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Abstract

Research data indicate that lutein and zeaxanthin intake can alleviate symptoms of different eye pathologies. Within the retina, lutein and zeaxanthin are concentrated in the macula, with as much as 25% of their total retinal content found in the outer segments of the rod photoreceptor neurons. Lutein and zeaxanthin are recommended at least as an appropriate cautionary measure, especially for patients with age-related macular degeneration, retinitis pigmentosa, cataracts and with low dietary intake of these carotenoids.

Keywords: Lutein, zeaxanthin, macular degeneration, retinitis pigmentosa, cataracts.

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Oxidative stress is well known to contribute to the onset and progression of a number of eye diseases, including at least some forms of retinal degeneration, particularly age-related macular degeneration (AMD), which is the most common cause of blindness in developed countries. Oxidative stress, especially that caused by UV light, also plays an important role in cataract development because it promotes oxidation of lens proteins. Therefore, a number of studies have assessed the effects of supplementation with several antioxidant nutrients, including lutein and zeaxanthin, on the risks of onset and progression of these diseases.

Although multiple carotenoid species are present in blood plasma, only lutein and zeaxanthin are able to cross the hemato-ophthalmic barrier and accumulate in the eye tissues, including the retina, where their concentration is 4 orders of magnitude higher than in the blood. These carotenoids are thought to protect the retina in a dual way: by filtering out the most damaging short-wavelength irradiation (blue light and UV) and by scavenging reactive oxygen species.

Within the retina, lutein and zeaxanthin are concentrated in the macula, with as much as 25% of their total retinal content found in the outer segments of the rod photoreceptor neurons, where the light receptor rhodopsin and enzymes of its downstream signaling cascade are located. Since rods are much more sensitive to light and therefore to photodamage than cone photoreceptors, the accumulation of carotenoids in rod outer segments suggests a direct function of lutein and zeaxanthin in rod protection from photodamage.

**Age-Related Macular Degeneration**

The effects of taking lutein and zeaxanthin supplementation on the content and spatial distribution of the macular pigment have been extensively studied. Although the results of studies conducted during the first years of this century appeared to be inconclusive, most studies of the last decade have reported at least some benefits of lutein and zeaxanthin supplementation. Examples of such studies are summarized below.

Taking a daily supplement of lutein, zeaxanthin and meso-zeaxanthin (a carotenoid that is formed from lutein directly in the retina and is a component of macular pigment along with lutein and zeaxanthin) for 8 weeks has been found to significantly increase the content of macular pigment (measured as optical density) as soon as 2 weeks after supplementation, both in healthy subjects and those with AMD. The authors also found that the spatial profile of macular pigment was atypical in some subjects, mainly those with AMD, and that supplementation restored the normal profile.

A more recent study investigated the effects of lutein and zeaxanthin on macular pigment and visual function in patients with early AMD. Daily intake of either 20 mg lutein alone or 10 mg lutein and 10 mg zeaxanthin was found to significantly increase the macular pigment content in comparison with the placebo group; the authors also reported a significant improvement in contrast sensitivity and a trend toward improvement in best-corrected visual acuity after 48 weeks of carotenoid supplementation. Furthermore, they found a significant correlation between these two parameters of visual function and the macular pigment content, suggesting that the increase in the latter underlies the improvement of visual function.

Similar results for the macular pigment content and contrast sensitivity have been reported by an independent study. Intriguingly, differential effects of lutein and zeaxanthin in patients with mild-to-moderate AMD have been reported: supplementation with either of the two carotenoids increased the macular pigment content, but lutein was more beneficial for rod-based monochromatic high-sensitivity vision, whereas zeaxanthin was more beneficial for cone-based color vision. Another important finding of the latter study was that equally dosed (i.e., atypical dietary ratio) lutein and zeaxanthin performed worse than each carotenoid individually, which emphasizes the importance of an optimal ratio between the two carotenoids (as implemented in Zealut-Dena).

Whereas the above studies provided evidence for the efficacy of lutein and zeaxanthin in restoring the content and spatial profile of macular pigment and improving at least some parameters of visual function in AMD patients, they have not addressed a separate question of whether lutein and zeaxanthin supplements may affect AMD onset or progression.
AREDS2, a large multicenter study conducted in 2006-2012, revealed that the protective effect of lutein and zeaxanthin supplementation was significant only in subjects whose dietary intake of these carotenoids was within the lowest quintile (which might in part explain inconclusive results of earlier studies). Moreover, lutein and zeaxanthin delayed progression of advanced AMD (categories 3-4), albeit only by 10%. Lutein (10 mg/day) and zeaxanthin (2 mg/day) have also been recommended as a replacement of β-carotene in the AREDS formulation (vitamins C and E, β-carotene, and zinc) because of the association of β-carotene with an increased incidence of lung cancer in former smokers. Taken together, the results of the AREDS2 study and available smaller studies suggest that lutein and zeaxanthin at the above doses (i.e., similar to their content in 1-2 Zealut-Dena capsules), would be beneficial for category 3 and 4 (i.e., advanced AMD) patients; potential long-term side effects (>5 years) of lutein and zeaxanthin supplementation have not yet been investigated.

Overall, although the benefits of taking lutein and zeaxanthin for different groups of AMD patients need further investigation, this supplement can be recommended at least as an appropriate cautionary measure, especially for patients with low dietary intake of these carotenoids.

Other Forms of Retinal Degeneration

Whereas the effects of lutein and zeaxanthin are best studied in AMD patients, some studies have assessed whether supplementation with these carotenoids would benefit patients with other forms of retinal degeneration.

Consistent with the results of the AMD studies, taking lutein (20 mg/day) for 6 months significantly increased the content of macular pigment in patients with retinitis pigmentosa and Usher syndrome (a combination of retinitis pigmentosa and a sensorineural hearing loss), choroideremia (a congenital X-linked retinal degeneration), CRB1-associated retinal degeneration, and ABCA4-associated retinal degeneration, but did not result in an improvement in central vision during the study periods, suggesting that either lutein has no benefit for patients with these diseases, or its effect takes longer than 6 months to develop.

A small-scale study on 13 retinitis pigmentosa patients reported beneficial effects of taking a higher dose of lutein (40 mg/day for 9 weeks, followed by 20 mg/day for 15 weeks). The authors found improvements in visual acuity and mean visual-field area, which were detectable as early as 2-4 weeks after the beginning of treatment and plateaued at 6-14 weeks. Curiously, blue-eyed participants benefited more from lutein intake than dark-eyed participants. The apparent discrepancies between the results of different studies are perhaps not surprising, because retinitis pigmentosa is a very heterogeneous group of diseases caused by mutations in several dozens of different genes, and in many cases the underlying genetic cause of retinal degeneration remains unknown. A tentative conclusion that can be made at present is that high doses and long treatment periods may be more beneficial for retinitis pigmentosa patients.

Cataract

The 5-year Beaver Dam Eye Study, which enrolled 1,354 subjects and was conducted between 1988 and 1995, found that lutein and zeaxanthin were the only carotenoids associated with the reduced risk of nuclear cataract development: their intake in the highest quintile reportedly reduced the risk by as much as half. These results were corroborated by two larger-scale studies conducted in the last quarter of the 20th century. The Nurses’ Health Study, which was conducted in the USA and Japan and enrolled female registered nurses, found that increased intake of lutein (≥6 mg/day) and zeaxanthin reduced the number of required cataract surgeries. Similar results were reported by the parallel Health Professionals Follow-Up Study, which enrolled male health professionals: this study found a decrease in the need for cataract surgeries as a result of increased intake of lutein and zeaxanthin (6.9 mg/day). However, some other studies at that time failed to find a significant association between the cataract risk and carotenoid supplementation, and a Food and Drug Administration review conducted in 2006 concluded that there was no reliable evidence for the ability of lutein and zeaxanthin to reduce the risk of cataracts. Nevertheless, a number of later studies have confirmed the beneficial effects of
these carotenoids, and a recent meta-analysis of 13 observational studies (18,999 participants in total) concluded that the blood levels of both lutein and zeaxanthin (the two carotenoid species were analyzed separately), but not those of three other carotenoids (β-carotene, lycopene, and β-cryptoxanthin), are inversely associated with risk of age-related cataract.

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References


