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THE IMPACT OF THE FUNCTIONAL FOOD COMPONENTS ON THE PROMOTION OF VISION

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ABSTRACT: The eye is a highly specialized organ, which we should care for if we want to maintain good eyesight throughout life into old age. Different ocular structures have been shown to require different nutrients levels. The ability to communicate food benefits to the eye is essential for the successful development of functional foods and their role in improving vision. However, the functional efficacy of foods often cannot be represented by food composition. Mounting evidence supports the observation that functional foods containing physiologically active components, either from plant or animal sources, may enhance eye health. Research into functional foods will not advance public health unless the benefits of the foods are effectively communicated to the consumer. The guidelines are intended to help ensure that research results about nutrition, food safety, and eye health are communicated in a clear, balanced, and non misleading manner. Those foods whose health eye benefits are supported by sufficient scientific substantiation have the potential to be an increasingly important component of a healthy eye and to be beneficial to the public and the food industry. The aim of this review article is to spot light and illustrate most studies made in this area in a trial to clarify the importance of different functional food components on the promotion of vision.

Keywords: Carotenoids**,** fatty acids, flavonoids, isothiocyanates, phytoestrogens, eye diseases.

INTRODUCTION

Functional food is a component of the usual diet that may provide health benefits beyond basic nutrients. Functional food is a natural or processed food that contains active components and important source in the prevention, management and treatment of chronic diseases (Danik,

2011).

The relation between functional food and eye is of a great importance and has its impact on the promotion of vision. The eye is a very special organ that needs nutritional care to stay healthy and perform its function with efficiency. During the last few decades, research from various institutes reported about the benefits of several nutrients and natural products present in food that can protect the eye from different diseases (Rasmussen and Johnson, 2013; Jalbert, 2013; Chew, 2013; Igor and Ahmad, 2014). Some of these studies are field surveys, which try to explore the nutritional state of the population particularly with regard to functional food components and the occurrence of signs or symptoms of different eye Diseases, and other studies are laboratory investigations that try to outline the metabolic process underlying the occurrences of these ocular manifestations (Smith, 2010; Chiu et al., 2014; Davidson et al., 2014).

Oxidation can sometimes produce reactive substances known as free radicals that can cause oxidative stress or damage to the cells. Antioxidants are capable of stabilizing free radicals before they can react and cause harm. Research suggests there is involvement of the resulting free radicals in a number of eye diseases. Consumption of antioxidants is thought to provide protection against oxidative damage and contribute positive health benefits (Abd El-Razek et al., 2012; Seham et al., 2013).

In the Research Institute of Ophthalmology (RIO), Giza, Egypt, most cases attending to the outpatient clinic are suffering from cataract and /or glaucoma. In the RIO, considerable research was carried out dealing with the effect of nutrients and natural compounds on the health

state of the eye and test the efficiency of functional food on either, individuals subjected to eye hazards or already suffering from early stages cataract and glaucoma, among these studies (Aziz et al., 2006; El-Sheikh et al.,2011; Abd El-Razek et al., 2011; Abd El-Razek et al.,2012; Seham et al., 2013). The previous studies recommended that zinc, iron and vitamin A should be included as nutritional supplement according to Recommended Daily Allowances (RDA) and also. El- Sheikh et al. (2011) suggested that garlic inhibits selenite-induced cataract formation by inhibiting lipid peroxidation, oxidative stress and act as anti-apoptotic agent that can delay progress of cataract formation. On the other hand, the previous studies suggested that onion, cactus pear and broccoli have antioxidant potential, able to protect human eye from free radical and maintain ocular function and prevent the onset or progression of cataract. Seham et al., (2013) and El-Sheikh et al., (2011) found that, consumption of broccoli and onion in cataractous group led to a significant decrease in serum total lipids, total cholesterol, triacylglycerols and low density lipoprotein cholesterol as well as significant decrease in malondialdehyde, nitric oxide and Fas ligand levels. On the other hand, dietary intake of broccoli or onion led to a significant increase in the activities and levels of catalase, superoxide dismutase and total antioxidant capacity and reduced glutathione, respectively as compared to selenite-induced cataract group.

Within the last 20 years, nutrition research has focused on both nutrients and non-nutritive compounds and their role in disease prevention and risk reduction.

Based on market research within the food industry, one third of consumers surveyed in 2011 planned to self-treat more and go to the doctor less. According to these and other data, consumers are looking more to foods for health benefits, especially consumers with higher education levels. According to the (2011) Functional foods/Foods for Health Consumer Trending Survey, 73% of consumers "believe that food and nutrition play a „great role" in maintaining and improving overall health," with

70% of those surveyed naming fruits and vegetables as the most recognized functional food. Among those surveyed, 80% of consumers agree that functional foods and beverages can help to maintain or improve health and wellness, including bone health (81%), heart and circulatory health (79 and 74%, respectively), immune health (79%), digestive health (78%), and eye health (66%). Although nutraceuticals are now available in European and American markets to help the people suffering from various chronic diseases such as atherosclerosis, diabetes, obesity, and others, yet nearly no one of these nutraceuticals up-till now is concerned with protection against eye diseases in Egypt. Researcher in the RIO will share in identifying the association between nutrition and eye diseases.

The aim of the current review article was to generate information related to functional food and eye. Also to illustrate most studies made in this area in a trial to clarify the importance of different functional food components on the promotion of vision.

Functional foods is defined as whole foods along with fortified, enriched, or enhanced foods that have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis at effective levels based on significant standards of evidence (Crowe and Francis, 2013) (Table 1).

Table (1): Functional Food Components (Background on Functional Foods).

Class/Components	Source*	Potential Benefit
Carotenoids		
Beta-carotene	Carrots, various fruits	Neutralizes free radicals
Lutein, Zeaxanthin	Kale, collards, spinach, corn, eggs, citrus	may contribute to maintenance of healthy vision
Lycopene	Tomatoes & processed	to maintenance of prostate health
Dietary (functional and total) Fibre		
Insoluble fibre	Wheat bran	to maintenance of a healthy digestive tract
Beta glucan**	Oat bran, oats, flour	may reduce risk of (CHD)
Whole grains**	Cereal grains	reduce risk of CHD and cancer; maintenance of healthy B.S levels.
Fatty Acids		
PUFAs,Omega-3—ALA	Walnuts, flax	maintenance of mental and visual function
DHA/EPA	Salmon, tuna, marine and other fish oils	reduced risk of CHD; may contribute to maintenance of mental and visual function
PUFAs–Conjugated (CLA)	Beef, lamb; some cheese	may contribute to maintenance of body composition and healthy immune function
Phenols		
Caffeic acid, Ferulic acid	Apples, pears, citrus fruits, & vegetables	may bolster cellular antioxidant defences; maintenance healthy vision and heart health
Flavonoids		
Anthocyanidins	Berries, cherries, red grapes	antioxidant defences; maintenance of brain
Flavanols-Procyanidins	Tea, chocolate, apples, grapes	maintenance of heart health
Flavanones	Citrus foods	neutralize free radicals; antioxidant defences
Flavonols	Onions, apples, tea, broccoli	neutralize free radicals and antioxidant defences
Proanthocyanidins	Cranberries, cocoa, apples, grapes, peanuts, cinnamon	may contribute to maintenance of urinary tract health and heart health
Isothiocyanates		
Sulforaphane	Cauliflower, cabbage, kale, horseradish broccoli,	may enhance detoxification of compounds and bolster cellular antioxidant defences
Plant Stanols/Sterols		
Free Stanols/Sterols**	Corn, soy, wheat, beverages.	may reduce risk of CHD
Polyols		
Sugar alcohols	gums , other food applications	may reduce risk of dental caries
Prebiotic/Probiotics		
Lactobacilli, Bifidobacteria	Yogurt, other dairy ,non-dairy .	improve gastrointestinal health and immunity
Phytoestrogens		
Isoflavones—Daidzein, Genistein	Soybeans and soy-based foods	to maintenance of bone health, healthy brain and immune function
Lignans	flax, rye, some vegetables	may contribute to maintenance of heart health and healthy immune function
Soy Protein**		

Chart adapted from International Food Information Council Foundation: Media Guide on Food Safety and Nutrition: 2004-2006. *Not a representation of all sources.

FUNCTIONAL FOODS AND IMPACT ON VISION
Carotenoids

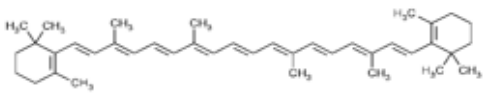


Fig. (1): β-carotene

Fig. (2):Lycopene

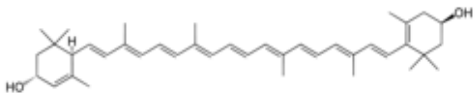


Fig. (3): Lutein

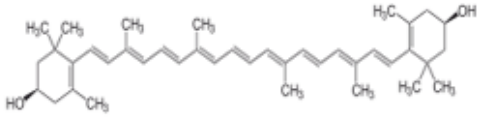


Fig. (4): Zeaxanthin

(adapted from http://en.wikipedia.org)

Carotenoids such as beta-carotein (figure 1) and lycopene (figure 2) are natural pigments with antioxidative functions that protect against oxidative stress. They are essential for humans and must be supplied through the diet. Karki et al. (2013) suggested that carotenoids consumption is inversely related to eye diseases such as age-related macular degeneration and cataracts. Carotenoids are the precursors for the visual pigment rhodopsin, and lutein (figure 3) and zeaxanthin (figure 4) must be accumulated in the yellow eye spot to protect the retina from excess light and ultraviolet damage (Sandmann, 2014).

Human intervention studies show that lutein supplementation results in increased macular pigment and improved vision in patients with age-related macular degeneration (AMD) and other ocular diseases (Ma et al., 2012; Aimjongjun et al., 2013). In the recent study by Huang and Lin (2014) who concluded that, the development of AMD might be affected by the daily intake of lutein+zeaxanthin and the serum concentrations of lutein and zeaxanthin and found that concentration of serum HDL might be related to the occurrence of AMD. To make sure that the concentration of lutein and zeaxanthin in the eye is strong enough to protect the macula we should eat foods such as spinach, cabbage, peas, peppers, oranges, kiwi and squash, or take a supplement (Stringham andHammond, 2005). The correlation between lutein and zeaxanthin intake and the risk of cataracts was studied and a statistically significant trend toward reduced risk of cataract extraction surgery with increased intake of lutein and zeaxanthin was found (Mares et al., 2010).

Dietary fibers

Dietary fiber is a mixture of many complex organic substances, which are resistant to hydrolysis by the digestive enzymes of man. Dietary fiber intakes average from 16.5 to 17.9 g/day for men and 12.1 to 13.8 g/day for women. Good sources of dietary fiber include fruits, no starchy vegetables, legumes, nuts, whole grains and bran products (Alaimo et al., 1994). Yagami et al. (1993) found that migration of acetylated hemicellulose from capillary hemodialyzer to blood, causing scleritis and/or iritis. Kaji et al., (2004) concluded that increased levels of (1, 3)-beta-D-glucan in tears were detected in the model of keratomycosis. Measuring the concentration of (1, 3) - beta-D-glucan in tears may be a reliable non-invasive method for the diagnosis of keratomycosis. Talbott et al. (2013) compared the effects of daily supplementation for with 250mg/day (β-1, 3/1, 6-Glucan with placebo 250 mg /day (rice flour) and found that, supplementation with β-1, 3/1, 6-Glucan for 4 weeks improved allergy symptoms. Ganesan et al. (2012) suggested that, the presence of diabetic retinopathy, and micro-albuminuria was associated with lower dietary-fiber intake.

Fatty acids

Fatty acid classification is based on the number of double bonds into: saturated and unsaturated fatty acids. Long chain poly unsaturated fatty acid (LCPUFA) includes the following:

a) Omega-3 fatty acids,

b) Alpha-linolenic acid (ALA),

c) Docosahexaenoic acid (DHA), d) Eicosapentaenoic acid (EPA) e) Linoleic acid (CLA).

Long chain polyunsaturated fatty acids (LCPUFA) namely arachidonic acid (ARA, 20:4n-6) and docosahexaenoic acid (DHA, 22:6n-3) are selectively incorporated, retained and highly concentrated in the phospholipid bilayer of retinal neural membranes.

The three types of omega-3 fatty acid involved in human physiology are α-linolenic acid (ALA) (found inplant oils) (Figure 5), eicosapentaenoic acid (EPA) (Figure 6) and docosahexaenoic acid (DHA) (both commonly found in marine oils) (Figure 7).

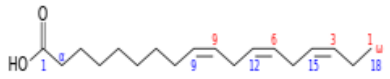


Fig. (5): Chemical structure of alpha-linolenic acid (ALA),

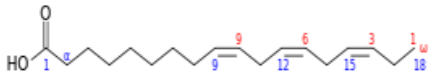


Fig. (6): Chemical structure of eicosapentaenoic acid (EPA)

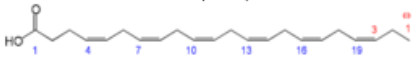


Fig. (7): Chemical structure of docosahexaenoic acid (DHA)

(Adapted from http://en.wikipedia.org)

Docosahexaenoic acid (DHA) is found in very high concentrations in the cell membranes of the retina. It accounts for over 50% of the fatty acids in the retina and plays a role in maintaining membrane fluidity to promote optimal visual processing (Johnson et al., 2008). DHA is found in the highest concentrations in the phospholipids of the outer segment disc membranes. Since the eye ishigh in reactive oxygen species and DHA is highly susceptible to oxidative damage, it must be protected by the antioxidants in the eye which include lutein, zeaxanthin, vitamin C and vitamin E (Table 2).

***ALA, alpha-linolenic acid; EPA, eicosapentaenoic acid, DHA, docosahexaenoic acid.**

Adequate Intake (AI) for Omega-3 Fatty Acids

Life Stage	Age	Source	Males (g/d)	Females (g/d)
Infants	0-6 months	ALA, EPA, DHA*	0.5	0.5
Infants	7-12 months	ALA, EPA, DHA	0.5	0.5
Children	1-3 years	ALA	0.7	0.7
Children	4-8 years	ALA	0.9	0.9
Children	9-13 years	ALA	1.2	1.0
Adolescents	14-18 years	ALA	1.6	1.1
Adults	19 years and older	ALA	1.6	1.1
Pregnancy	All ages	ALA	-	1.4
Breastfeeding	All ages	ALA	-	1.3

Spatially, vitamin E is the most likely candidate to protect the DHA in the retinal pigment

epithelium (RPE) since they both are found in the highest concentrations in the RPE and outer rod segments, but this relationship has not been well studied. A number of studies have demonstrated the effectiveness of lutein and DHA (Chucair et al., 2007;

Lien and Hammond, 2011). The levels of free fatty acids were significantly lower in the senile cataract group compared to that in the normal controls. Free fatty acids may be helpful in preventing senile cataract. Free fatty acid induced lens cell damage as a possible cause for age-dependent cataracts as well as a molecular link between systemic diseases such as diabetes and cataract formation was investigated. Nealon et al. (2011) demonstrate that, uptake of exogenous dietary fatty acids by the lens and their incorporation into phospholipids is minimal and this finding adds support to the hypothesis that once synthesized there is no active remodeling orturnover of fiber cell phospholipids. Bartlett and Eperjesi (2005) found that correlation between dietary fat and the risk of age-related macular degeneration and Gomes and Negrato (2014) emphasized that the use of alpha- lipoic acid as a potential therapeutic agent for many chronic diseases such as glaucoma.

Polyphenols

Polyphenols consist of a large number of molecules of heterogeneous structure. Their common feature is the presence of at least one hydroxyl-substituted aromatic ring system (Pfeilschifter et al., 2003). Black and green teas significantly inhibited diabetic cataracts, protect primary rat retinal pigment epithelial cells from H2O2- induced death and has protective effects on UVB radiation-induced corneal oxidative damage by causing a significant reductions in the biochemical pathway implicated in the development of the pathology (Vinson and Zhang, 2005; Cia et al., 2014; Chen et al., 2014).

Chlorogenic acid and caffeic acid (a polyphenol abundant in coffee) may have a preventive role in blood-retinal barrier breakdown in diabetic retinopathy by preserving tight junction protein levels and low Vascular endothelial growth factor. The inhibitory effect of caffeic acid was supported by lower malondialdehyde and nitric oxide with higher GSH levels in the treatment groups than in the control group (Turkoz et al., 2004; Shin et al., 2013). Li et al. (2003) studied the possible mechanism of ferulic acid on the proliferation of nerve cells of retinas *in vitro* and provide the principal for prevention and treatment of some degenerative retinal diseases.

Flavonoids

The basic structure of flavonoids is derived from the C15 body of flavone. Flavonoids can be divided into: flavonols, flavanones, flavones, flavanolols and flavanols (Ronald, 2005). The effect of flavonoids on ocular tissues was investigated. Several studies were found a correlation between flavonoids and eye health such as Christie et al. (2001) who suggested that flavonoid extracts are important for the health of the micro-blood vessel network. Park et al. (2004) and Park and Chiou (2004) concluded that the presence of OH groups at certain positions and the double bond at C2-C3 in the flavonoid molecules can affect the increment on ocular blood flow and retinal function recovery and O- methylation can increase ocular blood flow and retinal function.

Sulaiman et al. (2014) and Pescosolido et al. (2014) found that the multifunctional curcumin and the chalcone iso liquiritigenin have demonstrated promising anti- angiogenic effects in diabetic retinopathy and choroidal neovascularization. Also curcumin has effective in chronic anterior uveitis, glaucoma, age-related macular degeneration and dry eye syndrome.

Cornish et al. (2002), Osakabe et al. (2004) and Sasikala et al. (2013) reported that flavonoid rutin protect for the ocular surface and rat-lens crystallins in selenite- induced cataract.

Szabo et al. (2004) found that sour cherry seed flavonoid-rich extract showed a protective effect against reperfusion-induced injury through its ability to reduce the changes in concentrations of retinal ions through HO-1- related endogenous CO production in the ischemic/reperfused retina. Flavonoids have

also been shown to strengthen capillaries and to reduce bleeding in the retina. Chen et al. (2014) show that, the intake of luteolin, apigenin, myricetin, and quercetinas supplemental in treating retinal diseases should be accompanied by careful monitoring of the retinal function.

Fiore et al. (2010) found that, the intra vitreal injection of genistein could be considered a treatment alternative for ocular neovascularisation in selected cases. Genistein is an isoflavone found especially in soybeans. The isoflavonegenistein and the flavone apigenin on the other hand are showing potential in the prevention of retinal and choroidal angiogenesis with long-term administration (Sulaiman et al., 2014). The multifunctional curcumin and the chalcone isoliquiritigenin have demonstrated promising anti-angiogenic effects in mouse models of diabetic retinopathy and choroidal neovascularization respectively. Abd El-Razek et al. (2011) found that garlic inhibits selenite-induced cataract formation by inhibiting lipid peroxidation, oxidative stress and act as anti-apoptotic agent that can delay progress of cataract formation.

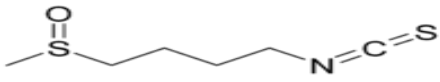
Isothiocyanates

Isothiocyanates are sulphur - containing phytochemicals with the general formula R-NCS (Figure 8). Isothiocyanates can be found in cruciferous vegetables such as broccoli, cauliflower, kale, turnips, collards, Brussels sprouts, cabbage, radish, and watercress. Bilberry is high in flavonoids known as anthocyanosides. Anthocyanosides is used by the rods in the eye for night vision and improve dark adaptation in people with poor night vision (Canter and Ernst, 2004). Ogawa et al. (2014) suggest that bilberry extract has protective effects against UVA-induced retinal damage and may prove useful as a prophylactic health food for the prevention of retinal diseases.

Plant stanols/sterols

The total plant sterol is composed of large number of individual sterols. The major dietary sources of plant sterols are seeds and oil. The intake of plant sterol is 200 to 400 mg/day (Jones et al., 1997). Kalariya et al. (2014)

Formula R-NCS



Sulforaphane

Fig. (8): Structure of Isothiocyanates (adapted from: http://en.wikipedia.org)

demonstrated that the plant sterol guggulsterone suppresses ocular inflammation in endotoxin-induced uveitis and suggesting that, the supplementation of guggulsterone could be a novel approach for the treatment of ocular inflammation. Kelly et al. (2010) suggested effects of plant sterols on vascular function.

Polyol and alcohol sugar

The sugar alcohol is "Polyol" This term refers to chemical compound containing three or more hydroxyl groups. Alcohol sugars are present in numerous berries, fungi, and algae. Diabetic eye complications are associated with the polyol pathway and attributed to and acts as anti-apoptotic agent that can reduce or even prevent progress of cataract formation. Proanthocyanidins, the active components in grape seed extract is very efficient to improve vision. Ha et al. (2014) suggests that muscadine grape polyphenols may provide a novel dietary strategy to prevent vision-threatening retinal diseases. Hyper glycaemic condition which is in turn and advanced glycation end products and cataract development. As shown in Figure 9, Aldose reductase is the principal enzyme of polyol pathway which plays a vital role in the development of cataracts (Takamura et al., 2003) and diabetic complications (Veeresham et al., 2014). Aldose reductase inhibitory activity can be screened by both in vitro and in vivo methods. The high intracellular levels of polyol induce histological change in the lens epithelial cells, which is considered the earliest event in sugar cataractogenesis (Kubo et al., 2004). Aldose reductase deficiency reduced retinal vascular changes in the mouse model of oxygen-induced

retinopathy. Also, aldose reductase can be a potential therapeutic target in ischemia-induced retinopathy (Fu et al., 2012). Shi et al. (2012) demonstrated that hesperidin attenuates retina and plasma abnormalities by anti-angiogenic, anti- inflammatory and antioxidative effects, as well as the inhibitory effect on polyol pathway and advanced glycation end products accumulation.

Prebiotic/probiotics

Probiotics and prebiotics are food ingredients that confer physiologic effects through the gastrointestinal tract. *Probiotics* have been defined as viable microorganisms that have a beneficial effect in the prevention and treatment of specific pathologic conditions. Prebiotics are non-digestible food ingredients that beneficially affect host health by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon.

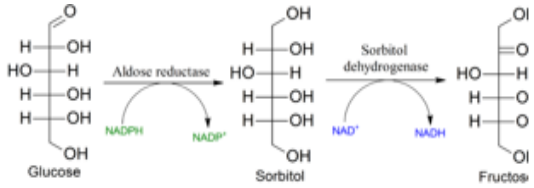


Fig (9): Polyol Pathway (adapted from: http://en.wikipedia.org)

Fang et al. (2013) demonstrated chitosan oligosaccharides significantly enhanced the recovery of retinal function, preserve dinner retinal thickness, and decreased retinal neurons loss in a dose-dependent manner. Chitosan administration demonstrated anti- oxidative effects by reducing luminol- and lucigenin-dependent chemiluminenscense levels and activating superoxide dismutase and catalase, leading to decreased retinal apoptosis. Also demonstrated that, chitosan oligosaccharides attenuates oxidative stress-induced retinal damages, probably by decreasing free radicals, maintaining the activities of anti-oxidative enzymes, and inhibiting the activation of nuclear factor-kappa B. A significant association was observed between lower intake of dairy products or calcium and adverse retinal vascular signs (Gopinath et al., 2014).

Phytoestrogens

Certain foods contain hormone-like compounds called phytoestrogens. Foods containing phytoestrogens include soy products, whole grains and legumes, lignin- rich foods like flaxseeds, millet and barley, lentils, kidney beans, lima beans, rye, clover, fennel, chickpeas, apples, alfalfa sprouts, celery, sarsley, beets, bokchoy, broccoli, cauliflower, carrots, cucumbers, mushrooms, and brussel sprouts. Lund et al. (2003) studied characterized dietary phytoestrogens' effect on retinal thickness in male and female. Long-Evans rats received either a phytoestrogens- rich diet or a diet low in phytoestrogens. These data suggest that phytoestrogens influence rat retinal characteristics in a sexually dimorphic manner (more robust effect in males vs. females) and that this influence can occur even in adulthood.

CONCLUSION AND RECOMMENDATIONS

As shown in this review article, mounting evidence supports the observation that functional foods containing physiologically-active components, either plant or animal source, may enhance eye health. All of the necessary nutrients and eye needed for maintaining and improving eyesight are in the food we eat. Therefore, an awareness of dietary sources of key nutrients important for ocular health is important for both the patient and health-care provider.

To date, the using a natural nutrient in the prevention of eye diseases has been entirely consistent. It is likely that nutrients are acting synergistically to provide protection. We believe the next decade will witness some major changes and more advanced search in the way to eat to impact vision. As previously discussed, there have been a number of important studies affirming the relationship of functional food and eye to treatment, prevention, and/or slowing progression of different eye diseases. A healthy diet including a variety of fresh fruit such as cactus pear, blackberry, guava, strawberry, and pomegranate; vegetables such as onion, garlic broccoli, legumes, lean meats, dairy, fish, and nuts, will have many benefits and will be a good source of the vitamins, minerals,

flavonoids and phenols which act as antioxidant and have a potential role to delay or stop the progress development of different eye diseases such as; of age-related eye health such as cataract, glaucoma, dry eye, age related macular degeneration, myopia and retinitis pigmentosa.

These observations have led to continuing research aimed at identifying specific bioactive components in foods, such as antioxidants, which may be responsible for improving and maintaining healthy eye. In the our institute (RIO), another study still now investigates to study the effect of functional food such as pomegranate, berries, guava, and ginkgo biloba to delay or prevent dry eye, cataract and glaucoma development.

Overall, there is much promise for development of functional foods that impact promotion of vision and eye health. Consumer education is important to promote the understanding the relation between nutrition and eye.

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