

**Excerpted
from the
Book**

NATURAL ASTAXANTHIN

THE SUPPLEMENT YOU CAN FEEL



BOB CAPELLI

TECHNICALLY REVIEWED BY LIXIN DING, PHD

Including excerpts from renowned health and nutrition experts
Dr. Joseph Mercola, Mike Adams "The Health Ranger", Suzy Cohen RPh,
Susan Smith Jones, PhD and more

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ASTAXANTHIN

**THE IMMUNE SYSTEM
MODULATOR**

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Astaxanthin, The Immune System Modulator

In the first chapter I mentioned that I haven't had a cold or flu since I started taking Astaxanthin. That was 17 years ago. I started taking another microalgae product called Spirulina about a year and a half after starting my Astaxanthin supplementation, but I already felt something had changed during that first year and a half since I went from two or three colds a year down to zero. So I'm inclined to believe that my outstanding immune system function is due to Astaxanthin.

I'm aware that such a dramatic change isn't typical for most Astaxanthin users. However, many people have told me that they get sick less often after starting to take Astaxanthin. And close to 30 medical research studies as well as a consumer survey validate these testimonials. The survey once again proved the 80/20 rule I talked about in Chapter 1.

Survey Says 80% of Consumers Improved Their Immune System with Astaxanthin

In conducting this survey, a medical doctor, a PhD and I employed an inclusive criterion for "Astaxanthin users." We started by polling 1584 people who had bought at least one bottle of Astaxanthin over the last seven years. Of the 423 people who responded, we disqualified 121 who hadn't used the product for at least a month or were not taking Astaxanthin at least three times per week.

The survey asked respondents to answer "true" or "false" to a series of statements about Natural Astaxanthin. Of the 302 qualified respondents, exactly 80% said it was "true" that their immune systems improved and/or they were getting fewer colds and flu since supplementing with Astaxanthin (Capelli et al., 2008). (Precisely 80% said "true" and 20% said "false"—the 80/20 rule can't get any more exact than that.)

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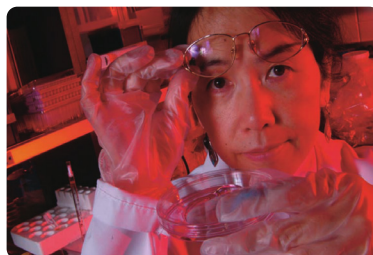
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Where it All Began: The Pioneering Work of Dr. Harumi Jyonouchi

Dr. Harumi Jyonouchi, a medical doctor and university professor, was working at All Children's Hospital at the University of South Florida when she began exploring the effects of Astaxanthin on the immune response and cancer prevention in the early 1990s. Dr. Jyonouchi truly was a pioneer of Astaxanthin research. Before she embarked on her immunity studies, very little research had been done on Astaxanthin. Her experiments were confined to pre-clinical trials in test tubes and rodents, but she published many different studies that set a great foundation for the immunity research that followed.

Dr. Jyonouchi did several experiments testing Astaxanthin against beta-carotene. In the 1980s and 1990s when I began working in the natural supplement industry, beta-carotene was all the rage as an immunity supplement. Yet in her experiments, Astaxanthin consistently far outperformed beta-carotene in every way. She also tested Astaxanthin against several other carotenoids and, as expected, it outclassed them as well. Let's briefly look at the important work she did, which set the stage for the human research that followed.



Pioneering investigator Harumi Jyonouchi, MD, the initiator of immunity research on Astaxanthin.

#1 Astaxanthin is superior to beta-carotene in immune modulation in vitro.

Dr. Jyonouchi tested beta-carotene against Astaxanthin in mouse cells and found that, while beta-carotene worked well, Astaxanthin was superior in all four parameters tested. The conclusion stated: "These results indicate that immunomodulating actions of carotenoids are not necessarily related to Pro-Vitamin A activity, because Astaxanthin, which does not have Pro-Vitamin A activity, showed more significant effects in these bioassays" (Jyonouchi et al., 1991).

#2 Astaxanthin enhances in-vitro antibody production to T-dependent antigens.

After moving to the University of Minnesota's School of Medicine, Dr. Jyonouchi examined the mechanism of action involved in enhancing antibody production. This experiment showed that Astaxanthin may be able to

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augment antibody production by affecting the initial stage of antigen presentation (Jyonouchi et al., 1993).

#3 Astaxanthin is superior to beta-carotene in preventing formation of cancer in mice. In her first animal trial in this area, Dr. Jyonouchi and her colleagues found Astaxanthin to be more effective than beta-carotene in preventing carcinogenesis in autoimmune-prone mice (Tomita et al., 1993).

#4 Astaxanthin enhances humoral immune response in old mice better than lutein or beta-carotene. The following year, Dr. Jyonouchi expanded the carotenoids she was testing and included both beta-carotene and lutein. She demonstrated that Astaxanthin performed better in older mice than both of its carotenoid cousins (Jyonouchi et al., 1994).

#5 Astaxanthin increases antibody response in vitro. An additional test-tube study corroborated earlier results showing that Astaxanthin has more profound effects than beta-carotene on antibody response in animal cells (Jyonouchi et al., 1995a).

#6 Astaxanthin enhances human immunoglobulin in culture more effectively than beta-carotene. Dr. Jyonouchi moved to human cells in this experiment and found that, again, Astaxanthin's effects in enhancing immunity in vitro were far superior to those of beta-carotene (Jyonouchi et al., 1995b).

#7 Astaxanthin enhances immunity in-vitro and was the sole carotenoid of several tested that performed as a T1-helper cell clone. This time, Dr. Jyonouchi's group tested Astaxanthin against several carotenoids: lutein, lycopene, zeaxanthin and canthaxanthin. As expected, Astaxanthin's effects in immune enhancement in vitro were the most potent. In fact, Astaxanthin was the only one of these antioxidant carotenoids that enhanced the number of antibody-secreting cells and performed as a T1-helper cell clone. Furthermore, both Astaxanthin and zeaxanthin successfully increased the number of immunoglobulin M cells while none of the other carotenoids had this effect (Jyonouchi et al., 1996).



A healthy immune system is essential to fight off germs.

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#8 Astaxanthin may exert anti-tumor activity through the enhancement of the immune response in mice. The year 2000 marked the final study from Dr. Jyonouchi's decade of pioneering research on Astaxanthin. This study was done in mice to test Astaxanthin's ability to suppress fibrosarcoma tumor growth. The mice were fed a diet containing 0.02% Astaxanthin (which equates to 40mcg per kg of their body weight). The mice in the Astaxanthin group had significantly lower tumor size and tumor weight than the control group. Improvements in blood immune markers were also noted in the Astaxanthin group (Jyonouchi et al., 2000).

The Preliminary Research of Drs. Chew & Park

You may remember Dr. Boon Chew from Chapter 2. He's a prolific researcher at Washington State University and is regarded as an expert on carotenoids. Along with long-time associate Jean Soon Park, Dr. Chew has added a great deal to the research of Astaxanthin, including a landmark human clinical trial on immunity.

In 1999, two early studies published by Drs. Chew and Park showed great potential for Astaxanthin to positively affect the immune response of mice. Like some of the research by Dr. Jyonouchi, the first study compared Astaxanthin to other carotenoids, in this case beta-carotene and canthaxanthin. The researchers focused on how these carotenoids fare against the growth of breast tumors in mice. They tested two different strengths of each carotenoid against placebo, starting the treatment feeds three weeks before the introduction of tumor cells. The result: "Mammary tumor growth inhibition by Astaxanthin was dose-dependent and was higher than that of canthaxanthin and beta-carotene." All three carotenoids showed some positive effects, with Astaxanthin demonstrating a clear advantage. Additionally, lipid peroxidation activity in the tumors was lower in mice fed the stronger dose of Astaxanthin but not in mice fed beta-carotene or canthaxanthin (Chew et al., 1999a).

Later that year, a mouse trial showed that both Astaxanthin and beta-carotene stimulate lymphocyte function while canthaxanthin had no effect (Chew et al., 1999b). Lymphocytes are white blood cells in the body that provide a baseline defense against infection and help to fight off disease. By stimulating the function

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of these disease fighters, Astaxanthin helps improve resistance to disease.

Another mouse study on tumor growth and immune response headed by Dr. Chew found corroborating results. Again, Astaxanthin was found to delay tumor growth, but only when the Astaxanthin feeding was started before tumor initiation. A corresponding modulation of the rodents' immune response was also found in the Astaxanthin treatment group (Nakao et al., 2010).

Moving up the mammal chain, Drs. Park and Chew did their next two experiments on cats and dogs. Both studies were done using similar methods, and both studies yielded similar results. The cat study showed that Astaxanthin improved immune function in multiple ways: it increased T helper cells, increased concentrations of plasma immunoglobulin G and immunoglobulin M, and heightened NK cell cytotoxic activity. The results showed increases in both the cell-mediated and humoral immune response in cats fed Astaxanthin (Park et al., 2011).

The dog study tested additional parameters and showed even more impressive results than the cat study. In addition to increases in several immune markers, Astaxanthin supplementation resulted in other important benefits. For one,

DNA damage was reduced in the dogs that were fed Astaxanthin, indicating a potential for cancer prevention. Additionally, C-reactive protein (CRP) was reduced, indicating a reduction in systemic inflammation (Chew et al., 2011).



Across a variety of mammal species, Drs. Chew and Park found Astaxanthin to have consistently positive effects on immune function.

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Landmark Human Clinical Trial Shows Immune Response Benefit

The promising pre-clinical research by Dr. Jyonouchi and the steady progression of mammal studies by Drs. Chew and Park led to a seminal human clinical trial. The study was done in healthy, young women averaging just over 20 years old. And, of course, the study was state-of-the-art: randomized, double-blind and placebo-controlled. The study lasted for eight weeks. The women were separated into three different groups: the control group took placebos every day, while the two treatment groups took either 2mg or 8mg of Natural Astaxanthin per day. The researchers assessed immune response at the beginning of the trial as a baseline, then halfway through the trial, and finally at the end of the trial after eight weeks of supplementation.

Landmark Clinical Trial Showed That Astaxanthin:

- Increased the total number of antibody-producing B cells
- Amplified natural killer cell cytotoxic activity
- Led to increased number of T cells
- Stimulated lymphocyte counts
- Significantly increased delayed-type hypersensitivity response
- Dramatically decreased DNA damage
- Reduced CRP, the key marker for systemic inflammation
(Park et al., 2010)

While these findings contain technical language, they can be summed up easily in plain English: just as Astaxanthin works through multiple pathways as an anti-inflammatory, an antioxidant and a cardiovascular aid, it also works through multiple pathways to support the immune system. Based on research reviewed in previous sections of this chapter, readers may have discerned a pattern emerging. Astaxanthin tends to improve individual health systems from a variety of angles at

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the same time. This may be why Astaxanthin is more effective than other nutrients (and why it is “The Supplement You Can Feel”).

One counterintuitive finding of this study was that the group supplementing with 2mg per day of Natural Astaxanthin showed slightly better results than the group taking 8mg per day. While the difference was not statistically significant, this result was unexpected, particularly since research on the many other health benefits of Natural Astaxanthin have generally found optimal results at levels significantly above 2mg per day. Further studies would be necessary to determine the optimum dosage for immune system modulation.

This research led to a patent for Drs. Chew and Park on the use of Astaxanthin to prevent DNA damage from oxidation. The patent states that administering as little as 2mg per day of Natural Astaxanthin over a four-week period is sufficient to reduce DNA damage by approximately 40% (Chew and Park, 2006).



The Washington State University landmark clinical trial showed multiple pathways for Astaxanthin's immune system benefits.

Additional Human Clinical Research

Improvement in Immunoglobulin, Pro-Oxidant/Antioxidant Balance and CRP Levels. Another clinical trial was done recently which further validates Astaxanthin's ability to improve the immune response in humans. This was the study done in Europe on young elite soccer players that I cited in the section on athletes. The 40 young men were randomly separated into two groups, one that took 4mg of Natural

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Astaxanthin each day for 90 days, and the other that took placebos.

This study found that, in the young athletes supplementing with Astaxanthin:

- ➔ **Immunoglobulin levels increased.** Immunoglobulins are proteins present in immune cells that function as antibodies, chemically combining with bacteria, viruses and foreign substances invading the body.
- ➔ **The Pro-Oxidant/Antioxidant balance decreased.** Pro-oxidants create more harmful free radicals in the body while antioxidants combat these destructive substances.
- ➔ **Plasma muscle enzyme levels decreased.** Muscle enzyme levels are a predictor of muscle disease and also cardiovascular problems.
- ➔ **CRP levels remained constant in the Astaxanthin group while they increased in the placebo group.**

The summary stated, “This study indicates that Astaxanthin supplementation improves immunoglobulin response and attenuates muscle damage, thus preventing inflammation induced by rigorous physical training. Our findings also point that Astaxanthin could show significant physiologic modulation in individuals with mucosal immunity impairment or under conditions of increased oxidative stress and inflammation” (Baralic et al., 2015).



Athletes' immune systems can become compromised by intense physical activity, but Astaxanthin can provide protection.

Astaxanthin Supplementation Leads to Improvements in Patients Suffering from an Auto-Immune Disorder. This study (also mentioned earlier) was done in Japan at the Tsurumi University School of Dental Medicine in patients suffering from an autoimmune disorder called Sjögren's syndrome. Sjögren's syndrome is a

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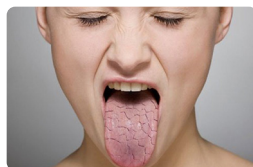
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systemic chronic inflammatory condition. What happens to people with Sjögren's is that lymphocytes infiltrate glands such as salivary and sweat glands. The result is symptoms such as dry mouth and eyes.

This study was done in three parts: in vitro, using a mouse model, and lastly as a human clinical trial with both patients suffering from Sjögren's syndrome and healthy subjects.

- ➔ In the in-vitro study, Astaxanthin partially suppressed hydrogen peroxide-induced oxidation in human salivary gland epithelial cells.
- ➔ In the mouse model, Astaxanthin helped keep the animals' mouths salivating after they were exposed to radiation.
- ➔ In both the healthy human group and the group with Sjögren's syndrome, Astaxanthin acted to increase salivary output and decrease the level of an oxidative stress marker (Yamada et al., 2010).

This study and the study on rheumatoid arthritis mentioned in the anti-inflammatory section were both done in patients with auto-immune disorders. Astaxanthin's benefits for these two different auto-immune conditions demonstrate that it modulates the immune response rather than simply boosting it—when the immune system needs a boost, it seems to enhance it; but when the immune system is overcharged, as in auto-immune diseases, it seems to reduce the self-destructive effects.



Auto-immune condition Sjögren's syndrome manifests as dry mouths and eyes.

Astaxanthin Suppresses Lymphocyte Activation in Human Cells of Patients Suffering from Allergic Rhinitis and Pollen-Related Asthma. Allergic rhinitis is commonly called hay fever. It is characterized by inflammation in the nose. Pollen-related asthma is also an allergic condition. Both of these disorders can lead to runny noses, sneezing and itching. This in-vitro study showed that Astaxanthin suppressed the activation of lymphocytes taken from people suffering from these conditions. This resulted in improved activity of antihistamines and led the researchers to suggest a dosing strategy for further trials (Mahmoud et al., 2012).

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For the Scientists (A quick review of some excellent supporting pre-clinical studies)

I covered many of the most important pre-clinical studies already in the first sections about Dr. Jyonouchi and Drs. Chew and Park. Other studies of interest have shown that Astaxanthin:

- Improved the tumor immune response in mice (Kurihara et al., 2002).
- Stimulated immune response in-vitro and in mice (Lin et al., 2015).
- Reduced immune liver injury in a rat model of autoimmune hepatitis (Li et al., 2015a).
- Slowed the spread of human liver cancer cells and induced cancer cell death in vitro (Li et al., 2015b).
- Slowed the growth of a human gastric cancer cell line (Kim et al., 2016).
- Improved the function of human neutrophils (a type of white blood cells) (Macedo et al., 2010).
- Changed the immune response to *H. pylori* bacteria (Akyon, 2002).
- Is superior to other carotenoids in enhancing immunity in vitro (Okai and Higashi-Okai, 1996).

It isn't only mammals whose immune systems are improved by Astaxanthin. I'll review a study in salmon in Chapter 5 and one in shrimp in Chapter 7 that both demonstrated huge improvements in survival rates of juveniles (which the authors attributed to improved resistance to disease and stress). In addition, a study in fish showed that Astaxanthin helps modulate their immune systems (Jagruthi et al., 2014).

In conclusion, I can't say that you won't get a cold or flu for 17 years like me if you start supplementing with Astaxanthin every day. But the research suggests that you're likely to see an improvement in your immune function with Astaxanthin supplementation. Though there haven't been as many clinical trials on immunity as on the other health benefits I've covered, the findings so far are compelling. The landmark study by Dr. Chew, coupled with a few other human clinical studies and many pre-clinical trials, lead to my recommendation that anyone wishing to improve their immune response should strongly consider supplementing with Natural Astaxanthin.