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REPORT

Carnosine: Exceeding Scientific Expectations

By Kirk Stokel

Almost ten years ago, *Life Extension*® published compelling data showing that supplementation with higher-dose **carnosine** induced a wide range of anti-aging effects, including marked reductions in lethal **glycation** reactions.

We reported on experimental findings in the 1990s demonstrating life span extending effects when **carnosine** was added to the diet.

Since then an enormous number of published scientific studies have corroborated the multiple beneficial effects of carnosine including protecting brain cells from toxic metal ion reactions that lead to dementia.

Carnosine is an amino acid compound found primarily in red meat. A typical red meat meal may provide **250 mg** of **carnosine**, but this is quickly degraded in the body by the **carnosinase** enzyme. What this means is that even if a person relied on red meat for their carnosine, it would not last long enough in the body to provide sustained protective effects. Supplementation with 1,000 mg a day of carnosine overwhelms the carnosinase enzyme, thus enabling one to maintain consistent blood levels of this critical nutrient.

In this article, we report on a new longevity study using **carnosine**.¹ Highly concentrated in brain and muscle tissue (including the heart), it turns out that carnosine strikes at *multiple* molecular targets to delay aging in laboratory animals and human tissues!²⁻⁴

This article uncovers new data about carnosine's ability to provide targeted support to vital tissues in the heart, brain, and eye.

A Groundbreaking Discovery

Dr. Sergey Stvolinsky, a highly-regarded anti-aging scientist at the Russian Academy, has studied carnosine for years. In 2010 he published some surprising results in the journal *Rejuvenation Research* about carnosine's effect on fruit flies.

Fruit flies are incredibly useful experimental animals, particularly for genetic and aging research, because of their very short life spans and rapid reproductive rates. Stvolinsky and his research team found that adding a tiny amount of carnosine to the flies' food supply produced an immediate **20% increase** in the average life span of male flies.⁵ Alone, carnosine had little effect on female flies' life span, but when combined with a water-soluble form of vitamin E, female flies experienced a **36% increase** in longevity as well.^{5,6}

Stvolinsky's work is indeed groundbreaking, but one is left with the question of why carnosine produces such dramatic effects and whether these results in insects have relevance for human life span. Let's look at carnosine's broad spectrum longevity benefits for some answers.

Cardiovascular Health Benefits

Oxidant stress eventually shortens our life span by contributing to the risk of atherosclerosis and its consequences such as heart attack and stroke. Carnosine's powerful antioxidant effects, coupled with its ability to scavenge both free radicals and damaged protein products, give it unique protective characteristics that have the potential to lengthen life span.⁷

Carnosine can inhibit sympathetic nervous system activity that otherwise promotes hypertension, thus diminishing obesity-associated blood pressure elevations.⁸ Its antioxidant properties protect heart muscle directly against toxins, even powerful chemotherapy agents that would otherwise pose serious risks to heart tissue.⁹ Its **anti-glycation** properties help prevent harmful modifications of LDL cholesterol molecules that contribute to early stages of arterial plaque formation, a benefit especially important in protecting blood vessels from diabetic damage.¹⁰

But even after substantial damage has been done, and arteries are clogged, carnosine offers potentially lifesaving benefits. When blood flow is obstructed, tissue is starved of oxygen and nutrients by the resulting ischemia. Even though the restriction of blood flow produces immediate damage, still more damage occurs when blood flow is restored and oxygen-rich blood floods the area. This double-hit is called *ischemia/reperfusion injury*, and accounts for much of the disability that follows a heart attack, stroke, or traumatic injury.

Carnosine protects against ischemia/reperfusion injury in a number of remarkable ways.¹¹ It protects brain cells after a stroke by reducing toxicity of the excitatory neurotransmitter glutamate.¹² Interestingly, treatment with carnosine significantly reduced the

amount of brain tissue involved in experimentally-produced strokes in mice.¹³ Perhaps more impressively, carnosine supplements protect animals' brains against localized ischemia in the first place.^{14,15} This discovery has been credited with increasing survival of experimental animals following stroke.¹⁶

Carnosine also prevents or reverses ischemia/reperfusion injury in liver and kidney tissue following injury or surgical procedures, helping to reduce complications.¹⁷⁻²¹ The more we learn about ischemia/reperfusion injury the more we find it contributes to long-term disability and reduces life span. Carnosine certainly deserves a place in a cardiovascular prevention program.

Combating the Dangers of Elevated Glucose

The destructive changes in vital enzymes and other proteins by glucose (the glycation process) is one of the major causes of aging and age-related tissue dysfunction.²² While this process is accelerated in diabetes due to constantly elevated glucose levels, it occurs in all of us, and the effects accumulate over time.²³ A substance that can prevent glycation in the first place, or one that can reverse existing protein glycation, would therefore be a powerful anti-aging compound.²²

Carnosine acts on multiple targets within cells and tissues to quench the chemical reactions that prevent proteins from functioning properly.^{22,24,25} One benefit discovered early from this process is a suppression of elevated blood pressure in diabetic animals.²² An animal study showed that carnosine decreases blood glucose levels indirectly through beneficial effects on the autonomic nervous system. This modulation of blood glucose levels makes damaging glycation reactions less likely to occur.²⁶

These benefits have immediate payoff in living organisms. Carnosine stabilizes red blood cell membranes against the damaging effects of glycation products in diabetes.²⁷ Additionally, it protects human LDL cholesterol from both oxidation and glycation, early events in the production of atherosclerosis.^{10,28} Astonishingly, carnosine supplementation in animals delays onset of diabetes and increases the mass of insulin-secreting pancreatic cells.²⁹

Novel Anti-Cancer Properties

The use of carnosine as a chemopreventive is in its infancy, but encouraging studies are rapidly emerging as scientists look for more ways to capitalize on its antioxidant, anti-inflammatory features. As an antioxidant, carnosine helps block the DNA damage that can lead to cancerous transformation in cultured cells—and it increases the life span of cells cultured from young subjects in the laboratory.³⁰ Carnosine also prevents release of inflammatory cytokines in intestinal cells, reducing a significant risk for colon cancers.³¹ Its ability to inhibit new metastases, and to interfere with cancer cells' energy metabolism, make it still more appealing as a potential anticancer nutrient.³²⁻³⁴

Safeguarding the Aging Brain

Brain tissue naturally contains high levels of carnosine, which is capable of reducing the oxidative, nitrosative, and glycemic stress to which the brain is especially vulnerable.^{7,35,36} Oxidation and glycation produce inflammation, and also contribute to cross-linking of proteins, including the Alzheimer's disease protein called amyloid-beta.³⁷ Carnosine can prevent that cross-linking, preserving normal neuronal function, and also helps minimize toxicity created by the high levels of metal ions that are present in certain areas of the brain.^{4,38-40}

Carnosine levels are significantly lower in patients with Alzheimer's and other neurodegenerative disorders, suggesting either that carnosine deficiency contributes to the disease, or, more likely, that the disease processes are using up protective carnosine.^{41,42} In either case, supplementation with carnosine could be expected to alleviate much of the cellular toxicity that contributes to these diseases, which is why animal and human studies now suggest an important role for carnosine supplementation in prevention of Parkinson's and Alzheimer's diseases.⁴³⁻⁴⁷

WHAT YOU NEED TO KNOW: CARNOSINE

- Carnosine lowers blood glucose, enhances insulin sensitivity, and may help prevent type 2 diabetes from emerging.
- Breakthrough research has shown that carnosine can dramatically extend the lifetimes of laboratory animals.
- Carnosine also extends lifetime of human cells in culture.
- Carnosine is a natural antioxidant and anti-glycation substance found in normal human tissues, predominantly in the brain and heart.
- By fighting oxidant and glucose-induced damage, carnosine blocks the central changes to cells and tissues that result in aging and age-related diseases.
- Carnosine helps prevent cardiovascular damage and brain injury through a host of mechanisms closely related to the interplay of glycation, oxidation, and inflammation.
- Carnosine should form a part of a comprehensive anti-aging supplement program.

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Blocking Cataract Formation

In addition to extending the quantity of life, carnosine can contribute to improved quality of life by reducing the risk and severity of cataracts in the eye.⁴⁸ The lens of the eye is highly sensitive to glycation of its proteins, which render it opaque. Carnosine's anti-glycation effects, therefore, provide prominent vision protection.⁴⁹ Carnosine in different delivery systems has been shown to reduce cataract formation in studies of diabetic animals, which, like diabetic humans, are prone to cataract development.⁵⁰⁻⁵²

WHY WE NEED SUPPLEMENTAL CARNOSINE

Carnosine levels in the body decline with age. Muscle levels decrease 63% between ages 10 to 70, which may account for the reduction in muscle mass and function seen in aging humans.¹

Carnosine acts not only as an antioxidant in muscle, but also as a pH buffer.² In this way it keeps on protecting muscle cell membranes from oxidation under the acidic conditions of muscular exertion.

Carnosine enables the heart muscle to contract more efficiently through enhancement of calcium response in heart cells.³ Muscle levels of carnosine correlate with the maximum life span of animal species.

Carnosine has been shown to rejuvenate connective tissue cells, which may explain its beneficial effects on wound healing. Damaged proteins accumulate and cross-link in the skin, causing wrinkles and loss of elasticity. The multiplicity of pathological effects caused by protein degradation places this problem beyond the scope of simple antioxidants.⁴ Carnosine is the most promising broad-spectrum shield against protein degradation.

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Summary

Growing scientific interest in longevity-boosting compounds has led to groundbreaking new research on carnosine. Highly concentrated in brain and muscle, carnosine is a natural antioxidant and glycation-fighting nutrient whose levels in the body naturally decline with age.

A 2010 study revealed that carnosine extends life span in laboratory animals, consistent with other recent findings that carnosine fights aging at multiple targets in heart, brain, skin, and other organ systems.

Carnosine's multiple and interrelated mechanisms of action mean that carnosine can provide benefits to cells and tissues throughout the body that would otherwise succumb to the pathologic effects of aging.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

CARNOSINE AT WORK

An obvious feature of carnosine is its powerful antioxidant effect, which may prevent age-related accumulation of free radicals and their disastrous impact on tissues.⁵³⁻⁵⁵

Carnosine is a dipeptide—that is, a small molecule composed of two amino acids, histidine and beta alanine. It continues to work to prevent oxidant damage even after cellular molecules are attacked. It prevents destructive effects of oxidized chemicals such as malondialdehyde (MDA) that are associated with brain cell death in neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.^{4,43}

A separate and equally important feature of carnosine is its ability to interfere with protein modifications by glucose and oxygen, two events that contribute powerfully to inflammation and aging.^{3,56} Carnosine also directly and indirectly inhibits release of inflammatory mediators such as cytokines and inducible nitric oxide synthase (iNOS), and is being closely studied for its ability to mitigate the inflammatory effects of viral infections such as influenza.⁵⁷

The sum of all these intracellular biochemical events helps to explain the remarkable explosion of literature on carnosine as a possible life span extender. A central biochemical characteristic of aging is the accumulation of proteins altered by chemical reactions with oxygen, nitrogen, and glucose.^{58,59} Carnosine's ability to interfere with that alteration may account for its observed ability to extend life span not only of fruit flies but also of "higher" laboratory animals and human tissue in culture.^{1, 2, 60-63}

A close-up look at carnosine's actions reveals a remarkable effect on telomeres, the DNA sequences at the ends of chromosomes that act as a sort of cellular "clock," largely controlling the aging process. As telomeres shorten with each cellular replication, the remaining life span of the cell is diminished.⁶⁴ Telomere shortening is induced by oxidative changes and other protein modifications of precisely the kind that carnosine can prevent.⁶⁵ Carnosine can therefore block telomere shortening and reduce aging effects in individual tissues.⁶⁶ For example, carnosine can prevent telomere shortening-induced cataracts in the lens of the eye.^{64,67,68}

CARNOSINE DOSAGE GUIDELINES

Most people consume relatively small amounts of carnosine in their diet. Based on a study showing that 250 mg of ingested carnosine from 7 oz. of hamburger meat was completely cleared from the blood of study volunteers within 5-6 hours by the carnosinase enzyme,⁶⁹ Life Extension recommends that individuals seeking its anti-aging effects supplement with at least 1,000 mg of carnosine daily to maintain optimal levels in the body.

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