

## **James L. Holly, M.D.**

### **Alpha Lipoic Acid**

**By: James L. Holly, MD**

Alpha lipoic, one of the five "members" of the antioxidant network, has been shown in clinical trials to:

- Provide powerful support for healthy blood sugar metabolism.
- Protect and even restore the functioning of nerves.
- Perhaps reverse kidneys damaged by years of high blood sugar exposure from diabetes.
- Lipoic acid is a nutrient with awesome potential, but those who are taking a conventional lipoic acid pill, are receiving only half the health-promoting, anti-aging benefits associated with this nutrient. The other half is worse than useless: it actually antagonizes the effects of the good half of the supplement.

### **The Three-dimensional structure of molecules**

The biological effects of many key molecules are defined not just by the sequence of the atoms that make them up, but their three-dimensional structure. One example of a molecule whose "handedness" is important to its function is alpha-tocopherol. As most health-conscious folks know, the alpha-tocopherol found in natural foods is "d-alpha tocopherol." But the synthetic form found in many drug-store supplements is "dl-alpha." The molecules in d- and dl-alpha-tocopherol are made up of the same atoms, put together in the same order. The difference is that the atoms in the molecules of the dl- mixture are twisted in different directions in space. These different "handednesses" are referred to as different "isomers" of the molecule.

### **Natural "isomers"**

Your body is designed in such a way that it can often make much better use of the natural isomer of a molecule than it can do with that molecule's synthetic look-alikes. Again, alpha-tocopherol is a great example: milligram for milligram, the d- form of the molecule is much better used and retained by the body than is the dl- mixture. Still, in the case of dl-alpha-tocopherol, there's nothing particularly dangerous about having those extra,

synthetic isomers in your supplement: they're just weaker, less effective imitations of the real thing.

### **Unnatural, Harmful Isomers -- Trans-fats**

In other cases, however, putting the wrong isomer into your body can actually harm you. Most health-conscious people have heard of trans-fats, but few people understand what they are, or why they're dangerous. Found in large quantities in most margarines, but also sprinkled throughout the processed-food universe, synthetic trans-fatty acids are actually just unnatural isomers of natural polyunsaturated fats. When you expose the natural "cis-" isomer of a polyunsaturated fat to a great deal of heat and pressure (as is done in the partial hydrogenation of vegetable oils), you can literally twist its structure, rearranging the molecule's orientation in space. Thus the synthetic trans- isomer is born.

### **Harm of the unnatural trans- isomer in fatty acids**

Changing a fatty acid from the cis- to the trans- form is a matter of a simple rotation of orientation, yet it completely alters the effects of the fat on your body. The crucial difference between the natural cis-isomers of polyunsaturated fats and their synthetic trans-forms was shown in a large study of the diet and health of over 80 000 female nurses in the United States. This study found that the total amount of fat in the nurses' diets did not affect their odds of heart attack, or of heart disease death. Instead, it found that it's the kind of fat that a person puts into his or her body that affects heart health.

When a woman in the study took 5% of the carbohydrate Calories in her diet, and replaced them with Calories from polyunsaturated fats in their natural cis- form, she cut her odds of a heart attack or a heart-disease death by an impressive 38%. But when a woman replaced just 2% of her carbohydrate Calories with trans-fatty acid isomers, she nearly doubled her risk of heart attack or death from heart disease (a 93% higher relative risk)! Frighteningly, scientists studying the same group of women have found that a similar pattern exists for risk of diabetes: the natural isomer is protective, while the artificial isomer puts a person at greater risk.

### **Alpha Lipoic Acid -- Most Products Sold: Mixture of the natural and the synthetic Isomers**

If you look on the label of conventional "lipoic acid" supplements, you'll see just that: "lipoic acid" or "alpha-lipoic acid," and the number of milligrams per capsule or tablet. What the label won't tell you is that you're actually getting a 50/50 mixture of two different, mirror opposite isomers of lipoic acid. Of the two isomers of lipoic acid present in conventional supplements, the isomer which is identical to the natural form of lipoic acid is the R(+)-lipoic acid. S(-)-lipoic acid is a purely artificial molecule. it does not exist in nature but is produced as a byproduct in the normal method of producing commercial lipoic acid.

## **Racemic Mixture**

A 50/50 mix of two mirror opposite isomers is called a "racemic compound" or "racemate." So the proper, scientific designation for the lipoic acid in conventional supplements is:

Rac-lipoic acid  
R,S-lipoic acid  
(±) lipoic acid

But because of industry conventions and the fact that until recently, lipoic acid was only available as the racemate, conventional "lipoic acid" supplement labels don't bother to tell you that you're getting a racemic compound, rather than the pure, natural R(+)-form of the nutrient.

## **Does the Racemate mixture in Lipoic Acid Supplements Make A Difference**

So does the fact that your lipoic acid is a "racemate" actually affect the value of the supplement? Does the presence of the S(-) form make any real difference? Yes, it does.

The S(-)-form that's taking up 50% of your supplement is not just a weaker cousin of the real thing, like the "other" isomers of alpha-tocopherol in the dl- product. In fact, S(-) lipoic acid is the R(+) isomer's.

When he reported his findings about the opposing effects of the two forms of lipoic acid on the energy-producing powers of mitochondrial particles, for instance, Dr. Guido Zimmer stated that "The S(-)-enantiomer ... part of the racemate, which is present as about a 50% impurity, needs to be eliminated.

When you look at the differences between the R(+)- and S(-)- forms of lipoic acid in terms of their:

- Effects on the body's metabolism of blood sugar, or
- Their protective and antioxidant activities, or
- Their effects on mitochondria
- The preliminary evidence on their effects on the aging process itself,

We expect you'll come to agree with Dr. Zimmer and other lipoic acid researchers who have shown that:

- There are cases where the S(-)-enantiomer is merely less effective than R(+)-Lipoic Acid – and
- Also cases where, at worst, the S(-)-form is just totally ineffective.
- There are also many cases in which the S(-)-enantiomer actually counteracts the benefits of R(+)-lipoic acid!

Dr. Tory Hagen, in *Mitochondrial Decay in Aging* supported that conclusion: "We're finding – and others are, too – that the R(+)-form – the natural form – is much more

powerful than the racemic mixture ... Hopefully ... companies are going to be producing on more of a clinical scale the R(+)-form of lipoic acid, because we're finding very significant effects using this, as opposed to the racemic mixture."

Dr. Ryan Streeper and colleagues reported in *The American Journal of Physiology*: "We have presented in this study new information indicating that this enhancement of glucose metabolism is stereospecific, with the R(+)-enantiomer being much more effective than the S(-)- enantiomer."

Dr. Bruce Ames, in *Strategies for Engineered Negligible Senescence* said. "Lipoic acid sold in a health food store is a synthetic mixture, a racemic mixture. And R[+]- is the natural form and S[-]- is an unnatural one ... And in our hands R[+]-works and S[-]- doesn't."

Dr. Lester Packer and colleagues, in *Free Radical Biology and Medicine* opined: "R[+]-LA [that is, R(+)-lipoic acid], and not a racemic mixture of R[+]-and S[-]- LA, should be considered a choice for therapeutic applications."

Dr. Guido Zimmer and colleagues, in *Methods in Enzymology* agreed: "The S[-]- enantiomer ... part of the racemate, which is present as about a 50% impurity, needs to be eliminated."

If you fit into one of the following categories and there are no contraindications (such as pregnancy), you should begin a supplement of the R Isomer of Alpha Lipoic Acid in the dosages mentioned last week:

1. You are over 40.
2. You are diabetic.
3. You have heart disease.
4. You are having problems with your memory.
5. You have chronic fatigue syndrome.
6. You have hepatitis.
7. You want to feel better, live better and be healthier longer.

Remember, it is your life and it is your health.