

LE Magazine May 2004

## COVER STORY

**The Role of Nutrition in Macular Degeneration**

By Dennis L. Gierhard, PhD



*Macular degeneration is the leading cause of blindness in people over the age of 55, affecting more than 10 million Americans. The disease occurs when the central portion of the retina (the macula) deteriorates, resulting in impaired vision or blindness. The good news is that leading researchers have identified specific dietary factors that can prevent, and even partially reverse, this devastating ocular disorder.*

*Zeaxanthin is one of 700 plant pigments called carotenoids that provide much of the color in nature and our diet. The carotenoids derive their name from the fact that the first pigment isolated, beta-carotene, was from carrots. Beta-carotene is an important source of vitamin A, which is critical to vision. Zeaxanthin and its closely related cousin, lutein, are called xanthophylls and are perhaps the third to seventh most prevalent carotenoids in the human diet (depending on fruit and vegetable selection).<sup>1,2</sup> Humans cannot synthesize these carotenoids and thus must obtain them from their diet. Zeaxanthin and lutein have been recently called “conditionally essential nutrients” because of their critical protective functions in the eye.<sup>3</sup>*

**Guarding Against Light Damage**

Plants synthesize zeaxanthin and lutein to harvest light energy and protect against excessive light. It now appears that humans also utilize these pigments to protect the eye from excessive interaction with the damaging effects of light. This function of zeaxanthin is analogous to a set of “nature’s sunglasses” for the tissues of the eye. In plants, lutein is most often used to help green leafy tissues harvest light safely.

While plants use zeaxanthin to safely harvest light, they more importantly use zeaxanthin to protect against harmful light levels. Dark green leafy vegetables contain large amounts of both pigments but have much more lutein compared to zeaxanthin. Zeaxanthin is more predominant in many of the yellow, orange, and red fruits and vegetables such as peppers, corn, and peaches.<sup>1-6</sup>

Both lutein and zeaxanthin absorb the very high-energy and most damaging portions of the light spectrum (ultraviolet blue). This absorption of the high-energy spectrum is critical to the protection of the lens, retina, and macular portions of the eye.<sup>1,5,7</sup>

**Protecting Against Free Radicals**

Lutein and zeaxanthin are fat-soluble antioxidants. Their structure effectively stops or “quenches” free-radical reactions and their potentially damaging by-products, which collectively are called “reactive oxygen species.” Zeaxanthin and lutein have a unique ability to stop light-accelerated or photo-oxidative reactive oxygen species that are particularly selective and damaging to the eye tissues and skin.<sup>1,5,7</sup>

Like other carotenoids, zeaxanthin is absorbed like a fat and its absorption is aided by the presence of fats in the accompanying meal. Because the bioavailability of carotenoids can be very poor, it is very important that the dietary supplements you consume have proven bioavailability (some sources may be as low as 5% bioavailable for these pigments).<sup>8</sup>

Zeaxanthin and lutein are transported from the intestine to the liver, where they are packaged for transport on the surface of blood lipoproteins to various body tissues such as the eye. There is good evidence that the xanthophylls protect lipoproteins—such as low-density lipoprotein (LDL)—and may reduce the earliest steps of atherosclerosis via their antioxidant and anti-inflammatory mechanisms.<sup>10-12</sup>

### Beyond Eye Protection: Other Health Benefits of Xanthophylls

- Reduced risks of several cancers (lung, prostate, breast, skin)<sup>5,9,12,13</sup>
- Inhibition of pre-malignant lesions and increased apoptosis in malignant tumors<sup>5,9,12,13</sup>
- Immune modulation and reduced risk of infection<sup>5,9,12-14</sup>
- Skin photo-protection and reduced sunburn (erythema) at high dietary intake levels<sup>15</sup>
- High levels are correlated with low levels of systemic inflammation markers like C-reactive protein<sup>10,11</sup>
- Reduction of numerous aging index biomarkers
- Decreased risk of cardiovascular disease, decreased lipoprotein oxidation, and early atherosclerosis lesions (possibly by reduced

The xanthophylls are concentrated in the adrenal, prostate, and breast glands and in the kidneys. The largest total quantities are stored in the liver and adipose (or fat) tissues. The xanthophylls' propensity to store in fat means that individuals who are obese or have a high body mass index (BMI) may have lower deposition of the xanthophylls in eye tissues and greater risk of degenerative eye disease. Both animal and human trial data suggest that lutein is affected more by this competition with fatty tissues, which may explain why in obese individuals zeaxanthin shows much greater ability to deposit in the eye than lutein.<sup>16</sup> Other health benefits attributable to both zeaxanthin and lutein are supported by data from laboratory, animal, and epidemiological studies, as shown below.

inflammatory response)<sup>12</sup>

- Decreased risk of type II diabetes progression
- Increased lung function
- Reduced oxidative (and macro- molecule) damage in numerous tissues<sup>9,12</sup>

## Discovering Lutein and Zeaxanthin in the Eye

Of the 20 or so carotenoids detected in our blood, only zeaxanthin and lutein are used selectively by the eyes.<sup>17-21</sup>

These two xanthophylls are found in almost all subsections of the eye,<sup>18,19</sup> but occur in concentrations nearly 1,000 times greater in the macula section of the retina than in any other tissue in the body.<sup>4</sup> This extremely high concentration creates a yellow spot that is visible to the trained professional and is called the "macula lutea." The xanthophylls that give the macula its striking color also are often referred to as the "macular pigments."

The American biochemist Dr. George Wald was the first to connect the xanthophylls with eye health in 1945 when he tentatively identified the macular pigment as lutein. (Dr. Wald later won a Nobel Prize for his research on the role of vitamin A in vision.<sup>23,24</sup>)

The modern era was initiated in 1985 when two Miami-based researchers, Bone and Landrum, determined that the macular pigment was actually two compounds, lutein and zeaxanthin.<sup>17</sup> This group, along with others, demonstrated that zeaxanthin was concentrated in the center of the retina, while lutein was more prominent at the edges.<sup>18,19,20</sup> In 1994, DSHEA legislation was passed and a group headed by Dr. Seddon at Harvard Medical School published epidemiological data that strongly suggested that people who consume fruits and vegetables containing zeaxanthin and lutein have reduced risks of advanced macular degeneration, the leading cause of acquired blindness in the elderly.<sup>22</sup> In 1997, a group at Tufts identified the same two pigments in the lens of the human eye in nearly equal proportions; at about the same time, epidemiological studies linked the same two pigments with reduced risk of cataract incidence, progression, and severity.<sup>25-31,32</sup>

## Macular Degeneration

Cataract is the leading cause of blindness worldwide and is one of the most costly items in the federal Medicare budget. The second serious vision problem is age-related macular degeneration.

Macular degeneration is the leading cause of acquired blindness and vision impairment among elderly Americans. It is estimated that up to 17 million elderly Americans have at least early signs of the disease called age-related maculopathy. The National Eye Institute estimates that nearly 1.7 million elderly Americans have the more advanced stage of macular degeneration, and a new case is diagnosed every three minutes. The prevalence of the disease increases with age, affecting one in six Americans aged 55 to 64 and one in three Americans over 75. Of the 1.7 million currently afflicted, nearly 85% have the most prevalent form of the disease, known as dry macular degeneration.<sup>2,33,34</sup>

Patients who are affected suffer a gradual loss of central vision due to the death of photoreceptor cells (rods and cones) and their close associates, retinal pigmented epithelium cells. Photoreceptors are the cells in the retina that actually "see" light and are essential for vision. Retinal pigmented epithelium cells are like the "nursemaids" for photoreceptor cells and are necessary for photoreceptor survival. The death of either of these cell types leads to the death of the other. The macula contains the highest concentration of cone-type photoreceptors that are responsible for providing color and fine detail in the center of the visual field. Thus, patients with macular degeneration gradually lose their central vision and with it, the ability to drive, read, and see the faces of loved ones. As bad as this may be, those suffering the disease can function at a reasonable level for many years.

However, another aspect of macular degeneration is even more devastating.

## Protecting the Eye's Structure

The eye is a highly complex organ that must safely harvest, control, focus, and react to light to produce vision. Light enters the anterior portion of the eye through the clear cornea and fluid-like aqueous humor, and is then focused by the clear lens before entering the gel-like vitreous. It must pass through a nerve layer of ganglions connected to photoreceptors (both rods and cones) where light signals are converted to electrical signals that are transported to the brain. Behind the photoreceptors are the "nursemaids" called retinal pigmented epithelium cells that feed and remove toxic waste from the constantly active photoreceptors. The retinal pigmented epithelium cells rest on a thin, connective, tissue-like support structure called Bruch's membrane, which also serves to create a blood-brain barrier for transport of nutrients, waste products, and critical oxygen. In the macula region of the retina, the choroidal blood supply should stay on its own side of this membrane.

With time, the aging eye accumulates greater photo-oxidative damage from its interaction with light. These events lead to two prevalent eye diseases: cataracts and macular degeneration.<sup>2,7,33-35</sup> Figures 1 and 2 on the following page show the major structures of

As the photoreceptor and retinal pigmented epithelium cells slowly degenerate, blood vessels tend to grow from their normal location in the choroid into an abnormal location beneath the retina. This abnormal new blood vessel growth is called choroidal neovascularization, or wet macular degeneration. Abnormal blood vessels leak and bleed, resulting in sudden and severe loss of central vision. Depending on the location, laser treatment can sometimes be given to destroy the blood vessels. When retinal cells are lost, they are not replaced and central vision loss can be profound. New drugs are currently under development for wet macular degeneration, but their availability may be years away.

the eye.

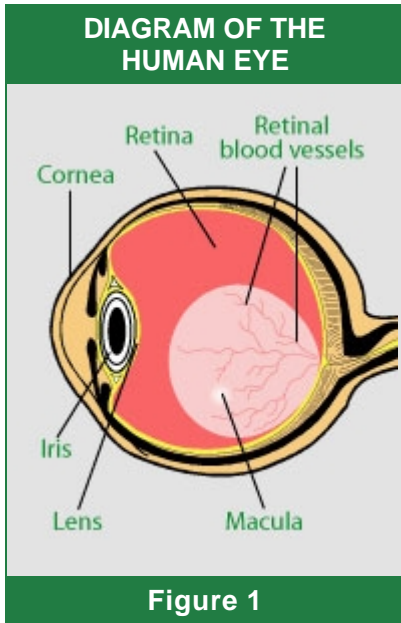


Figure 1

### Protecting the Lens and Macula

The high specific concentration of zeaxanthin and lutein in the macula gave scientists their first hint that nature has a purpose for these plant pigments in eye health.<sup>23,24</sup>

Within the retina, a significant portion of the xanthophylls reside in Henle's fiber, a layer of axons in the inner retinal layer where xanthophylls can filter light prior to light striking photoreceptors (rods and cones) and the very important retinal pigmented epithelium cells. This location would suggest a very strong role for the xanthophylls in filtering damaging light, particularly the most damaging blue part of the spectrum.

The exact center of the macula is where the highest concentrations of dietary zeaxanthin and a related isomer, meso-zeaxanthin, are found. In the peripheral retina, lutein dominates.<sup>18-21</sup> Current theory suggests that high macular pigment, particularly dietary zeaxanthin, protects the portion of the macula most critical to vision and most exposed to photo-oxidative damage.<sup>35</sup> Very high metabolic rates found in the fovea (the center of the macula) require extra antioxidant protection.<sup>7</sup>

Macular degeneration pathology often starts at the edges of the macula, where macular pigment concentrations start to decrease. Analyses of cadaver eyes have shown this direct link by contrasting macular pigment concentrations at distances from the macula's center

in eyes with macular degeneration with those in normal matched eyes.<sup>37</sup> These experiments found a significant drop in pigment concentrations in eyes with macular degeneration compared to normal matched eyes, a difference corresponding to the relative concentrations of zeaxanthin in the eyes.

To summarize, the eye concentrates just three xanthophylls—dietary zeaxanthin, non-dietary meso-zeaxanthin, and lutein—in the macula and other ocular tissues. Of the 16-20 carotenoids in the blood serum, only two are selected for deposition and hyper-concentration in the eye. This highly selective process is the most specific distribution in the entire field of carotenoid biochemistry.<sup>18-21,38</sup>

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#### How Many Xanthophylls Do We Need?

Determining a daily intake of lutein and zeaxanthin is problematic because food composition tables often do not analyze or report lutein and zeaxanthin separately, and comparisons of published data are often inconsistent. Despite the recommendation by many health agencies to eat at least five servings of fruits and vegetables per day, consumption varies widely.

Several major epidemiological studies have linked dietary carotenoid consumption with reduced risks of macular degeneration and cataract. The dietary gap between low- and high-risk individuals was equivalent to about 6 mg/day of lutein and zeaxanthin.<sup>22,25,29-32,39</sup> The data suggest that a difference of 4-5 mg/day in consumption of xanthophylls could influence the risks of contracting eye disease and may be a basis for a maintenance or preventive dosage.

For low-risk individuals, perhaps 3-6 mg/day of zeaxanthin may be extrapolated as a preventive dosage for degenerative eye diseases, though a dose as low as 0.5 mg/day over an entire lifetime may be sufficient. A number of other clinical trials are using 20-30 mg/day of zeaxanthin.

#### Differences Between Zeaxanthin and Lutein

Zeaxanthin and its chemical cousin, lutein, differ in several important ways. Lutein's three-dimensional structure is asymmetrical and bent, a perfect fit for its role in harvesting and transferring light energy in the photoreaction center of the chloroplast of a plant cell. As noted previously, this means that the human diet contains 5-20 times more lutein than zeaxanthin. In human blood serum, lutein is 3-10 times more predominant than zeaxanthin.<sup>1,2,5,6,38</sup> Zeaxanthin is a straight, symmetrical molecule that can perfectly transverse a biological membrane and influence and protect membrane-bound cellular functions more effectively than lutein, regardless of its orientation.<sup>42</sup> This may account for the ocular preference of zeaxanthin over lutein. This selective preference has also been seen recently in human cadaver brain.<sup>43</sup> This membrane spanning and greater antioxidant properties may also explain why the retina makes the unusual isomer meso-zeaxanthin (which is structurally closer) from the more abundant lutein. Most likely this is because the eye attempts to supplement the lower intake of preferred dietary zeaxanthin by converting lutein to meso-zeaxanthin, which is better than lutein but not as good as dietary zeaxanthin. This selective deposition and concentration of dietary antioxidants in the macula's center has also been demonstrated with vitamin E and selenium.<sup>7</sup>

A misconception among consumers is that they get enough dietary zeaxanthin from their lutein products. A second misconception, even among eye specialists, is that lutein is converted to zeaxanthin in the eye. In fact, lutein comes from marigold flowers and contains only a tiny amount of zeaxanthin compared to the 2:1 ratio seen in the section of the macula that seems to be protected. A second fact is that lutein is converted into a compromise structure, meso-zeaxanthin, in the eye.

#### Zeaxanthin's Protective Effects Against Eye Disease

The epidemiological evidence for a protective effect of zeaxanthin in eye health seems reasonably clear but not entirely consistent.<sup>3,4,7,9</sup> The surveys from both dietary and blood serum relations of zeaxanthin and eye disease progression of incidence show the normal inconsistencies. Most of the surveys, however, show a clear relationship to both macular degeneration and cataract for dietary intake of fruits and vegetables containing significant quantities of zeaxanthin and lutein. The blood serum relationship data have been less consistent but may have been clarified by the Medical Research Council in England last year.<sup>41</sup> Gale and colleagues completed analysis on fasting blood serum levels and analyzed lutein and zeaxanthin separately. They stated, for the first time, that the greatest increased risks of both wet and dry macular degeneration were correlated with low blood serum levels of zeaxanthin, not lutein.

With trials in Japanese quail and primates, the evidence from animal trials has recently become much stronger. In the early 1980s, researchers depleted primate diets of carotenoids and demonstrated retinal pathologies consistent with symptoms of macular degeneration. The studies were extended in the mid-1990s when Dr. C.K. Dorey and colleagues at Harvard Medical School and the Schepens Eye Institute established the Japanese quail as a model for studying degenerative eye disease and xanthophylls.<sup>16,44-46</sup> Using aging and light-insult models, Dr. Dorey was the first to show directly that the photo-protective effects

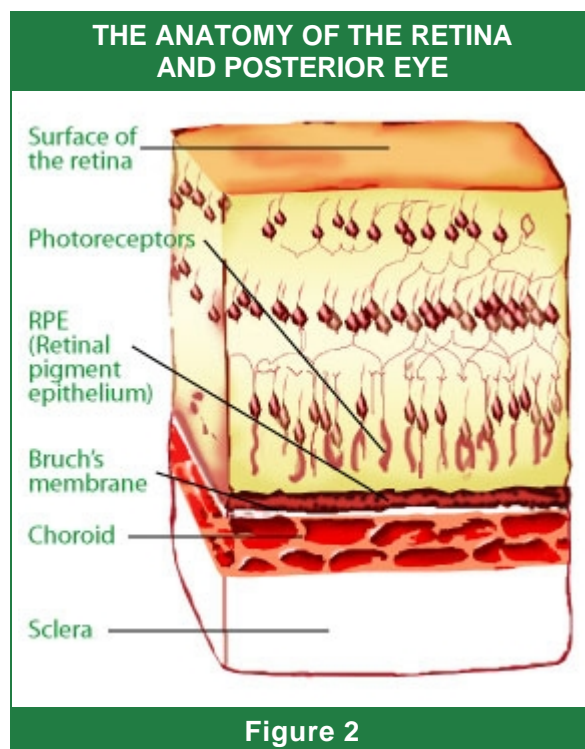


Figure 2

of zeaxanthin were related to the retinal levels of zeaxanthin that she controlled by feeding. This retinal protection extended to both rods and cones, and prevented the massive losses seen in late-stage dry macular degeneration. The team also went on to show that zeaxanthin:

- Protects the eye via reduced cell death
- Prevents age-related changes
- Showed a four times greater “retinal capture efficiency” compared to lutein
- Demonstrated for the first time that dietary manipulation could increase lens levels as much as fivefold, setting up a model for further work in cataract prevention.

Further results with primates have shown that zeaxanthin is more photo-protective (blue laser light insult) than lutein or meso-zeaxanthin.



### Increasing the Macular Pigment's Thickness

It is well established that higher intakes of zeaxanthin and lutein maintain the structure of the macula. The question doctors then asked is whether consumption of these plant extracts can increase the density or thickness of the macula. Human studies have produced fascinating findings indicating that it may be possible to reverse some of the age-related deterioration of the macula.

Doctors can now measure “macular pigment optical density” indirectly and noninvasively by at least six different techniques, though some of these techniques have been subject to criticism. The human trials that measured macular pigment optical density in response to lutein and zeaxanthin intake are summarized in the next column:

- Both food and supplements containing zeaxanthin and lutein are capable of raising retinal levels of the xanthophylls in most, but not all, volunteers. The reason for nonresponsive volunteers has not yet been delineated.<sup>4,47-51</sup>
- The retinal response is very slow relative to the blood serum response (months versus days), but appears to remain stable for months upon cessation of supplementation. This suggests that an intervention dosage may need to be significantly higher than a preventive or maintenance dosage and must be maintained to provide the maximum benefit.<sup>44-49</sup>
- Peak serum levels and ability to increase macular pigment optical density appear to be related, suggesting that high dietary intake may raise retinal levels faster and more effectively.<sup>5,47-51</sup>
- Factors other than peak blood serum levels appear to affect the ability to increase macular pigment optical density. These include many of the risk factors for macular degeneration but may also include genetics, obesity, and other serum or retinal transport/binding proteins for the xanthophylls.<sup>4,51</sup>
- To date, only one small trial has directly compared the ability of lutein and zeaxanthin to influence macular pigment optical density in humans where bioavailability was directly controlled.<sup>48</sup> In this trial, blood serum responses were equal, but more individuals had a retinal response to zeaxanthin.

The association between macular pigment optical density and risk factors for macular degeneration and cataracts is compelling. Reduced macular pigment optical density in the target population has been related to smoking, obesity/high BMI, age, lens density and opacity, gender, light iris, and poor zeaxanthin intake.<sup>1,2,4,7,9,47-51</sup>

### Top 10 Intriguing Facts about Zeaxanthin and the Eye

1. The human eye uses the same xanthophylls, zeaxanthin and lutein (to the exclusion of all others), that the plant world uses to harvest light and protect against excessive light levels.<sup>1,4</sup>
2. The macula selectively concentrates zeaxanthin and lutein at levels up to 1,000 times greater than found in any other body tissues.<sup>1,4</sup>
3. The macula selectively places zeaxanthin in its center where the greatest protection is needed and which is last to degenerate.<sup>18-20,36</sup>
4. The lens also selectively accumulates zeaxanthin and lutein.<sup>23</sup>
5. Biologically plausible theories for protection with zeaxanthin have been elucidated and are supported by direct experimental evidence in two animal models.<sup>16,44,45</sup>
6. The concentration of zeaxanthin and lutein in the retina can be increased by dietary manipulation.<sup>4</sup>
7. The evidence from epidemiological studies is relatively consistent in that high dietary intake of fruits and vegetables rich in xanthophylls reduces the risks of macular degeneration, lens opacity, onset of cataracts, and risks of cataract extraction.<sup>4</sup> A recent study suggests serum zeaxanthin is strongly associated with reduced risk of advanced macular

8. Reduced macular pigment optical density is related in most subpopulation studies to major risk factors for macular degeneration and cataracts.<sup>4</sup>

9. The 2001 AREDS results demonstrate that other dietary antioxidants can intervene in the late stages of macular degeneration, significantly increasing the credibility of one of the theorized protective mechanisms of zeaxanthin.<sup>40</sup> There is a good scientific basis for zeaxanthin acting synergistically with other proven dietary antioxidants.<sup>32,44,45,60</sup>

10. Early results from small clinical studies are consistent with a protective effect but not yet conclusive.

## Zeaxanthin and Other Eye Diseases

A half dozen smaller intervention trials using xanthophylls in degenerative eye disease have been completed. Several small trials have shown xanthophylls' positive impact on visual activity and drusen progression in early maculopathy,<sup>52,53</sup> on retinitis pigmentosa, and on visual activity and glare sensitivity in early age-related cataracts.<sup>54</sup> (Drusen are nodules beneath the retina in a layer called Bruch's membrane, which lies beneath the retina and the adjacent retina pigment epithelium layer). Dr. Stuart Richer and colleagues conducted a year-long trial of 90 males with dry macular degeneration, which showed improvements in glare recovery, contrast sensitivity, and near/distant visual activity.<sup>55</sup>



The results to date are promising, but larger and longer clinical trials will be necessary to clarify the benefits for patients and eye-care professionals before zeaxanthin supplements will receive an unqualified recommendation. The FDA will need to see statistically relevant data, and the medical community will need to see these functional improvements along with reduced progression of symptoms like area of atrophy, drusen and lipofuscin progression, and reduced risk of neovascularization or its progression.

Major trials on intervention in all stages of macular degeneration are in various stages of planning and execution. The largest of these may be the AREDSII trial, with more than 5,000 patients in late-stage macular degeneration. The National Eye Institute and National Institutes of Health are scheduled to begin this trial using lutein and zeaxanthin later this year. Zeaxanthin and lutein were not commercially available for the first trial.

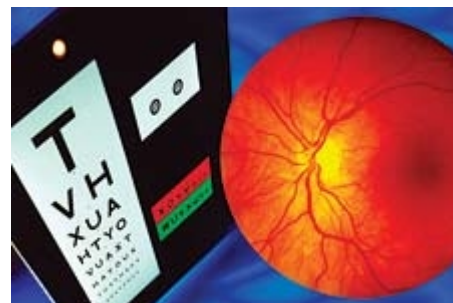
Finally, since zeaxanthin supplements were introduced, many patients who were hypersensitive to light (i.e., photophobic) are reporting dramatic decreases in this unpleasant phenomenon within months of initiating 20 mg/day doses of zeaxanthin. These observations are now being assessed objectively at two colleges of optometry.

## Dual Mechanisms of Action

There are currently two leading theories of how xanthophylls (lutein and zeaxanthin) may protect the eye: the first involves the xanthophylls' antioxidant mechanisms, while the second considers the xanthophylls' UV-blue light filtering properties. These mechanisms are not mutually exclusive, nor is either the only possible mechanism.<sup>1,3,4,7</sup>

Both lutein and zeaxanthin are capable of quenching free-radical reactions that create reactive oxygen species. These reactive oxygen species then react with cell membranes and macromolecules to create pathogenesis leading to many human degenerative conditions. In the eye tissues, these oxidative processes can be further enhanced by the presence of light (which accelerates photo-oxidation), extremely high metabolic rates (in the retina), and the highly polyunsaturated lipids found in the retina and other neural tissues. Both singlet oxygen and peroxy radicals are likely generated in eye tissues and quenched by the xanthophylls.

Light-driven photo-oxidation likely generates excited triplet-state species that also cause severe oxidative damage. As noted earlier, zeaxanthin is a better antioxidant and is more directly embedded in a manner to protect biological cell membranes than is lutein. Xanthophylls are particularly effective at lower oxygen tensions (concentrations) like the interior of a cell membrane or the center of lens tissue. The tocopherols are more effective at higher oxygen tensions. Thus it is highly likely the two lipophilic antioxidants are synergistic and complement ascorbates and the metal-containing enzyme-based antioxidant enzymes that are active in ocular tissues for protection against oxidative damage.



The very earliest steps in eye cells showing oxidative stress are the generation of lipoperoxides.<sup>56</sup> In 2000, these very early oxidation markers were shown to directly induce the pathways of angiogenesis or neovascularization.<sup>57,58</sup> This means that the

earliest step of oxidation may be capable of increasing the risk of progressing to wet macular degeneration.

The second biologically plausible mechanism is UV and blue-light filtering or absorption. The xanthophylls are excellent light filters and absorb that part of the UV and blue-light spectrum thought to be most damaging to the eye. In the lens, the xanthophylls absorb the UV light thought to be the principal initiator of oxidative stress that results in cross-linking of the component crystalline that in turn reduces the clearness of the lens. The xanthophylls would also reduce the amount of blue light reaching the retina. The absorption of blue light in the lens and from reflection in the retina would reduce light scatter and chromatic aberrations. This would suggest a more direct role in reducing visual effects like glare and starburst effects seen in early stages of these diseases.<sup>7</sup>



This blue-light filtering may directly reduce the photo-oxidation in the susceptible axons and likely reduces photo-oxidative damage directly in the photoreceptors and posterior retinal pigmented epithelium cells that support and maintain the photoreceptors.

In the critically important retinal pigmented epithelium cells insulted with blue light, zeaxanthin has been shown to prevent oxidative damage, apoptosis, DNA damage, and cell death. In these cell culture experiments, zeaxanthin shows synergy with the other cellular protectants vitamins C and E, glutathione, and melanin.<sup>60</sup>

### **Theories of Aging Explain Degenerative Eye Disease**

Readers of this magazine are aware of most theories of aging, and almost all are implicated in degenerative, age-related changes in the human eye. The eye has several special considerations. It must deal with light-accelerated degeneration, and the back of the eye has one of the highest oxygen levels, metabolic rates, and cellular turnover rates, as well as susceptible components (polyunsaturated lipids).<sup>7</sup> The back of the eye seems to be a microcosm for atherosclerosis susceptibility, and appears to be at the interface of the blood-brain barrier (i.e., neural retina). The lens is subject to constant ultraviolet insult, a low metabolic rate, and operating in a low oxygen context.

These two disparate and opposing functions are within an inch of each other inside the eye. Readers should also know that caloric restriction, the almost universal environmental anti-aging influence, has also been shown to slow degeneration or aging of the eye.

In addition to its role in the photo-oxidative mechanism of degenerative eye disease, it is likely that zeaxanthin also participates through other protective biological mechanisms. Because age-related eye degeneration is probably multi-etiological, it is likely zeaxanthin helps provide protection at multiple levels.<sup>1,4,7,35</sup>

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#### Summary and Prediction

Zeaxanthin is one of the newest antioxidants and has always been a naturally occurring component of the human diet.

A plausible theory is put forward to support others' speculation that zeaxanthin may be a "critically essential nutrient" for proper eye function and protection.<sup>3</sup> This theory suggests a need to change behaviors and increase dietary consumption of fruits and vegetables to decrease age-related degeneration of the eye. Some evidence suggests it may be more difficult to obtain higher levels of zeaxanthin from the diet than of lutein, indicating that supplementation may be desirable. There is good evidence that zeaxanthin is preferred by ocular tissues because it has unique properties and subtle structural differences compared to lutein that make it a better lipophilic antioxidant and photoprotectant.

Dietary supplementation with 3-6 mg/day of zeaxanthin may reduce the risk of contracting degenerative eye diseases. Significantly higher dietary intake of zeaxanthin (not the isomer meso-zeaxanthin) may be important for individuals with high risks for or advanced symptoms of macular degeneration and cataracts. Other health benefits associated with zeaxanthin also have been noted.



In the near future, we can expect more basic research, animal studies, and objective double-blind clinical trials attempting to clearly define zeaxanthin's importance in degenerative eye diseases. It is likely that high intake of dietary antioxidants and zeaxanthin will be shown to be a factor in reducing the risk and slowing the progression of degenerative eye diseases. Other important phytonutrients are also likely to act synergistically with zeaxanthin in slowing the aging effects in the eye. As science elucidates the most important degenerative mechanisms and genetics shines its light on inheritance issues and mechanisms, supplements will be on the market to address these needs. Looking out a little further in the future, it is likely that cataract prevalence and progression will benefit from combined research on zeaxanthin and advances in the nutritional biochemistry of the eye.<sup>33</sup> This advance could have a positive economic impact on growing Medicare expenditures tied to degenerative eye disease. Perhaps the same impact will be seen concerning diabetic complications of the eye and macular degeneration. With nearly 15 million dry macular degeneration sufferers in the US today and more on the way, a decreased incidence and progression rate would be welcome.

Pharmaceutical and biotechnology companies are developing cold laser and angiogenesis inhibitors for treating the ravaging effects of wet macular degeneration.<sup>35</sup> Almost all these treatments target single molecules or single pathways to prevent or destroy unwanted blood vessels. While zeaxanthin may be the single most critical nutrient for the eye, its value will most likely be in conjunction with high dietary intake of multiple nutrients. Eventually there will be a convergence of nutritional intervention (to prevent and modulate early insults and stresses of the eye) and sophisticated medical treatments (for very late and aggressive blood vessel growth of wet macular degeneration).

Future generations will be able to see those important things in life. In the meantime, you can eat healthy (lots of fruits and vegetables, decreased fats, and increased fish oil), increase your dietary intake of zeaxanthin and other antioxidants, stop smoking, lose those extra pounds, watch your risk factors for cardiovascular disease, and protect your eyes when in the sun.

#### About the Author

*Dr. Gierhart received his BS and MS degrees from Ohio State University in 1973 and 1974, and earned his PhD in Food and Industrial Microbiology from Cornell University in 1978. Before founding ZeaVision, Dr. Gierhart was founder and president of Applied Food Biotechnology, Inc., a food/feed ingredient company. Before founding Applied Food Biotechnology, Dr. Gierhart directed corporate research programs for two Fortune 500 food companies.*

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