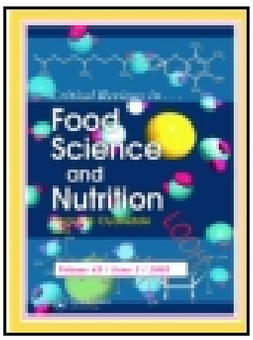

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Industrial potential of carotenoid pigments from microalgae: Current trends and future prospects

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ABSTRACT

Microalgae are rich source of various bioactive molecules such as carotenoids, lipids, fatty acids, hydrocarbons, proteins, carbohydrates, amino acids, etc. and in recent Years carotenoids from algae gained commercial recognition in the global market for food and cosmeceutical applications. However, the production of carotenoids from algae is not yet fully cost effective to compete with synthetic ones. In this context the present review examines the technologies/methods in relation to mass production of algae, cell harvesting for extraction of carotenoids, optimizing extraction methods etc. Research studies from different microalgal species such as *Spirulina platensis, Haematococcus pluvialis, Dunaliella salina, Chlorella* sps., *Nannochloropsis* sps., *Scenedesmus* sps., *Chlorococcum* sps., *Botryococcus braunii* and *Diatoms* in relation to carotenoid content, chemical structure, extraction and processing of carotenoids are discussed. Further these carotenoid pigments, are useful in various health applications and their use in food, feed, nutraceutical, pharmaceutical and cosmeceutical industries was briefly touched upon. The commercial value of algal carotenoids has also been discussed in this review. Possible recommendations for future research studies are proposed.

KEYWORDS

microalgae; carotenoids; processing; biological activities; applications

CHEMICAL COMPOUNDS STUDIED IN THIS ARTICLE

Neoxanthin (PubChem CID: 5281247); Violaxanthin (PubChem CID: 448438); Astaxanthin (PubChem CID:5281224); Lutein (PubChem CID: 5281243); Zeaxanthin (PubChem CID: 5280899); β-cryptoxanthin (PubChem CID: 5281235); α-carotene (PubChem CID: 6419725); β-carotene (PubChem CID: 5280489); Canthaxanthin (PubChem CID: 5281227); Fucoxanthin (PubChem CID: 5281239)

1. Introduction

Carotenoids are known for their industrial applications (Dufosse et al., 2005; Rodriguez-Amaya, 2016). While natural carotenoids are produced by plants (Giuliano et al., 2008; Ramel et al., 2012; Carbonell-Capella et al., 2014), synthetic ones are mainly by products from coal distillation. However, there is growing demand to phase out the use of synthetic carotenoids in many countries due to health considerations. Use of natural bioactive compounds in functional foods is beneficial as they will be able to protect cells from oxidative damage (Ranga Rao et al., 2013a, 2014a; Carbonell-Capella et al., 2014). They are also valuable in protecting deterioration of food products during the storage and processing. It is also a known fact that carotenoid pigments can influence signaling and regulation of many biological pathways (Stahl et al., 2002). More than 600 naturally occurring carotenoid pigments are identified and characterized and among them astaxanthin, β-carotene and lutein are considered to be important carotenoids for their potential applications in foods (Zhang et al., 2014). Microalgal species are also known to produce various bioactive compounds and fine chemicals (Pignolet et al.,2013; Phang et al., 2015; Ranga Rao et al., 2016). Certain algal species are exploited commercially for proteins, vitamins, pigments, fatty acids, lipids and phenolic compounds (Spolaore et al., 2006; Larkum et al., 2012). Table 1 shows recent review of literature on microalgal species for various uses. Recently, carotenoid pigments from algae have received more attention in health food applications (Guedes et al., 2011a; 2010b; Buono et al., 2014; Zhang et al., 2014). Among the algal species, *Haematococcus pluvialis, Dunaliella salina, Chlorella* sps, *Scenedesmus* sps, *Spirulina platensis, Botryococcus braunii*, and Diatoms are well known for the production of β-carotene, lutein, canthaxanthin, astaxanthin, and fucoxanthin (Lamers et al., 2008; Ranga Rao et al., 2010a; Zhang et al., 2014). However, the pigment composition of algae vary from species to species and also according to environmental conditions. It is observed that most of the algal species accumulate more amounts of pigments under stress conditions like nutrient deficiency (Ranga Rao et al., 2010b; Sarada et al., 2012). The present review provides information on the

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Table 1. Recent literature on microalgae and their use in various applications.

Micro algal species	Focus on	References
S. platensis, H. pluvialis, D. salina, Chlorella sps, *Nannochloropsis* sps, *Scenedesmus* sps, *Chlorococcum* sps, *B. braunii, Diatoms*	Carotenoid pigments, chemical structure, extraction and processing, commercial applications, carotenoid producing companies, global market, current trends and future prospects	Current article
Not specified algal species	Carotenoids, biosynthesis pathway, genetic engineering, transcription factors, metabolic engineering, nutritional fatty acids, lipids and carotenoids.	Coesel et al., 2008; Vigani et al., 2015; Odjadjare et al., 2015; Varela et al., 2015; Wang et al., 2015; Henriquez et al., 2016; Gong and Bassi, 2016; D Alessandro and Antoniosi Filho, 2016; Hamed, 2016; Minhas et al., 2016; Schweiggert and Carle, 2016; Bajhaiya et al., 2017;
H. pluvialis	Astaxanthin production, astaxanthin sources, stability, nutritional properties, commercial applications.	Ranga Rao et al., 2014a; Shah et al., 2016; Kishimoto et al., 2016; Bilbao et al., 2016; Panis and Carreon 2016
H. pluvialis, D. salina, Chlorella sps, *Scenedesmus* sps	Carotenoid health benefits.	Zhang et al., 2014
S. platensis, H. pluvialis, Chlorella sps, *Scenedesmus* sps, *Isochrysis* sps; *Nannochloropsis* sps, *Porphyridium* sps, *Tetraselmis* sps,	Bioactive molecules for livestock feed, poultry, aquaculture, and bioremediation	Yaakob et al., 2014a; Yaakob et al., 2014b; Roy and Pal, 2015
S. platensis	Nutritional, Medical applications	Eriksen, 2008; Kuddus et al., 2013; Hoseini et al., 2013
S. platensis, H. pluvialis, D. salina, Chlorella sps, *Scenedesmus* sps, *Isochrysis* sps	Functional properties of carotenoids; Functional ingredients; Novel food products	Gouveia et al., 2008; Plaza et al., 2009; Christaki et al., 2012; Vilchez et al., 2011; Buono et al., 2014;
H. pluvialis, D. salina, Chlorella sps, *Scenedesmus* sps, *Muriellopsis* sps,	Carotenoid production, process	Guedes et al., 2011a; 2011b; Del Campo et al., 2007
Chlorella sps, *Scenedesmus* sps, *Chlorococcum* sps, *Muriellopsis* sps	Lutein production	Fernandez et al., 2010.
S. platensis, H. pluvialis, D. salina, Chlorella sps, *Nannochloropsis* sps, *Isochrysis* sps	Commercial applications	Spolaore et al., 2006.
S. platensis, H. pluvialis, D. salina	Micro-organisms for pigments	Dufosse et al., 2005.
Diatoms	Pigments, fucoxanthin, biosynthesis pathway, biological properties, applications,	Lee et al., 2006; Kroger and Poulsen, 2008; Bozarth et al., 2009; Prestegard et al., 2009; Xia et al., 2013; Kuczynska et al., 2015; Fu et al., 2015; Lelyana, 2016; Guo et al., 2016; Medlin, 2016.

carotenoid pigments including pigment production, chemical structure, extraction process, and commercial applications from select algal species from Cyanophyceae, Chlorophycea, Rhodophyceae and diatoms. The select microalgal species include *S. platensis, H. pluvialis, D. salina, Chlorella* sps, *Nannochloropsis* sps, *Scenedesmus* sps, *Chlorococcum* sps, *Botryococcus braunii*, and Diatoms. Further, their market values and the future prospects of carotenoids are discussed.

2. Structure of carotenoids

Carotenoids are classified into two types based on their chemical structure. Oxygenated carotenoids are referred as xanthophyll's while other carotenoids are hydrocarbon carotenoids or simply referred as carotenoids. Carotenoids are fat soluble pigments and are tetraterpenoids (C_{40}). C_{40} carbon atoms are considered as the backbone of the carotenoid molecule. The content and composition of carotenoid pigments produced by microalgae species vary and are influenced by the culture conditions (Sarada et al., 2012; Ranga Rao et al., 2014a; Wells et al., 2016). Figure 1 shows common chemical structure of carotenoids in microalgae species.

3. Carotenoid pigments from microalgae

Microalgae are photosynthetic micro-organisms of around 30,000 species. Algal groups are classified as Cyanophyta(e.g. blue-green algae), Phaeophyta(e.g. brown algae), Rhodophyta (e.g. red algae) and Chlorophyta(e.g. green algae) based on their morphological features. However, based on the carotenoids, ten major classes of algae are identified (Table 2)

Though synthetic pigments are banned in many countries due to their adverse effects on human health, still they are used in various applications in many other countries (Mohammed and Mohd, 2011). The world demand of carotenoids is increasing due to consumer preference of natural carotenoids to synthetic ones. Based on the class to which the alga belongs and based on the species either carotenoids, or chlorophylls or phycobiliproteins may be dominant pigment in a particular alga. All these algae based pigments (Table 1) are used in various applications (Dufosse et al., 2005; Spolaore et al., 2006; Gantar and Svircev, 2008; Ceron et al., 2008; Ranga Rao et al., 2009; Ranga Rao et al., 2010b; Guedes et al., 2011a; 2011b; Pignolet et al., 2013; Yaakob et al., 2014a; Roy and Pal, 2015). Different stress conditions such as temperature, salinity, and irradiance may induce carotenoid production in algal species (Ranga Rao et al., 2010b; Sarada et al., 2012; Fu et al., 2014; Minhas et al., 2016). Accumulation of carotenoids in algae under nutrient deficiency culture conditions was reported by various authors (Orosa et al., 2001; Ranga Rao et al., 2010b; Sarada et al., 2012; Fu et al., 2013; Tran et al.,2014). Carotenoids from various microalgal species are discussed in the following section. Table 3, 4 and 5 summarizes culture conditions for carotenoid production, major carotenoid pigments, and their content for the selected microalgal species.

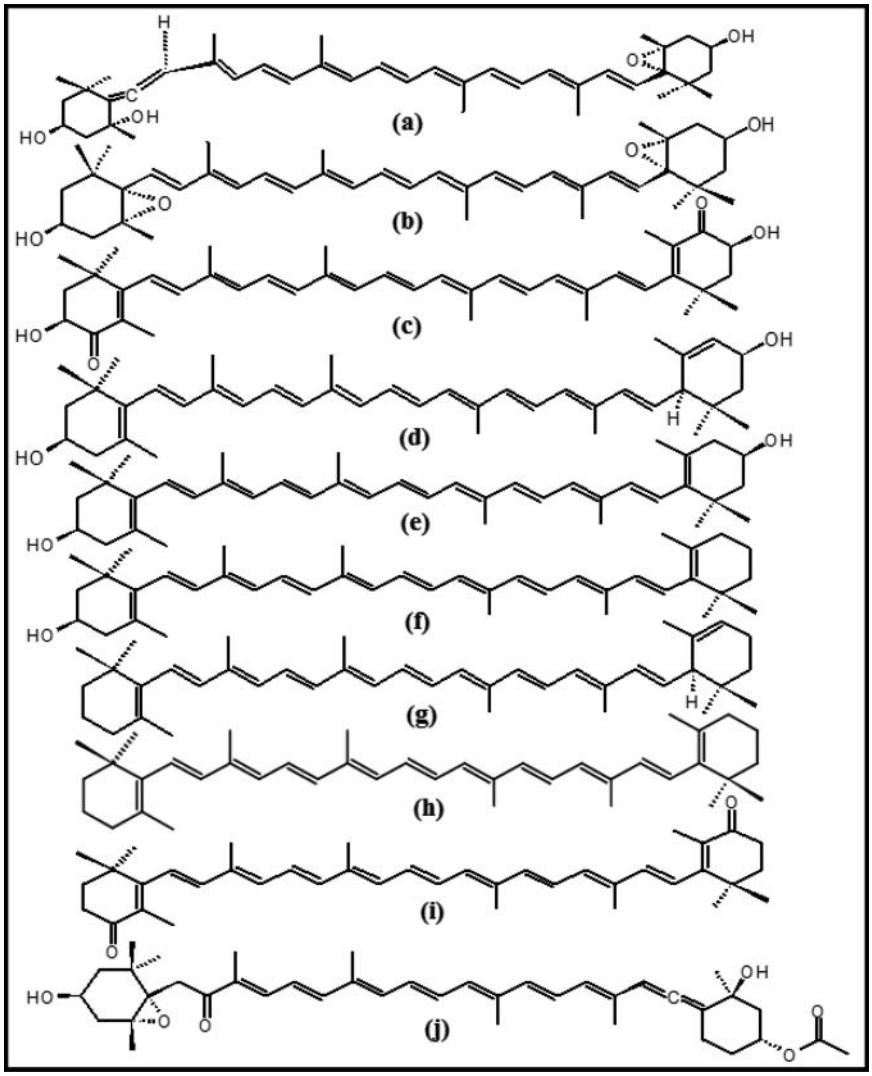

Figure 1. Common chemical structures of carotenoid pigments in microalgae. (a). Neoxanthin (3S,5R,6R,3′S,5′R,6′S)-6,7-didehydro-5′,6′-epoxy-5,6,5′,6′-tetrahydro-β,β-carotene-3,5,3′-triol), (b). Violaxanthin (3S,5R,6R,3′S,5′R,6′S)-5,6, 5′,6′-diepoxy-5,6,5′, 6′-tetrahydro-β,β-carotene-3,3′-diol), (c). Astaxanthin ((3S,3′S)-3,3′-dihydroxy-β,β-carotene-4,4′-dione), (d). Lutein (3R,3′R,6′R)-β,ε-carotene-3,3′-diol), (e). Zeaxanthin ((3R,3′R)-β,β-carotene-3,3′-diol), (f). β-cryptoxanthin ((3R)-β,β-caroten-3-ol), (g). α-carotene ((6′R)-β,ε-carotene), (h). β-carotene (β,β-carotene), (i). Canthaxanthin (β,β-carotene-4,4′-dione), and (j). Fucoxanthin ((3S,5R,6S,3′S,5′R,6′R)-5,6-epoxy-3,3′,5′-trihydroxy-6′,7′-didehydro-5,6,7,8,5′,6′-hexahydro-β,β-caroten-8-one 3′-acetate).

4. Select microalgal species for carotenoid pigments

4.1. Cyanobacteria (Cyanophycean forms)

4.1.1. Spirulina platensis

S. platensis is studied extensively as it contains high amount of protein ranging from 55 to 65% (Coca et al., 2014). *Spirulina* biomass is used commercially since it contains higher amounts of proteins, fatty acids including essential fatty acids and pigments (Hoseini et al., 2013). Carotenoid content of this alga was reported to vary from 0.1 to 0.4 mg/g (Ranga Rao et al., 2010a; Kumar et al., 2013). Carotenoids such as β-carotene, echinenone, β-cryptoxanthin, β-carotene-5,6-epoxide, 3-hydroxyechinenone, lutein, zeaxanthin, diatoxanthin, canthaxanthin, myxoxanthophyll, and oscillaxanthin were isolated and identified from *Spirulina* sps (Hanaa et al., 2003; Ranga Rao et al., 2010a; 2013b). Major carotenoids identified in *S. platensis* are β-carotene, zeaxanthin and β-cryptoxanthin (Ranga Rao et al., 2010a). In addition to carotenoids, *S. platensis* contains phycobiliprotein, the content of which varies based on the culture conditions (Simeunovic et al., 2012; Simeunovic et al., 2013). Upon consumption, these carotenoids help in controlling photo-oxidative damage of cells, immune enhancement, scavenging free radicals, hormone regulation, and enhancement of cell growth, cell maturation and multiplication (Eriksen, 2008).

4.2. Chlorophycean forms

4.2.1. Haematococcus pluvialis

H. pluvialis, green alga is well-known to produce astaxanthin and astaxanthin esters (Ranga Rao et al., 2013a). It is grown in autotrophic and heterotrophic culture conditions (Kang et al., 2005; Sarada et al., 2012). The carotenogenesis stage in this alga involves formation of thick walled aplanospores and accumulation of astaxanthin to a level of 2–4% of the dry weight (Ranga Rao et al., 2010a, 2013a, 2014a). Previously, we reported carotenoids in *H. pluvialis* as violaxanthin, astaxanthin, astaxanthin esters, lutein, zeaxanthin, α-carotene, and β-carotene (Ranga Rao et al., 2009, 2013a). Astaxanthin is permitted as color additive in fish feed by United States of Food and Drug

Table 2. Classification of algae and their carotenoid pigments.

Algae name	Scientific name	Carotenoid pigments
Blue-green algae	Cyanophyceae/Myxophyceae	Chlorophyll-a, β-carotene, c-phycoerythrin, c-phycoyanin,
Green algae	Chlorophyceae	Chlorophyll-a, chlorophyll-b, α-carotene, β-carotene, γ-carotene, lutein, siphonoxanthin and siphonein
Yellow-green algae	Xanthophyceae	Chlorophyll-a, β-carotene, diatoxanthin, diadinoxanthin, heteroxanthin
Golden-brown algae	Chrysophyceae	Chlorophyll-a, chlorophyll-c1, chlorophyll-c2 and fucoxanthin
Diatoms	Bacillariophyceae	Chlorophyll-a, chlorophyll-c, β-carotene, fucoxanhin, diatoxanthin and diadinoxanthin,
Cryptomonads	Crytophyceae	Chlorophyll-a, chlorophyll-c, α-carotene, diatoxanthin, phycoerythrin and phycocyanin
Dinoflagellates	Dinophyceae	Chlorophyll-a, chlorophyll-c2, β-carotene, peridinin and neoperidinin
Euglenoids	Euglenineae Euglenophyceae	Chlorophyll-a, chlorophyll-b, α-carotene, β-carotene, astaxanthin, antheraxanthin, diadinoxanthin and neoxanthin
Brown algae	Phaeophyceae	Chlorophyll-a, chlorophyll-c1, chlorophyll-c2, and β-carotene
Red algae	Rhodophyceae	Chlorophyll-a, r-phycocyanin, allo-phycocyanin, c-phycoerythrin, α-carotene, β-carotene

Administration (USFDA) (Pashkow et al., 2008). European countries have also approved astaxanthin as ingredient in human dietary supplement (Roche, 1987).

4.2.2. *Dunaliella salina*

D. salina is a motile green microalga which habitats lakes, oceans and brackish water bodies. It is a unicellular algal genus belonging to the family *Dunaliellaceae* (Feng et al., 2014; Lao et al., 2014). It is rich in carotenoids content that varies based on the culture conditions (Murthy et al., 2005; Tan and Suter, 2011; Fu et al., 2013; 2014; Tran et al., 2014). *Dunaliella* contains high amount of carotenoids (Fu et al., 2013). Thus, *Dunaliella* pro-vitamin A carotenes exhibit bright red color. Recently, carotenoids from *D. salina* are approved by USFDA as food color, and is recognized as safe natural colour (Dufosse et al., 2005; Yang et al., 2013). The provitamin-A carotenoids of *Dunaliella* are used as food additive (Hosseini and Shariati, 2009).

4.2.3. *Chlorella sps*

Chlorella is a green microalga producing good quantities of proteins, vitamins, minerals, carotenoids, and polysaccharides. (Sharma et al., 2012; Liu and Hu, 2013). *Chlorella* sps are also reported to produce xanthophylls such as violaxanthin, lutein and zeaxanthin, with lutein as the major carotenoid (Del Campo et al., 2004; Gouveia et al., 2006; Cha et al., 2008). *Chlorella vulgaris* and *Chlorella protothecoides* are mass cultivated both heterotrophically and autotrophically for biomass and carotenoid production (Shi et al., 2002; Wei et al. 2008; Seyfabadi et al., 2010; Campenni et al., 2013). In heterotrophic culture conditions, algal cells utilize organic carbon source available as energy whereas under autotrophic conditions cells collects the energy through photosynthesis (Larsdotter, 2006). *C. vulgaris* cells doubles in eight hours at a temperature of 20–35°C under autotrophic culture conditions (Gouveia et al., 1995). Carotenoids accumulation in *C. vulgaris* is affected by various factors such as light, salinity, nitrogen and phosphorus limitation (Gouveia et al., 1995; Zhang et al., 2017). Carotenoid pigments and their contents were reported to vary under different growth conditions (Safi et al., 2014; Abreu et al., 2012). *C. vulgaris* was grown in flat-plate photo-bioreactor, tubular photo-bioreactor and column photo-bioreactor for biomass, lipids, fatty acids, and pigments (Safi et al., 2014). Degen et al.,

Table 3. Possible carotenoid pigments from microalgae species.

Microalgae	Carotenoid pigments	References
S. platensis	Lutein, zeaxanthin, β-carotene,	Hanaa, 2003; Ranga Rao et al., 2010a; 2013a
H. pluvialis	Astaxanthin, astaxanthin esters, lutein, zeaxanthin, α-carotene, β-carotene, violaxanthin,	Sandesh Kamath et al., 2008; Ranga Rao et al., 2010a; 2013b
D. salina	Phytoene, β-carotene, lutein, zeaxanthin, *cis* and *trans* isomers,	Borowitzka and Borowitzka, 1989; Murthy et al., 2005; Dufosse et al., 2005; Borowitzka, 2010; Tan and Suter, 2011; Yang et al., 2013.
Chlorella sps; *Chlorella vulgaris; Chlorella protothecoides*	β-carotene, lutein, antheraxanthin, zeaxanthin, violaxanthin, canthaxanthin, astaxanthin, chlorophyll-a, chlorophyll-b, pheophytin-a, pheophytin-b	Gouveia et al., 1995; Shi et al., 2002;Pelah et al., 2004; Del Campo et al., 2004; Cha et al., 2008; Wei et al., 2008; Koo et al., 2012; Campenni et al., 2013; Liu et al., 2014; Zhang et al., 2014; Safi et al., 2014
Nannochloropsis sps	Zeaxanthin, astaxanthin, canthaxanthin	Lubian et al., 2000; Rebolloso-Fuentes et al., 2001; *Macias-Sanchez et al., 2005*; Forjan et al., 2007; Solovchenko et al., 2014.
Scenedesmus sps	Lutein, canthaxanthin isomer, canthaxanthin, astaxanthin, astaxanthin isomers, β-carotene, echinenone, adonirubin	Burczyk et al., 1981; Qin et al., 2008; Ceron et al., 2008; Sanchez et al., 2008; Pirastru et al., 2012, Ho et al., 2014.
Chlorococcum sps	Astaxanthin, astaxanthin esters, lutein,	Zhang and Lee, 1997; Zhang et al., 1997; Masojidek et al., 2000; Yuan et al., 2002;Sivathanu and Palaniswamy, 2012
B. braunii	Violaxanthin, astaxanthin, lutein, zeaxanthin, α-carotene, β-carotene	Grung et al., 1989; 1994; Okada et al., 1996; 1997; 1998; Muntean et al., 2008; Ranga Rao et al., 2010a; 2010b.
Diatoms- Phaeodactylum tricornutum, Hasle ostrearia; Haslea Karadagensis	Fucoxanthin, β-carotene, diadinoxanthin, diatoxanthin, violaxanthin, antheraxanthin, zeaxanthin, marennine, chlorophyll-a, chlorophyll-c,	Kraay et al., 1992; Prestegard et al., 2009; Bozarth et al., 2009; Peng et al., 2011; Gastineau et al., 2012; 2014; Kuczynska et al., 2015;Fu et al., 2015; Guo et al., 2016;Lelyana, 2016;

Table 4. Carotenoid content in the selected microalgae species.

Algal species	#Pigment (%)	#Major pigment or total carotenoids	References
Haematococcus pluvialis	3–7%	AX	Hata et al., 2001; Steinbrenner et al., 2001;Kang et al., 2005; Nobre et al., 2006; Ceron et al., 2007; Ranga Rao et al., 2011; 2014a; Regnier et al., 2015;
Chlorella vulgaris	12.5% TC	AX	Mendes et al., 1995; Cha et al., 2008
Chlorella vulgaris	55.5% TC	AX	Mendes et al., 2003; Singh and Gu, 2010; Chacon-Lee et al., 2010; Cha et al., 2010
Chlorella zofingiensis	0.7%	AX	Bar et al., 1995
Coelastrella striolata Var. multistriata	0.15%	AX	Abe et al., 2007
Dunaliella salina	3–13%	BC	El-Baz et al., 2002;
Chlorella zofingiensis	0.9%	BC	Bar et al., 1995
Coelastrella striolata Var. multistriata	0.7%	BC	Abe et al., 2007
Spirulina platensis	70–80% TC	BC	Miranda et al., 1998; El-Baky et al., 2003; Jaime et al., 2005; Ranga Rao et al., 2010
Chlorella pyrenoidosa	0.2–0.4%	LT	Wu et al., 2007
Botryococcus braunii	0.16%	LT	Tonegawa et al., 1998
Botryococcus braunii	75% TC	LT	Ranga Rao et al., 2006; 2007a; 2010a; 2010b; 2013b
Chlorella vulgaris	45% TC	LT CX	Mendes et al., 2003; Singh and Gu, 2010; Chacon-Lee et al., 2010; Cha et al., 2010
Phaeodactylum tricornutum	1.65%	FX	Ragni et al., 2007; Kim et al., 2012; Dambek et al., 2012
Isochrysis aff. galbana	1.8%	FX	Kim et al., 2012
Cylindrotheca closterium	0.5%	FX	Rijstenbil et al., 2003
Odontella aurita	2.2%	FX	Xia et al., 2013
Coelastrella striolata Var. multistriata	4.7%	CX	Abe et al., 2007
Chlorella zofingiensis	25% TC	CX	Bar et al., 1995
Chlorella vulgaris	36% TC	CX	Li et al., 2002; Singh et al., 2010; Chacon-Lee et al., 2010; Kong et al., 2012
Botryococcus braunii	0.17%	ECN	Tonegawa et al., 1998
Nannochloropsis sps	0.1%	TC	Lubian et al., 2000; Macias-Sanchez et al., 2005; Forjan et al., 2007; Nobre et al., 2013; Solovchenko et al., 2014
Scenedesmus sps	0.69%	TC	Qin et al., 2008; Ceron et al., 2008; Pirastru et al., 2012; Chan et al., 2013; Guedes et al., 2013; Ho et al., 2014;
Chlorococcum sps	0.25%	TC	Zhang and Lee, 1997; Zhang et al., 997;Masojidek et al., 2000; Yuan et al., 2002; Sivathanu and Palaniswamy, 2012;

#carotenoid contents in algae species varied upon their culture conditions; AX, astaxanthin; BC, β-carotene; LT, lutein; CX, canthaxanthin; ECN, echineone; TC, total carotenoids.

(2001) reported biomass productivity of 0.11 g/L/h when *C. vulgaris* was cultured in a flat panel photobioreactor under continuous light. High biomass productivity was obtained (up to 0.25 g/L/d) when *C. vulgaris* was grown in stirred bioreactor (Ogawa and Aiba, 1981; Martinez et al., 1991; Liang et al., 2009). *Chlorella* was widely cultivated for health food and nutrition supplements (Merchant and Andre, 2001; Merchant et al., 2002; Kitada et al., 2009). *Chlorella* contains very rigid cell wall and hence cells are processed in order to break the cell wall before using it as a food supplement in various applications (Tokusoglu and Unal, 2003). The bioavailability of carotenoids from *Chlorella* in humans is yet to be confirmed. However, as a good source of pro-vitamin A, the carotenoids from *Chlorella* could be converted in to vitamin A in humans.

4.2.4. Nannochloropsis sps

Nannochloropsis is a unicellular photosynthetic microalga with diameter of 2–3 μm and is found in marine, fresh and brackish waters (Brown, 1987). These species are non-motile, and cannot be distinguished by either light or electron microscopy. The characterization of this alga is done by rbcL gene and 18S rDNA sequence analysis (Starkenburg et al., 2014). The alga is known to produce various compounds such as fatty acids, lipids, including pigments such as zeaxanthin, astaxanthin and canthaxanthin (Rebolloso-Fuentes et al., 2001; Solovchenko et al., 2014). *Nannochloropsis* is considered as an important natural source in various applications due to its high essential fatty acids content (Hu and Gao, 2006; Gog et al., 2012; Nobre et al., 2013). *Nannochloropsis* is used as feed for fish larvae and rotifers (Bae and Hur, 2011).

4.2.5. Scenedesmus sps

Scenedesmus is a green microalga and is investigated for its possible applications in fish feed, as supplement in human nutrition, and in production of pharmaceutics (Yaakob et al., 2014a; Roy and Pal, 2015). It is one of the dominant species in freshwater bodies, lakes, and rivers (Mandotra et al., 2014). *Scenedesmus* sps are cultivated in continuous and semi-continuous culture mode using raceway and photobioreactors for obtaining high quantities of bioactive molecules (Wu et al., 2013; Abomohra et al., 2014). Physiological changes were observed in the cells under various culture conditions (Pancha et al., 2014). Under stress conditions, *Scenedesmus* accumulates β-carotene, astaxanthin isomers along with lutein and canthaxanathin (Burczyk et al., 1981; Ceron et al., 2008; Qin et al., 2008; Sanchez et al., 2008; Pirastru et al., 2012; Ho et al., 2014).

4.2.6. Chlorococcum sps

Chlorococcum is a green microalga, belonging to *Chlorophyta*, and is found in freshwater bodies and lakes. Under stress conditions *Chlorococcum* culture colour changes from green to orange as the cells accumulate secondary carotenoids (Zhang

Table 5. Culture conditions for carotenoid production in the selected microalgae using various photobioreactors.

Algal species	Culture conditions	Mode of cultivation and reactor	[#]Carotenoid productivity (mg/m^2/d or mg/L/d or mg/g/L/d)	Reference
Haematococcus pluvialis	T: 28°C; LI: 345 μmol photons/m^2/s	Batch (1L)	AX: 98 mg/g	Dominguez-Bocanegra et al., 2004;
	Day light cycle	Continuous chemostat, Tubular PBR (50 L)	AX: 8.0 mg/L/d	Garcia-Malea et al., 2009
	T: 15–25°C; LI: 2000 μmol photons/m^2/s	Enclosed PBR, outdoor (25000 L)	AX: 13 g/m^2/d	Olaizola, 2000
	T: 20–25°C; aeration: 1.5%v/v CO_2; day light	Glass column, batch mode; outdoor	AX: 17.1 mg/L/d	Wang et al., 2013
Dunaliella salina	T: 25°C; pH: 7.5 ± 0.5; LI: 281 ± 89 μmol photons/m^2/s	Semi-continuous outdoor, closed tubular PBR (55 L)	TC: 102.5 ± 33.1 mg/m^2/d;	Garcia-Gonzalez et al., 2005
	T: 30°C; pH: 7.5; LI: 200–1200 μmol photons/m^2/s	Continuous turbidostat, flat-panel PBR (2.5 L)	BC: 13.5 mg/L/d	Del Campo et al., 2001
	T: 30°C; pH:7.5; LI: 200–1200 μmol photons/m^2/s	Continuous turbidostat flat-panel PBR (1.9L) with in situ extraction	BC: 0.7–8.3 mg/L/d	Del Campo et al., 2001
Chlorella protothecoides	T: 28°C; pH: 6.5; LI: absence of light; heterotrophic	Batch (16 L)	LT: 10 mg/L/d	Wei et al., 2008
Chlorella zofingiensis;	T: 28°C; pH: 7; LI: 200 μmol protons/m^2/s; AF:50–100 L/h (1% v/v CO_2)	Batch (0.2 L)	LT: 3.4 mg/L/d	Kleinegris et al., 2011
Chlorella zofingiensis	T: 30°C; pH: 6.5; LI: darkness; SR: 130 rpm; heterotrophic	Batch (250 mL)	AX: 1.03 mg/L	Ip and Chen, 2005
Scenedesmus almeriensis	T: 30°C; pH:7.5; LI: 1700 μE/m^2/s; AF: 0.5 (v/v)/min/s; or T: 35°C; LI: 1900 μE/m^2/s	Continuous (2L) or Continuous outdoor, tubular PBR	LT: 4.9 mg/L/d; LT: 5.31 mg/m^2/d	Sanchez et al., 2008
Chlorococcum citriforme	T: 28°C; pH: 7; LI: 200 μmol protons/m^2/s; AF:50–100 L/h (1% v/v CO_2)	Batch (0.2 L)	LT: 1.05 mg/L/h	Kleinegris et al., 2011
Muriellopsis sp.	T: 28°C; pH:6.5; LI: 460 μmol photons/m^2/s;	Batch (0.2 L)	LT: 5.5 mg/g/L/d LT: 0.8–1.4 mg/L/d	Kleinegris et al., 2011
	T: 28°C; pH:7.0; LI: continuous 200 μmol photons/m^2/s; AF: 50–100 L/h (1%, v/v CO_2)	Continuous outdoor, tubular PBR (55 L); Semi continuous outdoor, open tank (100 L)	LT: 5.5 mg/g/L/d or LT: 100 mg/g/L/d	Garcia-Gonzalez et al., 2005

[#]carotenoid productivity in algal species varied upon their culture conditions; T, temperature; LI, light irradiance; AF, air flow; PBR, photobioreactors; TC, total carotenoids; AX, astaxanthin; LT, lutein; BC, β-carotene;

and Lee, 1997; Masojidek et al., 2000). *Chlorococcum* cells contain free astaxanthin, astaxanthin esters, free adonixanthin, adonixanthin esters, canthaxanthin, lutein, β-carotene and *cis*-isomers of keto-carotenoids (Zhang et al., 1997; Yuan et al., 2002). *Chlorococcum* produces high amounts of carotenoid esters like *Haematococcus pluvialis* (Ranga Rao et al., 2013a). Astaxanthin esters, free canthaxanthin and adonixanthin are the major pigments in *Chlorococcum* (Zhang and Lee, 1997; Sivathanu and Palaniswamy, 2012). *Chlorococcum* cells may be able to synthesize carotenoids from β-carotene via canthaxanthin and adonixanthin pathway (Yuan et al., 2002).

4.2.7. Botryococcus braunii

B. braunii is a Chlorophycean microalga and is found usually in fresh water reservoirs, ponds and brackish lakes (Metzger and Largeau et al., 2005). It is grouped into race'A', race 'B', and race 'L' based on hydrocarbons they produce (Banerjee et al., 2002; Ranga Rao et al., 2016). Apart from hydrocarbons, *B. braunii* produces carotenoids, lipids, and exopolysaccharides (Ranga Rao et al., 2007a, 2007b, 2012a, 2013a; Bayonaand Garces, 2014). Accumulation of carotenoids in race 'A', 'B' and 'L' of *B. braunii* was reported (Grung et al., 1989, 1994 Okada et al., 1996, 1997, 1998; Muntean et al., 2008; Ranga Rao et al., 2010). *B. braunii* culture changes to brown, red, orange, and pale yellow from green due to the carotenoids accumulation in the cells (Ranga Rao et al., 2016). Braunixanthin-1, braunixanthin-2, α-botryoxanthin, botryoxanthin-A, and botryoxanthin-B were isolated from 'B'race (Okada et al., 1996, 1991, 1998). Total carotenoids content in race 'A' was 0.28% as reported by Ranga Rao et al. (2010b). Carotenoid pigments such as lutein, violaxanthin, zeaxanthin, β-carotene and astaxanthin were reported in 'A' race (Muntean et al., 2008), and Ranga Rao et al (2006) reported lutein as major pigment in 'A' race. Recently, our research group reported carotenoid production and other molecules of interest from *B. braunii* for commercial applications (Ranga Rao et al., 2017)

4.2.8. Diatoms

Diatoms are prominent microalgal forms containing chlorophylls, carotenoids, fatty acids, lipids, and polysaccharides. The production of lipids, polysaccharides and pigments are regulated by abiotic stress factors and genetic modification of metabolic pathways (Perl et al., 1990; Lee et al., 2006; Prestegard et al., 2009; Peng, 2014). Diatoms have novel metabolic pathways in the evolutionary history of eukaryotes and show ecological success (Kuczynska et al., 2015). Diatoms are linked with the silicon metabolism involved in the biogeochemical cycling of silicon (Si) in the sea. The siliceous structures of their cell wall create unique morphologies which are used as taxonomic keys (Martin-Jezequel et al., 2000). Diatom cell physiology displays a significant difference in stationary, exponential and declining growth phases (Vidoudez and Pohnert, 2012). In both stationary and exponential growth phases, the influence of blue-green light and white light on accumulation of carotenoids in diatom species was reported (Sanchez-saavedra and voltolina, 2002; Brunet et al., 2014). Diatom cells accumulate high content of carotenoids under various stress conditions such as low and high irradiance, salinity, and nitrogen limitation (Xia et al., 2013). Diatoms contain chlorophylls and carotenoids which play a major role in photo-protection (Jeffrey and Vesk, 1997). The major component such as chlorophyll-a and chlorophyll-c together with fucoxanthin form fucoxanthin-chlorophyll protein complexes in diatoms species (Gelzinis et al., 2015). Fucoxanthin acts as light harvesting carotenoid pigment in diatoms which is usually found more in brown algal species. Carotenoids such as fucoxanthin, diadinoxanthin, diatoxanthin, zeaxanthin, β-carotene, astaxanthin, and violaxanthin were found in diatoms (Kuczynska et al., 2015). The carotenoid content in diatoms is different from that found in other algal species. The carotenoid composition is similar in various diatom species; however their levels among the species are varied. Carotenoid pigments from diatoms are used in health food applications (Bozar et al., 2009; Fu et al., 2015; Kuczynska et al., 2015). Changes in carotenoid content in diatom species under various culture conditions is presented in Table 6.

5. Extraction and processing of carotenoid pigments

Extraction and processing of carotenoid pigments from microalga is very challenging task as it involves harvesting of algal cells, processing, extraction and purification. Harvesting, analysis, extraction, purification and downstream processing of carotenoids from microalgae biomass are very important for commercialization process. Some of the microalgal cell walls are thick resisting easy disruption. Cell wall disruption can be achieved using any one or more of the several methods-mortar and pestle, two-phase extraction, milling, ultra-sonication, microwave, thawing, freezing, supercritical fluid extraction and also with edible oils. The selection of suitable extraction method depends on the specific algal species (McMillan et al., 2013). Carotenoids were extracted from *D. salina, H. pluvialis, S. platensis, B. braunii* and *Chlorococcum* sps cells with organic solvents using mortar and pestle (Zhang and Lee, 1997; Murthy et al., 2005; Sarada et al., 2006; Ranga Rao et al., 2013b). This method suits for bench scale process and not for scale-up process of industrial applications. Carotenoids extracted from the algal biomass using two phase extraction method of alkaline treatment were reported in different algal species (Sarada et al., 2006; Ceron et al., 2008; Ishida and Chapman, 2009). Extraction with ethanol and hexane allows easy removal of residual solvent and yielding extracts with high lutein content (Fernandez-Sevilla et al., 2010). Astaxanthin was extracted using dodecane and methanol solvent extraction method, and in this process free astaxanthin was recovered up to 85% (Kang and Sim, 2007). Another extraction method was developed for astaxanthin from *H. pluvialis* using vegetable oils. 90% of astaxanthin was recovered in olive oil extraction method (Kang and Sim, 2008). Carotenoid extraction with solvents was standardized to meet commercial specifications. However selective precipitation using supercritical CO_2 is a promising alternative. Carotenoids extraction from algal biomass is time consuming with many steps and requires large quantities of solvents which are expensive and harmful. Supercritical carbon-dioxide extraction method provides an efficient method for carotenoid extraction. This is a very rapid, efficient, non-flammable, non-toxic and an inexpensive extraction method. Carotenoids were extracted from various microalgal biomasses using supercritical carbon-dioxide (CO_2), with satisfactory results (Mendes et al.,

Table 6. Carotenoid pigments changes in diatoms species upon culture conditions.

Diatoms species	Culture conditions	Chl-a	Chl-c	BC	FX	DDX	DX	VX	References
Cyclotella meneghiniana	140 μmol photons/m^2/s; 40 μmol photons/m^2/s; 16 h: 8 h (L:D)	–	++	++	++	+	+	–	Alexandre et al., 2014
Cyclotella meneghiniana	140 μmol photons/m^2/s; Iron rich or replete medium	+	–	–	–	+++	+++	–	Beer et al., 2011
Cyclotella meneghiniana	40 μmol photons/m^2/s; Iron rich or replete medium	+	–	–	–	++	++	–	Brotas and Plante-Cuny, 2003
Pseudo-nitzschia multistriata	450 PFD with red and blue light ratio 0.25	+++	+	++	+++	+++	+++	–	Brunet et al., 2014
Pseudo-nitzschia multistriata	250 PFD with red and blue light ratio 0.25	+++	+	++	+++	+++	+++	–	Costa et al., 2013
Phaeodactylum tricornutum	300 μmol photons/m^2/s; 50 μmol photons/m^2/s; 14 h: 10 h (L:D)	–	+++	+	+++	+	+	–	Brunet et al., 2014
Phaeodactylum tricornutum	24 or 40 μmol photons/m^2/s with blue and white light,	+	++	++	++	++	–	+++	Costa et al., 2013
Phaeodactylum tricornutum	40 or 41 μmol photons/m^2/s with red and white light,	+	+++	+	+++	+++	–	+++	Costa et al., 2013
Phaeodactylum tricornutum	1250 μmol photons/m^2/s; 40 μmol photons/m^2/s; 12 h:12 h (L:D)	+++	++	++	++	+++	+	–	Domingues et al., 2012
Phaeodactylum tricornutum	24 or 40 μmol photons/m^2/s with blue and red light	+	–	–	–	+++	–	–	Jungandreas et al., 2014
Phaeodactylum tricornutum	24 or 40 μmol photons/m^2/s with blue and red light	++	–	–	–	+	–	–	Jungandreas et al., 2014
Cyclotella meneghiniana	700 or 40 μmol photons/m^2/s; 16 h: 8 h (L:D)	–	–	–	–	+++	+++	+++	Lohr et al., 1999
Odontella aurita	100 μmol photons/m^2/s with low or high nitrogen culture	–	–	–	+++	–	–	–	Xia et al., 2013

[#]Carotenoid pigments changes in diatoms species upon their culture conditions; Chl-a, chlorophyll-a; Chl-c, chlorophyll-c; BC, β-carotene; FX, fucoxanthin; VX, violaxanthin; DDX, diadinoxanthin; DX, diatoxanthin; "+", increase; "+++", decrease; "++", constant; "L", light, "D" dark; PFD, photon flux density.

1995; Careri et al., 2001; Macias-Sanchez et al., 2005; 2007; 2009). 80% of astaxanthin was recovered from *Haematococcus* cells when treated with hydrochloric acid at 80°C for 2 min. Similarly 70% of astaxanthin was recovered when cells were treated with 40% acetone at 80°C for 2 min (Kobayashi et al., 1997; Sarada et al., 2006). 95% of fucoxanthin in *Isochrysis galbana* was recovered using ethanol solvent extraction method (Kim et al., 2012).

Downstream processing is the most important step for algal carotenoid production and various strategies are available (Gong and Bassi, 2016). For cell harvesting, physical (Grima et al., 2003; Chen et al., 2011) or chemical methods (Uduman et al., 2010; Gorin et al., 2015; Hu et al., 2013; Pragya et al., 2013; McMillan et al., 2013; Utomo et al., 2013) can be used. Several extraction methods such as grinding (Hu et al., 2013), cryogenic grinding (Grima et al., 2003; Zheng et al., 2011), bead milling (Chan et al., 2013; Taucher et al., 2016), high pressure homogenizer (Kim et al., 2015), autoclave (Chan et al., 2013), microwave (McMillan et al., 2013; Pasquet et al., 2011; Zheng et al., 2011), enzymatic hydrolysis (Deenu et al., 2013; Kadam et al., 2013), pulsed electric field (Lai et al., 2014), alkaline treatment (Halim et al., 2012a; 2012b), ionic liquids (Park et al., 2015), conventional solvent extraction (Gil-Chavez et al., 2013), and supercritical carbon dioxide (Guedes et al., 2013; Yen et al., 2015; Liau et al., 2010) are used in carotenoid extraction. For cost effective downstream processing of carotenoids for food, feed and health application, an efficient method is to be adopted/developed based on the literature. Figure 2 presents downstream processing of carotenoids from algae for various applications.

6. Industrial application of carotenoid pigments

Carotenoids are natural pigments that occur widely in nature and shown to be beneficial in human health (Rao and Rao, 2007; Wells et al., 2016; Cooperstone and Schwartz, 2016). Various health benefits of carotenoids cover different ailments such as cancer (Sharoni et al., 2012), degenerative diseases (Ma et al., 2012; Aronow and Chew, 2014), cardiovascular diseases (Gaziano et al., 1995; Omenn et al., 1996), diabetes (Luvizotto et al., 2013), ulcer (Zhou et al., 2016). They also known to have ultraviolet light protection property (Stahl et al., 2000; Cesarini et al., 2003; Stahl and Sies, 2012). Carotenoids are bioactive compounds and play a part in important biological activities

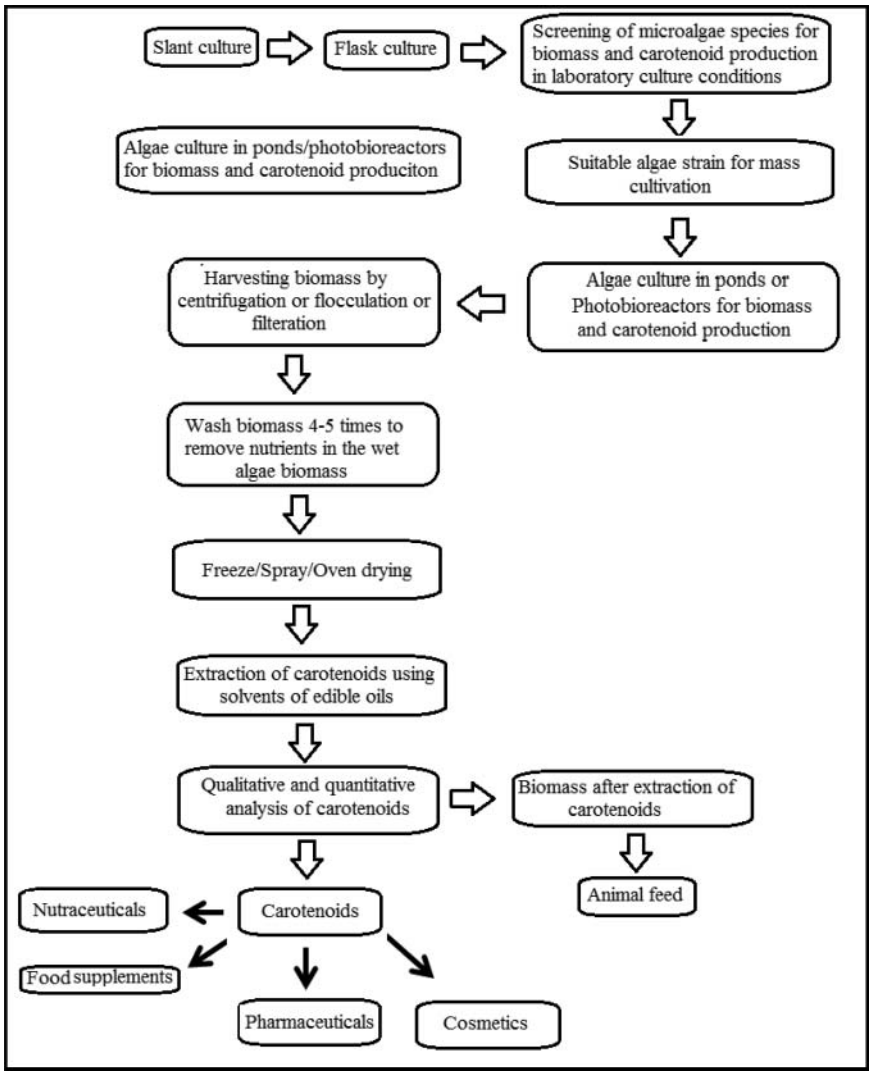

Figure 2. Processing of microalgal carotenoid pigments for commercial applications.

like bioavailability process (Castenmiller and West, 1998; Cooperstone et al., 2015), pro-vitamin A activity (Ross and Harrison, 2014), regulation of gene transcription (Palozza et al., 2003, 2012), induction of phase-II enzymes (Sharoni et al., 2004; Lian and Wang, 2008), antioxidant activity (Krinsky, 1989, 1991), alteration of immune function (Burton-Freeman et al., 2012), and also enhancement of gap junction communication (Stahl et al., 1997). Carotenoids are used in feed, food, and cosmeceutical applications (Vilchez et al., 2011; Tominaga et al.,2012; Ranga Rao et al., 2013a; Zhang et al., 2014; Yaakob et al., 2014a). Currently, the world demand for natural carotenoid pigments is increasing. Biotechnological process of β-carotene, astaxanthin, lutein, fucoxanthin and other pigments has high demand in the global market (*www.bccresearch.com*). Natural carotenoid pigments are preferred by the health market because they are mixture of cis/trans isomer forms, esters, and xanthophylls with high biological properties (Murthy et al., 2005; Hsu et al., 2008; Ranga Rao et al., 2013b). Microalgae rich in carotenoids are used as food colorants, food additives, and vitamin supplements (Zhang et al., 2014; Ranga Rao et al., 2014a). The most widely used algal species for this are *S. platensis, H. pluvialis, D. salina, B. braunii, Chlorella* sps, *Chlorococcum* sps, and *Scenedesmus* sps. Various cultivation systems (photo-bioreactors and raceway ponds) are used for mass cultivation of algae to obtain higher biomass yield and carotenoids for commercial applications (Olaizola, 2000; Del Campo et al., 2007; Ugwu et al., 2008; Chen et al., 2011; Ranga Rao et al., 2012a, 2012b; Havlik et al., 2013; Klok et al., 2014; Poonkum et al., 2015). Algae accumulate pigments in their biomass and also offer biological activities such as anti-oxidant activity, anti-cancer activity and anti-bacterial activity (Plaza et al., 2008, 2009; Buono et al., 2014). Among the algae species, β-carotene in *S. platensis;* β-carotene in and *D. salina*; astaxanthin and its esters in *H. pluvialis* and *Chlorococcum* sps; lutein in *Chlorella* sps and *B. braunii;* and fucoxanthin in diatoms have been used for commercial applications. Carotenoid pigments from algal species have been evaluated for biological properties in *in vitro* and *in vivo* models (Dufosse et al., 2005; Murthy et al., 2005; Vilchez et al., 2011; Zhang et al., 2014; Ranga Rao et al., 2014a).

Spirulina biomass is very interesting in food applications because of its nutritional properties (Eriksen, 2008; Hoseini et al., 2013). It is used as food supplements for humans, and as feed for animals as it contains nutritional constituents (Holman and Malau Adlui, 2013). It is also used in animal feed for pigmentation and for improvement of integumentary color of cultured fishes such as tilapia and sweet melt (Yaakob et al., 2014a). *S. platensis* has been used as a feed component in quality broilers and layer diets to enhance yolk color and flesh (Tan and Suter, 2011; Yaakob et al., 2014a). In *S. platensis*, β-carotene has been found to be the major carotenoid pigment (Del Campo et al., 2007). β-carotene is an important carotenoid which acts as pro-vitamin-A. It is used as color additive in foods and as an antioxidant. β-carotene from natural sources showed potential antioxidant properties compared to synthetic carotene (Murthy et al., 2005). *S. platensis* and *D. salina* are two algae which are the rich sources for β-carotene (Del Campo et al., 2007). Products derived from *D. salina* are either whole cell biomass or β-carotene extracts and are used for human consumption and also for animal feed (Spolaore et al., 2006; Gouveia et al., 2006). β-carotene from *D. salina* is used as natural colorant in foods and cosmetics (Hosseini and Shariati, 2009). β-carotene is the most efficient quencher and involved in the scavenging of reactive oxygen species, peroxyl radicals, singlet oxygen against lipid peroxidation (Stahl et al., 2005). It is also an efficient stimulator of gap junctional communication associated with cell differentiation, growth, apoptosis and also inhibition of lipid peroxidation (Palozza and Krinsky, 1992).

H. pluvialis, Chlorella sps and *Chlorococcum* sps are rich source for astaxanthin and its esters (Zhang et al., 1997; Gouveia et al., 2006; Ranga Rao et al., 2013b; Liu et al., 2014). Astaxanthin is a very valuable pigment, used as pigmentation source in aquaculture, nutraceutical, feed and food industries (Tominaga et al., 2012; Buono et al., 2014). Astaxanthin showed potential biological activities in *in vitro* and *in vivo* models (Sandesh Kamath et al., 2008; Ranga Rao et al., 2014a). Recently our research group has investigated biological activities of astaxanthin and astaxanthin esters against skin cancer in rat model, and the results showed better anticancer activity in both astaxanthin and astaxanthin esters treated animals (Ranga Rao et al., 2013a).

Chlorella sps are used as food supplements with various applications (Liu et al., 2014). It is used as nutritional supplements to the treatment of hypertension, fibromyalgia, and ulcerative colitis (Merchant and Andre, 2001). *Chlorella* sps showed potential antioxidant and anticancer properties in cell culture models (Gouveia et al., 2006; Cha et al., 2008). *C. vulgaris* is an important microalga used in biofuel, human nutrition, animal feed, food colorant, emulsifier agent, pharmaceuticals, and bio-fertilizers (Safi et al., 2014). *C. vulgaris* products are available in the form of capsules, tablets, extracts and powder in the market (Yamaguchi et al., 1996). *C. vulgaris* is rich in fatty acids, polysaccharides, pigments, vitamins, proteins, and is important in its use for nutraceutical purpose (Grobbelaar, 2003). *C. vulgaris* gives a better preservative activity compared to butylated hydroxytoluene and butylated hydroxyanisole (Rodriguez-Garcial and Guil-Guerrero, 2008). *C. vulgaris* accumulates pigments used as animal feed and showed an interesting pigmentation property for fish flesh and egg yolk in poultry industry (Gouveia et al., 1996; Gouveia et al., 2002). *C. vulgaris* showed protective activity against heavy metals and also harmful compounds by reducing oxidative stress in the tested animals (Vijayavel et al., 2007; Shim et al., 2008; Yun et al., 2011). The liquid extract of *C. vulgaris* used as bio-fertilizer in plants. It improved the seed germination, plant growth and productivity (Gonzalez and Bashan, 2000; Faheed and Abdel Fattah, 2008).

Nannochloropsis sps is used for nutraceutical applications as it contains vitamins, minerals, pigments, and polyunsaturated fatty acids (Markovits et al., 1992; Bishop and Zubeck, 2012; Nobre et al., 2013; Kent et al., 2015). *Scenedesmus* sps biomass is used as nutritional supplement for various applications (Ho et al., 2014; Kumar et al., 2015; Kent et al., 2015). Further, *Scenedesmus* sps is considered as potential source of feed stock for biofuel applications (Mandotra et al., 2014). *Chlorococcum* sps. is rich in carotenoids, polyphenols, fatty acids and showed potential biological activities in *in vitro* and *in vivo* models (Bhagavathy et al., 2011a, 2011b, 2012). Lutein accumulation in *B. braunii* and *Muriellopsis* sps. is exploited for commercial application (Del Campo et al., 2000, 2004; 2007; Ranga Rao

et al., 2010a; 2010b). Lutein and zeaxanthin are responsible for the coloration of the macula lutea in the retina, and are extremely important in ophthalmology for protection against age-related macular degeneration (Krinsky et al., 2003). *B. braunii* extracts showed potential anti-bacterial properties (Ranga Rao et al., 2010c). Antioxidant enzymes levels in rats were increased after feeding *B. braunii* as source of lutein (Ranga Rao et al., 2006, 2010a, 2013b).

Diatoms have great application in pharmaceutical, nutraceutical, and cosmeceutical industry (Perl et al., 1990; Lee et al., 2006; Prestegard et al., 2009) as they contain good quantities of chlorophylls, carotenoids, blue pigments, amino acids and fatty acids. There is much interest created for use of diatoms in health foods, pharmaceuticals, biofuels, and bioremediation applications (Bozarth et al., 2009). Diatom species also accumulates significant amount of fucoxanthin. Fucoxanthin is a carotenoid pigment with very high commercial value in the global market, and is used in biological activities such as anti-obesity, anti-oxidant, anti-angiogenic, anti-inflammatory, anti-cancer, photoprotective and neuro-protective activity (Pangestuti and Kim et al., 2011). Fucoxanthin may inhibit reactive oxygen formation, DNA damage, and apoptosis induced by hydrogen peroxide, and its antioxidant activity was comparable to α-tocopherol (Peng et al., 2011). Fucoxanthin showed anti-proliferative activity in human cell lines such as HL-60, PC-3, HT-29, DLD-1 and Caco-2 (Hosokawa et al., 1999; Asai et al., 2004). Fucoxanthin has the ability to reduce the nitric oxide levels, prostaglandin-E2, interleukin-6, tumor necrosis factor-α, histamine and interleukin-1β in *in vivo* models (Heo et al., 2008; Kim et al., 2010). Fucoxanthin is a promising bioactive compound which may help in the prevention of obesity through upregulation of uncoupling protein-1 (UCPI) which stimulates energy expenditure by thermogenesis (Maeda et al., 2005). Diatoms are rich in naviculan and domoic acid which showed anti-viral, neuroexcitatory, cytotoxic and blood platelet inhibitory activity (Perl et al., 1990; Lee et al., 2006; Prestegard et al., 2009). Marine diatom species such as *Haslea ostrearia* and *Haslea karadagensis* contain marennine (blue pigment) and showed anti-bacterial activity, anti-viral activity, and anti-oxidant activity in *in vitro* and *in vivo* experimental models (Gastineau et al., 2014). These unusual pigments accumulate in select diatoms species and these pigments have great potential applications in cosmetics and food supplements. Pigments from diatoms showed a major role in photo-protection (Wichuk et al., 2014; Fu et al., 2015; Kuczynska et al., 2015). Benefits of carotenoid pigments from algae are presented in Table 7.

7. Carotenoids market value and its manufactures

The importance and use of synthetic carotenoid pigments started declining due to their potential toxic effects. Nowadays, a transition has been stimulated towards green solutions and natural products and global market for natural products is estimated to reach $1.5 billion by 2020. One of the safe alternatives to synthetic pigments is carotenoids from microbial source (Dufosse et al., 2005; Yang et al., 2013). Naturally derived carotenoid pigments from microbial sources such as fungi, bacteria and algae have been exploited for commercial applications (Borowitzka, 2010). Carotenoid pigments such as astaxanthin, β-carotene, fucoxanthin and lutein from algae have received much more attention as they are shown to have potential use in nutraceuticals, pharmaceuticals, food, animal feed, dietary supplements, and cosmetics sector (Ranga Rao et al., 2014a; Bilbao et al., 2016; Lelyana, 2016). For nutritional importance, astaxanthin is considered as one of the best powerful antioxidant in nature that plays a major role in scavenging free radicals in human body (Roche, 1987; Guerin et al., 2003; Hussein et al., 2006; Park et al., 2010; Kent et al., 2015). The market value of carotenoids was expected to reach $1.53 billion by 2021. The demand for astaxanthin, β-carotene and lutein is now emerging in the global market. Astaxanthin is consumed by the salmon feed industry and the annual market value of the pigment is at $200 million with cost of $2500 per kg. Astaxanthin market for animal feed was $300 million, and for nutraceutical (as an antioxidant agent) was $30 million in 2009. It is expected to increase to $800 million and $300 million by 2020 for animal feed and for nutraceuticals respectively. Market value of β-carotene and lutein is expected to reach $334 and $309 million by 2018 respectively. The global market for fucoxanthin production was about 500 tonnes in 2015, and it is expected to reach at 5.3% CAGR by 2021(www.marketresearchstore.com).

Table 7. Benefits of carotenoid pigments from microalgae.

Carotenoid pigments	Benefits	References
Astaxanthin	Anti-oxidants, protect from UV rays, bioavailability, food colorant, animal feed, enhance immune functions, improve eye/skin health, anti-aging property, pharmaceutical, nutraceutical, cosmeceutical	Lorenz and Cysewski, 2000; Guerin et al., 2003; Higuera-Ciapara et al., 2003; Hussein et al., 2006; Lu et al., 2010; Park et al., 2010; Ranga Rao et al., 2010a; 2011; Choi et al., 2011; Kidd, 2011; Kim et al., 2011; Chan et al., 2012; Maoka et al., 2012; Chew et al., 2013; Dong et al., 2013; Huangfu et al., 2013; Ishiki et al., 2013; Yamashita, 2013; Yang et al., 2013; Ranga Rao et al., 2013a; 2014a;
β-carotene,	Vitamin A precursor, anti-oxidant, food color, malnutrition, prevent macular degeneration, skin burn from UV rays, depression, asthma, infertility, psoriasis, high blood pressure, pharmaceutical, cosmetics, animal feed, fish feed, pet foods	Fujii et al., 1993; Ben Amotz and Levy, 1996; Curtain, 2000; Kar, 2002; Murthy et al., 2005, Chidambara Murthy et al., 2005; Dufosse et al., 2005; Shaish et al., 2006; Mogedas et al., 2009; Ranga Rao et al., 2010a; Weber and Grune, 2012; Jayappriyan et al., 2013; Zhang et al., 2014; Donhowe and Kong, 2014;
Lutein, Zeaxanthin	Anti-oxidant, food colorant, fish feed, eye disease, health, age related macular degeneration, cataracts, pharmaceutical, nutraceutical, cosmetics, animal feed.	Landrum and Bone, 2001; Ranga Rao et al., 2006; Ceron et al., 2008; Fernandez-Sevilla et al., 2010; Ranga Rao et al., 2010a; Christaki et al., 2012; Maoka et al., 2012;
Fucoxanthin	Anti-oxidant, anti-viral, anti-diabetes, anti-obesity, anti-cancer, anti-inflammatory, anti-allergic, anti-osteoporotic	Maeda et al., 2009; Heo et al., 2010; Peng et al., 2011; Lee et al., 2013; Rokkaku et al., 2013;

As per the global carotenoids market analysis, Europe has a strong and potential market due to the increasing demand for animal feed, health supplements and Cosmetics. Involvement of leading cosmetic industries such as Unilever, L'Oreal, Henkel, and Beiersdorf are expected to improve the growth of carotenoid market value in the Europe market. Asia pacific region is projected to enhance the use of carotenoids in food supplements and animal feed in future. Several countries such as Japan, China and India are striving to improve the technology for carotenoid production economically to improve the market for carotenoids in Asia pacific region. A number of key vendors are playing a major role in producing carotenoid pigments across the globe such as Lycored, Divis Laboratories, Naturex SA, BASF Corporation, FMC Corporation, DSM Nutritional Products, Kemin Industries Inc., Allied Biotech Corp., Brenntag, Royal DSM N.V.Chr. Hansen A/S, Allied Biotech, Cognis, Carotech, D.D. Williamson & Co. Inc., Dohler Group, and ExcelVite SDN. BHD. Astaxanthin, β-carotene, fucoxanthin and whole cell biomass from algae are manufactured by various companies for commercial applications in food, feed, nutraceutical, pharmaceutical, and cosmeceutical sectors (Table 8).

8. Current trends and future prospects

Multi-steps are being considered towards screening, selection, production, cost and applications of carotenoids from microalgae. The important questions to be addressed are as follows: How to design micro-bioreactor technologies for emerging biotechnological applications to reduce bioprocess cost and time line? How to make a micro-photobioreactor design with high powered light emitting diodes (LEDs) with adjustable light intensity for massive carotenoid production and products for human health benefits? How to improve advanced sustainable engineering tools for proteomics, genomics, metabolomics and also applied for strain development for high value chemicals? How to make sustainable mass algal culture technologies with a control system for photosynthetic organisms for efficient biomass and carotenoid productivity? How to select mixed algal culture for high value compounds for health benefits? How to control potential predators in the open mass algal culture system (raceway/circular/photobioreactors)? How to develop early detection methods of controlling predators in mass algal culture? How to enhance the carotenoid production of the selected microalgae? How to develop sustainable technologies for carotenoid production of commercial process? How to enhance high quality carotenoid pigments in the global market for human consumption? How to exploit carotenoids for drug discovery and other novel applications? New integrated emerging technologies are required for microalgae to produce bioenergy molecules for health food applications. Novel technologies are required for cell harvesting, cell disruption, and downstream processing of microalgal carotenoid pigments. To save energy cost on the freeze or oven drier, wet extraction methods will have to be developed for carotenoids from algal biomass. The understanding of carotenoid structure, function relationships will enable researchers to tailor new microalgae carotenoids for biotechnological applications. Dueto the high cost of the currently available technologies for microalgal carotenoid pigments production on industrial scale, there is a requirement to develop sustainable cost effective process of the production of carotenoids to compete and replace the synthetic ones. Developments in microalgae research are expected through interaction between biotechnologists, biochemists, chemists, chemical engineers and as well as medical professionals. Micro algal carotenoids represent microorganisms capable of variety of important applications, there by presenting a fascinating field for future research. The carotenoids from algae can be scalable in cost effective manner, so that it can be continued to expand pigment production for the developing a new nutraceutical industry.

Table 8. List of companies producing carotenoid pigments and algae biomass.

Company name	Carotenoids or Biomass	Countries
E.I.D Parry Ltd.,	Astaxanthin	India
Algae Technologies	Astaxanthin	Israel
Mera Pharmaceuticals Inc.,	Astaxanthin	USA
Cyanotech Corporation	Astaxanthin	USA
Valensa International	Astaxanthin	USA
Fuji Chemicals Industry Co., Ltd.,	Astaxanthin	Japan, Sweden
Jingzhou Natural Astaxanthin Inc.,	Astaxanthin	China
Aquacarotene Ltd.,	β-carotene	USA
Cognis Nutrition and Health	β-carotene	Australia
Nikken Sohonsha Corporation	β-carotene	Japan
Tianjin Norland Biotech Co., Ltd.,	β-carotene	China
E.I.D Parry Ltd.,	β-carotene	India
Seambiotic	β-carotene	Israel
Muradel Pty Ltd.,	β-carotene	Australia
Cyanotech Corporation	β-carotene,	USA
AlgaNova International	Fucoxanthin	China
Leili Natural Products Co., Ltd.,	Fucoxanthin	China
Cyanotech Corporation	*Spirulina*	USA
E.I.D Parry Ltd.,	*Spirulina*	India
Hydrolina Biotech Pvt., Ltd.,	*Spirulina*	India
Nutrex Hawaii Inc.,	*Spirulina*	USA
Sun Chlorella Corporation	*Chlorella*	Japan
Yaeyama Shokusan Co., Ltd,.	*Chlorella*	Japan
Maypro Industries Inc.,	*Chlorella*	USA
Taiwan Chlorella Manufacturing Co., Ltd.	*Chlorella*	Taiwan
Far East Microalgae Ind Co., Ltd.	*Chlorella*	Taiwan
Roquette Klotze GmbH and Co. KG	*Chlorella*	Germany

9. Conclusion

Use of carotenoids from microalgae for health benefits is a promising field with large economic potential. Carotenoids from natural resources have been in demand in the global market. Microalgae species produce various carotenoid pigments. Major carotenoid pigments such as astaxanthin and astaxanthin esters in *H. pluvialis, Chlorococcum* sps and *Chlorella* sps, β-carotene in *D. salina, S. platensis*, and *Scenedesmus* sps, lutein in *B. braunii*, canthaxanthin in *Nannochloropsis* sps and fucoxanthin from diatoms were reported in microalgae. These carotenoids have high demand in the global market for health food applications. Astaxanthin and β-carotene have been well recognized in prevention and treatment of various diseases. There is lack of research studies on the astaxanthin esters, *cis* and *trans* forms of carotenoids, lutein and fucoxanthin in *in vitro* and *in vivo* models. Further, biochemistry, physiology, molecular genetics of carotenoid pigments needs to be investigated which will have major impact on the development and optimization of microalgae technologies. In view of this the genes encoding enzymes that are directly involved in specific carotenoid synthesis may be assessed. Further, mass algal cultivation systems

are required to be developed for production of high quality carotenoid pigments at economic cost. Currently, carotenoid pigments from algae are a very competitive, attractive, and the most popular growing field for bio-based economy. There is a need for better engineering tools to make the process better and cost effective manner.

Declaration of interest

The authors declare that they have no conflicts of interest.

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Author's contribution

ARR wrote the manuscript, GD involved in literature collection and chemical structures; GAR, RS, BPRN, BL, and SYP have been involved in improving the manuscript, and revising it critically. Finally all authors are in approval of the article submission.

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