

WHITE PAPER: COMPREHENSIVE OVERVIEW OF CAROTENOIDS FOR EYE HEALTH



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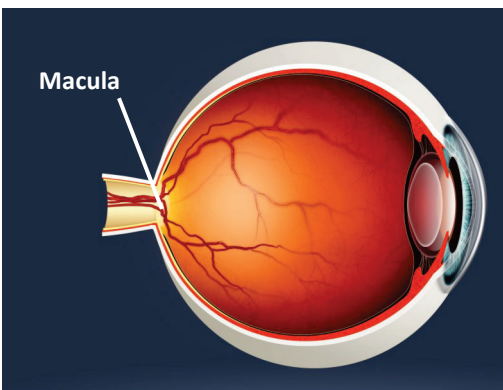
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Carotenoids are pigments responsible for the yellow to red colors in food and plants. More than 600 carotenoids are found in nature, but only a fraction have been found to play a role in health and disease. Carotenoids are not made by the body and must be supplied from food or supplements (Roberts 2009). Their concentration in blood is associated with a variety of positive health outcomes, yet over 95% of the U.S. falls short on the carotenoid health index (Donaldson 2011). This review will focus on two important carotenoids, lutein and zeaxanthin (RR-zeaxanthin and meso-zeaxanthin) isomers, and the role they play in eye health and disease, in addition to how the dietary supplement and food industry are developing creative ways to incorporate more of these vital nutrients into your diet.

Lutein and Zeaxanthin

Lutein and zeaxanthin are yellow-orange carotenoids—collectively called xanthophylls—that help filter blue light in targeted tissues (Britton 1995). Lutein and zeaxanthin are present in the eyes, skin, blood, brain and other tissues. Their selective placement in ocular tissue [concentrated ~1000-fold over that in blood] forms the macular pigment in the retina (Landrum 2001). The macular pigment helps protect against the photo-oxidative effects of ultraviolet [UV] radiation and high-energy blue light (Beatty 1999; Zuclich 2005). In the macula fovea, the ratio of lutein to two isomers of zeaxanthin (RR-zeaxanthin and meso-zeaxanthin) is roughly 1:1:1, while lutein dominates the outer edges of the retina (Whitehead 2006).

Lutein and zeaxanthin are the only carotenoids present in the retina and lens of the eye where their proposed function is to protect against oxidative stress (Khachik 1995; Sindhu 2010) due to exposure to solar radiation (Khachik 1997). These xanthophylls have



demonstrated the ability to block penetration of reactive oxygen into cell membranes (Subczynski 1991) and prevent oxidation of these highly susceptible areas (Sujak 1999). They can both neutralize most free radical species (Boileau 1999; Trevithick-Sutton 2006; Li 2010) and stimulate antioxidant enzymes (Sindhu



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Jeffrey Anshel, OD, FAAO is a 1975 graduate from the Illinois College of Optometry. He has written numerous articles and five books regarding nutritional influences on vision and computer vision concerns. Dr. Anshel is the principal of Corporate Vision Consulting, where he addresses the issues surrounding visual demands while working with computers. He also offers onsite consultations and seminars to corporations related to visual stress and productivity in the workplace. He lectures nationally to eye care providers on nutrition topics. Dr. Anshel is a Fellow of the American Academy of Optometry and President of the Ocular Nutrition Society. He maintains a private practice in Carlsbad, CA.



“The triple antioxidant combination of xanthophylls contributes to healthy vision and may provide broad-spectrum, antioxidative protection for an aging population...”

2010). Lutein and zeaxanthin are isomers that differ by the location of a single double bond (Sajilata 2008). Zeaxanthin exists in three forms wherein 3R, 3'R-zeaxanthin and 3R, 3'S-zeaxanthin (also referred to as *meso*-zeaxanthin) are the predominant forms present in the macula of the retina. Zeaxanthin has a stabilizing effect on cell membranes and appears to be more protective during prolonged sun exposure (Sujak 1999). Meso-zeaxanthin may have an even better antioxidant capacity than RR-zeaxanthin in preventing oxidation of membrane lipids (Bhosale 2005). The triple antioxidant combination of xanthophylls contributes to healthy vision and may provide broad-spectrum, antioxidative protection for an aging population (Ribaya-Mercado 2004; Thürmann 2005). Though these three xanthophylls found in the eye differ only slightly in structure, they are not redundant in regard to function. They appear to possess different photoprotective properties, packing a powerful protective punch.

Epidemiological data indicate that the average intake of lutein and zeaxanthin from dietary sources is in the range of 1 to 2 mg/day (approximately 0.01 to 0.03 mg/kg body weight/day). In general, the ratio of lutein to zeaxanthin in natural dietary sources is approximately 5:1 (Thurnham 2007). Numerous studies have demonstrated that increased dietary intake of lutein and zeaxanthin is associated with increased macular pigment density (MPOD) in healthy adults (Whitehead 2006; Thurnham 2007). MPOD is the thickness or density of the protective layer of carotenoids in the macula. As dietary intake increase, clinical research has shown that absorption and deposition of lutein and zeaxanthin in our visual center as well. Accordingly, some epidemiological studies have reported an inverse association between dietary intake, or serum and retinal levels of lutein and zeaxanthin, with the risk of developing ocular diseases such as age-related macular degeneration (AMD) and cataracts (Barker 2010; Lien and Hammond 2011; Wong 2011).

Long Term Supplementation

In addition to significantly increasing MPOD, long term supplementation with all three xanthophylls [10.6 mg meso-zeaxanthin, 5.9 mg lutein, 1.2 mg zeaxanthin] has demonstrated improvements in eyesight, including visual performance and acuity (Olmedilla 2003; Richer S 2004), reduced glare sensitivity (Stringham 2008), enhanced contrast sensitivity (Renzi 2010), improved vision in dim light (Kvansakul, 2006), and reduced chromatic blur (Rodriguez-Carmona 2006). During AREDS2 (Age-Related Eye Disease Study 2) , when the participants were ranked based on their dietary intake of lutein and zeaxanthin, it was observed that supplementation with lutein and zeaxanthin appeared to have a significant effect in participants with the lowest dietary intake levels. Within that group, lutein and zeaxanthin

was significantly associated with a 32 percent reduction in progression to cataract surgery. A significant reduction in any and/or cataract and/or severe cataracts was also observed with supplementation in participants with low dietary intakes of lutein and zeaxanthin. The presence of lutein plus zeaxanthin resulted in an 18% reduction in the risk of progression to advanced age-related macular degeneration (AAMD) and a 22% reduction in the risk of progression to neovascular AMD (Age-Related Eye Disease Study 2 Research Group, 2013). In another research study, sixty elderly veterans who took zeaxanthin [8 mg/day] for 12 months showed greater recognition of detail, improved 1.5 lines on the eye chart, experienced disappearance of blind spots, and improved ability to drive at night (Richer 2011). In a



randomized, double-blind, placebo-controlled study involving 120 Chinese drivers, supplementation with 20 mg/day lutein for 12 months showed a trend towards an increase in spectacle-corrected visual acuity; significant increases in serum lutein, MPOD, contrast and glare sensitivity—especially in mesopic [poorly-illuminated] conditions; and improved scores on driving subscale (Yuan 2013). Based on current research, lutein and zeaxanthin may have beneficial effects on one of the most costly and limiting age related concerns—vision loss.

Carotenoids For The Young

Of the approximately 30 carotenoids identified in human serum and breast milk, lycopene and β -carotene, together with lutein, are among the most abundant (Khachik 1997). Though not present in the eye, lycopene and β -carotene also possess light filtering and antioxidant characteristics (Rubin 2012). Recent research also suggests that these three dietary carotenoids together may play a crucial role in retinal development and function in infants (Bone 1985; Choi 2006; Izumi-Nagai 2007; Zimmer 2007) and response to oxidative stress and inflammation (Canfield 2003; Jewell 2004; Hammond 2008; Vogelsang 2009; Perrone 2010). Rubin (2012) research group were the first to report a comprehensive, randomized, controlled trial designed to assess feasibility and potential benefits of supplementing preterm infant formulas with lutein, lycopene and β -carotene.

Specifically, this trial demonstrated that lutein may improve neuro-retinal health in preterm infants at risk for poor eye health. Lutein supplemented preterm infants had greater rod photoreceptor sensitivity, suggesting a protective effect. These new findings in combination with some of the information we already knew about lutein's and zeaxanthin's roles in eye health lend to the theory that these xanthophylls help support eye health throughout the life span.

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What’s better? Lutein supplementation has been shown to be remarkably safe (Connolly 2011) even at very high doses (CFSAN 2011; Connolly 2011; Harikumar 2008; JECFA 2004; Ravikrishnan 2011; AREDS study 2). Both free lutein and lutein esters are GRAS-affirmed, and have been available in Europe and the US for many years (FDA2011;CFSAN2011).

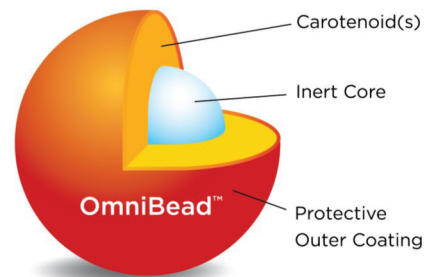
Delivering High Quality Carotenoids

Xanthophylls are selectively absorbed in the intestine, especially in conjunction with a fatty meal (Norkus 2010), but because of their highly unstable nature, can greatly benefit from the assistance of delivery systems. Understanding this need, eye health ingredient suppliers continue to develop technologies which support a wide array of delivery platforms. OmniActive Health Technologies is among such suppliers with their development of several patented technologies, including OmniBead™, a beadlet encapsulation process and UltraSOL™, a molecular dispersion process. OmniBead™ not only preserves the stability of highly labile carotenoids, but also allows for them to be successfully incorporated into a variety of finished products, such as tablets and capsules. For inclusion into gummies for dietary supplementation, as well as a variety of food and beverage applications, OmniActive also developed UltraSOL™ Nutrient System technologies, which provide greater dispersibility and bioavailability for both lutein and zeaxanthin, lipophilic nutrients normally difficult to incorporate in aqueous systems. UltraSOL™ technology is also designed to improve the bioavailability of poorly absorbed nutrients, such as lutein and zeaxanthin.

Through research and development, food technologists, with the assistance of innovative ingredient suppliers, have been able to stabilize lutein and zeaxanthin for the incorporation into functional foods. Their lipophilic (fat-loving) nature lends to their incorporation into foods containing fats which help stabilize and aid in absorption of these nutrients. Due to their continued efforts, food scientists have successfully incorporated lutein in to nutrition bars, powder drink mixes and candies.

Additional emerging technologies are focused on microencapsulation techniques, mucoadhesive polymers and/or phospholipid suspensions. These new delivery systems have been able to support targeted delivery, sustained release and safety of supplementation. They have also been shown to promote ease of transport through cell membranes, which may allow for increased bioavailability and efficiency of dosing.

Example of advanced delivery technology for carotenoids



For representative purposes only

Healthy Vision For A Lifetime

A life without vision is frankly unimaginable. Scientists have repeatedly demonstrated the protective effects of carotenoids in individuals of all ages, from infants to seniors, but there continues to be a communication gap as the concern remains strongest among the aging population, where it may be too late to take action. Increasing evidence



suggests early and consistent lutein and zeaxanthin intake may help maintain optimal eye health over a person’s lifetime. Though diets rich in fruits, vegetables and eggs increase tissue levels of lutein, zeaxanthin, lycopene and β-carotene, it may be difficult to achieve ideal amounts through dietary sources alone. Supplementing with products containing premium lutein and zeaxanthin such as the Lutemax® Lutein Esters, Lutemax® Free Lutein, Lutemax® 2020 lutein with enhanced levels of zeaxanthin isomers, or OmniXan® zeaxanthin from natural paprika or incorporating these ingredients into functional foods may be the best way to ensure protective levels of these

critical nutrients are achieved throughout the lifespan.

SPONSORED BY:

Lutein For Every Age™: *Lutein For Every Age is an award-winning, educational campaign created by OmniActive Health Technologies to raise awareness of the benefits of early and consistent lutein intake to maintain proper eye, skin, cognitive and general health throughout a lifetime.*



OmniActive Health Technologies: *OmniActive Health Technologies offers a range of quality ingredients, which are innovative and scientifically validated for dietary supplementation, nutritional fortification, functional food/beverage, coloring, flavor enhancement and personal care applications. We address complex challenges for customers in the dietary supplement, food and beverage space using technology-driven, sustainable solution with application support within a global regulatory framework. Whether you’re looking for a new ingredient to add to a finished product, or technology to enhance an existing ingredient, you’ll find unmatched innovation at OmniActive.*

Our core products are carotenoids, plant extracts and specialty functional ingredients. We leverage our international R&D strengths to deploy an array of state of the art manufacturing technologies in extraction, purification, isolation and delivery of nutritional actives. Our manufacturing operations are located at multiple sites in India and are cGMP and HACCP system compliant.

FOR INDUSTRY PURPOSES ONLY.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

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