



Antioxidant vitamins, minerals and cataract: current opinion

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Purpose of review

The purpose of this review is to assess the most recent findings and literature on the effect of minerals and antioxidant vitamins in the prevention of development and progression of cataract.

Recent findings

To retrieve most recent and relevant articles for this review, an intense and thorough search was conducted in databases and journal articles. Experts in the field of study were also contacted to know what the current opinions were in their practice. The data retrieved were qualitatively analysed and synthesized in order to arrive with the most objective conclusions. The result on the use of single antioxidant supplement did not show any significant effect on the cataract. A combination of antioxidant vitamins such as vitamins C and E may have a synergistic effect on cataract prevention; however, more studies need to be conducted to prove this.

Summary

There are still inconsistent results on the exact antioxidant and the required amount needed to prevent cataract. On the basis of the insufficient and inconsistent results of recent trials reviewed it is not clear that antioxidant vitamins and minerals nor that healthy diets prevent the development and progression of cataract.

Keywords

antioxidants, cataract, minerals, prevention, vitamins

INTRODUCTION

Cataract is defined as the opacification or clouding of the lens that leads to disruption in vision. It is the leading cause of reversible blindness worldwide affecting about 16 million people [1,2] with a rising incidence amongst the middle aged and aging population in the USA [3]. Cataract is a disabling condition that constitutes a major public health problem that has been estimated to progressively affect individuals in the USA rising from 20 million in the year 2000 to 30 million in 2020 [4]. Cataracts are noted in atopic disorders such as atopic keratoconjunctivitis or steroid induced lens opacifications [5].

Study purpose

There are very few good evidence-based studies to ascertain the effectiveness of antioxidant vitamins and minerals in the prevention of cataract. Most reviews have recommended that more randomized controlled trials should be carried out.

The purpose of this review is to assess the most recent findings and literature on the effect of

minerals and antioxidant vitamins in the prevention of development and progression of cataract.

THE HUMAN LENS

The human lens is a crystalline biconvex tissue made up of four layers: cortex, nucleus, capsule and sub-capsular epithelium layers. It contains specialized stratified epithelial cells having high cytoplasmic protein content and as it does not shed

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KEY POINTS

- More systematic reviews and meta-analysis to clinically analyse the effectiveness of antioxidant vitamins and minerals in the prevention of cataracts is highly recommended as only one study was identified to effectively address this review topic.
- In addition, some vitamins and minerals may have synergistic effects, as the use of vitamin E alone did not show any significant effect, although the combination with vitamin C did demonstrate a significant clinical effect.
- There is paucity of highly evidence-based studies such as randomized controlled studies on this subject hence, well controlled studies supported by federal programs such as those through the National Institutes of Health should be conducted.

its nonviable cells it becomes extremely susceptible to aging [6].

TYPES OF CATARACT

Based on anatomy of the eyes, cataracts are described as cortical, nuclear and subcapsular. However, they have also been described based on pathophysiology as: age related cataract (ARC), congenital, traumatic, radiation and secondary cataract. The most common type is ARC [7], with the nuclear cataract being the most common in elderly Americans [8]. ARC develops in persons 40 years or older especially in those more than 65 years [9].

CLINICAL PRESENTATION AND DIAGNOSIS OF CATARACT

Some of the clinical presentations of cataract include: blurry vision, double vision, sensitivity to light, visualising 'halos' of light, floaters or glares, decreased perception and so on. These changes commonly generate a visit to a primary care physician and then to an eye care specialist. Visual acuity is easily performed, although the more advanced level of examination using a slit lamp is done by the ophthalmologist/optometrist who can properly examine the anterior structures of the eye such as cornea, iris, lens and the anterior chamber (see Fig. 1 [10] and Fig. 2 [11]). An ophthalmoscope or slit lamp examination is used to magnify the anterior surface, but is also used to visualize the posterior structures behind the lens eyes after dilating the eyes. These techniques allow for proper visualization of eye structures including the lens.

Cortical, nuclear and posterior subcapsular cataracts are the three most common types that are

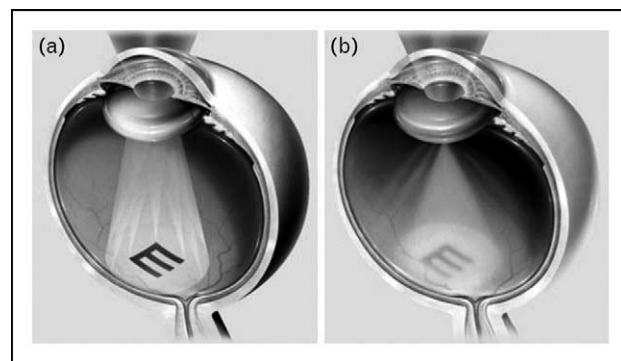


FIGURE 1. (a) It is showing light focus on normal lens. (b) It is showing light focus on a lens with cataract. Adapted with permission from [10].

graded according to severity using a four points grading system modified from the Lens Opacity Classification system (LOC II) (see Table 1) [12]. This has become ever more important as this system has been used for the approval of all new inhalational steroids (intranasal and pulmonary).

PATHOGENESIS AND RISK FACTORS

The eye lens is an avascular transparent complex structure made up of a thick basement membrane which envelopes a layer of cuboidal epithelial cells, (the lens epithelium) beneath the anterior capsule which receives its nourishment by diffusion from the aqueous and vitreous. The lens epithelium is located on the internal surface of the capsule. The cells of the lens epithelium continue to divide with age; thus, the lens grows in anterior–posterior thickness. The components of the nucleus and cortex include crystallins, which are tightly packed cells that have lost their nuclei and become packed by special transparent proteins and eventually make up the lens fibers. New lens cells are added to the margin of the lens throughout life from the lens epithelium; however, the cells at the lens cortex and nucleus do not undergo turnover or replacement, and are therefore the oldest cells in the body of an adult, thereby increasing the risk of lens opacification. The exact mechanism by which the lens opacifies is unknown, but various theories suggest that oxidative stress, inhibition of antioxidants and toxic injury may be linked to various risk factors that will assist public health campaigns on cataract prevention.

A recent clinic based prospective cohort study [13] investigated the possible risk factors associated with the development of cataracts in the Age-Related Eye disease study. The study recruited 4425 participants from 55 to 80 years old. They were followed up for about 10 years and the identified risk

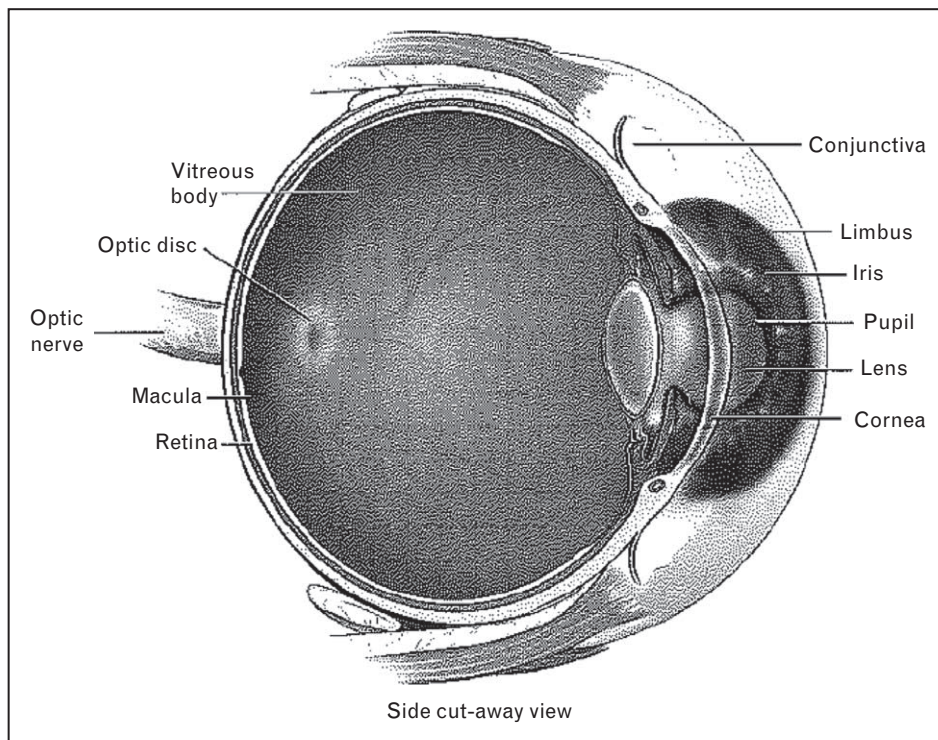


FIGURE 2. Showing anatomy of the human eye. Adapted with permission from [11].

factors found to be associated with the development of cataract were; age, smoking, diabetes mellitus, male sex, lower educational status and nonwhite race. Other risk factors identified in earlier conducted prospective studies include exposure to the ultraviolet (UV) rays of sunlight, nonuse of multivitamins, heavy alcohol consumption, long-term use of systemic or topical steroids for treatment of allergic conditions and poor nutritional status.

ATOPY AND CATARACT

The association between cataracts and atopic dermatitis was first reported in the 1940s[14–16],

leading to the development of ‘Andogsky syndrome’ (dermatogenic cataracts), although the clinical evidence seems to be more anecdotal as the only published studies investigating the association between atopy and cataractogenesis are population-based studies, cross-sectional, case reports and case series that are highly subject to selection and sampling bias. The incidence of cataract development in patients with atopic dermatitis has been reported to range between 5 and 38% [17,18].

Cataracts have been reported to be associated with exacerbation of atopic dermatitis or accelerated by long-standing corticosteroid (inhaled, oral,

Table 1. Showing grades of the three types of cataract according to severity

Cataract type	Grade 1	Grade 2	Grade 3	Grade 4
Nuclear yellowing and sclerosis of the lens nucleus	Mild	Moderate	Pronounced	Severe
Cortical measured as aggregate percentage of the intrapupillary space occupied by the opacity	10% of intrapupillary space is obscured	10–50% of intrapupillary space is obscured	50–90% of intrapupillary space is obscured	More than 90% of intrapupillary space is obscured
Posterior subcapsular measured as aggregate percentage of the posterior capsular area occupied by the opacity	3% of the posterior capsule area is obscured	30% of the posterior capsule area is obscured	50% of the posterior capsule area is obscured	More than 50% of the posterior capsule area is obscured

Adapted with permission from [12].

intranasal [19]) use [20] in both children and adults. A recent retrospective study showed only one atopic dermatitis subject out of 88 suffered from an atopic dermatitis-induced cataract and two of the 88 recruited participants were found to develop corticosteroid-induced cataract [17]. Other case reports have described bilateral cataracts ranging in children from as young as 6 years old [21] to a 36-year-old adult with concomitant long-term nasal steroid therapy for allergic rhinitis [19]. Although lenticular opacification is an important ocular complication in atopic dermatitis, the precise pathogenic mechanisms and risk factors for development of atopic cataract are not clear. Potential mechanisms of cataractogenesis include mechanical (habitual tapping and rubbing of the face), drug induced (corticosteroid therapy), elevated IgE [22] and perharps filaggrin mutation, whereas a more prevalent theory was related to increased oxidative stress generated by free radicals [23,24]. Corticosteroids have been associated with posterior subcapsular cataracts, whereas atopic dermatitis is associated with pathognomonic shield-shaped anterior subcapsular cataracts, but can also include posterior subcapsular cataracts [25].

Although cataractogenesis is associated with severe late stage atopic dermatitis, no study has successfully investigated the cause of the cataract from corticosteroid use or atopic dermatitis alone. Further studies are necessary to validate the correlation with distribution of skin lesions, clinical course of dermatitis, personal history of respiratory atopy, serum IgE levels or concomitant ichthyosis vulgaris.

OXIDATIVE STRESS AND ANTIOXIDANTS

Exposure to dietary mercury in fish has been implicated as one of the risk factors associated with the development of cataract on the lens. A recent population-based study was conducted in the Amazon community located in Brazil [26]. This community is known to have a high consumption of fish from the Tapaja River. A total of 211 participants greater than 40 years of age were recruited for the study. This is the first study to look at the relationship between high intake of mercury from fish and incidence of cataract. They looked at the damaging effect of mercury and the protective effect of selenium on the lens. This study suggested that selenium may have a protective effect on the oxidative damage caused by mercury on the lens.

The heavy metal Cadmium is shown to be associated with cataracts in heavy smokers in a population-based study conducted amongst 60 men diagnosed with cataract [27]. This study also demonstrated low levels of antioxidants such as

vitamins E, C and beta carotene in smokers when compared with nonsmokers.

CATARACT PREVENTION

Healthy diet has been investigated over the years for the prevention of cataract because of its high content of antioxidant vitamins and minerals and for potentially interfering with the oxidation of lens structures leading to cataract formation. Physicians do recommend certain approaches to help prevent development and progression of cataract thought to be associated with increased oxidative states. These include:

- (1) Wearing protective sunglasses against UV rays of sunlight;
- (2) Avoiding cigarette smoking;
- (3) Avoiding heavy alcohol consumption;
- (4) Eating healthy diets rich in vitamins and minerals;
- (5) Maintaining adequate weight with diet and exercise to prevent/control being overweight or obese;
- (6) Adequate control of diabetes for patients suffering from diabetes mellitus; and
- (7) Having a regular eye exam and reporting to a physician if any change in visual acuity is noticed.

RATIONALE FOR INTERVENTION

The US Food and Drug Administration (FDA) has not currently approved any medications or supplements for the treatment or prevention of cataract. The only recommended treatment for cataract so far is surgical intervention that is not readily available in most developing countries such as sub-Saharan Africa and Asia [28]. Surgery is also an expensive and invasive procedure, hence, there is a need for cheaper and less invasive approach as a solution to this public health burden.

MATERIALS AND METHODS

To retrieve most recent and relevant articles for this review, an intense and thorough search was conducted in databases and journal articles. Experts in the field of study were also contacted to know what the current opinions were in their practice.

NUTRITION AND CATARACT

Healthy diets and cataract prevention was demonstrated in a prospective cohort study [8]. Women aged between 50 and 79 years on the healthy eating

index from the women's health initiative adhering to US dietary guidelines were studied. The evidence revealed that diet rich in vitamins and minerals helped to reduce the incidence of commonly encountered cataract in the USA, specifically noting that cataract formation was lower in women who had high healthy eating index score. The highest prevalence was found in smokers and obese women.

ANTIOXIDANTS

Antioxidants are molecules that inhibit the destructive action caused by oxidative stress that leads to the release of free radicals causing cell death. Various vitamins and minerals have antioxidant capabilities and are commonly found in various foods, food supplements or multivitamin pills. The primary question arises as to the amount required for 'health' versus 'protection'. Antioxidants are grouped into fat and water-soluble compounds [29]. The lipid soluble antioxidants are protective of the lipophilic cell membranes, whereas the water soluble ones are protective of the cell cytoplasm.

ANTIOXIDANT MINERALS AND CATARACT

Minerals are naturally occurring chemical compounds of which selenium and zinc are the commonly studied minerals for the prevention of cataract. Selenium and zinc are trace elements, which are only required in small amounts for metabolism and critically integrated in the antioxidant enzyme – glutathione peroxidase system that may play a key protective role to the human eye lens. Zinc is one of the essential minerals with high public health importance, as its deficiency leads to numerous disease pathologies. A recently published comparative cross-sectional study assessed the relationship between zinc in serum and changes in the lens of diabetic and senile patients [30]. A total of 40 patients were included, 20 with senile cataracts and the other 20 with type 2 diabetic cataracts. The study concluded that there is a direct relationship between increased incidence of cataract in diabetics and zinc deficiency.

ANTIOXIDANT VITAMINS AND CATARACT

The antioxidants commonly investigated for the purpose of this review are vitamins A, C and E, beta carotenoids such as lutein and zeaxanthine. These have been reported as the only naturally occurring carotenoids in the human lens and macula [31] capable of absorbing damaging UV energy from sunlight. Lutein and zeaxanthin are present in highest concentrations in dark green leafy vegetables, as

well as corn, orange, pepper and tangerines. Natural vitamin E is shown to be twice as efficacious as synthetic vitamin E [32], as it contains more gamma than alpha tocopherol.

A randomized controlled trial [33^{*}] ($n = 11\,545$) compared antioxidant vitamins (400 IU of vitamin E, 500 mg of vitamin C) with placebo that demonstrated no significant effect on the incidence of cataract, even when each antioxidant was independently analyzed. Similar results were achieved by an earlier conducted prospective randomized-double masked placebo-controlled clinical trial [34] of patients ($n = 1193$) aged 55–80 years over a 4-year period who received either 500 IU of vitamin E containing soybean oil capsules or placebo. The result of the study showed that a 500 IU daily dose of vitamin E failed to reduce the incidence or progression of cataract. Whereas another study [35] using a higher dose, 3200 IU of synthetic vitamin E did show a reduction photocoagulation of the lens, hence, the development of cataract.

A recent review article [36] looked at the role of antioxidants such as vitamin C, lutein and zeaxanthine on the incidence and progression of cataracts and suggested that long-term antioxidant supplementation may impact the prevention of cataracts in smokers who are at a higher risk of oxidative stress. Although a population-based prospective cohort study in women suggested that vitamin C supplements increased the incidence of age-related cataracts [37] in women ($n = 24\,593$) 43–83 years of age. Another population-based study conducted in India described an association between lutein, zeaxanthine, retinol and vitamin C with cataract [38] in which participants ($n = 5638$) greater than 60 years old had a higher incidence of cataract and were depleted of vitamin C. An inverse relationship was found between vitamin C, lutein, zeaxanthine, retinoid and cataract. A more recent systematic review and meta-analysis [39^{*}] of randomized controlled trials (eight trials with $n = 107\,874$ participants) examining the effectiveness of antioxidant vitamins and mineral supplements in the prevention or development of age-related cataract concluded that there were no definitive studies nor enough evidence to support the use of antioxidant and minerals in the prevention of ARC, whereas other forms of cataract formation was not addressed.

CONCLUSION

Although the use of antioxidants appears to be logical in the prevention of potential oxidant-induced cataract formation, there are still limited and inconsistent results on the exact antioxidant

and the required amount needed to prevent cataract formation.

The results on the use of single antioxidant supplements have not shown any significant effect on the prevention of cataract. This might be because the studies comparing supplements used smaller doses that may have limited effect against cataract. On the basis of the insufficient and inconsistent results of recent trials reviewed, the present doses and combinations of antioxidants do not prevent the development and progression of cataract.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

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- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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This study included only randomized controlled studies making this article the first retrieved high level evidence-based Cochrane style reference for the review topic. It addressed the effect of antioxidants on ARC. The full manuscript was retrieved from the original authors and it is currently in the process of being published.