# ALPHA LIPOIC ACID

We are about to give you so much information about Alpha Lipoic Acid, it will make your head spin. We strongly suggest that you read every word of what follows. You will learn dozens of beneficial metabolic effects from Lipoic Acid, any one of which is in itself enough reason to supplement with it.

**IT IS ALMOST INCOMPREHENSIBLE THAT**
**ALL THESE BENEFITS COME FROM ONE ADAPTOGEN.**

You are richly supplied with Lipoic Acid in your Activator, Rejuvenator, Adapto-Max/Diphasic AM and Oxy-Max/Diphasic PM.

Antioxidant

- Alpha Lipoic Acid is a di-thiol antioxidant. It is reduced to the thiol form intracellularly. The di-thiol (two sulfur) character of its molecular structure is what gives it its anti-anabolic, anti-reductive stress activity in your ADAPTO-MAX/Diphasic AM.

- Lipoic Acid (like Carnosine and Quercetin) performs not only its own array of anti-INFLAM-AGING effects at the cellular lever, but also functions as what Gerontologists call a GLUTATHIONE INDUCER.

- Glutathione is "The Master Antioxidant", and the major defense against Endogenous INFLAM-AGING.

- Lipoic Acid not only restores glutathione and glutathione peroxidase as part of the anti-anabolic antioxidant defense system, it is also an important part of the anti-catabolic anti-oxidant system.

- This anti-oxidant function is shown in the research as an amazing effect at decreasing malondialdehyde, one of the principal end-products of age-related lipid peroxidation. Lipoic Acid also potentiates the antioxidant enzyme systems super oxide dismutase and catalase, and glutathione reductase. This extraordinary antioxidant is thus a key nutrient in your OXY-MAX.

- Lipoic Acid is an anti-oxidant in both fat and water soluble media, and is active both intra- and extra-cellularly.

- It particularly decreases iron-dependent lipid peroxidation. (Think Brain health.)

- Some of the most highly toxic products of lipid peroxidation inhibit mitochondrial respiration by inhibiting alpha ketoglutarate dehydrogenase and pyruvate dehydrogenase. This toxic inhibition is associated with decreased enzyme activity, which is induced by insufficient availability of lipoic acid sulfhydryl groups.

- Lipoic Acid has anti-INFLAM-AGING effects by attenuating the decrease in both enzymatic (e.g., SOD) and non-enzymatic (e.g., vitamin E) antioxidant levels with age.

- One interesting study compared the antioxidant effects of Lipoic Acid with those of alpha tocopherol (Vitamin E.) The results? Lipoic Acid effectively decreased LDL cholesterol oxidative susceptibility associated with atherosclerosis (but not quite as well as alpha tocopherol). Lipoic Acid decreased urine FZ-isoprostanes (but not quite as well as alpha tocopherol). Lipoic Acid decreased plasma protein carbonyl levels (which are a key marker for aging processes) (while alpha tocopherol had no effect whatsoever.)

- Oxidation of hemoglobin is prevented by both Lipoic Acid and vitamin E (but not by vitamin C).

- Lipoic Acid increases intra cellular Co-enzyme Q-10, and regenerates both vitamin C and vitamin E intracellularly.

- Lipoic Acid is a hydroxyl radical quencher (due to the di-sulfate bond in the di-thiol ring).

- Lipoic Acid has been shown to decrease oxidative stress associated with lead poisoning.

- Lipoic Acid has been shown to decrease the tendency to calcium oxalate kidney stones.

- Lipoic Acid increases lymphocyte T-Cell function.

Anti-INFLAM-AGING

- Lipoic Acid increases cyclo-oxygenase, which increases the oxidation of arachidonic acid, and increases the reduction of Prostaglandin PGG2 to Prostaglandin PGH2, which decreases inflammation of all types.

- A 600 mg daily dose of Lipoic Acid has shown consistently beneficial anti-inflammatory effects critical to meet the special needs of individuals suffering in Immuno-Neuro-Endocrine Stress caused by in a broad array of pathological conditions.

- With Lipoic Acid you are enhancing Adaptative Capacity through pumping up Vital Reserves by many mechanisms. LA is active against both anabolic and catabolic aspects of INFLAM-AGING. Thousands of studies have now been done on LA showing how it meets the extraordinary dietary supplement needs even of individuals with the most severe Immuno-Nuero-Endocrine Stress

- LA helps control the systemic inflammatory markers (INFLAM-AGING) indicating the special needs of individuals spanning the entire spectrum of health status. LA (as other ADAPTOGENS) is recommended with the recognition that the Immuno-Neuro-Endocrine Stress increases nutrient requirements.

- LA is effective in maintaining healthy liver detoxification functions (559 studies from the literature supporting this).

Heart and Vascular Health

- Skibska, et al. The protective effect of Lipoic Acid on selected cardiovascular diseases caused by age-related oxidative stress. Oxid Med Cell Longev, 2015.

  --- Many studies have confirmed that Lipoic Acid can improve vascular function and decrease the INFLAM-AGING burden. Lipoic Acid is thought to inhibit the Fenton-like reaction mechanism and inhibit the formation of OH-. As a consequence, lipid peroxidation is inhibited in mitochondria.

  A crucial regulator of vascular homeostasis is the renin-angiotensin-aldosterone system. A key role in maintaining vascular health is played by angiotensin II. It induces oxidative stress and creates superoxide anions primarily through the activation of NAD(P)H-oxidase in vascular cells and myocytes. In addition, angiotensin II activates intracellular signaling pathways and up-regulates many inflammation factors including chemokines, cytokines, and growth factors, which have been implicated in arterial INFLAM-AGING.

  LA reacts with ROS, normalizes NADPH-oxidase activity, and can prevent angiotensin II-induced macrophage, monocyte, and T-cell infiltrations. LA also blocks AT1 receptors, which improves endothelial function and preserves blood flow. The beneficial effects of LA against angiotensin II are linked not only to scavenging ROS, but also to NF-kappaB inhibition.

LA supplementation reduces serum cholesterol, prevents LDL cholesterol oxidation, reduces serum triglycerides and lipoprotein (a), as well as other oxidative biomarkers.

LA reduces the aortic expression of adhesion molecules and the accumulation of aortic macrophages and pro-inflammatory cytokines, resulting in reduced LDL level and triglyceride concentration while elevating HDL. LA may also initiate LDL receptor synthesis in the liver, resulting in increased return of cholesterol to the hepatic system and elevated synthesis of apoprotein A component for reversed cholesterol transport.

--- INFLAM-AGING of blood vessels increases the production of various inflammatory markers, such as monocyte MCP-1, adhesion molecules, cytokines such as TNF-alpha and IL-6. The elevated inflammation reduces endothelial nitric oxide availability, which impairs endothelium-dependent vasodilation. ROS binds NO and forms highly reactive and dangerous peroxynitrate (ONOO-). This ONOO- produces a cascade of changes, leading to increased tension within the blood vessels.

LA lowers the level of inflammation and thus prevents pathological changes to vessel cells, and normalizes blood pressure. LA inhibits the vascular overproduction of endothelin I, the main vasoconstrictor. LA is shown to be particularly effective in controlling vascular INFLAM-AGING when used in combination with L-carnitine.

--- Ischemia injury follows oxidative stress (Exogenous Aging). LA counteracts the damage caused by ischemia, providing protection by inhibiting ROS production, blocking inflammation, and reducing myocardium apoptosis.

LA prevents arrhythmias and protects heart cells from hypoxia-induced death. LA is found to enhance cardiac function by reducing infarct size, decreasing levels of myeloperoxidase, decreasing TNF-alpha, decreasing creatinine kinase and lactate dehydrogenase, while up-regulating the expression of several antioxidant enzyme genes.

--- In age-related oxidative stress, a reduced supply of energy from the mitochondria necessary for the contractile function of cardiomyocytes is found. LA targets mitochondrial function, increasing myocardial energy efficiency by up to 30% by increasing glucose oxidation and decreasing fatty acid metabolism. By several mechanisms, LA attenuates mitochondrial damage caused by oxidative stress and the aging process.

LA increases Glutathione and enhances SOD activity in mitochondria damaged by oxidative stress.

- Lipoic Acid improves reduced heart rate variability (a Sympathetic Imbalance indicator) at rest.

- Endothelial migration of monocytes is one of the first age-associated challenges to vascular health, along with the action of vascular adhesion molecules. These two fundamentals of INFLAM-AGING are stimulated by glycation end products, and are reversed by LA. (We have discussed the oxidative damage associated with glycation in many NUTRI-SPEC Letters.)

  Karunakaran, et al. Physiological effect and therapeutic application of alpha lipoic acid. Curr Med Chem, 2014. ----- Reactive oxygen species and reactive nitrogen species promote endothelial dysfunction in old age. LA has been studied intensively by chemists, biologists, and clinicians who have been interested in its role in energetic metabolism and protection from reactive oxygen species-induced mitochondrial dysfunction.

  Consequently, many biological effects of LA supplementation are attributed to its potent antioxidant properties. The reducing environments inside the cell help to protect from oxidative damage and the reduction-oxidation status of LA is dependent upon the degree to which the cellular components are found in the oxidized state.

  Although healthy young humans can synthesize enough LA to scavenge ROS and enhance endogenous antioxidants like Glutathione and vitamins C and E, the level of LA significantly declines with age, and leads to endothelial dysfunction. Furthermore, many studies report LA can regulate the transcription of genes associated with antioxidant and anti-inflammatory pathways.

- Lipoic Acid maintains arteriovascular health, and particularly lowers triglycerides by as much as 45%.

- Maintaining a healthy triglyceride level is one of your most important signs of vascular health. Nothing compares with Lipoic Acid in this regard. When you combine the Lipoic Acid in your Rejuvenator, Adapto-Max and Oxy-Max with your EAT WELL – BE WELL NUTRI-SPEC Fundamental Diet (avoidance of excess carbohydrate in general, and fructose in particular), you will offer your patients by far the most effective way to preserve vascular health.

  There have been many, many instances of NUTRI-SPEC practitioners lowering patients' triglycerides by more than 200 in a period of less than 6 months. You can as well. ----- The ultimate in maximizing cardiovascular health is your SOLID DNP (Stage Of Life INFLAM-AGING Defense Diphasic Nutrition Plan). Its synergistic combination of ADAPTOGENS and REJUVENINS is unmatched.

Energy Production; Exercise; Liver Health

- Lipoic Acid prevents oxidative stress in the liver, the heart, and in the gastrocnemius muscle in response to exercise.

- Lipoic Acid increases energy availability to the brain and to muscles during exercise.

- Lipoic Acid is also known as "acetate replacing factor," and as "pyruvate oxidation factor." As such, it is an important part of efficient oxidative energy production in the body.

- Lipoic Acid is a co-factor of mitochondrial dehydrogenase complexes. It activates lipid kinase, tyrosine kinase, and serine/threonine kinases, which increase the efficiency of glucose uptake for normal oxidative energy production.

- Lipoic Acid is a di-sulfate co-factor of dehydrogenases in oxidative phosphorylation.

- Lipoic Acid is an alpha keto-acid dehydrogenation co-enzyme. It is thus the link between lipid and carbohydrate metabolism. Lipoic Acid can also be considered the universal co-enzyme of alpha keto-acid oxidation.

- Lipoic Acid decreases the lactate to pyruvate ratio in cells (--- a critical benefit for your Anaerobic patients), and decreases lactic acid acidemia.

- LA is an essential mitochondrial co-enzyme. It increases oxygen consumption, increases metabolic activity, and increases mitochondrial membrane potential in hepatocytes of aged rats (= anti-INFLAM-AGING).

- Associated with this role as a metabolic activator, LA is effective in maximizing liver function.

- Lipoic Acid decreases nitric oxide synthesis (which is associated with septic or endotoxic shock) in the liver by improving carbohydrate metabolism in hepatocytes. [It is interesting to note that while LA decreases the damage from nitric oxide, administration of N-acetyl cysteine, in the absence of sufficient Glycine, it actually can increase the damage from nitric oxide.]

- Lipoic Acid reverses the age-related decrease in hepatocyte Glutathione and ascorbic acid.

- One study showed that LA combined with selenium decreased Hepatitis C, decreased cirrhosis, decreased portal hypertension and decreased esophageal varices.

- Liu, et al. Effects of lipoic acid on high-fat diet-induced alteration of synaptic plasticity and brain glucose metabolism. Sci Rep, 2017.

  **[Note the researcher's use of the term "high-fat diet (HFD). HFD is a term you will find repeatedly in the medical research literature in animal studies that involve feeding a high level of fat to create all sorts of metabolic disorders and diseases. Very often the fat that is stuffed into these poor critters is never clearly specified.**

  **You might jump to the conclusion that since these are studies distinguishing health from disease, that the fat in "high-fat" would be the "EVIL" saturated fats in meat, fish, poultry, eggs, and cheese --- the saturated fats that both health food mythology and medical mythology have been trying to convince us since the 1950s are responsible for all the diseases that afflict humankind.**

  **----- No, the dietary fat used in HFD is almost always corn oil. Zero saturated fat --- extremely high in polyunsaturates --- the HOHUM PUFAs (Heated, Oxidized, Hydrogenated Un-Metabolizable Polyunsaturated Fatty Acids). ----- We NUTRI-SPEC practitioners have been making war on HOHUM PUFAs for decades now. So now, from a NUTRI-SPEC perspective ...**

  **All these research studies that create every imaginable disease in lab animals by stuffing them with corn oil are proving our thesis --- that HOHUM PUFAs (corn oil, soy oil, canola oil, safflower oil, sunflower oil, etc.) are actually right up there with fructose sugar as a leading cause of morbidity and mortality in the Western World. In fact, as you will see as we discuss this particular study, the diseases caused by consuming vegetable oils are virtually identical to those caused by excess fructose intake --- abdominal obesity, fatty liver, elevated triglycerides + low HDL cholesterol (the #1 risk factor for heart attacks and strokes), Type II diabetes, and an increased risk of cancer.**
  **--- plus every inflammatory degenerative disease imaginable.)**

  One of the effects of HFD, in addition to obesity, fatty liver, elevated triglycerides, insulin resistance and eventually diabetes and all its sequelae --- is compromised brain synaptic plasticity. That loss of neuronal plasticity caused premature brain cell death, and a decrease in both learning capacity and memory. --- In this study, the HFD group of 3-month-old mice gained 40% more weight after 9 weeks than the control group. But the mice stuffed with HFD, but also supplemented with Lipoic Acid, showed only about half that weight gain --- indicating that Lipoic Acid protected against the metabolic damage of HFD.

--- The HFD group compared to the control group had 65% higher triglycerides and 113% higher glucose. But the HFD group supplemented with Lipoic Acid showed 20% less triglyceride increase and 23% less serum glucose increase. There was much less insulin resistance in the LA-protected group.

--- LA also protected mice against the decrease of brain glucose uptake caused by HFD. There was also protection by LA of the brain glucose transporter mechanisms.

--- Lipoic Acid also protected the brain against the oxidative damage caused by the HFD. LA protected the brain against the excitotoxicity of the HFD fatty acids, as shown by a lowering of the excess brain glycolytic activity of the HFD group.

--- Hippocampal synaptic plasticity (memory) is devastated by the HFD fatty acids, yet was significantly protected by Lipoic Acid.

- NMDA receptors in the brain are modulated by endogenous redox agents such as Glutathione and Lipoic Acid.

Supplementation and Dietary Sources:

- Molz, et al. Potential therapeutic effects of lipoic acid on memory deficits related to aging and neurodegeneration. Front Pharmacol, 2017. ----- This study highlighting the benefits of lipoic acid in the human diet, and of supplementation of humans as indicated by human studies and extrapolated from animal studies, clearly defines both the human absorption and safety of lipoic acid supplementation.

  --- The best dietary sources of Lipoic Acid are meat (particularly organ meats), as well as tomatoes. Lipoic Acid is very quickly and efficiently absorbed from the GI tract, and like the B vitamin family to which it properly belongs, it is also metabolized and excreted very quickly. However, unlike some of the B vitamins, there is the potential for significant storage capacity of Lipoic Acid in the human liver.

  There are no recommendations for daily Lipoic Acid intake in humans. However, a 600 mg daily dose of lipoic acid has consistently shown beneficial effects in individuals covering the full spectrum of health status. --- Clinical trials using Lipoic Acid to assess the adverse health effects in humans were performed in doses up to 2400 mg/day with no reported adverse effects.

- An additional advantage of Lipoic Acid is its solubility in both water and fat, which allows it to travel through all parts of the body. Because of its special properties, it is able to enter certain parts of the cell that most other antioxidants are not able to reach.