

Lutein and Zeaxanthin: Seeing into the Heart of the Matter

"...the effort to understand the health benefits of plant foods... is the characterization of their physiologically active constituents, phytochemicals... As our knowledge grows...we will learn how best to create new products through altering their concentrations, combinations and/or their bioavailability." -Functional Foods for Health Program, Department of Food Science and Human Nutrition, University of Illinois, Urbana, IL

Lutein and zeaxanthin are *carotenoid phytonutrients* integral to protecting vision and optimizing cardio-vascular health. ¹ Phytonutrients can be classified into seven major groups: *terpenes, amines, organosulfurs, phenols, polysaccharides, organic acids, and isoprenoid lipids*. The carotenoids, perhaps the most familiar of phytonutrients, are a subgroup of the fat soluble terpenes, along with the *chromanols, saponins and limonoids*.² Chemically carotenoids are classified in two main groups: *carotenes*, such as beta-carotene and lycopene, and *xanthophylls* like lutein, zeaxanthin, beta-cryptoxanthin, canthaxanthin, and astaxanthin.

Carotenoids function as membrane antioxidants due to their reactivity with singlet oxygen. In this article we will focus on two xanthophylls, *lutein* and *zeaxanthin*.

Leafy green vegetables, corn, and egg yolk are rich in the yellow colored lutein and its usual companion zeaxanthin, from which the color the former garners its name.³ Peaches, oranges, papaya, kiwi, squash, peas, lima beans, green beans, broccoli, Brussels sprouts, prunes, pumpkin, potatoes, sweet potatoes and honeydew melon also contain lutein and zeaxanthin. Marigold is so rich in lutein and zeaxanthin that it is the major source for supplementation.⁴ Egg yolk may be the most bioavailable source.⁵ Lutein and zeaxanthin, like all terpenes, are lipophilic, requiring fat for optimal uptake.⁶ It is not unlikely that the lutein in egg yolk provides greater bioavailability because of the yolk's rich lipid and phospholipid content which is ideal for liposome formation. (Liposomes are nanosized lipid vesicles in which oils, oil soluble nutrients, and fatty acids are absorbed in the small intestine and then taken up directly by the lymph system.) I should also point out that dietary fiber inhibits absorption of lutein by 40% to 75 %.⁷

Oh Say, Will You See?

Lutein and zeaxanthin are carotenoids without pro-vitamin A activity. They are the only carotenoids identified in the macula, the central part of the retina which controls fine vision. There they filter harmful blue light thereby inhibiting oxidative damage in the cell membranes. Such damage leads to macular degeneration, AMD, which affects over 30 million people worldwide, and is the leading cause of blindness in people over 50.⁸

Since there is no cure for AMD, prevention is crucial. Supplements and lutein-rich foods can increase the macular pigment density, which density has been shown to be associated with a lower risk of Age-related Macular Degeneration (AMD). Indeed, a stable intake of the carotenoids lutein and zeaxanthin could reduce the risk of age related macular degeneration by 43% in women under 75, says a new cohort study leader, Suzen Moeller, from the University of Wisconsin.⁹ *"This exploratory observation is consistent with a broad body of evidence from observational and experimental studies that suggests that these carotenoids (lutein and zeaxanthin) may protect against AMD,"* wrote Moeller.¹⁰

Nonetheless, it is still not clear whether lutein and zeaxanthin by themselves are responsible for the changes, as compared to the *total effect* of other carotenoids, phytonutrients and micronutrients consumed along with high lutein / zeaxanthin foods. *"More conclusive evidence from long-term prospective studies and clinical trials is needed to determine whether the intake of macular carotenoids themselves, or as markers of broader dietary patterns, can protect against intermediate AMD or delay progression in individuals who have early stages of the disease,"* said Moeller.¹¹ Also the effects appeared to be strongest on those with *life-long high intakes*. This suggests that just adding lutein to vitamin pills for people over 50 may not be as efficacious as more complete and balanced nutrition over a life time.

Let's Have a Heart to Heart

In America cardiovascular disease (CVD) is the leading cause of death. Researchers from the University of Southern California and University of California, Los Angeles, believe lutein may help to reduce the risk of CVD. A recently published article in the journal Circulation describes the effect of lutein on the progression of *atherosclerosis*.¹² Atherosclerosis is the thickening of arterial walls due to build-up of fatty plaque, a leading cause of CVD.

Investigators performed three separate studies. They demonstrated that increased lutein levels present in the blood serum had a desirable effect on arterial wall thickness. The higher the serum lutein levels, the less the arterial thickening, and the less the risk of CVD. A follow-up study also found higher serum lutein levels at baseline were associated with reduced arterial wall thickness progression over 18 months.¹³

In the prospective Health Professionals Study a high dietary intake of lutein had a modest association with a reduced risk of ischemic stroke.¹⁴ In the Tocopherol, β -Carotene Cancer Prevention (ATBC) Study conducted in Finland, lutein plus zeaxanthin was associated with a lower risk of subarachnoid hemorrhage.¹⁵ In the Atherosclerosis Risks in Communities Study, Iribarren, et al, noted that lutein plus zeaxanthin concentrations were inversely related to the extent of atherosclerosis.¹⁶

Magic Yellow Bullets?

Clearly nutrition has a significant role in the prevention of many chronic diseases such as CVD and AMD. It is well known that a greater intake of fruit and vegetables can help

prevent most of the common diseases of aging. However, as plant foods are chemically complex, it is difficult to pinpoint any single nutrient that is most responsible for their protective effects. Potential beneficial substances include vitamins and minerals, fiber, and phytonutrients. In a review by the Research Institute of Public Health, University of Kuopio, Finland, the role of main dietary carotenoids (lycopene, beta-carotene, alpha-carotene, beta-cryptoxanthin, lutein, and zeaxanthin) in the prevention of heart diseases is discussed. In their abstract the authors report, “Although it is clear that a higher intake of fruit and vegetables can help prevent the morbidity and mortality associated with heart diseases, more information is needed to ascertain the association between the intake of *single nutrients*, such as carotenoids, and the risk of CVD. *Currently, the consumption of carotenoids in pharmaceutical forms for the treatment or prevention of heart diseases cannot be recommended.*”¹⁷

Scanner or Scammer?

In the 1990's a device using a safe blue light and a technology called Raman Spectroscopy was made available for ophthalmologists. This tool could scan the retina to measure lutein and zeaxanthin to discern AMD risk. It was soon discovered that this laser scanner could also measure some carotenoids in the skin of the palm.

From this analysis the total antioxidant status cannot be determined as such, but an initial pilot study suggests that it nonetheless may be a good indicator of fruit and vegetable intake, antioxidant nutrition, and oxidative stress.¹⁸ *This of course presumes no skewing of the results via supplementation heavily weighted in carotenoids.* Such supplementation would increase scores, but would be more reflective of carotenoid status as such, and no longer as reflective of fruit and vegetable intake, antioxidant nutrition, and oxidative stress. Nonetheless, this easy-to-use portable tool, now available to doctors in general, including chiropractors, gives instant results and is non-invasive—requiring neither bodily fluids, tissue samples, nor a laboratory.

Scientific Supplementation

The current recommendation for lutein is as high as 6 mg a day. The average American is thought to consume 1-2 mg a day. Zeaxanthin recommended intake is 1 mg a day.¹⁹ Although lutein, sometimes along with zeaxanthin, is being added more and more to multi-vitamins, antioxidant pill formulas, or sold as separate product, we should keep the following quotes in mind which echo the conclusions above:

*"...fruits and vegetable phytochemical extracts exhibit strong antioxidant...activities ...from the combination of phytochemicals...the additive and synergistic effects of a "complex mixture" of phytochemicals...are responsible for these the benefits...no single antioxidant can replace the combination of natural phytochemicals...."*²⁰

*"...phytochemicals often appear in nature as families of related compounds (that)...may behave synergistically... and... activate metabolic enzymes...as a network"*²¹

We have already learned that marigold is the best plant source. Therefore it is likely wisest to provide several mg of marigold derived lutein and zeaxanthin in a 5 to 1 ratio in *a natural, complex matrix of a wide variety of carotenoids and other phytonutrients from all the seven major groups in a whole food base.*

To maximize bioavailability, carotenoid supplementation is best taken away from high fiber meals. But we need to consider yet another factor.

*"...antioxidants, which are found in many phytochemicals,... are biologically unstable, poorly soluble in water, and poorly distributed to target sites... we strongly advocate serious consideration of the bioavailability of dietary supplements... to improve their bioavailability using delivery systems such as liposomal formulations."*²²

Being lipophilic, carotenoid supplements should be taken with fat to allow for liposome formation. Liposomes are nanosized "fat bodies" that infuse non-water soluble fats so they can be absorbed.²³ They may also protect carotenoids from gastric juices, which can destroy 50% of ingested carotenoids.²⁴ Therefore, in order to maximize bioavailability and compliance simultaneously, the best solution may be to infuse the carotenoids in liposomes as well. In this way lutein can be supplemented without having to ingest fat at the same time, thereby enhancing compliance.

- 1.) Functional Foods and Nutraceuticals, March 2003, p. 64.
- 2.) Maher, J, Physiological Functions of Phytonutrients, Part 1, Dynamic Chiropractic, date, issue
- 3.) One food can contain several classifications of phytonutrients. For example, an orange contains terpenes (carotenoids and limonoids) and phenols (bioflavonoids).
- 4.) <http://en.wikipedia.org/wiki/Lutein>
- 5.) Chung H et al., Lutein Bioavailability Is Higher from Lutein-Enriched Eggs than from Supplements and Spinach in Men, J Nutr 2004;134:1887-1893
- 7.) Reidl, J. et al. Some dietary fibers reduce absorption of carotenoids in women. J Nutr 1999 Dec; 129 (12): 2170-6
- 6.) Roodberg AJ, et al. Amount of fat in the diet affects lutein esters but not of alpha carotene, beta carotene, and vitamin E in humans. Am J Clin Nutr 2000 May; 71(5):1187-93
- 8-11.) Moeller, S, The Carotenoids in Age-Related Eye Disease Study (CAREDS), AMA Archives of Ophthalmology (Vol. 124, pp. 1151-1162)
- 12.) Dwyer, J.H., et. al., Oxygenated Carotenoid Lutein and Progression of Early Atherosclerosis: The Los Angeles Atherosclerosis Study." *Circulation*. 2001;103:2922
- 13.) J. H. Dwyer, M. J. Paul-Labrador, J. Fan, A. M. Shircore, C. N. B. Merz, and K. M. Dwyer Progression of Carotid Intima-Media Thickness and Plasma Antioxidants: The Los Angeles Atherosclerosis Study *Arterioscler. Thromb. Vasc. Biol.*, February 1, 2004; 24(2): 313 - 319.
- 14.) Hirvonen T, Virtamo J, Korhonen P, Albanes D, Pietinen P. Intake of flavonoids, carotenoids, vitamins C and E, and risk of stroke in male smokers. *Stroke* 2000;31:2301-6.
- 15.) T Hirvonen, J Virtamo, P Korhonen, D Albanes, The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med* 1994;330:1029-35
- 16.) Iribarren C, Folsom AR, Jacobs DR Jr, Gross MD, Belcher JD, Eckfeldt JH. Association of serum vitamin levels, LDL susceptibility to oxidation, and autoantibodies against MDA-LDL with carotid atherosclerosis. A case-control study. The ARIC Study Investigators Atherosclerosis Risk in Communities. *Arterioscler Thromb Vasc Biol* 1997;17:1171-7.
- 17.) Sari Voutilainen, Tarja Nurmi, Jaakko Mursu and Tiina H Rissanen, Carotenoids and cardiovascular health, reprints not available. Address correspondence to S. Voutilainen, Research Institute of Public Health, University of Kuopio, PO Box 1627, 70211 Kuopio, Finland. E-mail: sari.voutilainen@uku.fi.
- 18.) Study conducted in collaboration with three major US universities to test skin carotenoid levels as an indicator of the overall antioxidant network presented at the annual meeting of the Federation of American Societies for Experimental Biology (FASEB) in San Francisco, California 04/06
- 19.) Seddon, J.M., et al., Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. *JAMA*, 1994. 272(18): p. 1413-20.

- 20.) Lui RH, J Nutr. Potential synergy of phytochemicals in cancer prevention: mechanism of action. Department of Food Science, Cornell University, Ithaca, NY 14853. 2004 Dec;134(12):3479S-85S.
- 21.) Heber D., Phytochemicals beyond antioxidation, J Nutr. 2004 Nov;134(11):3175S-3176S.
- 22.) Yoko Shojia, and Hideki Nakashimaa, Nutraceuticals and Delivery Systems, Journal of Drug Targeting, 12(6):385-391, 2004.
- 23.) Maher, J. H., Nano-Bio-Technology and Bioavailable Phytonutrition, Nutritional Perspectives, Volume 28, July 2005, <http://www.biopharmasci.com/downloads/NanoBioTechnologyandBioavailablePhytonutrition.pdf>
- 24.) MacSwan, R, Assessing the Bioavailability of Carotenoids from Seabuckthorn using In vitro Digestion, Poster Presentation, Scottish Crop Research Institute, Perth, Australia. "In conclusion, as the hydrophobic carotenoids are passively absorbed in the small intestine into the lymphatic system, any means of improving survival during gastric transit will markedly enhance carotenoid bioavailability."
http://www.scri.sari.ac.uk/posters/posters/McDougall_Carotenoid_%20SeaBuckthorn.pdf#search=%22lipd%20esters%