

## **Acetyl-L-carnitine and Alpha-lipoic acid**

Throughout the ages, people have searched for magical potions to reverse the aging process. Ponce de León was searching for the Fountain of Youth when he discovered Florida. And the 19th century was rife with anti-aging potions. In 1889, for example, a French scientist called Charles Eduardo Brown-Séquard claimed that drinking an extract of crushed dog testicle could restore youth and vigor to old men.

Acetyl-L-carnitine and alpha-lipoic acid are the latest in a long line of supplements promising to turn back the clock. This two-pronged ‘punch’ to ageing cells seemed to work, with the two supplements together producing better results than either one alone. In the mitochondria, alpha lipoic acid (ALA) can act both as an antioxidant, capable of recycling other antioxidant nutrients such as vitamin C and vitamin E, and as a coenzyme for key metabolic enzymes involved in energy production. In addition to its role as an antioxidant, alpha lipoic acid (ALA) also raises the levels within cells of a substance called glutathione, which is critical for neural function, and aids in glycolysis, the first stages of breaking down carbohydrates for energy.

The interest started when researchers in the Linus Pauling Institute at Oregon State University and the University of California at Berkeley found that they improved both the activity, energy level and cognitive function of old rats.

“After just a month, older rats whose diet was supplemented with these two compounds were about twice as active as our control rats, which remained largely inactive,” says Tory Hagen, an assistant professor in Oregon State University's Linus Pauling Institute.

Bruce Ames, a professor of biochemistry at the University of California at Berkeley says “The brain looks better, they are full of energy — everything we looked at looks more like a young animal.”

There are scores of different theories about aging. Some believe that aging is due to the normal wear and tear resulting from daily living. Others think that it is the result of a pre-programmed genetic plan, a process that begins at birth and continues until your “biological clock” runs down.

Ames falls in the wear and tear camp. He thinks that aging is at least partly due to a process called oxidative stress. One particularly vulnerable area appears to be the *mitochondria* (pronounced my-toe-kon-dree-a).

Your body is made up of millions of tiny cells. Think of each cell like a miniature city. Inside each city, you will find the power stations of the cell. They are called mitochondria. Of the oxygen consumed by an average cell, the mitochondria use most of it to help turn food into energy.

Unfortunately, mitochondria also appear to have a major design flaw — they leak electron. This, in turn, leads to an increase in the production of free radicals.

The antioxidant defenses of your body are usually adequate to prevent substantial tissue damage. However, an overproduction of free radicals (caused, for example, by intense exercise) or a drop in the level of the antioxidant defenses will lead to an imbalance between free radical generation and antioxidant protection.

This imbalance is known as *oxidative stress*.

Mitochondria are right in the neighborhood of the free radicals they just created. This means they are often the first victims.

It is ironic that the thing we most need to live — oxygen — is the very thing contributing to aging and some of the other problems associated with it, such as cancer and heart disease.

“Oxygen is a double-edged sword,” says Tory Hagen. “We need it to live and it’s essential to cell function. But oxygen can be converted into what we call reactive radical oxygen species, or free radicals.”

Bruce Ames and Tory Hagen have long had an interest in mitochondria as they relate to aging. They were intrigued by Italian research showing that acetyl-L-carnitine improved mitochondrial activity in older rats.

When Ames and Hagen tried the same experiment, there was a problem. The carnitine did improve mitochondrial health. But it also appeared to increase the level of free radicals. So, they decided to pair it with alpha-lipoic acid.

In one of the studies, Hagen, Ames and colleagues compared old rats to young rats, all fed acetyl-L-carnitine in their water and alpha-lipoic acid in their food.

“We significantly reversed the decline in overall activity typical of aged rats to what you see in a middle-aged to young adult rat 7 to 10 months of age,” Hagen says. “This is equivalent to making a 75- to 80-year-old person act middle-aged. We have only shown short-term effects, but the results give us the rationale for looking at these things long term.”

Supplementation has also been shown to improve both spatial and temporal memory. Pictures of brain cells show less decay in old rats fed a supplemented diet.

“It appears that some compounds, including carnitine and lipoic acid, can mask the metabolic problems caused by cellular aging and the natural oxidative process,” Hagen says. “If we can better understand the process of aging and how to influence it, we may be able to give people a way to maintain human health for as long as possible.”

The University of California have patented the use of acetyl-L-carnitine and alpha-lipoic acid as a way of “enhancing metabolism and alleviating oxidative stress.”

### **The bottom line**

Of course, the big problem is the lack of reliable research to show that these compounds benefit humans in the same way as rats.

Under certain circumstances, large doses of the popular antioxidants vitamin C and CoQ10 have been shown to increase oxidative stress. Whether alpha-lipoic acid and carnitine have any negative effects is a question that can only be answered by more human research.

Aging is a complex process. Different tissues may have fundamentally different mechanisms underlying their maintenance and repair. Most scientists believe that mitochondrial health is only one cog in the aging wheel.

Ames acknowledges he has not discovered the Fountain of Youth. “I do not want to over-hype it,” he cautions. “If you are an old rat, it looks very good. But we still have to wait for the results from the human trials. There is every reason to think it is going to work in people.”

### **The implications for human health**

These studies on rats caused a huge stir within the scientific community. Here was evidence that some of the processes of ageing could be slowed or even reversed, and the implications for human health and performance were enormous. In the months that followed, a number of human studies were started, many of which are still under way.

However, the question of whether the benefits observed in rats might also apply to humans will not be easy to determine. For one thing, the ageing process in humans is much slower than in rats, so the

seven-week supplementation period used in the rat studies would equate to around five years of supplementation in humans! Secondly, the amounts of acetyl L-carnitine (ALC)/alpha lipoic acid (ALA) used in the rat studies were very high – equivalent to 50g per day of acetyl L-carnitine (ALC) and 5g of alpha lipoic acid (ALA) for an 70 kilos adult. That’s around 50 times more than is typically available in acetyl L-carnitine (ALC)/ALA supplements found on the shelves of most health food stores!

One of the earliest studies examining the effect of acetyl L-carnitine (ALC) and alpha lipoic acid (ALA) in humans was carried out at San Francisco State University in 2001. In a double-blind, placebo-controlled study lasting 17 weeks, 18 healthy sedentary men aged 60-71 were randomised to one of two treatment régimes: a placebo tablet twice a day or 1,000mgs of acetyl L-carnitine (ALC) and 400mgs of alpha lipoic acid (ALA) in two divided doses. Both groups were then asked to perform a demanding sequence of exercises, after which blood was drawn and analysed for signs of exercise-induced oxidative stress (a potentially damaging by-product of energy production). To measure oxidative stress, the study evaluated nine different biomarkers: ammonia, beta-carotene, glutamine, glutathione, malondialdehyde, total antioxidant status (TAS), vitamin C, vitamin E-alpha tocopherol, and vitamin E-gamma tocopherol. For eight of these nine biomarkers, a majority of subjects in the treatment group recorded values indicating that levels of oxidative stress had fallen. By contrast, no such benefits were reported in the placebo group.