

# Why Tridocosaheenoína-AOX® is different from other sources of DHA?

- 01 Tridocosaheenoína-AOX® isn't a natural source of DHA. It's a molecule enzymatically synthesized, from DHA obtained from tuna fish. It shows a high bioactivity.
- 02 Its Biosynthesis process is conferring it special physiological characteristics, different from what normal Omega-3 oils are offering.
- 03 It imitates DHA-triglycerides present in human mother's milk, by attaching DHA in central (Sn-2) position of the glycerol backbone.
- 04 This is accelerating intestinal absorption, bioavailability, and conversion into DHA rich phospholipids being inserted into cell membranes.
- 05 It has been patented as a cell antioxidant: it stimulates intracellular glutathione synthesis, the main antioxidant in mammal cells.<sup>1</sup>
- 06 Bioactivity has been tested by means of *in vitro* human cell cultures (human pigmentary epithelium cells of the retina, and human skin cells).<sup>2</sup>
- 07 Trials in absorption and red blood cell membrane DHA availability have been done in healthy volunteers.<sup>17</sup>
- 08 Antioxidant plus anti-inflammatory clinical efficacy, and safety are **supported by more than 20 controlled\* clinical trials**, most of them double-blind and placebo- controlled:
  - Anti-inflammatory activity in Dry Eye due to diverse causes.<sup>3-6</sup>
  - In Dry Eye due to Meibomian Gland Dysfunction.<sup>7,8</sup>
  - Open trials of large series of patients with Dry Eye diagnosis.<sup>9-11</sup>
  - In patients suffering Expholiation Glaucoma.
  - In patients suffering Chronic Primary Glaucoma (trial ongoing).
  - In patients suffering Diabetic Retinopathy being supplemented:
    - Diabetic Macular Edema patients, in addition to iv ranibizumab.<sup>12</sup>
    - Effects on macular Microperimetry in NPDR patients.<sup>13</sup>
    - Versus placebo in NPDR patients in a prolonged follow-up.
  - In Kids suffering Attention Deficit Hyperactivity Disorder (ADHD).
  - In patients suffering Chronic Lymphatic Leukemia.
  - In patients suffering Amyotrophic Lateral Sclerosis.
  - In patients with DNA oxidative fragmentation of spermatozoa.<sup>14,15</sup>
  - Complex reaction time in female elite soccer players.<sup>16</sup>
  - Oxidative/anti-inflammatory protection in Triathletes.
  - Oxidative protection against intense exercise.<sup>17</sup>

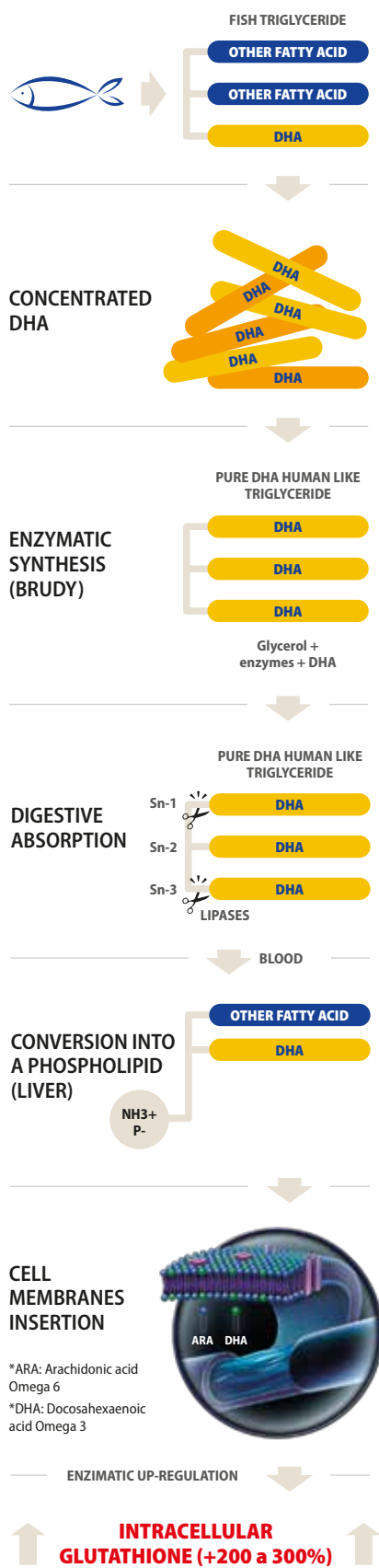
*\*Trials not showing bibliographic reference are either ongoing, or still pending to be published.*



# Tridocosahexaenoína-AOX® synthesis process

## Understanding the human physiology of DHA is fundamental

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3. Pinazo-Duran MD, et al; Effects of a Nutraceutical formulation based on the combination of antioxidants and  $\omega$ -3 essential fatty acids in the expression of inflammation and immune response mediators in tears from patients with dry eye disorders; Clin Int Aging 2013; 8:139-148.
4. Galbis-Estrada C, et al; Patients undergoing long-term treatment with antihypertensive eye drops responded positively with respect to their ocular surface disorder to oral supplementation with antioxidants and essential fatty acids; Clin Int Aging 2013; 8:711-19.
5. Ribelles Alfredo, et al; Ocular Surface and Tear Film Changes in Older Women Working with Computers; BioMed Research International 2015; Article ID 467039.
6. Carmen Galbis Estrada, et al; A metabolomic approach to dry eye disorders. The role of oral supplements with antioxidants and omega 3 fatty acids; Molecular Vision 2015; 21:555-567.
7. Andrea Oleñik, et al; A randomized, double-masked study to evaluate the effect of omega-3 fatty acids supplementation in meibomian gland dysfunction; Clinical Int Aging 2013; 8:1133-1138.
8. Andre a Oleñik, et al; Benefits of Omega-3 fatty acid dietary supplementation on health-related quality of life in patients with Meibomian Gland Disfunction; Clinical Ophthalmol 2014; 8:831-836.
9. Andrea Oleñik, 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;8:831-6.
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12. Maria Lafuente, et al; Combined intravitreal ranibizumab and oral supplementation with docosahexaenoic acid (DHA) and antioxidants for Diabetic Macular Edema: 2-year randomized single-blind controlled trial results; Journal of Retina 2016, 1-10, Ahead of print; DOI: 10.1097/IAE.0000000000001363.
13. Elena Rodríguez, et al; Suplementación dietética con ácido docosahexaenoico (DHA) en la retinopatía diabética no proliferativa: estudio prospectivo controlado de la función macular mediante microperimetría; Comunicación Congreso de la SERV, Viernes 3 Marzo, 2017.
14. JC Martinez-Soto, et al; Effect of dietary DHA supplementation on sperm DNA integrity; Fertility & Sterility 2010, S235-6.
15. JC Martinez-Soto, et al; Dietary supplementation with docosahexaenoic acid (DHA) improves seminal antioxidant status and decreases sperm DNA fragmentation; Systems Biology in Reproductive Medicine, 62(6):387-395, DOI: 10.1080/19396368.2016.1246623.
16. Guzman JF, et al; DHA- rich fish oil improves complex reaction time in female elite soccer players; Journal of Sports Sci Med 2011;10:301-5.
17. Carlos J Contreras; Modificación del daño oxidativo en un grupo de ciclistas tras consumir ácido docosahexaenoico a distintas dosis; Tesis Doctoral, Universidad Católica de Murcia, 2014.



## The 10 steps

to convert fish triglycerides into DHA-Triglycerides having DHA in central (Sn-2) position, as the ones mostly found in human maternal milk:

- 01 Obtaining tuna fish triglycerides.
- 02 Fatty acids different from DHA are eliminated.
- 03 Heavy metals and pollutants are eliminated by double distillation.
- 04 Concentrating DHA.
- 05 Ethanol is eliminated.
- 06 Triglycerides having central DHA are being synthesized.
- 07 Digestive lipases are only able to break bonds in Sn-1 and Sn-3 position.
- 08 Monoglycerides with central DHA are absorbed intact to blood.
- 09 They are converted inside the body into DHA rich phospholipids, and being inserted into cell membranes.
- 10 Stimulating oxidative protection of the cell (BRUDY TECHNOLOGY PATENT: DHA present in the cell membrane **stimulates glutathione synthesis**<sup>1,2</sup> up to 200-300% from its normal levels in the cell's cytoplasm). This is the main antioxidant, electron donor, in mammal cells.