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Carotenoids in Foods and their Effects on Human Health

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ABSTRACT

Carotenoids, responsible for the red, orange and yellow color in foods, consist a part of the pigment family that naturally present in vegetables and fruits. Six main carotenoids found in human blood serum and taken with the diet are β- and α-carotenes, lycopene, lutein, zeaxanthin, and β–cryptoxanthin. Many studies suggest that carotenoids have a positive effect on several diseases such as certain type of cancers, cardiovascular and ocular diseases, especially age related macular degeneration and cataract. The antioxidant properties of carotenoids may be responsible for their beneficial influence on human health. Human organisms are unable to synthesize carotenoids, therefore these compounds have to be supplied with the diet. Main carotenoid sources include carrots, green leafy vegetables, tomatoes, sweet potatoes, egg yolk and corn. In this study, carotenoids in foods and their effects on human health are reviewed.

Key Words: Carotenoids, α-Carotene, β-Carotene, Health

Gıdalardaki Karotenoidler ve İnsan Sağlığına Etkileri

ÖZET

Gıdalardaki kırmızı, turuncu ve sarı renklerden sorumlu olan karotenoidler, meyvelerde ve sebzelerde doğal olarak bulunan renk pigment ailesinin bir kısmını oluşturmaktadır. Diyetlerle alınan ve insan kanı serumunda bulunan temel 6 karotenoid şunlardır; β- ve α-karoten, likopen, lutein, zeaksantin ve β-kriptoksantin. Birçok çalışmada karotenoidlerin belirli kanser tipleri, kalp-damar, göz hastalıkları; özellikle de makula dejenerasyonu ve katarakt gibi hastalıklar üzerine olumlu etkilerinin olduğu ileri sürülmektedir. Karotenoidlerin antioksidan özelliklerinin de insan sağlığı üzerine yararlı etki sağladığı düşünülmektedir. İnsan organizması karotenoidleri sentezleyememekte, bu nedenle diyetlerle birlikte alınması gerekmektedir. Ana karotenoid kaynakları havuç, yeşil yapraklı sebzeler, domates, tatlı patates, yumurta ve mısırdır.

Anahtar Kelimeler: Karotenoidler, α-Karoten, β-Karoten, Sağlık

INTRODUCTION

The colour of food is perhaps the first attribute that consumers assess when determining the quality and appearance of a product, and therefore conditions its acceptability. In fruits and vegetables, colour is due mainly to three pigment families: chlorophylls, carotenoids and anthocyanins, which are responsible for green, red-yellow, and blue-violet colourations, respectively [1]. Neither chlorophylls nor carotenoids can be synthesized by animal tissues, though animal cells can chemically modify them for assimilation. Thus, these molecules must be obtained from food [2]. Carotenoid and chlorophyll molecules are also extracted and used as natural colorants and antioxidants [3-5] to restore the natural level of these molecules in food

products or to prepare fortified products [6]. Carotenoids which are C_{40} tetraterpenoids, are extremely widely distributed group of lipid-soluble pigments, found in all kinds of plants [7]. There are approximately 600 different carotenoids known to exist [8]. All natural sources of them are not present in our normal diet. It is estimated that we only have access to about 40 carotenoids that can be absorbed, metabolized, and/or used in our bodies. That number is reduced to 6 if we consider the carotenoid profile that is usually detected in human blood plasma [1].

Most of the carotenoids are composed of a central carbon chain of alternating single and double bonds and carry different cyclic or acyclic end groups. Their major biochemical functions are determined by the extended system of conjugated double bonds which is also responsible for their color [9].

Carotenoids are divided in two classes, carotenes containing only carbon and hydrogen atoms and oxocarotenoids (xanthophylls) which carry at least one oxygen atom β-Carotene, α-carotene, and lycopene are prominent members of the carotene group, whereas zeaxanthin, lutein, α- and β-cryptoxanthins, canthaxanthin and astaxanthin are important xanthophylls [10]. Carotenoids are natural pigments contributing to yellow, orange [yellow and orange fruits and vegetables contain hydrocarbon carotenes with substantial levels of cryptoxanthins and xanthophylls] and red pigmentations to plant tissues [red fruits and vegetables contain mainly lycopene]. The green vegetables had high contents of both xanthophylls and hydrocarbon carotenes [11].

Carotenoids can also be divided into provitamin A and non provitamin A compounds [12, 13]. Provitamin A carotenoids are β-Carotene, α–carotene and cryptoxanthins, while non provitamin A carotenoids are lutein, zeaxanthin and lycopene.

Several reports have demonstrated that plant pigments play important roles in health [14,15]; in fact, the potential health benefit of a diet rich in carotenoids have been indicated in recent studies reporting their role as antioxidant, and as agents preventing cardiovascular diseases and degenerative eyes pathologies [16, 17]; apart from the provitamin A value of the carotenoids with a β-ionone ring, numerous studies have also shown the anticancer activity of β -carotene and other carotenoids [18].

CHEMICAL STRUCTURE of CAROTENOIDS

The basic structure of a carotenoid molecule is a symmetrical tetraterpene skeleton formed by tail-to tail linkages of two geranylgeranyl diphosphate molecules [C_{20} unit] [6]. The chemical structure clearly indicates that carotenoids are lipophilic compounds, and, therefore, water-insoluble, except when very strongly polar groups, such as polysaccharides, esterify the carotenoid backbone [19, 20]. Their structural characteristic is a conjugated double bond system, which influences their chemical, biochemical and physical properties [21]. Carotenoid structures contain multiple conjugated double bonds that are responsible for their ability to efficiently scavenge free radicals [and these serve as antioxidants] and to absorb light in the visible region. These absorptions cause them to reflect their respective colours. Differences in the number of double bonds result in carotenoids ranging from colourless (owing to an insufficient number of conjugated double bonds) so bright red [22]. This unsaturated structure also causes carotenoids to be labile to oxygen, light and heat [23].

DIETARY CAROTENOIDS in FOODS

Major dietary carotenoids include the hydrocarbons, β-carotene, α -carotene and lycopene and the xanthophylls, or oxygen-containing carotenoids, β-cryptoxanthin, lutein and zeaxanthin [24].

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 [25, 26]. It is a strongly-colored red-orange pigment abundant in plants and fruits. Major sources of dietary β-carotene include green leafy vegetables as well as orange and yellow fruits and vegetables [24] such as carrots, sweet potatoes, mangoes, pumpkin, kale, spinach, apricots, pepper, cantaloupe, lettuce, and tomato paste. Absorption of β-carotene is enhanced if eaten with fats, as carotenes are fat soluble.

Lycopene

Lycopene, like other carotenoids, is a natural pigment synthesized by plants and microorganisms to absorb light during photosynthesis and to protect them against photosensitization [27]. Lycopene is a bright red carotene and carotenoid pigment and phytochemical found in tomatoes and other red fruits and vegetables, such as red carrots, red bell peppers, watermelons, and papayas [but not strawberries or cherries] [28]. Although lycopene is chemically a carotene, it has no vitamin A activity [29].

Dietary lycopene is derived predominately from tomatoes and tomato products [24]. Similar to the effect on β–carotene bioavailability, heating tomatoes in oil was found to be associated with an increase in lycopene absorption when compared to the absorption for unprocessed tomato juice [30]. Also, the lycopene bioavailability was greater from a single dose of tomato paste than it was from an equal lycopene dose from fresh tomatoes [31].

Lutein and Zeaxanthin

Lutein is a major carotenoid that is present in dark green leafy vegetables such as spinach, kale and in various fruits [32]. Chemically, lutein differs from other carotenoids. It has two hydroxyl groups, one on each side of the molecule [33]. Zeaxanthin is one of the most common carotenoid alcohols found in nature. It is

important in the xanthophyll cycle. Synthesized in plants and some micro-organisms, it is the pigment that gives paprika [made from bell peppers], corn, saffron, wolfberries, and many other plants and microbes their characteristic color [34].

Lutein and zeaxanthin have identical chemical formulas and are isomers, but they are not stereoisomers. The only difference between them is in the location of the double bond in one of the end rings [35]. In terms of food sources, human metabolism, and tissue storage, lutein and zeaxanthin are similar [24].

Foods considered good sources of lutein and zeaxanthin include fortified eggs, spinach, goji berry [wolfberries], kale, turnip greens, collard greens, romaine lettuce, broccoli, zucchini, kiwifruit, corn, garden peas, Swiss chard, Brussels sprouts and olive [36]. Though the values are relatively low in eggs, recent data suggest that lutein and zeaxanthin from this food source are highly bioavailable [37-39].

EFFECT of COLOUR PIGMENTS on HEALTH

Carotenoid pigments, which are abundant in many fruits and vegetables, have been studied lot a number of years because of their diverse roles in photobiology, photochemistry and photomedicine [40]. Epidemiological evidence has suggested that dietary β -carotene [and more recently lycopene [41, 42] may inhibit certain types of cancer [43, 44]. As well as cancer prevention, the potential anti-oxidant properties of carotenoids may help to inhibit the onset of other diseases that are believed to be initiated by free radicals. These include atherosclerosis, cataracts, and age-related macular degeneration [40]. In the human body, oxidants produced during normal metabolism and immune defense against infectious and chemical agents are responsible for damage to DNA, proteins and cellular tissues [45, 46]. This harmful oxidative damage is considered the major cause of aging and degenerative diseases such as cancer, cardiovascular disease, immune-system decline and cataracts. Compounds such as ascorbate, a-tocopherol and carotenoids are examples of antioxidants that have the ability to quench reactive oxygen species [46]. The physical properties of carotenoid molecules, particularly the conjugated carbon–carbon double bond system, permit the quenching of O_2. In vivo antioxidant activity is determined by carotenoid structure and concentration, as well as the nature and concentration of the reactive oxygen species. The localization of carotenoid molecules in biological tissues will also influence their ability to encounter and scavenge free radicals. Indeed, carotenoids are one of the most potent biological quenchers of singlet oxygen [47].

Cancer Prevention

In vitro and animal studies provide evidence that carotenoids may protect against several kinds of cancer [48]. These studies are in line with epidemiological studies demonstrating that an increased consumption of a diet rich in carotenoids is associated with a diminished risk for different kinds of cancer. This association appears to be most consistent for lung and stomach cancer [49, 50]. There are several mechanisms by which a carotenoid can function in cancer prevention. As a provitamin A, a carotenoid would have an effect on cellular differentiation and poliferation [51-53]. Moreover, the antioxidant function could prevent free radical-induced damage to cellular DNA and other molecules [54]. Immunomodulatory effects could enhance immune surveillance in tumorigenesis [55] and enhanced cell–cell communication would restrict clonal expansion of initiated cells [56].

There is a correlation between β-carotene serum levels and a diminished cancer risk as shown e.g. for lung cancer. However, most intervention trials with β-carotene as a component of a supplement did not show any effects regarding the risk for cancer [57, 58]. One exception is a study performed in China where protective effects were observed [59]. A recent systematic review and meta-analysis found that high dose β-carotene supplementation [20-30 mg/day] is associated with an increased risk of lung cancer in smokers and asbestos workers [60]. High doses of β-carotene supplementation cause prooxidant effect and these are related to adverse effect observed [61, 62].However lower dose β-carotene supplementation and dietary β-carotene are more protective than detrimental to lung cancer development [63, 60].

The prostate is the most frequent site of cancer in males in the United States, estimated to account for almost one-third of all diagnosed cases in 2010 [64]. In 1995, the Health Professional Follow-up Study, a prospective male cohort in the United States, found that lycopene intake, as well as the consumption of the raw tomatoes, tomato sauces, and pizza, were all significantly associated with a decreased risk of prostate cancer [65]. For reasons of decreased risk are not still not understood, lycopene preferentially accumulates in the prostate [66]. The xanthophylls [oxycarotenoids] lutein and zeaxanthin, carry desirable health-related properties, blockade mammary tumor growth [67-69].

The first experiments, performed around 1980, to show a preventive effect for carotenoids on experimental carcinogenesis in animals used the model of skin carcinogenesis in mice, and showed that β-carotene or canthaxanthin, a xanthophyll that contains two oxo groups, could delay the onset of tumors, or decrease their incidence or their multiplicity [70, 71]. Subsequently, many studies performed on rats, mice or hamsters have shown that β- carotene, canthaxanthin or, more recently, other carotenoids [α-carotene, lycopene, astaxanthin, fucoxanthin] could delay or reduce the onset of UV-induced skin tumors, chemically induced tumors in various sites [skin, mammary glands, buccal pouch, salivary glands, respiratory tract, lung, stomach, colon, pancreas, urinary bladder, liver], transplanted skin tumors, and spontaneous mammary and liver tumors [70, 71]. In these experiments, carotenoids were in some cases administered topically [skin, buccal pouch] or injected intraperitoneally, but in most cases they were included in the diet or

administered by gavage, at varying and often very high doses, that is, several g/kg diet. However, very low doses have also been shown to be active [71].

Cardiovascular Disease

Reactive oxygen species [ROS] and oxidative damage to biomolecules have been postulated to be involved in the causation and progression of several chronic diseases, including cancer and cardiovascular diseases, the two major causes of morbidity and mortality in Western world [11]. There is extensive evidence that oxidatively modified low-density lipoproteins [LDL] are involved in the initiation and promotion of atherosclerosis [72]. Cigarette smoking is a well-known risk factor for coronary atherosclerosis [73]. Atherogenesis may be due to foam cell production by the introduction of a source of free radicals that cause LDL oxidation [74]. Thus, protection from LDL oxidation by antioxidants may lead to protection against human coronary heart disease [11].

The antioxidant effect of carotenoids in LDL has been suggested to be the biological link between higher levels of dietary carotenoids and reduced risk for cardiovascular disease [75]. Carotenoids can reduce the risk of cardiovascular disease through reductions in low-density lipoprotein oxidation and oxidative stress at locations of plaque formations. Recent studies have established a link between increased intake of fruits and vegetables that are high in carotenoids with reduced incidences of mortality related to cardiovascular disease. Cohort studies involving a food frequency questionnaire and serum carotenoid data have established the preventative effects of dietary carotenoids on cardiovascular diseases in separate studies of populations in Italy [76], Japan [77], Europe [78] and Costa Rica [79]. Cardiovascular disease reductions were mostly associated with increased intakes of α -carotene, β–carotene and β-cryptoxanthin [80].

Ocular Disease

Lutein and zeaxanthin are two of major carotenoids found in human blood serum; however they are the only carotenoids present in the retina and lens [81]. Lutein is concentrated in the primate retina, where together with zeaxanthin it forms the macular pigment [82]. In the retina, lutein and zeaxanthin are mainly responsible or the yellow pigmentation collectively referred to as macular pigment [83]. The yellow pigments are postulated to participate in photo protection, and diminished MP might be related to retinal damage [84, 85]. Traditionally lutein is characterized by its blue light filtering and anti-oxidant properties. Eliminating lutein from the diet of experimental animals results in early degenerative signs in the retina while patients with an acquired condition of macular pigment loss [Macular Telangiectasia] show serious visual handicap indicating the importance of macular pigment. Whether lutein intake reduces the risk of age related macular degeneration (AMD) or cataract formation is currently a strong matter of debate and abundant research is carried out to unravel the biological properties of the lutein molecule [82]. Studies indicate that a high intake of a variety of vegetables, providing a mixture of carotenoids, is more strongly associated with reduced eye disease risk than intake of individual carotenoid supplements [86].

Age Related Macular Degeneration

Age related macular degeneration [AMD] is a leading cause of irreversible and unavoidable blindness in Western countries and it affects approximately 20% of the population above the age of 65 [87]. In addition to aging, genetic background, and cigarette smoking, dietary factors also contribute to the onset and progression of AMD [88, 89].It has been reported that a high serum carotenoid level and high dietary intake of lutein are associated with a lower relative risk of AMD [90].

Lutein and zeaxanthin are concentrated in the retina at the macula lutea and are responsible for the yellow color that gives the macula its name [24]. Lutein has been thought to provide protection to the photoreceptors in the centre of the macula from photochemical damage [87, 91]. Lutein and zeaxanthin are thought to protect the eye in two ways. One hypothesis is that the macular pigment filters blue light, which is particularly damaging to photoreceptors and to the retinal pigment epithelium [92, 93], and lutein and zeaxanthin absorb blue light. The second hypothesis is that these carotenoids act as antioxidants to limit the oxidant stress of the tissue that results from metabolism and light [83, 92, 94]. It has been shown that one of the ways light damages the retina is by generation of free radicals that lead to peroxidation of membrane lipids [92, 93].

Cataract

Lutein and zeaxanthin are the only two carotenoids that have been in the human crystalline lens [95]. Like the antioxidant enzymes found within the lens, the lipid-based lutein and zeaxathin, are primarily found in the metabolically active epithelium/outer of the lens [96], and in the vitro studies have shown that lutein can inhibit UV-B induced lipid peroxidation of cultured human lens epithelial cells which was ascribed to its anti-oxidant and blue light filtering properties [97].Hankinson et al. [98] reported that the rate of cataract surgery was associated with lower intakes of lutein rich foods such as spinach and other green vegetables and observational studies support an association between lutein intake and a lower incidence and progression of cataracts [99, 100]. These studies suggest that dietary lutein and zeaxanthin play a role in cataract prevention [24].

Other Diseases

Ischemia-reperfusion [I/R] in the intestine is known to be caused by oxidative injury of the intestinal mucosa which is extremely sensitive to ROS [101]. Intestinal I/R is a common clinical problem in the high morbidity and mortality following the settings of severe burns, circulatory shock and strangulation ileus [102]. The

physiological importance of an orally administered lutein depends on its availability for absorption and, subsequently, its interaction with target tissues. Appropriate accumulation of lutein in tissues may lead to protective effects against oxidative injury [103].

The mechanisms whereby lutein affects the immune response may differ from its action on inflammation [104]. During inflammation lutein is thought to scavenge reactive oxygen species generated during the inflammatory process. β-Carotene supplements are widely used as a so-called oral sun protectants [105]. However, studies demonstrating the protection of oral treatment with h-carotene against skin responses to sun exposure are scarce. The protective effects are thought to be related to the antioxidant properties of the carotenoid [10]. Since the skin is continuously exposed to light, it is prone to the light induced damage, a fact that has created a great deal of interest focusing on the protective role of lutein as a blue light filter and antioxidant in these tissues [106]. Evidence for the influence of β–carotene on indices of human fertility is suggestive but minimal, resting on a few small controlled human studies [107]. β–carotene may influence thyroid hormone status [108,109] Numerous case reports have inked anorexia nervosa, thyroid status, and unusually high serum concentrations of beta carotene[109]. These case reports are supported by evidence from two small controlled beta carotene depletion studies [108]. The mechanism for relating β–carotene to thyroid hormone status is unknown.

CONCLUSION

Carotenoids are not only the color pigments in foods but also bioactive substances that have favorable impact on human health. The protective effects of the carotenoids are thought to due to the provitamin A activity and/or antioxidant functions. The epidemiological studies show that the high consumption of carotenoid rich fruit and vegetable is associated with the decreased risk for cancer, cardiovascular disease, and eye disease. There is an inverse correlation between the β–carotene intake and lung cancer, however in the high risk groups like the smokers and as best workers, it has been reported that high dose β–carotene supplementation is associated with the increased risk of lung cancer. Lycopene is regarded to be a protective compound for some types of cancer, especially prostate cancer. High serum levels of carotenoids such as α- and β-carotenes, and β-cryptoxanthin were found to be significantly correlated with low hazard proportion for cardiovascular disease. It has been observed that sufficient lutein and zaexanthin intake with the diet significantly reduces the risk of AMD and cataract.

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