Astaxanthin from the Microalga Haematococcus – a superb natural antioxidant for human health


Algatechnologies (1998) Ltd. is an up and coming Israeli company and a global leader in solar-energy-based photobioreactor technology, devoted to exploiting the commercial potential of natural bioactives from microalgae.

Our first product, natural Astaxanthin, is a valuable bioactive ingredient for dietary supplements, nutraceuticals and cosmeceuticals.

Astaxanthin also enjoys a broad range of applications in the food industry and in the fish and animal feed arena.

Astaxanthin is produced by a patented biocontrolled growing process of the microalga Haematococcus pluvialis A1.

Astaxanthin – The “Jewel Antioxidant” among carotenoids

Carotenoids are lipid-soluble pigments, which participate as accessory pigments in the light-absorption process of photosynthetic organisms. To date, over 700 natural carotenoids have been identified. They are responsible for the orange and red colors in plants and algae, and for the wide range of blue, purple and reddish colors in aquatic animals. Only phytoplankton, algae, plants and certain bacteria and fungi synthesize carotenoids. Animals, including humans, must consume carotenoids as part of their diet and rely on this external supply.

Astaxanthin, a member of the carotenoid family, is a dark-red pigment which is the main carotenoid found in the marine world of algae and aquatic animals. Astaxanthin is present in many types of seafood, including salmon, trout, red sea bream, shrimp and lobster, as well as in birds such as flamingo and quail. This pigment is commercially produced from the microalga Haematococcus pluvialis, the richest known natural source for Astaxanthin.

Recent scientific findings indicate that Astaxanthin is a powerful antioxidant and can serve as a potent free-radical scavenger. Moreover, Astaxanthin has been found to provide many essential biological functions, including protection against lipid-membrane peroxidation of essential polyunsaturated fatty acids and proteins, DNA damage and UV light effects; it also plays an important role in immunological defense.

Oxygen is necessary for the metabolic production of energy in our bodies. Mitochondria, through the electron-transport chain, use oxygen to oxidize certain molecules and generate energy in the form of ATP. During this process, oxygen is reduced to water, producing several oxygen-derived free radicals or reactive oxygen species (ROS) which play an important role in various diseases. Normally, oxygen free radicals are neutralized by natural anti-oxidants such as vitamin E, or enzymes such as superoxide dismutase (SOD). However, ROS become a problem when either a decrease in their removal or their over-production occurs, resulting in oxidative stress. This stress, and the resultant damage, have been implicated in many diseases, and a wealth of preventive drugs and treatments are currently being studied.

Astaxanthin’s powerful anti-oxidant activity has been demonstrated in numerous studies showing the detrimental effects of free-radical-induced oxidative stress2-4 and Astaxanthin’s potential to target many important health conditions.

There is increasing testimonial evidence that Astaxanthin may be effective in enhancing general well-being, improving the quality of life and enhancing the immune system. Recent studies have shown enhanced immune response and decreased DNA damage in human subjects following Astaxanthin administration5. Astaxanthin is capable of crossing the blood-brain barrier in mammals6, a unique and important property in the realm of antioxidants. This characteristic allows Astaxanthin to extend its superior anti-oxidant activity to the central nervous system, which, being rich in unsaturated fatty acids is highly susceptible to oxidative damage by ROS7.

The efficacy of Astaxanthin in limiting the damage produced by ROS-induced oxidative stress and improving health parameters in the tissues and the body was demonstrated in a series of in-vitro experiments, in pre-clinical studies and in human models. The following is a list of diseases and conditions for which Astaxanthin has been shown to have beneficial effects, as described in numerous medical articles, patents and excellent reviews8-9 over the last 10 years:

- Age-Related Macular Degeneration: the leading cause of blindness in the aging population
- Alzheimer’s and Parkinson’s Diseases: two of the most important neurodegenerative diseases
- Cholesterol Disease: ameliorates the effects of LDL, the “bad” cholesterol
- Inflammatory; chronic viral and autoimmune diseases
- Dyspepsia
- Semen fertility improvement
- Muscle function
- Sunburn from UV light
- Normalization of cardiac rhythm
- Anti-hypertension agent
- Stress management
- Benign Prostatic Hyperplasia (BPH)
- Stroke: repairs damage caused by lack of oxygen.

A demand for natural Astaxanthin is now emerging in the fast-growing, multi-billion dollar nutraceutical market; in particular, increasing evidence suggests that Astaxanthin is a much more powerful anti-oxidant than vitamins C and E, or than other carotenoids such as beta-carotene, lycopene, lutein and zeaxanthin, among others.

The enhanced activity of Astaxanthin may stem from its molecular structure. Astaxanthin belongs to the xanthophyll group of carotenoids, or the oxygenated carotenoids (see other members of the group in Fig. 1). The hydroxyl and keto functional groups are responsible for its unique and important role in oxidative stress.

Fig 1: Members of the xanthophyll family
groups (see Fig. 1) present in the ending ionone ring of *Astaxanthin* may be responsible for its uniquely powerful anti-
oxidant activity and for its ability to span the membrane bilayers as a direct result of its more polar configuration relative to other carotenoids. Carotenoids with polar end groups like *Astaxanthin* span the lipid membrane bilayer with their end groups located near the hydrophobic-hydrophilic interface, where free-radical attack first occurs.

Haematococcus pluvialis is believed to accumulate the highest levels of *Astaxanthin* in nature. Commercially grown *Haematococcus pluvialis* can accumulate more than 40g of *Astaxanthin* per kilo of dry biomass (see Table 1).

### Table 1: Natural sources of *Astaxanthin*

<table>
<thead>
<tr>
<th>Astaxanthin natural sources</th>
<th>Astaxanthin concentration (ppm)</th>
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<tbody>
<tr>
<td>Salmonids</td>
<td>~ 5</td>
</tr>
<tr>
<td>Plankton</td>
<td>~ 60</td>
</tr>
<tr>
<td>Krill</td>
<td>~ 120</td>
</tr>
<tr>
<td>Arctic shrimp</td>
<td>~ 1200</td>
</tr>
<tr>
<td>Phaffia Yeast</td>
<td>~ 8000</td>
</tr>
<tr>
<td>Haematococcus pluvialis</td>
<td>~ 40,000</td>
</tr>
</tbody>
</table>

- Today is as an animal feed additive to impart coloration to salmonids (salmon and trout), as well as to red sea bream and tai. In natural habitats, salmonids obtain their coloration from natural food sources, including algae and crustaceans. However in fish farms, the absence of natural pigmentation sources results in salmonids with off-white coloration, imparting an artificial and unattractive look for consumers and making the fish difficult to market.
- Today, essentially all commercial *Astaxanthin* for aquaculture is produced synthetically from petrochemical sources, with an annual turnover of over $200 million, and a selling price of ~$2000 per kilo of pure *Astaxanthin*.
- Other developing applications for synthetic *Astaxanthin* include poultry and egg production.
- In recent years, there has been a growing trend toward using natural ingredients in all forms of food nutrients, resulting from increasing concerns for consumer safety and regulatory issues over the introduction of synthetic chemicals into the human food chain. This is also true for the nutraceutical and cosmeceutical markets.
- Good examples of commercially important naturally derived carotenoids are beta-carotene, lycopene, lutein and zeaxanthin, commercial carotenoids with antioxidant properties which have become popular ingredients in many vitamin and mineral supplements. Beta-carotene and lycopene can be produced both synthetically (from petrochemicals) and naturally. A decade ago, natural beta-carotene accounted for a tiny percentage of the total world market. Today, that market has increased several-fold and today, natural beta-carotene accounts for 15 to 20% of world demand. Virtually all nutraceutical producers use natural rather than synthetic carotenoids, and pay premium prices as much as five times that of the synthetic product.
- The demand for natural *Astaxanthin* is now emerging in the multi-billion dollar nutraceutical market, and increasingly, medical researchers believe that *Astaxanthin* may have significant pharmaceutical applications. While only a negligible part of today's market, the demand for such applications is expected to grow significantly in the near term as a result of numerous medical studies performed during the last 5 years in the area of *Astaxanthin* applications.
- This review supports the conviction that a daily dose of 4 to 6 mg of *Astaxanthin* is of tremendous importance for health management, by protecting body tissues from the oxidative stress caused by free radicals, among others.
- *Astaxanthin* producers have conducted several studies in recent years to demonstrate the safety of natural *Astaxanthin* derived from *Haematococcus* 16-18. A randomized, double-blind, placebo-controlled, 8-week trial designed to determine the safety of *Astaxanthin* in 35 healthy adults was published recently 19. Results revealed that healthy adults can safely consume 8mg of *Astaxanthin* per day from *Haematococcus pluvialis* extract. Based on recent findings, we believe that a daily dose of *Astaxanthin* will have an important influence in preventing a broad array of diseases. Moreover, small daily doses of *Astaxanthin* may prevent or delay the onset of some diseases, thus saving society significant sums of money.
production process is based on two distinct cultivation stages. The first is called the “Green Stage,” which starts indoors with a single-cell colony of the microalga, and continues outdoors in solar-powered photobioreactors. The aim of this stage is to produce plenty of viable, unstressed “green” algal cells by normal cell-division process (see Fig. 2). The “Green Stage” provides optimal growth conditions in order to achieve maximal biomass production rate. The second cultivation stage is the “Red Stage” (see Fig. 2), in which the algal cells synthesize and accumulate the pigment Astaxanthin. This stage starts by subjecting the cells to severe stress conditions, mainly high radiation intensity and changes in growth media. As a result, the Haematococcus cells start to form cysts by producing thick cell walls, and to synthesize and accumulate Astaxanthin in its esterified form. Cultivating the algal culture in closed systems allows an environmentally controlled process with less biological and chemical contamination. Following the “Red process”, the level of Astaxanthin in the “red cells” may reach up to ~4% of their dry weight. The Astaxanthin content of the “red cells” is correlated to the severity of the stress conditions, mainly to the light flux through the culture. In due time, the “red culture” is pumped to the down-processing area, where the cells are cracked (to render the pigment bioavailable), dried, and vacuum-packed. Haematococcus oleoresin is produced in an additional step, using the CO₂ Supercritical Fluid Extraction process. Increasingly, both consumers and regulatory agencies are requiring extracts that contain no residual solvents. U.S. Nutra of Eustis, FL, has the technology to extract Haematococcus with CO₂ and without any co-solvents. Very few companies commercially produce Astaxanthin from Haematococcus pluvialis. The Hawaiian companies Cyanotech Corporation and Merit Pharmaceuticals cultivate the algae using an open pond system for the “Red Stage.” The Japanese company Fuji Chemicals operates an indoor facility in Sweden and its “dome-shaped” bioreactors in Hawaii. The Israeli company Algatechnologies uses tubular solar-powered photobioreactors for both the “Green and Red stages” in closed, strictly controlled systems (Figs 3 and 4).

Table 2: Selected patents on Astaxanthin health and nutrition applications

<table>
<thead>
<tr>
<th>Patent number</th>
<th>Company</th>
<th>Patent title</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP0786990</td>
<td>US NUTRACEUTICALS</td>
<td>Use of Astaxanthin for retarding and ameliorating central nervous system and eye damage</td>
</tr>
<tr>
<td>EP12177996</td>
<td>ASTACAROTENE</td>
<td>Use of Astaxanthin for treatment of autoimmune diseases, chronic viral and intracellular bacterial infections</td>
</tr>
<tr>
<td>US6475547</td>
<td>ASTACAROTENE</td>
<td>Immunoglobulin-rich milk, Production and use thereof</td>
</tr>
<tr>
<td>WO00023064</td>
<td>ASTACAROTENE</td>
<td>Treatment of Dyspepsia</td>
</tr>
<tr>
<td>US6410602</td>
<td>ASTACAROTENE</td>
<td>Method of increasing the production and improving the quality of semen</td>
</tr>
<tr>
<td>US6335015</td>
<td>ASTACAROTENE</td>
<td>Method of the prophylactic treatment of Mastitis</td>
</tr>
<tr>
<td>US6262316</td>
<td>ASTACAROTENE</td>
<td>Oral preparation for the prophylactic and therapeutic treatment of Helicobacter Sp. infection</td>
</tr>
<tr>
<td>US6245818</td>
<td>ASTACAROTENE</td>
<td>Medicament for improvement of duration of muscle function or treatment of muscle disorders or diseases</td>
</tr>
<tr>
<td>US6054491</td>
<td>ASTACAROTENE</td>
<td>Agent for increasing the production of/in breeding and production mammals</td>
</tr>
<tr>
<td>US5744502</td>
<td>ASTACAROTENE</td>
<td>Method for increasing the production of/in breeding and production animals in the poultry industry</td>
</tr>
<tr>
<td>US6433025</td>
<td>CYANOTECH</td>
<td>Method for retarding and preventing sunburn by UV light</td>
</tr>
<tr>
<td>US6344214</td>
<td>CYANOTECH</td>
<td>Method for retarding and ameliorating fever blisters and canker sores</td>
</tr>
<tr>
<td>US6258855</td>
<td>CYANOTECH</td>
<td>Method of retarding and ameliorating carpal tunnel syndrome</td>
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<tr>
<td>EP1283038</td>
<td>SUNTORY LTD</td>
<td>Compositions normalizing circadian rhythm</td>
</tr>
<tr>
<td>WO030031556</td>
<td>ITAKURA HIROSHIGE</td>
<td>Medicinal compositions having effects of ameliorating eye diseases and holding eye functions</td>
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<tr>
<td>WO03003848</td>
<td>AANENSEN BERIT ANNIE</td>
<td>The use of di-esters of Astaxanthin for enhancing the growth of farmed fish</td>
</tr>
<tr>
<td>WO02094253</td>
<td>FUJI CHEM IND CO</td>
<td>Agents for relieving eye controlling function error</td>
</tr>
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<td>KR2000045197</td>
<td>PACIFIC CO LTD</td>
<td>Healthy nutrition composition containing Chitosan Oligosaccharide and Astaxanthin</td>
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<tr>
<td>WO02058683</td>
<td>LYCORED</td>
<td>Carotenoids as anti-hypertension agents</td>
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<td>NZ299641</td>
<td>SUNTORY AND ITANO</td>
<td>Use of Astaxanthin in pharmaceuticals for treating stress</td>
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<td>US6277417</td>
<td>TRIARCO</td>
<td>Method of inhibiting 5 Alpha-reductase with Astaxanthin</td>
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<td>US2003778304</td>
<td>ANDERSON AND PETTERSON</td>
<td>Method of inhibiting the expression of inflammatory Cytokines and Chemokines</td>
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<td>JP10276721</td>
<td>SUNTORY AND ITANO</td>
<td>Astaxanthin-containing food or drink</td>
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Algatechnologies produces its Astaxanthin from the microalgae Haematococcus pluvialis according to its patented biocontrolled growing process. The plant is located in the southern part of Israel, in the Arava Desert, near the resort city of Eilat, thus exploiting the unique environmental conditions.

The major parameters used to assess high-quality commercial Haematococcus biomass and oleoresins are high Astaxanthin content, the product, low levels of biological and chemical contamination, and excellent stability of the Astaxanthin in the product. Producing Astaxanthin in a closed system throughout the entire process (“Green” and “Red”) in an area with high solar-radiation intensity year-round, as in the case of Algatechnologies, yields high-quality commercial Haematococcus products (see Fig. 5). This algal biomass contains ~4% of its dry weight as Astaxanthin. The production of the algal biomass in flake form (as with Algatechnologies’ dry biomass), offers additional clear advantages when an extraction process is required for the production of high-quality oleoresin with ~10% Astaxanthin concentration.

Medical and nutraceutical applications of astaxanthin

Medical researchers have shown that Astaxanthin may have significant pharmaceutical applications. In-vivo pre-clinical studies and early-stage clinical trials have clearly indicated the possibility that Astaxanthin itself, or in conjunction with other components, behaves like a prophylactic and curing agent against various diseases and health conditions (see Tables 2 and 3).

Conclusions and Product Future

Numerous scientific papers indicate that natural Astaxanthin has great potential as a superb antioxidant with beneficial effects on various human diseases and physiological phenomena. The advanced commercial production of natural Astaxanthin from the microalgae Haematococcus pluvialis supplies the market with high-quality products rich in Astaxanthin, suitable for human applications. Further product development data will strengthen the scientific basis for the role of natural Astaxanthin as a unique and efficient anti-oxidant and for its use in human health.

The natural Astaxanthin market will become sophisticated and multi-product, and will include products for the food, food coloring, cosmetics and pharmaceutical industries as well.

Table 3: Selected articles on Astaxanthin applications for human and mammalian health

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reference</th>
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<tbody>
<tr>
<td>EYE HEALTH</td>
<td>6</td>
</tr>
<tr>
<td>JOINT HEALTH, MUSCLE ENDURANCE</td>
<td>6, 23 - 26</td>
</tr>
<tr>
<td>INFLAMMATION AND IMMUNE SYSTEM</td>
<td>27, 28</td>
</tr>
<tr>
<td>CARDIOVASCULAR, HEART, LIPID PEROXIDATION AND BLOOD FERTILITY</td>
<td>5, 29 - 46</td>
</tr>
<tr>
<td>CANCER</td>
<td>47 - 53</td>
</tr>
<tr>
<td>FERTILITY</td>
<td>49, 54 - 65</td>
</tr>
<tr>
<td>SUNBURN AND SKIN HEALTH, ANTI-AGING AND ANTI-WRINKLING</td>
<td>66, 67</td>
</tr>
<tr>
<td>BENIGN PROSTATIC HYPERPLASIA (BPH)</td>
<td>73</td>
</tr>
</tbody>
</table>

References

astaxanthin rich algal meal improves muscle endurance – a doubleblind study on male students. Unpublished study from the Kardinas Institute, Gustav-Adolfs-Street, Sweden.


Asteriou-Théry P. 216-22.


