Why the Lutein Source in Eye Vitamins Matters

Diane E Alexander, PhD

Technical Service Manager, Kemin Health, LC

Abstract

Eye care professionals are increasingly recommending eye vitamins to patients because a growing body of scientific evidence supports the benefits of good nutrition to reduce the risk for certain eye conditions and improve visual function. Eye care professionals expect that the eye vitamins they recommend will benefit the patients they serve. However, in order for ocular supplements to provide eye health benefits, the essential nutrients, including lutein, in eye vitamins should be bioavailable—so that they will be able to be delivered to the beneficial sites of action. Measurement of lutein and zeaxanthin in the macula via macular pigment optical density (MPOD) can help confirm the bioavailabilty of a lutein ingredient and indicate whether patients are getting enough lutein and zeaxanthin through their diet or supplementation regimen.

Keywords

Lutein, zeaxanthin, macular pigment, macular pigment optical density (MPOD), age-related macular degeneration (AMD)

Disclosure: Diane E Alexander, PhD, is an employee of Kemin Health, LC.
Received: December 9, 2010 **Accepted:** January 17, 2011 **Citation:** *US Ophthalmic Review*, 2011;4(1):86–9 *DOI: 10.17925/USOR.2011.04.01.86*
Correspondence: Diane E Alexander, PhD, Technical Service Manager, Kemin Health, LC, 600 East Court Avenue, Suite A, Des Moines, IA 50309. E: diane.alexander@kemin.com

Support: The publication of this article was funded by Kemin Health, LC.

Carotenoids—Lutein and Zeaxanthin

In general, carotenoids are yellow, orange, or red pigments that are soluble in lipids. Mammals utilize carotenoids for a variety of functions but are incapable of synthesizing them. Thus, carotenoids must be obtained solely from the diet. Of the 600 carotenoids found in nature, only dietary lutein and zeaxanthin are deposited in the macula. Meso-zeaxanthin is a compound derived from lutein that is also present in the macula—it is converted by the body from lutein rather than being introduced from dietary sources.

The lutein and zeaxanthin present together in the macula are known as macular pigment.[1] The macular pigment appears as a yellow tint in *Figure 1*. The intense deposition of the yellow-colored pigments in and around the fovea provided the basis for the clinical description of this area as the macula lutea or yellow spot. Lutein and zeaxanthin perform two primary functions in the macula. First, they filter high-energy, blue wavelengths of visible light as they enter the eye before they reach the photoreceptors.[2] By passively absorbing these wavelengths, the macular pigment limits photo-oxidative damage to tissues that results from the reactive oxygen species (ROS) produced by these short wavelengths of light. Second, the macular pigment functions as an antioxidant to directly protect the retina from damage caused by ROS. The macular pigment also protects vulnerable photoreceptors from damage caused by sunlight, indoor lighting, and even light emitted from computer monitors. In other words, lutein and zeaxanthin act like internal sunglasses for the eyes. This protection not only helps to maintain healthy vision now but also helps to reduce the risk for certain eye conditions.

Lutein and zeaxanthin are found naturally together in vegetables such as spinach, kale, broccoli, corn, green peas, and green beans as well as other foods such as eggs.[3,4] The bioavailability of lutein, unlike that of many other nutrients, is enhanced by chopping and cooking the food. This is likely due to the disruption of the strong interaction between chlorophyll and lutein molecules. It is difficult, however, to obtain beneficial amounts of lutein and zeaxanthin from diet alone. Interventional studies report that 10mg of lutein (specifically FloraGLO® brand lutein) per day is effective in improving vision and reducing the risk for certain eye conditions.[5] FloraGLO Lutein provides the same lutein as is found naturally in vegetables and other foods but is obtained from marigold flowers through a patented process as shown in *Figure 2*.

The average daily intake of lutein and zeaxanthin in the US from diet alone is estimated to be less than 2mg,[6] far below the 10mg per day clinically reported to reduce the risk for certain age-related eye conditions and improve visual function. How can we bridge the gap? As discussed earlier, increased consumption of foods with high concentrations of lutein such as dark green leafy vegetables, corn, and eggs can help increase lutein intake to 10mg per day. However, for many individuals changing dietary habits is not a practical option, which is why supplementing one's diet with lutein-fortified foods/beverages or eye vitamins containing FloraGLO is an easy, alternative way to bridge the dietary lutein gap. In fact, the FloraGLO Lutein found in ocular supplements has been shown to be approximately twice as bioavailable as the lutein in green vegetables, again due to the strong interaction between lutein and chlorophyll in leaves.[7,8]

When recommending eye vitamins to patients, it is expected that the products will deliver the health benefits promised on the label. However, the ingredients in these products should have demonstrated bioavailability to deliver on claims made on product packaging. Certain ingredients, including lutein, are unstable in their purified forms and must be wrapped in a protective coating for inclusion in the eye vitamin. Data indicate that these different coatings may significantly affect the bioavailability of the lutein ingredient.[9] Leading eye vitamin manufacturers choose FloraGLO as their lutein source because of its proven quality and safety profile, as well as its proven benefits for eye health. It is the most clinically researched lutein brand in the world and has over a dozen published studies demonstrating its absorption into the blood and increased lutein levels in the macula with daily supplementation at 10mg.

Macular Pigment Optical Density

The ability of the macular pigment to absorb or filter blue light is measured as macular pigment optical density (MPOD). MPOD is an optical indicator of the concentration of lutein and zeaxanthin in the macula and is becoming an accepted biomarker not only for predicting the risk for disease but also for visual function. In numerous studies, MPOD is linearly related to the levels of lutein in the serum and positively correlated with dietary intake of lutein and zeaxanthin. MPOD measurement is a relatively new technology, with only a few devices commercially available to evaluate MPOD; however, it has been well studied clinically. Over two dozen studies have been published demonstrating an increase in macular pigment following lutein and/or zeaxanthin supplementation at a range of 2–30mg per day or a high-carotenoid diet.[10–24] The degree of increase in MPOD levels following lutein or zeaxanthin supplementation varies, likely due to subject demographics, disease state, measurement method, diet, and supplementation regimen.

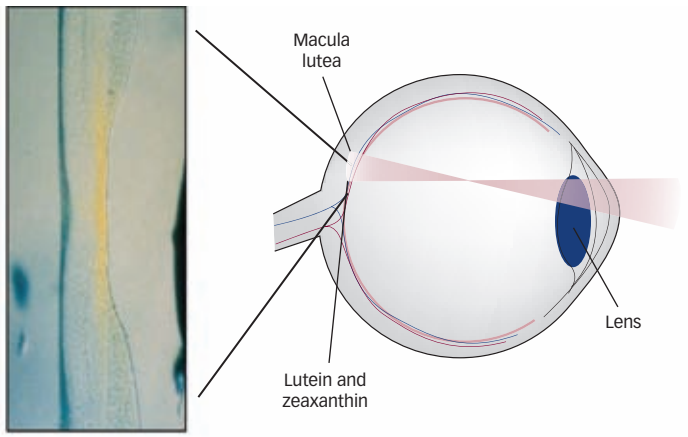
Macular pigment, likely via its blue-light-filtering property, has been shown in a number of clinical trials to enhance visual performance—the ability to perceive detail and carry out visual tasks. High levels of macular pigment contribute to improved visual acuity, glare tolerance and recovery, contrast sensitivity, chromatic aberration, and photophobia in healthy individuals as well as those diagnosed with age-related eye diseases.[15,17,25–30] One study conducted in healthy volunteers demonstrated a 58% increase in glare tolerance and a five-second reduction in photostress recovery time following daily supplementation with 10mg FloraGLO Lutein and 2mg OPTISHARP® (DSM IP Assets B.V. Ltd) Zeaxanthin for six months. Improvements in these parameters of visual performance can have a major impact on everyday activities. Glare can present a significant hazard to drivers at night because of the bright light from oncoming headlights; the reported five-second reduction in recovery time can thus significantly improve night-time driving safety. Glare is also a challenge for athletes and outdoor enthusiasts who rely on their vision to help them perform at their best.

Macular Pigment and Age-related Eye Conditions

Lutein has been associated with risk reduction for age-related macular degeneration (AMD) for over a decade. This link originated from an epidemiologic study from the Eye Disease Case Control (EDCC) Study group published in 1993, and a follow-up study by Seddon and colleagues on a subset of ADCC patients published in 1994.[31,32] The results indicated that the risk for developing AMD was 57% lower in individuals with the highest lutein and zeaxanthin intake compared with those with the lowest.[31] These epidemiologic studies provide evidence that consumption of lutein and zeaxathin from food is associated with a reduced risk for AMD. The National Eye Institute is currently evaluating the progression of AMD following supplementation with FloraGLO Lutein and OPTISHARP Zeaxathin in a large population diagnosed with early AMD, the second Age-related eye disease study (AREDS2).

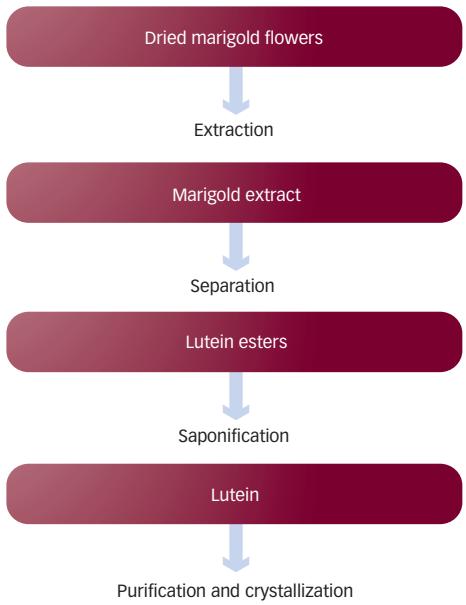
Nutritional intervention in the form of supplements was first evaluated by the National Eye Institute in AREDS. AREDS demonstrated that taking

Figure 1: Structure of the Human Eye



The diagram on the right shows the structure of the human eye. On the left is an unstained photomicrograph of a primate macula. The yellow coloration is due to high concentrations of lutein and zeaxanthin also known as the macular pigment. Reproduced with the permission of Max Snodderly.

Figure 2: FloraGLO® Lutein Production Schematic Diagram



FloraGLO® is a patented and purified free form of lutein that is naturally sourced from the petals of marigold flowers. The marigold extract is subjected to saponification, during which the esters are carefully removed from the lutein. This is followed by purification and crystallization, which yields purified lutein crystals.

a supplement containing beta-carotene, vitamins C and E, and the minerals zinc and copper reduced the risk for progression to advanced AMD by 29% and reduced visual acuity loss by 21%.[33] Lutein and zeaxanthin were not included in the AREDS study, in part because during the planning stages of the study in the early 1990s, lutein and zeaxanthin were not commercially available as ingredients. The in-progress follow-up study AREDS2 has added 10mg FloraGLO Lutein and 2mg OPTISHARP Zeaxanthin per day, alone or in combination with 1g of omega-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), to the original AREDS supplement formulation to assess their influence on progression to advanced AMD in individuals at high risk for the disease over the course of five years.[34] In addition to evaluating the rate of AMD progression, other simultaneously evaluated outcomes include the effects of supplementation on cognitive function, cataract development, cardiovascular disease, vision loss, and visual function. A subset of subjects will also have their MPOD measured to provide further insight into the relationship between MPOD levels and AMD progression.

There is a growing body of evidence that, although not conclusive, supports that lower levels of MPOD may be a risk factor for certain age-related eye conditions. Increased MPOD may provide greater protection against oxidative damage, which contributes in part to the manifestation of AMD. For example, risk factors for AMD including tobacco use, light iris color, advanced age, obesity, and female gender are associated with low levels of MPOD.[35] Significantly less macular pigment has been found in eyes at high risk for AMD because of advanced disease in the fellow eye compared with eyes with no known risk.[36,37] In a study measuring MPOD in 93 AMD eyes and 220 normal eyes, the results showed that AMD patients who were not taking lutein supplements had 32% lower MPOD than healthy subjects. Interestingly, AMD patients taking high-dose lutein supplements after their initial AMD diagnosis were found to have MPOD levels indistinguishable from those of control patients, although the study did not evaluate the effects of supplementation and increased MPOD on the progression of the disease.[38]

In addition to being present in the macula, lutein is also deposited in the lens, albeit at much lower concentrations.[39,40] The fact that oxidation of the lens is a major cause of cataracts suggests that antioxidant nutrients may play a role in cataract prevention. In support of this hypothesis, high lutein and zeaxanthin intake from dietary sources has been linked to the reduction in risk for cataract extraction in a number of epidemiologic studies.[29,41–45]

Nutritional intervention has also been shown to slow vision loss associated with retinitis pigmentosa. The National Eye Institute recommends that most adult patients with the common forms of retinitis pigmentosa take a supplement of 15,000IU of vitamin A daily under the supervision of their eye care professional. A study published in April 2010 suggests that the addition of 12mg per day of FloraGLO Lutein to this vitamin A regimen can slow the loss of midperipheral field sensitivity to a greater degree than vitamin A alone.[22] In fact, the authors of this study conclude that "the benefit of lutein supplementation on the long-term course of midperipheral visual field loss among patients also taking vitamin A and eating an oily fish diet would be three to 10 years of protection against further loss of sight."

Practical Application

MPOD has the potential to become a commonly tested biomarker to measure an individual's risk for eye disease and to assess visual function. Knowledge of an individual's MPOD level indicates whether he or she is getting enough lutein and zeaxanthin through their diet or supplementation regimen. Identification of individuals at low, medium, and high risk for eye disease can be made based on their MPOD level.[46] MPOD is typically measured on a logarithmic scale and values range from undetectable to over 1.0 optical density units (du). Experts agree that a central MPOD below 0.2du is considered low, between 0.2 and 0.5du is mid-range, and levels above 0.5du are high.[46] When compiling data from numerous studies across a diverse US population, nearly half of all Americans have low MPOD, indicating low concentrations of lutein and zeaxanthin in the macula.[47] As low MPOD is a risk factor for AMD, nearly half of the American population—approximately 133 million individuals—may be at risk for developing AMD later in life. For individuals with low MPOD, lifestyle changes such as maintaining a healthy bodyweight, stopping the use of tobacco products, and eating more dark green, leafy vegetables may increase MPOD levels. For those who may find these lifestyle changes difficult, taking a daily eye vitamin with FloraGLO Lutein is a proven method to significantly increase MPOD, thereby improving visual performance and reducing risk for certain age-related eye conditions.

Conclusion

The scientific literature shows that lutein and zeaxanthin are essential nutrients needed by our eyes daily. Lutein and zeaxanthin cannot be synthesized by the body, so these nutrients must be consumed from dietary sources or supplements. High concentrations of lutein and zeaxanthin in the macula reduce the risk for certain eye conditions and are also associated with improvements in visual function. Science suggests that 10mg lutein and 2mg zeaxanthin per day can increase MPOD levels to those associated with eye health benefits. Not all lutein in supplements are equivalent and, with the ability to measure MPOD, the bioavailability of a particular lutein ingredient is more easily confirmed. Recommending an eye vitamin containing a proven, high-quality lutein ingredient, such as FloraGLO, is critical to ensure that patients are getting the optimal eye protection associated with higher levels of MPOD. ■

1. Beatty S, Boulton M, Henson D, et al., Macular pigment and age related macular degeneration, *Br J Ophthalmol*, 1999; 83:867–77.
2. Snodderly DM, Brown PK, Delori FC, et al., The macular pigment. I. Absorbance spectra, localization, and discrimination from other yellow pigments in primate retinas, *Invest Ophthalmol Vis Sci*, 1984;25:660–73.
3. Mangels AR, Holden JM, Beecher GR, et al., Carotenoid content of fruits and vegetables: An evaluation of analytic data, *J Am Diet Assoc*, 1993;93:284–96.
4. Handelman GJ, Nightingale ZD, Lichtenstein AH, et al., Lutein and zeaxanthin concentrations in plasma after dietary supplementation with egg yolk, *Am J Clin Nutr*, 1999;70:247–51.
5. Literature review: Macular pigment and healthy vision, *Optometry*, 2009;80:591–7.
6. Centers for Disease Control and Prevention: National center for health statistics, National health and nutrition examination survey data 2001–2002. Available at: www.Cdc.Gov/nchs/about /major/nhanes/nhanes01-02.Htm (accessed February 9, 2011).
7. van het Hof KH, Brouwer IA, West CE, et al., Bioavailability of lutein from vegetables is 5 times higher than that of beta-carotene, *Am J Clin Nutr*, 1999;70:261–8.
8. Castenmiller JJ, West CE, Linssen JP, et al., The food matrix of spinach is a limiting factor in determining the bioavailability of beta-carotene and to a lesser extent of lutein in humans, *J Nutr*, 1999;129:349–55.
9. Beck M, Schalch W, Roos F, et al., Lutein bioavailability is matrix-dependent in powdered dietary supplements (abstract), EVER (European Association for Vision and Eye Research), Crete, Greece, 2010.

10. Francoise JL, Askew EW, Lang LC, et al., Serum and macular responses to antioxidant supplementation versus a carotenoid-rich dietary intervention in the elderly, *Curr Top Nutraceut Res*, 2006;4:69–78.
11. Aleman TS, Duncan JL, Bieber ML, et al., Macular pigment and lutein supplementation in retinitis pigmentosa and usher syndrome, *Invest Ophthalmol Vis Sci*, 2001;42:1873–81.
12. Cardinault N, Gorrand JM, Tyssandier V, et al., Short-term supplementation with lutein affects biomarkers of lutein status similarly in young and elderly subjects, *Exp Gerontol*, 2003;38:573–82.
13. Duncan JL, Aleman TS, Gardner LM, et al., Macular pigment and lutein supplementation in choroideremia, *Exp Eye Res*, 2002;74:371–81.
14. Johnson EJ, Chung HY, Caldarella SM, et al., The influence of supplemental lutein and docosahexaenoic acid on serum, lipoproteins, and macular pigmentation, *Am J Clin Nutr*, 2008;87:1521–9.
15. Kvansakul J, Rodriguez-Carmona M, Edgar DF, et al., Supplementation with the carotenoids lutein or zeaxanthin improves human visual performance, *Ophthalmic Physiol Opt*, 2006;26:362–71.
16. Morganti P, Fabrizi G, Bruno C, Protective effects of oral antioxidants on skin and eye function, *Skinmed*, 2004;3:310–6.
17. Richer S, Stiles W, Statkute L, et al., Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: The veterans last study (lutein antioxidant supplementation trial), *Optometry*, 2004;75:216–30.
18. Rodriguez-Carmona M, Kvansakul J, Harlow JA, et al., The effects of supplementation with lutein and/or zeaxanthin on human macular pigment density and colour vision, *Ophthalmic Physiol Opt*, 2006;26:137–47.
19. Schalch W, Cohn W, Barker FM, et al., Xanthophyll accumulation in the human retina during supplementation with lutein or zeaxanthin – the luxea (lutein xanthophyll eye accumulation) study, *Arch Biochem Biophys*, 2007;458:128–35.
20. Schweitzer D, Lang GE, Beuermann B, et al., Objektive bestimmung der optischen dichte von xanthophyll nach supplementation von lutein, *Ophtalmologe*, 2002;99:270–5.
21. Stringham JM, Hammond B, Macular pigment and visual performance under glare conditions, *Optom Vis Sci*, 2008;85:82–8.
22. Berson EL, Rosner B, Sandberg MA, et al., Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A, *Arch Ophthalmol*, 2010;128:403–11.
23. Aleman TS, Cideciyan AV, Windsor EA, et al., Macular pigment and lutein supplementation in abca4-associated retinal degenerations, *Invest Ophthalmol Vis Sci*, 2007;48:1319–29.
24. Richer S, Devenport J, Lang JC, Last II, Differential temporal responses of macular pigment optical density in patients with atrophic age-related macular degeneration to dietary supplementation with xanthophylls, *Optometry*, 2007;78:213–9.
25. Richer S, ARMD—pilot (case series) environmental intervention data, *J Am Optom Assoc*, 1999;70:24–36.
26. Massacesi AL, Faletra R, Gerosa F, et al., The effect of oral supplementation of macular carotenoids (lutein and zeaxanthin) on the prevention of age-related macular degeneration: A 18 month follow up study (abstract), *Invest Ophthalmol Vis Sci*, 2001;42:S234.
27. Bahrami H, Melia M, Dagnelie G, Lutein supplementation in retinitis pigmentosa: PC-based vision assessment in a randomized double-masked placebo-controlled clinical trial [NCT00029289], *BMC Ophthalmol,* 2006;6:23.
28. Cangemi FE, Tozal study: An open case control study of an oral antioxidant and omega-3 supplement for dry AMD, *BMC Ophthalmol*, 2007;7:3.
29. Olmedilla B, Granado F, Blanco I, et al., 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;19:21–4.
30. Wenzel AJ, Fuld K, Stringham JM, et al., Macular pigment optical density and photophobia light threshold, *Vision Res*, 2006;46:4615–22.
31. 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;272:1413–20.
32. The Eye Disease Case-Control Study Group, Antioxidant status and neovascular age-related macular degeneration, *Arch Ophthalmol*, 1993;111:104–9.
33. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins c and e, beta carotene, and zinc for age- related macular degeneration and vision loss: AREDS report no. 8, *Arch Ophthalmol*, 2001;119:1417–36.
34. Chew E, Age-Related Eye Disease Study 2 (AREDS2): A multi-center, randomized trial of lutein, zeaxanthin, and omega-3 long-chain polyunsaturated fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) in age-related macular degeneration. Ind # 74,781, version 5.1, 3 December 2007.
35. Nolan JM, Stack J, O' Donovan O, et al., Risk factors for age-related maculopathy are associated with a relative lack of macular pigment, *Exp Eye Res*, 2007;84:61–74.
36. Beatty S, Murray IJ, Henson DB, et al., Macular pigment and risk for age-related macular degeneration in subjects from a Northern European population, *Invest Ophthalmol Vis Sci*, 2001;42:439–46.
37. Bone RA, Landrum JT, Mayne ST, et al., Macular pigment in donor eyes with and without amd: A case-control study, *Invest Ophthalmol Vis Sci*, 2001;42:235–40.
38. Bernstein PS, Zhao DY, Wintch SW, et al., Resonance raman measurement of macular carotenoids in normal subjects and in age-related macular degeneration patients, *Ophthalmology*, 2002;109:1780–7.
39. Bates CJ, Chen SJ, Macdonald A, et al., Quantitation of vitamin E and a carotenoid pigment in cataractous human lenses, and the effect of a dietary supplement, *Int J Vitam Nutr Res*, 1996;66:316–21.
40. Yeum KJ, Taylor A, Tang G, et al., Measurement of carotenoids, retinoids, and tocopherols in human lenses, *Invest Ophthalmol Vis Sci*, 1995;36:2756–61.
41. 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;70:517–24.
42. 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;70:509–16.
43. Mares JA, Voland R, Adler R, et al., Healthy diets and the subsequent prevalence of nuclear cataract in women, *Arch Ophthalmol*, 2010;128:738–49.
44. Mares-Perlman JA, Brady WE, Klein BE, et al., Serum carotenoids and tocopherols and severity of nuclear and cortical opacities, *Invest Ophthalmol Vis Sci*, 1995;36:276–88.
45. Christen WG, Liu S, Glynn RJ, et al., Dietary carotenoids, vitamins C and E, and risk of cataract in women: A prospective study, *Arch Ophthalmol*, 2008;126:102–9.
46. Bernstein PS, Delori FC, Richer S, et al., The value of measurement of macular carotenoid pigment optical densities and distributions in age-related macular degeneration and other retinal disorders, *Vision Res*, 2010;50:716–28.
47. Wooten BR, Hammond BR, Macular pigment: Influences on visual acuity and visibility, *Prog Retin Eye Res*, 2002;21:225–40.