

An Overview on the Role of Macular Xanthophylls in Ocular Diseases

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Abstract: Macula lutea, is the center of the retina of the eye, contains high concentrations of lutein and zeaxanthin which can act as a filter against short-wavelength (blue) light. Lutein and zeaxanthin are the only carotenoids detected in human lens which exhibit highly strong free radical scavenging activity. Many epidemiological studies, clinical trials, animal experiments have suggested that lutein and zeaxanthin have anti-inflammatory potential with their high antioxidant properties. Several eye diseases including, age-related macular degeneration, uveitis and retinitis pigmentosa are caused by ocular inflammation. Some studies have shown that lutein and zeaxanthin could be protective, curative and preventive against ocular inflammation induced diseases and other ocular disorders such as cataract, glaucoma and choroideremia. The mechanisms responsible for these effects are absorption of near-ultraviolet and blue light, reduction of oxidative stress, inflammation and angiogenesis. Lutein and zeaxanthin can be taken from dietary supplements or a diet high in fruits, vegetables such as kale, spinach and turnip greens. The aim of this review is to evaluate the relationship between the consumption of lutein and zeaxanthin and eye diseases.

Keywords: Eye diseases; lutein; macular xanthophylls; ocular diseases; zeaxanthin. © 2018 ACG Publications. All rights reserved

1. Introduction

Carotenoids are naturally-occurring plant pigments and important constituents of a healthy diet with their established contribution to the antioxidant defense system in whole body especially in macula [1-3]. Carotenoids, which absorb a wavelength range of 350-550 nanometers (nm), are nonpolar organic pigments. Carotenoids divided into two major groups; orange pigments which are called carotenes and yellow pigments which are called xanthophylls [4]. The group of xanthophylls includes lutein, zeaxanthin, neoxanthin, violaxanthin, capsanthin, canthaxanthin, astaxanthin, echionine, flavoxanthin, alpha (α)- and beta (β)-cryptoxanthin [5]. It is widely thought that carotenoids

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can be protective against the formation and development of eye diseases due to their antioxidant properties [6-9].

Lutein and its stereo-isomer zeaxanthin are two carotenoids that belong to the xanthophylls subclass as shown in Figure 1. Lutein and zeaxanthin are the most dense compounds which are found at the center of the fovea that is the yellowish pigmented area called macula lutea. Due to the fact that it is referred to as macular pigment [10-15]. Macular pigment is located at the center of the retina and the site of highest visual acuity. Macula of the retina is yellow due to rich lutein and zeaxanthin content. Although the

function of macular pigment remains unclear, there are various possibilities. One of the claim is that lutein and zeaxanthin protect retina against oxidative stress from the damage of blue-light by inhibiting lipid peroxidation and c-fos gene expression [16,17]. The other is about antioxidant properties of lutein and zeaxanthin that are highly potent quenchers of singlet oxygens and other free radicals [18-20]. The near-ultraviolet and blue light filtering properties of macular pigment could be a result of free radical scavenging capacity and protective characteristics against the harmful effects of short wavelength light to the retina [21-26].

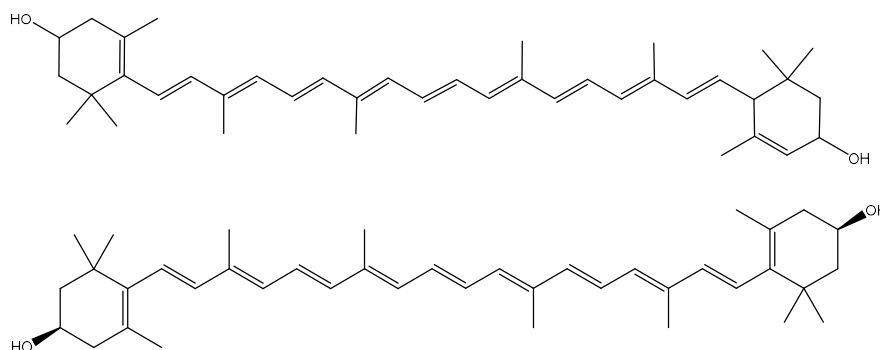


Figure 1. The molecular structure of lutein (above) and zeaxanthin (below).

U.S. National Library of Medicine National Center for Biotechnology Information (2017).

(The chemical structures of the compounds were drawn by using ChemDraw Professional Ver.16.0.1.44)

Recent epidemiological studies have suggested that lutein and zeaxanthin play roles in the reduction of the risk for inflammation-related eye disease, specifically age-related macular degeneration (AMD), uveitis, retinitis pigmentosa, scleritis and also cataracts, glaucoma, retinal ischemia, choroideremia, etc [27-33]. Low systemic and retinal levels of lutein and zeaxanthin are adversely associated with the risk of AMD and other eye related disease [34-37]. The mechanisms responsible for the effects of lutein and zeaxanthin include prevention of phototoxic damage by absorption of blue light, reduction of oxidative stress through free radical scavenging, antioxidant, anti-angiogenic, anti-inflammatory properties as shown in Figure 2 [38- 43].

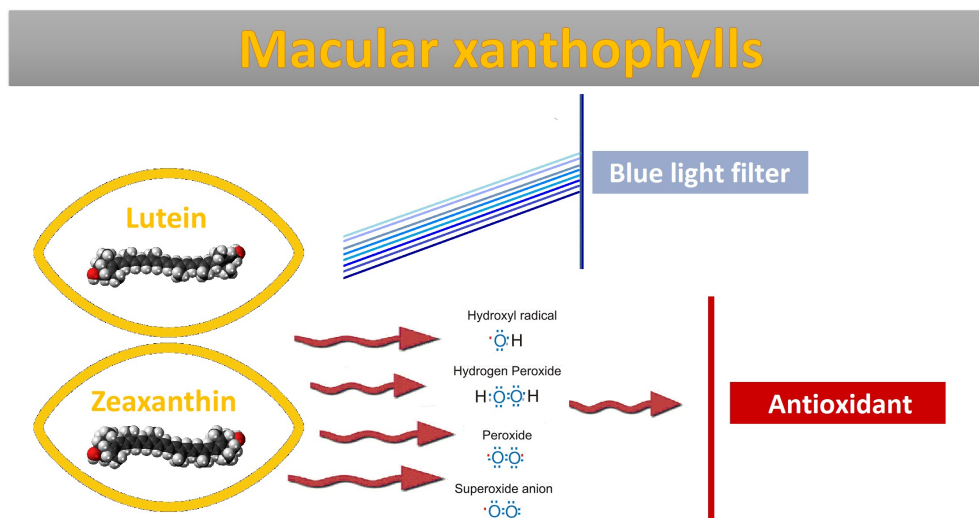


Figure 2. An overview for potential action mechanism of macular pigments (original).

Table 1. Common foods rich in lutein and zeaxanthin.

Food	Lutein + zeaxanthin (mg) per 100 g food	Food	Lutein + zeaxanthin (mg) per 100 g food
Arugula, raw	3.55	Lettuce, cos or romaine, raw	2.31
Balsam-pear, leafy tips, cooked, boiled, drained	2.63	Mustard greens, cooked, boiled, drained	10.4
Basil, fresh	5.65	Nuts, pistachio nuts, raw	2.9
Beans, fava, in pod, raw	1.81	Onions, spring or scallions (includes tops and bulb), raw	1.13
Beet greens, cooked, boiled, drained, with salt	1.81	Parsley, fresh	5.56
Broccoli raab, cooked	1.68	Peas, green, cooked, boiled, drained	2.59
Brussels sprouts, raw	1.59	Peppers, sweet, red, freeze-dried	5.79
Carrot, dehydrated	1.05	Pumpkin, raw	1.5
Chard, swiss, raw	11	Radicchio, raw	8.83
Chicory greens, raw	10.3	Rose Hips, wild (Northern Plains Indians)	2
Chrysanthemum, garland, raw	3.83	Spices, coriander leaf, dried	2.42
Collards, frozen, chopped, cooked, boiled, drained	10.89	Spices, paprika	18.94
Corn bran, crude	1.35	Spices, pepper, red or cayenne	13,15
Cornmeal, degermed, enriched, yellow	1.62	Spinach, frozen, chopped or leaf, cooked, boiled, drained	15.69
Cowpeas, young pods with seeds, raw	0.93	Squash, summer, all varieties, raw	2.12
Cress, garden, raw	12.5	Squash, summer, scallop, raw	2.31
Dandelion greens, raw	13.61	Stinging Nettles, blanched (Northern Plains Indians)	4.17
Drumstick leaves, cooked, boiled, drained	1.74	Sweet potato leaves, raw	14.72
Egg, yolk, dried	1.13	Taro leaves, raw	1.93
Grape leaves, raw	1.74	Tomatoes, sun-dried	1.42
Kale, frozen, cooked, boiled, drained, with salt	19.69	Turnip greens, raw	12.82
Lambsquarters, steamed (Northern Plains Indians)	6.16	Watercress, raw	5.76
Leeks, (bulb and lower leaf-portion), raw	1.9		

Data from the USDA National Nutrient Database for Standard Reference Release 28 (2015).

Lutein and zeaxanthin cannot be synthesized in mammals and must be obtained from the diet for distribution to various tissues, particularly the retina [10,11,12]. Lutein and zeaxanthin are found in

egg products, fruits and vegetables, especially green leafy plants, including, kale, spinach, turnip greens and collards highly as shown in Table 1 [11-15].

The recommended daily intake for lutein and zeaxanthin is 6 to 20 mg for adults to reduce the risk of ocular diseases [34,35]. Lutein and zeaxanthin are accumulated in lipophilic tissues such as adipose and liver tissue [44,45]. Lutein and zeaxanthin are absorbed with fat, which transport via high density lipoproteins (HDLs) mostly and low density lipoproteins (LDLs) lower [36,37]. Lutein and zeaxanthin, which are also called macular xanthophylls, show their effects by filtering high energy visible light, mostly with a peak of absorption at 446 nm and ultraviolet radiation lesser, inhibiting lipid peroxidation and reducing reactive species such as singlet oxygen and hydroxyl radical [46-48]. These carotenoids have several benefits on human health, including neuroprotective effects [49-51], anti-carcinogenic effects [52-55], anti-diabetic effects [56-58], cardioprotective effects [59- 61], protective effects on skin damages and ocular diseases [62-65]. Particularly, several studies showed the role of lutein and zeaxanthin in eye diseases. The studies we have chosen about this issue are listed in Table 2.

2. Role of Lutein and Zeaxanthin in Ocular Diseases

2.1. Role of Lutein and Zeaxanthin in Cataract

Occurrence of the cataractogenesis depends on some factors, including oxidative stress [66,67,68]. Consuming antioxidants by daily diet or as supplements may reduce this stress. Some studies indicate that there is a strong relationship between cataract development and lutein consumption [69-72].

Karppi et. al reported a study on the correlation between plasma lutein and zeaxanthin levels and the risk of age-related nuclear cataract. Samples were taken from Finnish men and women who had different lifestyles (education, body mass index (BMI), HDL-LDL levels), habits (smoking, alcohol consumption) and disease (hypertension, diabetes). The results of this study have shown that the risk of nuclear cataract in older people, with an average age of 70 years, decreased with high plasma lutein and zeaxanthin levels [69]. Another study was conducted on a Mediterranean population over the age of 60, suffering from several types of cataract such as nuclear, cortical, PSC, mixed and also cataract surgery. According to the results of this study, high plasma zeaxanthin levels were associated with lower risk of nuclear cataract significantly, whereas no relation with the other types of cataracts. Furthermore, high plasma lutein concentrations and total lutein levels were not related to any type of cataract markedly [70]. Aqueous humor samples were collected from 40 men and women with senile cataract development in both eyes during cataract surgery. These subjects had taken supplements containing lutein. After and before taking these supplements, some antioxidant enzyme levels, including superoxide dismutase (SOD), L-ascorbic acid, reduced GSH, superoxide scavenging capacity, the levels of hydrogen peroxide (H₂O₂) and total amount of hydroperoxides (TH, including H₂O₂ and the peroxides of lipids, peptides, proteins, nucleic acids and nucleotides) were measured in the aqueous humor and changes were determined. Superoxide scavenging capacity increased by taking lutein containing supplements in both men and women subjects. However, lutein intake caused an increase in the levels of H₂O₂ and a decrease in the levels of TH in postmenopausal females, whereas there were no huge differences in these levels in males. Although it is uncertain, it is thought that estrogen is the cause of the differences in these levels between the genders [71]. Vianna et al. conducted a study about using a dye containing trypan blue combined with lutein and zeaxanthin during cataract surgery. This combination was used during cataract surgery by phacoemulsification for screening anterior capsulorhexis in patients. The result of this study indicated that this combined dye might be an alternative for continuous circular capsulorhexis (CCC) in human due to its safe, effective and antioxidant profile [72]. The results of Chew et al.'s study was contrary to the most studies. More than 4000 people at the age of 73.1 meanly divided four treatment groups; placebo, lutein/zeaxanthin, DHA/EPA, lutein/zeaxanthin+DHA/EPA. In contrast to the other studies, this placebo-controlled, randomized study indicated that lutein and zeaxanthin supplementation had no significant beneficial or adverse effects on cataract surgery, any type of cataract and losing sight [73].

Table 2. Effects of lutein and zeaxanthin treatment on different eye diseases (original).

Reference	Study group	Participants	Health status	Treatment	Results
Karppi J. et al., 2012	Human	Group 1: 559 female Group 2: 1130 male	nuclear, cortical, posterior subcapsular cataracts (PSC), mixed and cataract surgery	lutein/zeaxanthin	Zeaxanthin treatment decreased the risk of nuclear cataract. No relation with the other types of cataract.
Hayashi R. et al., 2014	Human	Group 1: 18 male Group 2: 22 female	senile cataract	Ocuvite + Lutein®	Lutein-based treatment was effective in reducing oxidative stress.
Vianna L.M. et al., 2014	Human	Group 1:25 (25 eyes of 25 patients performed by 25 different surgeons) Group 2:docosahexaenoic acid (DHA)/eicosapentaenoic acid (EPA) 3 treated, 350 mg/650 mg (n=803) Group 3:lutein/zeaxanthin+DHA and EPA (n=794) Group 4:placebo (n=775)	cataract surgery	lutein and zeaxanthin	A lutein-based dye (s) could be an alternative dye for anterior capsulorhexis during cataract surgery.
AREDS-2, 2013	Human	Group 1:lutein treated 10 mg (n=26) Group 2:lutein treated 20 mg (n=27) Group 3:lutein (10 mg)+zeaxanthin (10 mg) (n=27) Group 4:placebo (n=28)	AMD	lutein and zeaxanthin	No beneficial or adverse effects was shown on subjects with cataract surgery, any type of cataract and losing sight.
Huang Y.M. et al., 2015	Human	Group 1:patients treated lutein-enriched egg yolk (n=52) Group 2:control (n=49)	early AMD	lutein and zeaxanthin	Lutein treatment caused increasing in macular pigment optical density (MPOD) and N1-P1.
Made S.M et al., 2014	Human	Group 1:patients with early AMD (n=51) Group 2:patients medium AMD (n=51) Group 3:control (wo AMD) (n=51)	AMD	lutein-enriched egg yolk	Plasma lutein concentrations in treated group were increased. The increases in serum total and LDL cholesterol levels were not significant.
Huang F.F. et al., 2014	Human	Group 1:lutein/zeaxanthin treated, 10 mg/2 mg (n=1044) Group 2:DHA and EPA 3, treated, 1.0 g (n=1068) Group 3:lutein/zeaxanthin+DHA and EPA (n=1079) Group 4:placebo (n=1012)	early-late AMD	lutein and zeaxanthin	Serum HDL levels were related with AMD development. No change in other levels.
AREDS-2, 2014	Human	Group 1:lutein treated, 12.5 mg/ml (n=18) Group 2:lutein treated, 25 mg/ml (n=18) Group 3:control (n=18) Group 4:model (n=18)	late AMD	lutein/zeaxanthin	Positive correlation was shown between lutein/zeaxanthin supplementation and progression of late AMD.
He R.R. et al., 2011	Male BALB/C mice	Group 1:lutein treated (n=9) Group 2:lutein treated with endotoxin-induced uveitis (EIU) (n=13) Group 3:control (n=9)	uveitis	lutein	Glutathione (GSH) and vitamin C levels were increased after lutein treatment.
Sasaki M. et al., 2009	C57BL/6 mice	Group 1:patients with open angle glaucoma (n= 40) Group 2:normal controls w/o ocular disease (n=54)	uveitis	lutein	Lutein supplementation caused improving in visual damages, rhodopsin levels and glial fibrillary acidic protein (GFAP) expressions.
Igras E. et al., 2013	Human	Group 1:women with glaucoma (n=77) Group 2:women wo glaucoma (n=507)	glaucoma (open angle)	lutein, zeaxanthin and mesozeaxanthin	MPOD levels were lower in patients with open angle glaucoma than control.
Giaconi J.A. et al., 2012	human		glaucoma	healthy diet contains lutein, zeaxanthin, vitamin A, C, E	Diet-enriched vitamin and carotenoids decreased the risk of glaucoma.

Hu B.J. et al., 2011	human	Group 1:patient supplied with lutein and zeaxanthin (n=30) Group 2:patients w/o lutein and zeaxanthin supplementation (n=30) Group 3:control (n=30)	diabetic retinopathy	lutein and zeaxanthin	Lutein and zeaxanthin concentrations in treated group were lower than control.
Lima V.C. et al., 2010	human	Group 1:control (nondiabetics) (n=14) Group 2:type 2 diabetes wo retinopathy (n=17) Group 3:type 2 diabetes with retinopathy (n=12) Group 1:control (n=9) Group 2:I/R (n=9)	diabetic retinopathy	lutein and zeaxanthin	Lutein and zeaxanthin treatment caused increasing MPOD levels more in nondiabetic patients than diabetics.
Dilsiz N. et al., 2006	Male Long-Evans rats	Group 3:tocopherol-treated (I/R+gamma tocopherol) (n=9) Group 4:lutein-treated (I/R+lutein) (n=8) Group 5:Trigonella-treated (I/R+Trigonella) (n=8) Group 6:Teucrium-treated (I/R+Teucrium) (n=8)	retinal ischemia	lutein	Lutein treatment improved malondialdehyde (MDA) levels and increased GSH.
Li S.Y. et al., 2012	Male C57BL/6N mice	Group 1:lutein treated (n=8) Group 2:sham control (n=8) Group 3:vehicle treated (n=8)	retinal ischemia	lutein	The levels of nuclear factor kappa B (NF-Kb), interleukin (IL)-1 β and cyclooxygenase (COX-2) reduced, no differences in tumor necrosis factor- α (TNF- α) and cell viability in lutein treated group.
Woo T.T. et al., 2013	Male Sprague-Dawley rats	Group 1:lutein treated (n=40) Group 2:vehicle treated (n=39)	retinal detachment	lutein	Lutein treatment improved caspase-3 and caspase-8 expression. No difference was found in caspase-9.
Li S.Y. et al., 2009	Male C57BL/6N mice	Group 1:lutein treated (n = 7) Group 2:vehicle treated (n = 11).	retinal ischemia	lutein	Lutein treatment improved in the levels of nitrotyrosine (NT) and poly-ADP-ribose (PAR).
Zhao D.Y. et al., 2003	human	Group 1:patients with retinitis pigmentosa (RP), choroideremia (CHM) and Stargardt macular dystrophy (n=30) Group 2:control (n=76)	RP, CHM Stargardt macular dystrophy	lutein and zeaxanthin	No differences was found in the levels of lutein and zeaxanthin in patients with RP and CHM, while lower levels in patients with Stargardt macular dystrophy.
Duncan J.L. et al., 2002	human	Group 1:patients with CHM (n=13) Group 2:normal vision (n=40)	CHM	lutein	No differences was found in progression of CHM

2.2. Role of Lutein and Zeaxanthin in AMD

A meta-analysis focused to determine the impacts of lutein and zeaxanthin supplementation on 1176 patients suffering from AMD. Lutein and zeaxanthin supplementation caused visual performance improvement in the patients with AMD compared to the placebo group [74]. Another meta analysis conducted by Wang et al. to evaluate the effects of lutein and zeaxanthin supplement on the conditions such as MPOD and visual acuity (VA). Three different groups: lutein-zeaxanthin, lutein-DHA and lutein-vitamin/mineral combinations were examined. MPOD and VA improved significantly in lutein treated group against placebo. Differences in the levels of MPOD were more severe than VA [75]. The effects of lutein and zeaxanthin on subjects with early AMD were investigated. Different concentrations of lutein and zeaxanthin (10 mg lutein, 20 mg lutein, 10 mg lutein + 10 mg zeaxanthin or placebo) were supplied to 112 patients for 2 years to enhance macular pigment levels and functional retinal changes. MPOD and N1-P1 response densities increased in lutein treated AMD groups. Also, retinal sensitivity was enhanced in the central retina meanly [76]. Eggs are extremely nutritious food that contain many vitamins, minerals, carotenoids including lutein and zeaxanthin. Patients over the age of 50 who had early symptoms of AMD consumed lutein-enriched egg yolk based buttermilk drink daily for a year. Plasma lutein concentrations in the treated group increased significantly while the increases in serum LDL and total cholesterol (TC) levels were not compared to the control [77]. Daily intake of lutein and zeaxanthin were calculated by asking questions about food consumption to the subjects with early/late AMD and without AMD. Also, serum concentrations of lutein, zeaxanthin and serum lipids, including serum TC, triglyceride (TG), HDL and LDL were measured and compared. Not all serum lipids, but serum HDL levels were associated with AMD development [78]. The Age-Related Eye Disease Study (AREDS) was conducted to evaluate the therapeutic effects of vitamin C, vitamin E, zinc with copper and β -carotene on AMD. Secondly, AREDS2 was performed and lutein/zeaxanthin was added to the first formulation to demonstrate the effects of them on AMD [73]. Both groups showed impairment on AMD. However the consumption of β -carotene can be a risk factor in the development of lung cancer for smokers, ex-smokers and subjects exposed to asbestos [74]. For all this, it was concluded that lutein/zeaxanthin supplements were better choices for treatment of AMD compared to β -carotene [79,80]. In a study among hospital patients in South India who were suffering from AMD, as the consumption of lutein and zeaxanthin increased, the risk of AMD decreased. In addition, the risk of AMD might reduce by taking cigarettes and alcohol [81].

2.3. Role of Lutein and Zeaxanthin in Uveitis

Lutein might play a protective and regulative role in mice suffered from the lipopolysaccharides (LPS)-induced uveitis. *BALB/C* mice were treated with different concentrations of lutein in drinking water for five days. Then uveitis formed in the eyes of these mice by applying LPS into the foot-pad. After the treatment, eyes were collected and several indicators were measured including, nitric oxide (NO), MDA, oxygen radical antioxidant capacity (ORAC), GSH, vitamin C levels, the enzymatic activities of SOD and glutathione peroxidase (GPx) in the eye homogenates. NO, MDA and ORAC levels decreased while the activities of SOD and GPx increased significantly in the eyes of the mice treated with lutein. Moreover, oral lutein intake improved the vitamin C and GSH levels in the eyes of the mice [82]. Sasaki M et al. conducted a study to evaluate the neuroprotective effects of lutein against retinal inflammation in mice with EUI. LPS was injected into the mice intraperitoneally (ip) to induce EUI, then lutein was administered by subcutaneous (sc) injection. It is suggested that lutein was a protective supplement on photoreceptor cells by decreasing production of reactive oxygen species which were causing visual damages, reduced rhodopsin (RHO) levels and induced GFAP expressions [83].

2.4. Role of Lutein and Zeaxanthin in Glaucoma

Igras et al. conducted a study to evaluate the relationship between macular pigments, oxidative damage and glaucoma. MPOD was higher in the control group (n=54) than patients with open angle glaucoma (n=40). Also glare was a problem for more than half of patients with glaucoma and not for the control group [84]. A strong relationship was found between eating habits and the development and progression of eye diseases. A healthy diet containing fruits and vegetables, which were rich in vitamin A, vitamin C, vitamin E, carotenoids such as lutein and zeaxanthin might lead to an increase of the risk of glaucoma among older African-American women [85]. The levels of MPOD were higher in subjects with open-angle glaucoma who had glaucomatous eyes without foveal involvement than with foveal involvement [86].

2.5. Role of Lutein and Zeaxanthin in Diabetic Retinopathy

Serum concentrations of lutein and zeaxanthin and the visual effects of them on subjects with/without non-proliferative diabetic retinopathy were investigated. Three groups of subjects; patients with non-proliferative diabetic retinopathy treated with lutein and zeaxanthin for three months, patients with non-proliferative diabetic retinopathy without any supplementation (diabetic retinopathy control group) and healthy subjects (control group) were investigated. Serum lutein and zeaxanthin concentrations in the control group were significantly higher than the treated group. Furthermore, foveal thickness decreased while contrast sensitivity increased significantly after the treatment compared with pre-medication [87]. There was a relationship between serum and dietary levels of lutein/zeaxanthin and MPOD [88]. Macular pigment and hemoglobin A1c (HbA1c) levels were compared in patients with type 2 diabetes (with/without retinopathy) and nondiabetics. MPOD values were higher while HbA1c levels were lower in nondiabetic subjects than diabetics. It can be considered that impaired glycemic control could cause defects in retinal absorption and dispersion of lutein and zeaxanthin [89].

2.6. Role of Lutein and Zeaxanthin in Retinal Ischemia

Retinal ischemia/reperfusion (I/R) causes irreversible structural and functional damages in retina resulting in neurodegeneration [90]. Lutein is used to protect retinal neurons against oxidative stress resulting in ischemia/reperfusion due to its potent antioxidant profile. The effects of several antioxidants such as α -tocopherol, lutein, *Trigonella foenum-graecum* Linn.) and *Teucrium multicaule* Montbret & Aucher ex Benth. were investigated in rats with ischemia-reperfusion injury. Lutein treatment caused a significant decrease in the levels of MDA as an indicator of lipid peroxidation and a considerable increase in GSH and also inhibition in the I/R-induced activation of caspase-3 [91]. Anti-inflammatory potential of lutein was investigated in *in-vivo* and *in-vitro* conditions. The levels of NF- κ B, IL-1 β , and COX-2 dramatically reduced, but not TNF- α and cell viability increased in lutein-treated Müller cells. Furthermore, lutein administration restored electroretinogram values caused by I/R injury controversially and also gliosis which was a formation of a glial scar was decreased [92]. Ip administration of lutein to Sprague-Dawley rats with retinal detachment minimized GFAP levels and remained the expression of RHO. Furthermore the treatment resulted in a reduction of caspase-3, cleaved caspase-8 expression and no difference in caspase-9 [93]. There had been significant increases in the levels of nitrotyrosine (NT) and poly-ADP-ribose (PAR) as a marker of apoptosis in mice with I/R injury treated with lutein [94].

2.7. Role of Lutein and Zeaxanthin in CHM and Other Eye Disease

The levels of lutein and zeaxanthin in patients with RP, CHM, Stargardt macular dystrophy and healthy subjects were compared by using resonance Raman spectroscopy. There was no significant difference between the patients with RP, CHM and the subjects who had no macular pathologic condition. Despite the fact that patients with Stargardt macular dystrophy showed lower levels of

macular carotenoids than the control groups [95]. The levels of macular pigments, the defects of rod-cone function and structure of central retina were determined. Foveal vision and macular pigment relation was evaluated after 6 months of oral lutein treatment. Serum macular pigment levels increased as a result of lutein supplementation while foveal sensitivity was stable in patients with CHM [96].

3. Conclusions

Carotenoids, which absorb a wavelength range of 350-550 nm are nonpolar organic pigments divided into two major groups; carotenes and xanthophylls [4]. The group of xanthophylls includes lutein, zeaxanthin, neoxanthin, violaxanthin etc [5]. Lutein and zeaxanthin are accumulated in lipophilic tissues such as adipose and liver tissue [44,45]. These are the only carotenoids called macular xanthophylls deposited in the human lens and found abundantly in the macula lutea which is the responsible area of vision [97,98]. Macula of retina is yellow due to rich lutein and zeaxanthin content. Lutein and zeaxanthin absorb near-ultraviolet and blue light, so macula is protected against phototoxic damage. Additionally, lutein and zeaxanthin have free-radical scavenging, anti-inflammatory and antitumor potential [99]. Based on this, lutein and zeaxanthin may be used to protect subjects against inflammatory diseases of the eye including, AMD, uveitis, RP, scleritis and also cataract, glaucoma, retinal ischemia, CHM, etc. The mechanisms of protective effects of lutein against retinal damage have not been revealed yet exactly. However, there are several aspects about the mechanism. One is that lutein and zeaxanthin protect retina against oxidative stress from the damage of blue-light by inhibiting lipid peroxidation and c-fos gene expression [16,17]. The other is about antioxidant properties of lutein and zeaxanthin that are highly potent quenchers of singlet oxygens and other free radicals [18,19,20]. With all this, further studies are necessary to quietly determine exact mechanisms of protective effects of these macular pigments.

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