

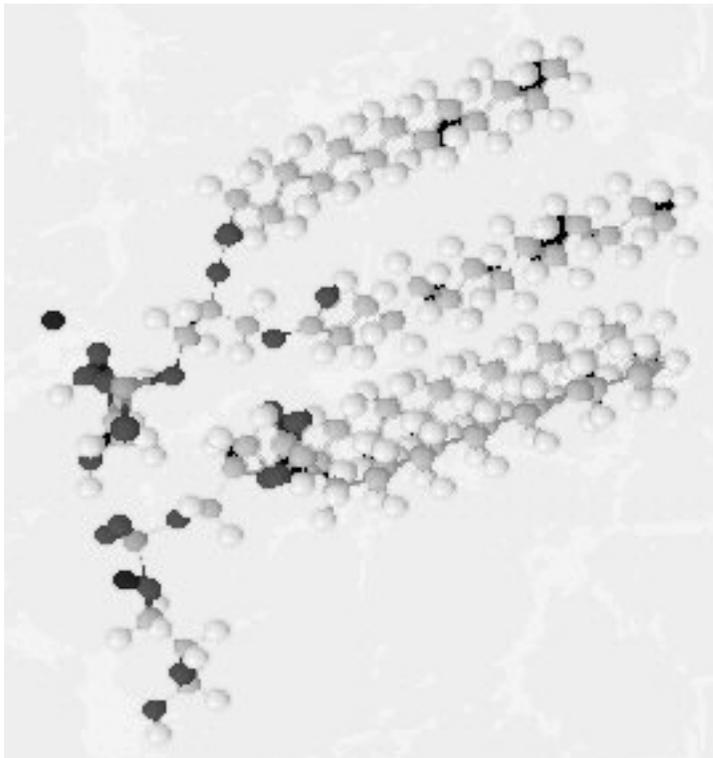
The Essentials of Essential Fatty Acids

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.^{1,2,3,4,5,6,7,8,9,10,11}

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



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.

EFA Deficiency

Why are EFAs, especially the omega-3s, deficient in modern diets? 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 steroids for sale 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. So 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 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 is transformed into eicosapentaenoic acid (EPA) and later into docosahexaenoic acid (DHA). The series three prostaglandins are formed from EPA. As well, EPA reduces the production of the bad prostaglandins from arachidonic acid.

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 know 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.¹²

Omega-3 fatty acids, found in fish oils (mainly EPA and DHA) and flaxseed oil, are useful in a wide variety of conditions.¹³ They have been shown to:

1. **Reduce oxidant stress¹⁴ (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.**^{15,16,17,18,19,20,21,22,23,24,25,26,27 28,29,30}
3. **Improve serum lipids and provide cardiovascular protection,**^{31,32,33,34,35}
4. **Provide protection against stress,³⁶ cognitive aging^{37,38} and depression.**³⁹
5. **Blood pressure, clotting, immune response, insulin resistance, and triglyceride levels are all positively affected by the omega-3s in EFA+.**⁴⁰
6. **May be effective in the prevention of coronary heart disease,^{41, 42} and headaches.**⁴³
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.**⁴⁴

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.⁴⁵ Another study found that EPA may prove an effective add-on treatment in schizophrenia.⁴⁶

There is even some evidence that the decrease in omega 3 consumption may be responsible for increasing homicide rates.⁴⁷

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:⁴⁸

There is no doubt that cerebral lipids, and EFA-derived LC-PUFAs in particular, have significant direct and indirect actions on cerebral function. 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. 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.

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, They have been shown to affect insulin sensitivity and growth hormone secretion, have anti-catabolic effects, both enhance weight loss and help keep the weight off, and influence exercise performance.

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.^{49,50} 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.⁵¹ Thus it is likely that omega-3 fatty acids from fish oil competitively inhibit the PGE sub 2 synthesis,^{52,53} 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.⁵⁴ 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.⁵⁵ 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)^{56,57} and decrease lipogenesis (body fat formation).^{58,59} 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.⁶⁰

A recent study⁶¹ 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.

Gamma linolenic acid

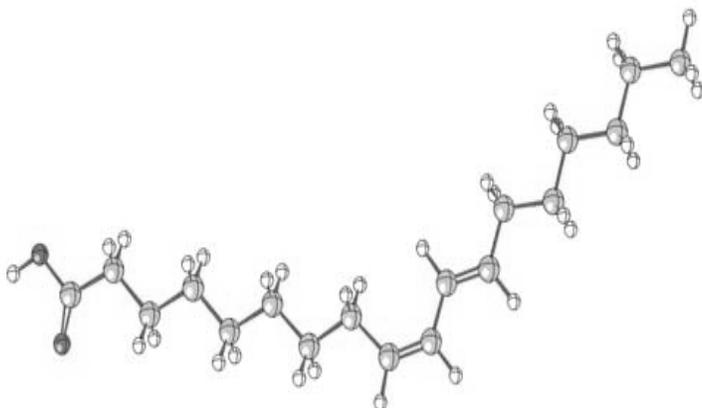
Gamma linolenic acid (GLA) is important for health and has suppressive effects on both acute and chronic inflammation, and effects on decreasing the response to anxiety and stress.^{62,63,64,65,66,67,68} It also works synergistically with some of the essential fatty acids to decrease inflammation and stress responses.^{69,70,71}

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 (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.⁷²

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.⁷³

Conjugated Linoleic Acid (CLA)



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^{74,75} and exhibits potent

antioxidant activity.⁷⁶ Studies have suggested that CLA may be cytotoxic to human cancer cells in vivo.⁷⁷

CLA has a wide range of biological effects.⁷⁸ It has potent antioxidant activity and has shown potential as an anticarcinogen. CLA has been shown to have significant anti-inflammatory properties⁷⁹ and to inhibit inflammatory mediators such as PGE2, IL-6, and TNF-alpha,^{80,81} and also acts as a COX-2 inhibitor.^{82,83}

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.^{84,85} 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.^{86,87,88,89}

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.⁹⁰

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.^{91,92} It likely does this by affecting various enzymes involved in lipid formation and to a lesser extent enhancing fat breakdown.^{93,94,95}

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.^{96,97,98}

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.^{99,100}

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.¹⁰¹

Adding to CLA's effects on body composition, another recent study found that CLA supplementation even increased fat oxidation and energy expenditure during sleep.¹⁰²

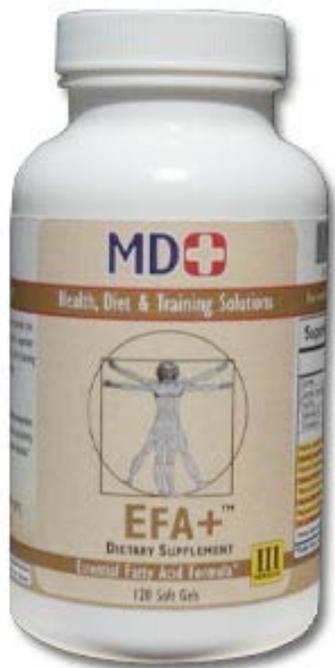
Conclusion

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



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.

The complex, scientifically based formulation provides much more than other essential fatty acid products.

Besides the essential fatty acids, EFA+ also contains numerous other ingredients that provide other benefits including weight and fat loss, and improvements in body composition.

EFA+ An Essential Fatty Acid Formulation, and More

Ingredients in EFA+

I formulated EFA+ to be a balanced geneza pharmaceuticals 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 man has consumed for most of his 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

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.^{105,106}

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.^{107,108}

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.¹⁰⁹

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.¹¹⁰ 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.¹¹¹ They have significant effects on nerve cell membranes, and are required for nerve growth and function.¹¹²

Policosanols are a blend of compounds isolated from natural plant waxes. Policosanols contain 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.

Policosanols help 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 policosanols, like some EFAs can significantly reduce both total cholesterol and LDL (bad) cholesterol.^{113,114,115,116}

As well, policosanols, 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.^{117, 118, 119} Octacosanol may also be useful for improving athletic performance as suggested by some studies.^{120, 121}

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.^{122,123,124,125,126} ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.¹²⁷

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^{128,129} 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.¹³⁰

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.^{131,132,133,134}

ALA is also useful in reversing mitochondrial dysfunction, especially in aging mitochondria.^{135, 136}

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 counterproductive inflammation in the body secondary to exercise, aging and various diseases.

EFA+ Nutritional Panel

Supplement Facts:		Serving Size: 4 Softgels			
		Servings Per Container: 30			
	Amount Per Serving	% Daily Value			
			Amount Per Serving		
			% Daily Value		
Calories	34		Glutathione (Reduced)	100 mg	*
Calories From Fat	34		Alpha Lipoic Acid	150 mg	*
Total Fat	3.8 g	6%	GLA (Gamma Linoleic Acid)	300 mg	*
Saturated Fat	0.4 g	2%	(from Borage Oil Extract)		
Cholesterol	0 mg	0%	Flaxseed Oil	1000 mg	*
			CLA (Conjugated Linoleic Acid)	150 mg	*
Vitamin A (as Retinyl Palmitate)	2,000 IU	40%	Omega-3 Fish Oil	1000 mg	*
Vitamin C (as Ascorbic Acid)	100 mg	167%	• EPA (Eicosapentaenoic acid)	330 mg	
Vitamin D (as Cholecalciferol)	100 IU	25%	• DHA (Docosahexaenoic acid)	220 mg	
Vitamin E (as d-Alpha Tocopheryl Acetate)	100 IU	333%			
Vitamin B3 (as Nicotinamide)	10 mg	50%			
Vitamin B6 (as Pyridoxine HCl)	10 mg	500%	EFA+ Proprietary Blend	470 mg	
Magnesium (as Magnesium Chelate)	100 mg	25%	Choline, Inositol, Methionine, Phosphatidylcholine,		
Zinc (as Zinc Monomethionine)	10 mg	67%	Leucidin (12% Phosphatidylcholine), Policosanol, Serine		
Other Ingredients: Gelatin, Water, Glycerin, Sorbitol, Natural Caramel Color, Titanium Oxide, Bees wax					
*Daily Value Not Established					

References:

-
- ¹ Carrero JJ, Fonolla J, Marti JL, Jimenez J, Boza JJ, Lopez-Huertas E. Intake of fish oil, oleic acid, folic acid, and vitamins B-6 and E for 1 year decreases plasma C-reactive protein and reduces coronary heart disease risk factors in male patients in a cardiac rehabilitation program. *J Nutr.* 2007 Feb;137(2):384-90.
 - ² Hosli I, Zanetti-Daellenbach R, Holzgreve W, Lapaire O. Role of omega 3-fatty acids and multivitamins in gestation. *J Perinat Med.* 2007;35 Suppl 1:S19-24.
 - ³ Gaullier JM, Halse J, Hoivik HO, Høy K, Syvertsen C, Nurminiemi M, Hassfeld C, Einerhand A, O'Shea M, Gudmundsen O. Six months supplementation with conjugated linoleic acid induces regional-specific fat mass decreases in overweight and obese. *Br J Nutr.* 2007 Mar;97(3):550-60.
 - ⁴ Mosley BS, Hobbs CA, Flowers BS, Smith V, Robbins JM. Folic acid and the decline in neural tube defects in Arkansas. *J Ark Med Soc.* 2007 Apr;103(10):247-50.
 - ⁵ Gariballa S, Forster S. Effects of dietary supplements on depressive symptoms in older patients: A randomised double-blind placebo-controlled trial. *Clin Nutr.* 2007 Jul 25; [Epub ahead of print]
 - ⁶ Hu J, Morrison H, Mery L, DesMeules M, Macleod M; Canadian Cancer Registries Epidemiology Research Group. Diet and vitamin or mineral supplementation and risk of colon cancer by subsite in Canada. *Eur J Cancer Prev.* 2007 Aug;16(4):275-91
 - ⁷ [No authors listed] Folic acid. Good for brain health. *Mayo Clin Health Lett.* 2007 Jul;25(7):6.
 - ⁸ Nykamp D, Kavanaugh ED, Wenker AP. Vitamins: the wise choice for women with cardiovascular disease. *Consult Pharm.* 2007 Jun;22(6):490-502.
 - ⁹ Tipoe GL, Leung TM, Hung MW, Fung ML. Green tea polyphenols as an anti-oxidant and anti-inflammatory agent for cardiovascular protection. *Cardiovasc Hematol Disord Drug Targets.* 2007 Jun;7(2):135-44.
 - ¹⁰ Houston MC. Treatment of hypertension with nutraceuticals, vitamins, antioxidants and minerals. *Expert Rev Cardiovasc Ther.* 2007 Jul;5(4):681-91
 - ¹¹ Machefer G, Groussard C, Vincent S, Zouhal H, Faure H, Cillard J, Radak Z, Gratas-Delamarche A. Multivitamin-mineral supplementation prevents lipid peroxidation during "the Marathon des Sables". *J Am Coll Nutr.* 2007 Apr;26(2):111-20.
 - ¹² Song C, Li X, Leonard BE, Horrobin DF. Effects of dietary n-3 or n-6 fatty acids on interleukin-1beta-induced anxiety, stress, and inflammatory responses in rats. *J Lipid Res.* 2003;44(10):1984-91.
 - ¹³ Schmidt GR. Therapeutics Of Fish Oil. Abstract of Meeting Presentation. ASHP Annual Meeting 1989;46:1-33.
 - ¹⁴ Mori TA, Puddey IB, Burke V, Croft KD, Dunstan DW, Rivera JH, Beilin LJ. Effect of omega 3 fatty acids on oxidative stress in humans: GC-MS measurement of urinary F2-isoprostane excretion. *Redox Rep* 2000;5(1):45-6.
 - ¹⁵ Siddiqui RA, Shaikh SR, Sech LA, Yount HR, Stillwell W, Zaloga GP. Omega 3-fatty acids: health benefits and cellular mechanisms of action. *Mini Rev Med Chem.* 2004;4(8):859-71.
 - ¹⁶ Trebble TM, Wootton SA, Miles EA, et al. Prostaglandin E2 production and T cell function after fish-oil supplementation: response to antioxidant cosupplementation. *Am J Clin Nutr* 2003;78: 376–82.

-
- ¹⁷ Mori TA, Beilin LJ. Omega-3 fatty acids and inflammation. *Curr Atheroscler Rep*. 2004;6(6):461-7.
- ¹⁸ Endres S, Ghorbani R, Kelly VE, et al. The effect of dietary supplementation with n-3 fatty acids on the synthesis of interleukin-1 and tumor necrosis factor by mononuclear cells. *N Engl J Med* 1989;320: 265–70.
- ¹⁹ Adam O, Beringer C, Kless T, et al. Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis. *Rheumatol Int* 2003;23: 27–36.
- ²⁰ Belluzzi A, Boschi S, Brignola C, Munarini A, Cariani G, Miglio F. Polyunsaturated fatty acids and inflammatory bowel disease. *Am J Clin Nutr* 2000;71S: 339S–42S.
- ²¹ Hardman WE. (n-3) fatty acids and cancer therapy. *J Nutr*. 2004;134(12 Suppl):3427S-3430S.
- ²² Nettleton JA, Katz R. n-3 long-chain polyunsaturated fatty acids in type 2 diabetes: a review. *J Am Diet Assoc*. 2005;105(3):428-40.
- ²³ Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. *J Am Coll Nutr*. 2002;21(6):495-505.
- ²⁴ Kremer JM, Lawrence DA, Petrillo GF, et al. Effects of high-dose fish oil on rheumatoid arthritis after stopping nonsteroidal antiinflammatory drugs. Clinical and immune correlates. *Arthritis Rheumatism* 1995;38:1107-1114.
- ²⁵ Esperson GT, Grunnet N, Lervang HH, et al. Decreased interleukin-1 beta levels in plasma from rheumatoid arthritis patients after dietary supplementation with n-3 polyunsaturated fatty acids. *Clin Rheumatol* 1992;11:393-395.
- ²⁶ Watkins BA, Li Y, Lippman HE, Seifert MF. Omega-3 polyunsaturated fatty acids and skeletal health. *Exp Biol Med (Maywood)* 2001;226(6):485-97.
- ²⁷ Tidow-Kebritchi S, Mobarhan S. Effects of diets containing fish oil and vitamin E on rheumatoid arthritis. *Nutr Rev* 2001;59(10):335-8.
- ²⁸ Kremer JM, Bigauoette J, Michalek AV, et al. Effects of manipulation of dietary fatty acids on clinical manifestations of rheumatoid arthritis. *Lancet* 1985;1:184-187.
- ²⁹ Herold PM, Kinsella JE. Fish oil consumption and decreased risk of cardiovascular disease: a comparison of findings from animal and human feeding trials. *Am J Clin Nutr* 1986;43:566-598.
- ³⁰ Kelley VE, Ferretti A, Izui S, Strom TB. A fish oil diet rich in eicosapentaenoic acid reduces cyclo oxygenase metabolites and supresses lupus in MRL-lpr mice. *J Immunol* 1985;134:1914-1919.
- ³¹ Ismail HM. The role of omega-3 fatty acids in cardiac protection: an overview. *Front Biosci*. 2005;10:1079-88.
- ³² Hjerkin EM, Seljeflot I, Ellingsen I, Berstad P, Hjerkmann I, Sandvik L, Arnesen H. Influence of long-term intervention with dietary counseling, long-chain n-3 fatty acid supplements, or both on circulating markers of endothelial activation in men with long-standing hyperlipidemia. *Am J Clin Nutr*. 2005;81(3):583-9.
- ³³ Phillipson BE, Rothrock DW, Connor WE, Harris WS, Illingworth DR. Reduction of plasma lipids, lipoproteins, and apoproteins by dietary fish oils in patients with hypertriglyceridemia. *N Engl J Med* 1985;312: 1210–6.
- ³⁴ Shahidi F, Miraliakbari H. Omega-3 (n-3) fatty acids in health and disease: Part 1--cardiovascular disease and cancer. *J Med Food*. 2004 Winter;7(4):387-401.
- ³⁵ Jacobson TA. Beyond lipids: the role of omega-3 Fatty acids from fish oil in the prevention of coronary heart disease. *Curr Atheroscler Rep*. 2007 Aug;9(2):145-53.

-
- ³⁶ Bourre JM. Dietary Omega-3 Fatty Acids and Psychiatry anabolic steroids for sale: Mood, Behaviour, Stress, Depression, Dementia and Aging. *J Nutr Health Aging*. 2005;11(1):31-36.
- ³⁷ Beyl RJ, Bax HC, Wahle KW, Starr JM, Deary IJ. Cognitive aging, childhood intelligence, and the use of food supplements: possible involvement of n-3 fatty acids. *Am J Clin Nutr*. 2004;80(6):1650-7.
- ³⁸ Maclean CH, Issa AM, Newberry SJ, Mojica WA, Morton SC, Garland RH, Hilton LG, Traina SB, Shekelle PG. Effects of omega-3 fatty acids on cognitive function with aging, dementia, and neurological diseases. *Evid Rep Technol Assess (Summ)*. 2005;(114):1-3.
- ³⁹ Su KP, Huang SY, Chiu CC, Shen WW. Omega-3 fatty acids in major depressive disorder. A preliminary double-blind placebo-controlled trial. *Eur Neuropsychopharmacol* 2003;13:267-71.
- ⁴⁰ Simopoulos AP. Essential fatty acids in health and chronic disease. *Am J Clin Nutr* 1999;70(3):560S-569S.
- ⁴¹ Hodgson JM, Wahlqvist ML, Boxall JA, Balazs ND. Can linoleic acid contribute to coronary artery disease?. *American Journal of Clinical Nutrition* 1993;58(2):228-234.
- ⁴² Cundiff DK, Lanou AJ, Nigg CR. Relation of omega-3 Fatty Acid intake to other dietary factors known to reduce coronary heart disease risk. *Am J Cardiol*. 2007;99(9):1230-3.
- ⁴³ Smith RS. The cytokine theory of headache. *Med Hypotheses* 1992;39(2):168-174.
- ⁴⁴ Hogstrom M, Nordstrom P, Nordstrom A. n-3 Fatty acids are positively associated with peak bone mineral density and bone accrual in healthy men: the NO2 Study. *Am J Clin Nutr*. 2007;85(3):803-7.
- ⁴⁵ Peet M, Horrobin DF. A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. *Arch Gen Psychiatry*. 2002;59(10):913-9.
- ⁴⁶ Emsley R, Myburgh C, Oosthuizen P, van Rensburg SJ. Randomized, placebo-controlled study of ethyl-eicosapentaenoic acid as supplemental treatment in schizophrenia. *Am J Psychiatry*. 2002;159(9):1596-8.
- ⁴⁷ Hibbeln JR, Nieminen LR, Lands WE. Increasing homicide rates and linoleic acid consumption among five Western countries, 1961-2000. *Lipids*. 2004;39(12):1207-13.
- ⁴⁸ Hallahan B, Garland MR. Essential fatty acids and mental health. *Br J Psychiatry*. 2005;186:275-7.
- ⁴⁹ Alexander JW, Saito H, Trocki O, Ogle CK. The importance of lipid type in the diet after burn injury. *Ann Surg* 1986;204:1-8.
- ⁵⁰ Trocki O, Heyd TJ, Waymack JP, Alexander JW. Effects of fish oil on postburn metabolism and immunity. *J Parent Enter Nutr* 1987;11:521-528.
- ⁵¹ Baracos V, Rodemann HP, Dinarello CA, Goldberg AL. Stimulation of muscle protein degradation and prostaglandin E sub 2 release by leukocytic pyrogen (interleukin-1). A mechanism for the increased degradation of muscle proteins during fever. *N Engl J Med* 1983;308:553-558.
- ⁵² Goodnight SH, Harris WS, Connor WE, Illingworth DR. Polyunsaturated fatty acids, hyperlipidemia and thrombosis. *Arteriosclerosis* 1982;2:87-111.
- ⁵³ Needleman P, Raz M, Minkes MS, et al. Triene prostaglandins: prostaglandin and thromboxane biosynthesis and unique biologic properties. *Proc Natl Acad Sci* 1979;76:944-948.
- ⁵⁴ Endres S, Ghorbani R, Kelley VE, et al. The effect of dietary supplementation with n-3 polyunsaturated fatty acids on the synthesis of interleukin-1 and tumor necrosis factor by mononuclear cells. *N Engl J Med* 1989;320:265-71.

-
- ⁵⁵ Dray F, Kouznetzova B, Harris D, Brazeau P. Role of prostaglandins on growth hormone secretion: PGE2 a physiological stimulator. *Advances in Prostaglandin & Thromboxane Research* 1980;8:1321-8.
- ⁵⁶ Awad AB, Zepp EA. Alteration of rat adipose tissue lipolytic response to norepinephrine by dietary fatty acid manipulation. *Biochem Biophys Res Comm* 1979;86:138-144.
- ⁵⁷ Parrish CC, Pathy DA, Parkes JG, Angel A. Dietary fish oils modify adipocyte structure and function. *J Cell Phys* 1991;148(3):493-502.
- ⁵⁸ Belzung F, Raclot T, Groscolas R. Fish oil n-3 fatty acids selectively limit the hypertrophy of abdominal fat depots in growing rats fed high-fat diets. *Am J Physiol* 1993;264(6 Pt 2): R1111-R1118.
- ⁵⁹ Parrish CC, Pathy DA, Angel A. Dietary fish oils limit adipose tissue hypertrophy in rats. *Metabolism: Clin Exp* 1990;39(3):217-19.
- ⁶⁰ Schirmer MA, Phinney SD. γ -Linolenate Reduces Weight Regain in Formerly Obese Humans. *J Nutr*. 2007;137(6):1430-5.
- ⁶¹ Portier K, de Moffarts B, Fellman N, Kirschvink N, Motta C, Letellierw C, Ruelland A, van Erck E, Lekeux P, Couder J. The effects of dietary N-3 and antioxidant supplementation on erythrocyte membrane fatty acid composition and buy anabolic steroids fluidity in exercising horses. *Equine Vet J* 2006;38(3):279-84.
- ⁶² Fan X, Chen H, Wang J, et al. Importance of dietary gamma-linolenic acid in human health and nutrition. *Journal of Nutrition* 1998;128: 1411-14.
- ⁶³ Furse RK, Rossetti RG, Seiler CM, Zurier RB. Oral administration of gamma-linolenic acid, an unsaturated fatty acid with anti-inflammatory properties, modulates interleukin-1 β production by human monocytes. *J Clin Immunol*. 2002;22(2):83-91.
- ⁶⁴ Tate G, Mandell BF, Laposata M, Ohliger D, Baker DG, Schumacher HR, Zurier RB. Suppression of acute and chronic inflammation by dietary gamma linolenic acid. *J Rheumatol*. 1989;16(6):729-34.
- ⁶⁵ Johnson MM, Swan DD, Surette ME et al. Dietary supplementation with gamma-linolenic acid alters fatty acid content and eicosanoid production in healthy humans. *Journal of Nutrition* 1997;127: 1435-44.
- ⁶⁶ Song C, Li X, Leonard BE, Horrobin DF. Effects of dietary n-3 or n-6 fatty acids on interleukin-1 β -induced anxiety, stress, and inflammatory responses in rats. *J Lipid Res*. 2003;44(10):1984-91.
- ⁶⁷ DeLuca P, Rossetti RG, Alavian C, Karim P, Zurier RB. Effects of gamma-linolenic acid on interleukin-1 β and tumor necrosis factor- α secretion by stimulated human peripheral blood monocytes: studies in vitro and in vivo. *J Invest Med*. 1999;47(5):246-50.
- ⁶⁸ Kapoor R, Huang YS. Gamma linolenic acid: an antiinflammatory omega-6 fatty acid. *Curr Pharm Biotechnol*. 2006 Dec;7(6):531-4.
- ⁶⁹ Barham JB, Edens MB, Fonteh AN, Johnson MM, Easter L, Chilton FH. Addition of eicosapentaenoic acid to gamma-linolenic acid-supplemented diets prevents serum arachidonic acid accumulation in humans. *J Nutr*. 2000;130(8):1925-31.
- ⁷⁰ Gillis RC, Daley BJ, Enderson BL, Karlstad MD. Eicosapentaenoic acid and gamma-linolenic acid induce apoptosis in HL-60 cells. *J Surg Res*. 2002;107(1):145-53.
- ⁷¹ Gueck T, Seidel A, Baumann D, Meister A, Fuhrmann H. Alterations of mast cell mediator production and release by gamma-linolenic and docosahexaenoic acid. *Vet Dermatol*. 2004;15(5):309-14.

-
- ⁷² Barham JB, Edens MB, Fonteh AN, Johnson MM, Easter L, Chilton FH. Addition of eicosapentaenoic acid to gamma-linolenic acid-supplemented diets prevents serum arachidonic acid accumulation in humans. *J Nutr* 2000;130(8):1925-31.
- ⁷³ Schirmer MA, Phinney SD. {gamma}-Linolenate Reduces Weight Regain in Formerly Obese Humans. *J Nutr*. 2007;137(6):1430-5.
- ⁷⁴ Ip C, Singh M, Thompson HJ, Scimeca JA. Conjugated linoleic acid suppresses mammary carcinogenesis and proliferative activity of the mammary gland in the rat. *Cancer Research* 1994;54(5):1212-5.
- ⁷⁵ Ip C, Scimeca JA, Thompson HJ. Conjugated linoleic acid. A powerful anticarcinogen from animal fat sources. [Review] *Cancer* 1994;74(3 Suppl):1050-4.
- ⁷⁶ Pariza MW, Ha YL, Benjamin H, et al. Formation and action of anticarcinogenic fatty acids. *Advances in Experimental Medicine & Biology* 1991;289:269-72.
- ⁷⁷ Shultz TD, Chew BP, Seaman WR, Luedecke LO. Inhibitory effect of conjugated dienoic derivatives of linoleic acid and beta-carotene on the in vitro growth of human cancer cells. *Cancer Letters* 1992;63(2):125-33.
- ⁷⁸ Bhattacharya A, Banu J, Rahman M, Causey J, Fernandes G. Biological effects of conjugated linoleic acids in health and disease. *J Nutr Biochem*. 2006;17(12):789-810.
- ⁷⁹ Zulet MA, Marti A, Parra MD, Martinez JA. Inflammation and conjugated linoleic acid: mechanisms of action and implications for human health. *J Physiol Biochem*. 2005;61(3):483-94.
- ⁸⁰ Luongo D, Bergamo P, Rossi M. Effects of conjugated linoleic acid on growth and cytokine expression in Jurkat T cells. *Immunol Lett* 2003;90:195– 201.
- ⁸¹ Eder K, Schleser S, Becker K, Korting R. Conjugated linoleic acids lower the release of eicosanoids and nitric oxide from human aortic endothelial cells. *J Nutr* 2003;133:4083–9.
- ⁸² Yu Y, Correll PH, Vanden Heuvel JP. Conjugated linoleic acid decreases production of pro-inflammatory products in macrophages: evidence for a PPAR gamma-dependent mechanism. *Biochim Biophys Acta*. 2002 15;1581(3):89-99.
- ⁸³ Cheng WL, Lii CK, Chen HW, Lin TH, Liu KL. Contribution of conjugated linoleic acid to the suppression of inflammatory responses through the regulation of the NF-kappaB pathway. *J Agric Food Chem*. 2004 14;52(1):71-8.
- ⁸⁴ DeLany JP, Blohm F, Truett AA, Scimeca JA, West D.B. Conjugated linoleic acid rapidly reduces body fat content in mice without affecting energy intake, *Am J. Physiol* 1999;276:R1172–R1179.
- ⁸⁵ Belury MA. Dietary conjugated linoleic acid in health: physiological effects and mechanisms of action. *Annu Rev Nutr* 2002;22:505–531.
- ⁸⁶ Gaullier JM, Halse J, Høye K, Kristiansen K, Fagertun H, Vik H, Gudmundsen O. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr*. 2004;79(6):1118-25.
- ⁸⁷ Eyjolfson V, Spriet LL, Dyck DJ. Conjugated linoleic acid improves insulin sensitivity in young, sedentary humans. *Med Sci Sports Exerc*. 2004;36(5):814-20.
- ⁸⁸ Steck SE, Chalecki AM, Miller P, et al. Conjugated Linoleic Acid Supplementation for Twelve Weeks Increases Lean Body Mass in Obese Humans. *J. Nutr*. 2007 137 (5).
- ⁸⁹ Blankson H, Stakkestad JA, Fagertun H, Thom E, Wadstein J, Gudmundsen O. Conjugated linoleic acid reduces body fat mass in overweight and obese humans. *J Nutr* 2000;130:2943-2948.

-
- ⁹⁰ Riserus U, Berglund L, Vessby B. Conjugated linoleic acid (CLA) reduced abdominal adipose tissue in obese middle-aged men with signs of the metabolic syndrome: a randomised controlled trial. *Int J Obes Relat Metab Disord.* 2001;25(8):1129-35.
- ⁹¹ Gaullier JM, Halse J, Høye K, et al. Conjugated linoleic acid supplementation for 1 y reduces body fat mass in healthy overweight humans. *Am J Clin Nutr* 2004;79:1118–1125.
- ⁹² Gaullier JM, Halse J, Høye K, Kristiansen K, Fagertun H, Vik H, Gudmundsen O. Supplementation with conjugated linoleic acid for 24 months is well tolerated by and reduces body fat mass in healthy, overweight humans. *J Nutr.* 2005;135(4):778-84.
- ⁹³ Park Y, Albright KJ, Storkson JM, et al. Changes in body composition in mice during feeding and withdrawal of conjugated linoleic acid, *Lipids* 1999;34(3):243-248.
- ⁹⁴ Pariza MW, Park Y, Cook ME. The biologically active isomers of conjugated linoleic acid, *Prog Lipid Res* 2001;40(4):283-298.
- ⁹⁵ Choi Y, Kim YC, Han YB, et al. The trans-10,cis-12 isomer of conjugated linoleic acid downregulates stearoyl-CoA desaturase 1 gene expression in 3T3-L1 adipocytes, *J Nutr* 2000;130 (8):1920-1924.
- ⁹⁶ Park Y, Albright KJ, Storkson JM, et al. Changes in body composition in mice during feeding and withdrawal of conjugated linoleic acid, *Lipids* 1999;34(3):243-248.
- ⁹⁷ Pariza MW, Park Y, Cook ME. The biologically active isomers of conjugated linoleic acid, *Prog Lipid Res* 2001;40(4):283-298.
- ⁹⁸ Choi Y, Kim YC, Han YB, et al. The trans-10,cis-12 isomer of conjugated linoleic acid downregulates stearoyl-CoA desaturase 1 gene expression in 3T3-L1 adipocytes, *J Nutr* 2000;130 (8):1920-1924.
- ⁹⁹ Cook ME, Miller CC, Park Y, Pariza M. Immune modulation by altered nutrient metabolism: nutritional control of immune-induced growth depression. *Poultry Science* 1993;72(7):1301-5.
- ¹⁰⁰ Miller CC, Park Y, Pariza MW, Cook ME. Feeding conjugated linoleic acid to animals partially overcomes catabolic responses due to endotoxin injection. *Biochem Biophys Res Comm* 1994;198(3):1107-12.
- ¹⁰¹ Gaullier JM, Halse J, Hoivik HO, Høye K, Syvertsen C, Nurminiemi M, Hassfeld C, Einerhand A, O'Shea M, Gudmundsen O. Six months supplementation with conjugated linoleic acid induces regional-specific fat mass decreases in overweight and obese. *Br J Nutr.* 2007;97(3):550-60.
- ¹⁰² Close RN, Schoeller DA, Watras AC, Nora EH. Conjugated linoleic acid supplementation alters the 6-mo change in fat oxidation during sleep. *Am J Clin Nutr.* 2007 Sep;86(3):797-804.
- ¹⁰³ Palacios A, Piergiacomini V, Catala A. Antioxidant effect of conjugated linoleic acid and vitamin A during non enzymatic lipid peroxidation of rat liver microsomes and mitochondria. *Mol Cell Biochem.* 2003; 250(1-2):107-13.
- ¹⁰⁴ Roberts WG, Gordon MH, Walker AF. Effects of enhanced consumption of fruit and vegetables on plasma antioxidant status and oxidative resistance of LDL in smokers supplemented with fish oil. *Eur J Clin Nutr.* 2003; 57(10):1303-10.
- ¹⁰⁵ Foulon T, Richard MJ, Payen N, Bourrain JL, Beani JC, Laporte F, Hadjian A. Effects of fish oil fatty acids on plasma lipids and lipoproteins and oxidant-antioxidant imbalance in healthy subjects. *Scand J Clin Lab Invest.* 1999; 59(4):239-48.
- ¹⁰⁶ Rakel DP, Rindfleisch A. Inflammation: nutritional, botanical, and mind-body influences. *South Med J.* 2005 Mar;98(3):303-10.

-
- ¹²⁵ Packer L, Tritschler HJ, Wessel K. Neuroprotection by the metabolic antioxidant alpha-lipoic acid. *Free Radic Biol Med* 1997;22(1-2):359-78.
- ¹²⁶ Podda M, Tritschler HJ, Ulrich H, et al. Alpha-lipoic acid supplementation prevents symptoms of vitamin E deficiency. *Biochem Biophys Res Commun*. 1994;204:98-104.
- ¹²⁷ Patrick L. Mercury toxicity and antioxidants: Part 1: role of glutathione and alpha-lipoic acid in the treatment of mercury toxicity. *Altern Med Rev*. 2002;7(6):456-71.
- ¹²⁸ Packer L. Alpha lipoic acid: a metabolic antioxidant which regulates NF- kappaB signal transduction and protects against oxidative injury. *Drug Metab Rev* 1998;30:245-75.
- ¹²⁹ Lee HA, Hughes DA. Alpha-lipoic acid modulates NF-kappaB activity in human monocytic cells by direct interaction with DNA. *Exp Gerontol*. 2002;37(2-3):401-10.
- ¹³⁰ Maroon JC, Bost JW. Omega-3 fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. *Surg Neurol*. 2006;65(4):326-31.
- ¹³¹ Faust A, Burkart V, Ulrich H, Weischer CH, Kolb H. Effect of lipoic acid on cyclophosphamide-induced diabetes and insulinitis in non-obese diabetic mice. *Int J Immunopharmacol*. 1994;16(1):61-6.
- ¹³² Burkart V, Koike T, Brenner HH, Imai Y, Kolb H. Dihydrolipoic acid protects pancreatic islet cells from inflammatory attack. *Agents Actions*. 1993;38(1-2):60-5.
- ¹³³ Lateef H, Aslam MN, Stevens MJ, Varani J. Pretreatment of diabetic rats with lipoic acid improves healing of subsequently-induced abrasion wounds. *Arch Dermatol Res* 2005;297(2):75-83.
- ¹³⁴ Thirunavukkarasu V, Nandhini AT, Anuradha CV. Fructose diet-induced skin collagen abnormalities are prevented by lipoic acid. *Exp Diabetes Res*. 2004;5(4):237-44.
- ¹³⁵ Arivazhagan P, Ramanathan K, Panneerselvam C. Effect of DL-alpha-lipoic acid on mitochondrial enzymes in aged rats. *Chem Biol Interact*. 2001 Nov 28;138(2):189-98.
- ¹³⁶ Palaniappan AR, Dai A. Mitochondrial ageing and the beneficial role of alpha-lipoic acid. *Neurochem Res*. 2007 Sep;32(9):1552-8.