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. We are going to give you literally 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 CAN COME FROM ONE ADAPTOGENIC NUTRIENT.

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. Because of its metabolically active sulfur, it has antioxidant activity as part of the glutathione system of antioxidants, as well as in the glutathione derivatives cysteine and n-acetyl-cysteine.

- Lipoic acid not only restores glutathione and glutathione peroxidase as part of your body’s anti-anabolic antioxidant defense system, it is also an important part of your 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 a key nutrient in your OXY-MAX.

- It particularly decreases iron-dependent lipid peroxidation.

- Lipoic acid has anti-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.)
- Lipoic acid has been shown to decrease oxidative stress associated with lead poisoning.

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

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

- 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 cataracts.

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

- Lipoic acid increases T-Cell function in cancer patients.
Anti-inflammatory === Anti-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 in a broad array of pathological conditions --- from vulvodynia to diabetic neuropathy to Alzheimer’s.

- With Lipoic Acid you are enhancing Adaptive 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 benefits such diverse conditions as peripheral neuropathy; the causes and effects of diabetes --- those effects including diabetic neuropathy, retinopathy, kidney failure, and poor wound healing; brain neuronal loss associated with increased oxidative stress; decreased cognitive function; obesity; non-alcoholic fatty liver disease; cardiovascular disease; high blood pressure; osteoporosis; glaucoma and cataracts. Also, lipoic acid is effective in improving liver detoxification functions (559 studies from the literature supporting this); reversing inflammatory bowel disease; protecting against cancer; controlling multiple sclerosis; and decreasing systemic inflammatory markers (INFLAM-AGING) covering a broad- spectrum of dis-ease.
Protection From: Heart Disease, Arteriosclerosis and High Blood Pressure


--- In atherosclerosis: Many studies have confirmed that lipoic acid can improve vascular function and decrease the atherosclerotic plaque 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 the pathogenesis of atherosclerosis 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 atherosclerotic plaque development. 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 reduces plaquing. 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 in 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.

--- In hypertension: High blood pressure 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 bind NO and form 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 reducing blood pressure when used in combination with L-carnitine.

--- In atherosclerosis-ischemic heart disease: Ischemia injury follows oxidative stress and can lead to significant morbidity and mortality. LA counteracts the damage associated with 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 ameliorate cardiac dysfunction 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 heart failure: 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 oxidation stress.

- Lipoic acid has been shown to improve cardiac autonomic neuropathy, which is diagnosed by reduced heart rate variability (a Sympathetic Imbalance indicator) at rest. (Tie this in with your NUTRI-SPEC clinostatic pulse response.)

- Endothelial migration of monocytes is one of the first steps in atherosclerosis, along with the action of vascular adhesion molecules. These two fundamentals of atherosclerosis 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 and contribute to the development of cardiovascular diseases such as atherosclerosis, diabetes, and hypertension. It 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 given to patients with coronary artery disease and essential hypertension has been shown to have a favorable influence on the fatty acid content of the blood.

- Lipoic acid, prevents atherosclerosis, and particularly lowers triglycerides.

- Lipoic acid has been shown in clinical studies to decrease elevated triglycerides by as much as 45%. (Elevated triglycerides (and not elevated cholesterol) is one of the few true independent risk factors for heart attacks and strokes.)

- As decreasing elevated triglycerides is one of your most important clinical goals, you must give your patients lipoic acid. Nothing compares with lipoic acid as a means to lower triglycerides, and it does so by several mechanisms. When you combine the lipoic acid in your Diphasic A.M. and Diphasic P.M. with your 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 lower deadly triglycerides.

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 do so as well. Doing so is as simple as either using your NUTRI-SPEC Metabolic Balancing or Sympathetic/Parasympathetic Support System on all your patients, and/or, implementing the Diphasic Nutrition Plan for your patients (and, of course, giving up all your favorite herbal remedies, “adrenal support” supplements, and mega doses of this and that).

- In spontaneously hypertensive rats, excess endogenous aldehydes (resulting from oxidative stress) bind sulphydryl groups of membrane proteins, altering membrane calcium channels and increasing blood pressure. Lipoic acid binds these excess aldehydes and actually decreases elevated blood pressure. Lipoic acid particularly decreases elevated systolic blood pressure, decreases excess cellular calcium, decreases elevated serum glucose and decreases elevated serum insulin, and decreases tissue aldehyde conjugates that are associated with tissue catabolism and premature aging. Lipoic acid also decreases adverse renal vascular changes associated with hypertension.
Energy Production; Exercise; Liver Metabolism & Protection

- 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.

- Lipoic acid is an essential mitochondrial co-enzyme. It increases oxygen consumption, increases metabolic activity, and increases mitochondrial membrane potential in hepatocytes of aged rats.

- Associated with this role as a metabolic activator, LA is effective in the treatment of liver disease.

- 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 glutathione or N-acetyl cysteine by themselves 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 lipoic acid combined with selenium decreased Hepatitis C, decreased cirrhosis, decreased portal hypertension and decreased esophageal varices.
Diabetes Protection

- There are over 700 studies in the medical literature defining the molecular mechanisms and therapeutic potential of lipoic acid in treating and preventing diabetes alone.

- In its antioxidant role, lipoic acid has been shown to decrease diabetic neuropathy.


It is a potent antioxidant with insulin-mimetic and anti-inflammatory activity. LA in the diet or as a supplement is quickly absorbed, transported to the intracellular compartments, and reduced to dihydrolipoic acid under the action of enzymes. LA, which plays an essential role in mitochondrial bioenergetic reactions, has drawn considerable attention as an antioxidant for use in managing diabetic complications such as retinopathy, neuropathy, and other vascular diseases.

- Papanas, et al. Efficacy of alpha-lipoic acid in diabetic neuropathy. *Expert Opin Pharmacother*, 2014. ----- Neuropathy is a serious complication of diabetes. The mechanisms of action of lipoic acid in diabetic neuropathy include: reduction of oxidative stress, along with improvement in nerve blood flow, nerve conduction velocity, and several other measures of nerve function. There is ample evidence from randomized double-blind placebo-controlled clinical trials and meta-analyses, suggesting that LA is efficacious and safe for diabetic neuropathy, and accomplishes clinically meaningful improvements. When compared with currently licensed analgesic drugs for diabetic neuropathy, LA is better tolerated, has more rapid onset of action, and improves paresthesia, numbness, sensory deficits and muscle strength in addition to neuropathic pain.

- Lipoic acid is an essential constituent of biological membranes. Another study shows that membrane fluidity and protein sulfhydryl reactivity of RBCs is decreased in diabetes, and is increased by LA supplementation.
A note on diabetic neuropathy: Studies have shown that in diabetic neuropathy the nerve is ischemic and hypoxic, with increased dependence on anaerobic metabolism. Lipoic acid increases glucose uptake and efficient oxidative metabolism and thus benefits the diabetic neuropathy.

Type II diabetics have increased fasting lactate and pyruvate concentrations in their blood. Furthermore, the increased lactate and pyruvate concentrations double after glucose loading in obese patients, but not in lean patients. Lipoic acid was shown to decrease excessive lactate and pyruvate levels in the serum of Type II diabetics. (These are generally your Ketogenic Imbalance patients.)
Brain & Nerve Protection; Dementia (including Alzheimer’s); Parkinson’s

- Above, we have highlighted the benefits of lipoic acid supplementation for pain, paresthesia, numbness, and neuromuscular weakness associated with diabetic neuropathy. But many studies show that other forms of nerve pain are also benefited by LA supplementation.

- Pessoa, et al. Emerging treatments for neuropathic pain. Curr Pain Headache Rep, 2015. ----- Neuropathic pain is a series of well-known conditions caused by diseases or lesions to the somatosensory system. With the better understanding of the pathophysiology of neuropathic pain, previously unexplored therapies have been used with encouraging results. Among those promising therapies are alpha-lipoic acid, acetyl-L-Carnitine and cannabinoids.

- Checchia, et al. Observational multicentric study on chronic sciatic pain. Eur Rev Med Pharmacol Sci, 2017. ----- Sciatic neuropathy is a multifaceted condition managed by means of a wide-spectrum of therapeutic options --- both physical and pharmacological therapies. This study was conducted in 44 Italian centers specializing in Physical Medicine, Rehabilitation, Orthopedics, Neurology, Neurosurgery, and Rheumatology. 394 patients with chronic low back pain and sciatica participated in the study. At baseline, patients received several different therapeutic options. A subgroup of 312 patients was treated with a combination of neurotrophic agents containing lipoic acid. After a 2 month follow-up, a general improvement in both perceived pain and functional disabilities was observed. There was significant improvement in the Pain Numeric Rating Scale, Roland-Morris Disability Questionnaire, and Brief Pain Inventory.


- Luchetti, et al. Observational multicentric survey on carpal tunnel syndrome. Eur Rev Med Pharmacol Sci, 2017. ----- This study reports the findings of the Management of Peripheral Neuropathies Study Group with carpal tunnel syndrome. A wide variability in the interventions prescribed and classified according to 3 categories (physical, pharmacological, and neurotrophic therapies) was evident. A subgroup of 303 patients was treated with a combination of neurotrophic agents containing alpha lipoic acid. At 2 month follow-up, a general improvement in symptoms and functional impairment was observed, with a reduction in the Boston Carpal Tunnel Questionnaire and in NRS (pain Numeric Rating Scale) for both nocturnal and diurnal pain of CTS.
Letizia, et al. Lipoic acid and superoxide dismutase in the management of chronic neck pain. Drugs R D, 2014. ----- Since oxidative stress plays a pathogenetic role in chronic neck pain, this study investigated whether a combination of lipoic acid and SOD might improve pain control and the efficacy of physiotherapy. One group of patients received physiotherapy alone, while the second group received physiotherapy plus supplementation with 600 mg ALA and 140 IU SOD daily in addition to physiotherapy. Pain was assessed by Visual Analog Scale and Neck Pain Questionnaire.

After 1 month, both groups experienced significant reduction in the VAS and NPQ scores. However, there was no further improvement in the physiotherapy alone group at 60 days, while the group supplemented with lipoic acid and SOD experienced continued improvement. At both 1 month and 60 days, more patients in the supplemented group than in the physiotherapy alone group reported their neck pain was improved.

Lipoic acid has been shown to decrease age-related memory loss.


[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 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 causes 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.

--- Lipoic acid 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.

- Mahboob, et al. Alpha-lipoic acid-mediated activation of muscarinic receptors improves hippocampus- and amygdala-dependent memory. Brain Res Bul, 2016. ----- This study used aluminum as a neurotoxin to damage the brains of test animals. Aluminum is neurotoxic --- crossing the blood brain barrier and accumulating in the brain and contributing to neurodegenerative disorders characterized by cognitive impairment. This study showed that lipoic acid protected against the aluminum-induced neurotoxicity, and protected the test animals from learning and memory deficits.

The mechanism by which lipoic acid protected the brain was by increasing expression of muscarinic receptor genes in the hippocampus and amygdala. From a NUTRI-SPEC standpoint --- muscarinic receptors are
Parasympathetic cholinergic. The indication is that the cognitive decline and memory loss elicited by aluminum is mediated via ImmunoNeuroEndocrine Stress of the Sympathetic system.

One particular manifestation of aluminum toxicity was an exaggerated fear response. In the lipoic acid treated group, fear extinction memory was “remarkably restored”, and the test animals demonstrated significant reduction of freezing (fear) response. The study concludes that lipoic acid protects against cognitive decline and enhances the cholinergic (anti-Sympathetic stress) system.

- Kahn, et al. The protective effect of alpha-lipoic acid against BPA-induced neurobehavioral toxicity. Neurochem Int, 2018. ----- BPA is a well-known xenoestrogen used in the manufacture of food packaging plastics. It is neurotoxic and causes behavioral deficits. This study tested the hypothesis that lipoic acid supplementation, already shown protective against heart disease, liver disease, diabetes, and neurological debility associated with aging, might also protect against the neurotoxicity of BPA.

It is demonstrated that lipoic acid protects against BPA-induced ROS generation and increased activity glial fibrillary acidic protein. LA also protected against cell death in astrocytes, and increased the neurospecific acetylcholinesterase activity and decreased the monoamine oxidase activity altered by BPA exposure, and protected against BPA-induced oxidative stress. Lipoic acid significantly replenished the declined neurobehavioral and cognitive performances as well as the decreased muscle coordination and alerted short-term recognition memory in mice exposed to BPA.

- Hager, et al. Alpha-lipoic acid as a new treatment option for Alzheimer's Disease --- a 48 months follow-up analysis. J Neural Transm Suppl, 2007. ----- Oxidative stress and neuronal energy depletion are characteristic biochemical hallmarks of Alzheimer's Disease. It is, therefore, conceivable that pro-energetic and antioxidant supplements such as lipoic acid might delay the onset or slow down the progression of the disease.

In a previous study, 600 mg lipoic acid was given daily to 9 patients with AD (also receiving a standard treatment with choline-esterase inhibitors) over an observation period of 12 months. The supplementation led to a stabilization of cognitive functions as demonstrated by constant scores in two neuropsychological tests. In this study, the analysis is extended to 43 patients over an observation period of 48 months.

In patients with mild dementia, the disease progressed extremely slowly in the lipoic acid supplemented group relative to the expected progression of the pathology, and in patients with moderate dementia, the cognitive decline advanced at twice the rate of those with mild dementia, but dramatically
slower than data reported for untreated patients or in patients on choline-esterase inhibitors in the second year of long-term studies.

- **NMDA receptors in the brain** are modulated by endogenous redox agents such as glutathione, lipoic acid, and PQQ.

- Parkinson’s Disease, ALS, Huntington’s Disease, Friedreich’s ataxia, and mitochondrial cytopathies and other neuromuscular diseases share to some extent the final common pathway leading to cell death through either necrosis or apoptosis. Compounds such as creatine monohydrate, and CoQ10 offer substantial neuroprotection against ischemia, trauma, oxidative damage, and neurotoxins. Miscellaneous agents, including alpha lipoic acid, beta-hydroxy beta-methylbutyrate, riboflavin, and nicotinamide, have also been shown to improve various metabolic parameters in brain and/or muscle.

- Lipoic acid is considered a universal antioxidant because it is an amphipathic substance. Lipoic acid and its reduced form, dihydrolipoic acid, act against ROS, reducing oxidative stress. Therefore, this antioxidant has been used in the treatment of many diseases, including a new perspective for the treatment of Parkinson’s Disease (PD).

- Coadministration of lipoic acid, a thiol antioxidant, abolished the toxic effects of a single dose of MPTP. Lipoic acid also attenuated dopaminergic cell loss seen after subchronic MPTP treatment. MPTP triggers death signaling pathway in vivo, and thiol antioxidants such as lipoic acid terminate this cascade and afford neuroprotection.

- An important biochemical feature of PD is a significant early depletion of the thiol antioxidant glutathione, which may lead to the degeneration of ROS, mitochondrial dysfunction, and ultimately to subsequent neuronal cell death. Pretreatment of PC12 cells with lipoic acid acts to prevent depletion of glutathione content and preserves the mitochondrial complex 1 activity which normally is impaired as a consequence of glutathione loss in PD.

- Lipoic acid and acetyl-l-carnitine are 2 mitochondrial antioxidants studied in a chronic rotenone-induced cellular model of PD. Both nutrients were found to be protective against mitochondrial dysfunction, oxidative damage, and accumulation of alpha-synuclein and ubiquitin. Most notably, it was found that combined lipoic acid and acetyl-l-carnitine worked at 100 to 1,000 times fold lower concentrations than they did individually. Pretreatment with combined lipoic acid and acetyl-l-carnitine increased mitochondrial biogenesis and decreased production of ROS through the up-regulation of peroxisome proliferator-activated receptor-gamma coactivator 1 alpha as a possible underlying mechanism. This study provided important
evidence that combining mitochondrial antioxidants at optimal doses might be an effective and safe prevention strategy for PD.
Supplementation:

- 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 shown consistently beneficial anti-inflammatory effects in a broad array of pathological conditions --- from vulvodynia to diabetic neuropathy to Alzheimer's. --- 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.

- Another qualitative consideration concerns the lipoic acid that you see as an ingredient in both your ADAPTO-MAX (Diphasic A.M.) and OXY-MAX (Diphasic P.M.) products. Alpha lipoic acid is available as a nutrient in both water soluble and fat soluble forms. Both forms are truly amazing in their biological effect, yet there are certain aspects of the effects of alpha lipoic acid which derive primarily from the fat soluble form. With your Diphasic Nutrition Plan you are getting alpha lipoic acid in both the water soluble (Diphasic A.M.) and in fat soluble (Diphasic P.M.) forms. Probably at least 90% of the alpha lipoic products available to you are in the water soluble form only. Only with NUTRI-SPEC can you be sure to be getting all the beneficial effects of alpha lipoic acid.