



UNIVERSIDAD COMPLUTENSE  
MADRID

## **Scientific evidence of RETICARE**

**Selection of scientific studies, reviews and doctoral thesis regarding  
blue-light phototoxicity and photo-protection through selective  
absorbance filters for visible radiation.**

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## SELECTION OF SCIENTIFIC STUDIES

**1. Noell, W.K., et al., Retinal damage by light in rats. Invest Ophthalmol, 1966. 5(5): p. 450-73.**

In 1965, Noell states that the retinae of albino rats can be irreversibly damaged when exposing them for hours or days to environmental light inside the intensity range of natural light. In pigmented rats, the damage can be the same as in albino ones when the pupils are dilated. –Animal testing.

**2. Ham WT Jr, Ruffolo JJ Jr, Mueller HA, Clarke AM, Moon ME. Histologic analysis of photochemical lesions produced in rhesus retina by short-wave-length light. Invest Ophthalmol Vis Sci. 1978. 17(10):1029-35.**

Retinal lesions caused by prolonged exposure (1,000 seconds) to low power levels of blue light (441 nm) on the cornea (62 mW) was evaluated by microscopy in 20 eyes of rhesus monkeys. Exposure took place in the time interval between 1 hour and 90 days. The results indicate that the exposure generates a non-thermal photochemical injury in the retinal pigment epithelium and it leads to a histological response with hypopigmentation, which requires 48 hours to appear. This type of injury helps explain solar retinitis and solar eclipse blindness, and it also has a significant relationship with age-dependent retinal degenerative changes.

**3. Ham, W.T., Jr., et al., Sensitivity of the retina to radiation damage as a function of wavelength. Photochem Photobiol, 1979. 29(4): p. 735-43.**

In 1979, Ham shows that the short visible-light wavelengths cause photochemical damage in the retina. – Animal testing.

**4. Sánchez-Ramos, C., et al., Role of Metalloproteases in Retinal Degeneration Induced by Violet and Blue Light. Retinal Degenerative Diseases. Advances in Experimental and Biology, 2010. 664: p.159-164.**

The results in this study shows that the exposure to long periods of light, in a circadian cycle, increases the expression of some MMP, which could have some harmful effects in the retina, as it shows the extracellular matrix damage. The increase in MMP expression could take place in order to avoid the accumulation of metabolic debris in the extracellular matrix. – Animal testing.

**5. Sparrow, J.R., A.S. Miller, and J. Zhou, Blue light-absorbing intraocular lens and retinal pigment epithelium protection in vitro. J Cataract Refract Surg, 2004. 30(4): p. 873-8.**

This is the first study to show the protective effect of intraocular lenses with yellow optic filters. In cells with the fluorophore A2E the cell survival is a  $41\pm 4\%$  lower, while cells free of that fluorophore A2E survive after being radiated with the different selected



radiations. However, in presence of intraocular lenses with short-wavelength selective absorption filters there is even a less cell death rate. – Study in-vitro.

**6. Yanagi, Y., et al., Effects of yellow intraocular lenses on light-induced upregulation of vascular endothelial growth factor. J Cataract Refract Surg, 2006. 32(9): p. 1540-4.**

This study concludes that an intraocular lens (IOL) with a selective absorption filter for blue light could be more protective against the photochemical damage induced by A2E, and inhibit the light-induced production of VEGF, than a conventional IOL with a UV filter.

**7. Rezai, K.A., et al., AcrySof Natural filter decreases blue light-induced apoptosis in human retinal pigment epithelium. Graefes Arch Clin Exp Ophthalmol, 2008. 246(5): p. 671-6.**

Lenses AcrySof with a natural filter (absorbance for short visible-light wavelengths) causes a significant reduction in the apoptosis induced by blue light. This is because of the short-wavelength light filtering, which reduces the energy reaching the cells. In patients with cataracts, with a high AMD risk, it must be considered the implantation of an intraocular lens with short-wavelength absorption filter to absorb the blue light.

**8. Hui, S., L. Yi, and Q.L. Fengling, Effects of light exposure and use of intraocular lens on retinal pigment epithelial cells in vitro. Photochem Photobiol, 2009. 85(4): p. 966-9.**

This study suggests that intraocular lenses which filter the short wavelengths can be more protective against the A2E-induced phototoxic damage; at the same time, they inhibit the generation of reactive oxygen species (ROS) and the production of VEGF, in comparison to a conventional intraocular lens with UV absorption.

**9. Kernt, M., et al., Cytoprotective effects of a blue light-filtering intraocular lens on human retinal pigment epithelium by reducing phototoxic effects on vascular endothelial growth factor-alpha, Bax, and Bcl-2 expression. J Cataract Refract Surg, 2009. 35(2): p. 354-62.**

Both types of intraocular lenses (IOL), those with a UV filter and those with an additional short-wavelengths absorbance filter, reduce the damage in the retinal pigment epithelium. This study supports the hypothesis that IOLs with blue-light absorption filters and prevents retinal damage.

**10. Mukai, K., et al., Photoprotective effect of yellow-tinted intraocular lenses. Jpn J Ophthalmol, 2009. 53(1): p. 47-51.**

The visible light causes photo-oxidation, and damage in intraocular tissues in-vitro. These results suggest that the effectiveness of tinted IOLs, which inhibit the tissue damage due to the visible light.



**11. Sánchez-Ramos C. Optic Filters blocking the negative effects of phototoxicity in the visible spectrum in the retina. Animal testing. Doctoral Thesis (Abstract) 2010**

The results of this doctoral thesis demonstrate the effectiveness of selective absorbance filters to neutralize the harmful effect of light on the retina, preventing changes that cause retinal damage. In this study, two different analysis are carried out, on one hand an structural analysis, where cells and retinal neurons affected are counted after exposure to light of different spectral composition and, on the other hand, a genetic study of proto-oncogenes, anti and pro-apoptotic genes, metalloproteases, calcium-binding proteins, the Trk-B, BDNF receptor and TIMP-1 and TIMP-2, all genes involved in the apoptotic process and retinal damage.

**12. Chamorro E. The effects of yellow intraocular lenses on retinal phototoxicity damage. Analysis of the macular thickness via Optical Coherence Tomography. Doctoral Thesis (Abstract) 2012**

It is an observational, descriptive and comparative study consisting of 3 phases separated by intervals of 2 and 5 years (2006, 2008, 2011), where differences in macular thickness between eyes was measured in each of the phases (cross-sectional studies) and differences in the evolution of macular thickness over time (longitudinal studies). The sample consists of individuals who have been implanted with a clear IOL in one eye and IOL with selective filter for blue light absorption in the contralateral eye. The main conclusion is the evidence of a decrease in macular thickness in eyes with clear intraocular implants after 5 years, while macular thickness in eyes with yellow IOLs have no macular thickness decreased during the same period of evolution.

**13. Chamorro, E., et al., Effects of Light-emitting Diode Radiations on Human Retinal Pigment Epithelial Cells In Vitro. Photochem Photobiol, 2013. 89(2): p. 468-73**

Paper about Neuro-Computing and Neuro-Robotics experiment on human retinal pigment epithelial cells exposed to LED lighting.

**14. Wu, J.M., S. Seregard, and P.V. Algvere, Photochemical damage of the retina. Survey of Ophthalmology, 2006. 51(5): p. 461-481.**

Bibliographical review on the retinal damage nature, the damage induced by the blue light, retinal-damage liable factors, etc.

**15. Algvere, P.V., J. Marshall, and S. Seregard, Age-related maculopathy and the impact of blue light hazard. Acta Ophthalmol Scand, 2006. 84(1): p. 4-15.**

Bibliographical review on phototoxicity induced by the blue light, retinal damage in pseudophakic eyes, as well as artificial-protection mechanisms.



**16. Zhu, X.-f., et al., Comparison of Blue Light-Filtering IOLs and UV Light-Filtering IOLs for Cataract Surgery: A Meta-Analysis. Plos One, 2012. 7(3).**

Bibliographical review on blue light filtering intraocular lens.

**17. Schwartz SG, Gombos DS, Schneider S: Light Toxicity in the Posterior Segment. In: Duane's Ophthalmology. Edited by Tasman W, Jaeger EA: Lippincott Williams & Wilkins; 2005.**

Bibliographical review on phototoxicity induced by the blue light.

**18. Behar-Cohen F, Martinsons C, Vienot F, Zissis G, Barlier-Salsi A, Cesarini JP, Enouf O, Garcia M, Picaud S, Attia D: Light-emitting diodes (LED) for domestic lighting: any risks for the eye? Prog Retin Eye Res 2011, 30(4):239-257.**

Bibliographical review on phototoxicity induced by Light-emitting diodes (LED).

**19. Sánchez-Ramos C, Bonnin-Arias C, Guerrero MC, et al. Light regulates the expression of the BDNF/TrkB system in the adult zebrafish retina. Microsc Res Tech. 2013. 76(1):42-9**

Paper regarding the effects of exposure for 10 days to white light and white light with a higher proportion of short wavelengths and blue light, circadian cycle (12 h light / 12 h dark) or 24 hours continuous as well as 10 days of total darkness, on expression of BDNF and TrkB in zebrafish retina.

**20. Sánchez-Ramos C, Guerrero MC, Bonnin-Arias C, et al. Expression of TRPV4 in the zebrafish retina during development. Microsc Res Tech. 2012. 75(6):743-8**

In this study the expression and distribution of TRPV4 is investigated in the zebrafish retina, from the first 3 days after fertilization (dpf) to 100 dpf.