



Biosynthesis and biomedical perspectives of carotenoids with special reference to human health-related applications



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ABSTRACT

Carotenoids are a group of versatile isoprenoid pigments, and bioactive constituents found predominantly in fruits and vegetables. Carotenoids play an essential role in the prevention of human diseases and thus facilitate to maintain a good health. They are effective health-promoting compounds, which are significant contributors to our diet and have been proposed to reduce the incidence of chronic diseases such as cardiovascular diseases, cancer, cataracts, and neural tube defects. They are an excellent scavenger of reactive oxygen species and contribute to immune the human body against various disorders and pathogenesis. Despite the above-mentioned roles, carotenoids impart different colors to our food and play a remarkable role in anti-oxidation as well as the main participant of provitamin A activity. Increasing research evidence suggests that proper intake of carotenoids reduce the risk of cardiovascular diseases, cancer and also promote eye health. The current review discusses the recent developments in biosynthesis, availability of carotenoids in fruits and vegetables along with their role in human and plant health. They also play key essential functions in plants, starting from photosynthetic pigments to potent anti-oxidant and their importance in gene regulation at the cellular level. The importance of carotenoids to prevent chronic human ailments including cancer, cardiovascular disorders, and its significance related to human eyesight as well as its role in plants have been discussed.

1. Introduction

Carotenoids are a very diverse group of natural pigments such as orange, yellow and red in fruit and vegetables, synthesized by plants, algae and some groups of bacteria (Namitha and Negi, 2010). On the basis of the functional group, carotenoids can be classified into two groups. Carotenoids that contain oxygen as functional groups are known as xanthophylls (zeaxanthin and lutein), and the carotenes, which are hydrocarbons (lack functional groups) included β -carotene and lycopene. Polar groups including keto, epoxy and hydroxyl combination can alter biological functions of carotenoids (Britton, 2008). Photosynthetic, as well as, some non-photosynthetic organisms (some fungi and bacteria) can synthesize carotenoids, but the human body cannot synthesize and consume these pigments only through diet (Ruiz-Sola and Rodríguez-Concepción, 2012). In plants, carotenoids and its derivatives participate in many valuable biological functions such as photosynthesis, phytohormones biosynthesis, photo-protection, etc. Whereas, in the human body, carotenoids along with other bioactive compounds have been proposed to enhance the anti-inflammatory and

antioxidant activity, immune responses and promote human health by preventing various reactive oxygen species (ROS) mediated-chronic diseases (Fig. 1) (Bilal et al., 2017; Centella et al., 2017; Monego et al., 2017; Sosa-Hernández et al., 2018). In our diet, the principal source of carotenoids is vegetables and fruits, which are essential for intercellular communication, antioxidant, and immune system activity. Previous studies demonstrated that high consumption of carotenoid-rich sources could minimize the incidence of cardiovascular diseases (CVDs), cancer, cataract formation and reduce the risk of age-related muscular disorders (Sharoni et al., 2012; Meyers et al., 2014). On the other hand, deficiency of carotenoids leads to the clinical signs of corneal aberrations including night blindness, xerophthalmia, corneal ulceration, keratomalacia, scarring and irreversible blindness (Sommer, 2008). Moreover, insufficient consumption of dietary sources of provitamin A carotenoids is associated with weakened innate immunity, which leads to visual disability in human (Stephensen, 2001). Antioxidant carotenoids including lycopene reduces the risk of CVDs in human and protects the cellular system from ROS and reactive nitrogen species (RNS) (Sathasivam and Ki, 2018).

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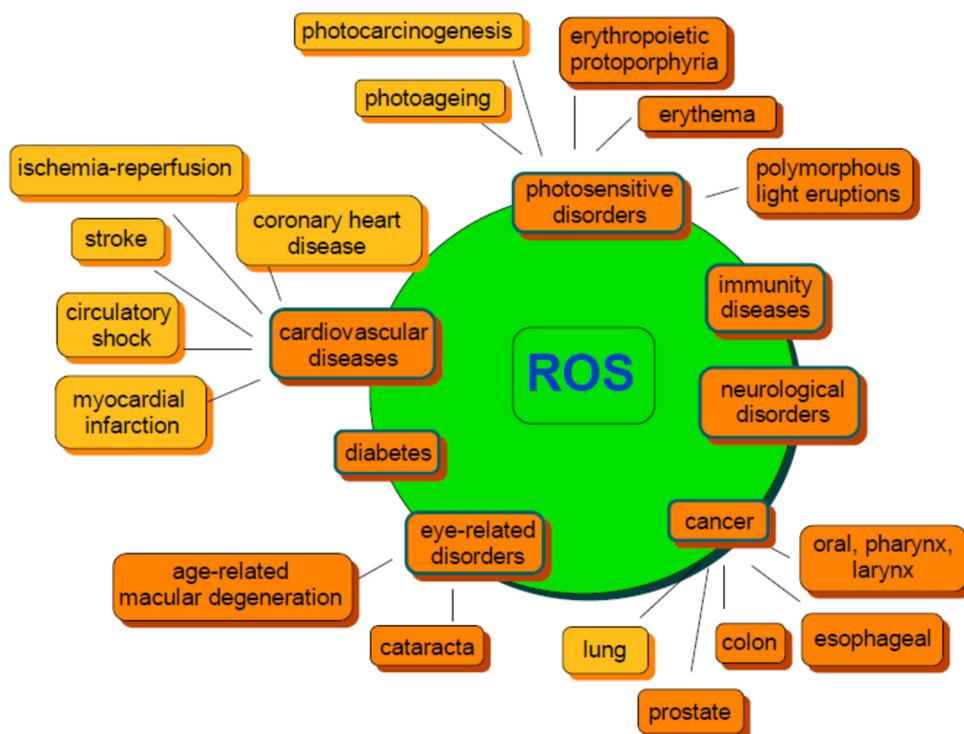


Fig. 1. Examples of ROS-mediated disorders. The orange color indicates the beneficial effect of carotenoids on disease risk development. The yellow color indicates that an equivocal effect was reported (Reproduced from Fiedor and Burdan, 2014), an open-access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).

Due to the versatile functions of carotenoids in feed, food, pharmaceutical industries, and cosmetics, strategies of carotenoids enhancement has been the focus of numerous studies. Recently, synthesis of carotenoids by plants and microorganisms at the molecular level as well as at biotechnological level has been revealed (Potrykus, 2001, 2003). The current review focuses on carotenoids biosynthesis, bioavailability, and role in the human body, as well as future research challenges in this context.

2. Food sources of carotenoids

In the diet, the primary sources of carotenoids are vegetables and fruits (Krinsky and Johnson, 2005; Carlsen et al., 2011). More than 50% of the total carotenoids reported in the human body are those that we consume in our diet (Fig. 2) (Khachik et al., 1997). Carotenoids availability can also be predicted from vegetables and fruits color such as orange-yellow vegetables and fruits are rich in α -carotene and the β -carotene. Orange, papaya, and mandarin are the rich sources of zeinoxanthin and α -Cryptoxanthin. Similarly, tomato and tomato products are enriched with lycopene pigment (red color). Green leafy vegetables (GLVs) are the rich sources of β -carotene (25–30%), lutein (nearly 45%), neoxanthin (10–15%) and violaxanthin (10–15%). But the exact concentration of each type of carotenoid differs among different vegetables (Lakshminarayana et al., 2005; Priyadarshani and Jansz, 2014). Yellow and orange vegetables are usually rich in β -carotene, whereas α -carotene is abundantly present in carrots. Other sources of α -carotene include dark green vegetables, such as spinach, broccoli, green beans, sweet potato, and pumpkin. Lutein and zeaxanthin are predominantly found in kale and spinach (Khoo et al., 2011).

For proper diet recommendation, the composition of carotenoids in different cultivars and part of plants will be useful for nutritional experts in this context. Although the main sources of carotenoids are well-known, other factors such as agriculture practices, seasonal variation, and food processing may affect the contents. Moreover, it has been reported that household cooking does not show any significant effect (Rao and Rao, 2007). Carotenoids composition of major vegetables and fruits are illustrated in Table 1. Recently, some underutilized vegetables have been proposed to be the rich source of carotenoids such as *Lactuca*

indica, *Moringa oleifera* and *Oenanthe javanica* (Andarwulan et al., 2012; Saini et al., 2014; Kongkachuichai et al., 2015). The leaves of *M. oleifera* contained the highest β -carotene (19.7 mg/100 g) among the most common leafy vegetables such as fenugreek, spinach, and amaranths (Bhaskarachary et al., 1995). Similarly, *M. pterygosperma* from Indonesia has been reported to contain β -carotene (14 mg/100 g) among the different underutilized vegetables (Andarwulan et al., 2012). Among the indigenous vegetables from Thailand, *L. indica* and *O. javanica* were documented to contain maximum contents of lutein and β -carotene (Kongkachuichai et al., 2015). Moringa leaves have advocated “tropics natural nutrition” by International non-governmental organizations (NGOs) such as Educational Concerns for Hunger Organization (ECHO) and Trees for Life.

Seed arils of achiote (*Bixa orellana*) and flower stigmas of saffron (*Crocus sativus*) are the most abundant sources of apocarotenoids (Rosati et al., 2009). However, paprika vegetables and citrus fruits also enriched with apocarotenoids. Apocarotenoids β -citaurin 2–7% has been reported in the pulp of citrus plants (Agócs et al., 2007). Similarly, 1.5% β -apocarotenoids has been recorded in *Cucumis melo* (Agócs et al., 2007). Gac fruit (*Momordica cochinchinensis*) arils and pulp were recognized as the richest sources of β -carotene (83.3 μ g/g fresh weight) and lycopene (408 μ g/g fresh weight), which are the major carotenoids (Agócs et al., 2007).

3. Carotenoids biosynthesis in plants

The carotenoids biosynthesis differs from species to species; however, all plants and photosynthetic algae share the common and primary metabolic pathway. Carotenoid biosynthesis in plants is associated with methylerythritol 4-phosphate (MEP) pathway, in which two molecules of geranylgeranyl diphosphate (GGPP) goes into condensation state and then changes into an intermediate 15-*cis*-phytoene in the presence of an enzyme called phytoene synthase (Fig. 3) (Cazzonelli and Pogson, 2010; Croteau et al., 2000; Gong and Bassi, 2016). The GGPE also serves as a precursor for other important metabolites like terpenes, tocopherols, gibberellins, ubiquinones, and chlorophylls. Four different sequential reactions are needed for 15-*Z*-phytoene to form lycopene by the action of two isomerases and two desaturases. Further,

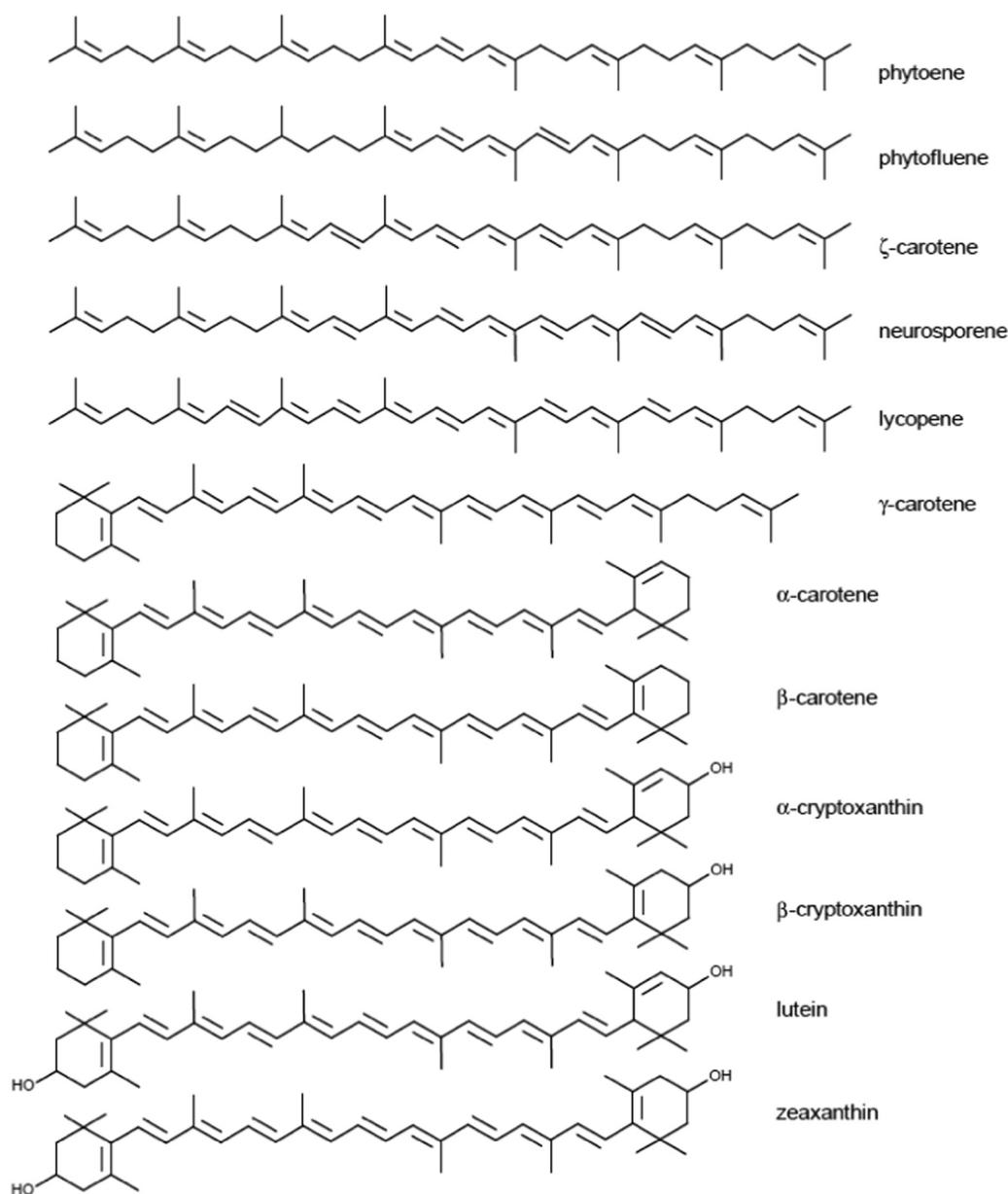


Fig. 2. Chemical structures of major carotenoids present in human plasma (Reproduced from Fiedor and Burda, 2014), an open-access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).

cyclization of lycopene with lycopene ϵ -cyclases (ϵ -LCY) and lycopene β -cyclases (β -LCY) to form δ -carotene and γ -carotene, respectively, is the critical branch-point in carotenoid biosynthesis. On one side, β -LCY enzyme adds a β -ionone ring to both ends of lycopene and origination of β -carotene takes place, while, on the other side for α -carotene formation β -LCY, as well as ϵ -LCY, adds one ϵ - and one β -ionone to lycopene which further leads to lutein (Send and Sundholm, 2007). Because of the unavailability of the β -ionone ring, lycopene has no provitamin A activity. In one branch, zeinoxanthin forms through the action of α -carotene upon β -ring hydroxylase, which further hydroxylated by a ϵ -ring hydroxylase to form lutein, while on the other branch, zeaxanthin can be produced by β -carotene hydroxylation in the presence of β -carotene hydroxylase enzymes. Zeaxanthin can also be further epoxidized into violaxanthin and antheraxanthin by the action of antheraxanthin epoxidase and zeaxanthin, respectively. Finally, violaxanthin can be further converted to neoxanthin by the action of another enzyme “neoxanthin synthase”. Some algae (*Haematococcus pluvialis*) and higher plants (*Adonis aestivalis*), can also accumulate ketocarotenoid

astaxanthin, which is mainly derived from the oxidation of zeaxanthin (Woods et al., 2011). *Capsicum annum* also accumulates two different types of keto-xanthophylls i.e. capsorubin and capsanthin, mainly account for the red color of *Capsicum* fruit. A single enzyme, called capsanthin-capsorubin (CCS) catalyzes and play a bi-functional role converting violaxanthin and antheraxanthin into capsorubin and capsanthin, respectively (Ariizumi et al., 2014). Phytoene, which is asymmetrical and colorless linear carotene, comprises three conjugated double bonds. The diversification in carotenoids is due to the chemical variations of phytoene, the first carotenoid molecule to be synthesized (Ajikumar et al., 2008). For α - and β -carotene structures, two different types of cyclization reactions are needed, while further transformations including epoxidation, glycosylation, hydroxylation, ketolation and oxygen cleavage may lead to diverse carotenoids family (Barredo, 2012). The chloroplast is speculated to be the site for carotenoids biosynthesis, associated with some specific steps in the cytoplasm and phytoene synthase (PSY) is the crucial enzyme for carotenoid biosynthesis (Mann et al., 2000). Different environmental stresses can up-

Table 1
Contents of major carotenoids in fruits and vegetables and their role in human health.

Carotenoids	Fruit sources	Vegetable sources	Bioactivities	References
Carotenes				
β -carotene	Apple, Banana, Peach, loquat, marolo, cherry Pineapple, red palm, apricot, Jambolão fruits (Brazil).	Broccoli, Brussels sprouts, Carrot, Cauliflower (var. White Rock), Chicory, Coriander leaves, Corn, Dandelion, Fenugreek, Lettuce, Pumpkin, Spinach, asparagus, beet greens, peas, cabbage, lettuce, okra Pumpkins (Cucurbita moschata Duch), amaranth, cowpea, sweet potato leaves, pumpkin, Carrot, Fenugreek, asparagus, beet greens, peas, lettuce, cabbage, okra Tomatoes, asparagus	Immunomodulatory effect, anticancer, positive effect on cardiovascular	(Bunea et al., 2012; Campbell and Padilla-Zakour, 2013; Delgado-Pelayo et al., 2014; Freitas et al., 2015; Lokesh et al., 2014; Maria et al., 2015; Pechinski and Kuregyan, 2014; Rodriguez-Amaya, 1999; Tanumihardjo, 2012)
α -Carotene	Banana, avocado, red palm Tangerines, peach, burti and apricot.		Anti-cancer, strong antioxidant, positive effect on blood composition	(Fraser and Bramley, 2004; Li et al., 2011; Lokesh et al., 2014; Murakoshi et al., 1992; Rodriguez-Amaya, 1999; Tanumihardjo, 2012)
Lycopene	Watermelon (Flesh), olive (Elaeagnus umbellata Thunb), red-fleshed papaya, guava, pitanga		Potent antioxidant. Anti-inflammatory, positive effect on prostate cancer, Enhance immune system	(Gajendragadkar et al., 2014; Gong et al., 2016; Martínez-Valdivieso et al., 2014; Mills et al., 2015; Stahl and Sies, 1996; Tanumihardjo, 2012)
Xanthophylls				
β -cryptoxanthin	Acerola (home garden, ripe), Apricot (var. hargrand), Jambolão fruits (Brazil), Peach (var. redhaven), Orange juice, Caja, nectarine, orange-fleshed papaya, pitanga	Broccoli, Brussels sprouts, Cauliflower (var. White Rock), Corn, Kale	Prevent lung cancer, improve the respiratory system and bone formation. Reduce cardiovascular diseases risk	(Aschoff et al., 2015; Kaulmann et al., 2014; Maria et al., 2015; Maurer et al., 2014; Mezzomo and Ferreira, 2016; Rodriguez-Amaya et al., 2008)
Lutein	Apple, Banana, Grapes, Jambolão fruits (Brazil), Mango, Papaya, Peach, Watermelon (Flesh), kiwi fruit	Broccoli, Brussels sprouts, Carrot, Cauliflower, Chicory, Dandelion, Drumstick leaves, fenugreek, Kale, Spinach, zucchini, squash, cabbage, lettuce	Prevent cardiovascular-related problems, eyesight, and age-related muscular disorders. Anti-tumor, anti-inflammatory, immunomodulatory, play a strong antioxidant role.	(Delgado-Pelayo et al., 2014; Fernández-García et al., 2016; Lokesh et al., 2014; Maria et al., 2015; Martínez-Valdivieso et al., 2014; Pechinski and Kuregyan, 2014; Rodriguez-Amaya et al., 2008; Sommerburg et al., 1998; Tanumihardjo, 2012)
Zeaxanthin	Apple, green (cv. green golden delicious, Apricot, Mango, Papaya, Peach, mamey, Pineapple, piquí, kiwi fruit, Grapes	Chicory, kale, lettuce, collard greens, cabbage, Dandelion, Drumstick leaves (cv. Bhagya), Fenugreek, Spinach, zucchini, corn, orange pepper, squash	Play Positive role in eye health (part of human eye Retina), has a stronger antioxidant activity promotes cardiovascular and respiratory system health.	(Guerin et al., 2003; Min and Min, 2014; Murillo et al., 2010; Rodriguez-Amaya, 1999; Sommerburg et al., 1998)

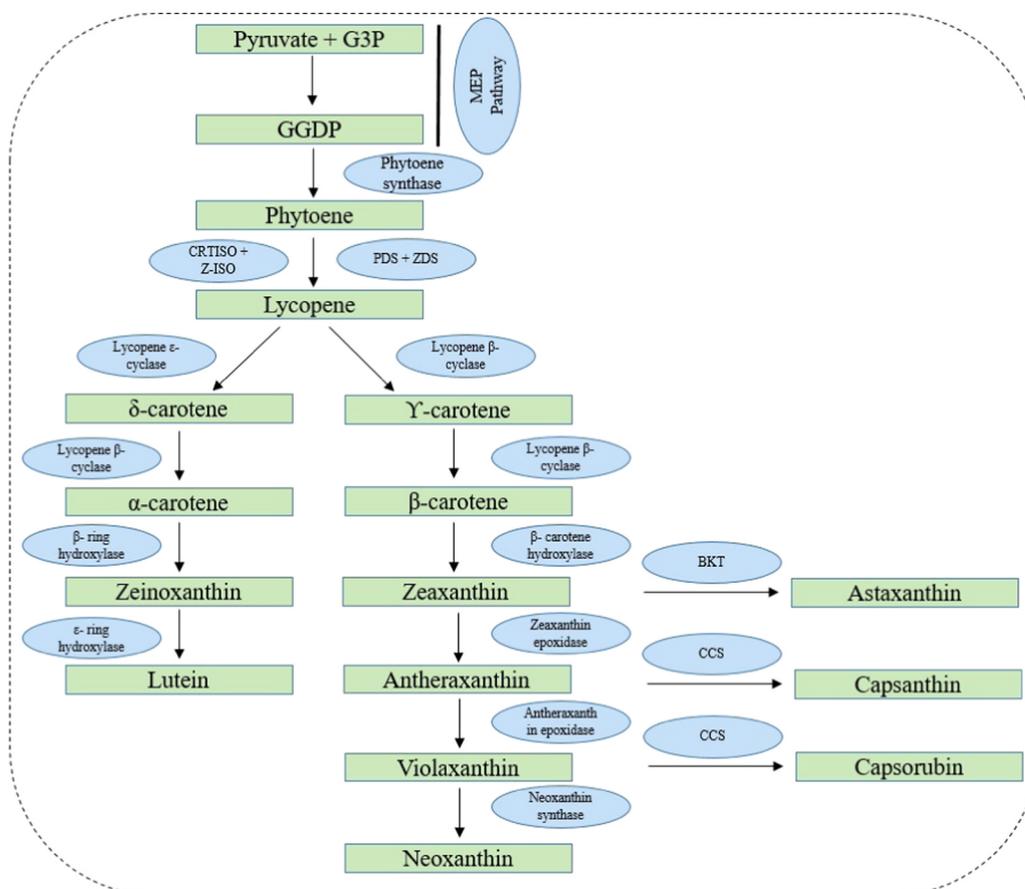


Fig. 3. Biosynthetic pathway of carotenoids in plants.

regulate the expression of *PSY* and other synthase genes (Nisar et al., 2015). The extension of the π -electron system is responsible for different colors of carotenoids and gives red, yellow and orange color to the plant tissues. For instance, lycopene and the β -carotene pigment are responsible for the typical color of a ripe tomato and orange color of carrots, respectively (McQuinn et al., 2015).

4. Role of carotenoids in human health

4.1. Carotenoids and cardiovascular disease

Cardiovascular disease is one of the significant and prime cause of death around the globe. Although in many countries, its mortality rate has been decreased but still, account for more than 40% of the total mortality (Menotti et al., 1999; Organization, 2005; Voutilainen et al., 2006). Approximately, more than 700 different types of carotenoids have been identified from various organisms including plants, animals, and microorganisms. Among the total carotenoid, only six carotenoids, i.e. α - and β -carotene, β -cryptoxanthin, zeaxanthin, lutein, and lycopene are the major constituents (95%) of human body total carotenoids (Table 1). A number of recent studies (especially preclinical and case-control studies) recommended that naturally occurring carotenoids have beneficial effects against CVDs presumably because of their antioxidant, anti-inflammatory, and antiproliferative properties (Palozza et al., 2010; Wang et al., 2014b). Carotenoids can play a central role in the reduction of risk of CVDs by reducing oxidative stress and low-density lipoprotein (LDL) oxidation at locations where plaque formations take place. A strong connection between high intake of different vegetables and fruits having a reasonable carotenoid content with less number of mortality rate caused by CVDs has been well established. Cohort studies, consists of serum carotenoid data along with food

frequency questionnaire have been done which revealed preventive effects of carotenoids against CVDs (Goyal et al., 2013; Krumholz et al., 2014; Tavani et al., 2006). Reductions in CVDs are mostly linked with the high intake of α - and β -carotene and also to some extent to β -cryptoxanthin (Touvier et al., 2005). It is reported that lifestyle including diet has a positive role to avoid CVDs (Perk et al., 2012). Various observational studies have been done regarding total carotenoid intake and CVDs outcomes and the association between CVDs risk factors, and carotenoid status has been confirmed (Krumholz et al., 2014). Carotenoids bioavailability may depend on various factors, but mainly their absorption is associated with bioavailability from food matrix as well as solubility in micelles (Boileau et al., 2002). Thus, carotenoids, especially β -carotene can play a significant role to reduce the risk of CVDs as they prevent oxidation of cholesterol in arteries, however, high doses of carotenoids may lead to pro-oxidant effect (Voutilainen et al., 2006; Martini et al., 2017). These beneficial effects of carotenoids on cardiovascular diseases can be attributed to its anti- and pro-oxidant activity. Nevertheless, still more data need to be collected to explain the detail mechanisms behind its protective function against cardiovascular diseases (Galasso et al., 2017).

4.2. Carotenoids—Role in eye health

Lutein, zeaxanthin, and meso-zeaxanthin are the major carotenoids responsible for macular pigment (MP) formation (Bergua, 2017). The yellow pigmentation (collectively called as MP) participates actively in photoprotection. Lutein and zeaxanthin are suggested to be consumed in 7:1 ratio usually, but their distribution in the human body is somewhat not reflective of this intake. In the blood serum, lutein concentration is approximately 10-times than that of zeaxanthin, but its accumulation in the macula decreases as twice of the total amount of

lutein present in the periphery of the retina, where zeaxanthin becomes predominant (Bone et al., 2007). It is hypothesized that MP performs two functions in the human eye: firstly, it acts as an optical filter to reduce the absorption of blue light, as a result, protect photoreceptor cells from light damage, secondly, acts as antioxidant to maintain cellular health by the neutralization of ROS (Aune et al., 2012). Zeaxanthin and lutein are the only carotenoids present in retina and lens, and antioxidant supplements could increase their intake. Many studies have been demonstrated to examine the response of the MP to increase zeaxanthin and lutein intake from different supplements (Kelly et al., 2017; Thurnham, 2007). As vertebrates cannot synthesize carotenoids, thus must be obtained in their diet to form their retinoids, like retinal, which is the main visual pigment (retinoic acid and retinol) (Lira et al., 2018; Sommer and Vyas, 2012). The fundamental precursor for retinoid is β -carotene which is also referred as provitamin A, to which two unsubstituted β -ionone rings are attached at both ends of the molecule (Grune et al., 2010; Shin et al., 2015). Deficiency of β -carotene in the human diet may cause night blindness and also keratomalacia and xerophthalmia and even total blindness (Hanson et al., 2017). Age-related Macular Degeneration (AMD) and cataract are two common age-related eye diseases in the world. It has been proposed that certain carotenoids can reduce the chances of cataract and macular degeneration probably by reducing the reactive oxygen species (Mohanty et al., 2002).

4.3. Carotenoids—Anticancer activities

It has been proposed that proper consumption of carotenoids in diet especially β -carotene and lycopene can reduce the incidence of cancer (Wan et al., 2014). The World Cancer Research Fund (WCRF) reported that increased carotenoids intake is directly or indirectly associated with reduced cancer risk. The report also summarized different evidence for foods having carotenoid contents at different sites. For aerodigestive tract cancers, i.e. (mouth, larynx, pharynx and lung cancer), evidence was rated as perhaps that food supplemented with high carotenoids content may play a protective role against cancer at these sites. Foodstuffs containing β -carotene were considered to have a protective role against oesophageal cancer, while such kind of association was unlikely for non-melanoma skin cancer and prostate cancer (Norat et al., 2014; Turati et al., 2015). Experimental studies suggested that carotenoids have not only the capability to inhibit tumor progression but they also reduce proliferation in estrogen receptor negative (ER⁻) as well as estrogen-receptor-positive (ER⁺) breast cancer cells (Eliassen et al., 2012; Prakash et al., 2001). Several mechanisms have been proposed for carotenoids to hinder carcinogenesis. β -carotene, α -carotene and β -Cryptoxanthin may reduce the incidence of cancer indirectly by their metabolism to retinol, which regulate cell growth and differentiation (Fisher et al., 2015; Simeone and Tari, 2004). By a number of different mechanisms, carotenoids may also act as direct anticarcinogenic agents, for example, enhanced immune system functioning, improved gap-junction communication or scavenging ROS (Fornelli et al., 2007). Supplementation of lutein, lycopene, astaxanthin, β -carotene, α -carotene and β -cryptoxanthin suggest a reduction in the risk of breast and prostate cancer. Carotenoids metabolism can affect blood concentrations, which may lead their correlation to reduction with dietary intake (Aune et al., 2012; Wang et al., 2014a). Certain lymphomas risk can also be reduced by increased carotenoid intake and the protective effects vary between the sexes. They show the ability to modify the expression of transcription factors and/or proteins involved in the apoptotic pathway and can stimulate apoptosis in tumor cells. Several mechanisms were suggested to cause the anticancer properties of carotenoids such as antioxidant activities (Ito et al., 2005; Abar et al., 2016; Monego et al., 2017).

4.4. Carotenoids role in plants

Being an essential structural component of photosynthetic machinery, carotenoids not only protecting the cells from oxidative damage, but also play a significant ecological role in attracting seed dispersers and pollinators due to imparting various colors to flowers, fruits, and leaves. Some important carotenoids such as violaxanthin and neoxanthin act as precursors for the biosynthesis of essential plant hormones. Strigolactone and abscisic acid (ABA) influence different processes such as regulation of seed dormancy, germination, maturation, morphogenesis, interaction with other hormones, root hair formation and plant adaptation with the environment (Matusova et al., 2005; Jia et al., 2017). ABA also mediates responses to different environmental stresses. For example, control the stomatal aperture as well as transpiration rate during drought stress (Chinnusamy et al., 2008). Blumenol and mycorradicin which are carotenoid-derived signaling molecules of C¹³ cyclohexenone derivatives and C¹⁴ apocarotenoids, respectively, have a crucial role in the symbiotic relationship with arbuscular mycorrhiza (AM) in the rhizosphere (Walter and Strack, 2011). The 3-hydroxy β -ionone (C¹³), which is a volatile carotenoid derivative, plays an essential role in biotic interactions as allelochemicals and also acts as feeding deterrents for various herbivorous insects (Gruber et al., 2009; Havaux, 2014). Apart from this, carotenoids and their derivatives endow fruits and flowers with fragrance and also improve the characteristic flavor of different nutritional crops. In the endosperm tissue of certain food crops, carotenoids give nutritional value and also play essential roles in photoprotection against heat stress and photo-oxidative damage via free radical detoxification and energy dissipation (Harjes et al., 2008; Havaux, 2014). Protecting cell organelles and their membranes from lipid peroxidation, UV, high temperature and ROS, carotenoid antioxidants increase light and heat stress tolerance (Havaux, 2014; Wu et al., 2015). Plants having low zeaxanthin contents show high sensitivity to heat and light stress, as zeaxanthin has a role in protecting thylakoid membranes against oxidative damage. Carotenoids also have a role in photosystem assembly, where they harvest light in the blue region across a broader range where the sun rays irradiate maximally and transfer energy to chlorophyll (Song et al., 2016; Walter and Strack, 2011). Carotenoids are also surrounded with different complexes of protein pigments (proposed as trimeric complex, LHCI), which work with the assistance of violaxanthin, neoxanthin, and lutein to transmit the energy to the photosynthetic process in chlorophyll (Dall'Osto et al., 2010, 2014). Strigolactones has a central role in rhizosphere as signaling molecules (e.g., mycorradicin and blumenin) and inhibit branching, which regulates plant architecture above ground (Tsuchiya et al., 2015; Umehara et al., 2008). Carotenoids are responsible for the formation of prolamellar bodies in etiolated seedlings, which define etioplasts to accelerate photomorphogenesis on illumination (Tsuchiya et al., 2015; Umehara et al., 2008).

5. Final remarks

Given noteworthy reactive oxygen scavenging and singlet oxygen quenching ability, carotenoids have appealed huge researcher's interest as potentially defensive agents against ROS-mediated human and plant disorders. To date, interventional, epidemiological, and clinical trials-based a large body of data from experiments with lycopene, β -carotene, lutein, and zeaxanthin demonstrated that the appropriate intake of carotenoids sources like vegetables, fruits or their supplements might considerably reduce the risk of chronic diseases. Moreover, the beneficial role of carotenoids intake in preventing several types of cardiovascular disorders, carcinogenesis, and eye-related syndromes has also been proved. However, more comprehensive clinical studies are required to fully establish the relationship of carotenoids administration with reduced ROS-mediated-disorder, due to some inconsistent results in previous reports. Although, the knowledge about the biological role

of carotenoids in protection and prevention of different disease have been established and understood. Similarly, the antioxidant activity of carotenoids has been well studied, but the exact mechanism underlying cell cycle regulation, cell differentiation, and apoptosis are still under scientific scrutiny. Future aspects of research include their bioavailability, supplementation versus dietary intake, metabolism, and mechanism of action. Ongoing areas of research in this direction also include human clinical trials and subject selection, which will increase our understanding about the functions of carotenoids and will help us to develop alternative strategies for the treatment and prevention of chronic diseases.

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Conflicts of interests

The authors declare that they have no competing interests.

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