Astaxanthin for Immune System Support

There has been some promising research on the effects of Natural Astaxanthin in enhancing immunity. A series of studies were conducted during the 1990's by Dr. Jyonouchi and various associates, first at the University of South Florida and later at the University of Minnesota's School of Medicine. The first study was in-vitro work on mouse and sheep blood, in which Astaxanthin was shown to have an immunomodulating effect as compared to beta carotene. "These results indicate that immunomodulating actions of carotenoids are not necessarily related to pro-vitamin A activity, because astaxanthin, which does not have pro-vitamin A activity, showed more significant effects" (Jyonouchi, et al, 1991). A follow up study in 1993 examined the mechanism of action for Astaxanthin's immunomodulating effects, and found it is related to enhancement of antibody production to T-cell dependent antigen (Jyonouchi, et al, 1993).

The following year, Dr. Jyonouchi went one step further by examining these invitro effects in live mice, and compared the effects of Astaxanthin this time with both beta carotene and lutein. The outcome was that all three carotenoids had significant immunomodulating action. In a group of old mice, Astaxanthin stood out beyond its carotenoid cousins as it partially restored antibody production to a greater extent than did lutein and beta carotene (Jyonouchi, et al, 1994).

The next study in this series was done in-vitro using samples from the blood of adult (human) volunteers, as well as blood from the umbilical cord of newborn babies. Testing was done with both beta carotene and Astaxanthin to check if they could increase immune markers in the blood. It was found that beta carotene had no effect, while Astaxanthin increased the production of two different forms of immunoglobulin. The researchers concluded: "This study has shown for the first time that astaxanthin, a carotenoid without vitamin A activity, enhances human immunoglobulin production in response to T-dependent stimuli" (Jyonouchi, et al, 1995).

The final study in this series measured Astaxanthin's and several other carotenoids' potency as immune enhancers. Astaxanthin did considerably more at equal dosage levels than all other carotenoids, including lutein, lycopene, zeaxanthin and canthaxanthin. Astaxanthin alone suppressed interferon-gamma production and increased the number of antibody-secreting cells with the use of primed spleen cells (Jyonouchi, et al, 1996).

Similar work was done the same year in Japan by other researchers, where Astaxanthin was again tested against beta carotene and canthaxanthin. Once more, it was found that Astaxanthin enhanced two different forms of immunoglobulin; canthaxanthin had a moderate effect and beta carotene had a slight effect at much higher doses. The release of inflammatory markers TNF-a and IL-1a were also enhanced. The summary ranked the cytokine inducing activities in this order: Astaxanthin>canthaxanthin>beta carotene (Okai and Higashi-Okai, 1996).

Another slant on the immune benefits of Astaxanthin is seen in a study involving Helicobacter pylori, a bacterium commonly found in the stomach that can lead to ulcers and ultimately, stomach cancer. There has been quite a lot of research on Astaxanthin's positive effects in reducing H. pylori. In this particular study, the author states that "Recent experimental studies, both in vivo and in vitro, have shown that vitamin C and astaxanthin, a carotenoid, are not only free radical scavengers but also show antimicrobial activity against H. pylori. It has been shown that astaxanthin changes the immune response to H. pylori by shifting the Th1 response towards a Th2 T-cell response" (Akyon, Y, 2002). Because Astaxanthin can actually change the immune response, it is very effective at reducing H. pylori, which can help prevent certain types of gastric cancer and other stomach ailments.

A professor at Washington State University named B.P. Chew, PhD has also been studying Astaxanthin's effects on the immune system. First he looked at how Astaxanthin boosted immunity in mice. He discovered that Astaxanthin and beta carotene both increased the lymphocyte function in mice's spleens. This was not true of canthaxanthin. Astaxanthin had an additional positive effect that beta carotene did not in that it also enhanced lymphocyte cytotoxic activity (Chew, et al, 2003).

After proving immune system enhancement in mice, Dr. Chew moved on to study the effect in humans. In a double blind, placebo controlled human clinical, Dr. Chew and his team showed that Astaxanthin is a strong immune system stimulator. The study showed that Astaxanthin:

- Stimulates lymphocyte proliferation
- Increases the total number of antibody producing B-cells
- Produces increased number of T-cells
- Amplifies natural killer cell cytotoxic activity
- Significantly increases delayed-type hypersensitivity response
- Dramatically decreases DNA damage

To summarize, these results show that Astaxanthin works through many different pathways to support healthy immune function in humans (Chew, et al, 2003).

Dr. Chew along with Dr. J.S. Park wrote a summary article entitled "Carotenoid Action on the Immune Response" in which they spoke very highly about Astaxanthin's advantages for tumor immunity. They stated that "Even though astaxanthin, canthaxanthin and beta carotene inhibited tumor growth, astaxanthin showed the highest anti-tumor activity" (Chew and Park, 2004).

Astaxanthin's positive effects on immunity have been corroborated in countless animal and in vitro studies involving many diseases such as cancer. While the volume of studies related to Astaxanthin's ability to prevent carcinogenesis and decrease tumor size in animals is too large to go into in depth here, we can examine a few of the more important studies: In one study, researchers transplanted tumor cells into mice and found that Astaxanthin inhibited the growth of the cancerous tumors in a dose-dependent fashion (Sun, et al, 1998). A similar study was done to see at what stage Astaxanthin would have its positive effects. It was found that when Astaxanthin supplementation was started both at one week and also at three weeks prior to the tumor inoculation, growth was inhibited. However, when the supplementation with Astaxanthin began at the same time as the tumor inoculation, the benefit was not found. The conclusion of this study was that Astaxanthin may work better in the early stages of tumor development, but not in the later stages. The researcher was very enthused with Astaxanthin's potential in cancer prevention, pointing out that the anti-tumor activity came at blood concentration levels that are achievable. The theory espoused by these researchers is that Astaxanthin's anti-tumor activity is related to its enhancement of the immune response (Jyonouchi, et al, 2000).

Other mice studies have also shown very promising results. One showed that Astaxanthin reduced the growth of transplanted breast tumors. This study was very interesting in that it tested Astaxanthin against two other carotenoids-beta carotene and canthaxanthin. The researchers found that "Mammary tumor growth inhibition by Astaxanthin was dose-dependent and was higher than that of canthaxanthin and beta carotene...Lipid peroxidation activity in tumors was lower (P < 0.05) in mice fed 0.4% astaxanthin, but not in those fed beta-carotene and canthaxanthin" (Chew, et al, 1999). Another favorable study demonstrated that Astaxanthin suppressed spontaneous liver carcinogenesis (Nishino, et al, 1999). Further studies have shown that introduction of carcinogens such as benzopyrene to mice was positively affected when they were fed Astaxanthin; two specific types of cancer that appeared in the control group were inhibited in the Astaxanthin group (Lee, et al, 1997 and Lee, et al, 1998). Research done at the Veterans Affairs Medical Center in Texas showed that Astaxanthin and beta carotene (but not lycopene) prevented UV-mediated carcinogenesis in mice (Black, H.S., 1998).

Astaxanthin was found to be an effective anti-tumor agent in a series of studies on mice and rats at the Gifu University School of Medicine in Japan (Mori, et al, 1997). One of these studies found that Astaxanthin significantly reduced both the incidence and the proliferation of chemically-induced bladder cancer in mice (Tanaka, et al, 1994). Two other studies showed the same effects in the oral cavity and the colon of rats; Astaxanthin reduced the incidence and the proliferation of cancers when carcinogenic chemicals were introduced (Tanaka, et al, 1995a and Tanaka, et al, 1995b). Lastly, a few different studies have shown Astaxanthin's positive effects on cancer of the liver in rats (Gradelet, et al, 1997, Gradelet, et al, 1998, Yang, et al, 1997 and Kurihara, et al, 2002).

Astaxanthin may also be very effective for autoimmune conditions such as rheumatoid arthritis. While there has not been a large amount of research in this area to date, in one very significant double blind, placebo controlled study, sufferers of rheumatoid arthritis in the treatment group showed marked improvement in pain and quality of life levels as the study progressed over eight weeks (Nir and Spiller, 2002). This is a very important study in that it demonstrates how the benefits of Astaxanthin can make a real difference in the here and now to people with debilitating diseases.

Mechanism of Action

In addition to the mechanisms demonstrated by Dr. Chew above (see bullet points on Page 2), Astaxanthin's outstanding properties as an anti-inflammatory also play a major role in its ability to enhance immune function. Due to the multitude of ways in which Astaxanthin combats inflammation, it is a very special anti-inflammatory indeed. Both in-vitro and in-vivo research has been done to uncover its mechanism of action as an anti-inflammatory. This mechanism has been further demonstrated in several double blind, placebo controlled human clinical trials on various inflammatory conditions.

Astaxanthin works to suppress different inflammatory mediators. Among these mediators are tumor necrosis factor alpha (TNF-a), prostaglandin E-2 (PGE-2), interleukin 1B (IL-1b) and nitric oxide (NO). In one experiment done with mice and also

in-vitro, Astaxanthin was shown to suppress TNF-a, PGE-2, IL-1b, NO as well as the Cox-2 enzyme and nuclear factor kappa-B (Lee, et al, 2003).

Another study done the same year was led by a researcher from Japan's Hokkaido University Graduate School of Medicine. Here, the researchers found similar results: Astaxanthin was shown in vitro to decrease the production of NO, PGE-2 and TNF-a. This study also looked at Astaxanthin's anti-inflammatory effect in the eyes of rats. The researchers induced uveitis (inflammation of the inner eye including the iris) and found that Astaxanthin had a "dose dependent ocular anti-inflammatory effect, by the suppression of NO, PGE-2 and TNF-a production, through directly blocking nitric oxide synthase enzyme activity" (Ohgami, et al, 2003).

While more human research would be welcome, it is evident from the vast amount of research already completed that Astaxanthin has outstanding immune enhancing effects, and may be an excellent aid in the prevention of cancer, in the reduction of tumors and in the treatment of people with inflammatory and autoimmune conditions.

References

- Akyon, Y. (2002). "Effects of antioxidants on the immune response of Helicobacter pylori." Clinical Microbiology and Infection. 8(7):438-41.
- Black, H. (1998). "Radical interception by carotenoids and effects on UV carcinogenesis." Nutrition and Cancer. 31(3):212-7.
- Chew, B., Park, J. (2004). "Carotenoid action on the immune reponse." The Journal of Nutrition. 134(1):257S-261S.
- Chew, B., Park, J., Chyun, J., Mahoney, M., Line, L. (2003). "Astaxanthin Stimulates Immune Response in Humans in a Double Blind Study." Presented at the Supply Side West International Trade Show and Conference, October 1-3, 2003.
- Chew, B., Wong, M., Park, J., Wong, T. (1999). "Dietary beta-carotene and astaxanthin but not canthaxanthin stimulate splenocyte function in mice." Anticancer Research. 19(6B):5223-7.
- Chew, B., Park, J., Wong, M., Wong, T. (1999). "A comparison of the anticancer activities of dietary B-carotene, canthaxanthin and astaxanthin in mice in vivo." Anticancer Research. 19(3A):1849-53.
- Gradelet, S., Le Bon, A., Berges, R., Suschetet, M., Astorg, P. (1998). "Dietary carotenoids inhibit aflatoxin B1induced liver preneoplastic foci and DNA damage in the rat: role of the modulation of aflatoxin B1 metabolism." Carcinogenesis. 19(3):403-411.
- Gradelet, S., Astorg, P., Le Bon, A., Berges, R., Suschetet, M. (1997). "Modulation of aflatoxin B1 carcinogenicity, genotoxicity and metabolism in rat liver by dietary carotenoids: evidence for a protective effect of CYP1A inducers." Cancer Lett. 114(1-2):221-223.
- Jyonouchi, H., Sun, S., Iijima, K., Gross, M. (2000). "Antitumor activity of astaxanthin and its mode of action." Nutrition and Cancer. 36(1):59–65.
- Jyonouchi, H., Sun, S., Mizokami, M., Gross, M. (1996). "Effects of various carotenoids on cloned, effector-stage Thelper cell activity." Nutrition and Cancer. 26(3):313-24.
- Jyonouchi, H., Sun, S., Gross, M. (1995). "Astaxanthin, a carotenoid without vitamin A activity, augments antibody responses in cultures including T-helper cell clones and suboptimal doses of antigen." J. Nutr. 125(10):2483-2492.

- Jyonouchi, H., Sun, S., Gross, M. (1995). "Effect of carotenoids on in vitro immunoglobulin production by human peripheral blood mononuclear cells: astaxanthin, a carotenoid without vitamin A activity, enhances in vitro immunoglobulin production in response to a T-dependent stimulant and antigen." Nutrition and Cancer. 23(2):171-183.
- Jyonouchi, H., Zhang, L., Gross, M., Tomita, Y. (1994). "Immunomodulating actions of carotenoids: enhancement of in vivo and in vitro antibody production to T-dependent antigens." Nutrition and Cancer. 21(1):47-58.
- Jyonouchi, H., Zhang, L., Tomita, Y. (1993). "Studies of immunomodulating actions of carotenoids. II. Astaxanthin enhances in vitro antibody production to T-dependent antigens without facilitating polyclonal B-cell activation." Nutrition and Cancer. 19(3):269-80.
- Jyonouchi, H., Hill, R., Tomita, Y., Good, R. (1991). "Studies of immunomodulating actions of carotenoids. I. Effects of beta-carotene and astaxanthin on murine lymphocyte functions and cell surface marker expression in in-vitro culture system." Nutrition and Cancer. 16(2):93-105.
- Kurihara, H., Koda, H., Asami, S., Kiso, Y., Tanaka, T. (2002). "Contribution of the antioxidative property of astaxanthin to its protective effect on the promotion of cancer metastasis in mice treated with restraint stress." Life Sciences. 70(21):2509-20.
- Lee, S., Bai, S., Lee, K., Namkoong, S., Na, H., Ha, K., Han, J., Yim, S., Chang, K., Kwon, Y., Lee, S., Kim, Y. (2003). "Astaxanthin Inhibits Nitric Oxide Production and Inflammatory Gene Expression by Suppressing IkB Kinase-dependent NFR-kB Activation." Molecules and Cells. 16(1):97-105.
- Lee, S. et al. (1998). "Inhibition of sarcoma-180 cell-induced mouse ascites cancer by astaxanthin-containing egg yolks." J. Kor. Soc. Food Sci. Nutr. 27, 163.
- Lee, S. et al. (1997). "Inhibition of benzo(a)pyrene-induced mouse forestomach neoplasia by astaxanthin containing egg yolks." Agric. Chem. Biotechnol. 40, 490.
- Mori, H., Tanaka, T., Sugie, S., Yoshimi, N., Kawamori, T., Hirose, Y., Ohnishi, M. (1997). "Chemoprevention by naturally occurring and synthetic agents in oral, liver, and large bowel carcinogenesis." Journal of Cellular Biochemestry. 27:35-41.
- Nir, Y., Spiller, G. (2002b). "BioAstin helps relieve pain and improves performance in patients with rheumatoid arthritis." Journal of the American College of Nutrition. 21(5):Oct, 2002.
- Nishino, et al, (1999). "Cancer prevention by carotenoids." Pure & Appl. Chem. 71, 2273.
- Ohgami, K., Shiratori, K., Kotake, S., Nishida, T., Mizuki, N., Yazawa, K., Ohno, S. (2003). "Effects of astaxanthin on lipopolysaccharide-induced inflammation in vitro and in vivo." Investigative Ophthalmology and Visual Science. 44(6):2694-701.
- Okai, Y., Higashi-Okai, K. (1996). "Possible immunomodulating activities of carotenoids in in-vitro cell culture experiments." International Journal of Immunopharmacology. 18(12):753–8.
- Sun, S. et al. (1998). "Anti-tumor activity of astaxanthin on Meth-A tumor cells and its mode of action." FASEB J. 12, A966.
- Tanaka, T., Kawamori, T., Ohnishi, M., Makita, H., Mori, H., Satoh, K., Hara, A. (1995a). "Suppression of azomethane-induced rat colon carcinogenesis by dietary administration of naturally occurring xanthophylls astaxanthin and canthaxanthin during the postinitiation phase." Carcinogenesis. 16(12):2957-63.
- Tanaka, T., Makita, H., Ohnishi, M., Mori, H., Satoh, K., Hara, A. (1995b). "Chemoprevention of rat oral carcinogenesis by naturally occurring xanthophylls, astaxanthin and canthaxanthin." Cancer Research. 55(18):4059-64.
- Tanaka, T., Morishita, Y., Suzui, M., Kojima, T., Okumura, A., Mori, H. (1994). "Chemoprevention of mouse urinary bladder carcinogenesis by the naturally occurring carotenoids astaxanthin." Carcinogenesis. 15(1):15-19.

Yang, Z. et al. (1997). "Protective effect of astaxanthin on the promotion of cancer metastases in mice treated with restraint-stress." J. Jpn. Soc. Nutr. Food Sci. 50, 423.