

The Role of Carotenoids in Human Health

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■ ABSTRACT

Dietary carotenoids are thought to provide health benefits in decreasing the risk of disease, particularly certain cancers and eye disease. The carotenoids that have been most studied in this regard are β -carotene, lycopene, lutein, and zeaxanthin. In part, the beneficial effects of carotenoids are thought to be due to their role as antioxidants. β -Carotene may have added benefits due its ability to be converted to vitamin A. Furthermore, lutein and zeaxanthin may be protective in eye disease because they absorb damaging blue light that enters the eye. Food sources of these compounds include a variety of fruits and vegetables, although the primary sources of lycopene are tomato and tomato products. Additionally, egg yolk is a highly bioavailable source of lutein and zeaxanthin. These carotenoids are available in supplement form. However, intervention trials with large doses of β -carotene found an adverse effect on the incidence of lung cancer in smokers and workers exposed to asbestos. Until the efficacy and safety of taking supplements containing these nutrients can be determined, current dietary recommendations of diets high in fruits and vegetables are advised. *Nutr Clin Care*. 2002;5:56–65 ■

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INTRODUCTION

Carotenoids are a family of compounds of over 600 fat-soluble plant pigments and provide much of the color we see in nature. For example, carotenoids are responsible for the red in tomatoes and the or-

ange in carrots. Apart from their aesthetic role, carotenoids are considered to be beneficial in the prevention of a variety of major diseases, including certain cancers and eye disease. The beneficial effects of carotenoids are attributed to a small portion of the hundreds of carotenoids found in nature, given that only about 2 dozen are found in human blood and tissue, and only 2 in the eye. The carotenoids that have been most studied in this regard are β -carotene, lycopene, lutein, and zeaxanthin. β -Carotene and lycopene belong to a class of carotenoids called carotenes and are very fat soluble. Lutein and zeaxanthin belong to a class of carotenoids called xanthophylls. Because xanthophylls contain at least 1 hydroxyl group, they are more polar than carotenes. Thus, β -carotene and lycopene tend to be predominately in LDL and HDL in the circulation, whereas lutein and zeaxanthin are more evenly distributed among the lipoproteins.¹ In part, the protection by carotenoids is thought to be through their antioxidant activity. Lutein and zeaxanthin are thought to have an additional role of absorbing damaging blue light that enters the eye.

FOOD SOURCES AND DIETARY INTAKES OF CAROTENOIDS

The estimation of carotenoid intakes has been made possible through the publications of the qualitative and quantitative carotenoid content of commonly consumed foods.^{2–4}

β -Carotene

β -carotene is the most widely studied carotenoid and is one of the major carotenoids in our diet and

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in human blood and tissues.^{5,6} Major sources of dietary β -carotene include green leafy vegetables as well as orange and yellow fruits and vegetables (Table 1). However, the bioavailability of β -carotene from green leafy vegetables such as spinach is thought to be low.⁷ Factors other than food vehicle are thought to be important in the bioavailability of β -carotene. These include cooking, chopping, and the presence of dietary fat, all of which improve the bioavailability.^{8,9} Of the 50 different carotenoids that can be metabolized into vitamin A, β -carotene has the highest pro-vitamin A activity. Typical dietary intakes of β -carotene in the United States are 0.5 to 6.5 mg per day.¹⁰ However, intakes much higher than this are possible through over-the-counter supplements that are commonly available in health food stores in doses of 3 to 20 mg per capsule.

Lycopene

Dietary lycopene is derived predominately from tomatoes and tomato products. In the United States, more than 85% of lycopene consumed is from tomato products, although other dietary sources include dried apricots, guava, watermelon, papaya, and pink grapefruit (Table 2).^{2,3,4} Similar to the effect on β -carotene bioavailability, heating tomato was found to be associated with an increase in lycopene absorption when compared to the absorption for unprocessed tomato juice.¹¹ Also, the lycopene bioavailability was greater from a single dose of tomato paste than it was from an equal lycopene dose from fresh tomatoes.¹² Interestingly, these studies support the findings of Giovannucci et al¹³

that the association between consumption of various tomato products and the risk of prostate cancer depends on the bioavailability of lycopene. That is, an association was found with the consumption of tomato paste or sauce and not with consumption of minimally processed tomato juice. Typical dietary intakes of lycopene in the United States are about 2 to 5 mg per day, which probably reflects a diet high in tomato and tomato products, eg, pizza.¹⁰ Supplemental lycopene is also available, usually in amounts of 5 to 10 mg per capsule.

Lutein and Zeaxanthin

The 2 foods that were found to have the highest amount of lutein and zeaxanthin are spinach and kale (Table 3).²⁻⁴ Other major sources include broccoli, peas, and Brussels sprouts. Another good source of lutein and zeaxanthin to consider is egg yolk. Though the values are relatively low in eggs, recent data suggest that lutein and zeaxanthin from this food source are highly bioavailable.^{14,15} Data on the lutein content of foods include zeaxanthin, ie, lutein plus zeaxanthin, making examination of specific effects of dietary lutein difficult. However, in terms of food sources, human metabolism, and tissue storage, lutein and zeaxanthin are similar. Intakes of lutein and zeaxanthin in the United States are generally lower than that of β -carotene or lycopene, but levels of approximately 3 mg per day can be easily achieved with a high fruit and vegetable diet.¹⁰ Although lutein and zeaxanthin are considered major carotenoids in the U.S. diet, data from the 1987 and 1992 National Health Interview Surveys suggest that there was a decline in lutein in-

Table 1. β -Carotene Content of Foods

Food	Content (mg/100g wet wt)*
Apricots, dried	17.6
Apricots, raw	3.5
Cantaloupe, raw	3.0
Carrots, cooked	9.8
Carrots, raw	7.9
Kale	4.7
Pepper, red	2.2
Pumpkin	3.1
Spinach, raw	4.1
Spinach, cooked	5.5
Sweet potato, cooked	8.8
Winter squash, cooked	2.4

*Edible portion.
Adapted from Mangels et al, 1993.

Table 2. Lycopene Content of Foods

Food	Content (mg/100g wet wt)*
Apricot, dried	0.9
Grapefruit, raw, pink	3.4
Guava, raw	5.4
Guava juice	3.3
Sun-dried tomato in oil	46.5
Tomato, cooked	3.7
Tomato, raw	3.1
Tomato juice	8.6
Tomato paste	6.5
Tomato sauce	6.2
Tomato soup, condensed	8.0
Watermelon, fresh	4.1

*Edible portion.
Adapted from Mangels et al, 1993.

Table 3. Lutein/Zeaxanthin Content of Foods

Food	Content (mg/100g wet wt)*
Broccoli, cooked	2.2
Brussels sprouts, cooked	1.3
Cabbage, white, raw	0.3
Corn, sweet, cooked	1.8
Egg yolk, med**	0.3
Kale, cooked	15.8
Lettuce, raw	2.6
Peas, green, cooked	1.4
Spinach, cooked	7.1
Spinach, raw	11.9

*Edible portion; **Handelman et al 1999; Surai et al 2000.
Adapted from Mangels et al, 1993.

take (from dark green leafy vegetables).¹⁶ Currently, there are a variety of supplement products available in health food stores that contain lutein in amounts of 6 to 25 mg per capsule. At this point, lutein is found in only one multivitamin product in much smaller amounts (0.25 mg/capsule).

CAROTENOIDS AND DISEASE RISK

Although epidemiological studies cannot provide evidence of causal relationship, they have proven useful in evaluating the possible protective effects of foods or food components in disease prevention. Observational epidemiologic studies have been very consistent in showing that people who consume higher dietary levels of fruits and vegetables have a lower risk of certain types of cancer. The results of 10 of 17 case-control studies show that a high intake of fruits and vegetables that are rich in carotenoids has been associated with decreased risk of cancer at a number of common sites. This association appears to be most consistent for lung and stomach cancer.^{2,17} Given the variability in study design and statistical analysis among the epidemiologic studies, the consistency of the relationship between fruit and vegetable intake and lung-cancer risk strongly suggests a real effect of fruit and vegetables on cancer prevention. It has been suggested that carotenoids are the chemopreventive agents in fruits and vegetables. There are several mechanisms by which a carotenoid can function in cancer prevention. As a pro-vitamin A, a carotenoid would have an effect on cellular differentiation and proliferation.¹⁸ Moreover, the antioxidant function could prevent free radical-induced damage to cellular DNA and other molecules.¹⁹ Immunomodula-

tory effects could enhance immune surveillance in tumorigenesis, and enhanced cell-cell communication would restrict clonal expansion of initiated cells.^{20,21}

β-Carotene

The epidemiologic observations, along with what is known about carotenoid function, have led to further study of the effect of β-carotene on cancer risk. Although other types of cancers have been evaluated, the relationship between β-carotene and lung cancer has been most studied and the data have been more consistent.²² Evidence for β-carotene as the chemoprotective agent in fruits and vegetables comes from prospective epidemiologic studies in which 11 of 15 have demonstrated a significant inverse relation of β-carotene intake and/or plasma level and risk of lung cancer (Table 4). Based on this kind of evidence, long-term, large, randomized intervention trials were designed to test the efficacy of high doses of β-carotene (20–30 mg/d) in the prevention of cancer. Surprisingly, the results from 2 trials provide possible evidence of harm from β-carotene supplements in relation to cancer among high-risk individuals such as smokers and asbestos workers and no effect (neither beneficial nor detrimental) in a generally well-nourished population.^{23–25} However, in the Linxian (Chinese) Cancer Prevention Study, it was found that supplementation with β-carotene, vitamin E, and selenium led to a significant reduction in total mortality (9%), especially from cancer (13%), particularly stomach cancer (21%). The positive results of the Chinese study may reflect the correction of a nutrient deficiency in this study population. Therefore, the usefulness of high doses of β-carotene in high-risk individuals needs to be reevaluated. It should be noted that, like the earlier epidemiologic studies that led to these intervention studies, there are recent studies that report a similar relationship between diet and/or blood β-carotene levels and cancer prevention.^{17,22,26–29} It is probable that β-carotene is serving as a marker of increased fruit and vegetable intake and therefore of all components that have cancer-prevention potential, eg, vitamin C, folic acid, and other carotenoids.

In a recent study, it was reported that a high-dose combination of antioxidants (including β-carotene and also vitamins C and E, and zinc) had no

Table 4. Prospective Studies on Dietary Intake or Plasma Levels of Carotenoids and Lung Cancer

Exposure Measured	Association	Relative Risk (high vs low)	Population	Reference
Carotenoid intake	decrease	0.14	men, U.S.	Shekell, 1981
Green salad & fruit	decrease	0.56	men & women, China	Long-de, 1885
Green, yellow vegetables	decrease	0.79 (men); 1.35 (women)	men & women, Japan	Hirayama, 1986
Carotenoid intake	n.s.	0.68	men & women, The Netherlands	Kromhout 1987
Carotenoid intake	decrease	0.72 (men); 0.67 (women)	men & women, U.S.	Paganini-Hill, 1987
Carotenoid intake	decrease	0.40 (non smokers) 0.93 (smokers)	Finland	Knekt, 1991
Fruit & green salad	decrease	0.26 (fruit) 0.65 (salad)	men & women California Adventists	Fraser, 1991
Plasma total carotene	n.s.		men & women, U.S.	Willett, 1984
Plasma β -carotene	decrease	0.43	men, U.S.	Connett, 1989
Plasma β -carotene	decrease	0.29	men, Japanese (Hawaii)	Nomura, 1985
Plasma β -carotene	decrease	0.41	men, U.K.	Wald, 1988
Plasma β -carotene	decrease	0.56	men & women, Swiss	Stahelin, 1991
Plasma β -carotene	n.s.	1.00	men & women, Finland	Knekt, 1990
Plasma β -carotene	decrease	0.45	men & women, U.S.	Comstock, 1991
Plasma β -carotene	decrease	0.33	men & women, U.S.	Orentreich, 1991

significant effect on the development or progression of cataract but significantly reduced the risk of age-related macular degeneration (AMD).³⁰ It was found that people at high risk for developing advanced stages of AMD (people with intermediate AMD or advanced AMD in one eye but not the other eye) lowered their risk by about 25% when treated with the high-dose combination. In the same high-risk group the nutrients reduced the risk of vision loss caused by advanced AMD by about 19%. For those subjects who had either no AMD or early AMD, the nutrients did not provide a measured benefit. Because single nutrients were not evaluated, specific effects could not be determined. However, it should be noted that β -carotene is not found in the lens or macula of the eye and, therefore, the result may be due to the other nutrients tested.^{31,32}

Lycopene

One of the earliest case-control studies examining the relationship between lycopene-rich foods and cancer risk reported that weekly tomato consumption was associated with a 40% reduction in risk for esophageal cancer.³³ Several studies have reported protective effects for diets rich in tomato products against gastric cancer, whereas others have found no relationship.³⁴⁻⁴⁰ A study of prospectively collected serum samples from a cohort was used to

compare serum micronutrients from those developing pancreatic cancer and matched controls.⁴¹ The greatest difference was observed for lycopene. However, because lycopene uptake and serum concentrations may be related to the digestibility of dietary lipids, diseases of the pancreas could significantly reduce absorption and perhaps confound such studies. In a single study examining the role of tomatoes, lycopene, and bladder-cancer risk, serum micronutrient profiles were quantitated, and only lycopene and selenium concentrations were found to be inversely related to risk.⁴² However, others have found no such relationship.⁴³⁻⁴⁵

Less consistent results have been observed for a relationship between estimated lycopene intake or serum lycopene concentrations and breast-cancer risk.^{46,47} A recent study of dietary intake interviews of 4,697 women in Finland showed no relationship between estimated intake of tomato products and breast-cancer risk.⁴⁸ However, a case-control study from Boston examined the relationship between breast adipose tissue lycopene concentrations and breast-cancer risk and an inverse association between lycopene and breast-cancer risk was observed.⁴⁹

In a study conducted in a cohort of Seventh Day Adventists, dietary and life-style factors were evaluated and related to subsequent risk of prostate cancer in a follow-up of 6 years. Multivariate analysis indicated that increasing age and previous prostate

problem were among the risk factors, whereas, unexpectedly, smoking and alcohol consumption were not. Among dietary factors, high tomato consumption of 5 or more per week was associated with a significantly decreased risk.⁵⁰ An inverse association between high intake of tomato products and prostate cancer risk was confirmed in an analysis of the U.S. Health Professionals Follow-up Study.¹³ A dietary frequency questionnaire was applied at baseline and related to the incidence of prostate cancer, which was assessed biennially. It was shown that lycopene intake but not the overall intake of fruits and vegetables was inversely related to prostate cancer risk. Among tomato-derived products, this association was strongest for tomato sauces, followed by tomatoes and pizza. No relationship was found for tomato juice. This might be explained by the low bioavailability of lycopene from unprocessed juice.¹¹ A summary of the epidemiologic studies evaluating lycopene and cancer risk is found in Table 5.

The reports of lycopene concentrations being relatively high in the prostate compared to other tissue suggests that this carotenoid may exert unique biological effects at this site that may be related to cancer prevention.⁵¹ Clinton et al⁵² have observed 14 to 18 different isomers of lycopene in the prostate. Approximately 80% of total lycopene is found as *cis* isomers in prostate tissue, compared to 50% in blood and 5-10% in foods.^{10,52} The biological significance of this is not known. *cis* Isomers differ in molecular shape from the all-*trans* form and, therefore, may differ in metabolism as has been reported for β -carotene.⁵³ A chemoprevention effect of lycopene remains to be determined.

Lutein

Lutein and zeaxanthin have been suggested to be protective against certain eye diseases. Given that lutein and zeaxanthin are the only carotenoids found in the retina and lens and that the retina and lens suffer oxidant damage, these two antioxidant nutrients may serve a unique role in the protection against eye disease.^{31,32}

Lutein and zeaxanthin are concentrated in the retina at the macula lutea and are responsible for the yellow color that gives the macula its name. Although the term macula lutea, or macula, originally

applied to the yellow pigment, it is now commonly used to refer to the corresponding region of the retina. This region includes the fovea, which is the region that is responsible for our highest visual acuity and contains the highest density of cone photoreceptors. Toward the periphery of the retina, the concentration of zeaxanthin declines rapidly, whereas the concentration of lutein declines gradually.⁵⁴⁻⁵⁶

Evidence from human studies suggest that dietary intake of carotenoids can lead to their accumulation in the retina and, therefore, may provide protection against retinal degeneration. In a recent prospective study, 11 subjects modified their usual daily diets by adding 60 grams per day of spinach (containing 11 mg lutein and 0.3 mg zeaxanthin) for 15 weeks.⁵⁷ Eight subjects had increases in serum lutein and macular pigment density, 2 subjects showed substantial increases in serum lutein but not macular pigment, and 1 subject showed no changes in serum lutein or macular pigment density. Although the results were varied, augmentation of macular pigment through dietary modification appears to be possible for many people. Similar to this study, Landrum et al⁵⁸ found that supplementation with lutein (30 mg/d for 140 days) resulted in increased serum levels of lutein and corresponding increases in the concentration of lutein in the macula on the human eye.

Population studies provide evidence to suggest that protection from AMD can be obtained from lutein (Table 6). Investigators from the Eye Disease Case-Control reported that patients in the group with the highest level of plasma lutein/zeaxanthin had a decreased risk for AMD.⁵⁹ In a subsequent study, the investigators found that protection from AMD was associated with dietary intake of specific carotenoids.⁶⁰ In this case-control study, AMD patients and matched control subjects (who had other eye problems) were divided into 5 groups on the basis on their intake of various nutrients from foods. The nutrient class that was found to have the strongest protective effect against AMD was carotenoids. Those in the highest quintile of carotenoid intake had a 43% lower risk of developing AMD compared to those in the lowest quintile. The authors then investigated which specific carotenoids were responsible for this effect. The strongest association with protection from AMD was found for lutein/zeaxanthin. Subjects who were in the highest quintile for their intake of lutein/zeax-

Table 5. Epidemiologic Studies Examining Tomato or Lycopene Intake or Plasma Level and Cancer

Exposure Measure	Type of Study	Cancer Examined	RR (95% Confidence Interval)	Reference
Raw tomato intake ≥1/wk vs <1/mo	case-control	esophagus	0.61 (0.43–0.86) men	Cook-Mozaffari, 1979
Tomato intake quartile 4 vs 1	case-control	stomach	1.08 (0.69–1.67) women	Franceschi, 1994
Tomato intake "high vs low"	case-control	stomach	0.43 (0.33–0.55)	
Tomato intake tertile 3 vs 1	case-control	stomach	0.82 (0.52–1.28) whites	Correa, 1885
Plasma lycopene	ecologic	stomach	0.56 (0.32–0.90) blacks	Buiatti, 1989
			0.70, P for trend < 0.001	
Tomato intake tertile 3 vs 1	case-control	stomach	regions high in lycopene have lowest cancer rates; low regions have highest rates	Tsugane, 1992
Tomato intake tertile 3 vs 1	case-control	stomach	1.24 n.s.	Tajima, 1985
Serum lycopene high vs lowest 2 tertiles	cohort	pancreas	1.02, n.s.	Ramon, 1993
Serum lycopene tertile 3 vs 1	cohort	bladder	0.16 (0.04–0.57)	Burney, 1991
Lycopene intake quintile 5 vs 1	case-control	bladder	P for trend < 0.02	Helzlsouer, 1989
Tomato intake tertile 3 vs 1	case-control	bladder	0.5, P for trend = 0.06	
Tomato intake > 0.29 vs ≤ 0.7/day	case-control	breast	0.7, P for trend = 0.27 (men)	Nomura, 1991
Plasma lycopene quartile 4 vs 1	case-control	breast	0.9, P for trend = 0.41 (women)	
Serum lycopene quintile 5 vs 1	case-control	bladder	no association	Riboli, 1991
Lycopene intake tertile 3 vs 1	cohort	bladder	0.71 (0.39–1.29) P for trend = 0.3	Bruemmer, 1996
Breast adipose lycopene (>0.51 vs ≤ 0.22 μmol/L)	case control	breast	0.62 (0.19–2.0) P = 0.43	Potischman, 1990
Tomato intake ≥5 vs <1/wk	cohort	prostate	1.0 (0.7–1.7)	London, 1992
Tomato product intake >10 vs <1.5 svgs/wk	cohort	prostate	~1.0	Jarvinen, 1997
			0.32 (0.11–0.94)	Zhang, 1997
			0.60 (0.37–0.97) P = 0.02	Mills, 1989
			0.65 (0.49–0.90) P = 0.01	Giovannucci, 1995

anthin had a 57% lower risk of advanced AMD compared to those in the lowest quintile. This odds ratio was calculated from a multivariate model, indicating that the reduction in odds associated with consumption of lutein/zeaxanthin was independent of effects from other carotenoids. A final analysis was performed by arranging the subjects on the basis of consumption of specific foods. In a multivariate model that included consumption of broccoli, cabbage-related vegetables, carrots, spinach or collard greens, sweet potatoes, and winter squash, only consumption of spinach was associated with protection from AMD. Subjects in the highest quintile for consumption of spinach had an 86% lower odds of advanced AMD.

It should be noted that not all studies have found an association between serum carotenoids and protection from AMD. For example, a case-control study that used the population for the Beaver Dam Eye Study found no such association for lutein or zeaxanthin, but did find a weak protective effect of serum lycopene (Table 6).⁶¹ However, this study included many fewer subjects than did the Eye Disease Case-Control Study.

Lutein and zeaxanthin are the only 2 carotenoids that have been identified in the human crystalline lens.³¹ Like the antioxidant enzymes found within the lens, the lipid-based lutein and zeaxanthin, are primarily found in the metabolically active epithelium/outer cortex of the lens, and therefore may

Table 6. Studies of Lutein and Age-Related Macular Degeneration

Exposure Measured	Association	Relative Risk (95% Confidence Interval)	Reference
Plasma lutein/zeaxanthin tertile 3 & 2 vs 1	decrease	risk reduced to 1/3 (tertile 3 vs 1)	EDCC, 1993
Lutein/zeaxanthin intake quintile 5 vs 1	decrease	risk reduced to 1/2 (tertile 2 vs 1) 0.4 (0.2-0.7)	Seddon, 1994
Serum lutein/zeaxanthin	n.s.	—	Mares-Perlman, 1995

have a preferential role in protecting against UV-induced oxidative damage.⁶² This function would be similar to the role that lutein and zeaxanthin play in the retina, where they are optimally located to reduce risk from blue light.³² Furthermore, foods rich in lutein and zeaxanthin, eg, spinach, appear to be preferentially related to reduced cataract risk when compared to foods rich in other carotenoids, such as β -carotene, eg, carrots.⁶³⁻⁶⁵

Lutein/zeaxanthin are thought to protect the eye in 2 ways. One hypothesis is that the macular pigment filters blue light, which is particularly damaging to photoreceptors and to the retinal pigment epithelium.^{66,67} In support of this hypothesis, lutein and zeaxanthin have been shown to absorb blue light.^{66,67} The second hypothesis is that these carotenoids act as antioxidants to limit the oxidant stress of the tissue that results from metabolism and light.^{66,68,69} It has been shown that one of the ways light damages the retina is by generation of free radicals that lead to peroxidation of membrane lipids.^{66,67} Carotenoids have long been known as powerful antioxidants.^{69,70}

CONCLUSIONS

Epidemiologic studies support for a protective role of carotenoids in prevention of certain major diseases, including certain cancers and eye disease. However, the results from such studies have not been entirely consistent. The reason for this may be explained by differences in the populations studied and differences in the study design and methods used to define both nutrient exposures and disease outcome. The hypothesis that these antioxidant nutrients may protect against the disease is a plausible one given the role of oxidative damage in the etiology of these diseases. It is not known at what stage the protective effect may be

important. The research to date has not sufficiently evaluated the effectiveness vs safety of nutrient supplements. But advocating the use of nutrient supplementation must be done with a cautionary note, given that there have been trials that have suggested that supplementation with β -carotene may have an adverse effect on the incidence of lung cancer in smokers and workers exposed to asbestos. Clearly, further trials are warranted to address the usefulness of nutrient supplementation in disease prevention.

It is likely that cancer and eye disease develops over many years and the etiology of these diseases is due to many factors. There are likely to be differences in the potential protective effect of antioxidant supplementation depending on the stage of the disease. Future research needs to take into account the stage at which oxidative damage, and therefore antioxidant supplementation, may be important. In the meantime, a healthy diet with a variety of fresh fruit and vegetables will have many benefits, will not do any harm, and will be a good source of the antioxidant nutrients implicated (but not proven) in the etiology of disease. There is no evidence that nutrient-dense diets high in fruits and vegetables, which provide known and unknown antioxidant components, are harmful. In fact, intake of fruits and vegetables is associated with reduced risk of death due to cancer, cardiovascular disease, and all causes. Thus, recommendations such as consuming a more nutrient-dense diet, ie, lower in sweets and fats, and increasing levels of fruit and vegetable intake do not appear to be harmful and may have other benefits despite their unproven efficacy in prevention or slowing disease. Until the efficacy and safety of taking supplements containing nutrients can be determined, current dietary recommendations of diets high in fruits and vegetables are advised.⁷¹

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