

Preventing Age-Related Macular Degeneration

(Lu)(Zx) Wu J, Cho E, Willett WC, Sastry SM, Schaumberg DA. Intakes of Lutein, Zeaxanthin, and Other Carotenoids and Age-Related Macular Degeneration During 2 Decades of Prospective Follow-up. *JAMA Ophthalmol.* 2015 Dec;133(12):1415-24. doi: 10.1001/jamaophthalmol.2015.3590. PMID: 26447482; PMCID: PMC5119484.

(Lu)(Zx) Liu R, Wang T, Zhang B, Qin L, Wu C, Li Q, Ma L. Lutein and zeaxanthin supplementation and association with visual function in age-related macular degeneration. *Invest Ophthalmol Vis Sci.* 2014 Dec 16;56(1):252-8. doi: 10.1167/iovs.14-15553. PMID: 25515572.

(Lu)(Zx) Wang X, Jiang C, Zhang Y, Gong Y, Chen X, Zhang M. Role of lutein supplementation in the management of age-related macular degeneration: meta-analysis of randomized controlled trials. *Ophthalmic Res.* 2014;52(4):198-205. doi: 10.1159/000363327. Epub 2014 Oct 25. PMID: 25358528.

(Lu)(Zx) Huang YM, Dou HL, Huang FF, Xu XR, Zou ZY, Lu XR, Lin XM. Changes following supplementation with lutein and zeaxanthin in retinal function in eyes with early age-related macular degeneration: a randomised, double-blind, placebo-controlled trial. *Br J Ophthalmol.* 2015 Mar;99(3):371-5. doi: 10.1136/bjophthalmol-2014-305503. Epub 2014 Sep 16. PMID: 25228440.

(Lu)(Zx) Age-Related Eye Disease Study 2 (AREDS2) Research Group, Chew EY, Clemons TE, Sangiovanni JP, Danis RP, Ferris FL 3rd, Elman MJ, Antoszyk AN, Ruby AJ, Orth D, Bressler SB, Fish GE, Hubbard GB, Klein ML, Chandra SR, Blodi BA, Domalpally A, Friberg T, Wong WT, Rosenfeld PJ, Agrón E, Toth CA, Bernstein PS, Sperduto RD. Secondary analyses of the effects of lutein/zeaxanthin on age-related macular degeneration progression: AREDS2 report No. 3. *JAMA Ophthalmol.* 2014 Feb;132(2):142-9. doi: 10.1001/jamaophthalmol.2013.7376. PMID: 24310343; PMCID: PMC4636082.

(Lu)(Zx) Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. *JAMA.* 2013 May 15;309(19):2005-15. doi: 10.1001/jama.2013.4997. Erratum in: *JAMA.* 2013 Jul 10;310(2):208. PMID: 23644932.

(Lu)(Zx) Ma L, Yan SF, Huang YM, Lu XR, Qian F, Pang HL, Xu XR, Zou ZY, Dong PC, Xiao X, Wang X, Sun TT, Dou HL, Lin XM. Effect of lutein and zeaxanthin on macular pigment and visual function in patients with early age-related macular degeneration. *Ophthalmology.* 2012 Nov;119(11):2290-7. doi: 10.1016/j.ophtha.2012.06.014. Epub 2012 Aug 1. PMID: 22858124.

(Lu)(Zx)(C)(Cu) Agrón E, Mares J, Clemons TE, Swaroop A, Chew EY, Keenan TDL; AREDS and AREDS2 Research Groups. Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2. *Ophthalmology.* 2021 Mar;128(3):425-442. doi: 10.1016/j.ophtha.2020.08.018. Epub 2020 Aug 25. PMID: 32858063; PMCID: PMC7902480.

(C)(E)(Zn) Chew EY, Clemons TE, Agrón E, Sperduto RD, Sangiovanni JP, Kurinij N, Davis MD; Age-Related Eye Disease Study Research Group. Long-term effects of vitamins C and E, β-carotene, and zinc on age-related macular degeneration: AREDS report no. 35. *Ophthalmology.* 2013 Aug;120(8):1604-11. e4. doi: 10.1016/j.ophtha.2013.01.021. Epub 2013 Apr 10. Erratum in: *Ophthalmology.* 2016 Dec;123(12):2634. PMID: 23582353; PMCID: PMC3728272.

(C)(E)(Zn) Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. *Arch Ophthalmol.* 2001 Oct;119(10):1417-36. doi: 10.1001/archophth.119.10.1417. Erratum in: *Arch Ophthalmol.* 2008 Sep;126(9):1251. PMID: 11594942; PMCID: PMC1462955.

(Glu) Qin L, Mroczkowska SA, Ekart A, Patel SR, Gibson JM, Gherghel D. Patients with early age-related macular degeneration exhibit signs of macro- and micro-vascular disease and abnormal blood glutathione levels. *Graefes Arch Clin Exp Ophthalmol.* 2014 Jan;252(1):23-30. doi: 10.1007/s00417-013-2418-0. Epub 2013 Jul 11. PMID: 23842712.

(Glu) Cohen SM, Olin KL, Feuer WJ, Hjelmeland L, Keen CL, Morse LS. Low glutathione reductase and peroxidase activity in age-related macular degeneration. *Br J Ophthalmol.* 1994 Oct;78(10):791-4. doi: 10.1136/bjo.78.10.791. PMID: 7803358; PMCID: PMC504938.

Scientific References

Bb Gerding H. Primäre oder sekundäre Prophylaxe der AMD mit Anthocyanen? [Primary or Secondary Prophylaxis of AMD with Anthocyanins?]. *Klin Monbl Augenheilkd.* 2009 Apr;226(4):216-9. German. doi: 10.1055/s-0028-1109326. Epub 2009 Apr 21. PMID: 19384768.

Preventing Diabetic / Hypertensive Retinopathy

Lu Zx Neelam K, Goenadi CJ, Lun K, Yip CC, Au Eong KG. Putative protective role of lutein and zeaxanthin in diabetic retinopathy. *Br J Ophthalmol.* 2017 May;101(5):551-558. doi: 10.1136/bjophthalmol-2016-309814. Epub 2017 Feb 23. PMID: 28232380.

C Tanaka S, Yoshimura Y, Kawasaki R, Kamada C, Tanaka S, Horikawa C, Ohashi Y, Araki A, Ito H, Akanuma Y, Yamada N, Yamashita H, Sone H; Japan Diabetes Complications Study Group. Fruit intake and incident diabetic retinopathy with type 2 diabetes. *Epidemiology.* 2013 Mar;24(2):204-11. doi: 10.1097/EDE.0b013e318281725e. PMID: 23348071.

Zn Miao X, Sun W, Miao L, Fu Y, Wang Y, Su G, Liu Q. Zinc and diabetic retinopathy. *J Diabetes Res.* 2013;2013:425854. doi: 10.1155/2013/425854. Epub 2013 Mar 17. PMID: 23671870; PMCID: PMC3647550.

Glu Cicik E, Tekin H, Akar S, Ekmekçi OB, Donma O, Koldaş L, Ozkan S. Interleukin-8, nitric oxide and glutathione status in proliferative vitreoretinopathy and proliferative diabetic retinopathy. *Ophthalmic Res.* 2003 Sep-Oct;35(5):251-5. doi: 10.1159/000072145. PMID: 12920337.

Bb Kim J, Kim CS, Lee YM, Sohn E, Jo K, Kim JS. Vaccinium myrtillus extract prevents or delays the onset of diabetes--induced blood-retinal barrier breakdown. *Int J Food Sci Nutr.* 2015 Mar;66(2):236-42. doi: 10.3109/09637486.2014.979319. Epub 2015 Jan 13. PMID: 25582181.

Bb Mills S, Bone K. 2005. *The Essential Guide to Herbal Safety.* St. Louis (MO): Churchill Livingstone.

Bb Blumenthal M. 2003. *ABC Clinical Guide to Herbs.* New York (NY): Thieme.

Scientific References

Bb Upton R, editor. 2001. *American Herbal Pharmacopoeia and Therapeutic Compendium: Bilberry Fruit Vaccinium myrtillus L.: Standards of Analysis, Quality Control and Therapeutics.* Santa Cruz (CA): American Herbal Pharmacopoeia.

Bb Morazzoni P, Bombardelli E. 1996. *Vaccinium myrtillus L.* *Fitoterapia* 67(1):3-29.

Qu Li R, Chen L, Yao GM, Yan HL, Wang L. Effects of quercetin on diabetic retinopathy and its association with NLRP3 inflammasome and autophagy. *Int J Ophthalmol.* 2021 Jan 18;14(1):42-49. doi: 10.18240/ijo.2021.01.06. PMID: 33469482; PMCID: PMC7790678.

Qu Chai GR, Liu S, Yang HW, Chen XL. Quercetin protects against diabetic retinopathy in rats by inducing heme oxygenase-1 expression. *Neural Regen Res.* 2021 Jul; 16(7):1344-1350. doi: 10.4103/1673-5374.301027. PMID: 33318415; PMCID: PMC8284280.

Preventing Cataract

Lu Zx Liu XH, Yu RB, Liu R, Hao ZX, Han CC, Zhu ZH, Ma L. Association between lutein and zeaxanthin status and the risk of cataract: a meta-analysis. *Nutrients.* 2014 Jan 22;6(1):452-65. doi: 10.3390/nu6010452. PMID: 24451312; PMCID: PMC3916871.

Lu Zx Ma L, Hao ZX, Liu RR, Yu RB, Shi Q, Pan JP. A dose-response meta-analysis of dietary lutein and zeaxanthin intake in relation to risk of age-related cataract. *Graefes Arch Clin Exp Ophthalmol.* 2014 Jan;252(1):63-70. doi: 10.1007/s00417-013-2492-3. Epub 2013 Oct 23. PMID: 24150707.

Lu Zx Karppi J, Laukkanen JA, Kurl S. Plasma lutein and zeaxanthin and the risk of age-related nuclear cataract among the elderly Finnish population. *Br J Nutr.* 2012 Jul 14;108(1):148-54. doi: 10.1017/S0007114511005332. Epub 2011 Oct 18. PMID: 22005336.

Lu Zx Moeller SM, Volland R, Tinker L, Blodi BA, Klein ML, Gehrs KM, Johnson EJ, Snodderly DM, Wallace RB, Chappell RJ, Parekh N, Ritenbaugh C, Mares JA; CAREDS Study Group; Women's Health Initiative. Associations between

Scientific References

age-related nuclear cataract and lutein and zeaxanthin in the diet and serum in the Carotenoids in the Age-Related Eye Disease Study, an Ancillary Study of the Women's Health Initiative. Arch Ophthalmol. 2008 Mar;126(3):354-64. doi: 10.1001/archophth.126.3.354. PMID: 18332316; PMCID: PMC2562026.

Lu **Zx** Vu HT, Robman L, Hodge A, McCarty CA, Taylor HR. Lutein and zeaxanthin and the risk of cataract: the Melbourne visual impairment project. Invest Ophthalmol Vis Sci. 2006 Sep;47(9):3783-6. doi: 10.1167/iops.05-0587. PMID: 16936087.

Lu **Zx** Delcourt C, Carriere I, Delage M, Barberger-Gateau P, Schalch W; POLA Study Group. Plasma lutein and zeaxanthin and other carotenoids as modifiable risk factors for age-related maculopathy and cataract: the POLA Study. Invest Ophthalmol Vis Sci. 2006 Jun;47(6):2329-35. doi: 10.1167/iops.05-1235. PMID: 16723441.

C Ravindran RD, Vashist P, Gupta SK, Young IS, Maraini G, Camparini M, Jayanthi R, John N, Fitzpatrick KE, Chakravarthy U, Ravilla TD, Fletcher AE. Inverse association of vitamin C with cataract in older people in India. Ophthalmology. 2011 Oct;118(10): 1958-1965.e2. doi: 10.1016/j.ophtha.2011.03.016. Epub 2011 Jun 25. PMID: 21705085; PMCID: PMC3185206.

C Dherani M, Murthy GV, Gupta SK, Young IS, Maraini G, Camparini M, Price GM, John N, Chakravarthy U, Fletcher AE. Blood levels of vitamin C, carotenoids and retinol are inversely associated with cataract in a North Indian population. Invest Ophthalmol Vis Sci. 2008 Aug;49(8):3328-35. doi: 10.1167/iops.07-1202. Epub 2008 Apr 17. PMID: 18421094.

C Valero MP, Fletcher AE, De Stavola BL, Vioque J, Alepuz VC. Vitamin C is associated with reduced risk of cataract in a Mediterranean population. J Nutr. 2002 Jun; 132(6):1299-306. doi: 10.1093/jn/132.6.1299. PMID: 12042450.

E Cui YH, Jing CX, Pan HW. Association of blood antioxidants and vitamins with risk of age-related cataract: a meta-analysis of observational studies. Am J Clin Nutr. 2013 Sep;98(3):778-86. doi: 10.3945/ajcn.112.053835. Epub 2013 Jul 10. PMID: 23842458.

Scientific References

Zn **GSE** Mani Satyam S, Kurady Bairy L, Pirasanthan R, Lalit Vaishnav R. Grape seed extract and zinc containing nutritional food supplement prevents onset and progression of age-related cataract in wistar rats. J Nutr Health Aging. 2014 May;18(5):524-30. doi: 10.1007/s12603-014-0020-8. PMID: 24886740.

Glu Lim JC, Grey AC, Zahraei A, Donaldson PJ. Age-dependent changes in glutathione metabolism pathways in the lens: New insights into therapeutic strategies to prevent cataract formation-A review. Clin Exp Ophthalmol. 2020 Nov;48(8):1031-1042. doi: 10.1111/ceo.13801. Epub 2020 Jun 15. PMID: 32462803.

Glu Wei Z, Caty J, Whitson J, Zhang AD, Srinivasagan R, Kavanagh TJ, Yan H, Fan X. Reduced Glutathione Level Promotes Epithelial-Mesenchymal Transition in Lens Epithelial Cells via a Wnt/ β -Catenin-Mediated Pathway: Relevance for Cataract Therapy. Am J Pathol. 2017 Nov;187(11):2399-2412. doi: 10.1016/j.ajpath.2017.07.018. Epub 2017 Aug 19. PMID: 28827139; PMCID: PMC5809338.

Lutein: **Lu** Zeaxanthin: **Zx** Vitamin C: **C** Vitamin E: **E** Zinc: **Zn** Copper: **Cu**
L-Glutathione: **Glu** Bilberry: **Bb** Grape Seed Extract: **GSE** Quercetin: **Qu**