THE EFFECT OF XANTHOPHYLL SUPPLEMENTATION UPON MACULAR PIGMENT AND GLARE/PHOTOSTRESS RECOVERY

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INTRODUCTION

Lutein and zeaxanthin along with their lutein-derived isomer, meso-zeaxanthin, are the only carotenoids found in the macula of the eye (1). In this location these carotenoids make up the macular pigment. They are present in the macula at more than 1000 times the amounts found in any other organ of the human body (2). Although these carotenoids have been shown to have a variety of activities in the human body, they are best known for their antioxidant and blue light filtering capacities in the eye (1). The latter two activities are important in helping protect the eye from over-exposure to short wavelengths of visible light (the blue wavelengths) focused upon the macula and believed to be involved in the genesis of age-related macular degeneration (AMD). However, the blue light filtering ability of lutein and zeaxanthin in the macula has also been credited with other activities aside from just protecting the macula from AMD, specifically visual performance functions including reduction in photophobias, reduction in photostress recovery time, reduction in glare disability, increased glare tolerance, improved chromatic contrast, and even improved visual acuity (3). These attributes are important because they affect visual quality and visual performance throughout a lifetime and not just vision in the latter stages of life.

Although improvements in visual function as related to intraocular yellow filters were first hypothesized by Wall and Judd as early as 1933 (4), it was not until 1981 that Nussbaum (5) related such improvements to macular pigment. Wooten and Hammond refined these hypotheses further in 2002 through the use of quantitative modeling (6). Support for these hypotheses were first found in the results obtained from clinical studies published in 2003 and 2004 in which subjects with AMD were supplemented with lutein and zeaxanthin (7, 8). Supplementation of those subjects resulted in increases in the amount of macular pigment present in their eyes as demonstrated by increased macular pigment optical density (MPOD) values. Furthermore, the increased MPOD values were found to be directly related to visual performance under glare light conditions. In 2003, Stringham, et al. (9) provided data showing that the visual discomfort from a glare light source was appreciably greater for wavelengths in the blue end of the visible light spectrum than for wavelengths in the mid-to-longer wavelengths (i.e., the green to red wavelengths). These authors also showed that subjects with higher MPOD values were able to tolerate exposure to greater amounts of short-wave light before averting their gaze than subjects with lower MPOD values. Additionally, they showed that this effect is most significant in the foveal area where macular pigment is highest and virtually negligible in the parafovea where MPOD is minimal. In order to verify these findings, these authors conducted a study in which they supplemented four subjects with lutein for 10 weeks during which they measured changes in MPOD values and photophobia thresholds (10). They found that photophobic thresholds increased in direct relation to increases in MPOD thereby showing that the
increases in macular pigment were most likely responsible for reducing discomfort related to glare. Although this study addressed discomfort glare, it did not extend those findings to disability glare.

It is important to understand that discomfort glare and disability glare are different (11). Glare discomfort is an instinctive effect causing a person to avert their gaze or squint because the intensity of the light entering the eye is uncomfortable. An example of discomfort glare is light reflected off the surface of a lake. No loss of vision is caused by glare discomfort. Alternatively, glare disability is the loss of vision caused by the fact that the intensity of the light induces a degradation of contrast between objects due to diffraction of light within the eyeball combined with a bleaching of photopigments (retinol) responsible for converting the absorbed light into neural impulses in the retina. This amounts to a virtual, albeit temporary, blinding of the subject to objects in their field of view with or without discomfort. An example of glare disability would be the inability to see objects on the road when driving at night because the driver of an oncoming car flashed their high beam headlights. Due to these differences, the above results obtained for glare discomfort (photophobias) are only suggestive of a relationship between MPOD and glare disability but cannot be used in support of such an effect.

Based upon this suggested relationship, Stringham and Hammond conducted a study to evaluate the relation between macular pigment and glare disability (12). Measuring both MPOD and glare energy (i.e., the amount of light a subject could withstand before losing sight of a target) as well as photostress recovery time (i.e., the time required to regain vision of a target after exposure to an intensely bright white light source) in a group of young healthy subjects, they found that MPOD was directly related to glare energy and inversely related to photostress recovery time. Those results showed that subjects with high MPOD values could see a target in their line of sight while simultaneously being exposed to more light than subjects with low MPOD values. Furthermore, the amount of time required to be able to see again a target after exposure to five seconds of extremely intense white light (i.e., photostress recovery time) was much shorter for subjects with high MPOD values when compared to subjects with low MPOD values. Taking this information to the next logical step, Stringham and Hammond conducted an open-label study in which a group of 40 young, healthy subjects were supplemented with 10 mg of FloraGLO® Lutein and 2 mg of OPTISHARP® Zeaxanthin for 6 months (13). MPOD, glare energy tolerance and photostress recovery time were measured at baseline and periodically throughout the study period. These researchers found significant increases in MPOD values and in tolerance to glare energy along with significant decreases in photostress recovery times in these supplemented subjects. Furthermore, the study showed that the changes in glare tolerance and photostress recovery were significantly related to the changes observed in MPOD values. A similar study conducted in a separate group of subjects but using different methodologies to deliver glare showed similar results (14).

GLARE 2 STUDY DESIGN AND RESULTS
Based upon the results from the above mentioned open-label study, a randomized, double-blind, placebo-controlled study was conducted (15). In this 12 month supplementation study, 115 young, healthy subjects were randomly assigned to take a tablet containing either 10 mg of FloraGLO Lutein (Kemin Foods, L.C.) combined with 2 mg of OPTISHARP Zeaxanthin (DSM Nutritional Products) daily or placebo. At baseline and at regular intervals throughout the study period, serum lutein and zeaxanthin, MPOD (at 0.17°, 0.5°, 1.0°, and 1.75° eccentricity), glare energy, and photostress recovery times were evaluated. Of the subjects randomized into the study, 109 returned for at least one follow-up visit. The data from these subjects were employed in the intention-to-treat data set (53 treated subjects and 56 placebo subjects) and analyzed with a linear mixed model regression. No statistical differences in baseline values were found between test groups in demographics, serum levels of lutein, zeaxanthin, lycopene, total carotenes, retinol, or total tocopherol, or MPOD values at each of the measured retinal eccentricity.
The results obtained from this study showed that serum levels of both lutein and zeaxanthin significantly increased as a result of supplementation compared to values for the placebo group as shown in Figure 1A. This significant increase was noted at the very first visit after beginning supplementation and continued throughout the supplementation period. It can be assumed that the increase was not a result of dietary changes since serum levels of lycopene and total carotenes did not change significantly in either test group throughout the study period. The increase in serum lutein and zeaxanthin levels was adequate to raise MPOD values at all the measured eccentricities in subjects taking these carotenoids as compared to subjects taking the placebo as shown in Figure 1B for 0.5° eccentricity. The slope of the linear regression line fitted to the MPOD results obtained as shown in Figure 1B indicates that the change per day in MPOD values for treated subjects was significantly higher than for those subjects in the placebo group. This statistically significant effect upon the slope of the change in MPOD per day of treatment was also found for subjects treated with lutein and zeaxanthin compared to placebo at each of the retinal eccentricities evaluated.

![Figure 1](image_url)  
**Figure 1.** Results from the GLARE2 Study. A) Serum levels of lutein and zeaxanthin along with the standard error of the mean (SEM) values for supplemented and placebo subjects. B) MPOD results measured at 0.5° eccentricity along with the SEM values for treated and placebo subjects.

Supplementation with lutein and zeaxanthin resulted in an increase of approximately 8% in glare disability energy (from 1.66 to 1.8 \(\mu W/cm^2\)) in the present study. When this increase is expressed in linear units (because energy difference is typically expressed in logarithmic units), this increase reflects an improvement of approximately 23%. However, despite this considerable increase, the difference between values for the treated and placebo groups did not reach statistical significance even though there was no change in this value amongst subjects in the placebo group. Photostress recovery time was reduced in subjects supplemented with lutein and zeaxanthin and was significantly lower when compared to placebo treatment. Although the recovery time remained unchanged in subjects treated with the placebo, it decreased by nearly 9 seconds over the treatment period in subjects taking lutein and zeaxanthin.

When MPOD values from all subjects were combined and the relationship between MPOD at 0.5° retinal eccentricity and glare disability or photostress recovery time was assessed, MPOD was found to be a significant predictor of visual function as shown in Table 1.

**DISCUSSION**

The results of the randomized, double-blind, placebo-controlled clinical study conducted in young, healthy subjects have confirmed the findings of previous studies (12, 14) and provided additional data supporting the effects of supplementation in terms of serum
levels of lutein and zeaxanthin as well as demonstrating continued improvement with longer supplementation duration. Significant increases in serum lutein and zeaxanthin were found as a result of supplementation with FloraGLO Lutein and OPTISHARP Zeaxanthin compared to baseline and placebo treatment. This increase in blood levels of lutein and zeaxanthin was accompanied by significant increases in MPOD values across the entire retinal area assessed (i.e., at 0.17º, 0.5º, 1º, and 1.75º retinal eccentricity).

Glare disability energy (the amount of light that subjects could withstand and still see the target) increased in supplemented subjects in the present study. This increase of approximately 8% was comparable to the increase of approximately 7% observed in the pilot study. Despite this similarity in the percentage, the increase was not found to be significant compared to placebo in the current study whereas it was significant in the previous study. However, the slight differences in the conditions under which glare disability was measured in the present study and the fact that a slight greater difference in MPOD over baseline was found in the pilot study help explain this lack of a significant difference. Furthermore, the study found a significant improvement in photostress recovery with lutein and zeaxanthin supplementation compared to baseline as well as to the placebo group. In fact, the 9-second improvement in photostress recovery time found in the present study is considerably longer than the 5-second improvement observed in the pilot study. Although a 9-second improvement may not seem like a significant period of time, an automobile traveling at 60 miles per hour (96.6 kg per hour) covers a distance of equivalent to about 2.5 football fields (792 feet or 241 meters) in this period of time. The inability to clearly and distinctly see oncoming traffic while traveling that distance or for that period of time helps put a real-world perspective upon the importance of this effect. It is not known whether the additional decrease in photostress recovery time found in the present study compared to the pilot study is solely the result of the longer supplementation time (12 versus 6 months). In addition to these visual performance parameters, this study also found that lutein and zeaxanthin supplementation resulted in significant improvements in chromatic contrast. Those results will be the subject of a separate document.

In conclusion, the results from all visual performance parameters measured in this new study were positively correlated to the MPOD measured in young, healthy subjects. Increases in MPOD resulted in decreased glare disability and reduced photostress recovery times. Supplementation of lutein and zeaxanthin to older subjects with AMD has been shown to have similar effects upon MPOD and visual performance to those observed in the present study (7, 8). Therefore, it is reasonable to postulate that improving MPOD values through lutein and zeaxanthin supplementation leads to better visual performance regardless of the age or the health of the eye. Given the premium that people place upon vision in daily life and everyday activities, daily dietary supplementation with lutein and zeaxanthin is an easy way to help maintain the health and performance of our eyes.

References