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Review

Potential Health Benefits of β-Cryptoxanthin: A Narrative Review With Implications for Precision Nutrition

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Abstract

β-cryptoxanthin is a provitamin A xanthophyll carotenoid that is abundant in human circulation, despite being derived from a relatively limited range of dietary sources, primarily citrus fruits, which contain approximately 0.5–10.0 mg per 100 g fresh weight. Owing to the polarity and the frequent occurrence associated with β-cryptoxanthin as esterified forms in foods, β-cryptoxanthin exhibits relatively high bioaccessibility and bioavailability. This review aims to provide a comprehensive overview of the current evidence regarding the biochemical characteristics, dietary sources, determinants of absorption, and potential health effects of β-cryptoxanthin, with particular emphasis on bone health and several cancer outcomes. Among the health outcomes examined, the evidence is most consistent for a beneficial role in skeletal health. In contrast, associations with cancer are heterogeneous and appear to depend on cancer type and population characteristics; inverse associations have been reported primarily for cancers of the upper aerodigestive tract, whereas most studies show no association with overall cancer incidence or mortality. Nonetheless, further research is required to investigate whether β-cryptoxanthin can be incorporated into evidence-based precision nutrition approaches that account for interindividual variability in metabolism, lifestyle, and disease risk.

Keywords: β-cryptoxanthin; absorption; antioxidants; bone health; cancers

1. Introduction

β-Cryptoxanthin, a xanthophyll carotenoid, is one of the most prevalent carotenoids found in human serum and tissues. It is commonly found in a variety of fruits and vegetables, particularly citrus fruits such as tangerines and oranges, and some tropical fruits such as mango and papaya. The average daily intake of β-cryptoxanthin is estimated to be approximately 0.3 mg [1]. Structurally, it is characterized by a hydroxyl group at the C3 position of the β-carotene ring, which distinguishes it from other carotenoids. While β-cryptoxanthin is a minor component in many dietary sources compared to other carotenoids, its bioavailability is relatively high. Hence, it is the fourth most abundant carotenoid in human serum, especially in populations with high citrus fruit consumption, such as Japan, Spain and the United States [2,3,4,5,6].

β-Cryptoxanthin is a major dietary pro-vitamin A carotenoid and several studies suggest that its conversion to retinol can be comparable to that of β-carotene [7,8]. As a precursor to vitamin A, which is essential for immune function, vision, and cell growth, β-cryptoxanthin contributes to combating vitamin A deficiency, a condition that remains a significant public health issue worldwide. In addition to its role in vitamin A synthesis, β-cryptoxanthin has garnered increasing attention due to its antioxidant properties and potential therapeutic effects in preventing various chronic diseases [9,10,11]. It plays a crucial role in protecting cells and tissues from oxidative damage, and its antioxidant properties have been linked to the prevention of several chronic diseases, including diabetes, obesity, metabolic syndromes and non-alcoholic fatty liver disease. Besides, epidemiological evidence suggests an inverse relationship between β-cryptoxanthin consumption and the risk of osteoporosis and several cancers [12,13,14,15].

β-Cryptoxanthin has garnered increasing attention due to its potential health-promoting and therapeutic effects. Its biological efficacy is largely determined by its bioaccessibility and bioavailability, which appear to be superior to those of many other carotenoids [16]. However, the determinants of its absorption and metabolic fate including host genetic polymorphisms, dietary matrix, and interactions with other nutrients remain insufficiently reviewed. Moreover, while observational or randomized controlled trials suggest protective effects against osteoporosis and multiple cancers [12,17,18], the molecular mechanisms underlying these associations are not fully elucidated, and findings across populations are sometimes inconsistent. Importantly, despite its promising bioavailability and health benefits, β-cryptoxanthin has received comparatively less research attention than other carotenoids such as β-carotene,

lutein, and lycopene. In recent years, precision nutrition has emerged as a promising approach to address interindividual variability in dietary responses by integrating genetic, metabolic, and lifestyle factors. β-Cryptoxanthin is a particularly relevant candidate in this context because its absorption, metabolism, and tissue distribution vary substantially among individuals. Understanding how β-cryptoxanthin interacts with host-specific factors, such as genetic polymorphisms, and with population characteristics, including sex and disease status, may help explain its heterogeneous health effects and support its use in personalized dietary strategies. Therefore, this present review aims to provide a comprehensive overview of current knowledge on β-cryptoxanthin, covering its biochemical properties, dietary sources, absorption and potential health benefits, with particular emphasis on evidence from epidemiological and interventional studies evaluating its roles in bone health and cancers. By synthesizing the recent advances, this review underscores the diverse physiological functions of β-cryptoxanthin and highlights the directions for future research into its health-promoting potential.

2. Biochemistry and Dietary Source of β-Cryptoxanthin

β-Cryptoxanthin is a naturally occurring xanthophyll carotenoid that appears widely in human blood and tissues despite being present in relatively few dietary sources. Biochemically, it belongs to a class of oxygenated carotenoids and contains a single hydroxyl group. Like other carotenoids, β-cryptoxanthin possesses an extended chain of conjugated double bonds that allows it to effectively quench reactive oxygen species. It also contains a β-ionone ring, enabling its conversion to vitamin A through enzymatic cleavage. β-Cryptoxanthin predominantly occurs as the all-trans form in foods and human circulation. Isolated β-cryptoxanthin is chemically unstable, readily undergoing oxidative degradation or geometric isomerization from the all-trans to cis forms (e.g., 9-cis-, 13-cis-, and 15-cis-β-cryptoxanthin) when exposed to light, heat, or oxygen [16]. In plant tissues, however, it is commonly present in esterified forms typically linked to palmitic, myristic, stearic, oleic and linoleic acids, which enhances its stability [19]. In mature citrus fruit, β-cryptoxanthin is found primarily as ester forms, with only a minor portion (approximately 5% to 20%) present in its free forms [20]. The chemical structures of β-cryptoxanthin isomers and esters are present in Fig. 1. The esterified species undergo hydrolysis during digestion, allowing the free carotenoid to be incorporated into mixed micelles and absorbed in the small intestine. Evidence suggests that β-cryptoxanthin is absorbed and retains with relatively high efficiency compared with many other carotenoids [9]. After absorption, it is transported in circulating lipoproteins and distributed to various tissues, including the liver, adipose tissues, and skin.

Citrus fruits and juices are the primary sources of this carotenoid, with sweet oranges, mandarins, and tangerines being especially abundant [21]. It was found that several mandarin cultivars contain substantial levels of β-cryptoxanthin, ranging from 0.5 to 10 mg per 100 g of fresh weight [22]. Other foods with moderate to high β-cryptoxanthin levels include papaya, persimmon, mango, pumpkin, red pepper, and certain varieties of sweet corn. The concentration of β-cryptoxanthin in plant foods varies depending on cultivar, environmental conditions, degree of ripeness, and post-harvest handling [23,24]. Seasonal variation is also evident, especially in citrus fruits, where β-cryptoxanthin levels tend to peak during their ripening period in autumn and winter [25,26]. Although food processing can reduce the amount of β-cryptoxanthin and the extent of loss depends on temperature, oxygen exposure, and the duration of processing. In some cases, it may also increase the bioaccessibility of β-cryptoxanthin by disrupting cellular structures. Quantitative data on β-cryptoxanthin intake at the population level are limited as few large-scale surveys have focused specifically on β-cryptoxanthin. Nevertheless, available dietary studies indicate marked geographical variation. Countries with high citrus consumption typically exhibit higher β-cryptoxanthin intake and correspondingly elevated plasma concentrations, whereas intake tends to be considerably lower in low-income regions where access to carotenoid-rich fruits is limited [2,3].

3. Absorption and Metabolism of β-Cryptoxanthin

The absorption and metabolism of β-cryptoxanthin depend on specific physiological processes. Before intestinal absorption, β-cryptoxanthin is liberated from the food matrix during digestion. In the presence of dietary triacylglycerols, phospholipids, and bile acids, β-cryptoxanthin is then incorporated into mixed micelles in the intestinal lumen. Micellization enables β-cryptoxanthin to disperse in an aqueous medium and promotes efficient interaction with the apical membrane of intestinal epithelial cells. Subsequently, these micelles are taken up by the enterocytes through active transport or passive diffusion [27,28,29,30]. For carrier-dependent absorption, the uptake of β-cryptoxanthin is mediated by the specific epithelial transporters [27,29], such as scavenger receptor class B type I (SR-BI), cluster determinant 36 (CD36) and intestinal transcription factor (ISX) [16,31,]. However, at high pharmacological doses, the uptake of β-cryptoxanthin occurs via passive diffusion [3,3,9,16,]. Within enterocytes, a fraction of the absorbed β-cryptoxanthin is converted to vitamin A (retinol) [16,]. This process is mediated by two dioxygenases: a central cleavage enzyme (β-carotene 15,15′-oxygenase 1, BCO1) and an asymmetric cleavage enzyme (β carotene-9′,10′-oxygenase 2, BCO2) [32]. BCO1 cleaves β-cryptoxanthin centrally into retinal, whereas BCO2 cleaves β-cryptoxanthin asymmetri-

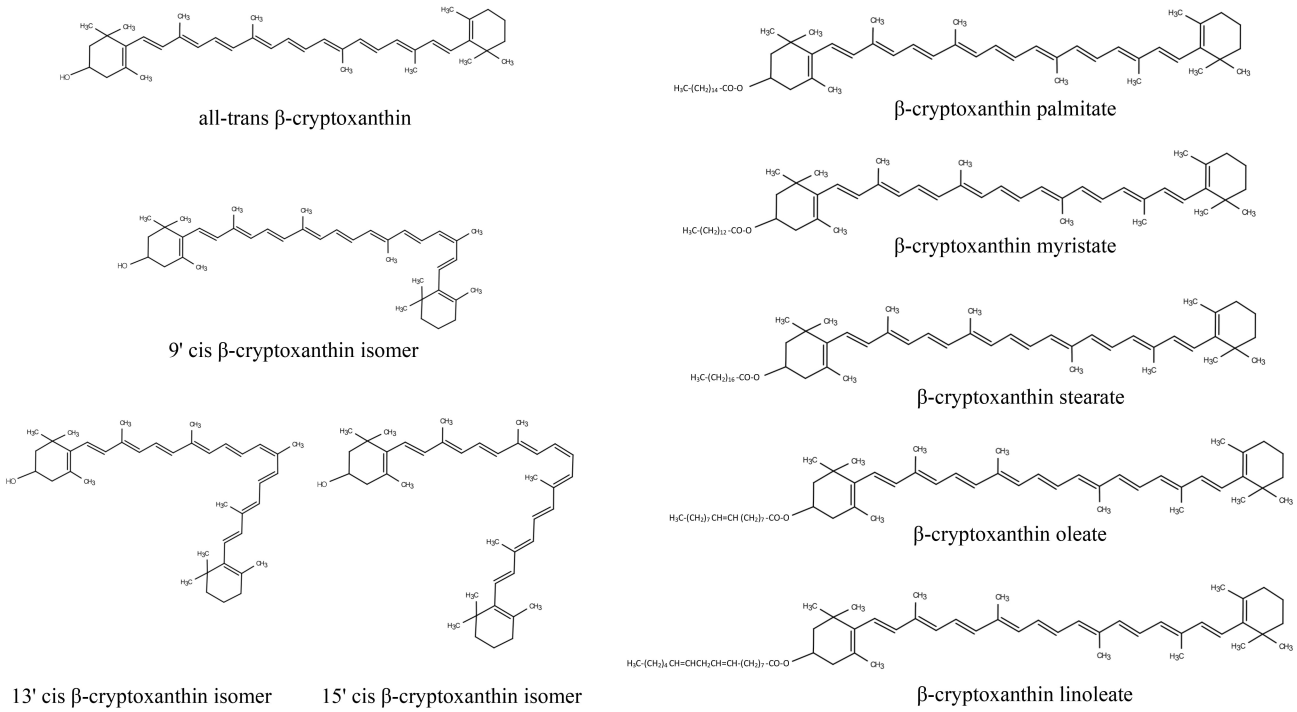

Fig. 1. Chemical structures of β-cryptoxanthin isomers and esters.

cally into apocarotenal, which is then cleaved into retinal and further hydrolyzed into retinol. The retinol is then converted into retinyl ester and assembled into chylomicrons, which are secreted into the lymphatic circulation [10]. After entering the bloodstream, β-cryptoxanthin is transported with lipoproteins to the liver for storage and metabolism or distributed to other tissues and organs (Fig. 2) [3,9,16,32]. One of the redistributed tissues is adipose tissue. Circulating carotenoids, carried by plasma lipoproteins, can be taken up by adipose tissue via receptors such as SR-BI and the low-density lipoprotein receptor. Afterwards, the carotenoids remain in adipocytes bound to the triglycerides in lipid droplets [33,34]. β-Cryptoxanthin is also found in the kidneys. In addition to lipoprotein-mediated uptake, megalin and cubilin are highly expressed in proximal tubule cells of the kidneys, where they play a role in the reabsorption of proteins and protein-bound molecules from the glomerular filtrate [35]. It is speculated that β-cryptoxanthin is redistributed to the kidneys via this pathway. Moreover, in a mouse model, following eight weeks of Satsuma mandarin extract consumption, detectable concentrations of β-cryptoxanthin were observed in the spleen and brain, with the highest levels in the liver, followed by the spleen, kidney, lung, heart, brain, and testis [36].

Although β-cryptoxanthin shares similar absorption and metabolism processes with other carotenoids (such as α-carotene, β-carotene, and lycopene), it has relatively higher bioavailability and bioaccessibility [16,37,38]. There are several reasons: (1) SR-BI preferentially promotes the absorption of β-cryptoxanthin [3,]; (2) β-Cryptoxanthin has higher polarity and can be more effectively dissolved in the lipid droplet [9]; (3) β-Cryptoxanthin exists on the outer surface of the micelles with higher hydrophilicity and solubility in the intestinal aqueous environment [9]. In addition, a study compared carotenoid plasma levels between the subjects with chronic cholestasis and the subjects who are generally healthy. The results showed that only the plasma level of β-cryptoxanthin was not lower than that of the control group [39], which may suggest that β-cryptoxanthin is less affected by specific diseases such as liver dysfunction and is more effectively absorbed and transported in comparison with other carotenoids.

There are several external and internal factors that influence the absorption and metabolism of β-cryptoxanthin. The first is food processing [3,]. Generally, mild and short-term cooking methods can improve its bioaccessibility by softening and breaking down cell walls, denaturing the proteins that are bound to the carotenoids, whereas harsh and long-term processing tends to isomerize and destroy carotenoids. An *in vitro* study investigating the bioaccessibility of carotenoids in raw, frozen and boiled red chili peppers revealed that the bioaccessibility of β-cryptoxanthin increased even after freezing or boiling [40]. Additionally, a study examined the effects of both high-pressure processing (HPP) and refrigerated storage on fruit smoothies [41]. They found the content of β-cryptoxanthin increased obviously at the beginning and then continue to decline. The rise in β-cryptoxanthin content likely stems from HPP's destruction of plant cell structures and dissociation of β-cryptoxanthin-protein complexes [42,43,44].

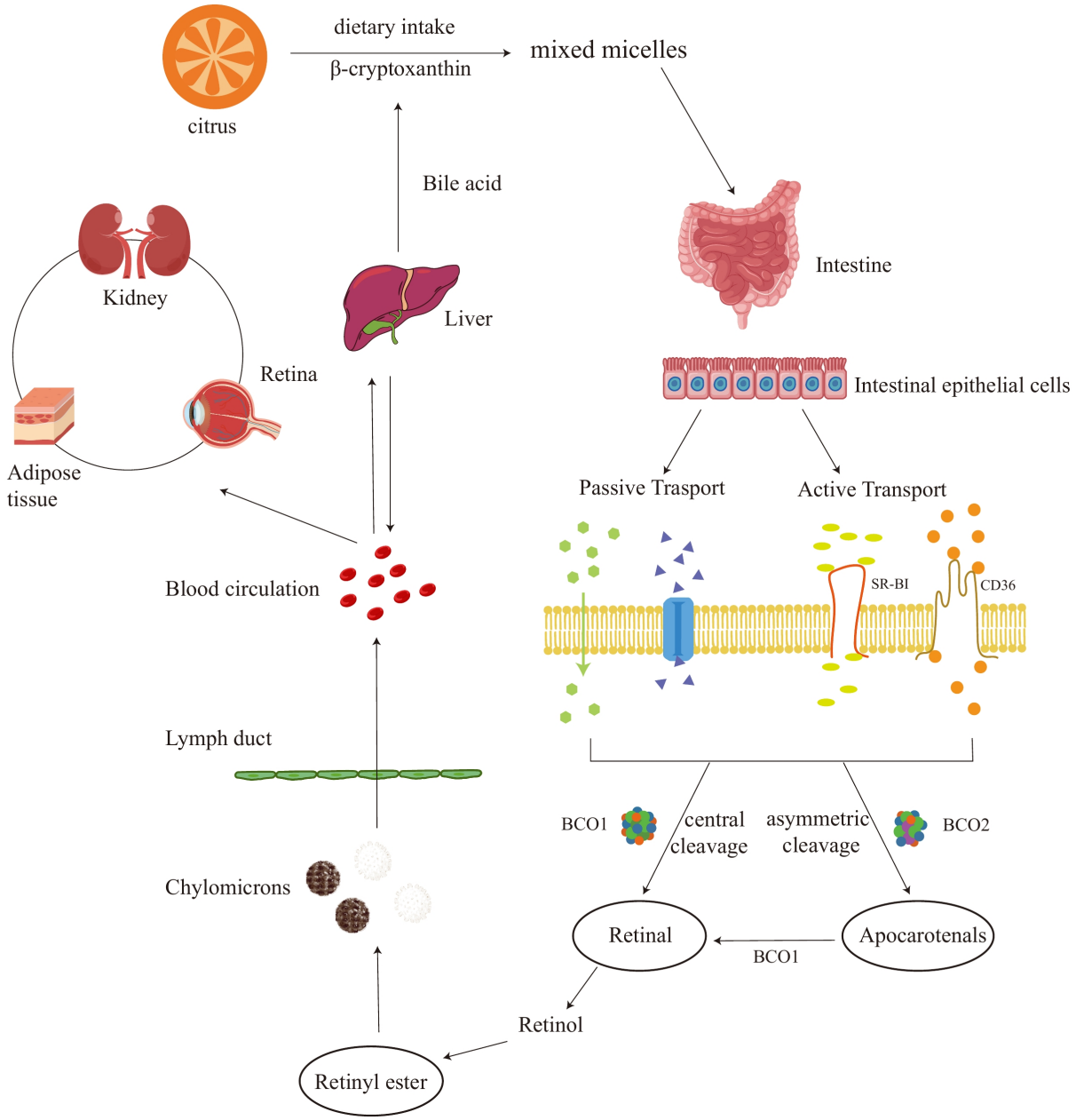

Fig. 2. Absorption and metabolism pathway of β-cryptoxanthin. Abbreviations: SR-BI, scavenger receptor class B type I; CD36, cluster determinant 36; BCO1, β-carotene 15,15′-oxygenase 1; BCO2, β carotene-9′,10′-oxygenase 2.

The decrease in content is mainly attributed to oxidation and isomerization during refrigerated storage [45,46]. Conversely, HPP alters the structure of the smoothie matrix, hindering the release of β-cryptoxanthin from the matrix and its micellization. The degradation of the smoothies matrix during storage enhances the release and micellization [43]. This explains why the bioaccessibility decreased first but gradually improved thereafter. In addition to processing, there are also other factors that affect the absorption and metabolism of β-cryptoxanthin. Iwata et al. [47] conducted an *in vivo* kinetic study of β-cryptoxanthin. When subjects co-consumed β-cryptoxanthin with fat-containing food, the absorption of β-cryptoxanthin was enhanced by 1.8 times, indicating that dietary fat can promote the absorption of β-cryptoxanthin. Dietary fiber may be another food component that affects the absorption of β-cryptoxanthin. Dietary fiber is capable of increasing the viscosity of intestinal contents, trapping bioactive components and inhibiting the activity of digestive enzymes. The release of β-cryptoxanthin from the food matrix becomes more difficult, accompanied by the decline of its micellization and bioaccessibility [41,48]. For internal factors, several aspects may be involved. As previously discussed, SR-BI enhances the uptake of β-cryptoxanthin by intestinal epithe-

lial cells [31], which means that variations in the gene encoding this protein can affect the levels of β-cryptoxanthin [49]. *SCARB1* is the gene that encodes SR-BI and single nucleotide polymorphism in this gene correlate significantly with the concentration of β-cryptoxanthin in human plasma [49,50]. It was observed that the plasma concentrations of β-cryptoxanthin were distinct among individuals with different alleles of SR-BI [50]. Some studies have shown potential interactions between carotenoids and intestinal microbiota even though we know little about this currently [51,52]. A study by Valdes et al. [53] demonstrated a significantly positive correlation between carotenoids and intestinal microbiota α-diversity (reflecting within-individual richness and evenness) and β-diversity (describing differences in microbial communities across individuals). Also, intestinal microbiota composition was reported to predict the circulating levels of carotenoids [53]. Since β-cryptoxanthin was included in this study's carotenoid analysis, the findings are applicable to the interaction between β-cryptoxanthin and the intestinal microbiota. These findings collectively highlight substantial interindividual variability in the absorption, metabolism, and tissue distribution of β-cryptoxanthin. Such variability, driven by genetic factors (e.g., SCARB1 polymorphisms), dietary composition, and gut microbiota, highlights the importance of β-cryptoxanthin in precision nutrition. Understanding these factors may help identify individuals who are more likely to benefit from β-cryptoxanthin-rich diets.

4. Potential Health Benefits of β-Cryptoxanthin

4.1 Improving the Bone Health

Age-related bone loss can lead to osteoporosis, which represents a major cause of morbidity and mortality in the elderly population, impairing both quality of life and life expectancy. Bone homeostasis is maintained by the balance between osteoblast-mediated bone formation and osteoclast-mediated bone resorption. Numerous studies suggest that β-cryptoxanthin can promote osteoblastic bone formation and inhibit bone resorption by osteoclasts. Hence, β-cryptoxanthin may prevent bone loss and has a unique effect on bone health [3,54,55,56].

4.1.1 Cellular Mechanisms

Existing studies have shown that β-cryptoxanthin can regulate the proliferation and differentiation of osteoblasts and osteoclasts at the cellular level. For osteoblasts, β-cryptoxanthin enhances transcriptional activity through signaling pathways such as protein kinase C or mitogen-activated protein kinase (MAPK). β-Cryptoxanthin also activates nuclear receptor pathways via retinoid X and retinoic acid receptors and upregulates transforming growth factor-β1 (TGF-β1) and insulin-like growth factor 1 (IGF-1) mRNA expression, thereby enhancing osteoblast and osteoprogenitor cell proliferation and differentiation and ultimately promoting bone formation [57]. In addition, emerging evidence suggests that β-cryptoxanthin may exert antioxidant effects through activation of the Keap1–Nrf2 signaling pathway, which enhances cellular antioxidant defenses and protects osteoblast function under oxidative stress conditions. For osteoclasts, β-cryptoxanthin inhibits the formation of inhibitor of nuclear factor kappa-B kinase (IKK) complexes, which prevents nuclear translocation. It also hinders receptor activator of nuclear factor-κB ligand (RANKL)–receptor activator of nuclear factor-κB (RANK) binding and downregulates the mRNA expression of cyclooxygenase-2 (COX-2) and microsomal prostaglandin E synthase-1 (mPGES-1). These actions reduce osteoclast formation, inhibit the differentiation of osteoclast precursors, and lower the number of mature osteoclasts. Notably, Nrf2 activation has also been reported to suppress osteoclastogenesis by attenuating oxidative stress and inhibiting RANKL-induced signaling pathways, suggesting an additional mechanism by which β-cryptoxanthin may inhibit bone resorption. In addition, in human periodontal ligament cells, β-cryptoxanthin can also reduce Interleukin-6 (IL-6) and Interleukin-8 (IL-8), and increase osteogenic growth peptide, further inhibiting excessive bone resorption [55]. In summary, these effects jointly improve bone health by promoting bone formation and inhibiting bone resorption. These proposed cellular mechanisms of β-cryptoxanthin in bone homeostasis are illustrated in Fig. 3.

4.1.2 Evidence From Preclinical Studies

In an *in vitro* experiment using rat femoral tissues, β-cryptoxanthin was found at 10^{-6} or 10^{-5} M range to suppress the bone resorption by increasing calcium content, alkaline phosphatase activity and deoxyribonucleic acid content. For instance, in the culture medium with a concentration of 10^{-6} M of β-cryptoxanthin added, the calcium content of the control group was 226.5 ± 5.3 mg/g dry bone, and the calcium content of the femoral diaphysis tissue was 272.2 ± 3.2 mg/g dry bone, $p < 0.01$ [58]. Another animal study showed that feeding rats β-cryptoxanthin at doses of 10, 25 or 50 μg per 100 grams of body weight could significantly increase the calcium content and alkaline phosphatase activity in the femoral diaphysis and epiphyseal tissues [59]. Researchers also observed similar effects of β-cryptoxanthin in other cell types. For instance, β-cryptoxanthin suppressed lipopolysaccharide (LPS)-induced osteoclast formation in bone marrow cell-osteoblast co-cultures [56]. In human periodontal ligament cells, β-cryptoxanthin increased the production of osteoprotegerin, a protein that prevents bone resorption by suppressing osteoclast formation. It also inhibited IL-6 and IL-8 production induced by mechanical stress and periodontopathogenic bacteria [60]. In a mouse periodontitis model, it inhibited mandibular alveolar bone resorption *in vitro* and reversed LPS-induced alveolar bone loss *in vivo*,

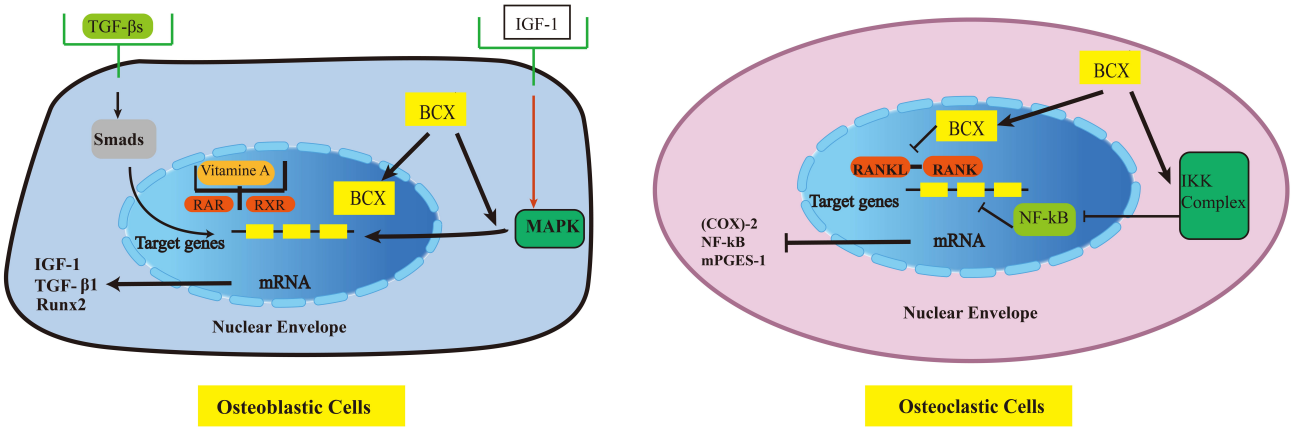

Fig. 3. The proposed roles of BCX in bone homeostasis. Abbreviations: BCX, β-cryptoxanthin; TGF-βs, transforming growth factor-βs; Smads, Smad proteins; IGF-1, insulin-like growth factor 1; TGF-β1, transforming growth factor-β1; MAPK, mitogen-activated protein kinase; RAR, retinoic acid receptor; RXR, retinoid X receptor; Runx2, Runt-related transcription factor 2; RANKL, receptor activator of nuclear factor-κB ligand; RANK, receptor activator of nuclear factor-κB; NF-κB, nuclear factor kappa-B; IKK, inhibitor of nuclear factor kappa-B kinase; COX-2, cyclooxygenase-2; mPGES-1, microsomal prostaglandin E synthase-1.

suggesting that β-cryptoxanthin may help prevent bone resorption in conditions like periodontitis.

4.1.3 Evidence From Human Studies

Regarding the impact of β-cryptoxanthin on bone health, researchers have conducted a series of clinical studies, including observational epidemiological studies and targeted intervention studies. The results of these studies have provided important evidence for the application of β-cryptoxanthin in supporting bone health. A previously published meta-analysis revealed that higher β-cryptoxanthin intake was associated with a significantly lower risk of osteoporosis (odds ratio [OR] = 0.79, 95% confidence interval [CI]: 0.70–0.90, $p = 0.0002$), and this effect remained statistically significant regardless of gender or ethnicity (i.e., Western vs. Asian populations) [61]. An observational epidemiological study, for the first time, verified a negative correlation between circulating β-cryptoxanthin levels and fracture risk, further providing biological support for its bone-protective effects [62]. A European population study using multiple regression analysis showed a positive association between dietary β-cryptoxanthin intake and broadband ultrasound attenuation, an indicator of bone mineral density ($p = 0.031$) [63]. From a broader population perspective, data from the National Health and Nutrition Examination Survey conducted from 2005 to 2018 showed that, regardless of gender, individuals in the highest quintile of β-cryptoxanthin intake had the lowest risk of osteoporosis (OR = 0.61; 95% CI: 0.39–0.97; $p = 0.037$) [12].

Regarding the impact of β-cryptoxanthin on bone health, in addition to epidemiological studies, several population-based intervention studies have also been conducted. A study involving 90 participants found that daily consumption of fruit juice containing β-cryptoxanthin (3.0 or 6.0 mg/day) for 28 or 56 days led to a significant increase in gamma-carboxylated osteocalcin concentration, compared with the pre-intake levels and those following placebo consumption. After 56 days of continuous consumption, the bone-specific alkaline phosphatase activity also increased significantly compared to the pre-intake levels [18]. Notably, the role of β-cryptoxanthin in bone health has also been explored in postmenopausal women. In a study involving 38 postmenopausal women, participants were administered 250 mL of a milk-based fruit beverage daily. The beverage was fortified with either β-cryptoxanthin (0.75 mg/day), phytosterols (1.5 g/day), or a combination of the two. The results revealed that only consumption of the beverage containing both β-cryptoxanthin and phytosterols led to a significant reduction in the levels of bone turnover markers, total cholesterol and low-density lipoprotein cholesterol [64]. This finding not only highlights the role of β-cryptoxanthin in maintaining bone health among postmenopausal women but also reveals the potential for synergistic effects when combined with other nutrients.

4.2 Prevention of Cancer

β-Cryptoxanthin has garnered considerable research interest because of its potential role in cancer etiology. Both its circulating levels and dietary intake have being investigated for their possible associations with carcinogenesis. However, epidemiological findings on this relationship remain inconsistent. This section summarizes the epidemiological evidence from prospective cohort and case-control studies examining the relationship between β-cryptoxanthin and a wide range of cancers, including those of the breast, gastrointestinal tract, respiratory system, genitourinary system, reproductive organs, liver, and head and

neck. The findings from human studies regarding the association between dietary β-cryptoxanthin intake and cancer risk, along with findings based on the β-cryptoxanthin levels in plasma or serum, are summarized in Table 1 (Ref. [65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106]) and Table 2 (Ref. [107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141]), respectively.

4.2.1 Association Between Dietary β-Cryptoxanthin Intake and Cancer Risk

Studies investigating the association between dietary β-cryptoxanthin intake and cancer risk have primarily focused on bladder and gastric cancers, with additional research examining other malignancies, including colorectal cancer, breast cancer, reproductive system–related cancers, and cancers of the oral cavity and throat. With respect to bladder cancer, most epidemiological studies consistently indicated that dietary β-cryptoxanthin intake was not significantly associated with bladder cancer risk [65,66,67,68,69]. However, a large prospective cohort study of 185,885 middle-aged and older adults (45–75 years) with a mean follow-up of 12.5 years reported a sex-specific association. Specifically, higher dietary β-cryptoxanthin intake was inversely associated with bladder cancer risk among women, whereas no significant association was observed among men [70]. Although the underlying mechanisms remain unclear, this sex-specific association may reflect differences in sex hormones, dietary patterns, carotenoid bioavailability, and residual confounding by smoking and other lifestyle factors. For instance, women were reported to exhibit greater efficiency in the absorption of β-cryptoxanthin; consequently, more efficient utilization may allow dietary intake to confer a stronger protective association against bladder cancer.

Regarding gastric cancer, seven studies (including five case-control studies and two cohort studies), with sample sizes ranging from several hundred to tens of thousands of participants, consistently reported no significant association between dietary β-cryptoxanthin intake and gastric cancer risk [71,72,73,74,75,76,77]. In contrast, a more recent case-control study published in 2022, involving 80 gastric cancer cases and 146 controls, reported an inverse association [78]. Notably, the discrepant findings may, at least in part, be attributable to methodological differences, including the substantially smaller sample size, the absence of female participants, and the exclusive use of hospital-based controls. No significant association was observed between dietary β-cryptoxanthin intake and colon cancer risk [79,80,81]. In contrast, a protective association with the rectal cancers, was reported in one study [82].

Neither breast cancer risk [83,84,85,86], breast cancer survival [87], nor the breast cancer mortality [88,89] was associated with dietary β-cryptoxanthin intake. With the exception of one study [90], the study populations were postmenopausal women with breast cancer; moreover, postmenopausal changes in estrogen levels may influence carotenoid metabolism and hormone-dependent breast cancer pathways, potentially contributing to the inconsistent findings. Similarly, no significant associations were observed between dietary β-cryptoxanthin intake and cancers of the reproductive system, including gynecological cancer [91], prostate cancer [92], and oncogenic Human papillomavirus (HPV) infection [93]. For cancers arising in the upper aerodigestive tract including the oral cavity and pharynx, larynx, and esophagus, an inverse association with dietary β-cryptoxanthin intake was consistently reported. Specifically, negative associations were observed for oral cavity and pharyngeal cancer [94], upper aerodigestive tract cancer [95], squamous cell carcinoma [96,97], laryngeal cancer [98], as well as for esophageal cancer in two independent studies [77,99].

Evidence regarding the association between dietary β-cryptoxanthin intake and several other cancer types remains limited. For lung cancer, one study reported an inverse association [100]. Hepatocellular carcinoma was reported not to be related to β-cryptoxanthin intake [101]. One case-control study reported inverse associations between dietary β-cryptoxanthin intake and pancreatic cancer [103], whereas two cohort studies observed no significant association [102,104], suggesting that differences in study design may partly account for the inconsistent findings. Findings for head and neck cancer are mixed. A case-control study involving 167 cases and 177 controls suggested a protective association [105]. However, a large prospective cohort study including 120,582 participants reported no significant association with a mean follow-up of 20.3 years [106].

4.2.2 Association Between Circulating β-Cryptoxanthin Concentrations and Cancer Risk

In addition to assessing the role of dietary β-cryptoxanthin intake in cancer, multiple studies have also examined the relationship between circulating β-cryptoxanthin concentrations and cancer risk. A majority of studies examining the relationship between cancer risk and plasma or serum β-cryptoxanthin levels reported either an inverse association or no association with cancer risk. The most frequently studied disease was breast cancer, with 12 studies conducted, 1 of which reported a negative association [107] and eleven of which reported no correlation [108,109,110,111,112,113,114,115,116,,117]. However, when the analysis was further stratified by body weight, higher circulating β-cryptoxanthin levels were found to be a protective factor for lean women (relative risk (RR) = 0.70) [116].

Five studies investigated the relationship between gastric cancer risk and blood β-cryptoxanthin levels [118,119,120,121,122], and four reported no association,

Table 1. Evidence from human studies on the association between dietary β-cryptoxanthin intake and cancer risk.

No	Study design	Subjects	Outcome	HR/OR/RR/IRR; 95% CI; *p*	Main results	Ref
1	Case-control study	322 bladder cancer cases, 239 controls, 2000–2003, America	Bladder cancer	OR = 0.87; 95% CI 0.50–1.53; $p = 0.65$	No correlation	[67]
2	Case-control study	1592 bladder cancer cases, 1592 controls, 1987–1996, America	Bladder cancer	OR = 0.83; 95% CI 0.64–1.08; $p = 0.21$	No correlation	[68]
3	Cohort study	88,796 subjects, 20 years of follow-up, NHS	Bladder cancer	RR = 1.09; 95% CI 0.73–1.63; $p = 0.97$	No correlation	[66]
4	Cohort study	27,111 subjects, aged 50–69 y, 11 years follow-up, 1985–1995, Finland	Bladder cancer	RR = 1.18; 95% CI 0.85–1.62; $p = 0.34$	No correlation	[69]
5	Cohort study	47,909 subjects, 10 years follow-up, 1985–1995, America	Bladder cancer	RR = 1.04; 95% CI 0.72–1.51; $p = 0.90$	No correlation	[65]
6	Cohort study	185,885 older (45–75 y) subjects, 12.5 years follow-up, America	Bladder cancer	HR = 0.47; 95% CI 0.28–0.77; $p < 0.01$	Negative correlation (women)	[70]
				HR = 0.97; 95% CI 0.74–1.30; $p = 0.85$	No correlation (men)	
7	Cohort study	120,852 subjects, aged 55–69 y, 6.3 years follow-up, Netherlands	Gastric cancer	RR = 0.80; 95% CI 0.60–1.20; $p = 0.14$	No correlation	[75]
8	Case-control study	124 esophageal adenocarcinoma cases, 124 distal gastric cancer cases, 449 controls, 1988–1993, America	Distal gastric cancer	OR = 0.60; 95% CI 0.30–1.20; $p = 0.08$	No correlation	[77]
9	Case-control study	120 gastric cancer cases, 360 controls, 1997–1999, Uruguay	Gastric cancer	OR = 0.80; 95% CI 0.40–1.61; $p = 0.55$	No correlation	[71]
10	Case-control study	415 gastric cancer cases, 830 controls, 2011–2014, Korea	Gastric cancer	OR = 0.77; 95% CI 0.54–1.10; $p = 0.14$	No correlation	[74]
11	Cohort study	82,002 subjects, aged 45–83 y, 1997–2005, Sweden	Gastric cancer	RR = 1.21; 95% CI 0.73–2.01; $p = 0.18$	No correlation	[76]
12	Case-control study	274 gastric cases, 463 controls, 1994–1996, Poland	Gastric cancer	OR = 1.06; 95% CI 0.68–1.65; $p = 0.79$	No correlation	[72]
13	Case-control study	230 gastric cancer cases, 547 controls, 1997–2007, Italy	Gastric cancer	OR = 1.01; 95% CI 0.62–1.66; $p = 0.86$	No correlation	[73]
14	Case-control study	80 gastric cancer cases, 146 controls, 2018–2019, Vietnam	Gastric cancer	OR = 0.34; 95% CI 0.14–0.79; $p = 0.02$	Negative correlation	[78]
15	Case-control study	1993 colon cancer cases, 2410 controls, 1991–1994, America	Colon cancer	OR = 1.02; 95% CI 0.83–1.27; $p = 0.08$	No correlation	[79]
16	Case-control study	402 colorectal cancer cases, 688 controls, 1989–1993, Canada	Colon cancer	OR = 0.96; 95% CI 0.66–1.40; $p = 0.14$	No correlation	[80]
17	Cohort study	191,004 subjects, 8.2 years follow-up, 1993–2002, America	Colorectal cancer	RR = 0.89; 95% CI 0.72–1.09; $p = 0.04$	No correlation	[81]
18	Case-control study	845 colorectal cancer cases, 845 controls, 2010–2013, China	Colorectal cancer	OR = 0.23; 95% CI 0.17–0.33; $p < 0.01$	Negative correlation	[82]
19	Cohort study	84,805 women subjects, 7.6 years follow-up, 1993–2000, America	Breast cancer	RR = 1.08; 95% CI 0.95–1.23; $p = 0.14$	No correlation	[84]
20	Cohort study	83,234 women subjects, 1980–1994, America	Breast cancer	RR = 0.89; 95% CI 0.70–1.13; $p = 0.34$ (pre-menopausal)	No correlation	[83]
				RR = 0.97; 95% CI 0.84–1.13; $p = 0.91$ (post-menopausal)		
21	Cohort study	56,837 women subjects, aged 40–59 y, 9.5 years follow-up, 1980–1993, Canada	Breast cancer	IRR = 0.88; 95% CI 0.6–1.13; $p = 0.59$	No correlation	[85]
22	Cohort study	36,664 women subjects, 9.4 years follow-up, Sweden	Breast cancer	RR = 1.02; 95% CI 0.82–1.26; $p = 0.99$	No correlation	[86]

Table 1. Continued.

No	Study design	Subjects	Outcome	HR/OR/RR/IRR; 95% CI; *p*	Main results	Ref
23	Cohort study	1235 breast cancer subjects, 1996–2002, LIBCSP	Breast cancer survival	HR = 1.13; 95% CI 0.53–2.41; *p* = 0.10 (pre-menopausal) HR = 0.82; 95% CI 0.53–1.28; *p* = 0.34 (post-menopausal)	No correlation	[87]
24	Cohort study	1982 subjects, 18 years of follow-up, America	Breast cancer mortality	RR = 0.86; 95% CI 0.63–1.19; *p* = 0.56	No correlation	[88]
25	Cohort study	4441 subjects, 1998–2007, America	Breast cancer mortality	HR = 0.81; 95% CI 0.45–1.45; *p* = 0.82	No correlation	[89]
26	Cohort study	516 postmenopausal breast cancer subjects, 80 months follow-up, America	Breast Cancer mortality	HR = 0.54; 95% CI 0.30–0.96; *p* ≤ 0.05	Negative correlation	[90]
27	Cross-sectional study	12,437-woman subjects aged over 20 years, 2007–2016, NHANES	Gynecological cancer	OR = 1.00; 95% CI 0.99–1.00; *p* > 0.05	No correlation	[91]
28	Case-control study	244 prostate cancer cases, 408 controls, aged 64–75 y, 2013–2015, Vietnam	Prostate cancer	OR = 1.29; 95% CI 0.79–2.09; *p* = 0.30	No correlation	[92]
29	Cohort study	120-woman subjects with oncogenic HPV, 141-woman subjects with any type of HPV, 1990s–2000s, YWHS	Oncogenic HPV	OR = 0.80; 95% CI 0.30–2.20; *p* > 0.05	No correlation	[93]
30	Case-control study	768 OCP cancer cases, 2078 controls, 1997–2009, Italy and Switzerland	OCP cancer	OR = 0.37; 95% CI 0.24–0.56; *p* < 0.01	Negative correlation	[94]
31	Case-control study	399 upper-aerodigestive-tract cancer cases, 393 controls, 1996–1997, Uruguay	Upper-aerodigestive-tract cancer	OR = 0.20; 95% CI 0.10–0.50; *p* < 0.01	Negative correlation	[95]
32	Cohort study	75,170 women subjects, 48,400 men subjects, 1984–2012, America	SCC	HR = 0.86; 95% CI 0.76–0.96; *p* < 0.01	Negative correlation	[96]
33	Case-control study	304 SCC cases, 743 controls, 1992–1997, Italy	SCC	OR = 0.50; 95% CI 0.30–0.80; *p* < 0.05	Negative correlation	[97]
34	Case-control study	527 laryngeal cancer cases, 1297 controls, 1992–2000, Italy and Switzerland	Laryngeal cancer	OR = 0.40; 95% CI 0.20–0.50; *p* < 0.01	Negative correlation	[98]
35	Case-control study	124 esophageal adenocarcinoma cases, 124 distal gastric cancer cases, 449 controls, 1988–1993, America	Esophageal adenocarcinoma	OR = 0.50; 95% CI 0.30–1.10; *p* = 0.05	*No correlation	[77]
36	Case-control study	234 Esophageal squamous cell carcinoma cases, 936 controls, 1996–2004, Uruguay	Esophageal squamous cell carcinoma	OR = 0.34; 95% CI 0.21–0.57; *p* < 0.01	Negative correlation	[99]
37	Case-control study	1105 lung cancer cases, 1449 controls, 1996–2002, Canada	Lung cancer	OR = 0.65; 95% CI 0.51–0.84; *p* < 0.01	Negative correlation	[100]
38	Case-control study	185 HCC cases, 412 controls, 1999–2002, Italy	HCC	OR = 1.11; 95% CI 0.84–1.45; *p* = 0.50	No correlation	[101]
39	Case-control study	326 pancreatic cancer cases, 652 controls, 1991–2008, Italy	Pancreatic cancer	OR = 0.66; 95% CI 0.39–1.09; *p* = 0.02	*No correlation	[102]
40	Clinic-based case-control design	384 pancreatic cancer cases, 983 controls, 2004–2009, America	Pancreatic cancer	OR = 0.55; 95% CI 0.37–0.82; *p* = 0.01	Negative correlation	[103]
41	Cohort Study	120,852 subjects, 16.3 years follow-up, 1986–2002, Netherlands	Pancreatic cancer	HR = 1.00; 95% CI 0.97–1.03; *p* = 0.73	No correlation	[104]
42	Case-control study	167 HNC cases, 177 controls, 1992–1994, America	HNC	OR = 0.30; 95% CI 0.15–0.60; *p* < 0.01	Negative correlation	[105]
43	Prospective cohort study	120,582 subjects, 20.3 years follow-up, Netherlands	HNC	RR = 0.73; 95% CI 0.47–1.14; *p* = 0.05	No correlation	[106]

Abbreviations: HR, Hazard Ratio; OR, Odds Ratio; RR, Relative Risk; CI, Confidence Interval; LIBCSP, Long Island Breast Cancer Study Project; HPV, Human papillomavirus; YWHS, Young Women's Health Study; HNC, Head and Neck Cancer; OCP, Oral Cavity and Pharyngeal; NHS, Nurses' Health Study; HCC, Hepatocellular Carcinoma; SCC, Squamous Cell Carcinoma; NHANES, National Health and Nutrition Examination Survey. *For these references, although quantile-based categorization (e.g., highest vs. lowest quintile) yielded a non-statistically significant inverse association (95% CI overlapping 1), the test for linear trend across quantiles suggested a significant inverse dose-response relationship.

Table 2. Evidence from human studies on the association between plasma or serum β-cryptoxanthin and cancer risk.

No	Study design	Subjects	Outcome	HR/OR/RR/IRR; 95% CI; *p*	Main results	Ref
1	Nested case-control study	100 breast cancers cases, 59 other cancer cases, 159 controls, 1994–2002, France	Breast cancer	OR = 0.83; 95% CI 0.71–0.96; *p* = 0.02	Negative correlation	[107]
2	Case-control study	270 breast cancer cases, 270 controls, 1985–1994, America	Breast cancer	OR = 1.68; 95% CI 0.99–2.86; *p* = 0.05	No correlation	[108]
3	Nested case-control study	1502 breast cancer cases, 1502 controls, 1992–1998, Europe	Breast cancer	OR = 0.70; 95% CI 0.45–1.10; *p* = 0.29 (ER–) OR = 0.84; 95% CI 0.51–1.37; *p* = 0.68 (ER+)	No correlation	[110]
4	Case-control study	105 breast cancer cases, 210 controls, 9.5 years follow-up, America	Breast cancer	RR = 0.60; 95% CI 0.30–1.20; *p* = 0.41	No correlation	[111]
5	Nested case-control study	286 breast cancer cases, 535 controls, 1993–2006, America	Breast cancer	OR = 1.36; 95% CI 0.85–2.16; *p* = 0.30 (trans-β-Cryptoxanthin) OR = 1.27; 95% CI 0.81–1.99; *p* = 0.28 (cis-β-Cryptoxanthin)	No correlation	[114]
6	Cohort study	5450 subjects, 8.0-year follow-up, 1993–2005, America	Breast cancer	HR = 1.16; 95% CI 0.81–1.65; *p* = 0.42 (age-adjusted) HR = 1.28; 95% CI 0.86–1.92; *p* = 0.23 (multivariate adjusted)	No correlation	[117,]
7	Nested case-control study	2188 breast cancer cases, 2188 controls, 1989–2010, NHS	Breast cancer	RR = 0.86; 95% CI 0.70–1.06; *p* = 0.12 RR = 0.70; 95% CI 0.53–0.92; *p* = 0.05	No correlation Negative correlation (lean women)	[116]
8	Nested case-control study	295 breast cancer cases, 295 controls, 1974–1989, America	Breast cancer	OR = 0.98; 95% CI 0.55–1.75; *p* = 0.67 (1974 cohort) OR = 0.70; 95% CI 0.29–1.73; *p* = 0.68 (1989 cohort)	No correlation	[112]
9	Nested case-control study	508 breast cancer cases, 508 controls, 1992–2002, America	Breast cancer	RR = 0.94; 95% CI 0.56–1.57; *p* = 0.91	No correlation	[113]
10	Nested case-control study	969 breast cancer cases, 969 controls, 1989–1998, America	Breast cancer	OR = 1.03; 95% CI 0.77–1.38; *p* = 0.32	No correlation	[115]
11	Case-control study	496 breast cancer cases, 496 controls, 1998–2007, America	Breast cancer	OR = 1.01; 95% CI 0.60–1.70; *p* = 0.65	No correlation	[109]
12	Nested Case-control study	511 gastric cancer cases, 511 controls, 1990–2004, Japan	Gastric cancer	OR = 0.71; 95% CI 0.43–1.17; *p* = 0.09	No correlation	[118]
13	Case-control study	191 gastric cancer cases, 570 controls, 12 years follow-up, China	Gastric cancer	OR = 0.90; 95% CI 0.51–1.58; *p* = 0.66	No correlation	[119]
14	Cohort study	3182 subjects, aged from 39–79, 10.5 years follow-up, 1988–1999, Japan	Gastric cancer	HR = 0.69; 95% CI 0.16–3.03; *p* = 0.75	No correlation	[120]
15	Stratified case-cohort study	590 esophageal, 395 gastric cardia, 87 gastric non-cardia cases, 1053 controls, 1986–1991, China	Gastric non-cardia cancer	RR = 0.88; 95% CI 0.76–1.00; *p* = 0.13	No correlation	[121]
16	Stratified case-cohort study	590 esophageal, 395 gastric cardia, 87 gastric non-cardia cases, 1053 controls, 1986–1991, China	Gastric cardia cancer	RR = 1.00; 95% CI 0.99–1.10; *p* = 0.23	No correlation	[121]
17	Case-control study	244 gastric cancer cases, 645 controls, 1992–1998, 10 European countries	Gastric cancer	OR = 0.53; 95% CI 0.30–0.94; *p* < 0.01	Negative correlation	[122]

Table 2. Continued.

No	Study design	Subjects	Outcome	HR/OR/RR/IRR; 95% CI; p	Main results	Ref
18	Cohort study	5477 subjects, 12 years follow-up, WHI	Colorectal cancer	HR = 1.10; 95% CI 0.67–1.83; p = 0.70	No correlation	[123]
19	Cohort study	3182 subjects, aged from 39–79, 10.5 years follow-up, 1988–1999, Japan	Colorectal cancer	HR = 0.70; 95% CI 0.19–3.00; p = 0.70	No correlation	[120]
20	Case-control study	538 colorectal cancer cases, 564 controls, 2010–2014, China	Colorectal cancer	OR = 0.44; 95% CI 0.29–0.66; p < 0.01	Negative correlation	[124]
21	Nested Case Control	207 lung cancer cases, 414 controls, 1997–2006, America	Lung cancer	OR = 0.33; 95% CI 0.15–0.73; p < 0.01	Negative correlation (men)	[125]
				OR = 1.58; 95% CI 0.59–4.23; p > 0.05	No correlation (women)	
22	Case-control study	211 lung cancer cases, 487 controls, 1989–1999, America	Lung cancer	OR = 0.32; 95% CI 0.13–0.78; p = 0.03	Negative correlation (men)	[126]
				OR = 1.00; 95% CI 0.22–4.48; p = 0.74	No correlation (women)	
23	Case control study	339 lung cancer cases, 678 controls, 1992–1999, China	Lung cancer	OR = 7.60; 95% CI 2.70–21.50; p < 0.01	Positive correlation (alcohol drinkers)	[127]
				OR = 0.80; 95% CI 0.30–2.00; p = 0.70	No correlation (non-drinkers)	
24	Prospective cohort study	10,382 subjects, aged over 20 years, 1988–2006, America	Lung cancer	RR = 0.56; 95% CI 0.33–0.96; p < 0.05	Negative correlation	[128]
25	Cohort study	3182 subjects, aged from 39–79, 10.5 years follow-up, 1988–1999, Japan	Lung cancer	HR = 0.66; 95% CI 0.18–2.36; p = 0.79	No correlation	[120]
26	Case-control study	242 bladder cancer cases, 204 controls, 1993–1997, MSKCC	Bladder cancer	OR = 0.90; 95% CI 0.81–1.00; p = 0.05	No correlation	[129]
27	Case-control study	111 bladder cancer cases, 111 controls, 1971–1995, America	Bladder cancer	OR = 0.41; 95% CI 0.20–0.88; p = 0.04	Negative correlation	[130]
				OR = 0.52; 95% CI 0.23–1.44; p = 0.15	No correlation (adjusted pack-years of cigarette smoking)	
28	Environment-wide association study	5163 cancer cases, 55,021 controls, 1999–2018, NHANES	Cancer	OR = 0.85; 95% CI 0.76–0.96; p < 0.01	Negative correlation	[131]
29	Nested case-control study	1305 kidney cancer cases, 1305 controls, 1980s–2000s, Europe	Kidney cancer	OR = 0.73; 95% CI 0.65–0.83; p < 0.01	Negative correlation	[132]
30	Cohort study	189 oncogenic HPV infections subjects, 1998–2003, America	Oncogenic HPV infections	HR = 1.64; 95% CI 0.99–2.73; p = 0.04	*No correlation	[133]
31	Cohort study	5477 subjects, 12 years follow-up, WHI	Colon cancer	HR = 0.91; 95% CI 0.52–1.58; p = 0.65	No correlation	[123]
32	Stratified case-cohort study	590 esophageal, 395 gastric cardia, 87 gastric non-cardia cases, 1053 controls, 1986–1991, China	Esophageal cancer	RR = 1.00; 95% CI 0.98–1.10; p = 0.57	No correlation	[121]
33	Case-control study	213 HCC cases, 1087 controls, 15 years follow-up, 1986–2001, China	HCC	OR = 0.85; 95% CI 0.48–1.51; p = 0.56	No correlation	[134]

Table 2. Continued.

No	Study design	Subjects	Outcome	HR/OR/RR/IRR; 95% CI; *p*	Main results	Ref
34	Nested case-control study	370 prostate cancer cases, 2470 controls, 1982–2005, America	Prostate Cancer	OR = 1.17; 95% CI 0.85–1.61; $p = 0.31$	No correlation	[135]
35	Nested case-control study	856 UCC cases, 856 controls, 1992–2005, Europe	UCC	IRR = 1.08; 95% CI 0.76–1.50; $p = 0.33$	No correlation	[136]
36	Cohort study	12,530 subjects, 1988–1994, America	Cancer mortality	HR = 0.90; 95% CI 0.70–1.15; $p = 0.47$	No correlation	[137]
37	Cohort study	13,293 subjects, 1988–2006, NHANES III	Cancer mortality	RR = 1.28; 95% CI 0.87–1.89; $p = 0.61$	No correlation	[138]
38	Cohort study	1054 subjects, aged 65 y+, 1994–2008, British	Primary cancer mortality	HR = 0.86; 95% CI 0.66–1.13; $p = 0.30$	No correlation	[139]
39	Cohort study	3254 subjects, aged 39–85 y, 11.7 years follow-up, Japan	Colorectal cancer mortality	HR = 0.80; 95% CI 0.38–1.67; $p = 0.55$	No correlation	[140]
40	Cohort study	3254 subjects, aged 39–85 y, 11.7 years follow-up, Japan	Gastric cancer mortality	HR = 0.58; 95% CI 0.28–1.18; $p = 0.14$	No correlation	[140]
			Liver cancer mortality	HR = 1.13; 95% CI 0.50–2.53; $p = 0.77$	No correlation	[140]
			Lung cancer mortality	HR = 1.01; 95% CI 0.66–1.56; $p = 0.96$	No correlation	[140]
41	Case-control study	125 premature mortality cases, 321 controls, 1988–2015, Japan	Cancer mortality	OR = 3.23; 95% CI 1.40–8.03; $p < 0.01$	Positive correlation (women)	[141]
				OR = 0.10; 95% CI 0.02–0.37; $p < 0.01$	Negative correlation (men)	

Abbreviations: HR, Hazard Ratio; OR, Odds Ratio; RR, Relative Risk; CI, Confidence Interval; MSKCC, Memorial Sloan-Kettering Cancer Center; NHS, Nurses' Health Study; NHANES, National Health and Nutrition Examination Survey; WHI, Women's Health Initiative; HCC, Hepatocellular Carcinoma; UCC, Urothelial Cell Carcinoma; ER, Estrogen Receptor. *For these references, although quantile-based categorization (e.g., highest vs. lowest quintile) yielded a non-statistically significant inverse association (95% CI overlapping 1), the test for linear trend across quantiles suggested a significant inverse dose-response relationship.

with one study showing an exception [122]. This case-control study, involving 244 gastric cancer cases and 645 controls from 10 European countries, revealed that higher plasma β-cryptoxanthin levels were associated with a reduced occurrence of gastric cancer (OR = 0.53). One possible explanation for this discrepancy is the considerable heterogeneity in the multi-country design and the more homogeneous population characteristics as this study included participants from 10 European countries, whereas the other four studies were conducted within a single country. Two cohort studies explored the relationship between the risk of colorectal cancer and plasma or serum β-cryptoxanthin levels but found no correlation [120,123]. Conversely, a case-control study involving 538 cases of colorectal cancer and 564 controls found that β-cryptoxanthin was a protective factor (OR = 0.44) [124].

Research on the association between blood β-cryptoxanthin levels and lung cancer risk presents a mixed pattern of results. Two studies reported that, when stratified by gender, plasma or serum β-cryptoxanthin was a protective factor for men but not for women [125,126]. A case-control study of 339 lung cancer cases and 678 controls in China, stratified by alcohol consumption, found that serum β-cryptoxanthin levels were associated with an increased risk of lung cancer among drinkers, an interesting contrast to its generally recognized health-protective role. No such association was observed among non-drinkers. This unexpected association may reflect an interaction between alcohol consumption and β-cryptoxanthin metabolism, in which alcohol-induced oxidative stress or metabolic alterations could diminish or even reverse its protective effects [127]. At the population level, the evidence is also mixed. One prospective cohort study of 10,382 subjects reported a protective association [128], while another 10.5-year follow-up cohort study of 3182 subjects concluded no correlation [120]. Collectively, evidence regarding the relationship between blood β-cryptoxanthin levels and lung cancer risk remains inconclusive, with findings varying by sex, population and lifestyle factors including alcohol consumption.

One case-control study conducted on bladder cancer revealed no correlation [129]. Another study reported blood β-cryptoxanthin levels might be the protective factor [130]. However, this association disappeared after adjusting for pack-years of cigarette smoking. For the risk of general cancer [131] and kidney cancer [132], the available results indicated that plasma or serum β-cryptoxanthin was considered a protective factor. In contrast, no statistically significant association was observed between plasma or serum β-cryptoxanthin levels and the incidence rates of colon cancer [123], esophageal cancer [121], oncogenic HPV infection [133], hepatocellular carcinoma [134], prostate cancer [135], or urothelial cell carcinoma [136].

In addition to evaluating the association between β-cryptoxanthin and cancer incidence, several epidemiological studies also examined its relationship with cancer mortality. Studies examining cancer mortality have consistently reported no association between plasma or serum β-cryptoxanthin levels and mortality outcomes, including overall cancer mortality [137,138], primary cancer mortality [139] and the mortality from colorectal, gastric, liver and lung cancers [140]. A case-control study involving 125 premature mortality cases and 321 controls found that, after being categorized by gender, the serum β-cryptoxanthin levels were associated with an increased risk of cancer mortality in women (OR = 3.23). In contrast, the association was reversed in men (OR = 0.10) [141]. Regarding this unexpected result, the authors proposed two possible explanations: the bone metabolism hypothesis and the potential toxicity of excessive β-cryptoxanthin intake. Overall, the heterogeneity observed across cancer studies may reflect underlying interindividual differences in β-cryptoxanthin metabolism, bioavailability, and interaction with lifestyle factors such as smoking and alcohol consumption. These findings highlight the importance of adopting a precision nutrition perspective, in which the potential protective effects of β-cryptoxanthin are evaluated in specific subpopulations rather than at the general population level.

5. Conclusions and Future Prospective

Despite the promising evidence summarized in this present review, several limitations should be considered. First, the majority of human studies are observational, limiting causal inference and leaving open the possibility of residual confounding from dietary patterns, smoking, alcohol consumption, adiposity, and other lifestyle-related factors. Second, both dietary intake estimates and circulating β-cryptoxanthin concentrations are imperfect indicators of biologically relevant exposure, as they are influenced by food composition variability, recent intake, absorption efficiency, host genetics and metabolic status. Moreover, because this article is a narrative review rather than a systematic review, the possibility of incomplete literature capture and selection bias should also be acknowledged. Nevertheless, this review highlights that β-cryptoxanthin is not merely a passive dietary antioxidant but a biologically active compound with tissue-specific actions. Among the health outcomes examined, evidence is most consistent for its beneficial role in skeletal health. Experimental studies collectively demonstrate that β-cryptoxanthin simultaneously stimulates osteoblast differentiation and activity while suppressing osteoclastogenesis and bone resorption. These mechanistic findings are complemented by epidemiological studies and human interventions showing favorable associations with bone mineral density, bone turnover markers, and reduced osteoporosis risk, suggesting that β-cryptoxanthin may contribute to bone homeostasis, particularly in aging populations.

In contrast, the relationship between β-cryptoxanthin and cancer risk appears to be inconclusive and population-dependent. While inverse associations have been observed for certain malignancies, most notably cancers of the upper aerodigestive tract, evidence across other cancer types remains inconsistent. Differences in study design, exposure assessment, population characteristics, and confounding factors such as smoking, alcohol intake, adiposity, and hormonal status likely contribute to the variability in reported outcomes. Importantly, the predominance of null findings for overall cancer incidence and cancer-related mortality indicates that β-cryptoxanthin should not be viewed as a broadly protective anticancer agent. Rather, its potential influence on carcinogenesis may be restricted to specific tissues or subpopulations and modulated by metabolic and lifestyle factors.

Moreover, substantial interindividual variability in circulating β-cryptoxanthin levels underscores the need to better characterize the determinants of absorption, metabolism, and tissue distribution. Genetic variation in carotenoid transporters and cleavage enzymes, interactions with dietary fat and fiber, and the role of the gut microbiota represent particularly important areas for future investigation. In summary, β-cryptoxanthin is an underexplored carotenoid with well-supported biological relevance to bone health, while associations with cancer risk differ according to population characteristics and cancer type. Future research is essential to determine whether β-cryptoxanthin can be effectively incorporated into evidence-based precision nutrition strategies that account for interindividual variability in disease risk and metabolic response.

Author Contributions

Conceptualization, YY, JW, RP; Investigation, YY, XW, TX, XZ; Writing—original draft preparation, YY, XW, TX, XZ; Writing—review and editing, YY, JW, RP; Supervision, YY, JW, RP; Funding acquisition, YY. All authors have read and agreed to the published version of the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflicts of Interest

The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGpt-5.2 in order to check spell and grammar. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication.

References

[1] Böhm V, Lietz G, Olmedilla-Alonso B, Phelan D, Reboul E, Bánati D, et al. From carotenoid intake to carotenoid blood and tissue concentrations - implications for dietary intake recommendations. Nutrition Reviews. 2021; 79: 544–573. https://doi.org/10.1093/nutrit/nuaa008

[2] Beltrán-de-Miguel B, Estévez-Santiago R, Olmedilla-Alonso B. Assessment of dietary vitamin A intake (retinol, α-carotene, β-carotene, β-cryptoxanthin) and its sources in the National Survey of Dietary Intake in Spain (2009-2010). International Journal of Food Sciences and Nutrition. 2015; 66: 706–712. https://doi.org/10.3109/09637486.2015.1077787

[3] Burri BJ, La Frano MR, Zhu C. Absorption, metabolism, and functions of β-cryptoxanthin. Nutrition Reviews. 2016; 74: 69–82. https://doi.org/10.1093/nutrit/nuv064

[4] Zhu CH, Gertz ER, Cai Y, Burri BJ. Consumption of canned citrus fruit meals increases human plasma β-cryptoxanthin concentration, whereas lycopene and β-carotene concentrations did not change in healthy adults. Nutrition Research (New York, N.Y.). 2016; 36: 679–688. https://doi.org/10.1016/j.nutres.2016.03.005

[5] van Kappel AL, Martínez-García C, Elmståhl S, Steghens JP, Chajès V, Bianchini F, et al. Plasma carotenoids in relation to food consumption in Granada (southern Spain) and Malmö (southern Sweden). International Journal for Vitamin and Nutrition Research. Internationale Zeitschrift Fur Vitamin- Und Ernahrungsforschung. Journal International De Vitaminologie et De Nutrition. 2001; 71: 97–102. https://doi.org/10.1024/0300-9831.71.2.97

[6] Fukushima Y, Taguchi C, Kishimoto Y, Kondo K. Japanese carotenoid database with α- and β-carotene, β-cryptoxanthin, lutein, zeaxanthin, lycopene, and fucoxanthin and intake in adult women. International Journal for Vitamin and Nutrition Research. Internationale Zeitschrift Fur Vitamin- Und Ernahrungsforschung. Journal International De Vitaminologie et De Nutrition. 2023; 93: 42–53. https://doi.org/10.1024/0300-9831/a000707

[7] Estévez-Santiago R, Olmedilla-Alonso B, Fernández-Jalao I. Bioaccessibility of provitamin A carotenoids from fruits: application of a standardised static in vitro digestion method. Food & Function. 2016; 7: 1354–1366. https://doi.org/10.1039/c5fo01242b

[8] Llopis S, Rodrigo MJ, González N, Genovés S, Zacarías L, Ramón D, et al. β-Cryptoxanthin Reduces Body Fat and Increases Oxidative Stress Response in *Caenorhabditis elegans* Model. Nutrients. 2019; 11: 232. https://doi.org/10.3390/nu11020232

[9] Jiao Y, Reuss L, Wang Y. β-Cryptoxanthin: chemistry, occurrence, and potential health benefits. Current Pharmacology Reports. 2019; 5: 20–34. https://doi.org/10.1007/s40495-019-00168-7

[10] Nishino A, Maoka T, Yasui H. Preventive Effects of β-Cryptoxanthin, a Potent Antioxidant and Provitamin A Carotenoid, on Lifestyle-Related Diseases-A Central Focus on Its Effects on Non-Alcoholic Fatty Liver Disease (NAFLD). Antioxidants (Basel, Switzerland). 2021; 11: 43. https://doi.org/10.3390/antiox11010043

[11] Shaaban HA, Abdel-Gawad HH, Sleem MM. Composition and Health Benefits of Carotenoids in Foods and Feeds. In Campos Chisté R, Helena de Aguiar Andrade E, Santana de Oliveira M (eds.) Carotenoids: Trends and Advances (pp. 227–244). Springer: Cham. 2024. https://doi.org/10.1007/978-3-031-75322-0_10

[12] Kan B, Guo D, Yuan B, Vuong AM, Jiang D, Zhang M, et al. Dietary carotenoid intake and osteoporosis: the National Health and Nutrition Examination Survey, 2005-2018. Archives of Osteoporosis. 2022; 17: 2. https://doi.org/10.1007/s11657-021-01047-9

[13] Wu S, Liu Y, Michalek JE, Mesa RA, Parma DL, Rodriguez R, et al. Carotenoid Intake and Circulating Carotenoids Are Inversely Associated with the Risk of Bladder Cancer: A Dose-Response Meta-analysis. Advances in Nutrition (Bethesda, Md.). 2020; 11: 630–643. https://doi.org/10.1093/advances/nmz120

[14] Aune D, Chan DSM, Vieira AR, Navarro Rosenblatt DA, Vieira R, Greenwood DC, et al. Dietary compared with blood concentrations of carotenoids and breast cancer risk: a systematic review and meta-analysis of prospective studies. The American Journal of Clinical Nutrition. 2012; 96: 356–373. https://doi.org/10.3945/ajcn.112.034165

[15] Männistö S, Smith-Warner SA, Spiegelman D, Albanes D, Anderson K, van den Brandt PA, et al. Dietary carotenoids and risk of lung cancer in a pooled analysis of seven cohort studies. Cancer Epidemiology, Biomarkers & Prevention : a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 2004; 13: 40–48. https://doi.org/10.1158/1055-9965.epi-038-3

[16] Burri BJ. Beta-cryptoxanthin as a source of vitamin A. Journal of the Science of Food and Agriculture. 2015; 95: 1786–1794. https://doi.org/10.1002/jsfa.6942

[17] Sui J, Guo J, Pan D, Wang Y, Xu Y, Sun G, et al. The Efficacy of Dietary Intake, Supplementation, and Blood Concentrations of Carotenoids in Cancer Prevention: Insights from an Umbrella Meta-Analysis. Foods (Basel, Switzerland). 2024; 13: 1321. https://doi.org/10.3390/foods13091321

[18] Yamaguchi M, Igarashi A, Uchiyama S, Sugawara K, Sumida T, Morita S, et al. Effect of β-crytoxanthin on circulating bone metabolic markers: intake of juice (Citrus unshiu) supplemented with β-cryptoxanthin has an effect in menopausal women. Journal of Health Science. 2006; 52: 758–768. https://doi.org/10.1248/jhs.52.758

[19] Ma G, Zhang L, Iida K, Madono Y, Yungyuen W, Yahata M, et al.

Identification and quantitative analysis of β-cryptoxanthin and β-citraurin esters in Satsuma mandarin fruit during the ripening process. Food Chemistry. 2017; 234: 356–364. https://doi.org/10.1016/j.foodchem.2017.05.015

[20] Mercadante AZ, Rodrigues DB, Petry FC, Mariutti LRB. Carotenoid esters in foods - A review and practical directions on analysis and occurrence. Food Research International (Ottawa, Ont.). 2017; 99: 830–850. https://doi.org/10.1016/j.foodres.2016.12.018

[21] González-Peña MA, Ortega-Regules AE, Anaya de Parrodi C, Lozada-Ramírez JD. Chemistry, Occurrence, Properties, Applications, and Encapsulation of Carotenoids-A Review. Plants (Basel, Switzerland). 2023; 12: 313. https://doi.org/10.3390/plants12020313

[22] Rodriguez-Amaya DB. Food carotenoids: chemistry, biology and technology. John Wiley & Sons: Hoboken, NJ. 2015.

[23] Mercadante AZ. 4.2 Carotenoids in foods: sources and stability during processing and storage. In Socaciu C (ed.) Food Colorants: Chemical and Functional Properties (pp. 213–240). CRC Press: Boca Raton, FL, USA. 2007.

[24] Boon CS, McClements DJ, Weiss J, Decker EA. Factors influencing the chemical stability of carotenoids in foods. Critical Reviews in Food Science and Nutrition. 2010; 50: 515–532. https://doi.org/10.1080/10408390802565889

[25] Xiang J, Nagaya T, Huang XE, Kuriki K, Imaeda N, Tokudome Y, et al. Sex and seasonal variations of plasma retinol, alpha-tocopherol, and carotenoid concentrations in Japanese dietitians. Asian Pacific Journal of Cancer Prevention : APJCP. 2008; 9: 413–416.

[26] Granado-Lorencio F, Olmedilla-Alonso B, Herrero-Barbudo C, Blanco-Navarro I, Pérez-Sacristán B. Seasonal variation of serum alpha- and beta-cryptoxanthin and 25-OH-vitamin D(3) in women with osteoporosis. Osteoporosis International : a Journal Established as Result of Cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2008; 19: 717–720. https://doi.org/10.1007/s00198-007-0470-5

[27] During A, Hussain MM, Morel DW, Harrison EH. Carotenoid uptake and secretion by CaCo-2 cells: beta-carotene isomer selectivity and carotenoid interactions. Journal of Lipid Research. 2002; 43: 1086–1095. https://doi.org/10.1194/jlr.m200068-jlr200

[28] Harrison EH. Mechanisms involved in the intestinal absorption of dietary vitamin A and provitamin A carotenoids. Biochimica et Biophysica Acta. 2012; 1821: 70–77. https://doi.org/10.1016/j.bbalip.2011.06.002

[29] Guo Z, Liu Y, Luo Y. Mechanisms of carotenoid intestinal absorption and the regulation of dietary lipids: lipid transporter-mediated transintestinal epithelial pathways. Critical Reviews in Food Science and Nutrition. 2024; 64: 1791–1816. https://doi.org/10.1080/10408398.2022.2119204

[30] von Lintig J, Moon J, Lee J, Ramkumar S. Carotenoid metabolism at the intestinal barrier. Biochimica et Biophysica Acta. Molecular and Cell Biology of Lipids. 2020; 1865: 158580. https://doi.org/10.1016/j.bbalip.2019.158580

[31] Borel P, Lietz G, Goncalves A, Szabo de Edelenyi F, Lecompte S, Curtis P, et al. CD36 and SR-BI are involved in cellular uptake of provitamin A carotenoids by Caco-2 and HEK cells, and some of their genetic variants are associated with plasma concentrations of these micronutrients in humans. The Journal of Nutrition. 2013; 143: 448–456. https://doi.org/10.3945/jn.112.172734

[32] Nagao A. Metabolism of Carotenoids in Mammals. Advances in Experimental Medicine and Biology. 2021; 1261: 67–78. https://doi.org/10.1007/978-981-15-7360-6_6

[33] Bonet ML, Canas JA, Ribot J, Palou A. Carotenoids in Adipose Tissue Biology and Obesity. Sub-cellular Biochemistry. 2016; 79: 377–414. https://doi.org/10.1007/978-3-319-39126-7_15

[34] Gouranton E, Yazidi CE, Cardinault N, Amiot MJ, Borel P, Landrier JF. Purified low-density lipoprotein and bovine serum albumin efficiency to internalise lycopene into adipocytes. Food and Chemical Toxicology : an International Journal Published for the British Industrial Biological Research Association. 2008; 46: 3832–3836. https://doi.org/10.1016/j.fct.2008.10.006

[35] Nielsen R, Christensen EI, Birn H. Megalin and cubilin in proximal tubule protein reabsorption: from experimental models to human disease. Kidney International. 2016; 89: 58–67. https://doi.org/10.1016/j.kint.2015.11.007

[36] Sugiura M, Ogawa K, Yano M. Absorption, storage and distribution of β-cryptoxanthin in rat after chronic administration of Satsuma mandarin (Citrus unshiu MARC.) juice. Biological & Pharmaceutical Bulletin. 2013; 36: 147–151. https://doi.org/10.1248/bpb.b12-00836

[37] Burri BJ, Chang JST, Neidlinger TR. β-Cryptoxanthin- and α-carotene-rich foods have greater apparent bioavailability than β-carotene-rich foods in Western diets. The British Journal of Nutrition. 2011; 105: 212–219. https://doi.org/10.1017/S0007114510003260

[38] Sugiura M, Ogawa K, Yano M. Comparison of bioavailability between β-cryptoxanthin and β-carotene and tissue distribution in its intact form in rats. Bioscience, Biotechnology, and Biochemistry. 2014; 78: 307–310. https://doi.org/10.1080/09168451.2014.878220

[39] Floreani A, Baragiotta A, Martines D, Naccarato R, D'odorico A. Plasma antioxidant levels in chronic cholestatic liver diseases. Alimentary Pharmacology & Therapeutics. 2000; 14: 353–358. https://doi.org/10.1046/j.1365-2036.2000.00729.x

[40] Pugliese A, O'Callaghan Y, Tundis R, Galvin K, Menichini F, O'Brien N, et al. In vitro investigation of the bioaccessibility of carotenoids from raw, frozen and boiled red chili peppers (Capsicum annuum). European Journal of Nutrition. 2014; 53: 501–510. https://doi.org/10.1007/s00394-013-0555-1

[41] Donda Zbinden M, Schmidt M, Vignatti CI, Pirovani MÉ, Böhm V. High-Pressure Processing of Fruit Smoothies Enriched with Dietary Fiber from Carrot Discards: Effects on the Contents and Bioaccessibilities of Carotenoids and Vitamin E. Molecules (Basel, Switzerland). 2024; 29: 1259. https://doi.org/10.3390/molecules29061259

[42] Ancos BAD, Sgroppo S, Plaza L, Cano MP. Possible nutritional and health-related value promotion in orange juice preserved by high-pressure treatment. Journal of the Science of Food & Agriculture. 2002; 82: 790–796. https://doi.org/10.1002/jsfa.1093

[43] López-Gámez G, Elez-Martínez P, Martín-Belloso O, Soliva-Fortuny R. Enhancing carotenoid and phenolic contents in plant food matrices by applying non-thermal technologies: Bioproduction vs improved extractability. Trends in Food Science & Technology. 2021; 112: 622–630. https://doi.org/10.1016/j.tifs.2021.04.022

[44] Westphal A, Schwarzenbolz U, Böhm V. Effects of high pressure processing on bioactive compounds in spinach and rosehip puree. European Food Research and Technology. 2018; 244: 395–407. https://doi.org/10.1007/s00217-017-2964-5

[45] Anese M, Bot F, Panozzo A, Mirolo G, Lippe G. Effect of ultrasound treatment, oil addition and storage time on lycopene stability and in vitro bioaccessibility of tomato pulp. Food Chemistry. 2015; 172: 685–691. https://doi.org/10.1016/j.foodchem.2014.09.140

[46] Meléndez-Martínez AJ, Esquivel P, Rodriguez-Amaya DB. Comprehensive review on carotenoid composition: Transformations during processing and storage of foods. Food Research International (Ottawa, Ont.). 2023; 169: 112773. https://doi.org/10.1016/j.foodres.2023.112773

[47] Iwata A, Fujiwara S, Matsubara S, Miyazaki K. Intake of β-cryptoxanthin with fat-containing food increases β-cryptoxanthin serum level and palmar yellowness in healthy adults. Nutrition Research (New York, N.Y.). 2019; 71: 65–71. https://doi.org/10.1016/j.nutres.2019.09.003
[48] Rodríguez-Roque MJ, de Ancos B, Sánchez-Vega R, Sánchez-Moreno C, Cano MP, Elez-Martínez P, et al. Food matrix and processing influence on carotenoid bioaccessibility and lipophilic antioxidant activity of fruit juice-based beverages. Food & Function. 2016; 7: 380–389. https://doi.org/10.1039/c5fo01060h
[49] Bohn T, Desmarchelier C, Dragsted LO, Nielsen CS, Stahl W, Rühl R, et al. Host-related factors explaining interindividual variability of carotenoid bioavailability and tissue concentrations in humans. Molecular Nutrition & Food Research. 2017; 61: 1600685. https://doi.org/10.1002/mnfr.201600685
[50] Borel P, Moussa M, Reboul E, Lyan B, Defoort C, Vincent-Baudry S, et al. Human plasma levels of vitamin E and carotenoids are associated with genetic polymorphisms in genes involved in lipid metabolism. The Journal of Nutrition. 2007; 137: 2653–2659. https://doi.org/10.1093/jn/137.12.2653
[51] Hailili G, Huang L, Shen J, Zheng Y, Yuan C. Dietary Carotenoids Intake and Gut Microbiome Signatures in Chinese Older Adults. Current Developments in Nutrition. 2025; 9: 106106. https://doi.org/10.1016/j.cdnut.2025.106106
[52] Mehta S, Huey SL, McDonald D, Knight R, Finkelstein JL. Nutritional Interventions and the Gut Microbiome in Children. Annual Review of Nutrition. 2021; 41: 479–510. https://doi.org/10.1146/annurev-nutr-021020-025755
[53] Valdes AM, Louca P, Visconti A, Asnicar F, Bermingham K, Nogal A, et al. Vitamin A carotenoids, but not retinoids, mediate the impact of a healthy diet on gut microbial diversity. BMC Medicine. 2024; 22: 321. https://doi.org/10.1186/s12916-024-03543-4
[54] Aziz E, Batool R, Akhtar W, Rehman S, Shahzad T, Malik A, et al. Xanthophyll: Health benefits and therapeutic insights. Life Sciences. 2020; 240: 117104. https://doi.org/10.1016/j.lfs.2019.117104
[55] Hirata N, Ichimaru R, Tominari T, Matsumoto C, Watanabe K, Taniguchi K, et al. Beta-Cryptoxanthin Inhibits Lipopolysaccharide-Induced Osteoclast Differentiation and Bone Resorption via the Suppression of Inhibitor of NF-κB Kinase Activity. Nutrients. 2019; 11: 368. https://doi.org/10.3390/nu11020368
[56] Matsumoto C, Ashida N, Yokoyama S, Tominari T, Hirata M, Ogawa K, et al. The protective effects of β-cryptoxanthin on inflammatory bone resorption in a mouse experimental model of periodontitis. Bioscience, Biotechnology, and Biochemistry. 2013; 77: 860–862. https://doi.org/10.1271/bbb.120791
[57] Yamaguchi M. Role of carotenoid β-cryptoxanthin in bone homeostasis. Journal of Biomedical Science. 2012; 19: 36. https://doi.org/10.1186/1423-0127-19-36
[58] Yamaguchi M, Igarashi A, Uchiyama S, Morita S, Sugawara K, Sumida T. Prolonged intake of juice (Citrus unshiu) reinforced with β-crypthoxanthin has an effect on circulating bone biochemical markers in normal individuals. Journal of Health Science. 2004; 50: 619–624. https://doi.org/10.1248/jhs.50.619
[59] Uchiyama S, Sumida T, Yamaguchi M. Oral administration of beta-cryptoxanthin induces anabolic effects on bone components in the femoral tissues of rats in vivo. Biological & Pharmaceutical Bulletin. 2004; 27: 232–235. https://doi.org/10.1248/bpb.27.232
[60] Nishigaki M, Yamamoto T, Ichioka H, Honjo KI, Yamamoto K, Oseko F, et al. β-cryptoxanthin regulates bone resorption related-cytokine production in human periodontal ligament cells. Archives of Oral Biology. 2013; 58: 880–886. https://doi.org/10.1016/j.archoralbio.2013.01.005
[61] Kim SJ, Anh NH, Diem NC, Park S, Cho YH, Long NP, et al. Effects of β-Cryptoxanthin on Improvement in Osteoporosis Risk: A Systematic Review and Meta-Analysis of Observational Studies. Foods (Basel, Switzerland). 2021; 10: 296. https://doi.org/10.3390/foods10020296
[62] Lu Y, Yang Z, Duan J, Li W, Tan W, Li Y, et al. Associations of serum vitamins, carotenoids, and retinyl esters with risk of hip and spine fractures. Nutricion Hospitalaria. 2025; 42: 1016–1030. https://doi.org/10.20960/nh.05938
[63] Hayhoe RPG, Lentjes MAH, Mulligan AA, Luben RN, Khaw KT, Welch AA. Carotenoid dietary intakes and plasma concentrations are associated with heel bone ultrasound attenuation and osteoporotic fracture risk in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk cohort. The British Journal of Nutrition. 2017; 117: 1439–1453. https://doi.org/10.1017/S0007114517001180
[64] Granado-Lorencio F, Lagarda MJ, Garcia-López FJ, Sánchez-Siles LM, Blanco-Navarro I, Alegría A, et al. Effect of β-cryptoxanthin plus phytosterols on cardiovascular risk and bone turnover markers in post-menopausal women: a randomized crossover trial. Nutrition, Metabolism, and Cardiovascular Diseases : NMCD. 2014; 24: 1090–1096. https://doi.org/10.1016/j.numecd.2014.04.013
[65] Michaud DS, Spiegelman D, Clinton SK, Rimm EB, Willett WC, Giovannucci EL. Fruit and vegetable intake and incidence of bladder cancer in a male prospective cohort. Journal of the National Cancer Institute. 1999; 91: 605–613. https://doi.org/10.1093/jnci/91.7.605
[66] Holick CN, De Vivo I, Feskanich D, Giovannucci E, Stampfer M, Michaud DS. Intake of fruits and vegetables, carotenoids, folate, and vitamins A, C, E and risk of bladder cancer among women (United States). Cancer Causes & Control : CCC. 2005; 16: 1135–1145. https://doi.org/10.1007/s10552-005-0337-z
[67] Brinkman MT, Karagas MR, Zens MS, Schned A, Reulen RC, Zeegers MP. Minerals and vitamins and the risk of bladder cancer: results from the New Hampshire Study. Cancer Causes & Control : CCC. 2010; 21: 609–619. https://doi.org/10.1007/s10552-009-9490-0
[68] Castelao JE, Yuan JM, Gago-Dominguez M, Skipper PL, Tannenbaum SR, Chan KK, et al. Carotenoids/vitamin C and smoking-related bladder cancer. International Journal of Cancer. 2004; 110: 417–423. https://doi.org/10.1002/ijc.20104
[69] Michaud DS, Pietinen P, Taylor PR, Virtanen M, Virtamo J, Albanes D. Intakes of fruits and vegetables, carotenoids and vitamins A, E, C in relation to the risk of bladder cancer in the ATBC cohort study. British Journal of Cancer. 2002; 87: 960–965. https://doi.org/10.1038/sj.bjc.6600604
[70] Park SY, Ollberding NJ, Woolcott CG, Wilkens LR, Henderson BE, Kolonel LN. Fruit and vegetable intakes are associated with lower risk of bladder cancer among women in the Multiethnic Cohort Study. The Journal of Nutrition. 2013; 143: 1283–1292. https://doi.org/10.3945/jn.113.174920
[71] De Stefani E, Boffetta P, Brennan P, Deneo-Pellegrini H, Carzoglio JC, Ronco A, et al. Dietary carotenoids and risk of gastric cancer: a case-control study in Uruguay. European Journal of Cancer Prevention : the Official Journal of the European Cancer Prevention Organisation (ECP). 2000; 9: 329–334. https://doi.org/10.1097/00008469-200010000-00007
[72] Lissowska J, Gail MH, Pee D, Groves FD, Sobin LH, Nasierowska-Guttmejer A, et al. Diet and stomach cancer risk in Warsaw, Poland. Nutrition and Cancer. 2004; 48: 149–159. https://doi.org/10.1207/s15327914nc4802_4
[73] Pelucchi C, Tramacere I, Bertuccio P, Tavani A, Negri E, La Vecchia C. Dietary intake of selected micronutrients and gastric cancer risk: an Italian case-control study. Annals of Oncology :

Official Journal of the European Society for Medical Oncology. 2009; 20: 160–165. https://doi.org/10.1093/annonc/mdn536
[74] Kim JH, Lee J, Choi IJ, Kim YI, Kwon O, Kim H, et al. Dietary Carotenoids Intake and the Risk of Gastric Cancer: A Case-Control Study in Korea. Nutrients. 2018; 10: 1031. https://doi.org/10.3390/nu10081031
[75] Botterweck AA, van den Brandt PA, Goldbohm RA. Vitamins, carotenoids, dietary fiber, and the risk of gastric carcinoma: results from a prospective study after 6.3 years of follow-up. Cancer. 2000; 88: 737–748.
[76] Larsson SC, Bergkvist L, Näslund I, Rutegård J, Wolk A. Vitamin A, retinol, and carotenoids and the risk of gastric cancer: a prospective cohort study. The American Journal of Clinical Nutrition. 2007; 85: 497–503. https://doi.org/10.1093/ajcn/85.2.497
[77] Chen H, Tucker KL, Graubard BI, Heineman EF, Markin RS, Potischman NA, et al. Nutrient intakes and adenocarcinoma of the esophagus and distal stomach. Nutrition and Cancer. 2002; 42: 33–40. https://doi.org/10.1207/S15327914NC421_5
[78] Sengngam K, Hoc TH, Hang DV, Tran Ngoan L. Trans-Lycopene and β-Cryptoxanthin Intake and Stomach Cancer in Vietnamese Men: A Pilot Case-Control Study. Asian Pacific Journal of Cancer Prevention : APJCP. 2022; 23: 861–865. https://doi.org/10.31557/APJCP.2022.23.3.861
[79] Slattery ML, Benson J, Curtin K, Ma KN, Schaeffer D, Potter JD. Carotenoids and colon cancer. The American Journal of Clinical Nutrition. 2000; 71: 575–582. https://doi.org/10.1093/ajcn/71.2.575
[80] Nkondjock A, Ghadirian P. Dietary carotenoids and risk of colon cancer: case-control study. International Journal of Cancer. 2004; 110: 110–116. https://doi.org/10.1002/ijc.20066
[81] Park SY, Nomura AMY, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN. Carotenoid intake and colorectal cancer risk: the multiethnic cohort study. Journal of Epidemiology. 2009; 19: 63–71. https://doi.org/10.2188/jea.je20080078
[82] Lu MS, Fang YJ, Chen YM, Luo WP, Pan ZZ, Zhong X, et al. Higher intake of carotenoid is associated with a lower risk of colorectal cancer in Chinese adults: a case-control study. European Journal of Nutrition. 2015; 54: 619–628. https://doi.org/10.1007/s00394-014-0743-7
[83] Zhang S, Hunter DJ, Forman MR, Rosner BA, Speizer FE, Colditz GA, et al. Dietary carotenoids and vitamins A, C, and E and risk of breast cancer. Journal of the National Cancer Institute. 1999; 91: 547–556. https://doi.org/10.1093/jnci/91.6.547
[84] Cui Y, Shikany JM, Liu S, Shagufta Y, Rohan TE. Selected antioxidants and risk of hormone receptor-defined invasive breast cancers among postmenopausal women in the Women's Health Initiative Observational Study. The American Journal of Clinical Nutrition. 2008; 87: 1009–1018. https://doi.org/10.1093/ajcn/87.4.1009
[85] Terry P, Jain M, Miller AB, Howe GR, Rohan TE. Dietary carotenoids and risk of breast cancer. The American Journal of Clinical Nutrition. 2002; 76: 883–888. https://doi.org/10.1093/ajcn/76.4.883
[86] Larsson SC, Bergkvist L, Wolk A. Dietary carotenoids and risk of hormone receptor-defined breast cancer in a prospective cohort of Swedish women. European Journal of Cancer (Oxford, England : 1990). 2010; 46: 1079–1085. https://doi.org/10.1016/j.ejca.2010.01.004
[87] Fink BN, Gaudet MM, Britton JA, Abrahamson PE, Teitelbaum SL, Jacobson J, et al. Fruits, vegetables, and micronutrient intake in relation to breast cancer survival. Breast Cancer Research and Treatment. 2006; 98: 199–208. https://doi.org/10.1007/s10549-005-9150-3
[88] Holmes MD, Stampfer MJ, Colditz GA, Rosner B, Hunter DJ, Willett WC. Dietary factors and the survival of women with breast carcinoma. Cancer. 1999; 86: 826–835. https://doi.org/10.1002/(sici)1097-0142(19990901)86:5<826::aid-cncr19>3.0.co;2-0
[89] Beasley JM, Newcomb PA, Trentham-Dietz A, Hampton JM, Bersch AJ, Passarelli MN, et al. Post-diagnosis dietary factors and survival after invasive breast cancer. Breast Cancer Research and Treatment. 2011; 128: 229–236. https://doi.org/10.1007/s10549-010-1323-z
[90] McEligot AJ, Largent J, Ziogas A, Peel D, Anton-Culver H. Dietary fat, fiber, vegetable, and micronutrients are associated with overall survival in postmenopausal women diagnosed with breast cancer. Nutrition and Cancer. 2006; 55: 132–140. https://doi.org/10.1207/s15327914nc5502_3
[91] Zhu G, Li Z, Tang L, Shen M, Zhou Z, Wei Y, et al. Associations of Dietary Intakes with Gynecological Cancers: Findings from a Cross-Sectional Study. Nutrients. 2022; 14: 5026. https://doi.org/10.3390/nu14235026
[92] Van Hoang D, Pham NM, Lee AH, Tran DN, Binns CW. Dietary Carotenoid Intakes and Prostate Cancer Risk: A Case-Control Study from Vietnam. Nutrients. 2018; 10: 70. https://doi.org/10.3390/nu10010070
[93] Peterson CE, Sedjo RL, Davis FG, Beam CA, Giuliano AR. Combined antioxidant carotenoids and the risk of persistent human papillomavirus infection. Nutrition and Cancer. 2010; 62: 728–733. https://doi.org/10.1080/01635581003693074
[94] Bravi F, Bosetti C, Filomeno M, Levi F, Garavello W, Galimberti S, et al. Foods, nutrients and the risk of oral and pharyngeal cancer. British Journal of Cancer. 2013; 109: 2904–2910. https://doi.org/10.1038/bjc.2013.667
[95] De Stefani E, Ronco A, Mendilaharsu M, Deneo-Pellegrini H. Diet and risk of cancer of the upper aerodigestive tract–II. Nutrients. Oral Oncology. 1999; 35: 22–26. https://doi.org/10.1016/s1368-8375(98)00061-x
[96] Kim J, Park MK, Li WQ, Qureshi AA, Cho E. Association of Vitamin A Intake With Cutaneous Squamous Cell Carcinoma Risk in the United States. JAMA Dermatology. 2019; 155: 1260–1268. https://doi.org/10.1001/jamadermatol.2019.1937
[97] Franceschi S, Bidoli E, Negri E, Zambon P, Talamini R, Ruol A, et al. Role of macronutrients, vitamins and minerals in the aetiology of squamous-cell carcinoma of the oesophagus. International Journal of Cancer. 2000; 86: 626–631. https://doi.org/10.1002/(sici)1097-0215(20000601)86:5<626::aid-ijc4>3.0.co;2-y
[98] Bidoli E, Bosetti C, La Vecchia C, Levi F, Parpinel M, Talamini R, et al. Micronutrients and laryngeal cancer risk in Italy and Switzerland: a case-control study. Cancer Causes & Control : CCC. 2003; 14: 477–484. https://doi.org/10.1023/a:1024991618398
[99] De Stefani E, Ronco AL, Boffetta P, Deneo-Pellegrini H, Acosta G, Correa P, et al. Nutrient intake and risk of squamous cell carcinoma of the esophagus: a case-control study in Uruguay. Nutrition and Cancer. 2006; 56: 149–157. https://doi.org/10.1207/s15327914nc5602_5
[100] Shareck M, Rousseau MC, Koushik A, Siemiatycki J, Parent ME. Inverse Association between Dietary Intake of Selected Carotenoids and Vitamin C and Risk of Lung Cancer. Frontiers in Oncology. 2017; 7: 23. https://doi.org/10.3389/fonc.2017.00023
[101] Polesel J, Talamini R, Montella M, Maso LD, Crovatto M, Parpinel M, et al. Nutrients intake and the risk of hepatocellular carcinoma in Italy. European Journal of Cancer (Oxford, England : 1990). 2007; 43: 2381–2387. https://doi.org/10.1016/j.ejca.2007.07.012
[102] Bravi F, Polesel J, Bosetti C, Talamini R, Negri E, Dal Maso L, et al. Dietary intake of selected micronutrients and the risk of pancreatic cancer: an Italian case-control study. Annals of

Oncology : Official Journal of the European Society for Medical Oncology. 2011; 22: 202–206. https://doi.org/10.1093/annonc/mdq302

[103] Jansen RJ, Robinson DP, Stolzenberg-Solomon RZ, Bamlet WR, de Andrade M, Oberg AL, et al. Nutrients from fruit and vegetable consumption reduce the risk of pancreatic cancer. Journal of Gastrointestinal Cancer. 2013; 44: 152–161. https://doi.org/10.1007/s12029-012-9441-y

[104] Heinen MM, Verhage BAJ, Goldbohm RA, van den Brandt PA. Intake of vegetables, fruits, carotenoids and vitamins C and E and pancreatic cancer risk in The Netherlands Cohort Study. International Journal of Cancer. 2012; 130: 147–158. https://doi.org/10.1002/ijc.25989

[105] Schantz SP, Zhang ZF, Spitz MS, Sun M, Hsu TC. Genetic susceptibility to head and neck cancer: interaction between nutrition and mutagen sensitivity. The Laryngoscope. 1997; 107: 765–781. https://doi.org/10.1097/00005537-199706000-00011

[106] de Munter L, Maasland DHE, van den Brandt PA, Kremer B, Schouten LJ. Vitamin and carotenoid intake and risk of head-neck cancer subtypes in the Netherlands Cohort Study. The American Journal of Clinical Nutrition. 2015; 102: 420–432. https://doi.org/10.3945/ajcn.114.106096

[107] Pouchieu C, Galan P, Ducros V, Latino-Martel P, Hercberg S, Touvier M. Plasma carotenoids and retinol and overall and breast cancer risk: a nested case-control study. Nutrition and Cancer. 2014; 66: 980–988. https://doi.org/10.1080/01635581.2014.936952

[108] Toniolo P, Van Kappel AL, Akhmedkhanov A, Ferrari P, Kato I, Shore RE, et al. Serum carotenoids and breast cancer. American Journal of Epidemiology. 2001; 153: 1142–1147. https://doi.org/10.1093/aje/153.12.1142

[109] Wang Y, Gapstur SM, Gaudet MM, Furtado JD, Campos H, McCullough ML. Plasma carotenoids and breast cancer risk in the Cancer Prevention Study II Nutrition Cohort. Cancer Causes & Control : CCC. 2015; 26: 1233–1244. https://doi.org/10.1007/s10552-015-0614-4

[110] Bakker MF, Peeters PH, Klaasen VM, Bueno-de-Mesquita HB, Jansen EH, Ros MM, et al. Plasma carotenoids, vitamin C, tocopherols, and retinol and the risk of breast cancer in the European Prospective Investigation into Cancer and Nutrition cohort. The American Journal of Clinical Nutrition. 2016; 103: 454–464. https://doi.org/10.3945/ajcn.114.101659

[111] Dorgan JF, Sowell A, Swanson CA, Potischman N, Miller R, Schussler N, et al. Relationships of serum carotenoids, retinol, alpha-tocopherol, and selenium with breast cancer risk: results from a prospective study in Columbia, Missouri (United States). Cancer Causes & Control : CCC. 1998; 9: 89–97. https://doi.org/10.1023/a:1008857521992

[112] Sato R, Helzlsouer KJ, Alberg AJ, Hoffman SC, Norkus EP, Comstock GW. Prospective study of carotenoids, tocopherols, and retinoid concentrations and the risk of breast cancer. Cancer Epidemiology, Biomarkers & Prevention : a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 2002; 11: 451–457.

[113] Sesso HD, Buring JE, Zhang SM, Norkus EP, Gaziano JM. Dietary and plasma lycopene and the risk of breast cancer. Cancer Epidemiology, Biomarkers & Prevention : a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 2005; 14: 1074–1081. https://doi.org/10.1158/1055-9965.EPI-04-0683

[114] Epplein M, Shvetsov YB, Wilkens LR, Franke AA, Cooney RV, Le Marchand L, et al. Plasma carotenoids, retinol, and tocopherols and postmenopausal breast cancer risk in the Multiethnic Cohort Study: a nested case-control study. Breast Cancer Research : BCR. 2009; 11: R49. https://doi.org/10.1186/bcr2338

[115] Tamimi RM, Hankinson SE, Campos H, Spiegelman D, Zhang S, Colditz GA, et al. Plasma carotenoids, retinol, and tocopherols and risk of breast cancer. American Journal of Epidemiology. 2005; 161: 153–160. https://doi.org/10.1093/aje/kwi030

[116] Eliassen AH, Liao X, Rosner B, Tamimi RM, Tworoger SS, Hankinson SE. Plasma carotenoids and risk of breast cancer over 20 y of follow-up. The American Journal of Clinical Nutrition. 2015; 101: 1197–1205. https://doi.org/10.3945/ajcn.114.105080

[117] Kabat GC, Kim M, Adams-Campbell LL, Caan BJ, Chlebowski RT, Neuhouser ML, et al. Longitudinal study of serum carotenoid, retinol, and tocopherol concentrations in relation to breast cancer risk among postmenopausal women. The American Journal of Clinical Nutrition. 2009; 90: 162–169. https://doi.org/10.3945/ajcn.2009.27568

[118] Persson C, Sasazuki S, Inoue M, Kurahashi N, Iwasaki M, Miura T, et al. Plasma levels of carotenoids, retinol and tocopherol and the risk of gastric cancer in Japan: a nested case-control study. Carcinogenesis. 2008; 29: 1042–1048. https://doi.org/10.1093/carcin/bgn072

[119] Yuan JM, Ross RK, Gao YT, Qu YH, Chu XD, Yu MC. Prediagnostic levels of serum micronutrients in relation to risk of gastric cancer in Shanghai, China. Cancer Epidemiology, Biomarkers & Prevention : a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 2004; 13: 1772–1780.

[120] Ito Y, Kurata M, Hioki R, Suzuki K, Ochiai J, Aoki K. Cancer mortality and serum levels of carotenoids, retinol, and tocopherol: a population-based follow-up study of inhabitants of a rural area of Japan. Asian Pacific Journal of Cancer Prevention : APJCP. 2005; 6: 10–15.

[121] Abnet CC, Qiao YL, Dawsey SM, Buckman DW, Yang CS, Blot WJ, et al. Prospective study of serum retinol, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin and esophageal and gastric cancers in China. Cancer Causes & Control : CCC. 2003; 14: 645–655. https://doi.org/10.1023/a:1025619608851

[122] Jenab M, Riboli E, Ferrari P, Friesen M, Sabate J, Norat T, et al. Plasma and dietary carotenoid, retinol and tocopherol levels and the risk of gastric adenocarcinomas in the European prospective investigation into cancer and nutrition. British Journal of Cancer. 2006; 95: 406–415. https://doi.org/10.1038/sj.bjc.6603266

[123] Kabat GC, Kim MY, Sarto GE, Shikany JM, Rohan TE. Repeated measurements of serum carotenoid, retinol and tocopherol levels in relation to colorectal cancer risk in the Women's Health Initiative. European Journal of Clinical Nutrition. 2012; 66: 549–554. https://doi.org/10.1038/ejcn.2011.207

[124] Huang J, Lu MS, Fang YJ, Xu M, Huang WQ, Pan ZZ, et al. Serum carotenoids and colorectal cancer risk: A case-control study in Guangdong, China. Molecular Nutrition & Food Research. 2017; 61: 10.1002/mnfr.201700267. https://doi.org/10.1002/mnfr.201700267

[125] Epplein M, Franke AA, Cooney RV, Morris JS, Wilkens LR, Goodman MT, et al. Association of plasma micronutrient levels and urinary isoprostane with risk of lung cancer: the multiethnic cohort study. Cancer Epidemiology, Biomarkers & Prevention : a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 2009; 18: 1962–1970. https://doi.org/10.1158/1055-9965.EPI-09-0003

[126] Ito Y, Wakai K, Suzuki K, Ozasa K, Watanabe Y, Seki N, et al. Lung cancer mortality and serum levels of carotenoids, retinol, tocopherols, and folic acid in men and women: a case-control study nested in the JACC Study. Journal of Epidemiology. 2005; 15 Suppl 2: S140–S149. https://doi.org/10.2188/jea.15.s140

[127] Ratnasinghe D, Forman MR, Tangrea JA, Qiao Y, Yao SX, Gunter EW, et al. Serum carotenoids are associated with increased lung cancer risk among alcohol drinkers, but not among

non-drinkers in a cohort of tin miners. Alcohol and Alcoholism (Oxford, Oxfordshire). 2000; 35: 355–360. https://doi.org/10.1093/alcalc/35.4.355

[128] Min KB, Min JY. Serum carotenoid levels and risk of lung cancer death in US adults. Cancer Science. 2014; 105: 736–743. https://doi.org/10.1111/cas.12405

[129] Hung RJ, Zhang ZF, Rao JY, Pantuck A, Reuter VE, Heber D, et al. Protective effects of plasma carotenoids on the risk of bladder cancer. The Journal of Urology. 2006; 176: 1192–1197. https://doi.org/10.1016/j.juro.2006.04.030

[130] Nomura AMY, Lee J, Stemmermann GN, Franke AA. Serum vitamins and the subsequent risk of bladder cancer. The Journal of Urology. 2003; 170: 1146–1150. https://doi.org/10.1097/01.ju.0000086040.24795.ad

[131] Li Z, Yu C, Hao J, Shu Y, Zhang J, Zhao K, et al. Identifying environmental factors and biological metrics associated with cancer prevalence and mortality: An environment-wide association study. Cancer Epidemiology. 2025; 97: 102828. https://doi.org/10.1016/j.canep.2025.102828

[132] Guida F, Tan VY, Corbin LJ, Smith-Byrne K, Alcala K, Langenberg C, et al. The blood metabolome of incident kidney cancer: A case-control study nested within the MetKid consortium. PLoS Medicine. 2021; 18: e1003786. https://doi.org/10.1371/journal.pmed.1003786

[133] Goodman MT, Shvetsov YB, McDuffie K, Wilkens LR, Zhu X, Franke AA, et al. Hawaii cohort study of serum micronutrient concentrations and clearance of incident oncogenic human papillomavirus infection of the cervix. Cancer Research. 2007; 67: 5987–5996. https://doi.org/10.1158/0008-5472.CAN-07-0313

[134] Yuan JM, Gao YT, Ong CN, Ross RK, Yu MC. Prediagnostic level of serum retinol in relation to reduced risk of hepatocellular carcinoma. Journal of the National Cancer Institute. 2006; 98: 482–490. https://doi.org/10.1093/jnci/djj104

[135] Graff RE, Judson G, Ahearn TU, Fiorentino M, Loda M, Giovannucci EL, et al. Circulating Antioxidant Levels and Risk of Prostate Cancer by TMPRSS2:ERG. The Prostate. 2017; 77: 647–653. https://doi.org/10.1002/pros.23312

[136] Ros MM, Bueno-de-Mesquita HB, Kampman E, Aben KKH, Büchner FL, Jansen EHJM, et al. Plasma carotenoids and vitamin C concentrations and risk of urothelial cell carcinoma in the European Prospective Investigation into Cancer and Nutrition. The American Journal of Clinical Nutrition. 2012; 96: 902–910. https://doi.org/10.3945/ajcn.111.032920

[137] Pu L, Zhang R, Wang X, Zhao T, Sun H, Han L. Associations of Serum Biomarkers of Fruit and Vegetable Intake With the Risk of Cause-Specific Mortality and All-Cause Mortality: A National Prospective Cohort Study. Frontiers in Nutrition. 2022; 9: 874943. https://doi.org/10.3389/fnut.2022.874943

[138] Shardell MD, Alley DE, Hicks GE, El-Kamary SS, Miller RR, Semba RD, et al. Low-serum carotenoid concentrations and carotenoid interactions predict mortality in US adults: the Third National Health and Nutrition Examination Survey. Nutrition Research (New York, N.Y.). 2011; 31: 178–189. https://doi.org/10.1016/j.nutres.2011.03.003

[139] Bates CJ, Hamer M, Mishra GD. Redox-modulatory vitamins and minerals that prospectively predict mortality in older British people: the National Diet and Nutrition Survey of people aged 65 years and over. The British Journal of Nutrition. 2011; 105: 123–132. https://doi.org/10.1017/S0007114510003053

[140] Ito Y, Suzuki K, Ishii J, Hishida H, Tamakoshi A, Hamajima N, et al. A population-based follow-up study on mortality from cancer or cardiovascular disease and serum carotenoids, retinol and tocopherols in Japanese inhabitants. Asian Pacific Journal of Cancer Prevention : APJCP. 2006; 7: 533–546.

[141] Fujii R, Suzuki K, Yamada H, Kawado M, Hashimoto S, Tsuboi Y, et al. Association between serum carotenoids and premature mortality in a population-based case-control study. Nagoya Journal of Medical Science. 2022; 84: 607–620. https://doi.org/10.18999/nagjms.84.3.607