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THE ASTAXANTHIN *Difference*

The science that separates the
red carotenoid among antioxidants



INGREDIENT MARKETPLACE

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The Astaxanthin Difference

Astaxanthin, a red carotenoid, is unique among antioxidants due to its molecular form, blood-brain transferability and powerful anti-inflammatory properties.

Sandy Almendarez examines this potent carotenoid and details human clinical research that substantiates astaxanthin's health benefits to inflammation, heart health, cognitive health, eye health, immunity, sports nutrition and skin health.



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The Future of Astaxanthin Research



As part of research for articles that discuss studies, INSIDER editors reach out to ingredient suppliers asking for the research they use to substantiate their products.

For this astaxanthin article, I did just that, and I got a mountain of evidence.

From Bob Capelli at AlgaeHealth, a division of BGG, I got a pdf of published abstracts of studies that was 565 pages. Each abstract was on its own page—minus a few pages for an introduction and table of contents, I estimate the pdf contained 560 studies. That is a lot of research. A lot of hours in labs were dedicated to the red carotenoid.

To keep this Digital Magazine a readable size, I focused on studies with human subjects, although a few in vitro studies were included to show antioxidant capacity of astaxanthin compared to other nutrients.

Human studies may be better for claims substantiation, while non-human studies may demonstrate the potential exciting future for astaxanthin research.

For example, mice and cell research has shown possible effects to weight management (*Biosci Biotechnol Biochem.* 2007 Apr;71(4):893-9), liver health (*PLoS One.* 2015 Mar 11;10(3):e0120440), lung health (*Acta Physiol Hung.* 2012 Jun;99(2):173-84) and more. As a lifelong asthmatic, I'm particularly excited about the lung health research.

Stay tuned to **INSIDER** for updates on astaxanthin research and other scientific developments; for now, supplement brands can turn to this Digital Magazine for insight on how current human studies show astaxanthin helps benefit immune health, eye health, skin health and more. This Magazine also explores sourcing methods and bioavailability issues to help brands choose the best astaxanthin for their products.

Sandy Almendarez

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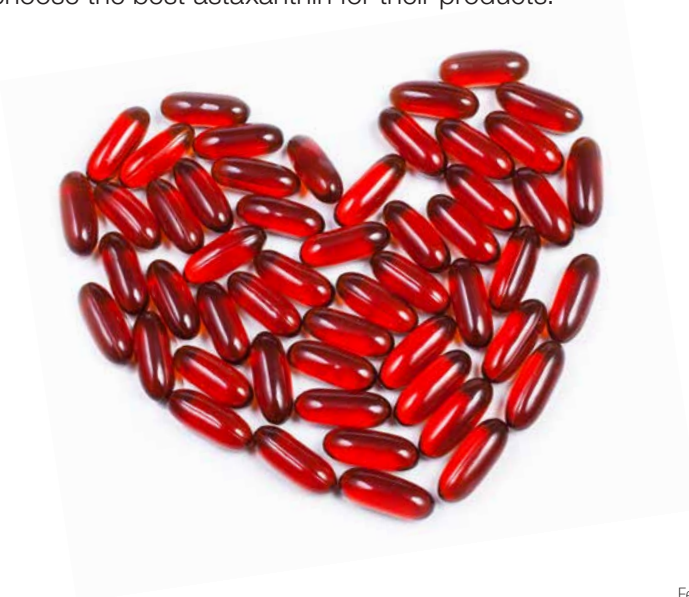
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The Astaxanthin Difference

The science that separates the red carotenoid among antioxidants

by Sandy Almendarez

INSIDER's Take

- Astaxanthin, a red carotenoid, is unique among antioxidants due to its molecular form, blood-brain transferability and powerful anti-inflammatory properties.
- The red pigment can, if not properly harvested and processed, lose its bioavailability and efficacy, so brands need to ensure proper manufacturing techniques.
- Human clinical research substantiates astaxanthin's benefits to inflammation, heart health, cognitive health, eye health, immunity, sports nutrition and skin health.

Distinguishable by its rich red color, astaxanthin is a powerful antioxidant from the family of carotenoids. Carotenoids are red, yellow and orange pigments created by plants, but they do much more than make tomatoes red (lycopene), marigolds yellow (lutein) and algae red (astaxanthin).

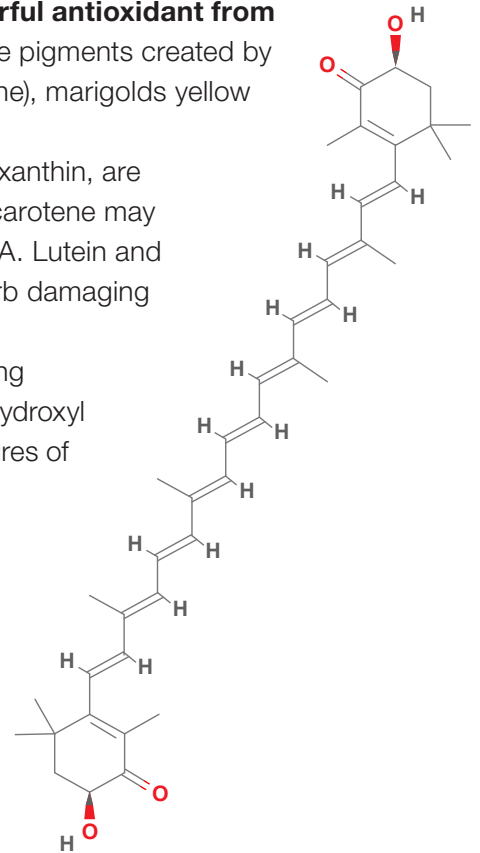
Carotenoids, such as beta-carotene, lycopene, lutein and zeaxanthin, are thought to benefit health due to their role as antioxidants. Beta-carotene may have added benefits due to its ability to be converted to vitamin A. Lutein and zeaxanthin may be protective in eye disease because they absorb damaging blue light that enters the eye.¹

But astaxanthin, a xanthophyll class carotenoid, is unique among carotenoids due to its molecular structure. "The presence of the hydroxyl and keto endings on each ionone ring explains some unique features of astaxanthin, such as its ability to be esterified, its high antioxidant potency and a more polar configuration than other carotenoids," explained Oran Ayalon, Ph.D., vice president for development and research, Algalo, Frutarom group.

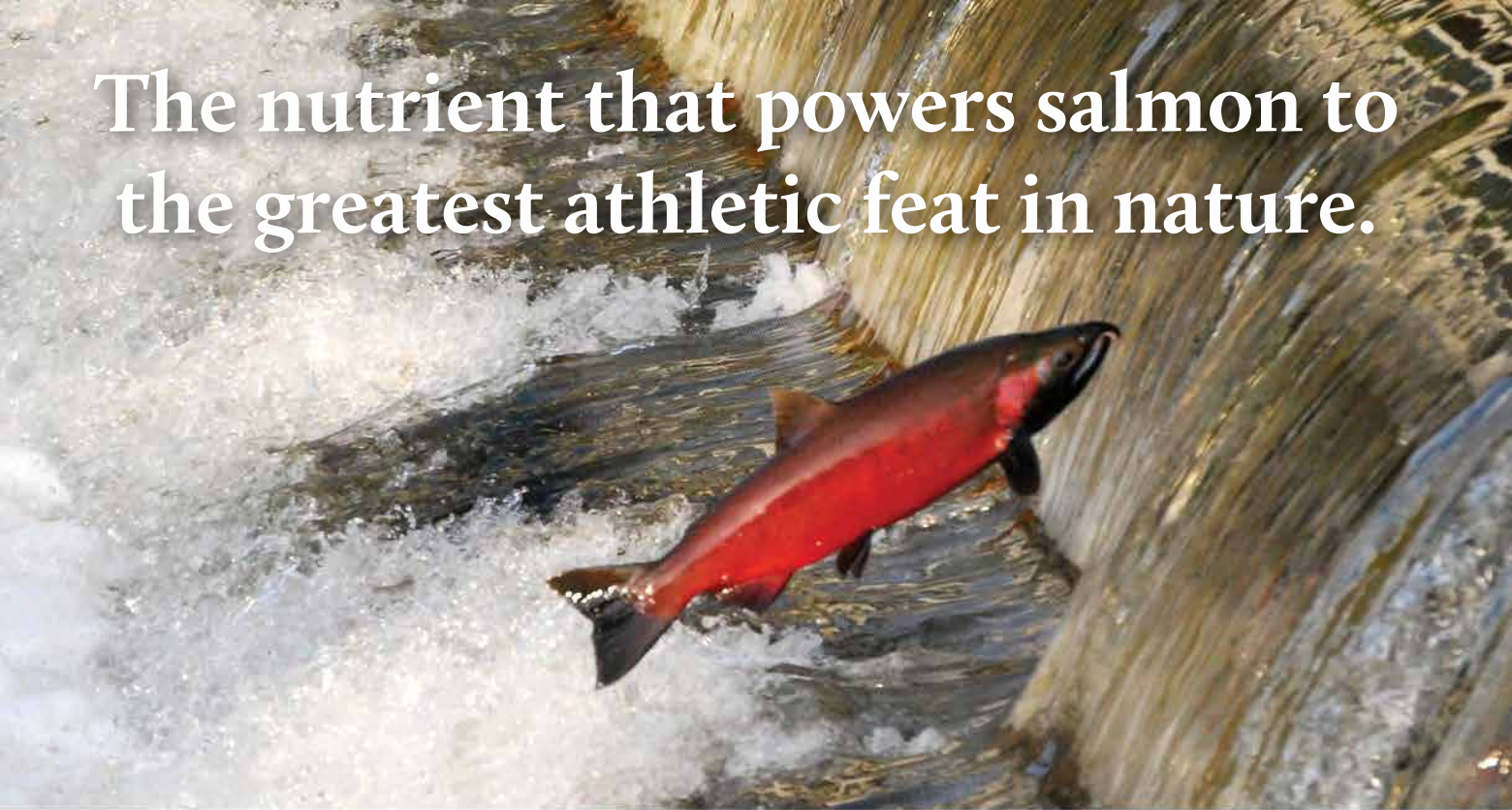
Astaxanthin's ability to span the entire cell membrane means it is both water and fat soluble. "This is unique because many nutrients are either lipid soluble (e.g., vitamin E) and protect the lipid/fat soluble part of our cells, or water soluble (e.g., vitamin C) and can only protect the water soluble part of our cells," said Gerald Cysewski, Ph.D., founder and CEO, Cyanotech.

Then, there's the blood-brain transferability. "Astaxanthin can cross the blood-brain and blood-retinal barriers to bring its anti-inflammatory and antioxidant protection to these vital organs, while other good antioxidant carotenoids like lycopene and beta-carotene can't get through these barriers," said Bob Capelli, executive vice president, global marketing, AlgaeHealth, a division of BGG.

These and others properties combine to make astaxanthin a powerful antioxidant. "It attaches itself onto cell membranes and spans the cell membrane bilayer of fat, where free radical attacks first occur, and inhibits the destruction of fatty acids and proteins in



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cell and mitochondrial membranes caused by lipid peroxidation,” said Steve Holtby, president and CEO, Soft Gel Technologies Inc. “Astaxanthin is different from beta-carotene in that it has two additional oxygenated groups on each of its ring structures, enhancing its ability to scavenge free radicals.”

Astaxanthin was identified as an extremely potent carotenoid as far back as the 1940s by French scientists, according to Cysewski. In vitro research completed in Japan in the 1990s expanded showed the activities of astaxanthin are approximately 10 times stronger than the other carotenoids that were tested, namely zeaxanthin, lutein, tunaxanthin, canthaxanthin and beta-carotene, and 100 times greater than alpha-tocopherol.²

A later in vitro study from the same researchers found astaxanthin’s antioxidant strength was 8,000 times more potent than vitamin C, 800 times more potent than coenzyme Q10 (CoQ10), 550 times more potent than green tea catechins, and 75 times more potent than alpha lipoic acid.³

An in vitro 2013 study, which included Bob Capelli, executive vice president, global marketing, AlgaeHealth, a division of BGG; and Gerald Cysewski, Ph.D., founder and CEO, Cyanotech as researchers, showed astaxanthin cultivated from



Microalga
Haematococcus
pluvialis was

14 times stronger than vitamin E
18 times stronger than French maritime pine bark
21 times stronger than synthetic astaxanthin
54 times stronger than beta-carotene
65 times stronger than vitamin C⁴

Growing Procedures

That 2013 study tested an astaxanthin harvested from *Haematococcus pluvialis*, a common source of natural astaxanthin. However, ingredient suppliers use different practices to extract the carotenoid from the algae. For example, BGG North America grows its microalgae using Himalayan water from the Tibetan Plateau in tube photobioreactors to ensure purity and prevent unwanted organisms from entering the algae media. “Our farm is the only astaxanthin farm in the world that has attained organic certification (from leading European firm Ecocert) as well as other key quality certifications,” Capelli said. BGG North America’s astaxanthin is 97 percent pure astaxanthin and can consistently attain levels of 6 to over 8 percent pure astaxanthin in its algae biomass, Capelli added.

Frutarom also sources its astaxanthin from *H. pluvialis*. “We harvest and dry the algal cysts, which are rich in esterified astaxanthin, without damaging the algae protective cell walls,” Ayalon said. “This ensures that the astaxanthin remains safe and protected, in its natural form and concentrated in globuli inside the cells throughout the process.” The algal cells (cysts) must be cracked to make the astaxanthin extractable or bioavailable from dried algal powder, he added. “Our unique cracking method, performed by

collisions of the algal cells themselves, without adding any other agent (such as glass beads), ensures that the product remains in its natural form and avoids the risks of foreign particles in the product.”

The astaxanthin used in Cyanotech’s BioAstin® Hawaiian Astaxanthin® is derived from *H. pluvialis* grown on the company’s 90-acre farm in Kona, Hawaii. “The astaxanthin in BioAstin is processed on our farm starting with cultivation, and then it’s processed through our very own CO₂ extraction facility,” Cysewski explained. Using chemical solvents such as hexane during the extraction process is easier and can reduce costs, Cysewski noted, but this method leaves a chemical residue in the finished product and makes it unstable. “The other and more superior method for extraction is using super critical high pressure CO₂. Super critical CO₂ extraction is a best practice among the top astaxanthin suppliers as it produces a pure and clean final extract, free of solvents.”

Natural Astaxanthin Verification Seal

In summer 2016, the supplement industry trade organization Natural Algae Astaxanthin Association (NAXA) launched the NAXA Verification Program (NAVP) to assure finished product manufacturers and consumers the astaxanthin they are purchasing is natural astaxanthin derived from *Haematococcus pluvialis*.

The program is open to NAXA member companies, and any company that purchases raw material from a member company that has qualified for the seal may use the seal on their finished product upon approval. The full line of Nutrex Hawaii’s BioAstin Hawaiian Astaxanthin® products were the first retail astaxanthin products to receive the verification seal in August 2016.

In July 2016, NAXA completed its first round of testing of retail astaxanthin products. Products that passed the testing are eligible for the NAXA Verified Seal. The NAVP used high-performance liquid chromatography (HPLC) to confirm that 10 of the 12 products the organization tested were correctly labeled as natural astaxanthin derived from *H. pluvialis*. Two of the products tested were not confirmed by HPLC to be astaxanthin derived from *H. pluvialis*.

“NAXA is pleased to confirm the majority of the market is representing itself accurately, and encourages consumers to demand accurate labeling,” said NAXA president Scott Steinfeld.

NAXA, formed in January 2014, aims to educate the public and industry on the health benefits of natural astaxanthin. The association was formed by three natural algae astaxanthin manufacturers—AstaReal, Algatechnologies Ltd. and Cyanotech Corp. The association now also includes Algae Health Sciences Inc. and Alphy Biotech. In May 2016, AstaReal withdrew its membership.

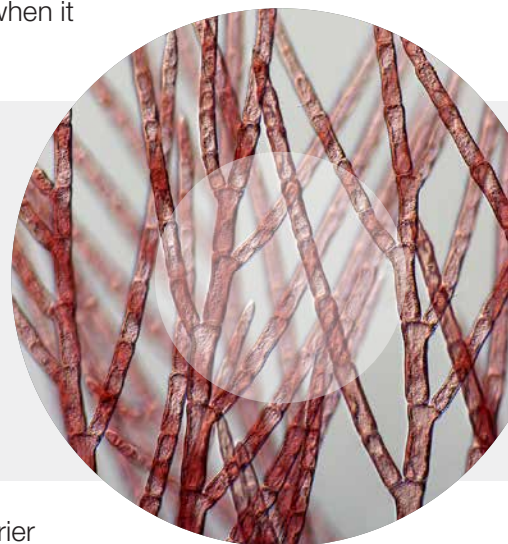
Delivery and Bioavailability

Astaxanthin is highly reactive with oxygen, so great care needs to be taken with the material once the astaxanthin has been extracted from the algae. “If exposed to oxygen, astaxanthin will oxidize into a degradation product called astacene and will lose all its benefits,” Cysewski warned.

Consumer variance also plays a role in efficacy and absorption. The natural range of absorption runs from as low as 5 percent to more than 90 percent, Capelli said. “So if Person A’s body only absorbs 5 percent, he may not get a good effect, even if he’s taking the upper dosage range of 12 mg per day. While if Person B’s body absorbs at the 90 percent level, she may get a fantastic result taking a minimum dose of 4 mg per day. Overall, we’ve seen in clinical trials as well as consumer surveys that about 80 to 85 percent of astaxanthin consumers can feel the difference if they take 4 to 12 mg of astaxanthin daily for at least two months.”

Regardless of personal absorption, carotenoids are better absorbed when taken with fat. A 2003 study reported astaxanthin had better absorption when it was added to a lipid than astaxanthin in formulas without fat.⁵

Astaxanthin is highly reactive with oxygen, so great care needs to be taken with the material once the astaxanthin has been extracted from the algae.



Thus, Cysewski said astaxanthin is typically blended in an oil carrier and then encapsulated in a softgel. “The oil helps protect the astaxanthin from oxidizing, as well as helping with absorption once consumed,” he noted. “The softgel also protects astaxanthin from oxygen and light.”

Ayalon added that the cracked algal cysts themselves are as good a delivery form as the oleoresin, which is astaxanthin dissolved in algal fatty acids. “Other factors that may affect astaxanthin’s bioavailability and hence its efficacy are the method and source of industrial production, and additional dietary factors, such as the presence of other carotenoids and smoking.”

Rodger Jonas, vice president of sales and business development, MTC Industries Inc., noted his company developed a patented self-emulsifying drug delivery system (SED DS) for its Astamax astaxanthin. “Our SED DS technology has been proven to increase bioavailability up to three times,” Jonas said. “It also improves clarity, improves stability and solubility.”



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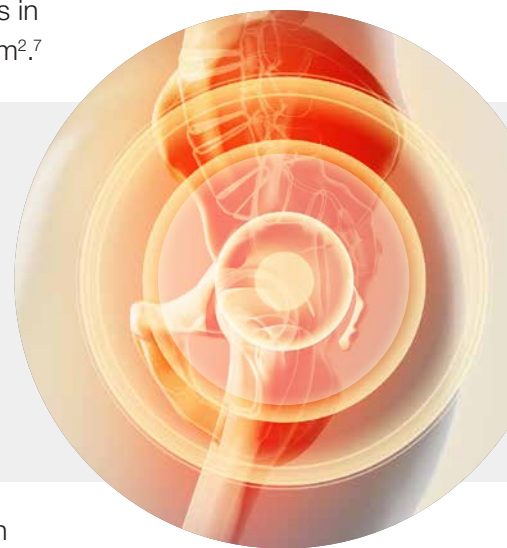
When manufacturing methods are effective, and bioavailability is realized, astaxanthin imparts a slew of benefits to humans, from athletic performance to heart health, skin health, eye health and more.

Inflammation: Research on inflammatory markers shows astaxanthin's antioxidant properties exert effects in humans.

Two capsules with 4 mg of astaxanthin (as Astaxin from AstaReal Inc.) daily for three months reduced the oxidative markers 12- and 15-hydroxy fatty acids significantly, but the placebo did not, in healthy non-smoking Finnish men, aged 19 to 33 years.⁶ The change of 15-hydroxy fatty acid was greater in the astaxanthin group, as compared with the placebo group, but not significantly. "Supplementation with astaxanthin may decrease in vivo oxidation of fatty acids in healthy men," the study authors wrote.

A randomized, double-blind, placebo-controlled study in Korea found astaxanthin reduced oxidative stress biomarkers and improved cholesterol levels in overweight subjects with body mass indexes of more than 25.0 kg/m².⁷

Research on inflammatory markers shows astaxanthin's antioxidant properties exert effects in humans.



The study participants had significantly lower low-density lipoprotein (LDL) cholesterol and apolipoprotein B (ApoB) levels after astaxanthin treatment supplementation for 12 weeks, compared with the start of study, whereas none of the lipid profiles were changed in the placebo group. Total antioxidant capacity was significantly higher in the astaxanthin group.

Heart Health: As the previous study shows, astaxanthin's anti-inflammatory effects lends itself to heart health benefits.

Consumption of marine animals that produce astaxanthin inhibited LDL oxidation and possibly contributed to the prevention of atherosclerosis, according to researchers from a 2000 study.⁸ In the experiment, the time it took LDL to oxidize was dose-dependently longer after consuming the seafood for 14 days compared with baseline. Results were best at a dose of 14.4 mg/d compared to 3.6 or 21.6 mg/d.

Twelve weeks of astaxanthin consumption dose dependently reduced triglycerides and increased high-density lipoprotein (HDL) cholesterol in correlation with increased adiponectin (a protein that helps regulate glucose levels) in non-obese subjects aged 25 to 60 years with high cholesterol (fasting serum triglyceride of 120 to 200 mg/dl)

and without diabetes or hypertension.⁹ Comparison tests showed 12 and 18 mg/d doses significantly reduced triglycerides, and 6 and 12 mg/d doses significantly increased HDL-cholesterol.

Cognitive Health: What affects the heart almost always also affects the brain, and the red carotenoid falls in line.

In 2009, researchers found a reduction in age-related decline in cognitive and psychomotor functions in subjects with age-related forgetfulness who received an extract of astaxanthin equivalent to 12 mg/d for 12 weeks to evaluate efficacy.¹⁰ Astaxanthin also improved markers of dementia and contributed to the prevention of dementia in a randomized, placebo-controlled human clinical trial.¹¹

Eye Health: As part of the brain, eyes also benefit from astaxanthin.

Astaxanthin (6 mg/d) reduced and prevented eyestrain caused by fatigue in healthy subjects in a double-blind, placebo-controlled, human, crossover study from 2006.¹² And astaxanthin supplementation at 5 mg/d for four weeks improved focus in visual display terminal workers compared to placebo in research from 2002.¹³

Dose-dependently, astaxanthin reduced the time it took healthy volunteers to focus their eyes in a 28-day study from 2004.¹⁴ Researchers found the 4 mg/d or 12 mg/d groups had significant changes compared to placebo. The effects weren't as prominent in subjects taking 2 mg/d. Administration of 6 mg/d (in a daily dosage of 2 capsules; 3 mg/capsule) of astaxanthin improved focus power and subjective symptoms of eyestrain in a double-blind, placebo-controlled study of healthy volunteers who complained of eye strain.¹⁵ Astaxanthin was also confirmed to be completely safe.

In two supplementation studies in healthy adult male volunteers, astaxanthin improved the ability to see fine detail and muscle fatigue that may lead to sports performance benefits.¹⁶ In both experiments, the treated groups ingested an astaxanthin capsule per day for 4 weeks (6 mg/d of astaxanthin) and the control groups received a placebo capsule. In the second study, the volunteers also ran 1,200 meters. In the nonrunners, deep vision and the critical flicker fusion (the ability to distinguish different flickers of light) were significantly improved in those who took astaxanthin. In the runners, serum lactic acid concentration was significantly lower two minutes after running in the astaxanthin group.

Sports Nutrition: Astaxanthin benefits athletes beyond eye health and lactic acid build up.

Competitive cyclists who took 4 mg/d of astaxanthin in capsule form experienced improved performance in their 20-km time trial, but similar athletes who took a placebo did not, in a 2011 study from Pennington Biomedical Research Center, Louisiana State University, Baton Rouge.¹⁷ The differences between the two groups were significant. Additionally, the astaxanthin group significantly increased power output, while the placebo group did not.


Algal meal capsules that contained 4 mg of astaxanthin (as AstaREAL® biomass from AstaReal Inc.) improved strength endurance in healthy paramedic students in a double-blind, placebo-controlled study from 2008.¹⁸ After six months of supplementation, the average number of squats increased by 27 (from 49 to 76), while subjects who took the placebo increased their squats by nine (from 46 to 55).

Five mg/d of astaxanthin ingestion for two weeks increased respiratory-circulatory function after healthy volunteers performed progressive loads of three exercises—30 percent heart rate max (HRM), followed by 50 percent HRM and 70 percent HRM—compared to a placebo.¹⁹ Additionally, sympathetic nervous activities during exercise and parasympathetic nervous activities during recovery increased significantly. Blood serum concentration of LDL cholesterol showed a significant decrease, while concentration of creatine phosphokinase increased significantly compared to the placebo group. The authors noted, “Those anti-fatigue and antioxidative functions might be promoted for humans to recover from the whole fatigue generated by exercise stress.”

Astaxanthin supplementation reduced salivary immunoglobulin A (sIgA, a stress marker) and muscle damage in trained male soccer players who were randomly assigned to take 4 mg of astaxanthin or placebo, thus preventing inflammation induced by rigorous physical training.²⁰ The researchers noted the findings suggested astaxanthin could show significant physiologic modulation in individuals with immune health impairment or under conditions of increased oxidative stress and inflammation.

Immune Health: Not only athletes benefit from the immune health properties of astaxanthin, as demonstrated in a 2010 randomized, double-blind, placebo-controlled study.²¹ Astaxanthin decreased DNA damage biomarkers and inflammatory markers, and enhanced immune response in young, healthy females who received 2 or 8 mg/d of astaxanthin. Plasma C-reactive protein (CRP) concentration (an inflammatory marker) was lower after eight weeks in subjects given 2 mg/d of astaxanthin. Dietary astaxanthin increased natural killer cell cytotoxic activity, and increased total T and B cell subpopulations, which are indicators of a healthy immune system.

Skin Health: Astaxanthin taken internally improved the beauty of the skin in two human clinical studies.²² Combining 6 mg/d orally and 2 ml/d in a topical application of astaxanthin showed improvements in skin wrinkle, age spot size and elasticity after eight weeks and in skin texture after four weeks in healthy female subjects. Further, the moisture content of the skin improved after eight weeks in 10 subjects who had dry skin. Another randomized, double-blind, placebo-controlled study found crow's feet wrinkle, elasticity and moisture were improved after 6 mg/d of astaxanthin in healthy male subjects for six weeks.

Human clinical research substantiates astaxanthin's health benefits to skin health, immunity, sports nutrition, eye health, cognitive health, heart health and inflammation. These studies demonstrate that the red carotenoid's unique amolecular form and blood-brain transferability make it a powerful ingredient in the health and nutrition market. 

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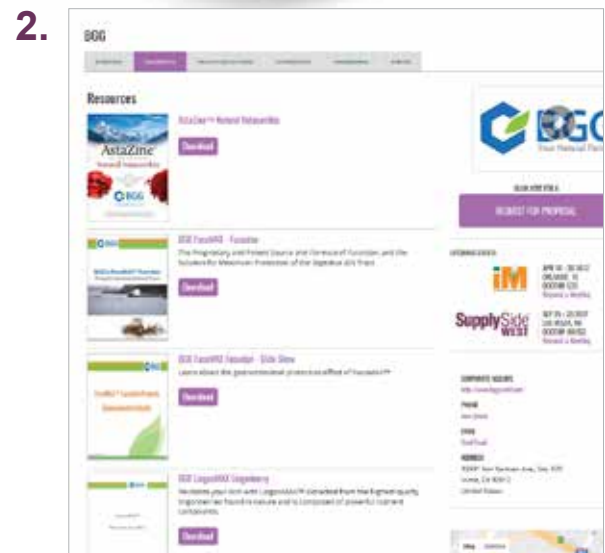
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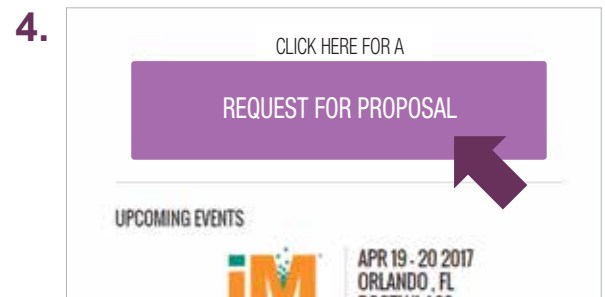
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Takeaways for Your Business

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in the astaxanthin space?

Check out these SupplySide and Vitafoods Global Storefronts to get more information
such as whitepapers, presentations, contacts and other content from suppliers offering
results for astaxanthin manufacturers and marketers.



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