeutic applications of bioactive food compounds obtained from microalgae. These bioactive compounds are extensively used for various physiological functions and play a vital role in ensuring good health and well being.

Pigments

Presence of different pigments and colors in each phylum is one of the most noticeable characteristics of microalgae.[48]Given their phylogenetic age, it is self-evident that they have evolved to produce pigments that are unique to them.[49] The different types of pigments isolated from microalgae have been proven to have numerous health benefits and hence have attracted the industries in producing various food and pharmaceuticals products in recent years using microlgal pigments as an active food additive. Table 2 summarizes the pigments of microalgae and their potential applications. These pigments are natural with zero toxicity and better health outcomes that make them a healthier choice compared to the synthetic food additives and colorants.

Table 1: Therapeutic applications of bioactive food compounds from microalgae

Microalgae	Bioactive compounds	Physiological Functions	Therapeutic Applications	References
Spirulina platensis	γ-Linolenic acid (GLA)	Maintains tissue integrity; delays aging	Immunity booster	40
	Vitamin C, vitamin K, vitamin B12, vitamin A & α-tocopherol	Antioxidant; forming blood cells; blood coagulation mechanism	Immunity booster	41
	Proteins	Anticoagulant; immunomodulatory	Health food supplement	41
Dunaliella salina	Proteins	Antimicrobial; Antiproliferative	Health food supplement; therapeutical	42
Haematococ -cus pluvialis	Short-chain fatty acids	Antimicrobial	Health food supplement	43
Chlorella vulgaris	Proteins		Health food supplement	44
	dietary fiber	Detoxify toxic metals and pesticides	Health food supplement; detoxifier	44
Porphyridium cruentum	Eicosapentaenoic acid (EPA)	Nutraceutical; antimicrobial; anti-inflammatory:	Baby and health food supplement	46
	Arachidonic acid (ARA)	Platelets aggregation; vasoconstrictive	therapeutics; health ingredient	46
	Vitamin C, vitamin K, vitamin B12, Vitamin A & α-tocopherol	Antioxidant; blood cell formation; blood clotting mechanism	Immune system	47
Aphanizomenon	Phenylethylamine	Prevents neurodegen-erative diseases	Healthfood supplement; therapeutical	45

Chlorophyll

Chlorophylls are green in colour, which are non-polar pigments with a porphyrin chain and are present in cyanobacteria, algae, and superior plants.[49] Chlorophylls contain tetrapyrrole with tightly bound magnesium atom. Chlorophylls are dimonant pigments in green algae (Chlorophyta).[10] Microalgae contain 0.5 to 1.0 % of chlorophyll per gram.[50] Chlorophyllin is a chlorophyll derivative in which sodium or copper replaces magnesium and the phytol chains are lost. Chlorophyllins are used in dietary supplements to control geriatric patients' body odor and studies have reported the antimutagenic and anticarcinogenic effects of chlorophyll and chlorophyllin.[50]

Table 2: Microalgal pigments and their potential applications

Microalgae	Pigment	pigment Colour	Applications	References
Spirulina platensis	Chlorophyll	Green	Pharmaceutical and cosmetics	10
	Phycocyanin	Blue-green	Dyes, beverages, whipped cream, hot cream and sweets), cosmetics, antiviral	61, 62
Dunaliella salina	β-Carotene	Yellow	Pro-vitamin A, an antioxidant food, additive E160a; egg yolk colorant	10
	Bixin	Yellowish to peach color	Food additive E160b (colorant); cosmetics	10, 61
	Lutein	Yellow-orange	Dietary additive E161b, gg yolk coloring, animal tissue pigmentation, medicinal (anti-macular degeneration), cosmetics (coloring)	64
Haematococcus pluvialis	Astaxanthin	Reddish-salmon	Livestock additive E161j, antioxidant, salmon and trout farming (color, immune response)	65
	Canthaxanthin	Golden-orange	Food additive E161 g, salmonid farming; tanning pills	66
Chlorella vulgaris	(α-Tocopherol)	Brown	Vitamin E, food additive E306, E307, E308. Antioxidant in cosmetics and foods,	63
	Chlorophyll	Green	Pharmaceutical cosmetics	10
Porphyridium cruentum	Phycoerythrin	Red	Antiviral	67
Aphanizomenon	Phycocyanin	Blue-green	Food dyes (beverages, ice cream, sweets),cosmetics, histochemical fluorescent markers, antibody marks against receptors and other biological molecules	61

Carotenoids

Among the lipid components of the microalgae, some lipophilic components are especially important in health industry.[51] Because of easy growing, non-competitive food production processes, and adaptation to the changing environmental conditions which in turn results in the production of wide range of secondary metabolites, microalgae have recently generated a high level of interest for different natural sources of carotenoids.[51] Carotenoid biosynthesis can be induced by regulation of crop circumstances or genetic engineering approaches.[52] In microalgae, carotenoids appear to be mainly photo-protective and light-processing pigments. Carotenoids have high potential antioxidant properties, and hence protect the harmful effects of excessive UV solar radiation and oxidative stress by scavenging free radicals.[10, 53]

Several groups of carotenoids are found to be effective against more than 60 diseases that are life-threatening including cancers, cardiovascular problems, premature aging, and arthritis.[54] The microalgae *H.pluvialis* is the primary source of carotenoid (β-carotene). *Dunaliella* extract has been sold as dietary supplements in numerous places since 1980.[55] The highest level of 9-cis-beta-carotene is found in *Dunaliella* amongst all the natural sources. Healthcare and consumer industries prefer natural beta-carotenes from microalgae as they are better absorbed in living organisms by a combination of trans and cis isomers than the beta carotenes synthesized by chemical processes.[56] Fortification of beta-carotene in soft drinks, cheese, butter and margarine is becoming popular in recent times.In addition, most cyanobacteria are α- carotene generators.[56]

The carotenoids are proven to have anticancer actions through activation of cell apoptosis and suppression of cell proliferation. In particular, beta-carotenes such as astaxanthin, canthaxanthin, and zeaxanthin help to reduce the size and number of liver neoplasms.[57] Astaxanthin has benefited humans through improved eye protection, strength and endurance, and also by preventing premature aging, inflammation and UV-A damages.[58] Several positive effects of astaxanthin on vision, growth, immune function, reproduction, and regeneration have brought in the usage of this pigment in human nutrition and animal feed.[43] Astaxanthin was approved in 1987 as a food preservative for utilization in aquaculture.[59]

H. pluvialis is a green freshwater microalga that can produce significant amounts of astaxanthin under oxidative stress. Currently, several companies grow algae on a wide scale using different methods to produce cysts with enriched astaxanthin.Using various methods of extraction, the *H.pluvialis* can yield about 70–94% of astaxanthin which is a boon to promote blue economy.[60]

Natural pigments isolated from microalgae have been proven to have numerous health benefits and have been utilized in many industrial products.Chlorophyll and phycocyanin from *S. platensis*, α-tocopherol and chlorophyll from *C. vulgaris* as well as phycocyanin from *Aphanizomenon* are vastly applied in food, cosmetics and pharmaceutical sectors.[10,61,62,63] Besides, *D. salina* contains pigments like β-carotene, bixin, and lutein. They are mostly yellow to orange in colour and are used in food additives and cosmetics, and also for animal tissue pigmentation.[10,61,64] Other than that, the reddish and golden orange pigments of *H. pluvialis* such as astaxanthin and cantaxanthin are widely as livestock additive for salmon and trout farming to produce coloured fish with enhanced antioxidant and immune properties.[65,66] Further, the phycoerythrin derived from *P. cruentum* has proven to have antiviral properties to be utilized as a neutraceutical agent.[67]

Conclusion

Currently the industrialized microalgae are primarily used as food, food additives, aquaculture feed, dyes, cosmetics, pharmaceuticals, and nutraceuticals. For human usage, only a small fraction of the total number of algal organisms are cultivated. There exist possibly numerous species of microalgae that nature has bestowed with good nutritional values and health benefits which remain under explored for their potential usage. Therefore, in the forth coming years, the potential of microalgal use in food intake, nutritional supplements, energy production, and much more is likely to intensify. Geographical use of microalgae for human nutrition will offer economically manageable and naturally produced healthy food for sustainable supply of food to meet the demand of growing population of the world.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

1. Lordan S, Ross R.P., Stanton C. Marine Bioactives as Functional Food Ingredients: Potential to Reduce the Incidence of Chronic Diseases. *Mar Drugs.* 2011;9(6):1056-1100. doi:10.3390/md9061056
2. Plaza M, Herrero M, Cifuentes A, Ibáñez E. Innovative Natural Functional Ingredients from Microalgae. *J Agric Food Chem.* 2009;57(16):7159-7170. doi:10.1021/jf901070g
3. Batista A.P., Gouveia L, Bandarra N.M., Franco J.M., Raymundo A. Comparison of microalgal biomass profiles as novel functional ingredient for food products. *Algal Res*. 2013;2(2):164-173. doi:10.1016/j.algal.2013.01.004
4. Siró I, Kápolna E, Kápolna B, Lugasi A. Functional food. Product development, marketing and consumer acceptance—A review. *Appetite.* 2008;51(3):456-467. doi:10.1016/j.appet.2008.05.060
5. Singh S, Kate B.N., Banerjee U.C. Bioactive Compounds from Cyanobacteria and Microalgae: An Overview. *Crit Rev Biotechnol.* 2005;25(3):73-95. doi:10.1080/07388550500248498
6. Borowitzka M.A. High-value products from microalgae—their development and commercialisation. *J ApplPhycol.* 2013;25(3):743-756. doi:10.1007/s10811-013-9983-9
7. Wijffels R.H., Kruse O, Hellingwerf K.J. Potential of industrial biotechnology with cyanobacteria and eukaryotic microalgae. *CurrOpinBiotechnol.* 2013;24(3):405-413. doi:10.1016/j.copbio.2013.04.004
8. Günerken E, D'Hondt E, Eppink M, Garcia-Gonzalez L, Elst K, Wijffels R. Cell disruption for microalgae biorefineries. *Biotechnol Adv.* 2015;33(2):243-260. doi:10.1016/j.biotechadv.2015.01.008
9. Becker A.E. Introduction. *Int J Eat Disord.* 2013;46(5):507-507. doi:10.1002/eat.22125
10. Koller M, Muhr A, Braunegg G. Microalgae as versatile cellular factories for valued products. *Algal Res.* 2014;6:52-63. doi:10.1016/j.algal.2014.09.002
11. Plaza M, Herrero M, Cifuentes A, Ibáñez E. Innovative Natural Functional Ingredients from Microalgae. *J Agric Food Chem.* 2009;57(16):7159-7170. doi:10.1021/jf901070g
12. Gouveia L, Marques A.E., Sousa J.M., Moura P, Bandarra N.M. Microalgae – source of natural bioactive molecules as functional ingredients. *Food Sci Tech Bull Funct Foods*. 2010;7(2):21-37. doi:10.1616/1476-2137.15884
13. Draaisma R.B., Wijffels R.H., (Ellen) Slegers P, Brentner L, Roy A, Barbosa M.J. Food commodities from microalgae. *CurrOpinBiotechnol.* 2013;24(2):169-177. doi:10.1016/j.copbio.2012.09.012
14. Leaf A. Health Claims: Omega-3 Fatty Acids and Cardiovascular Disease. *Nutr Rev.* 2009;50(5):150-154. doi:10.1111/j.1753-4887.1992.tb01310.x
15. Mahaffey K.R., Clickner R.P., Jeffries R.A. Methylmercury and omega-3 fatty acids: Co-occurrence of dietary sources with emphasis on fish and shellfish. *Environ Res.* 2008;107(1):20-29. doi:10.1016/j.envres.2007.09.011
16. Qu L, Ji X, Ren L, Nie Z, Feng Y, Wu W, Ouyang P, Huang H. Enhancement of docosahexaenoic acid production by *Schizochytrium* sp. using a two-stage oxygen supply control strategy based on oxygen transfer coefficient. *Lett ApplMicrobiol.* 2010;52(1):22-27. doi:10.1111/j.1472-765x.2010.02960.x
17. Soletto D, Binaghi L, Lodi A, Carvalho J, Converti A. Batch and fed-batch cultivations of *Spirulina* platensis using ammonium sulphate and urea as nitrogen sources. *Aquaculture*. 2005;243(1-4):217-224. doi:10.1016/j.aquaculture.2004.10.005
18. Becker E. Micro-algae as a source of protein. *Biotechnol Adv.* 2007;25(2):207-210. doi:10.1016/j.biotechadv.2006.11.002
19. Karawita R, Senevirathne M, Athukorala Y, Affan A, Lee Y, Kim S, Lee J, Jeon Y. Protective Effect of Enzymatic Extracts from Microalgae Against DNA Damage Induced by

H2O2. *Mar Biotechnol.* 2007;9(4):479-490. doi:10.1007/s10126-007-9007-3

20. Sheih I, Fang T.J., Wu T, Lin P. Anticancer and Antioxidant Activities of the Peptide Fraction from Algae Protein Waste. *J Agric Food Chem.* 2010;58(2):1202-1207. doi:10.1021/jf903089m
21. Hwang H, Kim I, Nam T. Effect of a glycoprotein from Hizikia fusiformis on acetaminophen-induced liver injury. *Food ChemToxicol.* 2008;46(11):3475-3481. doi:10.1016/j.fct.2008.08.032
22. Fleurence J. Seaweed proteins. *Trends Food Sci Technol*. 1999;10(1):25-28. doi:10.1016/s0924-2244(99)00015-1
23. Bermejo Román R, Alvárez-Pez J, AciénFernández F, Molina Grima E. Recovery of pure B-phycoerythrin from the microalga *Porphyridiumcruentum*. *J Biotechnol.* 2002;93(1):73-85. doi:10.1016/s0168-1656(01)00385-6
24. Stadnichuk I.N., Tropin I.V. Phycobiliproteins: Structure, functions and biotechnological applications. *Appl Biochem Microbiol.* 2017;53(1):1-10. doi:10.1134/s0003683817010185
25. Cho S, Lee H, Yu C, Kim M, Seong E, Ghimire B.K, Son E, Choung M, Lim J. Isolation and Charaterization of Bioactive Peptides from Hwangtae (yellowish dried Alaska pollack) Protein Hydrolysate. *PrevNutr Food Sci.* 2008;13(3):196-203. doi:10.3746/jfn.2008.13.3.196
26. Arad S, Levy-Ontman O. Red microalgal cell-wall polysaccharides: biotechnological aspects. *Curr Opin Biotechnol.* 2010;21(3):358-364. doi:10.1016/j.copbio.2010.02.008
27. Sekharam K, Venkataraman L, Salimath P. Structural studies of a glucan isolated from blue-green alga *Spirulina* platensis. *Food Chem*. 1989;31(2):85-91. doi:10.1016/0308-8146(89)90019-8
28. Ho S, Chen C, Chang J. Effect of light intensity and nitrogen starvation on CO2 fixation and lipid/carbohydrate production of an indigenous microalga Scenedesmus obliquus CNW-N. *Bioresour Technol.* 2012;113:244-252. doi:10.1016/j.biortech.2011.11.133
29. Cheng Y, Zheng Y, Labavitch J.M., Vander Gheynst J.S. The impact of cell wall carbohydrate composition on the chitosan flocculation of *Chlorella*. *Process Biochem.* 2011;46(10):1927-1933. doi:10.1016/j.procbio.2011.06.021
30. Harun R, Danquah M.K., Forde G.M. Microalgal biomass as a fermentation feedstock for bioethanol production. *J Chem Technol Biotechnol.* 2009:n/a-n/a. doi:10.1002/jctb.2287
31. Mohamed Z.A. Polysaccharides as a protective response against microcystin-induced oxidative stress in *Chlorella vulgaris* and Scenedesmusquadricauda and their possible significance in the aquatic ecosystem. *Ecotoxicology.* 2008;17(6):504-516. doi:10.1007/s10646-008-0204-2
32. Tannin-Spitz T, Bergman M, van-Moppes D, Grossman S, Arad S. Antioxidant activity of the polysaccharide of the red microalga Porphyridium sp. *J ApplPhycol.* 2005;17(3):215-222. doi:10.1007/s10811-005-0679-7
33. Napolitano G.E., Ackman R.G., Ratnayake W.M.N. Fatty Acid Composition of Three Cultured Algal Species (*Isochvysisgalbana, Chaetocerosgracilis* and *Chaetoceroscalcitrans*) Used as Food for Bivalve Larvae. *J World Aquac Soc.* 1990;21(2):122-130. doi:10.1111/j.1749-7345.1990.tb00532.x
34. Raposo M.F.D.J., De Morais A.M.M.B. Microalgae for the prevention of cardiovascular disease and stroke. *Life Sci.* 2015;125:32-41. doi:10.1016/j.lfs.2014.09.018
35. Marinova E.M., Yanishlieva N.V.L. Inhibited Oxidation of Lipids III: On the Activity of Ascorbyl Palmitate during the Autoxidation of Two Types of Lipid Systems in the Presence of α-Tocopherol. *Fett Wiss Technol.* 1992;94(12):448-452. doi:10.1002/lipi.19920941203
36. Herrero M, Ibáñez E, Cifuentes A, Reglero G, Santoyo S. *Dunaliella*salina Microalga Pressurized Liquid Extracts as Potential Antimicrobials. *J Food Prot.* 2006;69(10):2471-2477. doi:10.4315/0362-028x-69.10.2471
37. Wu L, Ho J.A., Shieh M, Lu I. Antioxidant and Antiproliferative Activities of *Spirulina* and *Chlorella* Water Extracts. *J Agric Food Chem.* 2005;53(10):4207-4212. doi:10.1021/jf0479517

38. Gouveia L, Marques A.E., Sousa J.M., Moura P, Bandarra N.M. Microalgae – source of natural bioactive molecules as functional ingredients. *Food Sci Tech Bull Funct Foods.* 2010;7(2):21-37. doi:10.1616/1476-2137.15884
39. Koyande A.K., Chew K.W., Rambabu K, Tao Y, Chu D, Show P. Microalgae: A potential alternative to health supplementation for humans. *Food Sci Hum Wellness.* 2019;8(1):16-24. doi:10.1016/j.fshw.2019.03.001
40. De Jesus Raposo M.F., De Morais R.M.S.C., De Morais A.M.M.B. *Health applications of bioactive compounds from marine microalgae. Life Sci.* 2013;93(15):479-486. doi:10.1016/j.lfs.2013.08.002
41. Andrade L.M. *Chlorella* and *Spirulina* Microalgae as Sources of Functional Foods, Nutraceuticals, and Food Supplements; an Overview. *MOJ Food Process Technol.* 2018;6(1). doi:10.15406/mojfpt.2018.06.00144
42. Darvish M, Jalili H, Ranaei-Siadat S, Sedighi M. Potential Cytotoxic Effects of Peptide Fractions from *Dunaliella*salina Protein Hydrolyzed by Gastric Proteases. *J Aquat Food Prod Technol.* 2017;27(2):165-175. do i:10.1080/10498850.2017.1414095
43. Matos J, Cardoso C, Bandarra N.M., Afonso C. Microalgae as healthy ingredients for functional food: a review. *Food Funct.* 2017;8(8):2672-2685. doi:10.1039/c7fo00409e
44. M. Bishop W, M. Zubeck H. Evaluation of Microalgae for use as Nutraceuticals and Nutritional Supplements. *J Nutr Food Sci*. 2012;02(05). doi:10.4172/2155-9600.1000147
45. Nuzzo D, Presti G, Picone P et al. Effects of the *Aphanizomenon*flos-aquae Extract (Klamin®) on a Neurodegeneration Cellular Model. *Oxid Med Cell Longev.* 2018;2018:1-14. doi:10.1155/2018/9089016
46. Cohen Z, Heimer Y. Production of Polyunsaturated Fatty Acids (EPA, ARA and GLA) by the Microalgae Porphyridium and *Spirulina*. *Industrial Applications of Single Cell Oils*. 1992. doi:10.1201/9781439821855.ch14
47. Antia N.J., Desai I.D., Romilly M.J. The tocopherol, vitamin K, and related isoprenoid quinone composition of a unicellular red alga (*Porphyridiumcruentum*)1. *J Phycol*. 1970;6(3):305-312. doi:10.1111/j.1529-8817.1970.tb02398.x
48. Gaignard C, Gargouch N, Dubessay P, Delattre C, Pierre G, Laroche C, Fendri I, Abdelkafi S, Michaud P. New horizons in culture and valorization of red microalgae. *Biotechnol Adv.* 2019;37(1):193-222. doi:10.1016/j.biotechadv.2018.11.014
49. Christaki E, Bonos E, Florou-Paneri P. Innovative Microalgae Pigments as Functional Ingredients in Nutrition. *Handbook of Marine Microalgae*. 2015:233-243. doi:10.1016/b978-0-12-800776-1.00014-5
50. D'Alessandro E.B., AntoniosiFilho N.R. Concepts and studies on lipid and pigments of microalgae: A review. *Renew Sustain Energy Rev.* 2016;58:832-841. doi:10.1016/j.rser.2015.12.162
51. Ahmed F, Fanning K, Netzel M, Turner W, Li Y, Schenk P.M. Profiling of carotenoids and antioxidant capacity of microalgae from subtropical coastal and brackish waters. *Food Chem.* 2014;165:300-306. doi:10.1016/j.*foodchem*.2014.05.107
52. Gouveia L, Marques A.E., Sousa J.M., Moura P, Bandarra N.M. Microalgae – source of natural bioactive molecules as functional ingredients. *Food Sci Tech Bull Funct Foods.* 2010;7(2):21-37. doi:10.1616/1476-2137.15884
53. Hamed I, Özogul F, Özogul Y, Regenstein J.M. Marine Bioactive Compounds and Their Health Benefits: A Review. *Compr Rev Food Sci Food Saf.* 2015;14(4):446-465. doi:10.1111/1541-4337.12136
54. Prasanna R, Sood A, Jaiswal P et al. Rediscovering cyanobacteria as valuable sources of bioactive compounds (Review). *ApplBiochemMicrobiol.* 2010;46(2):119-134. doi:10.1134/s0003683810020018
55. Mogedas B, Casal C, Forján E, Vílchez C. β-Carotene production enhancement by UV-A radiation in *Dunaliella*bardawil cultivated in laboratory reactors. *J BiosciBioeng.* 2009;108(1):47-51. doi:10.1016/j.jbiosc.2009.02.022
56. Tavani A, Braga C, La Vecchia C, Negri E, Russo A, Franceschi S. Attributable risks for

breast cancer in Italy: Education, family history and reproductive and hormonal factors. *Int J Cancer.* 1997;70(2):159-163. doi:10.1002/(sici)1097-0215(19970117)70:2<159::aid-ijc4>3.0.co;2-w

57. Sathasivam R, Ki J. A Review of the Biological Activities of Microalgal Carotenoids and Their Potential Use in Healthcare and Cosmetic Industries. *Mar Drugs.* 2018;16(1):26. doi:10.3390/md16010026
58. Gong M, Bassi A. Carotenoids from microalgae: A review of recent developments. *Biotechnol Adv.* 2016;34(8):1396-1412. doi:10.1016/j.biotechadv.2016.10.005
59. Dufossé L, Galaup P, Yaron A, Arad S.M, Blanc P, Chidambara Murthy K.N., Ravishankar G.A. Microorganisms and microalgae as sources of pigments for food use: a scientific oddity or an industrial reality?. *Trends Food Sci Technol.* 2005;16(9):389-406. doi:10.1016/j.tifs.2005.02.006
60. Milledge J.J. Commercial application of microalgae other than as biofuels: a brief review. *Rev Environ Sci and Biotechnol.* 2010;10(1):31-41. doi:10.1007/s11157-010-9214-7
61. Henrikson M. Work-Life Balance: Is There Such a Thing?. *NursWomens Health.* 2009;13(2):151-154. doi:10.1111/j.1751-486x.2009.01406.x
62. Liang S.X.T., Wong L.S., Dhanapal A.C.T.A., Balu P, Djearamane S. Therapeutic applications of *Spirulina* against human pathogenic viruses. *J ExpBiolAgric Sci.* 2021;9(Spl-1- GCSGD_2020):S38-S42. doi:10.18006/2021.9(spl-1-gcsgd_2020).s38.s42
63. Uquiche E, Antilaf I, Millao S. Enhancement of pigment extraction from B. brauniipretreated using CO 2 rapid depressurization. *Braz J of Microbiol*. 2016;47(2):497-505. doi:10.1016/j.bjm.2016.01.020
64. Nwachuku L.A. Slavery, institution of. *The Encyclopedia of Empire.* 2016:1-13. doi:10.1002/9781118455074.wbeoe296
65. Panis G, Carreon J.R. Commercial astaxanthin production derived by green alga Haematococcuspluvialis : A microalgae process model and a techno-economic assessment all through production line. *Algal Res.* 2016;18:175-190. doi:10.1016/j.algal.2016.06.007
66. Pulz O, Gross W. Valuable products from biotechnology of microalgae. *ApplMicrobiolBiotechnol.* 2004;65(6):635-648. doi:10.1007/s00253-004-1647-x
67. Mahendran M.S., Djearamane S, Wong L.S., Kasivelu G, Dhanapal A.C.T.A. Antiviral properties of microalgae and cyanobacteria. *J ExpBiolAgric Sci*. 2021;9(Spl-1- GCSGD_2020):S43-S48. doi:10.18006/2021.9(spl-1-gcsgd_2020).s43.s48