Blue Light Phototoxicity and the Importance of Meso-Zeaxanthin in Melanin Filtration

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Abstract

Macular ocular pigments are uniquely concentrated in the posterior pole, offering significant optical advantages and protection that other areas of the retina lack. Lutein and zeaxanthin are macular pigments that must be obtained from dietary sources such as green leafy vegetables, orange and yellow fruits and vegetables, whereas meso-zeaxanthin, a newly discovered carotenoid, is both produced by the body and found in certain aliments, an example being eggs from Mexico and California. The AREDS2 study brought attention to the potential of ocular health and preservation of vision of the xanthophyll carotenoids, specifically in age-related macular degeneration, which is the leading cause of progressive blindness in elderly in developed countries. The macula mediates central vision, provides sharpest visual acuity and facilitates best color discrimination, this is largely in part because of the higher concentration of cones to rods ratio. The human retina is protected from high density energy ultraviolet light by the cornea and lens, which absorb UV light below 400 nm. High frequency blue-light causes oxidative stress via excessive irradiation and oxygen molecule reconfiguration, due to this, it is more harmful to the RPE and the photoreceptors than other wavelengths of light. Blue-light irradiation generates superoxide anion, hydrogen peroxide, and singlet oxygen, these reactive oxygen species cause lipid peroxidation, enzyme inactivation and denaturation of proteins. In this review, we outline the biochemical properties of macular ocular pigments, the mechanism in which they absorb short-wavelength blue light, filter it and propagate it to the inner retinal layers. Macular ocular pigments also act as antioxidant molecules by neutralizing oxygen reactive species, with a subsequent neutralization of lipid peroxidation and chronic damage to the macula and fovea.

Keywords: Macular Ocular Pigment; Age-Related Macular Degeneration; Reactive Oxygen Species; Blue-Light; Meso-Zeaxanthin

Introduction

Vision is a complex physical, chemical and nervous process by which images from the external world can be interpreted by the occipital cortex of the brain. It is considered that the retina is the seeing part of the eye, by its facilitation of transformation of light into an electrical signal [1].

The name *macula lutea* (yellow spot) derives from the yellow color of the central retina. This color is due to the presence of carotenoid pigments, which are mostly located in the Henle fiber layer [1,2]. Previously, two major pigments were described – zeaxanthin (Z) and lutein (L). Lutein is more concentrated in rod-denser areas of the retina, whereas zeaxanthin is more concentrated in cone-dense areas (fovea). A recent carotenoid pigment meso-zeaxanthin (MZ) has been described [3]. Together these 3 carotenoids are collectively known as macular pigment (MP) [4].

In humans, L and Z are of dietary origin, found mostly in eggs and colored fruits and vegetables. MZ is mostly found in sea products and is also known to be produced in the body following isomerization of lutein.
Of the 14 carotenoids absorbed and used by the body, only L, Z and MZ are found in the macula. This preferential accumulation is thought to be the result of the functional needs of the macula [2,5] (Figure 1).

**Figure 1:** Schematic figure of the eye depicting the location of the macular ocular pigments, meso-zeaxanthin and zeaxanthin are densely located in the foveola, whereas lutein is located more peripherally. Meso-zeaxanthin is the most powerful of the three and is located in the Henle fiber layer.

**Blue light photo-toxicity**

Oxidative stress is a common contributor to many different neurodegenerative diseases, including but not limited to; diabetic retinopathy, glaucoma, retinal vein occlusion, and age related macular degeneration (AMD) [6]. The retina is highly vulnerable to oxidative stress because of its high levels of photosensitizers and its high consumption of oxygen [7,8]. Of the numerous factors associated with AMD, several are directly linked to inflammation and oxidative stress. These include: complement factor H polymorphism, complement C3, lipofuscin and its bis-retinoid; N-retinyllidene-N-retinylethanolamine (A2E) and complement component 2 [9,10]. There are major blue-light absorbing fluorophores of lipofuscin in the RPE believed to be associated with AMD pathogenesis [11]. Blue-light preferentially affects the RPE, whereas light of up to 500 nm wave-length affects the outer segments of the photoreceptors [12,13].

Several studies suggest that long-term history of exposure to light has impact on the incidence of AMD [14,15].

The exposure of retinal cells and RPE cells to blue light leads to preferential death of photoreceptors compared with other cell types, such as bipolar cells and Müller cells. Blue-light also induces dysfunction of the outer retinal-blood barrier (located in the RPE), with increased transcellular permeability, this dysfunction occurs before any ultrastructural evidence of cell damage [13].

Excessive light induces excessive activation of the visual cycle, which causes photoreceptor cell apoptosis. This role was supported by previous findings that antioxidants like N-acetyl-L-Cysteine [12] and lutein [16] can attenuate apoptosis and halt oxidative and inflammatory damage to the retina.

**Importance of Carotenoids in the retina**

It is widely known that age related macular degeneration is the major cause of irreversible blindness in the developed world. Cellular damage due to high levels of oxidative stress is linked to many retinal diseases. This is mostly related to the retina high oxygen metabolic rate [1]. The outer portion of the photoreceptors are high in concentration of polyunsaturated fats, and thus, are highly vulnerable to cellular damage caused by reactive oxygen species (ROS) [17] (Figure 2).

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Meso-zeaxanthin (MZ)

This carotenoid is found in high concentrations in ocular tissues, with peak concentrations in the fovea, it is almost non-existant in tissues other than the eye, which suggests specific ocular production of MZ. The dietary contribution of meso-zeaxanthin in a normal Western diet is almost negligible, owing to its location in turtle fat, seaweed, and fish skin [18].

A significant amount of MZ has been detected in commercially produced chicken eggs in Mexico, where it is commonly added to achieve desirable orange coloration [19].

Lutein and meso-zeaxanthin are almost identical biochemically, having the same stereo-chemistries at the 3 and 3’ positions with the only difference being the position of one double bond, this conformational similarity of MZ to L makes it more likely that L is its immediate precursor. Z and MZ differ in the hydroxyl group at the 3’ position.

Functional properties

The macular carotenoids are isomers with a common C₄₀H₅₆O₂ polyene backbone chain that allows electrons in their double bonds to easily delocalize. This system of conjugated carbon-carbon double bonds makes them effective smoothers of ROS and absorbers of damaging visible light (especially short wavelength light) [20]. ROS are radicals such as hydroxyl radical, peroxyl radical or hydrogen peroxide. The mechanism by which they damage the retina is by lipid peroxidation → DNA damage → protein and transmembrane glycoprotein oxidation. Among all ROS, hydroxyl radical is the most reactive [21].

Carotenoids react with ROS via oxidation, electron transfer and hydrogen abstraction. L,Z and MZ are very efficient at absorbing and transmitting excited energy when needed, releasing excess of energy as heat without chemical degradation [22].

Another proposed mechanism by which macular ocular pigment protects the eye is by reduction of oxygen stress-induced damage [21]. It is widely known that with age the RPE accumulates lipofuscin, and that N-retinyl-N-retinylidene ethanolamine (A2E) damages the RPE, the mitochondria and induces apoptosis of RPE cells when they are exposed to short-wavelength light [10].

Connolly et al commented on the safety of supplementation of MP in human subjects. None of the doses reported (both 30 mg/d to

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40 mg/d) were associated with any adverse effects. At the end of the study subjects demonstrated a statistically significant increase in serum concentrations of L, Z and MZ, with increase in central macular pigment concentration [5,21].

**Conclusion**

It is widely known that short wavelength light is hazardous for the retina and specially the macula. Carotenoids (macular ocular pigment) are highly effective in preventing reactive oxygen species inflammatory damage. Macular ocular pigment is necessary for optimal visual function. Supplementation can enhance visual performance in diseased eyes and help protect non-diseased eyes. MOP supplementation reduces the risk of AMD related progression, and protects against blue light phototoxicity by absorbing it and neutralizing the formation of ROS.

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**Conflict of Interest**

None.

**Bibliography**


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