

Chapter 5

Microalgae as Nutraceutical for Achieving Sustainable Food Solution in Future



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Abstract Of late, a spurt in the general awareness about the biological aspects of nutrition has been witnessed. The changing trend demands for high nutritional value products that can easily and rapidly be produced at large scales in a cost-effective manner. Microalgae constitutes a distinct group of unicellular photosynthetic organisms and a broad variety of eukaryotic algae containing a plethora of beneficial compounds such as carbohydrate, proteins, fatty acids, vitamins, carotenoids, phycobiliproteins, astaxanthin, and lutein. These compounds find application in the production of high-quality nutraceuticals that provide health benefits such as controlling blood pressure, boosting immune system, reducing coronary heart diseases, serving as anticancer agents, and acting as antioxidants. Besides, the benefits of using microalgae are its high productivity on arable and nonarable land, thus posing no threat to the agricultural crop production. Although the nutritional value and its commercialization is still in nascent stage, intense efforts are underway all over the world to explore untapped potential of microalgae that could lead to the solution of several problems through green technologies and open gateway to a multibillion dollar industry. This chapter gives an overview of microalgae and its diversity, nutritional value, and current challenges on its use as nutraceutical product.

Keywords Microalgae · Nutrition · Nutraceuticals · Green technology · Toxic metabolites

5.1 Introduction

The holistic development of any nation depends on the good health and well-being of its public. The frequent consumption of packaged and junk foods, fast eating food habits, long-scheduled work, sedentary lifestyle, etc. has resulted in a spurt

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in the prevalence of various diseases like carcinomas and heart-related disorders (Subudhi 2017). Therefore, there is an increasing global concern on the implementation of healthy foods in diet that will help to maintain a healthy lifestyle (Ranga et al. 2017). However, huge investment and capacity building are required to affirm to the food and nutritional security that often requires huge amount of farming land, livestock, and high density of natural resources. However, the current health policies demand the consumers to fend for themselves and entice them to attain maximum health benefits by spending minimum money (Lenoir-Wijnkoop et al. 2010). Therefore, a paradigm shift from traditional agriculture toward more sustainable solutions is the need of hour. To reduce the possibility of health problems, consumers prefer to use foods rich in adequate nutrients or nutraceuticals. Nutraceutical is a combination of two terms “nutrition” and “pharmaceutical,” a food stuff either in the form of fortified food or dietary supplement that has the capability to impart health benefits by strengthening the body’s response to ward off the infections and to get rid of diseases. Conventionally, these products are available in varied formulations. Nutraceutical are way more advantageous than the medicines as they are devoid of side effect, natural sources, easily available, and affordable. The term “nutraceutical” comprises several products such as vitamins, minerals, enzymes, antioxidants, probiotics, prebiotics, polyunsaturated fats, polyphenols, and spices (Chauhan et al. 2013). Depending upon their functions, nutraceuticals are grouped as dietary supplements, medicinal food, functional foods, etc. (Dillard and German 2000). On the basis of source of their origin, these are classified as products obtained from plants (vitamins, phytochemicals), animal (polysaccharides), or microorganisms (poly amino acids) (Pattanaik et al. 2019). Among the microorganisms, microalgae present a sustainable powerful reserve of number of functional ingredients for wide food applications (Pulz and Gross 2004). In general, the term “algae” circumscribes photosynthetic eukaryotic organisms. On the basis of their size, they can be classified as micro- and macroalgae. Macroalgae or seaweeds are multicellular organisms that include benthic marine organisms with variable sizes extending up to several meters (Markou et al. 2012). In contrast, the term microalgae, or microphytes, are microscopic photosynthetic algae and bacteria or cyanobacteria. Microalgae also have variable sizes, which can be as small as picometers (Waterbury 2006; Barsanti and Gualtieri 2006). The ecology of microalgae is also diverse, which ranges from marine to freshwater forms, and their photosynthetic mechanism resembles that of land-based plants. The microalgae have received an appreciable interest as sources of natural food, polysaccharides, fatty acids, and biomass due to its potentially simple and cost-effective cultivation techniques (Borowitzka 2013; Leu and Boussiba 2014; Aziz et al. 2017). Another major thrust for commercialization of microalgae is their generally regarded as safe (GRAS) status that has important relevance for products intended to be used for consumption purposes (Gangl et al. 2015). In contrast to plants, microalgae have higher growth rates (e.g., one to three doublings per day) and do not pose any competition for resources as they can be grown easily in open environment (Ng et al. 2015). In recognition of innumerable advantages of microalgae, several efforts are underway to promote them at biotechnological platforms, especially from genetic engineering point of view.

5.2 Indian Microalgal Diversity

India owing to its rich biodiversity, diverse ecologies, agronomic practices, and multitude of soil types is considered to be ideal for microalgal growth. The biodiversity-rich parts of the country like Eastern Ghats (Jena et al. 2005, 2008; Prasanna and Kaushik 2005; Rath and Adhikary 2005; Samantraray et al. 2002) and Chilika Lake in Odisha are also home to diverse species of microalgae (Adhikary 2000; Ratha et al. 2003; Rath and Adhikary 2005) and have been widely investigated. The investigation by Ratha et al. (2012) on qualitative distribution of microalgae in diverse ecological habitats from major biodiversity hotspots of India reported *Cyanophyceae* and *Chlorophyceae* as the abundantly found algal groups. Suresh et al. (2012) studied the microalgal diversity in Western and Eastern Ghats of Tamil Nadu and reported 97 species of microalgae. Kharkongar and Ramanujam (2014) reported a total of 85 taxa, including cyanobacteria and algal species belonging to diverse classes of algae with highest subaerial algal biodiversity in sacred grove compared to those of plantation and open disturbed forest. It is well reported in literature that the subaerial microhabitats are predominantly inhabited by members belonging to Trentepohliales and cyanobacteria since they can easily adapt to adverse environmental conditions by adopting different survival mechanisms, such as production of carotenoids in Trentepohliales and extracellular polymeric substances (EPS) sheath by cyanobacteria as a protective sheath (Urzi and Realini 1998; Tomaselli 2003). Singh and Sharma (2014) reported 19 microalgal taxa belonging to Cyanophyta (8 taxa), Chlorophyta (7 taxa), and Bacillariophyta (4 taxa) from Sheer Khad (stream), which is a tributary of Sutlej River, Himachal Pradesh. Severes et al. (2018) identified microalgae from Western Ghats regions of India. The panorama depicted by the microalgal biodiversity suggests their potential application in diverse fields, nutraceutical one of them, since they are proficient in producing high-value compounds even in the harsh environmental conditions.

5.3 Microalgae as Nutraceutical

The consumption of microalgae as a human food source or nutritional supplements is not new, but their use dates back to prehistoric times. The species of *Nostoc* find use in various parts across the world, where they are consumed in traditional ways. In Japan, cyanobacterium *Aphanothece sacrum* is consumed as a popular delicacy known as “suizenji-nori.” The microalgal biomass has gained immense popularity for the production of health-based food products, where it is being used exclusively for this purpose for over past few decades. Depending upon the organic composition, an array of products under different names are present in the market as nutraceuticals like dietary supplements, herbal preparations/products, traditional medicine, food supplements, or botanical supplements (Nicoletti 2012; Rajasekaran et al. 2008). The first-generation food supplements consist of primary metabolites,

whereas other substances, relevant to nutraceuticals, are secondary metabolites. The seaweeds contradict this simplified version of classification as they contain both the type of substances. Therefore, a new terminology “superfoods” was suggested (Bishop and Zubeck 2012). A third type of food supplement called as pharmafoods or functional foods is emerging because of their resemblance with ordinary foods in terms of physiological properties. These pharmafoods or functional foods probably can best harness the potential of microalgae in the future for a wide variety of different products after doing away with associated limitation such as poor aesthetics in the current utilizations (Nicoletti 2012).

5.4 Nutritional Components of Microalgae

Microalgae are repertoire of valuable compounds such as proteins, carbohydrates, polyunsaturated fatty acids (PUFAs), minerals, and vitamins that can not only heighten the nutritional content of food but also serve to provide benefits to the consumer (Table 5.1 and Fig. 5.1).

5.4.1 Microalgal Proteins

The essential amino acids (EAA) composition of algae is in sync with FAO requirements. *Chlorella vulgaris*, highly rich in protein content and desirable EAA composition, is popularly used as a food supplement (Becker 2007; Chronakis and Madsen 2011). Microalgae-based proteins have several advantages over other conventional protein sources, and they have scant land utilization compared to animal-based proteins (de Vries and de Boer 2010; Van Krimpen et al. 2013; Smetana et al. 2017), low water requirement, and ability to grow in saline water, among others (FAO 2010). Many species of microalgae produce proteins on par with egg, meat and milk, etc. (Gouveia et al. 2008a). Notably, red species of algae contain low concentrations of leucine and isoleucine, while brown algae species are often limited in methionine, cysteine, and lysine (Dawczynski et al. 2007; Mišurcová et al. 2014).

5.4.2 Microalgal Peptides and Protease Inhibitors

The bioactive peptides produced by the microalgae are known to possess anticancer, antiviral, antioxidant, and immunomodulatory effects. Proteases are a group of proteolytic enzymes with fine applications in food, detergents, and pharmaceutical industries. Their deregulation can result in serious health-related issues, and that is why both proteases and protease inhibitors find applications as therapeutic agents (Drag and Salvensen 2010).

Table 5.1 Microalgal species and products

Products	Producers	References
Food	<i>Chlorella</i> , <i>Spirulina maxima</i> , <i>Odontella aurita</i> , <i>Tetraselmis chunii</i> , <i>Aphanizomenon flos-aquae</i> , <i>Nostoc</i> , <i>Aphanothece sacrum</i> , <i>Spirogyra</i> , <i>Oedogonium</i> , <i>Haematococcus pluvialis</i> , <i>Isochrysis galbana</i> , <i>Porphyridium cruentum</i> , <i>Diacronema vlkianum</i> , <i>Scenedesmus</i> sp.	Valenzuela-Espinoza et al. (2002), Gantar and Svirčev (2008), Liu and Chen (2016), and Bleakley and Hayes (2017)
Feed	<i>Chlorella</i> , <i>Spirulina</i> , <i>Tetraselmis</i> , <i>Isochrysis</i> , <i>Pavlova</i>	Gouveia et al. (2008a), Yaakob et al. (2014), Mobin and Alam (2017)
Amino acid Mycosporine-like amino acids (MAA)	<i>Aphanizomenon</i> sp., <i>Chlorella luteoviridis</i> , <i>Chlorella minutissima</i> , <i>Chlorella sorokiniana</i> , <i>Chlorella sphaerica</i> , <i>Scenedesmus</i> sp., <i>Stichococcus</i> sp. <i>Chlamydomonas nivalis</i>	Xiong et al. (1999), Duval et al. (2000), Karsten et al. (2007), Chu (2012)
<i>Polyunsaturated fatty acids (PUFAs)</i> Eicosapentaenoic acid (EPA) Docosahexaenoic acid (DHA) α -Linolenic acid Arachidonic acid (AA) Linolenic acid	<i>Phaeodactylum</i> , <i>Nannochloropsis</i> , <i>Schizochytrium</i> <i>Cryptocodinium cohnii</i> , <i>Isochrysis galbana</i> , <i>Pavlova salina</i> , <i>Schizochytrium</i> <i>Botryococcus</i> sp., <i>Chlamydomonas moewusii</i> , <i>Chlorella vulgaris</i> , <i>Dunaliella</i> sp., <i>Micromonas pusilla</i> , <i>Muriellopsis</i> sp., <i>Nannochloris atomus</i> , <i>Pseudokirchneriella subcapitata</i> , <i>Scenedesmus acutus</i> , <i>Scenedesmus obliquus</i> , <i>Scenedesmus quadricauda</i> , <i>Tetraselmis suecica</i> <i>Nannochloris atomus</i> , <i>Porphyridium boryanum</i> <i>Botryococcus</i> sp., <i>Chlorella</i> sp., <i>D. bardawil</i> , <i>Tetraselmis primolecta</i> , <i>Tetraselmis tertiolecta</i> , <i>N. atomus</i> , <i>Neochloris oleoabundans</i> , <i>P. subcapitata</i> , <i>Scenedesmus obliquus</i> , <i>T. suecica</i>	Pereira et al. (2012), Adarme-Vega et al. (2014) Fried et al. (1982), Piorreck et al. (1984), Reitan et al. (1994), D'Souza and Loneragan (1999), Arisz et al. (2000), Becker (2004), Chiang et al. (2004), Poerschmann et al. (2004), Martinez-Fernandez et al. (2006), Patil et al. (2007) Reitan et al. (1994), Zhang et al. (2002) Fried et al. (1982), Piorreck et al. (1984), Reitan et al. (1994), D'Souza and Loneragan (1999), Arisz et al. (2000), Zhang et al. (2002), Chiang et al. (2004), Day et al. (2009), Gouveia and Oliveira (2009), Patil et al. (2007)
Vitamins	<i>Chlamydomonas eugametos</i> , <i>Chlorella pyrenoidosa</i> , <i>C. vulgaris</i> , <i>Chlamydomonas reinhardtii</i> , <i>Scenedesmus acutus</i> , <i>Scenedesmus obliquus</i> , <i>Scenedesmus quadricauda</i> , <i>C. protothecoides</i> , <i>Dunaliella tertiolecta</i> , <i>Prototheca moriformis</i> , <i>T. suecica</i>	Uhlik and Gowans (1974), Borowitzka (1988), Vilchez et al. (1997), Carballo-Cardenas et al. (2003), Matsukawa et al. (2000), Becker (2004)

(continued)

Table 5.1 (continued)

Products	Producers	References
Toxins Anatoxin and saxitoxin Microcystins Okadaic acid	<i>Flos-aquae</i> <i>Microcystis aeruginosa</i> <i>Dinophysis</i> sp.	Katircioglu et al. (2004), He et al. (2005)
Sterols	<i>Pyramimonas</i> cf. <i>cordata</i> , <i>T. suecica</i> , <i>D. salina</i> , <i>D. tertiolecta</i>	Ponomarenko et al. (2004), Cardozo et al. (2007), Luo et al. (2015)
Carotenoids Astaxanthin β -carotene Canthaxanthin Lutein	<i>C. nivalis</i> , <i>Chlamydocapsa</i> sp., <i>C. nivalis</i> , <i>C. vulgaris</i> , <i>Chromochloris zofingiensis</i> , <i>Coelastrrella striolata</i> , <i>Haematococcus</i> sp., <i>S. obliquus</i> , <i>Chlorella</i> sp., <i>Dunaliella</i> sp., <i>Pyramimonas</i> sp., <i>Tetraselmis</i> sp. <i>Chlorococccum</i> sp., <i>Chlamydocapsa</i> sp., <i>C. emersonii</i> , <i>C. fusa</i> , <i>C. vulgaris</i> <i>Neosporiocoocccum</i> sp., <i>Chlorococccum</i> sp., <i>Chlamydocapsa</i> sp.	Borowitzka (1988), Liu and Lee (2000), Lorenz and Cysewski (2000), Yuan et al. (2002), Kang et al. (2005), Remias et al. (2005), Zhekisheva et al. (2005), Jin et al. (2006), Abe et al. (2007), Chattopadhyay et al. (2008), Fujii et al. (2008), Leya et al. (2009), Chu (2012), Domínguez-Bocanegra et al. (2004) Rabbani et al. (1998), Egeland et al. (1995, 1997), Matsukawa et al. (2000), Hejazi and Wijffels (2003), Barbosa et al. (2005), Abe et al. (2007), Coesel et al. (2008), and Chu (2012) Sathasivam et al. (2012) and Wu et al. (2016) Yuan et al. (2002), Mendes et al. (2003), Pelah et al. (2004), Bhosale and Bernstein (2005), Abe et al. (2007), Chattopadhyay et al. (2008), Coesel et al. (2008) and Leya et al. (2009) Chen (1998), Egeland et al. (1995, 1997), Barbosa et al. (2005), Tukaj et al. (2003), Bhosale and Bernstein (2005), Blanco et al. (2007), Ceron et al. (2008), Cha et al. (2008), Matsukawa et al. (2000), Shi et al. (2006), Sanchez et al. (2008)
Polysaccharides Sulphated	<i>Porphyridium</i> sp.	Delattre et al. (2016), Xiao and Zheng (2016)
Phenolic and volatile compounds B-cyclostirol, α - and β -ionone, neophytadiene, nopole, phytol Pentadecane Heptadecane	<i>Chlorella</i> , <i>Nostoc</i> , <i>Anabaena</i> , <i>Tolypothrix</i> , <i>Chlamydomonas</i> , <i>D. salina</i> , <i>Synechocystis</i> sp., <i>Spirulina</i>	Plaza et al. (2010), de Morais et al. (2015)

(continued)

Table 5.1 (continued)

Products	Producers	References
Phycobiliproteins Phycocyanin Phycocerythrin Porphyridium Allophycocyanin Chlorophyll A	<i>Spirulina</i> , <i>A. flos-aquae</i>	Bishop and Zubeck (2012), Sonani et al. (2016)
Antioxidant	<i>Nostoc ellipsosporum</i> , <i>C. nivalis</i> , <i>Phaeodactylum tricornutum</i>	Mendiola et al. (2005), Wang et al. (2007), Jaime et al. (2007), Li et al. (2007), Ibáñez et al. (2008), Rodriguez-Garcia and Guil-Guerrero (2008)
Antibacterial Diterpenoid Nostocycline A Tenuocyclamides	<i>Nostoc commune</i> <i>Nosto</i> sp. <i>Nostoc spongiaeforme</i> <i>Spirulina platensis</i>	Asthana et al. (2009) Banker and Carmeli (1998), Ploutno and Carmeli (2000) Hayashi et al. (1996, 2008)
Antiviral Spirulina Nostoflan Antifungal Nostodione Nostocyclamide	<i>Nostoc flagelliforme</i> <i>Nostodione</i> <i>Nostoc commune</i>	Moore et al. (1988), Bhadury and Wright (2004)

Protease inhibitors are small molecules, and usually, peptides mimic the structure of a substrate and bind to enzymes. *Chlorella vulgaris* produces pepsin-hydrolyzed peptide with strong antioxidant activity and is resistant against gastrointestinal enzymes (Sheih et al. 2009a), besides containing a peptide with antiproliferative activity (Sheih et al. 2009b). Cyanobacteria also produce a set of potent metabolites in minute quantities (Janssen 2019). *Microcystis* has been known to produce aeruginosins, which helps to curtail the thromboembolic disorders by efficiently binding to serine proteases (Ersmark et al. 2008; Wang et al. 2009). The brackish water cyanobacterium *Nodularia spumigena* (Mazur-Marzec et al. 2013) and *Anabaena compacta* (Anas et al. 2012) are known to produce Spumigins, which inhibits trypsin-like serine proteases. The anabaenopeptins-cyclic hexapeptides act against exopeptidase, carboxypeptidase A (Murakami et al. 2000). The microginins have been shown to inhibit various exopeptidases (Welker and von Dohren 2006). Microginins are considered to be potential candidates for the development of new drugs for cardiovascular diseases as they are known to inhibit angiotensin-converting enzyme (ACE-I) and leucyl aminopeptidase (LAP) (Bagchi et al. 2016). The aerucyclamides have been reported to show activity against cancer cells and parasitic infections (Ishida et al. 2000; Portmann et al. 2008). The cyanopeptolins and aeruginosins show inhibitory action against serine proteases (Gademann and Portmann 2008; Hanessian et al. 2006). Ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCO), a heterohexadecamer structured protein, possesses functionally bioactive peptides known to cure cardiovascular diseases, diabetes, neurodegenerative disorders, and oxidative stress (Selvaraj et al. 2017).

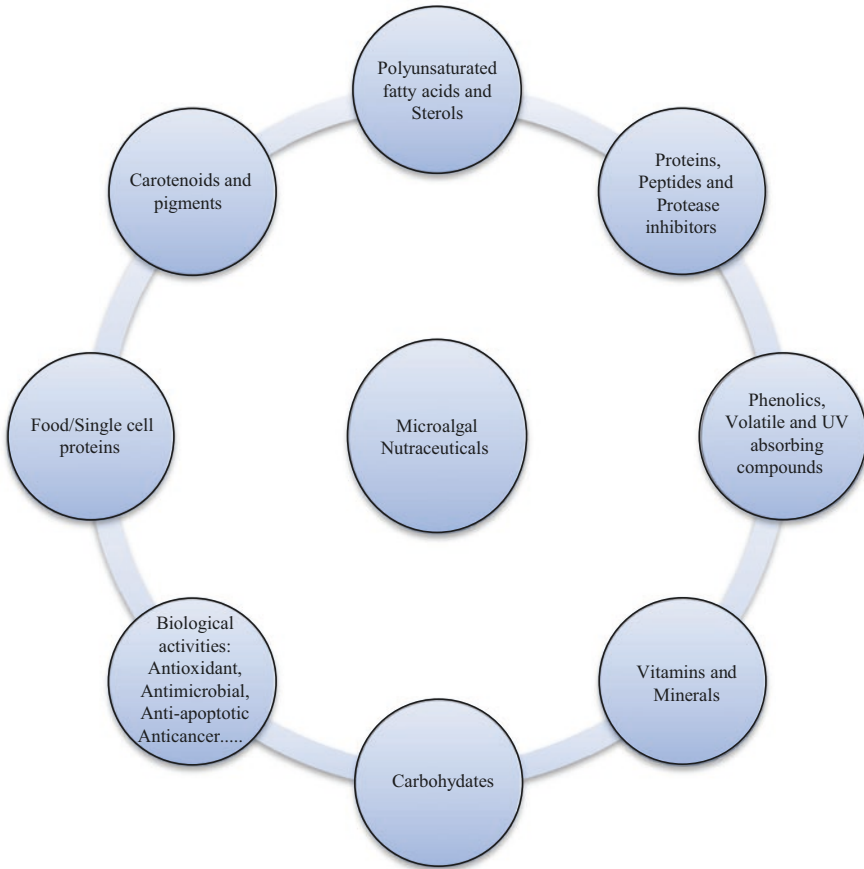


Fig. 5.1 Important microalgal nutraceuticals

5.4.3 *Microalgal Carbohydrates*

Carbohydrates constitute a wide variety of sugars or polysaccharides. Depending on the species, the microalgae produce discrete carbohydrates, e.g., glycogen, floridean starch, and amylopectin-like polysaccharides (Nakamura et al. 2005). Because of the absence of hemicelluloses and lignin, the algal biomass is amenable to easy digestion (Mussnug et al. 2010). The cultivation and environmental conditions as well as the microalgal species determine the biomass carbohydrate content. Microalgal polysaccharides are recognized to promote gut microflora growth and regulation of blood glucose as they constitute a part of prebiotic supplements (Ibañez and Cifuentes 2013). Many cyanobacteria and green algae are surrounded by a special mucilaginous covering around their cells or filaments composed of exopolysaccharides (EPS) and are termed as slimes, sheaths, and/or capsules

depending upon the species (Kumar and Adhikary 2018). EPS have received wide attention currently for their antimicrobial and anticarcinogenic roles (Mahendran et al. 2013, Bafanaa 2013). The cell wall polysaccharides from *Chlorella vulgaris* contain β -(1,3)-glucose, while the microalgal species contain heteropolysaccharides with different substituents (Raposo et al. 2014). The polysaccharides from *P. cruentum* are inhibitory against viruses, as well as bacteria (Huang et al. 2005; Raposo et al. 2014). The extracellular polysaccharides of *Rhodella reticulata* exhibit free radical scavenging and antioxidant activity (Chen et al. 2010a). Besides, EPS from red microalgae and *Arthrospira platensis* show antimicrobial and antioxidant activities (Rafika et al. 2011).

5.4.4 Microalgal Polyunsaturated Fatty Acids

Polyunsaturated fatty acids (PUFAs) which contain three or more double bonds play integral role in maintaining tissue integrity and imparting beneficial health effects, especially n-3 PUFAs, which are found to be effective in prevention or treatment of several ailments (e.g., heart-related disorders, various malignancies, and many more). Until recently, omega-3 and omega-6 fatty acids, the integral fatty acids, were mainly being derived from fish oil, but due to several concerns like overexploitation of marine sources, detection of toxic compounds in fishes, awful smell and taste, and oxidative instability, the interest has been deviated toward the exploitation of microalgae as an alternative source of PUFAs (Garcia et al. 2017). The three chief types of omega-3 fatty acids implicated in human health and physiology are α -linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). The microalgal species *Arthrospira* produce α -linolenic acid (ALA) and *Nannochloropsis*, *Phaeodactylum*, and *Nitzschia* produce EPA, while *Cryptocodinium* and *Schizochytrium* are the producers of DHA. The *Cryptocodinium cohnii* produces all the enzymes necessary for de novo synthesis of 22:6 ω -3 (Henderson and Mackinlay 1999). *Nannochloropsis* is another promising candidate for pharmaceutical-based applications because it accumulates high levels of PUFA (Udayan et al. 2017). Arachidonic acid (AA), derivative of omega-6 fatty acid is considered as a precursor of prostaglandin and leucotriene synthesis, which has major role to play in circulatory and CNS functions (Medina et al. 1997).

5.4.5 Microalgal Sterols

Sterols, which are required to regulate the membrane fluidity, reduce the LDL-cholesterol levels and promote cardiovascular health (Piironen et al. 2000; Volkman 2003; Silvestro et al. 2013; Alsenani et al. 2015). Microalgae are recognized to produce both saturated and unsaturated sterols such as brassicasterol, sitosterol, and stigmasterol (Kohlhase and Pohl 1988; Volkman 2003). *Glaucocystophyte* has been

reported to produce sitosterol, campesterol, and stigmasterol (Leblond et al. 2011), dinoflagellates produce 4 α -methyl sterols and 24-propylidenecholesterol (Thomson et al. 2004; Giner et al. 2009), and *Dunaliella tertiolecta* and *D. salina* produce sterols with in vivo neuromodulatory activities (Francavilla et al. 2012).

5.4.6 Microalgal Pigments

Microalgal pigments like chlorophylls (a, b, and c), phycobiliproteins, phycocyanin, phycoerythrin, β -carotene, lutein, and astaxanthin are important bioactive compounds (Zhang et al. 2016). Chlorophyll or its derived products are widely been used for health benefit characteristics such as antioxidant, therapeutic properties, neuroprotective action, and protection against chronic diseases (Pangestuti and Kim 2011; Galasso et al. 2019). Chlorophyll a and its mixture with chlorophyll b exhibit chemopreventive effects, antioxidant activity, promotion of cell arrest, and apoptosis (Mishra et al. 2011). Some of the most important carotenoids with health benefits are β -carotene, astaxanthin, lutein, and canthaxanthin. The antioxidant and therapeutic potentials of carotenoids include their role in prevention of diabetes, aging, cancer, obesity, and stroke, with higher provitamin A activity of β -carotene and lipid peroxidation activity of astaxanthin (Chidambara-Murthy et al. 2005; Lin et al. 2016; Raposo et al. 2001, 2013). β -Carotene and astaxanthin strongly prevent oxidative stress through scavenging of free radicals and also exhibit anticancer effect (Cuvelier 2001; Demming-Adams and Adams 2002; Uttara et al. 2009; Lobo et al. 2010). β -Carotene produced by *D. salina* and *D. bardawil* lower plasma cholesterol and atherogenesis (García-González et al. 2005). The vitamins C and E, β -carotene, and zinc have proved to be effective against age-related macular degeneration, which is responsible for causing blindness (Taylor et al. 2002). Astaxanthin by *Haematococcus pluvialis* and *Chlorella zofingiensis* prevents obesity and fatty liver disease (Lorenz and Cysewski 2000; Ikeuchi et al. 2007). Astaxanthin has protective effects against many diseases, like cancers, and prevents against *Helicobacter pylori* (Olaizola 2005; Ikeuchi et al. 2007; Kamath et al. 2008; Satoh et al. 2009; Yuan et al. 2011). Dried biomass of *Haematococcus pluvialis* which is a rich source of astaxanthin has been commercialized owing to its strong antioxidant activity. Astaxanthin-rich *Haematococcus* available as dietary supplement (Lorenz and Cysewski 2000) has strong antioxidant activity (Higuera-Ciapara et al. 2006). Zeaxanthin by *Microcystis aeruginosa*, *Nannochloropsis*, and *D. salina* helps in vision and antioxidant protection of the body (Jin et al. 2003; Chen et al. 2005). Lutein produced by *Chlorella zofingiensis*, *Chlorella protothecoides*, and *Muriellopsis* sp. has protective antioxidative effect (Kleinegris et al. 2010). Studies found that chances of cataract decreases on consumption of lutein/zeaxanthin-rich foods. Fucoxanthin is another microalgal pigment with nutraceutical abilities, which is associated with weight loss management (Abidov et al. 2010). The antioxidant and anti-inflammatory potential of phycocyanin and other pigments from red algae is also well documented (Kumar et al. 2014). Phycobiliproteins produced by

cyanobacteria and rhodophyta (Eriksen 2008; Watanabe and Ikeuchi 2013; Mulders et al. 2014) reduce oxidative stress by neutralizing the reactive oxygen species (ROS), which is possible due to their chemical structures and chelating properties (Roy et al. 2007; Eriksen, 2008; Stengel et al. 2011; Rodriguez-Sanchez et al. 2012; de Jesus Raposo et al. 2013). Phycocyanin and phycoerythrin are two well-known commercially important phycobiliproteins produced by *Spirulina* sp. and *Porphyridium* sp., respectively (Plaza et al. 2009; Rodriguez-Sanchez et al. 2012; Borowitzka 2013). Microalgae produce chlorophylls a, b, c, d, and f with variable absorption spectra and tonality (Chen et al. 2010b; Roy et al. 2011). Studies have shown that the antimutagenic effect of microalgae is conferred by chlorophylls (Ferruzi and Blakeslee 2007; Gouveia et al. 2008a).

5.4.7 Microalgal Vitamins

Microalgae form a part of human nutrition as it is a rich source of a number of vitamins. It has been reported that vitamin B₁₂ has a role to play in DNA repair and histone methylation, and it reduces the risk of breast cancer (Gruber 2016). *Nannochloropsis oculata*, *Chaetoceros calcitrans*, *Porphyridium cruentum*, and *Haslea ostrearia* are rich source of vitamin E (tocopherols) (Durmaz 2007; Bong and Loh, 2013; Santiago-Morales et al. 2018). Ascorbic acid is not only used as a food additive but also effective against diseases such as cancer and several infections (Boyera et al. 1998; Nunes-Alves et al. 2014). *Porphyridium cruentum* produces high quantities of vitamins E and C (ascorbic acid), as well as β -carotene (vitamin A) (Mus et al. 2013). The microalga *D. salina* produces vitamins A, B₁, B₂, B₃, B₆, B₇, and E (Hosseini Tafreshi and Shariati 2009). Microalgae is also known to contain vitamins D₂ and D₃ (Takeuchi et al. 1991; Rao and Raghuramulu 1996), together with provitamin D₃. Vitamin D and its metabolites are implicated in chemoprevention activities (Giammanco et al. 2015).

5.4.8 Microalgal Minerals

The mineral composition of microalgae which is determined by geographical range and environmental conditions varies extensively among marine and freshwater microalgae on a strain, species, and generic basis (Fox and Zimba 2018). Minerals are present either in the form of compounds or elemental form such as Zn, Ca, and Mg and have important role to play (Nose 1972). The mineral content of microalgae is sufficient to fulfill the recommended daily intake for adults (Alsenani et al. 2015). Significant quantities of Zn, K, Na, Fe, P, Mg, and Mn is produced by *Isochrysis* sp., *Sochrisis* sp., *Chlorella* sp., and *Dunaliella* sp. (Fabregas and Herrero 1986; Tokuşoglu and Ünal 2003). The mineral content produced by the microalgae fulfills the Recommended Dietary Allowances (RDA), prescribed for various minerals (USDA 2002; Tokuşoglu and Ünal 2003).

5.4.9 *Microalgal Phenolic and Volatile Compounds*

Phenolic compounds (PCs) or polyphenolics are secondary metabolites produced by microalgae in response to stress conditions (Cabrita et al. 2010; La Barre et al. 2010). Phenolic compounds like caffeic acid, ferulic acid, and p-coumaric acid, which are used as dietary supplements as they represent important classes of natural antioxidants (Stengel et al. 2011). *Chlorella* and *Spirulina* are known to produce an array of phenolic compounds in appreciable quantities like phloroglucinol, p-coumaric acid, ferulic acid, and apigenin, which are produced by *Chlorella* at 74,000 ng/g, 540 ng/g, 0.63 ng/g, and 9.9 ng/g and by *Spirulina* at 51,000 ng/g, 920 ng/g, 0.67 ng/g, and 6.0 ng/g, respectively (Goiris et al. 2014). The other microalgal species known to produce phenolic compounds are *Nostoc* sp., *Chlorella* sp., *Anabaena* sp., *Tolypothrix* sp., and *Chlamydomonas* sp. (Li et al. 2007; Hajimahmoodi et al. 2010) with phenolic contents of par or more than fruits and vegetables (Ismail et al. 2004; Hassimotto et al. 2005; Lin and Tang 2007).

The volatile compounds are also the secondary metabolites that are responsible for imparting characteristic odors to the water (Abd El-Baky et al. 2002). They have diverse structures and biological activities such as antibacterial, antifungal, antiviral, and anticancer. The biologically active volatile compounds are aldehydes, ketones, fatty acids, and isoprenylated and brominated hydroquinones (Mathew et al. 1995; Morimoto et al. 1995; Borowitzka 1997). The heptadecane and tetradecane produced by *Spirulina* are known to have antibacterial capacity (Ozdemir et al. 2004). *Dunaliella salina* produces antimicrobial compounds like β -cyclocitral, α - and β -ionone, neophytadiene, and phytol (Herrero et al. 2006).

5.4.10 *Microalgal UV-Absorbing Compounds*

The sizeable loss of ozone layer and consequent increment in ultraviolet (UV) radiation have resulted in a host of skin problems like extrinsic skin aging and wrinkles, mottled hyperpigmentation, dilated blood vessels, and loss of skin tone. All these skin-related disorders have ameliorated the interest in quest for natural photoprotective compounds (Lee et al. 2015). In aquatic environments, where microalgae figure prominently, the presence and role of UV-absorbing compounds like sporopollenin, scytonemin, and mycosporine-like amino acids (MAAs) have been documented. Their presumed antioxidant and skin protective strategies raise the interest for possible medicinal and cosmetic applications (Dionisio-Sese 2010). Xiong et al. (1997) observed that UV-B-tolerant chlorophyte species of *Characium terrestre*, *Enallax coelastroides*, *Scenedesmus* sp., *Scotiella chlorelloidea*, and *Spongiochloris spongiosa* contain produce large amounts of sporopollenin. The biopolymer has been reported to be present also in *Dunaliella salina* zygotes (Komaristaya and Gorbulin 2006). Microalgal scytonemin appears restricted to cyanobacteria, specifically in

the extracellular polysaccharide sheath of *Chlorogloeopsis* sp., *Scytonema* sp., and *Rivularia* sp. (Sinha et al. 1998). It is reportedly the most important UV-absorbing compound in *Lyngbya* cf. *aestuarii*, where its area content seems to follow the seasonal fluctuation of solar intensity (Karsten et al. 1998). MAAs are UV radiation-absorbing molecules and possess high molar extinction coefficients. Unlike sporopollenin and scytonemin, which are found in the cell wall or extracellular sheath of the microalgae, MAAs in microalgae are mostly intracellular. The presence of several MAAs in a species was observed in different chlorophytes, haptophytes, diatoms, and dinoflagellates grown in cultures or collected in a broad variety of aquatic habitats (Llewellyn and Airs 2010). MAAs also have been reported in several microalgae-invertebrate (sea anemone, coral, ascidian) symbiotic associations. Among the Chlorophytes, asterina and shinorine are produced by *Ankistrodesmus spiralis* and *Chlorella minutissima*; palythine, porphyra, and shinorine are produced by *Chlorella sorokiniana* and *Enallax coelastroides* (Xiong et al. 1999); and mycosporine-glycine is produced by *Pyramimonas parkeae* (Hannach and Sigleo 1998). Among the halophytes, mycosporine-glycine is produced by *Isochrysis* sp. and *Pavlova gyrans* (Hannach and Sigleo 1998); among the Diatoms, porphyra and shinorine are produced by *Chaetoceros* sp., *Corethron criophilumporphyra*, *Cosinodiscus centralisporphyra*, *Thalassiosira tumidaporphyra*, and *Porosira glacialis* (Helbling et al. 1996; Riegger and Robinson 1997). Among the Dinoflagellates, mycosporine-glycine, palythene, palythine, porphyra, and shinorine are produced by *Scrippsiella sweeneyae* (Taira et al. 2004); asterina, mycosporine-glycine, palythene, palythenic acid, palythine, palythinol, porphyra, shinorine, and usujirene are produced by *Alexandrium catenella*, *A. excavatum*, *A. minutum*, and *A. tamarense* (Carreto et al. 1990).

5.4.11 Microalgal Toxic Metabolites

Microalgal species are known to produce toxins called as microcystins; homo- and anatoxin-*a*, also known as Very Fast Death Factor (VFDF); and saxitoxins. The most prevalent are the microcystins, produced by the blooming *Microcystis aeruginosa*. The most toxic amino acid known is microcystin LR produced by *M. aeruginosa*, which is lethal for both animals and human (Khan et al. 2018); its degree of toxicity is determined by the length of amino acid chain (Jungblut and Neilan 2006). Cytotoxins are pharmacologically active compounds with various biological activities such as anticancer, antimicrobial, antiplasmodial, and immunosuppressive (Abdo et al. 2012; Rath and Priyadarshani 2013; Malathi et al. 2014; Mukund and Sivasubramanian 2014; Semary and Fouda 2015; Shaieb et al. 2014). *Amphidinium* sp. produce an active antimycotic and antiprotozoal agent called as karatungiols (Washida et al. 2006). *Dinophysis* sp. is known to produce a potent neurotoxin called as okadaic acid for the treatment of cognitive disorders (He et al. 2005).

5.4.12 *Microalgae as Food/Single Cell Protein*

Microalgae has been consumed for its high protein content since thousands of the year. For example, *Nostoc* and *Arthrospira* or *Spirulina* have been used in Asia and Africa, respectively (Chacòn -Lee and González-Maríno 2010). The most commonly consumed microalgae and with GRAS status are *Spirulina*, *Chlorella*, *Dunaliella*, *Haematococcus*, and *Schizochytrium* (Hayes et al. 2017). The microalgae-based foods are available as different formulations (Pulz and Gross 2004) or as fortified foods in the forms of confectionaries, refreshments, cereals, and beverages (Liang et al. 2004). Microalgae also serve as feed for animals (Gouveia et al. 2008a). Due to growing popularity of health foods, various food products are supplemented with microalgae. *Chlorella* and *Spirulina* are the popularly used microalgal species for the supplementation of pasta. Supplementation of pasta with *C. vulgaris* results in better nutritional value, enhanced sensorial properties, increased firmness, and improved swelling and water absorption (Fradique et al. 2010, Gouveia et al. 2007). *Isochrysis galbana* is another widely used species used for the supplementation of the food products. Supplementation of cookies with *I. galbana* is carried out to provide ω -3 PUFAs, besides exhibiting thermal resistance (Gouveia et al. 2008b). Phycocyanin extracts and whole *A. platensis* incorporation into cookies enhance the protein as well as fiber content (Singh et al. 2015). Supplementation of cookies with *Haematococcus pluvialis* provides antioxidant potential to the food product and also lowers the glycemic response (Hossain et al. 2017). *Spirulina platensis* is widely used in the supplementation of bread due to its antimicrobial activity, besides improving the protein content and mineral profile of the food product (Ak et al. 2016). *Arthrospira* is another popular supplement of the bread that helps to increase its protein content (Dinu et al. 2012; Achour et al. 2014; Ak et al. 2016). The techno-functional properties of microalgae are exploited as additives in food products (Caporgno and Mathys 2018). The property of microalgae to mimic fat molecules is utilized for its incorporation into emulsion resulting in reduction of percentage of oil as well as enhanced resistance to oxidation (Gouveia et al. 2006) and incorporation of microalgae into vegetarian desserts as coloring agents (Batista et al. 2008).

5.4.13 *Microalgal Biological Activities*

The microalgal metabolites have the following interesting biological activities:

5.4.13.1 **Antioxidant Activity**

Antioxidants are compounds that defend the body from the damage caused by potentially harmful molecules called as free radicals. The free radicals such as reactive oxygen and nitrogen species attack biomolecules like DNA and proteins,

causing several lethal diseases like carcinoma, cardiovascular, and brain-related disorders (Ngo et al. 2006). Microalgae produce several metabolites that have strong radical scavenging action, e.g., chlorophyll a (Cho et al. 2011); phycoerythrobilin (Yabuta et al. 2010); pigment fucoxanthin and its derivatives, auroxanthin, produced by *Undaria pinnatifida* (Sachindra et al. 2007); and carotenoids produced by *Dunaliella salina* (El-Baz et al. 2017).

5.4.13.2 Anticancer Activity

Cancer, also called as malignancy, is caused by uncontrolled growth and division of cells. There are more than 100 different cancer types, a few of them lethal in nature due to their metastatic activity (Kevin et al. 2018). Microalgae produce different types of carotenoids with significant anticancer activities, β -carotene, lutein, astaxanthin, violaxanthin, and fucoxanthin. Significant inhibition of the growth of human colon cancer cell lines and LoVo colon carcinoma cells by β -carotene has been reported by Palozza et al. (2005) and Pham et al. (2013). The inhibitory effect of astaxanthin on the growth of cancer cell lines and colorectal cancer (CRC) cell lines has been studied by Palozza et al. (2009). The antiproliferative effects of lutein and violaxanthin on human colon cell line HCT-116 was studied by Shi and Chen (2002), Cha et al. (2008), Pasquet et al. (2011), Fu et al. (2013), and Talero et al. (2015). Kumar et al. (2013a, b) have reported the antiproliferative effects of fucoxanthin against different cells lines such as SK-Hep-1 and BNL CL.2. Depending on the culturing conditions, e.g., nutrients, temperature (Ingebrigtsen et al. 2016; Lauritano et al. 2016), and growth phase (Ribalet et al. 2007), the bioactivity of microalgae may vary. Lauritano et al. (2016) demonstrated that diatom *Skeletonema marinoi* shows anticancer activity under nitrogen starvation conditions only. Microalgae produce a repertoire of polysaccharides with anticancer activities (Raposo et al. 2015). Many microalgae present a high content of therapeutic proteins and peptides (Talero et al. 2015).

5.4.13.3 Anti-Angiogenic Activity

Angiogenesis is completely a normal process, but under certain conditions, it may become pathological and cause malignancies, cardiovascular diseases, and many other lethal diseases (Cherrington et al. 2000; Armstrong et al. 2011). Fucoxanthin and fucoxanthinol suppress the angiogenesis process in rats (Sugawara et al. 2006) and significantly inhibit blood cell multiplication. Fucoxanthin also acts as therapeutic agent as it is effective against diabetes, impedes melanin formation (Shimoda et al. 2010), prevents photooxidation of DNA (Heo and Jeon 2009), and has also been reported to promote the synthesis of arachidonic acid and DHA content in mouse livers (Tsukui et al. 2009). Siphonaxanthin, an antiangiogenic agent, is also produced by some species of algae (Ganesan et al. 2010). Aerucyclamide, an antiplasmodial agent isolated from *M. aeruginosa*, is also a potential candidate to be used in pharmaceutical products (Pen et al. 2012).

5.4.13.4 Anti-obesity Activity

Obesity, an abnormal or excessive fat accumulation, is a major epidemic. It is associated with a number of metabolic syndromes, type 2 diabetes, cardiovascular disease, cancer, and aging (Kopelman 2000). The underlying mechanism that causes obesity is overgrowth of adipose tissue (Wang et al. 2008). Microalgae are known to produce anti-hyperlipidemic and fat-lowering agents. The fucoxanthin and fucoxanthinol predominantly produced by *Cylindrotheca closterium* and *Phaeodactylum tricoratum* not only inhibit differentiation of 3T3-L1 cells to adipocytes but also adipocyte differentiation (Hayato et al. 2006). The other biological activities fucoxanthin shows are anticancer, anti-oxidant, etc. (Maeda et al. 2007a; Kim et al. 2012). The fat in mouse feeds has been reported to be lowered by the activity of neoxanthin and fucoxanthin (Okada et al. 2008; Maeda et al. 2007b). The long-chain omega-3 fatty acid-rich oil obtained from *Aurantiochytrium* sp. KRS101 has been reported to decrease weight of obese animals treated with microalgal oil (Yook et al. 2015). Koo et al. (2019) documented that *Phaeodactylum* extract containing fucoxanthin exerts anti-obesity effects by promoting lipolysis and inhibiting lipogenesis.

5.4.13.5 Antimicrobial Activity

The antimicrobial activity of *Chlorella* was first demonstrated by Pratt in 1944 (Pratt et al. 1944). Microalgae owes its antimicrobial activity to several compounds like indoles, phenols, and fatty acids (Mayer and Hamann 2005; Mendiola et al. 2007). Microalgae also produce antifungal compounds like okadaic acid, ciguatera toxin, and karatungliols produced by *Prorocentrum lima*, *Gambierdiscus toxicus*, and dinoflagellate *Amphidinium*, respectively (Washida et al. 2006). *Microcystis aeruginosa* possess both antifungal and antibacterial activity (Khalid et al. 2010). *Dunaliella salina* and *Dunaliella primolecta* show inhibition to a large number of microorganisms like *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia* (Mendiola et al. 2008; Pane et al. 2015). Mudimu et al. (2014) observed an in vitro antifungal activity against *C. albicans* by *Heterochlorella luteoviridis* and *Porphyridium purpureum*. Ginsberg et al. (1947) first demonstrated the antiviral activity of algal polysaccharides against influenza B and mumps viruses. The cell wall sulfated polysaccharide of *Porphyridium* sp. is reported to act against *Herpes simplex* viruses types 1 and 2 (HSV 1, HSV 2) and *Varicella zoster* virus (VZV). *Scenedesmus obliquus* cells and protein extracts which were rich in Arg, Lys, Asp, Ala, and His have been found to be effective against Coxsackie B₃ virus (Afify et al. 2018).

5.4.13.6 Antiapoptotic Activity

Apoptosis is programmed cell death that helps the body to get rid of damaged or infected cells. It is mediated by intracellular proteolytic cascade, besides the activation and downregulation of proapoptotic and antiapoptotic genes, respectively

(Nappo et al. 2012), and stated that diethyl ether extract from marine diatoms *Cocconeis scutellum* resulted in 89.2% apoptosis. Suh et al. (2017) reported significant inhibition of carcinogenesis and induction of cellular apoptosis through upregulation of apoptotic genes by the ethanol extract of *Botrydiopsisidae* sp.

5.4.13.7 Cytotoxic Activity

Microalgae produce several groups of compounds that act as cytotoxic agents. *Cyanophora paradoxa* (Cp) produce pigments that can efficiently inhibit various carcinomas. The Cp water and ethanol microalgal extracts significantly inhibited the growth of cancer cell lines in vitro at 100 $\mu\text{g mL}^{-1}$ (Baudelet et al. 2013). Ávila-Román (2019) reported the cytotoxic activity of oxylipins (OXLs) isolated from *Chlamydomonas debaryana* (13-HOTE) and *Nannochloropsis gaditana* (15-HEPE) against UACC-62 (melanoma).

5.5 Safety, Market Potential, and Current Challenges

Notwithstanding the nutritional and health aspects of microalgae, high content of nucleic acids associated with them is a major concern. The metabolic conversion of nucleic acid to uric acid may lead to the development of gout or renal calculus (Gantar and Svirčev 2008). The other important issue is that genetic characteristics and technological approaches adopted for biomass productions determine the digestibility and overall nutritional value of microalgae. For instance, toxin production, i.e., hepatotoxins and neurotoxins, by some cyanobacteria when grown in open conditions, poses a threat of microalgal biomass getting contaminated with toxins and other contaminants (Grobelaar 2003).

Notwithstanding the acceptance of the use of microalgal biomass or myriad metabolites obtained from it, a small number of products can be seen in market. There are still a large number of avenue lying unexplored in this area and numerous challenges to be addressed to come up with innovative solutions. The most important challenge is to achieve high rate of microalgae production at economical scale. The commercial production of microalgae is being carried out in unsophisticated, low-productive man-made structures like artificial open ponds (Chisti 2007). Only a few species of microalgae such as *Spirulina*, *Chlorella*, and *Dunaliella* can be cultured in sustained open ponds. Despite the success of open systems, further advancements are required for closed system cultivation of microalgae. Closed photobioreactors such as tubular, flat panel, air lift, and bubble column which have been around for a long time are difficult to scale up and require high auxiliary energy, investment, and operation costs. The recovery and preservation of microalgae also require considerations. Microalgae cultures are usually very dilute suspensions with concentrations between less than 1 g/L (ponds) and 3–15 g/L (tubular or flat panel reactors) (Wijffels 2019). Thus, the recovery is a challenging task and is achieved by combining various operations such as sedimentation, flotation,

filtration, and centrifugation followed by preservation of microalgal cells in order to maintain the protein quality of the biomass and the activity of other compounds of interest (Table 5.2).

Table 5.2 Major microalgal products and producers

Product	Microalgal source	Producer	Reference
Astaxanthin (dietary supplement)	<i>Haematococcus pluvialis</i>	Cyanotech (Hawaii, USA), EID Parry (India), Mera Pharma (USA), US Nutra (USA), Bioreal (Sweden), Parry Nutraceuticals (India)	Cyanotech (2019), EID Parry (2019), Mera Pharma (2019), Bioreal (2019), and US Nutra (2019)
Astaxanthin (food ingredient/additive)	<i>Haematococcus pluvialis</i>	Algatech (Israel), Blue Biotech (Germany), Fuji Chemicals (Japan), Mera Pharma (USA), Bioreal (Sweden)	Algatech (2019), Bioreal (2019), Blue Biotech (2019), Fuji Chemical (2019), and Mera Pharma (2019)
<i>Spirulina</i> (dietary supplement)	<i>Spirulina</i> sp.	Cyanotech (Hawaii, USA), Earthrise (California, USA), Dainippon (Japan), EID Parry (India), Blue Biotech (Germany), Inner Mongolia Biomedical Eng (Mongolia), Panmol (Australia), <i>Spirulina Mexicana</i> (Mexico), Siam Alga Co (Thailand), Nippon <i>Spirulina</i> (Japan), Koor Foods Co (Israel), CBN <i>Spirulina</i> group Co., Ltd. (China), Beihai SBD Bio-Science Technology Co., Ltd. (China), Myanmar <i>Spirulina</i> (Myanmar), Blue Continent (NA)	Chacon-Lee and Gonzalez-Marino (2010), Tramroy (2011), Chen et al. (2015), Cyanotech (2019), Earthrise (2019), EID Parry (2019), US Nutra (2019), and Blue Biotech (2019)
<i>Chlorella</i> (dietary supplement)	<i>Chlorella</i> sp.	Blue Biotech (Germany), Earthrise (USA), Dainippon (Japan), Roquette Klotze (Germany), <i>Chlorella</i> Co. (Taiwan)	Chacon-Lee and Gonzalez-Marino (2010) and Blue Biotech (2019)
<i>Chlorella</i> (food supplement)	<i>Chlorella</i> sp.	Phycom (Netherlands), Dongying Diazen, Biological Engineering Co., Ltd. (China)	Chen et al. (2015)
EPA/DHA (omega-3) as dietary supplement	<i>Schizochytrium</i>	Flora Health (USA)	Flora Health (2019)
EPA/DHA (omega-3) as food ingredient)	<i>Cryptocodinium</i> , <i>Nannochloropsis</i> , <i>Schizochytrium</i>	Cellena (USA), Martek/DSM (USA/NL) Blue Biotech (Germany), Xiamen Huison Biotech Co. (China)	Tramroy (2011) and Blue Biotech (2019)

(continued)

Table 5.2 (continued)

Product	Microalgal source	Producer	Reference
β -Carotene (as additive/ vitamin)	<i>Dunaliella salina</i>	EID Parry (India), Cognis Australia (Australia), Natural Beta Technologies (Australia), Tianjin Lantai Laboratory (China), Nature Beta Technologies (Israel), Nikken Sohonsa (Japan), Aqua Carotene Ltd (Australia), Proalgen Biotech (India)	Carlsson et al. (2007), Chacon-Lee and Gonzalez-Marino et al. (2010), Tramroy (2011), Parry Nutraceuticals (2019), and Proalgen Biotech (2019)

5.6 Future Direction of Research

Although many compounds of high biological value and health benefits have already been discovered, microalgae still remain one of the most unexplored groups of organisms in the world, as around 97% of marine microalgal compounds are yet to be isolated and characterized (Guedes et al. 2011). This lack of information demands for intensive research in the area of bioprospecting that involves isolation, identification, and growth optimization of new and locally available microalgal strains. The discovery of hyper-producing strains and novel metabolites with various health benefits helps to improve the economics of nutraceutical production. Among the around 10,000 algae species that are believed to exist, only a few thousand strains are kept in collections, a few hundred are investigated for chemical content, and just handful microalgae, e.g., *Chlorella*, *Dunaliella salina*, and *Haematococcus pluvialis*, are cultivated in industrial quantities (Spolaore et al. 2006). The development of a number of transgenic algal strains boasting recombinant protein expression, engineered photosynthesis, and enhanced metabolism encourages the prospects of engineered microalgae (Rosenberg et al. 2008). The other key area of further research is the complete genome sequencing of high nutraceutical-producing microalgae. Although *C. reinhardtii* and 30 other organellar and whole algal genomes have reportedly been sequenced (Guarnieri and Pienkos 2015), but in order to understand and characterize the genes and enzymes involved in the production of nutraceuticals and the mechanisms that trigger the production of these metabolites, such as nutrient deprivation and biotic and abiotic stress, information on whole genome sequences is integral. Major advancements are also required to construct bioreactors or open pond systems, which are made of inexpensive and environmentally friendly materials, and development of less energy-demanding and inexpensive harvesting and extraction techniques as extraction and purification of microalgal biomass and nutraceutical compound add up to the major costs of microalgae production plants (Garcia et al. 2017). Intensive research is also required for the identification of phenolic and volatile compounds from microalgae, and furthermore, advanced techniques are required for the isolation of such compounds, since this information is missing till now due to the complexity of their isolation. Despite being rich in

proteins, the dried form of microalgae as food or food substitute has failed to attract the consumers due to the fishy smell and dark green color associated with these food products. To harness the benefits of nutritious proteins from microalgae, essential strategies are needed, which would be helpful to cover its smell or taste, for instance, microencapsulation techniques (Chacón-Lee and González-Mariño 2010).

5.7 Conclusion

Microalgae are known for their potential to produce food ingredients and bioactive compounds since ancient times. The microalgal biomasses are being widely cultivated to make the commercial formulation of functional foods and nutraceutical application. Microalgae contain many valuable compounds, which includes omega-3 fatty acids, vitamins, and pigment-protein complexes besides anticancer, antioxidative, cytotoxic, and anti-obesity activities. As research interests and investment in microalgae continue to grow in various parts of the world, their role in providing health benefits and nutrition will keep expanding, and these minuscule biofactories may bring about revolutionary changes in nutraceuticals in the future.

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