

Exploring the Potential of Microalgae as Food Supplements: A Comprehensive Review

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Microalgae, single-celled organisms rich in macro and micronutrients, emerge as promising dietary supplements for diverse organisms, ranging from humans to aquatic life. This comprehensive review explores various microalgal species suitable for food supplementation, detailing their nutritional compositions. Beyond dietary aspects, the review delves into the industrial, commercial, and environmental applications of microalgae. Examining the impact of microalgal supplementation on health parameters in different animal models reveals properties such as antioxidants, anti-diabetics, anti-carcinogenics, and immunomodulation, contributing to enhanced growth and productivity. Microalgae, with their nutrient-rich profiles, prove to be ideal dietary supplements, positively impacting the health, growth, and immunity of various organisms. This article underscores the multifaceted potential of microalgae as versatile food supplements and advocates for further exploration of their applications in sectors like food and industry.

Keywords: *Chlorella*, Dietary supplement, Microalgae, Nutrients, *Spirulina*

Introduction

Microalgae are the photosynthetic, single celled microorganism, that have gained attention for being a great nutritional source for humans, fishes, insects, and other livestock.¹ More than 40,000 algae species exist, mainly from two domain, which are prokaryotic unicellular cyanobacteria and multicellular eukaryotic algae (red, green, and brown algae).^{2,3} The most commonly studied microalgae include *Chlorella vulgaris*, cyanobacteria and *Spirulina*. Recently, Microalgae have fascinated more attention because of their property to produce broad range of essential compound for animal and human, which include Polyunsaturated Fatty Acids (PUFA), phenols, proteins, carotenoids, and polysaccharides. Microalgae produce a large amount of complete protein, polysaturated fatty acid and other essential nutrients and biomolecules.³ Algae are the ample source of proteins, carbohydrates, lipids, amino acids, vitamins, and minerals.² Algae are natural food source for honey bees⁴ and other animals. The 80% of lipid content is contributed by essential fatty acids such as linolic and palmitic acid.⁵ Malnutrition plays a vital role in mortality among organisms hence proper nutrition is required which can be provided in form of microalgae

supplementation. The most used microalgae as feed supplement are *Arthrospira* and *Chlorella*. *Chlorella* contains 50 to 60% protein as its dry weight.⁶ Essential amino acid required by different organisms like arginine, histidine, valine, lysine, and leucine are found in microalgae. Microalgae are a good source of not only macronutrient but also micronutrients like minerals and vitamins. Presence of all these nutrients, make microalgae a good source of nutrition. This paper presents a novel review of microalgae supplementation, offering a comprehensive analysis of their nutritional, industrial, and health-related significance. Highlighting diverse species' properties, from antioxidants to immunomodulators, it underscores their potential in enhancing health, growth, and immunity across various organisms. With a focus on novel properties and applications, including the presence of potent antioxidants like beta-carotene and astaxanthin, the review emphasizes the potential of microalgae, such as *Dunaliella* and *Haematococcus*, in promoting human health. Insights into gene expression, enzymatic activity, and therapeutic potential against conditions like cancer and hepatic fibrosis underscore the transformative impact of microalgae in health and nutrition. It advocates for further research in this area, indicating promising avenues for innovation in food and industry sectors. This review contributes to advancing our understanding and utilization of

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microalgae resources, showcasing their diverse applications and novel properties.

Types of Microalgae

Different microalgae that can be used as food supplement are *Chlorella*, *Dunaliella*, *Scenedesmus*, *Spirulina*, *Haematococcus*, and *Aphanizomenon*.

Chlorella: *Chlorella* is a green, unicellular algae found in fresh water belonging to class Chlorophyceae, order Chlorellales, and family Chlorellaceae. *Chlorella* is a rich source of nutrients. *Chlorella* contains 55 to 60% protein, 9–18% dietary fibre, 1–4% chlorophyll, vitamin, and minerals.⁷ They are also used for CO₂ bio fixation. Because of its nutritional properties it can be used as a dietary supplement for various organisms including human beings. *Chlorella* also poses therapeutic value. *Chlorella* is an efficient diet for increasing the colony nutrition, immunity, disease resistance and activity of bees.⁸ Hence nowadays there is more interest towards feeding algal based diet containing *Chlorella* to maintain proper nutritional requirements of animals because of its nutritional profile.

Dunaliella: *Dunaliella* is a unicellular, green, uninucleate microalga, which is a great source of zeaxanthin and beta carotene. It acts as an antioxidant. *Dunaliella* is composed of about 24 species including *Dunaliellabardawil*, *Dunaliellatertiolecta*, *Dunaliellasalina* and so on. *D. salina* was firstly announced by Dunal in saltern. Few *Dunaliella* species, mainly *D. salina* and *D. Bardawil* collect carotenoids in large amount under proper growth condition. Few species also collect Alpha-carotene, mainly at low temperature or in extreme condition. Due to the presence of Beta carotene, cell shows bright red colour.⁹ Different species of *Dunaliella* are found in a broad range of habitats from marine to hypersaline regions. *D. salina* is the most abundant species of *Dunaliella* due to presence of high content of beta carotene. *Dunaliella*, *Chlorella*, and *Spirulina* are mainly composed of carotenoid of the algae and plant origin. Beta-carotene enhance general well-being and obstruct the growth of cancer. Beta carotene have antitumor activity. *Dunaliella* assemble 8 to 14 g of beta-carotene of its dry weight.¹⁰ *Dunaliella* shows an anti-inflammatory and immunomodulatory property and they have positive effect on human on the treatment of cardiovascular disease. Carotenoid-biomass present in this alga, is used in food industry as a supplement for animals including humans.¹¹

Spirulina: It is a blue-green algae found in lakes, used as food supplement for years. It is used as a source of protein and vitamin for poultry and fishes. *Spirulina* has the presence of about 70% protein content, amino acids, vitamins, fatty acids, and minerals.¹² *Spirulina* has anti-diabetic, anti-cancer, radioprotective, antiviral, immunomodulatory, lipid modulating, and antioxidant properties. Interest is growing among researchers to use *Spirulina* as a nutrition enhancing supplement due to presence of good amount of protein and micronutrient content.¹³

Haematococcus: *H. pluvialis* is a unicellular microalgae found in freshwater belonging to family *haematococcaceae*. It is known for synthesis of high amount of astaxanthin.¹⁴ During stress conditions, *Haematococcuspluvialis* cell gets converted into red immobile cells also known as cyst by increasing their cell size, form thick cell wall, loose their flagella, and assemble astaxanthin.¹⁵ Astaxanthin is also identified as 3, 3-dihydroxy Beta carotene 4-4-dione which is a secondary carotenoid which is bright red in colour. Chemical composition of cells of *H. pluvialis* at the time of green phase is 1% lutein, whereas the lipid content is 20 to 25% and in red phase the lipid content is 32–37% and astaxanthin deposit is 1–5%.¹⁶ High amount of Beta carotene, lutein, Astaxanthin and fatty acid give many health benefits. Lutein and astaxanthin are natural antioxidants. Astaxanthin is most powerful carotenoid in the market. Carotenoid has anti-inflammatory, ant proliferative and antioxidant property. They all are used to protect against disease caused due to chronic inflammation and oxidative stress.¹⁷ Astaxanthin possess 500 times more antioxidant activity than vitamin E and have more potential to stop free radicle reaction as compare to beta carotene.¹⁶ Astaxanthin have therapeutic effect on humans. Furthermore, lutein is present in ocular tissue and support eye health. It decreases the age-related macular degeneration. Astaxanthin present in *Haematococcus* is safe to use as artificial diet with no negative effect on human health and can also be fed to different animals like fishes.¹⁸ Astaxanthin has beneficial effect on health to cure animal and human disease. It possesses various pharmacological effects like anti-inflammatory property, anti-diabetic effect, antioxidant property, cardiovascular and skin protective property.¹⁷ From last 30 years, ample

research has been done for astaxanthin production from *Haematococcus* microalgae.

Aphanizomenon: *Aphanizomenon floss* is a filamentous blue-green algae species, growing naturally in upper Kalmath Lake, Oregon. Genus *Aphanizomenon* belongs to order Nostocales. *Aphanizomenonis* (AFA) is used as food supplement for years. *Aphanizomenon* is a great source of various essential fatty acid like omega-3 fatty acid and omega-6 fatty acid which help to support the immune system and help in formation of myelin sheath around the nerve fibres in the brain.¹⁹ Intake of AFA help to treat diseases like Alzheimer's disease, enhance fertility, decreased tumour size and occurrence, enhance the immune response, improve stamina, improve digestion, enhance mental acuity, decrease cholesterol, and provide protection against radiation.²⁰ *Aphanizomenon* is a good source of PUFA, vitamin's, chlorophyll, minerals, carotenoids, and phycocyanin. *Aphanizomenon floss aquae* has powerful prebiotic compound that poses a positive effect on human health.²¹ *Aphanizomenon* have anti-inflammatory, anti-oxidant, hypolipidemic and radioprotective property. *Aphanizomenon* produces different form of cytotoxic, hepatotoxic and neurotoxic substances.²² AFA is vital source of blue photosynthetic pigment called phycocyanin. Phycocyanin possesses anti-oxidant and anti-inflammatory activities.²³

Phycocyanin is a strong anti-oxidant and anti-inflammatory compound. It is water soluble phycobiliprotein. Phycocyanobilin present in this microalga structurally resembles bilirubin and later work as strong scavenger of reactive oxygen species.²⁴ *Aphanizomenon* is utilized as dietary supplemented in lot of countries and phycocyanin is present as 15% of its dry weight. *Aphanizomenon* has both toxic and non-toxic form and the one found in lake is nontoxic algae. It consists of 68 minerals, 70 trace elements, 20 anti-oxidants, all amino acid, Beta vitamin and all-important enzymes.²⁵ However, there are many toxic effects of *Aphanizomenon* supplementation, and hence it is not an ideal food supplement.

Nutritional Composition of Different Types of Microalgae

Microalgae are a good source of several macro and micronutrients like proteins, carbohydrates, lipids, minerals, vitamins, and pigments. Presence of these nutrients makes microalgae an ideal food supplement. Along with the presence of primary metabolites like proteins, carbohydrates, polyunsaturated fatty acids, and vitamins, microalgae also compose of valuable secondary metabolites (Fig. 1). These secondary metabolites are the reason for the health benefits provided by microalgae. The secondary metabolites produced by microalgae are pigments, mycosporin like amino acids, and phytosterols.²⁶ The microalgal

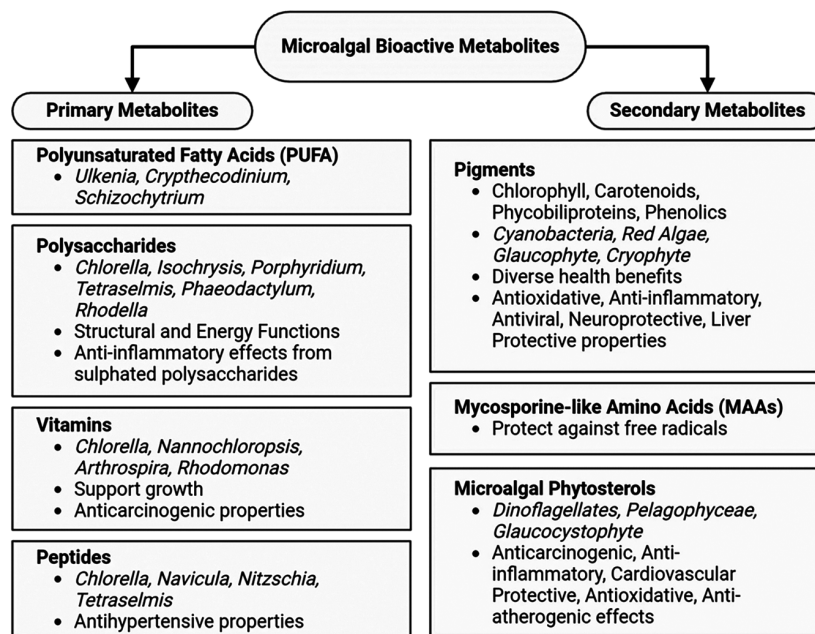


Fig. 1 — Bioactive metabolites present in microalgae: Various types of microalga showcase a spectrum of bioactive metabolites, from Polyunsaturated Fatty Acids to Phycobiliproteins, as microalgae unveil a potent arsenal for combating diseases and promoting overall well-being

metabolites possess antioxidant, anti-inflammatory, anticarcinogenic, and antimicrobial properties. Presence of these properties makes microalgae a potential food supplement.

Primary Bioactive Metabolites

Polyunsaturated Fatty Acids (PUFA): Omega-3 fatty acids and omega-6 fatty acids are the two types of PUFA. The microalgae are a good source of PUFA. *Ulkenia*, *Cryptocodinium*, and *Schizochytrium* are some chief producers of PUFA. PUFA helps to fight against cardiovascular diseases, obesity, arthritis, and diabetes and improve the brain and eye health.²⁷

Polysaccharides: Polysaccharides are mainly produced by microalgal genera like *Chlorella*, *Isochrysis*, *Porphyridium*, *Tetraselmis*, *Rhodella*, and *Phaeodactylum*. All these polysaccharides act as structural molecules, energy reservoirs, and perform protective functioning. These polysaccharides are divided into pectin, sulphated polysaccharides, homo-polysaccharides, hetero-polysaccharides, and glycoproteins.²⁸ The sulphated polysaccharides possess anti-inflammatory effects.

Vitamins: Vitamins are the important elements that support proper growth and development and are obtained through diet. Microalgae like *Chlorella*, *Nannochloropsis*, *Arthrospira*, and *Rhodomonas* produce different vitamins. Carotenes and retinol possess anti-carcinogenic property.²⁹

Peptides: Amino acids joined by peptide bonds are called peptides. Microalgae like *Chlorella*, *Navicula*, *Nitzschia*, and *Tetraselmis* produce peptides.³⁰ Microalgal peptides possess antihypertensive property.³¹

Secondary Bioactive Metabolites

Pigments: These are the secondary metabolites that provide colour to the organism. Pigments harvest the light energy to perform photosynthesis and give protection against oxidative damage. The pigments present in microalgae are chlorophyll, carotenoids, phycobiliproteins, and phenolics.³⁰ Carotenoids found in microalgae are beta-carotenes produced by *Scenedesmus* and *Dunaliella*³², lutein produced by *Chlorella*, fucoxanthin, astaxanthin produced by *Haematococcus*³⁰ and zeaxanthin produced by *Scenedesmus* and *Nannochloropsis*.

Phycobiliproteins: These are the hydrophilic proteins which absorb the light between a wavelength of 470

to 660 nm.³³ Phycobiliproteins are of four types which are phycoerythrins, phycocyanins, allophycocyanins, and phycoerythrocyanins. These are produced by cyanobacteria, red algae, glaucophyte, and cryophyte. Phycobiliproteins possess antioxidative, anti-inflammatory, neuroprotective, antiviral, and liver protective effects.³⁴

Mycosporine like Amino Acids (MAAs): MAAs are the molecules weighing less than 400 Da, and comprise of cyclohexanone or cyclohexenimine chromophores joined with one to two amino acids.³⁵ MAAs possess properties to protect against free radicals.

Phytosterols: These are the plant-based steroids comprising of two groups, the sterols and the stanols. Phytosterols are produced by microalgae like dinoflagellates, *Pelagophyceae* and *Glaucocystophyte*.³⁶ Microalgal phytosterols show anticarcinogenic, anti-inflammatory, cardiovascular protective, antioxidative, and anti-atherogenicity properties.³⁷

Applications of Microalgae

Microalgae have various commercial, industrial, and environmental applications (Fig. 2).

Commercial Applications

Microalgae has a commercial use in human health and nutrition, cosmetic industry, and biorefinery.³⁸ Microalgae produce better quality proteins as compared to plants. Microalgae produce sterols that can cure cardiovascular diseases.³⁹ Beta-carotene, mycosporine, carotenoids, and dimethylsulfonylpropionate produced by microalgae act as antioxidants. *Spirulina* supplementation possess immunomodulatory function and help in management of cardiovascular diseases, cancer, anemia, arthritis, and diabetes.⁴⁰ *Chlorella* being

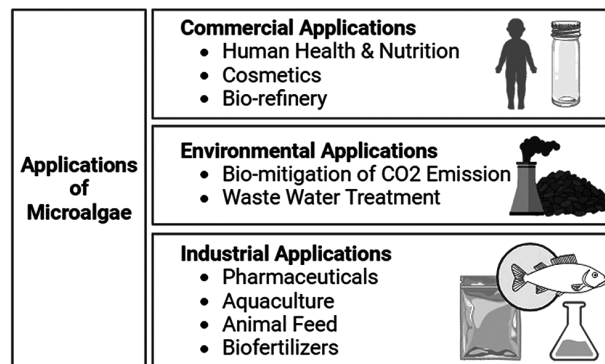


Fig. 2 — Applications of Microalgae: Microalgae has various commercial, environmental, and industrial applications

a rich source of protein, vitamins, and carotenoids helps in stimulation of immune system. *Nostoc sphaeroides* are used to enhance the property of various drugs.⁴¹ *Muriellopsis* species are used to cure degenerative diseases. Skin and hair care products contain microalgal extracts. Microalgae like *Chlorella* and *Arthrospira* are used for this purpose.⁴² This application of microalgae is due to its antioxidant, thickening, and water binding ability. Microalgal biomass can produce biofuels. Using biofuel instead of fossil fuel is a better option to prevent environmental pollution. Biofuels produced from algae compose of 10 to 45% of oxygen and low sulphur emission unlike petroleum, hence they are non-toxic and ecofriendly.²

Industrial Applications

Microalgae can be used in pharmaceuticals and aquaculture. It also has application as animal feed and biofertilizers. These are some of the industrial applications of microalgae. Microalgae can produce various bioactive compounds like antibiotics, pharmaceutically active compounds, toxins, growth regulators, and algicides. These bioactive compounds improve immunity, fertility, weight, and skin.⁴³ Microalgae being the primary producers are a main source of nutrition in aquaculture animals. The commonly fed species are *Chlorella*, *Pavlova*, *Nannochloropsis*, *Tetraselmis*, *Skeletonema* etc. In aquaculture, microalgae are used as fish feed, culture medium quality improver⁴⁴ and fish immune system stimulator.⁴³ Microalgae are rich in nutritional compounds and hence can be used as nutritional supplement. Microalgae is a good protein source for poultry animals. The algal biomass can be

implemented to produce bio-oil, charcoal, and syngas.⁴⁵ The biochar so produced can be used as a biofertilizer.⁴⁶ Cyanobacteria help to improve the physio-chemical properties of soil.

Environmental Applications

Microalgae have application in bioremediation as in bio-mitigation of CO₂ and in waste water treatment. The CO₂ produced due to burning of fossil fuels is a serious threat to the environment. Microalgae can fix CO₂ through photosynthesis.⁴⁷ Microalgae can be used in production of biofuel due to its capability to tolerate high concentration of CO₂.⁴⁸ Hence microalgae can be used efficiently for CO₂ mitigation.⁴⁹ Microalgae can be functional in treatment of domestic wastewater. Microalgal growth on waste water leads in eradication of heavy metals, pathogens, organic contaminants, and chemicals from the water.⁵⁰ The most used species are *Chlorella*, *Scenedesmus*, and *Spirulina*.⁵¹

Benefits of Microalgae Across Organisms

Microalga being a rich source of micro and macronutrients possess various health-modulating properties (Table 1) (Fig 3). *Chlorella* show antioxidant, anti-inflammatory, anti-tumorous and antimicrobial property.⁵² *Spirulina* possess antiviral, anticancer, anti-oxidant, and anti-inflammatory property.⁵³ Beta carotene present in *Dunaliella* possesses anti-cancerous properties. *Haematococcus* possess anti-bacterial, anti-tumor, anti-inflammatory and antibacterial property.⁵⁴ *Aphanizomenon* possess antioxidant and anti-inflammatory property.

Table 1 — Microalgae Supplementation Effects on Organisms

Phylum/ class	Organisms fed on microalgae	Microalgae used as supplement	Effects on health of organism
Nematodes	<i>C. elegans</i>	<i>Chlorella</i> , <i>Spirulina</i> , <i>Haematococcus</i>	Antioxidant effect, antidiabetic effect, increase longevity. ^{55,57,58}
Arthropoda	<i>Drosophila melanogaster</i> , honeybees	<i>Schizochytrium</i> , <i>Spirulina</i> , <i>Chlorella</i> , <i>Scenedesmus</i>	Antioxidant effect, enhanced gene expression and enzymatic activity, enhanced growth and immunity, increased productivity. ^{1,59-61, 65,67,70}
Pisces	Zebrafish, <i>A. ocellatus</i> , <i>O. mykiss</i> , Rainbow trout, dino fish	<i>Chlorella</i> , <i>Spirulina</i> , <i>Haematococcus</i> , <i>Tetraselmis</i>	Enhances growth, increase productivity, better immune functioning. ^{71,72,76-78}
Amphibians	Frogs	<i>Spirulina</i>	Enhance growth and productivity. ⁸¹
Aves	Broiler chickens	<i>Chlorella</i> , <i>Spirulina</i> , <i>Haematococcus</i> , <i>Dunaliella</i>	Immunomodulatory effect, enhance growth, increase productivity. ^{84,87}
Mammals	Humans, rats, cows, monkeys	<i>Chlorella</i> , <i>Dunaliella</i> , <i>Haematococcus</i> , <i>Spirulina</i> , <i>Aphanizomenon</i>	Anticarcinogenic effect, antioxidant effect, antidiabetic effect, enhance growth and reproductive health. ^{92,95,97,102,104,108,111,127}

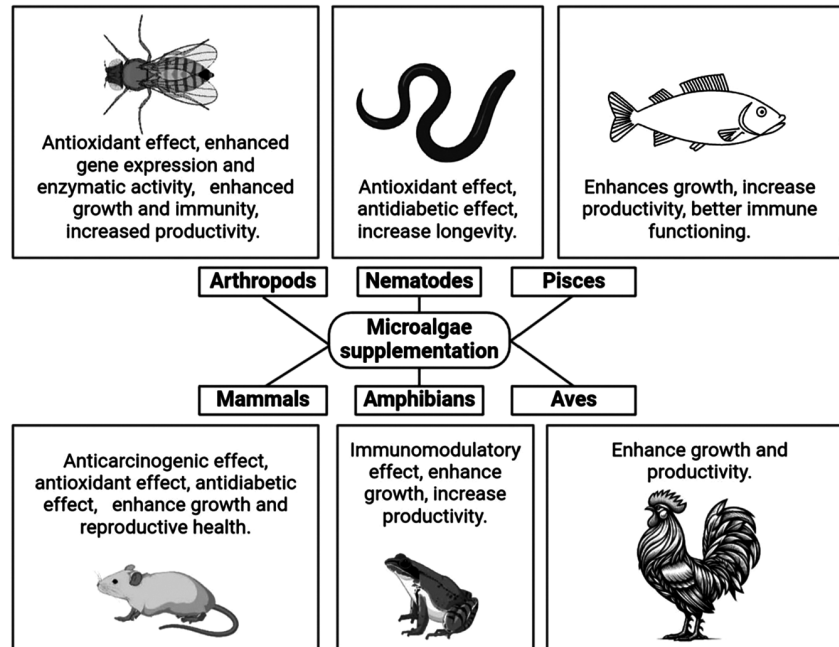


Fig. 3 — Microalgal Supplementation on Organisms: Microalgal supplementation elicits a range of health-enhancing effects, including anticarcinogenic, antioxidant, antidiabetic, and immunomodulatory impacts on organisms

Nematodes

Feed supplementation of *C. elegans* with microalgae increase the longevity of the nematode because of its antioxidant and antidiabetic activity. *Chlorella pyrenoidosa* possess anti-oxidant property by regulating the micro RNA and gut microbiota of *Caenorhabditis elegans*.⁵⁵ *Spirulina platensis* possess polysaccharide which can be used as a food supplement on *C. elegans* to fight against oxidative stress.⁵⁶ Treatment with oligosaccharide present in *U. lactuca* improve the glucose level and insulin resistance in *C. elegans*. The organism's life span was also enhanced. Hence it possesses anti-diabetic effect and can be used as a nutritional supplement to tackle hyperglycaemia.⁵⁷ The carotenoids found in *H. lacustris*, help to increase the longevity of *C. elegans*.⁵⁸ It also possesses anti-oxidant property.

Arthropoda

Microalgal supplementation shows antioxidant effect on *Drosophila melanogaster*. It also enhances the gene expression, growth, immunity, strength, and productivity in honeybees.

Antioxidant Property: Supplementation of fruit fly i.e. *Drosophila melanogaster* with 20% microalgae does not impact the physiological performance of fly and can be used as a food alternative to fulfil the dietary requirements of fly.¹ The DHA present in microalgae *Schizochytriummangrovei* show an anti-ageing

activity on *Drosophila melanogaster*.⁵⁹ *S. platensis* supplementation on *Drosophila melanogaster* show neuroprotective property. It shows that polyphenols present in *S. platensis* possess anti-oxidant property. *Chlorella pyrenoidosa* supplementation possess anti-aging property on *Drosophila melanogaster* due to presence of natural anti-oxidant compounds.⁶⁰

Gene Expression and Enzymatic Activity: Feed supplementation with microalgae help in the expression of several health promoting genes in the body of bees. A study by Jang *et al.*⁶¹ was done to see the impact of chlorella supplementation on the physiology of bees. Bees were given *Chlorella sorokinana* in different amount. The observation depicts that chlorella supplementation increased the longevity, muscle formation, development of glands and vitellogenin gene expression. The best outcome was observed in case of 2% chlorella concentration. Consumption of chlorella syrup increased the lipase activity and the gene expression of antioxidant like catalase and superoxide dismutase 1 in the adult bees. A high concentration of vitellogenin was seen in *chlorella* fed colonies. *Chlorella* supplemented diet does not affect the oxidative balance of bees hence can be used as a pollen supplement during dearth period.⁶² The impact of chlorella infused diet was seen on the biological characteristic of bees. The supplementation was done in the form of powder,

sugar solution and mixed with honey and sugar candy. The observation showed that there was a beneficial effect of this diet on the growth of colony. The transcript level of vitellogenin and fat deposition increased and TOR and INR2 transcript level were also enhanced. It influences the size of hypopharyngeal gland. There was a positive effect on the activity of base digestive enzyme of the midgut of bees.⁶³ Ricigliano *et al.*⁶⁴ supplemented honey bees with *Chlorella vulgaris* and *Arthrospira platensis*. The metabolomic results indicated an enhanced expression of antioxidant and heat shock proteins.

Growth and Development: Microalgal supplementation aids in proper growth and development in bees. A study by Nichols & Ricigliano⁶⁵ was done to see the benefits of algae on the bees and their use as an artificial diet. The bees were supplemented with chlorella microalgae and it is observed that the weight, length, and the diameter of the cells of queen increased significantly. Hence microalgae-based diet has a positive impact on development of bees. Nichols & Ricigliano⁶⁵ concluded that, microalgae-based diet has a beneficial effect on health of bees, and leads to an increase in productivity of bees. A study was conducted by Eremia *et al.*⁸ to see the impact of *Chlorella vulgaris* as an artificial diet for raising the queen. The results showed that supplementation enhanced the diameter, mass, and length of queen cells. Ricigliano *et al.*⁶⁶ fed varroa resistant bees with pollen and spirulina and observed that spirulina supplementation led to high body weight, less fat lipids and enhanced vitellogenin level. Spirulina as a pollen substitute diet for honey bees improves the nutritional state, body weight, lipid content, and vitellogenin protein.⁴

Immunity: Feeding bees with microalga help to enhance their immunity by production of antimicrobial peptides. *C. vulgaris* is not only nutritionally beneficial to bees but also prevent pathogenic infections as it possesses prophylactic properties.⁶⁷ Sulphate polysaccharides from algae can be used as nutritional supplement in prevention of nosemosis infections in honey bees.

Strength and Productivity: Microalgal supplementation increases the strength and overall productivity of bee colonies by enhancing the egg laying capacity of bees and larval development. *Spirulina* supplementation led to an improvement in brood production leading to a large and healthy colony of bees.⁶⁸ Bees

supplemented with *Scenedesmus quadricauda* increased the strength and productivity of bees by enhancing queen prolificacy and development of larva. A similar study shows the effect of feeding *Oocystisborgei* Snow on health of bees. The result depicted an increase in strength and productivity of bees. The egg laying by queen bees was increased. There was a positive impact on the larval and brood development.⁶⁹ Feed enriched with bioactive compounds supplemented from *Scenedesmus quadricauda*, *Scenedesmus apiculatus* and *Oocystisborgei* Snow depicted an increase in queen prolificacy, brood population, strength, immunity, wax production, and honey production.⁷⁰

Pisces

Different fish species when supplemented with microalgae possess better immune functioning. It also leads to better growth and development of fishes. The productivity is also increased.

Immunity: Supplementation of fish with different species of microalgae enhances the survival of fish during stress and infectious conditions by enhancing the immune response.⁷¹ Microalgal supplementation enhance the growth of Zebrafish. It regulates the gut microbiota and improve the immunity of the organism.⁷² Streptococcal infection in Zebrafish is reduced due to anti-bacterial property of supplemented microalgae.⁷³ *Chlorella* and *Tertselmis* supplementation in zebrafish help with the intestinal inflammation, caused due to soybean meal and infection caused by bacteria.⁷⁴ Feeding *D. salina* has a positive impact on immunological parameter and development of *A. ocellatus*.⁷⁵

Growth and Productivity: *Chlorella* supplementation on *Oncorhynchus mykiss* enhances the immunity, growth, and anti-oxidant capacity of fish.⁷⁶ *Chlorella* improves the quality of muscles in fish by reducing the inflammation and preventing the apoptosis in muscles.⁷⁷ In *O. niloticus*, *Chlorella* supplementation enhance the utilization of proteins, enhance the immunity, increase the activity of trypsin, perform anti-oxidant activity, and provide resistance against sodium nitrate.⁷⁸ *H. pluvialis* supplementation show a positive impact on the immune response, growth and heptamorphology of *Onchorhynchus mykiss*.⁷⁹ The reproductive potential and quality of eggs of rainbow trout was also enhanced.⁸⁰

Amphibians

There is an increment in the growth and immunity of amphibian species like frogs upon supplementation with microalgae. Dietary supplementation of *Spirulina* enhances the immunity and growth of Rugose Frog (*Hoplobatrachus rugulosus*). It also improves the hematological parameters of the organism.⁸¹ Dietary oxidants present in microalgae promote the growth of tadpole along with enhancing their immune response.

Aves

Microalgal supplementation enhances the growth and productivity of birds. It also enhances the immune functioning of birds.

Immunomodulatory Effect: *Chlorella* supplementation promotes growth and enhances the immunity of broilers. *Chlorella* supplementation increases the number of *Lactobacillus* in the intestine of bees which resulted in an enhanced immunity and improved body weights in the broilers.⁸² *Chlorella* supplementation enhances the antibody mediated immunity and promote growth in broilers.⁸³ Choi *et al.*⁸⁴ fed male and female broilers on recombinant chlorella supplement. They found that it increased the immunity of broilers with a rise in IgA antibody concentration in their body. The metabolism of nitrogen also increased. Research was done by Waldenstedt *et al.*⁸⁵, to see the impact of *Haematococcus pluvialis* on caecal campylobacter count, clostridial counts and tissue astaxanthin concentration in broiler chicken. It was observed that algal meal shows clostridium reducing effect, although campylobacter counts were unaffected. With more level of algal meal and when oil mix was sprayed onto the pellet, high tissue concentration of astaxanthin and total carotenoid were noticed. Awadh & Zangana⁸⁶ saw the impact of supplementing astaxanthin take out from algae *H. Pluvialis* on immunological aspects of broilers. It was observed that the supplementation enhanced the immune functioning of these broiler chickens.

Effect on Growth and Productivity: An experiment was conducted by Saadaoui *et al.*⁸⁷ to see the effect of microalgal supplemented diet in an alternative feedstock for livestock and poultry production and the observation showed that microalgae have huge capability as animal feed because in microalgae essential biomolecule are present like retinoids, vitamin, PUFA. They all increased the nutritional

quality of animal products. *Spirulina* supplementation increases the feed efficiency and weight of broiler chickens and influences the health of broilers. A study by Kharde *et al.*⁸⁸ showed that spirulina supplementation increased the mass and feed efficiency in broilers. Similar observation was made by Kaoud.⁸⁹ The probiotic and spirulina supplementation increased the weight and lowered the mortality and feed consumption ratio, hence improved the poultry production.

Other Effects: A research was done by Alghamdi *et al.*⁹⁰ to see the impact of *Dunaliella salina* and Spirulina mixture on immune response of fattening chicks, performance, kidney, lipid profile, liver markness. He concluded that Broiler chick after fed on artificial diet supplemented with *Dunaliella* and *Spirulina* combination enhanced immunity, liver function, kidney function, productivity performance, digestive enzyme, and lipid profile. According to Abd El-Hady⁹¹, *Spirulina* show a positive influence on the gut health of broiler chickens.

Mammals

Microalga supplementation on mammals like humans, rats, cattle, and monkeys possess various anticarcinogenic, antidiabetic, antioxidant, and reproductive effects (Fig. 4).

Anticarcinogenic Property: Otsuki *et al.*⁹² experimented on young man to see the influence of feeding chlorella on heart rate, blood pressure and pulse rate. The experiment concluded that the supplementation with *Chlorella* reduced the risk of stiffness in arteries of humans. *Chlorella* supplementation possesses immune system enhancing, medicinal, antioxidant, antidiabetic, and blood pressure modulating properties. It reduces the occurrence of cardiovascular diseases in humans.⁹³ *Dunaliella* possesses anti cancerous property. An experiment was done by Chiu *et al.*⁹⁴ to see the impact of *Dunaliella salina* as anti-inflammatory, anti-proliferative and pro-apoptotic. It was concluded that *D. salina* shows anticarcinogenic property. Another similar research was done by Martinezek *et al.*⁹⁵, to see the impact of *Dunaliella tertiolecta* on cancerous cells in humans. It was concluded that it possesses anti cancerous property. Another study done by Palozza *et al.*⁹⁶ to see the impact of astaxanthin rich *H. pluvialis* algae on human colon cancer cell growth concluded that *Haematococcus pluvialis* may prevent colon cancer in humans.

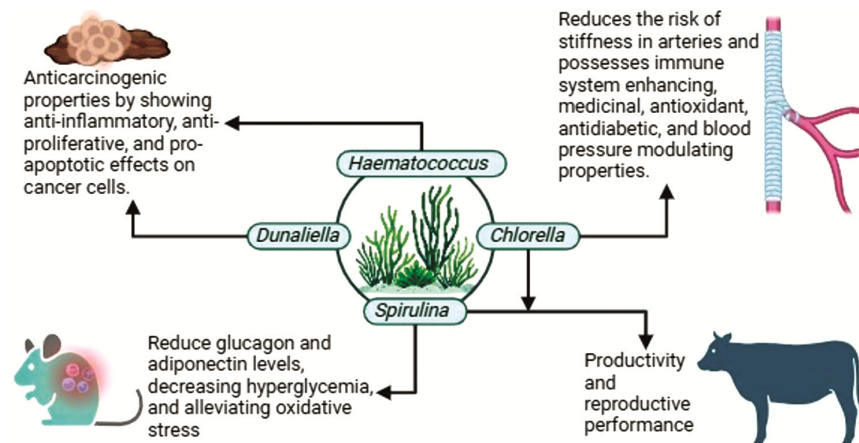


Fig. 4 — Microalga Supplementation Benefits in Mammals: Microalga provides a myriad of health benefits from anticarcinogenic and antidiabetic properties to enhanced growth and reproductive health.

Antidiabetic Property: Farouk *et al.*⁹⁷ saw the therapeutic effect of Crs-Df on obese rats. The experiment concluded significant decrease in glucagon and adiponectin level in serum of overweight rat. Study shows that combination of oral supplementation and CRF- DS have tendency to decrease problems associated with cardiac functioning in rats. *Spirulina* show antioxidant and antidiabetic effect in rats. Gargouri *et al.*⁹⁸ fed male Wistar rats on spirulina. A loss of body weight was observed in rats. The study also concluded that there was a decrease in hyperglycaemia in diabetic rats. The oxidative stress was also lower. Hence spirulina supplementation can be used to prevent diabetes. In a study by Yongchao *et al.*⁹⁹, on streptozotocin induced diabetes in rat it was concluded that *Haematococcuspluvialis* show anti-inflammatory and antioxidant property which help to reduce the chances of Streptozotocis induced diabetes in rats.

Antioxidant Property: An experiment was done by Guerin *et al.*¹⁰⁰, to see the effect of *Haematococcus* on health and nutritional parameters of humans. The result showed that *Haematococcus* supplementation may be beneficial and practical strategy in human health management. It was concluded that astaxanthin has strong antioxidant activity. Umemoto and Otsuki¹⁰¹ conducted an experiment to see the changes in amount of oxygen uptake in young men and women during cycling. It was noted that the *Chlorella* supplement treatment significantly raised the aerobic endurance capacity in individuals. There was a rise in the oxygen uptake by these individuals. Kalafati *et al.*¹⁰² concluded in their experiment that the supplementation with *Spirulina* increases the

oxidation of fat and exercise performance in humans. *Chlorella* supplementation has various positive impacts on the health of rats. Horii *et al.*¹⁰³ fed rats with *Chlorella* in combination with exercise training. It was noted that the rats had better exercise performance. The glucose and oxidative breakdown were also influenced. *Chlorella* supplementation had a beneficial impact on the metabolism of rats. Napolitano *et al.*¹⁰⁴ conducted an experiment on rats suffering from hypothyroidism. The *Chlorella* supplementation decreased the oxidative stress in the liver of the rats. Another research was done by Vanitha *et al.*¹⁰⁵, to see the impact of *Dunaliella bardawil*, a carotenoid producing alga on toxicity induced by CCl₄ in rats. Results concluded that with *D. bardawil* treatment, liver histopathology was less severe and it prevented damaged caused due to oxidative stress. El-Tantawy¹⁰⁶ concluded that spirulina has anti-apoptotic and antioxidant effect on lever damage caused by lead acetate. Another experiment was done by Farouk *et al.*¹⁰⁷ to see how *Haematococcus pluvialis* algae influence ageing in rats. It was concluded that astaxanthin rich *H. Pluvialis* has an antioxidant property and influence ageing related to hepatic changes in rats.

Growth and Productivity: *Chlorella* as a food supplement given to cattle enhances their economic value by various means. Khlolif *et al.*¹⁰⁸, saw the effect of *Chlorella vulgaris* as a supplement diet on Boer goat. It was concluded that supplementation of goats with *Chlorella vulgaris* had an increment on nutrient edibility, nutritive value of milk, milk production, ruminal fermentation, and efficiency of milk. Shams *et al.*¹⁰⁹ concluded that *Chlorella*

supplementation on suckling Friesian calves increased the albumin, globulin and protein content in the animal and enhanced the enzymatic activity in the liver. With increase in supplementation the gain in the average weight of calves was seen. Another study was done by Shams *et al.*¹¹⁰ to see the effect of *Chlorella vulgaris* on lactating Friesian cows' reproductive performance and concluded that *Chlorella* as a supplement for cows enhance their economic efficiency, reproductive trait and productive.

Reproductive Health: *Dunaliella* supplementation has various impacts on the health of livestock. *Dunaliella* supplementation showed improved development of ovarian follicles and influenced the reproductive potential of Boer goats.¹¹¹ Another experiment by Ciliberti *et al.*¹¹² concluded that *Dunaliella* show anti-proliferative effect in sheep during post-partum period. *Spirulina* supplementation influences the productivity in livestock in a positive way. Gaafar *et al.*¹¹³ observed that *spirulina* supplementation has a positive influence on the productivity and reproductive behaviour of cows. Kulpys *et al.*¹¹⁴ concluded that spirulina supplementation increases milk production in lactating cows. Kamada *et al.*¹¹⁵ concluded in their study that cows supplemented with astaxanthin obtained from *Haematococcus* has a great potential in increasing the production of progesterone from luteal cells.

Other Effects: Amato *et al.*¹¹⁶ studied the effect of *Aphanizomenon flos aquae* supplementations. It was observed that the supplementation had spasmolytic impact on colon contractility as it led to serotonin release. *Spirulina* poses different health benefits for humans. Daily consumption of *Spirulina* had a beneficial effect on immune response, allergic rhinitis, inflammation, hypertension, diabetes, and dyslipidaemia.¹¹⁷ A study was done by Yu *et al.*¹¹⁸ to conclude that *Spirulina* can be used as a great source of zeaxanthin to combat the problem of cataract in eyes of humans. Azlan *et al.*¹¹⁹ concluded in their experiment that *Chlorella* supplementation on Sprague-Dawley rats reduced 4-hydroxyalkenal and malondialdehyde amount and enhanced the function, strength, and mass of the muscles on the older rats. *Spirulina* supplementation can help with vitamin B12 deficiency.¹²⁰ *H. pluvialis* supplementation show antifibrotic effect hence it is effective treatment for hepatic fibrosis.¹²¹ Helal *et al.*¹²² observed that *Aphanizomenon flos-aquae* supplementation reduced

the body weight, increased the lipoprotein, testosterone, and protein levels. It prevents the biochemical alterations occurring in rats. *Aphanizomenon* supplementation protect against dysmetabolism induced by fat enriched diet, prevent oxidative stress and possess anti-inflammatory property.¹²³ Mohammed *et al.*¹²⁴, observed that AFA supplementation post carrageenan injection improves the liver functioning and hematological conditions in rats. It possesses strong anti-inflammatory activity. AFA reduce the pathological cellular injuries in the cells of cerebral cortex caused due to exposure to radiations.¹²⁵ According to Kumar *et al.*¹²⁶, consumption of astaxanthin and copper enhances the growth and immunity of Murrah buffalo heifers. It possesses antioxidant property and improves the functioning of liver. *Chlorella* supplementation on *Macaca mulatta* helps in better digestion, improves the metabolism, and increase the natural resistance in the organism.¹²⁷

Alzheimer's Disease (AD) is characterized by the accumulation of beta-amyloid (A β) plaques and Tau Neurofibrillary Tangles (NFTs), resulting in neuronal apoptosis and cognitive decline. *Chlorella* species, known for their functional properties, are being investigated for their potential in preventing neurodegenerative diseases. Our research highlights the antioxidant properties of *Chlorella Pyrenoidosa* hydrolyzed Protein (CPP) and suggests that CPPs, particularly CPP 1–3 kDa and CPP 3–10 kDa, show promise as therapeutic candidates for AD. In experimental mice, CPPs at 100 μ g/mL improved hippocampal cell density, spatial memory, and reduced inflammatory stress. These findings suggest that CPPs may mitigate AD pathology by reducing amyloid plaque and tau NFT accumulation, though further pre-clinical and clinical investigations are warranted for their therapeutic efficacy and safety profile validation.¹²⁸

Limitations

The potential use of microalgae as a food supplement is still not completely explored due to lack of proper knowledge regarding its dosage.²⁹ If diet is not used with standard protocol, it may show negative impact on the consumer so diet must be given with proper measurement to avoid any kind of miss happening. Proper monitoring of diet must be required to eliminate those substances from diet which do not meet the standard quality.¹²⁹ Despite

being a great source of different macro and micronutrients, microalgae like *Aphanizomenon* possess many toxic effects. Supplementation with microalgae led to several side effects like diarrhoea, abdominal discomfort, nausea, and rashes on skin. Hypothyroidism and renal failure were some major side effects despite the health benefits.¹³⁰ Hence a proper knowledge is required about the microalgal supplementation before consumption to prevent possible side effects. A proper consultation from specialist is necessary before consumption of microalgae as food supplement.

Future perspectives

Research can be done on different microalgal species that can be used as food supplement. Effect of different microalgae can be identified on different health aspects to find the most suitable one. Combinations of different microalgae can be used to see their combined effect on health parameters of different organisms. Nutritional compounds can be extracted from the microalgae and added as food supplements. Furthermore, studies can be done to see the therapeutic effect of microalgal supplementation on humans. Research regarding the appropriate dosage of supplementation can provide information to prevent toxicity and harmful effects caused due to supplementation. In future more applications of microalgae can be explored in different sectors like industrial sector. Microalgae can be used as a renewable source of energy as biofuel.

Conclusion

The exploration of applications of microalgae in different sectors, such as food and industry, highlights the vast potential of this natural resource. Abundant in complete proteins, polysaturated fatty acids, and essential nutrients, microalgae stand out as a great source of carbohydrates, proteins, lipids, amino acids, minerals, and vitamins. This review highlights the diverse health benefits of microalgae supplementation across various organisms, ranging from nematodes to mammals. Major findings include the antioxidant, anti-inflammatory, and immunomodulatory properties exhibited by different microalgae species, contributing to enhanced longevity, growth, and productivity in organisms. However, gaps in knowledge regarding optimal dosage and potential side effects elucidate the need for further research as well as standardization in microalgae

supplementation. Future directions for researchers include exploring the effects of different microalgae species combinations, identifying therapeutic applications in humans, and determining appropriate dosage regimens to prevent toxicity. The paper showcases the potential of microalgae as a valuable source of nutrition and suggests avenues for future research to maximize its benefits while minimizing potential risks.

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Conflict of interests

The authors declare no competing interests.

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