Chapter

Revisiting Microalgae as an Additive for Nutraceuticals: A Review

Kausthubh Sumanth, Sanjana Subramanya, Sourav Umashankar, Supriya Gummalam, Rajeswari Mallikarjunaiah, Ashwani Sharma and Nagashree Nagaraj Rao

Abstract

In order to meet the ever-growing global demands for food, healthcare, and energy, among other sources, the twenty-first century has seen a significant surge in the use of microalgae. They have seen applications in varied industries ranging from pharmaceuticals to energy to even the food industry, where its role as a source of proteins shines the most among other bioactive compounds. The microalgal biomass has the innate ability to grow in varied ecological conditions and has diverse compositions. While not economically competitive with fossil fuels or other renewable energy sources such as solar and wind, microalgal sources are technically viable, and a multitude of resources and time have been poured into the research of microalgal renewable fuels (biodiesel, ethanol, hydrogen, etc.). The rich diversity of microalgae, which is still underutilized, provides a variety of physiologically active metabolites of economic importance. These bioactive metabolites have antioxidant, antibacterial, antifungal, antiviral, anti-inflammatory, and anticancer properties. The microalgal biomass is a rich source of various compounds such as fatty acids, carotenoids, polysterols, and phenolics that can be utilized to synthesize pharmaceutical compounds and other nutraceuticals. Considering microalgae as a superfood, space food, functional food, strong agent for detoxification with high content of micro and macronutrients has found potential application in occupational, systematic, and life style disorders subsequently enhancing immunity. The path from algal research to the launching of new food products or dietary supplements is strongly affected by industrial, regulatory, and nutritional considerations. Our purpose is to review and assess what is known about different food components (i.e., proteins, polysaccharides, lipids, vitamins, minerals, and antioxidants, potential toxicants) in the context of improving knowledge about the efficacy of algal foods as nutraceuticals. This review will add be an asset for food, pharma, nutra, and cosmetic sector.

Keywords: microalgae, nutraceutical, bioactive, food, immunity

1. Introduction

1.1 Microalgae

Microalgae have a vast biodiversity and are an almost unexplored resource. Microalgae, also known as microphytes, are minute, microscopic algae that cannot be seen with the human eye. They are phytoplankton that live in both the water column and the sediment and can be found in both freshwater and marine systems [1]. Microalgae and bacteria form the foundation of the food web, providing energy to all trophic levels above them. Chlorophyll a concentrations are frequently used to quantify microalgae biomass, and they can be a good indicator of prospective production [2]. They are unicellular organisms that live individually, in chains, or in groups. Their diameters can range from a few micrometers to a few hundred micrometers depending on the species. Microalgae, unlike higher plants, lack roots, stems, and leaves. They've evolved to thrive in an environment dominated by viscous forces.

It is estimated that there are between 200,000 and 800,000 species in various genera, with roughly 50,000 species described [3]. Chemically, over 15,000 new chemicals derived from algal biomass have been identified [4]. Carotenoids, antioxidants, fatty acids, enzymes, polymers, peptides, toxins, and sterols are some examples [5]. Microalgae, capable of performing photosynthesis, are important for life on earth; they produce approximately half of the atmospheric oxygen [6] and develop photoautotrophically while using carbon dioxide as a greenhouse gas. Microalgae and cyanobacteria, collectively known as phytoplankton, dominate photosynthesis in the ocean [7]. Microalgae chemical composition is not a continuous factor; it fluctuates depending on a variety of circumstances, including species and growth conditions. Some microalgae have the ability to adapt to changes in environmental conditions by changing their chemical composition in response to variation in the environment. Their ability to substitute phospholipids with non-phosphorus membrane lipids in phosphorus-depleted settings is a particularly striking example [8]. Changing environmental parameters such as temperature, illumination, pH, CO_2 supply, and nutrients can help microalgae collect desired products to a great amount [9–20].

1.2 Major classification of microalgae

Chlorophyta: The phylum's members can be found in freshwater, marine, or even terrestrial habitats. It includes unicellular and multicellular organisms with chlorophylls a and b in a single chloroplast surrounded by two envelope membranes. Unicellular representatives of the phylum Chlorophyta, such as *Chlorella vulgaris*, *Dunaliella salina*, and *Haematococcus pluvialis*, are used in commercial manufacturing today and *Parietochloris incisa* and *Botryococcus braunii* have the ability to produce lipids and hydrocarbons respectively.

Rhodophyta: The phylum Rhodophyta is mostly made up of marine multicellular species, with a few freshwater or unicellular species thrown in for good measure. A huge single chloroplast is encircled by two envelope membranes with a single central pyrenoid, and cells are spherical with an eccentric nucleus. The brown-to-olive-colored unicells are coccoid, nonmotile, and have a single pyrenoid-containing chloroplast, and the mucilaginous sheath can be thickened unilaterally.

Haptophyta: Haptophyta algae are mostly marine and unicellular or colonial, while several freshwater species have been discovered. The two most well-known Haptophyta species utilised as feed microalgae in aquaculture are *Isochrysis* aff.

galbana (T-ISO) and *Pavlova salina*. All haptophytes have one or more pyrenoid-containing chloroplasts and an antapical nucleus, with the nuclear envelope connected to the chloroplast ER and a peripheral ER beneath the plasma membrane.

Dinophyta: Members of the phylum Dinophyta are unicellular and mostly marine, with a few freshwater species. Only around half of the Dinophyta are photosynthetic, with the remaining 50% being heterotrophs lacking chloroplasts. It is a marine, heterotrophic, colourless dinoflagellate with dinokont flagellation, in which the transverse flagellum is encircled by a medial encircling cingulum that is displaced and drops downhill [21].

1.3 Nutraceuticals

A nutraceutical, often known as a "bioceutical," is a pharmaceutical substitute that claims to have physiological benefits [22, 23]. A product that provides nutritional values as well as pharmaceutical values was coined as *nutraceutical* by Dr. Stephen DeFelic in 1989. There have been many definitions for this uprising term. The American

Cyanobacteria or blue-green algae
Gram-negative bacteria which can survive at some of the harshest habitats on earth. Some of them are known to be able to do nitrogen fixation along with carbon fixation both of which are essential for life on earth.
Prochlorococcus, Spirulina, Nostoc, Cyanothece, Anabaena

Glaucocytophytes
Uncommon unicellular eukaryotic algae that contain plastid which is structurally similar to cyanobacteria. Glaucocystophytes are one of the descendants of the product of early endosymbiosis.
Cyanophora, Glaucocystis, Peliaina, Gloeochaete

Rhodophytes or red algae
Mostly multicellular photosynthetic eukaryotes. They are characterized by their distinctive red color due to the presence of red pigments such as phycobilisomes in their chloroplast.
Batrachospermum, Chroodactylon, Compsopogon

Charophytes
Terrestrial and freshwater algae. They are notably having similar features as terrestrial plants, suggesting that the ancestors of charophytes gave rise to land plants.
Coleochaete, Micrasterias, Chara, Penium, Klebsormidium

Chlorophytes Chlorophytes or green algae
Photosynthetic eukaryotes which contain chlorophylls as their main photosynthetic pigments.
Haematococcus, Chlorella, Dunaliella, Graesiella, Scenedesmus

Euglenoids
Unicellular flagellated eukaryotes which exhibit both animal- and plant-like characteristics. Most Euglenoids are freshwater species while some are marine species.
Euglena, Discoplastis, Phacus, Colacium, Strombomonas

Dinoflagellates
Unicellular protists and are characterized by their relatively large nuclei, golden-brown-colored plastid and its unique method of swimming.
Gymnodinium, Karenia, Dinophysis, Alexandrium

Haptophytes
Unicellular photosynthetic microalgae with its chloroplast originated from the endosymbiosis of red algae. It usually has 2 equal or unequal flagella which allow it to be motile.
Chrysochromulina, Prymnesium, Pavlova, Diacronema

Cryptophytes
Motile, and photosynthetic unicellular organisms characterized by the presence of 2 flagella and are typically found in freshwater and marine habitat.
Guillardia, Campylomonas, Geminigera, Rhodomonas, Teleaulax

CLASSES OF ALGAE AND THEIR RESPECTIVE CHARACTERISTICS AND EXAMPLES [21]

Nutraceutical Association has defined the term as follows: "A nutraceutical is any substance conceived as a food, or part of a food which provides medical or health benefits, as well as the prevention and treatment of a disease" while according to the US Institute of Medicine, nutraceuticals include "any substance that is a food or part of a food which provides medicinal or health benefits including the prevention and treatment of disease, beyond the traditional nutrients it contains." Nutraceuticals, in general, have a favorable impact in improving customers' health and wellness. Therefore, health-promoting substances generated from food or food items to aid in the prevention or treatment of disease and/or dysfunction have also been considered as nutraceuticals.

2. Nutraceuticals from microalgae

2.1 Role of microalgae

Microalgae have been making its waves in the scientific community over the last few decades for the multitude of derivatives that can be obtained from them and the potential they hold in a vast number of fields. Microalgae have a massive biodiversity and are an essentially unexplored resource. It is believed that there are between 200,000 and 800,000 species in various genera, with approximately 50,000 species described [4]. Over 15,000 new chemicals derived from algal biomass have been chemically identified [5]. The various types of products include carotenoids, antioxidants, fatty acids, enzymes, polymers, peptides, toxins, sterols, etc. [6].

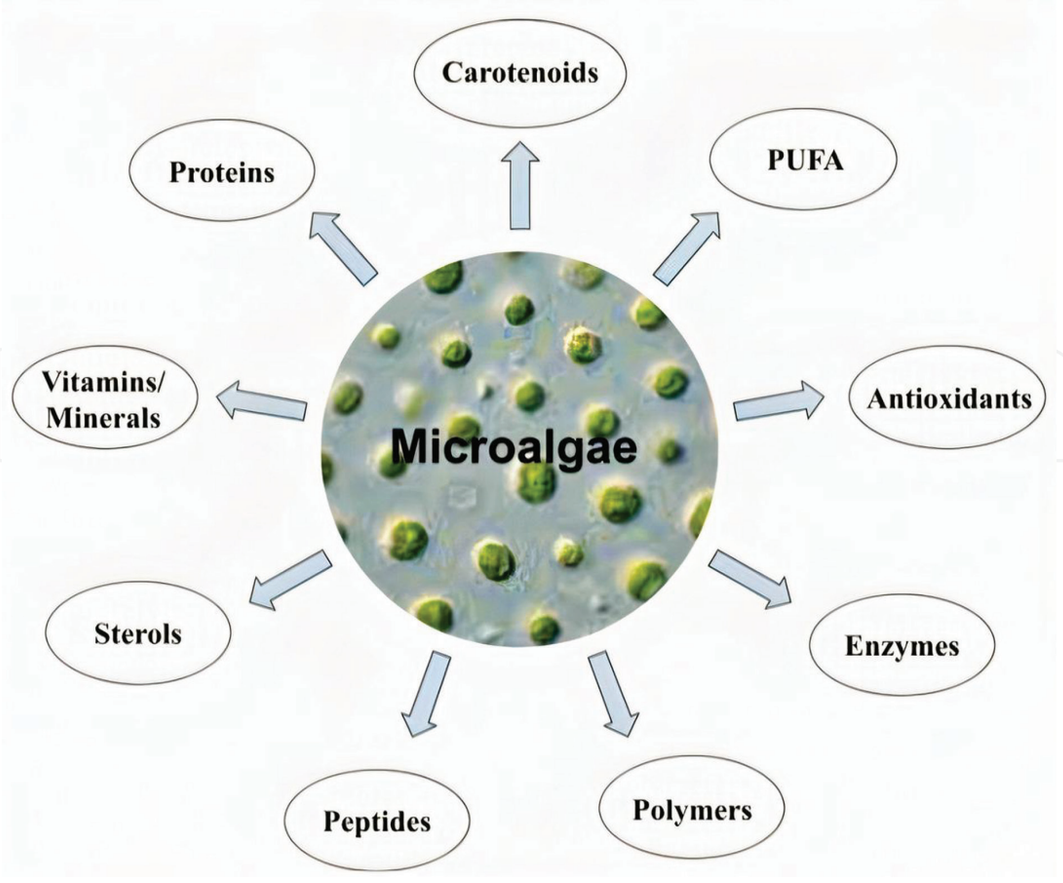

Figure 1.
An overview of nutraceuticals used from microalgae.

2.2 Microalgae and nutraceuticals

The market for nutraceuticals extracted from microalgae is dominated, if not composed majorly of products from around four species of microalgae—*Spirulina, Chlorella, Haematococcus,* and *Dunaliella*. Other species that are involved in nutraceutical production include *Odontella aurita, Schizochytrium sp, Phaeodactylum,* etc.

There are numerous essential compounds of interest (as show in **Figure 1**) that are and can be produced by means of these microalgae. These compounds are then further used for production of their respective functional and nutraceutical feed. Some of the important nutrients include

- Long-Chain Polyunsaturated Fatty Acids (PUFAs) – Arachidonic acid (AA), Eicosapentaenoic acid (EPA), etc.
    - These are defined as fatty acids with more than 18 carbon atoms and at least one double bond in their chemical structures. These can be synthesized as food supplements and are essential nutrients for humans and animals that are not produced internally. They have been recorded to have antimicrobial, anti-inflammatory, antioxidant properties.
- Pigments/Carotenoids – β-Carotene, Astaxanthin, etc.
    - Carotenoids and other pigment groups such as phycobilins are the most industrially produced algal pigments. Carotenoids are known to be strong antioxidants and to provide photoprotection to cells. Lately these algal carotenoids have been shown to have anticancer properties as well.
- Phenolic Compounds – Caffeic acid, *p*-coumaric acid, etc.
    - Phenolic compounds are one of the most significant types of natural antioxidants that may be used as dietary supplements. These molecules are primarily engaged in the defense against biotic stimuli and stress, such as grazing and UV radiation, bacteria colonization, or other fouling organisms, or metal contamination.
- Proteins/Amino Acids/Peptides – Lysine, Isoleucine, Tryptophan, etc.
    - Proteins being one of the major constituents of microalgae are now being studied as viable alternative protein sources. These compounds have been found to have hepatoprotective, anti-inflammatory, immunomodulating, anticancer, and antioxidant properties.
- Vitamins – Vitamin C, E, Riboflavin (B2), Pyridoxine (B6), etc.
    - Microalgae have shown good capability to produce important vitamins. *Spirulina* and *Chlorella* have been observed to produce quality bioavailable vitamin B12.
- Minerals – Zinc, Phosphorus, Potassium, etc.
    - Microalgae have the ability to accumulate trace elements and can be consumed as a daily nutritional supplement for minerals. Minerals provide significant

functions and are either incorporated into compounds or stay in their elemental state.

- Polysaccharides – Extracellular polysaccharides, sulfated polysaccharides, etc.
  - Microalgal polysaccharides have been reported to be rather complex polysaccharides such as immulina and other compounds that contain sugars such as galactose, xylose, fucose, etc.
- Sterols – Phytosterol, Poriferasterol, clionasterol, etc.
  - While sterols play a fundamental role in microalgae physiology, particularly with respect to their membrane integrity, they have gained popularity for their potential to lower LDL cholesterol and boost cardiovascular health.

Furthermore, sterols have been linked to anti-inflammatory and anti-atherogenicity, anticancer, and anti-oxidation actions, as well as protection against nervous system illnesses such as autoimmune encephalomyelitis, amyotrophic lateral sclerosis, and Alzheimer's disease.

2.3 Important microalgal species

2.3.1 Spirulina

Spirulina (classified as *Arthrospira sp*) is a prokaryotic cyanobacterium that has been commercially produced for over 30 years for a variety of applications such as fish food, vitamin supplements, aquaculture, medicines, and nutraceuticals. *Spirulina*, by means of photosynthesis, converts sunlight into a lot of life essential nutrients (Fatty Acids, Carbohydrates, proteins, etc.). It is often regarded as a superfood and is widely farmed to fulfill current demand, particularly in specially built raceway ponds and photobioreactors.

Spirulina is one of the algae being researched for large-scale commercial cultivation. *Spirulina* has 60–70% protein by weight (containing several amino acids) and up to 10 times more beta-carotene per unit mass than carrots. *Spirulina* is high in B vitamins, phycocyanin, chlorophyll, vitamin E, omega-6 fatty acids, and minerals.

2.3.2 Chlorella

Chlorella is a photoautotrophic, single-cell, spherical (2–10 m in diameter) green microalga with no flagella. It is simple to cultivate and produces massive amounts of biomass in a short period of time. It grows quickly and requires just CO2, water, sunshine, and a minimal quantity of minerals to thrive. They contain about 11–58% protein, 12–28% carbohydrate, and 2–46% lipids of its dry weight. Other composites include β-carotene, inositol, vitamin B6, vitamin B12, etc. *Chlorella* has been observed to lower cholesterol levels, decrease blood pressure, and even enhance the immune system.

2.3.3 Haematococcus

Haematococcus pluvialis (*H. pluvialis*) is a unicellular freshwater green microalgae that is most known for being the major producer of Astaxanthin, a red pigment that has shown innovative anti-inflammatory and antioxidant applications in human

nutrition. It has also been recently observed to have preventive powers for diabetes and certain neurodegenerative diseases. The Astaxanthin levels of *H. pluvialis* are around 1.5–3% of its dry weight making it the largest known natural source of the same.

2.3.4 Dunaliella

Dunaliella is a green unicellular algae that has been observed to contain large quantities of β-carotene, protein, and glycerol. *Dunaliella* has the ability to grow in a relatively vast array of conditions and does not need specific waters for its cultivation. The extraction of the nutritional compounds can take place through its thin cell wall. It is known for the production of many carotenoid pigments, and these pigments are potent free-radical scavengers that have shown to reduce levels of enzyme inactivation and lipid peroxidation.

2.4 Therapeutic applications of microalgal nutraceutical substances

Microalgae are known for being a fantastic source of protein, which enables it to meet the ever-growing demands of a growing population. Microalgae-derived protein products exhibit a high concentration of protein with complete essential amino acid profiles. Other than proteins, microalgae are known to contain crucial vitamins such as A, B12, C, D, E and minerals such as iron, calcium, potassium, and more. Foods derived from common microalgae species *Chlorella sp.* and *Spirulina platensis* are known for their high protein content and nutritional value and are available in form of capsules, powders, and liquids. These have great abilities to combat various types of diseases due to their antimicrobial, anti-inflammatory, anticancer, and immunosuppressive properties [24].

Generation of reactive oxygen species induced by prooxidants leads to oxidative stress and is a cause of swelling and lysis of mitochondria and mutagenic actions. They accelerate the aging process and contribute to various threatening chronic and degenerative diseases such as diabetes mellitus, rheumatoid arthritis, and cancer. Enzymatic and nonenzymatic antioxidants from microalgae have the capability to quench free radicals and have high radical scavenging activities [25]. The antimicrobial properties of microalgae-based food products are mainly due to its lipid composition. Fatty acids affect the membranes of microbes resulting in the damage of internal constituents. This has a direct impact on the cells' metabolism [26].

Monounsaturated and polyunsaturated fatty acids (PUFAs) in microalgae derived food products also contribute to their antibacterial properties. Microalgal fatty acids intrusively interfere with bacterial mechanisms and can result in fatal effects such as cell leakage, reduced uptake of nutrients and inhibition of cellular respiration. Antiviral and antifungal properties of microalgae food products are attributed to polysaccharides and lipid fractions respectively [27]. High concentrations of polyphenols, polysaccharides, and phycobiliproteins in microalgae-derived nutraceuticals are the reason for their exhibition of anticancer properties due to their abilities to induce apoptosis in tumor cells [28]. The biological response due to diverse factors such as pathogens, allergens, irritants is termed as inflammation, and this is mainly observed in damaged or infected cells and tissues [29]. Chronic inflammation can directly contribute to chronic illnesses such as diabetes, cardiovascular and neurodegenerative disorders, and several inflammatory responses are a direct consequence of oxidative stress. Anti-inflammatory compounds such as carotenoids produced by microalgae reinvigorate the body's immunity and accelerate healing [27].

Despite the obvious benefits, due to lack of awareness, microalgae are underexploited as a potential food source. There are a plethora of microalgal species that have the ability to produce therapeutic bioactive compounds with their respective functional properties, which are impacted by the varying biotic and abiotic stresses [27].

Carotenoids produced by microalgae have excellent therapeutic effects on humans due to their antioxidant properties, thus yielding protection against oxidative and free radical stresses [24].

They play a significant role in the inhibition of oxidative injury to cells and tissues. Two of the industrially important carotenoids include β-carotene and astaxanthin. The 9-cis-isomer of β-carotene has been observed to possibly prevent the advancement of artherosclerosis in humans. Studies have also evaluated the positive effects of β-carotene in cardiovascular health. Other than its addition in multivitamin tablets, β-carotene can also be used in food products such as cheese and butter. Astaxanthin is another important carotenoid that is known for its exceptional antioxidant properties. It has been proved to reduce oxidative stress and inflammation and aids in improving the immune system to combat cardiovascular diseases [27].

Another valuable bioactive compound extracted from the microalgal biomass is chlorophyll, which possesses powerful antioxidant and antimutagenic properties. Studies have demonstrated its wound healing properties and stimulation of tissue growth. Due to its facilitation of rapid oxygen and carbon dioxide interchange, it is used in the treatment of oral sepsis and ulcers. By trapping mutagens in the gastrointestinal tract, chlorophyll contributes to prevention of cancer [30]. Chlorophyll also consists of a component called chlorophyllin, which has the ability to target multiple carcinogen pathways and invade their cell cycle [24]. Despite the various benefits, utilization of chlorophyll for dietary needs has disadvantages of its own. Apart from being an expensive natural food dye, it is also unstable to changes in pH conditions, and to ensure its stability, it has to undergo chemical modification [30].

Carbohydrates from microalgae are in the form of reducing sugars such as sucrose, lactose, fructose, and polysaccharides. Despite limited food applications, microalgal polysaccharides have garnered attention due to their nontoxicity and biocompatibility [31]. They boost the immune system functionality and have the ability to block tumorigenesis. Polysaccharides such as immulina and immurella demonstrate great anticancer properties while β-1,3 glucan from *Chlorella* species alleviates gastric ulcers and atherosclerosis [27].

Most microalgae consist of polar lipids such as phospholipids and galactolipids in the exponential growth phase and then tend to accumulate triacylglycerols under stressful conditions [31]. In general, microalgae are rich in poly monounsaturated fatty acids, which play crucial roles in cellular metabolism, balancing of membrane fluidity and electron-oxygen transport. External administration of lipids is important for humans due to the lack of ability of synthesizing lipids for the maintenance of homoeostasis. Poly monounsaturated fatty acids have also been proven to decrease the prevalence of various chronic diseases and have demonstrated health benefits with respect to the nervous system [27]. Microalgal fatty acids have also shown therapeutic effects against inflammation and numerous cardiovascular diseases such as myocardial infarction and cardiac arrhythmia. Docosahexaenoic acid (DHA) shows excellent cardiovascular and nervous system benefits and is therefore used as a nutritional supplement in infant formula [32]. Species of microalgae such as *Cryptothecodininum cohnii* are cultivated in fermenters for the mass production of DHA [31].

Microalgal protein extraction has a lot of benefits regarding enhanced nutritional value, productivity, and efficiency [33]. Phycobiliproteins are hydrophilic complexes used in popsicles, gum, soft drinks, and dairy products. These pigments are found

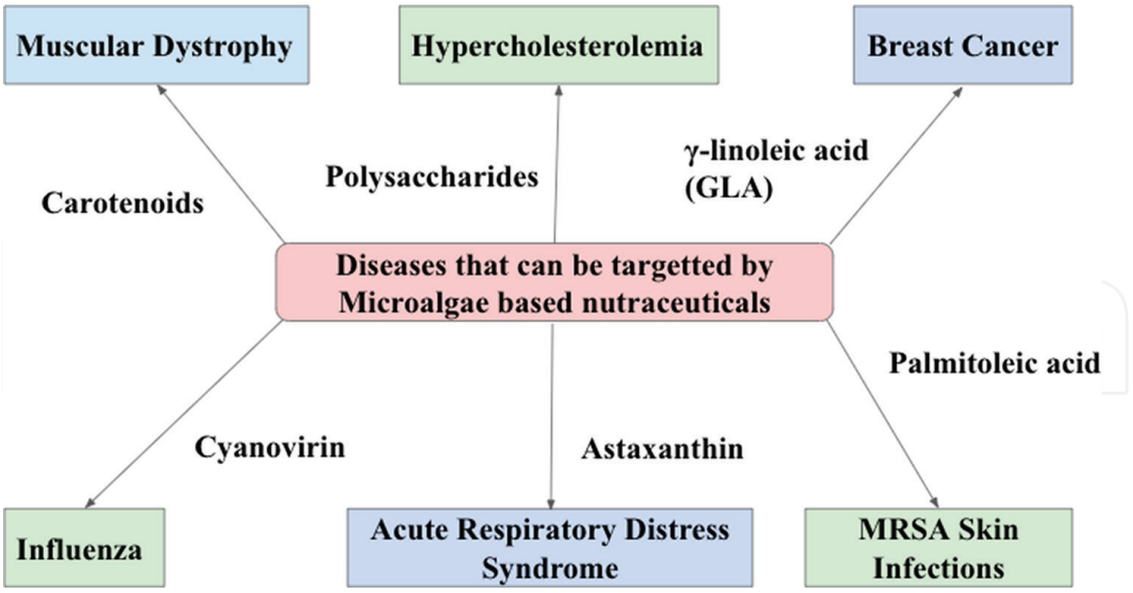

Figure 2.
This figure summarizes some of the various diseases that can be targeted by bioactive compounds derived from microalgae based food products [27, 35].

majorly in Cyanobacteria and have innate wound healing, antiviral, antioxidative properties and can act as neuroprotective agents. It also has the ability to function as an immunotoxin against B-cell lymphoma and also has an enhanced resistance to UV-induced stress [24, 27].

Microalgal species contain a plethora of vitamins (e.g., Pro-Vitamin A, Vitamin B12, Vitamin C, Vitamin D, Vitamin E), which are used as food supplements and are proven to help detoxify, revitalize cells and are involved in the activation of the immune system. The precursor of Vitamin A produced by microalgae has been seen to hinder the development of tumors in various types of cancers such as bladder, lung, and skin cancers. Cobalamin (Vitamin B12) has been demonstrated to aid in DNA repair, whereas ascorbic acid acts as an immunomodulatory agent for the prevention of severe diseases. Through the blockage of cell cycle progression, Vitamin D has demonstrated anticancer properties. Tocopherols and tocotrienols (Vitamin E) meanwhile have shown beneficial effects against atherosclerosis and pancreatic cancer [27, 34].

Microalgae consist of high levels of sterols and are components of the cellular membrane. The sterol composition is directly impacted by algal strain and the external conditions they are subjected to. Microalgae-derived sterols have been reported to demonstrate good anticancer, antioxidant, and anti-inflammatory properties. These have also been utilized as supplements for lowering cholesterol levels leading to the decrease in cardiovascular disease risks [27]. **Figure 2** summarizes some of the various diseases that can be targeted by bioactive compounds derived from microalgae based food products.

2.5 Challenges and future prospects

Despite the discovery of several compounds of high biological value and health benefits, microalgae continue to remain one of the most sparsely explored groups of organisms with an overwhelming majority of microalgal compounds yet to be isolated and identified. Although several thousand species of microalgae are believed to exist, only a small handful of these are currently cultivated and used for industrial applications.

This dearth of information calls for intensive research in the field of microalgal bioprospecting. These developments, however, give rise to a new set of challenges.

While the nutritional content of a few microalgal species has been thoroughly researched upon, their palatability, digestibility, and nutritional value ultimately depend upon the genetic makeup of the individual strains used, as well as the processes involved in large-scale biomass production. A major constraint in the use of large amounts of microalgae for human nutrition is the presence of excessive quantities of nucleic acids, which when metabolized in the human body to form urea may prove deleterious to human health. Microalgal cultivation strategies in the past include the use of natural lagoons or artificial ponds. While these open air systems are relatively economical, they suffer from a number of challenges including frequently varying climatic conditions, the prevalence of non-axenic cultures, etc. To combat these issues, the recent years have seen a rise in the use of closed systems. However, major constraints encountered with the use of closed culturing systems are the lack of inexpensive equipment and the inefficient use of light, both of which make scale-up problematic. Despite these challenges, closed reactors are promising candidates for the production of high-value nutraceuticals by microalgae including their production by recombinant technologies. Food safety is a highly pertinent matter in microalgal technology, particularly when open air systems are involved, and these products are thoroughly scrutinized by regulatory bodies in developed countries to determine their safety and efficacy prior to human consumption.

Despite being rich sources of proteins, microalgal foods and nutraceuticals have failed to carve a market niche for themselves due to the unpleasant odors and tastes associated with them, and better marketing strategies need to be developed to attract a larger consumer base There are also several considerations involving the specific doses to be prescribed to consumers. Proper labeling and marketing must be ensured to specify the quantities of all the ingredients, including details on allergenics and side effects.

Another key area of future research is the whole-genome sequencing of microalgal species producing high quantities of nutraceuticals to better understand the genes, enzymes, and metabolic pathways involved in nutraceutical production as well as the

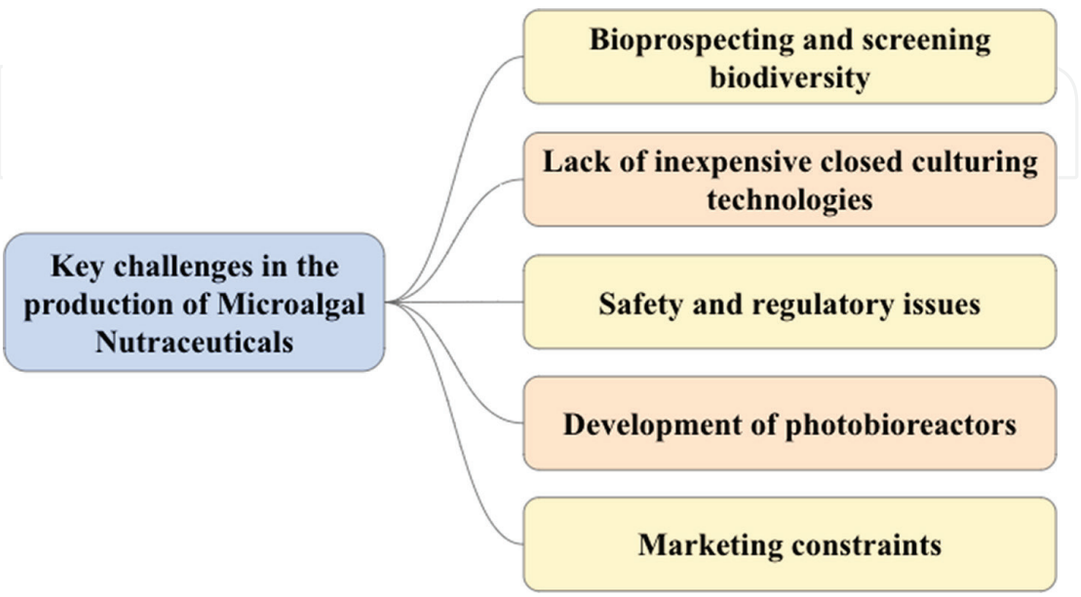

Figure 3.
Depicts challenges faced during microalgal nutraceuticals production.

mechanisms involved in the upregulation/downregulation of these genes and pathways. The development of engineered microalgae to boost protein expression, metabolism, photosynthesis, etc., is integral to large-scale production in the future. **Figure 3** depicts challenges faced during microalgal nutraceuticals production.

3. Conclusion

Microalgae have been used since time immemorial to provide food to humans and animals, but their nutritional largess has only been exploited very recently to provide high-value products on an industrial scale. Microalgae are currently used for pharmaceuticals, cosmetics, food and food additives, therapeutics, etc. While the effects of microalgae and their nutraceutical products have been tested worldwide to positive results, further health benefits are likely to be discovered with more intensive research. Advances in bioprospecting are required to further isolate and characterize microalgal compounds as they remain among the least explored groups of organisms on the planet. Other key areas of research include the development of efficient and economical microalgal cultivation technologies, metabolic engineering, genomics, and synthetic biology. Increased research and development will no doubt enable greater production as well as the identification and characterization of more microalgal species and continued investigation into their benefits for human health and nutrition.

Author details

Kausthubh Sumanth, Sanjana Subramanya, Sourav Umashankar,
Supriya Gummalam, Rajeswari Mallikarjunaiah, Ashwani Sharma
and Nagashree Nagaraj Rao*
Department of Biotechnology, R.V. College of Engineering, Bengaluru, Karnataka, India

*Address all correspondence to: nagashreenao@rvce.edu.in

References

[1] Thurman HV. Introductory Oceanography. New Jersey, USA: Prentice Hall College; 1997

[2] Thrush S, Hewitt J, Gibbs M, Lundquist C, Norkko A. Functional role of large organisms in intertidal communities: Community effects and ecosystem function. Ecosystems. 2006;**9**(6):1029-1040. DOI: 10.1007/s10021-005-0068-8. S2CID 23502276

[3] Starckx S. A place in the sun—Algae is the crop of the future, according to researchers in Geel Flanders Today. 2012. Available from: http://www.flanderstoday.eu/current-affairs/place-sun. [Accessed: February 15, 2021]

[4] Cardozo KH-M, Thais G, Barros MP, Falcão VR, Tonon AP, Lopes NP, et al. Metabolites from algae with economical impact. Comparative Biochemistry and Physiology C. 2006;**146**:60-78

[5] Ratha SK, Prasanna R. Bioprospecting microalgae as potential sources of "Green Energy"—challenges and perspectives. Applied Biochemistry and Microbiology. 2012;**48**(2):109-125

[6] Williams R. Microscopic algae produce half the oxygen webreathe. The Science Show. ABC, 2013. Retrieved 11 November 2020.

[7] Parker MS, Mock T, Armbrust EV. Genomic insights into marine microalgae. Annual Review of Genetics. 2008;**42**:619-645

[8] Bonachela J, Raghib M, Levin S. Dynamic model of flexible phytoplankton nutrient uptake. PNAS. 2012;**108**(51):20633-20638

[9] Cardozo KHM et al. Metabolites from algae with economical impact. Comparative Biochemistry and Physiology C: Toxicology and Pharmacology. 2007;**146**(1-2):60-78

[10] Ratha SK, Prasanna R. Bioprospecting microalgae as potential sources of 'Green Energy'—challenges and perspectives (Review). Applied Biochemical Microbiology. 2012;**48**(2):109-125

[11] Nilesh Hemantkumar J, Ilza Rahimbhai M. Microalgae and its use in nutraceuticals and food supplements. In: Microalgae—From Physiology to Application. IntechOpen; 2020

[12] de Raposo MF, de Morais RMSC, de Morais AMMB. Bioactivity and applications of sulphated polysaccharides from marine microalgae. Mar. Drugs. 2013;**11**(1):233-252

[13] Alsenani F, Ahmed F, Schenk P. Nutraceuticals from Microalgae. In: Nutraceuticals and Functional Foods in Human Health and Disease Prevention. CRC Press; 2015. pp. 673-684

[14] Nicoletti M. Microalgae nutraceuticals. Foods. 2016;**5**(3):54

[15] Kaur P. Microalgae as nutraceutical for achieving sustainable food solution in future. In: Environmental and Microbial Biotechnology. Singapore: Springer Singapore; 2020. pp. 91-125

[16] Andrade LM. Chlorella and Spirulina microalgae as sources of functional foods, nutraceuticals, and food supplements; An overview. MOJ Food Processing and Technology. 2018;**6**(1):62-65

[17] West MB, Zubeck HM. Evaluation of microalgae for use as nutraceuticals and nutritional supplements. Journal of Nutrition Food Science. 2012;**2**(5)

[18] García JL, de Vicente M, Galán B. Microalgae, old sustainable food and fashion nutraceuticals. Microbial Biotechnology. 2017;**10**(5)

[19] Paniagua-Michel J. Handbook of Marine Microalgae—Biotechnology Advances. pp. 255-267

[20] Singh Joginder, Vyas Ashish, Wang Shanquan, Prasad Ram. Microbial Biotechnology: Basic Research and Applications. 2020

[21] Heimann K, Huerlimann R. Microalgal classification. In: Handbook of Marine Microalgae. 2015. pp. 25-41

[22] Sarris J, Murphy J, Mischoulon D, Papakostas GI, Fava M, Berk M, et al. Adjunctive nutraceuticals for depression: A systematic review and meta-analyses. American Journal of Psychiatry. 2016;**173**(6):575-587. DOI: 10.1176%2Fappi.ajp.2016.15091228

[23] Maciej B, Maria PA, Vincenza GR, Cicero Arrigo FG, Atanasov Atanas G, Gani B, et al. The role of nutraceuticals in statin intolerant patients. Journal of the American College of Cardiology. 2018;**72**(1):96-118

[24] Koyande AK, Chew KW, Rambabu K, Tao Y, Chu D-T, Show P-L. Microalgae: A potential alternative to health supplementation for humans. Food Science and Human Wellness. 2019;**8**(1):16-24. DOI: 10.1016/j.fshw.2019.03.001

[25] Liu Z, Ren Z, Zhang J, Chuang C-C, Kandaswamy E, Zhou T, et al. Role of ROS and nutritional antioxidants in human diseases. Frontiers in Physiology. 2018;**9**:477. DOI: 10.3389/fphys.2018.00477

[26] de Morais MG, da Vaz B, de Morais EG, Costa JAV. Biologically active metabolites synthesised by microalgae. BioMed Research International. 2015;**2015**:835761

[27] Kiran BR, Venkata Mohan S. Microalgal cell biofactory-therapeutic, nutraceutical and functional food applications. Plants. 2021;**10**(5):836. DOI: 10.3390/plants10050836

[28] Martínez Andrade KA, Lauritano C, Romano G, Ianora A. Marine microalgae with anti-cancer properties. Marine Drugs. 2018;**16**(5). DOI: 10.3390/md Starckx 16050165

[29] Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018;**9**(6):7204-7218. DOI: 10.18632/oncotarget.23208

[30] Hosikian A, Lim S, Halim R, Danquah MK. Chlorophyll extraction from microalgae: A review on the process engineering aspects. International Journal of Chemical Engineering. 2010;**2010**:1-11. DOI: 10.1155/2010/391632

[31] Barkia I, Saari N, Manning SR. Microalgae for high-value products towards human health and nutrition. Marine Drugs. 2019;**17**(5):304. DOI: 10.3390/md17050304

[32] Koletzko B, Bergmann K, Brenna JT, Calder PC, Campoy C, Clandinin MT, et al. Should formula for infants provide arachidonic acid along with DHA – A position paper of the European Academy of Paediatrics and the Child Health Foundation. The American Journal of Clinical Nutrition. 2020;**111**(1):10-16. DOI: 10.1093/ajcn/nqz252

[33] Wang Y, Tibbetts SM, McGinn PJ Bonachela. Microalgae as sources of high-quality protein for human

food and protein supplements. Foods (Basel, Switzerland). 2021;**10**(12):3002. DOI: 10.3390/foods10123002

[34] Galasso C, Gentile A, Orefice I, Ianora A, Bruno A, Noonan DM, et al. Microalgal derivatives as potential nutraceut Comparative Biochemistry and Physiology ical and food supplements for human health: A focus on cancer prevention and interception. Nutrients. 2019;**11**(6):1226. DOI: 10.3390/nu11061226

[35] Debasis B, Harry P, Anand S. Nutraceuticals and functional foods in human health and disease prevention. Nutraceuticals from Microalgae. 2015;**9**:673-684