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Carotenoids: Structure and Function in the Human Body

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Chapter 27

Commercialization and Marketing Potential of Carotenoids



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27.1 Introduction

Carotenoids are isoprenoid molecules produced de novo in all photosynthetic entities and in some non-photosynthetic bacteria and fungi. The carotenoids share a common skeleton formed by two isoprenoid units linked in such a way that the molecule is linear and has inverted symmetry in the center and several c.d.b. in the chain. This basic skeleton of 40 carbon atoms can be modified by hydrogenation, dehydrogenation, cyclization, shortening or chain extension, isomerization, introduction of substituents or by a mixture of these methods. Some 1178 carotenoids have been properly characterized from 700 sources comprising of plants, algae, fungi and bacteria thus exhibiting huge structural diversity and range of physiochemical properties. Macroscopic fungi (e.g. *Blakeslea trispora* for β -carotene & lycopene) or microscopic fungi (e.g. *Rhodotorula* or *Xanthophyllomyces* for torulene & astaxanthin) are also a good source of carotenoids. The algal (e.g.

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Haematococcus pluvialis & *Dunaliella salina* for astaxanthin & β -carotene) and bacterial (e.g. *Flavobacterium* sp. for zeaxanthin) sources are also present. Supplements are usually used to obtain those carotenoids which food is usually deficient like astaxanthin, fucoxanthin and meso-zeaxanthin.

A wide range of pre-clinical and clinical investigations indicate that dietary carotenoids have significant health-promoting effects. Noticeable evidence exists for their ability to reduce the risk of major chronic disorders. It seems that they play roles in both the prevention and treatment of various human diseases and disorders. They are a key symbol of a suitable nutritional condition in birds and fishes suggesting a sign of fitness and consequently increasing sexual pull. In algae and higher plants, they maintain the configuration and task of the photosynthetic complex, quench the chlorophyll triplet states, scavenge ROS, dissipate of excess energy and help in harvesting light. As vital floral pigments, they attract pollinators and seed dispersers due to their striking rich color [1].

The universal carotenoids market volume was valued at USD 1.40 Billion in 2018 and is projected to reach USD 1.85 Billion by the end of 2026 growing at 3.57% compound annual growth rate (CAGR). The volume of world carotenoids consumption in 2007 was equal to 4193 metric tons and has increased within 10 years by about 1500 metric tons, thereby it was equal to 5693.6 metric tons in 2017. Carotenoids added to food totaled 4020.8 metric tons in 2017 [2]. The market of beverages with carotenoids added totaled 1609.8 metric tons (Euromonitor International). Non-food market consumed 63.0 metric tons of carotenoids in 2017 (Euromonitor International). The market prices of carotenoids can vary from 300 to 3000 USD per kg of β -carotene and from 2500 to 10,000 USD per kg of astaxanthin. Ketocarotenoids, such as astaxanthin or canthaxanthin, are amongst the most expensive carotenoids in market. They are abundantly present in algae, whereas they are rarely present in higher plants. They enjoy a characteristic keto functionality on 4 or 4' position on the β -ionone ring and can also possess OH groups on the 3 and 3' positions. The key commercial usages of ketocarotenoids are as feed additive in the aquaculture and poultry industry for color and nutritional value.

Various elements like safety, efficacy, price, and packaging volume among others drive the competition in the industry. The global carotenoids market is characterized by intense competitive conditions leading towards merging and acquisition of competitor companies. Subsequently, big pharmaceuticals corporations are taking over smaller companies to strengthen their position. Highest demand of carotenoids is in European and the USA markets. The carotenoids market ecosystem is given in Fig. 27.1. Niche markets exists where customers can pay premium price for health food ingredients like carotenoids.

The food product is the focus of rules in the USA, while the technology utilized to obtain the final food product is concentrated in Europe. The largest market for carotenoids is Europe and it is a home for prominent globally exporting carotenoids manufacturers based in Germany, Netherlands and Denmark. Germany, France, UK and Netherlands are the most significant states within the Carotenoids market in Europe. However, compared to the main regional markets of Japan and the US, the

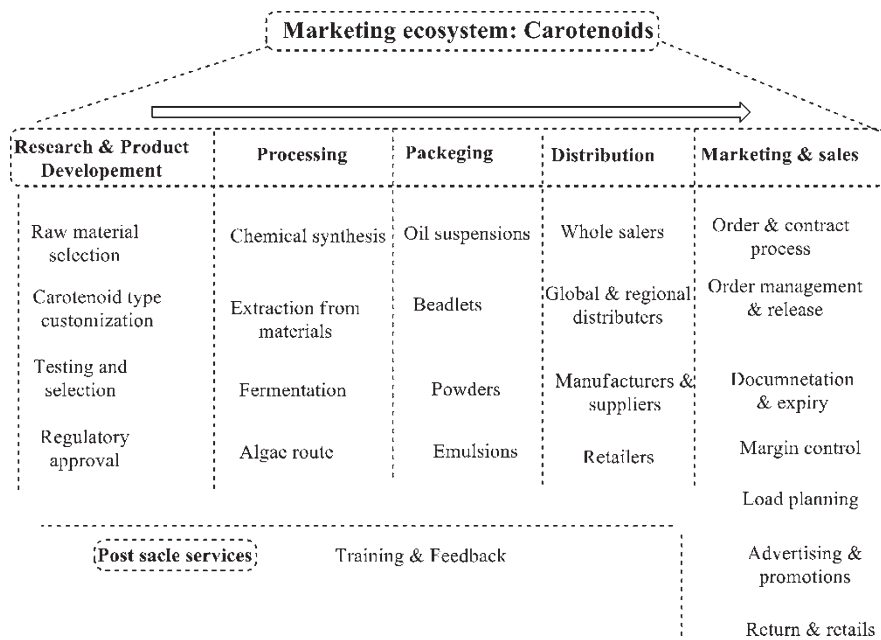


Fig. 27.1 Carotenoids market ecosystem

European markets are less-organized. Various elements limit development of this industry in EU. Food tagging, product devising, food handling, wrapping, advertising, registering and accrediting particulars are rigorously checked in the EU and are recognized as constraining the dimension of the buyer market. Factually the carotenoids markets have developed unevenly in Europe as majority of “Functional Foods” brands have sprung in merely a limited number of countries. Further, multinational food corporations usually offer single products instead of umbrella brands in the functional food (FF) market. North America is the second-largest carotenoids market after Europe. The Asia-Pacific carotenoids market is estimated to accrue commendable proceeds from cosmetics application, growing at a CAGR of 5% over the forthcoming years. Potential markets also exist in oil rich middle-eastern or Gulf States while African markets are not well-structured [2].

The world carotenoids industry is set to achieve over a 4% CAGR up to 2026, supported by rising demand for natural coloring agents, along with growth in end-use applications. Speaking of the application spectrum, the food and beverage application segment of the carotenoids market is estimated to advance at a lucrative pace and show massive growth in the upcoming years. Carotenoids are extensively used in various food and beverages as an additive for maintaining optimal vitamin A levels and boosting immunity, skin health, as well as vision. The Asia-Pacific carotenoids market is estimated to accrue commendable proceeds from cosmetics application, growing at a CAGR of 5% over the forthcoming years. Technological

advancements and burgeoning consumption in cosmetics and nutraceuticals are propelling overall regional demand.

27.2 Applications and Market

Carotenoids employed in animal and food-feed uses occupy the lion's share of market size. Carotenoids of plant sources are used in animal food applications as they can be ingested directly bypassing requirements of recovery while microbial sources need extraction and purification steps. Individual carotenoids market size is shown in Fig. 27.2. Similarly, Fig. 27.3 shows usage potential of carotenoids.

Carotenoids containing processed foods and supplements may contain structure and function claims like “promotes cardiovascular, prostate and skin health” in the US. The reason being that carotenoids in this form are considered as a kind of food under the Dietary Supplement Health and Education Act of 1994 (DSHEA). Such goods should accompany the disclaimer “these statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease” [3, 4]. In the EU, following are details of carotenoids under Commission Regulation (EU) 231/2012 (Table 27.1).

The Directive 87/552/EC in 1988, approved the use of astaxanthin @ 100 mg/kg in salmon and trout feed along with canthaxanthin. In 2004 under Regulation 258/97/EC, astaxanthin-rich oleoresin herbal capsules (@ 4 mg/capsule) were

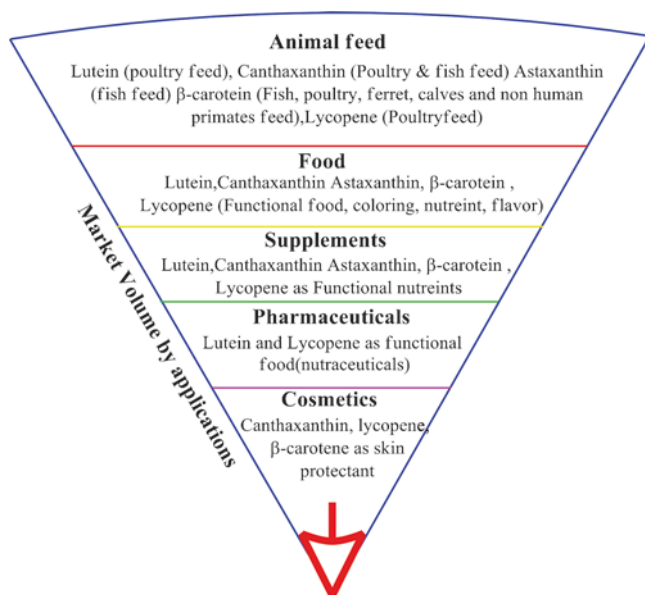


Fig. 27.2 Individual carotenoids market size

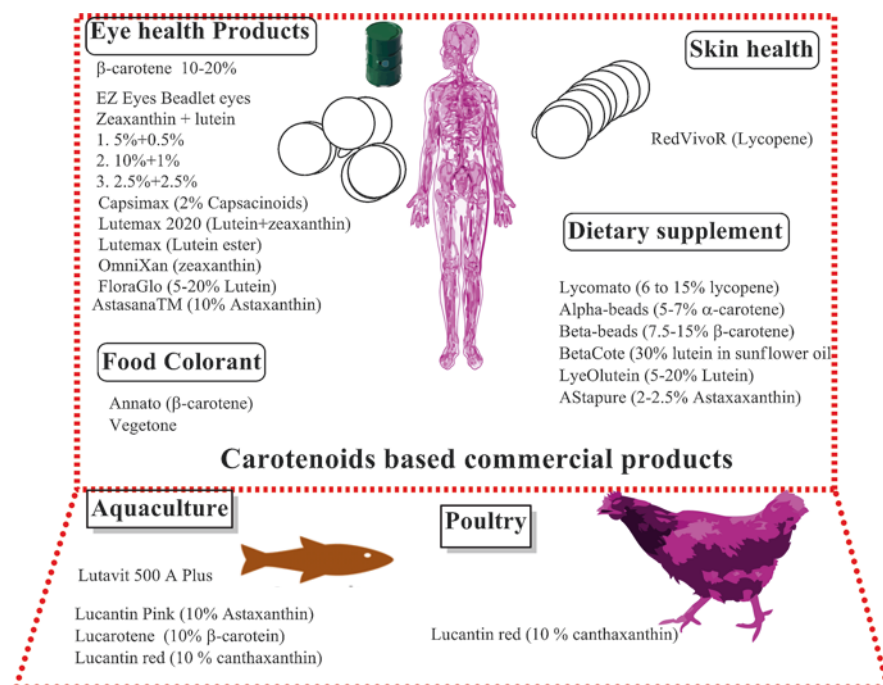


Fig. 27.3 Usage potential of individual carotenoids

Table 27.1 Carotenoids details in Commission Regulation (EU) 231/2012 [3, 4]

Carotenoids as food additive type	Color Index No	Production method
β -carotene (E160a)	75130	Chemically synthesis, extraction from plants, or production by the cultivation of <i>B. trispora</i> or <i>D. Salina</i>
Lycopene (E160d)	75125	Synthesized chemically, extracted from red tomatoes or obtained from <i>B. trispora</i> cultivation
Lutein (E161b)	–	Extraction from edible fruits, grass, Lucerne (<i>Medicago falcata</i>) and marigold
Zeaxanthin (E160a)	–	Algal-derived carotenoid preparations

permitted as a novel food ingredient and sold by Herbal Science International (Loughton, UK). Similarly, astaxanthin-rich oleoresin (AstaReal, Sweden) and astaxanthin-rich extracts (AlgaTechnologies, Israel) were permitted under this regulation. According to Regulation 1288/2004/EC, astaxanthin (E161z) obtained from *P. rhodozyma* is used in salmon and trout feed @ 100 mg/kg of the complete feed, while Regulation 393/2008/EC specifies astaxanthin dimethylsuccinate (E161j) for the same purpose. As per Regulation 721/2008/EC, astaxanthin acquired from *Paracoccus carotinifaciens* can be added to feed @ 100 mg/kg of complete feed along with canthaxanthin and adonirubin.

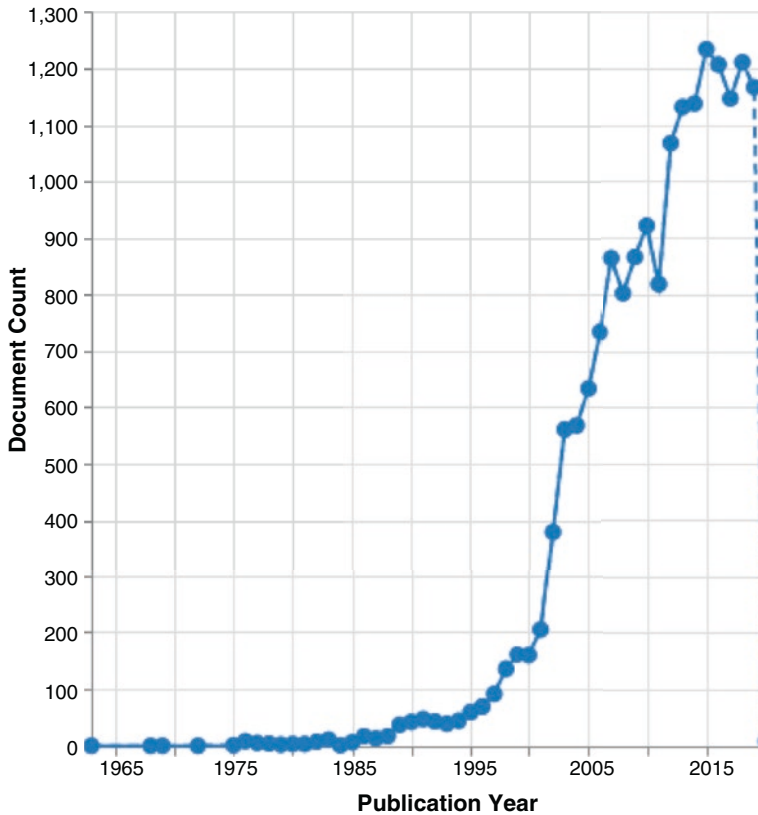


Fig. 27.4 Patents granted to carotenoids inventions with time scale

When “carotenoids” and “cosmetics” are used as keywords, 17,709 patents appear (Fig. 27.4), top owners (Fig. 27.5), top applicants (Fig. 27.6) and top inventors (Fig. 27.7) [5].

When “carotenoids” and “supplements, nutraceuticals” are used as keywords, 5524 patents appear (Fig. 27.8), top inventors (Fig. 27.9), top owners (Fig. 27.10), and top applicants (Fig. 27.11) [5].

When “carotenoids colors” are used as keywords, 31,731 patents appear (Fig. 27.12), top owners (Fig. 27.13), top inventors (Fig. 27.14), and top applicants (Fig. 27.15) [5].

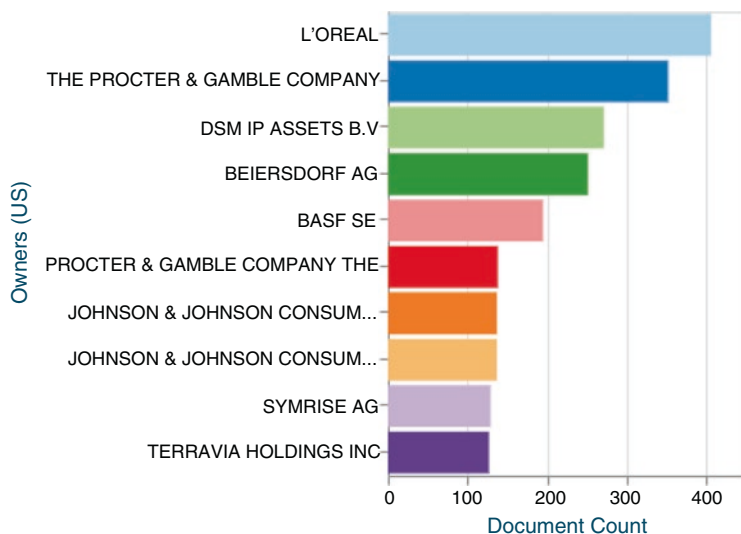


Fig. 27.5 Top owners of patented inventions

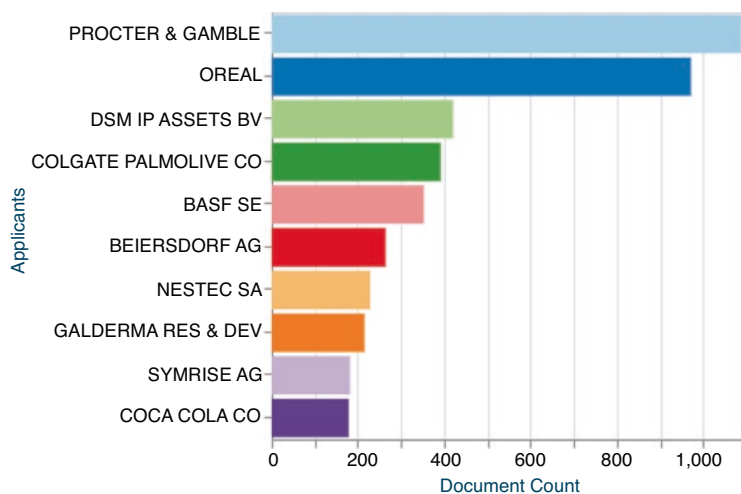


Fig. 27.6 Top applicants

27.3 Coloring Potential of Carotenoids

It is well-accepted saying that we also eat with our eyes, color is thus the first sensory interaction with food products, prior to taste and smell. Carotenoids help in enhancing the overall aesthetic appeal of food products by making them visually appealing. The salmonids characteristic “red, pink or orange” is due to their feed of

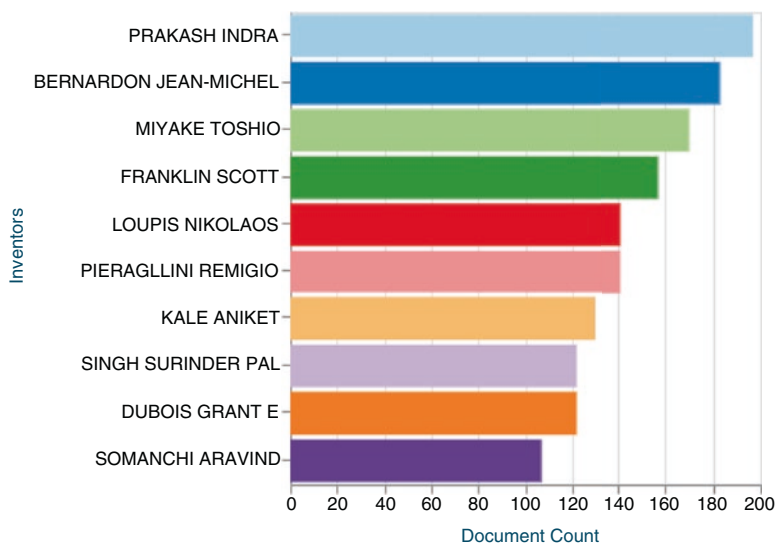


Fig. 27.7 Top Inventors

crustaceans or other fish with small crustaceans in their digestive system. Egg yolks are yellow because they accumulate carotenoids (largely lutein). At least 7 conjugated double bonds are needed for the carotenoid to impart color. Their role as food colorants have been comprehensively studied earlier. Currently, research focus is on microbial/biotechnological production of carotenoids as potential food and as precursors of aroma compound.

Achiote (*Bixa orellana* L.) accumulates several carotenoids derivatives (bixin and norbixin) in seeds and leaves. Annatto, the only carotenoid color obtained from the external coverings of the seeds of the Annatto tree fruits, is being used since decades in various forms. Demand for natural colors to pigment dairy foods with a reddish-orange hue is escalating. Increasing plantations in Asia and Latin America has led to overproduction thus leading to decreased prices for crude products. Annatto is used in the food sector to add yellow or orange color in a wide range of food products (e.g., processed meat, smoked fish, beverages). The most important color of annatto seeds is the *cis*-bixin (up to 80% of the entire color quantity), while norbixin (*cis* and *trans*) represent a insignificant portion of achiote seeds.

The consumption of β -carotene and lycopene as pigments in Food and Beverage division is increasing. β -carotene is extensively used in cheese, spreads, yogurts, soups, sauces, and bakery products, while lycopene is utilized in sauces and soups. Lycopene and canthaxanthin provide red dye for food and beverages are chiefly obtained from tomatoes. Astaxanthin or canthaxanthin are added to animal feed in farmed salmons and trout, giving their meat the characteristics color of the species in nature. In the poultry industry, lutein, bixin, and capsanthin are used to impart typical yellow-red color to chicken skin and egg yolk; for which the natural sources are marigold, achiote, and pepper, respectively. Sales of natural food colors like

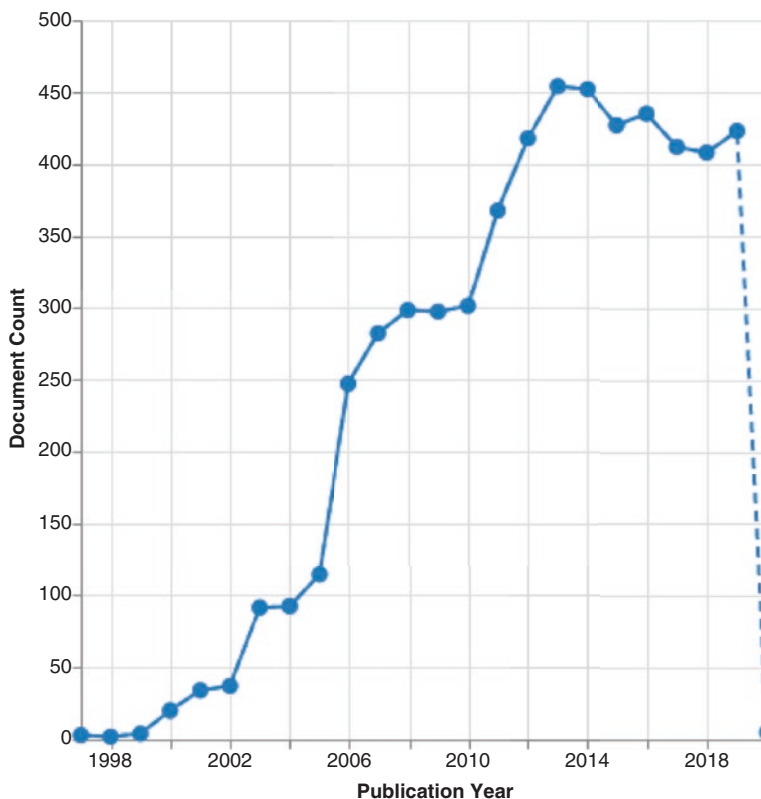


Fig. 27.8 Patented Inventions containing carotenoids over time

carotenoids are growing globally due to growing demand for clean label products. Natural colors are five times expensive than synthetic analogs, particularly for confectionary items, where this difference can reach up to 20 times. Requirement of more raw materials is a key reason for increased cost of natural colors. Cost is also influenced as increased quantity of natural color is required for the production of looked-for color.

27.4 Carotenoid-Based Commercial Products

The carotenoid-based commercial products available as supplements in the market are for (1) provitamin A potential (2) powerful antioxidant and lipid peroxidation preventing action (3) bone and skin health (anti-aging), physical stamina (sports nutrition), vision, and immune system augmentation (4) cancer, cardiovascular, neuronal, and gastrointestinal protecting capacity and (v) animal nutrition (particularly for poultry and fish).

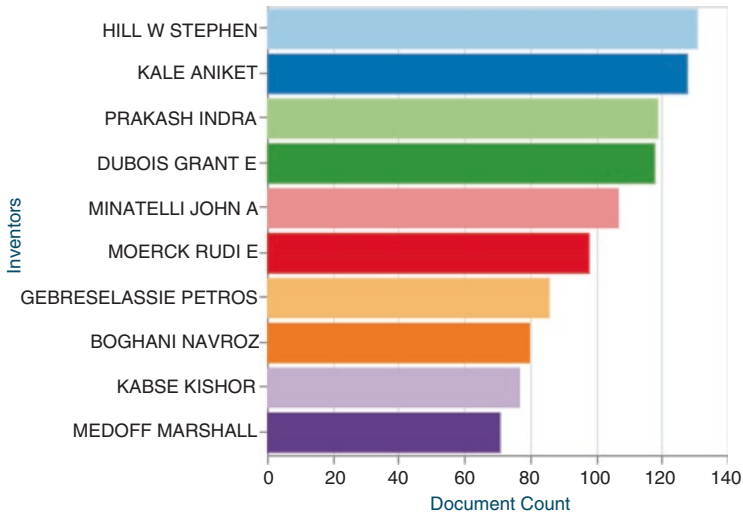


Fig. 27.9 Top inventors

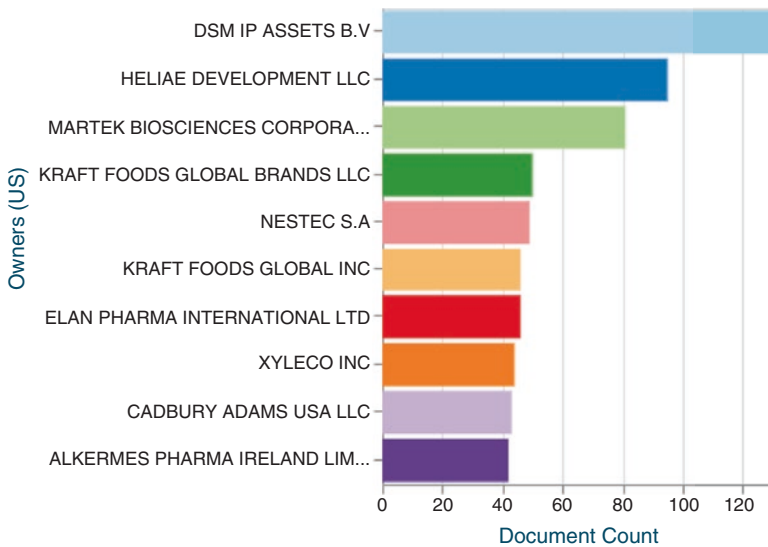


Fig. 27.10 Top owners

Recently, striking red–orange coloration of ornamental aquaculture animals, such as freshwater crustaceans and fishes, is a prevalent advertising element. Astaxanthin and canthaxanthin, are mainly used as nutritional supplements to improve skin pigmentation. Further, carotenoids increase the health and reproduction of ornamental animals, including better embryonic and larval growth, maturation, increased immune response, and photoprotection. Aquaculture feed is the most

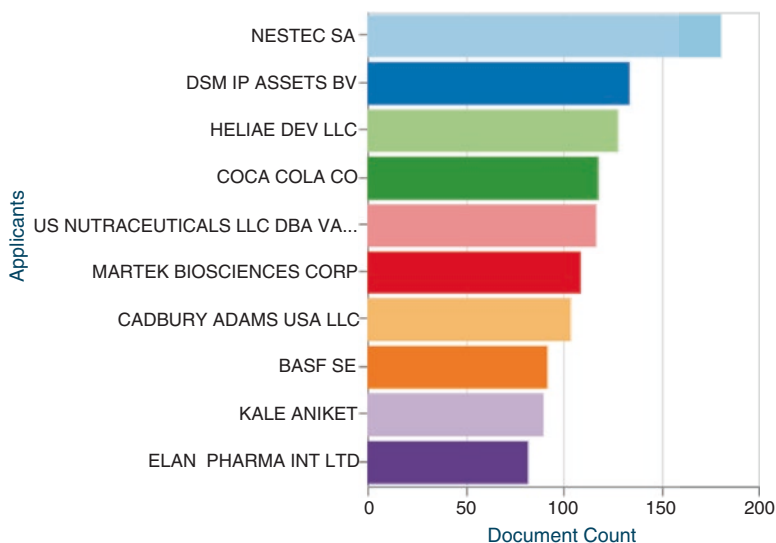


Fig. 27.11 Top applicants

significant segment that is responsible for the substantial revenue earned by astaxanthin and related carotenoids [3, 4].

27.5 Food/Feed Potential

Animal feed and food & beverage (F&B) segments are presently the leading markets for carotenoids worldwide. By 2026 end, F&B business is expected to exceed US\$ 2400 million income. The F&B market volume is estimated to grow markedly in near future, due to large-scale usage as food additives worldwide. Animal feed segment, which makes up almost 41% of the total carotenoids market share in terms of size, will grow significantly in coming years. Animals need carotenoids as they cannot make them hence carotenoids are added to animal feed.

Carotenoids are not developed alike in essentially all food groups. Carotenoids products are chiefly demanded in the dairy, confectionery and soft-drinks. The orange-red-brown color of French cheese *vieux-pan* is due the carotenoid (added to increase aesthetic value) produced by *Brevibacterium linens*. In Russia, natural pigments such as lutein are added to infant formulas to increase children's health. In Japan, *Undaria pinnatifida*, fucoxanthin rich seaweed, is marketed as pasta component.

Their use in animal feeds acts as a main precursor for amino acids in animal feeds and improves feed coloration, consequently enhancing their palatability besides increasing the looks of meat, meat products and fish. Feed area is a big segment where carotenoids are required to color fish, broilers and eggs. Suitable fish

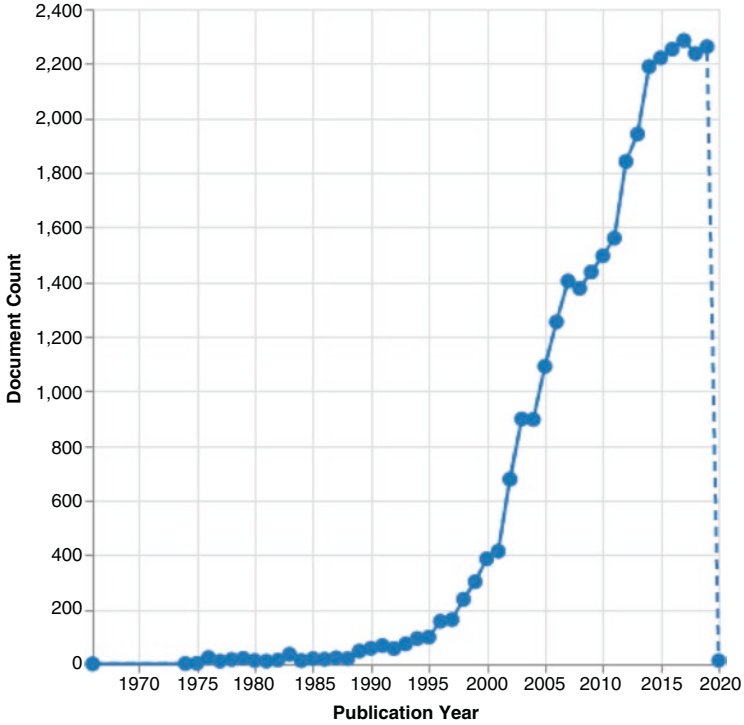


Fig. 27.12 Patented Inventions of carotenoids over time period

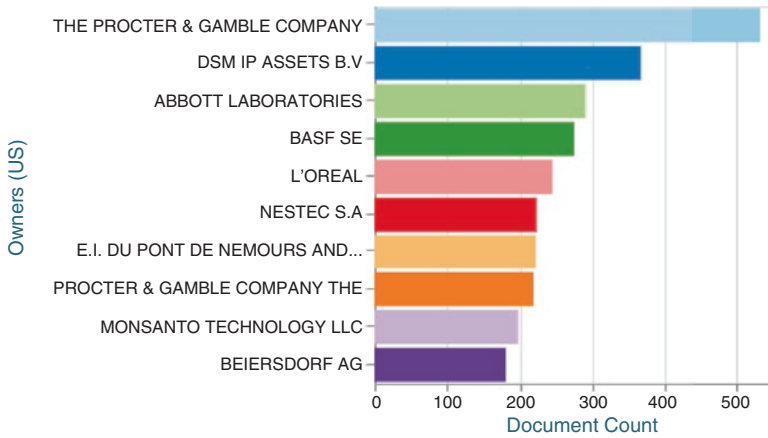


Fig. 27.13 Top owners

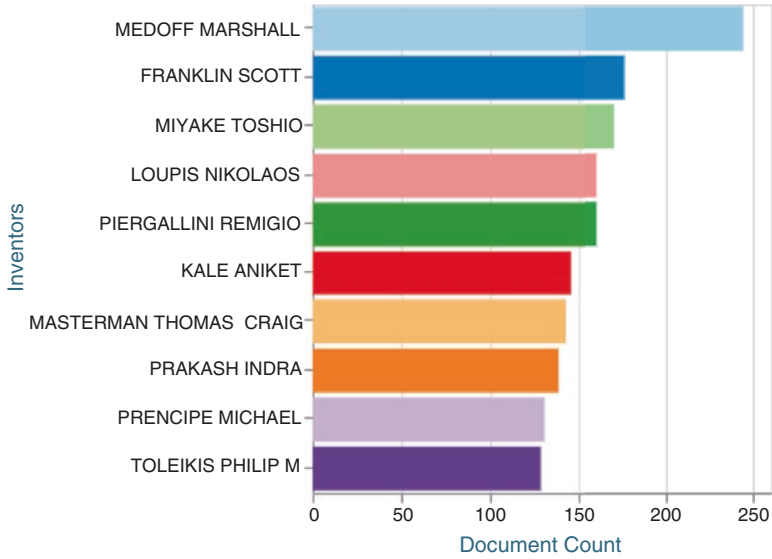


Fig. 27.14 Top inventors

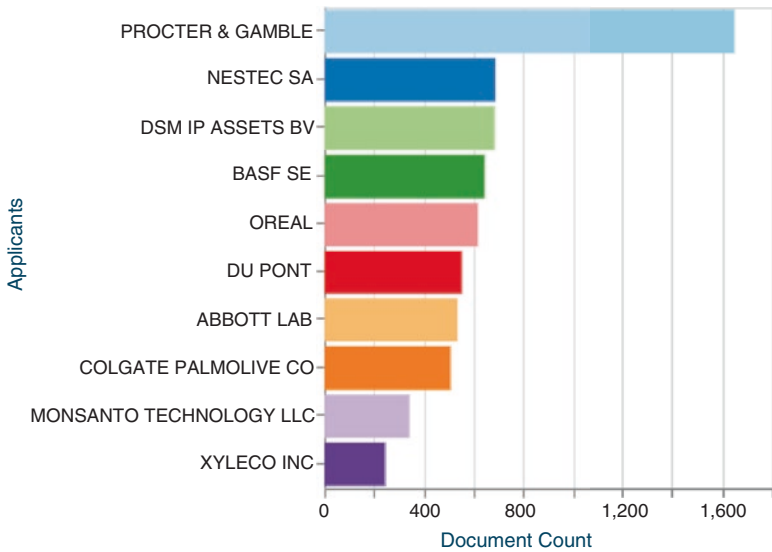


Fig. 27.15 Top applicants

flesh pigmentation and an economically feasible product cannot be obtained without them. Approximately 15–25% of the total feed costs linked with aquaculture production are because of the price of the needed carotenoid feed supplements. There are two chief uses for carotenoids in feed additives. Use of astaxanthin or

canthaxanthin to acquire the pink color of the flesh in salmon and trout farming. Carotenoids are used in poultry for the skin and egg yolk pigmentation [6].

27.6 Functional Foods Potential

Their antioxidant potential makes them one of highly purchased product in the over-the-counter sector. Despite the general socio-demographic and behavioral trends favoring carotenoids as FF, peculiar challenges exist in their formulation and marketing. Legally nutraceuticals including carotenoids occur in an in-between domain between pharmaceuticals and food. In nearly all European countries, they are typically regulated by discrete bodies and are subject to different rules, hence a “grey zone” surfaces with an increased degree of uncertainty. The factual processes, requirements and regulatory organizations linked with market entry differ substantially between the two domains. Definition glitches chiefly exist for goods aimed for prevention of nutrition-related ailments and/or to provide health (“health claims”). In the EU and allied national legislations, it is presently not allowed to utilize disease-related traits in customer knowledge or goods flyers for Functional Food. Hence, manufacturers attempt to encompass the nature of claims allowed for Functional Food. Another central success element is the expense for this category of food as compared to “conventional” food products. The common success elements for the advertising of food such as taste, convenience traits, a certain product range and different packaging volumes are valid for FF as well. It is advised to oblige high-size delivery outlets (superstores, wholesale stores & discount merchants) that are central food sales channels in most European countries. Buyers assume FF in such retail channels and are not keen to drive to particular shops merely to buy such FF products. This policy should not eliminate offering particular delivery outlets (pharmacies and health food shops) the equivalent or adapted FF product. As FF warrant good health and/or stop/manage particular disorders suitably, their formulation and marketing is rather compound, expensive and challenging as exceptional requirements have to be met. Noteworthy research efforts are required for all this. This starts with identification of likely carotenoids, evaluating their physiological impact, designing a proper food matrix keeping in mind bio-availability and prospective modifications during food processing, and clinical trials for product’s effectiveness to get endorsement for claims of improving health. Businesses require new techniques of recognizing critical technologies at an initial phase of product brand. Merely systematic studies do not make a product popular in emporium. The product should be in a suitable shape so that the customers can receive it easily. Consequently it is essential to sightsee which ailments users are worried about so that the carotenoid product can be fruitful in the market.

Certainly, strong suggestions exist indicating association between carotenoid ingestion and ‘good health.’ But is it only due to carotenoids? We are still far away from answering this question. In studies using cell and animal models (CAM), carotenoids impact various molecular and cellular mechanisms. It is however difficult to directly associate existing experimental data to human pathophysiology.

First, the findings of many studies require an accurate analysis of the processes by which carotenoids exercise neuro-protective effects. Their antioxidant potential can be one of the reason as increased oxidative stress is one of the characteristic pathologies in neurodegenerative ailments. However, the mechanisms by which carotenoids prevent neuro-inflammation and trigger autophagy have not been well-studied. Second, clinical application studies in human are necessary to observe the causal relationship of the carotenoid effect in human. It is also possible to deduce the connection between carotenoid ingestion and the onset of disease through comparative studies of races taking different diets. Finally, it is possible that merely enhancing the carotenoids intake exercises only limited protective effects to neurons. Hence future studies evaluating other neuro-protective reagents/treatments that exhibit synergistic effects in combination with carotenoids in neurodegenerative ailments will be vital in finding real treatments [7].

27.7 Market Growth Drivers

The carotenoids market growth is primarily driven by

1. The all-natural trend resonating in the global marketplace coupled with increasing demand for naturally obtained colorants like carotenoids in the nutraceutical industry due to their positive impact on various human organs and systems.
2. The alternative treatment methods for diabetes, eye disorders, and other lifestyle diseases are witnessing robust popularity. There is increased expenditure on medical and healthcare insurance facilities coupled with increased life expectancy of aging population. The increasing inclination towards functional foods and dietary supplements is also boosting this industry.
3. Increasing application in personal care and cosmetics especially in face care (anti-aging) and skin care (whitening agents & sun screen) are also a major factor in growth of carotenoid industry.
4. Increasing health awareness thanks to easy access to the information leading to self-care movement among consumers is a key driver in growth of industry. Participants of space science and operations, acknowledgement of FF like carotenoids is increasing due to improving health value and eating routines in long-term flights and tasks.
5. Amendment in government rules and liability are a key driver of growth of carotenoids industry.

27.8 Challenges

1. Deficiency of technical know-how may hinder entry of new players in market.
2. Toxicity symptoms due to the higher carotenoids intake is a key challenge in growth of industry. Currently carotenoids are being considered as a substitute to

antibiotics. Wide use of antibiotics in animal feed has created drug resistance in animals and humans. Hence carotenoids like β -carotene are focus of research to help animals grow by boosting their immunity.

3. Rigid government policies and shortage of awareness in emerging economies is hampering growth of carotenoids industry.
4. Adulteration of natural carotenoids colorants by colors from other sources is a major challenge being faced by food industry.
5. Ingredient compatibility during food manufacturing impacts ingredient interaction. Further, oil-based colors including carotenoids can stain permanently, creating difficulties for F&B processors. Cold storage to retain integrity of natural colors is challenging as opening and closing of storage unit can contaminate and degrade product. The fortified drinks are in high demand. However, fortification can cause unwanted color interactions degrading colors.
6. Procurement of natural colors from different geographical regions where they are grown is an emerging challenge. For example, annatto is chiefly obtained from Latin America and most fruit-based colors originate from Europe. Hostile climatic situations in these areas can upset their supply and hence price.
7. In the last decade, there has been substantial progress in increasing pro-vitamin A carotenoid content in maize. However, maize carotenoid quality during storage depends on temperature and humidity and minute changes in them can degrade carotenoids.

27.9 Production Methods

Carotenoids can be achieved via industrial fermentation using microorganisms, extraction from plants, and chemical synthesis.

Industrial production of carotenoids is done by

- (i) biotechnological processes using filamentous fungi, yeasts, bacteria or microalgae
- (ii) solid-liquid extraction from plants
- (iii) Chemical synthesis

Currently, carotenoids produced by chemical synthesis lead the international commerce [3, 4]. Biotechnological production however is now becoming method of choice due to two strategies (1) isolation after fermentative production in a micro-organism and (2) genetic engineering to synthesize the desired carotenoid in plants. There is competition between synthetic and naturally-obtained carotenoids. The biotechnological production is considered superior due to availability of range of microorganisms in nature, flexibility in the usage of substrates and agro-industrial wastes and the option to regulate operational conditions like temperature, pH,

dissolved oxygen, and light intensity. These organisms can produce carotenoids from fats and other basic organic metabolic building units. Fatty tissues of animals store carotenoids and entirely carnivores get these molecules from animal fat.

Carotenoids are being made by chemical synthesis since first synthesis in 1950 by Karrer, Eugster, Inhoffen, and Milas. In 1954, synthetic β , β -carotene was made on industrial level. Nearly all key carotenoids including lycopene, canthaxanthin, astaxanthin, β , β -carotene, β -apo-8'-carotenal, β -apo-8'-carotene, and cytranaxanthin have been synthesized either by Wittig reactions or Grignard compounds [8]. Synthetic carotenoids are made from various approaches including reactions of dehydration and elimination, specific condensation of carbonyl compounds and homo-dimerization reaction, and selective coupling reaction of Csp²–Csp². Chemical synthesis using petrochemical-derived precursors is the preferred production method. Table 27.2 indicates main products of famous companies [2].

The chemical synthesis of over 200 carotenoids has been reported. β -carotene obtained from natural sources is merely 2% of the total global market and remaining from the chemical synthesis. Various rubrics determine strength of both synthetic and natural production.

27.9.1 Yields

Very small quantity of carotenoids is obtained from natural sources including plants, animals, and micro-organisms. The maximum producing algal strains yield <10% of carotenoids per DW.

27.9.2 Cost

They are quickly created synthetically utilizing low-cost labor and low-priced chemicals and inexpensive harvesting and extraction. The expenses of algae-based carotenoid can range > \$7500/kg while its synthetic equivalent can cost half of this amount.

Table 27.2 Main products of famous companies

Company	Country of origin	Main products
BASF SE	German	Lucantin [®] , Lucarotin [®]
DSM	Dutch	Carophyll [®]
Döhler Group	Germany	–
Chr. Hansen	Denmark	NutriPhy [®]
Kemin Industries	USA	Kem Glo [™]

27.9.3 Choice of Type

Carotenoid of choice can be manufactured by synthetic way. The algal astaxanthin is >95% esterified while synthetic astaxanthin can be obtained in both esterified and unesterified forms. However due to their chiral nature, natural and synthetic carotenoids cannot be distinguished in a laboratory.

27.9.4 Pros and Cons of Both Methods

The total annual production in nature is estimated at over 1000 million tons. Synthetic carotenoids controlled the source landscape with a market value of 200 million US\$ in 2018 and by 2026; they are anticipated to surpass US\$ 4700 million income. Synthetic carotenoids account for 90% of the total market while remaining 10% are obtained from natural sources. Synthetic market is dominated by two main companies, the BASF and DSM, which produce 55% of the global market while remaining 45% demand is met by small players.

Synthetic carotenoids have certain alluring traits as compared to natural analogs. Synthetic carotenoids are more stable as they are particularly designed to decrease oxidation or isomerization. They are available as colloidal suspension, emulsification, and dispersion colloids to make carotenoids application in food easier. Despite these advantages, they are less effective with regard to their health-promoting characteristics and are therefore less appreciated and wanted. They manifest high toxicity, carcinogenicity, and teratogenicity characteristics and health-conscious customers are hesitant to use them. The emerging modern standards for a healthy lifestyle and ecofriendly approaches has increased the quest of natural colors as alternatives to synthetic analogs. Hence biomass (vegetables, fruits, yeast and microorganisms) is used as carotenoids source. However naturally sourced carotenoids need complex extraction stages, are more hydrophobic, unstable, experience seasonal fluctuations, and are limited in supply. The yield from natural hosts is very less, commonly a few mg/kg of raw material. Further, plants or microbes commonly yield mixtures of these compounds with same physical and chemical properties e.g. α - and β -carotenes. Thus, their production from natural sources is challenging and quite expensive from process economics and sustainable land-use perspective. Chemical synthesis is also very costly due to structural complexity [9].

27.10 Recent Commercial/Corporate Developments

- ExcelVite announced the collaboration with USP in April 2019 for the publication of new Plant Carotenes Monograph.

- In March 2019, GacLife, solutions by nature beverage brand launched five new daily health beverages, which include the highest amount of antioxidant carotenoids to provide powerful antioxidant protection for the whole body.
- In March 2019, Kemin Industries, Inc. introduced Organic KEM GLO for North American Egg Producers. It is a USDA-certified organic additive that enables organic egg producers to intensify the color of egg yolks. It utilizes the natural characteristics of paprika to evenly distribute color throughout the feed, delivering consistent egg color pigmentation and density.
- In August 2018, BASF Animal Nutrition introduced Lucantin NXT product line in the EU 28 market. Lucantin NXT products offer outstanding stability, longer shelf life, and high homogeneity, while maintaining the efficacy of egg yolk and broiler skin coloring.
- In July 2018, Nutrex Hawaii has received United States Pharmacopeia (USP®) Verified Mark for BioAstin® Hawaiian Astaxanthin® which is the first dietary supplement brand of astaxanthin to receive USP verification. Nutrex Hawaii is the only producer of naturally grown Hawaiian Astaxanthin using open pond technology
- In February 2018, KnipBio established SCP strain for Astaxanthin production. The enterprise declared that it has developed its single-cell protein-based meal containing bio-astaxanthin.
- In January 2018, NextFerm Technologies Ltd., an Israel based biotech start-up company has developed two kinds of products using their fermentation technology—NextFreeze™, a new and improved baker's yeast strain and AstaFerm™ phaffia yeast astaxanthin. NextFerm's AstaFerm™ is a whole astaxanthin extract of *Phaffia rhodozyma*. The Company is aiming to commercialize AstaFerm™ astaxanthin in the market at the last quarter of 2018, and will be available in 10% oil and 5–10% free flowing CWD powder forms.
- DSM & Kemin Industries have partnered to launch natural zeaxanthin as Optisharp® in 2014.

27.11 Overall Scenario

In 2024 the consumption of Natural Carotenoids is estimated to be 2699.8 MT. Western Europe followed by US are likely to be the largest market for natural colors. FDA has approved list of natural colorants including annatto, caramel, β -carotene for use in cosmetics. The capsanthin, astaxanthin, β -carotene, lutein,

Table 27.3 Market share by key carotenoids

Carotenoid	Revenue generated (million) 2017	Expected in 2022 (million)	CAGR (%)	Market share (%)
Capsanthin	USD300	USD385	5.1	20
Astaxanthin	USD288.7	USD426.9	8.1	16

annatto, lycopene, and canthaxanthin together share nearly 90% of the total market value. Astaxanthin and β -carotene are the two most recognized carotenoids and make up almost half of the global carotenoid market. Table 27.3 indicates market share by key carotenoids [3, 4].

27.12 Active Organizations

The positive endorsements by research institutes has greatly impacted the adoption of carotenoid-rich food by customers. International Carotenoid Society, IBERCAROT (the Ibero-American network for the study of carotenoids as FF components), Spanish Carotenoid Network (CaRed), and Eurocaroten are working to increase the carotenoids information and research.

27.13 Key Manufacturers/Players

The market for carotenoids is highly competitive due to existence of numerous players. Moreover, more than half of the market is accounted by two major players DSM and BASF. BASF and DSM occupy the market of β -carotene, astaxanthin, and canthaxanthin, while small companies dominate lutein and lycopene market. These manufacturers are facing stiff competition from the Indian and Chinese manufactures of carotenoids.

The main players in the market comprise FMC Corporation, Chr. Hansen A/S, Kemin Industries, Inc., Allied Biotech Corporation, Cyanotech Corporation, Carotech Berhad, Döhler Group, BASF SE, D.D. Williamson & Co., Inc., Koninklijke DSM N.V., ExcelVite Sdn. Bhd., Brenntag AG, DSM Nutritional Products, Divis Laboratories, Naturex SA, Lycored Ltd. and, Algatechnologies, Ltd.

27.14 Carotenoids Type

Beta-carotene and astaxanthin are dominating in global marketplace while novel and unconventional carotenoids are expected to register higher growth rates. The global market has ample scope of innovative pigments that provide enhanced functionalities – for instance, Phycocyanin from *Arthrospira* extracts was approved for use in candy, chewing gum, and other types for confection in the U.S. in 2013 and 2014 by FDA.

27.15 Product Type

The worldwide carotenoids market is fractioned on the basis of product kind, application, source, and area (Fig. 27.16).

Based on the product type, β -carotene is one of the hit products between 2019 and 2026. By 2026 end, β -carotene is anticipated to beat US\$2000 million income. The astaxanthin, β -carotene, and lutein together occupy almost 60% of total market value. Astaxanthin accounted for a considerable market share in 2019. Synthetic β -carotene chiefly manufactured by BASF or DSM (Heerlen, Netherlands) accounts for 90% of the market while the residual 10% is obtained from natural sources. Aquacarotene Ltd., Cognis Australia Pty Ltd. (a BASF subsidiary) and Nature Beta

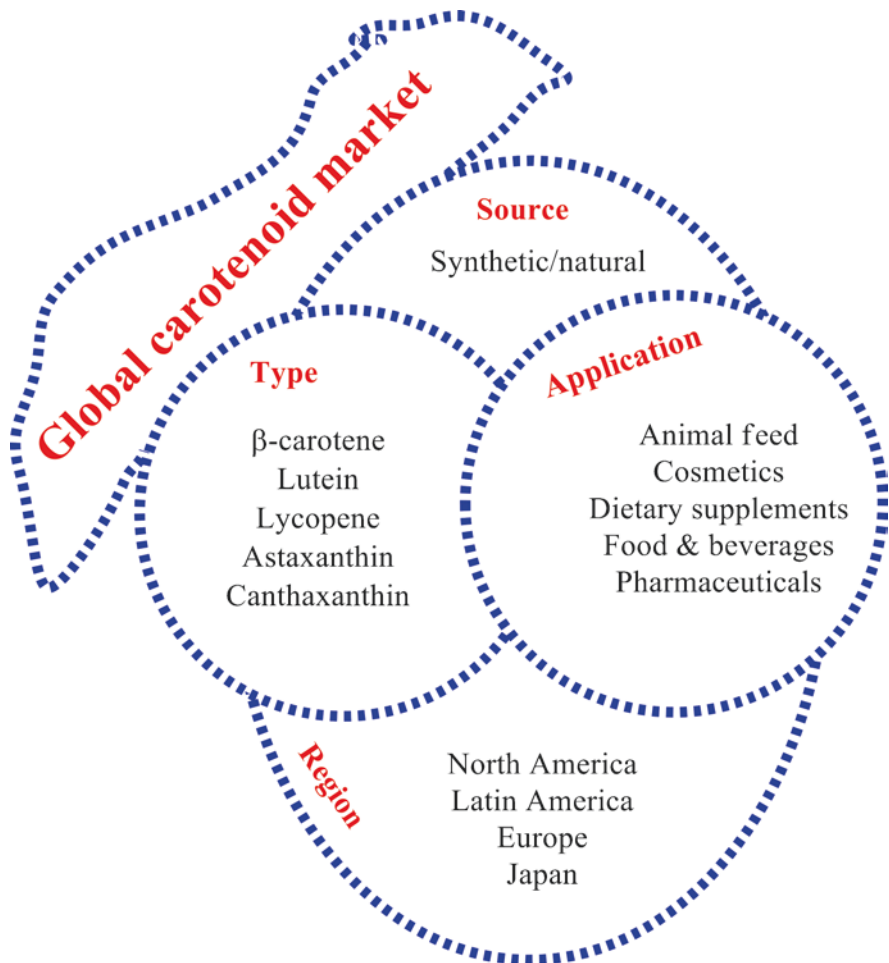


Fig. 27.16 Key segments of carotenoids market

Technologies Eilat use *D. salina* at one of the biggest algal farms in Australia and Israel, respectively to produce β -carotene. Similarly DSM and Vitatene use *B. trispora* while Biotrend of Portugal use *Sphingomonas* for β -carotene production. The ripe tomatoes and *B. trispora* are the key commercial sources of lycopene although synthetic lycopene (96% pure) is also available in markets [3, 4].

27.16 Price

Prices of all kinds of formulation and origin have dropped substantially owing to the Chinese companies with first-rate products. The egg-pigmentation segment is developing moderately while the spice market is growing quickly. Astaxanthin was the highest priced, @ \$2000 per kg for the synthetic compound and about \$7000 per kg for natural analog.

27.17 Geographic

Germany leads the European market of Carotenoids for Food & Beverage applications while Spain shows the slowest CAGR. China forms the single biggest market for carotenoids in Asia-Pacific while the Japanese market for carotenoids is expected to nurture rapidly. Their demand in Australia is expected to be the slowest from 2019 to 2024. South Korean market demand for Carotenoids in terms of product is the largest for β -Carotene. Geographically, the carotenoids market is fragmented into Asia Pacific Excluding Japan (APEJ), Japan, North America, Europe, Latin America, and the Middle East and Africa (LAMEA). In terms of value, Asia-Pacific and LAMEA collectively contributed more than one-third share in the global market in 2018. LAMEA market will grow significantly due to increasing per capita income and consciousness of the benefits of FF. Carrots are as the chief source of β -carotene in several European countries. Lutein is chiefly obtained from peas in UK and Ireland, and from spinach in other states. Asia-Pacific is projected to grow at the highest CAGR due to rising per capita income coupled with rising demand for dietary supplements in the region and higher adoption of carotenoids in Indian and Indonesian F&B industry.

27.18 Individual Carotenoids

27.18.1 Beta Carotene

It is an organic, strongly colored red-orange color which is amply present in plants and fruits. β -carotene obtained from *Blakeslea trispora* is used for the pigmentation of butter and margarine, cakes, milk products, and soft drinks. The β -carotene segment, the carotenoid of highest value, is estimated to develop at a compound annual growth rate (CAGR) of 5.1% from 2019 to 2026. The β -carotene market is currently oversupplied. Synthetic type rules the market and expectations that fermentation-derived type will fetch a bigger market stake has not been met, with algal β -carotene almost vanishing from the market [10, 11].

Beta carotene has tremendous health benefits as a provitamin A and is also popular as a colorant for food and beverages applications. Increasing preference towards naturally derived ingredients and cleaner label solutions has instigated the natural beta carotene segment's growth. Beta-carotene market has gained significant momentum over the last few years, due to superior properties of the ingredient such as promoting eye health, healthy skin, and preventing cardiovascular disease. The infusion of this ingredient in diet and supplements has directed product demand across the globe and amplified the carotenoid's industry size. Women, focusing on adopting a healthy and natural diet for the skin rejuvenation, are the foremost target consumers in the natural β -carotene market. As Australia is a geologically important region for the natural beta carotene market, neighboring regions have automatically become target markets. Lower freight costs and storage costs have opened avenues for the natural beta carotene market in Australia's neighboring regions. South Korea makes up nearly 50% of the natural beta carotene demand produced in Australia. India and China have demonstrated immense market potential in fortified beverages market which concurrently aids the natural beta carotene market to grow. The growing demand for natural beta carotene in the fortified food industry is mainly nourished by the research divisions of the natural beta carotene manufacturers.

β -carotene is largely used as colorant for beverage and food applications. In 2017, BASF SE launched a 10% beta carotene powder, Lucarotin 10 CWD (Cold Water Dispersible)/O (Orange) Plus. In the United States, this product replaced azo dyes yellow 5 and 6 in beverages, soups, confections, and nutrition products. In US, β - (95% pure) is allowed as a colorant under 21 CFR 73.95 and 21 CFR 166.110 and a pro-vitamin A nutrition supplement under 21 CFR 182.5245 and 21 CFR 184.1245 [12].

Beverage manufacturers have launched various ready-to-drinks (RTD) containing β -carotene, nature-identical being the most predominant form. For instance, Vitatine which is an antibiotic subsidiary signed an exclusive agreement with B & D Nutritional Ingredient which will bring its natural β -available in the United States for application in food and beverages and dietary supplement industry. Also, beverage brand GacLife has launched the world's first line of gac-based wellness

products with functions for skin and vision care. Gac fruit is a fruit found in certain Southeast Asian regions and comprises of high concentration of carotenoids.

27.18.2 Lycopene

Permission obtained for Lycopene from the European Commission for use as a food additive and coloring instrument long-ago but this endorsement could not increase the market size. However, use in traditional supplement sector has augmented. Amounts have declined as numerous Asian dealers sell lycopene obtained from tomatoes with adequate quality. The lycopene product segment is anticipated to witness rapid growth in the future, owing to the high usage of it in cosmetic and pharmaceutical products. Lycopene is efficient in preventing ailments, such as age-related macular degeneration, diabetes, and also protects skin against sunburn. Lycopene industry worth USD 15 million in 2015, will grow significantly in near future due to usage in cosmetics and pharmaceuticals industry.

The hydrophobic character of most carotenoids causes their aggregation and crystallization in aqueous medium, a typical example of lycopene crystals in chromoplasts of tomatoes. A lycopene-based supplement is Lycosome (made by Lycotec, UK) employing lycopene micelles to entrench a whey protein isolate, enhancing its delivery and efficiency. Due to its powerful antioxidant potential and high solubility in aliphophilic milieu such as the skin, natural lycopene is also employed in cosmetic goods. Generally recognized as safe (GRAS) certificate has been issued by the FDA to three products of BASF Corporation and Lyc-O-Mato (LycORed Ltd). Tomato lycopene competes with synthetic analog. Tomato lycopene is employed as a nutraceutical and to red color the food. The Tomat-O-Red (LycORed) comprises tomato lycopene achieved from oleoresin in crystallized form to provide a fine dispersion in water [13].

Mega manufacture of natural lycopene initiated in Israel in the mid-1990s when LycORed (a company) initiated its extraction from tomatoes. Today many companies including LycORed (Israel), Parry Nutraceuticals and Perennial Lifesciences (India), Lycotec (U.K.), Pierre (Italy), and Xi'an Miracle Biotechnology and North China Pharmaceutical (China) are active in this business [13, 14].

27.18.3 Astaxanthin

The current global annual market of astaxanthin is around 250 tons worth \$447 million and it is growing rapidly. Due to strong antioxidant potential, it is the third carotenoid in terms of high added value [9]. Its consumption is increasing in aquaculture business for coloring fish and shrimp. Algal astaxanthin is increasingly being used in food supplements. The well-ordered tube systems for creation and usage of microbes that can yield astaxanthin in the dark has multiplied its

production. The older adult population face vision damage increasing demand for astaxanthin, as it is useful for eyes. It is also used in the cosmetics sector due to its UV and anti-aging potential.

27.18.4 *Canthaxanthin*

It provides a red tone in egg yolks, salmonid fishes and shrimp. Canthaxanthin contributed almost 10% of the global carotenoids market share in 2015, and is expected to observe a surge in next few years due to broad usage in cosmetics sector due to its anti-tanning capacity.

Canthaxanthin market trends have shown modest growth lately, primarily driven by increasing consumer preference for foodstuffs such as fruits and vegetables, dairy, baby food, meat, breakfast cereals, snacks, and bakery and confectionery. canthaxanthin also has enormous applications in the cosmetic industry and is used as an artificial tanning agent. However, stringent regulations enforced by the FDA on the use of canthaxanthin in tanning pills might restrict revenue contribution from this segment.

27.18.5 *Lutein and Zeaxanthin*

The lutein market flourished until 2004. Since then, the market has developed moderately. Lutein is estimated to grow substantially in the near future due to its high demand in pharmaceutical, food, dietary supplements, nutraceuticals, and animal feed sector. Zeaxanthin obtained permission for sale in 2012 is unlocking a considerable market growth.

Table 27.4 Various sources of key carotenoids

Carotenoid	Plant source	Algae source	Bacteria	Fungi
Lutein	Marigold flowers	<i>Chlorella</i> Spp.	<i>Gordonia alkanivorans</i>	–
β -carotene	Carrot, Palm oil fruit	<i>D. salina</i>		<i>Blakeslea trispora</i>
Lycopene	Tomato fruit			<i>Fusarium sporotrichioides</i>
Capsanthin	Red pepper			
Astaxanthin		<i>H. pluvialis</i>		
Bixin	Annatto (<i>B. orellana</i>) seeds			

27.18.6 Microbial Platforms for Carotenoids Production

Microbial-derived carotenoids metabolites have led to a paradigm shift in carotenoids research leading to new aspects about the impact and role of these metabolites in absorption and biological activity. Plants are the main source of natural carotenoids. Xanthophylls containing acetylene functional groups are unique to algae. Table 27.4 indicates various sources of key carotenoids.

The microbial production of carotenoids has numerous benefits. As from minimum land, water, nutrients and labor, considerably 5–10 times greater growth rate can be achieved. The lutein quantity of dehydrated marigold petals (0.02–2.8 g/100 g) is comparable to microalgae biomass (0.24–0.74 g/kg). Additionally operating dynamics like stress-driven adaptive process influencing the carotenoids contents in microbes can be additionally enhanced for higher yields. The price of the microbial generation can be considerably decreased by using the agro-industrial wastes as cheap substrates. In fact all conditions of production can be regulated and optimized, particularly knowing the metabolic route of each microorganism used [3, 4].

27.19 Algal Production

The market volume of carotenoids obtained from algae has grown five times since the start of the century and its growth has fairly matured now. Algae-based carotenoids are produced on a smaller scale with a bigger market potential, chiefly in Asia, the USA and Australia. While the production is expensive, the quality of carotenoids obtained is superior to those obtained from chemical synthesis or from plants. It is chiefly since the molecules obtained from the algal biomass are more effective for food applications than their synthetic analogs. Earlier market pundits were skeptic about integration of algae-derived carotenoids into market due to great investment needed for open ponds, photobioreactors and allied facilities. However, all these fears were baseless [3, 4].

Natural astaxanthin is economically achievable and competitive with synthetic analog, which has a manufacturing price of USD1000/Kg. In China, astaxanthin can be obtained from *H. pluvialis* @ USD718/Kg, with a cost of algae biomass of merely USD18/Kg. *Xanthophyllomyces dendrorhous* and *Scenedesmus* sp. are used to produce astaxanthin for utilization in the feed and nutraceutical businesses for the production of salmonids (salmon, rainbow trout) and for the development of egg yolk coloring. *Haematococcus pluvialis* accumulates astaxanthin inside their extraplastidial lipid bodies at a concentration of approximately 4% on a wet weight basis and approximately 300 tons of *Haematococcus* biomass are created yearly as a natural source of astaxanthin.

The most relevant natural source and process to obtain β -carotene is the culture of *Dunaliella salina*, which can accrue up to 12% of β -carotene on a dry weight basis subject to the cultivation settings. Industrial creation of β -carotene from

microalgae originated in the 1980s in Israel, Australia, and the United States and expanded later to other countries including India and China.

Key European Algal Production companies are Algalif, Fermentalg, Allmicroalgae Natural Products, BDI-BioLife Science, Qualitas Health, Earthrise, Triton, and A4F. The Cyanotech, established in 1983 dominates the algae-based carotenoid industry and is generating astaxanthin (and cultivating *Haematococcus* and *Spirulina*) for years. Sphera (Italy) has combined with AlgaTechnologies Ltd. (Israel) consenting AlgaTechnologies to nurture algae and harvest astaxanthin and fucoxanthin and Sphera for their encapsulation. The Beijing Ginko Group (BGG), famous for its algal manufacturing plant in Yunnan province, has linked with Natural Astaxanthin Association (NAXA) for the manufacturing of the “world’s first organic astaxanthin”. Moreover, BGG has teamed up with Solix (USA) to found a new company centered in Colorado aiming on the mining of ingredients from algae [2]. The Israeli company Algaennovation has entered into agreement with an Icelandic geothermal plant to obtain eco-friendly electricity, hot and cold water and CO₂ energy for its microalgae farm in Iceland.

Microalgal carotenoids namely astaxanthin and β -carotene are being currently commercialized. The production cost of astaxanthin from *Haematococcus pluvialis* in 718 USD per kg as compared to 1000 USD per kg of synthetic with a market price of over 2000 USD/kg. The *H. pluvialis* can yield astaxanthin at >4% per DW, which is encouraging than the bacterium *Paracoccus carotinifaciens* (2.2% DW), the yeast *Phaffa rhodozyma* (<0.5% DW) of (3R, 3'R)-astaxanthin and shrimp/crab shells (<0.025% DW).

27.20 Conclusions

The hopeful endings stemming from of preclinical studies (CAM) are challenged or at least reduced moving to case-control trials. This limited disappointment is complicated and complicated to address. Different dosages regimes used in animal versus clinical studies, the complex metabolism and biotransformation of carotenoids in the intestine and tissues, the likelihood that dissimilar ingredients of supplemented mixtures can network producing antagonistic, synergistic, or additive influences are some of the opinions. However, another matter contributing confusion is the difference between prevention and therapy. Prevention infers low doses for long time (years), while therapy is linked with upper dosages for smaller time duration. Establishment of new and adequate CAM is essential suggesting more well-organized and prevention-targeted clinical studies. Funding This research was funded by the Deanship of Scientific Research at Princess Nourah bint Abdulrahman University through the Fast-track Research Funding Program.

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