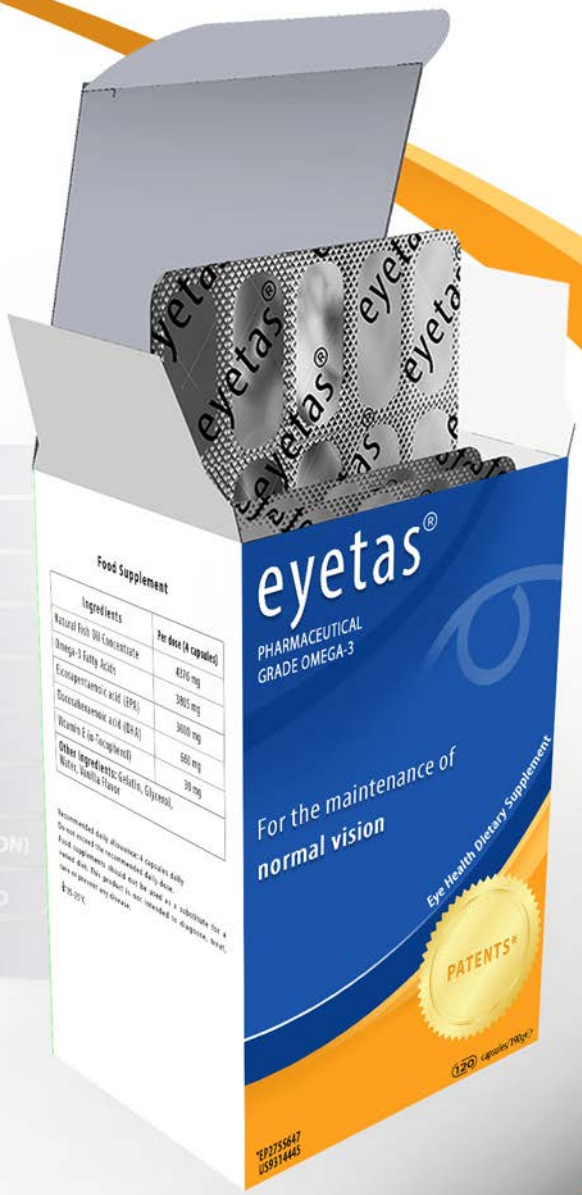

eyetas®
Nutritional · Innovative · Eye Health




97%
EPA and DHA
Moleculary
Distilled
Omega-3
Ultra
Purified
Therapeutic
Dose
EPA/DHA
3.7g
EPA/DHA

1 eyetas® MECHANISM OF ACTION

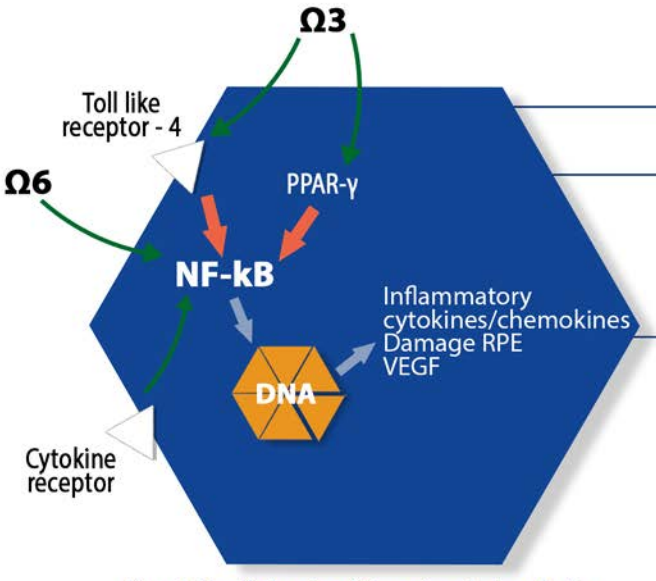


Figure 1: Simplified version of Omega-3 mechanism of action
Fig. adapted from Sears B, Ricordi C. 2012

TISSUE DAMAGE REPAIR

REGENERATION

IMPROVES VISION - CLINICALLY TESTED

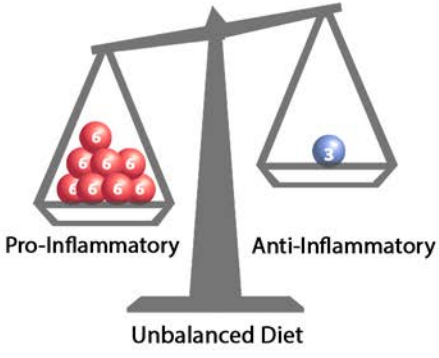
- ✓ Age-related macular degeneration – Wet and Dry
- ✓ Macular dystrophies e.g. Stargardt's disease
- ✓ Diabetic retinopathy
- ✓ Glaucoma
- ✓ Photoreceptor damage e.g. Aging retina
- ✓ Moderate to severe dry eyes
- ✓ Optic neuropathies

Some ocular diseases are believed to be caused by unresolved chronic inflammation. This inflammation is below the threshold of perceived pain.

Eicosanoids are the hormones which increase inflammation and are produced by Omega-6 fatty acids, mainly the arachidonic acid (AA). Specialized proresolving lipid mediators – resolvins, protectins, and maresins – are the hormones that resolve inflammation and are produced by Omega-3 fatty acids, mainly the eicosapentaenoic acid (EPA).[2] EPA fatty acids are required to reduce the production of eicosanoids and increase the production of resolvins.

1. Sears B, Ricordi C. Role of fatty acids and polyphenols in inflammatory gene transcription and their impact on obesity, metabolic syndrome and diabetes. Eur Rev Med Pharmacol Sci. 2012 Sep 1;16(9):1137-54.
2. Serhan CN. Pro-resolving lipid mediators are leads for resolution physiology. Nature. 2014 Jun;510(7503):92-101.
* Kim KY, et al. DRP1 inhibition rescues retinal ganglion cells and their axons by preserving mitochondrial integrity in a mouse model of glaucoma. Cell death & disease. 2015 Aug;6(8). cited in LaFee S. Promise of Gene Therapy for Glaucoma Shines Bright in Award-Winning Image. UCSan Diego. 2016 Oct 17 [Online]. Available from: https://ucsdnews.ucsd.edu/pressrelease/promise_of_gene_therapy_for_glaucoma_shines_bright_in_award_winning_image: [Accessed 19th Feb 2019].
* *Burns C. 2017 Dec 06. [Online]. Available from: https://unsplash.com/photos/QaGNhezu_5Q: [Accessed 19th Feb 2019].

OMEGA-6 vs OMEGA-3



*A blood ratio of **AA/EPA<2** must be maintained to have reduced inflammation. This is achieved by taking* eyetas® *capsules orally.*

TIME COURSE OF ACUTE INFLAMMATION

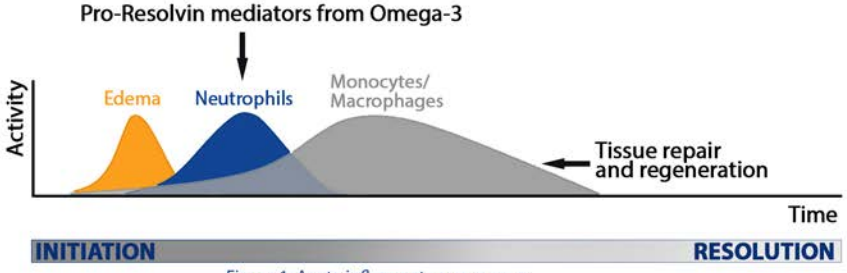


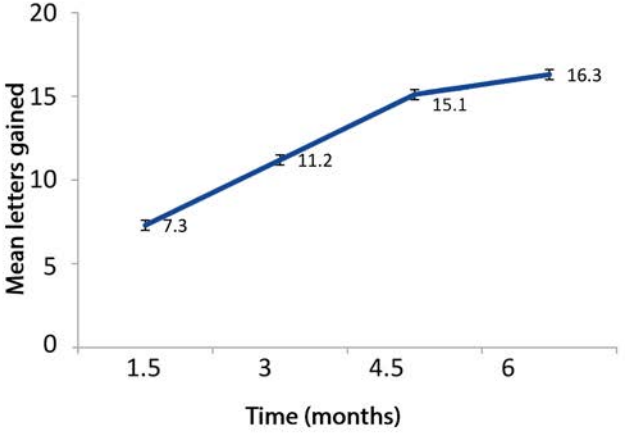
Figure 1: Acute inflammatory response
Fig. adapted from Serhan CN. 2014

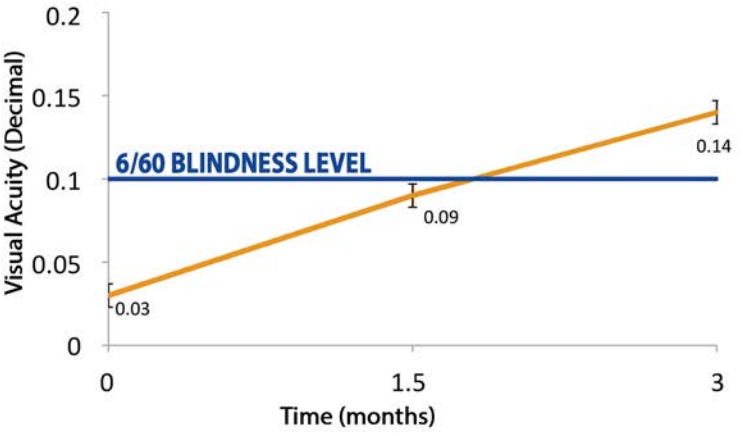
Although an acute inflammatory response is protective for the body and normally self-limited, chronic low-grade inflammation associated with some ocular diseases is sustained and harmful. The resolution of inflammation involves the termination of neutrophil recruitment, removal of the pro-inflammatory cytokines and chemokines, stimulation of macrophage-mediated clearance, and tissue repair and regeneration.

1. Serhan CN. Pro-resolving lipid mediators are leads for resolution physiology. Nature. 2014 Jun;510(7503):92-101.

DRY AGE-RELATED MACULAR DEGENERATION

OMEGA-3 IMPROVES VISION IN PATIENTS WITH DRY AGE-RELATED MACULAR DEGENERATION (AMD)





The effect of Omega-3 supplementation on visual acuity (VA) in patients with dry AMD[1]

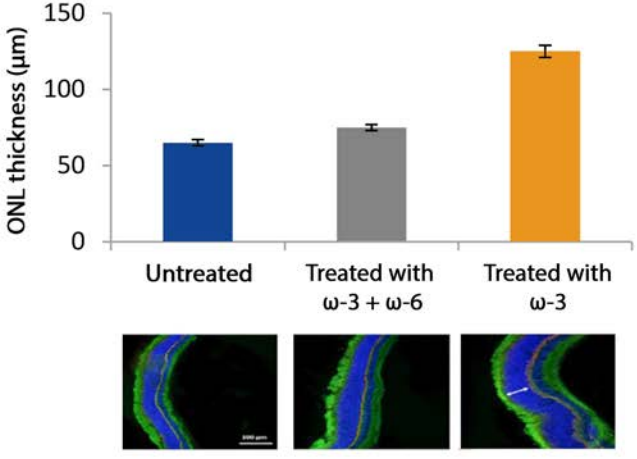
- ✓ VA improved by 16.3 letters in a period of 6 months in 49 patients (61 eyes) with dry AMD
- ✓ VA of 9 blind patients (12 eyes with initial VA of <6/60) improved above levels of blindness within 3 months

Diets rich in Omega-3 appear protective against AMD. Donor eyes with AMD and their age-matched controls were examined and their retinal lipid profiles were related with systemic biomarkers of lipid intake. The systemic AA/EPA ratios correlated well with retinal AA/EPA ratios. The AMD donors had significantly higher retinal levels of AA/EPA ratio than their age-matched controls, and the serum AA/EPA ratio was likewise higher relative to the age-matched controls.[2]

Fish consumption and the risk of AMD appear linearly related in a recent meta-analysis and systematic review. The results demonstrated that fish consumption can reduce the risk for AMD.[3] *Epidemiological studies are also in agreement that consumption of Omega-3 rich foods are associated with a lower risk of AMD.*[4-6]

1. Georgiou T, Prokopiou E. The New Era of Omega-3 Fatty Acids Supplementation: Therapeutic Effects on Dry Age-Related Macular Degeneration. J. of Stem Cells. 2015 Jul 1;10(3):205-215.
2. Gorusupudi A, et al. Associations of human retinal very long-chain polyunsaturated fatty acids with dietary lipid biomarkers. J. of lipid res. 2016 Mar;57(3):499-508.
3. Zhu W, et al. Fish Consumption and Age-Related Macular Degeneration Incidence: A Meta-Analysis and Systematic Review of Prospective Cohort Studies. Nutrients. 2016 Nov 22;8(11).
4. Cho E, et al. Prospective study of dietary fat and the risk of age-related macular degeneration. The Am. J. of Clin. Nutr. 2001 Feb 1;73 (2): 209-218.
5. Seddon JM, et al. Dietary fat and risk for advanced age-related macular degeneration. Arch. of Ophthalmol. 2001 Aug 1;119(8):1191-1199.
6. SanGiovanni JP, et al. The relationship of dietary lipid intake and age-related macular degeneration in a case-control study: AREDS Report No. 20. Arch. of Ophthalmol. 2007; 125 (5): 671-679.

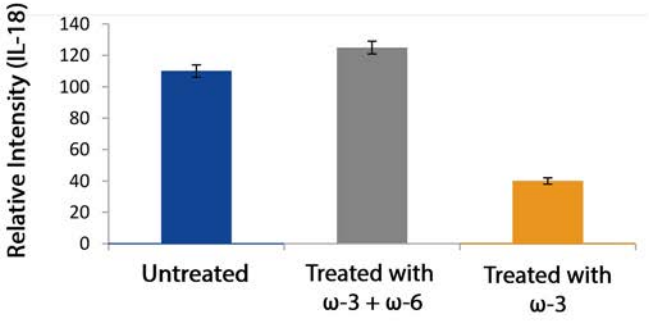
RETINAL OUTER NUCLEAR LAYER (ONL) THICKNESS INCREASES IN OMEGA-3 FED MICE MODEL WITH DRY AMD



Mice model with dry AMD were treated with Omega-3 + Omega-6, or with Omega-3 only[1]

- ✓ Animals were randomly allocated in groups of 22-24 and the ONL thickness was examined. One group treated with Omega-3 and Omega-6 and the other with Omega-3 only. Both treatment groups exhibited significantly larger ONL thicknesses than the untreated animals with more pronounced effect in the Omega-3 treated group ($p<0.05$ and $p<0.001$ respectively)
- ✓ The Omega-3 group had significantly larger ONL thickness compared with the untreated or the Omega-3 and Omega-6 group ($p<0.001$)
- ✓ Their corresponding representative ocular photomicrographs are presented

EFFECT OF TREATMENT ON INFLAMMATORY RESPONSE

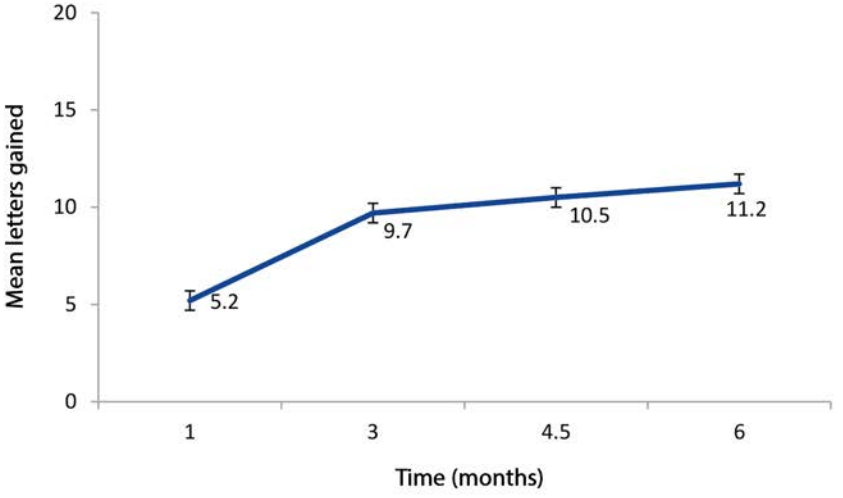


Retinal tissues were evaluated to identify any difference in the protein levels of Interleukin-18 (IL-18)[1]

- ✓ A 4-fold reduction in the IL-18 was observed in the Omega-3 treated group compared to the untreated group ($p<0.001$)

1. Prokopiou E, et al. Therapeutic potential of Omega-3 fatty acids supplementation in a mouse model of dry macular degeneration. BMJ Open Ophthalmol. 2017 Jun 1;1(1):e000056. doi:10.1136.

OMEGA-3 IMPROVES VISION IN MACULAR DYSTROPHIES



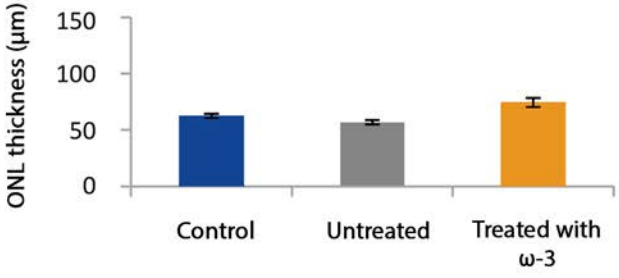
The effect of Omega-3 on VA in 21 patients (41 eyes) with macular dystrophies[1]

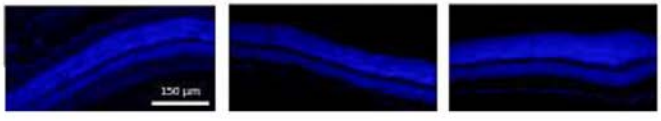
- ✓ Nine patients had Stargardt's disease, 6 patients had Retinitis Pigmentosa and 6 patients had Cone dystrophy
- ✓ VA gradually improved by 11.2 letters at 6 months following supplementation with Omega-3
- ✓ The mean blood levels of AA/EPA ratio pre-treatment was 9.9, while during treatment with Omega-3, the ratio was reduced to 1.4

Red blood cell membrane and adipose tissue lipids were analyzed as an indication of short-term and long-term dietary fatty acid in a family with autosomal dominant Stargardt's macular dystrophy. When adipose lipids were analyzed, there was a significant inverse relationship between phenotypic severity and the level of EPA. When red blood cell lipids were analyzed, there were significant inverse relationships between phenotypic severity and levels of EPA and DHA.[2]

1. Georgiou T, Prokopiou E. Role of Omega-3 fatty acids for eye health. Hedge MV, et al. Omega-3 fatty acids, Switzerland: Springer;2016; 251-261.
2. Hubbard AF, et al. Association of adipose and red blood cell lipids with severity of dominant Stargardt macular dystrophy (STGD3) secondary to an ELOVL4 mutation. Arch. of Ophthalmol. 2006 Feb 1;124(2):257-63.

REGENERATIVE POTENTIAL FROM OMEGA-3 IN MICE MODEL OF STARGARDT'S DISEASE

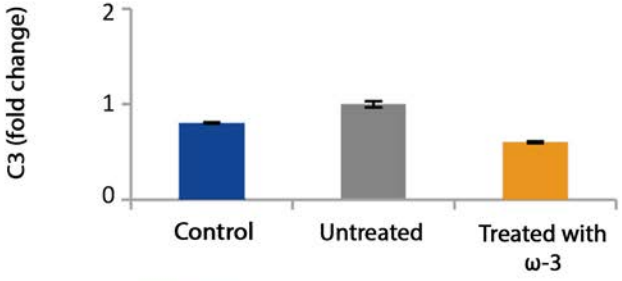


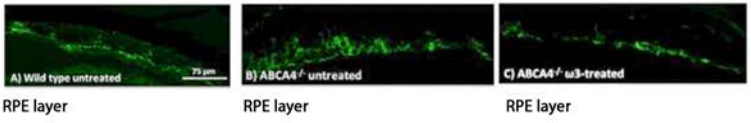


Therapeutic effects of Omega-3 in mice model of Stargardt's disease when AA/EPA blood ratio is maintained <1.5[1]

- ✓ The thickness of the retinal ONL was significantly greater in the Omega-3 treated mice compared to either of the other groups (untreated Stargardt's mice model: $p<0.01$, Control wild mice: $p<0.05$)
- ✓ Representative ocular photomicrographs are seen below the graph

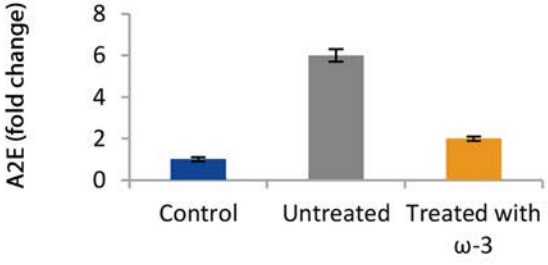
COMPLEMENT C3 AND LIPOFUSCIN COMPONENT A2E ARE REDUCED FOLLOWING OMEGA-3 SUPPLEMENTATION





Complement C3 plays a key role in the activation of the complement system[1]

- ✓ C3 was reduced in the Omega-3 treated group than the untreated group ($p<0.05$)
- ✓ Their corresponding representative ocular photomicrographs of C3 (green) immunofluorescence are shown



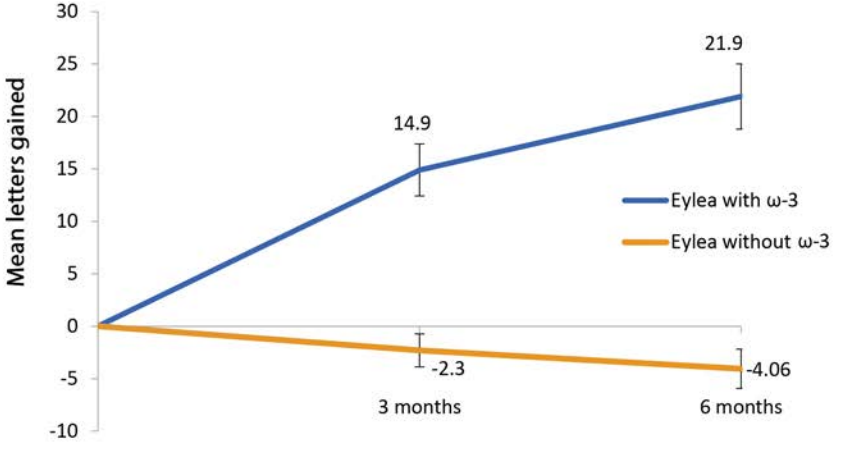
Omega-3 effect on A2E bisretinoid levels[1]

- ✓ Levels of A2E in the mice treated with Omega-3 were approximately 4 times lower than in the untreated group

1. Prokopiou E, et al. Omega-3 fatty acids supplementation: Therapeutic potential in a mouse model of Stargardt disease. IOVS. 2018 Jun 1;59(7):2757-2767.

WET AGE-RELATED MACULAR DEGENERATION

EYLEA INJECTIONS COMBINED WITH OMEGA-3 PROVIDE BETTER VISUAL OUTCOME IN WET AMD



Patients with wet AMD and not responding to Avastin injection were treated with Eylea injection with or without Omega-3[1]

- ✓ Total of 29 patients (35 eyes) with wet AMD who received Eylea injections were examined at 3 and at 6 months
- ✓ Fifteen patients (17 eyes) had Eylea injections alone while 14 patients (18 eyes) had Eylea injections in combination with Omega-3 supplementation
- ✓ Patients receiving Eylea injections with Omega-3 gained 21.9 letters and 45% had no macular oedema on OCT scan at 6 months whereas patients receiving Eylea injections alone lost 4.06 letters and 6% had no macular oedema on OCT scan at 6 months ($p<0.01$)

Higher levels of Omega-3 and lower levels of Omega-6 fatty acids are associated with a lower risk of exudative AMD.[2]

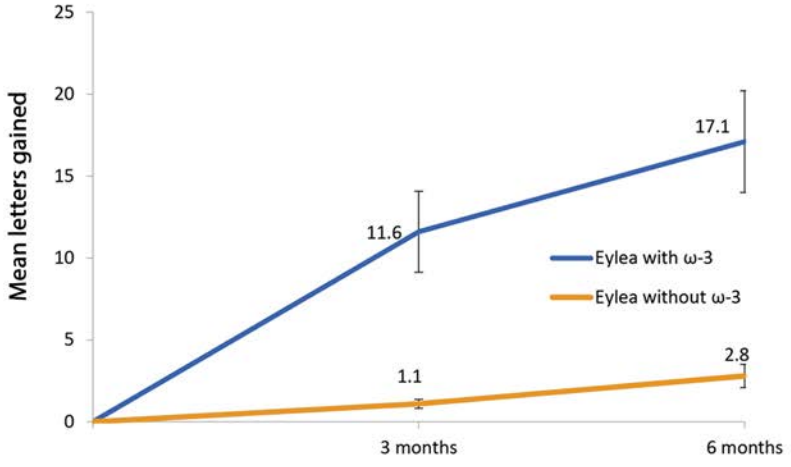
Serum levels of EPA are associated with a significantly lower risk of choroidal neovascular AMD in a study of 290 patients with wet AMD and 144 controls without AMD. The red blood cell membrane levels of EPA and DHA, which represent long term levels of PUFAs, are associated strongly with a lower risk for choroidal neovascular AMD.[3] Similarly, in a recent cross-sectional case-controlled study, neovascular AMD was associated with lower circulatory levels of Omega-3 and higher levels of Omega-6 fatty acids.[4]

In a randomized clinical trial, Omega-3 supplementation combined with anti-VEGF intravitreal injections were associated with decreased vitreal VEGF-A levels compared to anti-VEGF injections alone in neovascular AMD patients.[5]

Omega-3 reduce choroidal neovascular AMD in a mouse model. The levels of VEGF and leukocytes infiltration were also reduced in the retina and choroid in the Omega-3 fed mouse model.[6]

1. Georgiou T, et al. The use of high dose Omega-3 fatty acids in patients with macular oedema due to wet age related macular degeneration and diabetic retinopathy. 9th Euretina winter meeting. Prague 2019.
2. Leung H.H. et al. Increase in omega-6 and decrease in omega-3 polyunsaturated fatty acid oxidation elevates the risk of exudative AMD development in adults with Chinese diet, Free Radical Biology&Medicine (2019), doi: https://doi.org/10.1016/j.freeradbiomed.2019.10.007.
3. Merle BM, et al. Circulating omega-3 fatty acids and neovascular age-related macular degeneration. IOVS. 2014 Mar 1;55(3):2010–2019.
4. LK Ng et al. Dietary Habits, Fatty Acids, and Carotenoid Levels Are Associated with Neovascular Age-Related Macular Degeneration in Chinese. Nutrients 2019; 11,1720;doi:10.3390/nu11081720
5. Rezende FA, et al. Omega-3 Supplementation Combined With Anti–Vascular Endothelial Growth Factor Lowers Vitreal Levels of Vascular Endothelial Growth Factor in Wet Age-Related Macular Degeneration. Am. J. of Ophthalmol. 2014 Nov 1;158(5): 1071–1078.
6. Yanai R, et al. Cytochrome P450-generated metabolites derived from Omega-3 fatty acids attenuate neovascularization. Proc. of the National Acad. of Sci. 2014 Jun 12;111(26):9603-8.

EYLEA INJECTIONS COMBINED WITH OMEGA-3 PROVIDE BETTER VISUAL OUTCOME IN DIABETIC RETINOPATHY (DR)



Patients with DR not responding to Avastin injections were treated with Eylea injections with or without Omega-3[1]

- ✓ Total of 19 patients (27 eyes) with DR who received Eylea injections were examined at 3 and at 6 months
- ✓ Ten patients (16 eyes) had Eylea injections alone while 9 patients (11 eyes) had Eylea injections in combination with Omega-3 supplementation
- ✓ Patients receiving Eylea injections with Omega-3 gained 17.1 letters and 82% had no macular oedema on OCT scan at 6 months whereas patients receiving Eylea injections alone gained 2.8 letters and 0% had no macular oedema on OCT scan at 6 months ($p<0.01$)

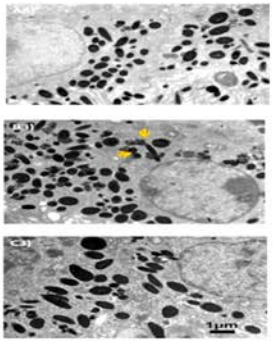
3482 participants with type 2 diabetes, taking at least 2 weekly servings of oily fish at baseline showed a 48% relatively reduced risk of incident sight-threatening diabetic retinopathy compared with those not meeting this target.[2]

A mouse model of oxygen-induced retinopathy has shown that increasing Omega-3 tissue levels reduces pathological angiogenesis. These results indicate that enriching the sources of Omega-3 may be an effective therapeutic approach to help prevent proliferative retinopathy.[3]

Omega-3 fatty acids have great potential to prevent the progression of diabetic retinopathy, due to their wide range of protective properties, such as anti-inflammatory, antiangiogenic, and antioxidant. They decrease the formation of free radicals and they remarkably prevent the initiation of retinal angiogenesis by downregulating the expressions of various angiogenic agents such as VEGF, MMPs and COX-2.[4]

1. Georgiou T, et al. The use of high dose Omega-3 fatty acids in patients with macular oedema due to wet age related macular degeneration and diabetic retinopathy. 9th Euretina winter meeting. Prague 2019 .
2. Sala-Vila A, et al . Dietary Marine ω-3 Fatty Acids and Incident Sight-Threatening Retinopathy in Middle-Aged and Older Individuals With Type 2 Diabetes: Prospective Investigation From the PREDIMED Trial. JAMA Ophthalmol. 2016 Oct 1;134(10):1142-1149.
3. Connor MK, et al. Increased dietary intake of Omega-3-polyunsaturated fatty acids reduces pathological retinal angiogenesis. Nature Med. 2007 Jul;13(7):868-873.
4. Behl T, Kotwani A. Omega-3 fatty acids in prevention of diabetic retinopathy. J. of Pharm and Pharmacol. 2017 Aug;69(8):946-954.

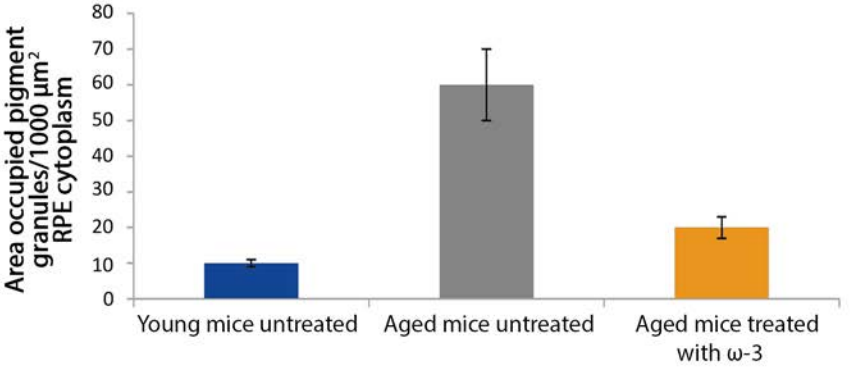
OMEGA-3 PROTECTS THE RETINA FROM AGE-RELATED MACULAR DEGENERATION IN WILD AGED MICE



Young mice untreated

Aged mice untreated

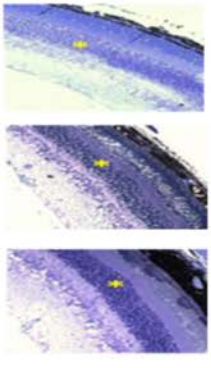
Aged mice treated with ω-3



Reduction of lipofuscin in Omega-3 treated aged mice[1]

- ✓ The production of free radicals which create metabolic waste products in the aged retina, including a substance called lipofuscin were investigated in Omega-3 fed aged mice
- ✓ Levels of lipofuscin and melanolipofuscin granules were reduced in the Omega-3 treated aged mice compared to the untreated aged mice ($p<0.05$)
- ✓ Their corresponding representative ocular photomicrographs of the RPE cell are presented. Unusual granules of irregular shape and electron density (yellow arrows) accumulated in the RPE cytoplasm of the untreated mice

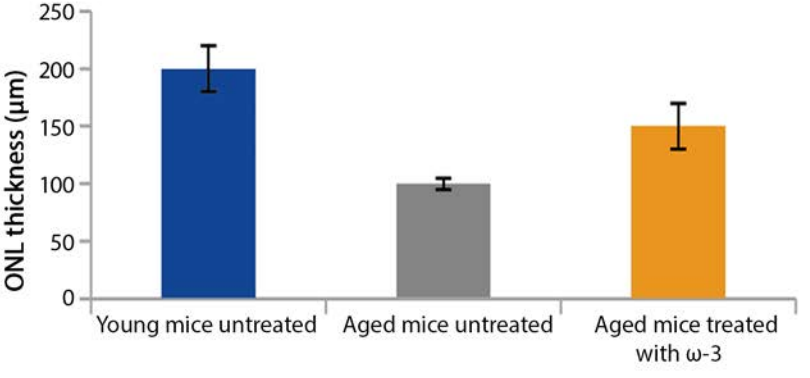
OMEGA-3 PROTECT THE PHOTORECEPTOR LAYER



Young mice untreated

Aged mice untreated

Aged mice treated with ω-3

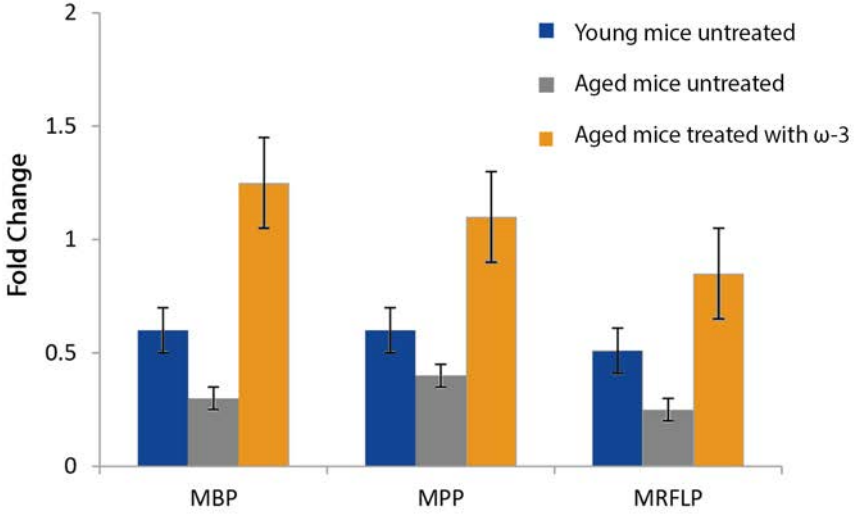


Retinal ONL thickness increases in Omega-3 treated aged mice[1]

- ✓ Greater retinal ONL thickness was observed in the Omega-3 treated aged mice at different fields around the entire retinal section compared to the untreated aged mice ($p<0.05$)
- ✓ Their corresponding representative ocular photomicrographs are presented. Asterisk (*) points out the retinal ONL

1. Prokopiou E, et al. Omega-3 Fatty Acids Supplementation Protects the Retina from Age-Associated Degeneration in Aged C57BL/6J mice. BMJOO. 2019 Nov.

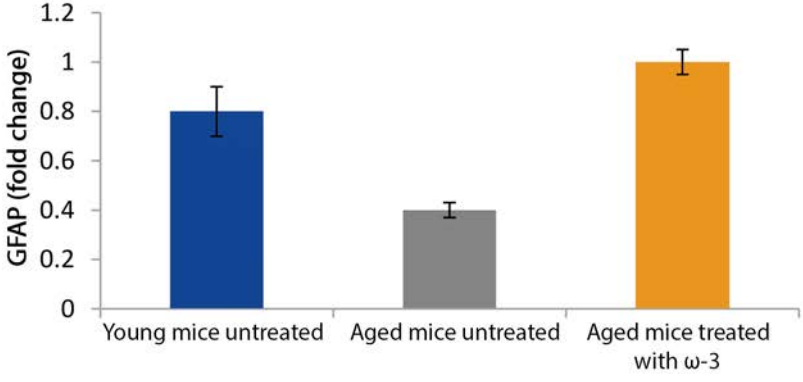
INCREASE OF MYELIN-RELATED PROTEINS FOR BETTER OPTIC NERVE FUNCTION



Omega-3 increase expression of myelin proteins in Omega-3 treated aged mice[1]

- ✓ Increase in myelin basic protein (MBP), myelin proteolipid protein (MPP) and myelin regulatory factor-like protein (MRFLP) in the Omega-3 treated aged mice compared to the untreated aged mice was detected ($p<0.05$)

INCREASE OF ASTROCYTES PROVIDES RETINAL GANGLION CELL (RGC) REPAIR

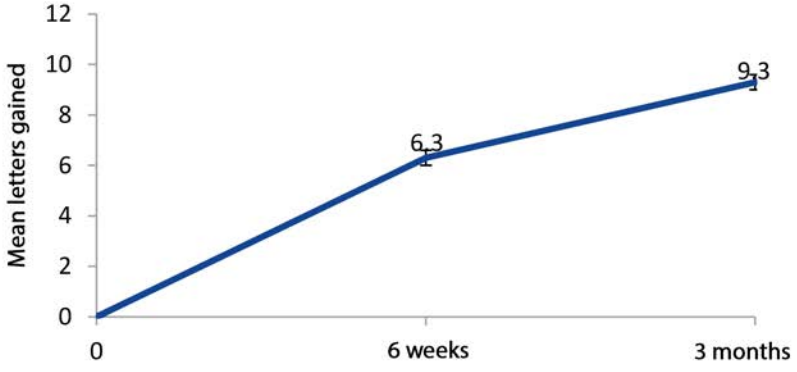


Increase in Glial fibrillary acidic protein (GFAP) in Omega-3 treated aged mice[1]

- ✓ GFAP represents astrocyte function. Increase in GFAP is associated with increase of astrocytes, which are responsible for providing support to neurons and repair of RGCs
- ✓ Increase in GFAP in the Omega-3 treated aged mice was detected compared to the untreated aged mice ($p<0.05$)

1. Prokopiou E, et al. Omega-3 Fatty Acids Supplementation Protects the Retina from Age-Associated Degeneration in Aged C57BL/6J mice. BMJOO. 2019 Nov.

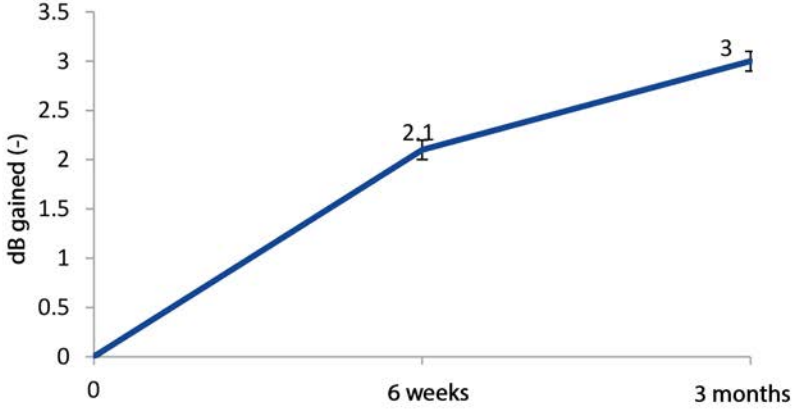
VISUAL ACUITY IMPROVES WITH OMEGA-3 SUPPLEMENTATION



The effect of Omega-3 on VA in patients with severe glaucoma[1]

✓ Eighteen patients (24 eyes) with advanced glaucoma had improvement in VA by 9.3 letters after 3 months of Omega-3 supplementation

VISUAL FIELD IMPROVES WITH OMEGA-3 SUPPLEMENTATION

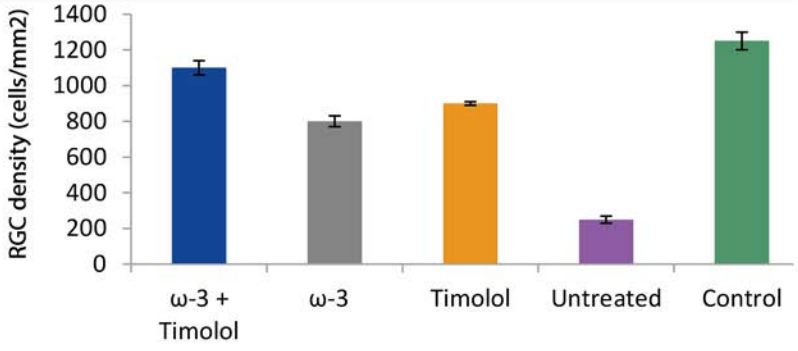


Visual field improvement is evident following Omega-3 in glaucoma patients[1]

✓ An improvement of the Mean Deviation of the visual field loss by 3.04dB ($p<0.01$) on the Humphrey Field Analyser was observed

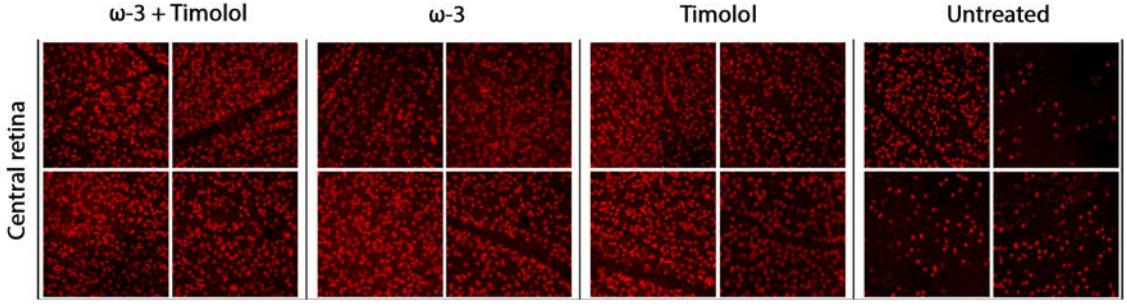
1.Georgiou T, et al. Neuro-rescuing glaucomatous damage. Eurotimes. 2015 Oct: 2-4.

RETINAL GANGLION CELL SURVIVAL IN OMEGA-3 FED MICE MODEL OF GLAUCOMA



Neuroprotective effects of Omega-3 supplementation alone or in combination with Timolol eye drops in hereditary glaucoma mice model[1]

- ✓ Twenty mice with hereditary glaucoma were assigned per group
- ✓ Higher density of surviving RGCs is seen when Omega-3 is combined with Timolol drops, compared with treatment with Timolol drops or Omega-3 alone ($p < 0.05$)
- ✓ Density of RGCs in the Omega-3 and Timolol, Omega-3 alone and Timolol alone groups were higher than those in the untreated group ($p<0.01$)
- ✓ Representative photomicrographs of the flat-mounted central retinas in each group are seen below



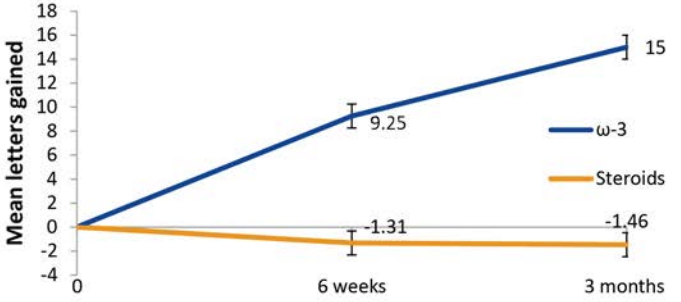
The association between daily dietary intake of Omega-3 and the prevalence of glaucoma in the U.S was examined in 3865 participants. The results showed that daily dietary intake of EPA and DHA was associated with lower likelihood of glaucomatous optic neuropathy.[2]

Patients with primary open angle glaucoma were compared with their healthy siblings and found that the glaucoma patients had reduced EPA and DHA fatty acids.[3]

1. Kalogerou M, et al. Omega-3 Fatty acids protect retinal neurons in the DBA/2J hereditary glaucoma mouse model. Exp. Eye Res. 2017 Dec 16;167:128-139.
2.Wang YE, et al. Association of Dietary Fatty Acid Intake With Glaucoma in the United States. JAMA Ophthalmol. 2018 Feb 1;136(2):141-147.
3.Ren H, et al. Primary open-angle glaucoma patients have reduced levels of blood docosahexaenoic and eicosapentaenoic acids. Prostaglandins, Leukotrienes and Essential Fatty Acids. 2006 Mar 1;74(3):157-163.

NON ARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY (NAION)

IMPROVEMENT OF VISUAL ACUITY WITH OMEGA-3 FATTY ACIDS

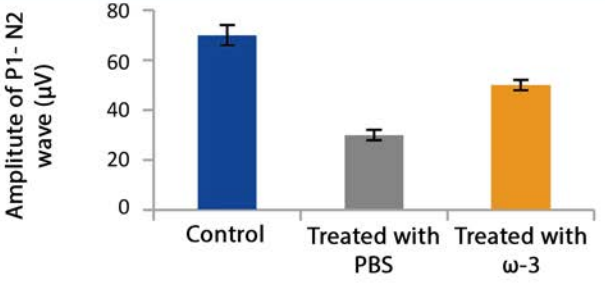


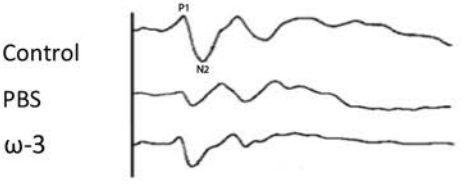
The effect of Omega-3 supplementation on VA in patients with NAION[1]

- ✓ Twenty six patients (27 eyes) with NAION were examined at 6 weeks and 3 months following diagnosis. Thirteen patients (13 eyes) received steroids within 2 weeks of the acute reduction in VA (IV 1g/daily of methylprednisolone for 3 days followed by 20mg prednisolone orally for 1 month). Thirteen patients (14 eyes) received oral supplementation of Omega-3
- ✓ VA was preserved in the Omega-3 group. Patients taking Omega-3 had improvement in VA by 15 letters at 3 months while patients receiving steroids lost on average 1.5 letters

A study investigated the effects of increased production of Omega-3 on retinal ganglion cell survival after optic nerve crush injury in adult mice. It was found that increased production of Omega-3 in mice enhanced retinal ganglion cell survival.[2]

NEUROPROTECTIVE EFFECTS OF OMEGA-3 IN A RAT MODEL OF ANTERIOR ISCHEMIC OPTIC NEUROPATHY (rAION)



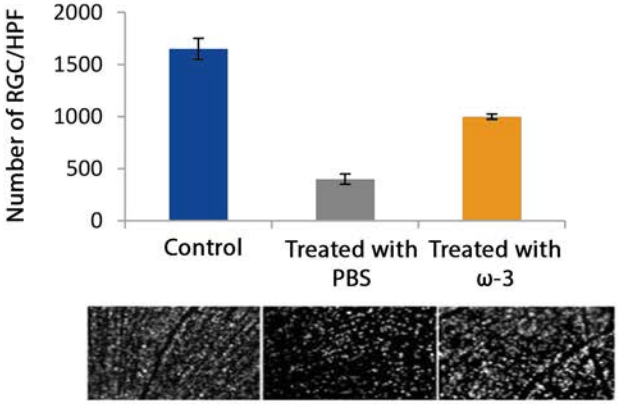


Electrodiagnostic evaluation of the injured optic nerves in the rAION model[3]

- ✓ The amplitude of P1-N2 waves in the Omega-3 treated group were significantly higher than those in the Phosphate-buffered saline (PBS) treated group
- ✓ Visual function is preserved in the Omega-3 fed rAION. The electrodiagnostic results are presented

1. Georgiou T, et al. Non-arteritic anterior ischaemic optic neuropathy. Ophthalmol. Times Europe. 2014 Dec; 2-4.
2. Peng S, et al. Increased production of Omega-3 fatty acids protects retinal ganglion cells after optic nerve injury in mice. Exp. Eye Res. 2016 Jul 1;148:90-96.
3. Georgiou T, et al. Neuroprotective Effects of Omega-3 Polyunsaturated Fatty Acids in a Rat Model of Anterior Ischemic Optic Neuropathy. IOVS. 2017 Mar 1;58(3):1603-1611.

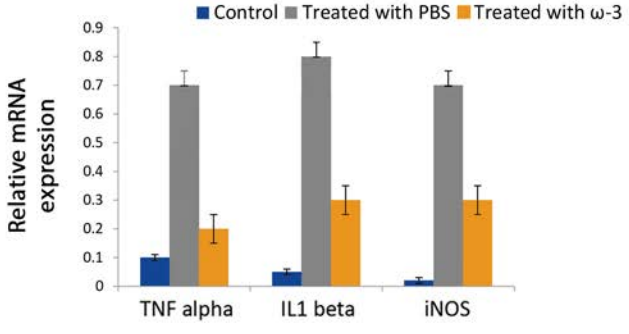
PROTECTION OF RETINAL GANGLION CELLS



Administration of Omega-3 or Phosphate-buffered saline (PBS)[1]

- ✓ Omega-3 preserved a higher density of RGCs in both central and mid peripheral retinas in contrast to treatment with PBS
- ✓ Their corresponding representative images of flat mounted central retinas are shown below the graph

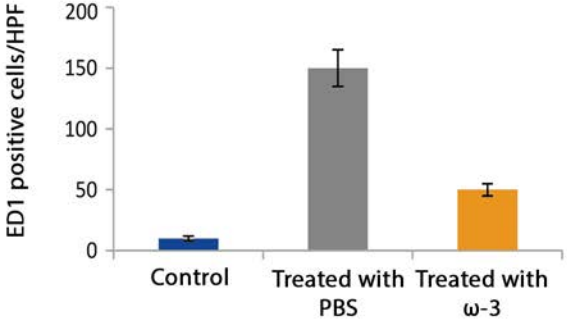
EFFECT OF TREATMENT ON INFLAMMATORY RESPONSE



Relative mRNA expression levels of TNF-a, IL-1b and iNOS in the optic nerve tissues[1]

- ✓ All factors were reduced after treatment with Omega-3 compared to PBS treatment ($p<0.05$)

MACROPHAGE RECRUITMENT DECREASES



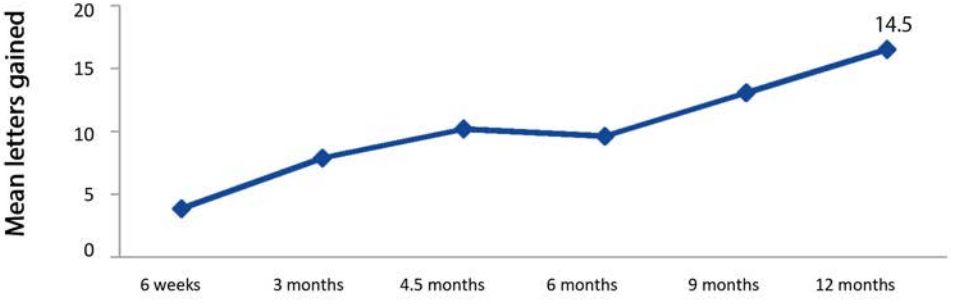
Immunohistochemistry evaluation of macrophage recruitment to the ON[1]

- ✓ The macrophage recruitment was decreased 3.170-fold in the Omega-3 compared to the PBS-treated group

1. Georgiou T, et al. Neuroprotective Effects of Omega-3 Polyunsaturated Fatty Acids in a Rat Model of Anterior Ischemic Optic Neuropathy. IOVS. 2017 Mar 1;58(3):1603-1611.

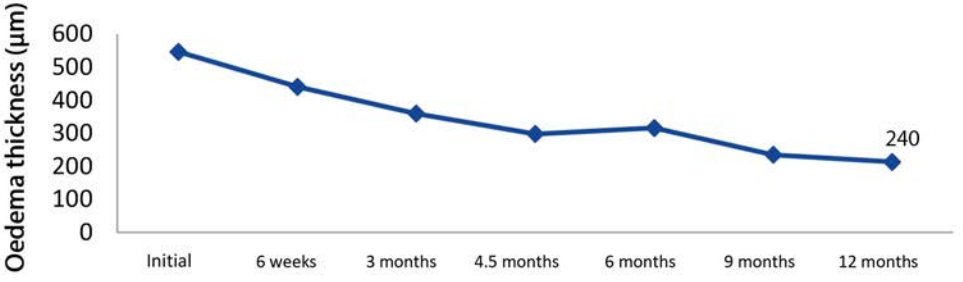
MACULAR OEDEMA SECONDARY TO CHRONIC UVEITIS AND BRANCH RETINAL VEIN OCCLUSION

IMPROVEMENT OF VISUAL ACUITY WITH OMEGA-3 FATTY ACIDS



The role of Omega-3 fatty acids on visual acuity in patients with macular oedema[1]

✓ VA improved by 14.5 letters in a period of 12 months in 5 eyes with BRVO and 8 eyes with chronic uveitis with macular oedema ($p<0.05$)



The effectiveness of Omega-3 supplementation on macular oedema thickness[1]

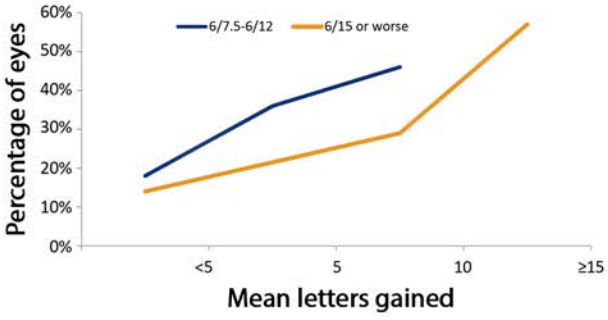
✓ Significant reduction in OCT oedema thickness observed when compared to the initial thickness at all time points ($p<0.05$)

Dietary Omega-3 fatty acids suppress inflammation in mice with experimental autoimmune uveitis.[2] The mechanism by which Omega-3 attenuate inflammation in uveitis is through their anti-inflammatory action on dendritic cells.[3]

In an animal model of acute ocular inflammation, oral EPA administration(50 mg/kg/day) showed significant reduction of inflammation, through a decrease of inflammatory cytokines and chemokines, such as MCP-1 and IL-6 in the retina and choroid. In addition there was significant decrease in leukocyte adhesion to the retinal vessels and leukocyte infiltration into the vitreous cavity. The study also demonstrated that the level of transcription factor NF-κB was significantly suppressed by EPA in the inflamed retina and choroid.[4]

1. Georgiou et al. High-Dose Omega-3 Fatty Acids for Cystoid Macular Oedema due to Chronic Uveitis or Branch Retinal Vein Occlusion. EVER. 2013 Aug. doi.org/10.1111/j.1755-3768.2013.S057.
2. Shoda H, et al. Dietary Omega-3 Fatty Acids Suppress Experimental Autoimmune Uveitis in Association with Inhibition of Th1 and Th17 Cell Function. PLoS ONE 2015 Sep 22;10(9):e0138241.
3. Uchi et al. Dendritic Cells Mediate the Anti-Inflammatory Action of Omega-3 Long-Chain Polyunsaturated Fatty Acids in Experimental Autoimmune Uveitis. PLoS One 2019 July 23; 14(7):e0219405.
4. Suzuki M et al. Eicosapentaenoic acid suppresses ocular inflammation in endotoxin-induced uveitis. Molecular Vision 2010;16:1382-1388.

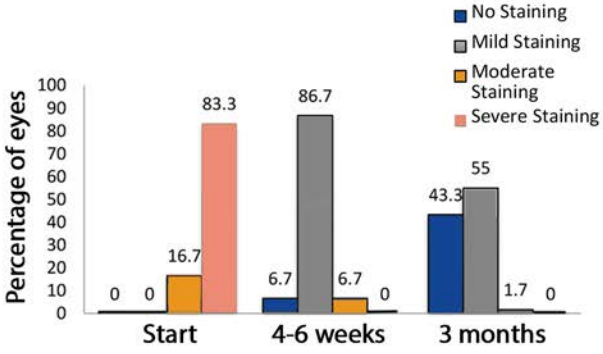
VISUAL ACUITY IMPROVES WITH OMEGA-3 IN PATIENTS WITH MODERATE TO SEVERE DRY EYES



The effect of Omega-3 on VA in patients with moderate to severe dry eyes[1]

- ✓ Patients with severe dry eyes who had not responded to other standard treatment with baseline VA of 6/7.5-6/12 and 6/15 or worse showed significant improvement in VA of up to 15 or more letters at 3 months following Omega-3 supplementation ($p<0.05$)
- ✓ Eyes with worse initial VA (6/15 or worse) showed greater improvement ($p<0.05$)

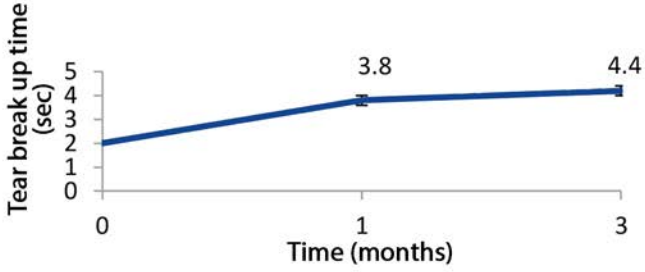
REDUCTION IN CORNEAL FLUORESCEIN STAINING WITH OMEGA-3



The effect of Omega-3 on corneal staining[1]

- ✓ Corneal fluorescein staining scores of severity in eyes with moderate or severe staining, showed increasing percentage of the eyes with no or mild staining, during and after supplementation with Omega-3 ($p<0.001$)

IMPROVEMENT IN TEAR FILM BREAK-UP TIME (TBUT)



Effect of Omega-3 on TBUT for assessing evaporative dry eyes[1]

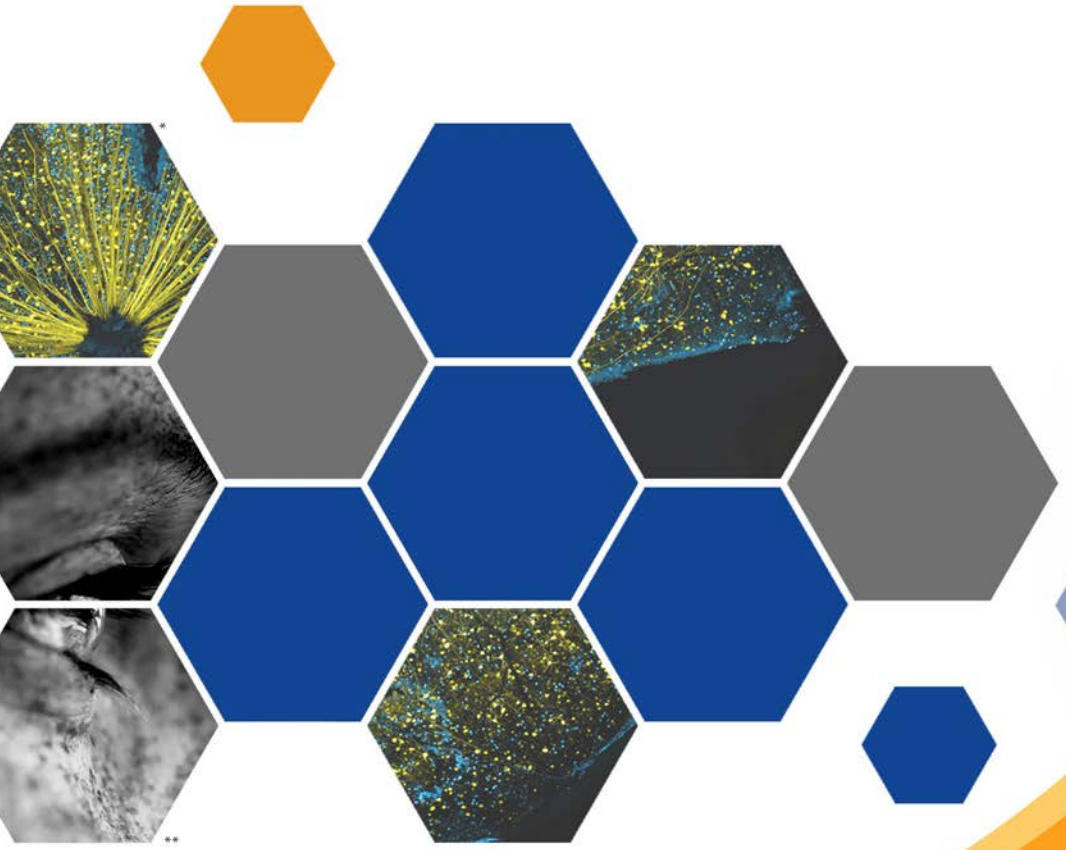
- ✓ Increase in TBUT, up to 4.4 seconds, observed in patients with severe dry eyes in 3 months following supplementation with Omega-3 ($p<0.001$)

> *A meta-regression analysis of 17 randomised controlled studies with 3363 patients, proved the effectiveness of Omega-3 fatty acid supplementation on the significant improvement of dry eyes, including reduced corneal fluorescein staining, reduced dry eye symptoms and increased tear break up time.*[2]

1. Georgiou T, et al. Role of Omega-3 fatty acids for eye health. Hedge MV, et al. Omega-3 fatty acids, Switzerland: Springer;2016; 251-261.
2. Giannaccare G, et al. Efficacy of Omega-3 Fatty Acid Supplementation for Treatment of Dry Eye Disease: A Meta-analysis of randomized Clinical Trials. Cornea. 2019 Jan 29.

why eyetas®?

- ✓ The only patented oral therapy for improving vision in retinal and optic nerve diseases
- ✓ Protects and improves the function of the retinal photoreceptors and the retinal ganglion cells
- ✓ Ultra concentrated fish oils with more than 95% EPA and DHA
- ✓ Advanced formulation with virtually no environmental toxins



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