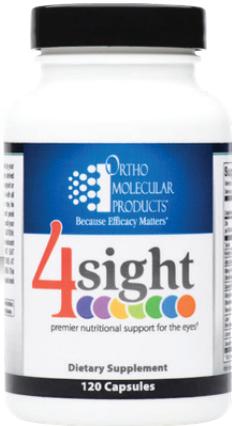


# 4SIGHT



## CLINICAL APPLICATIONS

- Provides Key Antioxidant Support for Eyes
- Supports Macular Health
- Increases Ocular Circulation

## EYE HEALTH

4Sight was formulated with a specific blend of botanicals, nutrients, antioxidants and minerals, shown in research to support healthy eye function. The formula provides key antioxidant support as well as key nutrients to care for and maintain the long-term health of the eyes.

### Overview

In the US, eye health is a major concern for those over 60 years of age. The eye is the most susceptible organ to oxidative damage caused by light, toxins (smoke), atmospheric oxygen and abrasion. As ultraviolet and blue light pass through the retina to the photoreceptors (rods and cones) and the pigmented epithelial (PE) cells, reactive oxygen species (free radicals) are generated. If there are insufficient antioxidants available to neutralize free radicals, the eye undergoes excessive oxidative damage.

### Alpha Lipoic Acid<sup>†</sup>

Alpha lipoic acid (ALA) is a potent, versatile antioxidant that is both water- and fat-soluble. ALA has been shown to inhibit aldose reductase, which prevents sorbitol-induced leakage of important antioxidants from eye tissues and recharges ALA vitamin C, E and glutathione. Used clinically in Russia, animal studies have shown ALA has the potential to reach high concentrations in and be protective to the ocular lens of rats.<sup>1,2</sup> Recent studies have shown lipoic acid increases insulin-stimulated glucose disposal both in whole body and in skeletal muscle,<sup>3</sup> thus helping to promote healthy blood sugar levels. One study, using oral dosing, showed that ALA increases insulin sensitivity by 27%.<sup>4</sup> Other research has found that a dose of 600 mg/day of ALA over 3 months helped promote healthy

blood fats by 36% and provided key antioxidant support.<sup>5</sup> ALA has also been shown to increase the GLUT4 pathway, a primary passageway for glucose to enter the cell and be used for metabolic energy. In addition, ALA has been shown to increase nerve conductivity in related neuropathy.

### Ginkgo Biloba<sup>†</sup>

Ginkgo biloba extract is a well-studied botanical that increases cerebral blood flow and protects neurons from a variety of conditions and oxidant-induced damage.<sup>6,7</sup> It scavenges NOS (Nitric Oxide Species) and ROS (Reactive Oxygen Species), supports mitochondrial function, inhibits NMDA receptor activation, antagonizes PAF (Platelet Activating Factor), and stimulates the release of NOS to support cerebral blood flow.<sup>8</sup> It has been shown to provide key antioxidant support for eyes.<sup>9,10,11</sup>

### Carotenoids: Lutein, Zeaxanthin, Lycopene<sup>†</sup>

Lutein and zeaxanthin are carotenoid pigments whose role in eye health is well-established from epidemiological, clinical and interventional studies.<sup>12</sup> Epidemiologic research shows a connection between high levels of lutein and zeaxanthin in eye tissues and enhanced eye function and visual acuity.<sup>13</sup> Lutein and zeaxanthin supplementation has been shown to protect the lens protein, lipid and DNA from oxidative damage and improves intracellular redox status when under oxidative stress.<sup>14</sup> Increased dietary intake of carotenoids, especially lutein and zeaxanthin, protect the eye from oxidative stress.<sup>15</sup> A 12-month intervention including 145 patients divided into a placebo group, and 2 groups given capsules of lutein, zeaxanthin, DHA and EPA each day, found that over 12 months, the supplements significantly improved plasma antioxidant

<sup>†</sup>These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

capacity, circulating macular xanthophyll levels and the optical density of the macular pigment.<sup>16</sup>

### Zinc†

A vital coenzyme for eye tissue, zinc is a necessary component in antioxidant enzymes including superoxide dismutase, glutathione peroxidase and catalase. Studies on monkeys with oxidative stressed retinas showed a 60% reduction in the activity of catalase and glutathione peroxidase as well as a 4-fold reduction in zinc concentration compared with controls.<sup>17</sup> The enzymes responsible for digesting rod outer segments and preventing the build-up of lipofuscin, a lipid-containing residue caused by normal “wear and tear” that can impair vision, are significantly less active in older individuals. These important enzymes can be stimulated by adding zinc.<sup>18,19</sup>

### Bilberry†

Bilberry extract contains a high amount of the antioxidants known as anthocyanidins, similar to those found in grape seeds. Bilberry has a long history of use in eye health. Its activities include inhibition of aldose reductase and improving capillary permeability. Bilberry has been shown to protect against an oxidative stress-induced immune response in the mouse uvea<sup>20</sup> and to support night vision.<sup>21</sup> The extract has also been found to support renewal and homeostasis of corneal cells.<sup>22</sup>

### Quercetin†

A flavonoid found in a variety of herbs, vegetables and fruits, quercetin provides key antioxidant support for eyes.<sup>23,24,25</sup>

### Taurine†

Taurine concentration is high in the retina and is required for retinal tissue growth. It has been shown to protect rod outer segments from oxidative damage<sup>26</sup> and to protect lens tissue from radiation. Researchers have suggested possible functions for taurine in the retina include protection of the photoreceptor, regulation of Ca<sup>2+</sup> transport and regulation of signal transduction.<sup>27</sup>

### Directions

2 capsules per day or as recommended by your health care professional.

### Does Not Contain

Gluten, yeast, artificial colors and flavors.

### Cautions

If you are pregnant or nursing, consult your physician before taking this product.

## Supplement Facts<sup>V2</sup>

Serving Size 2 Capsules

Servings Per Container 60 & 120

2 capsules contain	Amount Per Serving	% Daily Value
Zinc (as TRAACS® Zinc Bisglycinate Chelate)	15 mg	136%
Taurine	400 mg	*
N-Acetyl-L-Cysteine USP	200 mg	*
Alpha Lipoic Acid	150 mg	*
Bilberry Fruit Extract (Standardized to contain 25% Anthocyanidins)	150 mg	*
Quercetin Dihydrate	100 mg	*
<i>Ginkgo biloba</i> Leaf Extract (Standardized to contain 24% Ginkgo Flavone Glycosides and 6% Terpene Lactones)	60 mg	*
Lutein	30 mg	*
Lycopene	6 mg	*
Zeaxanthin	1.5 mg	*

\* Daily Value not established

ID# 557060 60 Capsules

ID# 557120 120 Capsules

†These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

**eFFICACY**  
the power of e

## References

1. Maitra I, Serbinova E, Tritschler HJ, Packer L. Stereospecific effects of R-lipoic acid on buthione sulfoximine-induced cataract formation in newborn rats. *Biochem Biophys Res Commun* 1996; 221(2):422-9.
2. Li Y, Liu YZ, Shi JM, Jia SB. Alpha lipoic acid protects lens from H<sub>2</sub>O<sub>2</sub>-induced cataract by inhibiting apoptosis of lens epithelial cells and inducing activation of anti-oxidative enzymes. *Asian Pac J Trop Med*. 2013 Jul;6(7):548-51.
3. Lee,WJ, Song,KH, Koh,EH, Won,JC, Kim,HS, Park,HS, Kim, MS, Kim,SW, Lee,KU, Park,JY: Alpha-lipoic acid increases insulin sensitivity by activating AMPK in skeletal muscle. *Biochem Biophys Res Commun* 332:885-891, 2005.
4. Osler,ME, Zierath,JR: Minireview: adenosine 5'-monophosphate-activated protein kinase regulation of fatty acid oxidation in skeletal muscle. *Endocrinology* 149:935-941, 2008.
5. Ruderman,NB, Saha,AK, Kraegen,EW: Minireview: malonyl CoA, AMP-activated protein kinase, and adiposity. *Endocrinology* 144:5166-5171, 2003.
6. Ahlemeyer B, Krieglstein J. Neuroprotective effects of Ginkgo biloba extract. *Cell Mol Life Sci*. 2003 Sep;60(9):1779-92.
7. Ahlemeyer B, Krieglstein J. Pharmacological studies supporting the therapeutic use of Ginkgo biloba extract for Alzheimer's disease. *Pharmacopsychiatry*. 2003 Jun;36 Suppl 1:58-14. Review.
8. Ponto LL, Schultz SK. Ginkgo biloba extract: review of CNS effects. *Ann Clin Psychiatry*. 2003 Jun;15(2):109-19.
9. Droy-Lefaix MT, Vennat JC, Besse G, Doly M. Effects of Ginkgo biloba extract (EGb 761) on chloroquine induced retinal alterations. *Lens Eye Toxic Res* 1992; 9(3-4):521-8.
10. Droy-Lefaix MT, Cluzel J, Menerath JM, et al. Antioxidant effect of a Ginkgo biloba extract (Egb 761) on the retina. *Int J Tissue React* 1995; 17(3):93-100.
11. Szabo ME, Droy-Lefaix MT, Doly M. Direct measurement of free radicals in ischemic/reperfused diabetic rat retina. *Clin Neurosci* 1997; 4(5):240-5.
12. Abdel-Aal el-SM, Akhtar H, Zaheer K, Ali R. Dietary sources of lutein and zeaxanthin carotenoids and their role in eye health. *Nutrients*. 2013 Apr 9;5(4):1169-85.
13. Koushan K, Rusovici R, Li W, Ferguson LR, Chalam KV. The role of lutein in eye-related disease. *Nutrients*. 2013 May 22;5(5):1823-39.
14. Gao S, Qin T, Liu Z, Caceres MA, Ronchi CF, Chen CY, Yeum KJ, Taylor A, Blumberg JB, Liu Y, Shang F. Lutein and zeaxanthin supplementation reduces H<sub>2</sub>O<sub>2</sub>-induced oxidative damage in human lens epithelial cells. *Mol Vis*. 2011;17:3180-90. *Epub* 2011 Dec 7.
15. Seddon JM, Ajani UA, Sperduto RD, et al. Dietary carotenoids, vitamin A, C and E and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. *JAMA* 1994; 272(18):1413-20.
16. Arnold C, Winter L, Fröhlich K, Jentsch S, Dawczynski J, Jahreis G, Böhm V. Macular xanthophylls and ω-3 long-chain polyunsaturated fatty acids in age-related macular degeneration: a randomized trial. *JAMA Ophthalmol*. 2013 May;131(5):564-72.
17. Nicolas MG, Fujiki K, Murayama K, et al. Studies on the mechanism of early onset macular degeneration in cynomolgus monkeys. II. Suppression of metallothionein synthesis in the retina in oxidative stress. *Exp Eye Res* 1996; 62(4):399-408.
18. Cingle KA, Kalski RS, Bruner WE, et al. Age-related changes of glycosidases in human retinal pigment epithelium. *Curr Eye Res* 1996; 15(4):433-8.
19. Wyszynski RE, Bruner WE, Cano DB, et al. A donor-age-dependent change in the activity of alpha-mannosidase in human cultured RPE cells. *Invest Ophthalmol Vis Sci* 1989; 30(11):2341-7.
20. Yao N, Lan F, He RR, Kurihara H. J Protective effects of bilberry ( *Vaccinium myrtillus* L.) extract against endotoxin-induced uveitis in mice. *Agric Food Chem*. 2010 Apr 28;58(8):4731-6.
21. Canter PH, Ernst E. Anthocyanosides of *Vaccinium myrtillus* (bilberry) for night vision--a systematic review of placebo-controlled trials. *Surv Ophthalmol*. 2004 Jan-Feb;49(1):38-50.
22. Song J, Li Y, Ge J, Duan Y, Sze SC, Tong Y, Shaw PC, Ng TB, Tsui KC, Zhuo Y, Zhang KY. Protective effect of bilberry (*Vaccinium myrtillus* L.) extracts on cultured human corneal limbal epithelial cells (HCLEC). *Phytother Res*. 2010 Apr;24(4):520-4.
23. Bito T, Roy S, Sen CK, et al. Flavonoids differentially regulate IFN gamma-induced ICAM-1 expression in human keratinocytes: molecular mechanisms of action. *FEBS Lett*. 2002 Jun 5;520(1-3):145-52.
24. Amasheh M, Schlichter S, Amasheh S, Mankertz J, Zeitz M, Fromm M, Schulzke JD. Quercetin enhances epithelial barrier function and increases claudin-4 expression in Caco-2 cells. *J Nutr*. 2008 Jun;138(6):1067-73.
25. Penissi AB, Rudolph MI, Piezzi RS. Role of mast cells in gastrointestinal mucosal defense. *Biocell*. 2003 Aug;27(2):163-72.
26. Lombardini JB. Taurine: retinal function. *Brain Res Rev* 1991; 16(2):151-69.
27. Lombardini JB. Taurine: retinal function. *Brain Res Brain Res Rev*. 1991 May-Aug;16(2):151-69.