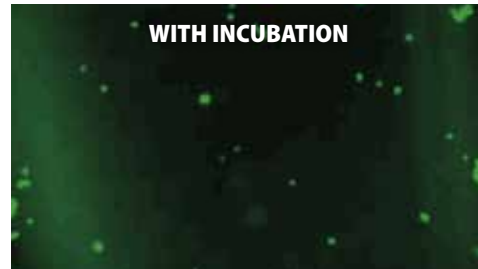
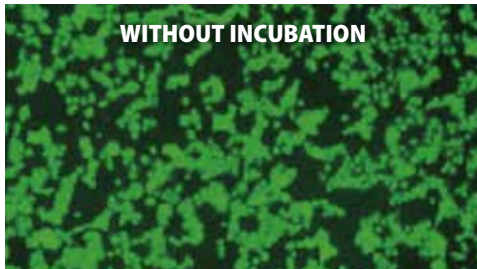
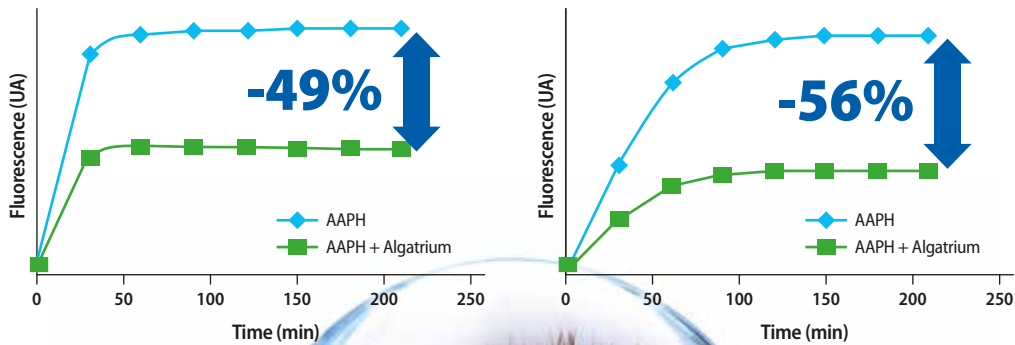


Tridocosahexaenoina-AOX[®] raises cellular oxidative protection by inducing extra synthesis of glutathione¹



Oxidative stress induced in ARPE-19 cells incubated and not incubated in Tridocosahexaenoina-AOX[®]



IMPLICATIONS FOR THE OCULAR SURFACE

SELF CLINICAL EXPERIENCE¹⁻⁹



Tridocosahexaenoina-AOX®

Reduces oxidation in the epitheliums¹

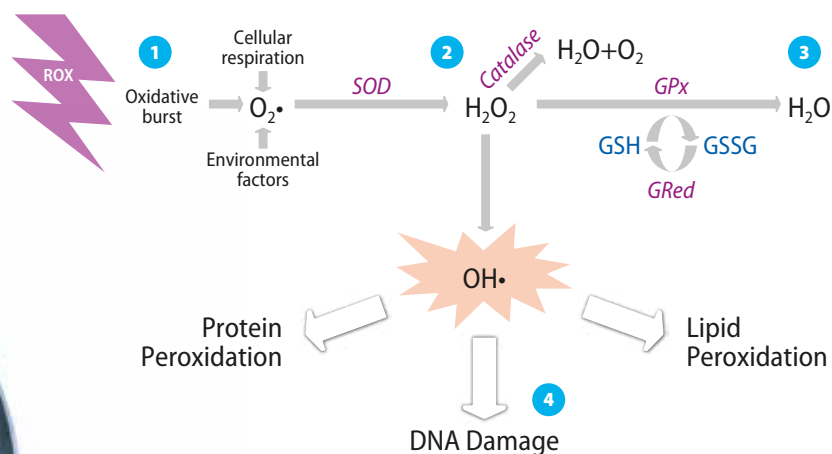
The incubation of human retinal pigment epithelium cells (ARPE-19 cells) in Tridocosahexaenoina-AOX® reduces the oxidative stress induced by 50%¹ because it stimulates the intracytoplasmic synthesis of Glutathione (Brudy Patent), making the cells more resistant to oxidation degeneration.

The fluorescence of intracytoplasmic Oxygen Free Radicals (ROX) in human retinal ARPE-19 cells is reduced by 49 to 56% with the previous incubation in Tridocosahexaenoina-AOX® due to stimulation in the synthesis of Glutathione, which grows between 200 to 300%. (Cover image).

Glutathione is the main antioxidant in mammal cells

It is an electron-donating protein, produced by cells for their oxidative self-protection, to prevent the formation of the hydroxyl radical (OH) derived from ROX, which damages DNA, proteins and cell lipids.

Enzymatic mechanisms for the removal of oxygenated free radicals in the cell



GSH: Reduced Glutathione; GSSG: Oxidized Glutathione; SOD: Superoxide dismutase; GPx: Glutathine Peroxidase; GRed: Glutathione Reductase; ROX: Oxygenated free-radicals.

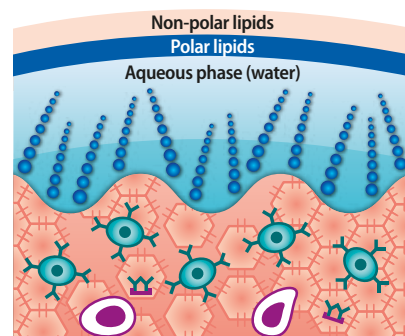
Corneoconjunctival epithelium is the only one directly exposed to environmental and luminic oxidation



Improvement in the stability of the lacrimal lipid layer¹⁻⁹

- Tridocosaheanoina-AOX[®] is incorporated into membrane phospholipids of the meibomian cells that make up the **polar lipid monolayer** in the tear.

- The 6 double bonds present in DHA are making it more fluid, flexible and stable.



- **Polar lipids** (in blue) are responsible for the stability of the lipid film (TBUT) and support the **non-polar lipids from the cytoplasm** (in black) responsible for the antievaporative effect.

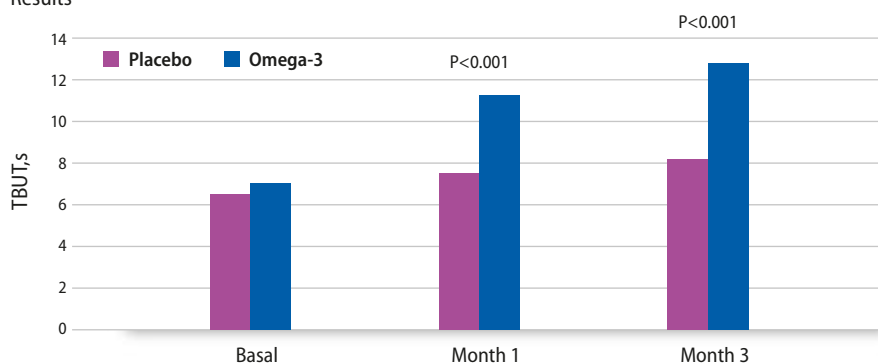
Components of meibum

Waxes	35%
Sterol esters	30%
Polar lipids	16%
Diesters	8,5%
Triglycerides	4%
Free fatty acids	2%
Free sterols	2%



It improves the Tear Break-up time¹⁻⁹

Results



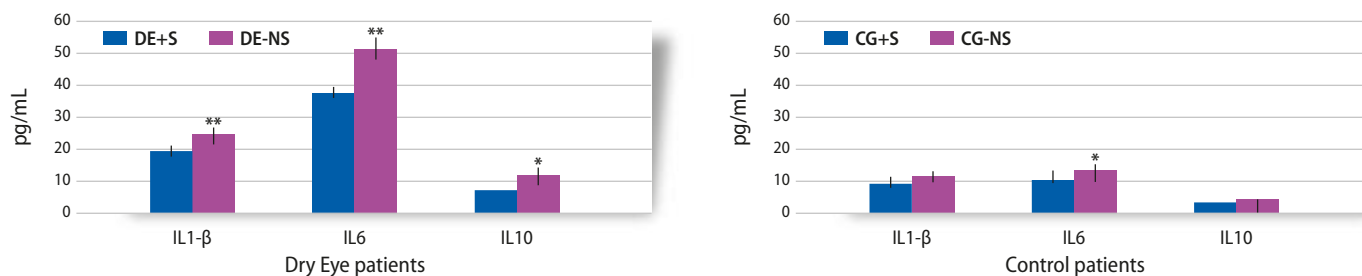
Effect of Tridocosaheanoina-AOX[®] versus Placebo supplementation on the Tear Break-up Time (TBUT) in N = 60 patients suffering Meibomian Gland Dysfunction, 50% randomized to receive either 1g/day x 90 days of Tridocosaheanoina-AOX[®] or Placebo.²

Tridocosaheanoina-AOX[®] supplementation improves the quality of life in patients suffering meibomian gland dysfunction³

It alleviates ocular surface inflammation^{4,5,6}

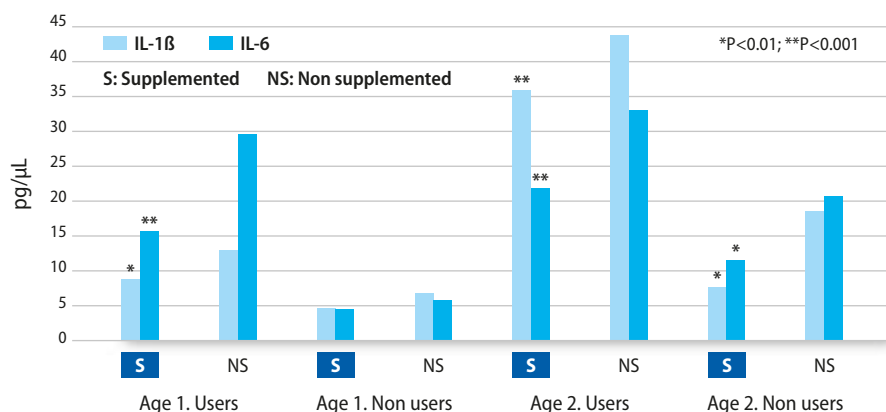
DHA inhibits the activation of Nuclear Factor ($\kappa\beta$) and cytokine synthesis.^{4,5,6}

Effect of oral supplementation on the expression of cytokines in tears⁴



Synthesis of Tear cytokines is significantly reduced in (n=30) patients suffering moderate dry eye, and in (n=36) healthy controls, 50% of them being Supplemented (1g/day; BRUDYSEC 3 caps/day) or not at random with Tridocosahexaenoine-AOX during 90 days. A statistical significant lower tear levels of IL-6, IL-1B, and IL-10 are detected in the actively supplemented Dry Eye patients (DE+S) and in the actively supplemented Controls (CG+S) compared with the non supplemented Dry Eye patients (DE-NS) and the non supplemented group of Controls (CG-NS) (*P<0.01, **p<0.001). Significant improvements of all clinical variables are also detected. (S: supplemented patients; NS: non supplemented patients).

Citokines present in tears (women intensive computer screen users)⁶

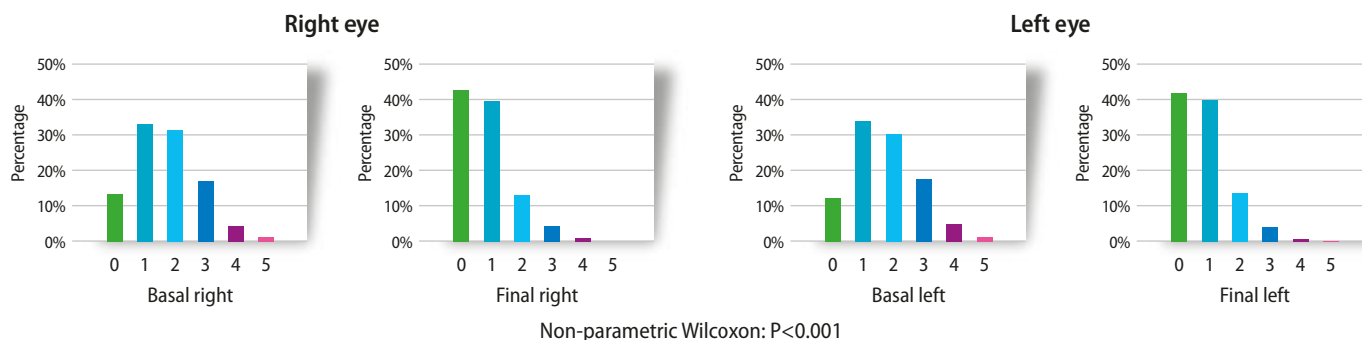


Expression level of inflammatory markers (IL-6 and IL-1B) in reflex tears of n=83 women intensive users of computer screens, and in n=65 women non users (Controls). They are analyzed in two different age ranks (Age 1: 40-52 years; Age 2: 53-65 years), 50% randomly assigned either to receive or not supplementation with Tridocosahexaenoina-AOX[®] (1g/day; BRUDYSEC 3 caps/day) during 90 days. *P<0.01; **P<0.001

Active supplementation had a positive influence on the ocular surface pathology, showing evident and significant improvements of the clinical signs and symptoms derived from the abusive use of screen computers.⁶

It improves Oxford Test scoring^{7,8}

Oxford Test⁷



Evolution in the Oxford test scoring in N= 1419 patients suffering dry eye, being users of artificial tears, being supplemented with Tridocosahexaenoina-AOX[®] (1g/day; BRUDYSEC 3 caps/day) during 90 days. After 90 days supplementing, the more severe basal scorings: 2, 3, 4 and 5, are evolving towards less severe final scorings: 0 and 1.⁷

It improves hydration of the ocular surface¹⁻⁸

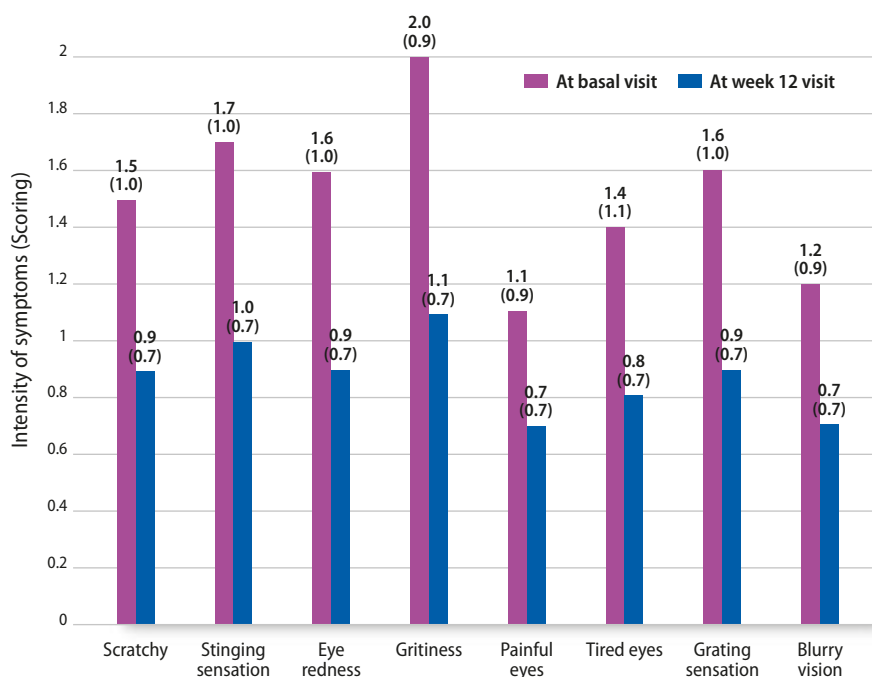
Schirmer test	Basal (mm) Average (SD)	Week 12 (mm) Average (SD)	P value
Right Eye	9,69 (4,02)	11,0 (3,70)	<0.001
Left Eye	9,81 (4,06)	12,1 (1,87)	<0.001

N= 1255 glaucoma patients suffering Dry Eye supplemented with Tridocosahexaenoina-AOX® (1g/day; BRUDYSEC 3 caps/day) during 90 days.⁸

Schirmer test	Basal (mm) Average (SD)	Week 12 (mm) Average (SD)	P value
Right Eye	9,06 (4,40)	11,0 (4,43)	<0.001
Left Eye	9,24 (4,62)	11,2 (4,64)	<0.001

N=1419 Dry Eye diagnosed patients being supplemented with Tridocosahexaenoina-AOX® (1g/day; BRUDYSEC 3 caps/day) during 90 days.⁷

It improves annoying symptoms of dryness¹⁻⁹



Evolution of symptoms in (N= 905) patients with diagnosis of dry eye supplemented with Tridocosahexaenoina-AOX® (1g/day; BRUDYSEC 3 caps/day) during 90 days.⁹



BRUDYLAB®

BRUDYSEC 1,5g

In the dietary treatment of dry eye



DOSING	1st month	2nd month	From 3rd month and on
Number of capsules/day	3	2	1

(1) P. Bogdanov, et al; Docosahexaenoic Acid Improves Endogen Antioxidant Defense in Arpe-19 Cells; IOVS, ARVO Journals; May 2008, Vol.49, 5932. doi:

(2) A. Oleňik, et al; A randomized, double-masked study to evaluate the effect of omega-3 fatty acids supplementation in meibomian gland dysfunction; Clinical Interventions in Aging 2013; 8:1133–38.

(3) Andrea Oleňik, et al; Benefits of Omega-3 fatty acid dietary supplementation on health-related quality of life in patients with Meibomian Gland Dysfunction; Clinical Ophthalmol 2014; 8:831-836.

(4) M. Dolores Pinazo-Durán, et al; Effects of a nutraceutical formulation based on the combination of antioxidants and ω -3 essential fatty acids in the expression of inflammation and immune response mediators in tears from patients with dry eye disorders; Clinical Int Aging 2013; 8:139-148.

(5) C. Galbis-Estrada, et al; Patients undergoing long-term treatment with antihypertensive eye drops responded positively with respect to their ocular surface disorder to oral supplement with antioxidants and essential fatty acids; Clin Int Aging 2013;8:711-9.

(6) A. Ribelles, et al; Ocular Surface and Tear Film Changes in Older Women Working with Computers; BioMed Research International 2015; Article ID 467039.

(7) J. Gatell-Tortajada, et al; Oral supplementation with a nutraceutical formulation containing omega-3 fatty acids, vitamins, minerals, and antioxidants in a large series of patients with dry eye symptoms: results of a prospective study; Clin Int Aging 2016; 11:571-578.

(8) Jesús Tellez-Vazquez, et al; Omega-3 fatty acid supplementation improves dry eye symptoms in patients with glaucoma: results of a prospective multicenter study; Clin Ophthalmol 2016; 10:617-626.

(9) Oleňik A, et al; Effectiveness and tolerability of dietary supplementation with a combination of omega-3 polyunsaturated fatty acids and antioxidants in the treatment of dry eye symptoms: results of a prospective study; Clinical Ophthalmology 2014;8 169–176.

