



Lutemax
LUTEIN &
ZEAXANTHIN **2020**



PROTECTIVE ROLE OF LUTEIN & ZEAXANTHIN ISOMERS AGAINST HIGH-ENERGY BLUE LIGHT EXPOSURE: A NEED ACROSS ALL AGE GROUPS

Interest in supplements for eye health is increasing quickly and evident in the category's growth of 9% in 2018, well above the industry standard and expected to be a \$530 million industry by 2021. An aging population continues to contribute to the category but the explosive growth in eye health is driven by the "modern condition" and the needs of the 21st century consumer. And as consumers spend more time sheltering in place, the COVID pandemic is serving as an unexpected driver for digital device use. Working and schooling from home, entertainment and staying socially connected is increasing user rates higher and faster than before. Post-COVID, those numbers are expected to remain high as these situational activities transform into lasting behaviors.

Quick Stats The Blue Light Whitespace

73% of consumers report concern about prolonged exposure to blue light from digital devices

64% are interested in supplements to help protect against blue light

25% of the US general population comprises the new eye health consumer



Adults nearly spend half of the day interacting with media—approximately 11 hours



84% of teens have their own cellphones and average 7 hours per day of use



Just over half of US children—53% — now own a smart phone by age 11 and spend more than 4 hours on them each day



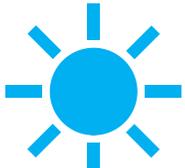
Nearly half of the population spends 5 or more hours using their smartphone

A “DIGITAL” LIFESTYLE INCREASES BLUE LIGHT EXPOSURE: A CONCERN & OPPORTUNITY



These statistics are a small example of our exposure to blue light. Including other sources of blue light (sunlight, television, laptops, etc.) the amount of exposure can be substantially higher. And factoring in consumers' concerns represent how relevant blue light is becoming. This new eye health consumer is most receptive to taking supplements that proactively help their children and family deal with the consequences of a modern, digital lifestyle. And as they become more educated on the sources and potential consequences of blue light exposure, their intent to purchase almost doubles. Blue light is a white space opportunity for the modern lifestyle: to provide a frontline defense against prolonged exposure from all sources – sunlight and digital devices – by supplementing with nature's most effective eye nutrients, the macular carotenoids.

BLUE LIGHT & EYE HEALTH: THE CONSEQUENCES OF INCREASING EXPOSURE



The light the human eye responds to is a narrow band of electromagnetic radiation between 390 to 700 nanometers and within this band, blue light makes up some of the highest energy - between 400 to 500 nanometers. Unlike UV-light exposure, which is almost exclusively from the sun, blue light is emitted from a multitude of sources including sunlight, digital devices (e.g. computers/laptops, smartphones, television screens) and energy-efficient indoor lighting, specifically compact fluorescent and LED bulbs. Therefore, compared to UV-light, daily exposure to blue light from both outdoor and indoor sources can be significantly greater.

Absorption of UV vs blue light

Absorption of almost all ambient UV-light occurs primarily in the cornea and crystalline lens and results of long-term exposure can manifest within the outer layers of the eye as cataracts. Blue light, however, penetrates deeper into the eye and has the potential to damage retinal structures through photochemical and photo-oxidative reactions in the retinal pigment layer. Therefore, UV-light from the sun may be less of a causative factor for conditions associated with retinal damage (such as AMD) and there are several studies to suggest this.



Effects of short-term vs long-term exposure

Short-term exposure of blue light manifests as eye fatigue, eye strain and headaches, whereas long-term exposure may lead to gradual loss of visual function. In a mouse model, it was shown that damage from high-energy blue light can occur within three hours of exposure with significant photoreceptor loss after three weeks. The mechanisms by which blue light damages the eye are multifactorial but primarily mediated through photo-oxidative reactions and the generation of reactive oxygen species (ROS). Due to its high metabolic rate and exposure to high-energy blue light, the retinal pigment epithelial cells (RPE) are a primary target of photo-oxidative damage.



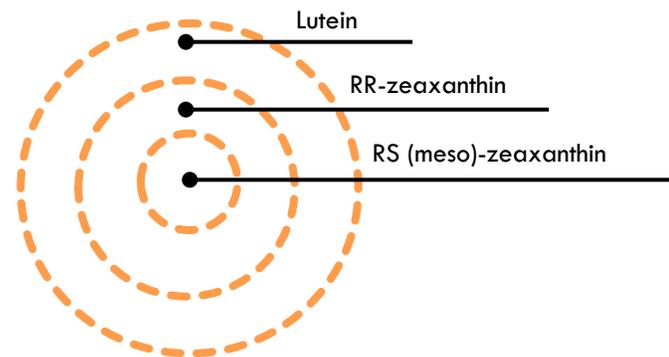
THE DAMAGING EFFECTS OF BLUE LIGHT ARE CUMULATIVE

A vicious cycle

Damage to the RPE is a vicious cycle of oxidative stress and inflammation: oxidative stress triggers an inflammatory response and, in turn, inflammation enhances the production of reactive oxygen species (ROS). Without adequate protection, increased oxidative stress inactivates a major proteolytic pathway called the ubiquitin-proteasome pathway (UPP). The UPP functions to degrade unneeded or damaged proteins in all cells and plays a major role in the regulatory mechanism central to cellular processing that includes inflammation, immune and stress responses, and antigen processing. A fully functioning UPP is required for cells to cope with various stress, including oxidation. However, extensive oxidative insults, as seen in RPE exposed to blue light, can impair UPP, resulting in the accumulation of damaged proteins, dysregulated cell processing and increased inflammation. Since the RPE is a major source of pro-inflammatory mediators and a primary target of photo-oxidative impairment of UPP, the formation of ROS from high-energy blue light may contribute to inflammation and eye-related issues, like AMD.

The macular carotenoids: Preferential protectors against blue light

The damaging effects of blue light is a cumulative process and often the result of a lack of protection by endogenous mechanisms and antioxidants. Several nutrients play critical roles in protecting the retina from photo-oxidative damage and perhaps none are more important than the macular carotenoids: lutein and the zeaxanthin isomers.



macular carotenoids are deposited in specific areas of the retina

Lutein and the two zeaxanthin isomers – RR-zeaxanthin (3R,3'R-zeaxanthin) and RS-zeaxanthin (3R,3'S-zeaxanthin)—are the only three carotenoids found in the eye, specifically in the macula—the area of the retina responsible for highest visual performance and susceptible to the greatest amount of photo-oxidative damage. The location of their respective areas of deposition is highly specific: lutein is preferentially deposited in the peripheral macula, RR-zeaxanthin in the mid-peripheral macula and RS-zeaxanthin in the center of the macula. Increased dietary intake of lutein and zeaxanthin is associated with increased macular pigment density (MPOD – the thickness or density of the protective layer of carotenoids in the macula) in healthy adults. Epidemiological studies have reported an inverse association between dietary intake of lutein and zeaxanthin and the risk of developing age-related eye diseases such as AMD and cataracts.

SCIENCE SHOWS THE NEED FOR A 3-IN-1 FORMULA

Science says three > one

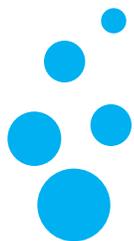
Researchers, including Bone and Snodderly, have established that the basic biology of the macular carotenoids is protecting the retina and supporting visual performance by acting as blue light filters, quenching ROS and inhibiting lipid peroxidation of cellular membranes generated from photo-oxidation. Bian et.al also suggest that aside from its primary role as an antioxidant, lutein and the zeaxanthin isomers mitigate the inactivation of UPP and partially reverses photo-oxidation-induced inflammation of RPE. Ensuring optimal levels of all three carotenoids is critical to protecting the eye against high-energy blue light. Lutein and the zeaxanthin isomers absorb different wavelength bands of light and together, the three absorb a broader spectrum of high-energy blue light, which offers greater protection of retinal tissue. Supplementation with zeaxanthin resulted in increased levels in the macula and protected against light-induced photoreceptor death. After long-term deficiency, supplementation with lutein or zeaxanthin protected the fovea from blue light damage. Long-term supplementation with all three carotenoids has demonstrated improvements in eyesight, including visual performance and acuity, reduced glare sensitivity, enhanced contrast sensitivity, improved vision in dim light, and reduced chromatic blur.

The specialized locations and functions of each macular carotenoid suggests that the best way to support eye health and visual performance is to consume all three macular carotenoids through diet or supplementation. Given that the average US dietary intake of lutein and zeaxanthin is far below levels shown in research to be beneficial (less than 2 mg lutein and 0.5 mg zeaxanthin), supplementation may be a more viable approach to maintain optimal levels of the macular carotenoids and protect the eyes against high-energy blue light.

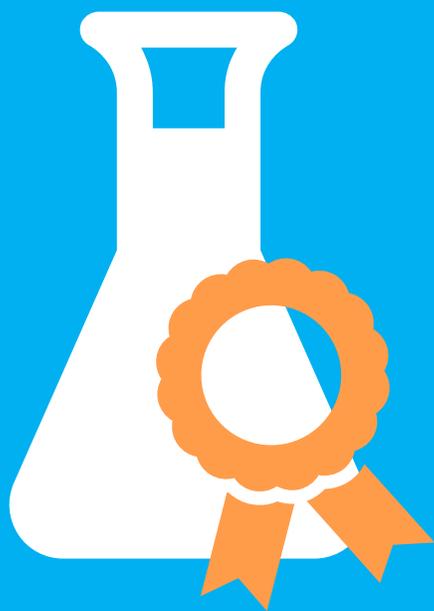
Why just lutein isn't enough

While lutein is a potent antioxidant that provides a significant amount of the total carotenoid content of the eye, healthy eyes require more than lutein alone and a formula containing all three macular carotenoids (lutein, RR- & RS [meso]-zeaxanthin) offers greater protection of retinal tissue. Another advantage of a complete macular carotenoid formula is that it improves serum and retinal uptake, increases macular pigment optical density faster than demonstrated in previous studies and, therefore, confers greater antioxidant protection.





LUTEMAX 2020®: A BALANCED MACULAR CAROTENOID MATRIX TO HELP PROTECT AGAINST BLUE LIGHT



The award-winning science

Multiple randomized, double-blind, placebo-controlled studies using young, healthy subjects, and additional in vitro/in vivo research support the effectiveness of Lutemax 2020 supplementation to support the needs of the 21st century eye-health consumer:

Better bioavailability. Supplementing with Lutemax 2020 significantly increases serum lutein and zeaxanthin concentrations resulting in a rapid, dose-dependent increase in MPOD in as little as 8-weeks. Spatial profile of the macular pigment was also improved with increased central deposition.

Improved visual performance. Increases in MPOD improves lateral inhibitory processes, which corresponds to improved contrast sensitivity, the ability to distinguish between an object and its background or detect differences between similar shades of light and dark. Contrast sensitivity is especially important under conditions of low light, fog, or bright light conditions. Supplementation with Lutemax 2020 also significantly improved photostress recovery and disability glare thresholds (i.e. the ability of the eyes to “see” and recover under bright light conditions).

Blue light protection--an in vitro model. Lutemax 2020 enhanced catalase activity and inhibits cholinesterase, enzymes associated with increased antioxidant protection during exposure to sources of ultraviolet and high-energy blue light and reducing eye fatigue, respectively.

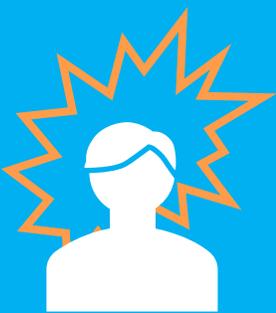
Reducing oxidative stress from blue light—an animal model. Lutemax 2020 provided functional and morphological preservation of photoreceptors against light damage by mitigating oxidative and endoplasmic reticulum stress.

The B.L.U.E Study. This first human clinical trial examining the effects of supplementation with macular carotenoids during prolong blue light exposure from various sources including digital devices. The significance of this study follows.

THE B.L.U.E. STUDY DEMONSTRATES BENEFITS OF LUTEMAX 2020 FOR DIGITAL DEVICE USERS

The B.L.U.E. study (an acronym for Blue Light User Exposure) is the first of its kind to demonstrate how macular carotenoids support visual function and reduce the symptoms of prolonged screen time, including sleep quality, eye strain and fatigue and headache frequency. B.L.U.E. was a 6-month randomized, double-blind, placebo-controlled trial in young healthy subjects exposed to 6-hours per day of screen time and supplementing with Lutemax2020 (20mg L/4 mg Zi) or placebo.

The result show that MPOD, indicators of visual performance (contrast sensitivity, disability glare, photo-stress recovery, visual processing speed), and symptoms resulting from prolonged blue light exposure (headache frequency, eye strain, eye fatigue and sleep quality) all significantly improved. The B.L.U.E. study and prior studies with Lutemax 2020, demonstrate a direct link between supplementation with macular carotenoids and their ability to provide a frontline defense against persistent blue light exposure.



Lutemax 2020 B.L.U.E. Study Outcomes

MPOD	26% increase
Contrast Sensitivity	19% improvement
Disability Glare	44% improvement
Photostress Recovery	33% improvement
Eye Strain	29% decrease
Eye Fatigue	28% decrease
Neck Strain	5% decrease
Headache Frequency	34% decrease
Sleep Quality	20% improvement



A CLINICALLY DEMONSTRATED HEALTH BENEFIT SOLUTIONS

Lutemax 2020 is a complete macular carotenoid formula containing lutein with zeaxanthin isomers in a balanced 5:1 ratio—as found naturally in the diet—and contains significantly higher levels of zeaxanthin isomers than other lutein ingredients. Clinical research has shown that Lutemax 2020 delivers multiple benefits for vision and cognitive health. In addition to a diet rich in fruits and vegetables, Lutemax 2020 is a convenient and effective way to optimize adequate intakes of lutein and the zeaxanthin isomers.

- USP & Non-GMO Project Verified
- FDA GRAS notified
- Winner: NutrAward Best Functional Ingredient 2018
- Manufactured under a fully vertically integrated supply chain



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VersaBead

FOR IMPROVED
BIOLAVAILABILITY & ABSORPTION

VersaBead takes all the science-backed benefits of Lutemax 2020 and provides improved formulation capabilities to meet the growing demand for blue light protection across different applications, including tablets, capsules, powders, gummies, foods beverages and beyond.



OmniActive Health Technologies offers a wide range of scientifically validated, sustainable solutions from natural sources to address complex challenges for customers in the dietary supplement and functional food and beverage space. OmniActive brings added value, with a focus on healthy living as well as healthy aging through IP-protected, science-backed branded health benefit solutions that consumers demand in top categories such as: active wellness and physical performance; metabolic health and weight wellness; vision, cognition and mental wellness; and daily energy and productivity performance.



Early and consistent macular carotenoid intake may help maintain healthy eyes of all ages. 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 macular carotenoid intake to maintain proper vision, cognition and mental wellbeing throughout a lifetime. For more info, visit LuteinForEveryAge.org.



What's Your B.L.U.E.?™ (Blue Light User Exposure) is an award-winning initiative based on scientific research and OmniActive's clinical studies to spread awareness of high-energy blue light exposure, its sources and ways to help protect the eyes from its effects with the support of the macular carotenoids. For more information, visit WhatsYourBlue.info.

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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.

1. NBJ Condition Specific Report 2019.
2. Top Trends Report, Supply Side East 2019.
3. OmniActive Consumer Insights Survey n=500 consumers.
4. Nielsen Insights 2018
5. Common Sense Media. Smartphone use by Tweens and Teens, 2019
6. Statista 2020
7. The 2013 GALLUP Study of U.S. Eye Health - - Basic Survey. Multisponsor Surveys, Inc.
8. The Lowdown on Blue Light: Good vs. Bad, and Its Connection to AMD. *Rev of Opt.* 2014; http://www.reviewofoptometry.com/continuing_education/tabviewtest/lessonid/109744/
9. Pew Research 2012. www.pewinternet.org/2012/04/13/digital-differences.
10. Gutnick AL, Robb M, Takeuchi L, Kotler J. Always Connected: The New Digital Media Habits of Young Children 2011.
11. Zero to Eight: Children's Media Use in America 2013.
12. GFK. (2014). Teen's Time Spent Online Grew 37% Since 2012, Outpacing Other Age Groups [press release]. Retrieved from <http://www.gfk.com/us/news-and-events/press-room/press-releases/documents/1-16-14-teen-internet.pdf>
13. eMarketer 2014.
14. Klepeis, et.al. *J Exp Anal & Env Epid.* 2001; 11:231-252.
15. Taylor et.al *Arch Ophthalmol.* 1992; 110:99-104.
16. Roberts. *J Photobiol B.* 2001; 64: 136-143.
17. Arnault et al. *Plos One.* 2013; 8: 71398.
18. Bush EM, Gorgels TGMF, van Norren D. *Vision Res.* 1999; 39: 1233-1247.
19. Q. Bian, et al. Lutein and zeaxanthin supplementation reduces photo-oxidative damage and modulates the expression of inflammation-related genes in retinal pigment epithelial cells. *Free Radic Biol Med.* 2012; 53(6): 1298–1307.
20. Haas AL, Warms JV, Hershko A, Rose IA. Ubiquitin-activating enzyme. Mechanism and role in protein-ubiquitin conjugation. *The Journal of Biological Chemistry.* 1982; 257 (5): 2543–8.
21. JC Merriam. The concentration of light in the human lens. *Trans Am Ophthalmol.* 1996; 94: 803-918.
22. MT Coroneo. Albedo concentration in the anterior eye: a phenomenon that locates some solar diseases. *Ophthalmic Surg.* 1990; 21: 60-66.
23. Bone RA, Landrum JT, Friedes LM, Gomez CM, Kilburn MD, Menendez E, Vidal I, Wang W. Distribution of lutein and zeaxanthin stereoisomers in the human retina *Exp Eye Res.* 1997; 64(2):211-8.
24. Whitehead AJ, Mares JA, Danis RP. Macular pigment: a review of current knowledge. *Arch Ophthalmol.* 2006; 124: 1038-45.
25. Thurnham, DI. Macular zeaxanthins and lutein - a review of dietary sources and bioavailability and some relationships with macular pigment optical density and age-related macular disease. *Nutr Res Rev.* 2007; 20: 163-79.
26. Seddon JM, Ajani UA, Sperduto RD, Hiller R, Blair N, Burton TC, Farber MD, Gragoudas ES, Haller J, Miller DT, et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. *Jama.* 1994; 272:1413–1420.
27. Bone RA, Landrum JT, Dixon Z, Chen Y, Llerena CM. Lutein and zeaxanthin in the eyes, serum and diet of human subjects. *Exp Eye Res.* 2000; 71:239–245.
28. Mares-Perlman JA, Fisher AI, Klein R, Palta M, Block G, Millen AE, Wright JD. 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; 153:424–432.
29. Bone RA, Landrum JT, Guerra LH, Ruiz CA. Lutein and zeaxanthin dietary supplements raise macular pigment density and serum concentrations of these carotenoids in humans. *J Nutr.* 2003; 133(4):992-8.
30. Thurnham DI, Howard AN. Studies on RS-zeaxanthin for potential toxicity and mutagenicity. *Food Chem Toxicol.* 2013; 59:455-63.
31. Stringham JM, Garcia PV, Smith PA, McLin LM, Foutch, BK. *Invest Ophthalmol Vis Sci.* 2011; 52:7406–7415.
32. Billsten HH, Bhosale P, Yemelyanov A, Bernstein PS, Polivka T. Photophysical properties of xanthophylls in carotenoproteins from human retinas. *Photochem Photobiol.* 2003; 78(2):138-45.
33. Li B, Ahmed F, Bernstein PS. Studies on the singlet oxygen scavenging mechanism of human macular pigment. *Arch Biochem Biophys.* 2010; 504(1):56-60.
34. Nolan JM, Meagher K, Kashani S, Beatty S. What is RS-zeaxanthin, and where does it come from? *Eye (Lond).* 2013; 27(8):899-905.
35. 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; 65(1): 57-62.
36. Olmedilla B, Granado F, Blanco I, (2003) Lutein, but not alpha-tocopherol, supplementation improves visual function in patients with age-related cataracts: a 2-y double-blind, placebo-controlled pilot study. *Nutr.* 2003; 19: 21-4.
37. 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.
38. Stringham JM, Hammond BR Jr. Macular pigment and visual performance under glare conditions. *Optom Vis Sci.* 2008; 85(2):82–88.
39. Renzi LM, Hammond BR. The effect of macular pigment on heterochromatic luminance contrast. *Exp Eye Res.* 2010; 91: 896-900.
40. Kvensakul 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.
41. Rodriguez-Carmona M, Kvensakul 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.
42. Chew E and SanGiovanni JP. Lutein. *Encyclopedia of Dietary Supplements.* Marcel Dekker. 2005.409-420.
43. Snodderly DM. *Am J Clin Nutr.* 1995; 62 (suppl): 1448S-61S. 2. Bone RA, et al. *Exp Eye Res.* 1997; 64: 211-218.
44. Stringham J. Macular Carotenoids, psychological stress, and general health in young adults. *EJO.* 2015; 25(4): e59-e73.
45. Juturu V, Deshpande J, Ghanam K, Doyle L. Soluble lutein inhibits cholinesterase and reduces ultraviolet radiation-induced inflammation and immunosuppression: In vitro model." *EJO.* 2015: 24(4): e59-e73.
46. Yu M, Yan W, Beight C. Lutein and Zeaxanthin Isomers Protect against Light-Induced Retinopathy via Decreasing Oxidative and Endoplasmic Reticulum Stress in BALB/cJ Mice. *Nutrients.* 2018, 10, 842.
47. Stringham JM, Stringham NT, O'Brien KJ. Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure. *Foods.* 2017, 6, 47; doi:10.3390.