

## Review Article

# You Are What You Eat: Preventive Roles of Antioxidant Phytochemicals on Age-related Eye Diseases

---

### ABSTRACT

**Aim:**What we eat plays a vital role in human health with no exception to the eye which results to either good or poor vision. This review aimed at determining how what we eat affect age-related eye diseases and the role of antioxidants in phytochemical compound in preventing age-related eye diseases.

**Study Design:** A non-systematic review and evaluation of published literatures was done through web search engines such as PubMed and Google Scholar using Mendeley reference library for citation.

**Methodology:**A total of 48 articles were reviewed using the key words such as “you are what you eat,” Age-related eye diseases, Antioxidants, Phytochemical compounds, Oxidative Stress and Free Radicals

**Result:** Increased consumption of energy-dense foods such as refined grains, processed meats, added sugar and saturated fatty foods might increase the risk of obesity, insulin resistance, chronically elevated blood glucose, chronic systemic inflammation, oxidative stress, and increased protein damage leading to initiation and progression of systemic diseases such as diabetes, hypertension, heart related diseases, as well as age-related eye diseases such as cataract, glaucoma, diabetic retinopathy, and macular degeneration. Findings also showed that many botanical compounds such as curcumin, lutein and zeaxanthin, ginseng, and many more, present in food exhibit strong antioxidative, anti-inflammatory, and antiapoptotic properties that helps in ameliorating the destructive roles of oxidative stress.

**Conclusion:** Phytochemicals with proven antioxidant and anti-inflammatory activities, such as carotenoids and polyphenols, could be of benefit in preventing age-related eye diseases. Consumption of products containing these phytochemicals is recommended to provide noninvasive alternatives for protection, prevention and treatments of the major systemic and age-related eye diseases.

*Keywords:* Age-related eye diseases, Antioxidants, Oxidative Stress, Free Radicals, Cataract, Glaucoma, Diabetic Retinopathy, Age-related Macular Degeneration

## 1. INTRODUCTION

Healthy eating result to healthy living, and unhealthy eating results to ill health, diseases and death [1]. Modification towards a healthier diet (nutrient-rich and less energy-dense foods) is encouraged by the World Cancer Research Fund (WCRF) to promote prevention of various cancers [1]. Increased consumption of energy-dense foods such as refined grains, processed meats, added sugar and saturated fatty foods might increase the risk of obesity [2]. The health of the eye is dependent on the health of the body [3].

Healthy eyes provide good vision, which is essential for an enjoyable and productive lifestyle. The World Health Organization (WHO) report on visual impairment in 2010 identifies the principal causes of visual impairment as shown in Figure 1 below [4], [5]. Cataract, age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy are the main causes of blindness as well as progressive and irreversible vision loss worldwide as shown in Figure 2 below [6]. There are many fruits and vegetables that contain phytochemicals with antioxidants activities but little evidence is available to identify the different antioxidants present in this food. This review aimed at determining how what we eat affect age-related eye diseases and the role of identified antioxidants present in phytochemical compound in preventing age-related eye diseases.

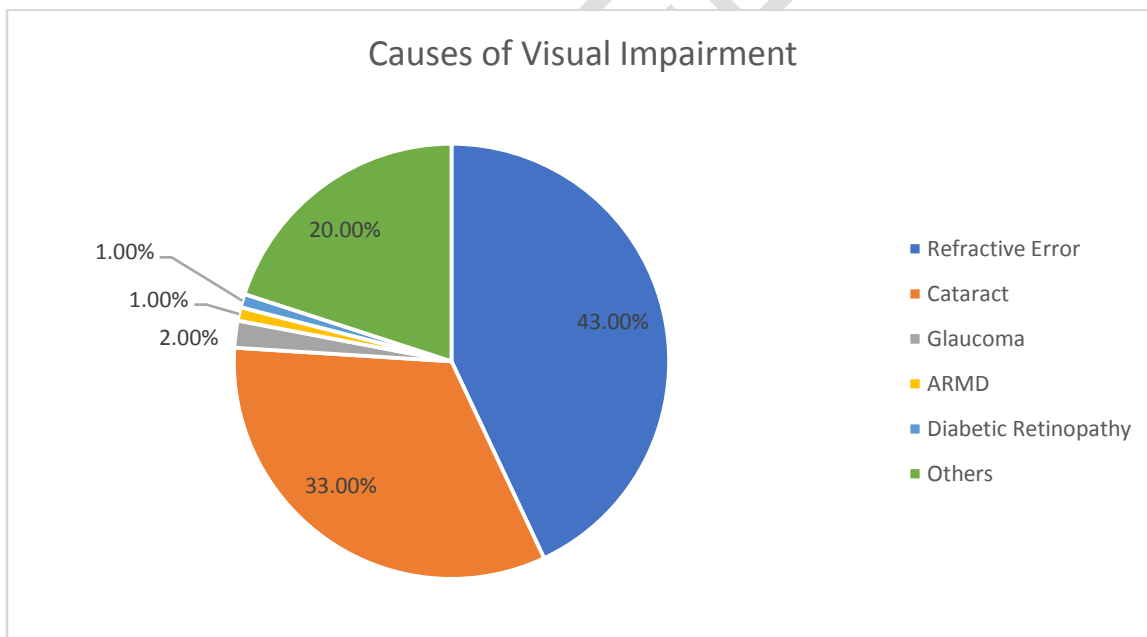


Figure 1: causes of visual impairment [4], [5]

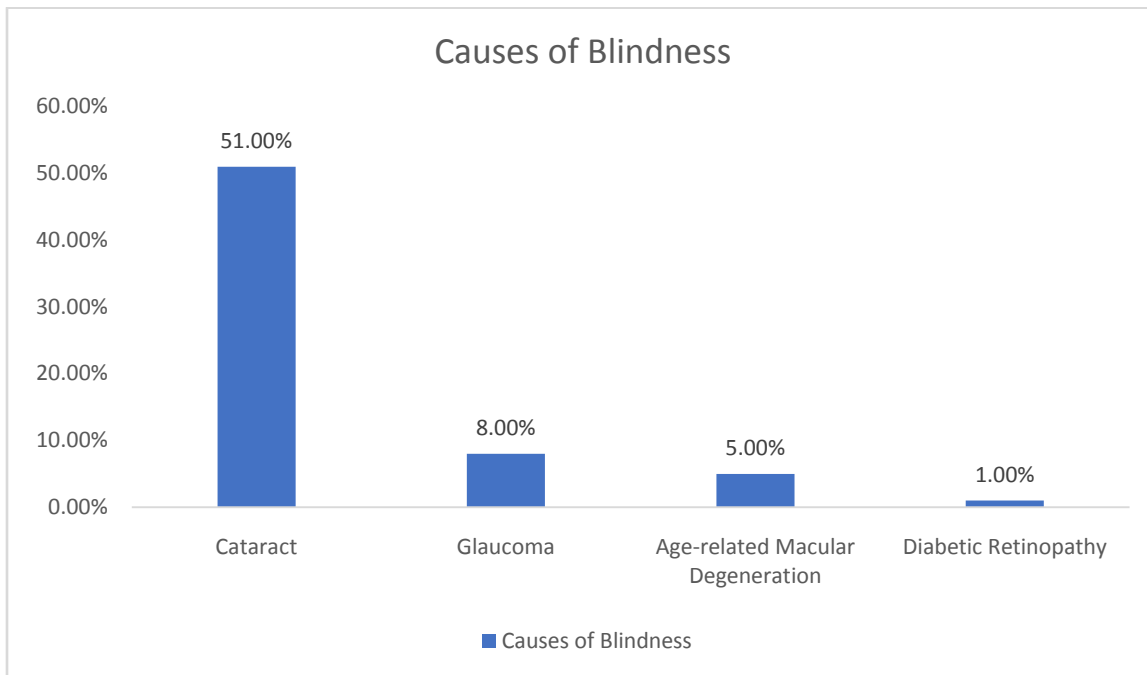


Figure 2: Causes of Age-related Macular Degeneration[6]

## 2. MATERIALS AND METHODS

This followed a non-systematic review approach. The search and evaluation of published literatures globally, in sub-Saharan Africa and in Nigeria was done through search engines including PubMed, google scholar using Mendeley reference library for citation. The published literatures were searched using the key words such as "you are what you eat," Age-related eye diseases, Antioxidants, Phytochemical compounds, Oxidative Stress and Free Radicals. A total of 48 articles were reviewed. The references were also screened for relevant articles. Other key words relating to role of phytochemicals, antioxidants, free radicals, carotenoids, polyphenols, carbohydrates, proteins and diabetes on age-related eye diseases were searched for and reviewed appropriately for important information.

## 3. RESULTS AND DISCUSSION

### 3.1 Unhealthy Consumption of Food and Its Effect on Ocular Health

Carbohydrates being the major source of food in Nigeria vary greatly in structure and function and have wide-ranging physiological effects on the eye [7]. The structure of the carbohydrate determines the rate of monosaccharide release and absorption. Simple sugars and highly branched starches, such as those found in refined flour, are rapidly digested and absorbed, resulting in a quick and substantial increase in blood glucose concentration, mirrored by a rise in insulin. Frequent consumption of rapidly digested carbohydrates can lead to insulin resistance and eventual exhaustion of the pancreas' ability to maintain glucose homeostasis, leading to chronically elevated blood glucose, which has far reaching

effects including increased gut permeability, chronic systemic inflammation, oxidative stress, and increased protein damage due to advanced glycation end products (AGEs), which have been associated with many diseases including retinopathy [7]. Diabetes (*Diabetes mellitus*) arises as a chronic ailment when the pancreas does not produce enough insulin or when the body cannot efficaciously use the insulin (hormone that regulates blood sugar) it produces [8]. Raised blood sugar (hyperglycemia) is a common consequence of uncontrolled diabetes [7]. Therefore, Diabetes is a major cause of blindness and vision loss [8]. The eye is particularly vulnerable to damage from direct and indirect effects of chronically elevated blood glucose due in part to its limited capacity for cellular turnover, limited roles for glucose transporters, and the high metabolic activity of the retina [9]. Hyperglycemia has been clearly associated with cell damage and apoptosis via an accumulation of AGEs, increased metabolism leading to reactive oxygen species (ROS) accumulation, decreased glutathione and protein kinase C activation resulting in Diabetic Retinopathy (DR), age-related macular degeneration (AMD), and cataracts [9]. Finally, the effects of hyperglycemia on eye health may be mediated by systemic health conditions including dyslipidemia, which is associated with the formation of deleterious lipid droplets in the eye, as well as chronic low-grade inflammation, which triggers immune hyperactivity in retinal cells [9]. People with diabetes benefit from high protein diets due to better blood glucose control, and therefore less insulin is required. Diets rich in plant protein, white meat, or fish protein, as compared with red meat protein, improve the levels of total cholesterol in people with Type 2 Diabetes [10].

### **3.2 Roles of Oxidative stress in Age-related Eye Diseases**

Oxidative stress defined as an imbalance between oxidants and antioxidants in favor of the oxidants, potentially leads to tissue damage [11]. Oxidative stress can damage lipids, proteins, enzymes, carbohydrates and DNA in cells and tissues and can lead to cell death induced by RNA or DNA fragmentation and lipid peroxidation [11], [12]. Free radicals, also referred to as oxidants are molecules in the body with unpaired electrons as a result of weak chemical bond splitting, hence are unstable and ready to bond with other molecules with unpaired electrons. They include Reactive Oxygen Species (ROS) such as superoxide anion radicals ( $O^{\cdot -}$ ), hydrogen peroxide ( $H_2O_2$ ), lipid hydro-peroxides, and hydroxyl free radicals ( $\cdot OH$ ) [11]. Endogenous sources of ROS include metabolic and other organic processes such as mitochondrial peroxisomes, lipoxygenases and NADPH oxidase, while exogenous sources include ultraviolet radiation, ionizing radiations, chemotherapeutics, inflammatory cytokines, environmental toxins (such as smoke) and growth factors [11]. Laboratory and epidemiological studies have implicated oxidative stress in the pathogenesis of several eye conditions such as corneal disease, cataract, primary open glaucoma, macular degeneration, diabetic retinopathy and retinitis pigmentosa [11]. The eye is particularly vulnerable to oxidative stress due to its exposure to light, rich content of mitochondria, high concentration of polyunsaturated fatty acids, and high metabolic rate of photoreceptors [6], [13]. Due to

the disequilibrium between the production and neutralization of ROS, it results in oxidation of cellular constituents and ultimately malfunctions and degeneration of retinal tissues [6]. Endogenous aerobic metabolism is common in all age-related eye diseases characterized by oxygen reduction [12]. Oxidative stress caused by photo-oxidation and high metabolic rate plays a crucial role in the pathogenesis of age-related eye diseases by activating nuclear factor kappa B (NF- $\kappa$ B), vascular endothelial growth factor (VEGF), and lipid peroxidation which leads to the production of inflammatory cytokines, angiogenesis, protein and DNA damage, and apoptosis [14], these result to chronic and irreversible age-related eye diseases such as; age-related macular degeneration (AMD)- caused by the damage in the retinal pigment epithelium (RPE) and photoreceptors; cataracts-caused by damage to the protein, DNA and membrane fibre which lead to loss of lens transparency due to imbalance in electrolytes; diabetic retinopathy-caused by endothelial cell dysfunction, disruption of blood retinal barrier; glaucoma-caused by the alteration of human trabecular mesh-work in the drainage of the aqueous humor resulting to an increase in intraocular pressure (IOP) [6].

### **3.3 Ocular Structures Susceptible to Oxidative Stress**

**3.3.1 Retina:** The retina is highly susceptible to oxidative stress due to its rich content of polyunsaturated fatty acids and oxygen and its heavy exposure to light. In addition, oxidative stress can be involved in the production of severe inflammation by increasing the pro-inflammatory cytokines in the retinal tissue. These cytokines degrade the retinal blood barrier (RBB) and produce vascular cell death and apoptosis through tumor necrosis factor-  $\alpha$ , chemotactic proteins, intercellular adhesion molecule 1, and interleukin (IL) 1 $\beta$  [6].

**3.3.2 Cornea:** Oxidative stress plays a major role in the propagation of cellular injury that results in anterior eye disorders such as dry eyes, conjunctivochalasis, UV light-induced and tobacco smoke-induced ocular surface epithelial damage [15]. Histochemical and biochemical findings in corneas of albino rabbits have suggested that ROS-generating oxidases (xanthine oxidase and D-amino acid oxidase) contribute to corneal damage evoked by UV rays [16]. Cejkova *et al* found that increased UV radiation leads to a profound decrease in corneal antioxidants, resulting in oxidative injury of the cornea [17].

**3.3.3 Crystalline Lens:** The lens is under threat by oxidation. Biochemical evidence demonstrates that proteins and lipids undergo oxidative damage by free radicals [3].

### **3.4 Major Age-related Eye Diseases**

Age-related Macular Degeneration (AMD), glaucoma, cataract, and other retinal diseases, including diabetic retinopathy (DR) and retinitis pigmentosa (RP), are the major causes of blindness around the world, and are associated with aging [11]. In many cases of eye diseases, oxidative stress due to reactive oxygen or nitrogen species and lipid peroxidation

lead to ocular cell death. In addition, many pathogenic pathways include inflammatory factors such as the tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) and nuclear factor-kappa B (NF- $\kappa$ B) [18].

**3.4.1 Cataract:** Cataract is the second most pervasive cause of age-related vision loss accounting for 51% of world blindness[9] among people over 40 years of age predominantly in developing countries due to improper nutrition (e.g., lack of carotenoids in diet) and infectious diseases [19]. Although it can be treated surgically, this is cost-prohibitive in many developing nations, where there are insufficient numbers of surgeons to meet the challenge. Oxidative stress, aging and smoking are known to cause cataract [20]. Prevention through lifestyle intervention of micronutrient or vitamins consumption may be the only viable treatment option [9]. Age-related opacification is usually attributable to aggregation and precipitation of the normally well-ordered and soluble crystalline lens proteins, a phenomenon believed to result in part from crosslinking that occurs when amino groups react with open-chain sugars or glycolytic intermediates to form so-called advanced glycation end products [21]. Production of ROS and reduction of endogenous antioxidants both contribute to cataract formation. However, the crystalline lens has several mechanisms to protect its components from oxidative stress and to maintain its redox state [11]. These include enzymatic pathways and high concentration of ascorbate and reduced glutathione [11]. Lipid peroxidation (LPO) as well as significant increase in superoxide dismutase activity and protein level have been proposed as a causative factor of cataract (nuclear cataracts) [11]. The development of cataract has been associated with a number of systemic diseases, including cardiovascular, diabetic, renal and gastrointestinal (diarrhoea), and with increased mortality [3].

**3.4.2 Age-related Macular Degeneration (AMD):** AMD is a chronic retinal disease, commonly present among populations of age 50 or older, resulting in loss of central vision due to degeneration of photoreceptor and RPE cells in the macula which are essential in providing sharp and clear vision [18]. AMD is the leading cause of legal blindness with limited treatment options in industrial countries with an estimated 196 million people between the ages of 30–97 affected by AMD around the world [9], and costs many billions of dollars worldwide [19]. There are two types of AMD—dry (atrophic) and wet (neovascular or exudative) [19]. In most cases AMD starts as —'Dry', which then progresses slowly in approximately 20% cases to —'Wet' stage. The retina is highly susceptible to photochemical damage from the continuous exposure to UV. Short wavelength radiation and blue light induce significant oxidative stress to the RPE [22]. The retina is susceptible to oxidative stress due to its high oxygen consumption, high proportion of polyunsaturated fatty acids and its exposure to visible light [23]. RPE cells are prone to ROS from intense oxygen metabolism, accumulation of iron ions in the cells, sunlight exposure and tobacco smoke [24]. Systemic hypertension is a risk factor for age-related retinal macular degeneration (AMD) [3]. ROS including free radicals are responsible for apoptotic cell death and the development of pathological changes in AMD [25]. Study to investigate the molecular and cellular effects of cigarette smoke on human

RPE showed evidence of oxidative damage to the RPE and therefore, contributes to AMD pathogenesis [26]. The macular pigment formed by two dihydroxy carotenoids, lutein and zeaxanthin is a natural barrier protecting the macula against oxidative stress [27]. Although, there is no known treatment for dry AMD, research findings by Janik-Papis *et al* (2009) have demonstrated that a diet poor in antioxidant micronutrients (vitamin C, E, carotenoids, zinc) and low plasma levels of antioxidants may favor the development of the AMD [24]. San Giovanni and Chew (2005) have reported that omega-3 long-chain polyunsaturated fatty acids exhibit cytoprotective and cytotherapeutic actions providing anti-angiogenic and neuroprotective mechanisms within the retina and this may have a protective role against ischemic, light, oxygen, inflammatory, and age-related pathology of the vascular and neural retina [28].

**3.4.3 Glaucoma:** Glaucoma is described as a group of eye conditions leading to the interruption of visual information from the eye to the brain. In most cases of glaucoma, an increased pressure in the eye, commonly known as intraocular pressure (IOP), causes damage to the optic nerve via retinal ganglion cell (RGC) apoptosis [29]. Glaucoma is the fourth major age-related eye disease, affecting an estimated 76 million people across the globe [9]. The mechanism(s) of disease progression of glaucoma are not well understood, but the result is a loss of peripheral vision from damage to the optic nerve and a measurable increase in intraocular pressure [29]. A systematic review by Francisco *et al* (2020) found that some micronutrients like selenium and iron may be associated with increased risk for glaucoma, while components of dark-green leafy vegetables, specifically glutathione, flavonoids, and nitric oxide, were significantly associated with decreased risk for glaucoma [9]. With regard to primary open angle glaucoma (POAG), Izzotti *et al* (2006) found that oxidative DNA damage was significantly increased in the trabecular meshwork (TM) as well as in retinal cells and appears to be involved in the neuronal death affecting the optic nerve in glaucomatous patients compared to controls [29]. Fernandez-Durango *et al* (2008) found an increase in the expression and enzymatic activity of nitric oxide synthase (NOS) isoenzymes and nitrotyrosine in the TM of patients with POAG. The increase correlated with visual field defects which may serve as a maker of oxidative stress in the progression of cell death of the TM in patients with POAG [30].

**3.4.4 Diabetic retinopathy:** Diabetic Retinopathy (DR) occurs in individuals suffering from both type 1 and type 2 diabetes [7]. It is estimated that 140 million individuals are affected with DR [18]. The pathology is triggered by changes in the retinal blood vessels which may swell or leak and growth of new abnormal vessels may be detected on the retinal surface [18]. There are four stages in the DR pathology: mild non-proliferative retinopathy, moderate non-proliferative retinopathy, severe non-proliferative retinopathy, and proliferative retinopathy [18]. There are no treatments required for the first three stages; however, in order to prevent progression of the disease in these stages, patients are required to control their blood sugar, blood pressure, and blood cholesterol [9]. In cases of proliferative retinopathy, laser surgery is needed to control leaking fluids [18]. The laser treatment helps shrink the abnormal blood vessels, but in cases of severe

bleeding a vitrectomy is required to remove the blood from the center of the eye [18]. Vitamin E may prevent ROS-induced lipid peroxidation and thereby limit the development of diabetic complications in the eyes [31].

**3.4.5 Retinitis Pigmentosa:** Retinitis Pigmentosa (RP), a heterogeneous group of inherited retinal disorders characterized by progressive photoreceptor apoptosis, is the leading cause of inherited retinal degeneration-associated blindness worldwide [32]. RP is a less common disease, affecting only 1 in 4000 people in the United States [18]. It is a disease in which one of a variety of mutations selectively causes rod photoreceptor cell death, followed by gradual death of cone cells resulting in blindness [32]. Although, RP is commonly considered to be genetic in origin, oxidative stress plays a role in its pathogenesis, and protection from oxidative damage may be a treatment strategy in RP [32]. However, previous studies in mice suggested that high doses of antioxidants, such as vitamin A palmitate, may slow the disease [18].

### **3.5 Phytochemical Compounds/Antioxidants in Diets that Prevent Age-related Eye Diseases**

Numerous natural plant (phytochemical) compounds contain active ingredients or produce secondary metabolites that have beneficial properties, including anti-inflammation, antioxidation, protection against apoptosis, and restoration of the body's homeostasis disease [6]. As the pathologic mechanisms of major blinding diseases, such as age-related macular degeneration (AMD), diabetic retinopathy (DR), cataracts, and glaucoma, often involve inflammation- and oxidative stress-mediated cell death, evidences are accumulating on the potential benefits of botanical compounds in diets to improve or prevent these visions threatening eye diseases [18]. Preventive intervention may, therefore, be the most effective course of action against these age-related ocular diseases [18]. Experimental studies have found that fruit and vegetable consumption contribute to preserving vision and even reversing visual impairment [6]. These beneficial effects have been attributed to the presence of some phytochemical compounds with bioactive properties, such as polyphenols and carotenoids [6]. Carotenoids and polyphenols are plant-based molecules that have shown potent antioxidant and anti-inflammatory activities in several animal models of disease [6]. Nutritional epidemiology has provided insights into the major age-related eye diseases, of which, multiple reviews indicate effects of individual food components through supplementation with whole foods, micronutrients, or macronutrients [9]. AMD onset and progression are associated with low levels of carotenoids, antioxidant vitamins, and omega-3 fatty acids, and reduced intake of fruit, vegetables, and fish [9]. Studies demonstrated that high intake of vitamin A, vitamin, C, zinc, copper, and carotenoids could reduce the progression of AMD by approximately 25% [9]. Age-related cataract has also been associated with vitamin and carotenoid status [9]. Nutrients such as vitamins A, C, and E, lutein, zeaxanthin, and  $\beta$ -carotene were associated with reduced cataract risk in cohort studies[9], [33].

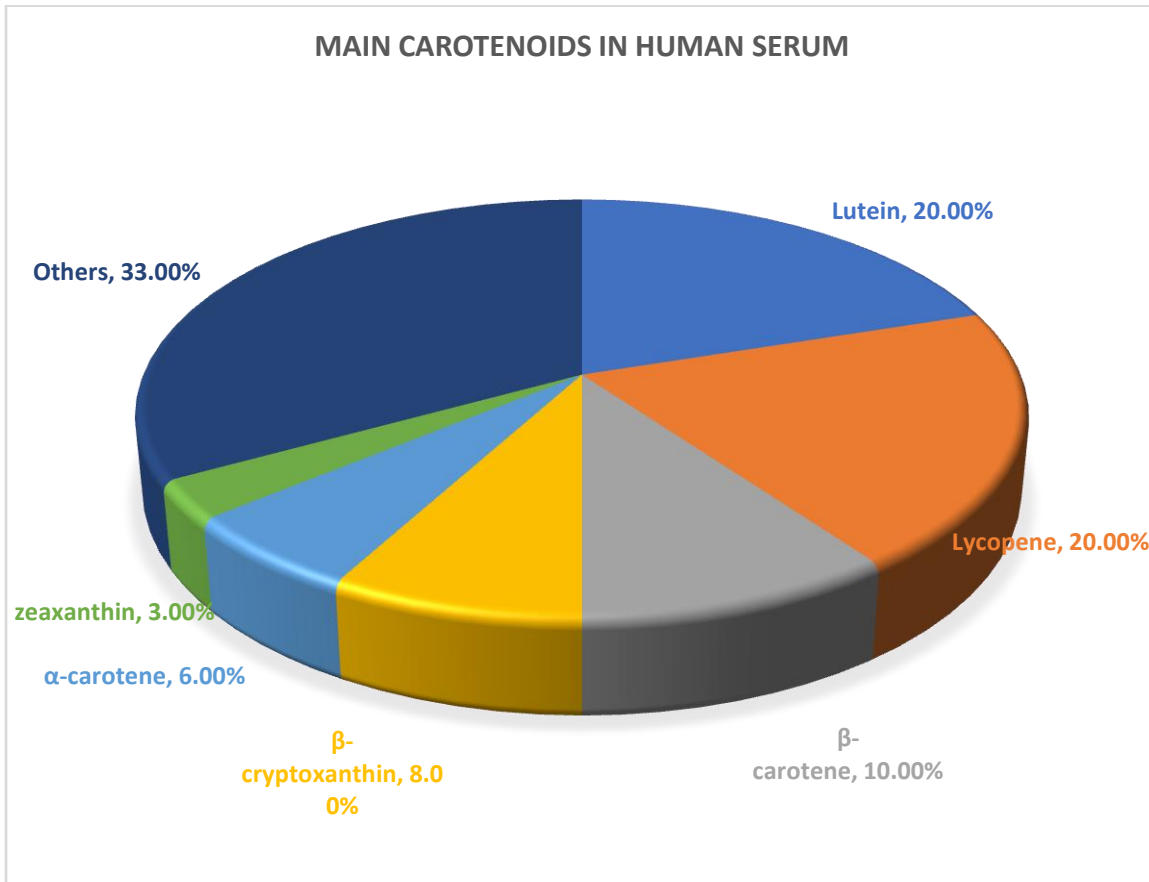
The Age-Related Eye Disease Study (AREDS), sponsored by the US Federal Government's National Eye Institute, found that supplementation with vitamin C (452 mg daily dosage), vitamin E (400 IU daily dosage), vitamin A [( $\beta$ -carotene)

28,640 IU daily dosage], zinc (69.6 mg daily dosage) and copper (1.6mg daily dosage) at levels well above the recommended daily allowances reduced the risk of developing advanced AMD by about 25% at 5 years compared with a placebo group [34]. Copper was added to prevent copper-deficiency anemia, a condition associated with high levels of zinc intake [34]. Diets rich in lutein and zeaxanthin may also reduce risk [34].

### **3.6 Nutritional Antioxidants for Prevention of Age-Related Eye Diseases**

Antioxidants are molecules which scavenge free radicals and prevent the tissue damage caused by them [4], [9]. Antioxidants detoxify oxidants in order to protect cells from free radical destruction and to maintain physiological homeostasis [11]. Antioxidants (oxidant scavengers) include non-enzymatic, low molecular weight compounds such as ferritin, ascorbate, alpha-tocopherol and glutathione as well as various enzymatic compounds such as superoxide dismutase (SOD), catalase and glutathione reductase are also present in the body and in many foods or food supplements [11]. Protective effect of antioxidant on lens tissue and supplementation with vitamin C and lutein/zeaxanthin has been associated with a decreased risk of cataract formation in multiple observational studies especially for individuals exposed to high oxidative stress such as heavy smokers and those with poor nutrition [35]. High-dose antioxidants lowered the progression of lens opacities [36]. Micronutrients supplementation enhances antioxidant defense and might retard AMD or modify the course of the disease [27]. Omega-3 long chain polyunsaturated fatty acids reduce the effects of environmental exposures that activate the molecules implicated in the pathogenesis of vaso-proliferative and neurodegenerative retinal diseases [28]. Consumption of diets high in vitamins C and E and carotenoids, particularly the xanthophylls, prevent the development of cataract and AMD [37]. A high intake of phytochemical lutein and zeaxanthin is safe and has been associated with reducing risks of eye diseases [38]. Phytochemical nutrients such as green tea (*catechins*, *anthocyanins*), *resveratrol*, and *Ginkgo biloba*, have been shown to ameliorate ocular oxidative stress [12]. Supplementation of dietary plant natural products has demonstrated preventive and therapeutic effects because of its capacity to scavenge free radicals, reduce enzymes involved in ROS production, neutralizes the oxidation reaction that occurs in photoreceptor cells, reduce opacification of the suppressed lens and apoptosis of the retinal pigment epithelium as well as inhibition of the inflammatory markers and blood-retinal barrier and improve ocular blood flow [14]. Major natural plant sources of antioxidants are classified into carotenoids and polyphenols.

**3.6.1 Carotenoids:** Carotenoids are divided into three classes of xanthophylls, carotenes, and lycopene [6]. Percentage of main carotenoids in human serum is shown in figure 3 below [19].



**Fig. 3: Percentage of main carotenoids in human serum [19]**

**3.6.2 Polyphenols:** Polyphenols being the secondary metabolites of plants with natural antioxidants and neuro-protective properties, contribute to mitochondrial restoration and inhibit the trigger of the apoptosis pathway [39]. Polyphenols can directly interact with various enzymes, resulting in anti-inflammatory [40], antimicrobial, anti-viral, anti-aging, anticancer properties and they also show neuroprotective effects [41]. Polyphenols can inhibit the characteristic uncontrolled ocular angiogenesis in AMD by restoring the retinal structure and increasing the RPE function and choroidal blood flow, inhibit oxidative stress, block the production of pro-inflammatory cytokines, attenuate vascular leakage and neovascularization in the retina of diabetic patients [6].

Different categories of plant source antioxidants (carotenoids and polyphenols) are classified as shown in Table 1 below.

(Table 1)

**Table 1: Different categories of plant source antioxidants (carotenoids and polyphenols)**

Type of Antioxidants	Descriptions	Functions	Food Sources
<b>Carotenoids</b>			
Lutein and Zeaxanthin	Main dietary carotenoids in yellow spot of the human retina, impart yellow or orange color to various foods, common xanthophylls in green leafy vegetables [19]	Decreased risk of AMD[34], protect the macula and photoreceptor outer retinal segments from oxidative stress by triggering the antioxidant cascade that disables reactive oxygen species, act as light filters in the eye and absorb blue-light entering the retina, improves visual function in older male patients with AMD [18]	kale, spinach, corn, kiwi, or red grapes [42], cantaloupe, pasta, corn, carrots, orange/yellow peppers, fish, salmon, eggs yolks, broccoli, peas and lettuce [19]
<b>β-Cryptoxanthin</b>	pro-vitamin A	They are involved in vision improvement and prevention of night blindness in humans	corn, oranges, peaches, papaya, watermelon, and egg yolk [19], [43].
<b>β-carotene</b>	Orange pigment commonly found in fruits and vegetables, dietary source of provitamin A	3–6 mg/day of β-carotene from food sources is associated with a lower risk of various chronic diseases <sup>31</sup> . Dietary intake in combination with vitamin C and E decreased AMD risk and reduced the risk of neovascular AMD [14]	carrot, orange, mangoes, papaya, kale, spinach, pumpkin, pepper, sweet potatoes, lettuce, romaine [34]
<b>Lycopene</b>	Naturally water-insoluble dietary carotenoid	It has anticancer, antioxidant, anti-inflammatory, neuroprotective and osteoprotective effects. Prevent oxidative stress, angiogenesis, ameliorate diabetic retinopathy in diabetes-induced optic neuropathy [14]	Tomatoes, watermelon, pink grapefruit and papaya [42]
<b>Polyphenols</b>			
<b>Flavonoids</b>			
<b>Ginkgo Biloba Extract</b>	Ginkgo leaves contain two main active ingredients, flavonoids and terpenoids [18]	Protection against free radical damage and lipid peroxidation. Conserves mitochondrial metabolism and ATP production in tissues. Scavenge and prevent production of nitric oxide. It has good therapeutic potential in cases of patients with glaucoma, normal tension glaucoma and with normal IOP. It acts as a neuroprotectant and prevent damage to retinal ganglion cells [18]	<b>Ginkgo Biloba Extract</b>
<b>Anthocyanins</b>	Water-soluble flavonoid pigments	Reduce inflammation, aging, neurological diseases, cancer, and diabetes. Increased expression of the glutathione-related enzymes and NADPH, inhibit oxidative stress-induced apoptosis caused by H <sub>2</sub> O <sub>2</sub> in retinal pigment epithelium [12], reduced risk of type 2 diabetes, improved neuroprotection, reduced risk of AMD, normalized visual field in glaucoma patients, improve ocular blood flow [44].	Black currant, blueberry, maqui berry, black soybean seeds, apple, cherry, grape, strawberry [44]
<b>Quercetin</b>	Plant polyphenols from flavonoids	Inhibit pro-inflammatory molecules, directly inhibit intrinsic apoptosis pathway, reduced cellular damage, reduced ROS production by ascorbate/Fe <sup>+2</sup> -induced oxidative stress in retinal cell cultures [18]. Protects against hydrogen peroxide-induced cataracts and diabetes-induced retinal lesions [6]. It exhibits	Black and green teas, <i>Brassica</i> vegetables, many types of berries, red wine, Ginkgo biloba, Hypericum Perforatum, and Sambucus

		anticarcinogenic, anti-inflammatory, antiviral, anti-hypertensive, antioxidant effects, inhibit lipid peroxidation and platelet aggregation, and stimulate mitochondrial biogenesis [45], [46]. Quercetin-inhibits ROS, VEGF, apoptosis of the neurons, and protects RPE cells [14]	Canadensis [41], red onions, apples, tomato
<b>Epigallocatechin gallate</b>	Main flavonoid present in green tea, representing more than 50% of the whole number of polyphenols	Inhibit ROS-generating enzymes, protect endothelial cell against H <sub>2</sub> O <sub>2</sub> -mediated oxidative stress, modulate antioxidative enzyme activity (SOD, GST), protect neuronal cells from glycation-induced neurotoxicity [6]. Leaves extract possess anticataract effect [47], protect retinal neurons from injuries due to high IOP [48], inhibits angiogenesis, protects against mitochondrial dysfunction, reduces vascular leakage and permeability in VEGF, reduces apoptosis of retinal ganglion cells [14].	Green tea [47]
<b>Stilbenes</b>			
<b>Resveratrol</b>	A natural phytoalexin polyphenol that is found in more than 70 species of plants, herbs, fruits, or vegetables	Inhibition of platelet aggregation, synthesis of proinflammatory and procoagulant eicosanoids, and inhibition of endothelin synthesis, which activates vasoconstriction [41]. Reduced diabetes-induced early vascular lesion, vascular endothelial growth factor, and oxidative stress, improve blood flow and prevent damages to vessels and apoptosis of optic nerve cells in patients suffering from glaucoma [18]. It inhibit lipid peroxidation, reduces inflammatory molecules and increases glutathione (GSH) [14]	Mulberries, peanuts, grape, and berry skins, red wine [41]
<b>Other Polyphenols</b>			
<b>Kaempferol</b>	It is a ubiquitous polyphenol, present in fruits and vegetables	antioxidant, antiinflammatory, cardioprotective, and anticancer properties [41].	Green leafy vegetables, such as spinach, kale, and herbs including dill, chives, and tarragon [41]
<b>Ferulic Acid</b>	It is a common polyphenolic molecule most abundantly present in vegetables	It possesses excellent antioxidant properties [41]	artichokes, eggplants, and in maize bran. it is an effective component of Chinese medicinal herbs such as Angelica Sinensis, Cimicifuga Heracleifolia, and LignsticumChuangxiong[41]
<b>Curcumin</b>		Exhibits anti-inflammatory, antioxidant, anti-tumor, chemosensitizing, epatoprotective, lipid-modifying, and neuroprotective effects, ameliorate neurodegenerative diseases [41]. Curcumin-inhibits LPO, ROS and VEGF, suppresses oxidative stress, decreases pro-inflammatory cytokines, reduces DNA damage by decreasing NFkB activation, increase antioxidant enzymes [14].	turmeric spice [41]

UNDER PEER REVIEW

## 4. CONCLUSION

What we eat plays a vital role in human health with no exception to the eye. Healthy eating result to healthy living and good vision. Unhealthy eating results to ill health, diseases, poor vision and death. Several major eye diseases in particular, AMD, glaucoma, cataract, and other retinal pathologies are age-related and results from oxidative stress and inflammatory activities. Researchers have discovered several active phytochemical ingredients having strong antioxidative, anti-inflammatory, and antiapoptotic properties to prevent or reduce the effects of free radical (oxidants) activities in causing damage to ocular structures. Consumption of diets high in vitamins C and E and carotenoids, particularly the xanthophylls, prevent the development of cataract, AMD and other age-related eye disease.

## CONSENT

Not required.

## ETHICAL APPROVAL

Not required.

## REFERENCE

- [1] World Cancer Research Fund, "Our cancer prevention recommendations," *World Heal. Organ.*, 2018.
- [2] Jacobs I, "Dietary intake and breast cancer risk in black South African women : the South African Breast Cancer study," *Br. J. of Nutrition*, vol. 121, pp. 591–600, 2019, doi: 10.1017/S0007114518003744.
- [3] Phelps-Brown NA, Bron AJ, Harding JJ, and Dewar HM, "Nutrition supplements and the eye," *Eye*, vol. 12, no. 1, pp. 127–133, 1998, doi: 10.1038/eye.1998.21.
- [4] Moyegbone JE, Nwose EU, Nwajei SD, Odoko JO, Agege EA, and Igumbor EO, "Epidemiology of visual impairment: focus on Delta State, Nigeria," *Int. J. Community Med. Public Heal.*, vol. 7, no. 10, pp. 4171–4179, 2020, doi: 10.18203/2394-6040.ijcmph20204392.
- [5] Moyegbone JE, "Prevalence and Pattern of Visual Impairment among Adult Population in Mangu Local Government Area of Plateau State, Nigeria," *Ophthalmol. Res. An Int. J.*, vol. 18, no. 2, pp. 18–29, 2023, doi: 10.9734/or/2023/v18i2381.
- [6] Bungau S, "Health Benefits of Polyphenols and Carotenoids in Age-Related Eye Diseases," *Oxid. Med. Cell. Longev.*, vol. 2019, pp. 1–22, 2019, doi: <https://doi.org/10.1155/2019/9783429>.
- [7] Dias J, "Nutritional quality and health benefits of vegetables: a review," *Food Nutr Sci*, vol. 3, pp. 1354–1374, 2012.
- [8] da JCDias S and Imai S, "Vegetables Consumption and its Benefits on Diabetes," *J. Nutr. Ther.*, vol. 6, pp. 1–10, 2017, doi: 10.6000/1929-5634.2017.06.01.1.
- [9] Francisco SG, "Dietary Patterns, Carbohydrates, and Age-Related Eye Diseases," *Nutrients*, vol. 12, pp. 1–19, 2020, doi: doi:10.3390/nu12092862.
- [10] Pfei AFH, Pedersen E, Schwab U, Ris U, and Aas A, "The Effects of Different Quantities and Qualities of Protein Intake in People with Diabetes Mellitus," *Nutrients*, vol. 12, pp. 1–12, 2020.
- [11] Oduntan OA and Mashige KP, "A review of the role of oxidative stress in the pathogenesis of eye diseases," *S Afr Optom*, vol. 70, no. 4, pp. 191–199, 2011.
- [12] Rhone M and Basu A, "Phytochemicals and age-related eye diseases," *Nutr. Rev.*, vol. 66, no. 8, pp. 465–472, 2008, doi: 10.1111/j.1753-4887.2008.00078.x.
- [13] Lawrenson JG and Downie LE, "Nutrition and Eye Health," *Nutrients*, vol. 11, pp. 11–14, 2019, doi: 10.3390/nu11092123.

- [14] Ikonne UE, Ikpeazu OV, and Ugboogu AE, "The potential health benefits of dietary natural plant products in age related eye diseases," *Heliyon*, vol. 6, p. e04408, 2020, doi: 10.1016/j.heliyon.2020.e04408.
- [15] Dogru M, "The role of oxidative stress and inflammation in dry eye disease," *Cornea*, vol. 28, pp. S70–S74, 2009.
- [16] Cejková J, Stipek S, Crkovska J, Ardan T, and Midelfart A, "Reactive oxygen species (ROS)-generating oxidases in the normal rabbit cornea and their involvement in the corneal damage evoked by UVB rays," *Histol Histopathol*, vol. 16, pp. 523–533, 2001.
- [17] Cejková J, Stipek S, Crkovska J, Ardan T, Platenik JCC, and Midelfart A, "UV rays, the pro-oxidant / anti-oxidant imbalance in the cornea and oxidative eye damage," *Physiol Res*, vol. 53, pp. 1–10, 2004.
- [18] Huynh T, Mann SN, Mandal NA, Mcgee DA, Boulevard SLY, and City O, "Botanical Compounds : Effects on Major Eye Diseases," *Evidence-Based Complement. Altern. Med.*, pp. 1–12, 2013, doi: <http://dx.doi.org/10.1155/2013/549174> Review.
- [19] Akhtar H, Zaheer K, and Ali R, "Dietary Sources of Lutein and Zeaxanthin Carotenoids and Their Role in Eye Health," *Nutrients*, vol. 5, pp. 1169–1185, 2013, doi: 10.3390/nu5041169.
- [20] Richer S, "Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: The Veterans LAST study (Lutein Antioxidant Supplementation Trial)," *Optometry*, vol. 75, pp. 216–230, 2004.
- [21] Chiu C, "Carbohydrate intake and glycemic index in relation to the odds of early cortical and nuclear lens opacities," *J Clin Nutr*, vol. 81, pp. 1411–1416, 2005.
- [22] Chalam K, Khetpal V, Rusovici R, and Balaiy S, "A review: role of ultraviolet radiation in age-related macular degeneration," *Eye Contact Lens*, vol. 37, pp. 225–232, 2011.
- [23] Beatty S, Koh H, Henson D, and Boulton M, "The role of oxidative stress in the pathogenesis of age-related macular degeneration," *Surv Ophthalmol*, vol. 45, pp. 115–134, 2000.
- [24] Janik-Papis K, "Role of oxidative mechanisms in the pathogenesis of age-related macular degeneration," *Klin Ocz.*, vol. 111, pp. 168–173, 2009.
- [25] Roehlecke C, Schaller A, Knels L, and Funk R, "The influence of sublethal blue light exposure on human RPE cells," *Mol Vis*, vol. 15, pp. 1929–1938, 2009.
- [26] Bertram K, Baglole C, Phipps R, and Libby R, "Molecular regulation of cigarette smoke induced oxidative stress in human retinal pigment epithelial cells. Implications for age-related macular degeneration.,", *Am J Cell Physiol*, vol. 297, pp. 1200–1210, 2009.
- [27] Drobek-Slowik M, Karczewicz D, and Safranow K, "The potential role of oxidative stress in the pathogenesis of the age-related macular degeneration (AMD)," *Postep. Hig Med Dosw*, vol. 61, pp. 28–37, 2007.
- [28] SanGiovanni J and Chew E, "The role of omega-3 long chain polyunsaturated fatty acids in health and disease of the retina," *Prog Retin. Res*, vol. 24, pp. 87–138, 2005.
- [29] Izzotti A, Bagnis A, and Saccà S, "The role of oxidative stress in glaucoma," *Mutat Res*, vol. 612, pp. 105–114, 2006.
- [30] Fernández-Durango R, "Expression of nitrotyrosine and oxidative consequences in the trabecular meshwork of patients with primary open-angle glaucoma," *Invest Ophthalmol Vis Sci*, vol. 49, pp. 2506–2511, 2008.
- [31] Baynes J, "Role of oxidative stress in development of complications in diabetes," *Diabetes*, vol. 40, pp. 405–412, 1991.
- [32] Komeima K, Rogers B, and Campochiaro P, "Antioxidants slow photoreceptor cell death in mouse models of retinitis pigmentosa," *J Cell Physiol*, vol. 213, pp. 809–815, 2007.
- [33] Moyegbone JE, "Effects of Antioxidant Vitamins ACE and Iron Supplements on Visual Impairment among Primary and Secondary School Children in Delta State , Nigeria," *Acta Sc. Ophthalmol*, vol. 6, no. 8, pp. 30–41, 2023, doi: 10.31080/ASOP.2022.06.0662.
- [34] Rasmussen HM and Johnson EJ, "Nutrients for the aging eye," *Clin. Interv. Aging*, vol. 8, pp. 741–748, 2013.
- [35] Fernandez M and Afshari N, "Nutrition and prevention of cataracts.," *Curr Opin Ophthalmol*, vol. 19, pp. 66–70, 2008.
- [36] Mares J, "High-dose antioxidant supplementation and cataract risk," *Nutr Rev*, vol. 62, pp. 28–32, 2004.
- [37] Jacques P, "The potential preventive effects of vitamins for cataract and age-related macular degeneration," *Int J Vitam Nutr Res*, vol. 69, no. 3, pp. 198–205, 1999, doi: 10.1024/0300-9831.69.3.198.
- [38] Tan J, Wang J, Flood V, and Mitchell P, "Dietary fatty acids and the 10-year incidence of age-related macular degeneration: the Blues Mountain Eye Study," *Arch Ophthalmol*, vol. 127, pp. 656–665, 2009.
- [39] Claudio S, "Can Polyphenols in Eye Drops Be Useful for Trabecular Protection from Oxidative Damage?," *J. Clin. Med.*, vol. 9, no. 3584, pp. 1–14, 2020, doi: doi:10.3390/jcm9113584.
- [40] Pires TC, Caleja C, Santos-buelga C, Barros L, and Ferreira IC, "Vaccinium myrtillus L. Fruits as a Novel Source of Phenolic Compounds with Health Benefits and Industrial Applications - A Review," *Curr. Pharm. Des.*, vol. 26, pp. 1917–1928, 2020, doi: 10.2174/1381612826666200317132507.
- [41] Favero G, Moretti E, Kristína K, Vladimíra T, and Rezzani R, "Evidence of Polyphenols Efficacy against Dry Eye Disease," *antioxidants*, vol. 10, no. 190, pp. 1–17, 2021, doi: <https://doi.org/10.3390/antiox10020190>.
- [42] Sommerburg O, Keunen J, Bird A, and Kuijk VF, "Fruits and Vegetables That Are Sources for Lutein and

- Zeaxanthin: The Macular Pigment in Human Eyes,” *Br. J. Ophthalmol.*, vol. 82, no. 8, pp. 907–910, 1998.
- [43] Chandrika U, Jansz E, Wickranasinghe SMD, and Warnasuriya N, “Carotenoids in yellow and red-fleshed papaya (*Carica papaya* L),” *J. Sci. Food Agric*, vol. 83, pp. 1279–1282, 2003.
- [44] Kalt W, “Recent Research on the Health Benefits of Blueberries and Their Anthocyanins,” *Adv. Nutr.*, vol. 11, pp. 224–236, 2020.
- [45] Li Y, “Quercetin, inflammation and immunity,” *Nutrients*, vol. 8, p. 167, 2016.
- [46] Javadi F, “The effect of quercetin on plasma oxidative status, C-reactive protein and blood pressure in women with rheumatoid arthritis,” *Int. J. Prev. Med*, vol. 5, pp. 293–301, 2014.
- [47] Gupta K, Halder N, Srivastava S, Trivedi D, Joshi S, and Varma S, “Green tea (*Camellia sinensis*) protects against selenite induced oxidative stress in experimental cataractogenesis,” *Ophthalmic Res.*, vol. 34, no. 2, pp. 258–263, 2002.
- [48] Falsini B, “Effect of epigallocatechin-gallate on inner retinal function in ocular hypertension and glaucoma: a short-term study by pattern electroretinogram,” *Graefe’s Arch. Clin. Exp. Ophthalmol.*, vol. 247, no. 9, pp. 1223–1233, 2009.

UNDER PEER REVIEW