Astaxanthin

Boosts muscle performance

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SUMMARY

Oxidative stress has harmful effects on muscle health causing muscle pain, weakness and fatigue. Astaxanthin is a strong antioxidant which by reducing oxidative stress will support muscle function. Results from human and model studies have shown that astaxanthin increases muscle endurance, lowers lactic acid and might prevent muscle atrophy in aging. The effects of astaxanthin on muscle are explained by its ability to protect membranes from oxidation and thereby enhance mitochondrial function and reduce inflammation and muscle damage.

INTRODUCTION

Oxidative stress: increased by aging and physical activity

An imbalance between reactive free radicals and antioxidant defense leads to an oxidative stress state. Physical activity generates more free radicals due to greater stress on muscle fibers and an increased metabolism (**1**). Up to 5% of the total oxygen consumed by mitochondria will end up as free radicals. Intensive training leads to higher oxygen consumption and therefore can increase the generation of free radicals up to 100 times. Although endogenous antioxidants are directly increased by strenuous exercise, their protection against oxidative stress is not adequate during later recovery (**2**). Furthermore, reduced levels of antioxidants have been suggested to be a factor in the process of muscle atrophy and a cause for why muscle mass is gradually lost with age, which weakens our body and makes us more prone to falls and injuries and to age-related illnesses exacerbated by inactivity (**3**).

Oxidative stress: negative effects on muscle

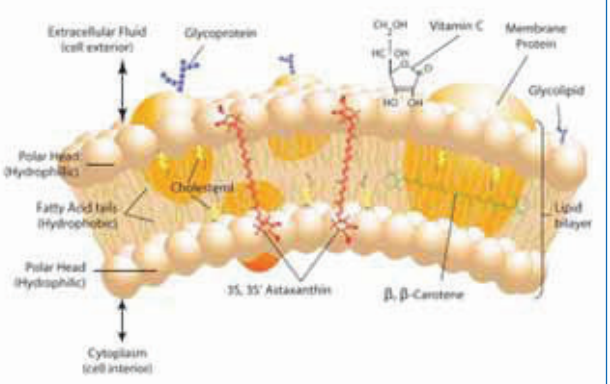
Oxidative stress damages proteins, lipids, DNA and alters the function of muscle cells (**1**). Increased oxidative stress triggers inflammation by activating pro-inflammatory cytokines which leads to muscle pain, stiffness and injuries. In addition, oxidative stress damages mitochondrial membranes, which reduces their capacity to generate energy. Mitochondria provide as much as 95% of the body´s energy, primarily by burning carbohydrates and fats. As a consequence of reduced mitochondrial function, the muscles will be supplied with less energy causing muscle fatigue; this is a major factor in muscle atrophy in aging (**1,3**). Moreover, oxidation of the red blood cell (RBC) membranes, followed by poorer motility and a reduced blood flow, might lower their ability to transport oxygen out to muscles. It has been demonstrated that physical activity increases oxidation of the RBC membranes (**4,5**). Oxidation of RBCs and impaired mitochondrial function might finally result in lowered aerobic capacity, which increases lactic acid and exhaustion. In addition, increased oxidative stress might alter muscle contraction and damage enzymes in the aerobic and anaerobic pathways resulting in declined muscle power and fatigue (**1**).

Astaxanthin as antioxidant

Several clinical studies have reported that astaxanthin from the alga *Haematoccus pluvialis* has benefits on muscle function and endurance. Astaxanthin is related chemically to other lipid antioxidants of the carotenoid family such as lutein, zeaxanthin, beta-carotene and lycopene. It is found typically in seafood such as salmon and crabs.

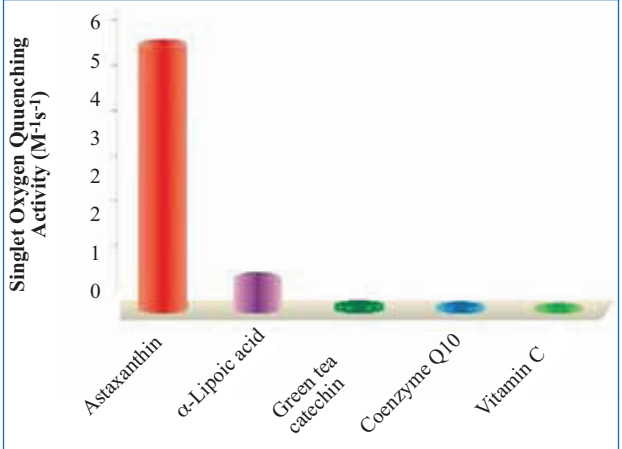
Astaxanthin is fat soluble and, as can be seen in *Figure 1*, its unique molecular structure enables it to stretch through the cell membrane in a way that no other antioxidant can (**6**). Nishida *et al* (**7**) found that astaxanthin had the greatest capacity to quench singlet oxygen as compared with several other antioxidants (***Fig 2***). In other *in vitro* systems, astaxanthin has shown antioxidant capacity up to 500 times higher than vitamin E and 10 times

Figure 1 *How astaxanthin, β-carotene and vitamin C are positioned in the phospholipid cell membrane*



The unique molecular structure of astaxanthin enables it to be positioned both inside and outside the cell membrane affording better protection to the membrane as compared to β-carotene or vitamin C. These can only be positioned, respectively, inside or outside the lipid bilayer. Figure taken from (**6**). Copyright Bioreal

Figure 2 *Capacity of different antioxidants to quench free radical singlet oxygen*



Quenching activities of common hydrophilic and lipophilic antioxidants against singlet oxygen was measured by chemiluminscence detection. Data taken from (**7**)

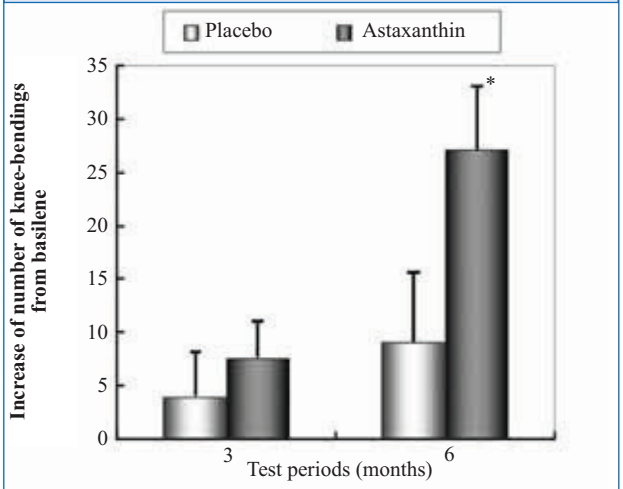
higher than β-carotene (**8**). Unlike many other antioxidants, astaxanthin has been classified as a pure antioxidant and does not show any pro-oxidative effects (**9**). Other antioxidants may show pro-oxidative effects under certain conditions, which increase oxidative stress and cause damage on cells.

STUDIES ON ASTAXANTHIN

Effect of astaxanthin on muscle endurance

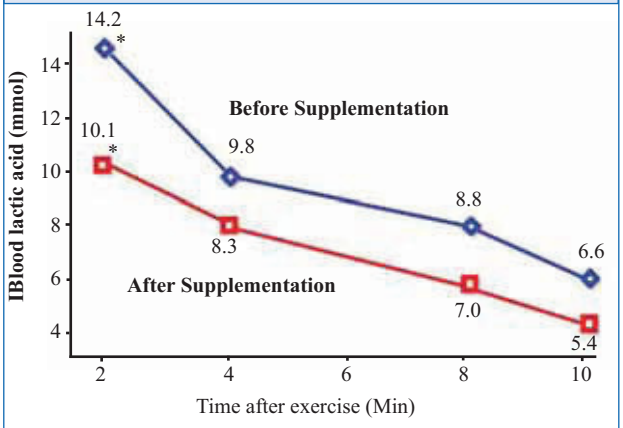
A randomized, double-blind study has shown that astaxanthin increases muscle endurance (**10**). Forty-two healthy men were supplemented with 4 mg astaxanthin/day for 6 months. Standardized exercise tests demonstrated that the average number of knee bends performed increased only in the astaxanthin treated group at three months, and by six months significant improvements were observed (***Fig 3***). In addition, Sawaki *et al* (**11**) demonstrated that a daily dose of 6 mg astaxanthin/day for 4 weeks resulted in lower levels of lactic acid during a 1,200 meter sprint (***Fig 4***).The formation of lactic acid is a result of insufficient oxygen to muscles and leads to fatigue; a lower level of lactic acid will, therefore, improve endurance.

Figure 3 *Effect of astaxanthin on muscle endurance in young men*



Increased number of knee bends in healthy young men receiving placebo or 4 mg of astaxanthin per day. Data are expressed as means ± SD;
*p<0.05, Student t-test. Data taken from (**10**)

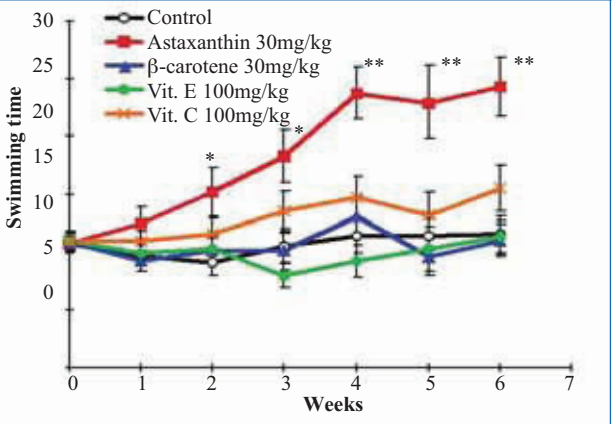
Figure 4 *Effect of astaxanthin on blood lactic acid in runners*



The amount of blood lactic acid after a 1,200m run before and 4 weeks after 4 mg/day of astaxanthin. Data are the means ± SD, *p<0.05, paired t-test.
Data taken from (**11**)

The effect of astaxanthin on muscle endurance is further supported by studies on mice. Ikeuchi *et al* (**12**) found that mice supplemented with astaxanthin for 5 weeks could swim for a significantly longer time to exhaustion as compared to placebo and other antioxidants (***Fig 5***). In the astaxanthin group, blood lactate concentration was significantly lower than the control group while at the same time muscle and liver glycogen were higher (data

Figure 5 *Effect of different antioxidants on swimming time to exhaustion in mice*

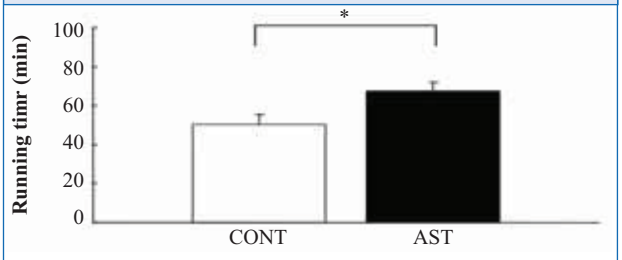


Mice were supplemented with different antioxidants and placebo for 6 weeks. Data are the means ± SD; *p<0.05; **p<0.01, ANOVA. Data taken from (**12**)

not shown). Another study by Aoi *et al* demonstrated similar results (**13**).

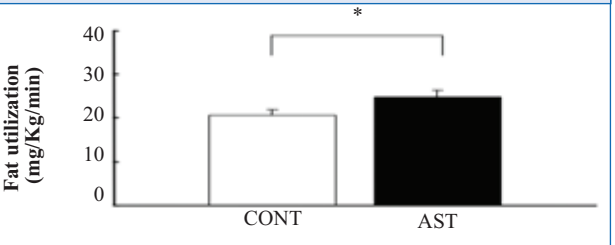
Running time to exhaustion for mice fed astaxanthin was significantly longer compared to control group as shown in *Figure 6*. Plasma lactate was significantly increased by exercise, an effect that was prevented by the addition of astaxanthin to the diet. Additionally, astaxanthin increased muscle glycogen and increased fat utilization (***Fig 7***).

Figure 6 *Effect of astaxanthin on treadmill running performance in mice*



The mice were treated with astaxanthin or placebo for 4 weeks. Both groups performed treadmill running at 30m/min and running time to exhaustion was measured. Values are the means ± SD (n=8); *p<0.05, Student t-test. Data taken from (**13**)

Figure 7 *Effect of astaxanthin on fat utilization in mice*



The effect of astaxanthin or placebo on fat utilization during exercise. Both groups performed treadmill running at 25m/min for 60 min after 4 weeks of supplementation. Fat utilization was calculated from the respiratory exchange ratio (RER) and oxygen consumption. Values are the means ± SD (n=8); *p<0.05, Student t-test. Data taken from (**13**)

A better fat utilization during exercise contributes to a reduced level of lactic acid. It has been shown that astaxanthin enhanced fat burning by protecting the mitochondrial membrane bound enzyme, carnitine palmitoyltransferase I (CPT I), which plays an important role in the entry of fatty acids into the mitochondria (**13**).

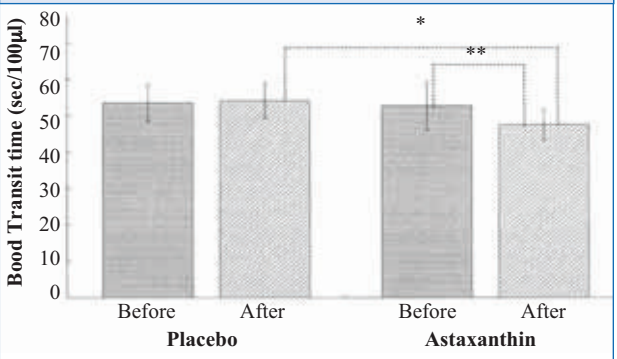
A randomized, double blind study on humans has confirmed that astaxanthin increases fat utilization during exercise (**14**). In that study, 32 subjects were supplemented with 2 x 6 mg astaxanthin/day, or placebo, for 6 weeks. The subjects were instructed to perform continuous exercise for a 40-min period 3 times per week during this 6-week period. After the 6 weeks, it was found that the astaxanthin group had a significantly reduced percentage of body fat while there were no difference in the placebo group These results indicated that astaxanthin increases muscle endurance and reduces lactic acid during intensive training by promoting the use of fat and sparing glycogen.

Effect of astaxanthin on aerobic power

Muscle cells are dependent on oxygen that is used by mitochondria to generate ATP and energy from carbohydrates and fats. If the muscle does not have a sufficient amount of oxygen, it will resort to anaerobic metabolism with increased lactic acid production and muscle fatigue.

Two studies showed that astaxanthin was able to improve oxygen transport by reducing the oxidation of RBCs thus enhancing blood flow. In the first study, a double blind, randomized study (**15**), twenty male subjects received 6 mg of astaxanthin or placebo for ten days. Blood samples were taken before and after the treatment period and the blood transit time were measured by channeling the blood through a micro channel array. The results showed that the group treated with astaxanthin had a transit time 10% significantly lower than the placebo group (***Fig 8***). The authors conclude that this effect was due to the ability of astaxanthin to protect blood cells from oxidation and thus improve blood rheology.

Figure 8 *Effect of astaxanthin on human blood flow*



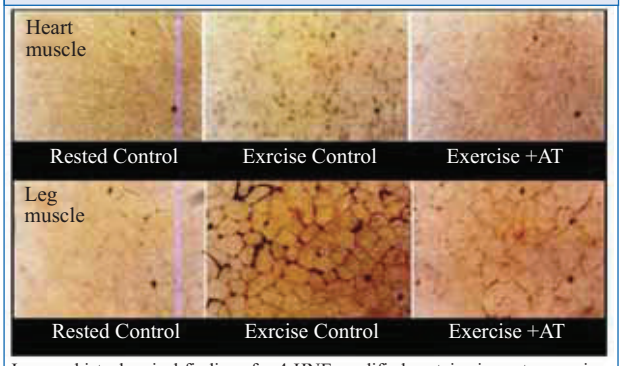
Twenty men received 6 mg/day of astaxanthin or placebo for ten days. Blood samples were taken before and after the treatment period and the blood transit time was measured by a micro channel array. Values are the means ± SD; *p<0.05; **p<0.01, paired t-test. Data taken from (**15**)

In a recent randomized, double blind study on humans (**16**), it was demonstrated that astaxanthin is taken up by the RBCs and reduces the oxidation of the RBC membrane. In this study, a total of thirty healthy subjects received 0 mg (placebo), 6 mg or 12 mg of astaxanthin per day for 12 weeks. The content of astaxanthin was increased both in plasma and in the RBCs among the subjects that were supplemented. Oxidation of the RBC membranes was significantly reduced by both doses of astaxanthin compared to placebo. These results indicate that astaxanthin can enhance the transportation of oxygen by reducing the oxidation of RBCs and thus improve blood flow.
In other studies, Wolf *et al*, (**17**) demonstrated that astaxanthin stimulates mitochondrial respiration by maintaining a higher membrane potential in mitochondria, thus increasing, oxygen consumption. The effect is enhanced mitochondrial function followed by a better energy supply to muscles. These results indicate that astaxanthin boosts aerobic power by increasing oxygen transport to muscles and enhancing the capacity of mitochondria.

Effect of astaxanthin on muscle oxidation and inflammation

Astaxanthin not only protects mitochondria and RBCs from oxidation, but it also protects heart and skeletal muscle cells from damage. In a study on mice (**18**), it was found that exercise increased oxidation and inflammation in heart and leg muscle while supplementation with astaxanthin contributed to significantly prevent the damage to both muscles (***Fig 9***).

Figure 9 *Effect of astaxanthin on exercise-induced gastrocnemius and cardiac muscle damage*



Immunohistochemical findings for 4-HNE-modified proteins in gastrocnemius and heart in mice after intensive exercise. Exercise increases muscle damage and destroys the cell membranes (shown in black). Supplementation of astaxanthin for 3 weeks reduces the muscle damage. Data taken from (**18**)

The anti-inflammatory effect of astaxanthin was further established in a randomized, double-blind, placebo controlled study on 42 subjects who were supplemented with 0 mg (placebo), 2 mg or 8 mg of astaxanthin for 8 weeks (**19**). The groups treated with astaxanthin showed significantly reduced DNA damage caused by oxidation and plasma C-reactive protein (data not shown). C-reactive protein increases in the blood as a result of inflammation. According to these results, astaxanthin may lower muscle pain, stiffness and fatigue by reducing inflammation and oxidation in muscles.
It is found in *in vitro* studies in mice that astaxanthin acts as an anti-inflammatory by inhibiting free radicals in the cell membrane that otherwise trigger NF-κB (20), a transcription factor that activates pro-inflammatory cytokines.

Effect of astaxanthin on risk of muscle atrophy

Since astaxanthin seems to be able to protect muscle cells from damage, it may be hypothesized that astaxanthin prevents muscle weakness (sarcopenia) in aging. In a study on mice, long-term dietary astaxanthin intake was found to prevent muscle atrophy by reducing oxidative stress and degenerative proteins (**21**). Mice were supplemented with astaxanthin or placebo for one year. After the treatment period, the weight of the soleus muscle was significantly higher for the astaxanthin group compared to placebo. The levels of degenerative proteins, e.g. cathepsin L and ubiquitinated myofibrillar protein, were also significantly lower compared to the placebo group. The results indicate that astaxanthin increases muscle mass by protecting muscle cells from damage. In addition, astaxanthin might prevent muscle atrophy by improving the function of mitochondria, since dysfunction is described as a major factor (**3,17**).

CONCLUSION

The interest of astaxanthin is growing among researchers and new findings about muscle health and endurance continue to appear. The results indicate that astaxanthin protects muscle cells and membranes from oxidative damage; in addition, it improves muscle endurance and lowers lactic acid mainly by improving fat utilization, mitochondrial function and reducing oxidation of RBCs. Studies further demonstrate that astaxanthin decreases inflammation which might reduce muscle pain and also shows potential for preventing muscle atrophy.

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