

### **Liposomal Carnosine Is Essential for Detoxing Linoleic Acid**

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#### **STORY AT-A-GLANCE**

- > Carnosine is a dipeptide found in meat. The highest concentrations of carnosine are found in your muscles, brain, central nervous system and gastrointestinal tract
- > If you're a vegetarian or vegan, you will have lower levels of carnosine in your muscles.
  This is one reason why many strict vegans who do not properly compensate for this tend to have trouble building muscle
- > Carnosine binds to advanced lipoxidation endproducts (ALEs) that form from oxidized seed oils in your diet, making it a crucial aid in the detoxification of linoleic acid (LA)
- > Thanks to its ability to scavenge 4-hydroxynonenal (4HNE), carnosine is also protective against obesity, diabetes, cardiovascular disease and Alzheimer's disease, just to name a few
- > The best way to optimize your carnosine level is to eat organic grass fed beef. When it comes to carnosine supplements, your best bet is liposomal versions as they have the highest bioavailability

Carnosine is a dipeptide found in meat. It's not found in any plant foods. Dipeptide means it's made up of two amino acids, in this case beta-alanine and histidine. The highest concentrations of carnosine are found in your muscles, brain, central nervous system<sup>1</sup> and gastrointestinal tract,<sup>2</sup> which gives you an indication of its potential importance.

Unfortunately, it's also one of the top 10 most common nutrient deficiencies, especially among vegans. If you're a vegetarian or vegan, you will have lower levels of carnosine in your muscles. This is one reason why many strict vegans who do not properly compensate for this tend to have trouble building muscle.

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### **Carnosine's Physiological Roles**

Carnosine has several physiological roles and benefits. For example, it:<sup>3</sup>

Provides athletic benefits – Approximately 99% of carnosine is found in muscle tissue where it facilitates lactic acid detoxification, improves muscle contraction and muscle relaxation and enhances endurance

Alleviates diabetic nephropathy by protecting podocyte and mesangial cells<sup>4</sup>

Modulates energy metabolism in macrophages and microglia by restoring and/or enhancing the basal conditions

Has antioxidant properties and scavenges reactive oxygen species (ROS) and aldehydes created by peroxidation of fatty acid cell membranes during oxidative stress<sup>5</sup>

Regulates the activity of stem cells

Modulates glucose metabolism

Enhances the degradation and/or scavenging of nitric oxide (NO)

Promotes wound healing

# Opposes glycation<sup>6</sup> Slows down the aging process by prolonging the life of cells and preserving cellular homeostasis<sup>7</sup> Regulates osmotic pressure Modulates glutamate production and transport Modulates brain metabolism Chelates heavy metals<sup>8</sup> Acts as a pH buffer<sup>9</sup>

Protects olfactory receptor neurons in the elderly

## **Beef, Liposomal Carnosine and Precursors Are the Best Sources**

Interestingly, a June 2023 paper<sup>10</sup> in the medical journal Pharmaceuticals reviewed the science behind carnosine with the aim of developing new delivery systems for carnosine-based drugs. As noted in this paper:

"Because of its well-demonstrated multimodal pharmacodynamic profile, which includes anti-aggregant, antioxidant, and anti-inflammatory activities, as well as its ability to modulate the energy metabolism status in immune cells, this dipeptide has been investigated in numerous experimental models of diseases, including Alzheimer's disease, and at a clinical level.

The main limit for the therapeutic use of carnosine is related to its rapid hydrolysis ... [This is the] reason why the development of new strategies, including the chemical modification of carnosine or its vehiculation into innovative drug delivery systems (DDS), aiming at increasing its bioavailability and/or at facilitating the site-specific transport to different tissues, is of utmost importance."

Delivery systems currently in use or in development include intraperitoneal injections, intranasal sprays and oral administration of various nanoformulations. But while the drug industry is keen on figuring out how to profit from carnosine by making it into a drug, you certainly don't need a drug to get these benefits.

Simply eating organic grass fed beef is one of the most efficient ways to raise your carnosine level.<sup>11</sup> This is one of many reasons why cultured beef is not a viable substitute for real beef. Not only does fake beef lack carnosine but also B vitamins, retinol, long-chain omega-3 fatty acids, taurine, creatine and bioavailable forms of iron and zinc.<sup>12</sup>

Most carnosine supplements aren't very effective either because the carnosine is rapidly broken down into its constituent amino acids by certain enzymes. Your body then reformulates those amino acids back to carnosine in your muscles.

An exception to this is liposomal carnosine, which appears to work quite well. Another alternative is to supplement with beta-alanine, which is the rate limiting amino acid in the formation of carnosine. According to a 2021 paper,<sup>13</sup> daily intake of beta-alanine can raise the carnosine content of skeletal muscle by as much as 80%.

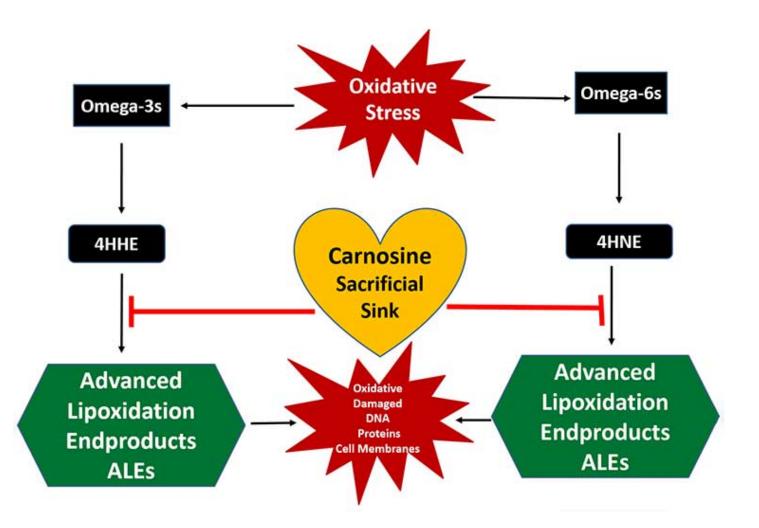
### **Carnosine Protects Against LA-Induced Oxidative Stress**

One benefit not expounded upon in the Pharmaceuticals paper is carnosine's ability to reduce LA-induced oxidative stress. While your body will slowly eliminate stored LA over time, provided you reduce your intake, carnosine can help reduce the oxidative damage caused by LA while your body is cleaning itself out. I take liposomal carnosine every day before meals to help detoxify LA.

# <sup>66</sup>Carnosine binds to ALEs like a magnet and acts as a sacrificial sink. It's basically a substitute target for these profoundly damaging molecules.<sup>99</sup>

The omega-6 fat LA is highly susceptible to oxidation, and as the fat oxidizes it breaks down into harmful sub-components such as ALEs and oxidized LA metabolites (OXLAMs). These ALEs and OXLAMs are what cause most of the damage.

Carnosine binds to ALEs like a magnet and acts as a sacrificial sink. It's basically a substitute target for these profoundly damaging molecules. In this way, carnosine allows your body to excrete the ALEs from your body before they damage your mitochondria, DNA or proteins. (Another molecule that protects against LA-induced damage is carbon dioxide). The illustration below shows how carnosine works in this regard.



### **Carnosine May Be Protective Against a Wide Range of Diseases**

A more detailed explanation of how carnosine protects against reactive oxygen species (ROS) and how that helps protect against oxidative stress-related pathologies is given in a 2021 paper in the journal Antioxidants:<sup>14</sup>

"A study that examined the effect of carnosine on oxidative stress in human kidney tubular epithelial (HK-2) cells indicated that carnosine decreased NADPH oxidase (NOX) 4 expression and increased total superoxide dismutase (T-SOD) activity, thus reducing the production of intracellular ROS, relieving the oxidative stress of cells, and ultimately inhibiting the mitochondrial pathway of apoptosis.

Ability of carnosine to protect against pathologies characterized by oxidative stress has been shown in a number of conditions ... Carnosine changes the reactivity of superoxide anion by forming a charge-transfer complex with the superoxide radical and also by reducing the efficiency of hydroxyl radicals, creating a compound less reactive than the hydroxyl radical.

One of the mechanisms to protect organisms from oxidative stress is the chelation of transition metals, preventing them from participating in deleterious processes involving ROS ... Interestingly, when comparing metals involved in free radical generation, carnosine was found to have a greater antioxidant activity coupled with copper than iron ...

At physiological concentrations, carnosine directly reacts with superoxide anion similar to ascorbic acid. In physiological conditions, carnosine was found to reduce oxidative damage and to improve antioxidant activity of different antioxidative enzymes ...

Experiments on aged rats showed that therapy with 250 mg/kg/carnosine per day significantly decreased oxidative stress and increased activity of antioxidative enzymes ... In similar model of aged rats, carnosine increased liver vitamin E, which further demonstrates its importance in defending the organism from free radicals. Rising data indicate that carnosine acts as a scavenger of reactive and cytotoxic carbonyl species including 4-hydroxynonenal (HNE). HNE is an aldehyde generated endogenously by lipid peroxidation of unsaturated fatty acids that act as 'toxic second messengers,' extending the harmful potential of free radicals.

HNE is considered an important biomarker of oxidative stress and accumulating data indicate that it may modulate signaling pathways of cell proliferation, apoptosis, and inflammation."

### How Carnosine Protects Against Alzheimer's

As noted in the Pharmaceuticals paper,<sup>15</sup> one of the pathologies that carnosine is protective against is Alzheimer's disease. In my November 2021 interview with Tucker Goodrich, he explained the role of HNE, specifically, in Alzheimer's, and why it's so important to get rid of it.

"In heart failure, Alzheimer's, and AMD [age-related macular degeneration], one of the things they see is an inability of the cell to produce enough energy. The mitochondria are getting damaged. HNE does that damage. It damages 24% of the proteins in the cell, primarily around energy production.

One of the ways your cells produce energy is they basically ferment glucose into pyruvate outside of the mitochondria. This is a perfectly normal part of metabolism and they produce something called pyruvate. A molecule called pyruvate dehydrogenase takes pyruvate into the mitochondria and converts it to acetyl-CoA so the mitochondria can burn it very efficiently for fuel.

Well, one of the things HNE does is it breaks pyruvate dehydrogenase, and they see this in Alzheimer's where their cells are no longer able to produce enough energy. This is why your cells are dying in Alzheimer's.

The beta amyloid plaques in Alzheimer's disease are induced by HNE. There's a great model that came out of Harvard a couple of years ago showing that.

Even the critical, the most important part of the mitochondria, complex 5, – ADP synthase – which is what takes all the energy coming from your mitochondria and turns it into ATP, which is what fuels the rest of your body – is damaged by HNE. This is a huge issue. There's no more fundamental problem in aging and health than protein damage."

Carnosine is the most effective scavenger of HNE, so optimizing your level can go a long way toward protecting against the HNE-induced damage that promotes Alzheimer's.

## Carnosine — A Promising Therapeutic for Obesity-Related Conditions

Elevated HNE has also been found in obese and diabetic patients,<sup>16</sup> so there's reason to suspect carnosine can be important in the treatment of these conditions as well. Another disease where elevated HNE plays a role is atherosclerosis. As noted in the 2021 Antioxidants paper:<sup>17</sup>

"... emerging studies have indicated that these reactive aldehydes are more than simply markers of oxidative stress.

Rather, it is suggested that these reactive species may play a significant pathogenic role in obesity-associated disorders such as insulin resistance and a carnosine analog alleviates the production or enhances the removal of reactive carbonyl species, providing promising new therapeutic compounds for cardiovascular and metabolic diseases related to obesity."

### Take Control of Your Health by Lowering Your LA Intake

As detailed in several previous articles, the evidence strongly suggests excessive LA is driving most if not all modern diseases, including heart disease and cancer. Fortunately, the solution is simple. Just lower your LA intake.

The easiest way to do this is to use an online nutritional calculator such as Cronometer to calculate your daily intake. Cronometer will tell you how much omega-6 you're getting from your food down to the 10th of a gram, and you can assume 90% of that is LA. Anything over 10 grams is likely to cause problems. I keep my intake below 5 grams a day.

Since there's no downside to limiting your LA, you'll want to keep it as low as possible, which you do by avoiding high-LA foods. Keep in mind you'll never be able to get to zero, and you wouldn't want to do that either. You do need some LA, but since it's found in most foods, and since you need only small amounts, there's really no way to end up with a deficiency.

### **Sources and References**

- 2, 4, 5, 6, 7, 8, 9, 13, 14, 16, 17 Antioxidants July 2021; 10(7): 1037
- <sup>11</sup> Science Direct, Carnosine; Nutritional Supplements and Metabolic Syndrome
- <sup>12</sup> Animal Frontiers April 15, 2023

<sup>• &</sup>lt;sup>1, 3, 10, 15</sup> Pharmaceuticals June 2023; 16(6): 778