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REVIEW

Emerging industrial applications of microalgae: challenges and future perspectives

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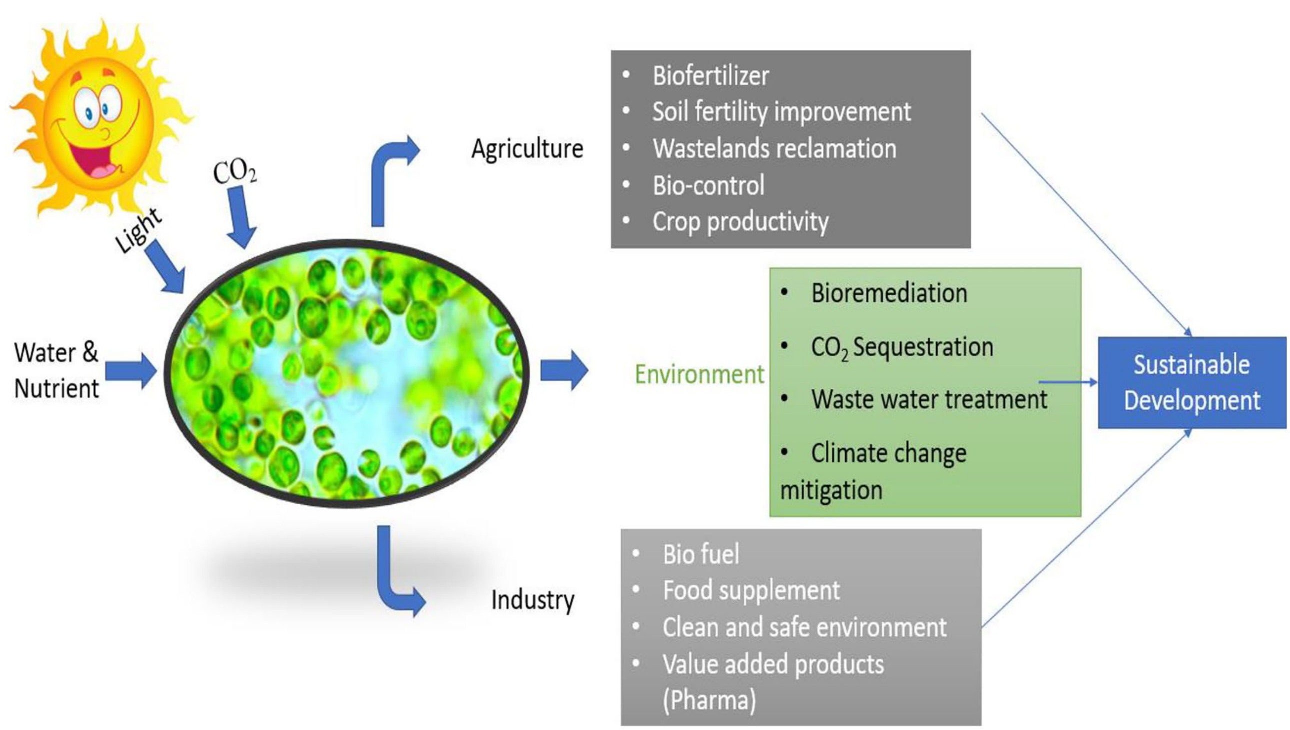
Abstract
Microalgae are unicellular photosynthetic organisms that have been recently attracted potential interests and have applications in food, nutraceuticals, pharmaceuticals, animal feed, cosmetics, and biofertilizers industry. Microalgae are rich in a variety of high-value bioactive compounds which have potential benefits on human health and can be used for the prevention and curing of many disease conditions. But scale-up and safety issues remain a major challenge in the commercialization of microalgal products in a cost-effective manner. However, techniques have been developed to overcome these challenges and successfully selling the products derived from microalgae as food, cosmetics and pharmaceutical industries. Microalgae are rich in many nutrients and can be used for the production of functional food and nutraceuticals, safety and regulatory issues are major concerns and extensive research is still needed to make microalgae a commercial success in the future. Many practical difficulties are involved in making the microalgal food industry commercially viable. The present review focuses on the industrial applications of microalgae and the challenges faced during commercial production.

Graphic abstract



Keywords Microalgae · Functional foods · Nutraceuticals · Pharmaceuticals · Cosmetics

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Introduction

Microalgae are the ancestors of present-day land plants and primary members of the aquatic ecosystem. Microalgae are unicellular microorganisms capable of photosynthesis and to generate chemical energy from solar energy. Microalgae are capable of the production of a major amount of oxygen in the atmosphere. These organisms have rapid growth and produce more biomass rich in bioactive compounds in comparison with higher plants. Microalgae process the ability to adapt to adverse environmental conditions, do not compete with agricultural lands and can even cultivate in waste or saline water. Since early 1500 BC, algal biomass has been used as a major dietary component and medicine. The first microalgae used as a medicine dates back 2000 years to overcome famine disease [1]. Microalgae have the capacity to generate a variety of high-value bioactive compounds like carbohydrates, proteins, lipids, essential fatty acids, pigments, vitamins, antioxidants etc. [2]. For these reasons, microalga has been extensively used in food, cosmetics, biofuels, feed, nutraceutical and pharmaceutical industries (Fig. 1) [3–5]. It has also been used in bioremediation, CO_2 mitigation, bioremediation of wastewater, and biofuel production [6, 7]. But the production of energy derivatives using microalgae is not cost-efficient if it is not joined with other high-value metabolite production. The major disadvantages of the commercialization of microalgal products are small market size, high cost of production, low biomass and product accumulation in large-scale cultivation and high regulatory constraints [8] [9]. But recent economic studies have proved that the development of microalgal industries is a progressing market field. The worldwide market of microalgal products is expected to exceed $75 million USD in revenues by 2026 (Microalgae market 2020).

Over the last few years, microalgal bioactive compounds have been attracted more funding and research activities. The different types of high-value metabolites with nutraceutical and pharmaceutical importance extracted and purified

Fig. 1 Industrial applications of microalgae

from microalgae include polysaccharides, proteins, polyunsaturated fatty acids, polyphenols, vitamins, minerals, carotenoids etc. [10–12]. The metabolites derived from microalgae have proven roles for the treatment and prevention of many disease conditions like diabetes, cardiac, autoimmune, rheumatoid arthritis, anemia, obesity, dementia, and other neurodegenerative diseases [13, 14].

From literatures, it is evident that microalgae have been considered as a food supplement from ancient times itself. During AD 1300, people from Mexico have reported to use *Spirulina* as a food ingredient. It is also reported that people from Africa have also included *Spirulina* in their daily diet. Population from South America, Mongolia, and China has been used *Nostoc* as a food supplement. In Spain, people prepared a dry cake known as 'tecuitlatl' from blue-green algae. From ancient times, *Spirogyra* has been used as a food ingredient in countries like India, Burma and Vietnam [15]. Japanese people also used edible cyanobacteria to prepare their native food 'Suizenji-nori'. Hence it is clear that modern biotechnological developments using microalgae have started years ago. In 1952, the University of Stanford in the United States conducted the first Algal mass culture symposium which opened a new way for the industrialization and commercialization of microalgae.

In 1960s, Japan has started a company named Nihon *Chlorella* for the mass cultivation of *Chlorella* for food applications [16]. Then in 1970s, a company named Sosa Texcoco S.A has started *Arthrospira* cultivation facility in Lake Texcoco, Mexico. [16]. In Asia, 46 large-scale microalgal cultivation factories have started in 1980s producing more than 1000 kg of microalgae per month. Then, the large-scale cultivation of *Dunaliella salina* was started for beta carotene production and became one of the major producers of microalgal metabolites. India also started cultivating microalgae in large-scale industries [1]. In recent years, there is rapid growth in the algal biotechnology industries (Table 1). Microalgal biomass production market has reached about 5000 tons of dry matter/year and has a turnover of ~ $\$1.25 \times 10^9$ USD per year [1].

But the major disadvantage of large-scale microalgal cultivation systems is low biomass production and difficulties in product recovery, which increases the cost of cultivation and final product prize. Researchers are still focused on the development of new methods to enhance the production of biomass from microalgae and decrease the commercial cultivation cost of microalgae [2, 12]. Microalgal high-value metabolites are also used in several industries for the development of nutraceuticals, pharmaceuticals, cosmetic products, aquaculture and poultry feed, and as biofertilizers [2]. Thus, the present study deals with the recent developments of algal biotechnology and the emerging industrial applications of microalgae, the major challenges and future applications of microalgal products in the global market.

Microalgae as major players in food industry

The primary source of protein for food and feed has been plant-based proteins. Microalgae have emerged as an available renewable natural source of protein. More than 70% of the world biomass is the food chain basis for these microalgae. Compounds like protein, carbohydrates, and lipids are produced. In 1960s, Japan started the first commercial cultivation of *Chlorella* [31]. The enrichment of high-value metabolites in microalgae will improve the growth and development of the algal-based food industry, which focuses on the processing and use of microalgae for novel functional food products (Table 2). While it is calculated that between 200,000 and 800,000 microalgae exist in nature, but only a few can be used in human nutrition [32]. An innovative unique concept is microalgae as a source of bulk proteins. Microalgae-based proteins, with many benefits over other protein sources commonly used greatly contributing to satisfy the population and demand for protein. High-quality proteins are produced by *Chlorella* and *Arthrospira*, with both species possessing high content of essential amino acids for human growth and development (EAAs) [33, 34].

Microalgae are the source of many useful compounds in addition to proteins with health advantages, that can improve the nutrition value of dietary supplements [35]. In addition to a good protein source, *Arthrospira*, *Chlorella*, and *Nannochloropsis* have also been identified as major producers of carbohydrates and lipids [36, 37]. GRAS (Generally Recognized as Safe) status is given for *Arthrospira*, *Chlorella*, *Dunaliella*, *Haematococcus*, *Schizochytrium*, *Porphyridium cruentum*, and *Crypthecodinium cohnii* [15]. Some products extracted from microalgae are sold like the phycocyanin blue colorant from *Arthrospira*, DHA from *C. Cohnii*, and β-carotene from *Dunaliella* [38]. Even amongst the numerous forms of microalgae-compounds, some microalgae with powerful antioxidants are possibly the most significant for industrial uses. It is also possible to incorporate milk products with microalgae to provide bioactive compounds [39]. Peptides derived from microalgae have been linked to health-promoting activities in humans. Moreover, high-value metabolites from microalgae also facilitate the growth of the appropriate bacteria [40, 41].

The application of microalgae as food additives would not only deliver nutrient value, but will also assist in improving sustainability issues, considering the increasing population and our modern diet, behaviors, and health. Recent studies demonstrated the use of microalgae in gluten-free bread [42]. Including several amino acids, *Spirulina* contains 70% protein by weight and contains more beta-carotene than that in carrots per unit mass.

Table 1 Companies involved in the industrial production of microalgal food products

Microalgae	Natural habitat	Cultivation conditions	Bioactive compound	Application	Companies involved	References
Chlorella vulgaris	Freshwater	Autotrophic, mixotrophic and heterotrophic mode of growth	Lutein	Dietary supplement, feed	Algae 4 Future (A4F) (Portugal) E.I.D Parry (India) Chlorella Co. (Taiwan) Necton (Portugal)	[17–20]
Spirulina platensis	Freshwater	High alkalinity	Phycocyanin	Food ingredient, food colorant, dietary supplement, fluorescent markers	Algae 4 Future (A4F) (Portugal) E.I.D Parry (India) Chlorella Co. (Taiwan) Necton (Portugal) DIC Lifetec (Japan) Ocean Nutrition (Canada) Wonder Labs (USA)	[17–22]
Chlamydomonas sp.	Freshwater	Mixotrophic and auxotrophic growth	Terpenoids	Pharmaceuticals and cosmetics	Algae 4 Future (A4F) (Portugal)	[17, 23]
Dunaliella salina	Hypersaline water	Halophilic	Beta carotene	Food supplement, food colorant, pharmaceuticals, feed additive	BASF (USA) Wonder Labs (USA) Nikken Sohonsa Co. (Japan) Solzyme Inc. (San Fransisco)	[22, 24–26]
Haematococcus pluvialis	Freshwater	Mesophilic, stress conditions	Astaxanthin	Food supplement, feed additive, antioxidant	Algatech (Israel) E.I.D Parry (India) Blue Biotech (Germany) AstaReal Co. (Japan)	[18, 27–29]
Labosphaera incisa	Freshwater	Mesophilic	Omega 6 fatty acids (Arachidonic acid)	Food supplement, infant formulae	Algae 4 Future (A4F) (Portugal)	[17]
Nannochloropsis sp	Marine	Mesophilic	Omega 3 fatty acids (Eicosapentaenoic acid)	Food supplement, infant formulae, pharmaceuticals, aquaculture	Martek biosciences (USA) Cyanotech (USA)	[30]
Phaeodactylum tricornutum	Marine	Mesophilic	Omega 3 fatty acids (Eicosapentaenoic acid)	Food supplement, antioxidant, colouring agent, feed additive	Algae 4 Future (A4F) (Portugal) Algatech (Israel)	[17, 27]

Spirulina is also rich in nutrients like vitamin B, phycocyanin, chlorophyll, vitamin E, omega 6 fatty acids, and several minerals. Because of these properties, *Spirulina* is reported as the highly consumed microalgae in the world [43]. Because of all these reasons, WHO has labelled *Spirulina* as a ‘super food’ and also considered as a ‘space food’ by the National Aeronautics and Space Administration (NASA). It has been reported that *Spirulina* contains 670% more protein than tofu and 180% more calcium than milk [44]. *Spirulina* is more readily absorbed by the body when consumed in diet and maintains a normal level of nutrients and vitamins in the body. It is also considered as a perfect food for children with malnutrition, pregnant and lactating women. Hainan Simai Enterprising Ltd, located in China is the major producer of *Spirulina* in the world [43] and produces 200 tons of dried biomass per year and accounts for 10% of the global production.

Chlorella is another protein-rich microalga consumed globally. *Chlorella* contains 60% proteins along with other high-value bioactive compounds. Extracts from *Chlorella* biomass showed effective anticancer, antimicrobial, and other health-promoting activities [61]. The protein concentrations of these organisms are three times higher than that of beef. *Chlorella* has been mainly consumed as pills, tablets, and powder. It is also incorporated in many other functional foods like bread, biscuits, noodles, sweets and

Table 2 Role of microalgae in various functional food products

Name of food product	Microalgal species used	Addition	Benefits	References
Biscuit	*Spirulina platensis*	0.3,0.6 and 0.9%	Good sensory and nutritional profiles	[45]
	Spirulina platensis, Chlorella vulgaris, Tetraselmis suecica, Phaeodactylum tricornutum	2 and 6% w/w	High protein, phenolic and antioxidant content	[46]
	Isochrysis galbana	1 and 3% w/w	High color stability and good profile of polyunsaturated fatty acids	[47]
Cookies	*Haematococcus pluvialis*	Astaxanthin powder: 5, 10 and 15% w/w	Lower glycemic response, high phenolic content and antioxidant activity	[48]
	Chlorella vulgaris	0.5,1, 2 and 3% w/w	Increased color, protein and carbohydrate content	[49]
Bread	*Spirulina fusiformis*	1 and 3% w/w	Increased protein content	[50]
	Spirulina platensis	10% w/w	Increased protein, calcium, iron and magnesium content	[51]
	Isochrysis galbana, Tetraselmis suecica, Nannochloropsis gaditana, Scenedesmus almeriensis	0.47% w/w	Change in bread color and green yellow tonalities	[52]
Processed cheese	*Chlorella sp.*	0.5 and 1% w/w	Decreased meltability and hardness, yellowish green color, improved texture	[53]
Yogurt	*Chlorella sp.*	0.25% *Chlorella* powder and 2.5–10% *Chlorella* extract powder	Increased sensory and storage properties	[54]
Frozen yogurt	*Spirulina platensis*	3 g/L	Increased lactic acid production and increased nutritional value of milk. Increased trace elements, vitamins and other bioactive compounds	[41]
Fermented milk	*Spirulina platensis*	0.1–0.8%	Increased survival of acidophilus-bifidus-thermophilus (ABT) starter culture and nutritional quality	[40]
Probiotic fermented milks	*Spirulina platensis* *Chlorella vulgaris*	0.3, 0.5 and 0.8%	Increased viability and sensory characteristics of probiotics	[39]
Vegetarian food gels	*Spirulina* and *Haematococcus*	0.75% w/w	Increased gelling and rheological properties	[55]
	Spirulina maxima and *Diacronema vlkianum*	0.1–1% w/w	Increased PUFA content and favorable texture characteristics	[56]
Pasta	*Chlorella vulgaris* and *Spirulina maxima*	0.5–2% w/w	Increased firmness of pasta, attractive color (orange and green), increased nutritional and sensory qualities	[57]
	Isochrisis galbana and *Diacronema vlikianum*	0.5, 1 and 2% w/w	Increased omega 3 fatty acid content and high resistance of pasta to thermal treatment	[58]
	Spirulina	5, 10, 20 and 100 g w/w	Increased protein content, phenolic content and antioxidant activity	[59]
	Dunaliella salina	1,2 and 3% w/w	Increased protein, iron, calcium, magnesium and potassium content. Increased polyunsaturated and pigment content	[60]

beer. AlgaVia is the major producer of protein and lipid-rich *Chlorella* flour.

Antioxidants derived from microalgae are more effective than other synthetic and plant-based antioxidants. The potential antioxidants derived from microalgae are carotenoids, polyphenols, phycobiliproteins, and vitamins [62]. Vitamin C is regarded as the major antioxidants produced in chloroplast and is found abundantly in *Dunaliella, Chlorella, Chaetoceros* and *Skeletonema* [63]. In microalgae, the accumulation of antioxidants occurs during their cultivation in closed photoreactors as a mechanism to prevent cell damage. Antioxidant activities of microalgal extracts are getting more attractive in functional foods and also in beverages.

Microalgae can be considered a natural source of food colorants due to the abundance of photosynthetic pigments present in it; hence, it is widely used as food coloring agents. Pigments derived from microalgae also have neuroprotective, anti-oxidant and hepatoprotective effects and it is used in nutraceutical, pharmaceutical, cosmetic and aquaculture industries. In Brazil, chlorophyll extracted from *Spirulina* have been used as a natural colorant in food industry. In poultry feed, consumption of *Chlorella vulgaris* increases the pigmentation of egg yolk [64]. *Dunaliella* contains a high amount of beta carotene and it is more readily absorbed in the body when compared to synthetic pigments. Powder from *Dunaliella* biomass is commonly used as food and feed additives [2]. In comparison to other medicinal properties, β-carotene naturally occurs with its all-trans, 9-cis, 13-cis, and 15-cis isomers [65] Consumption of microalgae rich in astaxanthin by fish increase the red color of the flesh and contains high amounts of vitamin E because of its antioxidant activities. *Haematococcus pluvialis* is the major producer of astaxanthin.

Microalgal lipids are high-value energy-rich compounds with many health benefits. Omega 3 fatty acids are long chain polyunsaturated fatty acids (LC-PUFAs) which have important roles in brain development, memory and learning. Docosahexaenoic acid (DHA) and Eicosapentaenoic acid (EPA) are two major omega 3 fatty acids derived from microalgae. Currently fish and fish-derived oils are considered as the major sources of omega 3 fatty acids, but microalgae are the primary producers of these fatty acids in the aquatic ecosystem. Fish derived essential fatty acids have many practical disadvantages and it contains toxic contaminants like mercury. Microalgae can be considered as ecofriendly and safe sources of DHA and EPA. DHA oil from microalgae is used in pharmaceuticals, infant formulas, baby food and dietary supplements due to its health-promoting effects [14]. Martek, USA is the major producer of DHA from *C.cohnii* in the form of a single cell oil DHASCO [2]. *Nannochloropsis* is the potential candidate for EPA production with emerging industrial applications. It is an edible microalga which can be used in functional food and in animal feeds. EPA productivity of *Nannochloropsis* is highly dependent on cultivation conditions and researchers are focused to enrich EPA productivity of *Nannochloropsis* in an ecofriendly and cost-effective manner [2, 11, 12, 62]. *Phaeodactylum tricornutum* is also considered for commercial production of EPA. DHA rich *Isochrysis galbana* have been incorporated into biscuits for enhancing its nutrient profile [66]. Hens consuming omega 3 fatty acid enriched microalgae have been reported to enhance the polyunsaturated fatty acid content in their egg yolks and is commercially profitable [62].

Concerns associated with microalgal food industry

Application of microalgae either as a direct food supplement or constituents in food products and dietary supplements are still in conflict because of the industrial, regulatory and nutritional considerations [67]. The factors taken into consideration while using microalgae in the food industry are digestion and bioavailability, metal toxicity, allergenicity, toxic secondary metabolites, and synthetic compounds, cyanotoxins, radioisotopes, contamination of biomass with pathogens, and safety and regulatory issues [35]

Digestibility and bioavailability

Bioavailability can be defined as the combination of bioactivity and bio-accessibility. Bioactivity is the process of uptake of nutrients into the tissues, its physiological effects, and subsequent metabolism. The term bio-accessibility refers to the transport of nutrients across the digestive epithelium, release of food constituents from the matrix, and the major changes occurred during the digestion process [68]. Most available research works are focused on the short-term in vitro experiments for studying the bioactivity of algal foods in which the clear idea of the food value of algal nutrients and its composition is limited. Mainly the fate and behavior of the food components and nutrients from the algae in the gut is not clearly studied. Also, the data on the biological effects of algal nutrients on the dietary intake and bioactivity of the gut microbiota are lacking. Therefore, it is indeed necessary to study the digestion and transformation of microalgae and its subsequent nutrients in the human system.

The process of digestion starts in the mouth with the help of salivary amylase. However, the role of saliva from humans on microalgae and its bioactive metabolites were not clearly studied. Unlike the ruminants, humans lack the enzymes to digest polysaccharides in cellulose and hemicellulose and the undigested material is called as dietary fiber. These materials will be moved to the large intestine. Cian et al. [73] reported that the carbohydrate and proteins from algae that is not processed completely in the small intestine stimulate the immune responses in humans indirectly by enhancing the responses gut microbiota [69]. Duffy et al. [74] showed important health benefits of microalgal-derived foods on bacterial fermentation and digestion [70].

The capacity of gut microbiomes is not similar in all humans and the fermentation of consumed algal polysaccharides will be different in humans from different countries. In Japanese people, the presence of enzymes that degrade polysaccharides was reported in the *Bacteroides plebeius* which is absent in Americans [71]. The presence of these enzymes is the result of the horizontal gene transfer (HGT) from a marine bacterium *Zobellia galactinvorans* which is reported to present in the surface of the edible red seaweed 'nori' [72]. Thomas et al., in 2012 reported HGT as the reason specific gene cluster present in the gut microbiota which helps in the digestion of alginates from brown algae [73]. Moreover, a study conducted in Spanish people also shows the presence of gut microbes with the enzymes porphyranases and agarose 4-glycanohydrolase (agarases) [71]. These differences clearly show the different dietary history, food practices, and gut microbiota which makes the digestibility and bioavailability of food and dietary products from algae more complex [74, 75]. Therefore, it is very important to understand the bioavailability of nutrients and functional foods from microalgae.

Similar to plants, microalgae have a very complex cell wall structure and the components are very difficult to degrade. Hence, bioavailability studies have a crucial role to understand the processing and absorption of metabolites and components from food materials. It is also important to study the host and microbiome co-metabolism in the intestine together with the study of the degree of fermentation in the gut [35]. Vast literature is available on microalgae and macroalgae-derived nutraceuticals and functional foods [2]. But there, quantitative analysis on human health and metabolism is still unknown. The traditional analytical approaches provide less information about the interaction and regulation of microbial flora and its fermentation mechanisms. The complexity and nature of algal cell wall, presence of soluble fibers, altered metabolite and biomass composition based on the harvest season, changes in metabolite profiles during environmental variations, differences in food preparation and biomass processing methods, anthropogenic factors, etc. significantly contribute to the bioavailability of nutrients and functional foods from algae [76]. Future studies using improved molecular and genetic methods, xenobiotic animal models, studies of enhanced gastrointestinal digestion, etc. will give new insights on how the bioactive compounds derived from algae currently used in food industries and its bioavailability in humans and other animal models.

Heavy metal toxicity

The microalgal high-value metabolite synthesis can be improved by the uptake of metals but the excessive uptake will cause heavy metal toxicity. There is a conflict in using microalgae as a food source due to the heavy metal uptake for their growth and metabolite production. However, the information on how algal metals are bioactive or bio-accessible in human digestion is lacking and there are no proper quantification approaches available to study the bioavailability of metals.

Continuous exposure to the inorganic forms of arsenic (iAs) such as arsenite (As III), arsenate (As V) increases the chances of different types of cancers such as lung, urinary tract and skin cancers [77]. iAs is present in all types of seafood's and they enter into the cells with the help of aquaporins and phosphate transporters [78]. According to the guidelines of WHO, the permissible concentration of inorganic As in potable water is 10 $\mu g\ L^{-1}$ [79]. Over 50 types of As were identified in marine food products but the exact As content in marine foods cannot be used to calculate the potential health impacts on humans because aquatic organisms possess efficient systems to detoxify iAs to nontoxic forms [80]. Fish and mollusks convert iAS to arsenobetaine which after consumption by humans excreted as arsenobetaine which is not toxic [80].

Algae convert iAs to arsenosugars, and when there is a deficiency of phosphate, iAs again converted into As-phospholipids which helps in the function of the algal cell wall membrane [81]. Dimethylarsinic acid (DMA) is the major type of algal arsenosugars found in humans and listed as potential carcinogenic agents by IARC 2012 [77]. Raml et al. [81] reported that invitro trials using human HepG2 cell lines resulted in DMA toxicity at testing levels higher than that normally found in the urine [82]. However, algae (micro and macroalgae) are capable of accumulating As in comparison with other aquatic organisms [83]. Higher accumulation of As by algal cells will cause toxicity to food products derived from algae and will be a serious threat to human health. Brown macroalgae such as *Laminaria sp*. and *Sargassum sp.* are reported to contain a significant amount of iAS in their cells [84, 85]. Studies conducted by Nakamura et al. (2008), showed that, the uncooked sea weed *Sargassum fusiforme* (also known as hijiki) contains high levels of iAS (60 $\mu g\ g^{-1}$ dry wt) in comparison to the cooked hijiki (0–4-2.8 $\mu g\ g^{-1}$ [86]. The major concerns regarding the toxicity of As to humans are the major form of As in the dietary supplement, metabolism of As in specific individuals and the bioavailability of As on cooking [86, 87]. Nakamura et al. (2008) showed that the consumption of iAS at higher levels would increase the susceptibility to skin cancers [88]. Huang et al. [89] reported 3.5–291 g/L of As pollution in a group of *Mozambique Tilapia* fish in Taiwan, which causes the accumulation of iAs in humans via consumption of these fish [89]. Ground water and fertilizers are the two important routes through which As is accumulated in the edible microalgae *Spirulina platensis* [90]. In addition to this, eutrophication and increasing concentrations of As due to different industrial and human activities in the water environment also leads to the higher accumulation of As by algae and subsequent toxicity of algal-derived food products. But there are only limited reports are available about the toxicity of As in microalgal food products and its negative effects on human health. Wang et al. [91] reported that supplementation of 150 g/L of As in the cultivation medium of *Spirulina platensis* exceeded the normal reference range (1.0 mg/kg) proposed by the National Standard of Health Functional Food Products in China [91]. They had also reported that the higher risk of As contamination can be reduced by the addition of phosphorous to the cultivation medium.

Bromine (Br) toxicity is also a major problem associated with the intake of foods derived from algae. But its toxic effects on human health is not well recognized. Boyer et al. [92] reported that excessive intake of Br can create many health problems [92]. In countries like China, Korea, and Japan, excessive seafood intake including macroalgae have shown to increase the Br concentrations of human female subjects [93]. However, future research should be carried out to study the risk of heavy metal toxicity in algal food products and developing strategies to eliminate the threats to humans and animals on the consumption of algae. Experiments in terms of all aspects are indeed necessary specifically beyond toxicity tests of in vitro cell cultures and moving on to animal studies to identify the risk of consuming the micro or macroalgae-derived food products.

Allergic reactions and toxicity from algal food products

Relatively less information is available on the allergic reactions of algae and related functional food products. Le et al. [94], reported the anaphylactic reaction for the first time in a 17-year-old male after the intake of *a* tablet containing *Spirulina* [94]. He had developed symptoms of tingling of lips, angioedema of the face, nausea, abdominal pain, wheezing, rashes on arms and trunks, and breathing difficulties after ingestion of 300 mg *Spirulina* tablet. However, the original details of the *Spirulina* and its purity were not mentioned in the tablet. Consumption of native *Spirulina* with *Microcystis* and other toxin-producing blue-green algae caused toxicity in humans. 'Whole algalin protein' (wap) produced from edible microalgae *Chlorella protothecoides* by the company Solazyme, Inc. was shown to cause allergies in tested animal models [95]. Kainic acid, a type of amino acid which is structurally similar to glutamate can act as neurotransmitters in the brain. The red algae *Palmaria palmata* (dulse) and *Digenia simplex* were reported to produce kainic acid. Kainic acid at higher concentrations is neurotoxic, which is often used to make disease models in experimental animals [35]. Safety standards are not available for humans regarding the consumption of kainic acid [96]. Blue-green algae supplements (BGAS) are widely sold in markets due to their health benefits like weight loss, detoxification, enhanced energy, immunity etc. [97]. BGAS are available in the form of powders, capsules and pills which are natural in origin and considered as safe. However, the negative effects of BGAS are also reported which include nausea, diarrhea, vomiting, gastrointestinal disturbances etc. Moreover, presence of cyanotoxins is reported in some BGAS products. Even though, *Spirulina* is considered nontoxic edible microalgae, traces of dihydrohomoanatoxin-a and epoxyanatoxin-a have been reported in some of the *Spirulina*-based BGAS [98]. Figure 2, shows the side effects of different types of cyanobacterial toxins on human health. Iwasa et al. [99] reported that consumption of *Spirulina*-associated BGAS can cause liver damage in middle-aged people in Japan [99]. BGAS often reported to contain traces of microcystins (MCs) which are toxic to humans [100]. Due to the public concerns regarding the side effects of BGAS, more cautionary statements have been amended regarding the certification of such products in markets. In USA, the tolerable daily intake (TDI) of BGAS is at the level of 1 μg MCeq g^{-1} and Switzerland allows the daily consumption of 2 μg MC L^{-1} for adults and subsequent lower amounts for infants and children's [101]. Based on the average body weight i.e., infants (5 kg), children (20 kg) and adults (50 kg) can tolerate a maximum consumption of 0.2. 0.8 and 2.4 μg MCs per day respectively [102].

Algal toxins are also reported to cause different poisoning symptoms such as paralytic shellfish poisoning (PSP), amnesic shellfish poisoning (ASP), neurotoxic shellfish poisoning (NSP), diarrhic shellfish poisoning (DSP) etc. which can cause negative effects on human health (Table 3) [103].

Applications of microalgae in cosmetics

The major advantage of microalgae being used in cosmetic industries is their capacity to regenerate and adaptation under adverse environmental conditions by counteracting the cell-damaging activities and prevention of free radical formation. These abilities of microalgae are used in cosmetics industries to replace synthetic products with negative effects on the skin. In cosmetics, microalgae can either directly use or can be used based on the activity of bioactive compounds. Microalgae have been used in hair care products, products used for regeneration, anti-aging and peelers for skin irritation [115]. *Arthrospira* and *Chlorella* have been used in sunscreen creams and lotions. Major algae used in the

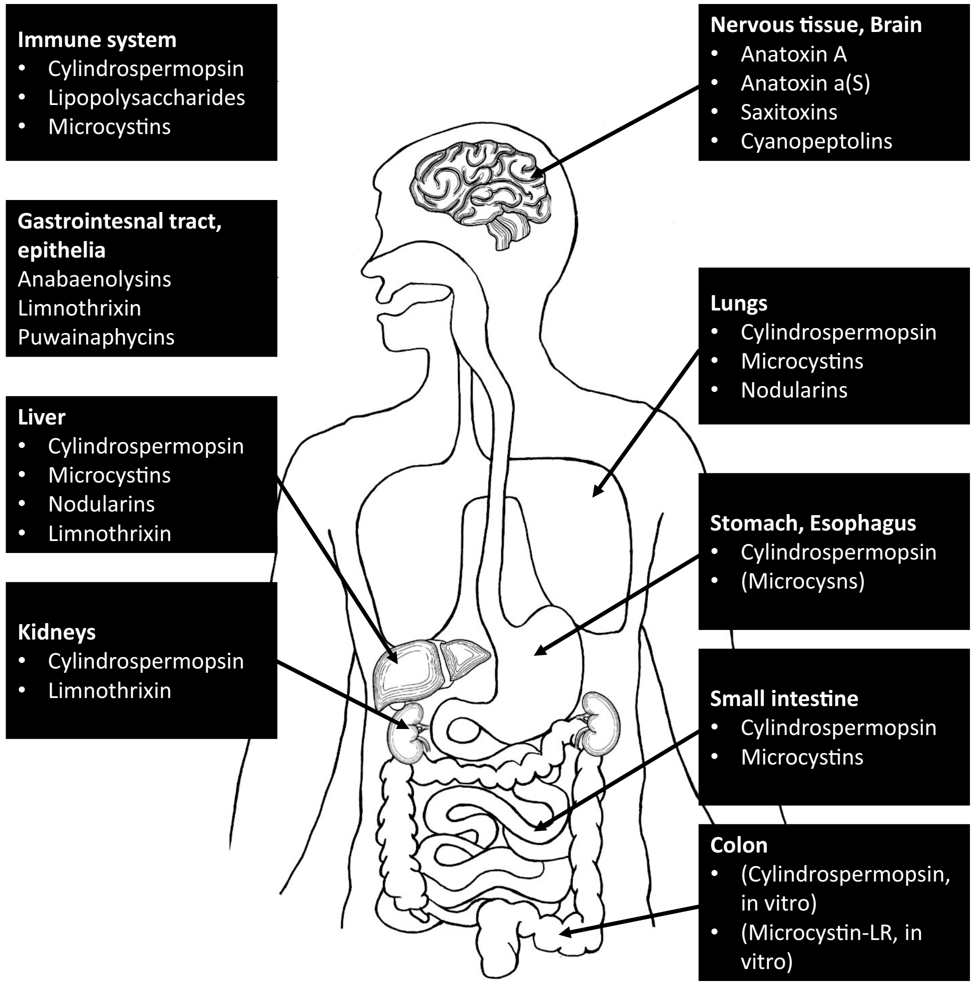

Fig. 2 Health problems associated with consumption of cyanobacterial toxins

production of cosmetics are *Arthrospira, Chlorella, Nannochloropsis, Dunaliella, Spirulina, Anacystis, Ascophyllum, Alaria, Chondrus, Mastocarpus* etc. [116]. These algae help to prevent wrinkle formation, enhances collagen synthesis and also helps to reduce vascular imperfections (Table 3). Ocean Pharma company in Germany produced a skin care product from the extracts of microalgae named 'Skinicer' for preventing aging of the skin. Pepha Tight produced by Pentapharma (Switzerland), using extracts of marine microalgae *Nannochloropsis* also used to maintain the youthful properties of the skin. Phytomer company in France used extracts of *Chlorella vulgaris* for improving natural protection of skin. The cosmetics industry uses extracts from microalgae which are high in pigments, PUFAs, phycobiliproteins and carbohydrates which can be used to make lotions, creams and ointments [116]. Mycosporine like amino acids (MAAs) are small natural molecules synthesized by marine microbes as an adaptation for their high sunlight environments. MAAs have good antioxidant properties. MAAs produced from *Dunaliella, Spiruluna* and *Chlorella* have the potential to incorporate into sunscreens to reduce the damage induced by ultraviolet rays [2]. Microalgae *Odontella aurita* also showed potential free radical scavenging activity to maintain youthful skin [117] (Table 4).

Therapeutic applications

Microalgae are rich in metabolites such as beta-carotene, astaxanthin, eicosapentaenoic acid, polyphenols, terpenoids etc. promoting their role in the pharmaceutical industry [118, 119]. These microalgal metabolites and pigments have gained the attention of researchers and scientists for their potential in pharmaceutical and therapeutic uses. Recently, the development of genomic and transcriptomic analysis for the improved microalgal bioactive compound production with the help of genetic engineering tools has been considered as an emerging field of research [120]. Microalgae are also known to synthesize immunological proteins, such as monoclonal antibodies and either accumulate them in their cytoplasm or release in surrounding media [121].

Table 3 Potential toxins from cyanobacteria and its short term and long-term effects on human health

Toxin	Producer	Short term health effects	Long term health effects	References
Microcystins	*Microcystis, Anabaena, Planktothrix* *Nostoc* *Oscillatoria* *Anabaenopsis*	Gastrointestinal (GI) disorders, liver inflammation, hemorrhage, pneumonia, skin irritation and blistering, fever and flu-like symptoms, atypical pneumonia	Tumor promoter and liver failure leading to death	[104, 105]
Nodularins	*Nodularia*	GI disorders, liver inflammation, hemorrhage, pneumonia, dermatitis	Cancer and liver damage leading to death	[106]
Saxitoxins	Dinoflagellates: *Protogonyaulux* *Alexandrium,* *Gymnodinium,* *Pyrodinium,* Cyanobacteria: *Anabaena,* *Aphanizomenon* *Cylindrospermopsis* *Lyngbya*	Paralytic shell fish poisoning (PSP), sometimes lead to temporary blindness	Long term health effects are unknown	[107]
Anatoxins	*Anabaena,* *Aphanizomenon* *Cylindrospermopsis* *Lyngbya* *Plantothrix, Oscillatoria,* *Microcystis*	Skin irritations, speaking difficulties, lung disorders	Paralysis, tremors, convulsions and cardiac arrhythmia leading to death	[108]
Cylindrospermopsins	*Cylindrospermopsis* *Aphanizomenon* *Umezakia* *Raphidiopsis* *Anabaena*	GI disorders, liver inflammation, hemorrhage, pneumonia, dermatitis	Malaise, Cancer, anorexia and liver damage leading to death	[109]
Lipopolysaccharides (LPS)	*Anacystis* *Anabaena* *Spirulina* *Microcystis* *Oscillatoria* *Phormidium* *Schizothrix*	Skin rashes, gastrointestinal, respiratory and allergic reactions	Long term health effects are unknown	[110]
Beta methyl amino alanines (BMAAs)	*Limnothrix, Daphnia Magna* *Aphanizomenon*	Damage to neurons	Potential link to neurodegenerative disorders like Alzheimer's and Parkinson's	[111, 112]
Aplysiatoxins	*Lyngbya* *Schizothrix* *Oscillatoria*	Dermatitis	Cancer	[113]
Lyngbyatoxin	*Lyngbya*	Skin and GI tract disorders		[114]

Pharmaceutical proteins production by microalgae

Expression of human CL4 monoclonal antibody (mAb) was carried out with *P. tricornutum* and was evaluated in vitro against the targeted hepatitis B surface antigens [122]. The produced mAb was also found to bind to the Fcγ receptors in humans, as confirmed by cellular binding and surface plasmon resonance assays [123]. *P. tricornutum* has also been used for the expression of recombinant mAb against Marburg virus (MARV) which is pathogenic to humans. Various analysis has confirmed the efficient expression, secretion into medium and functioning of the recombinant mAb against MARV [124]. Microalgae lack the machinery for N-glycosylation and it has been also explored for the production of immunoglobulin A (IgA) mAb in *C. reinhardtii* for countering glycoprotein D of herpes simplex virus [125]. Positive organization of human IgG1 has been performed in the *Chlamydomonas reinhardtii* against *Bacillus anthracis* antigen PA83 wherein the antigen was successfully targeted by the assembled mAb both in cell lines and in animal models [126].

Immunotoxins or toxin-conjugated Abs are hybrid proteins that are made by the chemical or genetic conjugation of antibody fragments with eukaryotic toxins [127, 128]. Microalgae are also able to produce immunotoxins using specific mechanisms. These toxin conjugated Abs approach specific tumor cells, release the toxins, and trigger apoptosis by hindering the translation mechanism of the target cells [129]. *C. reinhardtii* chloroplast has been used for the production of a single-chain variable fragment against the CD22 antigen of B-cell surface receptor of exotoxin A from *Pseudomonas aeruginosa*. To increase the half- life of this immunotoxin in serum, human IgG1 domains were assembled between αCD22 and PE40 followed by the expression of the resultant construct into *C. reinhardtii* chloroplast, therefore providing a more stable and functionally efficient immunotoxin [130, 131]. The treatment of live cell lines of Burkitts lymphoma with variable concentrations of different immunotoxins was conducted to study the lethality of immunotoxins expressed in microalgae [131]. The outcome suggested the potential inhibition of proliferation of CA-46 and Ramos cells by αCD22PE40 and αCD22CH32PE40 molecules whereas without the PE40 toxin αCD22 was unable to restrict the proliferating B or T cells. Moreover, subcutaneous injection of αCD22PE40 and αCD22CH23PE40 inhibited tumor propagation in mice models [131].

Erythropoietin from humans had been successfully expressed in the nuclear region of *C. reinhardtii* with the activity of *hsp70A/rbcS2* [132]. Almost 8 times increase in cell number of Nb2-11 rat lymphoma cell line was observed after 4 days when treated with about 100 ng HGH from the cell extract of modified *C. reinhardtii* [133]. Trypsin-modulating oostatic factor (TMOF) is a hormone produced in mosquito which can restrict trypsin biosynthesis in the organisms' gut. *Chlorella desiccata* with the expression of TMOF can prove to be a lethal tool for mosquito larvae since these microalgae are a food source for the larvae [134]. The control of the mosquito population by the use of such transgenic microalgae can be considered as an efficient method to control the spread of fatal diseases transmitted by mosquitoes, such as malaria, dengue and yellow fever in a cost-efficient manner. *Chlamydomonas* has been used as a candidate for the successful expression of the Human immuno virus (HIV) protein. Although the effectiveness of the recombinant protein was not evaluated but it has presented opportunities for the development of a microalgae-based oral vaccine for AIDS [135]. Another novel idea towards the development of an edible vaccine against infectious bursal disease (IBD) was introduced when IBD virus protein VP2 (a strong IBD vaccine candidate) was successfully expressed into *Chlorella pyrenoidosa,* an edible microalga [136].

Polyphenols are a class of metabolites investigated therapeutic role in diseases, such as diabetes, hyperlipidemia, hypertension and even cancer [137, 138]. Polyphenols obtained from marine algae are hydrophilic and polar compounds with molecular weight in the range 162 Da to 650 kDa [139]. Another type of polyphenol is bromophenol, known for their antidiabetic effects. Marine algae from Rhodomelaceae family are a major source of these polyphenols. CYC27 is a synthetic marine bromophenol derivative extracted from red alga *Rhodomela confervoides.* CYC27 imparts antidiabetic effects by controlling triglyceride and cholesterol levels in serum, enhancing insulin sensitivity, and promoting phosphorylation of RNA binding proteins [140]. Similar inhibitory effects on serum triglyceride, cholesterol, and plasma glucose levels are dissplayed by bromophenol analogue extracted from red alga [141]. HPN inhibits PTP1B which is a negative regulator and a potential therapeutic target of insulin signaling pathway (Table 5).

Microalgal polysaccharides contain high quantity of dietary fibers which, if consumed, helps in the prevention of many disease conditions [142]. Alginate is a well-known algal polysaccharide which aids in obesity control and reduces the absorption of nutrients through gut thereby reducing energy intake and promoting satiation [143]. Fucoidan, a derivative of fucan (sulfated polysaccharides), is an algal polysaccharide which reportedly has potential applications in glycemia and lipedema prevention [144]. Fucoidan and alginate are also utilized for encapsulation and delivery of drugs, such as insulin [145]. Another group of therapeutic metabolites produced by microalgae are terpenoids, for e.g., Fucoxanthin, known for its anti-oxidant and anti-obesity properties. Restricted accumulation of adipose tissues, regulation of lipid metabolism, and enhanced insulin sensitivity are some other functions of Fucoxanthin [146]. Fatty acids extracted from microalgae shows therapeutic potential by increasing insulin sensitivity and other health promoting effects [147, 148]. Alkaloids from *S. thunbergii* inhibit the accumulation of lipid by suppressing SREBP-1c, PPARγ C/EBPα expression [149].

Microalgae as animal feed

Many studies are available regarding the utilization of different types of microalgae as animal feed. Ever since the population of meat consumers has relatively increased, there has been an increasing need to develop and maintain livestock to obtain improved quality and quantity of meat. The market for meat is constantly growing and the vegetarians now contribute to only about 21.8% of the world population [150, 151]. So, to meet the rising meat demands, microalgae are now being used as animal feed resulting in improvement in the quality (in some cases quantity as well) of the meat. It has been reported that out of the total microalgae biomass

Table 4 Production of cosmetics from microalgae and their major skincare products and activities [2, 116–118]

Organism	Major producers	Products	Activity
Spirulina	Optimum Derma Acidate, (ODA, Britain), Ferenes cosmetics	Skin whitening facial mask, Algae mask	Improves moisture balance of skin, immunity, complexion and reduce wrinkles
Spirulina maxima	Ocean Pharma (Germany)	Skinicer	Skin regeneration and natural Protection
Chlorella vulgaris	Phytomer (France)	Phytomer	Strengthens skins natural protection and neutralizes inflammation
Nannochloropsis oculata	Pentapharm Ltd (Switzerland)	Pepha-Tight	Improves skin tightening properties
Dunaliella salina	Pentapharm Ltd (Switzerland)	Pepta-Ctive	Stimulates skin proliferation and energy metabolism of skin
Anacystis nidulans	Estee Lauder (USA) Solazyme (France)	Photosomes Algenist	Improves skin immunity and sun protection
Spirulina platensis	Exsymol S.A.M (Monaco) Sanatur GmbH (Germany)	Protulines	Prevents early skin ageing and wrinkle formation

Table 5 Potential applications of microalgae in aquaculture and associated health benefits

Microalgal species	Bioactive compound	Fish	Improved characteristics in fish	Health benefits	References
Thraustochytrium sp.	EPA and DHA	Catfish, Atlantic salmon, Pacific white shrimp	Increased growth rate, weight gain and flesh quality	Improved immune system and disease resistance	[177, 178]
Chlorella sp.	Astaxanthin, omega 3 fatty acids	Freshwater prawns	Increased nutritional profile	Increased antioxidant activity	[179, 180]
Spirulina platensis	Protein, Vitamin, Phycocyanin	Tilapia, Carp, Yellow tail cichlid, Rainbow trout	Increased growth and survival rate	Improved immune system, antioxidant activity and disease resistance	[181]
Nannochloropsis sp.	EPA	Tilapia, Pacific white shrimp, Rainbow trout	Increased growth, high digestibility	Immunomodulatory effects, brain and eye health	[182, 183]
Phaeodactylum tricornutum	Protein	Atlantic salmon	Improved growth performance, nutrient profile and digestibility	Improved intestinal absorption and immunity	[184]
Tetraselmis chuii	Protein	Shrimp	Improved antioxidant activity	Enhanced antioxidant activity	[185]

produced, about 30% is used as animal feed or in animal feed preparations [152]. Various species of microalgae, such as *Schizochytrium, Chlorella, Arthrospira, Isochrysis, Porphyridium*, *Pavlova* and *Nannochloropsis* have been either utilized as feed or supplemented in animal feed [153]. The fatty acids, pigments, and other metabolites from microalgae can ameliorate the feed and enhance the physical and chemical characteristics of the meat including its colour and antioxidant properties. Consumption of microalgae as/in the feed also elevates animal physiology [33, 154]. *Arthrospira platensis* (*Spirulina*) is a blue-green microalga frequently used in feed supplements for both humans and animals. It is rich in nutrients, such as β- carotene, vitamins B-complex and E, proteins and is highly digestible to the low carbohydrate content, making it a suitable supplement or feed for livestock [155, 156].

Feed for cattle

An increase in omega 3 fatty acids in milk is observed on feeding dairy cattle with lipid encapsulated microalgal supplements, with no negative impact on the yield of milk [157]. Supplementation with about 10 g algae per kg of dry matter feed for dairy cows reduced the content of milk fat and positively altered the fatty acid composition causing increased conjugated linolenic acid (CLA) and DHA concentrations [158]. Lipid encapsulation of microalgae averts dehydrogenation in cattle rumen [157]. Consumption of microalgae supplemented rapeseed feed by lactating cows resulted in an increase in milk yield and energy content along with higher concentrations of protein and lactose [159]. However, contradictory results were observed on feeding Holstein cows fed with microalgal biomass [158]. Increase in milk yield and energy content with more lactose and proteins was also observed when lactating Damascus goats fed with microalgae [160]. Change in fatty acid composition with increase in omega-3 fatty acids had been observed in goats and their milk with microalgae feed [161].

More microbial protein and branched fatty acids were observed in the rumen of *Bos indicus* when the cattle fed on tropical grasses supplemented with *Spirulina platensis* and *Chlorella pyrenoidosa* [162]. Use of *Spirulina* as feed supplement for different breeds of Australian sheep resulted in the growth and increase in body weight along with an overall improved physiology of the sheep [163]. Anti-inflammatory properties depending upon the fed dose were shown by *Dunaliella tertiolecta* when sheep was fed with it [164]. Feed intake in cattle and other bovine may also reduce by the consumption feed supplemented with microalgae [165].

Feed for poultry and pigs

Red algae, such as *Porphyra, Gracilaria, Kappaphycus* and brown algae like *Laminaria, Undaria* and *Hizikia fusiforme* are traditionally used as food supplements for humans and show potential to be used as animal feed too owing to their rich nutritional profile. Live weight of pigs revealed an increment of up to 10% on feeding upon diet supplemented with *Laminaria digitata* [166]. The supplementation of chicken feed with red microalgae *Porphyridium sp.* carotenoid content which is evident from the darker color of egg yolk along with about 10% reduction in cholesterol content of the yolk [167]. However, the use of a high concentration of microalgae in feed for a long time can impart negative effects especially on the skin color and egg yolk of poultry animals [152]. More weight gain and feed efficiency with reduced intake were observed in broiler chickens while reduced feed intake and higher feed efficiency along with 7% decrease in body weight and 13% reduction in average daily weight gain was observed in pigs feeding upon *Desmodesmus sp.* supplemented diet [168]. An increase in DHA and EPA content in chicken egg has been reported at wash out duration with the feeding of *Nannochloropsis gaditana* at 5% and 10% concentration [169, 170]. Green microalgae *Nannochloropsis oceanica* with removed fat content showed slight stimulation of protein synthesis in muscles and liver of broiler chickens [171]. When fed to anaemic pigs, these defatted *Nannochloropsis oceanica* biomass increased haemoglobin in blood and enhanced growth [172].

Microalgae in aquaculture

Microalgae are considered as potential candidates in aquaculture to increase the nutritional value of fish to induce specific biological activities. Microalgae are important in the nutrition of fish larvae during the developmental stages [173]. Diets rich with microalgae have the ability to fulfill the nutritional needs for growth, metabolism and reproduction of bivalve mollusks [174]. Bivalve shellfish cannot synthesize omega 3 fatty acids as their own, therefore is necessary for bivalve shellfish to consume essential omega 3 fatty acids for proper growth. The commonly used microalgal species in aquaculture are *Tetraselmis, Chlorella, Isochrysis, Pavlova, Chaetoceros, Thalassiosira, Nannochloropsis, Phaeodactylum* etc. [43, 175]. For use in aquaculture, microalgae should fulfill certain parameters like no toxicity to the fish species, high nutritional content, proper size, readily available cell wall etc. for easy digestibility [176]. High protein, essential fatty acids and vitamin content are also important parameter for using microalgae in aquaculture. In aquaculture, bioactive compounds from microalgae can be divided into three classes. First class includes the use of carbohydrate and protein-rich microalgae to replace the traditional feed which can reduce the aquaculture cost. In the second class, antioxidant-rich microalgae were used to increase the immunity of aquatic organisms and thereby overcoming the side effects of antibiotics usage. Third class used for the enhancement of growth of ornamental or special fish. Astaxanthin-rich microalgae were used to increase the flesh and fish color in the salmon culturing industry.

Microalgae as fertilizers

Biofertilizers are the substances that facilitate nutrient availability and uptake by plants. They not only promote plant growth but also prevent entry and invasion by pathogen and pests as well as aid in the decomposition of organic residues. Microalgal metabolites can be efficiently used to produce biofertilizers/biostimulants, which promote the growth and metabolism of higher plants [186, 187]. Chemical fertilizers that are traditionally used to improve plant growth are among the major contributor to soil and water pollution. The aim of pollution reduction along with the fulfillment of global food demand has led to huge support in favor of biostimulants and biofertilizers as a cleaner and sustainable alternative in agriculture. They are safer and cleaner alternatives as they are biodegradable and non-toxic. Biostimulant activity is shown by phytohormones, such as indole acetic acid, gibberellic acid, cytokinins, abscisic acid, and others which are synthesized by microalgae like *Nannochloropsis sp., Chlorella sp.,* *Scenedesmus sp.* etc. [186]. Biofertilizers derived from microalgae should conserve the stimulants present in the biomass and should satisfy the market parameters and nutrient transport [188].

Biofertilizers are generally produced by chemical hydrolysis or enzymatic method. Acidic hydrolysis of biomass produces biofertilizer but the end product quality is not up to the mark. The enzymatic method is better in terms of quality of the final product if an efficient cell disruption method is employed such that no biomass residues remain in the end product. Production of microalgae-based biofertilizers by enzymatic method requires adequate knowledge and selection of enzymes and operating parameters along with the quality control of the final product as per the stated regulations.

Cyanobacteria promote the soil characteristics in terms of organic content, nitrogen enrichment, soil moisture, helps in the aggregation of soil particles, phosphates, etc. [189]. Cyanobacteria helps to increase the humus content in the soil and will be helpful for the growth of plants by facilitating proper mixing with soil. Cyanobacteria also helps to fix nitrogen in the soil and thereby promoting plant growth by transporting organic and inorganic nutrients from the soil. Natural and anthropogenic activities cause the degradation of biological soil crusts. Recovery process from the crusts may take a longer time but it can be reduced by inoculation of cyanobacteria.

Currently, organic fertilizers for small-scale farmers have become a problem of economic instability and for solving this issue many biological approaches and technologies play a crucial role which lowers the cost and helps to improve the fertility of the soil. Cyanobacteria are considered as a very good example of a source of organic biofertilizer which contains naturally occurring ingredients.

Apart from cyanobacteria with heterocysts, unicellular non-heterocystous cyanobacteria such as, *Aphanothece*, *Gloeocaosa*, *Oscillatoria*, and *Plectonema* has also reported which can be used as biofertilizer [190]. For the optimum nitrogen fixation process, an inadequate supply of oxygen and dark light is not favorable. Blue-green algae with heterocysts will have light-dependent nitrogenase enzyme activity and also helps to fix atmospheric N_2 [190].

Some countries like Vietnam, China, and India use cyanobacteria in the soil as an alternative source of nitrogen for rice cultivation. Apart from nitrogen, it is also responsible for the availability of phosphorus to the crop and plants, because it solubilizes the insoluble form of phosphate [191]. The growth and metabolism of crops get enhanced by the use of the combination of growth-promoting bacteria, cyanobacteria. It also regulates the concentration of the micronutrients as well as nitrogen, phosphorus, and potassium content in grains [189].

Conclusion and future perspectives

There are several drawbacks of using microalgae large-scale industrial applications. Harvesting of microalgae in larger scale has several practical limitations. Moreover, there are chances of bacterial contamination in microalgal culture in open cultivation systems. Such bacteria can be toxic which affects the growth and survival of aquatic organisms. Therefore, it is indeed necessary to address the challenges regarding biomass safety, economic viability and harvesting methods to facilitate the industrialization of microalgae-based aquaculture. It is also necessary to study the life cycle analysis and economic performance of using microalgae as aquaculture feed in a natural environment. Therefore, it is very necessary to study further on the economic and lifecycle analysis as well as the cultivation of microalgae in a cost-effective manner for future applications. There is indeed a wide range of applications of microalgae in biotechnology. In terms of nutritional value, microalgal high-value metabolites are on-demand but commercial development is still on early stages due to high production costs, technical difficulties in downstream processing, and sensory and palatability problems during the development of functional foods. Microalgal nutraceuticals and pharmaceutical production industries are facing many practical difficulties in terms of successful biomass and product development in a cost effective manner. The major problem associated with commercial microalgal production is low biomass production. Methods involving mixotrophic cultivation, use of cheap low carbon sources, industrial and municipal wastewater as cultivation medium, and growth-promoting substances can be used to achieve high biomass production. With the development of efficient large-scale cultivation systems, microalgal biotechnology can satisfy the challenging requirements of food, feed, nutraceuticals, pharmaceuticals, and biofertilizers. Due to increasing population rates and emerging of new diseases, the general nutritional needs for the society are continuously increasing which can be satisfied by microalgae. It is also important to study the safety aspects of microalgal food products in a broad manner.

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Declarations

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