

# Stabilized R-Lipoic Acid

The Highly Effective Form of Lipoic Acid • By Cristiana Paul, M.S.

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## Lipoic Acid Chemical Forms: the R and S Isomers

Alpha-Lipoic Acid (or thioctic acid) is synthesized from the amino acid Cysteine and Octanoic acid in plants and animals as both the R and S isomer with a great majority as R-Lipoic Acid and only trace amounts of S-Lipoic Acid.

When Alpha-Lipoic Acid is synthesized in a laboratory, a 50/50 racemic mixture of the R and S enantiomers results in what we call R/S Lipoic Acid, which is the most popular form of commercially available Lipoic Acid (also named RAS Lipoic Acid or All Racemic Lipoic Acid). Our patients know it as simply Alpha Lipoic Acid. New technological advancements have allowed for the stabilization and isolation of the RLA (R-Lipoic Acid isomer), which is believed to account for all the benefits seen from studies with R/S Lipoic Acid. Supplementing with pure RLA, thus eliminating the presence of SLA (S-Lipoic Acid isomer), creates new opportunities for intensive nutritional support because SLA is believed to interfere with the effectiveness of RLA.<sup>16-21, 25</sup>

## How is Stabilized R-Lipoic Acid Different From Other R-Lipoic Products on the Market?

R-Lipoic Acid is a highly unstable compound that easily polymerizes into a sticky rubber or glue-like substance if it is not prepared, stored and processed correctly. This may adversely affect bioavailability. Stable RLA is a non-hygroscopic, non-polymeric potassium salt form of RLA. The capsules are heat stable, characterized by fast dissolution rates, high solubility and absorption. They are also free of residual solvents and moisture.

There are wide variations in the R/S ratios and total polymer contents of raw material and finished products now on the market. Few supplement companies have experience with RLA and are unaware of the myriad of problems associated with its encapsulation and stability. Designs for Health's Stabilized R-Lipoic Acid is the only stable and highly bioavailable form of R-Lipoic Acid available on the market.

## R-Lipoic Benefits

Lipoic acid, also known as thioctic acid, is a disulfide compound that is a cofactor in vital energy-producing reactions in the body. It is also a potent biological antioxidant, both water and fat soluble.

It is made endogenously in humans and so it is not an essential nutrient. However, many physiological states, such as excessively high blood glucose levels, diabetic polyneuropathy, cataract, liver pathologies and toxic metal load, make Lipoic acid conditionally essential. In addition, extensive research indicates that the many roles of alpha-lipoic acid may result in various health benefits, as reviewed below.

R/S-Lipoic acid has been studied for over 30 years and it is approved in Germany as a drug for the treatment of polyneuropathies, such as diabetic and alcoholic polyneuropathies, and liver disease.<sup>1</sup>

Recent studies have investigated the effectiveness of RLA versus SLA forms in order to identify their specific effects. It was suspected that, RLA being the majority of the natural form produced in the body, would have a stronger impact than SLA and the results of the research have indeed confirmed this.<sup>16-21, 25</sup>

## Bioavailability

Compared to SLA, RLA causes 50% higher peak plasma levels of lipoic acid and 60-85% higher total absorption.<sup>12</sup> Feeding lipoic acid to animals at risk of cataract caused a 2-7 fold higher uptake of RLA versus SLA in the lens content of lipoic acid, and reduced the development of experimentally produced cataract by 50%.<sup>19</sup>

## Boosts Energy Production/Mitochondrial Cofactor

RLA is the majority of lipoic acid found in nature and therefore likely to fit better as a cofactor for mitochondrial enzymes pyruvate and alpha-ketoglutarate dehydrogenase.<sup>5</sup> SLA cannot bind well to these enzymes and actually inhibits them.<sup>20</sup> Thus the S-form can oppose the action of the R-form. In the aging rat heart, RLA stimulated ATP production, whereas SLA inhibited it.<sup>3</sup>

RLA supplementation improves metabolism, measured as oxygen consumption in liver cells, and improves ambulatory activity in supplemented animals, bringing old treated animals to the level of young animals.<sup>3</sup> Pre-treatment of brain cells with RLA leads to the restoration of the mitochondrial activity lost due to glutathione depletion.<sup>6</sup>

## Enhanced Glucose Metabolism

RLA, significantly increases insulin sensitivity, glucose transport, metabolic rate and reduces the gain in body fat associated with aging.<sup>10-11</sup> R-Lipoic Acid has insulin-mimetic effects in glucose uptake in insulin resistant cells and may have therapeutic implications in restoring glucose availability in tissues such as the skeletal muscle.<sup>13, 16</sup>

The RLA was found to enhance insulin-stimulated glucose transport and non-oxidative/oxidative glucose metabolism by as much as 64%, while SLA had no effect. Also, RLA decreased insulin by 17% while SLA increased it by 15%.<sup>16</sup>

RLA, through its positive effects on cellular energy metabolism, attenuates metabolic dysfunction associated with advanced glycation end products (AGEs). AGEs accumulate on long-lived proteins, including beta-amyloid plaques in Alzheimer's disease and contribute to neuronal dysfunction and cell death.<sup>21</sup>

## Antioxidant Properties

RLA increases cellular and mitochondrial antioxidant activity, and was able to eradicate the age related changes in animal models. This effectively attenuates the reported age-related increase in oxidative stress.<sup>3</sup>

RLA significantly increases or recycles other antioxidants including Coenzyme Q10, vitamin C, vitamin E and glutathione.<sup>3, 5, 6, 11</sup> RLA protects lipids against peroxidation and reverses stress damage in the heart.<sup>7</sup>

## Anti-inflammatory Effect

RLA, a membrane permeable antioxidant, prevents the up-regulation of the AGE-induced gene expression responsible for regulating nitric oxide (NO) production. NO oxidizes nitrates and proteins which are markers of a chronic neuroinflammatory condition. This mechanism is relevant for Alzheimer's disease and for many chronic inflammatory conditions.<sup>24</sup> RLA reduces inflammation, and is more potent by a factor of 10 over R/S-LA.<sup>17</sup>

## Metal Chelator

RLA was more effective than the SLA in a battery of metal chelation tests. One hypothesis of the cause of diabetic complications involves overloading by transition metals which implicates the RLA as more effective in treating diabetic neuropathy.<sup>2</sup>

## Neuroprotection

RLA improves memory, reverses cognitive dysfunction, and protects the brain from neurodegeneration associated with aging. This may be due to its effect on increased ATP production, chelating, antioxidant and anti-glycating capacity.<sup>6, 7</sup>

## Summary of SLA (S-Lipoic Acid) Properties

Until recently it was believed that SLA was physiologically inactive. Results from studies performed in vitro and with animals comparing the R with the S or R/S LA are warranting the use of pure RLA over the racemic ALA, whenever possible. SLA cannot bind with critical mitochondrial enzymes and inhibits ATP production.<sup>20</sup> At high concentrations, S-Lipoic acid inhibits mitochondrial metabolism. It is metabolized in the outer cell membrane or cytoplasm which may interfere with RLA's ability to penetrate the inner mitochondrial membrane, thus limiting energy production.<sup>20</sup> SLA does not improve glucose disposal and slightly increases insulin levels.<sup>16</sup>

SLA has some positive benefits, but no advantage over the pure R form. SLA can function as an antioxidant but it recycles 38 times slower than RLA.<sup>14</sup> It also has some metal chelating properties, yet inferior to the R form.<sup>16</sup> Although toxicity studies have proven SLA to be safe up to very high levels, it is clear that SLA is not a metabolically preferred molecule.

\*Enantiomers are a set of molecules identical in composition yet with a different spatial conformation which confers them different chemical and physiological properties.

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