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- [1] Mardin, C. (2002). Age-related macular degeneration. **Orphanet**, 1, 1-5.
- [2] Williams, R. A., Brody, B. L. and Thomas, R. G. (1998). The psychosocial impact of macular degeneration. **Archives of Ophthalmology**, 116, 514-520.
- [3] Comer, G. M., Ciulla, T. A., Heier, J. S. and Criswell, M. H. (2005). Future pharmacological treatment options for nonexudative and exudative age-related macular degeneration. **Expert Opinion on Emerging Drugs**, 10(1), 119-135.
- [4] Comer, G. M., Ciulla, T. A., Criswell, M. H. and Tolentino, M. (2004). Current and future treatment options for nonexudative and exudative age-related macular degeneration. **Drugs and Aging**, 21(15), 967-992.
- [5] Mainster Ma Fau - Ham, W. T., Jr., Ham Wt Jr Fau - Delori, F. C. and Delori, F. C. (1983). Potential retinal hazards. Instrument and environmental light sources. **Ophthalmology**, 90(8), 927-932.
- [6] Taylor, H. R., West, S., Munoz, B., Rosenthal, F. S., Bressler, S. B. and Bressler, N. M. (1992). The long-term effects of visible light on the eye. **Archives of Ophthalmology**, 110(1), 99-104.
- [7] Matsui, H., Lin, L.-R., Singh, D. P., Shinohara, T. and Reddy, V. N. (2001). Lens epithelium-derived growth factor: Increased survival and decreased DNA breakage of human RPE cells induced by oxidative stress. **Investigative Ophthalmology & Visual Science**, 42, 2935-2941.
- [8] Noell, W. K. (1980). Possible mechanisms of photoreceptor damage by light in mammalian eyes. **Vision Research**, 20(12), 1163-1171.
- [9] Gorgels, T. G. and van Norren, D. (1995). Ultraviolet and green light cause different types of damage in rat retina. **Investigative Ophthalmology & Visual Science**, 36(5), 851-863.
- [10] Patton, W. P., Chakravarthy, U., Davies, R. J. H. and Archer, D. B. (1999). Comet assay of UV-induced DNA damage in retinal pigment epithelial cells. **Investigative Ophthalmology & Visual Science**, 40(13), 3268-3275.
- [11] Tratsk, K. and Thanos, S. (2003). UV irradiation causes multiple cellular changes in cultured human retinal pigment epithelium cells. **Gracfe's Archive for Clinical and Experimental Ophthalmology**, 241(10), 852-859.

- [12] Age-Related Eye Disease Study Research Group. (2001). A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta carotene for age-related cataract and Vision Loss: AREDS Report No. 9. **Archives of Ophthalmology**, 119(10), 1439-1452.
- [13] Richer, S., Stiles, W., Statkute, L., Pulido, J., Frankowski, J., Rudy, D., et al. (2004). 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**, 75(4), 216-229.
- [14] Snodderly, D. (1995). Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. **The American Journal of Clinical Nutrition**, 62(6), 1448-1461.
- [15] Khachik, F., Beecher, G. R., Goli, M. B., Lusby, W. R. and Smith Jr, J. C. (1992). Separation and identification of carotenoids and their oxidation products in the extracts of human plasma. **Analytical Chemistry**, 64(18), 2111-2122.
- [16] Khachik, F., Spangler, C. J., Smith Jr, J. C., Canfield, L. M., Steck, A. and Pfander, H. (1997). Identification, quantification, and relative concentrations of carotenoids and their metabolites in human milk and serum. **Analytical Chemistry**, 69(10), 1873-1881.
- [17] Schalch, W. (1992). Carotenoids in the retina-a review of their possible role in preventing or limiting damage caused by light and oxygen. **EXS**, 62, 280-298.
- [18] Leung, I. Y. F. (2008). Macular pigment: New clinical methods of detection and the role of carotenoids in age-related macular degeneration. **Optometry** 79(5), 266-272.
- [19] Kvensakul, J., Rodriguez Carmona, M., Edgar, D. F., Barker, F. M., Köpcke, W., Schalch, W., et al. (2006). Supplementation with the carotenoids lutein or zeaxanthin improves human visual performance. **Ophthalmic and Physiological Optics**, 26(4), 362-371.

- [20] Olmedilla, B., Granado, F., Blanco, I. and Vaquero, M. (2003). Lutein, but not α -tocopherol, supplementation improves visual function in patients with age-related cataracts: A 2-y double-blind, placebo-controlled pilot study. **Nutrition**, 19(1), 21-24.
- [21] Norren, D. V. and Vos, H. (1990). Sunlight and age-related macular degeneration. **Archives of Ophthalmology**, 108(12), 1670-1671.
- [22] Kaurola, J., Taalas, P., Koskela, T., Borkowski, J. and Josefsson, W. (2000). Long-term variations of UV-B doses at three stations in northern Europe. **Journal of Geophysical Research**, 105, 20813-20820.
- [23] Chucair, A. J., Rotstein, N. P., SanGiovanni, J. P., During, A., Chew, E. Y. and Politi, L. E. (2007). Lutein and zeaxanthin protect photoreceptors from apoptosis induced by oxidative stress: Relation with docosahexaenoic acid. **Investigative Ophthalmology & Visual Science**, 48(11), 5168-5177.
- [24] Wrona, M., Rózanowska, M. and Sarna, T. (2004). Zeaxanthin in combination with ascorbic acid or α -tocopherol protects ARPE-19 cells against photosensitized peroxidation of lipids. **Free Radical Biology and Medicine**, 36(9), 1094-1101.
- [25] Marmorstein, A. D. (2001). The polarity of the retinal pigment epithelium. **Traffic**, 2(12), 867-872.
- [26] Boulton, M. and Dayhaw-Barker, P. (2001). The role of the retinal pigment epithelium: Topographical variation and ageing changes. **Eye**, 15, 384-389.
- [27] Dornonville de la Cour, M. (1993). Ion transport in the retinal pigment epithelium. A study with double barrelled ion-selective microelectrodes. **Acta ophthalmologica Supplement**, 209, 1-32.
- [28] Baehr, W., Wu, S. M., Bird, A. C. and Palczewski, K. (2003). The retinoid cycle and retina disease. **Vision Research**, 43(28), 2957-2958.
- [29] Finnemann, S. C. (2003). Focal adhesion kinase signaling promotes phagocytosis of integrin-bound photoreceptors. **The EMBO Journal**, 22(16), 4143-4154.
- [30] Bost, L. M., Aotaki-Keen, A. E. and Hjelmeland, L. M. (1992). Coexpression of FGF-5 and bFGF by the retinal pigment epithelium in vitro. **Experimental Eye Research**, 55(5), 727-734.

- [31] Slomiany, M. G. and Rosenzweig, S. A. (2004). Autocrine effects of IGF-I-induced VEGF and IGFBP-3 secretion in retinal pigment epithelial cell line ARPE-19. **American Journal of Physiology Cell Physiology**, 287(3), 746-753.
- [32] Walsh, N., Valter, K. and Stone, J. (2001). Cellular and subcellular patterns of expression of bFGF and CNTF in the normal and light stressed adult rat retina. **Experimental Eye Research**, 72(5), 495-501.
- [33] Ciulla, T. A., Harris, A. and Martin, B. J. (2001). Ocular perfusion and age-related macular degeneration. **Acta Ophthalmologica Scandinavica**, 79(2), 108-115.
- [34] Kimura, K., Isashiki, Y., Sonoda, S., Kakiuchi-Matsumoto, T. and Ohba, N. (2000). Genetic association of manganese superoxide dismutase with exudative age-related macular degeneration. **American journal of ophthalmology**, 130(6), 769-773.
- [35] Hamdi, H. K., Reznik, J., Castellon, R., Atilano, S. R., Ong, J. M., Udar, N., et al. (2002). Alu DNA polymorphism in ACE gene is protective for age-related macular degeneration. **Biochemical and Biophysical Research Communications**, 295(3), 668-672.
- [36] Allikmets, R., Singh, N., Sun, H., Shroyer, N. F., Hutchinson, A., Chidambaram, A., et al. (1997). A photoreceptor cell-specific ATP-binding transporter gene (ABCR) is mutated in recessive Stargardt macular dystrophy. **Nature Genetics**, 15(3), 236-246.
- [37] Handa, J. T., Verzijl, N., Matsunaga, H., Aotaki-Keen, A., Luttj, G. A., Te Koppele, J. M., et al. (1999). Increase in the advanced glycation end product pentosidine in Bruch's membrane with age. **Investigative Ophthalmology & Visual Science**, 40(3), 775-779.
- [38] Li, W., Yanoff, M., Li, Y. and He, Z. (1999). Artificial senescence of bovine retinal pigment epithelial cells induced by near-ultraviolet in vitro. **Mechanisms of Ageing and Development**, 110(3), 137-155.
- [39] Watzke, R. C., Soldevilla, J. D. and Trune, D. R. (1993). Morphometric analysis of human retinal pigment epithelium: Correlation with age and location. **Current Eye Research**, 12(2), 133-142.

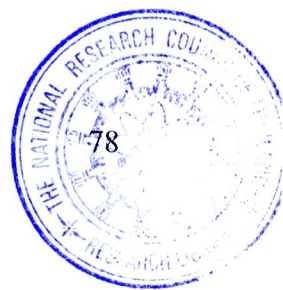
- [40] Ross, R. D., Barofsky, J. M., Cohen, G., Baber, W. B., Palao, S. W. and Gitter, K. A. (1998). Presumed macular choroidal watershed vascular filling, choroidal neovascularization, and systemic vascular disease in patients with age- related macular degeneration. **American Journal of Ophthalmology**, 125(1), 71-80.
- [41] Beatty, S., Koh, H. H., Phil, M., Henson, D. and Boulton, M. (2000). The role of oxidative stress in the pathogenesis of age-related macular degeneration. **Survey of Ophthalmology**, 45(2), 115-134.
- [42] Alder, V. A. and Cringle, S. J. (1985). The effect of the retinal circulation on vitreal oxygen tension. **Current Eye Research**, 4(2), 121-129.
- [43] Bazan, N. G. (1989). The metabolism of omega-3 polyunsaturated fatty acids in the eye: the possible role of docosahexaenoic acid and docosanoids in retinal physiology and ocular pathology. **Progress in Clinical and Biological Research**, 312, 95-112.
- [44] Gaillard, E. R., Atherton, S. J., Eldred, G. and Dillon, J. (1995). Photophysical studies on human retinal lipofuscin. **Photochemistry and Photobiology**, 61(5), 448-453.
- [45] Tate Jr, D. J., Miceli, M. V. and Newsome, D. A. (1995). Phagocytosis and H₂O₂ induce catalase and metallothionein gene expression in human retinal pigment epithelial cells. **Investigative Ophthalmology & Visual Science**, 36(7), 1271-1279.
- [46] Augood, C. A., Vingerling, J. R., de Jong, P. T., Chakravarthy, U., Seland, J., Soubrane, G., et al. (2006). Prevalence of age-related maculopathy in older europeans: The european eye study (EUREYE). **Archives of Ophthalmology**, 124(4), 529-535.
- [47] Mitchell, P., Smith, W., Attebo, K. and Wang, J. J. (1995). Prevalence of age-related maculopathy in Australia. The blue mountains eye study. **Ophthalmology**, 102(10), 1450-1460.
- [48] Smith, W., Attebo, K. and Wang, J. J. (1997). Gender, oestrogen, hormone replacement and age-related macular degeneration: results from the blue mountains eye study. **Australian and New Zealand Journal of Ophthalmology**, 25, 13-15.

- [49] Schachat, A. P., Hyman, L., Leske, M. C., Connell, A. M. S., Wu, S. Y. and (1995). Features of age-related macular degeneration in a black population. The Barbados Eye Study Group. **Archives of Ophthalmology**, 113(6), 728-735.
- [50] Gregor, Z. and Joffe, L. (1978). Senile macular changes in the black African. **The British Journal of Ophthalmology**, 62, 547-550.
- [51] Weiter, J. J., Delori, F. C., Wing, G. L. and Fitch, K. A. (1985). Relationship of senile macular degeneration to ocular pigmentation. **American Journal of Ophthalmology**, 99, 185-187.
- [52] Beatty, S., Boulton, M., Henson, D., Koh, H. H. and Murray, I. J. (1999). Macular pigment and age related macular degeneration. **The British journal of Ophthalmology**, 83(7), 867-877.
- [53] Bone, R. A., Landrum, J. T. and Tarsis, S. L. (1985). Preliminary identification of the human macular pigment. **Vision Research**, 25, 1531-1535.
- [54] Nussbaum, J. J., Pruett, R. C. and Delori, F. C. (1981). Historic perspectives. Macular yellow pigment. The first 200 years. **Retina**, 4, 296-310.
- [55] Reading, V. and Weale, R. (1974). Macular pigment and chromatic aberration. **American Journal of Optometry and Archives of American Academy of Optometry**, 64, 231 - 234.
- [56] Kirschfeld, K. (1982). Carotenoid pigments: their possible role in protecting against photooxidation in eyes and photoreceptor cells. **Proceedings of the Royal Society of London**, 216, 71 - 85.
- [57] Bone, R. A. and Landrum, J. T. (1984). Macular pigment in Henle fiber membranes: a model for Haidinger's brushes. **Vision Research**, 24, 103 - 108.
- [58] Seddon, J., Ajani, U., Sperduto, R., Hiller, R., Blair, N. and Burton, T. (1994). Dietary carotenoids, vitamin A, C, and E, and advanced age-related macular degeneration. **Journal of the American Medical Association**, 272, 1413 - 1420.
- [59] Vingerling, J. R., Dielemans, I., Bots, M. L., Hofman, A., Grobbee, D. E. and De Jong, P. T. (1995). Age-related macular degeneration is associated with atherosclerosis: The Rotterdam study. **American journal of epidemiology**, 142(4), 404-409.

- [60] Klein, R., Clegg, L., Cooper, L. S., Hubbard, L. D., Klein, B. E., King, W. N., et al. (1999). Prevalence of age-related maculopathy in the Atherosclerosis Risk in Communities Study. **Archives of Ophthalmology**, 117, 1203-1210.
- [61] Goldberg, J., Flowerdew, G., Smith, E., Brody, J. A. and Tso, M. O. (1988). Factors associated with age-related macular degeneration. An analysis of data from the first national health and nutrition examination survey. **American Journal of Epidemiology**, 128(4), 700-710.
- [62] Kahn, H. A., Leibowitz, H. M., Ganley, J. P., Kini, M. M., Colton, T., Nickerson, R. S., et al. (1977). The framingham eye study. **American journal of Epidemiology**, 106(1), 17-32.
- [63] Klein, R., Klein, B. E. and Franke, T. (1993). The relationship of cardiovascular disease and its risk factors to age-related maculopathy. The Beaver Dam Eye Study. **Ophthalmology**, 100, 406-414.
- [64] Willett, W. (1994). Diet and health: what should we eat? **Science**, 264(5158), 532-537.
- [65] Klein, R., Klein, B. E. and Moss, S. E. (1992). Diabetes, hyperglycemia, and age-related maculopathy. The Beaver Dam Eye Study. **Ophthalmology**, 99(100), 1527-1534.
- [66] Chiu, C. J. and Taylor, A. (2011). Dietary hyperglycemia, glycemic index and metabolic retinal diseases. **Progress in Retinal and Eye Research**, 30(1), 18-53.
- [67] Delcourt, C., Cristol, J. P., Léger, C. L., Descomps, B. and Papoz, L. (1999). Associations of antioxidant enzymes with cataract and age-related macular degeneration: The POLA study. **Ophthalmology**, 106(2), 215-222.
- [68] Group, E. D. C.-C. S. (1992). Risk factors for neovascular age-related macular degeneration. **Archives of Ophthalmology**, 110, 1701 - 1708.
- [69] Ferris, F. (1983). Senile macular degeneration: review of epidemiological features. **American Journal of Epidemiology**, 118, 132 - 151.
- [70] Klein, R., Klein, B. E. K., Linton, K. L. P. and DeMets, D. L. (1993). The Beaver Dam Eye Study: The relation of age-related maculopathy to smoking. **American Journal of Epidemiology**, 137(2), 190-200.

- [71] Hammond, B., Wooten, B. and Snodderly, D. (1996). Cigarette smoking and retinal carotenoids: implications for age-related macular degeneration. **Vision Research**, 36, 3003 - 3009.
- [72] Ham, W. T., Mueller, H. A., Ruffolo, J. J., Guerry, D. and Guerry, R. K. (1982). Action spectrum for retinal injury from near-ultraviolet radiation in the aphakic monkey. **American Journal of Ophthalmology**, 93, 299-306.
- [73] Young, R. (1988). Solar radiation and age-related macular degeneration. **Survey of ophthalmology**, 32, 252 - 269.
- [74] Tso, M. O. (1985). Pathogenetic factors of aging macular degeneration. **Ophthalmology**, 95, 628-635.
- [75] Jaques, P. (1999). The potential preventive effects of vitamins for cataract and age-related macular degeneration. **International Journal for Vitamin and Nutrition Research**, 69, 198 - 205.
- [76] Robison, W. G., Kuwabara, T. and Bieri., J. G. (1982). The roles of vitamin E and unsaturated fatty acids in the visual process. **Retina**, 263-281,
- [77] Landrum, J. T. and Bone, R. A. (2001). Lutein, zeaxanthin, and the macular pigment. **Archives of Biochemistry and Biophysics**, 385(1), 28-40.
- [78] Mares-Perlman, J. A., Fisher, A. I., Klein, R., Palta, M., Block, G., Millen, A. E., et al. (2001). Lutein and zeaxanthin in the diet and serum and their relation to age-related maculopathy in the third national health and nutrition examination Survey. **American Journal of Epidemiology**, 153, 424 - 432.
- [79] Sommerburg, O., Keunen, J. E., Bird, A. C. and van Kuijk, F. J. (1998). Fruits and vegetables that are sources of lutein and zeaxanthin: the macular pigment in human eye. **The British Journal of Ophthalmology**, 82, 907 - 910.
- [80] Prommuak, C., De Eknankul, W. and Shotipruk, A. (2008). Extraction of flavonoids and carotenoids from Thai silk waste and antioxidant activity of extracts. **Separation Science and Technology**, 62(2), 444-448.
- [81] Dwyer, J. H., Navab, M., Dwyer, K. M., Hassan, K., Sun, P., Shircore, A., et al. (2001). Oxygenated carotenoid lutein and progression of early atherosclerosis : The Los Angeles atherosclerosis study. **Circulation**, 103(24), 2922-2927.

- [82] Michaud, D. S., Feskanich, D., Rimm, E. B., Colditz, G. A., Speizer, F. E., Willett, W. C., et al. (2000). Intake of specific carotenoids and risk of lung cancer in 2 prospective US cohorts. **The American Journal of Clinical Nutrition**, 72(4), 990-997.
- [83] Johnson, E. J. (2002). The role of carotenoids in human health. **Nutrition in Clinical Care**, 5, 47-79.
- [84] Demmig-Adams, B., Gilmore, A. M. and Adams Iii, W. W. (1996). In vivo functions of carotenoids in higher plants. **Federation of American Societies for Experimental Biology**, 10(4), 403-412.
- [85] Timberlake, C. F. and Henry, B. S. (1986). Plant pigments as natural food colours. **Endeavour**, 10(1), 31-36.
- [86] Quackenbush, F. W. (1973). Use of heat to saponify xanthophyll esters and speed analysis for carotenoids in feed materials: collaborative study. **Journal Association of Official Analytical Chemists**, 56(3), 748-753.
- [87] Moran, N. A. and Jarvik, T. (2010). Lateral transfer of genes from fungi underlies carotenoid production in aphids. **Science**, 328(5978), 624-627.
- [88] Sakudoh, T., Sezutsu, H., Nakashima, T., Kobayashi, I., Fujimoto, H., Uchino, K., et al. (2007). Carotenoid silk coloration is controlled by a carotenoid-binding protein, a product of the Yellow blood gene. **Proceedings of the National Academy of Sciences of the United States of America**, 104(21), 8941-8946.
- [89] Tabunoki, H., Higurashi, S., Ninagi, O., Fujii, H., Banno, Y., Nozaki, M., et al. (2004). A carotenoid-binding protein (CBP) plays a crucial role in cocoon pigmentation of silkworm (*Bombyx mori*) larvae. **FEBS Letters**, 567(2-3), 175-178.
- [90] Jouni, Z. E. and Wells, M. A. (1996). Purification and partial characterization of a previous term-lutein-binding protein from the midgut of the silkworm *Bombyx mori*. **Journal of Biological Chemistry**, 271, 14722-14726.
- [91] Ravikrishnan, R., Rusia, S., Ilamurugan, G., Salunkhe, U., Deshpande, J., Shankaranarayanan, J., et al. (2011). Safety assessment of lutein and zeaxanthin (Lutemax™ 2020): Subchronic toxicity and mutagenicity studies. **Food and Chemical Toxicology**, 49(11), 2841-2848.



- [92] Christensen, R. (2004) The Electronic States of Carotenoids. In: The Photochemistry of Carotenoids. **Springer Netherlands**, 8, 137-159.
- [93] Bone, R. A., Landrum, J. T., Friedes, L. M., Gomez, C. M., Kilburn, M. D., Menendez, E., et al. (1997). Distribution of lutein and zeaxanthin stereoisomers in the human retina. **Experimental Eye Research**, 64, 211 - 218.
- [94] Bone, R. A. and Landrum, J. T. (2004). Heterochromatic flicker photometry. **Archives of Biochemistry and Biophysics**, 430(2), 137-142.
- [95] Bone, R. A., Landrum, J. T., Fernandez, L. and Tarsis, S. L. (1988). Analysis of the macular pigment by HPLC: retinal distribution and age study. **Investigative Ophthalmology & Visual Science**, 29, 843 - 849.
- [96] Yeum, K. J. and Russell, R. M. (2002). Carotenoid bioavailability and bioconversion. **Annual Review of Nutrition**, 22(1), 483-504.
- [97] van het Hof, K. H., West, C. E., Weststrate, J. A. and Hautvast, J. G. A. J. (2000). Dietary factors that affect the bioavailability of carotenoids. **The Journal of Nutrition**, 130(3), 503-506.
- [98] Parker, R. S., Swanson, J. E., You, C. S., Edwards, A. J. and Huang, T. (1999). Bioavailability of carotenoids in human subjects. **The Proceedings of the Nutrition Society**, 58(01), 155-162.
- [99] Wang, W., Connor, S. L., Johnson, E. J., Klein, M. L., Hughes, S. and Connor, W. E. (2007). Effect of dietary lutein and zeaxanthin on plasma carotenoids and their transport in lipoproteins in age-related macular degeneration. **The American Journal of Clinical Nutrition**, 85(3), 762-769.
- [100] O'Neill, M. E. and Thurnham, D. I. (1998). Intestinal absorption of β -carotene, lycopene and lutein in men and women following a standard meal: response curves in the triacylglycerol-rich lipoprotein fraction. **The British Journal of Nutrition**, 79, 149-159.
- [101] Kritchevsky, S. B. (1999). β -Carotene, carotenoids and the prevention of coronary heart disease. **The Journal of Nutrition**, 129(1), 5-8.

- [102] Ascherio, A., Rimm, E. B., Hernán, M. A., Giovannucci, E., Kawachi, I., Stampfer, M. J., et al. (1999). Relation of consumption of vitamin E, vitamin C, and carotenoids to risk for stroke among men in the united states. **Annals of Internal Medicine**, 130(12), 963-970.
- [103] Holick, C. N., Michaud, D. S., Stolzenberg-Solomon, R., Mayne, S. T., Pietinen, P., Taylor, P. R., et al. (2002). Dietary carotenoids, serum β -carotene, and retinol and risk of lung cancer in the alpha-tocopherol, beta-carotene cohort study. **American Journal of Epidemiology**, 156(6), 536-547.
- [104] Martin, K. R., Wu, D. and Meydani, M. (2000). The effect of carotenoids on the expression of cell surface adhesion molecules and binding of monocytes to human aortic endothelial cells. **Atherosclerosis**, 150(2), 265-274.
- [105] Ribaya Mercado, J. D., Garmyn, M., Gilchrest, B. A. and Russell, R. M. (1995). Skin lycopene is destroyed preferentially over β -carotene during ultraviolet irradiation in humans. **The Journal of Nutrition**, 125(7), 1854-1859.
- [106] Stahl, W. and Sies, H. (2002). Carotenoids and protection against solar UV radiation. **Skin Pharmacology and Applied Skin Physiology**, 15(5), 291-296.
- [107] Kowluru, R. A., Menon, B. and Gierhart, D. L. (2008). Beneficial effect of zeaxanthin on retinal metabolic abnormalities in diabetic rats. **Investigative Ophthalmology & Visual Science**, 49(4), 1645-1651.
- [108] Sundelin, S. P. and Nilsson, S. E. (2001). Lipofuscin-formation in retinal pigment epithelial cells is reduced by antioxidants. **Free Radical Biology and Medicine**, 31(2), 217-225.
- [109] Krinsky, N. I., Landrum, J. T. and Bone, R. A. (2003). Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye. **Annual Review of Nutrition**, 23, 171-201.
- [110] Khachik, F., Bernstein, P. S. and Garland, D. L. (1997). Identification of lutein and zeaxanthin oxidation products in human and monkey retinas. **Investigative Ophthalmology & Visual Science**, 38(9), 1802-1811.

- [111] Woodall, A. A., Britton, G. and Jackson, M. J. (1997). Carotenoids and protection of phospholipids in solution or in liposomes against oxidation by peroxy radicals: Relationship between carotenoid structure and protective ability. **Biochimica et Biophysica Acta**, 1336(3), 575-586.
- [112] Wisniewska, A. and Subczynski, W. K. (2006). Accumulation of macular xanthophylls in unsaturated membrane domains. **Free Radical Biology and Medicine**, 40(10), 1820-1826.
- [113] Roca, A., Shin, K. J., Liu, X., Simon, M. I. and Chen, J. (2004). Comparative analysis of transcriptional profiles between two apoptotic pathways of light-induced retinal degeneration. **Neuroscience**, 129(3), 779-790.
- [114] Greenstein, V. C., Chiosi, F., Baker, P., Seiple, W., Holopigian, K., Braunstein, R. E., et al. (2007). Scotopic sensitivity and color vision with a blue-light-absorbing intraocular lens. **Journal of Cataract and Refractive Surgery**, 33(4), 667-672.
- [115] Snodderly, D. M., Auran, J. D. and Delori, F. C. (1984). The macular pigment. II. Spatial distribution in primate retinas. **Investigative Ophthalmology & Visual Science**, 25(6), 674-685.
- [116] Junghans, A., Sies, H. and Stahl, W. (2001). Macular pigments lutein and zeaxanthin as blue light filters studied in liposomes. **Archives of Biochemistry and Biophysics**, 391(2), 160-164.
- [117] Sparrow, J. R., Miller, A. S. and Zhou, J. (2004). Blue light-absorbing intraocular lens and retinal pigment epithelium protection in vitro. **Journal of Cataract and Refractive Surgery**, 30(4), 873-878.
- [118] Sujak, A. and Gruszecki, W. I. (2000). Organization of mixed monomolecular layers formed with the xanthophyll pigments lutein or zeaxanthin and dipalmitoylphosphatidylcholine at the argon-water interface. **Journal of Photochemistry and Photobiology B, Biology**, 59(1-3), 42-47.
- [119] Sommerburg, O., Keunen, J. E., Bird, A. C. and van Kuijk, F. J. (1998). Fruits and vegetables that are sources for lutein and zeaxanthin: The macular pigment in human eyes. **The British Journal of Ophthalmology**, 82(8), 907-910.

- [120] The Eye-Disease Case Control Study, G. (1993). Antioxidant status and neovascular age-related macular degeneration. **Archives of Ophthalmology**, 111, 104 - 109.
- [121] Moeller, S. M., Parekh, N., Tinker, L., Ritenbaugh, C., Blodi, B., Wallace, R. B., et al. (2006). Associations between intermediate age-related macular degeneration and lutein and zeaxanthin in the carotenoids in age-related eye disease study (CAREDS): Ancillary study of the women's health initiative. **Archives of Ophthalmology**, 124(8), 1151-1162.
- [122] Vincenzo, P., Massimiliano, T., Geltrude, G., Monica, V., Sandro, S. and Stefano, P. (2008). Carotenoids and antioxidants in age-related maculopathy italian study : Multifocal electroretinogram modifications after 1 year. **Ophthalmology**, 115, 324-333.
- [123] Dagnelie, G., IsZorge, F. and McDonald, T. M. (2000). Lutein improves visual function in some patients with retinal degeneration: a pilot study via the Internet. **Optometry**, 71(3), 147-164.
- [124] Le Marchand, L., Hankin, J. H., Bach, F., Kolonel, L. N., Wilkens, L. R., Stacewicz-Sapuntzakis, M., et al. (1995). An ecological study of diet and lung cancer in the South Pacific. **International Journal of Cancer**, 63(1), 18-23.
- [125] Granado, F., Olmedilla, B., Gil-Martínez, E. and Blanco, I. (1998). Lutein ester in serum after lutein supplementation in human subjects. **The British Journal of Nutrition**, 80(05), 445-449.
- [126] González de Mejía, E., Ramos-Gómez, M. and Loarca-Piña, G. (1997). Antimutagenic activity of natural xanthophylls against aflatoxin B1 in *Salmonella typhimurium*. **Environmental and Molecular Mutagenesis**, 30(3), 346-353.
- [127] Madronich, S., McKenzie, R. L., Björn, L. O. and Caldwell, M. M. (1998). Changes in biologically active ultraviolet radiation reaching the Earth's surface. **Journal of Photochemistry and Photobiology B, Biology**, 46(1-3), 5-19.
- [128] Kulms, D. and Schwarz, T. (2000). Molecular mechanisms of UV-induced apoptosis. **Photodermatology, Photoimmunology & Photomedicine**, 16(5), 195-201.

- [129] Kochevar, I. E. (1990). UV-induced protein alterations and lipid oxidation in erythrocyte membranes. **Photochemistry and Photobiology**, 52(4), 795-800.
- [130] Ham, W. T., Mueller, H. A. and Sliney, D. H. (1976). Retinal sensitivity to damage from short wavelength light. **Nature**, 260(5547), 153-155.
- [131] West, S. K., Rosenthal, F. S., Bressler, N. M., Bressler, S. B., Munoz, B. and Fine, S. L. (1989). Exposure to sunlight and other risk factors for age-related macular degeneration. **Archives of Ophthalmology**, 107, 875 - 859.
- [132] Cruickshanks, K. J., Klein, R. and Klein, B. E. (1993). Sunlight and age-related macular degeneration. The Beaver Dam Eye Study. **Archives of Ophthalmology**, 111, 514 - 518.
- [133] Pham, T. Q., Rochtchina, E., Mitchell, P., Smith, W. and Wang, J. J. (2009). Sunlight-related factors and the 10-year incidence of age-related maculopathy. **Ophthalmic Epidemiology**, 16(2), 136-141.
- [134] Madronich, S., McKenzie, R. L., Björn, L. O. and Caldwell, M. M. (2003). Changes in biologically active ultraviolet radiation reaching the earth's surface. **Photochemical & Photobiological Sciences**, 2, 5-15.
- [135] Mosmann, T. (1983). Rapid colorimetric assay for cellular growth and survival: Application to proliferation and cytotoxicity assays. **Journal of Immunological Methods**, 65(1-2), 55-63.
- [136] Li, K., Wong, D., Hiscott, P., Stanga, P., Groenewald, C. and McGalliard, J. (2003). Trypan blue staining of internal limiting membrane and epiretinal membrane during vitrectomy: Visual results and histopathological findings. **British Journal of Ophthalmology**, 87(2), 216-219.
- [137] Tsuchiya, M., Suematsu, M. and Suzuki, H. (1994). In vivo visualization of oxygen radical-dependent photoemission. **Methods in Enzymology**, 233, 128-140.
- [138] Sharikabad, M. N., Østbye, K. M., Lyberg, T. and Brørs, O. (2001). Effect of extracellular Mg²⁺ on ROS and Ca²⁺ accumulation during reoxygenation of rat cardiomyocytes. **American Journal of Physiology - Heart and Circulatory Physiology**, 280(149-1), 344-353.

- [139] Wallin, B., Rosengren, B., Shertzer, H. G. and Camejo, G. (1993). Lipoprotein oxidation and measurement of thiobarbituric acid reacting substances formation in a single microtiter plate: Its use for evaluation of antioxidants. **Analytical Biochemistry**, 208(1), 10-15.
- [140] Prohaska, J. R. and Ganther, H. E. (1977). Glutathione peroxidase activity of glutathione S transferases purified from rat liver. **Biochemical and Biophysical Research Communications**, 76(2), 437-445.
- [141] Kakkar, P., Das, B. and Viswanathan, P. N. (1984). A modified spectrophotometric assay of superoxide dismutase. **Indian Journal of Biochemistry and Biophysics**, 21(2), 130-132.
- [142] Wong, R. C., Ngo, T. T. and Lenhoff, H. M. (1981). Formation of blue chromophore from oxidative coupling of aminoantipyrine with chromotropic acid in the presence of peroxide and horseradish peroxidase. **International Journal of Biochemistry**, 13(2), 159-163.
- [143] Guzikowski, A. P., Naleway, J. J., Shipp, C. T. and Schutte, R. C. (2000). Synthesis of a macrocyclic rhodamine 110 enzyme substrate as an intracellular probe for caspase 3 activity. **Tetrahedron Letters**, 41(24), 4733-4735.
- [144] Lakshminarayana, R., Raju, M., Krishnakantha, T. P. and Baskaran, V. (2005). Determination of major carotenoids in a few Indian leafy vegetables by high-performance liquid chromatography. **Journal of Agricultural and Food Chemistry**, 53(8), 2838-2842.
- [145] Gurr, J. R., Wang, A. S. S., Chen, C. H. and Jan, K. Y. (2005). Ultrafine titanium dioxide particles in the absence of photoactivation can induce oxidative damage to human bronchial epithelial cells. **Toxicology**, 213(1-2), 66-73.
- [146] Singh, S., Shi, T., Duffin, R., Albrecht, C., van Berlo, D., Höhr, D., et al. (2007). Endocytosis, oxidative stress and IL-8 expression in human lung epithelial cells upon treatment with fine and ultrafine TiO₂: Role of the specific surface area and of surface methylation of the particles. **Toxicology and Applied Pharmacology**, 222(2), 141-151.

- [147] Voinov, M. A., Pagán, J. O., Morrison, E., Smirnova, T. I. and Smirnov, A. I. (2011). Surface-mediated production of hydroxyl radicals as a mechanism of iron oxide nanoparticle biotoxicity. **Journal of the American Chemical Society**, 133(1), 35-41.
- [148] Shukla, R. K., Sharma, V., Pandey, A. K., Singh, S., Sultana, S. and Dhawan, A. (2011). ROS-mediated genotoxicity induced by titanium dioxide nanoparticles in human epidermal cells. **Toxicology in vitro**, 25(1), 231-241.
- [149] Kulms, D., Pöppelmann, B., Yarosh, D., Luger, T. A., Krutmann, J. and Schwarz, T. (1999). Nuclear and cell membrane effects contribute independently to the induction of apoptosis in human cells exposed to UVB radiation. **Proceedings of the National Academy of Sciences**, 96(14), 7974-7979.
- [150] Bongarzone, E. R., Pasquini, J. M. and Soto, E. F. (1995). Oxidative damage to proteins and lipids of CNS myelin produced by in vitro generated reactive oxygen species. **Journal of Neuroscience Research**, 41(2), 213-221.
- [151] Siu, T. L., Morley, J. W. and Coroneo, M. T. (2008). Toxicology of the retina: advances in understanding the defence mechanisms and pathogenesis of drug and light induced retinopathy. **Journal of Clinical & Experimental Ophthalmology**, 36(2), 176-185.
- [152] Ashkenazi, A. and Dixit, V. M. (1998). Death Receptors: Signaling and Modulation. **Science**, 281(5381), 1305-1308.
- [153] Rosette, C. and Karin, M. (1996). Ultraviolet light and osmotic stress: activation of the JNK cascade through multiple growth factor and cytokine receptors. **Science**, 15, 1194-1197.
- [154] Rehemtulla, A., Hamilton, C. A., Chinnaiyan, A. M. and Dixit, V. M. (1997). Ultraviolet Radiation-induced Apoptosis Is Mediated by Activation of CD-95 (Fas/APO-1). **Journal of Biological Chemistry**, 272(41), 25783-25786.
- [155] Pintea, A., Rugina, D. O., Pop, R., Bunea, A. and Socaciu, C. (2011). Xanthophylls protect against induced oxidation in cultured human retinal pigment epithelial cells. **Journal of Food Composition and Analysis**, 24(6), 830-836.

- [156] Lornejad-Schäfer, M. R., Lambert, C., Breithaupt, D. E., Biesalski, H. K. and Frank, J. (2007). Solubility, uptake and biocompatibility of lutein and zeaxanthin delivered to cultured human retinal pigment epithelial cells in tween40 micelles. **European Journal of Nutrition**, 46(2), 79-86.
- [157] Pintea, A., Preda, D., Braicu, C., Bunea, A. and Socaciu, C. (2007). Lutein and zeaxanthin uptake in cultured retinal pigmented epithelial cells. **Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca Veterinary Medicine**, 14, 238-243.
- [158] Mesley, R. J., Pocklington, W. D. and Walker, R. F. (1991). Analytical quality assurance. A review. **Analyst**, 116(10), 975-990.
- [159] Lakshminarayana, R., Aruna, G., Sangeetha, R. K., Bhaskar, N., Divakar, S. and Baskaran, V. (2008). Possible degradation/biotransformation of lutein in vitro and in vivo: isolation and structural elucidation of lutein metabolites by HPLC and LC-MS (atmospheric pressure chemical ionization). **Free Radical Biology and Medicine**, 45(7), 982-993.
- [160] Kanofsky, J. R. and Sima, P. D. (2006). Synthetic carotenoid derivatives prevent photosensitised killing of retinal pigment epithelial cells more effectively than lutein. **Experimental Eye Research**, 82(5), 907-914.
- [161] Kalariya, N. M., Ramana, K. V., Srivastava, S. K. and van Kuijk, F. J. G. M. (2011). Post-translational protein modification by carotenoid cleavage products. **BioFactors**, 37(2), 104-116.
- [162] Mortensen, A. and Skibsted, L. H. (1997). Free radical transients in photobleaching of xanthophylls and carotenes. **Free Radical Research**, 26(6), 549-563.
- [163] Krinsky, N. I. and Johnson, E. J. (2005). Carotenoid actions and their relation to health and disease. **Molecular Aspects of Medicine**, 26(6), 459-516.
- [164] Becker, E. M., Ntouma, G. and Skibsted, L. H. (2007). Synergism and antagonism between quercetin and other chain-breaking antioxidants in lipid systems of increasing structural organisation. **Food Chemistry**, 103(4), 1288-1296.

- [165] Veerman, E. C. I., Nazmi, K., Van 't Hof, W., Bolscher, J. G. M., Den Hertog, A. L. and Nieuw Amerongen, A. V. (2004). Reactive oxygen species play no role in the candidacidal activity of the salivary antimicrobial peptide histatin 5. **Biochemical Journal**, 381(2), 447-452.
- [166] Mantena, S. K. and Katiyar, S. K. (2006). Grape seed proanthocyanidins inhibit UV-radiation-induced oxidative stress and activation of MAPK and NF-[kappa]B signaling in human epidermal keratinocytes. **Free Radical Biology and Medicine**, 40(9), 1603-1614.
- [167] Zigler, J. S. and Goosey, J. D. (1984). Singlet oxygen as a possible factor in human senile nuclear cataract development. **Current Eye Research**, 3(1), 59-65.
- [168] Valko, M., Izakovic, M., Mazur, M., Rhodes, C. J. and Telser, J. (2004). Role of oxygen radicals in DNA damage and cancer incidence. **Molecular and Cellular Biochemistry**, 266(1), 37-56.
- [169] Foote, C. S. (1968). Mechanisms of photosensitized oxidation. There are several different types of photosensitized oxidation which may be important in biological systems. **Science (New York, NY)**, 162(857), 963-970.
- [170] Bonini, M. G., Rota, C., Tomasi, A. and Mason, R. P. (2006). The oxidation of 2',7'-dichlorofluorescein to reactive oxygen species: A self-fulfilling prophesy? **Free Radical Biology and Medicine**, 40(6), 968-975.
- [171] Conn, P. F., Schalch, W. and Truscott, T. G. (1991). The singlet oxygen and carotenoid interaction. **Journal of Photochemistry and Photobiology B: Biology**, 11(1), 41-47.
- [172] Santocono, M., Zurria, M., Berrettini, M., Fedeli, D. and Falcioni, G. (2006). Influence of astaxanthin, zeaxanthin and lutein on DNA damage and repair in UVA-irradiated cells. **Photochemistry and Photobiology**, 85(3), 205-215.
- [173] Chang, C. and Zheng, R. (2003). Effects of ultraviolet B on epidermal morphology, shedding, lipid peroxide, and antioxidant enzymes in Cope's rat snake (*Elaphe taeniura*). **Journal of Photochemistry and Photobiology B, Biology**, 72(1-3), 79-85.

- [174] Kowluru, R. A., Menon, B. and Gierhart, D. L. (2008). Beneficial effect of zeaxanthin on retinal metabolic abnormalities in diabetic rats. **Investigative Ophthalmology and Visual Science**, 49(4), 1645-1651.
- [175] Chow, C. K. (1991). Vitamin E and oxidative stress. **Free Radical Biology and Medicine**, 11(2), 215-232.
- [176] Mortensen, A. and Skibsted, L. H. (1997). Relative stability of carotenoid radical cations and homologue tocopheroxyl radicals. A real time kinetic study of antioxidant hierarchy. **FEBS Letters**, 417(3), 261-266.
- [177] Ryhänen, T., Mannermaa, E., Oksala, N., Viiri, J., Paimela, T., Salminen, A., et al. (2008). Radicol but not geldanamycin evokes oxidative stress response and efflux protein inhibition in ARPE-19 human retinal pigment epithelial cells. **European Journal of Pharmacology**, 584(2-3), 229-236.
- [178] Foussal, C., Lairez, O., Calise, D., Pathak, A., Guilbeau-Frugier, C., Valet, P., et al. (2010). Activation of catalase by apelin prevents oxidative stress-linked cardiac hypertrophy. **FEBS Letters**, 584(11), 2363-2370.
- [179] Zhu, L., Liu, Z., Feng, Z., Hao, J., Shen, W., Li, X., et al. (2010). Hydroxytyrosol protects against oxidative damage by simultaneous activation of mitochondrial biogenesis and phase II detoxifying enzyme systems in retinal pigment epithelial cells. **The Journal of Nutritional Biochemistry**, 21(11), 1089-1098.
- [180] Tate Jr, D. J., Miceli, M. V. and Newsome, D. A. (1999). Zinc protects against oxidative damage in cultured human retinal pigment epithelial cells. **Free Radical Biology and Medicine**, 26(5-6), 704-713.
- [181] Katiyar, S. K. and Meeran, S. M. (2007). Obesity increases the risk of UV radiation-induced oxidative stress and activation of MAPK and NF-[kappa]B signaling. **Free Radical Biology and Medicine**, 42(2), 299-310.
- [182] O'Connor, I. and O'Brien, N. (1998). Modulation of UVA light-induced oxidative stress by [beta]-carotene, lutein and astaxanthin in cultured fibroblasts. **Journal of Dermatological Science**, 16(3), 226-230.

- [183] Krishnaswamy, R., Devaraj, S. N. and Padma, V. V. (2010). Lutein protects HT-29 cells against deoxynivalenol-induced oxidative stress and apoptosis: Prevention of NF-[kappa]B nuclear localization and down regulation of NF-[kappa]B and cyclo-oxygenase - 2 expression. **Free Radical Biology and Medicine**, 49(1), 50-60.
- [184] Arthur, J. R. (2000). The glutathione peroxidases. **Cellular and Molecular Life Sciences**, 57(13-14), 1825-1835.
- [185] Polte, T. and Tyrrell, R. M. (2004). Involvement of lipid peroxidation and organic peroxides in UVA-induced Matrix Metalloproteinase-1 expression. **Free Radical Biology and Medicine**, 36(12), 1566-1574.
- [186] Black, A. T., Gray, J. P., Shakarjian, M. P., Laskin, D. L., Heck, D. E. and Laskin, J. D. (2008). Distinct effects of ultraviolet B light on antioxidant expression in undifferentiated and differentiated mouse keratinocytes. **Carcinogenesis**, 29(1), 219-225.
- [187] Sies, H. (1993). Ebselen, a selenoorganic compound as glutathione peroxidase mimic. **Free Radical Biology and Medicine**, 14(3), 313-323.
- [188] Holl, V., Coelho, D., Silbernagel, L., Keyser, J. F., Waltzinger, C., Dufour, P., et al. (2000). Prevention of nitrogen mustard-induced apoptosis in normal and transformed lymphocytes by ebselen. **Biochemical Pharmacology**, 60(11), 1565-1577.
- [189] Zhang, C., Baffi, J., Cousins, S. W. and Csaky, K. G. (2003). Oxidant-induced cell death in retinal pigment epithelium cells mediated through the release of apoptosis-inducing factor. **Journal of Cell Science**, 116(10), 1915-1923.
- [190] Seko, Y., Pang, J., Tokoro, T., Ichinose, S. and Mochizuki, M. (2001). Blue light-induced apoptosis in cultured retinal pigment epithelium cells of the rat. **Graefe's Archive for Clinical and Experimental Ophthalmology**, 239(1), 47-52.
- [191] Sparrow, J. R. and Cai, B. (2001). Blue light-induced apoptosis of A2E-containing RPE: Involvement of caspase-3 and protection by Bcl-2. **Investigative Ophthalmology & Visual Science**, 42(6), 1356-1362.

- [192] Rezai, K. A., Gasyna, E., Seagle, B. L. L., Norris Jr, J. R. and Rezaei, K. A. (2008). AcrySof Natural filter decreases blue light-induced apoptosis in human retinal pigment epithelium. **Graefe's Archive for Clinical and Experimental Ophthalmology**, 246(5), 671-676.
- [193] Xu, J. Y., Wu, L. Y., Zheng, X. Q., Lu, J. L., Wu, M. Y. and Liang, Y. R. (2010). Green tea polyphenols attenuating ultraviolet B-induced damage to human retinal pigment epithelial cells *in vitro*. **Investigative Ophthalmology & Visual Science**, 51(12), 6665-6670.
- [194] Thomson, L. R., Toyoda, Y., Delori, F. C., Garnett, K. M., Wong, Z. Y., Nichols, C. R., et al. (2002). Long term dietary supplementation with zeaxanthin reduces photoreceptor death in light-damaged Japanese Quail. **Experimental Eye Research**, 75(5), 529-542.
- [195] Stahl, W., Junghans, A., De Boer, B., Driomina, E. S., Briviba, K. and Sies, H. (1998). Carotenoid mixtures protect multilamellar liposomes against oxidative damage: Synergistic effects of lycopene and lutein. **FEBS Letters**, 427(2), 305-308.
- [196] Böhm, F., Edge, R., Lange, L. and Truscott, T. G. (1998). Enhanced protection of human cells against ultraviolet light by antioxidant combinations involving dietary carotenoids. **Journal of Photochemistry and Photobiology B: Biology**, 44(3), 211-215.
- [197] Miller, N. J., Sampson, J., Candeias, L. P., Bramley, P. M. and Rice-Evans, C. A. (1996). Antioxidant activities of carotenes and xanthophylls. **FEBS Letters**, 384(3), 240-242.

APPENDIX

Table 1 Effect of UV-B on ARPE-19 cell viability at 12 h. after UV-B exposure
(For the Figure 3)

UV-B Dose (mJ/cm ²)	% cell viability			Mean ± SEM
	N1	N2	N3	
0	10.00	100.00	100.01	100.00± 0.01
20	89.53	85.81	90.99	88.78 ± 1.54
40	82.57	85.88	74.98	81.14 ± 3.23
80	73.26	85.00	66.84	75.03 ± 5.32
100	76.37	70.77	64.66	70.60 ± 3.38
120	66.89	68.84	59.15	64.96 ± 2.96
150	62.44	61.56	55.32	59.78 ± 2.24
200	57.29	68.65	54.34	60.10 ± 4.36
250	57.15	61.11	51.27	56.51 ± 2.86
500	58.30	69.92	50.78	59.67 ± 5.57

Table 2 Effect of UV-B on ARPE-19 cell viability at 24 h. after UV-B exposure
(For the Figure 3)

UV-B Dose (mJ/cm ²)	% cell viability			Mean ± SEM
	N1	N2	N3	
0	100.00	100.00	100.01	100.00± 0.01
20	92.63	92.63	107.80	96.30 ± 5.87
40	79.26	79.26	98.46	86.01 ± 6.24
80	76.37	76.37	83.68	75.73 ± 4.78
100	63.40	63.40	73.81	66.21 ± 3.84
120	58.59	58.59	61.07	59.75 ± 0.72
150	53.03	53.03	56.23	55.05 ± 1.02
200	47.14	47.14	52.10	50.86 ± 1.89
250	47.79	47.79	49.34	49.13 ± 0.72
500	55.56	55.56	51.54	54.07 ± 1.27

Table 3 Effect UV-B on ARPE-19 cell viability at 24 h. after UV-B exposure investigated by MTT and Trypan blue assay (For the Figure 4)

MTT assay	% cell viability				Mean	±	SEM
UV-B (mJ/cm ²)	N1	N2	N3	N4			
0	99.99	99.99	100.00	99.99	99.99	±	0.00
20	102.85	85.19	96.94	94.13	94.78	±	4.25
40	98.22	74.63	92.72	72.47	84.51	±	7.44
80	84.01	76.14	87.96	67.99	79.03	±	5.11
150	80.82	48.84	-	-	64.82	±	-

Trypan blue	% cell viability				Mean	±	SEM
UV-B (mJ/cm ²)	N1	N2	N3	N4			
0	100.00	100.00	100.00	100.00	99.99	±	0.00
20	90.74	97.54	64.77	-	94.78	±	4.25
40	77.78	66.39	62.12	-	84.51	±	7.44
80	72.22	54.92	36.36	-	79.03	±	5.11
150	38.00	-	-	36.75	79.03	±	

Table 4 Effect of silk lutein extract, maligold or trolox (10 μ M) for 24 h on UV-B irradiated ARPE-19 cell viability at 24 h. after UV-B exposure (For the figure 5A)

UV-B (mJ/cm ²)	No antioxidant			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
0	100.00	100.00	100.00	100.0	±	0.00
20	68.37	89.62	76.92	78.3	±	6.17
40	55.35	66.04	68.38	63.3	±	4.01
80	46.51	51.89	59.83	52.7	±	3.87
UV-B (mJ/cm ²)	Silk lutein extract (10 μM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
0	101.86	82.55	135.04	106.48	±	5.33
20	70.47	64.47	85.47	73.47	±	6.25
40	53.02	78.62	85.47	72.37	±	9.87
80	54.42	61.32	52.99	56.24	±	2.57

Table 4 (Cont.)

UV-B (mJ/cm ²)	C-lutein (10 μM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
0	93.95	92.77	99.15	95.29	±	1.96
20	62.79	74.29	83.76	73.61	±	6.06
40	46.98	72.33	67.95	62.42	±	7.82
80	53.02	63.68	52.56	56.42	±	3.63
UV-B (mJ/cm ²)	Trolox (10 μM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
0	97.67	99.06	111.11	102.61	±	4.27
20	71.86	77.04	94.02	80.97	±	6.69
40	62.33	74.29	76.92	71.18	±	4.49
80	56.28	71.54	51.28	59.70	±	6.09

Table 5 Effect of with silk lutein, trolox or their combination (50 μ M) for 24 h on UV-B irradiated ARPE-19 cell viability at 24 h after UV-B exposure (For the Figure 5B)

UV-B (mJ/cm ²)	No antioxidant			Mean	± SEM
	% cell viability				
	N1	N2	N3		
0	100.00	100.00	100.00	100.00	± 0.00
20	90.74	97.54	64.77	84.35	± 9.98
40	77.78	66.39	62.12	68.76	± 4.67
80	72.78	54.92	36.36	54.35	± 11.98
UV-B (mJ/cm ²)	Silk lutein extract (50 μM)			Mean	± SEM
	% cell viability				
	N1	N2	N3		
0	114.81	108.20	115.15	112.72	± 2.26
20	100.00	61.48	74.24	78.57	± 11.33
40	101.85	68.85	69.70	80.13	± 10.86
80	85.19	55.08	54.55	64.94	± 10.13

Table 5 (Cont.)

UV-B (mJ/cm ²)	C-lutein (50 μM)			Mean	± SEM
	% cell viability				
	N1	N2	N3		
0	83.33	78.69	45.45	69.16	± 11.93
20	85.19	65.57	36.36	62.37	± 14.18
40	50.00	55.74	34.85	46.86	± 6.23
80	60.00	58.03	21.21	46.41	± 12.61
UV-B (mJ/cm ²)	Trolox (50 μM)			Mean	± SEM
	% cell viability				
	N1	N2	N3		
0	112.96	97.54	95.45	101.99	± 5.52
20	100.00	83.61	84.09	89.23	± 5.39
40	96.30	79.92	70.45	82.22	± 7.55
80	72.22	62.70	60.61	65.18	± 3.57

Table 6 Effect of silk lutein, trolox or their combination (50 μ M) for 24 h on UV-B irradiated ARPE-19 cell viability at 24 h. after UV-B exposure (For the Figure 7)

UV-B (mJ/cm ²)	No antioxidant			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
0	100	100	100.00	100.00	±	0.00
20	74.29	111.43	81.97	89.23	±	13.86
40	54.29	81.43	59.02	64.91	±	10.25
80	38.57	58.57	60.66	52.60	±	8.62

UV-B (mJ/cm ²)	Trolox (50 μM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
0	108.57	124.29	91.80	108.22	±	11.49
20	88.57	87.14	78.69	84.80	±	3.78
40	57.14	80.00	68.85	68.67	±	8.08
80	52.86	82.86	72.13	69.28	±	10.75

Table 6 (Cont.)

UV-B (mJ/cm ²)	S-lutein (50 μM)			Mean	± SEM
	% cell viability				
	N1	N2	N3		
0	97.14	101.43	104.92	101.16	± 2.75
20	84.29	87.14	91.80	87.74	± 2.68
40	78.57	74.29	78.69	77.18	± 1.77
80	50.00	64.29	77.05	63.78	± 9.57
UV-B (mJ/cm ²)	Lutein+Trolox (50 μM each)			Mean	± SEM
	% cell viability				
	N1	N2	N3		
0	107.14	98.57	88.52	88.52	± 6.59
20	72.86	92.86	90.16	90.16	± 7.67
40	62.86	78.57	68.85	68.85	± 5.61
80	71.43	61.43	65.57	65.57	± 3.55

Table 7 Effect of pretreatment with silk lutein extract (50 μ M) for 2, 4, 12 and 24 h in culture ARPE-19 cell viability at 24 h after UV-B exposure. (For the Figure 8)

UV-B (0 mJ/cm ²)	Control		Mean±SEM		
	% cell viability				
	N1	N2			
2 h	100.01	99.99	100.00	±	0.01
4 h	100.00	99.99	100.00	±	0.01
12 h	100.01	100.00	100.00	±	0.00
24 h	100.01	100.00	100.00	±	0.00
UV-B (40 mJ/cm ²)	Lutein (50 μM)		Mean±SEM		
	% cell viability				
	N1	N2			
2 h	51.70	80.19	65.94	±	20.15
4 h	60.83	59.20	60.01	±	1.16
12 h	52.03	62.50	57.27	±	7.40
24 h	50.58	64.44	57.51	±	9.80
UV-B (40 mJ/cm ²)	Control		Mean±SEM		
	% cell viability				
	N1	N2			
2 h	38.99	46.53	42.76	±	5.33
4 h	45.83	47.20	46.51	±	0.96
12 h	45.95	47.92	42.76	±	1.39
24 h	43.61	56.11	49.86	±	8.84

Table 8 Effect of UV-B induced intracellular ROS in ARPE-19 cell at 0.5, 1, and 24 h after UV-B exposure (For the figure 10)

UV-B (mJ/cm ²)	ROS level (ratio of control) 30 min			Mean±SEM		
	N1	N2	N3			
0	1.00	1.00	1.00	1.00	±	0.00
20	1.67	1.61	1.49	1.59	±	0.05
40	1.98	2.19	2.09	2.09	±	0.06
80	3.07	3.06	2.85	2.99	±	0.07

UV-B (mJ/cm ²)	ROS level (ratio of control) 60 min			Mean±SEM		
	N1	N2	N3			
0	1.00	1.00	1.00	1.00	±	0.00
20	1.38	1.22	1.30	1.30	±	0.05
40	1.56	1.34	1.33	1.41	±	0.08
80	2.09	1.61	1.40	1.70	±	0.20

UV-B (mJ/cm ²)	ROS level (ratio of control) 24 min			Mean±SEM		
	N1	N2	N3			
0	1.00	1.00	1.00	1.00	±	0.00
20	1.24	1.18	1.20	1.21	±	0.02
40	1.18	1.15	1.31	1.21	±	0.05
80	1.35	1.17	1.31	1.28	±	0.06

Table 9 Effect of UV-B induced lipid peroxidation in ARPE-19 at 24 h after UV-B exposure (For the figure 12)

UV-B (mJ/cm ²)	MDA level (ratio of control) control			Mean±SEM		
	N1	N2	N3			
0	1.00	1.00	1.00	1.00	±	0.00
20	1.35	0.97	1.51	1.28	±	0.07
40	1.96	1.35	2.22	1.84	±	0.11
80	4.08	1.93	2.00	2.67	±	0.52

Table 10 Effect of pretreatment with silk lutein extract (50 µM), standard lutein (50 µM) or trolox (50 µM) or their combination (25 µM each) for 4 h in culture ARPE-19 cell viability at 24 h. after UV-B exposure (For the figure 9A)

UV-B (0 mJ/cm ²)	(Antioxidant 25 μM)			Mean	± SEM
	% cell viability				
	N1	N2	N3		
Control	100.00	100.00	100.00	100.00	± 0
Silk lutein	113.25	116.22	116.25	115.24	± 1.0
Std. lutein	121.29	113.56	92.95	109.27	± 8.5
Trolox	120.48	101.80	111.25	111.18	± 5.4
Silk lutein+Trolox	131.33	72.29	102.50	102.04	± 17.0
Std. lutein+Trolox	112.90	99.15	100.00	104.02	± 4.4

Table 10 (Cont.)

UV-B (40 mJ/cm ²)	(Antioxidant 25 μM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
Control	51.81	51.35	57.50	53.55	±	2.0
Silk lutein	77.11	71.17	70.00	72.76	±	2.2
Std. lutein	68.72	77.97	68.72	71.80	±	3.1
Trolox	86.75	72.07	72.50	77.11	±	4.8
Silk lutein+Trolox	80.72	74.77	68.75	74.75	±	3.5
Std. lutein+Trolox	106.45	82.20	68.72	85.79	±	11.0

Table 11 Effect of pretreatment with silk lutein (50 µM), standard lutein (50 µM) or trolox (50 µM) and their combination (25 µM each) for 4 h in culture ARPE-19 cell viability at 24 h. after UV-B exposure (For the figure 9B)

UV-B (0 mJ/cm ²)	(Antioxidant 50µM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
Control	100.00	100.00	100.00	100.00	±	0
Silk lutein	113.25	116.22	116.25	115.24	±	1.0
Std. lutein	121.29	113.56	92.95	109.27	±	8.5
Trolox	120.48	101.80	111.25	111.18	±	5.4
Silk lutein+Trolox	131.33	72.29	102.50	102.04	±	17.0
Std. lutein+Trolox	112.90	99.15	100.00	104.02	±	4.4

Table 11 (Cont.)

UV-B (40 mJ/cm ²)	(Antioxidant 50 μM)			Mean	± SEM	
	% cell viability					
	N1	N2	N3			
Control	51.81	51.35	57.50	53.55	±	2.0
Silk lutein	77.11	71.17	70.00	72.76	±	2.2
Std. lutein	68.72	77.97	68.72	71.80	±	3.1
Trolox	86.75	72.07	72.50	77.11	±	4.8
Silk lutein+Trolox	80.72	74.77	68.75	74.75	±	3.5
Std. lutein+Trolox	106.45	82.20	68.72	85.79	±	11.0

Table 12 Effect of pretreatment with silk lutein (50 µM), standard lutein (50 µM) or trolox (50 µM) or their combination (25 µM each) for 4 h in ROS production in ARPE-19 cell at 24 h after UV-B exposure (For the figure 11)

UV-B (0 mJ/cm ²)	ROS level (ratio of control)			Mean	± SEM	
	N1	N2	N3			
Control	1.00	1.00	1.00	1.00	±	0.00
Silk lutein	0.76	0.81	0.81	0.79	±	0.02
Std. lutein	0.64	0.79	0.81	0.75	±	0.05
Trolox	0.73	0.73	0.76	0.74	±	0.01
Silk lutein+Trolox	0.72	0.74	0.78	0.75	±	0.02
Std. lutein+Trolox	0.61	0.70	0.75	0.69	±	0.04

Table 12 (Cont.)

UV-B (40 mJ/cm ²)	ROS level (ratio of control)			Mean	± SEM
	N1	N2	N3		
Control	2.21	2.23	2.05	2.16	± 0.06
Silk lutein	2.01	1.84	1.77	1.87	± 0.07
Std. lutein	1.42	1.50	1.69	1.54	± 0.08
Trolox	2.09	1.75	1.59	1.81	± 0.15
Silk lutein+Trolox	1.97	1.75	1.65	1.79	± 0.09
Std. lutein+Trolox	1.26	1.37	1.54	1.39	± 0.08

Table 13 Effect of pretreatment with silk lutein (50 µM), standard lutein (50 µM) or trolox (50 µM) or their combination (25 µM each) for 4 h in lipid peroxidation in ARPE-19 cells at 24 h after UV-B exposure (For the figure 13)

UV-B (0 mJ/cm ²)	MDA level (ratio of control)			Mean	± SEM
	N1	N2	N3		
Control	1.00	1.00	1.00	1.00	± 0.00
Silk lutein	0.84	0.79	0.92	0.85	± 0.04
Std. lutein	0.75	0.70	0.88	0.78	± 0.05
Trolox	0.74	1.10	0.99	0.94	± 0.11
Silk lutein+Trolox	0.69	0.77	1.06	0.84	± 0.11
Std. lutein+Trolox	1.00	1.00	1.00	1.00	± 0.00

Table 13 (Cont.)

UV-B (40 mJ/cm ²)				Mean ± SEM		
	N1	N2	N3			
Control	1.90	1.94	1.51	1.78	±	0.14
Silk lutein	0.95	1.29	1.33	1.19	±	0.12
Std. lutein	0.77	0.78	1.12	0.89	±	0.11
Trolox	1.06	1.34	1.16	1.19	±	0.08
Silk lutein+Trolox	0.91	1.19	1.46	1.19	±	0.16
Std. lutein+Trolox	0.76	0.90	1.04	0.90	±	0.08

Table 14 Effect of pretreatment with silk lutein extract (50 µM), standard lutein (50 µM) or trolox (50 µM) or their combination (25 µM each) for 4 h SOD activity in ARPE-19 cell at 24 h after UV-B exposure (For the figure 15)

UV-B (0 mJ/cm ²)	SOD activity			Mean ± SEM		
	N1	N2	N3			
Control	100.00	100.00	100.00	100.00	±	0.00
Silk lutein	100.34	94.78	95.23	96.79	±	1.78
Std. lutein	99.89	93.32	86.76	93.32	±	3.79
Trolox	100.56	81.43	83.34	88.44	±	6.08
Silk lutein+Trolox	100.75	86.00	87.95	91.57	±	4.62
Std. lutein+Trolox	101.10	82.88	93.68	92.55	±	5.29

Table 14 (Cont.)

UV-B (40 mJ/cm ²)				Mean	±	SEM
	N1	N2	N3			
Control	80.28	79.80	90.90	83.66	±	3.62
Silk lutein	98.76	81.18	97.02	92.32	±	5.59
Std. lutein	102.07	89.24	75.15	88.82	±	7.77
Trolox	100.02	85.33	89.72	91.69	±	4.36
Silk lutein+Trolox	100.64	70.23	99.21	90.03	±	9.91
Std. lutein+Trolox	100.69	75.94	80.16	85.60	±	7.65

Table 15 Effect of UV-B on catalase activity in ARPE-19 cell at 1, 4, and 24 h after UV-B exposure (For the figure 16)

UV-B (0 mJ/cm ²)	CAT unit/mgprotein			Mean	±	SEM
	N1	N2	N3			
1 h	38.9	31.7	20.9	30.5	±	5.2
4 h	39.2	31.2	30.4	33.6	±	2.8
24 h	40.0	50.9	36.1	42.3	±	4.4

UV-B (40 mJ/cm ²)	CAT unit/mgprotein			Mean	±	SEM
	N1	N2	N3			
1 h	39.00442	40.46241	39.24697	39.57	±	0.45
4 h	37.45923	37.08043	36.3528	36.96	±	0.32
24 h	34.44244	23.42445	23.64247	27.17	±	3.64

Table 16 Effect of pretreatment with silk lutein extract (50 µM), standard lutein (50 µM) or trolox (50 µM) and their combination (25 µM each) for 4 h on catalase activity in ARPE-19 cell at 1 h after UV-B exposure (For the figure 17A)

UV-B (0 mJ/cm ²)	CAT unit/mgprotein			Mean	±	SEM
2 h	N1	N2	N3			
Control	29.02747	23.41628	31.74722	15.49	±	4.44
Silk lutein	25.09773	25.32937	25.7763	14.14	±	3.20
Std. lutein	23.0729	27.26699	33.00626	13.34	±	4.17
Trolox	25.92619	25.45745	32.47212	15.55	±	2.58
Silk lutein+ Trolox	27.04897	25.57736	24.39463	13.10	±	0.92
Std. lutein+Trolox	31.01141	24.98599	31.54555	15.93	±	2.64

UV-B (40 mJ/cm ²)	CAT unit/mgprotein			Mean	±	SEM
2h	N1	N2	N3			
Control	32.38219	33.64123	35.66878	28.06	±	2.45
Silk lutein	28.68954	24.68622	25.41385	25.40	±	0.20
Std. lutein	31.17492	24.31287	34.5896	27.78	±	2.88
Trolox	25.58281	29.63791	23.96949	27.95	±	2.26
Silk lutein+Trolox	23.7106	27.39507	29.10105	25.67	±	0.77
Std. lutein+Trolox	32.47757	17.86777	20.27957	29.18	±	2.10

Table 17 Effect of pretreatment with silk lutein (50 μM), standard lutein (50 μM) or trolox (50 μM) and their combination (25 μM each) for 4 h on catalase activity in ARPE-19 cell at 24 h after UV-B exposure. (For the figure 17B)

UV-B (0 mJ/cm ²)		CAT unit/mgprotein			Mean $\pm$ SEM	
24 h	N1	N2	N3			
Control	33.54	33.41	35.66	34.20	$\pm$	0.73
Silk lutein	38.43	35.18	43.03	38.88	$\pm$	2.28
Std. lutein	34.15	27.95	34.98	32.36	$\pm$	2.22
Trolox	34.60	30.88	32.88	32.79	$\pm$	1.07
Silk lutein+Trolox	44.54	34.86	39.95	39.78	$\pm$	2.79
Std. lutein+Trolox	36.91	40.15	35.85	37.64	$\pm$	1.29

UV-B (40 mJ/cm ²)		CAT unit/mgprotein			Mean $\pm$ SEM	
24 h	N1	N2	N3			
Control	25.11	18.55	25.37	23.01	$\pm$	2.23
Silk lutein	32.99	27.94	37.58	32.84	$\pm$	2.79
Std. lutein	30.34	23.04	35.39	29.59	$\pm$	3.59
Trolox	27.17	28.64	31.64	29.15	$\pm$	1.32
Silk lutein+ Trolox	30.09	35.47	36.61	34.06	$\pm$	2.01
Std. lutein+Trolox	23.62	28.90	34.75	29.09	$\pm$	3.21

Table 18 Effect of pretreatment with silk lutein extract (50 μM), standard lutein (50 μM) or trolox (50 μM) and their combination (25 μM each) for 4 h on glutathione peroxidase activity in ARPE-19 cell at 24 h after UV-B exposure (For the figure 18)

UV-B (0 mJ/cm ²)		GPx unit/mgprotein			Mean $\pm$ SEM	
24 h	N1	N2	N3			
Control	5.00	3.74	4.87	4.54	$\pm$	0.40
Silk lutein	3.96	5.58	5.20	4.92	$\pm$	0.49
Std. lutein	1.36	3.96	6.36	3.90	$\pm$	1.44
Trolox	1.41	3.16	6.16	3.58	$\pm$	1.39
Silk lutein+Trolox	1.54	3.23	5.15	3.31	$\pm$	1.04
Std. lutein+Trolox	3.26	4.12	4.07	3.81	$\pm$	0.28

UV-B (40 mJ/cm ²)		GPx unit/mgprotein			Mean $\pm$ SEM	
24 h	N1	N2	N3			
Control	5.81	9.09	9.57	8.16	$\pm$	1.18
Silk lutein	3.54	5.71	4.92	4.72	$\pm$	0.64
Std. lutein	4.82	4.29	5.03	4.71	$\pm$	0.22
Trolox	4.60	5.96	5.13	5.23	$\pm$	0.40
Silk lutein+Trolox	5.13	6.19	5.38	5.56	$\pm$	0.32
Std. lutein+Trolox	3.23	4.92	5.03	4.39	$\pm$	0.58

Table 19 Effect of pretreatment with silk lutein extract (50 µM), standard lutein (50 µM),trolox(50 µM) or their combination (25 µM each) for 4 h caspase 3 activity in ARPE-19 cell at 24 h after UV-B exposure (For the figure 19)

UV-B (0 mJ/cm ²)	Fluorescent value			Mean	± SEM
	N1	N2	N3		
Control	52619	60908	65582	56764	± 3790
Silk lutein	60518	61498	70104	61008	± 3045
Std. lutein	57531	68625	67941	63078	± 3589
Trolox	53094	68015	68229	60554	± 5010
Silk lutein+Trolox	60040	67714	67557	63877	± 2532
Std. lutein+Trolox	62674	79429	69331	71051	± 4871

UV-B (40 mJ/cm ²)	Fluorescent value			Mean	± SEM
	N1	N2	N3		
Control	95498	88461	81129	91979	± 4148
Silk lutein	69376	75749	69730	72562	± 2068
Std. lutein	70147	80172	65867	75160	± 4239
Trolox	66542	80620	64896	73581	± 4990
Silk lutein+Trolox	58687	78735	67991	68711	± 5792
Std. lutein+Trolox	65386	78251	63604	71818	± 4614

Table 20 Effect of pre-incubation of silk lutein extract (25 µM) standard lutein (25 µM) with and without vitamin E in culture serum free DMEM/12 for 4 h analysis by HPLC (For the figure 20)

Lutein with trolox	% lutein remaining			Mean	±	SEM
	N1	N2	N3			
Silk lutein	106.67	93.33	100.00	100.00	±	3.85
Std. lutein	116.35	105.59	106.51	109.49	±	3.44

Lutein without trolox	% lutein remaining			Mean	±	SEM
	N1	N2	N3			
Silk lutein	80.00	70.00	86.67	78.89	±	4.84
Std. lutein	75.35	94.45	71.83	80.54	±	7.03

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