Traditionally, support of vision and eye health is not one of the first clinical issues that we as functional and alternative medicine practitioners focus on when considering which nutritional supplements to recommend to our patients. However, as the US population continues to demonstrate, more and more people are living longer in spite of exponential increases in chronic illness — and they are also experiencing a dramatic rise in metabolic imbalances that adversely affect vision. Fortunately, we are also witnessing a dramatic rise in the publication of research papers that make it clear that lifestyle modification with emphasis on improved diet and ingestion of key nutrients can have a massive positive impact on vision-related metabolic imbalances that are associated with aging. Therefore, we are excited to be introducing to you our eye-health support product — OculoSelect™ along with a recommendation that we now routinely ask your patients about vision along with your usual questions about gut health, stress, toxicology, etc.

As you will see in the enclosed technical bulletin, OculoSelect™ contains many of the nutrients you would ordinarily expect to see in an eye support product, two of which I will be discussing in detail below. However, it also contains one substance you might not expect based on the labels of the usual eye support products in the marketplace. As you can probably guess (if you are a regular reader of these newsletters) this substance is curcumin — but not just conventional curcumin but the highly bioavailable form of curcumin we use in so many of our products that are designed to optimize health in chronically ailing individuals — Meriva®. Why? As we all know, chronic inflammation has been firmly established as part of the common currency of all chronic illnesses including those chronic illnesses that impact vision.

A discussion on curcumin and its impact on eye health will follow shortly. However, I would first like to review research on what are probably the key constituents of any quality vision support product, including OculoSelect™, the carotenoid compounds lutein and zeaxanthin. As you will see below, for OculoSelect™ we opted to use the outstanding standardized product Lutemax® 2020 as a source of lutein and zeaxanthin.

**Lutemax® 2020 — The source of lutein and zeaxanthin in OculoSelect™**


> “Lutemax™ 2020 is a lutein and zeaxanthin (including meso-isomer) enriched product obtained from Marigold flowers.”

As a basic overview, why is Lutemax® 2020 a key factor in OculoSelect™? Consider the following quote from the above-mentioned paper:

> “The active constituents of Lutemax 2020™, trans-lutein, and zeaxanthin and meso-zeaxanthin are found in the macula of the
eye. Lutein and zeaxanthin are commonly found in the human diet and there is a safe history of consumption of these components. Thus, there is sufficient qualitative and quantitative scientific as well as history of use evidence to support the safety-in-use of lutein/zeaxanthin.”

**Why are lutein, zeaxanthin, and meso-zeaxanthin so important for eye health?**

Of course, the above quote only begins to tell the story of why Lutemax® 2020 is included in OculoSelect™. For a more complete understanding I would now like to review the paper “Lutein, zeaxanthin, and meso-zeaxanthin: The basic and clinical science underlying carotenoid-based nutritional interventions against ocular disease” by Bernstein et al (Bernstein PS et al. Prog Retinal Eye Res, Vol. 50, pp. 34-66, 2016). To begin, consider the first line of the abstract:

“The human macula uniquely concentrates three carotenoids: lutein, zeaxanthin, and meso-zeaxanthin. Lutein and zeaxanthin must be obtained from dietary sources such as green leafy vegetables and orange and yellow fruits and vegetables, while meso-zeaxanthin is rarely found in the diet and is believed to be formed at the macula by metabolic transformations of ingested carotenoids.”

What is the primary beneficial function of these carotenoids in the eye? As you can probably guess, they are powerful and potent antioxidants. Bernstein et al comment:

“Macular carotenoids may neutralize the reactive oxygen species (ROS) generated due to various free radical reactions in the eye and other tissues. Lutein and zeaxanthin are very efficient at absorbing and transmitting excited energy when needed, and they can harmlessly release the energy as heat without chemical degradation.

The potential for generation of ROS in the retina is high. The outer retina, especially membranes of the outer segments of the photoreceptors, has high concentrations of polyunsaturated fatty acids that are susceptible to photo-oxidation. ROS are produced by absorption of UV and blue light by a photosensitizing compound or molecule (e.g. lipofuscin, protoporphyrin, or cytochrome). Carotenoids are potent scavengers of free radicals (e.g., superoxide anion and hydroxyl radical) and are particularly efficient at neutralizing singlet oxygen. These carotenoid molecules have the ability to vibrate away their triplet-state energy as heat.

Similar to their roles in plants, lutein, zeaxanthin, and meso-zeaxanthin act as protective antioxidants in the eye. These eye protective nutrients undergo oxidation and a series of transformations to protect the macula.”

**How are dietary carotenoids such as lutein and zeaxanthin absorbed and metabolized?**

The next quote I would like to feature from the Bernstein et al paper relates to the absorption and metabolism of lutein and zeaxanthin:

“Most dietary carotenoids are consumed and embedded within a food matrix. When they reach the gut, they will be released from the food matrix through the action of various enzymes including esterases which will cleave xanthophyll esters. The free carotenoids are then solubilized into micelles before being taken up by the intestinal mucosal cells where they are cleaved by the carotenoid cleavage enzymes, BCO1 and/or BCO2, to form vitamin A and other metabolites or packaged into chylomicrons. Then carotenoids and their metabolites will be secreted into the lymphatic and portal circulations for transport to the liver, where xanthophyll carotenoids such as lutein and zeaxanthin are loaded onto their relevant transporters to be carried to the retina and other tissues through the circulation system. In the human serum, water soluble lipoproteins are responsible for carrying carotenoids, retinoids, vitamin E, and plasma lipids.”

Interestingly, HDL lipoproteins, levels of which are often suboptimal in many patients with vision issues, are extremely important in the delivery of carotenoids to the retina:

“HDL is the smallest and densest of all plasma lipoproteins, playing a critical function in cholesterol metabolism with an important role in removing cholesterol from peripheral tissues, a process known as reverse cholesterol
transport. In the bloodstream, all carotenoids are detectable in all lipoprotein classes to varying degrees, but lutein and zeaxanthin are primarily associated with HDL, consistent with their less hydrophobic nature relative to the carotenes; however, the specific components of HDL responsible for carotenoid binding remain to be identified. The Wisconsin hypoalpha mutant (WHAM) chicken, a natural animal model of HDL deficiency, has a >90% reduction in plasma HDL. When these chickens are fed a high-lutein diet, lutein levels increase in plasma, heart, and liver, but not in retina, suggesting that HDL is critical for delivery of carotenoids to retinal tissue.”

The impact of lutein and zeaxanthin on macular health

Up to this point the quotes presented have focused on the relationship between lutein, zeaxanthin, and health of the retina in general. However, lutein and zeaxanthin also have an important role to play in the macular portion of the retina, which is of major clinical significance due to the high incidence of macular degeneration in the US. Specifically, to fully understand the role of lutein and zeaxanthin on macular health another key aspect of macular physiology must be discussed, macular pigment (MP). To begin this discussion, consider the following quote from the Bernstein et al paper:

“There is a growing and evidence-based consensus that MP is important for optimal visual performance because of its blue light-filtering properties and consequential attenuation of chromatic aberration, veiling luminance, and blue haze, and it has been hypothesized that MP may protect against age-related macular degeneration (AMD) because of the same optical properties and because of the antioxidant capacity of the three macular carotenoids. Also, it has been found that MP levels correlate with concentrations of lutein and zeaxanthin in the brain. This had led to researchers to speculate that the carotenoids that comprise MP may also play a role in the brain (the retina is part of the central nervous system), but the mechanisms whereby carotenoids may play a role in brain health are not known.”

Based on several studies that suggest lutein and zeaxanthin supplementation may increase MP, thereby improving macular health, Bernstein et al conclude the following:

“In conclusion, there is a biologically plausible rationale, supported by MP’s light-filtering properties, which suggest that augmentation of MP will enhance visual function and comfort by attenuation of the effects of chromatic aberration and light scatter. Indeed, clinical trials have repeatedly shown that supplementation with the macular carotenoids lutein, zeaxanthin, and meso-zeaxanthin results in augmentation of MP, and consequential benefits in visual performance such as improved contrast sensitivity and reduced glare disability. The importance of these findings extends to those involved in vision-dependent-specialized activities, such as pilots, vehicle drivers, military personnel, and athletes.”

Preventive use of lutein and zeaxanthin supplementation: Prenatal use and use with infants

Much of the literature on lutein and zeaxanthin supplementation focuses on age-related visual disorders. However, research on these nutrients has also presented compelling information about their use with infants and during pregnancy. Bernstein et al state:

“Although most clinical studies including carotenoids have focused on the prevention of degeneration or oxidative damage, the influence of carotenoids on normal visual function is also of great interest. Reports from adult populations indicate that carotenoid supplementation may increase normal visual performance. These suggest a role for carotenoids in enhancing visual function and suggest a potential role for carotenoid supplementation and MP in normal visual development in infants.”

The next series of quotes discuss the use of lutein and zeaxanthin during pregnancy:

“Maternal carotenoid status during the gestational period may impact infant macular development, and prenatal supplementation may play a role in maximizing visual development. As shown by us, maternal...
serum zeaxanthin levels correlate with infant macular pigment optical density (MPOD) in term infants shortly after birth. This suggests a key role for maternal nutrition and macular development in utero.”

The next quote discusses retinopathy of prematurity (ROP):

“Similar to the prevention of macular degeneration, the role of carotenoids in the prevention of oxidative damage in retinopathy of prematurity (ROP) is also promising. Preliminary studies suggest a potential role for carotenoids in decreasing oxidative stress.”

With this information in mind, Bernstein et al make the following recommendation:

“An examination of current literature would suggest that prenatal supplementation starting early in pregnancy would have some impact, due to presence of carotenoids in retinal tissue as early as 20 weeks gestation, but supplementation during later stages may have even greater clinical impact on the treatment or prevention of retinopathy of prematurity.”

More information on the impact of lutein and zeaxanthin on eye health

The next paper I would like to review, “Lutein and zeaxanthin isomers in eye health and disease” by Mares (Mares J. Ann Rev Nutr, Vol. 36, pp. 571-602, 2016), focuses on clinical applications of lutein and zeaxanthin that were not addressed in significant detail by the Bernstein et al paper. The paper begins by discussing all the structures in the eye that contain lutein and zeaxanthin:

“Lutein is the most abundant isomer in vision-related tissues (the eye and brain). Nearly all human ocular structures except the vitreous, cornea, and sclera contain lutein (L), zeaxanthin (Z), and metabolites. The highest concentration of L and Z in the eye is in the macula of the retina. Only humans (and nonhuman primates) have a macula with a central fovea, and concentrations of L and Z in the central fovea are 100-fold higher than elsewhere in the eye.”

Lutein and zeaxanthin can also be found in the lens and other eye structures:

“L and Z and oxidized metabolites are also the only carotenoids present in the lens of the eye. The most light-exposed and metabolically active lens tissue of the epithelial/cortical lens layers contains about 75% of the L/Z. The center (nuclear) region has lower levels. Approximately ten percent of the L and Z in the eye is contained in ciliary body, which is the metabolically active tissue responsible for aqueous humor formation; defects in aqueous humor flow contribute to the major form of glaucoma.”

Functions of lutein and zeaxanthin

The Bernstein et al paper primarily focused on the antioxidant capabilities of lutein and zeaxanthin in terms of their functions. Mares points out additional functions:

“Light absorption. Macular carotenoids are estimated to absorb 40 to 90% of incident blue light (depending on concentration); this absorption protects the retina from light-related damage and reduces light scatter.”

“Protection against inflammation. Evidence indicates that L also protects against inflammation, a pathogenic mechanism in many ocular diseases that can affect many regions of the eye. Possible mechanisms include preventing the increase in oxidation-induced cytokines and upregulating the expression of inflammation-related genes. L may also indirectly influence ocular inflammation by reducing systemic inflammation via reducing factor D, a rate-limiting enzyme of the alternative complement activation pathway.”

“Other functions. Evidence suggests that carotenoids can play a role in cell-to-cell communication, through intracellular membrane structures known as gap junctions, which can play a role in homeostasis. However, this role has not, to this author’s knowledge, been specifically investigated in ocular tissues.

The presence of L and Z in membranes and their unique alignment decrease membrane fluidity, which could influence many membrane functions in photoreceptors and other parts of the neural retina and brain.”

Still another function is the following:
“The presence of L and Z throughout the neural retina and brain supports the possibility that L might play a role in preserving long-chain polyunsaturated-rich neural tissue and ultimately enhance the transmission of visual impulses to the brain.”

Variability in the accumulation of lutein and zeaxanthin in retinal tissues

The following quote makes it clear that the amounts of lutein and zeaxanthin in the retina will vary considerably from patient to patient:

“Levels of L and Z in the serum and macula vary between individuals more than tenfold, whether assessed in autopsy tissues by high-performance liquid chromatography or by noninvasive assessment of macular pigment optical density (MPOD). A substantial amount of evidence…suggests numerous dietary, metabolic, and genetic influences on L and Z absorption, transport in the blood, and accumulation in the eye. Consistent with this idea, responses to dietary supplementation with L and Z are quite variable between individuals. Dietary supplementation with macular carotenoids for 6 to 24 months has been observed to increase MPOD in 36% to 95% of subjects, with many studies suggesting estimates between these two extremes.”

Why the extreme variability? Mares points out:

“The large interindividual variability in response to supplementation suggests there are many exogenous and endogenous influences on uptake, transport, and retinal capture of L and Z. Several recent reviews detail the many dietary and host phenotypes and genotypes that influence the absorption of L and Z, their transport in the blood, and their uptake and stabilization in the retina.”

The next few quotes focus on the specific factors that affect uptake and utilization of lutein and zeaxanthin.

Absorption – “Some of the variability in MPOD levels appears to be the result of variable absorption. A large body of evidence indicates that the serum response to ingested L and/or Z is highly variable (similar to that of other carotenoids).”

Part of this variability is due to differences in bioavailability from various foods:

“Grinding or cooking foods (which may release carotenoids from the food matrix) and consuming L or Z with a fat source increases blood response. The context of food matters. For example, L and Z are more bioavailable in eggs than in spinach. Recent evidence suggests that this higher bioavailability may be the result of carotenoid presence within the lipid matrix of the egg and/or increased transfer to blood high-density lipoproteins (HDLs). In contrast to other carotenoids, at least half of these more polar carotenoids are carried on HDLs.”

Again, please note the importance of HDL cholesterol in the transport of lutein and zeaxanthin to the retina. Therefore, when considering use of OculoSelect™, also keep in mind use of lifestyle modifications and other Moss Nutrition products that will address causes of low HDL (chronic inflammation, insulin resistance, sarcopenia, chronic, low-grade metabolic acidosis, etc.).

Transport and tissue distribution – “Carotenoid efflux from the enterocytes occurs via their secretion in chylomicrons and transport to the liver, where they are repackaged into lipoproteins and distributed throughout the body.”

Of course, concerning this issue of distribution, our primary goal with OculoSelect™ is to optimize transport of the lutein, zeaxanthin, and meso-zeaxanthin to the eye. As you will see from the quotes below, obesity and diabetes can significantly compromise transport of these carotenoids to the eye:

“Adipose tissue is a storage tissue for carotenoids. Current evidence suggests that the metabolic status of individuals might influence the distribution of carotenoids between adipose tissue and the eye. A large body of evidence indicates that obesity and diabetes are associated with lower levels of serum carotenoids and lower macular pigment optical density (MPOD). Moreover, we recently observed a strong linear and inverse relationship between MPOD and metabolic syndrome risk scores composed of
these and other phenotypes (e.g., serum triglycerides >3mmol/L, use of cholesterol-lowering medications, history of hypertension) and of genotypes related to low HDL levels."

Why is lutein and zeaxanthin lower in the serum and eye with a metabolic syndrome type profile? Mares suggests:

“At least three possible explanations exist for lower levels of L and Z in serum and MPOD in individuals with metabolic syndrome phenotypes. First, a large body of evidence indicates that metabolic syndrome phenotypes are associated with higher oxidative stress and inflammation, which could increase the turnover of carotenoids. Second, larger body fat compartments may shift the distribution of carotenoids away from the blood and retina and into adipose tissue. Third, interesting recent evidence suggests that carotenoid status and/or carotenoid cleavage enzymes directly influence adiposity.”

More on lutein and zeaxanthin in relationship to neonatal development

The Bernstein et al paper briefly commented on the importance of optimal lutein and zeaxanthin levels during neonatal development in terms of lifelong eye health. The following quotes from the Mares paper provide much more detail, particularly in relationship to breast milk content.

“Significant direct relationships between L and Z concentrations in the macula and age from birth to seven years have been observed. Premature human infants and monkeys born to mothers raised on L- and Z-free diets do not have macular pigment. Accumulation of macular L and Z is likely to depend on maternal L and Z status, and this hypothesis has been supported by evidence from a small sample that indicated direct relationships between maternal serum Z and infant macular pigment optical density (MPOD) levels. More studies are needed to confirm this finding. Recent evidence indicates that MPOD is higher in older women with early-life exposure to L and Z in breast milk, which contains higher concentrations than formulas made from cow’s milk. (Cow’s milk was the predominant source of formula for infants not breast fed in the 1920s to 1940s.) These data suggest that levels later in life may be influenced by L and Z exposure in the first years.”

As I hope you can see from the above quote, when considering use of OculoSelect™, particularly in relation to dose, a long term history that includes method of feeding during infancy will be very helpful. For, even though vision symptomatology may have begun later in life, the physiologic conditions that laid the groundwork for these symptoms may have had its onset decades before.

What is it about breast milk that makes it so beneficial to eye health later in life? To answer this question, consider the following:

“Breast milk appears to selectively concentrate these carotenoids, particularly in early lactation. L and Z are proportionally more prevalent in breast milk than in maternal serum. The molar ratio of carotenoids in human milk to maternal plasma was observed to be highest for L relative to other carotenoids. Currently, carotenoids are not routinely added to infant formulas, and they were not added to any formulas prior to about 2012. L and Z were the most abundant carotenoids in samples of human milk in one multinational study, but not in five of nine countries in other multinational studies to date. Breast-milk carotenoids are related to maternal serum carotenoids, which are influenced not only by diet but also likely by conditions known to influence serum carotenoid levels, such as obesity, smoking, and alcohol use and markers of inflammation. L in breast milk appears to be approximately fourfold more bioavailable than L in infant formulas to date.”

Visual issues impacted upon by lutein and zeaxanthin supplementation

Visual acuity – The quote below indicates that many studies indicate a positive impact of lutein and zeaxanthin supplementation:

“Results of some but not all intervention studies indicate improvements in visual acuity when L and/or Z are supplemented alone or,
more often, in conjunction with other antioxidants and/or omega-3 fatty acids.”

Of course, OculoSelect™ already contains other antioxidants. However, based on the above quote, consider use of any of our Omega 3 products, EPA/DHA Select™ and EPA/DHA HP Select™, when supplementing OculoSelect™.

**Contrast Sensitivity** – “Contrast sensitivity is the ability to detect contrasts in levels of lightness or darkness of an object, or of colors, relative to the objects background.”

Can lutein and zeaxanthin supplementation be helpful with this issue? Mares states:

“Supplements containing L and Z at various amounts and taken for three months to three years have improved contrast sensitivity in most previous studies, including in young, healthy subjects, in people with early and/or advance age-related macular degeneration, and in individuals with diabetes. Four of five randomized, placebo-controlled trials of solely L and/or Z isomers in >50 subjects observed improvements in spatial contrast sensitivity; results of one other trial did not. The long-term influences of L and Z status on contrast sensitivity in later life would include not only these short-term effects but also protection against age- and disease-related changes.”

**Photostress recovery and glare reduction** – “A considerable body of observational evidence suggests that higher levels of macular pigment reduce the impact of bright lights by shortening the time needed to recover from bright lights (photostress recovery) and by enhancing the ability to see in conditions of glare (lower glare disability), as might occur from oncoming headlights while driving at night.”

With the above in mind, how well did supplementation with lutein and zeaxanthin work? Mares notes:

“One in four randomized trials in more than 50 people indicated a benefit of L and/or Z supplements on glare disability; one of three trials found beneficial effects on photostress recovery.”

**Visual processing speed** – Mares points out the following in relation to lutein and zeaxanthin supplementation:

“Improved critical flicker-frequency thresholds, visual motor reaction time, and visual processing speed have been observed in adults 18 to 32 years of age who received Z supplements, alone or with L and omega-3 fatty acids, for only four months. Increases in about 0.09 MPOD units through supplementation were estimated to significantly improve visual processing speed in these young, healthy adults.”

**Age-related macular degeneration** – As we all know, this is one of the major vision-related maladies plaguing middle-aged and older individuals in the US today. Can lutein and zeaxanthin supplementation be of benefit? Mares points out:

“Strong evidence indicates that L and Z protect against the development of age-related macular degeneration (AMD), the leading cause of blindness in persons over 40 years of age in the United States.”

What is the minimum dose of lutein and zeaxanthin needed to have a positive impact on AMD?

“In summary, L and Z intakes of 5 to 6 mg/day are associated with lowering the risk of developing AMD, and supplemental intakes at 12 mg/day (in the absence of beta-carotene but in the presence of other antioxidants) slowed AMD progression in people who already had intermediate AMD.”

(Each capsule of OculoSelect™ contains 10 mg of lutein and 2 mg of zeaxanthin).

**Cataracts** – Mares points out:

“A large body of evidence from longitudinal observational studies supports a protective association of L and Z in diet and/or serum with the subsequent prevalence or incidence of cataract (except in well-nourished samples), particularly for opacities in the nuclear (central) region of the lens, where opacities develop slowly over a lifetime.”
What about dosage? Interestingly, cataracts is one condition where it appears very little lutein and zeaxanthin is needed:

“…the body of evidence from different study types suggests that L and Z are likely to be two dietary components that protect against nuclear cataract, but if this is the case, the level needed to protect against lens opacity development is likely to be in the range of 0.5 to 1 mg/day, which is below the average intake in American adults.”

Glaucoma and diabetic retinopathy – “An early body of research suggests that L and Z might help prevent the development and progression of glaucoma and diabetic retinopathy, which are more common in people with diabetes.”

Curcumin and the eye

As I mentioned above, as with virtually all chronic ailments in our society today, chronic inflammation plays an integral role in all the visual issues discussed thus far in this monograph. Because of this, as I also mentioned, it should come as no surprise that we included a potent anti-inflammatory compound, curcumin in the form of Meriva®, in OculoSelect™.

Evidence that curcumin can be helpful for eye disorders can be found in the paper “Curcumin: Therapeutical potential in Opthalmology” by Pescosolido N et al (Pescosolido N et al. Planta Med, Vol. 80, No. 4, pp. 249-254, 2014). In this paper the authors state:

“Experimental and clinical data obtained so far indicate that oral supplementation with curcumin is well tolerated and has been shown to be safe in humans. It could reduce symptoms and signs of eye discomfort after a few weeks of treatment. Most studies demonstrated its potential therapeutic role and its efficacy in eye relapsing diseases, such as dry eye syndrome, allergic conjunctivitis, anterior uveitis, glaucoma, maculopathy, and ischemic and diabetic retinopathy.”

Furthermore:

“In light of its angiogenesis-modulating profile and anti-inflammatory properties, curcumin has great potential in the treatment of inflammatory and neovascular proliferative diseases of the retina.”

Some final thoughts

As I mentioned in the beginning of this monograph, most people, which includes the general public and health care practitioners, both allopathic and alternative, do not immediately think of nutrition and nutrient supplementation when confronted with age-related vision issues. As suggested by this review, it may be time to reevaluate this mindset. Hopefully, those of you who are ophthalmologists and opticians, if you are not employing nutritional supplementation in your practices, will consider routine use of OculoSelect™. For those of you whose primary clinical focus is not vision-related issues, it is my hope that you will make questions about visual impairment a more routine part of your history with middle-aged and older patients. In addition, when vision issues are elucidated by patients, it is my hope that both a referral to a competent vision practitioner and a recommendation of OculoSelect™ will also become routine.

OculoSelect™ - Moss Nutrition

Contents: 60 and 120 Vegetarian Capsules