Astaxanthin—the Ultimate Anti-Aging Nutrient

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Astaxanthin is perhaps the very best nutrient for anyone over the age of 40 to take on a daily basis. The clinically validated benefits of Natural Astaxanthin in areas that most concern people as they age are quite comprehensive; practically every concern for people approaching middle age and beyond is at least to some extent addressed by this single supplement: Cardiovascular health, eye & brain health, skin health & UV protection, immunity, energy & strength levels, aches & pains, cellular health—research indicates that Natural Astaxanthin addresses all of these and more. It is our opinion that every consumer over the age of 40 should be supplementing with at least 4mg of Natural Astaxanthin every day. And even people under the age of 40 should consider Astaxanthin as a great preventive supplement.

At the very heart of Astaxanthin's benefits against aging are its foundational properties of being the world's strongest and highest quality natural antioxidant and being a safe and natural, broad spectrum anti-inflammatory. As a result of these attributes, Astaxanthin has demonstrated the ability to protect our cells and the DNA within our cells from the onslaughts of oxidation and inflammation. In fact, these properties are the primary mechanisms of action from which most of Astaxanthin's varied health benefits emanate.

In order to fully understand Astaxanthin's benefits against aging, we will first review related research that shows anti-aging properties in each of the categories we mentioned above. This review will focus on human research; however, in a few cases we will cite relevant pre-clinical research (which will be limited to a small handful of studies). Then we will look at research specific to Astaxanthin's ability to protect vital parts of our cells such as DNA and the mitochondria. Lastly, we will round out this paper by examining Astaxanthin's antioxidant and anti-inflammatory characteristics that further demonstrate its ability to protect the cells in our bodies.

Human Clinical Research Reveals Anti-Aging Benefits of Astaxanthin

There have been approximately one hundred human clinical trials showing a variety of health benefits for Natural Astaxanthin. Most of these areas of research are directly related to concerns that people face in middle age and beyond. While a thorough review of all this research is not possible within the confines of this paper, we will examine some of the most relevant areas of research and delve into the most exciting research within each area.

Eye Health

As anyone who is 50 or older knows, the eyes change with age. Many people who never required corrective lenses as children or in their 20's and 30's find themselves going to the optometrist for a pair of reading glasses in their mid-40's. And as people get older, much more serious issues such as age-related macular degeneration, cataracts and glaucoma become increasingly prevalent. What we need as an ounce of prevention for our aging eyes and brains is a combination supplement: A strong antioxidant and broad spectrum anti-inflammatory that can get through the blood-brain barrier and enter the brain. Then, once in the brain, it must be able to get through the blood-retinal barrier to bring its antioxidant and anti-inflammatory protection to the eyes. Fortunately, Astaxanthin has exhibited these abilities in university and private research which began over 60 years ago in Europe and has continued since then, primarily in the USA and Japan (Grangaud, 1951; Massonet, 1958; Tso and Lam, 1996; Capelli and Cysewski, 2014). There are several human clinical trials that validate a variety of eye health benefits; let's examine some of the best human trials that have shown Natural Astaxanthin's diverse positive effects on the eyes.

Eye Fatigue, Eye Accommodation and Eye Strain. Eye fatigue (which is known medically as "Asthenopia") is becoming more prevalent due to extensive use of computers and other visual display terminals. This can manifest as eye strain, blurring and diplopia (a disorder of vision in which two images of a single object are seen because of unequal action of the eye muscles – also called double vision). Accommodation is a critical function of the eyes. This is the process by which the eye changes optical power to focus on a particular object as the viewing distance varies. An extensive series of human clinical trials have shown that Natural Astaxanthin has positive benefits for all of these conditions.

An early study in this area was done in Japan. It was a state-of-the-art study—a double blind, placebo-controlled human clinical study. After four weeks of supplementation with 5 mg of Astaxanthin per day (extracted from Haematococcus algae meal) the authors reported a 46% reduction in the number of eye strain subjects. They also found higher accommodation amplitude (the adjustment in the lens of the eye that allows it to focus) in subjects who used visual display terminals (Nagaki, 2002).

The next study we'll look at tested two different dosage levels of Natural Astaxanthin for eye fatigue. Results showed positive effects at 4 mg per day, but found a better result at 12 mg per day (Nakamura, 2004). This study showed that the optimum dose was above 4mg per day, but there was no conclusion as to whether the optimum would be 12mg or somewhat higher or lower. Much of the research since then has centered on 6mg per day as the optimum dose for eye health.

Another group of researchers found similar results in their own human clinical study. This double blind study was done to evaluate Astaxanthin's effect on eye fatigue and visual accommodation. Forty subjects were divided into placebo and treatment groups, with the treatment group receiving 6 mg of Astaxanthin for four weeks. The results showed that three separate visual parameters were found to have statistically significant benefits from Astaxanthin supplementation. This study established an optimum daily dose for eye fatigue of at least 6 mg per day (Nitta, 2005). A study the following year corroborated these results. This study concluded that taking 6mg of Natural Astaxanthin per day has the effects of reducing and preventing eye strain and accommodative dysfunction (Iwasaki, et al, 2006). This study was interesting in the sense that it showed both a preventative as well as a therapeutic potential for Astaxanthin for eye conditions such as strain and accommodation.

This preventative role is displayed in a clinical study done on subjects whose eyes were healthy, with no signs of fatigue or strain. Both the treatment and the placebo groups were subjected to heavy visual stimuli to induce eye fatigue, and it was found that the treatment group recovered more quickly. This clearly indicates that Natural Astaxanthin may serve not only to treat eye fatigue in those that already suffer from it, but also to prevent eye fatigue from occurring in healthy people (Takahashi and Kajita, 2005).

Additional studies have shown that 6 mg per day of Natural Astaxanthin supplementation for four weeks can reduce eye soreness, dryness, tiredness and blurred vision (Shiratori, 2005; Nagaki, 2006; Capelli and Cysewski, 2014).

Other Human Research. A study was done in Japan with subjects comprised of twenty year old, healthy men. The treatment group was given 6 mg of Natural Astaxanthin per day for four weeks. Statistically significant improvement was found in two different parameters—visual acuity (the ability to see fine detail) and depth perception. Depth perception in particular saw a remarkable improvement by 46% in the group supplementing with Natural Astaxanthin (Sawaki, et al, 2002).

It is very important to have sufficient blood flow to the eyes and the retina to ensure they are healthy and functioning properly. A human clinical study examined the ability of Astaxanthin to improve retinal capillary blood flow. Eighteen subjects were given 6 mg per day of Natural Astaxanthin and another eighteen people were given a placebo. After four weeks it was found that the Astaxanthin group had improved retinal capillary blood flow as compared to the placebo group (Yasunori, 2005). The final study we'll review in this section showed a different benefit for using Natural Astaxanthin related to blood flow. This double-blind, placebo-controlled study examined Astaxanthin's effect on blood flow to the vascular layer of the eye. Increased blood flow velocity was found in subjects taking Astaxanthin (Saito, et al, 2012). It appears that Astaxanthin can increase blood flow and can also increase the speed at which the blood is flowing to the eyes.

Brain Health

The incidence of age-related neurological problems is one of the fastest growing health issues facing the world's aging population. In fact, with the possible exceptions of skin cancer and diabetes, we have seen the incidence of maladies affecting the brain increase quicker than any other ailment over the last few decades. Certainly, a preventive food supplement that is safe and natural that could help prevent age-related neurological issues would be a logical recommendation for everyone who is approaching middle age. Fortunately, according to some great research over the last few years, it appears that we may have found just that in Natural Astaxanthin. There have been many pre-clinical studies on how Astaxanthin can support the brain, eyes and central nervous system. In fact, animal research in this area began in the late 1940's in France and was published as doctoral theses by two scientists who were certainly way ahead of their time (Grangaud, 1951; Massonet, 1958). Limiting our review to human research, we'll look at three of the recent studies showing benefits for our brains:

All three of these human clinical trials were done in Japan, a country that has embraced Natural Astaxanthin as an outstanding preventative supplement for several years already. The first study took elderly subjects with age-related forgetfulness and administered 12 mg of Astaxanthin each day for 12 weeks. The researchers found efficacy for age-related decline in cognitive and psychomotor function (Satoh, 2009).

The second study was randomized, double-blind and placebo-controlled in human volunteers. After 12 weeks at either 6 mg or 12 mg daily Astaxanthin dosages, subjects were found to have decreased levels of phospholipid hydroperoxides (which accumulate in people suffering from dementia), as well as improved erythrocyte antioxidant status. The researchers concluded that Astaxanthin supplementation may contribute to the prevention of dementia in humans as we age (Nakagawa, et al, 2011).

The last study we'll review related to brain health incorporated a larger subject pool than the first two studies. This randomized double-blind, placebo-controlled study took healthy people who were either middle age or elderly who complained of age-related forgetfulness. The study

included 96 subjects who were randomly assigned to take either placebo, 6mg of Natural Astaxanthin per day, or 12mg of Natural Astaxanthin per day. The study duration was twelve weeks; however, several tests were performed on the subjects every four weeks during the study. In this study, the 12mg dose appeared to work somewhat better than the 6mg dose. Improvements in cognitive tests such as the CogHealth battery score and the Groton Maze Learning Test were found to increase in the 12mg group, while a lower level of improvement was noted in the 6mg group. The authors concluded, "The results suggested that Astaxanthin-rich *Haematococcus pluvialis* extract improves cognitive function in healthy aged individuals" (Katagiri, et al, 2012).

Aches & Pain: The Anti-Inflammatory Effects of Astaxanthin

There have been several human clinical trials showing that Astaxanthin reduces pain in joints, tendons and muscles in groups of patients suffering from chronic conditions as well as in healthy young men doing intense exercise. The variety of studies are strong support for Natural Astaxanthin's far-ranging anti-inflammatory effects—whether the pain is in the joints, the tendons or the muscles, Astaxanthin seems to be able to reduce it and make people feel better. But we must warn our Readers—don't expect Astaxanthin to work fast. You'll have to use Astaxanthin at least two weeks and more likely four to as much as eight weeks to get the desired results. Fortunately, although Natural Astaxanthin takes longer to work than prescription anti-inflammatories and over-the-counter pain remedies, it is completely safe. It does not share the serious side effects that the quicker pain pills all have.

The other point we must warn our readers about is this: About 15 – 20% of the people who take Astaxanthin for pain don't obtain their desired results. This isn't very different from other anti-inflammatory products you find in a drug store; most of those don't work for 100% of the people 100% of the time either. The reason this happens with Astaxanthin is most likely due to different people's bodies having a different capacity to absorb carotenoids. Astaxanthin is a carotenoid, the family of molecules that includes other health-giving nutrients like lutein, lycopene, zeaxanthin and the most famous carotenoid, beta-carotene. When absorption of carotenoids is studied in humans, researchers find a huge disparity in people's ability to assimilate them. The range is massive—from about 5% absorption level up to over 90% absorption. So what is probably happening when someone takes Astaxanthin for a few months and doesn't feel a reduction in pain is that they are most likely in the very low absorption range. Their body may only be absorbing 5% of the Astaxanthin in the capsule they're taking. So even if they're taking 12mg per day (which is generally the upper level recommended by most brands), their body isn't feeling the effects because so little is getting into their bloodstream. Meanwhile, a person whose body is absorbing at the upper end of the range is getting practically all the Astaxanthin they consume into their bloodstream where it can work its magic. This person could take as little as 2mg – 4mg per day and get an excellent result for painful conditions. Fortunately, with over 80% of people finding great results in the normal dosage range of 4mg – 12mg per day, and considering that these benefits happen without any dangerous side effects, there is little reason for most people to try other remedies that may be unsafe such as over-the-counter medications

and prescription anti-inflammatory drugs. Now, let's examine some of the human clinical trials showing how Natural Astaxanthin can reduce aches and pain, increase mobility and generally improve the quality of life for people suffering from joint or tendon pain.

Reduction of C-Reactive Protein. Before we get started looking at the painful conditions Astaxanthin has been shown to reduce, let's first look at the main test used to measure inflammation in our bodies. The marker used by doctors to measure how much silent (also called "systemic") inflammation is occurring in a person's body is called C-reactive protein (CRP). Silent inflammation has been singled out as a leading cause of many different diseases, most of them life threatening. In fact, the two leading causes of death in most countries, cardiovascular disease and cancer, have both been attributed to silent inflammation. (As an example, the American Heart Association has indicated that CRP levels may be a better indicator of heart disease than cholesterol levels.) In addition to heart disease and cancer, neurological conditions such as Alzheimer's and Parkinson's, diabetes, ulcers, asthma and many more serious diseases are all closely linked to silent inflammation. And while silent inflammation does not cause people to feel pain, it is important to appreciate the effect of Astaxanthin in reducing silent inflammation to have a full understanding of its anti-inflammatory activities.

A double-blind, placebo-controlled human clinical trial was done to test Natural Astaxanthin's effect on CRP levels in healthy volunteers. The subjects took either 12mg per day of Natural Astaxanthin or a placebo for eight weeks. CRP levels were measured before and after the eight week supplementation period. Results were very good—in only eight weeks people taking Astaxanthin reduced their CRP levels by over 20%; meanwhile, people taking placebo saw a slight increase in their CRP levels (Spiller, et al, 2006a).

A team of researchers from Washington State University led by long-time carotenoid researcher Boon Chew, PhD did a multi-faceted study on Natural Astaxanthin primarily to test its effect on the human immune response. They used young women in this randomized, double-blind and placebo-controlled study. They measured immune markers as well as DNA damage, oxidative stress levels and CRP. The results were positive on all markers. In fact, at a dose of only 2mg per day they found a statistically significant decrease in CRP levels after eight weeks of supplementation (Park, et al, 2010).

In addition to the studies on CRP above, a company experimenting with Astaxanthin production back in 2006 publicized a human clinical trial on patients with CRP levels that were high enough to place them in a high risk category for cardiovascular disease. The patients took Natural Astaxanthin or placebo for three months, after which their CRP levels were again measured. Nearly half of the people taking Astaxanthin fell out of the high risk category while none of those taking placebo did (Mera, 2006).

Rheumatoid Arthritis. Rheumatoid arthritis is a much more debilitating disease than osteoarthritis in most cases. This is a disease where the person's immune system attacks itself, a condition called an "auto-immune" disorder. Rheumatoid arthritis is a chronic condition that is more difficult for doctors to address than osteoarthritis. For example, many people who use

drugs to treat rheumatoid arthritis find them ineffective. And regrettably, as with most prescription drugs, many people experience dangerous side effects.

Fortunately, Natural Astaxanthin has been shown to be very effective in reducing pain and increasing satisfaction with the ability to perform daily activities in these patients suffering from rheumatoid arthritis. In this double-blind, placebo controlled study, people in the treatment group took 12mg per day of Astaxanthin over the course of eight weeks. Results showed a steady trend toward improvement in both pain levels and satisfaction from the beginning of the study to a midway point after four weeks, and then increasing improvement during the last four weeks of the study. During the first month, subjects found slight improvements on average. But by the end of eight weeks, the pain scores had dropped by 35% and the satisfaction scores improved by 40% in the group taking Astaxanthin (Nir and Spiller, 2002a).

Carpal Tunnel Syndrome. A disease with no cure, carpal tunnel syndrome (abbreviated as "CTS" and also known as "repetitive stress injury" in some countries) affects up to 2% of Americans at any given time. CTS is common among people working in repetitive situations like cash register operators, some manual laborers and people working all day on computers. This is a debilitating condition that causes pain in the wrists. It also causes numbness and can sometimes even cause paralysis of the wrists. Treatment usually consists of putting splints on the wrists to immobilize them. Doctors will try splints for a period of time, and if improvement doesn't occur the next step in most cases is wrist surgery. Regrettably, in many cases, surgery doesn't work well. This is a disease that obviously needs an alternative solution.

Natural Astaxanthin may be just that—an alternative to surgery for people suffering from carpal tunnel syndrome. As we mentioned above, there is no cure for CTS. We want to make it clear that Astaxanthin cannot cure this disease either; however, a clinical trial showed excellent results in treating the pain that CTS causes.

Patients suffering from CTS were randomly separated into two groups. One group took 12mg per day of Natural Astaxanthin and the other group took a placebo. Similar to the study on rheumatoid arthritis, this study also lasted eight weeks with a mid-term assessment of pain levels after four weeks.

Perfectly mimicking the results found by people with rheumatoid arthritis, the group of CTS sufferers taking Astaxanthin had good results after four weeks, but much more significant results after the full eight-week course of treatment. Pain levels were measured as well as the duration of pain. After eight weeks, these dropped by 41% and 36% respectively. Some of the people taking Astaxanthin reported that they were able to make major changes in their lifestyle due to the positive effects they experienced (Nir and Spiller, 2002b).

Tennis Elbow (Tendonitis). We've seen that Natural Astaxanthin can help people with serious painful conditions like rheumatoid arthritis and carpal tunnel syndrome. Another painful condition that is very difficult for physicians to treat is tendonitis. Tendonitis can affect many

different areas of the body. An area that is commonly affected with tendonitis in athletes is the arms. And, perhaps the most famous instance of this is known as "tennis elbow."

The repetitive motion of hitting tennis balls with a racket can manifest as tennis elbow, which causes a loss of grip strength in the hands and pain while gripping objects in the hand. The clinical researcher responsible for studying Astaxanthin's effects on rheumatoid arthritis and carpal tunnel syndrome did a different kind of study on people suffering from tennis elbow. His name is Gene Spiller, PhD. Dr. Spiller tested people's grip strength and the pain in their hands from tennis elbow before and after Astaxanthin supplementation. Once again, he separated the tennis elbow sufferers into two different groups randomly. The first group took 12mg per day of Natural Astaxanthin for eight weeks, while the other group took an identical placebo. The results for people supplementing with Astaxanthin were outstanding: On average, their grip strength increased by almost double in only eight weeks. The average increase was 93% to be exact, and there was also a decrease in their self-assessment of pain in their hands. Dr. Spiller concluded that using Natural Astaxanthin may alleviate pain and increase mobility. "This improvement may greatly improve the standard of living for those who suffer from such joint disorders" (Spiller, et al, 2006b).

Joint Soreness After Exercise. The first human clinical trial to test Astaxanthin's effectiveness against pain and inflammation was done on a different population of people than Dr. Spiller used in his experiments. If you analyze Dr. Spiller's excellent research, you find that he focused on people who were already living in pain—people suffering from chronic painful conditions like rheumatoid arthritis, carpal tunnel syndrome and tendonitis. A clinical trial performed at the University of Memphis back in 2001 under supervision of Andrew Fry, PhD looked at Natural Astaxanthin's effect on healthy men who were performing strenuous exercise.

This study used a much lower dose of Astaxanthin—only 4mg per day. Additionally, this study ran for a very short period of time—only three weeks. Dr. Fry wanted to see if Astaxanthin could help prevent the soreness that usually occurs after intense exercise. The men who participated in this study were training regularly with weights. The subjects used a resistance-training apparatus for strenuous knee exercises during the three week treatment period and took either 4mg of Natural Astaxanthin or placebo every day.

The young men taking placebo had significant joint pain in their knees immediately after performing the exercises. This pain was tested 10 hours after the heavy exercises, and then again at 24 hours and 48 hours after. Whether immediately afterward or at the various test times up to and including 48 hours afterward, the pain persisted for those who took placebo. But the young men who were taking 4mg of Astaxanthin every day showed no change in knee soreness right after exercise. This pain-free state remained consistent at the three other test times of 10, 24 and 48 hours after exercise (Fry, A., 2001). This is a fantastic result in particular when you consider that the dosage was the lowest level commonly recommended and that the study only ran for three weeks.

As you probably remember from the studies on rheumatoid arthritis and carpal tunnel syndrome, after four weeks there was an improvement in pain levels, but it became much more pronounced

after eight weeks as the Astaxanthin concentrated throughout the body. In this study, the results were much quicker and at one third the dosage. The reason for this is not clear, but may have to do with the fact that the subjects did not start with painful conditions and were athletic. In any event, it is very important to understand that Natural Astaxanthin appears to both reduce pain in people who suffer from chronic conditions, but also prevents pain in people who are exercising heavily. The implications for not only the millions suffering from arthritis and tendonitis but also for athletes as well as regular people doing heavy work on a daily basis are extremely promising.

Muscle Soreness After Exercise. The trial that Dr. Fry did at University of Memphis was originally focused on another painful condition. In fact, the main goal Dr. Fry had with the study was to see if Natural Astaxanthin could help prevent the soreness in muscles that occurs after doing heavy exercise. This condition is called "Delayed Onset Muscle Soreness," and it affects athletes, weight lifters, people doing hard physical work, and perhaps most notably, weekend warriors. Thankfully, the results he found about Astaxanthin preventing joint soreness are much more significant than his original goal. There is no doubt that joint pain caused by strenuous exercise is a much more serious condition than muscle pain that often occurs after a heavy workout. Pretty much everyone has had muscle soreness after a tough day in the garden or a long game of volleyball at the beach, and people are all highly aware that it's just a temporary condition that will go away in a couple days. But sore joints are a much more troubling issue that are certainly a greater concern than normal muscle soreness.

In any event, Dr. Fry did not immediately find a statistically significant result showing that Astaxanthin could prevent muscle soreness. But years later, Dr. Fry reexamined the data and found that in a subset of the subjects in this trial, Astaxanthin did have an excellent result in preventing muscle soreness after heavy exercise. The people that were positively affected were those whose muscles had high fiber content (Fry, et al, 2013). So basically, it appears that Natural Astaxanthin can prevent joint soreness after heavy exercise in most people, but it can only prevent muscle soreness after heavy exercise in some people.

Cardiovascular Health

Natural Astaxanthin has been clinically validated to support cardiovascular and heart health. There are currently well over forty published medical research studies outlining Astaxanthin's cardioprotective properties. These properties may help people prevent heart disease and may also help people with heart disease to minimize their risk of a heart attack or stroke. There are several distinct potential cardiovascular benefits that have been demonstrated through this extensive research (Capelli and Cysewski, 2014).

The main focus of the human clinical research has been on Natural Astaxanthin's ability to improve blood lipid profiles by decreasing low density lipoprotein (LDL, bad cholesterol) and triglycerides, and by increasing high density lipoprotein (HDL, good cholesterol). A human

clinical trial in Japan found a very promising effect on LDL (bad cholesterol) both in test tubes and in human volunteers. They began with an in-vitro test which showed that Astaxanthin dose-dependently prolonged the oxidation lag time of LDL. The test was then repeated in humans at doses ranging from as low as 1.8 mg per day to as high as 21.6 mg per day for fourteen days. This study found that all four doses positively affected LDL oxidation lag time—at 1.8 mg per day it was 5% longer; at 3.6 mg per day it was 26% longer; at 14.4 mg per day it was 42% longer; but at the highest dose of 21.6 mg per day the upward trend stopped and the lag time was 31% longer. This suggests that the optimum dose for blood lipid profiles is significantly less than 21.6 mg per day. The researchers concluded that consumption of Astaxanthin "inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis" (Iwamoto, et al, 2000; Capelli and Cysewski, 2014).

Another placebo-controlled human clinical study on 61 volunteers with mild hyperlipidemia showed benefits for improving blood lipid profiles and also for increasing adiponectin in the serum. Doses were varied at 6mg, 12mg and 18mg per day over a 12-week supplementation period. Blood lipid improvements were seen in significantly increased levels of HDL (good) cholesterol and significantly decreased triglyceride levels (Yoshida, et al, 2008).

In a human clinical trial done in Eastern Europe, researchers took men with high cholesterol and supplemented them with 4 mg of Astaxanthin per day for one month. The average decrease in cholesterol levels was excellent in such a short period of time: Subjects supplementing with Astaxanthin showed an average decrease of triglycerides of 24% and an average decrease in LDL cholesterol as well as total cholesterol of 17% (Trimeks, 2003).

A randomized double-blind study was done on healthy men in Finland at the Research Institute of Public Health to test the effect of Astaxanthin on lipid peroxidation. Subjects in the treatment group were given 8mg of Natural Astaxanthin each day for three months. At the end of the study, the researchers found that Natural Astaxanthin significantly reduced the levels of two hydroxy fatty acids in the subjects' blood plasma (Karppi, et al, 2007).

Lastly, in a clinical study related to blood pressure improvement, researchers gave human volunteers a dosage of 6 mg of Astaxanthin per day. This study only lasted for ten days, yet at the end of the ten day period, a significant improvement in blood flow was found in the treatment group (Miyawaki, H, 2005). Blood flow improvement can have a positive effect on different conditions related to cardiovascular health, including blood pressure as well as prevention of atherosclerosis.

Skin Health & UV Protection

The benefits of Natural Astaxanthin for skin fall into three distinct categories. First of all, as amazing as it may seem, the daily consumption of 4mg of Astaxanthin can improve the appearance and the quality of skin within two months. Secondly, Astaxanthin has demonstrated that it not only can improve the appearance and quality of the skin, but it can also improve the health of the skin as well. And lastly, after Astaxanthin has had time to accumulate in the skin, it

has demonstrated a protective effect against the ongoing ravages from ultraviolet light exposure. Let's briefly examine each of these three categories of skin benefits.

Skin Appearance and Quality. One of its most amazing attributes is that Astaxanthin has demonstrated that it can improve the quality and appearance of the skin when taken internally. A landmark clinical trial done in the USA in 2006 reported that Natural Astaxanthin has several different benefits for skin quality and beauty. Forty-six middle aged women were divided into two groups—one group taking 4mg of Natural Astaxanthin per day and the other group taking placebo. Results were examined in a variety of ways such as measurement by dermatological devices; visual assessment by a dermatologist; before and after pictures; and self-assessment. All results showed noticeable and statistically significant benefits. This study found that, as an internal beauty pill, Natural Astaxanthin:

- Fights wrinkles
- Improves skin elasticity
- Increases skin moisture levels
- Reduces visible signs of UV-aging within four to six weeks of use
- Maintains a youthful appearance (Yamashita, 2006)

Some other human clinical studies in this area have been performed. One was an open-label study involving 30 healthy female subjects for 8 weeks. Significant improvements were observed by combining 6mg per day oral supplementation and 2 ml (78.9 μM solution) per day topical application of Natural Astaxanthin. Results showed improvements in wrinkles, age spot size, elasticity, skin texture, moisture content of corneocyte layer and also in the condition of the corneocyte. These results suggest that by combining oral supplementation and topical treatment, Natural Astaxanthin may improve skin condition in all layers including the corneocyte layer, the epidermis, the basal layer and the dermis (Tominaga, et al, 2012).

It's interesting to note that Natural Astaxanthin works very well as an internal beauty supplement when combined with tocotrienols, a Vitamin E component that has also shown some remarkable properties for improving human health in its own right. In fact, in just four weeks, a dose as low as 2mg per day of Astaxanthin was effective when combined with tocotrienols in a human clinical trial done in Japan. Results included reduction of fine wrinkles, increased skin elasticity and also increased skin moisture levels (Yamashita, 2002).

Skin pigmentation can be an unsightly problem as we age when it is irregular, as evidenced by a common occurrence associated with aging: Age spots. In a model of skin pigmentation done in Japan, Astaxanthin was found to dose-dependently inhibit the stem cell factor-associated stimulation of pigmentation. In fact, at the highest dosage, Astaxanthin was found to almost completely inhibit this pigmentation (Nakajima, et al, 2012).

Skin Health. Skin cancer is one of the fastest growing diseases in the world today, ranking right at the top with age-related neurological disease and diabetes. In an extremely interesting study, Natural Astaxanthin has shown that it is more effective than Synthetic Astaxanthin in inhibiting

skin cancer in rats. In fact, the natural forms tested were effective in reducing UV-induced tumor incidence by 96% and 88%, while the synthetic form only attained 66%. Other markers tested were also much more positive in the Natural Astaxanthin groups. The researchers hypothesized that "the better anti-cancer potency of Natural Astaxanthin could be due to increased bioavailability" (Rao, et al, 2013).

In a study that is extremely relevant to several aspects of our discussion in this paper, Astaxanthin showed anti-cancer potential in a mouse study which used UV radiation to induce carcinogenesis. This study tested two other carotenoids in addition to Astaxanthin. The results showed that, while both Astaxanthin and beta-carotene showed cancer preventative properties, lycopene had no effect (Black, 1998).

Lastly, in an area of research that is related to most of the benefits we'll examine throughout this paper and which we'll describe in more detail later, Astaxanthin was shown to be effective against DNA damage. In this particular study, benefits were found in three separate skin components. DNA damage is commonly considered a root cause of carcinogenesis. This led the researchers to theorize that Astaxanthin may be useful in preventing the formation of skin cancer (Lyons and O'Brien, 2002).

UV Protection. Pre-clinical research has shown that Astaxanthin can effectively protect skin from the ravaging effects of UV exposure. There have been several studies on UV exposure and the end result of this exposure, photo-aging. An early study using hairless mice measured the effects of Astaxanthin as well as beta-carotene and retinol in preventing UV damage. Astaxanthin performed better than beta-carotene either by itself or in combination with retinol. In fact, it was extremely proficient at preventing photo-aging of the skin (Savoure, et al, 1995).

In addition, Astaxanthin was also found to be effective in protecting skin cells from UV-induced oxidative stress. In fact, an early study demonstrated in-vitro that Astaxanthin is 100 times stronger than beta-carotene and, remarkably, 1000 times stronger than lutein in protecting cells against UVA light-induced oxidative stress (O'Connor and O'Brien, 1998).

Energy and Performance

Astaxanthin is an excellent nutrient for athletes and active people as it can help them in several important ways. While there have not been studies in these areas specifically done on older subject pools, there have been several different human clinical trials demonstrating a variety of benefits applicable for active people. There is ample evidence in these studies that leads us to believe that people in middle age and beyond should also derive benefits from Astaxanthin supplementation in the areas of energy and performance. Among this research are studies done at universities and at leading research institutions. One of the most exciting studies was sponsored by Gatorade®, the world's leading company in sports drinks. The research encompasses work done in USA, Japan and Europe. Along with these human clinical trials are

twenty-five supporting pre-clinical trials done in mammals and in-vitro; however, in the interest of brevity we will limit our review to the human clinical research.

Muscle Inflammation and Recuperation in Elite Soccer Players. Soccer is the world's sport—the most closely followed competitive sport in most countries around the globe. This study looked at the effect of Astaxanthin supplementation on elite soccer players in Europe. The study was randomized and placebo-controlled; it spanned 90 days of supplementation. Shane Starling, a leading nutraceutical industry journalist summed up the results very well:

> "They gave 4mg of Astaxanthin daily to 40 young, trained soccer players and found via plasma testing better results for the Astaxanthin group in inflammation, immune system function and muscle recuperation…the researchers said the study showed Astaxanthin 'attenuates muscle damage, thus preventing inflammation induced by rigorous physical training'" (Starling, 2015).

Concluding the study, the researchers hypothesized that the mechanism of action may be that Astaxanthin "protects the cell membranes against free radicals generated during heavy exercise, thus preserving the functionality of muscle cells" (Baralic, et al, 2015).

Gatorade® Sponsored Study Finds Competitive Cyclists Made Faster with Higher Power Output by Astaxanthin. When a company like Gatorade pays to do a study on how an ingredient affects competitive athletes, you can bet that they were fairly certain of the outcome before commissioning the study and making the investment. Gatorade looked at the existing research on Astaxanthin as the world's strongest natural antioxidant and as a proven broad spectrum anti-inflammatory, and they reviewed the earlier human trials on athletes and supporting pre-clinical trials, and then decided to sponsor this study to see if Natural Astaxanthin could make competitive cyclists faster and stronger. As expected, Astaxanthin worked great.

This study lasted only four weeks, a relatively short time for Astaxanthin to concentrate in the bodies of the athletes and improve their race times. It also was done at the very minimum dose generally recommended by Astaxanthin experts: 4mg per day. The researchers tested the cyclists in a 20 kilometer (about 12.5 miles) time trial before the supplementation began and again at the end of four weeks of supplementation. We must keep in mind that these were not average people, but highly trained, competitive cyclists. Even marginal improvement from a supplement regimen after just four weeks would be an excellent result in this particular group of subjects.

At the end of four weeks, the placebo group showed no improvement in their cycling times. However, the cyclists taking Natural Astaxanthin were on average 5% faster. In addition, the power output in these athletes increased by 15% on average (Earnest, et al, 2011). In just four weeks and at the very lowest generally recommended dosage, Astaxanthin made these competitive cyclists significantly faster and stronger. Any athlete would love to have these fantastic results from taking just one small capsule each day. (We'd like to see more research in

this area, but with a longer study duration and at the upper range of dosage of 12mg per day—the results would most likely be even more dramatic following this model.)

Recovery from Exercise and Muscle Fatigue. A randomized, double-blind, placebo-controlled crossover study in Japan measured recovery from exercise in healthy volunteers. The researchers had both groups do progressively greater loads in a stepwise exercise. Again, the dosage was low (5mg per day), and remarkably, the study duration was extremely short (2 weeks). Examination was done of respiratory-circulatory function as well as blood analysis. They also measured sympathetic nervous activities during exercise and parasympathetic nervous activity during recovery.

All parameters tested showed significant improvements in the treatment group taking Natural Astaxanthin. Metabolism during exercise became more efficient, respiratory-circulatory ability improved, and anti-fatigue and antioxidant profiles were augmented. These results led the researchers to conclude that recovery ability from exercise stress may be improved by taking Astaxanthin. Additional benefits from blood analyses were found: The Astaxanthin group had significantly less LDL cholesterol in their bloodstream and significantly higher creatine phosphokinase (Nagata, et al, 2003).

Increased Strength and Endurance Improvement in Healthy Men. Natural Astaxanthin is the power generator that allows salmon to make their heroic upstream swim. Astaxanthin is found at the highest concentration in the animal world in salmon. Within the salmon, the Astaxanthin concentrates in the muscles to allow the salmon to swim up raging rivers for over a week straight. This is the greatest endurance feat in all of nature, and it is fueled by Natural Astaxanthin.

Based on this fact, researchers in Sweden did a six month clinical trial on healthy men to see if Astaxanthin would have the same effect in humans that it does in salmon. They had the men do deep knee bends to exhaustion after a warm-up period. Again, the study featured a very low dose of Astaxanthin—only 4mg per day—but fortunately the study lasted six months, so the Astaxanthin had time to concentrate throughout the treatment group's bodies. Results showed that Astaxanthin increased strength and endurance by 62% in six months. The placebo group also showed improvement of 22%, which is normal for young people who are participating in sports over a six month period. But the relation between the two groups is what really counts—strength and endurance increased three times faster in the men taking Natural Astaxanthin compared to the group taking placebo. The lead researcher, Dr. Curt Malmsten, summarized the results:

> "The marked improvement in strength/endurance would seem very interesting, since it cannot be explained by improved fitness (step-up test) or improved lactic acid tolerance (Wingate test). Furthermore, since there was no significant increase in body weight, an increased muscle mass cannot be used to explain this positive effect. Because of this, Astaxanthin seems to have the beneficial effect on strength/endurance.

> This is the first study in humans to show that Astaxanthin supplementation has a positive effect on physical performance. The result of this study is supported by earlier findings that Astaxanthin supplementation in mice increases swimming time before exhaustion, and that biomarkers of muscle fatigue decrease in humans after exercise due to Astaxanthin supplementation.
>
> Further studies need to be designed to find the explanations to the mechanisms behind the increased muscle endurance. It can be hypothesized that Astaxanthin protects the membrane structures of the cells, like the mitochondrial membrane against oxidative stress generated during heavy exercise and thereby preserves the functionality of the muscle cells" (Malmsten and Lignell, 2008).

Reduced Muscle Fatigue from Lactic Acid Buildup During Exercise. Lactic acid builds up during physical exertion and causes burning in the muscles and fatigue. A study in Japan had healthy adult men take 6mg of Astaxanthin daily for four weeks. They had both the placebo and the Astaxanthin group run 1200 meters and tested their lactic acid levels before and after running at the beginning of the study (before supplementation began). They repeated this at the end of the study and found a statistically significant reduction in lactic acid buildup due to exercise. The result was excellent—a 28.6% reduction in lactic acid on average from taking 6mg of Natural Astaxanthin per day for a month (Sawaki, et al, 2002).

Reduction of Respiratory Parameters and Improvement of Energy Metabolism. This Japanese double-blind crossover study tested several different parameters after working volunteers on a treadmill. The study only lasted two weeks, yet improvements in respiratory metabolism and energy metabolism were indicated. The study concluded that Astaxanthin supplementation may also contribute to the enhancement of lipid metabolism as LDL cholesterol decreased markedly after exercise (Tajima and Nagata, 2004).

Reduced Free Radical Production in Elite Soccer Players. The same group of researchers from Europe who did the first study we reviewed on elite soccer players did two preliminary human clinical trials before starting on their landmark study. The first of these preliminary studies tested whether Astaxanthin can reduce free radical production after intense two-hour long exercise. The treatment group took Astaxanthin for 90 days; as expected, the results were promising for Astaxanthin. The conclusion stated "Supplementation with Astaxanthin could prevent exercise induced free radical production and depletion of non-enzymatic antioxidant defense in young soccer players" (Djordjevic, et al, 2012).

Improvement of Oxidative Status in Elite Soccer Players. The second preliminary clinical trial on elite European soccer players validated the results of the first preliminary trial: Astaxanthin supplementation led to improvement in the athletes' oxidative status (Baralic, et al, 2013).

Immunity

Another major issue with aging is that our immune systems stop functioning at peak performance. Fortunately, a landmark human clinical trial done by leading carotenoid researcher Boon Chew, PhD showed that, at an extremely low dose of only 2mg per day, Natural Astaxanthin is effective in boosting immune markers in healthy women (Park, et al, 2010). Dr. Chew is an extremely well-published and highly respected researcher from Washington State University. He has done extensive research on carotenoids, much of which has focused on their ability to positively affect the immune response of humans and other mammals. He has also broadly researched inflammation and oxidation in relation to age-related diseases. Dr. Chew's focus on immunity, inflammation and oxidation has naturally led him to deeply investigate carotenoids, and specifically to focus on Natural Astaxanthin. Dr. Chew, along with colleagues such as Jean Soon Park, PhD, has uncovered some fascinating properties of Natural Astaxanthin, one of which is related to DNA damage which we'll look at in the next chapter.

Dr. Chew began researching Natural Astaxanthin's effects on immunity back in the late 1990's. His team did a study comparing the effects of various carotenoids on immunity in mice which was published in 1999. This study found that Astaxanthin and beta-carotene both increased lymphocyte function in the mice, but canthaxanthin did not have this effect. Astaxanthin performed better than beta-carotene in another important way—it enhanced the lymphocyte cytotoxic activity. This was Dr. Chew's first realization that Natural Astaxanthin has a much better effect on immunity than other carotenoids, which led him to continue research on Astaxanthin's immune boosting potential (Chew, et al, 1999a). This study was accompanied by another study by the same group published that year that again leads to the conclusion that Astaxanthin is superior to other carotenoids in boosting immunity, this time against cancer. In this study, Astaxanthin was found to be significantly more effective in preventing the growth of breast cancer tumors in mice than both beta-carotene and canthaxanthin (Chew, et al, 1999b).

Drs. Chew and Park have investigated Astaxanthin's effect on immunity in other mammals besides rodents. They have validated Astaxanthin's benefits for the immune systems of both dogs and cats in two separate studies. Each of these studies investigated dose-dependency in these animals. They measured several different immune markers in the blood of the animals before the experiment started, and then after twelve weeks of either Astaxanthin supplementation or a control diet. In the study on cats, they tested three different dosage levels. Astaxanthin had the expected results in cats—it showed a significant improvement on several different immune system markers in their bloodstream. It demonstrated a multiple pathway method of action which was similar to what was found in the earlier research in mice. The conclusion of this study was that "Astaxanthin heightened the cell-mediated and humoral immune response in cats" (Park, et al, 2011).

The dog study was even more impressive than the excellent cat study referenced above. It lasted 16 weeks instead of 12, and tested some additional parameters above and beyond immune markers. Both damage levels to DNA and systemic (also known as "silent") inflammation were tested. This study also tested three different dosage levels. All of the different markers tested in dogs showed positive benefits from Astaxanthin supplementation. "Astaxanthin heighted cell-mediated and humoral immune response and reduced DNA damage and inflammation in dogs" (Chew, et al, 2011).

Landmark Human Clinical Trial: After proving that Natural Astaxanthin improves immunity in mice, dogs and cats, it is only logical that it should show some benefit for immunity in humans as well. Fortunately, Dr. Chew headed a landmark clinical trial in humans that validated this theory. This study tested the effect of Astaxanthin on the immune systems of healthy female volunteers. There were three different groups assigned in this randomized, double-blind, placebo-controlled study. One group took placebo for eight weeks, while the other groups took either 2mg per day of Natural Astaxanthin or 8mg per day. Measurements were taken at baseline at the commencement of the study, then again at week 4 and finally at the end of the study after eight weeks of supplementation had passed. This study revealed that Astaxanthin improved a variety of blood immune markers in humans. Conclusions revealed that:

- Astaxanthin is a strong immune system stimulator
- Astaxanthin increases the total number of antibody producing B-cells
- Astaxanthin increases the number of T-cells
- Astaxanthin amplifies natural killer cell cytotoxic activity
- Astaxanthin significantly increases delay-type hypersensitivity response
- Astaxanthin stimulates lymphocyte proliferation
- Additionally, Astaxanthin decreases DNA damage significantly
- Unexpectedly, immune markers in the subjects taking 2 mg per day improved slightly more than in the subjects taking 8 mg per day (Chew, et al, 2003; Park, et al, 2010; Capelli and Cysewski, 2014)

It is very interesting to note this last result: Natural Astaxanthin had a slightly better effect on the immune system of healthy women at the lower dose tested of 2mg per day compared to a dose four times that strength of 8mg per day. Immunity is the only area of research in which we've seen such a low dose having a great effect. Furthermore, this is one of only a small handful of cases where a lower dose has proven more effective than a higher dose. Generally, all of the research on Natural Astaxanthin's benefits in humans has shown benefits in the 4mg per day to 12mg per day range, with a few outlying studies showing benefits at dosages as high as 20mg or more per day. And the present study would have been even more interesting if it had investigated whether 2mg per day was more effective than 4mg or 6mg. Since this study only analyzed results at 2mg and 8mg per day, we conclude for now that 2mg per day is the optimum dosage for people exclusively seeking to improve their immunity. Yet, in spite of this study, the general consensus among doctors and researchers involved with Natural Astaxanthin is that most people derive excellent overall health benefits in the range of 4mg – 12mg per day.

Other Human Clinical Research. Some very interesting research that corroborated Dr. Chew's landmark clinical trial on immunity has been going on in Europe over the last few years related to Astaxanthin's effects on athletes. We cited three studies above from a group of researchers that looked at how Natural Astaxanthin positively affects elite soccer players. Two of these studies did not test any markers related to immunity; however, the third study, which was done earlier this year, showed a result that is very relevant to immune system modulation along with other results that are of great interest to athletes and to people faced with aging.

This study randomly assigned 40 elite soccer players to either a placebo group or a group that took 4mg per day of Astaxanthin. Measurements in both groups were tested at baseline before the study began. The study lasted 90 days, after which the same measurements were tested again. Results were excellent from both an anti-aging viewpoint as well as from an immunity viewpoint:

- Subjects supplementing with Astaxanthin resulted in an increase in immunoglobulin as measured in their saliva.
- The pro-oxidant / antioxidant balance decreased in the Astaxanthin group.
- Plasma muscle enzyme levels were reduced by Astaxanthin supplementation.
- The placebo group showed an increase in high sensitivity C-reactive protein levels (this is the primary marker for systemic inflammation in the body) but the Astaxanthin group showed no such increase.

For the purposes of this chapter, immunoglobulin levels are our primary interest from this study as they are a key marker of immune system function. Immunoglobulin are a class of proteins found in the cells and serum of the immune system. They are essential to a healthy immune response since they function as antibodies in our bodies—they combine with pathogens such as bacteria and viruses which are subsequently rendered harmless. By increasing immunoglobulin, Astaxanthin is providing our immune system with the fuel it needs to fight off disease. This finding is very different from the findings of Dr. Chew's research, and it adds additional validation to Astaxanthin's far-ranging benefits for the human immune response. The soccer player study concluded "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 out that Astaxanthin could show significant modulation in individuals with mucosal immunity impairment or under conditions of increased oxidative stress and inflammation" (Baralic, et al, 2015).

Finally, while not directly testing immune markers, another human clinical trial on patients suffering from an autoimmune disorder called "Sjogren's syndrome" is of interest in our present discussion. This study measured Astaxanthin's effects on saliva secretion in both patients with this autoimmune disease and also in healthy subjects. The salivary system is of interest in discussing immunity because salivary glands help protect us from many different microbes which attack us through our mouths. Fortunately, results of this study showed that Astaxanthin can increase salivary output in both patients suffering from the autoimmune disease as well as in healthy people (Yamada, et al, 2010).

Protection of our Cells by Astaxanthin

The most obvious ways that Astaxanthin protects the cells in our bodies are through its antioxidant and anti-inflammatory activity. These are in-depth topics that we've reserved for the last chapters of this paper. And as we mentioned above, these two properties are at the very root of all the health benefits that Astaxanthin bestows on consumers. But there are also many studies on two very important components of our cells showing that Astaxanthin has a protective effect: These two components are DNA and the mitochondria.

Prevention of DNA Damage. DNA is the main constituent of chromosomes in all living organisms. It carries genetic information which makes us who we are. Damage to DNA has profound implications to our cells; in fact, when DNA is damaged, it can have grave effects up to and including development of a cancerous cell line (Moorhead, et al, 2005). A supplement that can help prevent DNA damage is certainly a powerful preventive medicine to keep us living long, healthy lives.

For our discussion of how Natural Astaxanthin can prevent DNA damage, we once again turn to Drs. Chew and Park. They hold a patent on preventing DNA damage from oxidation through the use of Astaxanthin. As amazing as this may seem, the findings from their research show that using only 2mg of Natural Astaxanthin each day over four weeks can reduce DNA damage by approximately 40% (Chew and Park, 2006). This is really a phenomenal result—in only one month and at an incredibly low dosage level of only 2mg per day, Natural Astaxanthin can effectively prevent DNA damage by close to half.

In addition to their patent, Drs. Park and Chew published a randomized, double-blind, placebo-controlled human clinical trial in 2010 that outlines the effects of 2mg of Natural Astaxanthin supplementation on several parameters including oxidative stress, inflammation, immune response as well as DNA damage. This study concluded that "dietary Astaxanthin decreases a DNA damage biomarker and acute phase protein, and enhances immune response in young healthy females" (Park, et al, 2010).

While the research of Drs. Chew and Park is excellent and clearly demonstrates Astaxanthin's prevention of DNA damage, one wonders once again how much damage could be prevented over a longer period of time than just one month as Astaxanthin accumulates throughout the cells in our bodies. And it would be very interesting to see how Astaxanthin performs on DNA damage at a dosage level toward the 12mg per day upper end of the recommended range. We suspect that the effect would be much more pronounced than the 40% result that was found at 2mg per day for one month.

Supporting Pre-Clinical DNA Research. In addition to the human research done by Drs. Chew and Park, a flurry of pre-clinical studies has been performed related to DNA damage over the last ten years. Here are some of the most exciting ones:

- Astaxanthin shows a neuroprotective effect in rat retinal cells and aids against oxidative stress, glutamate stress and DNA damage (Yamagishi and Aihara, 2014)
- Astaxanthin enhances a DNA repair enzyme and is a novel candidate for cancer prevention (Kavitha, et al, 2013)
- Astaxanthin improves oxidative stress markers and an indicator of oxidative DNA damage in mouse cells and may be developed as an antioxidant drug to treat diabetic retinopathy (Dong, et al, 2013)
- Astaxanthin modulates age-associated mitochondrial disfunction in dogs which is attributed to alleviating oxidative damage to cellular DNA and protein (Park, et al, 2013)
- Astaxanthin reduces DNA damage in rat liver cells (Turkez, et al, 2014)
- Astaxanthin may protect against oxidative impairment and DNA damage (Zhao, et al, 2011)
- Astaxanthin heightens the immune response and reduces DNA damage and inflammation in dogs (Chew, et al, 2011)
- Astaxanthin improves oxidative stress and DNA damage in rats (Tripathi and Jena 2010)
- Astaxanthin protects retinal cells against oxidative stress and reduces an indicator of DNA damage in mice (Nakajima, et al, 2008)
- Astaxanthin inhibits cytotoxic and genotoxic effects and restores DNA damage in mouse cells (Tripathi and Jena, 2008)
- Astaxanthin protects against DNA damage in human neuroblastoma cells (Santocono, et al, 2007)
- Astaxanthin reduces DNA damage in UVA-irradiated cells (Santocono, et al, 2006)

Astaxanthin's Effects on the Mitochondria: Mitochondria are commonly known as the "powerhouse of the cell." To put it simply, mitochondria are responsible for energy production in our cells. There is already a great deal of research on how Astaxanthin can protect and benefit the mitochondria, which is probably why it is so effective at increasing energy levels and boosting strength and endurance in human clinical trials. There are many supporting pre-clinical studies about how astaxanthin can positively affect mitochondria as well. We'll review some of the most relevant of these studies here:

- In a study done at University of Pittsburgh's School of Medicine, Astaxanthin protected against mitochondrial dysfunction and reactive oxygen species in a mouse model of Parkinson's disease and also in-vitro (Lee, et al, 2011).
- In perhaps the earliest study on Astaxanthin's effects on the mitochondria, Japanese researchers at Kochi Medical School found that Astaxanthin protects the mitochondria of rats better than a-tocopherol (Kurashige, et al, 1990).
- In a study done at Washington State University under the auspices of the famous carotenoid researcher Boon Chew, PhD, Astaxanthin prevented age-related mitochondrial dysfunction in dogs (Park, et al, 2013).

- Astaxanthin extended the lifespan of C. elegans (a model organism used in longevity studies) by protecting the mitochondria and the nucleus of the cells (Yazaki, et al, 2011).
- Astaxanthin can protect mitochondria that are subjected to oxidative stress. This study's abstract summarized the study very well:

  > "Mitochondria combine the production of energy with an efficient chain of reduction-oxidation (redox) reactions but also with the unavoidable production of reactive oxygen species. Oxidative stress leading to mitochondrial dysfunction is a critical factor in many diseases, such as cancer and neurodegeneration and lifestyle-related diseases. Effective antioxidants thus offer great therapeutic promise…Astaxanthin at nanomolar concentrations was effective in maintaining mitochondria in a reduced state. Additionally, Astaxanthin improved the ability of mitochondria to remain in a reduced state under oxidative challenge. Taken together, these results suggest that Astaxanthin is effective in improving mitochondrial function through retaining mitochondria in a reduced state" (Wolf, et al, 2009).
- Astaxanthin was found capable of protecting the mitochondrial membrane and preventing DNA damage and cell-death in-vitro in a university study done in Taiwan (Chan, et al, 2009).
- Cells subjected to heat stress in-vitro were protected by Astaxanthin, which the researchers attributed to Astaxanthin's positive effect on the mitochondria (Kuroki, et al, 2013).
- In different studies on Astaxanthin's effects on the mitochondria, it was found to be effective in benefiting various organs in different ways. The organs positively affected include:
  - Liver (Ma, et al, 2011; Song, et al, 2011).
  - Kidneys (Manabe, et al, 2008)
  - Heart (Nakao, et al, 2010)
  - Brain and central nervous system (Liu and Osawa, 2009; Liu, et al, 2009; Lu, et al, 2010)

The World's Strongest & *Highest Quality* Natural Antioxidant

Astaxanthin has been tested head-to-head in many experiments on antioxidant strength against several other carotenoids and antioxidants; it has consistently come out as the very strongest of all natural antioxidants in these tests regardless of the type of test. For example, whether examining free radical elimination or singlet oxygen quenching, Astaxanthin's power as an antioxidant comes out far beyond the capacity of other antioxidants. This is really amazing when you think about it, since many of the antioxidants Astaxanthin has been tested against are closely related molecules in the carotenoid family. Yet Astaxanthin usually comes out superior by at least a power of ten. And when comparing with vitamin antioxidants such as Vitamin C and Vitamin E, Astaxanthin has been shown to be as high as 550X to 6000X stronger.

Yet, as we'll examine below, it is not only that Astaxanthin is so much stronger than other antioxidants that makes it unique; Astaxanthin also has four remarkable qualitative properties that demonstrate its superiority over other antioxidants. When taking together both its quantitative and qualitative properties, it quickly becomes crystal clear that Astaxanthin is the best antioxidant we can take to supplement our diets and would provide anyone with a healthy dose of preventative antioxidant protection.

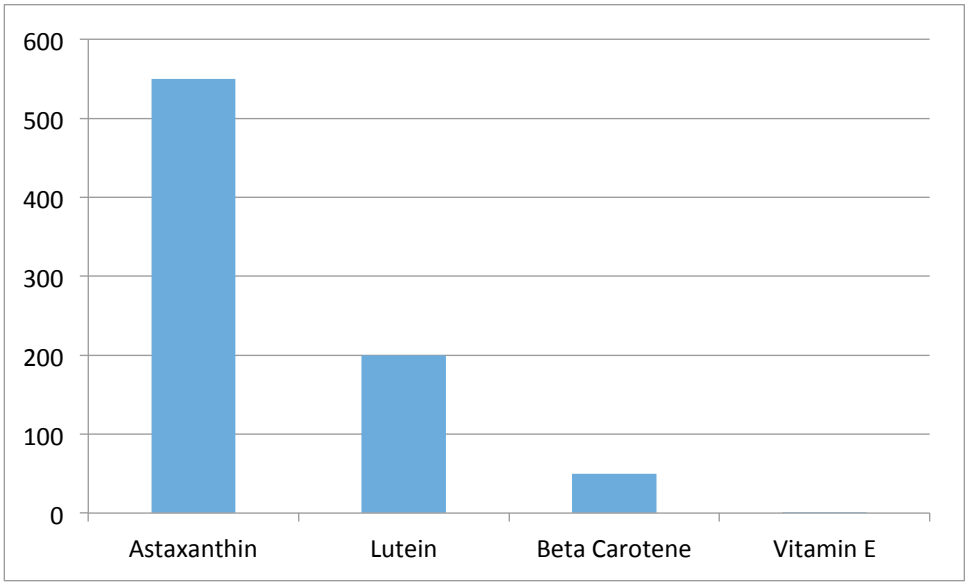
Quantitative Differences Between Astaxanthin and Other Antioxidants: As far back as the 1940's, scientists had discovered the antioxidant abilities of carotenoids and had isolated Astaxanthin as being extremely potent. Research in France in 1946 found that Astaxanthin and beta-carotene were both powerful antioxidants, with Astaxanthin being the stronger of the two (Herisset, A., 1946).

By the 1990's, Astaxanthin's powerful antioxidant activity was becoming widely accepted. A paper published in Japan in 1991 set the platform for the flurry of research that would follow:

> "Astaxanthin, one of the dominant carotenoids in marine animals, showed both a strong quenching effect against singlet oxygen and a strong scavenging effect against free radicals. These effects are considered to be defense mechanisms in the animals for attacking these active oxygen species. The activities of Astaxanthin are approximately 10 times stronger than those of other carotenoids that were tested, namely zeaxanthin, lutein, tunaxanthin, canthaxanthin and beta-carotene, and 100 times greater than a-tocopherol. Astaxanthin also showed strong activity as an inhibitor of lipid peroxidation mediated by these active forms of oxygen. From these results, Astaxanthin has the properties of a 'Super Vitamin E'" (Miki, et al, 1991).

Dr. Miki must have been extremely impressed to call Astaxanthin a "Super Vitamin E." During that period in the early 1990's, Vitamin E was considered by many to be the most beneficial nutrient for both topical application and internal consumption. However, in finding that Astaxanthin was 10 times stronger as an antioxidant than its carotenoid cousins and 100 times stronger than Vitamin E, he must have felt that it deserved such a venerable title.

Many other experiments have been done since Dr. Miki's, all with the same results—Astaxanthin remains the most powerful natural antioxidant found to date. The volume of studies is far too great to review in their totality in a paper of this scope, so we will look at a few of the most important studies which will enable our Readers to get a general idea of Astaxanthin's superior antioxidant strength. The first study we'll examine was also done in the 1990's and also in Japan. This study focused on singlet oxygen quenching. It pitted Astaxanthin against several other antioxidants including carotenoids such as lutein and beta carotene, and it also tested Astaxanthin against Vitamin E. The results were heavily favored toward Astaxanthin; lutein got within the same realm as Astaxanthin in this particular test, but beta carotene and particularly Vitamin E were far weaker than Astaxanthin.



Singlet Oxygen Elimination (Shimidzu, Goto, Miki, 1996)

In singlet oxygen elimination, results of this study found Astaxanthin to be:

- 550 times stronger than Vitamin E
- 11 times stronger than beta-carotene
- 2.75 times stronger than lutein (Shimidzu, et al, 1996)

One of the authors of this study was Dr. Miki, the original researcher who did the oft-times quoted study from 1991 showing Astaxanthin to be phenomenally stronger than other antioxidants and calling it a "Super Vitamin E." As a great fan of Astaxanthin, Dr. Miki participated in another study of Astaxanthin's strength against singlet oxygen many years later in

2007. This time they pitted Astaxanthin against a completely different set of antioxidants. The antioxidants evaluated in this study were Coenzyme Q10, green tea catechins, alpha lipoic acid and Vitamin C. The main difference between this study and Dr. Miki's earlier work is that the results were even more slanted in Astaxanthin's favor.

Many people consider CoQ10 an excellent antioxidant. And among vitamins, Vitamin C is also fairly highly regarded as an antioxidant. Yet when tested against Astaxanthin for their ability to eliminate singlet oxygen, Astaxanthin wasn't just superior—it was incredibly more potent.

Singlet Oxygen Quenching (Nishida, Yamashita, Miki, 2007)

As you can see from the chart above, none of the other antioxidants were even remotely close to Astaxanthin's capacity to eliminate harmful singlet oxygen. The closest of the four was alpha lipoic acid, yet Astaxanthin was still 75 times more potent. Results showed that Astaxanthin is:

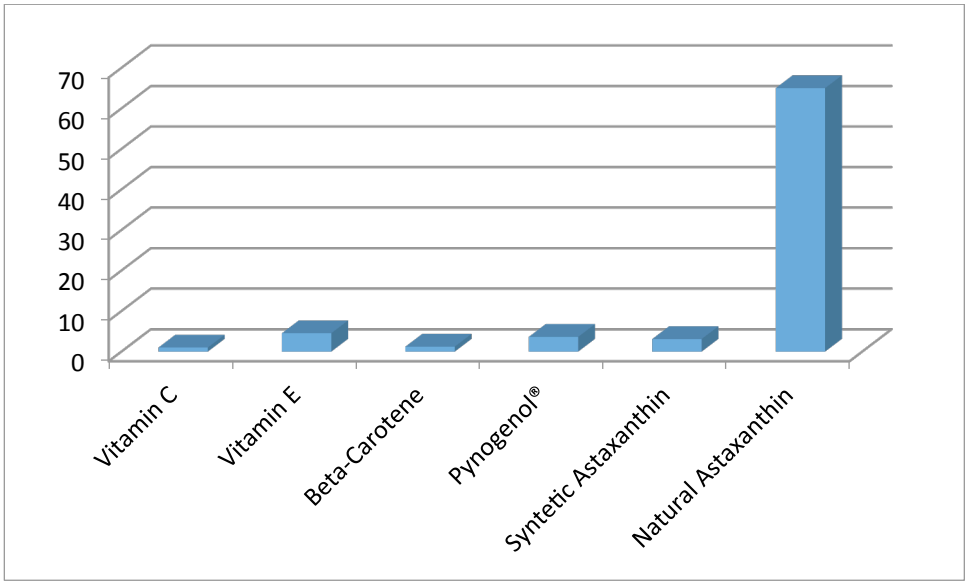
- 8000 times more potent than Vitamin C
- 800 times more potent than CoQ10
- 550 times more potent than Green Tea Catechins
- 75 times more potent than Alpha Lipoic Acid (Nishida, et al, 2007)

The last antioxidant research we'll review here was done at Creighton University by a leading antioxidant and nutritional supplement researcher, Debasis Bagchi, PhD. Professor Bagchi is very well respected in his field with almost 300 publications including several books and hundreds of peer-reviewed studies. Incredibly, Dr. Bagchi's work has been cited by his colleagues over 12,000 times.

When comparing antioxidants, it is very important to analyze them head-to-head and to test them in different experiments. A single test of, for example, Astaxanthin versus Vitamin E as a singlet oxygen eliminator is not a comprehensive view of the two different molecules' antioxidant

capacity. Singlet oxygen are without a doubt extremely harmful to our cells over time, but they are just one of many different types of oxidants that wreak havoc in our bodies. The research in the 1990's focused primarily on Astaxanthin as a singlet oxygen eliminator, so Dr. Bagchi decided to look at Astaxanthin from a different angle: He tested Astaxanthin head-to-head against other well-known antioxidants by measuring their ability to scavenge free radicals in a very well designed experiment.

While this research was originally done in 2001, Dr. Bagchi and his co-author Dr. Gerald Cysewski had great foresight and decided to test both Natural Astaxanthin and Synthetic Astaxanthin in this study even though Synthetic Astaxanthin was not available at the time as a human nutritional supplement. He pitted the natural and synthetic versions of Astaxanthin against Vitamin E, Vitamin C, beta-carotene, and he also included the trademarked supplement Pycnogenol® in the mix as it was claiming to be an extremely powerful antioxidant in its marketing literature. Although this was a completely different way to measure antioxidant strength from the earlier Miki studies, and this set of antioxidants included two completely new molecules—Synthetic Astaxanthin and Pycnogenol®—Natural Astaxanthin again came out the undisputed champion with antioxidant strength ranging from 14X greater than Vitamin E to 65X greater than Vitamin C.



Free Radical Elimination (Capelli, Bagchi, Cysewski, 2013)

Natural Astaxanthin was again far more potent than all other antioxidants. The results showed that, in free radical quenching, Natural Astaxanthin is:

- 14X stronger than Vitamin E
- 18X stronger than Pycnogenol®
- 21X stronger than Synthetic Astaxanthin
- 54X stronger than beta-carotene

- 65X stronger than Vitamin C (Capelli, et al, 2013a)

This university-based research led by one of the world's leading experts in the field did three very important things:

- It proved the consistency of Astaxanthin's superior antioxidant strength regardless of how it is analyzed.
- It quantitatively proved that Astaxanthin is much stronger than other antioxidants that were claiming to be extremely powerful at that time such as Pycnogenol®.
- It showed how incredibly different *Natural* Astaxanthin is from *Synthetic* Astaxanthin.

We see by the relationship between Astaxanthin and Vitamin E in the studies cited above how important it is to use more than one method of measuring antioxidant strength. In the singlet oxygen experiments in the 1990's, Astaxanthin was proven to be 550X stronger than Vitamin E. Yet, when Dr. Bagchi tested the two as free radical scavengers in 2001, Astaxanthin was shown to be 14X stronger. While 14X is still quite impressive, it is a far cry from 550X. So the question comes up as to which number is accurate. The answer is that both of these numbers are accurate, and Astaxanthin is 14 times better than Vitamin E in eliminating free radicals and 550 times better than Vitamin E in specifically eliminating singlet oxygen. It would be impossible to accurately give an exact number when comparing the two in "antioxidant strength," but if we had to, Dr. Miki's original estimate of 100X back in 1991would probably be just about right. Which may be why Dr. Miki simplified things and started calling Astaxanthin a "Super Vitamin E."

A final, critical finding of this study is the clear superiority of Natural Astaxanthin to its distant relative, Synthetic Astaxanthin in antioxidant strength. While a full review of the vast differences between these two molecules would be too comprehensive for this paper, it is important that our Readers understand that these are two completely distinct molecules. In fact, other than sharing the same chemical formula, they are almost exact opposites in all other respects. The primary differences between the two are:

- **Shape**: The Natural Astaxanthin molecule's stereochemistry is unique (it is shaped differently than the Synthetic Astaxanthin molecule).
- **Esterification**: Natural Astaxanthin is 95% esterified (it has a fatty acid molecule attached to either one or both ends of the molecule). Synthetic Astaxanthin is exclusively "free" Astaxanthin and does not have fatty acid molecules attached to it.
- **Synergy**: Natural Astaxanthin from *Haematococcus pluvialis* microalgae comes complexed in nature with supporting carotenoids. There are consistently small amounts of other antioxidant carotenoids present in the carotenoid fraction such as lutein, beta-carotene and canthaxanthin which help provide a synergistic effect when ingested. Synthetic Astaxanthin does not contain supporting carotenoids.
- **Source**: Synthetic Astaxanthin is synthesized from petrochemicals in an elaborate process. Natural Astaxanthin is extracted from natural *Haematococcus pluvialis* microalgae.
- **Safety**: Natural Astaxanthin has an extensive portfolio of human safety studies and a history of over 15 years of safe use as a commercially-sold nutritional supplement. Synthetic Astaxanthin has never been directly tested in humans for safety. (This is an

overriding concern due to serious safety issues that have surfaced with related synthetic carotenoids when ingested by humans.)

- **Efficacy**: Synthetic Astaxanthin has also never been shown to have <u>any</u> health benefit in human clinical research; basically, no one knows if it will have any health benefit at all as a human nutritional supplement. Natural Astaxanthin has been shown to have diverse health benefits in approximately 100 human clinical trials.
- **Dosage**: In the event that Synthetic Astaxanthin is ultimately proven safe for long-range human consumption, dosages would logically be at least 20 times greater than corresponding dosages of Natural Astaxanthin due to its vastly inferior antioxidant profile (Capelli, et al, 2013a), which would most likely put Synthetic Astaxanthin out of reach economically for most consumers.

<u>Qualitative Differences Between Astaxanthin and Other Antioxidants</u>: Astaxanthin is not only an incredibly powerful antioxidant, it is also a unique antioxidant in terms of how it works in our bodies. There are four distinct ways we can see these qualitative properties. While each of these independently would be a critical differentiator from other antioxidants in terms of health value and efficacy, the four of these taken together form a critical mass of evidence of Astaxanthin's superior qualitative antioxidant properties. Each of these on its own is very impressive, and while hard to pick the most important or least, below we list these qualitative differences in the order of their relative importance in our opinion:

1. **Spans the cell membrane to protect the entire cell**: A general rule of antioxidants is: "Lipid soluble antioxidants protect the lipid (oil) soluble part of our cells, and water soluble antioxidants protect the water soluble part of our cells." So when we ingest Vitamin C which is water soluble, its antioxidant properties are useful in one part of our cells, and when we ingest Vitamin E which is oil soluble, its antioxidant properties are useful in the remaining part of our cells. The shape of the Astaxanthin molecule allows it to span the cell membrane and have one end of the molecule in the lipid soluble part of the cell and the other end of the molecule in the water soluble part of the cell. This gives Astaxanthin the distinctive characteristic of being able to protect the entire cell. And Astaxanthin has been found capable of travelling throughout the entire body, into the bloodstream, muscle tissue, skin, as well as various critical organs (Capelli and Cysewski, 2014). This double feature of being able to get throughout the body and being able to protect the entire cell makes Astaxanthin a super-effective antioxidant and anti-inflammatory for humans.

2. **Never a Pro-Oxidant**: A lot of very good antioxidants can, under certain conditions, turn into oxidants and start harming our cells. This is what happened in the famous "Finnish Smokers Study" on beta-carotene published in the prestigious "New England Journal of Medicine" in 1994. This study tested consumption of synthetic beta-carotene, which (like Synthetic Astaxanthin) is completely different from the natural form. Heavy smokers (who were smoking on average three packs of cigarettes each day) were supplemented with synthetic beta-carotene and found after time to have a slightly higher incidence of cancer. This was amazing to all involved since dozens of epidemiological studies as well as pre-clinical research showed that beta-carotene has cancer-preventative

properties (Moorhead, et al, 2005). What was happening was that the beta-carotene was turning into a pro-oxidant in the smokers' bodies because smoking depleted their Vitamin C levels. In the absence of Vitamin C, the beta-carotene molecules had no supporting antioxidants to pass off the supercharged free radicals caused by smoking, so they "changed teams" and became oxidants. This caused additional cellular damage, which in turn increased the incidence of cancer (Heinonen and Albanes, 1994). "Without Vitamin C, beta-carotene can catch the destructive energy of a free radical and itself become a damaging molecule. In this situation, beta-carotene has entered a 'pro-oxidant' state. If Vitamin C is available this pro-oxidant state will quickly be converted back to an antioxidant state without damage to cells" (Malila, et al, 2006; Capelli and Cysewski, 2014).

Many other excellent antioxidants besides beta-carotene can become pro-oxidants under certain conditions. For example, well-known vitamin antioxidants such as Vitamins C & E, zinc, and even carotenoid antioxidants such as lycopene and zeaxanthin can all become pro-oxidants (Martin, et al, 1999). Fortunately, Astaxanthin can never become a pro-oxidant and cause damage to our cells (Beutner, et al, 2000).

3. **Crosses the blood-brain barrier and blood-retinal barrier**: A lot of very good antioxidants cannot help protect our eyes and brains. Even carotenoid antioxidants that are closely related to Astaxanthin such as beta-carotene and lycopene cannot get through these barriers that are present to protect our most vital organs from foreign matter and contaminants. Since our brains are the control center for everything we think and do, an antioxidant that cannot protect the brain seems to be of little value to us. Fortunately, Astaxanthin can get through the blood-brain barrier to protect our brains. When it reaches our brains, it can then travel through the blood-retinal barrier to help protect our eyes. Some of the earliest research on Astaxanthin back in the 1940's and 1950's showed Astaxanthin's ability to get into the brains and eyes of rats (Grangaud, 1951; Massonet, 1958); meanwhile, many human clinical studies have been completed over the last several years to confirm Astaxanthin's diverse health benefits for the eyes and brain (Capelli and Cysewski, 2014). And once present in the eyes and brain, it is not only Astaxanthin's antioxidant activity that is working prophylactically, but also its broad spectrum anti-inflammatory properties are providing additional protection to these vital organs. This one-two punch against oxidation and inflammation is exactly what brains and eyes need to stay healthy and function well.

4. **Bonds with muscle tissue**: As we mentioned above, Astaxanthin can get throughout the entire body and into all the critical organs. It can also bond with muscle tissue to protect muscles from increased levels of oxidation and inflammation and keep the muscles functioning smoothly.

If Astaxanthin only had one distinct advantage over other antioxidants, it would be unjustified to call it the "Highest Quality Natural Antioxidant;" however, with four important, documented advantages over more commonplace antioxidants, we feel it's perfectly warranted and that Astaxanthin has earned this title. Coupled with its broad spectrum anti-inflammatory properties, it becomes clear that Astaxanthin is unquestionably the most useful antioxidant to consume as a

dietary supplement and is highly recommended for everyone over the age of 40 as a preventative anti-aging supplement.

A Safe & Natural, Broad-Spectrum Anti-Inflammatory

It is difficult to say whether Astaxanthin's anti-inflammatory properties or its antioxidant power is more important with regards to anti-aging and cellular health; both create benefits that can help prevent many of the maladies associated with aging. Fortunately Astaxanthin is quite capable in both respects, leading to a variety of distinct advantages for anyone approaching middle age or beyond.

Astaxanthin works as an anti-inflammatory through multiple pathways. The various mechanisms of action for Astaxanthin as an anti-inflammatory have been demonstrated in several studies (Lee, et al, 2003; Ohgami, et al, 2003; Choi, et al, 2008; Kishimoto, et al, 2010). This research has consistently shown that Astaxanthin works on a variety of different causes of inflammation. In fact, there is evidence that it works on six different inflammatory markers, but that it works in a gentle, broad-spectrum manner. This is in distinct contrast to anti-inflammatory drugs such as Celebrex® and Vioxx® as well as over-the-counter anti-inflammatories such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs including Tylenol®, Motrin®, Alleve®, etc.) and aspirin, all of which target a single inflammatory marker, but in an intense manner. Inflammatory markers gently reduced by Astaxanthin include:

- Prostaglandin E-2
- Interleukin 1b
- Interleukin 6
- Tumor Necrosis Factor-A
- Nitric Oxide
- Cox 1 & 2 enzymes (Lee, et al, 2003; Ohgami, et al, 2003; Choi, et al, 2008; Kishimoto, et al, 2010)

Natural Astaxanthin has never been reported to have any side effect or contraindication in hundreds of medical research studies as well as over 15 years of commercial consumer use. There are countless safety studies such as acute toxicity and chronic toxicity studies showing that Natural Astaxanthin is completely safe and has absolutely no adverse side effects or contraindications (Capelli and Cysewski, 2014). Meanwhile, prescription anti-inflammatory drugs as well as over-the-counter anti-inflammatories all have serious side effects. Over-the-counter anti-inflammatory NSAIDs such as Tylenol, Motrin and Alleve can all cause serious liver problems, while aspirin can harm the stomach lining and cause ulcers. The prescription drugs such as Vioxx and Celebrex are even more dangerous; Vioxx was taken off the market several years ago after causing an increase in heart disease and premature death in many consumers, while Celebrex remains on the market albeit with extensive warnings about its potential for adverse cardiovascular events.

Natural Astaxanthin is completely different from these other drugs. It takes significantly longer to work, but it has no side effects. The prescription and over-the-counter drugs can work the same day to combat pain, while Astaxanthin usually takes at least two and up to six or eight

weeks to show effects; but once it starts working, users report that Natural Astaxanthin has the same positive effects on painful inflammatory conditions as the anti-inflammatory drugs, but without any side effects.

In addition to several human clinical trials, two consumer surveys have validated Natural Astaxanthin's ability to combat painful inflammatory conditions. In fact, one of these consumer surveys asked users to compare Natural Astaxanthin's anti-inflammatory effects to prescription and OTC anti-inflammatories and found that Natural Astaxanthin has similar results to those non-natural drugs:

- A survey of people with joint, muscle or tendon pain found that:
    - 84% had positive results from using Natural Astaxanthin
    - 83% experienced less pain
    - 60% had increased mobility
    - When asked how Natural Astaxanthin's effects compared to other anti-inflammatories found in the drug store:
        - 75% said that Natural Astaxanthin works the same or better than over-the-counter pain medications such as aspirin, Tylenol, Alleve or Motrin
        - 64% said that Natural Astaxanthin works the same or better than prescription anti-inflammatories such as Celebrex or Vioxx (Capelli, et al, 2008).
- In a consumer survey of 247 Natural Astaxanthin users, "over 80% of those reporting back pain and symptoms from osteoarthritis or rheumatoid arthritis reported an improvement from Astaxanthin supplementation. Astaxanthin supplementation was also reported to improve symptoms of asthma and enlarged prostate. All of these conditions have an inflammation component which is closely tied to oxidative damage" (Guerin, et al, 2002).

To summarize, it appears from these consumer surveys that Natural Astaxanthin works about as well as prescription and OTC anti-inflammatories. It does, however, take considerably longer to work. But the critical distinction is that Natural Astaxanthin has never been reported to have any side effects or contraindications—it is completely safe and natural—while OTC pain pills and prescription anti-inflammatories all have serious side effects under certain conditions, some that can end up killing you (Capelli and Cysewski, 2014). So the crucial decision is left up to the consumer: Do you want fast results that may end up seriously hurting you, or would you rather wait about a month for the same results and be safe and healthy?

Astaxanthin's Anti-Inflammatory Mechanisms of Action: Back in 2003, scientists working concurrently but independently in Japan and Korea were honing in on Astaxanthin's broad-spectrum mechanisms of action for combatting inflammation. Although they were not corresponding or sharing information, and even though they used very different paths to get there, both groups of researchers arrived at similar conclusions. This was the start, but other studies since then have further substantiated the early findings. Below is a summary of some of the most significant research in this area:

1. First Study Proving Mechanism of Action: Researchers at Japan's Hokkaido Graduate School of Medicine were the first to prove Astaxanthin's multiple mechanisms for controlling inflammation. They did their research in test tubes and also in rats, focusing on the rats' eyes. They found that Astaxanthin reduced three key causes of inflammation: Nitric oxide (NO), tumor necrosis factor alpha (TNF-a) and prostaglandin E-2 (PGE-2) (Ohgami, et al, 2003).
2. Second Mechanism of Action Study: Later the same year, Korean researchers working independently found similar results to the Ohgami study in vitro and ex-vivo. In harmony with the Ohgami results, they found that Astaxanthin suppresses the inflammatory mediators nitric oxide, prostaglandin E-2 and tumor necrosis factor alpha. But they also demonstrated Astaxanthin's positive effects on three other inflammatory markers: Interleukin 1B (IL-1b), COX-2 enzyme and nuclear factor kappa-B (Lee, et al 2003).
3. Further Validation: Several years later, scientists from Korea University further validated the earlier results finding broad-spectrum anti-inflammatory activity (Choi, et al, 2008).
4. "Remarkable" Results: Japanese researchers referred to Astaxanthin's anti-inflammatory activity as "remarkable" and found a statistically significant reduction in the six different inflammatory markers tested (Kishimoto, et al, 2010).
5. Inhibition of Mast Cells: Mast cells are the key initiators of inflammation. Research at Kyoto University showed an inhibitory effect of Astaxanthin in rats' mast cells (Sakai, et al, 2009).
6. In the most recent study in this area, Astaxanthin was found to be effective at protecting against UV-induced inflammation in a broad-spectrum manner. In fact, cell death that is frequently caused by UV exposure was significantly decreased in the Astaxanthin-treated cells (Yoshihisa, et al, 2014).

As we discussed in the first chapter of this paper, there have been several human clinical trials showing that Astaxanthin reduces pain in joints, tendons and muscles in groups of patients suffering from chronic conditions as well as in healthy men doing intense exercise. Please refer to the discussion starting on Page 6 for a thorough review of this research.

Conclusion

The body of evidence for Astaxanthin's benefits for anti-aging has attained critical mass. On a cellular level, it can protect our cells extremely efficiently and from many different pathways. It is very well documented as the world's strongest natural antioxidant. Yet it is not only Astaxanthin's supreme antioxidant power that make it so effective, but also its four distinct qualitative properties which clearer separate it from other antioxidants as well:

- Unlike other antioxidants, it can span the cell membrane and protect the entire cell, both the water-soluble part as well as the lipid-soluble part.
- It can never become a pro-oxidant and start causing oxidation like so many otherwise good antioxidants do under certain conditions.
- It can cross the blood-brain and blood-retinal barriers to bring its intense antioxidant protection to our most vital organs, our brains and eyes.
- It can bond with muscle tissue to protect them and keep them functioning at their highest levels.

In addition to its effectiveness in quenching singlet oxygen and other free radicals, Natural Astaxanthin is also a very safe and very effective anti-inflammatory. It has been shown to reduce systemic inflammation, the silent killer that is a root cause of many life-threatening diseases. And it has also shown that it can reduce acute inflammation which manifests in pain in the joints and tendons.

And finally in our discussion of Astaxanthin on a cellular level, a great deal of research has been done showing benefits of Astaxanthin specific to key parts of our cells. It can prevent damage in DNA and protect the mitochondria, which are two additional valuable characteristics of this fascinating molecule.

So, what does all this mean? Astaxanthin's multi-pronged approach of neutralizing oxidation, reducing inflammation, preventing DNA damage and protecting the mitochondria means that Natural Astaxanthin can help combat many of the problems associated with aging. Areas in which multiple human clinical trials have been successfully performed that indicate health benefits against aging include:

- ❋ Eye Health
- ❋ Brain Health
- ❋ Joint & Tendon Health
- ❋ Cardiovascular Health
- ❋ Skin Health & UV Protection
- ❋ Energy & Performance
- ❋ Immune System Modulation

It is for these reasons that we highly recommend the preventative use of 4mg – 12mg per day of Natural Astaxanthin for all people over the age of 40.

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