Dietary Zeaxanthin – The Other Macular Pigment

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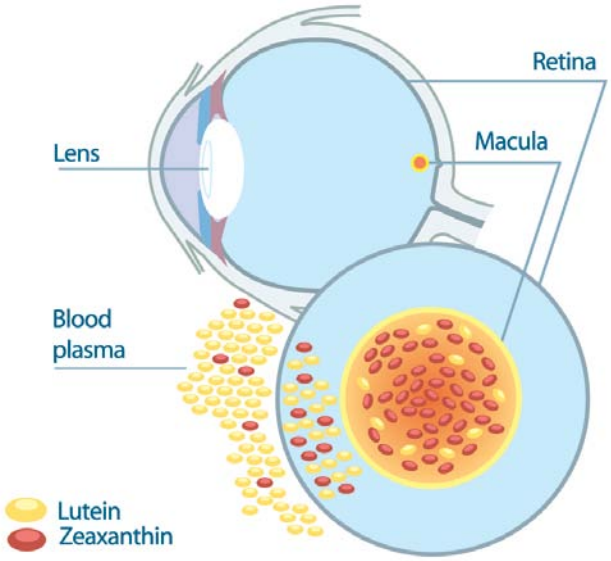
Dietary Zeaxanthin is the second xanthophyll obtained from our diet and accumulated in very specific ways in the human retina, lens and brain. Xanthophylls, unlike Beta-carotene, do not convert to vitamin A derivatives.

In the 1980's, research showed that zeaxanthin selectively accumulated in the center of the macula, suggesting an important function separate from the previously identified macular pigment: lutein. At first glance, the structures of these two pigments look remarkably similar and this similarity made separate analyses of foods and blood serum very difficult.



The difficulty in analyses resulted in many studies grouping the two together. A second problem is that the commercial source of lutein -- marigold flowers -- produces 3-10% zeaxanthin, and thus all lutein trials also included zeaxanthin. Some products claim this minute amount by listing it on the label.

The human diet contains 5-10 times more lutein than zeaxanthin because the bent structure of lutein is used in more plants to help harvest energy from

light. Zeaxanthin is also capable of this plant function but it is used more often by plants to protect against excessive light damage.

In the US diet, major sources of zeaxanthin are corn, peppers and egg yolks. While zeaxanthin is also found in dark green leafy vegetables, it is perhaps 20 times less abundant than lutein. The selective uptake of zeaxanthin in the macula spurred researchers in the 1990's to examine its effects separately from lutein, which required the development of separate sources and processes of manufacturing. Early studies at Harvard Medical School demonstrated in animal models that zeaxanthin was essential to the retina for protection against excessive light and the ravages of aging. While lutein sources were available in 1995, no commercial source of zeaxanthin was available until 2001, which partially explains the disparity in awareness.

In 1994, a classic epidemiological study demonstrated that dietary levels of at least 6mg of lutein and zeaxanthin reduced risks for AMD. Because most Americans do not eat the 5-13 servings of fruits and vegetables recommended by many health organizations, there is a minimum dietary gap of 5-6 mg/day of both macular pigments. While this observation has become a basis for recommendations, it is not necessarily optimum. Animal and human studies have shown that maximum retinal deposition is effected by higher dietary intake, peak blood levels and individual response. These studies suggest that significantly higher intake should be recommended for those at highest risks for AMD. The US and world food safety organizations have established an upper acceptable daily intake of around 160mg for the typical US male. While higher

intake of colorful fruits and vegetables should always be recommended, it should be augmented with zeaxanthin greater than 6 mg/day (10-30mg) for those at higher AMD risks.

The highest natural source of zeaxanthin was recently established to be Chinese wolfberry (Goji berries.) Interestingly, Chinese herbalists have been recommending these berries for more than 2000 years for "vision problems."

Epidemiology studies on zeaxanthin analyzed separately have suggested that zeaxanthin may be more important than lutein for several related vision issues. Zeaxanthin also preferentially accumulates in human lens and brain. Studies of dietary zeaxanthin levels show an inverse relationship with cataracts and cognition in the elderly. The macular pigments together have shown additional benefits in improving photophobia, glare recovery, macular stress tests, mesopic vision, blue-yellow threshold detection, mERG, contrast sensitivity and dark adaptation (night vision). A recent unpublished study has shown a 75% improvement in contrast sensitivity with a dietary zeaxanthin-based supplement in young, healthy females in as short a time as 3 months.

Epidemiology has also shown health benefits for cardiovascular disease and some cancers. Basic research studies have confirmed that in cell culture and animal models, zeaxanthin does absorb harmful blue light, reduces retinal oxidative biomarkers and, most importantly, reduces retinal inflammatory bio-markers. In other animal studies it reduces drusen and lipofuscin, and the toxic

effects of these two compounds often seen in retinal photographs. Very recently, basic studies have demonstrated that dietary zeaxanthin normalizes the key angiogenic molecule, VEGF, induced by various insults. These basic studies help to explain why high dietary intake reduces the risk of wet AMD.

While many epidemiology studies from around the world have shown that lutein plus zeaxanthin reduce the risks of AMD, four studies from Europe have evaluated zeaxanthin separately and concluded dietary zeaxanthin may be more important.

A British study published by Gale in 2003 concluded that in 380 patients that low serum level of zeaxanthin doubled the risk of AMD, and that this relationship was stronger than serum lutein. This study was followed in 2006 by a French study (POLA) showing in 899 subjects that high serum zeaxanthin reduced AMD risk 93% and nuclear cataract risks by 77%. These results were significantly greater than serum lutein. Several papers published out of Ireland in 2007 and 2008 on 828 healthy Irish showed that major risk factors for AMD were inversely associated with macular pigment levels and demonstrated that zeaxanthin intake levels were independently related to age. They also suggested that poor retinal uptake of zeaxanthin might be a major risk factor for AMD. This conclusion becomes more intriguing when considered with soon-to-be-released results suggesting that there are genetic deficiencies of the protein responsible for selective uptake of zeaxanthin (GST-1) in AMD cadaver eyes. Finally, in 2008 a major multi-center European trial (Eureye) demonstrated that low serum

zeaxanthin and high lifetime sunlight exposure combined to increase by four times the risk of AMD.

Two devices based on Heterochromatic Flicker Photometry (HFP) have been introduced to the optometrists for use in AMD prevention. These devices can measure retinal levels of these protective pigments, and when combined with retinal photographs and lifestyle questionnaires, can help the ECP assess the risk and tailor prevention recommendations to include dietary intervention, supplement prescription and compliance monitoring. Recently it has been demonstrated that an experimental objective device can measure retinal zeaxanthin levels separate from lutein. This device opens up the possibility of directly relating macular zeaxanthin levels to beneficial visual effects.

There is great confusion currently in the marketplace by the introduction of non-dietary meso-zeaxanthin, often without labeling it as meso. Meso-zeaxanthin is found only in the human retina. It is not found in the human diet or blood. Primate studies have recently confirmed that it is converted only in the retina from lutein (in the absence of dietary source or true zeaxanthin). It is felt that this conversion to meso validates the importance of dietary zeaxanthin. The body has developed a compromise molecule in response to a low intake of the preferred dietary zeaxanthin. Meso-zeaxanthin is sourced from outside the US and is manufactured by harsh chemical treatment of lutein. The FDA has reviewed the safety of lutein and dietary zeaxanthin multiple times; the same cannot be said for meso-zeaxanthin. The bioavailability and stability of lutein and

zeaxanthin are extremely sensitive to formulation so careful attention to a quality source is recommended.

In summary, the selective deposition of zeaxanthin in the center of the macula challenged scientists. Subsequent research has suggested that zeaxanthin, while less well known, could be the most critical eye nutrient.