

## The Final Development Related Microbial Pigments and the Application in Food Industry

Filiz YANGILAR<sup>1\*</sup>, Pınar Oğuzhan YILDIZ<sup>2</sup>

<sup>1</sup>Department of Nutrition and Dietetics, Faculty of Health Sciences, Erzincan University, 24000, Erzincan, Turkey

<sup>2</sup>Department of Food Engineering, Faculty of Engineering, Ardahan University, 75000, Ardahan, Turkey

(Geliş Tarihi/Received: 29.01.2016, Kabul Tarihi/Accepted: 18.04.2016)

### ABSTRACT

The successful marketing of natural pigments derived from microorganisms and microalgae or extracted from flowering plants, both as food colorants and nutritional supplements, reflects the presence, and importance of markets in which consumers are willing to pay a premium for “natural healthy ingredients”. As known, pigments present in natural products have antioxidant, antimicrobial and antimutagenic activities. The most commonly used food grade pigments are chemical compounds containing nitrite and nitrate salts and these synthetic compounds have carcinogenic and teratogenic effects. As colorant substances, natural pigments are very important. Natural pigments sourced from ores, insects, plants and animals were the colorants used since prehistoric period. The industry is now able to produce some microbial pigments for applications in food, pharmaceuticals, cosmetics and textiles. Microorganisms and microalgae as sources of pigments for food use: an industrial reality. The utilization of agro-industrial residues for pigment production may represent an added value to the industry and an environmental-friendly way for waste management. It is emphasized in the present review that is microbial pigments therapeutic potential and assess the potential roles of in food industry.

**Keywords:** microbial pigments; food industry, biological properties

## Mikrobiyal Pigmentler ile İlgili Son Gelişmeler ve Gıda Endüstrisindeki Uygulama Alanları

### ÖZET

Mikroorganizmalardan/alglerden veya bitki özütlerinden elde edilen doğal renk maddeleri hem gıda renk bileşenleri hem de gıda katkı maddeleri olarak tüketici isteklerini karşılayan “doğal sağlıklı katkı maddesi” olarak başarılı market uygulamaları yansıtmaktadır. Bilindiği gibi, antioksidant, antimikrobiyal ve antimutajenik aktiviteye sahip olan renk maddeleri doğal ürünler olarak tercih edilmektedir. Karsinojenik ve teratojenik özelliğe sahip sentetik bileşiklerden nitrit ve nitrat tuzlarını içeren kimyasal bileşikler en fazla kullanılan sentetik gıda renk maddeleridir. Renk maddeleri olarak doğal pigmentler çok önemlidir. Doğal renk madde kaynakları tarih öncesi zamandan beri kullanılan bitki, hayvan ve böceklerden elde edilen renklendiricilerdir. Günümüzde endüstriyel olarak gıdalarda, farmakolojide, kozmetik ve tekstilde kullanılmak üzere bazı mikrobiyal renk maddeleri üretilmektedir. Mikroorganizmalar ve alglerden endüstriyel olarak elde edilen renk maddeleri gıda üretiminde kullanılan renk maddeleri kaynağıdır. Renk üretimi için tarım-ziraat atıklarının uygulanabilirliği sanayi ve atık yönetiminde çevre dostu bir yöntem olarak ilave bir etki sunabilir.

Sunulan derlemede mikrobiyal pigmentlerin terapötik etkileri ve gıda endüstrisindeki potansiyel rolleri vurgulanmıştır.

**Anahtar kelimeler:** mikrobiyal pigment, gıda endüstrisi, biyolojik özellikleri

## 1. Introduction

Microalgae play an important role in the marine biological system. With their photosynthetic ability, they are the major producer of biomass and organic compounds in the oceans (Shimizu, 1993) and including the production of specialty compounds and nutritional supplements (Dunahay et al., 1996). Microalgae are a highly heterogeneous group of organisms and to be called a microalga, the organism to be small (usually microscopic), unicellular (but can be colonial with little or no cell differentiation), colourful (wherefore pigments), occur mostly in water and most likely be photoautotrophic. The microalgae, as a group, a potentially rich source of a vast array of chemical products with applications in the feed, food, nutritional, cosmetic, pharmaceutical and fuel industries (Schwartz et al., 1990; Kay and Barton, 1991; Borowitzka, 1992; Vilchez et al., 1997; Olaizola, 2003; Metzger and Largeau, 2005; Carvalho et al., 2006; Chisti, 2007; Chisti, 2008; Eriksen, 2008; Xu et al., 2009).

Live microalgae have been the traditional food for many animals in aquaculture. However, their mass cultivation on-site can represent 30% of a production cost (Coutteau and Sorgeloos, 1992; Knuckey et al., 2006). Alternatives that are potentially more cost-effective have been investigated including microcapsules, dried microalgae, yeasts or yeast-based diets and bacteria (Robert and

Trintignac, 1997; Knauer and Southgate, 1999; Langdon and Onal, 1999; Knuckey et al., 2006).

Microalgae are tremendous valuable microorganisms because they are the light-harvesting "cell factories" that convert carbon dioxide into biomass or a variety of bioactive compounds. The all microalgae which many can grow heterotrophically but photoautotrophs, requiring mainly sun, water and inorganic nutrients for growth. Compared to higher plants, microalgae are simple in structure, being unicellular, filamentous or colonial, and energy is directed via photosynthesis into growth and reproduction (Walker et al., 2005; Xu et al., 2009).

The microalga species are capable of synthesizing all amino acids; they can provide the essential ones to humans and animals (Guil-Guerrero et al., 2004). However, to fully characterize the protein and determine the amino acid content of microalgae, information on the nutritive value of the protein and the degree of availability of amino acids should be given (Becker, 1988). Carbohydrates in microalgae can be found in the form of starch, glucose, sugars and other polysaccharides, and their overall digestibility is high, which is using dried whole microalgae in foods or feeds (Becker, 2004). The average lipid content of algal cells varies between 1% and 70% but can reach

90% of dry weight under certain conditions (Metting, 1996).

**Table 1.** General composition of different micro algae (% of dry matter)

<b>Alga</b>	<b>Protein</b>	<b>Carbohydrates</b>	<b>Lipids</b>
<i>Anabaena cylindrica</i>	43–56	25–30	4–7
<i>Aphanizomenon flos-aquae</i>	62	23	3
<i>Chlamydomonas reinhardtii</i>	48	17	21
<i>Chlorella pyrenoidosa</i>	57	26	2
<i>Chlorella vulgaris</i>	51–58	12–17	14–22
<i>Dunaliella salina</i>	57	32	6
<i>Euglena gracilis</i>	39–61	14–18	14–20
<i>Porphyridium cruentum</i>	28–39	40–57	9–14
<i>Scenedesmus obliquus</i>	50–56	10–17	12–14
<i>Spirogyra</i> sp.	6–20	33–64	11–21
<i>Arthrospira maxima</i>	60–71	13–16	6–7
<i>Spirulina platensis</i>	46–63	8–14	4–9
<i>Synechococcus</i> sp.	63	15	11

Algal lipids are composed of glycerol, sugars or bases esterified to saturated or unsaturated fatty acids (12 to 22 carbon atoms). Microalgae also represent a valuable source of almost all vitamins (e.g., A, B1, B2, B6, B12, C, E, nicotinate, biotin, folic acid and pantothenic acid) (Becker, 2004; Spolaore et al., 2006).

The algal biotechnology mainly connected to choosing the right alga with relevant properties form specific culture conditions and products (Table 2; Pulz and Gross, 2004).

### **1. Final Development Related Microbial Pigments**

Natural pigments were the only source of colour available and were widely used and traded, providing a major source of wealth creation around the globe before the emergence of synthetic pigments. It has been used for purposes such as the colouring of natural fibres, fur and leather (Venil et al., 2013). The art of dyeing is of based on old and many of the dyes go back into prehistory.

**Table 2.** Microalga species with high relevance for biotechnological applications

Species/group	Product	Application areas	Basins/reactors
<i>Spirulina platensis/Cyanobacteria</i>	Phycocyanin, biomass	Health food, cosmetics	Open ponds, natural lakes
<i>Chlorella vulgaris/Chlorophyta</i>	Biomass	Health food, food supplement, feed surrogates	Open ponds, basins, glass-tube PBR
<i>Dunaliella salina/Chlorophyta</i>	Carotenoids, $\beta$ -carotene	Health food, food supplement, feed	Open ponds, lagoons
<i>Haematococcus pluviialis/Chlorophyta</i>	Carotenoids, astaxanthin	Health food, pharmaceuticals, feed additives	Open ponds, PBR
<i>Odontella aurita/Bacillariophyta</i>	Fatty acids	Pharmaceuticals, cosmetics, baby food	Open ponds
<i>Porphyridium cruentum/Rhodophyta</i>	Polysaccharides	Pharmaceuticals, cosmetics, nutrition	Tubular PBR
<i>Isochrysis galbana/Chlorophyta</i>	Fatty acids	Animal nutrition	Open ponds
<i>Phaedactylum tricornutum/Bacillariophyta</i>	Lipids, fatty acids	Nutrition, production	Open ponds, basins
<i>Lyngbya majuscula/Cyanobacteria</i>	Immune modulators	Pharmaceuticals, nutrition	

\* PBR – photo bioreactor

In Europe, it was applied to during the Bronze Age. The earliest written record of the use of natural dyes was found in China dated 2600 BC. In Indian subcontinent, dyeing was known as early as in the Indus Valley period (2500 BC) and has been substantiated by findings of coloured garments of cloth and traces of madder dye in the ruins of Mohenjo

daró and Harappa civilization (3500 BC). In Egypt, mummies have been found wrapped in coloured cloth. Chemical tests of red fabrics found in the tomb of King Tutankhamen in Egypt showed the presence of alizarin, a pigment extracted from madder. The cochineal dye was used by the people of Aztec and Maya culture period of Central and North

America. The 4th century AD, dyes such as wood, madder, weld, Brazil wood, indigo and a dark reddish-purple were known. Brazil was named after the wood found there (Frankel, 1993; Aberoumand, 2011). Henna was used even before 2500 BC, (Freund et al., 1988; Aberoumand, 2011) while saffron is mentioned in the Bible (Frick & Meggos, 1988; Aberoumand, 2011). Use of natural bio colorants in food is known from Japan in the shoso in text of the Nara period (8<sup>th</sup> century) contains references to coloured soybean and adzuki-bean cakes, so it appears that coloured processed foods had been taken at least by people of some sections. Study of colour intensified, since late 19th century (Aberoumand, 2011).

They were also used to colour cosmetic products and to produce inks, water colours and artist's paints (Cristea & Vilarem, 2006; Venil et al., 2013). Historical developments in colour were demonstrated in Table 3. Since the introduction of synthetic dyes by Perkin in 1856 (Joshi et al., 2003; Venil et al., 2013), many convenient and cheap synthetic pigments have appeared, and the use of natural dyes has decreased due to the relatively cheaper synthetic pigments (Zollinger, 1991; Venil et al., 2013). Throughout the 20th century, naturally occurring organic pigments have been almost completely displaced by synthetic molecules such as phthalocyanines that range from blue

to green, aryl ides that are yellow to greenish or reddish-yellow and quinacridones ranging from orange to violet (Lomax & Learner, 2006; Venil et al., 2013). Advances in organic chemistry enabled mass production of these compounds relatively cheaper thereby allowing them to displace natural product pigments, whose procurement is often more challenging. Applications of synthetic pigments are in the textile industry, leather tanning industry, paper production, food technology, agricultural research, light harvesting arrays, photo electrochemical cells and in hair colourants (Venil et al., 2013).

The synthetic pigments are consistently decreased under pressure of new rules and from the consumers. Table 4 shows the natural pigments available in the world market (Durán et al., 2002). Nowadays there is a great interest of the market for the microbial pigments; because of widely used synthetic pigments have harmful issues associated with the workers of industry as well as consumer. The success of any pigment produced by fermentation depends upon its acceptability in the market, regulatory approval, and the size of the capital investment required bringing the product to market. Microbial pigments are not only used as food colorant, flavouring agent and dyeing agents they are widely applied in medicinal aspects. Apart from food and textile colouring

**Table 3.** Historical developments in colour

Year	Development
1886	Perkin's mauve pigment was discovered and coal tar dyes were synthesized
1884	<i>Monascus</i> sp. was traditionally cultivated and utilized in the orient for making red rice wine, red shao hsing wine and red Chinese rice
1954	The first carotenoid pigment from <i>Cryptococcus</i> was marketed
1963	Production of carotenoid pigments from <i>Rhodotorula</i> sp. started
Early 1970s	Astaxanthin was isolated from <i>Phaffia rhodozyma</i> (in honour of Prof. Herman Jan Phaff) grown on exudates of deciduous trees in Japan and Alaska
Late 1970s and early 1980s	Production of beta carotene from <i>Dunaliella salina</i> took place
1985	Betatene limited corporation was established for cultivation of <i>D. salina</i> on large scale for producing natural beta carotene products

they have been used in clinical therapy to lower the blood cholesterol concentration, e.g. Anti-Diabetic Activity, Anti-Inflammation. A few years ago, some expressed doubts about the successful commercialization of fermentation-derived food grade pigments because of the high capital investment requirements for fermentation facilities and the extensive and lengthy toxicity studies required by regulatory agencies. Public perception of biotechnology-derived products should also be taken into account. Some fermentative food grade pigments are in the market and also the algae-derived or vegetable extracted pigments are successful marketed (Kumar et al., 2015).

### 3. Microbial Pigments Obtained from Different Ecosystems

Microorganisms by produce food grade pigments like carotenoids, melanins, flavins, quinones, and more specifically monascins, violacein, indigo, etc. Fermentation derived ingredients in the food industry are increasing the year. Production of food grade pigments by microbial fermentation is at a developing stage (Clydesdale, 1993; Dharmaraj et al., 2009). Especially carotenoids are widely used as food colourants (Klaui, 1981) and pigments in feeds (Marusich & Bauernfeind, 1981; Simpson et al., 1981).

**Table 4.** Natural pigments available in the world market

Pigments	CODE <sup>22</sup>
<b>YELLOW</b>	
Curcumin	E 100
Riboflavin	E 101
Annatto (carotenoids)	E 160
Xathophills (cathaxenthines)	E 161
<b>RED</b>	
Carminic acid	E 120
Beetroot Red (betaine)	E 162
Anthocyanine	E 163
<b>GREEN</b>	
Chlorophylle	E 140
Chlorophyllins	E 141
Greee S	E 142
<b>BROWN</b>	
Caramel colour	E 150
Ammonium sulfite caramel	E 150
<b>BLACK</b>	
Carbo medicinalis	E 153

More than 600 different carotenoids are synthesized by plants and microorganisms (Park et al., 2007). In addition to this, a number of microorganisms that includes *Serratia* and *Streptomyces* produce carotenoids in good amount (Kim, 1997; Dharmaraj et al., 2009). While the majority of microbes reported produce carotenoids constitutively, some organisms belonging to *Myxococcus* (Browning et al., 2003), *Streptomyces* (Takano et al., 2006),

*Mycobacterium* (Rilling, 1962), *Agrobacterium* (Yokoyama & Miki, 1995) and *Sulfolobus* (Hemmi et al., 2003), form these pigments when the cells are illuminated. The two *Streptomyces* sp., *Streptomyces setonii* and *Streptomyces griseus* are designated as cryptic since the conditions for carotenoid production in these organisms are unknown (Kato et al., 1995; Schumann et al., 1996; Krügel et al., 1999).

The red pigment includes monascorubramine and rubropunctamine that are the nitrogen analogues of the orange pigment. The yellow pigment includes monascin and ankaflavin (Zhou et al., 2009). The stained marble was found to contain red-pigmented heterotrophic bacteria belonging to the genera *Micrococcus*, *Halococcus*, and *Flavobacterium*, as well as the red yeast *Rhodotorula minuta*, and some photosynthetic microorganisms (Konkol et al., 2009).

Nowadays some fermentative food grade pigments from filamentous fungi exist in the market: *Monascus* pigments, Arpink red™ from *Penicillium oxalicum*, riboflavin from *Ashbya gossypii*, lycopene and  $\beta$ -carotene from *Blakeslea trispora*. Fungal hydroxyanthraquinoid (HAQN) pigments are widespread in nature (plants, insects, lichens) and have also been found abundantly in microorganisms, particularly in filamentous fungi belonging to the genera *Penicillium* sp. and *Aspergillus* sp., with different colour hues (Dufosse' et al., 2014). Some strains among *Talaromyces* species (formerly *Penicillium* sp.) viz. *Talaromyces aculeatus*, *T. funiculosus*, *T. pinophilus*, and *T. purpuro* genus have been discovered to produce *Monascus* like polyketide azaphilone (MPA) pigments without coproducing citrinin or any other known mycotoxins using

chemotaxonomic rationale (Teng & Feldheim, 2001; Dufossè et al., 2014).

Algae can be categorised into Chlorophyceae (green), Rhodophyceae (red), Pheophyceae (brown) according to their colours. Among the significant pigments produced by algae are chlorophyll a, b and c,  $\beta$ - carotene, Astaxanthin, Phycocyanin, Xanthophyll and Phycoerythrin which are frequently used in food, pharmacology, textile and cosmetics (Anonymous, 2015). Traditionally natural pigments have been extracted from natural sources such as plant and insect tissues, but obtaining pigments through microbial fermentation is also possible. Some bacteria, yeasts, basidiomycetes fungi and microalgae are known to produce pigments (Arad and Yaron, 1992; Ogihara et al., 2001; Davoli and Weber, 2002; Ginka et al., 2004; Zhang et al., 2006; Mapari et al., 2008), but high costs and low productivity are significant bottlenecks for commercial production (Hejazi and Wijffels, 2004; Hailei et al., 2011). A natural pigment as Astaxanthin produced from microalgae is a strong bioactive material (Yeum & Russell, 2002). The red microalgae are characterized by their accessory pigments which are red or blue. The pigment list's obtained from microorganisms is given in Table 5 (Malik et al., 2012).

**Table 5.** List of pigment producing microorganisms.

Microorganism (s)	Pigments/Molecule	Colour/appearance
<b>Bacteria</b>		
<i>Agrobacterium aurantiacum</i>	Astaxanthin	Pink- red
<i>Paracoccus carotinifaciens</i>	Astaxanthin	Pink-red
<i>Bradyrhizobium</i> sp.	Canthaxanthin	Dark- red
<i>Flavobacterium</i> sp., <i>Paracoccus zeaxanthinifaciens</i>	Zeaxanthin	Yellow
<i>Achromobacter</i>		Cream
<i>Bacillus</i>		Brown
<i>Brevibacterium</i> sp		Orange yellow
<i>Corynebacterium michigannise</i>		Greyish to creamish
<i>Corynebacterium insidiosum</i>	Indigoidine	Blue
<i>Rugamonas rubra</i> , <i>Streptovercillium rubrreticuli</i> , <i>Vibrio</i> <i>gaogenes</i> , <i>Ateromonas rubra</i>	Prodigiosin	Red
<i>Rhodococcus maris</i>		Bluish- red
<i>Xanthophyllomyces dendrorhous</i>	Astaxanthin	Pink-red
<i>Haloferax alexandrinus</i>	Canthaxanthin	Dark- red
<i>Staphylococcus aureus</i>	Staphyloxanthin Zeaxanthin	Golden Yellow
<i>Chromobacterium violaceum</i>	Violacein	Purple
<i>Serratia marcescens</i> , <i>Serratia rubidaea</i>	Prodigiosin	Red
<i>Pseudomonas aeruginosa</i>	Pyocyanin	Blue-green
<i>Xanthomonas oryzae</i>	Xanthomonadin	Yellow
<i>Janthinobacterium lividum</i>	Violacein	Purple
<b>Algae</b>		
<i>Dunaliella salina</i>	$\beta$ -carotene	Red
<i>Chlorococcum</i>	Lutein	
<i>Hematococcus</i>	Canthaxanthin	
<b>Fungi</b>		
<i>Aspergillus</i> sp.		Orange-red
<i>Aspergillus galucus</i>		Dark-red
<i>Blakeslea trispora</i>	$\beta$ -carotene	Cream
<i>Helminthosporium catenarium</i>		Red
<i>Helminthosporium avenae</i>		Bronze
<i>Penicillium cyclopium</i>		Orange
<i>Penicillium nalgeovensensis</i>		Yellow
<i>Fusarium sporotrichioides</i>	Lycopene	Red
<i>Haematococcus pluviialis</i>	Astaxanthin	Red
<i>Monascus</i> sp.	Monascorubramin	Red Orange
	Rubropunctatin	
<i>Monascus purpureus</i>	Monascin Ankaflavin	Red Yellow
<i>Monascus roseus</i>	Canthaxanthin	Orange-Pink
<i>Monascus</i> sp.	Ankaflavin	Yellow
<i>Penicillium oxalicum</i>	Anthraquinone	Red
<i>Blakeslea trispora</i>	Lycopene	Red
<i>Cordyceps unilateralis</i>	Naphtoquinone	Deep blood-red
<i>Ashbya gossypi</i>	Riboflavin	Yellow
<i>Mucor circinelloides</i> , <i>Neurospora crassa</i> and <i>Phycomyces</i> <i>blakesleeanus</i>	$\beta$ -carotene	Yellow-Orange
<i>Penicillium purpurogenum</i> , <i>Paecilomyces sinclairii</i>		Red
<i>Pacilomyces farinosus</i>	Anthraquinone	Red
<b>Yeast</b>		
<i>Cryptococcus</i> sp.		Red
<i>Saccharomyces neoformans</i> var. <i>nigricans</i>		Melanin black
<i>Phaffia rhodozyma</i>	Astaxanthin	Pink-red
<i>Rhodotorula</i> sp. <i>Rhodotorula glutinis</i>	Torularhodin	Orange-red
<i>Yarrowia lipolytica</i>		Brown
<b>Actinomycetes</b>		
<i>Streptovercillium rubrreticuli</i>	Prodigiosin	Red
<i>Streptomyces echinoruber</i>	Rubrolone	Red

In addition, microalgae are preferred since they can be cultured easily and fast when mixed with plants and they are also demanded for their high rate of carotenoid production, high bio-compatibility and benefits (Turkcan & Okmen, 2012).

#### **4. Antioxidant Activities of Microalga**

Nowadays, there has been a surge in research on the potential role of antioxidants in the treatment of atherosclerosis, heart disease, liver disorders, neurodegenerative dysfunction, cancer, and diabetes mellitus (Madhavi et al., 1996; Finkel and Holbrook, 2000; Ajitha et al., 2001; Mukund, 2013). For this aim, the functional foods are widely preferred by consumers due to the functional ingredient from the traditional foods that possess ingredients which are able to provide a useful action for human health. These natural ingredients are chosen by consumers and usually extracted from natural sources (plants, food by-products or even algae and microalgae). Among many ingredients in natural sources, antioxidants compounds are being the most studied (Hadzri et al., 2014). Antioxidants play an important role to protect the human body against oxidative damage caused by free radicals. Oxidative free radicals are highly reactive to attack molecules by capturing electrons and thus modifying chemical structures. The free radicals are generated through the oxidation of carbohydrates, fats and proteins through both aerobic and anaerobic processes. Over-production of the free radicals is responsible

for tissue injury (Gomathi et al. 2013; Kalidasan et al., 2015). Some algae are noted as rich sources of natural antioxidants (Chkhikvishvili & Ramazanov, 2000; Huang & Wang, 2004). Algae contains many biotic compounds such as phenolic compounds, alkaloids, plants acid, terpenoides and glycosides and they are used as antioxidants, anti-bacterial, antiviral and anti-carcinogenic (Demirel et al., 2009; Ansari and Nikhil, 2014). Polyphenolic compounds are among the interesting antioxidant compounds isolated from marine resources, including micro and microalgae. The most polyphenols isolated from marine sources and referenced in the literature are of macro and microalga origin (Amann et al., 1991). The intensity of the antioxidant activity of these complex polyphenols is related to the degree of polymerization of the polyphenol. Algal biomass and algae-derived compounds have a very wide range of potential applications, from animal feed and aquaculture to human nutrition and health products. There has been very limited information on antioxidant activity of microalgae (Herrero et al., 2005; Murthy et al., 2005; Tannin-Spitz et al., 2005). The microalga cells can be controlled, so that some of these contain no herbicides and pesticides, or any other toxic substances, by using clean nutrient media for growing the microalgae (Li & Chen, 2001; Li et al., 2002). The value of microalgae as a source of natural antioxidants is further enhanced by the relative ease of purification of target compounds (Li et al., 2001; Li et al., 2007). Some of the seaweeds are considered to be a

rich source of antioxidants (Lim et al., 2002). For example, chlorophylls, carotenoids, tocopherol derivatives such as vitamin E, and related isoprenoids that are structurally related to plant-derived antioxidants were found in some marine organisms (Takamatsu et al., 2003; Duan et al. 2006). In addition to fruits and vegetables, the carotenoids from microalgae have also demonstrated antioxidant properties (Jahnke, 1999; Maoka, 2011). Carotenoids possess other bioactivities and are thought to be active agents for the prevention of cancer cardiovascular diseases, and macular degeneration (Stierle et al., 1988; Balakrishnan et al., 2014). Seaweeds are considered to be an important source of bioactive compounds, as they are able to produce a great variety of secondary metabolites characterized by a broad spectrum of biological activities. Compounds with cytostatic, antiviral, anthelmintic, antifungal, and antibacterial activities have been detected in green, brown and red algae (Newmann et al., 2003; Ambreen et al., 2012; Yıldız et al., 2014). *Spirulina* boost the immune system and enhance the body's ability to generate new blood cells to prevent disease and cancer (Mathew et al. 1995; Danaraddi, et al., 2016).

The pigments, phenolics, antioxidant and vitamins from microalgae are given in Table 6 (de Jesus Raposo and de Morais, 2015). Especially carotenoids in general, and those from marine microalgae in particular, are excellent antioxidants, which can be exogenously supplied to the cells. Some of the most known and studied carotenoids

produced by microalgae include  $\beta$ -carotene from *Dunaliella salina*, astaxanthin from *Haematococcus pluvialis*, canthaxanthin from *Coelastrella striolata*, but also the less known, but not less effective, fucoxanthin from several diatoms, such as *Phaeodactylum tricornutum*, and *Isochrysis galbana* (Gross et al., 2002; Bhatt, 2008; Helmersson et al., 2009; Riccioni, 2009; Fassett et al., 2011; Bian et al., 2012; Speranza et al., 2012; de Jesus Raposo and de Morais, 2015).

### **5. The Application in Food Industry**

Colour is a vital quality attribute of foods, and plays an important role in sensory and consumer acceptance of products that consumers assess when determining the quality and appearance of a product, and therefore conditions its acceptability (Fernández-García et al., 2012). Based on the origin, food colours can be classified as natural, nature identical and synthetic. The use of colour in food has been a common practice since ancient time. With globalization in the research trends, colorants have been used for many years in the pharmaceutical industry in order to add colour to many medicinal products, as well as to ensure the same colour for all the batches of a given product (Rowe et al., 2003; Sanjay et al., 2007). Colours of foods create physiological and psychological expectations and attitudes that are developed by experience, tradition, education and environment (Stich et al., 2002; Dharmaraj et al., 2009). Natural pigments which are often

commercially available in powder, oil-soluble emulsion, or water-soluble emulsion forms (Caro et al., 2012) and synthetic are used extensively in the food, cosmetic and pharmaceutical industries (Mapari et al., 2005).

Concerns over potential toxicity of some synthetic pigments have led to increased interest in pigments derived from natural sources (Downham & Collins, 2000; Mapari et al., 2005; Silveira et al., 2008; Hailei et al., 2011). Natural colorants or dyes derived from flora and fauna are believed to be safe because of non-toxic, non-carcinogenic and biodegradable in nature. Therefore the present trend throughout the world is shifting towards the use of eco-friendly and biodegradable commodities, the demand for natural colorants are increasing day by day. Natural pigments are sourced from ores, insects, plants and microbes. Among microbes, bacteria have immense potential to produce diverse bio-products and one such bio-product is pigments (Venil et al., 2013). Some bacteria, yeasts, basidiomycetes fungi and microalgae are known to produce pigments (Ginka et al., 2004; Zhang et al., 2006; Mapari et al., 2008), but high costs and low productivity are significant bottlenecks for commercial production (Hejazi & Wijffels, 2004).

Ascomycetes fungi of the genus *Monascus* have been used to produce a natural food colorant when grown on rice (Liu et al., 2005); however, *Monascus* derived pigments contain citrinin, and the production of mycotoxin limits the use of *Monascus* as a

producer of food colorants (Liu et al., 2005; Hailei et al., 2011). Some species of the genus *Monascus* have long been used in East Asia as a natural food colorant for red rice wines, red soybean cheeses, and meat and fish products. Typical *Monascus* pigments are red, orange and yellow (Kim et al., 2006). Basidiomycete fungi may produce melanin from phenols and catechol precursors, characterized by a dark brown colour, in contrast to the true black appearance of melanin from the polyketide monomer 1.8 dihydroxynaphthalene (DHN) (Tudor et al., 2013). A natural pigment, Astaxanthin, produced from microalgae is a strong bioactive material and frequently used to be supplementary food to give more yellowish colour to egg's core and antioxidant in food (Yeum & Russell, 2002).

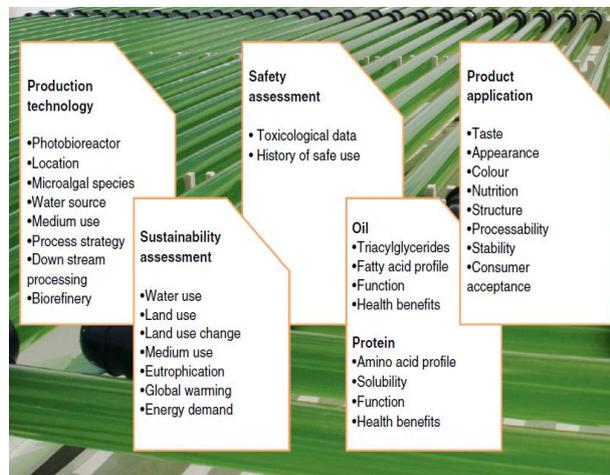
Nowadays, fermentative production of food-grade pigments particularly carotenoids from microorganisms are available in the market. To name a few, pigments from *Monascus* sp. (Blanc et al., 1994; Fabre et al., 1993; Hajjaj et al., 1999), astaxanthin from *Xanthophyllomyces dendrorhous* (Cruz & Parajo, 1998; An et al., 2001; Johnson & An, 2008), Arpink red colour from *Penicillium oxalicum* (Sardaryan, 2002; Sardaryan et al., 2004), riboflavin from *Ashbya gossypii* (Jacobson & Wasileski, 1994; Stahmann et al., 2000; Santos et al., 2005;),  $\beta$ -carotene from *Blakeslea trispora* (Lampila et al., 1985; European Commission, 2000; Enrique et al., 2005) and lycopene from *Erwinia uredovora* and *Fusarium sporotrichioides* (Jones et al., 2004; Leathers et al., 2004). In addition to this, a number of microorganisms that includes *Serratia* and *Streptomyces* produce

carotenoids in good amount (Kim et al., 1997; Dharmaraj et al., 2009).

**Table 6.** Pigments, phenolics and antioxidant vitamins from microalgae

Phytochemicals	Microalgae	Concentration	References
	<i>Dunaliella salina</i>	10–13% DW	El-Baz et al. (2002)
Carotenoids	<i>Chlorella zofingiensis</i>	50% total carotenoids	Bar et al. (1995)
β-carotene	<i>Arthrospira</i>	80% total carotenoids	Patel et al. (2005); Miranda et al. (1998)
Astaxanthin	<i>H. phuvialis</i>	Up to 4% DW	Steinbrenner and Hartmut (2001)
	<i>Arthrospira</i>		El-Baky et al. (2003)
Canthaxanthin	<i>C. zofingiensis</i>	25% total carotenoids	Bar et al. (1995)
	<i>Arthrospira</i>		El-Baky et al. (2003)
Lutein			
Phycobiliproteins			
C-phycoerythrin	<i>Arthrospira</i>	Up to 20% DW	Sarada et al. (1999); Patel et al. (2005)
Phycocyanin			
Phycocyanin	<i>Porphyridium</i>	80% total phycobiliproteins	Reboloso-Fuentes et al. (2000)
Phenolics (acids)			
Synapic	<i>Arthrospira</i>		Miranda et al. (1998)
Gallic	<i>Phaeodactylum</i>		Goiris et al. (2012)
trans-Cinnamic	<i>Tetraselmis Chlorella</i>		
Chlorogenic	<i>Neochloris, Isochrysis</i>		
Quimic	<i>Botryococcus</i>		
Caffeic			
Antioxidant vitamins			
Vitamin E (α-tocopherol) D	<i>Dunaliella</i>	12.1 mg/L	El-Baz et al. (2002)
	<i>Haslea, Chlorella</i>		
	<i>D. tertiolecta</i>	116.3 mg/kg DW	Miranda et al. (1998)
	<i>T. suecica</i>	442 mg/kg DW	Fabregas and Herrero (1990)
Vitamin C (ascorbic acid)	<i>Isochrysis</i>	885 mg/kg DW	Bandarra et al. (2003) El-Baz et al. (2002)
	<i>Dunaliella</i>	24.6 mg/L	
	<i>P. cruentum</i>		Sarrobot and Dermoun (1991)
	<i>D. tertiolecta</i>	163.2 mg/kg	
	<i>T. suecica</i>	191.0 mg/kg DW	
Other vitamins: Provitamin A	<i>P. cruentum</i>		Sarrobot and Dermoun (1991)
	<i>D. salina</i>		El-Baz et al. (2002)
B complex: thiamine, riboflavin, pyridoxine, folic acid, (cyano) cobalamin	<i>Dunaliella, Chlorella</i>		Fabregas and Herrero (1990)

An overview of the most important elements, which need to be considered to enable successful production and application of food commodities from microalgae, is showed in Fig. 1 (Draaisma et al., 2013).



**Fig. 1.** Food commodities from microalgae: overview of key features, which need to be considered to enable successful sustainable, cost effective and safe product applications.

The orange pigment includes monascorubrin and rubropunctatin, possessing the oxo-lactone ring. The red pigment includes monascorubramine and rubropunctamine that are the nitrogen analogues of the orange pigment. The yellow pigment includes monascin and ankaflavin (Zhou et al., 2009). Among these pigments, the red pigment (monascorubramine and rubropunctamine) is of high demand, especially for its use in meat products to substitute nitrites (Fabre et al., 1993). The red pigment is also reported to have the potential for therapeutic use particularly when produced in red rice (Lin et al., 2008; Mukherjee and Singh, 2011). While Rommier (1868) studied its dyeing properties on silk and wool, most recent studies determined that xylindein inhibits plant

germination without any hazardous effects on cultivated crops (Shibata et al., 2007; Tudor et al., 2013).

## 6. Conclusions

As food colourants are bio-accessibility of bioactive compounds that are of interest to the food scientists, nutritionists and food industries due to their positive impact on human health and their economic benefits. However, the number of approved colourant for food industry is limited. In addition the need for the studies related to the activities and contents of microbial pigments obtained from different ecosystems increases consistently. It is also thought that the studies related especially to pigments to be used as colourants in food and additive materials can contribute greatly to the subject. While the use of microalgae in functional foods and animal feed could soon reach the level of mass products, their use in pharmaceutical applications appears to lie more in the future.

## 7. References

- Aberoumand A. 2011. A Review Article on Edible Pigments Properties and Sources as Natural Biocolorants in Foodstuff and Food Industry. *World Journal of Dairy & Food Sciences*, 6 (1), 71-78, 2011.
- Ajitha M., Rajnarayana K. 2001. Role of oxygen free radicals in human diseases. *Indian Drugs*, 38, 545-554.
- Amann R., Springer, N. Ludwig, W., Gortz, H.D., Schleifer K.H. 1991. Identification *in situ* and phylogeny of uncultured

- bacterial endosymbionts. *Nature*, 351, 161-164.
- Ambreen A., Hira K., Ruqqia A., Sultana V. 2012. Evaluation of biochemical component and antimicrobial activity of some seaweeds occurring at Karachi coast. *Pakistan Journal of Botany*, 44 (5), 1799-1803.
- An G.H., Jang B.G., Cho M.H. 2001. Cultivation of the carotenoid – Hyperproducing mutant 2A2N of the red yeast *Xanthophyllomyces dendrorhous* (*Phaffia rhodozyma*) with molasses. *Journal of Bioscience and Bioengineering*, 92, 121–125.
- Anonymous. 2015. “<http://www.gidacilar.net/fonksiyonel-gidalar/fonksiyonel-gidalarda-mikroalglerin-nutrasotik-olarak-kullanilmasi-2115.html>”, (Access date, 2015).
- Ansari I., Nikhil K. 2014. Algal approach for Sustainable Development: A Critical Review. *International Journal of Engineering and Technical Research*, 2 (4), 83-85.
- Arad S.M., Yaron A. 1992. Natural pigments from red microalgae for use in foods and cosmetics. *Trends Food Science and Technology*, 3, 92-97.
- Balakrishnan D., Kandasamy D., Nithyanand P. 2014. A review on Antioxidant activity of marine organisms. *International Journal of ChemTech Research*, 6, 3431-3436.
- Bandarra N.M., Pereira P.A., Batista I., Vilela M. 2003. Fatty acids, sterols and  $\alpha$ -tocopherol in *Isochrysis galbana*. *Journal of Foods Lipids*, 10, 25–34.
- Bar E., Rise M., Vishkautsan M., Arad S. 1995. Pigment and structural changes in *Chlorella zofingiensis* upon light and nitrogen stress. *Journal of Plant Physiology*, 146, 527–34
- Becker E.W. 2007. Micro-algae as a source of protein. *Biotechnology Advances*, 25, 207–210.
- Becker E.W. 1988. Micro-algae for human and animal consumption, p. 222–256. In Borowitzka, M.A. and Borowitzka, L.J. (ed.), *Micro-algal biotechnology*. Cambridge University Press, Cambridge.
- Becker W. 2004. Microalgae in human and animal nutrition, p. 312– 351. In Richmond, A. (ed.), *Handbook of microalga culture*. Blackwell, Oxford.
- Bhatt D.L. 2008. Anti-inflammatory agents and antioxidants as a possible “third great wave” in cardiovascular secondary prevention. *American Journal of Cardiology*, 101, 4–13.
- Bian Q., Gao S., Zhou J., Qin J., Taylor A., Johnson E.J., Tanq G., Sparrow J.R., Gierhart D., Shanq F. 2012. Lutein and zeaxanthin supplementation reduces photooxidative damage and modulates the expression of inflammation-related genes in retinal pigment epithelial cells. *Free Radical Biology and Medicine*, 53, 1298–1307
- Blanc P.J., Loret M.O., Santerre A.L., Pareilleux A., Prome D., Prome J.C., Laussac J.P., Goma G. 1994. Pigments

- of *Monascus* spp. Journal of Food Science, 59, 862–865.
- Borowitzka, M.A. 1992. Algal biotechnology products and processes—matching science and economics. Journal of Applied Phycology, 4 (3), 267-279.
- Browning D.F., Whitworth D.E., Hodgson D.A. 2003. Light induced carotenogenesis in *Myxococcus xanthus*: functional characterization of the ECF sigma factor CarQ and antisigma factor CarR. Molecules Microbiology, 48 (1), 237-251.
- Caro Y., Anamale L., Fouillaud M., Laurent P., Petit T., Dufosse L. 2012. Natural hydroxyanthraquinoid pigments as potent food grade colorants: an overview. Natural Products and Bioprospecting, 174–19.
- Carvalho A.P., Meireles L.A., Malcata F.X. 2006. Microalgal reactors: a review of enclosed system designs and performances. Biotechnology Progress, 22 (6), 1490-1506.
- Chisti Y. 2007. Biodiesel from microalgae. Biotechnology Advances, 25 (3), 294-306.
- Chisti Y. 2008. Biodiesel from microalgae beats bioethanol. Trends in Biotechnology, 26 (3), 126-131.
- Chkhikvishvili I.D., Ramazanov Z.M. 2000. Phenolic substances of brown algae and their antioxidant activity. Applied Biochemistry and Microbiology, 36, 289–291.
- Clydesdale F.M. 1993. Color as a factor in food choice. Critical Review Food Science and Nutrition, 33 (1), 83-101.
- Cristea D, Vilarem G. 2006. Improving light fastness of natural dyes on cotton yarn. Dyes Pigments, 70, 238–45.
- Cruz J.M., Parajo J.C. 1998. Improved astaxanthin production by *Xanthophyllomyces dendrorhous* growing on enzymatic wood hydrolysates containing glucose and cellobiose. Food Chemistry, 63, 479–484.
- Coutteau P., Sorgeloos P. 1992. The use of algal substitutes and the requirement for live algae in the hatchery and nursery rearing of bivalve molluscs: an international survey. Journal of Shellfish Research, 11, 467-467.
- Danaraddi S., Koneru A., Hunasgi S., Ramalu S., Vanishree M. 2014. Natural ways to prevent and treat oral cancer. Journal of Oral Research and Review, 6 (1), 34.
- Davoli P., Weber R.W.S. 2002. Carotenoid pigments from the red mirror yeast, *Sporobolomyces roseus*. Mycologist, 16, 102–108.
- de Jesus Raposo M.F., de Moraes A.M.M.B. 2015. Microalgae for the prevention of cardiovascular disease and stroke. Life Sciences, 125, 32-41.
- Demirel Z., Yilmaz-Koz F.F., Karabay-Yavasoglu U.N., Ozdemir G., Sukatar A. 2009. Antimicrobial and antioxidant activity of brown algae from the Aegean Sea. Journal of the Serbian Chemical Society, 74 (6), 619-628.

- Dharmaraj S., Ashokkumar B., Dhevendaran K. 2009. Food-grade pigments from *Streptomyces* sp. isolated from the marine sponge *Callyspongia diffusa*. Food Research International, 42 (4), 487-492.
- Draaisma R. B., Wijffels R. H., Slegers P. E., Brentner L. B., Roy A., Barbosa M. J. 2013. Food commodities from microalgae. Current Opinion in Biotechnology, 24, 169-177.
- Downham A., Collins P. 2000. Colouring our foods in the last and next millennium. International Journal of Food Science and Technology, 35 (1), 5-22.
- Duan X.J., Li W.W., Zhang X.M., Wang B.G. 2006. Evaluation of antioxidant property of extract and fractions obtained from a red alga, *Polysiphonia urceolata*. Food Chemistry, 95, 37-43.
- Dufosse L., Fouillaud M., Caro Y., Mapari S.A.S., Sutthiwong N. 2014. Filamentous fungi are large scale producers of pigments and colorants for the food industry. Current Opinion Biotechnology, 26, 56-61.
- Durán N, Teixeira M.F.S., de Conti R., Esposito E. 2002. Ecological-Friendly Pigments from Fungi. Critical Reviews in Food Science and Nutrition, 42(1), 53-66.
- Dunahay T.G., Jarvis E.E., Dais S.S., Roessler P.G. 1996. Manipulation of microalga lipid production using genetic engineering. In Seventeenth Symposium on Biotechnology for Fuels and Chemicals (pp. 223-231). Humana Press.
- El-Baky H.H., El Baz F.K., El-Baroty G.S. 2003. *Spirulina* species as a source of carotenoids and a-tocopherol and its anticarcinoma factors. Biotechnology, 2 (3), 222-240.
- El-Baz F.K., Abdoul-Enein A.M., El-Baroty G.S., Youssef A.M., El-Baky H.H.A. 2002. Accumulation of antioxidant vitamins in *Dunaliella salina*. Journal of Biological Sciences, 2 (4), 220-223.
- Enrique A., Papp T., Breum J., Arnau J., Arturo P. 2005. Strain and culture conditions improvement for  $\beta$ -carotene production with *Mucor*. In Microbial Processes and Products (pp. 239-256). Humana Press.
- Eriksen N.T. 2008. The technology of microalgal culturing. Biotechnology Letters, 30 (9), 1525-1536.
- European Commission. 2000. Opinion of the scientific committee on food on  $\beta$ 2-carotene from *Blakeslea trispora*, SCF/CS/ ADD/COL, pp. 158.
- Fabre C.E., Santerre A.L., Loret M.D., Baberian R., Parailleux A., Goma G., Blanc P.J. 1993. Production and food application of the red pigments of *Monascus ruber*. Journal of Food Science, 58, 1099-103.
- Fabregas J., Herrero C. 1990. Vitamin content of four marine microalgae: potential use as source of vitamins in nutrition. Journal of Industrial Microbiology, 5, 259-64.

- Fassett R.G., Coombes J.S. 2011. Astaxanthin: A potential therapeutic agent in cardiovascular disease. *Marine Drugs*, 9, 447–465.
- Fernández-García E., Carvajal-Lérída I., Jarén-Galán M., Garrido-Fernández J., Pérez-Gálvez A., Hornero-Méndez D. 2012. Carotenoids bioavailability from foods: From plant pigments to efficient biological activities. *Food Research International*, 46 (2), 438-450.
- Finkel T., Holbrook N.J. 2000. Oxidants, oxidative stress and the biology of ageing. *Nature*, 408, 239–247.
- Frankel E.N. 1993. In search of better methods to evaluate natural antioxidants and oxidative stability in food lipids. *Trends Food Sci. Technol.*, 4, 220-225.
- Freund P.R., Washam C.J., Maggion M. 1988. Natural color for use in foods. *Cereal Foods World*, 33, 553-559.
- Frick D., Meggos H. 1988. FD&C colors. *Food Technology*, 7, 49-56.
- Fuentes M. R., Fernández, G. A., Pérez, J. S., Guerrero, J. G. (2000). Biomass nutrient profiles of the microalga *Porphyridium cruentum*. *Food Chemistry*, 70(3), 345-353.
- Ginka F., Emilina S., Dora B. 2004. Use of wheat ultrafiltrate as a substrate for production of carotenoids by the yeast *Rhodotorula rubra*. *Applied biochemistry and biotechnology*, 112, 133-142.
- Gomathi V., Sithranga Boopathy N., Kayalvizhi K., Saravanakumar K., Kathiresan K. 2013. Antioxidant Properties of Mangrove-Derived thraustochytrids. *Journal of Biotechnological Sciences*, 1 (2), 108–112.
- Gross G.J., Hazen S.L., Lockwood S.F. 2006. Seven day oral supplementation with Cardax TM (disodium disuccinate astaxanthin) provides significant cardioprotection and reduces oxidative stress in rats. *Molecular and Cellular Biochemistry*, 283 (1), 23–30.
- Goiris K., Muylaert K., Fraeye I., Foubert I., De Brabanter J., De Cooman L. 2012. Antioxidant potential of microalgae in relation to their phenolic and carotenoid content. *Journal of Applied Psychology*, 24 (6), 1477–86
- Guil-Guerrero J.L., Navarro-Juárez R., López-Martínez J.C., Campra-Madrid P., Rebolloso-Fuentes M.M. 2004. Functional properties of the biomass of three microalgal species. *Journal of Food Engineering*, 65 (4), 511–517.
- Jacobson G., Wasileski J. 1994. Production of food colorants by fermentation. In A. Gabelman (Ed.), *Bioprocess production of flavor, fragrance, and color ingredients* (pp. 205–237).
- Jahnke L.S. 1999. Massive carotenoid accumulation in *Dunaliella bardawil* induced by ultraviolet-A radiation. *Journal of Photochemistry and Photobiology B: Biology*, 48 (1), 68–74.
- Johnson E.A., An G.H. 2008. Astaxanthin from microbial sources. *Critical Reviews on Biotechnology*, 11, 297–326.

- Jones J.D., Hohn T.M., Leathers T.D. 2004. Genetically modified strains of *Fusarium sporotrichioides* for production of Lycopene and  $\beta$ -Carotene. Society of Industrial Microbiology Annual Meeting, San Diego, USA, 91.
- Joshi V.K., Attri D., Bala A., Bhushan S. 2003. Microbial pigments. Indian Journal of Biotechnology, 2, 362-9.
- Hadzri H.M., Yunus M.A.C., Zhari S., Rithwan F. 2014. The Effects of Solvents and Extraction Methods on the Antioxidant Activity of *P. niruri*. Journal Technology (Sciences & Engineering), 68 (5), 47-52.
- Hailei W., Zhifang R., Ping L., Yanchang G., Guosheng L., Jianming Y. 2011. Improvement of the production of a red pigment in *Penicillium* sp. HSD07B synthesized during co-culture with *Candida tropicalis*. Bioresource Technology, 102 (10), 6082-6087.
- Hajjaj H., Blanc P.J., Groussac E., Goma G., Uribe Larrea J.L., Loubiere P. 1999. Improvement of red pigment/citrinin production ratio as a function of environmental conditions by *Monascus ruber*. Biotechnology and Bioengineering, 64, 497-501.
- Hejazi M.A., Wijffels R.H. 2004. Milking of microalgae. Trends Biotechnology, 22 (4), 189-194.
- Helmersson J., Arnlöv J., Larsson A., Basu S. 2009. Low dietary intake of  $\beta$ -carotene,  $\alpha$ -tocopherol and ascorbic acid is associated with increased inflammatory and oxidative stress status in a Swedish cohort. British Journal of Nutrition, 101, 1775-1782.
- Hemmi H., Ikejiri S., Nakayama T., Nishino T. 2003. Fusion-type lycopene  $\beta$ -cyclase from a thermoacidophilic archaeon *Sulfolobus solfataricus*. Biochemical and Biophysical Research Communications, 305 (3), 586-591.
- Herrero M., Martin-Alvarez P.J., Senorans F.J., Cifuentes A., Ibanez E. 2005. Optimization of accelerated solvent extraction of antioxidants from *Spirulina platensis* microalga. Food Chemistry, 93, 417-423.
- Huang H.L., Wang B.G. 2004. Antioxidant capacity and lipophilic content of seaweeds collected from the Qingdao coastline. Journal of Agricultural and Food Chemistry, 52, 4993-4997.
- Kalidasan K., Sunil K.S., Narendran R., Kathiresan K. 2015. Antioxidant activity of mangrove-derived marine thraustochytrids. Mycosphere, 6 (5), 602-611.
- Kato F., Hino T., Nakaji A., Tanaka M., Koyama Y. 1995. Carotenoid synthesis in *Streptomyces setonii* ISP5395 is induced by the gene crtS, whose product is similar to a sigma factor. MGG, Molecular and General Genetics, 247 (3), 387-390.
- Kay R.A., Barton L.L. 1991. Microalgae as food and supplement. Critical Reviews in Food Science & Nutrition, 30 (6), 555-573.

- Knauer J., Southgate P.C. 1999. A review of the nutritional requirements of bivalves and the development of alternative and artificial diets for bivalve aquaculture. *Reviews in Fisheries Science*, 7(3-4), 241-280.
- Kim S.W., Seo W.T., Park Y.H. 1997. Enhanced synthesis of trisporic acid and  $\beta$ -carotene production in *Blakeslea trispora* by addition of a non-ionic surfactant, Span 20. *Journal of Bioscience and Bioengineering*, 84 (4), 330-332.
- Kim C., Jung H., Kim Y.O., Shin C.S. 2006. Antimicrobial activities of amino acid derivatives of *Monascus* pigments. *FEMS Microbiology Letters*, 264 (1), 117-124.
- Klaur H. 1981. Carotenoids as colorants and vitamin A precursors", Bauernfeind JC Ed. Academic Press, 73, 1397.
- Knuckey R.M., Brown M.R., Robert R., Frampton D.M. 2006. Production of microalgal concentrates by flocculation and their assessment as aquaculture feeds. *Aquacultural Engineering*, 35 (3), 300-313.
- Konkol N., McNamara C., Sembrat J., Rabinowitz M., Mitchell R. 2009. Enzymatic decolorization of bacterial pigments from culturally significant marble. *Journal of Cultural Heritage*, 10 (3), 362-366.
- Krügel H., Krubasik P., Weber K., Saluz H.P., Sandmann G. 1999. Functional analysis of genes from *Streptomyces griseus* involved in the synthesis of isorenieratene, a carotenoid with aromatic end groups, revealed a novel type of carotenoid desaturase. *BBA Molecular and Cell Biology of Lipids*, 1439 (1), 57-64.
- Kumar A., Vishwakarma H.S., Singh J., Dwivedi S., Kumar M. 2015. Microbial pigments: production and their applications in various industries. *IJPCBS* 5(1), 203-212.
- Lampila L.E., Wallen S.E., Bullerman L.B., Lowry S.R. 1985. The effect of *Blakeslea trispora* strain and type of whey on the production of  $\beta$ -carotene and other parameters. *Lebensm Wiss Technology*, 18, 366-369
- Langdon C., Önal E. 1999. Replacement of living microalgae with spray-dried diets for the marine mussel *Mytilus galloprovincialis*. *Aquaculture*, 180 (3), 283-294.
- Leathers T.D., Jones J.D., Hohn T.M. 2004. System for the sequential, directional cloning of multiple DNA sequences. US patent, 6, 696, 282.
- Li H.B., Chen F. 2001. Preparative isolation and purification of astaxanthin from the microalga *Chlorococcum* sp. by high-speed counter-current chromatography. *Journal of Chromatography A*, 925, 133-137.
- Li H.B., Chen F., Zhang T.Y., Yang F.Q., Xu G.Q. 2001. Preparative isolation and purification of lutein from the microalga *Chlorella vulgaris* by high-speed counter-current chromatography. *Journal of Chromatography A*, 905, 151-155.

- Li H.B., Jiang Y., Chen F. 2002. Isolation and purification of lutein from the microalga *Chlorella vulgaris* by extraction after saponification. *Journal of Agricultural and Food Chemistry*, 50, 1070–1072.
- Li H.B., Cheng K.W., Wong C.C., Fan K.W., Chen F., Jiang Y. 2007. Evaluation of antioxidant capacity and total phenolic content of different fractions of selected microalgae. *Food Chemistry*, 102, 771–776.
- Lim S.N., Cheung P.C.K., Ooi V.E.C., Ang P.O. 2002. Evaluation of antioxidative activity of extracts from a brown seaweed, *Sargassum siliquastrum*. *Journal of Agricultural and Food Chemistry*, 50 (13), 3862–3866.
- Lin Y.L., Wang T.H., Lee M.H., Su N.W. 2008. Biologically active components and nutraceuticals in the *Monascus*-fermented rice: a review. *Applied Microbiology and Biotechnology*, 77, 965-73.
- Liu B.H., Wu T.S., Su M.C., Chung C.P., Yu F.Y. 2005. Evaluation of citrinin occurrence and cytotoxicity in *Monascus* fermentation products. *Journal of Agriculture Food Chemistry*, 53, 170-175.
- Lomax S.Q., Learner T. 2006. A review of the classes, structures, and methods of analysis of synthetic organic pigments. *J Am Inst Conservation*, 45, 107–25.
- Madhavi D.L., Deshpande S.S., Salunkhe D.K. 1996. Food antioxidants: Technological, toxicological. Health perspective. New York: Marcel Dekker.
- Malik K., Tokkas J, Goyal S. 2012. Microbial Pigments: A review. *International Journal of Microbial Resource Technology*, 1 (4), 361-365.
- Maoka T. 2011. Carotenoids in marine animals. *Marine Drugs*, 9 (2), 278-293.
- Mapari S.A., Nielsen K.F., Larsen T.O., Frisvad J.C., Meyer A.S., Thrane U. 2005. Exploring fungal biodiversity for the production of water-soluble pigments as potential natural food colorants. *Current Opinion Biotechnology*, 16 (2), 231-238.
- Mapari S.A.S., Hansen M.E., Meyer A.S., Thrane U. 2008. Computerized screening for novel producers of *Monascus*-like food pigments in *Penicillium* species. *Journal of Agriculture Food Chemistry*, 56, 9981-9989.
- Marusich W.L., Bauernfeind J.C. 1981. Oxycarotenoids in poultry feeds. *Carotenoids as Colorants and Vitamin A Precursors*. (ed. J. C. Bauernfeind), Academic Press, New York, pp. 319-462.
- Mathew B., Sankaranarayanan R., Nair P.P., Varghese C., Somanathan T., Amma B.P. et al. 1995. Evaluation of chemoprevention of oral cancer with *Spirulina fusiformis*. *Nutrition Cancer*, 24, 197-202.

- Metting F.B. 1996. Biodiversity and application of microalgae. *Journal of Indian Microbiology*, 17, 477-489.
- Metzger P., Largeau C. 2005. *Botryococcus braunii*: a rich source for hydrocarbons and related ether lipids. *Applied Microbiology and Biotechnology*, 66 (5), 486-496.
- Miranda M.S., Cintra R.G., Barros S.B., Mancini-Filho J. 1998. Antioxidant activity of the microalga *Spirulina maxima*. *Brazilian Journal of Medical and Biological Research*, 31, 1075-1079.
- Mukherjee G., Singh S.K. 2011. Purification and characterization of a new red pigment from *Monascus purpureus* in submerged fermentation. *Process Biochemistry*, 46 (1), 188-192.
- Mukund S., Sivasubramanian V., Kumar N.S. 2013. In vitro Antioxidant Activity and Enzymatic and Non-Enzymatic Antioxidant Potential of *Chroococcus turgidus*. *Journal of Pharmaceutical Research and Development*, 5 (5), 112-120.
- Mukund S. 2013. In-vitro antioxidant activity and enzymatic and non-enzymatic antioxidant potential of *chroococcus turgidus*. *International Journal of Pharmaceutical Research and Development*, 5 (5), 112-120.
- Murthy K.N.C., Vanitha A., Rajesha J., Swamy M.M., Sowmya P.R., Ravishankar G.A. 2005. In vivo antioxidant activity of carotenoids from *Dunaliella salina* – a green microalga. *Life Sciences*, 76 (12), 1381-1390.
- Newmann D.J., Cragg G.M., Snader K.M. 2003. Natural products as source of new drugs over the period 1981-2002. *Journal of Natural Products*, 66, 1022-1037.
- Ogihara J., Kato J., Oishi K., Fujimoto Y. 2001. PP-R, 7-(2-hydroxyethyl)-monascorubramine, a red pigment produced in the mycelia of *Penicillium* sp. *AZ. Journal of Bioscience Bioengineering*, 91, 44-47.
- Olaizola M. 2003. Commercial development of microalgal biotechnology: from the test tube to the marketplace. *Biomolecular Engineering*, 20 (4), 459-466.
- Park P.K., Kim E.Y., Chu K.H. 2007. Chemical disruption of yeast cells for the isolation of carotenoid pigments. *Separation and Purification Technology*, 53 (2), 148-152.
- Patel A., Mishra S., Pawar R., Ghosh P.K. 2005. Purification and characterization of C-phycoerythrin from cyanobacterial species of marine and freshwater habitat. *Protein Expression and Purification*, 40, 248-255
- Pulz O., Gross W. 2004. Valuable products from biotechnology of microalgae. *Applied Microbiology and Biotechnology*, 65, 635-648.
- Riccioni G. 2009. Carotenoids and cardiovascular disease. *Current Atherosclerosis Reports*, 11, 434-439.
- Rilling H.C. 1962. Photoinduction of carotenoid synthesis of a *Mycobacterium* sp. *Biochimica*

- et *Biophysica Acta* (BBA), 60 (3), 548-556.
- Robert R., Trintignac P. 1997. Substitutes for live microalgae in mariculture: a review. *Aquatic Living Resources*, 10 (05), 315-327.
- Rommier M.A. 1868. Sur une nouvelle matiere colorante appelee xylindeine et extraite de certains bois morts. *Comptes rendus hebdomadaire des séances del'Academie des Sciences III* (Paris), 66, 108-110.
- Rowe R.C., Sheskey P.J., Weller P.J. 2003. *Handbook of Pharmaceutical Excipients*. Fourth ed. Pharmaceutical Press and American Pharmaceutical Association.
- Sanjay K.R., Kumaresan N., Naidu K.A., Viswanatha S., Narasimhamurthy K., Kumar S.U., Vijayalakshmi G. 2007. Safety evaluation of pigment containing *Aspergillus carbonarius* biomass in albino rats. *Food Chemical Toxicology*, 45 (3), 431-439.
- Santos M.A., Mateos L., Stahmann K.P., Revuelta J.L. 2005. Insertional mutagenesis in the Vitamin B2 producer fungus *Ashbya gossypii*. In J. L. Barredo (Ed.), *Methods in biotechnology: Microbial Processes and Products* (pp. 283-300).
- Sarada R., Pillai M.G., Ravishankar G.A. 1999. Phycocyanin from *Spirulina* sp: influence of processing of biomass on phycocyanin yield, analysis of efficacy of extraction methods and stability studies on phycocyanin. *Process Biochemical*, 34, 795-801.
- Sardaryan E. 2004. Food supplement. US Patent 0105864 A1.
- Sardaryan E. 2002. Strain of the microorganism *Penicillium oxalicum* var. *Armeniaca* and its application. US Patent 6, 340, 586 B1.
- Sarrobot, B., Dermoun D. 1991. Extraction et valorisation de molecules à haute valeur ajoutée chez la microalgue *Porphyridium cruentum*. Premier Colloque Scientifique Français sur la Biotechnologie des Microalgues et des Cyanobactéries Appliquée au Thermalisme. Amélie-les-Bains, France: Centre d'Études Nucléaires de Cadarache, 109-114.
- Stahmann K.P. et al. 2000. Three biotechnical processes using *Ashbya gossypii*, *Candida famata*, or *Bacillus subtilis* compete with chemical riboflavin production. *Applied Microbiology and Biotechnology*, 53, 509-516.
- Schumann G., Nürnberger H., Krügel H., Sandmann G. 1996. Activation and analysis of cryptic genes for carotenoid biosynthesis from *Streptomyces griseus*. *Molecular Genetics and Genomics* MGG, 252 (6), 658-666.
- Schwartz R.E., Hirsch C.F., Sesin D.F., Flor J.E., Chartrain M., Fromtling R.E., Harris G.H., Salvatore M.J., Liesch J.M., Yudin K. 1990. Pharmaceuticals from cultured algae. *Journal of*

- Industrial Microbiology, 5 (2-3), 113-123.
- Spolaore P., Joannis-Cassan C., Duran E. Isambert A. 2006. REVIEW. Commercial Applications of Microalgae. Journal of Bioscience and Bioengineering, 101 (2), 87-96.
- Steinbrenner J., Hartmut L. 2001. Regulation of two carotenoids biosynthesis genes coding for phytoene synthase and carotenoid hydroxylase during stress-induced astaxanthin formation in the green alga *Haematococcus pluvialis*. Plant Physiology, 125, 1810-7.
- Stich E., Chaundry Y., Schnitter C. 2002. Colour, you eat with your eyes. International Food Ingredients, 1, 6-8.
- Shibata M., Sakaki T., Miyauchi S., Wakamatsu K., Mukae K. 2007. U.S. Patent No. 2007/0274956A1, Washington, DC.
- Shimizu Y. 1993. Microalgal metabolites. Chemical Review, 93 (5), 1685-1698
- Silveira S.T., Daroit D.J., Brandelli A. 2008. Pigment production by *Monascus purpureus* in grape waste using factorial design. LWT-Food Science and Technology, 41 (1), 170-174.
- Simpson K.L., Katayama T., Chichester C.O. 1981. Carotenoids in fish feeds. Carotenoids as colorants and vitamin A Precursors, 4, 463-538.
- Speranza L., Pesce M., Patruno A., Franceschelli S., de Lutiis M.A., Grilli A., Felaco M. 2012. Astaxanthin treatment reduced oxidative induced pro-inflammatory cytokines secretion in U937: SHP-1 as a novel biological target. Marine Drugs, 10, 890-899.
- Stich E., Chaundry Y., Schnitter C. 2002. Colour, you eat with your eyes, International Food Ingredients, 1, 6-8.
- Stierle A.C., Cardellina J.H., Singleton F.L. 1988. A marine *Micrococcus* produces metabolites ascribed to the sponge *Tedania ignis*. Experientia, 44, 1021.
- Takano H., Asker D., Beppu T., Ueda K. 2006. Genetic control for light-induced carotenoid production in non-phototrophic bacteria. Journal of Indian Microbiology and Biotechnology, 33 (2), 88-93.
- Takamatsu S., Hodges T.W., Rajbhandari I., Gerwick W.H., Hamann M.T., Nagle D.G. 2003. Marine natural products as novel antioxidant prototypes, Journal of Natural Products, 66, 605-608.
- Tannin-Spitz T., Bergman M., van-Moppes D., Grossman S., Arad S. 2005. Antioxidant activity of the polysaccharide of the red microalga *Porphyridium* sp. Journal of Applied Phycology, 17, 215-222.
- Teng S.S., Feldheim W. 2001. Anka and anka pigment production. Journal of Indian Microbiology and Biotechnology, 26 (5), 280-282.
- Tudor D., Robinson S.C., Cooper P.A. 2013. The influence of pH on pigment formation by lignicolous fungi. International Biodeterioration and Biodegradation, 80, 22-28.

- Turkcan O., Okmen G. 2012. Microbial Carotenoids. Turkish Journal of Science Review, 5 (1), 115-122.
- Venil C.K., Zakaria Z.A., Ahmad W.A. 2013. Bacterial pigments and their applications. Process Biochemistry, 48 (7), 1065-1079.
- Vilchez C., Garbayo I., Lobato M.V., Vega J. 1997. Microalgae-mediated chemicals production and wastes removal. Enzyme and Microbial Technology, 20 (8), 562-572.
- Walker T.L., Purton S., Becker D.K., Collet C. 2005. Microalgae as bioreactors. Plant Cell Reports, 24 (11), 629-641.
- Xu L., Weathers P.J., Xiong X.R., Liu C.Z. 2009. Microalgal bioreactors: challenges and opportunities. Engineering in Life Sciences, 9 (3), 178-189.
- Yeum K.J., Russell R.M. 2002. Carotenoid bioavailability and bioconversion", Annual Review Nutrition, 22 (1), 483-504.
- Yildiz G., Dere E., Dere S. 2014. Comparison of the antioxidative components of some Marine macroalgae from Turkey. Pakistan Journal of Botany, 46 (2), 753-757.
- Yokoyama A., Miki W. 1995. Composition and presumed biosynthetic pathway of carotenoids in the astaxanthin-producing bacterium *Agrobacterium aurantiacum*. FEMS Microbiology Letters, 128 (2), 139-144.
- Zhang H.C., Zhan J.X., Su K.M., Zhang Y.X. 2006. A kind of potential food additive produced by *Streptomyces coelicolor*: characteristics of blue pigment and identification of a novel compound k-actinorhodin. Food Chemistry, 95, 186-192.
- Zhou B., Wang J., Pu Y., Zhu M., Liu S., Liang S. 2009. Optimization of culture medium for yellow pigments production with *Monascus anka* mutant using response surface methodology. European Food Research Technology, 228: 895-901.
- Zollinger, H. 1991. Color chemistry: syntheses, properties, and applications of organic dyes and pigments. 3rd edn. Zurich: Wiley-VCH.