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Carotenoids

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Carotenoids form one of the most important classes of plant pigments and play a crucial role in defining the quality parameters of fruit and vegetables. Carotenoids are of great interest due to their essential biological functions in both plants and animals. Herein, the review article discuss how carotenoids synthesised in plants leading to different types, their role in plants and biological activities to human and all details concerning the most important carotenoids in our life

Keyword: Carotenoids, Classification, Biosynthesis, Function, β-Carotene

1. Introduction

Without pigments we're nothing. Life presents us with a kaleidoscope of colors. From the green grass of home to a forest's ruddy autumn hues, we are surrounded by living color. Living things obtain their colors, with few exceptions, from natural pigments. In addition to their role in coloration, natural pigments carry out a variety of important biological functions[1].

Plants play an important aesthetic function by providing flowers with a broad spectrum of colors[2]. Plant pigments are important in signalling, as in attracting pollinating and dispersal agents, and repelling herbivores. They are also important for humans, attracting our attention and providing us with nutrients. Plant pigments are important clues to humans and other herbivorous animals in helping identify plants find plant parts such as fruit, leaves, stems, roots, or tubers and determine stages of plant development such as ripeness or overall senescence. It was realized early in this century that many of these pigments play a positive role in human health. Plant pigments are obviously physiologically important, and recent research suggests novel protective mechanisms, both photo-protective and anti-oxidative. Plant pigments are economically important, in determining the colours and patterns of attractive flowers and valuable fruits. They are also important nutritionally, with an understanding of emerging new roles in nutrition and in aiding health[3]. All of these reasons were a motivation for production a review about one of the most important plant pigments; carotenoids.

1.1Carotenoids

Carotenoids form one of the most important classes of plant pigments and play a crucial role in defining the quality parameters of fruit and vegetables [4].

They are found principally in plants, algae, and photosynthetic bacteria, where they play a critical role in the photosynthetic process. They also occur in some non-photosynthetic bacteria, yeasts, and molds, where they may carry out a protective function against damage by light and oxygen[1,5].

Carotenoids are responsible for many of the red, orange, and yellow hues of plant leaves, fruits, and flowers, as well as the colors of some birds, insects, fish, and crustaceans. Some familiar examples of carotenoid coloration are the oranges of carrots and citrus fruits, the reds of peppers and tomatoes, and the pinks of flamingos and salmon[6]. Some 600 different carotenoids are known to occur naturally, and new carotenoids continue to be identified[1,7]. They are partially responsible for fall coloration after the leaf chlorophyll has been destroyed[8].

Animals are unable to synthesise carotenoids de novo, and rely upon the diet as a source of these compounds[9].

1.2 Classification

Carotenoids are classified according to the structure as follows:

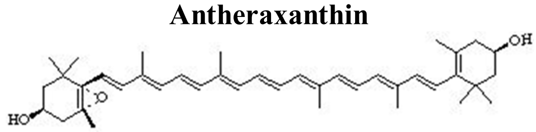
1. The hydrocarbon carotenoids which are known as carotenes example β-carotene
2. The oxygenated carotenoids which are derivatives of these hydrocarbons known as xanthophylls, examples of these compounds are a zeaxanthin and lutein (hydroxy), spirilloxanthin (methoxy), echinenone (oxo), and antheraxanthin (epoxy)[10].

1.3 Structure

Carotenoids are lipid-soluble C40 tetraterpenoids. The majority carotenoids are derived from a 40-carbon polyene chain, which could be considered the backbone of the molecule. This chain may be terminated by cyclic end-groups (rings) and may be complemented with oxygen-containing functional groups.

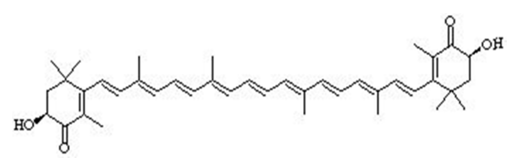
In nature, carotenoids are predominantly present in the all-*trans* configuration. However, processing fruits and vegetables produces a 10% to 39% increase in *cis*-isomers. [11] The degree of isomerisation is directly correlated with the intensity and duration of the heating process. However, when Rock *et al.* fed processed vegetables to subjects, no increase in 9-*cis*-b-carotene plasma concentrations was observed. Rather, the plasma response was characterized by an increase of all *trans*-*β*–carotene, due to isomerization of *cis*-isomers to all *trans*-*β*-carotene or a rapid tissue uptake[12].

Antheraxanthin



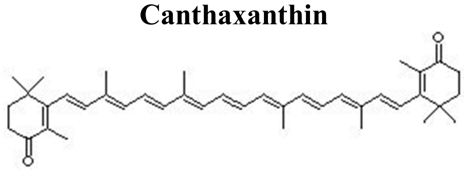
Present in many plants, especially maize

Astaxanthin



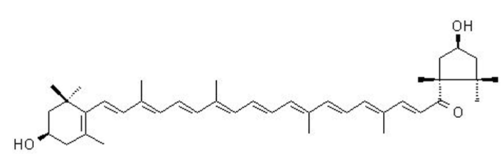
Present in: salmon, shrimp, lobster, and flamingo

Canthaxanthin



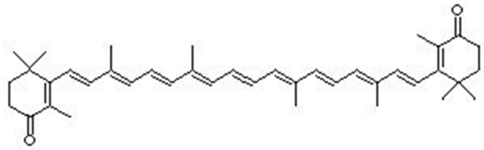
Present in: salmon, shrimp, flamingo feathers

Capsanthin



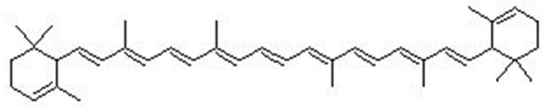
Present in: peppers, paprika

α-Carotene



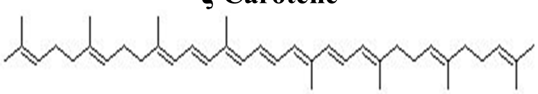
Present in carrots, most green plants

ε-Carotene



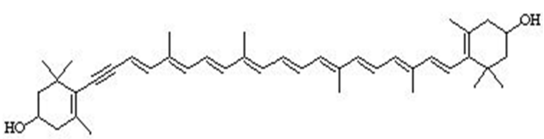
Present in most green plants

ζ-Carotene



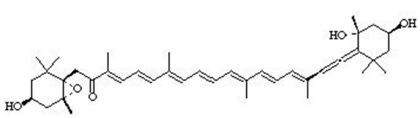
Present in many plants

Diatoxanthin



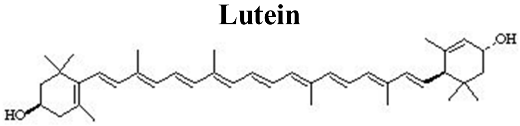
Present in algae and corals

Fucoxanthinol



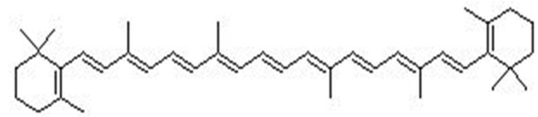
Present in many algae and seaweed

Lutein



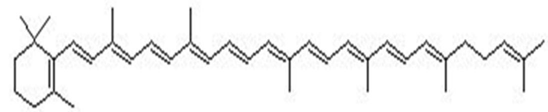
Present in many green plants

ß-Carotene



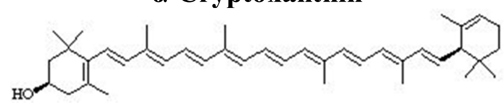
Present in carrots and most other plants

γ-Carotene



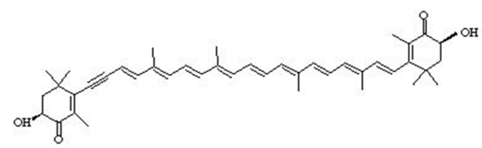
Present in many plants, often with ß-carotene

α-Cryptoxanthin



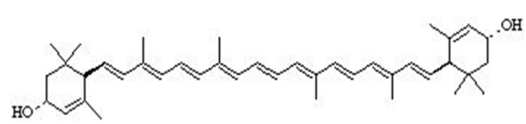
Present in many coloured plants as maize and papaya

7,8-Didehydroastaxanthin



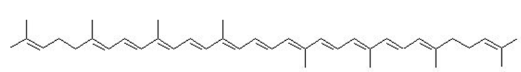
Present in: salmon and crustaceans

Lactucaxanthin



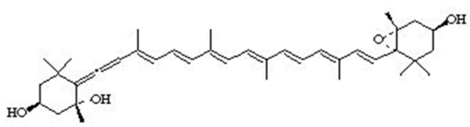
Present in algae

Lycopene



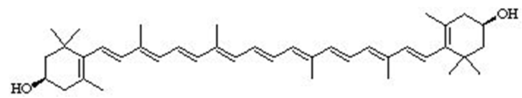
Present in many plants, especially in tomato

Neoxanthin



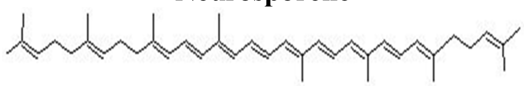
Present in the chloroplasts of most plants

Zeaxanthin



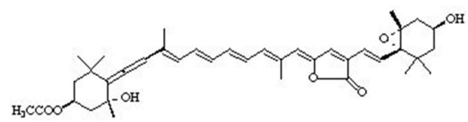
Present in many plants, especially in maize

Neurosporene



Present in many plants, intermediate between carotene and lycopene

Peridinin



Present in the chloroplasts (green particles) of compound most plants

1.4 Biosynthesis

In the plastids, where carotenoid biosynthesis takes place, IPP is synthesized through the plastid-specific DOXP (1-deoxyxylulose 5-phosphate) pathway.

1. The carotenoid pathway is catalyzed by phytoene synthase (PSY), resulting in the condensation of two C-20 geranylgeranyl diphosphate (GGPP) molecules to form phytoene.
2. Four desaturation reactions, two each catalyzed by the membrane associated phytoene desaturase (PDS) and ζ-carotene desaturase (ZDS), result in the formation of the pink lycopene from the colorless phytoene.
3. The cyclization of lycopene represents a branch point in the pathway, and two products can be formed depending on the position of the double bond on the cyclohexane ring.

   a. On one hand, lycopene β-cyclase, for which there are two forms in tomato, one specific to green tissues (LCY-B) and the other to chromoplasts (CYC-B), first produces γ-carotene containing one β-ring which is subsequently converted to β-carotene by the same enzyme.

   b. On the other hand, lycopene ε-cyclase (LCY-E) produces δ-carotene. The formation of α-carotene, the precursor for lutein, involves formation of a β-ring on δ-carotene by lycopene β-cyclase.

4. The α- and β-carotenes are the precursors for the xanthophylls, which are oxygenated carotenoids generated by β- and ε-ring specific hydroxylases.
5. β-carotene is converted to zeaxanthin by the carotenoid β-ring hydroxylases (HYD-B), encoding a nonheme diiron enzyme for which there are two genes in *Arabidopsis*. The hydroxylation of the ε-ring is carried out by the carotenoid ε-ring hydroxylase (HYD-E), a cytochrome

P450 enzyme, CYP97C1, encoded by the *Arabidopsis LUT1* locus.

6. In addition to displaying activity toward the ε-ring, LUT1 can also hydroxylate the β-ring. Hydroxylation of the β-ring of α-carotene is also mediated by a P450 enzyme (E. Wurtzel, personal communication). Lutein is the main carotenoid present in the petals of marigold, and the broad range of colors that characterize marigold flowers is due to the very different levels of this xanthophyll.
7. The formation of ketocarotenoids, such as, for example, astaxanthin, requires the addition of keto groups in each β-ring of zeaxanthin[13].

1.5 Function

1. For plant life: carotenoids are essential for plant life, providing important photoprotective functions during photosynthesis; light harvesting and prevention of photo-oxidative damage, and serving as precursors for the biosynthesis of the phytohormone abscisic acid (ABA). They have a role in attraction of pollinators[4,14].

2. For human: of the over 600 carotenoids found in nature, about 40 are present in a typical human diet. Of these carotenoids, only 14 and some of their metabolites have been identified in blood and tissues[15].

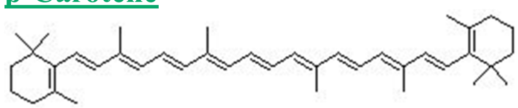
Their function as antioxidants in the plant shows interesting parallels with their potential role as antioxidants in foods and humans[4]. The antioxidant actions of carotenoids are based on their singlet oxygen quenching properties and their ability to trap peroxyl radicals[16]. The best documented antioxidant action of carotenoids is their ability to quench singlet oxygen. This results in an excited carotenoid, which has the ability to dissipate newly acquired energy through a series of rotational and vibrational interactions with the solvent, thus regenerating the original unexcited carotenoid, which can be reused for further cycles of singlet oxygen quenching. The quenching activity of a carotenoid mainly depends on the number of conjugated double bonds of the molecule and is influenced to a lesser extent by carotenoid end groups (cyclic or acyclic) or the nature of substituents in carotenoids containing cyclic end groups[17]. It has been known for many years that carotenoids ‘‘bleach’’ i.e., lose their color, when exposed to radicals or to oxidizing species. This process involves interruption of the conjugated double bond system either by cleavage or by addition to one of the double bonds. Cleavage can be detected by characterizing the products that are formed, which frequently are carbonyls [18] or epoxides[19]. Because of their role as antioxidants, carotenoids have been suggested to be protective against coronary vascular disease. One contributor to the development of coronary vascular disease is the oxidation of low-density lipoproteins (LDL). When LDL is oxidized it is readily taken up by foam cells in the vascular endothelium where it contributes to the development of atherosclerotic lesion[20,21].

This hypothesis is supported by the observational epidemiological studies that report that foods rich in carotenoids and antioxidant vitamins are associated with reduced risk of cardiovascular disease[22]. Many epidemiologic studies have associated high carotenoid intake with a decrease in the incidence of chronic disease. However, the biological mechanisms for such protection are currently unclear. Multiple possibilities exist: certain carotenoids

1) Can be converted to retinoids (i.e. have pro-vitamin **A** activity).
2) Can modulate the enzymatic activities of lipoxygenases (proinflammatory and immunomodulatory molecules).
3) Can have antioxidants properties which are well above what is seen with vitamin **A**,
4) Can activate the expression of genes which encode the message for production of a protein, connexin[43], which is an integral component of the gap junctions required for cell to cell communication. Such gene activation is not associated with antioxidant capacity and is independent of pro-vitamin **A** activity[23].

Other health benefits of carotenoids that may be related to their antioxidative potential include enhancement of immune system function[24], protection from sunburn[25], and inhibition of the development of certain types of cancers[26].
In summary, carotenoids may act as antioxidants and may exhibit chemopreventive anti-atherosclerotic effects and anticancer effects in some specific animal models, using specific carcinogens.

β-Carotene



β-Carotene: β,β-Carotene

β-carotene is the most widely studied carotenoid and is one of the major carotenoids in our diet and in human blood and tissues[27].

Colour: yellow to orange.
Source: Beet root, apricots, cantaloupe, carrots, pumpkin, sweet potato, pink grapefruit, tomatoes, watermelon, mango, papaya, peaches, prunes, squash and oranges whereas green fruits and vegetables such as green beans, broccoli, brussel sprouts, cabbage, kale, kiwi, lettuce, peas and spinach[28] *Capsicum annuum* var. *lycopersiciforme rubrum*[29], *rosa mosqueta* hips (*Rosa rubiginosa*, *Rosa eglanteria*)[30].

Medicinal uses

- **Vitamin A**

Beta-carotene is a pro-vitamin which the body converts into vitamin A[31]. β-Carotene is the most abundant form of vitamin A in fruits and vegetables[32]. The other two carotenoids with vitamin A activity, α-carotene and β-cryptoxanthin are not prevelant in food. β–carotene is an effective source of vitamin A in both conventional food and dietary supplements[33].
Absorption of β-carotene and other carotenoids from vegetables is usually (5-30%) of the absorption from synthetic supplements, due to the food matrix surrounding β-carotene. This matrix of fiber or protein must first be broken down by mastication, gastric acid, pancreatic enzymes, and bile acids[34].
In the small intestinal enterocyte, β-carotene can be transformed into vitamin A mainly as retinyl ester (20-75%) through cleavage of the β-carotene molecule. The majority of conversion to vitamin A takes place, not in the liver, but in the intestinal mucosa[35]. This cleavage depends on the vitamin A content of the meal and the vitamin A status of the individual[36]. In vitamin A-depleted subjects, synthetic β-carotene had 50% of the potency of retinol; in other words, 2 mg β-carotene was equivalent to 1 mg vitamin A[37]. However, β-carotene has not been shown to precipitate vitamin A toxicity, and it has been demonstrated in several species that, when dietary β-carotene increases, the regulatory mechanisms limit vitamin A production from carotenoids[18]. β-carotene not converted to vitamin A is absorbed by the lymphatics, having been incorporated into chylomicrons as intact β-carotene or other non-vitamin A products of β-carotene cleavage[38].

- **Immune response**

There is growing evidence from *in vitro* and *in vivo* laboratory animal studies that β-carotene can protect phagocytic cells from autooxidative damage, enhance T and B lymphocyte proliferative responses, stimulate effector T cell functions, and enhance macrophage, cytotoxic T cell and natural killer cell tumoricidal capacities, as well as increase the production of certain interleukins[39]. A recent study in HIV-infected women reported lower serum concentrations of lycopene, α-carotene, and β-carotene, especially in those with low counts of CD-4 helper cells[40].
Both β-carotene and selenium are deficient in a significant percentage of both HIV and AIDS patients. Their roles as antioxidants in HIV/AIDS appear to be related to both direct immune modulation and inhibition of cytokine and NF-kB activation, inhibiting HIV replication. Beta carotene has been shown to act directly as an immunomodulator by increasing natural killer cell function and improving CD4 count. As an antioxidant, beta carotene appears to support

enzymatic defence systems involved in minimizing oxidative damage.

- **Antioxidant**

The fact that LDL is a major transporter of β-carotene and lycopene in the circulation[41] and that these carotenoids have the capacity to trap peroxyl radicals and quench singlet oxygen lends support to this hypothesis.

β-Carotene is a scavenger of peroxyl radicals, especially at low oxygen tension. This activity may be also exhibited by others carotenoids. The interaction of carotenoids with peroxyl radicals may proceed via an unstable β-carotene radical adduct [42, 43]. Carotenoid adduct radicals have been shown to be highly resonance stabilized and are predicted to be relatively unreactive. They may further undergo decay to generate non radical products and may terminate radical reactions by binding to the attacking free radicals[43]. Carotenoids act as antioxidants by reacting more rapidly with peroxyl radicals than do unsaturated acyl chains. In this process, carotenoids are destroyed[44].

Carotenoids partially or completely protect intact cells (e.g. human liver cell line HepG2) against oxidant-induced lipid peroxidation, and the protective effect is independent of provitamin A activity[45]. Further, in both normal and transformed thymocytes, β-carotene acted as an antioxidant at 150 mm Hg pO2, inhibiting radical-induced lipid peroxidation. However, upon increasing the pO2 to 760 mmHg, b-carotene lost its antioxidant activity in normal thymocytes and actually exhibited a dose-dependent prooxidant effect in the tumor thymocytes[46]. These data point out a key role of the oxygen tension on the antioxidant/prooxidant effects of beta-carotene[49]. High carotenoid concentrations may also result in a prooxidative effect, which may be modified by interactions with other nutrients[47].

- **Cancer**

Research emphasizing the biology of carotenoids was initiated after Peto *et al.* suggested that β-carotene might be the primary anticancer agent in fruits and vegetables[48]. It could be hypothesized that beneficial effects of β-carotene occur at physiologic or dietary levels of intake, whereas harmful effects in some subpopulations can be seen if pharmacologic levels are given.

Proponents believe that beta-carotene helps to neutralize free radicals, which are believed to lead to cancer[31]. A diet rich in beta-carotene-rich fruits and vegetables or high blood levels of beta-carotene are associated with a reduced risk of cancer at a number of common sites, such as lung and stomach[49]. Animal studies have indicated that beta-carotene can delay or prevent induction of sarcomas and skin cancer in mice exposed to carcinogens[50].

The inhibitory effects of the newly-developed forms of beta-carotene - water-soluble and liposomal-have been studied in rats and mice bearing tumors induced in 4 models of carcinogenesis. Water-soluble beta-carotene failed to influence the carcinogenesis in the mammary gland and esophagus in rats; however, it significantly inhibited carcinoma development in murine vagina and cervix uteri (47%). Liposomal beta-carotene significantly inhibited lung adenomas (46.4%) and mammary carcinomas (55.6%) in the urethane-treated mice[51]. In a conducted double-blind placebo-controlled trial to evaluate the chemopreventive potential of either vitamin

Four studies in the USA, Canada, and Italy have shown that beta-carotene, as a single agent, completely or partially reduces oral leukoplakia in 44-71% of patients. Another study, in India, reported that 14% of patients responded completely to beta-carotene; the percentage with partial improvement was not given. The extent to which a reduction in oral leukoplakia will lead to a reduction in the incidence of oral cancer is unknown[52].

Numerous studies have shown that a high intake of carotenoid rich fruit and vegetables is associated with a decreased risk of cancer[53].

A large study examining the effects of beta-carotene and alpha-tocopherol on prostate cancer revealed that "beta-carotene apparently increased the risk of clinically evident prostate cancer only in drinkers, and that the increase was dose related to alcohol intake[55].

- **Lung cancer**

The relationship between β-carotene and lung cancer has been most studied and the data have been more consistent[49]. Evidence for β-carotene as the chemoprotective agent in fruits and vegetables comes from prospective epidemiologic studies in which 11 of 15 have demonstrated a significant inverse relation of β-carotene intake and/or plasma level and risk of lung cancer[27].

Smoke has been invoked as a pro-oxidant, and it has been suggested that in the presence of high concentrations of β-carotene, cigarette smoke might led to oxidative destruction of β-carotene, resulting in the formation of oxidized metabolites that might facilitate carcinogenesis[55].

Conaway *et al.* showed that β-carotene treatment did not inhibit a total tumor formation in the lungs of female A/J mice treated with the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone[56]. However, high doses of β-carotene significantly retarded the malignant progression. While the most direct way to reduce lung cancer risk is not to smoke tobacco, smokers should avoid high-dose β-carotene supplementation.

2. Conclusion

This article reviews carotenoids in general and beta carotene in particular for their role in human health. Carotenoids world is very interesting, starting from its biosynthesis till its medicinal uses. Their biological activities play important roles in the prevention and treatment of many diseases and so, human health is greatly affected by the presence of these pigments.

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