Antiox Version IV

Cutting-Edge Supplement with potent Antioxidant, Anti-inflammatory, Health Body Composition and Performance Effects

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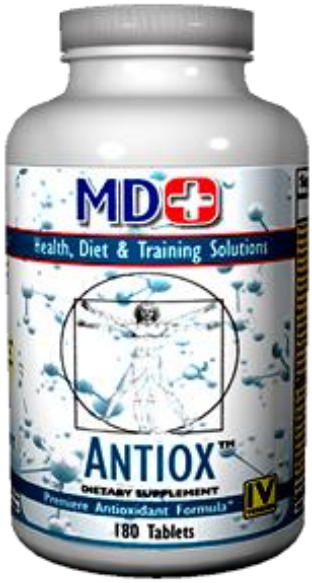

Antiox version IV is the most complete and most effective antioxidant formula available on the market today. It combines more than 60 potent natural antioxidants that effectively neutralize free radicals and improve health, immunity, body composition, strength, and physical and mental performance.

Antiox version IV - https://metabolicdiet.com/product/antiox/.

Formulated by Mauro Di Pasquale, B.Sc. (Hons), M.D.

The information below on the new Antiox version IV is in near final draft form and will be expanded and revised on a regular basis as more information is available both on an academic and in the treanches levels. For now, this latest information will give you the flavor of just what Antiox will do for you in helping you achieve your health, body composition and performance goals.

Introduction

Antioxidants form a front-line defense against cell damage caused by free radicals, which are involved in muscle, joint and tendon damage and inflammation, degenerative arthritis and even in the aging process. The use of antioxidants can reduce free radical damage that occurs when we exercise and can also attenuate the ongoing damage to injured tissues caused by free radicals, thus accelerating the healing process.

Antioxidants, such as vitamins C and E (see under Vitamins below), selenium, green tea, reduced glutathione and N-acetyl-cysteine (NAC) can play an important role in reducing inflammation and fatigue, decreasing tissue damage, and in both preventing and treating injuries.

Various antioxidants, such as vitamin E, have been found to be useful in the treatment of some forms of arthritis[1] and in dealing with the oxidative stress of exercise.[2] As well, oxidative damage has been shown to contribute to the pathogenesis of injuries and arthritis, and the use of antioxidants, such as NAC,[3] shown to have therapeutic value for reducing endothelial dysfunction, inflammation, fibrosis, invasion and cartilage erosion.

A study found that a combination of 2 antioxidants, selenomethionine and epigallocatechin-gallate (the main antioxidant in green tea extract), had beneficial effects on catabolic and anabolic gene expression of articular chondrocytes.[4] The authors of the study concluded that “Our data provide insights into the mechanisms whereby ECGg and selenium modulate chondrocyte metabolism. Despite their differential mechanisms of action, the 2 compounds may exert global beneficial effects on articular cartilage.”

Antiox version IV Nutrition Panel

Supplement Facts:

Serving Size: 6 Tablets
Servings Per Container: 30

	Amount Per Serving	% Daily Value
Vitamin A (Beta Carotene)	10,000 IU	200%
Vitamin C (Ascorbic Acid)	400 mg	667%
Vitamin E (dl-Alpha Tocopherol Acetate)	200 IU	667%
Vitamin B1 (Thiamin HCL)	10 mg	666%
Vitamin B2 (Riboflavin)	10 mg	588%
Niacinamide	25 mg	125%
Vitamin B6 (Pyridoxine HCL)	10 mg	500%
Folic Acid	400 mcg	100%
Vitamin B12 (Cyanocobalamin)	100 mcg	1667%
Biotin	1000 mcg	333%
d-Calcium Pantothenate	10 mg	100%
Calcium (Calcium Phosphate)	250 mg	25%
Magnesium (Citrate)	200 mg	50%
Zinc (Optizinc – Zinc monomethionine)	15 mg	100%
Selenium (Sodium Selenite and Selenomethionine)	50 mcg	70%
Copper (Gluconate)	200 mcg	10%
Manganese (Sulfate)	5 mg	250%
Bioperine (*Piper nigrum*) (fruit)	5 mg	*
L-Taurine	250 mg	*
L-Methionine	200 mg	*
Ginkgo Biloba Leaf Extract	200 mg	*
Grape Skin Extract	200 mg	*
Green Tea Extract (*Camellia sinensis*) (leaf)	200 mg	*
Creatine Monohydrate	200 mg	*
Eleuthero Root Extract	200 mg	*
Quercetin Dihydrate	120 mg	*
Milk Thistle Seed Extract	100 mg	*
N-Acetyl Cysteine	100 mg	*

	Amount Per Serving	% Daily Value
Alpha Lipoic Acid	100 mg	*
Turmeric Root Extract	100 mg	*
Panax Ginseng Root Extract	100 mg	*
Cranberry Juice Powder	100 mg	*
Rosemary Leaf Extract	100 mg	*
Superoxide Dismutase	62.5 mg	*
Ferulic Acid	60 mg	*
Cinnamon Bark Extract	60 mg	*
Schizandra Berry Extract	60 mg	*
L-Glutamine	60 mg	*
Pomegranate Fruit Extract	60 mg	*
Betaine HCL	50 mg	*
Grape Seed Extract	50 mg	*
L-Carnosine	50 mg	*
Rutin	50 mg	*
Bilberry Fruit Extract	40 mg	*
Hawthorn Berry Extract	30 mg	*
Ginger Root Powder	30 mg	*
Pine Bark Extract (*Pinus strobus*)	25 mg	*
Phosphatidylserine Complex	20 mg	*
Lutein	5 mg	*
Lycopene	5 mg	*

Antiox™ Proprietary Complex 816.5 mg

Citrus Bioflavanoids Complex, Garlic Bulb Powder (*Allium sativum*), Omega 3 Fish Oil Powder, L-Carnitine, Coenzyme Q10, Glutathione (Reduced) L-Cysteine HCL, Resveratrol, Astaxanthin, Zeaxanthin

Other Ingredients: Cellulose, Stearic Acid, Magnesium Stearate, Hypromellose, Modified Cellulose Gum, Silicon Dioxide

***Daily Value Not Established**

Antiox version IV

Antiox is so much more than just the usual antioxidant supplement. Because of the mix of ingredients, it also has other beneficial effects including decreasing inflammation, protecting muscle from microtears, apoptosis of muscle fibers, and damage from pro-oxidants stemming from oxidative phosphorylation and ATP formation, improving recovery, and helping to improve body composition and exercise/sports performance.

All you have to do is look at the nutritional supplement panel to see how truly unique Antiox is and how much it can do to prevent the counter-productive aspects of exercise while enhancing exercise's beneficial effects.

Antiox contains the several antioxidants, including vitamin C, beta-carotene, vitamin E, zinc, selenium, pycnogenol, resveratrol, astaxanthin, zeaxanthin, various amino acids and various herbs. However, it also contains many other antioxidants that give it a full rounded effect without an overemphasis on just a few isolated antioxidants and contains other ingredients that facilitate the formation of endogenous antioxidants as well as complement the antioxidant and health benefits of Antiox.

For example, various nutrients are necessary for priming the endogenous antioxidant systems including some minerals as copper, zinc and selenium (all present in Antiox) that contribute to the antioxidant defense system by acting as co-factors for antioxidant Cu-Zn superoxide dismutase and glutathione peroxidase activities.

A recent study emphasized the importance of selenium in maintaining endogenous antioxidant production. Selenium is important for the selenium-dependent endogenous antioxidant glutathione peroxidase (GPx). This selenium-dependent GPx reduces lipid hydroperoxides to their corresponding alcohols and water and so maintains intracellular redox status. [5]

Selenium is required as a cofactor for the synthesis of this enzyme, and data suggest that reduced blood selenium concentrations are associated with an increased cardiovascular incidence, certain cancers, and all-cause mortality.

Overall, Antiox contains over 60 nutrients that have antioxidant activity and/or increase endogenous antioxidant activity. As well, many of these ingredients have other properties that result in beneficial effects on health, energy metabolism, body composition and performance.

Having this large mix of antioxidants, as well as plant and herbal extracts, and supporting nutrients, makes Antiox not only more natural than other antioxidants on the market but also makes it more effective and bypasses the problems associated with using just a few antioxidants by themselves.

Studies have shown that a complex mixture of ingredients, including plant and herbal extracts, are synergistic in their effects on metabolism and their health and performance benefits. For example, a review paper published in 2017 concluded that herbal synergism often found in polyherbal formulations were found effective to combat disease heterogeneity as found in complex pathogenesis of Alzheimer's disease.[6]

As such, Antiox, with its individual antioxidants as well as full and partial plant extracts, and fruit complexes, provides the most complete full spectrum antioxidant effects one would expect from a combination of single antioxidants and natural extracts from herbs, plants, and fruits. In fact, I've made Antiox more like a super antioxidant and anti-inflammatory food rather than a nutritional

supplement since it contains so many ingredients, not just a mix of the most effective antioxidants but also many complex herbal, and plant extracts.

Antioxidants Enhance the Anabolic Effects of Exercise

Before I continue with information on oxidative stress and antioxidants, I want to make one thing clear - antioxidants as supplied by Antiox does not impair the anabolic effects of exercise.

Exercise damages skeletal muscle, with the extent of the damage depending on the intensity and duration of resistance, aerobic and sports specific exercise. The damage to muscle is caused by both mechanical and oxidative stress.

While some people feel that the use of antioxidant supplements are-counter-productive in that they decrease the exercise induced mechanical muscle injury and more importantly the subsequent inflammatory response, that leads to a response by the body to repair the damage and increase muscle hypertrophy, this is not the case.

Many studies have shown that the inflammatory response secondary to high mechanical muscle fiber stimulation after intense exercise mediates the initial steps involved in regeneration, healing, and muscle hyperplasia and hypertrophy.

However, studies have shown that antioxidants do not effect muscle fiber stimulation secondary to exercise, which leads to a beneficial effect on muscle mass and strength, **but can decrease excessive muscle fiber damage and oxidative stress, which are counter-productive and not needed for the hypertrophic and performance enhancing response to exercise**.[7],[8],[9] As such, it is unlikely that the use of antioxidants by athletes will impair the repair, hypertrophic, and performance enhancing response secondary to counter-productive muscle fiber damage and microtears in the musculoskeletal system that can lead to injuries and decrease the beneficial effects of exercise.

On the other hand, the use of antioxidants does affect some counter-productive processes that occur in the body secondary to intense and/or prolonged, exhaustive exercise, including fibrosis, mitochondrial damage, muscle fiber cell apoptosis, irreparable structural damage, and immune system dysfunction, which inhibit the ability of muscle to hypertrophy, and decrease both short and long term exercise performance.

Antiox has ingredients that reduce inflammation and severe muscle damage although productive muscle damage secondary to exercise is not unduly affected so that the secondary anabolic response is not diminished but in fact due to other ingredients is increased. In other words, Antiox decreases oxidative damage and inflammation without blocking the beneficial cellular adaptation to exercise.

More on this below under the Ergogenic Effects of Antioxidants.

In the next section, I'll cover some of the ingredients in Antiox and what they're all about. After that I'll go into details about oxidative stress, antioxidants and other information that you'll find useful in understanding oxidative stress and antioxidants.

Some of the Ingredients in Antiox version IV

There are a variety of antioxidants that are commercially available, including vitamins C and E, selenium, beta-carotene, glutathione, superoxide dismutase, gamma oryzanol, coenzyme Q10, cysteine, and histidine dipeptides (such as carnosine). Antiox contains over 60 ingredients with antioxidant and anti-inflammatory activity. We'll discuss some of these below.

Glutathione

Glutathione (gamma-glutamylcysteinylglycine) is one of the most effective endogenous and exogenous antioxidants. In both in rats and humans it has been found that exhaustive physical exercise causes a change in glutathione redox status in blood and that antioxidant administration, i.e., oral vitamin C, N-acetyl-L-cysteine, or glutathione, is effective in preventing oxidation of the blood glutathione pool after physical exercise in rats[10].

In one study, the changes of glutathione status, oxidative injury, and antioxidant enzyme systems after an exhaustive bout of treadmill running and/or hydroperoxide injection in male rats were studied[11]. In this study, concentrations of total and reduced glutathione in muscle were significantly increased after exhaustive exercise. Concentrations of glutathione-related amino acids glutamate, cysteine, and aspartate were also significantly increased. As well, endogenous antioxidant enzymes such as glutathione peroxidase, glutathione reductase, superoxide dismutase, and catalase activities were significantly elevated in muscle after exhaustive exercise. Overall, this study shows that exhaustive exercise can impose a severe oxidative stress on skeletal muscle and that glutathione systems and antioxidant enzymes are important in coping with free radical-mediated muscle injury.

Glutathione, a potent endogenous antioxidant that protects major organs from oxidant injury, may not be present in adequate amounts during intense exercise. Since glutathione reserves may be increased with supplements, nutrition strategies that include the provision of GSH monoester may lend additional support to musculoskeletal and other tissues that are at risk for injury from oxygen free radicals during catabolic states[12].

N-Acetylcysteine

N-acetyl-L-cysteine (or NAC) is the N-acetyl derivative of L-cysteine (a non-essential amino acid) and a reduced thiol donor. As with other amino acids, only L-isomers are biologically active. While Antiox also contains smaller amounts of cysteine, NAC is thus the preferred form for oral use for systemic effects while cysteine is more useful for use by the gastrointestinal tract.[13]

Cysteine serves as a component of coenzyme A which is involved in carbohydrate and fat metabolism. Cysteine is also a precursor of taurine. Numerous studies have shown the clinical use of NAC supplements in chronic[14] but apparently not acute[15] pulmonary problems. NAC is marketed in European and other countries for use in chronic pulmonary diseases.

NAC has been shown to have hepatoprotectant effects against various liver toxic compounds such as alcohol, acetaminophen, carbon tetrachloride, and drugs used in cancer chemotherapy.[16] Much of the protective effects are due to NAC's antioxidant properties and its ability to increase cellular levels of glutathione.

As well, NAC and other reducing agents have been shown to be useful for the treatment of AIDS and the wasting seen in AIDS patients since they have been shown to decrease viral replication and to inhibit the action of inflammatory cytokines.[17,18]

Aside from protein synthesis, cysteine/NAC is an essential component of glutathione (L-gamma-glutamyl-L-cysteinylglycine - one of the main cellular antioxidants). NAC and cysteine also act as potent antioxidants both by themselves[19] or in concert with glutathione and other antioxidants.[20]

NAC, because of its potent antioxidant properties, may prove useful in decreasing the oxidative stress seen with exercise.[21] Human studies performed by Dr. Lester Packer of the University of California at Berkeley, and presented at the 1996 American College of Nutrition meeting in San Francisco found that supplementation with NAC improved exercise performance times and reduced oxidative stress by preserving glutathione levels during exercise.

Since oxidative stress is considered a causal factor in human muscle fatigue and overtraining,[22] this finding is extremely important because it provides evidence of positive effects of amino acid supplementation on human exercise performance and recovery. If this response were to continue for an adequate time period, then enhanced results from resistance training (faster increase in muscle mass and strength) could be expected.

Studies in the last decade have shown that the most promising thiol donors are L-cysteine, NAC, glutathione and alpha lipoic acid, have significant effects on exercise performance.[23,24,25,26,27,28,29,30]

Of these the prototypical compound in this category is N-acetylcysteine (NAC), a reduced thiol donor with antioxidant properties, which has effects both directly and indirectly by inhibiting glutathione oxidation and supporting reduced glutathione synthesis and resynthesis.

NAC infusion in well trained individuals increased each of muscle NAC, total and reduced glutathione, cysteine and cystine, and substantially enhanced performance during prolonged exercise.[31] Oral use of NAC has recently been demonstrated to enhanced handgrip performance.[32]

A recent study looked at the possible interaction between ROS and Na^+,K^+-pump activity in skeletal muscle, and a possible role in fatigue during exercise.[33] The results showed that the antioxidant NAC attenuates muscle fatigue, in part via improved K^+ regulation and attenuating the decline in Na+,K+ pump activity, and point to a role for ROS in muscle fatigue.

In fact the effects of NAC on fatigue was examined in a paper in which the author felt that taking NAC may constitute doping. ****

Selenium

Selenium is an essential trace element that provides antioxidant protection in concert with vitamin E (both in Antiox). Several selenoproteins have been identified, but only one, glutathione peroxidase (SeGSHpx), a selenoenzyme, has a known function, that of neutralizing toxic lipid hydroperoxides[34]. Selenium, however has several metabolic effects not associated with glutathione peroxidase[35].

Many of the nutrients have multiple actions in the body. For example, selenium also has significant anti-inflammatory properties and involved in thyroid health and function.[36,37]

Vitamin C

Vitamin C is essential to proper collagen synthesis, and this is evident in the vitamin C deficiency disease scurvy, in which the collagen fibers synthesized in the body cannot form fibers properly, resulting in lesions, blood vessel fragility and poor wound healing.

Vitamin C has been shown to have some anticatabolic effects that likely involves decreasing exercise induced cortisol but may also have some effects through its antioxidant action. Conversely, some of the anticatabolic effects of antioxidants may be mediated through a decrease in cortisol.

Antioxidants may be of some use in training induced muscle ischemia and injury. Research shows that exercise can adversely affect muscle tissue by increasing the formation of free radicals. These free radicals can then lead to muscle fatigue, inflammation and muscular damage.[38] During normal conditions free radicals are generated at a low rate and neutralized by antioxidant enzymes in the liver and skeletal muscle and other systems. Unfortunately, the increase in free radicals caused by exercise accompanies a simultaneous decrease in the supply of antioxidants to handle them. Vitamin E, for instance, can be severely decreased by training thus depleting muscle of its major antioxidant force.[39]

A study examined the potential protective effect of pretreatment with corticosteroids or antioxidants (ascorbic acid or allopurinol) in rabbits with reperfusion-induced damage to skeletal muscle after ischemia.[40] In this study 4 hours of limb ischemia induced by a pneumatic tourniquet, followed by reperfusion for 1 hour, caused a considerable amount of ultrastructural damage to the anterior tibialis muscles accompanied by a rise in circulating creatine kinase activity. Pretreatment of animals with depomedrone by a single 8 mg bolus injection led to a preservation of the anterior tibialis structure on both light and electron microscopy. High-dose continuous intravenous infusion with ascorbic acid (80 mg/hr) throughout the period of ischemia and reperfusion also preserved skeletal muscle structure, although allopurinol in various doses had no protective effect.

These data are fully compatible with a mechanism of ischemia/reperfusion-induced injury to skeletal muscle, involving generation of oxygen radicals and neutrophil sequestration and activation. They also indicate that damage to human skeletal muscle caused by prolonged use of a tourniquet is likely to be reduced by simple pharmacological interventions.

Vitamin C is necessary for collagen synthesis and is a strong antioxidant with beneficial effects on pro-inflammatory cytokines.[41] Research on vitamin C shows that it may have important effects in reducing pain and inflammation secondary to exercise. In one study 400 mg daily of vitamin C reduced post exercise pain and inflammation.[42] Vitamin C is involved in the enzymatic hydroxylation of proline to form 4-hydroxyproline, an amino acid that is an integral part of collagen and elastin.

Vitamin E

One of the most effective and central antioxidants is alpha-tocopherol (vitamin E). It appears to have an important role as both a primary antioxidant and as a compound that enhances the effect of both endogenous and exogenous antioxidants.

Vitamin E, a lipophilic chain-breaking antioxidant which inhibits lipid peroxidation in isolated mitochondrial membranes and protects membranes from oxidative damage, performs an antioxidant role in biological membranes by acting as a one-electron reductant[43]. The primary oxidation product of vitamin E is the tocopheroxyl radical. Reduction of the tocopheroxyl radical can occur by reactions

with water-soluble anti-oxidants such as ascorbate or glutathione, resulting in the recycling of vitamin E[44].

It has been shown that free radical-mediated lipid peroxidation and glutathione depletion may be involved in the toxic manifestations of various compounds[45]. It has also been shown that vitamin E may largely modulate the expression of toxicity by glutathione depleting agents. Experiments carried out with vitamin E deficient or supplemented diets indicate that the pathological phenomena occurring as a consequence of glutathione depletion depend on hepatic levels of vitamin E[46].

According to one study, deficiency in vitamin E may be related to arterial lesions[47]. Vitamin E can mitigate some of the adverse effects of fat in diets. The lipid peroxidation caused in the liver, heart and intestine by a diet containing autoxidized oil was suppressed when the same tocopherol level as fresh soybean oil was added to the diet[48]. Uptake of oxidatively modified low-density lipoprotein (LDL) by cells in the arterial wall is believed to be an important early event in the development of atherosclerosis.

This lipid peroxidation mechanism, which can readily be rationalized by the known chemistry of the alpha -tocopheroxyl radical and by the radical isolating properties of fine emulsions such as LDL, explains how reagents which reduce the alpha -tocopheroxyl radical (i.e. vitamin C and ubiquinol-10) strongly inhibit lipid peroxidation in vitamin E-containing LDL[49].

Level of plasma tocopherol (vitamin E) which has free radical scavenging properties rises significantly during intensive exercise[50]. Mobilization of tocopherol could help to prevent lipoperoxidation phenomena occurring in exercising skeletal muscle. A combination of vitamin E and coenzyme Q10 (both in Antiox) was found to attenuate exercise induced lipid peroxidation and muscular damage.[51]

Green Tea Extract

The constituents of green tea are polyphenolic compounds termed catechins. The most abundant catechin in green tea is (–)-epigallocatechin 3-gallate (EGCG) although others are also present in lesser quantities.

Green tea extract, besides being rich in antioxidants, also has significant effects on inflammation and the musculoskeletal system.[52],[53],[54] For example green tea catechins have been shown to inhibit inflammation and cartilage degradation, and have therapeutic effects on a variety of musculoskeletal problems including arthritis.[55],[56],[57],[58],[59],

Green tea extract may well prove to be more useful than green tea itself. A recent study found that green tea extract supplements retain the beneficial effects of green and black tea and allow larger doses of tea polyphenols to be used without the side effects of caffeine associated with green and black tea beverages.[60]

Rutin and Quercetin

These two flavonoids have been shown in studies to have significant anti-inflammatory activity in cases of both acute and chronic inflammation.[61] A review article concluded that there is evidence to suggest that flavonoids may be beneficial to connective tissue for several reasons, which include the limiting of inflammation and associated tissue degradation, the improvement of local circulation, as

well as the promoting of a strong collagen matrix. [62] These compounds also have significant antioxidant properties.

Quercetin may have properties that downregulate or inhibit cyclooxygenase-2 safely.[63] As well, studies have shown that quercetin has beneficial effects on exercise, especially on exercise induced muscle damage.[64][65] A recent study found that **"Fourteen days of Q supplementation seems able to attenuate the severity of muscle weakness caused by eccentric-induced myofibrillar disruption and sarcolemmal action potential propagation impairment."[66]**

Turmeric

Curcumin, the active component of turmeric, is documented to have anti-inflammatory and antioxidative benefits.[67] As an antioxidant, curcumin reduces the activity of certain enzymes, inhibiting all branches of the arachidonic acid cascade. Thereby, these plant extracts reduce inflammation.

Turmeric exhibits marked anti-inflammatory action and has been shown to be as effective as some anti-inflammatory drugs. For example, in a double-blinded trial, post-surgical patients receiving curcumin experienced reductions in stiffness and joint swelling comparable to the effects of phenylbutazone, a potent anti-inflammatory drug.[68]

Of all the spices and herbal preparations it seems that only the spice turmeric has any anti-inflammatory effects. This was the conclusion of a study of a variety of Ayurvedic and herbal preparations, which was presented recently at the 9th Asia Pacific League of Associations for Rheumatology Congress.

In this study, a variety of herbal and Ayurvedic preparations were tested in rats. The rats were fed oral doses of the varied herbal and Ayurvedic recipes. Only turmeric showed anti-inflammatory effects when tested on irritated paws of the rats.

Several studies have shown the effectiveness of curcumin, especially when coupled with piperine which increases absorption of curcumin (both are in Antiox) on exercise induced muscle damage and soreness, and recovery as well as on improving body composition and exercise performance. [69][70][71][72][73][74][75] In one study the combination of curcumin and piperine resulted in an improvement of in sprint mean power output 24 hours post-exercise.[76]

As well, other studies have shown the value of curcumin in the prevention and treatment of neurological dysfunction such as Alzheimer's disease and other neurological diseases.[77][78]

Resveratrol

Resveratrol is a potent anti-oxidant with significant anti-aromatase activity.[79][80] Researchers have shown that resveratrol may have significant anti-aging effect and extend lifespan and healthspan.[81]

As well, resveratrol has been shown to decrease fatigue. enhances body composition and both physical and mental performance, and improves testicular function.[82][83][84][85][86][87][88][89][90][91][92]

Studies have also shown that resveratrol, and the B vitamins in Antiox, can counteract some of the detrimental effects of environmental pollution especially first, second, and third hand cigarette smoke and air pollution. [93][94][95]

Both the ingredient resveratrol and grape seed extract that contains resveratrol and many other beneficial ingredients, are in Antiox.

Carnosine

Carnosine, a dipeptide made up of the amino acids alanine and histidine (histidyl-alanine or beta-alanyl-l-histidine) was added to Antiox because of its many beneficial effects. It has been shown to have significant antioxidant, anti-inflammatory, anti-ischemic properties, increases healing, enhances the immune system, improves skeletal muscle function, and provides health and anti-aging effects.[96,97,98,99,100,101,102,103,104,105,106,,107,108,109,110,111]

It also inhibits glycation, a destructive protein/sugar reaction that occurs in the body and which contributes to aging through a number of mechanisms including the breakdown of connective tissue, a loss of elasticity, and a decrease in cellular hydration. Carnosine, along with alpha lipoic acid, provides protection against glycation and premature aging.

Carnosine also works well with other ingredients in Antiox. For example carnosine, chromium and cinnamon and polyphenols, all in Antiox, have shown beneficial effects on body composition and insulin sensitivity.[112113]

Coenzyme Q10 (ubiquinone-10)

Coenzyme Q10 acts as an electron carrier of the respiratory chain in mitochondria. Under the various forms of stress and inflammation, demand for coenzyme Q10 increases which must be met by dietary intake in order to optimize mitochondrial function.

As well, it has been shown that the reduced form of coenzyme Q10 is an important physiological lipid-soluble antioxidant that scavenges free radicals generated chemically within liposomal membranes.[114,115] It has also been shown that it reduces oxidative stress associated with strenuous exercise in rats, healthy adults and young athletes.[116117118119] As noted above, vitamin E and ubiquinone increase physical working capacity of experimental animals.[120]

Generation of free radicals and subsequent lipid peroxidation have been proposed to contribute to delayed tissue damage. One study has found that ascorbate and ubiquinol levels were decreased after trauma.[121] In this study, changes in tissue levels of ubiquinol, but not ascorbate reflected the degree of trauma. The authors suggest that ubiquinol levels may provide a useful marker of the oxidative component of the secondary injury response.

Beta carotene

Beta carotene is the most popularly known carotenoid, although over 600 carotenoids from natural sources that have been characterized. Of these less than 60 can be converted to vitamin A. Many dietary carotenoids, both with and without provitamin A activity, are found in the blood and tissues of humans. Carotenoids, however, have biological actions apart from their function as precursors of vitamin A.

Studies have shown that particular carotenoids enhance the immune system, inhibit mutagenesis, reduce nuclear damage, protect against photo-induced tissue damage, and quench highly reactive singlet oxygen under certain conditions and can block free radical-mediated reactions[122].

Although Beta-Carotene is only one of the nutritionally active carotenoid (making up 15-30% of total serum carotenoids) it is often the only carotenoid considered in antioxidant regimens. Using only synthetic beta carotene without any of the associated carotenoids, although theoretically beneficial may show some adverse effects. For example, in epidemiological studies, the intake of carotenoids from natural sources such as certain fruits and vegetables has been associated with a decreased incidence of certain cancers especially lung cancer.

The main problem with epidemiological associations is that because they do not show cause and effect, it is difficult to properly interpret the data and draw proper conclusions. For example while one study shows that dietary beta carotene and vitamin E supplements reduce the risk of lung cancer in nonsmoking men and women[123], another study shows that the use of beta carotene in smokers may actually increase the incidence of lung cancer.

The synthetic all-trans isomer of beta carotene was recently shown to possess antioxidant properties towards the formation of oxidized low density lipoprotein. The all-trans isomer of beta -carotene is more effective in inhibiting the susceptibility of lipoproteins to lipid peroxidation and in reducing the cellular uptake of oxidized LDL by macrophages[124].

Taurine

Taurine, a sulfur-containing amino acid and the second most abundant amino acid, and the most abundant free amino acid, found in skeletal muscle tissue, has many properties that can enhance the training effect, including its abilities to increase growth hormone, protect joints, and protect the liver, as well as its antioxidant and anabolic effects. Taurine has also been shown to have insulin like effects and to help control cell volume. The volumizing effect on muscle cells is felt to lead to an increase in protein synthesis.

Over the years oral taurine administration has been shown to help muscle cramping in patients with liver cirrhosis and myotonic dystrophy. Several studies have suggested that it may also help to alleviate muscle cramps occurring during and after exercise. But there’s more to the story.

One study on rats has shown that oral taurine supplementation may increase muscle performance and reduce muscle injury caused by exercise.[125] The aim of the study was to determine if increasing muscle levels of taurine would decrease free radical damage after exercise-induced injury. The authors found that first of all taurine levels rose in muscle after supplementation, and secondly that running performance was improved by the taurine supplementation. Thus it appears taurine supplementation may facilitate exercise performance and reduce some of the counterproductive muscle injury caused by exercise.

Another study also in rats showed that taurine is useful for reducing physical fatigue and muscle damage during exercise training, presumably due to its antioxidant effects and the beneficial effects that taurine has on metabolism and on muscle and cardiac functions.[126]

And yet another study found that taurine may attenuate exercise-induced DNA damage and enhance the capacity of exercise due to its cellular protective properties.[127] Taurine, along with carnosine has also shown protective effects on testicular injury.[128]

And as if that weren't enough, there is some evidence to show that taurine may enhance training further by decreasing training induced fatigue. One paper has shown that Na+-K+-ATPase activity is depressed with fatigue, regardless of training state, suggesting that this may be an important determinant of fatigue.[129] Another paper associated fatigue and training with reduced Ca2+-ATPase activity.[130] Previous studies have shown that taurine stimulates Na+-K+-ATPase activity and also the pumping rate of the Ca2+-activated ATPase pump.

While the evidence is circumstantial at present and a direct study linking the two research findings needs to be done, it's quite possible that supplemental taurine, besides all the positive effects we know it has, may also reduce exercise induced fatigue.

On a preventative level, taurine administration has been shown to increase taurine concentrations in skeletal muscles, reduce the decrease in taurine concentration in skeletal muscles on exercise, and up-regulates physical endurance.[131]

For more information on taurine have a look at my updated 2019 article at https://metabolicdiet.com/wp-content/uploads/2017/product_pdf/Taurine.pdf.

Alpha Lipoic Acid

Alpha lipoic acid (ALA) has potent antioxidant properties intrinsically and secondary to its ability to increase levels of intra-cellular glutathione, and its ability to recycle other antioxidants such as vitamin C, vitamin E and glutathione.[132,133,134,135,136] ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.[137]

Alpha lipoic acid also has significant anti-inflammatory properties and has been shown to inhibit IL-1, a proinflammatory cytokine and also inhibit the synthesis of PGE2 by inhibiting COX-2 activity.[138]

This latter mode of action, along with similar effects from CLA, simulates the anti-inflammatory effects of the present class of NSAIDS such as Celebrex, Advil, Aleve, etc. As well, Antiox contains fish oil containing DHA and EPA, which has also been shown to have effects similar to the anti-inflammatory prescription and OTC drugs.[139]

ALA has other beneficial effects, such as decreasing both the pro-inflammatory cytokines, decreasing secondary cortisol elevations, and improving the lipid profile and cardiovascular risk factors.[140141142143]

It has been shown to inhibit cross-linking among proteins, a process that contributes to the aging process in the body and especially in collagen-heavy tissues such as skin. Alpha-lipoic acid activates a collagen-regulating factor known as AP-1 that turns on enzymes that digest glycation-damaged collagen and thus make the skin more supple and youthful looking.

Besides having potent antioxidant and anti-inflammatory effects, ALA also has significant anabolic and body composition effects secondary to its beneficial effects on insulin sensitivity and growth hormone and IGF-I secretion, all factors involved in maintaining, repairing and regenerating musculoskeletal tissues.[144,145,146,147148]

ALA is also useful in reversing mitochondrial dysfunction, especially in aging mitochondria.[149],[150]

Zinc

Exercise can lead to an increased need for certain nutrients. For example, one study found that there is an increase in selenium requirements with exercise.[151] Problems can arise from exercise induced mineral loss, which is further enhanced by the finding that many of us don't consume adequate amounts of many essential minerals.

Studies have shown that many athletes, and female athletes, in particular, consume diets that have been found to be inadequate for certain key minerals such as zinc, magnesium, copper, and iron. The combination of strenuous exercise and compromised mineral status ultimately leads to low endurance capacity, depressed immune function, and the development of a variety of disease conditions.

One study looked at the effects of zinc deficiency on physical performance and found that low dietary zinc was associated with impaired cardiorespiratory function and impaired metabolic responses during exercise.[152]

Zinc deficiency in humans is widespread[153] and athletes may be particularly prone to lower plasma zinc levels.[154] Zinc is a constituent of more than a hundred fundamentally important enzymes, so zinc deficiency has many negative effects on almost every body function.[155] As well, zinc deficiency can adversely affect the reproductive hormones and as such impair athletic efforts.[156]

Zinc deficiency adversely affects protein synthesis. In one study the effects of zinc deficiency in rats, on the levels of free amino acid in urine, plasma and skin extract were investigated.[157] Zinc deficiency adversely affected skin protein synthesis. Especially where a deficiency may be present, supplemental zinc has resulted in an increase the secretion of growth hormone and IGF-I,[158] and testosterone[159] and to raise plasma testosterone and sperm count.[160,161]

A study looking at the effects of zinc supplementation on wrestlers found that the results obtained at the end of the study indicate that zinc supplementation (as well as several other ingredients in Antiox including NAC and ALA) prevents production of free radicals by **activating the endogenous antioxidant system**.[162] This activation is important as it coincides with the effects of exercise, which also activates the endogenous antioxidant system and leads to endogenous antioxidants that enhance the beneficial effects of exercise on body composition and performance. The authors concluded that "physiologic doses of zinc supplementation to athletes may beneficially contribute to their health and performance."

It's been shown that there is an improvement in insulin resistance with **zinc** supplementation and that zinc is involved in controlling some of the aspects of obesity.[163] Zinc also improves calcium metabolism and thus the beneficial effects that calcium has on fat metabolism.

Magnesium

Magnesium, besides complementing the effects of calcium on obesity[164] and other functions, also has important effects on its own. Magnesium is involved in numerous processes that affect muscle function including oxygen uptake, energy production and electrolyte balance. Low levels of magnesium promote inflammation[165166] and impact on the body's ability to handle stress.[167] These functions are useful in alleviating the release of pro-inflammatory cytokines, and decreasing both insulin resistance and inappropriate cortisol secretion.

There is evidence that marginal magnesium deficiency impairs exercise performance and increases oxidative stress. As well, strenuous exercise increases urinary and sweat losses that may increase magnesium requirements.[168]

Recent surveys have shown that a significant number of individuals are magnesium deficient based on their intake. Athletes in sports with weight classes are especially vulnerable to magnesium deficiency due to their weight loss practices. As such, in these athletes, and others who are magnesium deficient or whose levels are marginal, magnesium supplementation would have beneficial effects on exercise performance.

A recent study found that magnesium supplementation improved alactic anaerobic metabolism, even though the athletes were not magnesium-deficient.[169] Another study found that magnesium supplementation increased strength performance.[170] As well, magnesium may prove effective for muscle cramps.[171]

Magnesium has been shown to influence testosterone levels as well as the anabolic peptide IGF-1.[172][173] As well, magnesium has been shown to work along with zinc and B6 (both of which are present in Antiox) to produce a significant anabolic effect.[174]

Other Antioxidants

Many other compounds, some touted as ergogenic aids, have shown significant antioxidant properties.

Gamma oryzanol, another compound widely used by athletes, while not having any significant anabolic effects, does have some antioxidant activity[175].

Cysteine (decreases cross linkage of proteins), **taurine**[176] (may have a protective effect in joints by decreasing the degradation of hyaluronic acid), histidine dipeptides[177], pantothenic acid, copper, zinc, selenium.

Cinnamon has been shown to have significant antioxidant, anti-inflammatory, and anti-obesity effects. A recent study found that the use of cinnamon results in fewer molecules involved in the body's fat-storing process and more antioxidant and anti-inflammatory molecules that protect the body from the damages of stress.[178]

Antioxidant Interactions

Many antioxidant compounds act in concert with both other exogenous compounds and with endogenous antioxidants. For example ubiquinol-10 spares alpha-tocopherol when both antioxidants are present in the same liposomal membranes and that ubiquinol-10, like alpha-tocopherol, does not interact with reduced glutathione[179].

Generation of free radicals and subsequent lipid peroxidation have been proposed to contribute to delayed tissue damage. One study has found that ascorbate and ubiquinol levels were decreased after trauma[180]. In this study, changes in tissue levels of ubiquinol, but not ascorbate reflected the degree of trauma. The authors suggest that ubiquinol levels may provide a useful marker of the oxidative component of the secondary injury response.

In some cases antioxidants act synergistically. For example water based antioxidants such as Vit C can act in concert with lipophilic antioxidants such as Vit E. In one study Vit E and Vit C acted synergistically to inhibit the oxidation of human low density lipoprotein (LDL)[181]. In another study, the combination of vitamins E and C produced a protective effect on parinaric acid peroxidation exceeding the sum of their individual contributions[182].

Many antioxidants have a vitamin E-sparing action. The water-soluble antioxidant vitamin C can reduce tocopheroxyl radicals directly or indirectly and thus support the antioxidant activity of vitamin E[183,184]. In one study, vitamin C and other compounds (including ascorbyl palmitate, propyl gallate, butylated hydroxytoluene, hydroquinone and glutathione) blocked the oxidation of platelet tocopherol. In this same study, it was shown that the use of exogenous natural and/or synthetic antioxidants can prevent the oxidation of endogenous antioxidants[185].

Oxidative Stress

Oxidative stress occurs when the generation of reactive oxygen species (ROS) in a system exceeds the system's ability to neutralize and eliminate them. This condition can arise from a lack of antioxidant capacity and/or an excessive production of ROS.

The end result is an excess of ROS that in turn can damage cellular lipids, proteins and DNA, and causing problems with cellular function. As such, oxidative stress may contribute to a number of diseases and in the aging process.[186]

Free Radicals and Tissue Damage

In the past few decades there has been an intense amount of investigation on the role of free radicals in disease and aging, and on the role of antioxidants on attenuating the damaging effects of free radicals.

Free radicals are highly reactive molecules with unpaired electrons. These radicals play an important part in many physiological processes, including the metabolism of food and the utilization of energy substrates during exercise. These free radicals arise from endogenous metabolic processes and increase with physical (such as exercise) and emotional stress. Free radicals can also arise in the body as a result of exposure to environmental pollutants[187188189].

The most common free radicals are the superoxide anion and the free radicals derived from its interaction with other molecules. Superoxide radicals are generated from cellular respiratory-chain oxygen use and by a number of other enzyme systems.[190191] It has been proposed that the superoxide radical (along with its derivatives, such as singlet oxygen and the hydroperoxyl, hydroxyl, and alkoxyl radicals) and other free radicals initiate the peroxidation of membrane lipids, which results in cellular damage[192].

Also it is felt that the peroxidation of low-density lipoproteins (LDL) and their subsequent cytotoxicity is involved in atherogenesis. One study has shown that there may be a synergistic effect of HDL and antioxidant molecules (such as vitamin E and catechin) for the protection of cells against oxidized LDL, and for the preventative modification of LDL[193]. As well, there is evidence to show that over time there is substantial oxidant-induced DNA damage[194].

In reaction to free-radical reactions and lipid peroxidation that occur in living cells, highly efficient enzymatic and nonenzymatic systems for scavenging free radicals have evolved. The antioxidant

enzymatic system consists largely of superoxide dismutase (SOD), catalase, and glutathione peroxidase, which detoxify, respectively, the superoxide radical, hydrogen peroxide, and lipid hydroperoxides.[195][196] In addition to these enzymes, various free-radical scavengers are present, such as the micronutrient selenium, which is a component of glutathione peroxidase, ubiquinols (reduced coenzyme Q), ascorbate (vitamin C), and alpha-tocopherol (vitamin E), cysteine, glutathione, and possibly uric acid.[197][198]

It has been postulated that free radicals that are produced during normal metabolism react with cellular components, leading to molecular damage and eventually to the death of vital cells and the aging and death of the organism[199]. For example, the free radical theory of aging[200] states that endogenous free radical reactions cause or contribute significantly to: cancer, atherosclerosis, hypertension, Alzheimer's disease, amyloidosis, immune deficiency, arthritis, diabetes and Parkinson's Disease, among others. Proponents of this free-radical theory have advocated the use of various antioxidants in the diet to interrupt free-radical chain reactions and thus prevent or attenuate cellular damage and aging.[201]

Antioxidants

Antioxidants are compounds that prevent or limit the formation of ROS and their effects on biological structures. Antioxidant defense involves multiple strategies, enzymatic or non-enzymatic.

Antioxidants function to prevent or minimize peroxidative damage in biological systems. Studies have suggested that adequate antioxidant defense can protect the body from the high free radical concentrations that are unavoidable at the present time[202].

Non-enzymatic compounds include tocopherols, carotenes, ascorbate, glutathione, ubiquinols, and flavonoids. As well, there are the micronutrient elements such as selenium and zinc which are important as integral constituents of protective enzymes via special amino acids (e.g. selenomethionine) or structural components (e.g. Zn-metallothionein).[203] Overall, these low-molecular-mass antioxidant molecules add to the enzymatic defense system provided by superoxide dismutases, catalase, thioredoxin reductases, and glutathione peroxidases.

The Ergogenic Effects of Antioxidants

Studies have shown conflicting results on the use of antioxidant supplements by athletes and anyone interested in improving body composition and performance. The problem lies not so much in the studies themselves but in the study parameters. The studies using a small number of antioxidants, especially vitamins C and E, and studies looking at exercise done in moderation, will usually result in the conclusion that the use of antioxidants are counter-productive for improving body composition and performance.[204][205]

They reach this conclusion because the protocols do not take into account the duality of exercise. Practiced in moderation, exercise increases the production of endogenous antioxidants that are capable of handling the damaging effects of exercise and oxidative stress on metabolism and the musculoskeletal system. Under these conditions the use of exogenous antioxidants can be counter-productive or productive depending the genetic and epigenetic makeup of the athlete.

However strenuous exercise and exercise under less than optimal conditions, causes cell damage and oxidative stress that often overwhelms the endogenous antioxidants and results in damaged

muscle, loss of muscle cells, fibrotic changes within skeletal muscle, and cumulative microtears and other changes that increase the possibility of injuries and overtraining.

Antioxidants form a front-line defense against cell damage caused by free radicals, which are involved in muscle, joint and tendon damage and inflammation, degenerative arthritis and even in the aging process. The use of antioxidants can reduce free radical damage that occurs when we exercise[206] and can also attenuate the ongoing damage to injured tissues caused by free radicals, thus accelerating the healing process.[207] As well, antioxidants have been shown to enhance aerobic performance.[208]

Antioxidants, such as vitamins C and E (see under Vitamins below), selenium, green tea, reduced glutathione and N-acetyl-cysteine (NAC) can play an important role in reducing inflammation and fatigue, decreasing tissue damage, and in both preventing and treating injuries.

Various antioxidants, such as vitamin E, have been found to be useful in the treatment of some forms of arthritis[209] and in dealing with the oxidative stress of exercise.[210] As well, oxidative damage has been shown to contribute to the pathogenesis of injuries and arthritis, and the use of antioxidants, such as NAC,[211] shown to have therapeutic value for reducing endothelial dysfunction, inflammation, fibrosis, invasion and cartilage erosion.

One study found that a combination of 2 antioxidants, selenomethionine and epigallocatechin-gallate (the main antioxidant in green tea extract), had beneficial effects on catabolic and anabolic gene expression of articular chondrocytes.[212] The authors of the study concluded that “Our data provide insights into the mechanisms whereby ECGg and selenium modulate chondrocyte metabolism. Despite their differential mechanisms of action, the 2 compounds may exert global beneficial effects on articular cartilage.”

Supplementing endogenous antioxidants with supplementation is especially important in intense exercise which can overwhelm the intracellular antioxidant systems and can result in damage to the musculoskeletal and other systems in the body. For example, oxidative stress, the result of the overwhelming of the endogenous antioxidant system, can lead to damage to the reproductive system and decrease sex hormone production over the long term.[213],[214]

Supplemental exogenous antioxidants interact with endogenous antioxidant to provide protection from the increase in free radicals produced by exercise.

Exogenous supplementation may be useful in all forms of exercise, or they may actually be counterproductive in that they may impair the natural increase in endogenous antioxidants. If the exercise intensity is only mild to moderate supplemental antioxidants may, by decreasing the stimulus to enhance the endogenous antioxidant system, be somewhat counterproductive.

However, supplemental antioxidants are crucial in those that perform acute and chronic intense and/or exhaustive exercise and training since this intensity of training produces excessive free radical production and irreparable oxidative damage that overwhelms the endogenous antioxidant system resulting in irreparable tissue damage, an increase proneness to injury, and ill health.

So while skeletal muscle has an amazing capacity to adapt and repair itself, significantly increased levels of physical activity (intense training, chronic long duration exercise and overtraining) exposes the limitation of adaptation to tissue damage and will lead to some degree of maladaptation and musculoskeletal tissue changes that are counter-productive to both skeletal muscle function and performance.

As well, various nutrients are necessary for priming the endogenous antioxidant systems. For example, some minerals as copper, zinc and selenium (all present in Antiox) contribute to the antioxidant defense system by acting as co-factors for antioxidant Cu-Zn superoxide dismutase and glutathione peroxidase activities.

But Antiox contains much more than the usual antioxidants. It includes a mix of antioxidants and other supporting nutrients that makes other antioxidant supplements pale in comparison.

For example, Antiox contains quercetin, which has been shown to increase brain and muscle mitochondrial biogenesis and exercise tolerance, and thus may enhance athletic performance.[215]

Antiox also contains alpha lipoic acid (see above), which has been shown to enhance insulin sensitivity, decrease post exercise lactic acid concentrations, and have potent antioxidant and anti-inflammatory properties.[216]

Overall, Antiox contains over 60 nutrients that have antioxidant activity and/or increase endogenous antioxidant activity. As well, many of these ingredients have other properties that result in beneficial effects on health, energy metabolism, body composition and performance.

Free Radicals and Exercise

Oxygen consumption greatly increases during exercise, which leads to increased free radical production. The body counters the increase in free radical production through the antioxidant defense system. When free radical production exceeds clearance oxidative damage occurs. Free radicals formed during chronic exercise may exceed the protective capacity of the antioxidant defense system, thereby making the body more immune to disease and injury.

Antioxidants have been shown to be useful in many different conditions. Certain preparations have been postulated to retard the aging process by reducing the peroxidation of fatty acids secondary to enhancing the antioxidant enzymes to inhibit free radical activity. Although one such study showed significant effects of certain compounds on some physical symptoms, levels of endogenous antioxidants and hormonal levels (especially serum testosterone) in elderly men[217], little is known about the use of such compounds and other antioxidants in retarding the aging process.

Data from many studies show that free radicals play important roles in carcinogenesis[218,219] (in a role as natural inhibitors which may act on cancer initiation or promotion) and aging. It has also been shown that antioxidants act as protective agents in carcinogenesis[220], protect against heart disease[221,222], and may attenuate the effects of aging[223]. Administration of antioxidants (vitamins C, E and A) has been found useful for the prevention of postoperative complications[224].

Studies have shown that antioxidative treatment by vitamins could be an important regimen in the reduction of reperfusion damage. In three separate studies, inhibition of lipid peroxidation by antioxidants improved the function of the transplanted kidney[225], liver[226], and heart[227].

Experimental evidence suggests that oxidative stress due to the accumulation of free radicals plays a role in the pathogenesis of cataracts and that the process can be prevented or ameliorated by antioxidants, such as Vit C and E[228,229,230,231]. Low antioxidant levels may also be a risk factor for rheumatoid arthritis[232], and myocardial infarction[233].

A study has shown that oxygen-derived free radicals contribute to myocardial injury after cardioplegic arrest and that antioxidant therapy should improve myocardial protection[234]. Another study found that low plasma vitamins E and C seems to lead to increased risk of angina in Scottish men[235]. Low plasma vitamin E predisposes to angina, and smoking may increase the risk of angina by lowering plasma vitamin C levels in Scottish men.

There is a growing amount of data available on the physiological and pathological effects of free radicals on the musculoskeletal system. It has been shown that exercise can adversely affect muscle tissue by increasing the formation of free radicals, leading to lipid peroxidation and tissue damage.

Exercise results in free radical formation and muscle damage and inflammation. Muscular contraction produces reactive oxygen intermediates that contribute to muscular fatigue[236]. Skeletal muscle oxygen utilization greatly increases during high intensity exercise along with an increased rate of ATP utilization that exceeds the rate of ATP generation. The subsequent metabolic stress results in a markedly enhanced rate of production of oxygen free radicals from semiquinone and xanthine oxidase.

Studies have shown that training causes a substantial decrease in vitamin E concentration in the proliferating muscle mitochondrial membranes, thus depleting muscle mitochondria of their major lipid antioxidant[237]. Since vitamin E is the major cellular, lipid-soluble, chain- breaking antioxidant, these findings indicate increased free radical reactions in the tissues of exercising animals.

A study found that high altitude exposure adversely affects glutathione metabolism and antioxidant defense mechanisms and these changes can be ameliorated through supplementation of NAC and vitamin E.[238] Another study found that NAC prevents impairment to exposure to hypobaric hypoxia.[239]

During normal conditions free radicals are generated at a low rate and subsequently taken care of by the well-developed scavenger and antioxidant systems. It has been shown that exercise training imposes an oxidative stress to the body and induces increases in skeletal muscle antioxidant enzymes particularly glutathione peroxidase[240],[241]. It is thought that free radical damage to proteins accelerates overall protein catabolism. However, in most circumstances it is felt that most cells are in possession of sufficient antioxidants to control protein damage, so that changing radical fluxes do not greatly change intracellular protein turnover rates[242].

Thus under normal exercise conditions antioxidant enzymes in liver and skeletal muscle are capable of adapting to exercise to minimize oxidative injury caused by free radicals[243]. However, a greatly increased rate of free radical production may exceed the capacity of the cellular defense system. Consequently, a substantial attack of free radicals on the cell membranes may lead to a loss of cell viability and to cell necrosis and could initiate the skeletal muscle damage and inflammation caused by exhaustive exercise[244].

It is possible that therapies based on anti-oxidant supply may be valuable in these cases. For example in the thyrotoxic myopathy and cardiomyopathy, which are the major complications of hyperthyroidism, hyperthyroid muscular tissues may undergo several biochemical changes that predispose them to free radical-mediated injury[245].

It has been shown that vitamin E protects against thyroxine-induced acceleration of lipid peroxidation in cardiac and skeletal muscles in rats[246]. The results of this study also suggest that vitamin E protects against lipid peroxidation in hyperthyroid heart and skeletal muscle independently of the changes in oxidative enzymes and antioxidant enzymes.

Exercise training seems to increase muscle antioxidant enzymes and reduced glutathione[247]. Many reports show that vitamin E levels decrease in the muscle and increase in plasma during exercise. Studies of vitamin E deficiency and supplementation strongly suggest that this vitamin is of protective value during exercise.

It's well known that muscle fatigue with exercise is caused at least in part by oxidative stress and that the use of antioxidants can delay the muscle fatigue. Oxidants produced by exercise depress muscular force by decreasing the contractile response leading to premature fatigue.

In one study, it was shown that free radicals appeared to contribute to fatigue in oxidative skeletal muscle[248]. As well animal studies have shown that the use of compounds that neutralize free radicals can enhance aerobic performance.[249]

Several antioxidants, and especially **NAC** have been shown to decrease fatigue and have a positive effect on endurance.[250] For example, two recent studies found that NAC attenuates fatigue during whole body exercise[251] and during hand grip exercise.[252]

A recent study concluded that **"natural supplementation with Pycnogenol, with proper hydration, good training and nutritional attention may improve training and performances both in normal subjects and in semi-professional athletes performing at high levels in difficult, high-stress sports such as the triathlon."**[253]

Peroxidation of myocardial-membrane phospholipid is considered an important pathogenic component of heart muscle damage in ischemia and reperfusion. Membrane alpha-tocopherol (vitamin E) in the heart can modulate such damage and protect against it[254]. There is evidence that vitamins C and E and beta-carotene may protect against lipid peroxidation damage in muscle tissue. In one study use of these three compounds led to reduced CPK and LDH levels, indicating a decrease in muscle tissue damage.[255]

It would seem logical to assume that as a result of the vast amount of information now available about antioxidants that they would lessen tissue damage and speed recovery and thus might in the long term lead to increased performance. Antioxidants may be useful for athletes by reducing the destructive effects of free radicals on skeletal muscle as well as other tissues and organs, especially the liver and the central and peripheral nervous systems. Increasing levels of antioxidants prior to intensive exercise may have significant effects in reducing muscle injury and catabolism.

It has been shown that antioxidants might be useful in the biological preparation of endurance athletes. One study has demonstrated the antioxidant effects of a new compound, containing selenium, vitamin E, glutathione and cysteine, prepared as tablets[256]. In this study 3 weeks of antioxidant treatment induced significant increase of the nonproteic -SH and significant decrease of the lipid peroxides in comparison with placebo treatment. In another study the use of an antioxidant vitamin mixture (ascorbate, alpha -tocopherol, and beta -carotene) lowered markers of lipid peroxidation at rest and after exercise[257].

Several human and animal studies suggest that strenuous exercise may promote free radical production, leading to lipid peroxidation and tissue damage. On the other hand, there is evidence that vitamins C and E and beta-carotene may protect against such damage. Thus, concordance between the health benefits of exercise and nutrition and a compensatory role of antioxidant nutrients against the potentially harmful effects of exercise suggests that nutrition and exercise should form important components of any regimen for prevention of chronic diseases and/or promotion of optimal health[258].

Result suggests the involvement of the oxygen free radicals generated from the xanthine oxidase pathway in the pathogenesis of the ischemic injury of the rat brain[259]. Xanthine oxidase, which catalyzes hypoxanthine to xanthine and xanthine to uric acid as the last steps of ATP degradation. These reactions catalyzed by xanthine oxidase are considered to be a source of free radicals and may play important roles in the pathogenesis of cerebral ischemic injury[260].

The existence of a xanthine oxidase system in skeletal muscle could produce favorable conditions for oxy-radical formation through hypoxanthine degradation, which may contribute to the known muscle tissue injury[261].

It is possible to decrease the peroxidation of skeletal muscle-membrane phospholipid and thus decrease the oxidant radical portion of muscle injury and disease processes. In one recent study, the spontaneous lipid peroxidation in liver, kidney and heart decreased with increasing levels of dietary antioxidants[262].

Results of some studies have shown that some degree of autoxidation occurs in trauma. It appears that in blunt trauma the synthesis and regeneration capacity of glutathione are intact but that the levels of the consumable antioxidants, ascorbic acid, and alpha-tocopherol are compromised[263]. It is conceivable that the use of antioxidants might decrease the repercussions of musculoskeletal injuries or the microtrauma associated with overtraining.

Antioxidants form a front line defense against cell damage caused by free radicals, which are involved in muscle, joint and tendon damage and inflammation, degenerative arthritis and even in the aging process. The use of antioxidants can reduce free radical damage that occurs when we exercise and can also attenuate the ongoing damage to injured tissues caused by free radicals, thus accelerating the healing process.

Antioxidants, such as vitamins C and E, selenium, green tea, reduced glutathione, N-acetyl-cysteine (NAC), and many others can play an important role in reducing inflammation and fatigue, decreasing tissue damage, and in both preventing and treating injuries.

Various antioxidants, such as vitamin E, have been found to be useful in the treatment of some forms of arthritis[264] and in dealing with the oxidative stress of exercise.[265] As well, oxidative damage has been shown to contribute to the pathogenesis of injuries and arthritis, and the use of antioxidants, such as NAC,[266] shown to have therapeutic value for reducing endothelial dysfunction, inflammation, fibrosis, invasion and cartilage erosion.

A study found that a combination of 2 antioxidants, selenomethionine and epigallocatechin-gallate (the main antioxidant in green tea extract), had beneficial effects on catabolic and anabolic gene expression of articular chondrocytes.[267] The authors of the study concluded that “Our data provide insights into the mechanisms whereby ECGg and selenium modulate chondrocyte metabolism. Despite their differential mechanisms of action, the 2 compounds may exert global beneficial effects on articular cartilage.”

Why Studies Vary on Their Findings

A scan of the literature shows a variety of studies that seem at odds on the effects of antioxidants on health, body composition, training, and performance. There are several reasons these discrepancies, including the use of only one or two antioxidants at one time (vitamin C and vitamin E are the most common), differences in subjects used (for example those who exercise for fitness or fun versus

those who train hard including but not exclusive to competitive bodybuilders and power athletes, and most elite athletes in any sport), and a multitude of differences in protocols.

Also, few studies take into account possible gene polymorphisms and epigenetic influences that can affect the degree of oxidative stress and damage, and the effects of antioxidants on the response to exercise.[268],[269]

The bottom line is that if you're serious about your training, whether for personal or competitive reasons, Antiox will give you anabolic, body composition, performance, recovery, injury protection, and other benefits that will help you reach your goals.

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