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**REVIEW ARTICLE**

# The Effect of Nutrition and Supplements on Ocular Health

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## Abstract

Nutrition is a subject of interest in many fields of medicine. So ophthalmologists have also attempted to find possible ways to preserve vision through diet and supplements. Ocular disorders such as cataracts, age-related macular degeneration and glaucoma are the leading causes of visual impairment and blindness in the world, so most of the studies have focused on these major disorders and nutritions containing antioxidant such as vitamin C and E. Zexanthin/luteins and omega 3 have been the main substances studied in this relation. Although benefits of the regimens with high amounts of antioxidants were observed in reducing progression of cataract, age-related macular degeneration and so on, as many of these studies have been observational, the cause and effect relationship cannot be definitely concluded and multiple cohort prospective studies will be desired to evaluate the exact role of nutrition. Somehow, a healthy diet which means the diet which increases our health can be achieved in regimens with low saturated fatty acids and rich in fresh fruits, vegetables and fish. On the whole, even though they may not affect disease progression, they are generally good for overall health.

**Keywords:** Nutrition; Supplement; Ocular health

## Introduction

Ocular disorders such as cataracts, age-related macular degeneration (ARMD) and glaucoma are the leading causes of visual blindness in the world. Currently, cataract extraction is the most common surgical procedure performed. It has been estimated that if the progression of cataracts could be delayed by at least 10 years, the number of cataract surgeries would be approximately reduced by 45 percent per year.[1] On the other hand, the severity and irreversibility of ARMD and glaucoma have caused interest in finding a modality to prevent or retard cataract formation. In this respect, nutrition modification is one promising subject which seems to be effective to fulfill our desire to some extend; however, the evaluation of the exact effects of nutrition on such long lasting ocular disorders, which are manifested as people age, is not practical anyway.[2] As a result, multiple observational cohort and misanalysis studies were performed to investigate any effect of nutrition on modulation of those ocular disorders. Considering the eye as a certain area of the body with heavy exposure to light, the oxidative damage mediated by light exposure remains as the main cause of ocular problems.[3-5] Oxidation is a process that allows free radicals to alter the genetic structure of a cell leading to disastrous chronic diseases in humans. However, any substance consumption which neutralizes this process of oxidation will protect human cells from damage. The question remaining to be answered is what substances and with what amount to be included in daily nutrition to gain optimal effect. Other issues concern the cost effectiveness of such regimens.[6]

As studies on this issue have come up with conflicting results, we attempted to have an overview of the nutritional substances pertaining to ocular health, the main sources of obtaining them, and the possible effect of these regimens in each ocular disorder.

## Materials and Methods

The Pubmed databases were searched from 1993 to 2008, using the search term (nutrition), (nutrition and ocular health), (nutrition and eye), (nutrition and eye disease/ ocular disorder/cataract/age related macular

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disease or glaucoma) and (sources and caretenoid/zexanthin/lutein/vitamin C or vitamin E). In addition, English abstracts of articles which are non-English and of significant interest were included**.**

*Nutritional substances and their main sources*

Multiple kinds of carotenoids (plant pigments) give each fruit and vegetable its special colors. Such carotenoids as zeaxanthin and lutein, which give color from yellow to orange, provide a bright red hue to foods such as tomatoes, watermelon and pink grapefruit. Spinach, peas and many yellow/orange fruits and vegetables are rich in lutein. Corn, orange, peppers and certain leafy greens provide zeaxanthin. Lutein and zeaxanthin, however, can be found in many of the same foods and are often considered together as one value in the literature.

See the Tables below for food sources of lutein and zeaxanthin

| FOOD SERVING SIZE | LUTEIN (MG) |
|---|---|
| Spinach, cooked 1 cup | 13.3 |
| Savoy cabbage, shredded 1 cup | 10.2 |
| Greens, cooked 1 cup | 8.4 |
| Broccoli, cooked 1 cup | 3.4 |
| Peas, cooked 1 cup | 3.2 |
| Spinach, raw 1 cup | 1.8 |
| Butter head lettuce 1 cup | 0.9 |
| Green pepper, sliced 1 cup | 0.9 |

* Provided by American Optometric Association

*Vitamin C*

Vitamin C is an essential water-soluble vitamin considered as an important antioxidant which works to protect cells from damaging in the face of free radicals. Many fruits and vegetables are excellent sources of vitamin C.

See the Table below for a list of good food sources of vitamin C

| FOOD SERVING SIZE | VITAMIN C (MG) |
|---|---|
| Papaya 1 medium | 188 |
| Orange juice 6 ounces | 93 |
| Strawberries 1 cup (8 whole) | 84 |
| Grapefruit juice 6 ounces | 70 |
| Cantaloupe, cubed 1 cup | 68 |
| Mango 1 medium | 57 |
| Green peppers, raw 1/2 cup | 45 |
| Broccoli, raw 1/2 cup | 41 |
| Cauliflower, raw 1/2 cup | 23 |
| Tomato 1 medium | 23 |

*Provided by American Optimetric Association

*Vitamin E*

Vitamin E is a fat-soluble vitamin. Alpha-tocopherol is the most active form of vitamin E that may protect the body against free radicals. Vegetable oils and nuts are also the good dietary sources of vitamin E.

See the Table below for a list of good food sources of vitamin E.

| FOOD SERVING SIZE | VITAMIN E MG/ (IU) |
|---|---|
| Almonds 1 ounce | 5.0 (7.5) |
| Safflower Oil 1 tablespoon | 3.1 (4.7) |
| Corn Oil 1 tablespoon | 1.9 (2.9) |
| Turnip Greens 1/2 cup | 1.6 (2.4) |
| Mango 1 fruit | 1.5 (2.3) |
| Peanuts 1 ounce | 1.3 (2.1) |
| Broccoli 1/2 cup | 1.0 (1.5) |
| Pistachio Nuts 1 ounce | 0.8 (1.2) |

*Provided by American Optometric Association

*Omega-3 Poly Unsaturated Fatty Acid (PUFA)*

The primary food source of omega-3 is sea food, especially cold water fish such as salmon, sardines and tuna.[7-10]

*Age-related macular degeneration (ARMD) and nutrition*

Age-related macular degeneration (ARMD) is a common cause of decreased vision and blindness in patients with the mean age over 40. The cause of ARMD remains unknown and the pathophisiologic mechanism of the damage of the retinal cells is beyond the scope of this text; however, numerous epidemiological studies have suggested a relationship between nutritional factors and ARMD.[11-16] As an instance, the relationship of lipid and ARMD is expected since certain kinds of lipids present in the retina have properties capable of reducing cell damage that may be encountered in patients with advanced ARMD.[17] A daily diet high in n-3 polyunsaturated fat, especially from fish, may have protection against both forms of early and late ARMD. Also, people with the highest versus lowest quantities of 3-polyunsaturated fat as well as omega-3 fatty acids have a lower risk of developing neovascular ARMD and such substances may even hinder the progression of this event.[18,19] The blue mountain Eye Study of more than 2000 Australian adults found that those whose diet was enriched in omega 3 fatty acid were less prone to developing both early and late ARMD.[17] A recent case control study on 4000 individuals also

reported the benefits of regimens of omega -3 on abolishing the process of progression to neovasculr type.[20] Moreover, as found in many studies, docosahexaenoic acid (an omega-3 polyunsaturated fatty acid) found more in the retina than pigmented epithelium, has especial functional properties in photoreceptors.[16-18,21] The other compound is oleic acid or olive oil that was reported to be used as a suitable fat source to increase the absorption of dietary lutein in the management of age-related macular degeneration.[22] An analysis by NHANES (National Health and Nutrition Examination Survey) showed the relationship between blood vitamin level and reduction in the incidence of early ARMD. The mechanism by which this finding was interpreted was related to the anti-inflammatory effect of vitamin D, leading to the establishment and reduction of the growth of new blood vessels.[23] On the other hand, the eye is particularly sensitive to oxidative stress because of direct exposure to light. Antioxidants, such as vitamin E, C or zinc, clearly have a protective and beneficial effect on ARMD.[21] Individuals randomly assigned to receive antioxidants and zinc reduced their risk of aggravation of ARMD and loss of visual acuity.[24,25] A previous study implied that the use of high doses of a combination of antioxidants (vitamin C, vitamin E, and beta carotene) and zinc reduced the risk of progression of advanced ARMD by about 25% in participants who had at least a moderate risk of developing ARMD.[17] Also, levels of serum vitamin D were inversely associated with early ARMD but not advanced ARMD. This provides evidence that vitamin D may protect against ARMD.[26] Those with intermediate risk of age-related macular degeneration or advanced age-related macular degeneration in one eye are recommended to take the supplements. In Age-Related Eye Disease Study (AREDS), it has been proved to be promising in the prevention of advanced age-related macular degeneration by 25%. The formulation used by them was made of vitamins C, E, beta-carotene and zinc.[27] Subsequently a cocktail of antioxidants (supplements of vitamins C and E, beta carotene, and zinc) has been shown to reduce the risk of developing advanced (wet) ARMD by about 25%. In individuals with unilateral advanced ARMD, the combination of antioxidants studied in AREDS -- vitamins C and E, beta carotene, and zinc-- reduced the risk of developing advanced ARMD in the other eye.[28] The AREDS ARMD study also indicated that, compared with placebo, both the combination of antioxidants plus zinc and zinc alone considerably reduced the risk of advanced ARMD in persons at risk of progression. They claimed that the combination of antioxidants and zinc had the most benefit, reducing the risk of development of moderate visual acuity loss (OR, 0.73; 99% CI, 0.54-0.99) and also advanced ARMD.[29,30] However, the formulation of zinc and antioxidants is only recommended for persons at high risk, determined by a dilated eye examination by an ophthalmologist. This therapy is not a cure that resolves ARMD completely, but these are important in demonstrating a benefit for patients with early ARMD, before the development of advanced disease, as well as those who have already developed advanced disease in one eye.[31] Development of ARMD appears to have several carbohydrate-related mechanisms as it was shown that a reduction in the dietary glycemic index (dGI), a modifiable risk factor, may provide a way in reducing the risk of ARMD.[32]

In other words, higher dGI is associated with a greater risk of age-related macular degeneration (ARMD). Those at risk of ARMD progression, especially those at high risk of advanced ARMD may benefit from consuming a smaller amount of carbohydrates especially of the refined type.[33] It has been argued that the xanthophylls carotenoids lutein and zeaxanthin may protect the eyes against the age-related macular degeneration (ARMD). Macular pigment optical density (MPOD) is directly related to dietary consumption of lutein and zeaxanthin and also to their serum concentrations.[34-37] Many studies suggest that people with ARMD have lower concentrations of lutein and zeaxanthin in the macula than those without ARMD.[38,39] Suzan et al. (2006) studied the association between intermediate ARMD and lutein and zeaxanthin in the carotenoids in Age-Related Eye Disease Study (CAREDS). They selected women aged 50 to 79 years with intake of lutein plus zeaxanthin above the 78th (high) and below the 28th (low) percentiles, in whom the presence of AMD was determined by fundus. They concluded that diets rich in lutein plus zeaxanthin may protect against intermediate AMD in healthy women younger than 75 years.[40] In this regard, three mechanisms were interdicted by which lutein and zeaxanthin would protect against ARMD by absorbing the blue light, by quenching free radicals (reviewed by Landrum and Bone), or by increasing the membrane stability. Also, It has been hypothesized that lutein and zeaxanthin protect the macula against photo oxidative damage by their function as antioxidants and/or optical filters.[40,41] Observational and clinical trials support the safety of higher

intakes of the lutein and zeaxanthin and their roles in improving clinical features of ARMD in patients.[42] Also, it was reported that dietary lutein/zeaxanthin intake was inversely associated with neovascular ARMD.[19] Moreover, the increase in the serum levels of lutein/zeaxanthin correlates with increases in the serum levels of their metabolites that have previously been detected in the ocular tissues. Elderly human subjects with and without ARMD can safely take supplements of lutein up to 10 mg/d for 6 months with no apparent toxicity or side effects.[43] However, in cigarette smokers, a high rate of lung cancer was documented in those receiving beta carotene supplements.[44,45] So, except in cigarette smokers, carotenoids have been advocated as potential therapeutic agents in treating age-related macular degeneration (ARMD).[44-47]

*Cataract and nutrition*

Cataracts are opacities of the lens in the eye that result in decreased visual acuity in the elderly. According to literature regarding many experimental and observational researches, antioxidants, such as vitamin E, C or zinc, probably have a protective effect on cataract by their antioxidant properties.[21,30] Moreover, the lens contains carotenoids, lutein and zeaxanthin, which have been shown to have antioxidant properties. It has been hypothesized that increasing the intake of lutein and zeaxanthin may prolong the onset of age-related cataracts.[48] In an experimental study on animals with sodium selenite induced cataract, L-cysteine and vitamin C were highly effective in preventing and retarding the process of cataractogenicity of this substance by maintaining the soluble protein concentrations of the lens.[49] In previous studies, it was reported that women in the group with high dietary levels of lutein and zeaxanthin had a 23% lower prevalence of nuclear cataract compared with those with low levels but the final results were in favor of only moderate association of those regimens and prevalence of nuclear cataract in older patients.[50-53] Consequently, it was said that supplementation with vitamin C, lutein, zeaxanthin, or a multivitamin may help only certain populations in prevention of cataract, but it will probably affect the progression of cataracts in most patients.[54] Christen et al. (2008) in a study on women reported that higher dietary intakes of vitamin E from food and supplements were associated with significantly decreased risk of cataract.[53] Although in observational studies high levels of antioxidants especially vitamin E was found to be associated with lower rates of nuclear cataract, in other prospective randomized placebo controlled clinical trails, the Age Related Eye Disease Study (AREDS) and recent vitamin E, cataract and Age Related Maculopathy Trial, it was found that neither the combination of vitamin E, C and ß carotene nor vitamin E alone was effective in this relation.[55] Furthermore, osmotic stress caused by accumulation of polyols within the lens has been shown to be associated with glucose-induced cataractogenesis. Taurine has an antioxidant capacity and its level in diabetic cataractous lens is markedly decreased. Higgines et al. (2007) claimed that pretreatment of the lense with 30 miliMole taurine significantly reversed the level of protein carbonylation and reduced glutathione (GSH) compared to the control group. Therefore, taurine might spare GSH and protect ional effect on the lens in the face of oxidative stress induced by a high concentration of glucose.[57]

According to the nutritional lipid profile, higher dietary intake of omega-3 polyunsaturated fatty acids (n-3 PUFA) was associated with a reduced incidence of nuclear cataract as dietary fat may affect the lens cell membrane composition and function, and these are related to age-related cataract.[58] In addition, higher alpha-linolenic acid (ALA) intake was associated with a greater age-related change in the lens nuclear density.[59] Suzan et al. studied the association between age-related nuclear cataract and lutein and zeaxanthin in the diet and serum in the carotenoids in the Age-Related Eye Disease Study (CAREDS). They reported that diets rich in lutein and zeaxanthin are moderately associated with decreased prevalence of nuclear cataract in older patients as patients in the group with high dietary levels of lutein and zeaxanthin had a 23% lower prevalence of nuclear cataract compared with those with low levels.[60] Conversely, an Italian trial which randomized more than 1000 older adults to a daily multivitamin supplement or placebo reported that while supplements reduced the risk of nuclear cataract by 34 percent, it increased the risk of posterior subcapsular cataract.[61]

*Glaucoma and Nutrition*

Glaucoma is one of the common causes of blindness in the elderly population. Increasing dietary omega-3 reduces IOP with age because of increased outflow facility, probably as the result of an increase in docosanoids. So, dietary formulations may provide a modifiable factor for IOP regulation. This can reduce the risk for glaucoma and lead to a role in treatment of the disease.[35] A higher intake of certain fruits

and vegetables enriched in vitamins may result in decreased risk of glaucoma.[36]

*Dry Eye and Nutrition*

The women health study (WHS) found that women with a higher dietary intake of omega-3 fatty acids were less prone to dry eye.[62] The mechanism by which this result could be interpreted may be related to the anti-inflammatory effect of Omega-3 found in maibomian gland. The same result was observed in patients with sjôgrens by abolishing lacrimal gland inflammation. So, it was recommended to use fish oil as a main source of this substance especially in regions with low intake of fish. However, caution is recommended as these supplements may not be useful for health by increasing bleeding time and interfering with COXZ-2 inhibitors.[63,64]

*Summary*

Nutrition is a subject of interest in all fields of medicine. Accordingly, in the field of ophthalmology attempts have been made to find possible ways to preserve vision through diet and supplements. In spite of several studies in this field,[65-70] the most famous was the Age Related Eye Disease Study (AREDS), a randomized trial that reported the benefit of supplementation with antioxidants and zinc in patients with intermediate ARMD or loss of vision in one eye as a result of advance disease. Age Related Eye Disease Study (AREDS) is important since it revealed a certain effect of supplementation on abolishing specific disease progression in specific groups of patients. The effect of nutrition on ocular health has not been neglected any way though most of the studies were observational and this made it difficult to make a definite conclusion about what to eat or what supplements to use as pills. Moreover, the results of some of the recent prospective cohort studies, while not confirming the previous results, may conversely give different conclusions. In other words, as stressed by Dr Chew, "most of those studies tell us that there may be something there, but still need to do well–conducted randomized controlled trails.[65,71,74]

As previously mentioned, since the eyes are more vulnerable to light and oxidative damage by light, trends are towards nutrition with high antioxidative properties such as vegetables containing beta carotene zexanthine /lutein, vitamin C, E and also those with high amounts of unsaturated fatty acid and omega 3 such as fish oil. Researchers hope that antioxidants might at least slow disease progression if not effective on prevention. Although the results of the first AREDS are currently used as a guideline in treatment of patients with ARMD, it is impossible to know if the relation of diet and disease progression is a real cause and effect one until cohort studies confirm it.[72,73] "Fortunately a randomized trial called ARDES-2 is investigating the effect of these nutrients on the development of ARMD. Enrolment has begun and the results will be available in about five years. Therefore, "The results from ARDES-2 which is looking for cataract will be available in 2012. They are going to study the effect of lutein/Zexanthin and omega 3 fatty acid on cataract following 4000 participants in five years.[74] Somehow, a health diet which means the one that increases the life health can be achieved in regimens with low saturated fatty acids and enriched in fresh fruits, vegetables and fish .We can state briefly that even though they may not affect disease progression, they are generally good for overall health. It would be better to obtain these substances through natural foods and include them in the daily regimens rather than through supplements, since many fat soluble supplements such as vitamin E are risky for health. In addition, other supplements containing Beta carotene increase the risk of lung cancer in asbestoses workers and cigarette smokers. Also, combination of selenium, Beta carotene and vitamin E has been found to increase the risk of esophageal cancer.[75,76] Despite these arguments, researchers still work on making pills proper for ocular health.

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