Chapter

Role of Carotenoids in Cardiovascular Disease

Arslan Ahmad, Sakhawat Riaz, Muhammad Shahzaib Nadeem, Umber Mubeen and Khadija Maham

Abstract

Carotenes are fat-soluble pigments found in a variety of foods, the majority of which are fruits and vegetables. They may have antioxidant biological properties due to their chemical makeup and relationship to cellular membranes. And over 700 carotenoids have been found, with—carotene, lutein, lycopene, and zeaxanthin is the most significant antioxidant food pigments. Their capacity to absorb lipid peroxides, reactive oxygen species (ROS) and nitrous oxide is likely linked to their anti-oxidative properties (NO). The daily requirements for carotenoids are also discussed in this chapter. Heart disease is still a prominent source of sickness and mortality in modern societies. Natural antioxidants contained in fruits and vegetables, such as lycopene, a-carotene, and B-carotene, may help prevent CVD by reducing oxidative stress, which is a major factor in the disease's progression. Numerous epidemiological studies have backed up the idea that antioxidants might be utilized to prevent and perhaps treat cardiovascular illnesses at a low cost. Supplements containing carotenoids are also available, and their effectiveness has been proven. This article provides an overview of carotenoids' chemistry, including uptake, transport, availability, metabolism, and antioxidant activity, including its involvement with disease prevention, notably cardiovascular disease.

Keywords: carotenoids, antioxidants, cardiovascular disease, free radicals, CVD prevention

1. Introduction

There are presently around 700 carotenoids known, although only about 50 of them are being digested by humans [1, 2]. Carotenoids are present in large concentrations in adipose tissue (80–80% of total), liver (8–12%), and muscles (2–3%) in healthy adults, but in fewer amounts in all other areas [3]. overall amount and levels of various carotenoids inside a person's bloodstream are mostly determined by their daily average diet. Carotenoids and polyenes are abundant in green leafy vegetables and various multicolored fruits [4]. The bulk of dietary carotenoids is digested by the stomach and enters the bloodstream in humans. People's blood contains B-carotene, a-carotene, cryptoxanthin, lycopene, and lutein [5]. Carotenoids circulate in the circulation alongside lipoproteins, notably LDL (low-density lipoprotein fraction) [6]. However, a large amount of ingested B-carotene and other provitamins. A carotenoid is transformed

to the retina, primarily in the gut wall, but also some proportion in the stomach and intestines [7]. In the human diet, fresh vegetables are currently the primary source of carotenoids [8–10]. Lutein might perform an important role in hypertension and symptoms of acute permeability in those with heart problems, high cholesterol, and/or hyperglycemia, according to a literature review and meta-analysis [11].

Carotenoids may be found in a variety of fruits and are also available as a nutritional supplement [12, 13]. Cardiovascular abnormalities have subsequently been a major source of worry across the world since they affect a large portion of the global population, and an elevated death rate has been reported in individuals aged 30 and above [14, 15]. Numerous researches have looked at carotenoids' possible cardioprotective and antioxidant capabilities [16, 17]. Individuals with cardiovascular disease may benefit from the anti-inflammatory properties of lutein, which may help to alleviate their symptoms [18]. ROS-induced reactive damage can arise in lipid peroxidation products, this may hasten the onset of atherosclerosis, the condition that causes heart attacks and ischemic strokes [19].

2. Chemistry of carotenoids and their dietary sources

Carotenoids can be found in a variety of foods, although the majority of carotenoids in the diet are derived from strongly colored vegetables, fruits, and juices.

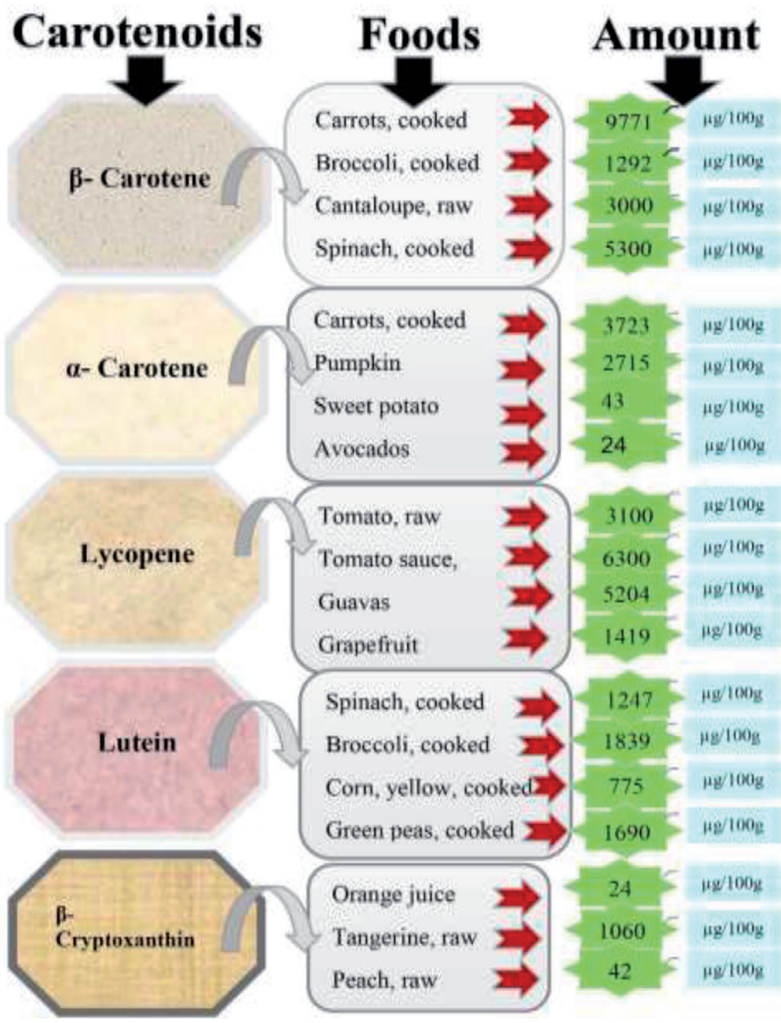

Figure 1.
United States donators of carotenoids rich foods and per capita.

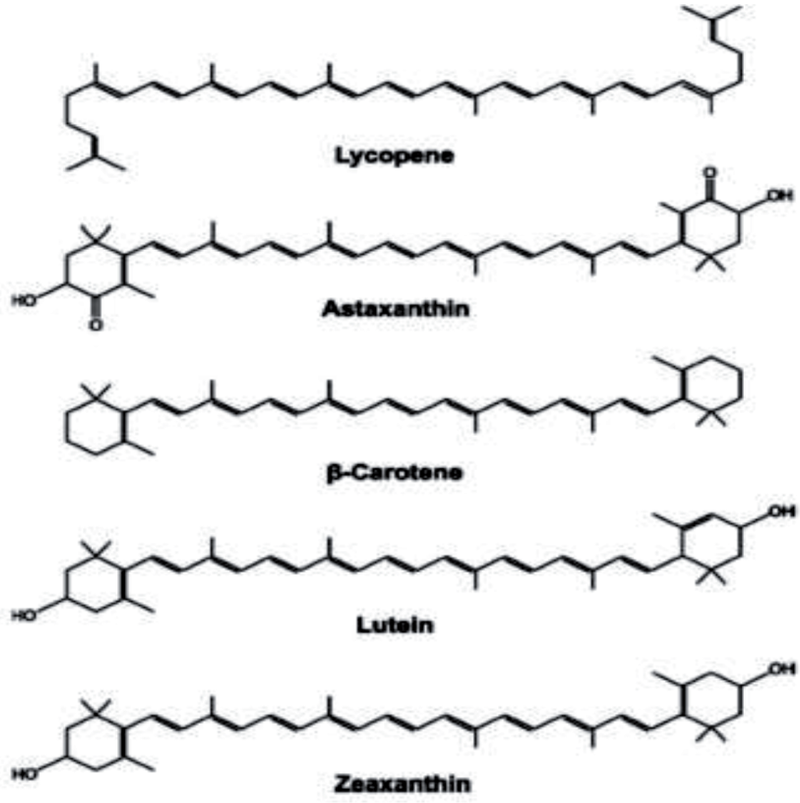

Figure 2.
Chemical structure of common carotenoids.

Carotenes supplied as food colorings to foods during the process, milk and dairy fat-containing meals, eggs, seafood, and carotenoids provided as food colorings to foods during handling can also supply trace amounts. The principal sources of carotenoids in the United States are shown in **Figure 1**. The data is derived from Median values using current HPLC procedures [20].

B-cryptoxanthin is present in orange fruits, lutein in green leafy vegetables, and lycopene in tomatoes and tomato derivatives, while B-carotene and a-carotene are both found in yellow-orange veggies and fruits. Multicomponent or mixed meals (e.g., soup, stew) generally contain a considerable proportion of carotenoid-rich foods, which is a practical element to address in dietary evaluation [21, 22]. Seasonality may be a key factor of the kind and amount of dietary carotenoids consumed in populations or cultural groups that consume fruits and vegetables in seasonal patterns [23, 24]. Most carotenoids have a polyisoprenoid structure, which means they have a lengthy connected network with the double bonds and are essentially bilaterally symmetrical around the central doubled bond [25]. Multiple carotenoids are generated by cyclizing the end groups and adding oxygen functionalities to the basic structure, which gives them their distinctive hues and antioxidant characteristics. The structure of several carotenoids is shown in **Figure 2**.

3. Carotenoids and cardiovascular health

3.1 Lycopene

The most frequent pigment present in human blood is lycopene. That's just a non-cyclic-carotene analog with 11 linked doubled bonds and two distinct doubling

bonds arranged in a linear arrangement [25]. This natural pigment is produced by bacteria and plants. Tomatoes are one of the most potent antioxidants, having a respiration activity that is greater than the total beta-carotene and 10 twice that of -tocopherol [26]. This is owing to the high quantity of linked diamines in the product. The adrenals, testicles, liver, and sex organs all contain lycopene [27]. Unlike some other carotenoids, lycopene content in the blood and organs does not correspond well with the total fruit and veggies diet [28].

According to the oxidative hypothesis, preventing LDL from being damaged is the first stage in the production of fibrils and atherosclerosis plaques, which leads to its absorption by monocytes inside the artery wall and the formation of plaque [29]. Oxidative alterations include triglyceride destruction, phospholipid oxidation, and subsequent oxidation of Apolipoprotein B, in addition to unsaturated fatty acids [30].

3.2 Lycopene absorption

Lycopene can mainly be found in its all-trans stereoisomer"s natural form [31]. Lycopene is perhaps the most abundant pigment in blood serum, with a duration of 2–3 days [32].

Fragmentation of the lycopene-rich feed solution, cooking temperature, and the incorporation of lipids as well as other fat compounds, such as other carotenoids, all impact lycopene absorption from food components. Carotenoids, like other lipid-soluble medicines, are digested via a chylomicron-mediated process in the gastrointestinal system [33]. Humans absorb 10–30% of the lycopene they eat in their diet [34, 35]. Sauce, tomato puree, and tomato aqueous extracts capsules all absorb lycopene as well [34, 36]. Lycopene levels are greatest in the testicles, adrenals, prostate, chest, and liver in humans [37, 38]. Lycopene is metabolized and broken down in the tissues. Many oxidizing lycopene forms, as well as polarized intermediates, have recently been isolated and identified [39]. **Table 1** shows the lycopene content of several foods [37, 40]. According to studies, 10–30% of lycopene taken in the diet is absorbed in the body [41].

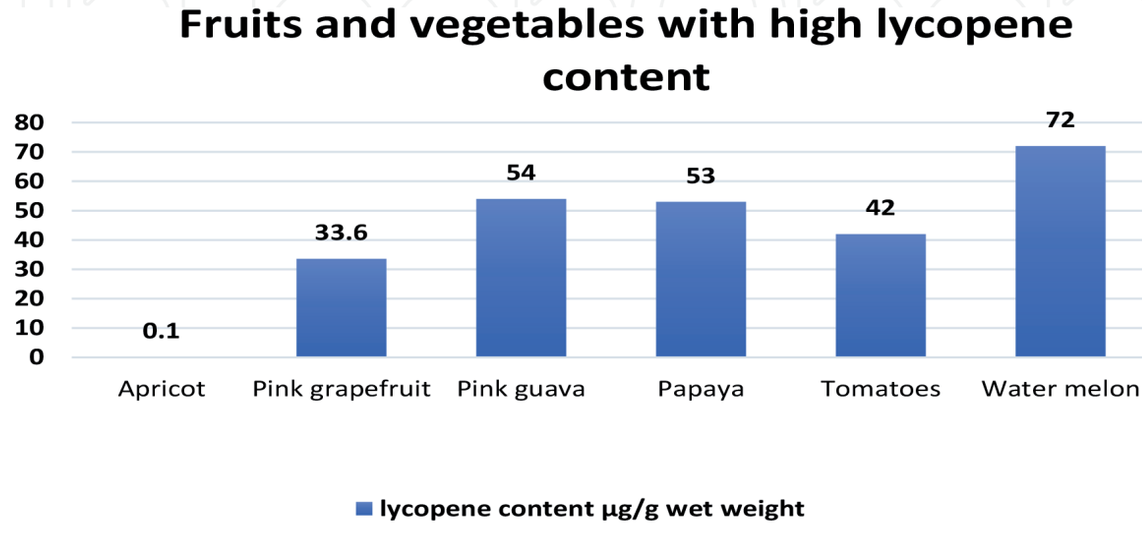

Table 1.
Fruits and vegetables with high lycopene content [37, 40].

3.3 Lycopene and CVD

A lower incidence of cardiovascular disease has been attributed to the Mediterranean diet. Tomatoes, tomato derivatives, lycopene, and other pigments are abundant [42, 43]. In 499 patients with CVD (Mayo cordial infection, strokes, CVD mortality, or revascularization therapies), increased plasma lycopene levels were linked to a decreased risk of cardiovascular disease in the Physicians' Health Study [44]. Lower blood lycopene levels were connected to an increased risk of death in a demographic study comparing Lithuanian and Swedish populations with different heart disease mortality rates [45]. Inflammation is considered to have a part in the development of atherosclerotic disease, which accounts for around 80% of all heart disease cases. In studies, high levels of cytokine production in blood plasma were associated with the onset of cardiac problems [46].

In a research of 139 sick people, oxygenated carotenoids (zeaxanthin, lutein, carotenoids, B-cryptoxanthin, a-carotene, and b-carotene) were found to be reduced in both patient groups (39 with acute illness, 50 with cardiovascular events, and 50 control participants) [47]. In a Japan inhabitants research of 3061 people, there was a link between high blood carotenoids (a-carotene, a-carotene, lycopene, total carotene levels) and a decreased hazard ratio for mortality risk [48]. Upon 60 days of tomato diet intake, a study of CHD (chronic heart disease) patients found a significant improvement in plasma key anti-oxidative enzymes (lipid oxidation rate, dismutase, glutathione peroxidase) compared with control, implying that or more elements of veggies could have medicinal beneficial health effects. In a 3-month study, six healthy guys were given 60 mg of lycopene each day. At the completion of the medication term, their plasma LDL cholesterol level had dropped by 14% [49]. For 1 week, 19 smoke-free healthy people (10 men, 9 women) received lycopene via normal tomatoes and nutraceuticals (20–150 mg/d) in a designed cross nutritional controlled trial [50]. The goal of Thiess and coworkers' randomized clinical experiment was to see how lycopene consumption affected the levels of cardiovascular risk indicators in healthy people. According to the data, taking 10 mg of lycopene every day for 12 weeks did not influence raised blood concentrations. The levels of Apolipoprotein A-I and Apoprotein B-100 were constant. Although the findings were not significant, both the diastolic (DBP) and systolic (SBP) blood pressures were reduced by 3.2 and 0.3 mmHg, respectively [51].

3.4 B-carotene

This group includes the xanthophyll compounds lutein and zeaxanthin. Macula lutea pigments are made from the macula lutea plant's natural dyes. Certain pigments seem to be essential for the physiological function of the eye. They protect against cataracts and macular degeneration caused by aging. These qualities are owed to their antioxidant properties first and foremost [52]. **Figure 1** shows that zeaxanthin has the same composition as lutein and is its derivative. From one of the final b-ion rings, the placement of a double bond changes between the two compounds: zeaxanthin is between C50 and C60, whereas lutein's is between C40 and C5. Leafy foods, along with colorful veggies, are high in lutein. Two of the most prevalent sources are spinach and greens. Lutein can also be present in egg yolks, thanks to the practice of feeding chickens plant-based foods. Corn and red peppers, for example, contain zeaxanthin [53, 54]. Xu and colleagues looked into the efficacy of lutein supplements here on activation of proinflammatory mediators and blood lipids in atherosclerotic

subjects. The levels of monocyte chemotaxis protein type 1 in the blood of several individuals who received lutein at a dosage of 20 mg/d for 3 months were decreased (MCP-1). LDL blood cholesterol values were also found to be lower in these individuals [55]. The China Coronary Finding provides evidence that lutein has a protective effect on atherosclerosis. Patients with early stages of atherosclerosis had lower blood lutein concentrations than healthy individuals, according to the study. Plasma lutein content is seen to be negatively linked to the thickness of carotid endothelial tissue (CIMT). The high amount of zeaxanthin in the blood was also shown to be inversely related to right main aorta stiffness and pulse velocity (PWV), both of which are markers of cardiovascular risk [56]. In the 39,876 women who were investigated, there was no link between serum lutein and zeaxanthin contents but also cardiovascular events [57].

3.5 Beta carotene absorption

β-Carotene is a strong fat-soluble nutraceutical that may be found in many fruits and vegetables. β-carotene converts to two molecules of vitamin A, resulting in a higher vitamin A supply [58, 59]. Cardiovascular, cancer, neurological, immunological, rheumatoid arthritis, cataracts, and aging have all been proven to be prevented by β-carotene [60–62]. The effectiveness of tagged β-carotene absorption varies greatly between clinical investigations, ranging from 3 to 80%, but quite often around 10 and 30% [63, 64]. It might be related to β-carotene's varied bioavailability, or it could be owing to the enterocyte's delayed absorption or transit. It's worth noting that the absorption of β-carotene was commonly evaluated after a little meal. In humans, though, our stomach may retain β-carotene from the initial meal for eventual release during the subsequent period [65].

On the other hand, carotenoid binding vehicles may impact carotenoid absorption routes. Blended micelles were most likely separated from the majority of the bolus in the unstirred water of such a glycocalyx region before touching the boundary layer, whereupon carotenoid could be ingested passively or via a transporter-dependent method [66]. Phytofluene, β-carotene, and lutein accumulation are comparable to as well as much bigger than phytoene ingestion in differentiated Caco-2 cell monolayers, albeit lycopene ingestion was the lowest [67, 68]. Uptake efficiency appears to be linked to carotenoid polarity and flexibility in the same manner as bioavailability is. This might be because hydrophilic, pliable pigments have such a stronger attraction for lipids carriers and plasma membrane, resulting in more absorption. According to an IOM report from 2001 [69], the Supplemental and dietary β-carotene absorbing rate ranges from 5 to 26% (spinach) (raw carrots). β-carotene and lycopene are the most abundant carotenoids in human adipocytes, accounting for 20.2 and 18.5% of total carotenoids, respectively, with substantial inter-individual variability [70].

3.6 Beta-carotene and CVD

In a recent meta-analysis of all-cause mortality in 25,468 men and women, the relative risk (RR) for those with the highest vs. lowest blood beta-carotene levels was 0.69 (95% confidence interval: 0.59–0.80). (6137 deaths) [71]. According to the NHANES III study of 16,008 people, some in the top tertile of serum beta-carotene seemed to have a 25% lower risk of mortality (95% CI: 10–37%) than those in the lowest quintile (4225 deaths) [72]. Many investigations, along with a recent meta-analysis, suggest that circulating beta-carotene and overall mortality are negatively

correlated [73–75]. In contrast, a meta-analysis of observational studies found that supplementation with b-carotene raises the odds of cardiovascular mortality from a tiny proportion [76]. Increased nutritional consumption of a-carotene and b-carotene was linked to a reduced risk of CVD mortality in the Zutphen Elderly research [77]. High serum concentrations of a-carotene and b-carotene, lycopene, or carotenoids, according to Japanese population-based follow-up studies, can lower the risk of mortality rates [78, 79].

The development of cardiovascular disorders is undoubtedly aided by peroxidation and chronically low irritation in the cardiovascular system. This pathogenesis of CVD and coronary disease has been related to oxidatively damaged low-density lipoproteins. An injection of such a free radical source that promotes LDL oxidation into foam cells appears to cause thermogenesis. An injection of such a free radical source into foam cells that stimulates LDL oxidation appears to trigger thermogenesis. Antioxidants may prevent cholesterol levels from degradation, lowering the risk of cardiovascular diseases in humans. Because β-carotene and lycopene are mostly found in LDL, they have a significant role in preventing oxidation [80]. The addition of b-carotene to LDL in situ was already found to lower the oxidation sensitivity of LDL [81].

Carotenoids have antioxidant properties and promote lymphocyte proliferation, which would boost immunological activity. The modification of vascular NO bioavailability owing to carotenoids' lowering action is another intriguing technique for explaining how carotenoids assist prevent CVD. In a model of vascular inflammation, high beta-carotene concentrations are connected to a large rise in NO level or absorption, as seen by an increase in cGMP level. In endothelial cells, increased NO release resulted in the enzyme inhibition of NF-kB-dependent binding proteins [82]. Endothelial NO bioavailability is therefore thought to be important to endothelial function and overall vascular health. In a rat model of atherosclerosis, further study reveals that a 9-cis-beta-carotene-rich diet can protect heart disease by lowering non-HDL plasma cholesterol levels, inhibiting liver fibrosis growth and inflammation [83].

3.7 Astaxanthin absorption

Astaxanthin, or 3,3′-dihydroxy-, ′ β-carotene-4,4′-dione, is a red-orange marine carotenoid present inside a wide range of microorganisms and marine animals [61, 62]. Soft gels, capsules, lotions, energy beverages, oils, and extracts containing astaxanthin have already entered the market as nutritional supplements [84]. As for other liposome carotenoids, astaxanthin is considered to go through a complicated digesting and absorption process that includes liberation from food material, transport to a stomach organic phase, creation into micelles under solvation via pancreas hydrolases but also bile acids, transit through the villi, uptake by enterocytes, and inclusion into chylomicrons allowing transportation to the lymphatic vessels and bloodstream [58, 85]. The gastrointestinal system, particularly the duodenum, absorbs almost no carotenoids into enterocytes, and bioavailability refers to the fraction of the ingested dosage retained into micelles. [86].

However, because of its weak water solubility and corrosiveness, oral astaxanthin's bioavailability is restricted. The pharmacokinetics of astaxanthin in rats were dose-independent between 100 and 200 mg/kg. Oral astaxanthin intake in the gastrointestinal tract followed a flip-flop pattern, according to Choi et al. [87]. The structure of astaxanthin has a role in its bioavailability. In vitro and rat, experiments demonstrated that a single ingestion of 100 mg mixed isomers resulted in a greater plasma level of cis-astaxanthin, particularly the 13-cis isomer, than diet [88–90].

Osterlie et al. looked at the dispersion of astaxanthin in different lipid fragments and found that 36–64% plasma astaxanthin accumulated in chylomicron-containing very-low-density lipoproteins, with the rest distributed almost evenly between low-density lipoprotein 29% and high-density lipoprotein 24% [90].

3.8 Astaxanthin and CVD

Microalgae, plankton, krill, fish, and other seafood are all members of the xanthophyll family. Microalgae, plankton, krill, fish, and other seafood contain astaxanthin, a red soluble pigment. In the marine environment, it can be found in microalgae, plankton, krill, fish, and some other seafood. It's the pigment that gives salmon and crustaceans their characteristic colors [91]. Even though chronic damage is still a biomarker conducted in a range of diseases, astaxanthin has shown promise in the prevention and treatment of malignancies, inflammatory diseases, metabolic disease, kidney disease, nephropathy, spleen, and digestive diseases, neurodegenerative diseases, and even cardiovascular disease. According to Pashow et al., astaxanthin might help with myocardial injury, oxidation LDL, re-thrombosis following angioplasty, or other cardiac issues including fibrillation. Astaxanthin is a strong anti-oxidant and FR's remover, and a reactive oxygen species (ROS) and nitrogen-oxygen species (NOS) quencher (NOS) [92]. During an eight-week study, Park looked at the effects of astaxanthin supplementation (0, 2, and 8 mg per day) on oxidative stress. People taking 2 mg a day for 8 weeks had a decreased hs-CRP, a primary predictor of heart disease. After 4 weeks of therapy, DNA damage as determined by serum 8-hydroxy-2?-deoxyguanosine was also reduced [93].

3.9 Lutein and zeaxanthin carotene absorption

The xanthophyll pigment astaxanthin (AST) is present in a variety of marine animals and microalgae [28]. Anti-inflammatory and antioxidant capabilities, as well as the ability to improve cardiovascular and immune system health, as well as prevent diabetes and neurological illnesses, are all found in AST [94–98]. In green foods, the lutein-to-zeaxanthin ratio ranges from 12 to 63, with kale having the highest concentration, whereas the ratio in yellow-orange fruits and vegetables is between 0.1 and 1.4 [99]. Dark green algae, that are consumed by fish, are rich in astaxanthin and fucoxanthin. Capsanthin is most commonly found within the pepper. β-Cryptoxanthin is a provitamin A that may be found inside a variety of vegetables, but it's especially abundant in corn, oranges, peaches, papaya, watermelon, and egg yolk. [100, 101].

Carotenoids should be digested then delivered into the blood to assert and provide their physical effects. Carotenoids seem to be either lipid-soluble or hydrophilic, indicating they are accessible in fats and immiscible, just like the human digestive tract. When compared to the hydrocarbon carotenoids (α-, β-carotene, and lycopene), lutein and zeaxanthin have hydroxyl groups and are thus polar molecules. To calculate the advantages, a thorough understanding of carotenoid release, absorption, transit, and storage in the eye is required. The quantity and type of dietary fat, that assists in the solvation of releasing carotenoids, and also phospholipids, soluble fiber, and indeed the nature of carotenoids, are all key determinants in lutein and zeaxanthin absorption from food [102–104]. Many phases are engaged in the intake of carotenoids released from food: (i) dispersion inside the stomach colloid so it can be integrated into fat droplets, (ii) followed by translocation to micelles holding bile salts, biliary phospholipids, dietary lipids, as well as other substances.

Food item	Lutein µg/g	Zeaxanthin µg/g
Parsley	64.0–106.5	64.0–106.5
Red pepper	2.5–85.1	5.9–13.5
Corn chips	61.1	92.5
Corn	21.9	10.3
High lutein bread	36.7	3.3
High lutein muffin	26.1	3.7
Durum wheat	5.4	0.5

Table 2.
Lutein and zeaxanthin sources [107–110].

The intestinal cell collects the dissolved carotenoids and distributes them into the blood. In vitro transfer of lutein, zeaxanthin, and β-cryptoxanthin from fruits (orange, kiwi, grapefruit, and sweet potato) was nearly 0%, compared to 19 and 38%, respectively, from spinach and broccoli [105]. The primary carotenoids detected in maize milling fractions are lutein and zeaxanthin, which account for nearly 70% of total carotenoids [106]. **Table 2** lists foods that are high in lutein and zeaxanthin [107–110].

3.10 Zeaxanthin and CVD

With a 40-carbon hydroxylated structure, zeaxanthin is just an oxygenation non-provitamin A carotenoid [111]. The macular lutea, a yellow-colored region of the retina that supports the central vision and includes lutein and zeaxanthin, is a yellow-colored section of the retina that contains lutein and zeaxanthin. Zeaxanthin may protect proteins, lipids, or DNA from oxidative stress via influencing various cellular antioxidant mechanisms, in addition to immediately reducing superoxide radicals. Glutathione is a potent antioxidant found within tissues that defends them from oxidation [112]. Taking supplements with zeaxanthin or a-tocopherol lowers metabolized glutathione (GSSG) levels while raising internalized reduced glutathione (GSH) levels and the GSH/GSSG ratio, particularly during redox balance. By regulating glutathione production and hence glutathione levels, zeaxanthin functions as an antioxidant, either directly or indirectly. As a result, the internal redox state improves in oxidative stress, and susceptibility to H_2O_2-induced cell death decreases [113].

Beta-carotene and zeaxanthin, which are inversely related to right main artery stiffness, pulse speed, and deformability, are implicated in both ocular and cardiovascular health. Both the Beijing and Los Angeles atherosclerosis studies discovered an opposite relation between serum lutein and initial CVD, although subsequent follow-up trials revealed that greater serum zeaxanthin concentrations may defend from early arteriosclerosis [114]. Zeaxanthin may help vascular health, according to these studies.

3.11 Lutein and CVD

With chemically similar formulas, it's an isomer of the carotenoid zeaxanthin. It, like zeaxanthin, is exclusively found in foods like yellow maize, egg yolk, orange juice, honeydew melon, and other fruits, and must be gotten by supplements or diet [113]. The ubiquitous nuclear transcription factor NF-kB, which is implicated in a range of

pathogenic reactions, is blocked by lutein [115], as well as the kB inhibitor's degradation (I-kB) [48]. It also has a significant potential to scavenge ROS [116, 117]. NF-kB can begin to migrate into the nucleus when I-kB is released from the NF-kB complex by lutein, reducing inducible transcription of genes and the activation of cytokines markers such cytokines, chemokines, and iNOS [118]. Lutein inhibits the production of TNF-alpha, interleukin 6 (IL-6), prostaglandin 2 (PGE-2), monocyte chemotactic protein 1 (MCP-1), and macrophage inflammatory protein 2 (MIP-2) [119].

According to this study, plasmatic lutein shows a negative correlation with oxidative stress, implying that it has significant oxidative and anti-inflammatory effects on aortic tissue, potentially preventing atherosclerotic [120]. Several studies have found that lutein levels in individuals with atherosclerosis were considerably lower than in normal and that they were indirectly correlated to arterial tightness [121]. The cardiac and blood vessel preventive actions of lutein have also been connected to the management of hypertension. A rise in systolic blood pressure and unintentional hypertension was often negatively proportional to a larger amount of this carotenoid. Some with greater lutein values had lower serum blood pressure but a decreased risk of future hypertension, independent of whether or not they smoke [122]. By lowering peroxidation and myocyte apoptosis, lutein prevents the myocardium from ischemia damage [123]. By avoiding contractile dysfunction, limiting myocardial damage may lower CAD morbidity and mortality [124].

3.12 Oxidative stress and antioxidants activity

The onset and evolution of a range of disorders, including cardiovascular issues, have been related to oxidative stress. ROS are important biological variables that can influence a wide range of physiological and disease-related conditions [125]. Cancer, reactive arthritis, osteoarthritis, aging, neurological, and cardiac illnesses are all connected to oxidative stress. Given the evidence linking oxidative stress to a wide range of human illnesses, measuring oxidative stress biomarkers is critical for assessing health and detecting the onset of oxidative stress-related disorders [126]. Hypercholesterolemia is also a disease that is closely connected to peroxidation. FH individuals reported greater levels of reactive oxygen species than normolipidemic patients, as per an inter observational study involving 132 individuals with high cholesterol (FH). MDA concentration seems to be much higher in FH, suggesting a higher oxidative stress state, according to the International Federation of Clinical Chemists (IFCC) standard range (>1.24 g/L) [127]. Various demographic studies have examined the association between higher nutritional carotene intake and thus the environment's effects on cardiovascular disease prevention [128–131].

Circulating carotenoid concentrations, for example, have been associated with inflammatory markers, increased lipid peroxidation, and vascular dysfunction, that has all been connected to CVD [132–134]. Secondly, pigments and minerals have a phytonutrient-like impact on endothelial dysfunction and irritation, decreasing the risk of atherosclerosis. [135]. The finding of a link between carotene, peroxidation, and inflammation has been aided by several in vitro studies, notably those that used subsystem [136]. Carotenoids exhibit anti-oxidant and anti-inflammatory properties in vascular cells, as shown in **Figure 3**.

Nitrogen oxide may combine with O^{2-} to generate peroxynitrite (ONOO-) under oxidative conditions, resulting in decreased NO bioavailability, vascular dysfunction, increased lipid oxidation, and chronic inflammatory responses. Nitrogen oxide may combine with oxygen to generate peroxynitrite (ONOO-) during oxidative

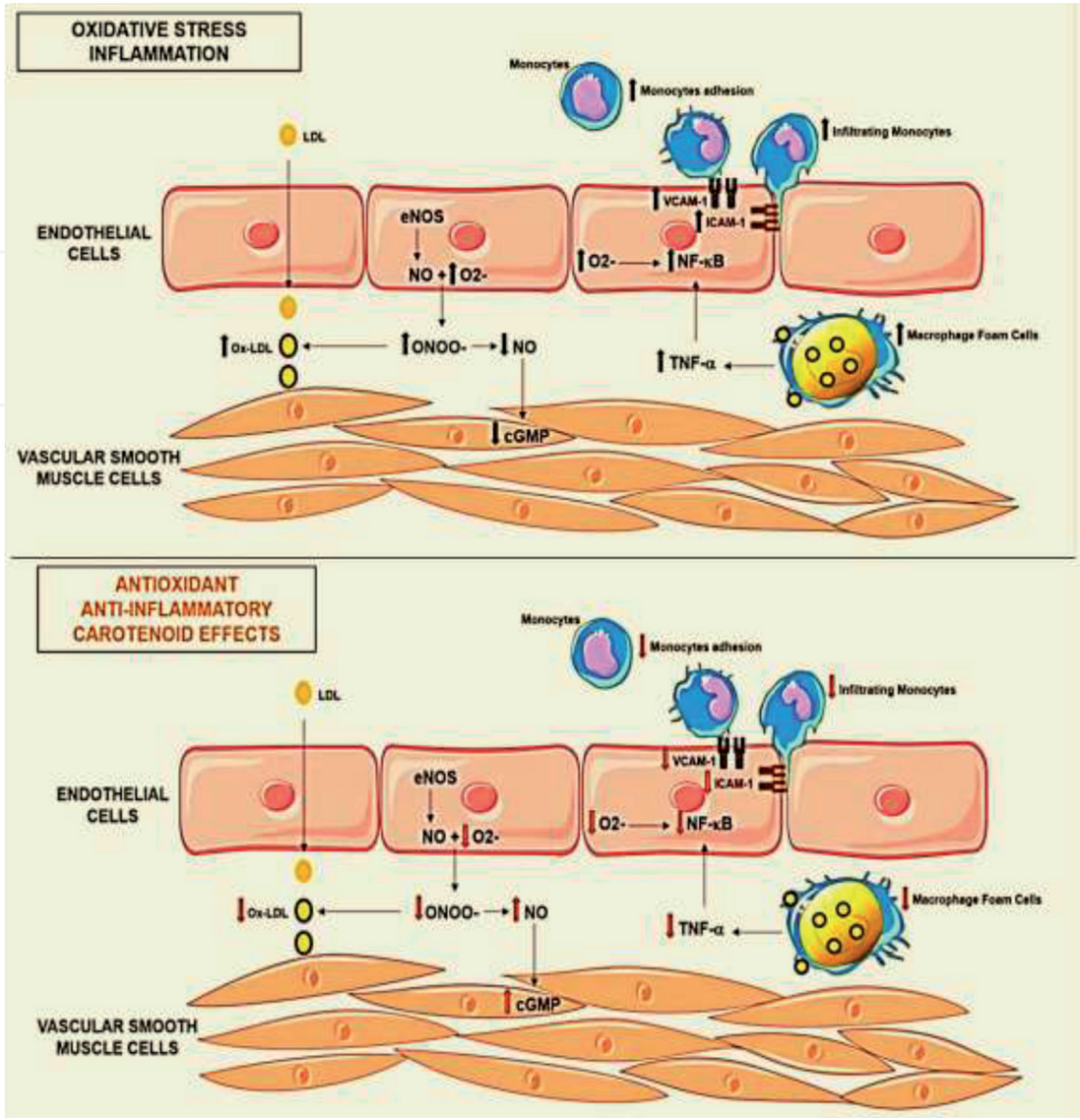

Figure 3.
Carotenoids have a beneficial effect on endothelial dysfunction and overall vascular health [137].

conditions, resulting in decreased NO bioavailability, vascular dysfunction, increased lipid oxidation, and chronic inflammatory responses. All of these actions create a negative cycle, and the antioxidant and anti-inflammatory capabilities of carotenoids may be harmed as a result. TNF-, tumor necrotic lesions factor-alpha; NF-B, nuclear factor kappa-light-chain-enhancer of activated B cells; ICAM-1, intercellular adhesion molecule 1; VCAM-1, vascular cell adhesion molecule 1; TNF-, tumor necrosis factor-alpha; NF-B, nuclear factor kappa-light-chain-enhancer of activated B cells; ICAM-1, intercellular adhesion molecule 1; TNF-, tumor necrosis factor-alpha; NF-B, nuclear factor kappa-light-chain-enhancer of activated B cells; ICAM-1, intercellular adhesion molecule 1; eNOS, endothelial nitric oxide synthase; NO, nitric oxide; O_2-, superoxide anion; ONOO-, peroxynitrite; eNOS, endothelial nitric oxide synth cGM.

Antioxidants are chemicals that prevent or restrict oxidative damage by inhibiting the action of reactive oxygen species. Intrinsic antioxidant components present in body cells include chronic damage, catalase, and glutathione peroxidase. Antioxidants found in foods include vitamin C, vitamin C, polyphenols, and carotenoids [138]. To help avoid chronic diseases like cancer and cardiovascular disease, current dietary

guidelines recommend consuming more antioxidant-rich plant foods like fruits and vegetables [139].

3.13 ROS and RNS production by nitric oxide synthases

The conversion of L-arginine to L-citrulline and nitric oxide is catalyzed by nitric oxide synthases (NOS)., but they can create superoxide under uncoupling conditions:

NOS + L-arginine + O_2 + NADPH − → NO + citrulline + NADP+ NOS(Fe(II) heme) + O_2 − → NOS(Fe(III)heme) + O_2 •− [140].

Two NOS isoforms, neuronal NOS (NOS1) and endothelial NOS (eNOS, NOS3), are generated in cardiomyocytes constantly, whereas inducible NOS (NOS2) is lacking in the healthy heart but can be triggered by pro-oxidants [141]. It was discovered that hypertrophied myocytes had a higher amount of iNOS [142]. Because NOSs may produce both RNS and ROS, their effects on the cardiovascular system can be complex—they can enhance or reduce heart damage. Because nitric oxide is an EDRF (endothelium-derived relaxing factor), its effects must primarily benefit the heart. The diffusion-controlled interaction of nitric oxide with superoxide, on the other hand, produces the very reactive peroxynitrite. To avoid heart damage, the equilibrium of superoxide/nitric oxide must be maintained. During pathological changes in the heart, the interplay of major enzymatic ROS generators contributes to this balance. In dogs with pacing-induced heart failure, NO synthases and xanthine oxidase was shown to be important in the modulation of myocardial mechanical efficiency, and overexpression of XO relative to NOS contributed to mechanoenergetic uncoupling [143].

4. Conclusion

Fruits and vegetables are rich in carotenoids. Carotenoids have long been regarded to be beneficial to one's health. Nearly 700 carotenoids have been discovered. The most regularly referenced carotenoids in this chapter were a-carotene, b-carotene, lutein, lycopene, and zeaxanthin. Their absorption, transportation, needs, and chemistry were all discussed. Cardiovascular diseases are a significant public health issue. Carotenoids-rich meals may help to reduce the progression of coronary heart disease, according to the study reviewed in this chapter. Oxidative stress is responsible for a wide range of degenerative diseases, including cardiovascular issues. The pathogenesis of CVD is heavily influenced by oxidative stress. We looked at the significance of carotenoids in endothelial function and vascular health in general in this chapter. We also discussed how carotenoids may be obtained from a variety of fruits and vegetables. The etiology of atherosclerosis is aggravated by oxidative stress. Throughout this chapter, we looked at the significance of carotenoids in endothelial function and vascular health in general.

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Conflict of interest

There is no conflict of interest as declared by all authors.

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Author details

Arslan Ahmad[1*], Sakhawat Riaz[1], Muhammad Shahzaib Nadeem[1], Umber Mubeen[1] and Khadija Maham[2]

1 Department of Home Economics, Government College University Faisalabad, Faisalabad, Pakistan

2 Department of Nutritional Science, Government College University Faisalabad, Faisalabad, Pakistan

*Address all correspondence to: ahmadarslan784@gmail.com

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