

REPORT

Why Lutein and Zeaxanthin Are Becoming So Popular

By Heather S. Oliff, PhD

For decades, scientists have tried to determine why people who eat more vegetables and fruits have such low rates of degenerative disease.

After evaluating hundreds of carotenoids found in red, yellow, and orange plants, researchers have zeroed in on lutein and zeaxanthin. They have discovered that these two carotenoids provide broad-spectrum effects, including protection against atherosclerosis and a reduced risk of certain cancers.

The benefit that doctors are focusing on most is the ability of these carotenoids to help maintain the structure of the macula. Considering the magnitude of today’s macular degeneration epidemic, it is no wonder that so many aging people are taking steps to ensure that they obtain enough lutein and zeaxanthin.



LUTEIN AND ZEAXANTHIN DEFINED

Lutein and zeaxanthin are classified as xanthophyll carotenoids. Zeaxanthin is the stereoisomer of lutein—that is, it possesses the same chemical structure but in a different configuration. As such, lutein and zeaxanthin are often measured and reported as a single group, though they may have different functions in the body. Unlike other carotenoids, lutein and zeaxanthin are not sources of vitamin A because they are not converted to vitamin A; rather, lutein and zeaxanthin are lipid-soluble antioxidants. Lutein and zeaxanthin are found in the liver, ovaries, pancreas, kidneys, spleen, testes, adrenals, and many eye tissues. Some of these sites use the xanthophylls, while others may store them for future use.<sup>1</sup>

SOURCES OF LUTEIN AND ZEAXANTHIN

The most important sources of lutein and zeaxanthin are fruits and vegetables. While most people associate lutein and zeaxanthin with dark green, leafy vegetables, they are found in high concentrations in a rainbow of fruits and vegetables, and in egg yolks, as shown in Table 1.

Of 35 fruits and vegetables examined for their lutein and zeaxanthin content, corn was found to have the greatest quantity of lutein and orange pepper the most zeaxanthin.<sup>2</sup> Lutein is found in many fruits and vegetables, while zeaxanthin is present in only a small number of fruits and vegetables.<sup>2</sup> In fact, most dark green vegetables contain only traces of zeaxanthin.<sup>2</sup> Cooking green, leafy vegetables reduces their lutein content,<sup>3</sup> while eating whole spinach leaves rather than chopped spinach improves lutein absorption from the intestinal tract.<sup>4</sup> One study, however, found that vegetable juice provides better lutein absorption than raw or cooked vegetables.<sup>5</sup> The greatest quantities of lutein and zeaxanthin are found in egg yolk.<sup>2</sup>

Because most Americans do not eat enough fruits and vegetables—and a considerable number are leery of eating too many egg yolks—many people may not be obtaining enough xanthophylls through dietary sources. A recent study reported that cheddar cheese can be successfully fortified with lutein.<sup>6</sup> Just as milk fortified with vitamin D increased vitamin D consumption, cheese fortified with lutein may boost lutein consumption. Lutein and zeaxanthin can also be consumed as dietary supplements.

The availability of carotenoids in the plasma is vital for long-term

Table 1: Foods Rich in Lutein and Zeaxanthin

	Lutein (Molecular Weight %)	Zeaxanthin (Molecular Weight %)
Corn	30	25
Egg yolk	54	35
Kiwi	54	0
Pumpkin	49	0
Zucchini	47	5
Spinach	47	0
Yellow squash	44	0
Red seedless grapes	43	10
Peas	41	0

maintenance of adequate tissue levels of carotenoids.<sup>2</sup> Plasma levels of micronutrients are correlated to the risk of certain disorders.<sup>2</sup> For example, low plasma levels of lutein and zeaxanthin are associated with an increased risk of age-related macular degeneration (ARMD).<sup>7</sup> Serum levels of lutein and zeaxanthin may be altered by diet, lifestyle, and physiology.<sup>8</sup> The Third National Health and Nutrition Examination Survey (1988-1994) examined 7,059 Americans who were at least 40 years old.<sup>8</sup> The survey determined that lower serum lutein and zeaxanthin levels are found in women, Caucasians, smokers, heavy drinkers, the physically inactive and overweight, those with a high waist-to-hip ratio, and those who have a lower dietary intake of lutein and zeaxanthin.<sup>8</sup> Fortunately, nearly all of these factors can be modified by making healthy lifestyle changes that enhance serum levels of lutein and zeaxanthin.

### UNIQUE PROPERTIES

Understanding the mechanism of action of lutein and zeaxanthin helps to explain their value for cancer prevention, cardiovascular health, and healthy eyes. Lutein and zeaxanthin are antioxidants that destroy harmful free radicals generated by exposure to light,<sup>9</sup> which initiates oxidative damage in the eyes and skin. These xanthophylls provide protection against free radicals that can damage cells and DNA, and thus cause cancer.

Lutein and zeaxanthin may also improve the cytotoxic action of anti-cancer chemotherapy drugs.<sup>10</sup> Multidrug resistance proteins, which are found in most malignant tumors, are important contributors to chemotherapy drug failure. Researchers studying lymphoma and breast cancer cells discovered that lutein inhibits the action of multidrug resistance proteins,<sup>10</sup> thus enhancing chemotherapy. They also found that zeaxanthin could induce apoptosis (death) of the cancer cells.<sup>10</sup> While more research is needed, this exciting new finding provides hope for better therapeutic outcomes.

Cucumber	38	4
Butternut squash	37	0
Green pepper	36	3
Red grapes	33	4
Celery	32	2
Orange juice	15	20
Honeydew	17	18
Orange pepper	8	37
Orange	7	15
Mango	2	16

Amounts shown are for a five-gram piece of fruit or vegetable. Adapted from: Sommerburg O, Keunen JE, Bird AC, et al.<sup>2</sup> These values may vary with the cultivar.<sup>44</sup>



### SKIN CANCER

Malignant melanoma is the most dangerous type of skin cancer, and its incidence is rapidly increasing. Risk factors include sun exposure and having a fair complexion that burns easily.

One of the largest case-controlled studies investigating the association between diet and melanoma reported that high intake of lutein from fruits and vegetables significantly reduces the risk of melanoma.<sup>11</sup> Scientists believe these xanthophyll carotenoids prevent melanoma by protecting the skin against sun damage.<sup>11</sup> Because tissue levels rather than plasma levels of xanthophylls provide this protection, eating lutein-containing foods on the day of sun exposure may not necessarily be protective, but daily consumption of such foods will be beneficial.

### BREAST CANCER

Because lutein and zeaxanthin are deposited in breast tissue, scientists are studying possible associations between breast cancer prevention and xanthophylls. While the study findings to date are inconclusive, some researchers have reported that lutein and zeaxanthin can protect against breast cancer.

A long-term study of 83,234 healthy women evaluated the relationship between breast cancer and carotenoid intakes.<sup>12</sup> The researchers found that intake of lutein and zeaxanthin from food and supplements may reduce the risk of breast cancer in premenopausal women. The association was particularly strong among women with a higher risk for breast cancer, as determined by a family history of the disease or alcohol use (defined as at least one alcoholic drink per day).<sup>12</sup> The authors concluded that consuming fruits and vegetables high in lutein and zeaxanthin may reduce the risk of breast cancer among premenopausal women.<sup>12</sup> Similarly, another study of 540 women found an increased risk of breast cancer in women with very low intakes of lutein due to a poor diet or lack of supplementation.<sup>13</sup>

## CARDIOVASCULAR HEALTH

A major contributor to coronary heart disease is atherosclerosis, which is initiated by free radical oxidation of low-density lipoprotein (LDL) and causes arteries to occlude (close up).<sup>14</sup> This oxidation damages the endothelial cells lining the arterial walls. The damaged cells subsequently initiate an inflammatory response and the release of adhesion molecules, which attract cells that form fatty plaques in the artery.<sup>14</sup>



A study using human aortic endothelial cells found that lutein can inhibit the expression (molecular formation) of adhesion molecules on the cell surface.<sup>15</sup> Therefore, both this mechanism and lutein's antioxidant capability could enable lutein present in plasma to protect against atherosclerosis. In fact, research on humans and mice has found that increased lutein intake protects against the progression of early atherosclerosis.<sup>16</sup> Plasma levels rather than tissue levels of lutein are important for cardiovascular health, and thus regular dietary intake of lutein may protect against the progression of atherosclerosis.

## HEALTHFUL EGG YOLKS

Chicken egg yolks are the most abundant dietary source of lutein and zeaxanthin, but many people remain concerned about the cholesterol content of egg yolks. LDL cholesterol is a known contributor to atherosclerosis. Cholesterol, triacylglycerol, and phospholipids make up the yolk's lipid matrix, and lutein and zeaxanthin are dispersed within this matrix.<sup>17</sup> The yolk's lipid matrix permits the body to absorb lutein and zeaxanthin efficiently.<sup>17</sup> While consuming either 1.3 cooked egg yolks or 60 grams of cooked spinach daily increases plasma lutein levels to a similar amount, egg yolk intake also increases plasma zeaxanthin levels while spinach intake does not.<sup>17</sup> Interestingly, one study reported that corn, which is very high in zeaxanthin, does not increase plasma zeaxanthin.<sup>17</sup> The bioavailability of lutein in egg yolk may be greater than that of lutein and lutein ester supplements.<sup>18</sup>

Many recent studies report that daily egg consumption does not increase risk for coronary heart disease.<sup>19</sup> Further supporting this finding is that while egg intake has declined over the past 30 years, coronary heart disease is still the leading cause of death in the US.<sup>19</sup> Hence, the nutritional benefits of consuming egg yolk may simply outweigh related concerns about dietary cholesterol intake.<sup>19</sup> For healthy individuals, consuming egg yolks may be beneficial by increasing lutein and zeaxanthin intake,<sup>2</sup> and may help prevent atherosclerosis. While egg yolk is no longer considered a "forbidden food,"<sup>19</sup> consuming 1.3 egg yolks per day is not recommended for people with elevated cholesterol or established coronary heart disease, as this could increase plasma cholesterol and risk for ischemic heart mortality.

## HEALTHY EYES

Most people associate carrots (a rich source of beta-carotene) with eye health. Carrots are important for vision, though beta-carotene has not been detected in the eye lens, which is important for focusing vision.<sup>20</sup> In fact, lutein and zeaxanthin are the predominant carotenoids in the eye lens and macula, the area in the eye's retina that contains cells that are important for color vision.<sup>21</sup> For this reason, lutein and zeaxanthin play a critical role in maintaining normal vision.



In the eye, lutein and zeaxanthin are known as the macular pigments, which are important for absorbing visible light, reducing light scatter in the eye, and providing antioxidant protection. Light is necessary for vision, but is also dangerous—capable of destroying cells or their components by photo-oxidation.<sup>22</sup> Lutein and zeaxanthin can filter the high-energy blue and blue-green wavelengths of light from the visible-light spectrum.<sup>9</sup> Filtering blue light has two important functions: it reduces chromatic aberration (poor image color) and prevents blue light-induced oxidation. In other words, these blue wavelengths, which allow a person to see the color blue, are similar to the invisible ultraviolet A and B wavelengths in that they can induce cell damage in the eyes. Phototoxic damage contributes to the pathophysiology of macular degeneration and cataract.

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#### MACULAR DEGENERATION

As the name implies, macular degeneration occurs when the macula is damaged and breaks down. The macula produces central vision and color vision, and is vital for visual acuity. Thus, macular degeneration causes a gradual destruction of sharp, central vision, which is needed for reading, driving, watching television, and so forth. Macular degeneration causes permanent blindness and is the leading cause of blindness in people over the age of 50. Increased exposure to blue light or sunlight increases the risk of age-related macular degeneration (ARMD).<sup>23</sup> While there is no cure for macular degeneration, lutein and zeaxanthin may slow the disease's progression or even help prevent it.

A scientific review of the literature indicates that lutein and zeaxanthin could modulate the course of ARMD.<sup>23</sup> Most risk-analysis studies evaluate the combination of lutein and zeaxanthin, and show that higher dietary intake of lutein and zeaxanthin is associated with reduced risk for ARMD.<sup>7,24,25</sup> However, other conflicting data do not support this association.<sup>26,27</sup> Among the explanations researchers provide for this disparity: consumption of lutein and zeaxanthin in some study populations may have been too low to have influenced the risk of ARMD; statistically, there may not have been enough patients who progressed from early to late macular degeneration to determine efficacy; and evaluating lutein and zeaxanthin together rather than separately may have obscured evidence that one xanthophyll is more effective than the other.<sup>26-28</sup>



Considering that they have different distribution patterns within the eye—zeaxanthin is the dominant macular pigment in the central macula and lutein is more prevalent in the peripheral retina—lutein and zeaxanthin may have different functions.<sup>28</sup> Zeaxanthin may be more important for preventing macular degeneration. One study of 380 adults aged 66-75 found that those with the lowest plasma concentrations of zeaxanthin had twice the risk of ARMD compared to those with the highest zeaxanthin plasma concentrations.<sup>28</sup> By contrast, plasma concentrations of lutein had no significant correlation with risk for macular degeneration.<sup>28</sup>

#### IMPORTANCE OF MACULAR PIGMENT DENSITY

A low density of macular pigment permits greater blue light damage to the eye and increases the risk for ARMD. An autopsy study reported that ARMD patients had lower levels of macular pigments than patients without ARMD.<sup>29</sup> Similarly, another study reported that eyes with ARMD had significantly less macular pigment than healthy eyes.<sup>30</sup> The authors concluded that the low macular pigment caused the macular degeneration rather than the reverse (degeneration causing the low macular pigment).<sup>30</sup>

A sign of early ARMD is loss of visual sensitivity to blue and green light.<sup>31</sup> Older adults aged 60-84 with lower macular pigment density reportedly have lower visual sensitivity. Older people with high macular pigment density reportedly have visual sensitivity comparable to younger people aged 24-36.<sup>32</sup> Thus, high macular pigment density may help retain youthful visual sensitivity and retard age-related declines in visual function.<sup>32</sup>

#### WAYS TO INCREASE MACULAR PIGMENT DENSITY



Macular pigment density can be increased by consuming foods and supplements that are rich in lutein and zeaxanthin.<sup>33-36</sup> Ingested lutein and zeaxanthin may be transported from the blood into the retina in the same proportions found in the blood.<sup>37</sup> Consuming lutein ester can increase macular pigment density in patients with early ARMD, so even people with diseased macula can accumulate lutein and possibly zeaxanthin.<sup>36</sup>

Obese men and women have a higher risk of ARMD and also have lower macular pigment density.<sup>1</sup> Obese people may have lower macular pigment density than the non-obese because they typically have poor dietary habits and may not consume enough foods containing lutein and zeaxanthin.<sup>1</sup> Also, body fat may compete with the retina for uptake of lutein and zeaxanthin. A larger quantity of body fat may draw more xanthophylls away from the serum and prevent their deposition in the

retina.<sup>1</sup> People with very low body fat have higher levels of serum carotenoids,<sup>38</sup> which could translate to higher macular pigment density. This is yet another benefit of losing excess weight.

## CATARACT

A cataract is a clouding of the eye lens, causing loss of vision. The lens is necessary to adjust the eye's focus so that vision is sharp. Symptoms of a cataract include cloudy or blurry vision, problems with light (as when car headlights, glare from lamps, and sunlight seem too bright), and faded color vision. The most common cause of cataract is aging. Oxidative damage caused by tobacco smoke, light exposure, and inadequate intake of dietary antioxidants is also thought to play a central role in cataract formation.<sup>32</sup> The symptoms, along with the etiology, highlight the importance of xanthophylls in preventing cataract.



Eating foods rich in xanthophylls is associated with a decreased risk of cataract.<sup>39-41</sup> Not only are xanthophylls important for preventing cataracts, but research shows that consuming xanthophylls can slow the progression of cataracts. Visual acuity and glare sensitivity significantly improve in patients with age-related cataracts who take lutein supplements.<sup>42</sup> And patients with the highest intake of lutein and zeaxanthin have a lower risk of cataract extraction surgery compared to those with the lowest intake.<sup>39,40</sup>

Lutein and zeaxanthin protect lens cells from damaging ultraviolet light, a leading cause of cataract formation. When treated with xanthophylls, human lens epithelial cells exposed to ultraviolet B (UVB) light were protected from lipid peroxidation.<sup>43</sup> Xanthophyll treatment also significantly decreased UVB-induced oxidative stress.<sup>43</sup> These findings suggest that lutein and zeaxanthin protect against cataract by preventing sunlight-induced oxidative stress.

## CONCLUSION

A wealth of scientific research demonstrates the benefits of a diet rich in fruits, vegetables, and eggs.

The antioxidants lutein and zeaxanthin have the power to protect eyes and vision, while helping prevent eye disorders. Xanthophylls provide optimal nutrition for ocular health by protecting the eyes from light-induced oxidative damage, which triggers macular degeneration and cataract. They can also protect against certain types of cancer, including skin cancer and breast cancer. Lutein and zeaxanthin likewise can help prevent atherosclerotic build-up by inhibiting fatty plaque formation and endothelial cell damage.

Tissue and plasma levels of xanthophylls can be increased by eating foods rich in lutein and zeaxanthin, taking dietary supplements, and maintaining a healthy weight.

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## References

1. Hammond BR, Jr., Ciulla TA, Snodderly DM. Macular pigment density is reduced in obese subjects. *Invest Ophthalmol Vis Sci.* 2002 Jan;43(1):47-50.
2. Sommerburg O, Keunen JE, Bird AC, van Kuijk FJ. Fruits and vegetables that are sources for lutein and zeaxanthin: the macular pigment in human eyes. *Br J Ophthalmol.* 1998 Aug;82(8):907-10.
3. Micozzi MS, Beecher GR, Taylor PR, Khachik F. Carotenoid analyses of selected raw and cooked foods associated with a lower risk for cancer. *J Natl Cancer Inst.* 1990 Feb 21;82(4):282-5.
4. Faulks RM, Hart DJ, Brett GM, Dainty JR, Southon S. Kinetics of gastro-intestinal transit and carotenoid absorption and disposal in ileostomy volunteers fed spinach meals. *Eur J Nutr.* 2004 Feb;43(1):15-22.
5. McEligot AJ, Rock CL, Shanks TG, et al. Comparison of serum carotenoid responses between women consuming vegetable juice and women consuming raw or cooked vegetables. *Cancer Epidemiol Biomarkers Prev.* 1999 Mar;8(3):227-31.
6. Jones ST, Aryana KJ, Losso JN. Storage stability of lutein during ripening of cheddar cheese. *J Dairy Sci.* 2005 May;88(5):1661-70.
7. Antioxidant status and neovascular age-related macular degeneration. Eye Disease Case-Control Study Group. *Arch Ophthalmol.* 1993 Jan;111(1):104-9.
8. Gruber M, Chappell R, Millen A, et al. Correlates of serum lutein + zeaxanthin: findings from the Third National Health and Nutrition Examination Survey. *J Nutr.* 2004 Sep;134(9):2387-94.

9. Krinsky NI. Possible biologic mechanisms for a protective role of xanthophylls. *J Nutr.* 2002 Mar;132(3):540S-2S.
10. Molnar J, Gyemant N, Mucsi I, et al. Modulation of multidrug resistance and apoptosis of cancer cells by selected carotenoids. *In Vivo.* 2004 Mar-Apr;18(2):237-44.
11. Millen AE, Tucker MA, Hartge P, et al. Diet and melanoma in a case-control study. *Cancer Epidemiol Biomarkers Prev.* 2004 Jun;13(6):1042-51.
12. Zhang S, Hunter DJ, Forman MR, et al. Dietary carotenoids and vitamins A, C, and E and risk of breast cancer. *J Natl Cancer Inst.* 1999 Mar 17;91(6):547-56.
13. Toniolo P, Van Kappel AL, Akhmedkhanov A, et al. Serum carotenoids and breast cancer. *Am J Epidemiol.* 2001 Jun 15; 153(12):1142-7.
14. Alexander RW. Theodore Cooper Memorial Lecture. Hypertension and the pathogenesis of atherosclerosis. Oxidative stress and the mediation of arterial inflammatory response: a new perspective. *Hypertension.* 1995 Feb;25(2):155-61.
15. Martin KR, Wu D, Meydani M. The effect of carotenoids on the expression of cell surface adhesion molecules and binding of monocytes to human aortic endothelial cells. *Atherosclerosis.* 2000 Jun;150(2):265-74.
16. Dwyer JH, Navab M, Dwyer KM, et al. Oxygenated carotenoid lutein and progression of early atherosclerosis: the Los Angeles atherosclerosis study. *Circulation.* 2001 Jun 19;103(24):2922-7.
17. Handelman GJ, Nightingale ZD, Lichtenstein AH, Schaefer EJ, Blumberg JB. Lutein and zeaxanthin concentrations in plasma after dietary supplementation with egg yolk. *Am J Clin Nutr.* 1999 Aug;70(2):247-51.
18. Chung HY, Rasmussen HM, Johnson EJ. Lutein bioavailability is higher from lutein-enriched eggs than from supplements and spinach in men. *J Nutr.* 2004 Aug; 134(8):1887-93.
19. Herron KL, Fernandez ML. Are the current dietary guidelines regarding egg consumption appropriate? *J Nutr.* 2004 Jan; 134(1):187-90.
20. Yeum KJ, Taylor A, Tang G, Russell RM. Measurement of carotenoids, retinoids, and tocopherols in human lenses. *Invest Ophthalmol Vis Sci.* 1995 Dec;36(13):2756-61.
21. Moeller SM, Jacques PF, Blumberg JB. The potential role of dietary xanthophylls in cataract and age-related macular degeneration. *J Am Coll Nutr.* 2000 Oct;19(5 Suppl):522S-7S.
22. Kirschfeld K. Carotenoid pigments: their possible role in protecting against photooxidation in eyes and photoreceptor cells. *Proc R Soc Lond B Biol Sci.* 1982 Aug 23; 216(1202):71-85.
23. Mozaffarieh M, Sacu S, Wedrich A. The role of the carotenoids, lutein and zeaxanthin, in protecting against age-related macular degeneration: A review based on controversial evidence. *Nutr J.* 2003 Dec 11;2(1):20.
24. Seddon JM, Ajani UA, Sperduto RD, et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. *JAMA.* 1994 Nov 9;272(18):1413-20.
25. Mares-Perlman JA, Fisher AI, Klein R, et al. Lutein and zeaxanthin in the diet and serum and their relation to age-related maculopathy in the third national health and nutrition examination survey. *Am J Epidemiol.* 2001 Mar 1;153(5):424-32.
26. Mares-Perlman JA, Klein R, Klein BE, et al. Association of zinc and antioxidant nutrients with age-related maculopathy. *Arch Ophthalmol.* 1996 Aug;114(8):991-7.
27. VandenLangenberg GM, Mares-Perlman JA, Klein R, Klein BE, Brady WE, Palta M. Associations between antioxidant and zinc intake and the 5-year incidence of early age-related maculopathy in the Beaver Dam Eye Study. *Am J Epidemiol.* 1998 Jul 15; 148(2):204-14.
28. Gale CR, Hall NF, Phillips DI, Martyn CN. Lutein and zeaxanthin status and risk of age-related macular degeneration. *Invest Ophthalmol Vis Sci.* 2003 Jun;44(6):2461-5.

29. Bone RA, Landrum JT, Mayne ST, Gomez CM, Tibor SE, Twaroska EE. Macular pigment in donor eyes with and without AMD: a case-control study. *Invest Ophthalmol Vis Sci.* 2001 Jan;42(1):235-40.
30. Landrum JT, Bone RA, Kilburn MD. The macular pigment: a possible role in protection from age-related macular degeneration. *Adv Pharmacol.* 1997;38:537-56.
31. Beatty S, Boulton M, Henson D, Koh HH, Murray IJ. Macular pigment and age related macular degeneration. *Br J Ophthalmol.* 1999 Jul;83(7):867-77.
32. Hammond BR, Jr., Wooten BR, Snodderly DM. Preservation of visual sensitivity of older subjects: association with macular pigment density. *Invest Ophthalmol Vis Sci.* 1998 Feb;39(2):397-406.
33. Hammond BR, Jr., Johnson EJ, Russell RM, et al. Dietary modification of human macular pigment density. *Invest Ophthalmol Vis Sci.* 1997 Aug;38(9):1795-801.
34. Landrum JT, Bone RA, Joa H, Kilburn MD, Moore LL, Sprague KE. A one year study of the macular pigment: the effect of 140 days of a lutein supplement. *Exp Eye Res.* 1997 Jul;65(1):57-62.
35. Berendschot TT, Goldbohm RA, Klopping WA, van de Kraats J, van Norel J, van Norren D. Influence of lutein supplementation on macular pigment, assessed with two objective techniques. *Invest Ophthalmol Vis Sci.* 2000 Oct;41(11):3322-6.
36. Koh HH, Murray IJ, Nolan D, Carden D, Feather J, Beatty S. Plasma and macular responses to lutein supplement in subjects with and without age-related maculopathy: a pilot study. *Exp Eye Res.* 2004 Jul;79(1):21-7.
37. Bone RA, Landrum JT, Friedes LM, et al. Distribution of lutein and zeaxanthin stereoisomers in the human retina. *Exp Eye Res.* 1997 Feb;64(2):211-8.
38. Curran-Celentano J, Erdman JW, Jr., Nelson RA, Grater SJ. Alterations in vitamin A and thyroid hormone status in anorexia nervosa and associated disorders. *Am J Clin Nutr.* 1985 Dec;42(6):1183-91.
39. Chasan-Taber L, Willett WC, Seddon JM, et al. A prospective study of carotenoid and vitamin A intakes and risk of cataract extraction in US women. *Am J Clin Nutr.* 1999 Oct;70(4):509-16.
40. Brown L, Rimm EB, Seddon JM, et al. A prospective study of carotenoid intake and risk of cataract extraction in US men. *Am J Clin Nutr.* 1999 Oct;70(4):517-24.
41. Lyle BJ, Mares-Perlman JA, Klein BE, Klein R, Greger JL. Antioxidant intake and risk of incident age-related nuclear cataracts in the Beaver Dam Eye Study. *Am J Epidemiol.* 1999 May 1;149(9):801-9.
42. Olmedilla B, Granado F, Blanco I, Vaquero M. Lutein, but not alpha-tocopherol, supplementation improves visual function in patients with age-related cataracts: a 2-y double-blind, placebo-controlled pilot study. *Nutrition.* 2003 Jan ;19(1):21-4.
43. Chitchumroonchokchai C, Bomser JA, Glamm JE, Failla ML. Xanthophylls and alpha-tocopherol decrease UVB-induced lipid peroxidation and stress signaling in human lens epithelial cells. *J Nutr.* 2004 Dec;134(12):3225-32.
44. Kopsell D, Kopsell D, Curran-Celentano J. Carotenoid variability among kale and spinach cultivars. *Hortscience.* 2004;39(2):34.