

# Technical Bulletin 01 - Antioxidant

## AstaREAL<sup>®</sup> astaxanthin

### The powerful and well substantiated *antioxidant*

Supported by full spectrum research from laboratory... to pre clinical... to human clinical

Outlined below

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## 1. Antioxidant capacity of astaxanthin as determined by laboratory testing methods

- Total **ORAC 14,779**

Ou, B. *et al.*, *J Agric and Food Chem*, **2001**, 49 (10): 4619-4626.  
Huang, D. *et al.*, *J Agric and Food Chem*, **2002**, 50 (7): 1815-1821.  
Ou, B. *et al.*, *J Agric and Food Chem*, **2002**, 50 (10): 2772-2777.  
Zhang, L. *et al.*, *Free Radic. Bio Med*, **2007**, 43 (suppl. 1): S17.  
Dubost, N.J. *et al.*, *Food Chem*, **2007**, 105 (2): 727-735  
Zhang, L. *et al.*, *J Agric and Food Chem*, **2009**, 57(7): 2661-2667.  
Ou, B. *et al.*, Method for Assaying the Antioxidant Capacity of A Sample. US Patent 7,132,296 B2.

- **Lipid peroxidation and Radical Oxygen Specie quenching of astaxanthin by model assay systems**

**Martin H D et al.** Chemistry of carotenoid oxidation and free radical reactions. *Pure appl chem*. 1999; 71(12):2253-2262.  
**Miki W.** Biological functions and activities of animal carotenoids. *Pure & appl chem*. 1991; 63(1):141-146.  
**Mortensen A et al.** Comparative mechanisms and rates of free radical scavenging by carotenoids antioxidants. *FEBS Letters* 1997; 418:91-97.  
**Mortensen A, et al.** relative stability of carotenoids radical cations and homologue tocopheroxyl radicals. A real time kinetic study of antioxidant hierarchy. *FEBS Letters* 1997; 417:261-266.  
**Naguib Y M A.** Antioxidant activities of Astaxanthin and related carotenoids. *J agric food chem*. 2000; 48:1150-1154.  
**Nishida Y et al.** Quenching Activities of Common Hydrophilic and Lipophilic Antioxidants against Singlet Oxygen Using Chemiluminescence Detection System. *Carotenoid Science*. 2007; 11:16-20.  
**Shimidzu N et al.** Carotenoids as singlet oxygen quenchers in marine organisms. *Fisheries science* 1996; 62(1):134-137.  
**Tomoaia-Cotisel M et al.** Intermolecular interactions in lipid/carotenoid monolayers. *Biochem J* 1987; 248 :877-882.

## 2. In-Vitro Antioxidant Studies establishing astaxanthin mechanisms of action

- **Cell culture studies:**

**Ben-Dor A et al.** Carotenoids activate the antioxidant response element transcription system. *Mol cancer therapeutics* 2005; 4(1):177-186.  
**Kishimoto Y et al.** Astaxanthin suppresses scavenger receptor expression and matrix metalloproteinase activity in macrophages. *Eur J Nutr*. 2010; 49(2):119-26. Epub 2009 Sep 26.  
**Kim YJ et al.** Protection against oxidative stress, inflammation, and apoptosis of high-glucose-exposed proximal tubular epithelial cells by astaxanthin. *J Agric Food Chem*. 2009; 57(19):8793-7.  
**Mahmoud F F et al.** In vitro effects of astaxanthin combined with ginkgolide B on T lymphocyte activation in peripheral blood mononuclear cells from asthmatic subjects. *J Pharmacol sci* 2004; 94:129-136.  
**Rebrin I, Zicker S et al.** Effect of antioxidant-enriched diets on glutathione redox status in tissue homogenates and mitochondria of the senescence-accelerated mouse. *Free radical biology & medicine* 2005; 39:549-557.  
**Tatsuzawa H et al.** Quenching of singlet oxygen by carotenoids produced in *Escherichia coli* – attenuation of singlet oxygen-mediated bacterial killing by carotenoids. *FEBS Letters* 2000; 484:280-284.  
**Tominaga K et al.** Protective Effects of Astaxanthin against Singlet Oxygen Induced Damage in Human Dermal Fibroblasts In-vitro *Food Style* 21 Vol. 13 No. 1/2009 p84-86.

## - **Model membrane studies** demonstrating **astaxanthin** mechanisms of action

**Cantrell A et al.** Singlet oxygen quenching by dietary carotenoids in a model membrane environment. Archives of biochemistry and biophysics 2003; 412:47-54.

**Goto S et al.** Efficient radical trapping at the surface and inside the phospholipid membrane is responsible for highly potent antiperoxidative activity of the carotenoids Astaxanthin. Biochimica et biophysica acta 2001; 1512:251-258.

**McNulty H P et al.** Differential effects of carotenoids on lipid peroxidation due to membrane interactions: X-ray diffraction analysis. Biochimica et biophysica acta 2007; 1768:167-174.

## 3. **Pre Clinical In-vivo Antioxidant Studies** exploring and demonstrating in-vivo utilization and function of **astaxanthin** within a biological system

**Hussein G et al.** Astaxanthin ameliorates features of metabolic syndrome in SHR/NDmcr-cp. Life sciences 2007; 80:522-529.

**Hussein G et al.** Astaxanthin, a carotenoids with potential in human health and nutrition. J Nat prod 2006; 69:443-449.

**Jyonouchi H et al.** Immunomodulating actions of carotenoids: Enhancement of in vivo and in vitro antibody production to T-dependent antigens. Nutr Cancer 1994; 21:47-58.

**Lee S-J et al.** Astaxanthin inhibits nitric oxide production and inflammatory gene expression by suppressing I $\kappa$ B kinase-dependent NF- $\kappa$ B activation. Mol Cells 2003; 16(1):97-105.

**Naito Y et al.** Prevention of diabetic nephropathy by treatment with Astaxanthin in diabetic db/db mice. BioFactors 2004; 20:49-59.

**Naito Y et al.** Microarray profiling of gene expression patterns in glomerular cells of Astaxanthin-treated diabetic mice: A nutrigenomic approach. Int J Mol Med 2006; 18:685-695.

**Nishigaki I et al.** Suppressive effect of astaxanthin on lipid peroxidation induced rats. J Clin Biochem Nutr. 1994; 16:161-6.

**Ohgami K et al.** Effects of Astaxanthin on lipopolysaccharide-induced inflammation in vitro and in vivo. Invest Ophthal Vis Sci 2003, 44(6):2694-2701.

**Suzuki Y et al.** Suppressive effects of Astaxanthin against rat endotoxin-induced uveitis by inhibiting the NF- $\kappa$ B signalling pathway. Experimental eye research 2006; 82:275-281.

**Uchiyama K et al.** Astaxanthin protects  $\beta$ -cells against glucose toxicity in diabetic db/db mice. Redox report 2002; 7(5):290-293.

## 4. **Human Clinical In-vivo Antioxidant Studies** demonstrating **astaxanthin** antioxidant efficacy and function within the human body

**Comhaire F H et al.** Combined conventional/antioxidant « astaxanthin » treatment for male infertility : a double blind, randomized trial. Asian J Androl 2005; 7(3):257-262.

**Hashimoto H et al.** Effect of astaxanthin consumption on superoxide scavenging activity in aqueous humor. Translated from Atarashii Ganka (Journal of the Eye). 2009; 26(2):229-234.

**Iwamoto T et al.** Inhibition of low-density lipoprotein oxidation by Astaxanthin. J Atheroscler Thromb 2000; 7(4):216-222.

**Karppi J et al.** Effects of astaxanthin supplementation on lipid peroxidation. Int J for Vitamin and Nutrition Research 2007; 77(1):3-11.

**Park J S et al.** Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans. Nutrition & Metabolism 2010, 7:18

**AstaREAL astaxanthin is GRAS** (generally recognized as safe) for use as an ingredient in the food categories of baked goods, beverages, cereals, chewing gum, coffee, tea, dairy product analogs, frozen dairy desserts and mixes, hard candy, milk products, processed fruits and fruit juices, processed vegetables and vegetable juices and soft candy at a use level to provide 0.1 milligram (mg) astaxanthin per serving.

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3 Terri Lane, Unit 12, Burlington, NJ 08016  
Tel: 609 386 3030 Fax: 609 386 3033  
Email: [contact@fujihealthscience.com](mailto:contact@fujihealthscience.com)