

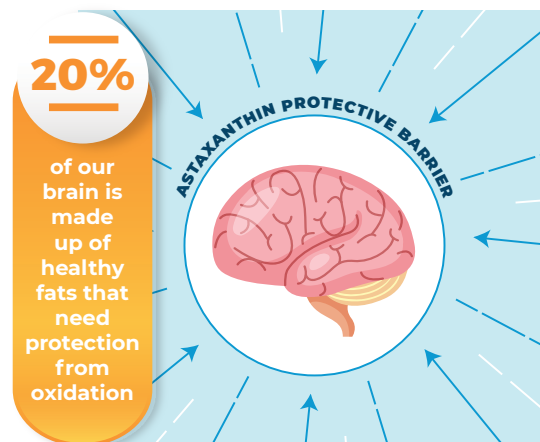
SUPPORT COGNITIVE FUNCTION WITH ASTAREAL® ASTAXANTHIN

Benefits of natural astaxanthin for a healthy & alert brain

WHY THE BRAIN NEEDS ASTAREAL® ASTAXANTHIN

The brain contains more than 100 billion neurons that are long enough to circle the globe 4.5 times. Healthy fats in our diet, including omega-3s and omega-6s, make up a large part of the brain. They are found in foods like fish, flax seeds, and walnuts. The most abundant omega fatty acids in the brain are DHA, and arachidonic acid, which together make up one fifth of the brain's dry weight and help support neuron and brain health.

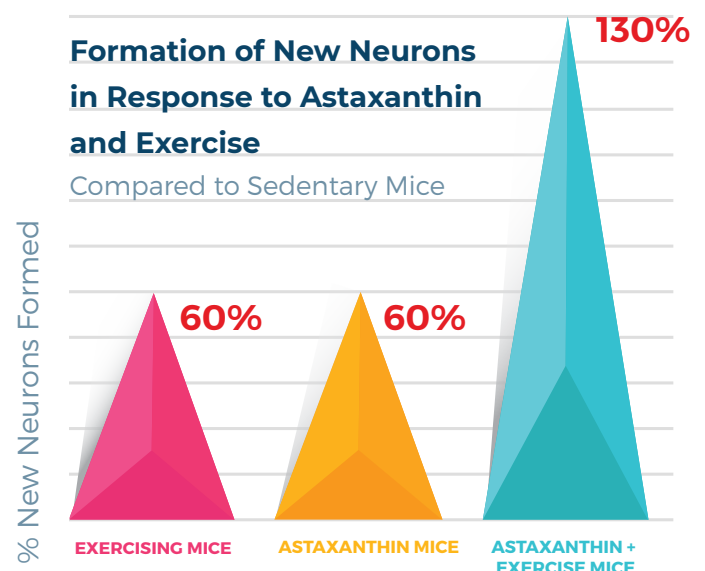
However, these healthy fats are easily oxidized to form toxic byproducts. It's important to protect healthy fats from oxidation, since they play important roles in cognitive function. For example, **DHA and arachidonic acid stimulate neurogenesis in the hippocampus**, the part of the brain known as the gateway to memory.



Natural astaxanthin is one of nature's strongest antioxidants, and it is able to cross the blood brain barrier to access neurons and neutralize free radicals that cause oxidation in the brain. Natural astaxanthin has been shown in studies to promote memory, reaction time, and cognitive function.

STUDY SHOWS ASTAXANTHIN SUPPORTS NEUROGENESIS IN MICE

Exercise is known to promote Adult Hippocampal Neurogenesis (AHN), and studies suggest that astaxanthin may boost this effect. Exercising mice experienced more neurogenesis than sedentary mice, and exercising mice taking AstaReal® Astaxanthin showed a further increase in "newborn" neurons in the hippocampus compared to both exercising and sedentary mice without astaxanthin.



ASTAREAL® ASTAXANTHIN PROMOTES BRAIN HEALTH AND FIGHTS FATIGUE

Clinical studies with AstaReal® Astaxanthin support the following suggested structure/function claims for brain health:

- AstaReal® Astaxanthin supports healthy blood pressure associated with lower stroke risk¹
- AstaReal® Astaxanthin fights mental and physical fatigue²

REFERENCES

1. Iwabayashi M *et al.* Anti-aging medicine. 2009 6(4):15-21.
2. Hongo *et al.* Japanese Pharmacology & Therapeutics. 2017 Jan; 45:61-72

DOSAGE

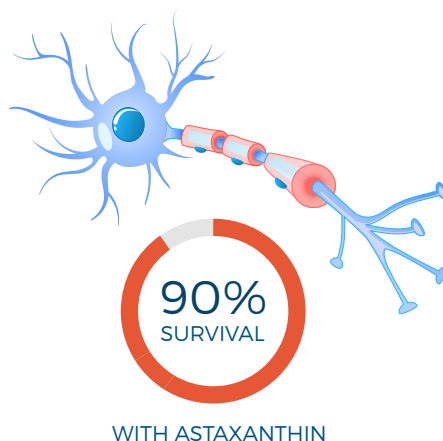
- 12 mg/day
- 12 mg/day

*These are suggested structure/function claims based on AstaReal studies. These suggested structure/function claims have not been verified for promotional use by a regulatory team. We encourage you to review the studies together with your regulatory affairs team to confirm their suitability for promotional applications.

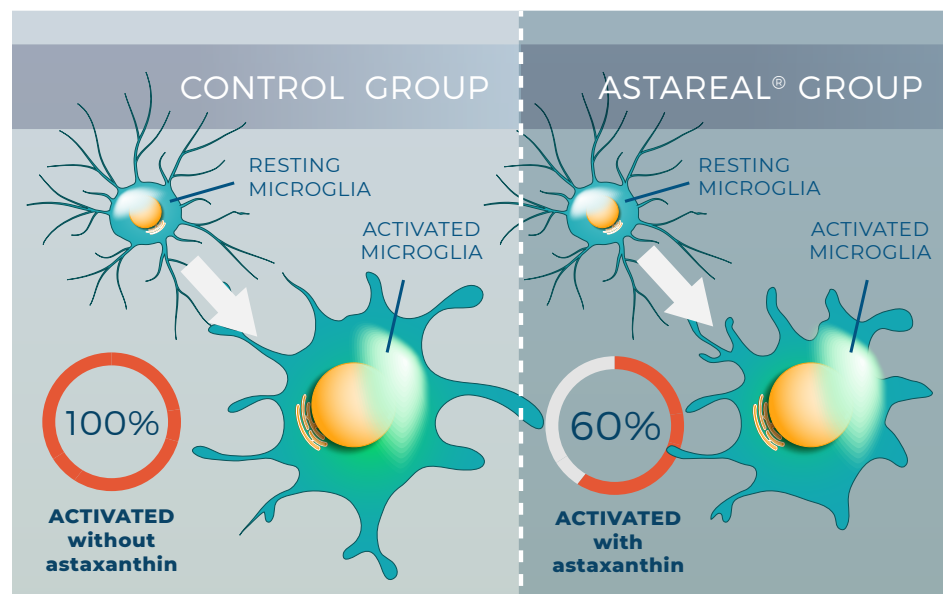
ANTIOXIDANT AND ANTI-INFLAMMATORY PROPERTIES OF ASTAXANTHIN IN BRAIN CELLS

Hydrogen peroxide (H_2O_2) is produced in excess in the brain after a stroke where it generates hydroxyl radicals, inactivates cell enzymes, and induces programmed cell death in neurons.

To see if astaxanthin could help protect neurons, cortical neuronal cells in a petri dish were treated with H_2O_2 in the presence or absence of astaxanthin. Only 64% of neurons survived H_2O_2 exposure without antioxidant protection. When the cells were treated with astaxanthin before being exposed to H_2O_2 , neuronal survival increased to 90% compared to H_2O_2 treated cells in the absence of antioxidant ($p < 0.01$).



ASTAXANTHIN SUPPRESSES BRAIN CELL INFLAMMATION IN VITRO



The brain has specialized immune cells called microglia that lay dormant until they sense infection or injury. Microglia can be activated to induce a temporary inflammation signal that is turned off again once the infection or injury has been resolved. However, in aging individuals microglia are in a perpetually semi-active state that leaks free radicals and inflammatory signals. These leaky microglia activate the master regulator of inflammation, known as NF- κ B, which triggers chronic inflammation and bulging neurons that may lead to neurodegenerative diseases if left unchecked.

When microglia were cultured in a petri dish and an infection was simulated using bacterial endotoxin, 100% of the NF- κ B was found in an activated, pro-inflammatory state. When microglia were pre-treated with astaxanthin before exposure to bacterial endotoxin, only 60% of the NF- κ B was activated ($p < 0.01$). This shows that astaxanthin can modulate inflammation in immune cells of the brain in vitro.

NATURAL ASTAXANTHIN FOR COGNITIVE FUNCTION

Clinical studies with Natural Astaxanthin support the following suggested structure/function claims for brain health:

- AstaReal® Astaxanthin decreases oxidized red blood cells, which are associated with dementia when present at high levels¹
- Natural Astaxanthin promotes reduction in age-related forgetfulness, multitasking and alertness²
- Natural Astaxanthin promotes faster reaction times (choice reaction, mid and episodic memory, spatial attention)^{3,4}

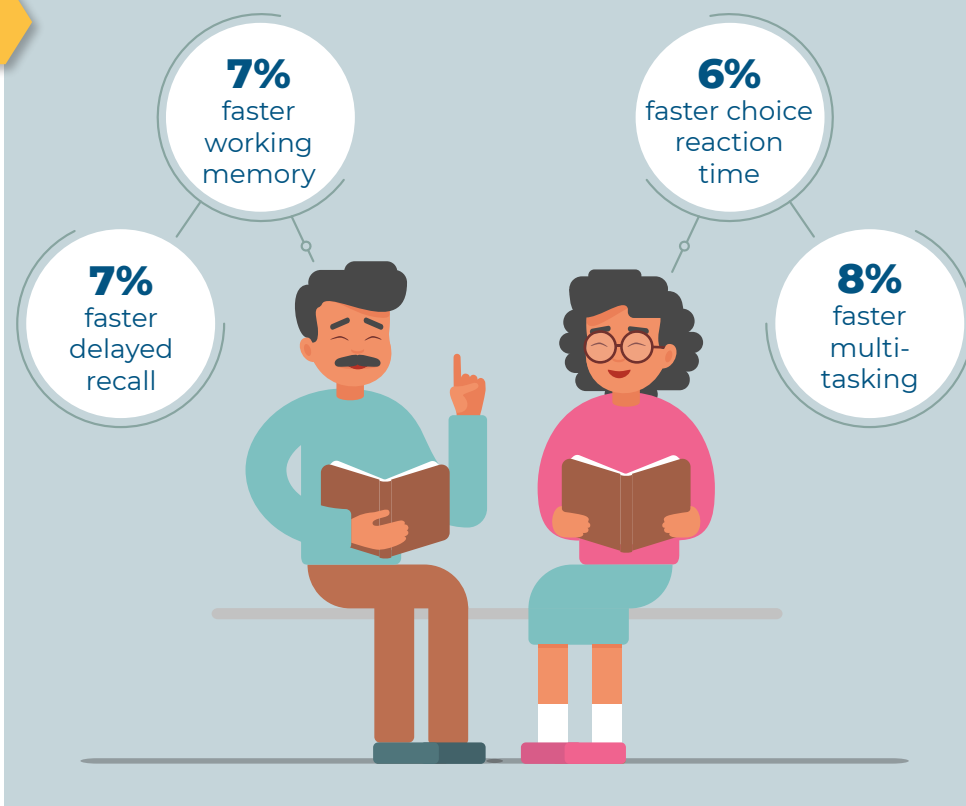
REFERENCES

- | REFERENCES | DOSAGE |
|---|-----------|
| 1. Nakagawa <i>et al.</i> , British Journal of Nutrition (2011), 105, 1563-1571. 6. | 12 mg/day |
| 2. Zanotta <i>et al.</i> , Neuropsychiatric Disease and Treatment 2014;10: 225-230. | 2 mg/day |
| 3. Katagiri <i>et al.</i> , J Clin Biochem Nutr. 2012;51(2):102-7. | 12 mg/day |
| 4. Satoh, A. <i>et al.</i> , J. Clin. Biochem. Nutr., 44, 280-284, May 2009. | 12 mg/day |

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ASTAREAL® ASTAXANTHIN SUPPORTS COGNITIVE FUNCTION

1



Katagiri *et al.* 2012 published a double blind, randomized, placebo-controlled study in which 96 healthy participants (mean age 56) supplemented with 0mg (n=31), 6mg (n=29), or 12 mg (n=29) natural astaxanthin daily for 12 weeks. Cognitive functions were measured using response times to a battery of CogHealth tasks performed on a computer. The group supplementing with 12 mg/day natural astaxanthin exhibited 6% faster choice reaction time ($p<0.1$), 7% faster working memory ($p<0.05$), 7% faster delayed recall ($p<0.1$), and 8% faster multitasking ($p<0.1$) compared to baseline.

2

Zanotta *et al.* 2014 reported an open label study with 98 subjects (mean age 71) with mild cognitive impairment. Subjects supplemented with a formulation including 2 mg/day natural astaxanthin, Bacopa monnieri, bacosides, phosphatidylserine and vitamin E for 60 days. Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) went from 13.7 ± 5.8 at baseline, to 9.7 ± 4.9 on day 60 ($p<0.001$). A significant improvement was also found in the Clock Drawing Test (CDT) score, from 8.5 ± 2.3 to 9.1 ± 1.9 ($p<0.001$).

3*

Satoh *et al.* 2008 published an open-label clinical study with 10 healthy adults (50-69 years old) exhibiting age-related forgetfulness. Participants took 12 mg/day natural astaxanthin for 12 weeks. Brain function was assessed using the CogHealth test after 12 weeks of supplementation. Participants exhibited a 17.5% increase in simple reaction time, 8% faster choice reaction time, 17% faster multitasking, 14% faster working memory, and 9% faster delayed recall compared to baseline ($p<0.05$). A 6.5% improvement in accuracy during working memory tasks after 12 weeks of supplementation compared to baseline was also observed ($p<0.05$).

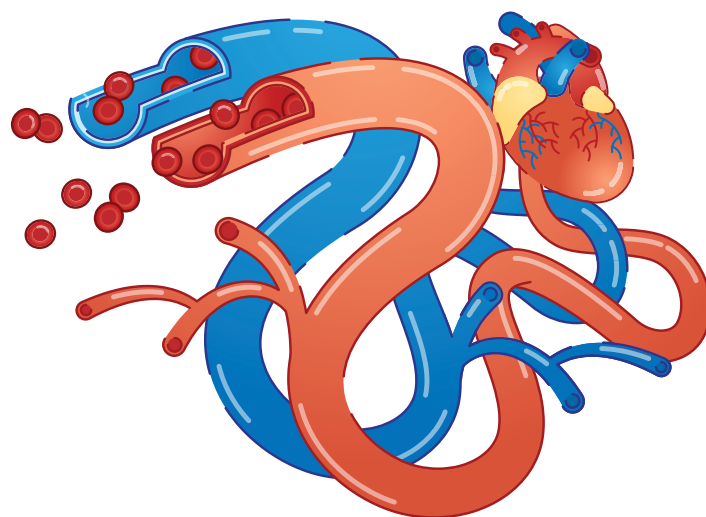
4*

Hongo *et al.* 2016 reported in a randomized, double-blind, placebo-controlled study of 39 healthy subjects (20-64 years old) given control softgels (n=19) or 12 mg AstaReal® Astaxanthin and 20 mg tocotrienol (n=20) for 8 weeks. AstaReal® Astaxanthin reduced perceived symptoms of fatigue, including, mental fatigue and improved clarity of thinking, concentration, motivation and mood. After 8 weeks, the control group made an average of 3.2 ± 1.1 mistakes in the second round of calculations as compared to the first round of calculations ($p < 0.05$). The AstaReal® Astaxanthin group, who reported less mental fatigue, did not see a similar decline in accuracy; averaging only 0.2 ± 0.8 more wrong answers in the second round of calculations as compared to the first round ($p < 0.05$).

* Study conducted using AstaReal material

ASTAREAL® ASTAXANTHIN SUPPORTS BLOOD FLOW FOR A NOURISHED BRAIN

Blood carries oxygen and nutrients to the brain, making good cardiovascular health critical for a healthy brain and robust cognitive function. As we age, changes in vascular structure and function lead to reduced blood flow, decreased capillary density, as well as thicker and more rigid blood vessel walls.



1* Iwabayashi *et al.* 2009 reported on an open label study of 35 post-menopausal women supplementing with 12 mg/day AstaReal® Astaxanthin for 8 weeks. The study found that lower limb vascular resistance, indicative of blood vessel flexibility, improved by nearly 4% after 4 weeks of supplementation ($p < 0.05$).

2* Nagaki *et al.* 2005 published a double blind placebo controlled study of 36 healthy subjects (average age 41), supplementing with 0 or 6 mg/day AstaReal® Astaxanthin for 4 weeks. The AstaReal® group ($n=18$) exhibited increased retinal capillary blood flow of 9-11% compared to baseline ($p < 0.01$).

3* Saito *et al.* 2012 found in a double blind placebo controlled study of 20 subjects (average age 38) that the test group ($n=10$) supplementing with 12 mg/day AstaReal® Astaxanthin for 4 weeks exhibited a 15% increased blood flow velocity at the macula compared to baseline ($p < 0.05$).

4* Miyawaki *et al.* 2008 published a single blind study of 20 subjects supplementing with 0 mg/day ($n=10$; average age 51) or 6 mg/day AstaReal® Astaxanthin ($n=10$; average age 57) for 10 days. The *ex vivo* blood transit time through a capillary was shortened by 10% in the AstaReal® group compared to placebo ($p=0.05$).

5* Oxidative modification of red blood cells produces phospholipid hydroperoxides (PLOOH), which may reduce oxygen carrying capacity. High PLOOH levels have been associated with an increased incidence of dementia. Nakagawa *et al.* 2011 published a double blind placebo controlled study in which 30 healthy individuals (average age 56) supplemented with 0, 6, or 12 mg/day AstaReal® Astaxanthin for 12 weeks. After 12 weeks, total PLOOH levels decreased in both astaxanthin groups compared to placebo ($p < 0.05$) with a 40% decrease in the 6 mg/day group ($n=10$) and a 48% decrease in the 12 mg/day group ($n=10$) ($p < 0.01$).

ASTAREAL® ASTAXANTHIN PROMOTES NOURISHING BLOOD FLOW

Clinical studies with AstaReal® Astaxanthin support the following suggested structure & function claims for blood flow*:

- AstaReal® Astaxanthin promotes good circulation^{1,7}
- AstaReal® Astaxanthin helps alleviate oxidative stress^{2, 3, 4, 5, 6, 8, 9}

References	DOSAGE
1. Nagaki Y. <i>et al.</i> 2005. Journal of Clinical Therapeutics and Medicines, 21(5): 73-78.	6 mg/day
2. Hashimoto H. <i>et al.</i> 2009. Atarashii Ganka (Journal of the Eye), 26 (2):229-234.	6 mg/day
3. Hashimoto H. <i>et al.</i> 2013. Journal of Clinical Biochemistry and Nutrition, 53(1): 1-7.	6 mg/day
4. Hashimoto H. <i>et al.</i> 2016. Journal of Clinical Biochemistry and Nutrition, 59(1): 10-15.	6 mg/day
5. Hashimoto H. <i>et al.</i> 2011. Rinsho Ganka (Jpn J Clin Ophthalmol), 65(4): 465-470.	6 mg/day
6. Karppli, J. <i>et al.</i> Int. J. Vitam. Nutr. Res. 77(1): 3-11, 2007.	8 mg/day
7. Saito M. <i>et al.</i> 2012. Graefes Arch Clin Exp Ophthalmol. 250(2):239-45.	12 mg/day
8. Iwabayashi M. <i>et al.</i> 2009. Anti-Aging Medicine. 6(4):15-21.	12 mg/day
9. Yamada T. <i>et al.</i> J. Clin. Biochem. Nutr., 47: 130-137, 2010.	12 mg/day

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WHY CHOOSE ASTAREAL® ASTAXANTHIN



THE GLOBAL PIONEER

The first company in the world to commercially produce natural astaxanthin - AstaReal® is the only brand backed by 30+ years of research and innovation.



THE LEADING EXPERT

AstaReal® is an expert in natural astaxanthin cultivation, R&D and clinical science.



THE AUTHORITY IN HUMAN CLINICAL STUDIES

The only brand of natural astaxanthin backed by over 60 human clinical studies.



UNRIVALED PRODUCT QUALITY

Two state of the art, in-door production sites in the USA and Sweden producing a consistent and stable supply of natural astaxanthin products with unrivaled levels of product quality and purity. AstaReal® is USP, Non-GMO, ISO, HACCP, Halal, and Kosher certified, NSF GMP Registered, and has approved Health Canada claims.



TRULY INTERNATIONAL

Our partners benefit from access to talented, high performance local teams of technical, marketing, and regulatory experts with an in-depth knowledge of your target region.



BE YOU, JUST HEALTHIER

The AstaReal® group has established other initiatives that are in line with our corporate philosophy of making the world healthier with natural astaxanthin. These include community health and wellness programs, a global symposium focusing on natural astaxanthin and sponsorship grants for groups and individuals.



MADE IN THE USA

From cultivation to extraction, AstaReal® Astaxanthin is made in the USA to ensure the best quality and traceability. Our proprietary closed, indoor cultivation technique is unique to the industry and the only one of its kind in North America.



To learn more about natural astaxanthin and your health visit www.astaxanthin.net

AstaReal, Inc.
3 Terri Lane, Unit 12
Burlington, NJ 08016 USA
T: 1-609-614-6904

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