

Lipoic acid is known by a variety of other names. These include alpha-lipoic acid, thioctic acid, 1,2-dithiolane-3-pentanoic acid, 1,2-dithiolane-3-valeric acid, as well as 6,8 thioctic acid. Scientists and health professionals have attempted to categorize it as a glucose optimizer, antioxidant, neurological enhancer, mitochondrial recharger and even an anti-aging remedy. The fact of the matter is that it performs all of these functions to varying but credible degrees. Perhaps this is the reason why lipoic acid is one of the few supplements to slowly and gradually emerge from the fringes of alternative health circles to occupy a solid foothold among health professionals and astute supplement-users alike. Slowly and gradually are operative words here because lipoic acid is the type of nutrient that has demonstrated its worth in a subtly ubiquitous fashion, quietly appearing and reappearing in a variety of crucial metabolic functions.

What Is Lipoic Acid?

Lipoic acid is, biochemically speaking, a sulfur-containing coenzyme which was isolated in 1950 by Dr. Lester Reed of the Department of Chemistry at the University of Texas. From 1950 until the late 1980's, lipoic acid was studied

almost exclusively for its effect on glucose and the cellular mechanism of action that made such an effect possible. Since then, it has come to be categorized under the ever-expanding definition of antioxidant, and the focus of its study has broadened to include these properties. Listed below are the most abundant dietary sources of lipoic acid found in nature:³⁷

Dietary Sources of Lipoic Acid		
Food	Serving	Lipoic acid/per serving (in micrograms)
Beef kidney	3 ounces (85g)	32
Beef heart	3 ounces (85g)	19
Beef liver	3 ounces (85g)	14
Spinach	1 cup raw (30g)	5
Broccoli	1 cup raw (71g)	4
Tomato	1 medium (123g)	3
Peas	1 cup raw (145g)	7
Brussel sprouts	1 cup raw (88g)	3
Rice bran	1 cup (118g)	11
Egg yolk	1 large (17g)	0.3

At this point it must be noted that in the majority of human clinical trials, the amount of lipoic acid used is between 200 and 800 milligrams.

What Does Lipoic Acid Do?

The fundamental pillars of lipoic acid's overall function can arguably be simplified down to two; a glucose metabolizer and an antioxidant. Lipoic acid has also been examined for its ability to generally enhance the mitochondria, to improve neurological function, and to provide an important degree of overall resistance against the aging process. However, these added benefits can effectively be categorized as residual advantages or sub-categories of the two all-encompassing capacities of glucose metabolism and antioxidant activity.

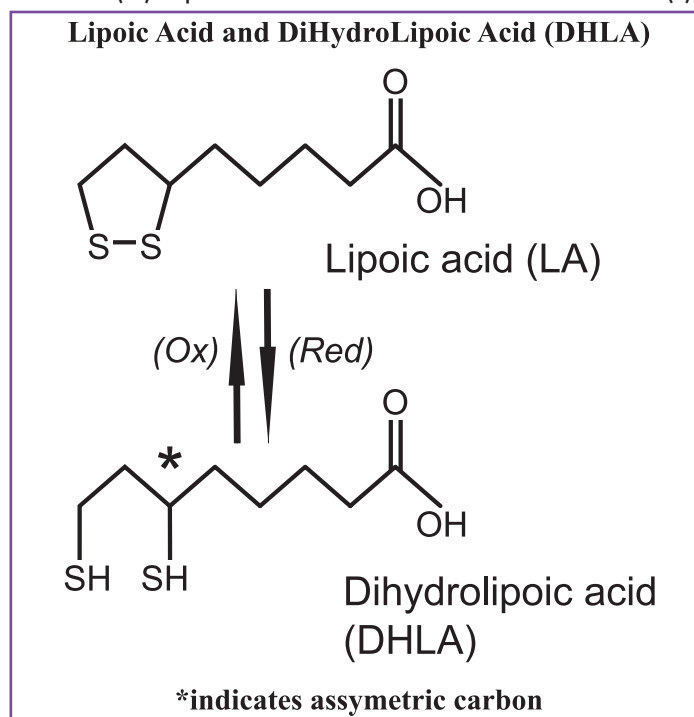
Lipoic acid is generally known for being essential in the oxidation of alpha-keto acids in metabolism, especially pyruvate. It is more specifically regarded as a coenzyme in the oxoglutarate dehydrogenase complex of the citric acid cycle. Furthermore, as nutrients and subsequent micronutrients (including antioxidants) are converted for usage at the cellular level by the mitochondria, supplemental lipoic acid simultaneously becomes converted by the mitochondria to its effective metabolite, dihydrolipoic acid (DHLA).

Lipoic acid is unique among anti-oxidants in that it is both water-soluble and fat-soluble. Like the thiol antioxidant

glutathione, lipoic acid is part of a redox couple, with lipoic acid itself being the oxidized precursor of the reduced form metabolite known as DiHydroLipoic Acid (DHLA). Dietary sources of lipoic acid, most notably red meat and spinach, are readily converted to DHLA by the pyruvate dehydrogenase enzyme complex (PDH). Unlike glutathione, for which only the reduced form (GSH) is an anti-oxidant, both the oxidized and reduced forms of lipoic acid are anti-oxidants. Lipoic acid is effective against hydroxyl radicals, hypochlorous acid and singlet oxygen, but not against hydrogen peroxide or superoxide. DHLA, on the other hand, is effective against hydroxyl, superoxide, peroxy reactive oxygen species and hypochlorous acid, but not against hydrogen peroxide or singlet oxygen. From a limited perspective, DHLA's antioxidant properties are superior to those of lipoic acid. DHLA can regenerate Vitamin C and Vitamin E from their oxidized forms.¹ Furthermore, DHLA (like coenzyme Q₁₀) has two hydrogens to donate in the contention against Reactive Oxygen Species (ROS), thus possessing the ability to neutralize free radicals without becoming one in the process.

What is Lipoic Acid's Overall Mechanism of Action?

Lipoic acid is absorbed from the small intestine and distributed to the liver via the portal circulation and to various tissues in the body via the systemic circulation. It is comprised of two isomers that are also enantiomers. One is R(+)- lipoic acid and the other is S(-)- lipoic acid. Only the natural R(+)- lipoic acid enantiomer is bioactive. The S(-)-



lipoic acid enantiomer is purely an artificial creation that only exists as a result of the manufacturing process to create commercial lipoic acid supplements. R(+)-lipoic acid readily crosses the blood-brain barrier and is found, after its distribution to the various body tissues, intracellularly, intramitochondrially and extracellularly.² It has been found to exhibit antioxidant activity in all of these environments, not to mention the aqueous and lipophilic ones.³

As previously mentioned, R(+)-lipoic acid is metabolized to its reduced form, dihydroLipoic acid (DHLA), by the pyruvate dehydrogenase enzyme complex (PDH). DHLA forms a redox couple only with the R(+)-lipoic acid enantiomer. It is also metabolized to lipoamide, which functions as the R(+)-lipoic acid cofactor in the multienzyme complexes that catalyze the oxidative decarboxylations of pyruvate and alpha-ketoglutarate.⁴

Exogenous lipoic acid has been shown to increase ATP production and aortic blood flow during reoxygenation after hypoxia in a working heart model. It is thought that this is due to its role in the oxidation of pyruvate and alpha-ketoglutarate in the mitochondria, which enhances energy production. This activity, probably more so than its antioxidant properties, may account for its possible benefit in diabetic polyneuropathy.⁵

R(+)-lipoic acid has been found to decrease urinary isoprostanes, Oxidised LDL Cholesterol (O-LDL) and plasma protein carbonyls - which are all markers of oxidative stress.⁶ With regard to R(+)-lipoic acid's vaunted antioxidant capability, it appears to fundamentally initiate the recycling of other pivotal biologic antioxidants, particularly vitamins E and C, glutathione and coenzyme Q₁₀. Finally, both R(+)-lipoic acid and DHLA are effective in the specific chelation of heavy metals such as zinc, iron and copper.⁷

PART ONE: R(+)-ENANTIOMER VS S(-)-ENANTIOMER; Why This Distinction is So Important.

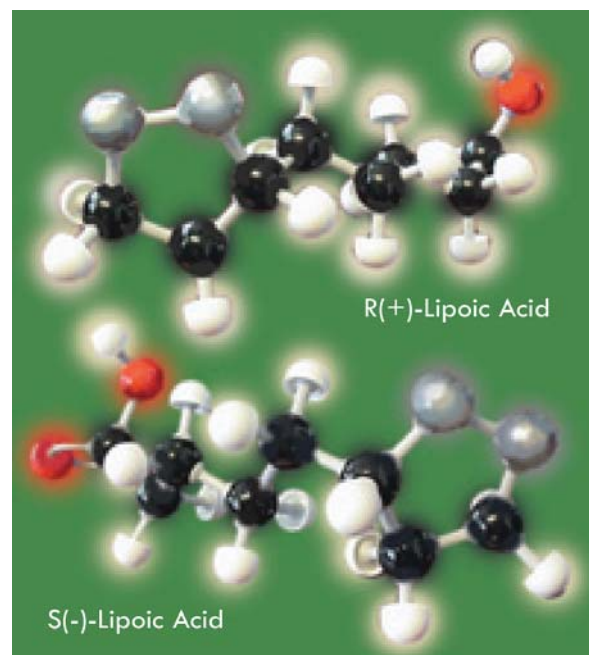
Prior to any discussion about the importance of one enantiomer over another, it is important to explicate the concept of what these enantiomers are based upon. That concept is called chirality, and it is found throughout the natural world. Very simply put, chirality means "handedness" - meaning the existence of left/right opposition. For example, your left hand and right hand are mirror images and therefore "chiral". To fully appreciate the

potency of this metaphor, it is important to emphasize how each of your hands have identical numbers of fingers, thumbs and palms, yet their relative arrangement makes them different in both structure and function. The term Chiral is derived from the Greek name kheir meaning "hand" and apparently was coined by Lord Kelvin in 1904, in his "Baltimore Lectures on Molecular Dynamics and the Wave Theory of Light" in which he stated ..."I call any geometrical figure, or group of points, chiral, and say it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself." Perhaps a more ideal metaphor can be borrowed from Lord Kelvin himself: try to imagine the physical existence of a mirror image of any object. Although superficially identical, the complete structural arrangements of the two objects would run inversely to each another. As the number of carbons with asymmetry (chirality) increase in a molecule, the number of possible optical isomers (enantiomers) also increases. With one asymmetric carbon, 2 isomers...with two asymmetric carbons, 4 isomers, with three asymmetric carbons, 8 isomers...that is, the number of isomers is 2^n , where n = number of asymmetric atoms.⁸ Every time such a carbon is artificially synthesized, a pair of isomers (or enantiomers) is created - one natural and bioactive, the other artificial and for the most part, relatively inert.

Vitamin E is a popular and excellent example of the importance of chirality. Vitamin E contains three asymmetric carbons allowing for up to eight possible optical isomers (or enantiomers) to be formed (see Holistic International Volume 1 Issue 4). These are the natural "d" forms of alpha-tocopherol, beta-tocopherol, gamma-tocopherol, and delta-tocopherol, as well as their artificial mirrored counterparts, namely the "dl" versions of the aforementioned tocopherols. The latter form comprises half the vitamin E content of much of the commercially available vitamin E supplements because they are the result of artificially synthesized versions of this vitamin. Natural sources of vitamin E, such as soy, palm or wheat germ oil will contain only the natural, bioactive "d" versions. In the case of vitamin E, however, the synthetic "dl" enantiomers which comprise half of any supplement utilizing artificial sources of this vitamin are not specifically harmful. They are simply not absorbed as well as the "d" enantiomers, in effect "watering down" the vitamin E supplement.

There are other examples where artificial enantiomers can in fact be harmful. One such example is the distinction between the natural cis isomer and the synthetic trans isomer of polyunsaturated fatty acids. When the natural cis isomer is exposed to the heat and pressure of the manufacturing

process of hydrogenated vegetable oils, the cis isomer is actually twisted out of its original proportions, creating the artificial trans isomer. The difference between the natural cis isomer and the trans isomer is simply a matter of alternating a point of reference within the respective atomic structures of each fatty acid. The problem, however, is that even such a simple alteration at the molecular level completely alters the effect of the fatty acid in the human body. This phenomenon was aptly demonstrated in a truly massive study involving 80,000 nurses in the United States. The purpose of this study was to determine if the type of fat in a diet was more important than the actual amount of fat with specific regards to heart health. Not only did this study determine the former to be true, but it also found that the natural cis isomer also offered a degree of protection against the risk of Type II diabetes, while the artificial trans isomer actually increases that risk.⁹



The Two Lipoic Acids

Now that we have grasped the macro explanation of why the natural enantiomer is the perfunctory first choice for most molecules, a detailed micro explanation of why it is preferable in the case of lipoic acid is also in order.

As mentioned earlier, lipoic acid is converted in the mitochondria into its effective metabolite dihydrolipoic acid (DHLA). The specific enzyme that is actually responsible for this conversion process is called the pyruvate dehydrogenase enzyme complex or PDH. In order for this conversion process to be initiated, PDH must recognize and be stimulated by lipoic acid. Since the PDH is purely endogenous (and therefore natural), it will easily recognize the natural R(+)- enantiomer and follow suite with the

conversion to dihydrolipoic acid (DHHLA). The S(-)-enantiomer on the other hand, being an artificial counterfeit with no real place in nature, will not be so easily recognized by PDH for conversion to DHHLA. This is not to say that the ersatz S(-)- enantiomer isn't capable of managing at least some conversion to dihydrolipoic acid, because it does possess enough of a similarity to the R(+)- enantiomer to do just that. However, it cannot do it very well or in quantities anywhere approaching that of the natural R(+)-enantiomer. The fact of the matter is that the rate at which the PDH enzyme can convert the R(+)- enantiomer into DHHLA is at least twenty-four times faster than the rate at which it can do the same for the S(-)- form.¹⁰

In some types of cells, the PDH enzyme will refuse to accept the S(-)- enantiomer for DHHLA conversion altogether. Furthermore, high quantities of the S(-)- enantiomer will actually compromise the ability of the PDH enzyme to convert even the natural R(+)- enantiomer into dihydrolipoic acid (DHHLA).¹¹ Pursuant to the S(-)- enantiomer's handicapped ability to recruit the mitochondrial enzyme complex (PDH) for the conversion to DHHLA, S(-)- lipoic acid must resort to unorthodox means to manage even its very limited conversion rate. To do this, S(-)- lipoic acid effectively usurps the activity of an enzyme which was never designed for DHHLA conversion, and that enzyme is called glutathione reductase. This enzyme is of course essential for the recycling of another critically ubiquitous antioxidant known as glutathione, from its reduced (GSH) form to its oxidized (GSSH) form. If the resources of glutathione reductase are continuously taxed by the limited conversion to DHHLA of the S(-)- enantiomer of lipoic acid, then logic dictates that this enzyme's ability to recycle glutathione will be compromised. Any action that compromises the operation of glutathione is one that ought to be avoided. R(+)- lipoic acid, for its part, imposes no such strains on glutathione reductase and is readily accepted by the PDH mitochondrial enzyme complex to perform the function assigned to it by evolutionary nature - to convert to DHHLA and begin its mitochondrial cascade of events.

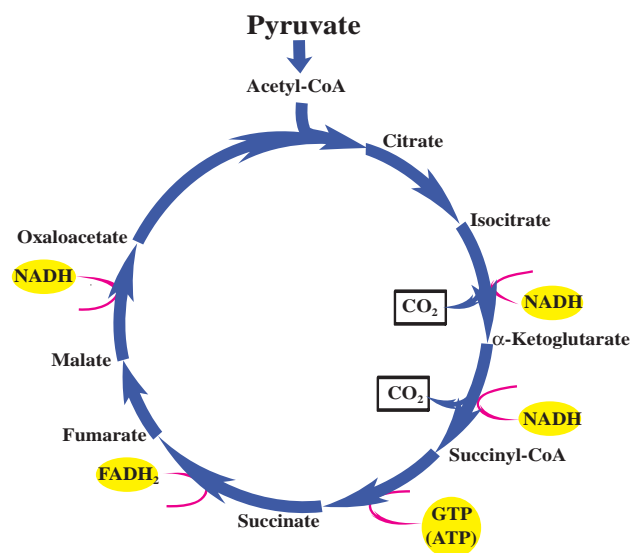
Dihydrolipoic Acid (DHHLA) Is The Next Logical Step - Or Is It?

There is a great deal of information and research to suggest that dihydrolipoic acid (DHHLA) is in fact the active metabolite of lipoic acid. It therefore stands to reason that if DHHLA is the active ingredient of lipoic acid, why not simply isolate it (in supplement form) and then take it in place of lipoic acid? Although simplistic, this is not an unfair question.

The answer is essentially twofold; firstly, there seems to be a fairly clear delineation of duties between R(+)-lipoic acid and dihydrolipoic acid (DHHLA). This delineation of duties is based on the fact that R(+)-lipoic acid is effective against singlet oxygen free radicals where DHHLA is not, while DHHLA can be effective against hydrogen superoxide free radicals where R(+)-lipoic acid is not.¹² Right from the beginning, supplemental DHHLA in its isolated form automatically negates the ability to quench singlet oxygen free radicals, compromising the spectrum of lipoic acid's central role as an antioxidant.

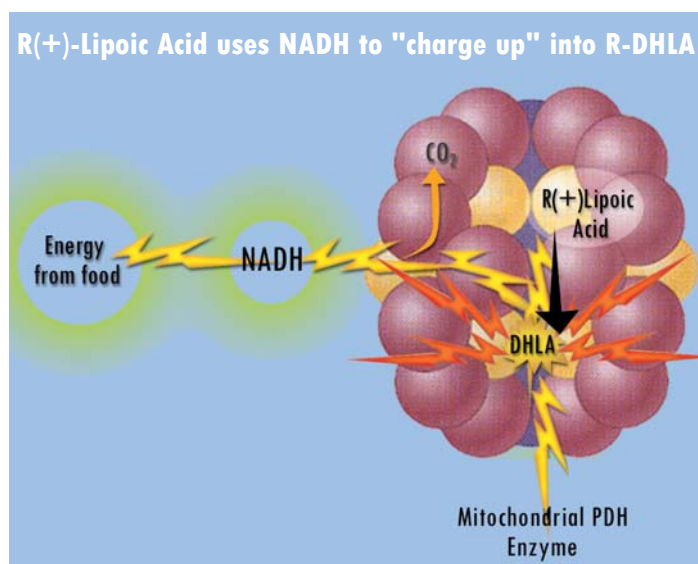
R(+)-lipoic acid is effective against singlet oxygen free radicals where DHHLA is not

Dihydrolipoic acid's shortcomings are even more glaringly apparent when we consider the other central role of its precursor(R+lipoic acid), namely that of glucose metabolism. This happens as a result of the decarboxylation process that oxidates pyruvate and alpha-ketoglutarate using the NAD⁺/NADH conversion process as a catalyst. It is the R(+)-enantiomer of lipoic acid that is responsible for modulating this NAD⁺/NADH conversion process.¹³ This conversion process is a direct catalyst (and as a result a significant influence) for the conversion of pyruvic acid to lactic acid prior to its oxidation by acetyl-coenzyme A in addition to its subsequent participation in the Krebs cycle.¹⁴ The Krebs Cycle is one of the body's fundamental biological operations for glucose metabolism, and as previously stated, relies heavily on the NAD⁺/NADH conversion process as a catalyst, a process mediated not by DHHLA but by R(+)-lipoic acid.



The Krebs Cycle

A further examination of the NAD⁺/NADH conversion process reveals more shortcomings of supplemental dihydrolipoic acid taken in the absence of its R(+)-lipoic acid precursor. Excess electrons from the NAD⁺/NADH conversion process are utilized by the pyruvate dehydrogenase mitochondrial enzyme complex (PDH) to convert R(+)-lipoic acid into dihydrolipoic acid (DHLA). Consuming supplemental R(+)-lipoic acid provides the body with more of this molecule than is immediately required for mitochondrial energy production. The result is that more DHLA is synthesized from it, and this 'surplus' dihydrolipoic acid is simply released into the cell and subsequently to the surrounding fluid where it can be systemically utilized for its antioxidant cascade.¹⁵ Furthermore, proper and efficient use is being made of the excess electrons by the pyruvate dehydrogenase mitochondrial enzyme complex (PDH) to convert R(+)-lipoic acid into dihydrolipoic acid (DHLA). However, if there is no R(+)-lipoic acid for PDH to convert to DHLA, what happens to the extra electrons from the NAD⁺/NADH conversion process?



What happens is that these excess electrons are greeted by a PDH mitochondrial enzyme complex that cannot use them, because it is missing the necessary R(+)- lipoic acid it needs to produce DHLA. The end result is that these surplus electrons simply spin out of control and form superoxide radicals from inside the mitochondria itself.¹⁶

These electrons that we are speaking of are all a result of the conversion of Nicotinamide Adenine Dinucleotide from its oxidized form (NAD⁺) to its reduced form, namely NADH. The "H" simply represents a hydrogen atom, itself consisting of one proton and one electron. This extra hydrogen atom is usurped by the PDH mitochondrial enzyme to convert R(+)- lipoic acid into dihydrolipoic acid (DHLA). A concurrent result, however, is an NAD⁺/NADH ratio that is

more favourable to NAD⁺. This is important for a number of reasons, not the least of which is that NAD⁺ is the form of Nicotinamide Adenine Dinucleotide that is readily available as an energy source for the mitochondria. Furthermore, improving the ratio of NAD⁺ to NADH has direct implications in diabetes. This is due to the close association between an unfavourable ratio of NAD⁺ to NADH and an inhibition of cellular glucose uptake and utilization.³⁸ In fact, such a ratio has been linked not only to diabetes but also to ischemia conditions as well. Furthermore, a low NAD⁺/NADH ratio also promotes the formation of Reactive Oxygen Species (ROS) and can be traced to a number of other unfavourable metabolic conditions.³⁹

Glucose metabolism relies heavily on the NAD⁺/NADH conversion process as a catalyst, a process mediated not by DHLA but by R(+)-lipoic acid

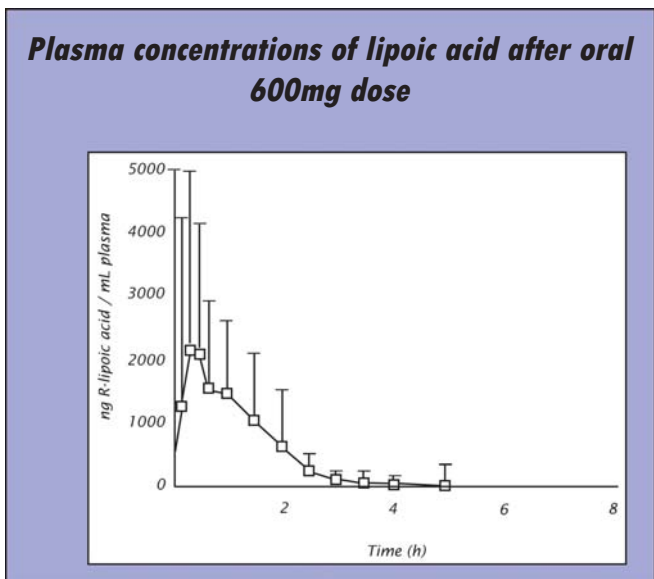
Then there is the issue of bioavailability. Even R(+)- lipoic acid itself is a very unstable molecule that requires a careful, high-quality approach to manufacturing in order to insure efficacy. Its melting point is a surprisingly low 46-49 degrees Celsius.¹⁷ This is an important point to consider when the average human body temperature is approximately 36.5 degrees Celsius. Using these facts as a source of concern for the stability of dihydrolipoic acid as a stand-alone supplement is by no means unwarranted.

GLUCOSE METABOLISM; Longer is Better

Lipoic acid was first isolated in order to study its effects on glucose metabolism, which is an extraordinary capability for an antioxidant. As a matter of fact, R(+)- lipoic acid's insulin sensitivity-enhancing capabilities are so potent that it is prescribed as a drug for Type II diabetics in Germany.¹⁸ The heart of this potential seems to lie in the ability of R(+)-lipoic acid to increase the cell's basal glucose uptake capacity.¹⁹ This means that R(+)-lipoic acid can open the cells insulin receptors known as transmembrane receptors (belonging to the large class of tyrosine kinase receptors)- even in the absence of insulin! R(+)-lipoic acid therefore increases insulin sensitivity from the cellular surface, which is where the transmembrane receptors are located-and not at the mitochondrial level. (Incidentally, this latter point is yet another reason why DHLA alone, which begins its work at the mitochondrial level, would be void of R(+)-lipoic acid's glucose metabolism benefits).

One study of 20 type II diabetics found that oral administration of 1,200 mg of lipoic acid for 4 weeks significantly improved measures of glucose metabolism.²⁰ Another placebo-controlled human study of 72 type II diabetics found that oral lipoic acid at doses of 600 mg/day, 1,200 mg/day or 1,800 mg/day for 4 weeks improved insulin sensitivity by 25%.²¹ It is also more than noteworthy to emphasize that all of these studies were conducted using the racemic form of lipoic acid, 50% of which is composed of the artificial S(-)- enantiomer. Insofar as insulin sensitivity is concerned, this ersatz lipoic acid twin (depending on which cell is examined) is either only partially effective²² or not effective at all.²³ Increased insulin resistance (or inversely, decreased insulin sensitivity) develops to some degree in most people in a manner concurrent with the aging process. R(+)- lipoic acid's glucose-dispersing abilities are therefore one of the reasons why it has become almost standard-issue in any anti-aging regimen.

However, in order for type II diabetics to seriously consider R(+)-lipoic acid as a possible alternative to traditional forms of treatment, it must offer sustained relief over significant periods of time. This would allow these people the freedom to fulfill their daily responsibilities at work or school, etc, as unencumbered as possible by the constant need for self-medication. One of the current limitations of R(+)-lipoic acid is the speed at which it is absorbed by the bloodstream. The plasma half-life of R(+)-lipoic acid is generally considered to be around 22 minutes. In fact, studies have shown that R(+)- lipoic acid is not only rapidly and completely absorbed into the bloodstream between 30 minutes to an hour after ingestion, but that its peak plasma levels decline equally sharply, dropping 50% within thirty minutes of reaching that peak.²³

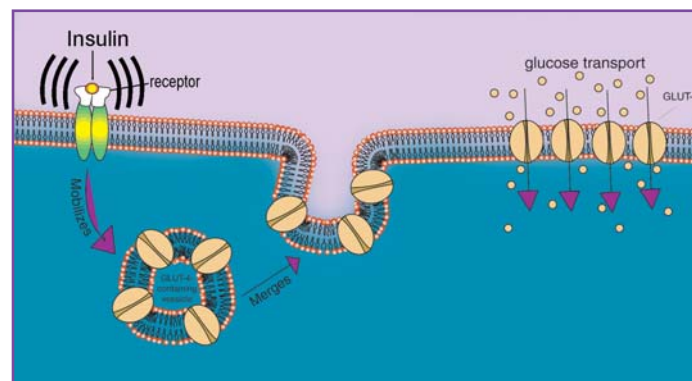


Not only does this not bode well for type II diabetics, but it also spells inconvenience for anyone looking at R(+)-lipoic acid as an alternative (or adjunct) to standard pharmaceutical treatments for metabolic syndrome, or Syndrome X. By some estimates, the latter may affect as much as 25% of the North American population!²⁴ Insulin resistance is the most significant common denominator between the two conditions, and Syndrome X is a medically expedient term defined by the American Heart Association as "a multiplex risk factor for cardiovascular disease".²⁵ The spectrum of conditions encompassed by this definition is as follows:²⁶

- > Abdominal obesity
- > Atherogenic dyslipidemia
- > Raised blood pressure
- > Insulin resistance \pm glucose intolerance
- > Proinflammatory state
- > Prothrombotic state

There is obviously a great deal of overlap between these conditions, none more so than with insulin resistance.

As potent as R(+)-lipoic acid is for increasing insulin sensitivity, its short plasma half-life is an Achilles heel that needs to be addressed. The good news for diabetics is that it is being addressed, and the results have produced several lipoic acid formulations with various excipients or delivery systems that prolong the enhanced sensitivity of the insulin receptors.



How the cell takes in blood sugar

The human trials involving these formulations have demonstrated a dramatic and sustained lowering of blood glucose levels. One such formulation was composed of 300 milligrams of racemic lipoic acid in an excipient base of calcium phosphate, starch, cellulose ethers polycarboxylic acid, and magnesium stearate. These tablets were administered to a group of eight type II diabetic patients

whose ages ranged from 45 to 82, with each patient given 2 such tablets in the morning before breakfast and one more 6 to 8 hours later. The average glucose level of these patients prior to the administration of the controlled release racemic acid formulation was 176.5 mg/dl. After the treatment, that average glucose level dropped to 128.5 mg/dl, an average decrease of 48 mg/dl or just over 27%.²⁷ A follow-up study using the same formulation and procedure among three more type II diabetic patients produced even more impressive results. Their average blood glucose level dropped from 342 mg/dl to 158 mg/dl, an average decrease of 184 mg/dl or just over 46%.²⁸

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It must be noted that these studies were conducted under the auspices of the corporation securing the patent for controlled release lipoic acid. However, there have been more objective, independent studies conducted as well. One of the most encompassing of these was conducted at the Northern California Diabetes Institute at the Seton Medical Center in Dale City, California. Its intentions were two-fold: to determine the pharmacokinetics of a controlled-release lipoic acid supplement and then to determine its safety, tolerability, and effectiveness in patients with type 2 diabetes.

The first part of the study involved 12 human subjects of average health receiving either a single 600 milligram dose of controlled release lipoic acid or a single dose of conventional lipoic acid of the same potency. The plasma profile of lipoic acid was determined 24 hours after the administration of the doses to each group, and pharmacokinetic analyses were then performed. The time to maximal plasma concentration (of lipoic acid) was measured for each group, and the controlled release lipoic acid group measured 1.25 hours (on average) to reach maximal plasma concentration.²⁹ This was approximately 2.5 times longer than the time required for the conventional lipoic acid to reach maximal plasma concentration.³⁰

For the second part of the study examining safety, tolerability and efficacy for diabetics, 21 patients with type 2 diabetes were given 900 mg of controlled-release lipoic acid daily for 6 weeks, followed by 1,200 mg of controlled-

release lipoic daily for an additional 6 weeks. Active treatment was followed by a 3-week washout period. Throughout the study, patients continued to take their prestudy antidiabetic medications, which included metformin (Glucophage[®]), sulfonylureas (Amaryl[®], glyburide, and Glucotrol[®]), acarbose (Precose[®]), troglitazone (Rezulin[®]), and insulin (either as monotherapy or in combination). Controlled release lipoic acid was evaluated for safety and tolerability as well as for effects on glycemic control. There were no appreciable side effects or changes in either liver or kidney function or hematologic profiles noted after the administration of the controlled-release lipoic acid.³¹ Furthermore, in 15 of the 21 type II diabetes patients, plasma fructosamine levels were reduced from an average of 313 micromoles per litre of plasma to an average of 283 micromol/L after 12 weeks of treatment with controlled-release lipoic acid.³²



This demonstrates the capability of lipoic acid (or more accurately R(+)-lipoic acid) to be an effective adjunct to conventional type II diabetes medication as well as a possible alternative on its own, which was itself demonstrated in the previously-mentioned patent application studies.

ANTIOXIDANT ACTIVITY; The Centerpiece Can Now Play Longer

The importance of R(+)-lipoic acid as an antioxidant requires no further elaboration here. However, it is definitely worth noting that just as the prolonged effects of R(+)-lipoic acid's glucose metabolizing properties can benefit diabetics, the prolonged effects of its antioxidant potential can benefit everyone.

The body's intake and production of free radicals is obviously a ceaseless, lifelong process, comparable to (and partly dependent on) methylation in its frequency. This means that under optimal circumstances, the body would require constant protection from an antioxidant as critical as R(+)-lipoic acid. However, we are all too familiar by now with R(+)-lipoic acid's notoriously short plasma half-life. In fact, conventional lipoic acid supplements are almost entirely flushed out of the body within three hours of taking them.³³

So unless we consume additional R(+)-lipoic acid capsules every three hours, we are only protecting ourselves for a small part of the day. The importance of continuous protection was demonstrated by an experiment in which racemic lipoic acid was administered to laboratory rodents in large, single-serving, daily dosages. The scientists then subjected them to an artificially-induced "stroke" by cutting off their blood supplies. When the animals received their lipoic acid two hours before their blood supplies were interrupted, it provided them with a measure of protection from significant brain cell death. This protection was not

seen in the laboratory animals not administered with the supplement.³⁴ However, lipoic acid failed to offer any significant neural protection if it was administered either four or six hours prior to the artificially-induced "strokes".³⁵

Conventional lipoic acid supplements are almost entirely flushed out of the body within three hours of taking them

The aforementioned experiment is testimony not only to R(+)-lipoic acid's legendary capacity as an antioxidant, but also for the additional protection it provides through its ability to chelate heavy metals such as iron, copper, and cadmium, which can turn relatively 'mild' free radicals into more insidious ones.³⁶ It is this metal chelating facet of the antioxidant cascade that is most directly associated with R(+)-lipoic acid's lesser known ability to protect brain and nerve cells. As we have seen, the importance of the consistency of that protection is difficult to understate.

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