

## MVM, EFA+, and Antiox

Increasingly over the past few decades research is showing that supplementing your diet with vitamins, minerals, antioxidants, essential fatty acids and other ingredients can keep you out of harms way, help deal with certain diseases, provide a foundation for optimal health, and improve mental and physical performance.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16</sup>

Some of these effects are due to correcting frank and marginal deficiencies while others are due to the beneficial effects of the nutrients themselves at higher than recommended daily intake.

Low intakes of various nutrients can lead to marginal deficiencies. Low intake is a problem in a significant proportion of athletes, especially those watching weight and body composition and thus do not consume sufficient amounts of many nutrients from foods alone. These deficiencies can be exacerbated by exercise since exercise can increase the need for certain nutrients.

For example, lower than normal intake of magnesium along with strenuous exercise that has been shown to increase the rate of magnesium loss via sweat and urine, can lead to a marginal deficiency. This in turn can impair energy metabolism, muscle function, oxygen uptake and electrolyte balance.<sup>17, 18</sup>

Some ingredients aren't strictly necessary but help as far as providing benefits for improving body composition and exercise performance. For example, quercetin, which is present in my Antiox, has been shown to increase brain and muscle mitochondrial biogenesis and exercise tolerance, and thus may enhance athletic performance.<sup>19</sup>

Alpha lipoic acid (in Antiox and EFA+) has been shown to enhance insulin sensitivity, decrease post exercise lactic acid concentrations, and have potent antioxidant and anti-inflammatory properties.<sup>20</sup>

Many of the nutrients have multiple actions in the body. For example selenium also has significant anti-inflammatory properties.<sup>21</sup>

There can also be marked health and in some cases treatment benefits to making sure you're not marginally deficient in any of the vitamins, minerals, and fatty acids.<sup>22, 23, 24, 25</sup> For example low intakes of certain vitamins are associated with increased risk of certain cancers.<sup>26</sup>

The essential fatty acids are also necessary for optimal health as well as helping to maximize body composition and performance.

Overall, there is substantial evidence that the use of the three foundation supplements, **MVM**, **EFA+**, and **Antiox** can provide both short and long term benefits. For more information on each of the supplements in the Foundation trio read or download the PDF information pieces in the store.

### The Importance of Nutrients found in MVM, EFA+, and Antiox

## Vitamins and Minerals

Vitamins and minerals, widely used by athletes and the general population are useful in correcting specific deficiencies that interfere with maximal physical performance. For example thiamin, vitamin C, sodium and iron<sup>27,28,29,30,31</sup>), and may be useful under certain conditions as in cases where greater requirements for sodium, potassium, magnesium and iron may be present in athletes who train for prolonged periods of time in hot weather.<sup>32</sup>

Many studies have shown that certain vitamins and minerals improve athletic performance. For example, a recent study found that a multiple vitamin and mineral supplement improved recovery of skeletal muscle as far as maximal force contraction.<sup>33</sup> Another study found that vitamin-mineral supplementation was found to attenuate cardiac and muscle damage markers while also enhancing antioxidant levels and reducing membrane LPO levels.<sup>34</sup>

Metabolic processes, including the all important production of energy, are dependant not only on the macronutrients (proteins, fats, and carbohydrates) but also on micronutrients. Many vitamins and minerals act as vital coenzymes and cofactors in cellular energy generation.<sup>35</sup> For example, mitochondrial functions are compromised by insufficient dietary intake of B vitamins and/or increased B vitamin needs.<sup>36,37</sup>

Frank deficiencies resulting in deficiency diseases are somewhat rare today in the industrialized world, marginal vitamin and mineral deficiencies are common.<sup>38</sup> These deficiencies are due to a variety of factors including poor diets (due for example to dieting, rushed meals, and unhealthy food choices), eating disorders, emotional or physiological stress (including intensive exercise), unhealthy lifestyles (including smoking, chronic alcohol abuse), certain diseases, malabsorption, and abnormal metabolism.<sup>39</sup>

While it's well known that frank deficiencies result in well documented diseases, even mild micronutrient deficiencies can result in a lack of well-being and general fatigue, reduced resistance to infections, increased incidence of various diseases, and impaired physical and mental performance.<sup>40,41,42,43,44,45</sup>

Certain vitamins and minerals have been shown to be important for athletic performance. For example, a study examined the effect of thiamine supplementation on exercise-induced fatigue.<sup>46</sup> The authors concluded that thiamine supplementation significantly suppressed the increase in blood glucose in the normal thiamine group and significantly decreased the number of complaints shortly after exercise in the subjective fatigue assessment of 30 items. Vitamin B6 is an essential co-factor necessary for the metabolism of protein and a useful supplement to take with any protein product. Usual dose for athletes is 25 mg daily.

In one study marginal deficiencies of thiamine, riboflavin, vitamin B6 and vitamin C resulted in decreased physical performance.<sup>47</sup> A recent 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.<sup>48</sup>

As well, it's been shown that physical activity is not only affected by marginal deficiencies but that it also depletes micronutrient status. For example, it's been found that riboflavin levels remain stable if no exercise is done but decrease with exercise.<sup>49</sup> In one study it was found that riboflavin levels decreased with increasing levels of exercise and that these levels were restored when dietary riboflavin was increased.<sup>50</sup>

Vitamin B6, which is also lost as a result of exercise, is transformed by the body to pyridoxyl-5-phosphate (PLP), the active coenzyme form of vitamin B-6 and cofactor for over 100 enzyme-catalyzed reactions, including aminotransferases (involved in amino acid metabolism) and glycogen phosphorylase (involved in glycogenolysis).

Studies have shown that PLP levels increase during exercise, which in turn leads to an increase in its breakdown and excretion.<sup>51,52</sup> As an example, it was calculated that marathon runners lose about 1 mg vitamin B6 during a marathon, equivalent to the DRI for an adult.<sup>53</sup>

As a result, it has been suggested that persons who exercise frequently may be at risk for riboflavin and pyridoxine deficiency and likely should supplement with both.<sup>54</sup>

In a review on the nutrition of children and adolescents engaged in high-level sports activities, the authors recommended mineral and vitamin supplementations. They feel that for minerals, perspiration losses may be associated with dietary deficiency and possible vitamin deficiencies concern B1, B2, B6, B9, B12, C and D vitamins.<sup>55</sup>

But there's more to it than just preventing marginal deficiencies. The use of some supplements can actually prevent certain conditions and problems both in the short and long term.

For example, using a daily broad spectrum multiple vitamin and mineral supplement has benefits that are just now being documented.

In the past, the emphasis was generally away from using multiple ingredients in the hope to correcting any marginal deficiencies, improving health, decreasing mortality, preventing and/or delaying age related disorders. There is also evidence that the use of a multivitamin may have significant anti-aging effects and improve lifespan. For example, a recent study found that multivitamin use is associated with longer telomere length – a shortening of telomere length is a marker of aging.

There's no doubt that a broad spectrum multi will have more effects on those who have a lower nutritional intake from food.

For example, the use of a multiple vitamin and mineral supplement is now recommended for all pregnant women as it has been shown to be more beneficial than the use of just a few nutrients such as iron and folic acid.<sup>56</sup>

The authors of the study did a meta-analysis of 11 randomized trials on prenatal supplementation, some comparing multivitamins with no supplementation and others comparing multivitamins with folic acid and/or iron supplementation. They found a significant reduction in the risk of low birth weight children with the use of multivitamins as compared to the use of iron-folic acid supplementation.

And closer to home, a recent study found that the use of 500 mg of vitamin C actually prevented complex regional pain syndromes (reflex sympathetic dystrophy or RSD) a serious condition that sometimes occurs after wrist fractures.<sup>57</sup>

In this study Four hundred sixteen adult patients (18 years or older) with a unilateral or bilateral wrist fracture (total 427 fractures) seen in the emergency department were randomly assigned to receive 50 days of placebo or vitamin C (daily doses of 200 mg, 500 mg or 1500 mg), regardless of whether the fractures were treated surgically or with immobilization. The study demonstrated that vitamin C taken at 500 mg a day for 50 days after the wrist fracture was effective in preventing RSD.

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.<sup>58</sup> 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.

The bottom line is that anyone who exercises should be taking a good daily multiple vitamin and mineral supplement, to make sure that they're not suffering from any marginal deficiencies, to make use of higher levels of certain nutrients that may offer physiological benefits, and as a preventative measure for some conditions and diseases.

## MVM version VI



**MVM is a comprehensive, specially balanced, multiple vitamin and mineral formula, with added ingredients, designed to promote body composition and athletic performance.**

MVM is the most complete multiple vitamin and mineral supplement on the market for anyone and especially for those who are interested in health, weight loss, body composition and athletic performance.

While the general medical consensus for the general population over the years was that you could get all you needed from food, that has changed.

The use of MVM is even more important for those who exercise, as we'll point out below.

# MVM version VI Supplement Panel

<b>Supplement Facts:</b>				Serving Size: 4 Tablets		Servings Per Container: 30	
	Amount Per Serving	% Daily Value		Amount Per Serving	% Daily Value		
Vitamin A (as Palmitate)	2500 IU	50%	Copper (as Copper Gluconate)	500 mcg	25%		
Beta-Carotene	10000 IU	200%	Manganese (as Manganese Gluconate)	5 mg	250%		
Vitamin C (as Ascorbic Acid and Calcium Ascorbate)	500 mg	830%	Chromium (as Chromium Amino Acid Chelate)	50 mcg	40%		
Vitamin D3 (as Cholecalciferol & Calcifediol)	1200 IU	300%	Molybdenum (as Sodium Molybdate)	10 mcg	15%		
Vitamin E (as d-Alpha Tocopherol Succinate)	400 IU	1330%	Potassium (as Potassium Phosphate and Aspartate)	199 mg	6%		
Vitamin K1 (as Phytonadione)	100 mcg	125%	Bioperine® (Black Pepper Extract (Piper Nigrum))	5 mg	*		
Vitamin K2 (as 50/50% MK-4 and MK-7)	80 mcg	100%	Boron (as Amino Acid Chelate)	2 mg	*		
Vitamin B1 (as Thiamine Mononitrate)	50 mg	3330%	DigeZyme™ (Aspergillus Oryzae)	100 mg	*		
Vitamin B2 (as Riboflavin)	50 mg	2940%	L-Taurine	150 mg	*		
Vitamin B3 (as Niacin, Niacinamide & Inositol Hexanicotinate)	90 mg	450%	Choline Bitartrate	150 mg	*		
Vitamin B6 (as Pyridoxine HCL & Pyridoxal-5-Phosphate)	50 mg	2500%	Betaine (Trimethylglycine)	100 mg	*		
Folate (as Folinic Acid)	1000 mcg	250%	Panax Ginseng Extract (Root)	100 mg	*		
Vitamin B12 (as Methylcobalamin)	500 mcg	8330%	Acetyl-L-Carnitine	100 mg	*		
Biotin	300 mcg	100%	Alpha Lipoic Acid	100 mg	*		
Pantothenic Acid (as d-Calcium Pantothenate and Pantethine)	50 mg	500%	Inositol Hexanicotinate	75 mg	*		
Calcium (as Calcium Phosphate, Citrate and Ascorbate)	400 mg	40%	L-Carnosine	50 mg	*		
Iron (as Ferrous Fumarate)	10 mg	55%	N-Acetyl-L-Cysteine	50 mg	*		
Phosphorus (as Calcium, Magnesium and Potassium Phosphate)	300 mg	30%	Citrus Bioflavonoids Complex	50 mg	*		
Iodine (as Potassium Iodide & Kelp)	150 mcg	100%	PABA (Para-Aminobenzoic Acid)	50 mg	*		
Magnesium (as Magnesium Phosphate and Aspartate)	300 mg	75%	Coenzyme Q10	40 mg	*		
Zinc (as Zinc Monomethionine Aspartate and Picolinate)	18 mg	120%	Lutein	5 mg	*		
Selenium (as L-Selenomethionine & Sodium Selenite)	50 mcg	70%	Astaxanthin	4 mg	*		
				<b>MVM Proprietary Formula – 1542 mg</b>			
				Glutamine Peptides (from Casein), Lactobacillus Acidophilus 150B/G, Green Tea Extract,			
				Phosphatidylcholine, Phosphatidylserine (from Non-GMO Sunflower Lecithin), L-Lysine, Quercetin,			
				Ganoderma Lucidum, L-Glutamic Acid, Grape Seed Extract, Turmeric Extract, Pine Bark Extract,			
				Astragalus Root, Ginkgo Biloba Extract, Hesperidin, Rutin, Schizandra Berry Extract, Milk Thistle			
				Extract (80% Silymarin), Beet Extract (root), Pomegranate extract, Spirulina.*			
<b>Other Ingredients: Rice Bran, Microcrystalline Cellulose, Hydroxypropylmethyl Cellulose, Croscarmellose Sodium, Glycerin.</b>							
<b>*Daily Value not established</b>							

## MVM version VI

Version VI of MVM represents the ongoing improvement of the best multiple vitamin and mineral supplement available anywhere.

In keeping with the aim of maximizing health and meeting the needs of those who exercise and who are looking to improve body composition, the formulation for MVM has been improved, with more of some of the ingredients, and over a few dozen new ingredients.

For example, **vitamin D** has been increased from 400 IU to 800 IU since it's been shown we need more vitamin D than was once thought and that marginal deficiencies of vitamin D are common. Vitamin D along with Calcium are intimately involved in skeletal homeostasis. But each do much more. Vitamin D has several vital functions outside this established role. Vitamin D has been shown to have important implications for general health, immunity, cognitive function, body composition, and athletic performance.<sup>59, 60, 61, 62, 63</sup>

**Vitamin K (as phytonadione)** has been added as it's been shown to maintain normal blood coagulation, decrease bone loss, maintain bone strength, and improve vascular health. It also may have roles in mitochondrial electron transport, protein synthesis, neuroprotection and immunity.

Rather than go through all the ingredients in MVM, have a look at the above Supplement Panel to see for yourself the complexity and sophistication of the MVM formulation. As well read the information below to see just how MVM is right for you.

## **Ingredients in MVM**

### **Minerals**

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

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.<sup>64</sup> 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.

A recent 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.<sup>65</sup>

### **Zinc**

Zinc deficiency in humans is widespread<sup>66</sup> and athletes may be particularly prone to lower plasma zinc levels.<sup>67</sup> Zinc is a constituent of more than a hundred fundamentally important enzymes, so zinc deficiency has many negative effects on almost every body function.<sup>68</sup> As well, zinc deficiency can adversely effect the reproductive hormones and as such impair athletic efforts.<sup>69</sup>

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.<sup>70</sup> 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,<sup>71</sup> and testosterone<sup>72</sup> and to raise plasma testosterone and sperm count.<sup>73,74</sup>

A recent 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.<sup>75</sup>

### **Magnesium**

Lower than normal intake of magnesium along with strenuous exercise that has been shown to increase the rate of magnesium loss via sweat and urine, can lead to a marginal deficiency. This in turn can impair energy metabolism, muscle function, oxygen uptake and electrolyte balance.<sup>76,77</sup>

Magnesium supplementation has been shown to increase protein synthesis and strength.<sup>78</sup> In another study the authors felt that insulin sensitivity can be improved by reduction of excessive body weight, regular physical activity and, possibly, by correcting a subclinical magnesium deficiency.<sup>79</sup>

## **Calcium**

Calcium permits the contractile filaments of the muscle cell -actin filaments and myosin filaments- to associate and produce the force that generates movement. When the nerve cell innervating a muscle cell signals that cell to contract, calcium is released from the sarcoplasmic reticulum into the region of the contractile filaments, thereby permitting contraction to occur. In one study calcium was shown to be effective in prolonging time of onset of fatigue in striated muscle.<sup>80</sup>

Several studies have shown that calcium plays a key role in body weight regulation and especially on fat metabolism (with possible effects on lipolysis, fat oxidation, lipogenesis, energy expenditure, and appetite suppression) and thus is a useful supplement for those looking to decrease weight and body fat.<sup>81828384858687888990</sup>

For example, Zemel et al. (2002) looked at the effects of calcium supplements on obese adults who were dieting. They found that a high-calcium diet (1200-1300 mg/day) resulted in greater weight and fat loss in humans compared to a low-calcium diet (400-500 mg/day).

Another study published in November 2004 found that a high intake of calcium may hinder weight and fat regain.<sup>91</sup> The study found that after putting mice on a low calorie diet and producing weight and body fat loss, that those on a low calcium diet regained their weight after 6 weeks. However, for those on a high calcium diet it was a different story. They found that the high calcium diets produced significant increases in lipolysis, decreases in fatty acid synthase expression and activity, and reduced fat regain. They also found that increasing calcium through the use of dairy products had significantly greater effects on fat regain.

## **Chromium**

It has been shown through various studies that chromium is an essential element involved in carbohydrate and lipid metabolism. Since the need for chromium increases with exercise,<sup>92</sup> and modern refined foods are low in chromium, there may be a need for chromium supplementation in athletes and other active people,<sup>93</sup> and especially in those wanting to lose weight and/or improve their body composition.<sup>94</sup>

Insufficient dietary chromium has been linked to maturity-onset diabetes and cardiovascular diseases, with supplemental chromium resulting in improvements of risk factors associated with these diseases.<sup>95,96,97</sup>

One of the most frustrating aspects of being overfat is that your body has become conditioned to converting excess calories, especially if combined with high carbohydrate intake, into body fat. Part of the problem with this fat conditioning involves insulin. The problem is that as you gain more body fat you become more insulin resistance so that you need more insulin to do the same job as when you

had less body fat. This increase in insulin decreases your ability to use body fat as fuel, and stores more energy as body fat. The end result is a fatter you.

Chromium helps to increase insulin sensitivity and thus your body's ability to burn off body fat as a preferred fuel, and decreases body fat production. Along with its effects on muscle, chromium picolinate has been shown to have significant effects on body composition.<sup>98,99,100</sup>

Although most diets just barely provide the RDA for chromium, for many it's not enough to make up for daily losses, especially if they exercise.

### **Chromium and Conjugated Linoleic Acid (CLA)**

It's been shown that combining chromium with CLA (see below for information on CLA) enhances insulin sensitivity and body composition even more when used together. A recent study found that CLA alone lowered body weight, total body fat mass, and visceral fat mass, the last of which decreased further with the combination of CLA and Chromium.<sup>101</sup>

### **Potassium**

Potassium is one of the essential dietary minerals. While most diets supply an adequate amount of potassium, athletes may have increased needs since it is one of the electrolytes lost in sweat. While it is important for athletes to replace the increased electrolytes lost due to sweating, it is especially important to replace potassium.

Even mild potassium deficiency can lead to fatigue and decreased performance,<sup>102</sup> while a significant deficiency can lead to cardiac problems. Muscular fatigue is manifested by a decline in force- or power-generating capacity and may be prominent in both submaximal and maximal contractions. Disturbances in muscle electrolytes play an important role in the development of muscular fatigue. Unfortunately, surprisingly little research has been carried out to investigate the effects of exogenous potassium on training intensity and muscle hypertrophy.

Studies with isolated animal muscle fibers have shown that potassium may help alleviate muscle fatigue. KCl- or caffeine-induced release of Ca<sup>2+</sup> from intracellular stores has been shown to decrease fatigue by reversing long-lasting interference in excitation-contraction coupling.<sup>103</sup>

Since some studies have implicated the decline of the intracellular to extracellular potassium gradient and extracellular K<sup>+</sup> accumulation during activity is an essential factor of muscle fatigue,<sup>104</sup> it might be argued that excessive potassium accumulation at the surface of the muscle cell might increase fatigue. A recent study investigated the role of K<sup>+</sup> in muscle fatigue by testing whether an increased extracellular K<sup>+</sup> concentration in unfatigued muscle fibers caused a decrease in force similar to the decrease observed during fatigue.<sup>105</sup> The authors concluded that exogenous potassium does not cause accumulation of K<sup>+</sup> at the surface of the sarcolemma that is sufficiently large to suppress force development during fatigue.

It has been shown that potassium deficiency can result in lower GH and IGF-I levels and that potassium replacement restores these levels. The problem appears to be at the pituitary level rather than the muscular level since the use of GHRH did not correct serum levels.<sup>106</sup> As well a recent study has shown that potassium deficiency inhibits protein synthesis.<sup>107</sup>

## **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.<sup>108,109,110,111,112</sup> ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.<sup>113</sup>

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.

ALA's ability to decrease both the pro-inflammatory cytokines<sup>114,115</sup> and secondary cortisol elevations, 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, EFA+ contains fish oil with substantial amounts of DHA and EPA, which has also been shown to have effects similar to the anti-inflammatory prescription and OTC drugs.<sup>116</sup>

ALA 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 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.<sup>117,118,119,120</sup>

ALA is also useful in reversing mitochondrial dysfunction, especially in aging mitochondria.<sup>121, 122</sup>

## **Antioxidants**

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<sup>123</sup> and can also attenuate the ongoing damage to injured tissues caused by free radicals, thus accelerating the healing process. As well, antioxidants have been shown to enhance aerobic performance.<sup>124</sup>

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<sup>125</sup> and in dealing with the oxidative stress of exercise.<sup>126</sup> As well, oxidative damage has been shown to contribute to the pathogenesis of injuries and arthritis, and the use of antioxidants, such as NAC,<sup>127</sup> 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.<sup>128</sup> 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.<sup>129, 130</sup>

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 counter productive.

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

Excessive free radical production and oxidative damage secondary to chronic long duration exercise and/or overtraining leads to irreparable oxidative damage, potentially resulting in the development or progression of ill health and/or disease.

As well, various nutrients are necessary for priming the endogenous antioxidant systems. For example, some minerals as copper, zinc and selenium (all present in MVM and 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.<sup>131</sup>

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.<sup>132</sup>

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.

# Antiox Version IV Supplement Panel

<b>Supplement Facts:</b>		<b>Serving Size: 6 Tablets</b>			
		<b>Servings Per Container: 30</b>			
	<b>Amount Per Serving</b>	<b>% Daily Value</b>			
			<b>Amount Per Serving</b>		
			<b>% Daily Value</b>		
Vitamin A (Beta Carotene)	10,000 IU	200%	Alpha Lipoic Acid	100 mg	*
Vitamin C (Ascorbic Acid)	400 mg	667%	Turmeric Root Extract	100 mg	*
Vitamin E (d-Alpha Tocopherol Acetate)	200 IU	667%	Panax Ginseng Root Extract	100 mg	*
Vitamin B1 (Thiamin HCL)	10 mg	666%	Cranberry Juice Powder	100 mg	*
Vitamin B2 (Riboflavin)	10 mg	588%	Rosemary Leaf Extract	100 mg	*
Niacinamide	25 mg	125%	Superoxide Dismutase	62.5 mg	*
Vitamin B6 (Pyridoxine HCL)	10 mg	500%	Ferulic Acid	60 mg	*
Folic Acid	400 mcg	100%	Cinnamon Bark Extract	60 mg	*
Vitamin B12 (Cyanocobalamin)	100 mcg	1667%	Schizandra Berry Extract	60 mg	*
Biotin	1000 mcg	333%	L-Glutamine	60 mg	*
d-Calcium Pantothenate	10 mg	100%	Pomegranate Fruit Extract	60 mg	*
Calcium (Calcium Phosphate)	250 mg	25%	Betaine HCL	50 mg	*
Magnesium (Citrate)	200 mg	50%	Grape Seed Extract	50 mg	*
Zinc (OptiZinc - Zinc monomethionine)	15 mg	100%	L-Carnosine	50 mg	*
Selenium (Sodium Selenite and Selenomethionine)	50 mcg	70%	Rutin	50 mg	*
Copper (Gluconate)	200 mcg	10%	Bilberry Fruit Extract	40 mg	*
Manganese (Sulfate)	5 mg	250%	Hawthorn Berry Extract	30 mg	*
Bioperine (Piper nigrum) (fruit)	5 mg	*	Ginger Root Powder	30 mg	*
L-Taurine	250 mg	*	Pine Bark Extract ( <i>Pinus strobus</i> )	25 mg	*
L-Methionine	200 mg	*	Phosphatidylserine Complex	20 mg	*
Ginkgo Biloba Leaf Extract	200 mg	*	Lutein	5 mg	*
Grape Skin Extract	200 mg	*	Lycopene	5 mg	*
Green Tea Extract ( <i>Camellia sinensis</i> ) (leaf)	200 mg	*	<b>Antiox™ Proprietary Complex 816.5 mg</b>		
Creatine Monohydrate	200 mg	*	Citrus Bioflavonoids Complex, Garlic Bulb Powder ( <i>Allium sativum</i> ),		
Eleuthero Root Extract	200 mg	*	Omega 3 Fish Oil Powder, L-Carnitine, Coenzyme Q10, Glutathione (Reduced)		
Quercetin Dihydrate	120 mg	*	L-Cysteine HCL, Resveratrol, Astaxanthin, Zaccanthin		
Milk Thistle Seed Extract	100 mg	*			
N-Acetyl Cysteine	100 mg	*			
<b>Other Ingredients: Cellulose, Stearic Acid, Magnesium Stearate, Hypromellose, Modified Cellulose Gum, Silicon Dioxide</b>					
<b>*Daily Value Not Established</b>					

## Some of the Ingredients in Antiox

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 antioxidants. 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<sup>133</sup>.

In a 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<sup>134</sup>. 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<sup>135</sup>.

### 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. The main difference between dietary supplements of NAC and cysteine is stability. Supplements of cysteine, but not NAC, are readily oxidized (inactivated) in the gastrointestinal tract, and can lead to toxic side effects.<sup>136</sup> NAC is thus the preferred form for oral use.<sup>137</sup>

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<sup>138</sup> but apparently not acute<sup>139</sup> 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.<sup>140</sup> 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.<sup>141,142</sup>

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<sup>143</sup> or in concert with glutathione and other antioxidants.<sup>144</sup>

NAC, because of its potent antioxidant properties, may prove useful in decreasing the oxidative stress seen with exercise.<sup>145</sup> 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 also reduced oxidative stress by preserving glutathione levels during exercise.

Since oxidative stress is considered a causal factor in human muscle fatigue and overtraining,<sup>146</sup> 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.<sup>147, 148, 149, 150, 151, 152, 153, 154</sup>

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.<sup>155</sup> Oral use of NAC has recently been demonstrated to enhanced handgrip performance.<sup>156</sup>

A recent study looked at the possible interaction between ROS and Na<sup>+</sup>,K<sup>+</sup>-pump activity in skeletal muscle, and a possible role in fatigue during exercise.<sup>157</sup> The results showed that the antioxidant NAC attenuates muscle fatigue, in part via improved K<sup>+</sup> regulation and attenuating the decline in Na<sup>+</sup>,K<sup>+</sup> 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. Several selenoproteins have been identified, but only one, glutathione peroxidase (SeGSHpx), a selenoenzyme, has a known function, that of neutralizing toxic lipid hydroperoxides<sup>158</sup>. Selenium, however has several metabolic effects not associated with glutathione peroxidase<sup>159</sup>.

For example, one study found that there is an increase in selenium requirements with exercise.<sup>160</sup>

## 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.<sup>161</sup> 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.<sup>162</sup>

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.<sup>163</sup> 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.<sup>164</sup> 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.<sup>165</sup> 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<sup>166</sup>. 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<sup>167</sup>.

It has been shown that free radical-mediated lipid peroxidation and glutathione depletion may be involved in the toxic manifestations of various compounds<sup>168</sup>. 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<sup>169</sup>.

According to recent studies, deficiency in vitamin E may be related to arterial lesions<sup>170</sup>. 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.<sup>171</sup> 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 radicalisolating 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<sup>172</sup>.

Level of plasma tocopherol (vitamin E) which has free radical scavenging properties rises significantly during intensive exercise<sup>173</sup>. Mobilization of tocopherol could help to prevent lipoperoxidation phenomena occurring in exercising skeletal muscle.

### **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.<sup>174,175,176</sup> 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.<sup>177,178,179,180,181</sup>

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.<sup>182</sup>

### **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.<sup>183</sup> A recent 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.<sup>184</sup> These compounds also have significant antioxidant properties.

Quercetin may have properties that downregulate or inhibit cyclooxygenase-2 safely.<sup>185</sup>

## **Turmeric**

Curcumin, the active component of turmeric, is documented to have anti-inflammatory and antioxidative benefits.<sup>186</sup> 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.<sup>187</sup>

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.

As well, turmeric has also been shown to have protective effects against chemical damage to connective tissue.<sup>188</sup>

## **Carnosine**

Carnosine, a dipeptide made up of the amino acids alanine and histidine (histidyl-alanine) was added to Antiox because of its many beneficial effects. It has been shown to have significant antioxidant and anti-inflammatory properties, increase healing, enhance the immune system, and provide anti-aging effects.<sup>189,190,191,192,193,194</sup>

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 has beneficial effects on exercise performance by helping to overcome muscle fatigue, likely due its effectiveness as a buffering agent, and perhaps its antioxidant, chelating,, and enzyme regulating effects.<sup>195</sup>

Carnosine levels tend to be higher in athletes such as sprinters<sup>196,197</sup> and in bodybuilders<sup>198</sup> These studies also show that intramuscular carnosine may be an effective physiological H<sup>+</sup> buffer and that there is a significant relationship between the carnosine concentration in human skeletal muscle and high intensity exercise performance. A recent study found that beta-alanine supplementation increased muscle carnosine levels<sup>199</sup> and resulted in an improvement in exercise performance.<sup>200</sup>

## **Coenzyme Q10 (ubiquinone-10)**

Coenzyme Q10 (CoQ10) acts as an electron carrier of the respiratory chain in mitochondria. As well, it has been shown that the reduced form of coenzyme Q10 is an important physiological lipid-soluble antioxidant and scavenges free radicals generated chemically within liposomal membranes.<sup>201,202</sup> It has also been shown that vitamin E and ubiquinol increase physical working capacity of experimental animals.<sup>203</sup>

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.<sup>204</sup> 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.

A recent study found that the combination of creatine, CoQ10, and lipoic acid (all in Antiox) had beneficial effects on mitochondrial disorders, resulting in lower plasma lactate levels and improved cellular energy levels.<sup>205</sup>

## **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<sup>206</sup>.

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<sup>207</sup>, 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<sup>208</sup>.

## **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.

A recent study on rats has shown that oral taurine supplementation may increase muscle performance and reduce muscle injury caused by exercise.<sup>209</sup> 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.

The most recent study to date found that taurine decreases oxidative stress in skeletal muscle after eccentric exercise.<sup>210</sup>

A 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.<sup>211</sup> Another study found that taurine may attenuate exercise-induced DNA damage and enhance the capacity of exercise due to its cellular protective properties.<sup>212</sup>

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.<sup>213</sup>

There is some evidence to show that taurine may enhance training further by decreasing training induced fatigue. A recent paper has shown that Na<sup>+</sup>-K<sup>+</sup>-ATPase activity is depressed with fatigue, regardless of training state, suggesting that this may be an important determinant of fatigue.<sup>214</sup> Another recent paper associated fatigue and training with reduced Ca<sup>2+</sup>-ATPase activity.<sup>215</sup> Previous studies have shown that taurine stimulates Na<sup>+</sup>-K<sup>+</sup>-ATPase activity and also the pumping rate of the Ca<sup>2+</sup>-activated ATPase pump.

A recent study found that taurine administration reduced the decrease in taurine in skeletal muscles in exercise, increased duration of running time in rats, and was considered to reduce exercise-induced muscle fatigue.<sup>216</sup> Also taurine supplementation has been shown to increase skeletal muscle force production, protects muscle function and reduce oxidative stress.<sup>217</sup>

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.

### **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.<sup>218,219,220,221,222</sup> ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.<sup>223</sup>

Alpha lipoic acid also has a number of useful and diverse properties. In a review<sup>224</sup> the author states “LA improves glycemic control, polyneuropathies associated with diabetes mellitus, and effectively mitigates toxicities associated with heavy metal poisoning. As an antioxidant, LA directly terminates free radicals, chelates transition metal ions (e.g. iron and copper), increases cytosolic glutathione and vitamin C levels and prevents toxicities associated with their loss.”

ALA 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.

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, EFA+ contains fish oil with substantial amounts of DHA and EPA, which has also been shown to have effects similar to the anti-inflammatory prescription and OTC drugs.<sup>225</sup>

ALA’s actions on decreasing both the pro-inflammatory cytokines<sup>226,227</sup> and because of its effects on decreasing secondary cortisol elevations.

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 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.<sup>228,229,230,231</sup>

ALA is also useful in reversing mitochondrial dysfunction, especially in aging mitochondria.<sup>232,233</sup>

## **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<sup>234</sup>.

Cysteine (decreases cross linkage of proteins), taurine<sup>235</sup> (may have a protective effect in joints by decreasing the degradation of hyaluronic acid), histidine dipeptides,<sup>236</sup> pantothenic acid, copper, zinc, selenium.

Over two dozen antioxidants from various plants, herbs, and fruits are included in Antiox as they have also been shown to have significant antioxidant activity and health benefits.

## **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<sup>237</sup>.

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<sup>238</sup>. 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)<sup>239</sup>. 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<sup>240</sup>.

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<sup>241,242</sup>. 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<sup>243</sup>.

# Essential Fatty Acids

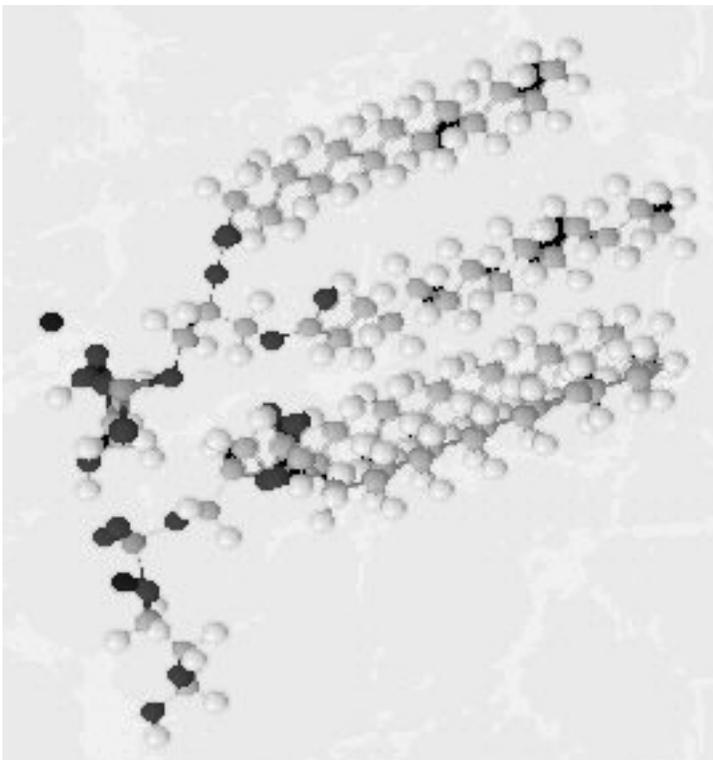
## Introduction

Increasingly over the past few decades research is showing that supplementing your diet with essential fatty acids (EFAs) can keep you out of harms way, help deal with certain diseases, provide a foundation for optimal health, and improve body composition, and mental and physical performance.<sup>244, 245, 246, 247, 248, 249, 250, 251</sup>

As well, some other fatty acids and companion compounds have also been shown to have significant effects on health and body composition and can work additively or even synergistically with the essential fatty acids.

## Dietary Fats

Figure 1  
Triglyceride Molecule



Dietary fats are essential for normal metabolism and good health. Not only are they necessary for the proper absorption, transportation and function of the fat-soluble vitamins A, D, E, and K, fats are used by the body to produce cellular components, hormones and other compounds that are essential to the proper functioning of the body. As well, a moderate intake of fat is essential for maximizing body composition and decreasing body fat.

But while all fats, including saturated fatty acids, have an important role in energy metabolism and body functions, the most important fats are the essential fatty acids (EFAs) since the body needs them to survive.

While the human body can manufacture most of the fats it needs from other fats, carbohydrates and protein, including cholesterol, saturated fatty

acids and unsaturated fatty acids, there are two groups of fatty acids, called essential fatty acids, based on linoleic acid (omega 6 group – which includes gamma linolenic acid or GLA) and alpha-linolenic acid (omega 3 group which includes eicosapentaenoic acid or EPA, and later into docosahexaenoic acid or DHA, which cannot be manufactured in the body.

The body cannot make an omega-3 or omega-6 fatty acid because human metabolism cannot add a double-bond to a fatty acid that is more than 9 carbons away from the delta end. For the same reason, the body cannot interconvert omega-3 and omega-6 fatty acids.

Unfortunately, for various reasons, many people are EFA challenged.

## EFA Deficiency

There are documented reasons for essential fatty acid deficiency under special circumstances.<sup>252</sup> For example a recent study found that children with food allergy managed with restricted intake of foods such as milk, egg, fish and vegetables are at risk of developing a deficiency in EFA and particularly in omega3 long-chain polyunsaturated fatty acids.<sup>253</sup>

However, it seems that a deficiency may exist in a good part of the general population that is eating normally. So the question is why are EFAs, especially the omega-3s, deficient in modern diets? The answer may be as simple as the diet itself, which may not include enough EFA containing foods, especially fish.<sup>254, 255, 256, 257, 258, 259</sup>

But there is more to it than that. Modern large scale methods of growing food is also at fault as it has decreased the n-3 fatty acid content in many foods: green leafy vegetables, animal meats, eggs, and cultured fish.<sup>260</sup>

Part of the problem is the food that's given to livestock and poultry. It's a lot different from the natural food that these animals would normally consume in the wild or even in the past.

For example, while both omega-3 (alpha-linolenic acid) and omega-6 (linoleic acid) are plentiful in the leafy plants consumed by roaming animals, providing nearly equal ratios of these EFAs, that's no longer the case when they're switched from grass to grains.<sup>261</sup> The result is that the fat in wild game and grazing ruminant contains roughly seven times more omega-3 fatty acids than animals raised for commercial meat.

Another reason is that processing or cooking can decrease plasma levels of essential fatty acids and can also change healthy EFAs into unhealthy trans-fatty acids.<sup>262</sup> So the meat, fish, and eggs that we consume today that's already low in omega-3s is even more depleted once it reaches our tables.

As well, we consume a lot of vegetable oils most of which are rich in omega-6 fatty acids and poor in the omega-3s. Increasing levels of omega-6 fatty acids also decreases the conversion of alpha linolenic acid to the longer chain omega-3 fatty acids, including DHA and EPA.<sup>263</sup>

The increased omega-6/omega-3 ratio common to our modern diets, but not to man during most of his existence,<sup>264, 265</sup> can give rise to disturbances in cellular structure and function, and an increase in systemic inflammation, which can lead to dysfunction and disease.

The realization of decreasing levels of omega-3s and increasing levels of omega-6s in our diets has led to recent attempts to modify existing foods to help correct this imbalance.<sup>266, 267, 268, 269, 270, 271, 272, 273</sup>

So although you can get the EFAs you need from food, you have to know what you're doing and what you're eating (and perhaps more importantly what you're eating was eating), and even then, although you're trying to eat right, you likely will still need to supplement your diet with some of the essential fatty acids.

# The Secrets of EFAs: How the Omegas Work

Alpha linolenic acid is the principal essential fatty acid in the omega-3 family and linoleic acid takes the lead in the omega-6 series. In a healthy body with sound nutrition, various metabolic conversions take place transferring the raw dietary materials into usable, biologically potent EFAs and other compounds.

Alpha linolenic acid can be transformed into eicosapentaenoic acid (EPA) and EPA can be converted into docosahexaenoic acid (DHA), although the rate of conversion of alpha-linolenic acid into EPA is relatively inefficient, at 5–10% and is inhibited by linoleic acid.<sup>274, 275</sup> The series three prostaglandins are formed from EPA. As well, EPA reduces the production of the bad prostaglandins from arachidonic acid.<sup>276</sup>

The omega-6 linoleic acid converts to gamma linolenic acid (GLA). Both the EPA and the GLA synthesized from dietary sources undergo another conversion, resulting in hormone-like biochemical compounds known as eicosanoids. These substances aid in virtually every body activity, from vital organ functioning down to intracellular processes, including helping to regulate inflammation and blood pressure as well as heart, gastrointestinal, and kidney functions.

As such, their use can be preventative and therapeutic for various conditions including some types of cancer, and cardiovascular, neurological and musculoskeletal diseases. Because of their anti-inflammatory properties they are effective anti-aging nutrients. As well, they can be used as an aid for weight loss and for improving body composition.

## Omega 3 Fatty Acids

Omega-3 fatty acids are long chain polyunsaturated fatty acids that have biological functions because they are converted to a number of active substances in the body such as prostaglandins and leukotrienes and are involved in a number of metabolic events. Linolenic acid is an essential fatty acid since it cannot be synthesized in the body. Other omega-3 fatty acids can, however, be synthesized from linolenic acid.

Omega 3 and omega 6 fatty acids are precursors for hormones and determine the composition of our cell membranes, influencing the production of pro- and anti-inflammatory substances.<sup>277</sup>

Omega-3 fatty acids, found in fish oils (mainly EPA and DHA) and flaxseed oil, are useful in a wide variety of conditions:<sup>278, 279</sup> They have been shown to:

- 1. Reduce oxidant stress<sup>280</sup> (oxidative stress or free radical damage is a factor of importance in the development of inflammatory events).**
- 2. Suppress the production of pro-inflammatory compounds in the body and therefore influence inflammatory conditions such as arthritis, diabetes, inflammatory bowel disease, cancer, autoimmune disorders, and aging.**<sup>281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297</sup>
- 3. Improve serum lipids and provide cardiovascular protection,**<sup>298, 299, 300, 301, 302</sup>
- 4. Provide protection against stress,<sup>303</sup> cognitive aging<sup>304, 305</sup> and depression.<sup>306</sup>**
- 5. Blood pressure, clotting, immune response, insulin resistance, and triglyceride levels are all positively affected by the omega-3s in EFA+.**<sup>307</sup>
- 6. May be effective in the prevention of coronary heart disease,<sup>308, 309</sup> and headaches.<sup>310</sup>**
- 7. Aid in weight and fat loss, especially when combined with CLA (see below).**

## 8. Be positively associated with peak bone density in young men.<sup>311</sup>

While it's generally known that EFAs are good for the cardiovascular system and for arthritis, it's not as well known the EFAs can affect mental health. In fact, a deficiency in EFAs or too little omega 3 fatty acids can lead to decreased mental health, depression and even aggressive tendencies.

EFAs have been shown to assist in treating depression and other mental health conditions. Low levels of omega-3 EFAs are common in depression. In one 2002 study, researchers found that treatment with EPA improved outcomes in patients with persistent depression.<sup>312</sup> Another study found that EPA may prove an effective add-on treatment in schizophrenia.<sup>313</sup>

There is even some evidence that the decrease in omega 3 consumption may be responsible for increasing homicide rates.<sup>314</sup>

Part of omega-3's effectiveness in treating brain disorders and the reason why lack of omega 3's results in some mental aberrations may be linked to its role in neurotransmission and brain development. DHA in particular is crucial for proper brain function, and pregnant women are advised to consume adequate levels for fetal brain development.

A recent paper published in 2005 concluded:<sup>315</sup>

There is no doubt that cerebral lipids, and EFA-derived LC-PUFAs in particular, have significant direct and indirect actions on cerebral function.<sup>316</sup> Not only does the lipid composition of neural membranes affect the function of their embedded proteins, but also many LC-PUFAs are converted to neurally active substances.

There is good evidence that psychiatric illness is associated with depletion of EFAs and, crucially, that supplementation can result in clinical amelioration.<sup>317</sup> As well as challenging traditional views of aetiology and therapeutics in psychiatry, the clinical trial data may herald a simple, safe and effective adjunct to our standard treatments for many disabling conditions.<sup>318, 319, 320, 321, 322</sup>

## EFAs and Body Composition and Exercise Performance

Besides all the health benefits above, the EFAs may also be useful in improving body composition and exercise performance as they have been shown to affect insulin sensitivity and growth hormone secretion, have anti-catabolic effects, and both increase lipolysis and decrease lipogenesis.<sup>323, 324, 325, 326,</sup>

Fish oil may, through perhaps more than one mechanism, have anti-catabolic properties. By extrapolating from burn injury studies, there is the possibility of modifying the catabolic processes secondary to training through the use of fish oil.<sup>327,328</sup> There is the possibility that fish oil may modulate PGE sub 2-mediated muscle proteolysis.

Studies have shown that the mechanism of interleukin-1 (IL-1)-induced muscle proteolysis involves PGE sub 2 synthesis.<sup>329</sup> Thus it is likely that omega-3 fatty acids from fish oil competitively inhibit the PGE sub 2 synthesis,<sup>330,331</sup> resulting in less muscle proteolysis. Furthermore, it has been shown that fish oil feeding in healthy volunteers can reduce the in vitro production of IL-1 and tumor necrosis factor by macrophages.<sup>332</sup> Thus, the reduction of IL-1 level may represent another mechanism by which fish oil moderates muscle proteolysis.

Omega-3 fatty acids may increase growth hormone secretion since they are involved in the formation of prostaglandin E1, which in turn is involved in GH release.<sup>333</sup> As well, to add to the possible benefits in improving exercise performance and body composition,

Several studies have shown that fish oil increases insulin sensitivity, the breakdown of body fat and the use of fat as a primary energy source. As such, besides decreasing inflammation and increasing cardiovascular health, they also provide substantial weight and fat loss benefits.

LNA, EPA, and DHA can enhance lipolysis (body fat breakdown)<sup>334,335</sup> and decrease lipogenesis (body fat formation).<sup>336,337</sup> The combined breakdown of stored body fat and decrease in additional body fat can have very positive results for the dieter. You actually end up making less and breaking down more body fat when using these oils.

As well, a recent study found that GLA reduced weight regain in humans following major weight loss, suggesting a role for essential fatty acids in fuel partitioning in humans prone to obesity.<sup>338</sup>

A recent study<sup>339</sup> in horses found that n-3 fatty acids laced vitamin supplement induced changes in membrane composition, which modulated the decrease in erythrocyte membrane fluidity seen during exercise, and therefore found to be potentially beneficial in exercising horses.

Another recent study found that DHA + EPA-induced increases in stroke volume and cardiac output imply that dietary supplementation with these fatty acids can increase oxygen delivery during exercise.<sup>340</sup>

## Gamma Linolenic Acid

Gamma linolenic acid (GLA) is important for health and has suppressive effects on both acute and chronic inflammation, and effects on decreasing the response to anxiety and stress.<sup>341,342,343,344,345,346,347</sup> It also works synergistically with some of the essential fatty acids to decrease inflammation and stress responses.<sup>348,349,350</sup>

GLA is needed by the body for the manufacture of certain hormone-like substances called Prostaglandins. These substances have beneficial regulatory effects on the immune system, circulation and the menstrual cycle. Their purpose is to help control and regulate cell growth and to maintain hormonal balance. Also helps to maintain healthy skin.

The use of EPA with GLA decreases some of the possible inflammatory effects of using GLA supplements. That's because GLA can be a precursor for arachidonic acid (AA, a "bad" type of prostaglandin that increases platelet aggregation and inflammation) and the addition of EPA reduces AA accumulation in some cells and tissues secondary to GLA supplementation.<sup>351</sup>

A recent study found that GLA reduced weight regain in humans following major weight loss, suggesting a role for essential fatty acids in fuel partitioning in humans prone to obesity.<sup>352</sup>

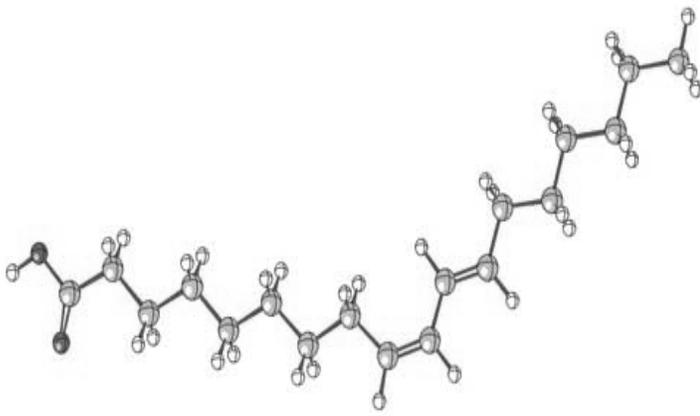
## Conjugated Linoleic Acid (CLA)

Figure 2

CLA Molecule

Used with permission of Lance H. Baumgard, PhD

[http://ag.arizona.edu/pubs/general/resrpt2003/article3\\_fig3.jpg](http://ag.arizona.edu/pubs/general/resrpt2003/article3_fig3.jpg)



Conjugated Linoleic Acid (CLA), while not an essential fatty acid, has significant effects on body composition. It's a mixture of isomers of linoleic acid, which is found preferentially in dairy products, meat, and in cheese, milks and yogurt that have undergone heat treatment.

CLA has been shown to have properties above and beyond those of linoleic acid. It has shown potential as a powerful anticarcinogen<sup>353,354</sup> and exhibits potent antioxidant activity.<sup>355</sup> Studies have suggested that CLA may be cytotoxic to human cancer cells in vivo.<sup>356</sup>

CLA has a wide range of biological effects.<sup>357</sup> It has potent antioxidant activity and has shown potential as an anticarcinogen. CLA has been shown to have significant anti-inflammatory properties<sup>358</sup> and to inhibit inflammatory mediators such as PGE<sub>2</sub>, IL-6, and TNF-alpha,<sup>359,360</sup> and also acts as a COX-2 inhibitor.<sup>361,362</sup>

Studies in animals and humans indicate that CLA supplementation decreases body fat and increases lean muscle mass. The increase in lean muscle mass is most pronounced in individuals who are exercising regularly.

CLA appears to reduce the ability of fat cells to take up fats from the bloodstream; it also inhibits the formation of new fat cells. CLA also helps cells burn fat at a higher rate, while fueling and preserving muscle, leading to a reduction in fat and an increase in lean muscle mass.

Numerous physiological effects in relation to body-weight control have been attributed to CLA in animals. In different animal models, CLA has been shown to reduce body fat and to increase lean body mass.<sup>363,364,365</sup> But CLA has marked effects in humans as well and has been found to decrease body fat mass and support muscle mass in overweight humans.<sup>366,367,368,369</sup>

For example, a study published in the International Journal of Obesity found that those who were given CLA for a four week period had significant decreases in abdominal fat.<sup>370</sup>

As well, a recent study concluded that long term CLA supplementation not only helps to decrease body fat but also helps to maintain weight loss in the long term. A recent long term study found that a mixture of the two CLA isomers significantly lowered body fat mass in overweight humans at both 1 and 2 years.<sup>371,372</sup> It likely does this by affecting various enzymes involved in lipid formation and to a lesser extent enhancing fat breakdown.<sup>373,374,375</sup>

As well, CLA seems to have significant effects on weight regain, as it reduces fat uptake into adipocytes by decreasing the formation of fat and but not affecting fat breakdown. It likely does this by affecting various enzymes involved in lipid formation rather than enhancing fat breakdown, known as lipolysis.<sup>376,377,378,379</sup>

Thus there is an overall increase in fat breakdown since the two processes are usually in dynamic equilibrium with as much fat being produced as is broken down. Decreasing fat formation changes the dynamics to one of overall increased fat breakdown and subsequently a decrease in overall body fat.

Of equal importance, for those wishing to maximize lean body mass, is the possible anti-catabolic effects of CLA.<sup>380,381</sup>

The most recent study in a series of studies of the effects of CLA confirmed and expanded on the findings of the previous studies: CLA reduces body fat mass in specific regions of the body, especially the abdominal area in both men and women, and maintains or increases lean body mass.<sup>382</sup>

Adding to CLA's effects on body composition, another recent study found that CLA supplementation even increased fat oxidation and energy expenditure during sleep.<sup>383</sup>

## **Conclusion**

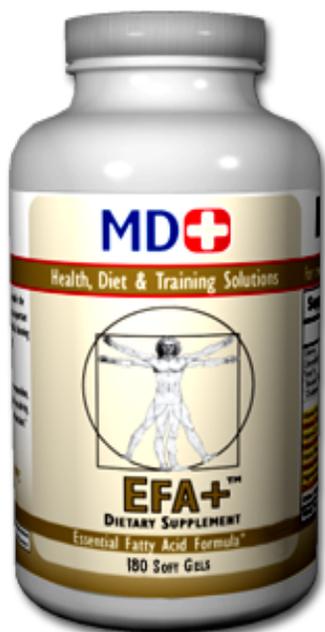
The bottom line is that the essential fatty acids, and some non essential fatty acids such as CLA, have significant effects on body composition, training, recovery, and can also increase overall health and well being.

# MD+

# EFA+ Version V



## Essential Fatty Acids – Plus



EFA+ is an enhanced essential fatty acid formula containing optimum levels of the essential fatty acids as well as several other additive and synergistic ingredients.

Besides the essential fatty acids, EFA+ also contains several other ingredients that along with the essential fatty acids provide a host of other benefits including:

1. Decreasing inflammation
2. Weight and fat loss
3. Improvements in body composition
4. Enhancing exercise/sports performance
5. Increased well-being and cognition
6. Protection of the brain from toxins

The information presented here focuses on the basics and on the specifics of the ingredients in EFA+. For more detailed information on Essential Fatty Acids see my article – the Essentials of Essential Fatty acids.

The many benefits of EFA+ include:

1. **Effects on body composition – improved metabolism, increased insulin sensitivity, enhanced weight loss mostly as fat loss, and retention of muscle mass, with the potential of increased muscle hypertrophy and strength.**

- 2. Improved intensity of training and more efficient recovery.**
- 3. Decreased inflammation in the body thus providing cardiovascular, neural, musculoskeletal, and hormonal (including testosterone and growth hormone) health benefits.**
- 4. Improved immune system functioning.**
- 5. Improved serum lipid (cholesterol, triglycerides) profile including cholesterol levels.**
- 6. Improved mental health.**
- 7. Anti-aging effects.**
- 8. Neuroprotection by preserving the blood-brain barrier.**

## **Dietary Fats and Essential Fatty Acids**

### **A. Introduction**

Dietary fats are essential for normal metabolism and good health. Not only are they necessary for the proper absorption, transportation and function of the fat-soluble vitamins A, D, E, and K, fats are used by the body to produce cellular components, hormones and other compounds that are essential to the proper functioning of the body. As well, a moderate intake of fat is essential for maximizing body composition and decreasing body fat.

But while all fats, including saturated fatty acids, have an important role in energy metabolism and body functions, the most important fats are the essential fatty acids (EFAs) since the body needs them to survive.

While the human body can manufacture most of the fats it needs from other fats, carbohydrates and protein, including cholesterol, saturated fatty acids and unsaturated fatty acids, there are two groups of fatty acids, called essential fatty acids, based on linoleic acid (omega 6 group – which includes GLA) and alpha-linolenic acid (omega 3 group which includes EPA and DHA), which cannot be manufactured in the body.

The body cannot make an omega-3 or omega-6 fatty acid because human metabolism cannot add a double-bond to a fatty acid that is more than 9 carbons away from the delta end. For the same reason, the body cannot interconvert omega-3 and omega-6 fatty acids.

Unfortunately, for various reasons, many people are EFA challenged.

### **B. EFA Deficiency**

EFAs, especially the omega-3s (including DHA and EPA) are frequently deficient in modern diets.<sup>384385</sup> Part of the problem is the food that's given to livestock and poultry. It's a lot different from the natural food that these animals would normally consume in the wild or even in the past.

So, while both omega-3 (alpha-linolenic acid) and omega-6 (linoleic acid) are plentiful in the leafy plants consumed by roaming animals, providing nearly equal ratios of these EFAs, that's no longer the case when they're switched from grass to grains. The result is that the fat in wild game and grazing ruminant contains roughly seven times more omega-3 fatty acids than animals raised for commercial meat.

Another reason is that processing or cooking changes healthy EFAs into unhealthy trans-fatty acids. As such, the meat and eggs that we consume today that's already low in omega-3s is even more depleted once it reaches our tables.

As well, we consume a lot of vegetable oils most of which are rich in omega-6 fatty acids and poor in the omega-3s.

The increased omega-6/omega-3 ratio common to our modern diets, but not to man during most of his existence, can give rise to disturbances in cellular structure and function, and an increase in systemic inflammation, which can lead to dysfunction and disease.

So, although you can get the EFAs you need from food, you must know what you're doing and what you're eating (and perhaps more importantly what you're eating was eating), and even then, although you're trying to eat right, you likely will still need to supplement your diet with some of the essential fatty acids.

## C. Omega 3 Fatty Acids

The omega-3s like alpha-linolenic acid (LNA) and eicosapentaenoic and docosahexaenoic acids (known as EPA and DHA respectively) increase fatty acid oxidation (burning of fat), basal metabolic rates, and lower cholesterol.

Omega-3 fatty acids also provide an anabolic effect by increasing the binding of IGF-1 to skeletal muscle and improving insulin sensitivity, even on diets high in fat which tend to decrease insulin sensitivity.<sup>386</sup> As well, fish oils may also have important implications for women prone to osteoporosis since they appear to decrease calcium excretion.<sup>387</sup>

Omega-3s also stimulate prostaglandin production. Prostaglandins are chemical messengers that regulate activity in body cells on a moment-to-moment basis and are involved in critical functions like blood pressure regulation, insulin sensitivity, immune system and anti-inflammatory responses. They're also involved in a myriad of other functions, many of which have yet to be fully identified.

If you have a problem producing prostaglandins or experience an imbalance between the different kinds of prostaglandins, overall health can be affected. EFA deficiency can lead to many problems including cardiovascular, hormonal, neurological, musculoskeletal, and immune dysfunction.

## What's New in EFA+ version V?

EFA+ has been totally reformulated to contain three times higher levels of DHA and EPA, as well as the addition of other beneficial oils including olive and krill oils. It also contains several new ingredients and higher levels of the vitamins and minerals. **All these changes are intended to increase the health, body composition and performance effects of EFA+.**

To hold all the changes and added ingredients, EFA+ version V now has 180 capsules Instead of 120 capsules per bottle.

## Ingredients in EFA+

I formulated EFA+ to be a balanced combination of essential fatty acids (EFAs), and other ingredients that work additively and synergistically to maximize the beneficial effects of the essential fatty acids on health, inflammation and body composition.

As far as the essential fatty acids, EFA+ consists largely of the omega 3 family of essential fatty acids, so as to even out the omega 6/omega 3 ratio to one that is closer to the ratio that humans have consumed for most of their existence. Bringing the ratio into line enhances cellular function, decreases inflammation, and improves body composition, health and well-being.

EFA+ contains pharmaceutical grade fish oil with higher levels of EPA and DHA. It's important to include these longer carbon chain omega 3s for two reasons. First of all as first of all the formation of EPA and DHA from ALA is limited and secondly while fish is one method of getting these oils, most sources recommend that fish consumption be limited to two to three servings weekly because so many fish are tainted with mercury, PCBs and other contaminants.

High-quality, purified fish oil, as found in EFA+ are contaminant free and present a viable alternative to frequent consumption of fish.

But there are many more active ingredients in EFA+ that enhance its effects. For example, the co-factors zinc, magnesium, Vitamins. C, B3 and B6 must be present for the benefits of the essential fatty acids to be realized.

Some of the added vitamins and minerals, besides optimizing the use of the essential fatty acids, also have other beneficial properties related to the effects of the essential fatty acids. For example vitamins B3 and B6 have significant antioxidant properties and also beneficial effects on serum cholesterol and triglycerides. Magnesium and zinc are also heart friendly and have beneficial effects on the immune, cardiovascular and neuromuscular systems.

EFA+ also contains several lipotropic factors and other ingredients, including conjugated linoleic acid, L-carnitine, methionine, serine, choline and inositol that optimize the utilization, transport and metabolism of fat, working to decrease body fat, normalize serum lipids including cholesterol, enhance energy levels, and fight inflammation in the body.

The antioxidants present in EFA+ serve several purposes. First of all they help preserve the natural state of the EFAs by protecting them from oxidative damage and becoming rancid while in the capsule so that what you get are all the good effects that EFA+ has to offer and none of the bad.

That's one of the reasons why EFA+ combines several antioxidants, including **vitamin A, vitamin C, vitamin E, conjugated linoleic acid (CLA), alpha lipoic acid,** and **glutathione**, with fish oil and other sources of essential fatty acids.<sup>388, 389</sup>

As well, the association of antioxidants with the omega-3 essential fatty acids, such as the fish oil and other ingredients found in EFA+, act in concert to enhance the beneficial effects of the essential fatty acids on inflammation and on the immune and cardiovascular systems.<sup>390,391</sup>

On top of all this the antioxidants counteract some of the adverse effects that these essential fatty acids might have. For example, although it's been shown that fish oil increases oxidation of LDL cholesterol, the "bad" cholesterol in the body that's been implicated in cardiovascular disease, it has also been shown that the use of antioxidants counteracts this negative effect of fish oil.<sup>392,393</sup>

## Omega-3, 6 and 9 Oils

EFA+ contains omega 3, 6 and 9 fatty acids, including EPA and DHA, the longer chain fatty acids found mostly in fish oil. The plant based oils are mechanically pressed under low heat, light and oxygen-free environment ensuring the extremely high quality of the formula. As well, pharmaceutical grade fish oil is used in the formulation. The formula is mercury free and free of harmful trans fatty acids.

The emphasis in EFA+ is on the omega 3 essential fatty acids and on GLA, an important omega 6 fatty acid, but EFA+ also contains omega 6 linoleic acid as part of flax seed oil and oleic acid, an omega-9 fatty acid, which is also present as a natural constituent of flax seed oil.

## Conjugated Linoleic Acid and Gamma linolenic acid (GLA)

Both CLA and GLA have health and body composition effects and are included in EFA+.

The use of EPA with GLA (as in EFA+) decreases some of the possible inflammatory effects of using GLA supplements. That's because GLA can be a precursor for arachidonic acid (AA, a "bad" type of prostaglandin that increases platelet aggregation and inflammation) and the addition of EPA reduces AA accumulation in some cells and tissues secondary to GLA supplementation.<sup>394</sup>

## Choline, Phosphatidylcholine, Phosphatidylserine, Serine and Policosanol

Choline, phosphatidylcholine, phosphatidylserine, and serine are involved in phospholipid metabolism and augment the effects of the EFAs on cell wall structure and integrity, as well as molecular signaling properties.<sup>395</sup> These ingredients are needed for cell membrane integrity and to facilitate the movement of signaling compounds between cells and the movement of fats in and out of cells.<sup>396</sup> They have significant effects on nerve cell membranes, and are required for nerve growth and function.<sup>397</sup>

Policosanols are a blend of compounds isolated from natural plant waxes. Policosanol contains several long chain fatty alcohols, including octacosanol, hexacosanol and triacontanol. Animal and in-vitro research has shown that these compounds may support the cardiovascular system and inhibit lipid peroxidation as well as support macrophage activity.

Policosanol helps lower cholesterol levels by slowing the body's own production of cholesterol in the liver, as well as reducing the risk of blood clots and enhancing circulation. Some studies have shown that policosanol, like some EFAs can significantly reduce both total cholesterol and LDL (bad) cholesterol.<sup>398,399,400,401</sup>

As well, policosanol, due mainly to the abundant octacosanol, has several other beneficial effects including increasing muscle endurance, increasing the efficiency of blood flow, and helping to stabilize cell membranes.<sup>402,403,404</sup> Octacosanol may also be useful for improving athletic performance as suggested by some studies.<sup>405,406</sup>

## 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.<sup>407,408,409,410,411</sup> ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.<sup>412</sup>

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.

ALA's ability to decrease both the pro-inflammatory cytokines<sup>413,414</sup> and secondary cortisol elevations, 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, EFA+ contains fish oil with substantial amounts of DHA and EPA, which has also been shown to have effects similar to the anti-inflammatory prescription and OTC drugs.<sup>415</sup>

ALA 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 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.<sup>416,417,418,419</sup>

ALA is also useful in reversing mitochondrial dysfunction, especially in aging mitochondria.<sup>420, 421</sup>

### The many benefits of EFA+ include:

- Effects on body composition – improved metabolism, enhanced weight and fat loss and retention of muscle mass.
- Increased insulin sensitivity.
- Decreased inflammation in the body thus providing cardiovascular, neural, musculoskeletal, and hormonal (including testosterone and growth hormone) health benefits.
- Improved serum lipid (cholesterol, triglycerides) profile including cholesterol levels.
- Improved immune system functioning.
- Improved mental health.
- Anti-aging effects.

### Bottom Line

The bottom line is that EFA+ is a multi-purpose formulation designed to provide the full gamut of all the essential fatty acids and supporting ingredients that are so important in optimizing your metabolism, enhancing weight loss, body composition, and the anabolic and fat burning effects of exercise, boosting your immune system and decreasing counter productive inflammation in the body secondary to exercise, aging and various diseases.

# EFA+ version V Nutritional Panel

<b>Supplement Facts:</b>		<b>Serving Size: 6 Softgels</b>	
		<b>Servings Per Container: 30</b>	
	<b>Amount Per Serving</b>	<b>% Daily Value</b>	
	<b>Amount Per Serving</b>	<b>% Daily Value</b>	
Calories	48		Omega-3 Fish Oil (Ultra High Concentrate) 2650 mg *
Calories From Fat	48		EPA (Eicosapentaenoic acid) 980 mg
Total Fat	5.3 g	8%	DHA (Docosahexaenoic acid) 760 mg
Vitamin A (as Palmitate)	3000 IU	60%	Flaxseed Oil 1500 mg *
Vitamin C (as Ascorbic Acid and Calcium Ascorbate)	200 mg	335%	GLA (Gamma Linoleic Acid) (Borage Oil Extract) 500 mg *
Vitamin D3 (as Cholecalciferol & Calcifediol)	400 IU	100%	Conjugated Linoleic Acid (CLA) 300 mg *
Vitamin E (as d-Alpha Tocopherol Succinate)	200 IU	665%	Alpha Lipoic Acid 150 mg *
Vitamin B3 (as Niacinamide & Inositol Hexanicotinate)	20 mg	100%	Acetyl-L-Carnitine 150 mg *
Vitamin B6 (as Pyridoxine HCL & Pyridoxal-5-Phosphate)	15 mg	750%	Glutathione (Reduced) 100 mg *
Zinc (as Zinc Monomethionine Aspartate)	15 mg	100%	Astaxanthin 950 mcg *
Total Omega-3 Fatty Acids (as EPA, DHA, and ALA)	2580 mg	*	<b>EFA+™ Proprietary Complex 1690 mg*</b>
			Olive Oil, Krill Oil, Glycerophosphocholine (Alpha-GPC), Choline, Citicoline (CDP-Choline), Phosphatidylcholine, Phosphatidylserine, Inositol, Methionine, Policosanol, Serine.
<b>Other Ingredients: Gelatin, Vegetable Glycerin, Water, Natural Color.</b>			
<b>*Daily Value Not Established</b>			

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