



## **Carnosine - Anti Ageing from the Inside to Out**

What is Carnosine?.....	2
Carnosine - Anti Ageing from the Inside Out.....	2
From the Inside.....	2
Carnosine .....	2
What is it? .....	2
How does it work? .....	3
How soon will I notice the difference?.....	3
Other Benefits.....	3
Carnosin - A Summary .....	4
How does Carnosine rejuvenate cells?.....	4
L-Carnosine - Pharmacology and biochemistry.....	4
In Summary .....	6
L-Carnosine - A Short Historic Review .....	6
This History of Carnosine as a medicine and dietary supplement.....	7
How Carnosine Works .....	9
L-Carnosine - "The Super Peptide" .....	9
Age-related conditions that carnosine may be useful for include:.....	9
Side-effects:.....	10
Carnosine - A Multi-Potent Super-Antioxidant.....	10
Carnosine - Metal Chelation Therapy.....	12
What does it mean in plain English?.....	12
Vaccinations & Mercury .....	12
EDTA Chelation Therapy & Atherosclerosis .....	13
Personal Experience.....	13
In Summary .....	13
Carnosine - Protection from Age Related Diseases (Prevention of Glycation)	
.....	14
Then what is this glycation?.....	14
Carnosine - Carbonylation - Beyond antioxidants .....	15
How does carnosine do this?.....	16
High Strength Carnosine 90 Caps x 500mg.....	18
How to Order .....	18
Online.....	18
Ordering by post.....	18
Order Form .....	19

## What is Carnosine?

### Carnosine - Anti Ageing from the Inside Out

When most of us consider using anti-ageing treatments, we immediately think about using topical skin care products. We can spend £'s on creams offering miraculous cures, only to find the effects are minimal or temporary at best. Good skin starts from the inside and literally grows outwards and although we can certainly make a difference by using creams we can't ignore the possibilities of what can be done from the inside out.

Informed scientists have always looked at ways in which the ageing process can be affected from the inside, examining the elements which contribute towards the ageing process and seeking a solution based on real science and not on cosmetic promises.

Carnosine can slow down skin ageing. In fact, it can rejuvenate skin cells.



#### From the Inside

One of the reasons why older people and animals look different than younger ones has to do with changes in the proteins of the body. Proteins are the substances responsible for the daily functioning of living organisms, which gives protein deterioration its dramatic impact on the body's function and appearance. Many lines of research over the last decade have converged on protein modification as a major pathway for aging and degenerative diseases. These modifications result from **oxidation** (by free radicals) and interrelated processes such as protein-sugar reactions (**glycation**).

#### Carnosine

Set to become one of the most important new anti-ageing supplements on the market, Carnosine's main ingredient Carnosine is not new. It is an amino acid occurring naturally in the body, which was discovered more than 100 years ago. In use in Russia for many years, its specific anti-ageing properties have only recently become clear to Western researchers.

#### What is it?

Carnosine addresses the biochemical paradox of life:

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*"The elements that make and give life - oxygen, glucose, lipids, protein, trace metals - also destroy life"*

Carnosine (not to be confused with 'Carnitine') is a combination of two amino acids (building blocks of proteins), alanine and histidine. It is naturally present in tissues like muscle and brain, but its concentration falls with advancing age.

## How does it work?

Carnosine works in a number of important ways:

### Antioxidant - Free Radical Protection

Firstly, it is an **antioxidant**, protecting our cells from free radical damage. Used together with vitamin E and other antioxidants, it has an optimum effect.

### Extending cell life span - Glycosylation

Secondly, it may reduce the destruction of valuable proteins and DNA by sugar molecules, a process known as **glycosylation**. The significance of this process has only recently been appreciated. Abnormal combinations of sugar and proteins are very toxic, contributing to several age-related diseases such as diabetes, heart disease, stroke, Alzheimer's dementia and skin ageing. Carnosine may help prevent damage from glycosylation, ridding the system of any abnormal substances and leaving it free to function optimally.

### Chelates metals in the Body

Thirdly, it is a toxic **metal binder** - it reacts with toxic by-products of our metabolism and eliminates them from the body. It stabilises the cells, making them more resistant to injury, and boosts the immune system.

## How soon will I notice the difference?

Early trials of the product in Scandinavia are reporting visible skin, vitality and energy improvements within two months of commencement.

## Other Benefits

Carnosine is believed to offer many benefits including **anti-ageing**, **longevity**, **Skin Rejuvenation**, **Muscle ageing, muscle disorders**, **Sexual Potency**, **Cataracts**, **Diabetes**, **Cardiovascular**, **Neurological and psychiatric disorders** and **other health benefits**

### Energy and Endurance

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Given to Russian athletes and Swimmers for many years Carnosine has remarkable energy and endurance benefits with many users claiming a considerable daily energy uplift.

## Carnosin - A Summary

Interest in Carnosine has increased markedly over the last few years and many experts are predicting it will become the fundamental daily treatment for people of all ages, but in particular those approaching 40 and beyond. In America and the UK, anti-ageing specialists and nutritionist are recommending it as a valuable supplement. There are no known side effects or incompatibility with other drugs.

Laboratory research on cellular senescence (the end of the life cycle of dividing cells) suggests that these facts may not be coincidences. CARNOSINE has the remarkable ability to rejuvenate cells approaching senescence, restoring normal appearance and extending cellular life span.

## How does Carnosine rejuvenate cells?

We do not yet know the full answer, but CARNOSINE'S properties may point up key mechanisms of tissue and cell aging, as well as the anti-aging measures that counteract them

Carnosine normally comes in a capsule form. No side effects are reported, and it can be used together with other supplements.

## L-Carnosine - Pharmacology and biochemistry

Carnosine is a 100 % natural substance, a so-called dipeptide, formed of two amino acids ( $\beta$ -alanyl-L-histidine). It is often called a neuropeptide due to its brainprotective properties.

Carnosine is found naturally in healthy muscles, hearth, brain, liver, kidneys and other tissues. The muscles contain about 20  $\mu\text{mol/g}$  dry weight. The more meat contains carnosine, the longer is its shelf life, as carnosine - a superb antioxidant - prevents it from going rancid.

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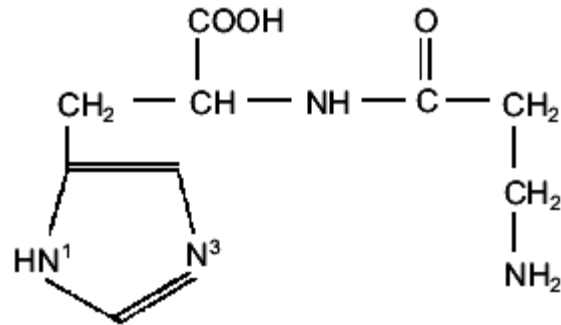
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*Figure 1. Chemical formula of L-Carnosine (NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CONHCH(C<sub>4</sub>H<sub>5</sub>N<sub>2</sub>)CO<sub>2</sub>H )*

Carnosine acts together with other biological **antioxidants**, e.g., vitamin E and vitamin C, zinc and selenium, and it spares their consumption in the tissues. Persons with latent vitamin E deficiency consume carnosine more than normally. [It is stressed that the intake of vitamin E is deficient in a major part of the general population, as suggested by epidemiological studies world wide.]

In the human body, the enzyme carnosine synthetase, forms carnosine from the amino acids alanine and histidine. This reaction occurs mainly in the brain and in the musculature. Another group of enzymes, called dipeptidases or carnosinases, in turn inactivate carnosine in the blood and other tissues.

Meat is the main dietary source of carnosine. High doses of carnosine are necessary for therapeutic effect because the body naturally degrades carnosine with the enzyme carnosinase. Absorption of carnosine from food is 30 to 70 % (depending on the amount of various amino acids in the meal) and that of pure L-carnosine greater than 70%. A greater part of the absorption occurs in the small intestine (jejunum, but not in the ileum). From the blood carnosine moves into the muscles, brain and other tissues. The human plasma does not contain measurable quantities of carnosine, in other words a blood test does not detect a possible deficiency state.

*[In contrast, equine plasma contains carnosine over 100 µmol/l. As a result of muscle injuries the content in the plasma increases, and determination of plasma carnosine can be used for detection of muscle injuries.]*

The biological functions of carnosine are:

- buffering the effects of lactic acid in the muscles (the pH remains neutral even in heavy physical exercise, such as sport sprints)
- pluripotent antioxidative actions
- ability to inactivate reactive oxygen species, scavenge free radicals
- aldehyde-sequestering
- prevention of glycation
- prevention of carbonylation of proteins, i.e., 'carnosinylation')
- function as neurotransmitter
- protection of proteasomes
- chelation of metals

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## In Summary

Carnosine is an aldehyde scavenger, which is also able to remove the rubble (ultimate de-linking damaged proteins, sugars and phospholipids) and act as a key member in the building of the new more impervious towers. As a dietary supplement, carnosine is a possible modulator of diabetic complications, atherosclerosis, Alzheimer's disease, Parkinson's disease, epilepsy, autism, dyslexia, AD/HD, schizophrenia and related syndromes, as we will discuss later in this section in more detail.

Copper and zinc are released during normal synaptic activity. However, in the presence of a mildly acidic environment which is a characteristic of Alzheimer's disease, they reduce to their ionic forms and become toxic to the nervous system. Research has shown that carnosine can buffer copper and zinc toxicity in the brain.

Carnosine has also been shown, *in vitro* (in the test tube), to inhibit non-enzymic glycosylation and cross-linking of proteins induced by reactive aldehydes, including aldose and ketose sugars, certain triose glycolytic intermediates, and malondialdehyde (MDA, a lipid peroxidation product). Carnosine also inhibits formation of MDA-induced protein-associated advanced glycosylation end products (AGEs) and formation of DNA-protein cross-links induced by acetaldehyde and formaldehyde.

The lipid peroxidation product malondialdehyde forms adducts with proteins that are detected during routine assays for protein carbonylation

## L-Carnosine - A Short Historic Review

Carnosine was discovered and its structure determined in the very beginning of the 20th century by the Russian scientist W. S. Gulewich. It was the first and the simplest example of biologically active peptides (actually a dipeptide), opening the long list of widespread natural protein regulators of metabolism. The first decades were dedicated to studies of structure, distribution, and properties of the compound. The it was understood that carnosine has a direct relation to the function of excitable tissues like muscles and the brain.

In 1953 another Russian scientist, S.E. Severin showed that carnosine effectively buffered lactic acid, produced by working muscles, and that adding carnosine substantially increased the contractility and endurance of the muscles. As the carnosine is consumed, the muscles accumulate lactic acid, the pH decreases, and the muscles get tired. When carnosine is added, the muscles recover almost immediately and contract like they never had been exhausted. This is known as the "*Severin phenomenon*".

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Everybody who has some experience in sports, has experienced how physical fatigue feels, and he or she will understand the immense importance of supplementation with carnosine in sports event.

Widespread interest in this natural nontoxic substance has only recently been increased, fueled by dramatic Australian and British discoveries about its antiaging actions. Carnosine's antiageing properties have only been extensively studied during the past few years even though we've known about it for almost a century. However, the most striking research came in 2002 from the USA where Dr Michael Chez's team reported data on the carnosine's dramatic effects on autistic children ([view report](#)).

At this writing, the **MEDLINE** data base includes over 900 published studies on carnosine.

## **This History of Carnosine as a medicine and dietary supplement**

A wide range of therapeutic uses have been proposed for this remarkable substance. As early as 1935, carnosine was recognized as a treatment for polyarthritis. Carnosine has the remarkable ability to down-regulate cellular and enzymatic processes when in excess, and up-regulate them when suppressed.

Several recent studies suggest that a combination of zinc and carnosine provide gastric mucosal protection against various irritants and are effective as antiulcerogenic substances (Odashima et al. 2002).

For example, carnosine decreases platelet aggregation in patients with abnormal clotting tendencies ("thins the blood"), and increases platelet aggregation in patients with low clotting indices. Carnosine has protective effects on blood cell membranes, enhancing their survival, and has demonstrated cell membrane-stabilizing effects, offering protection against chemical-induced hemolytic anemia.

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Table 1. Carnosine as complementary therapy

Disorder/disease	Year of commencement
1. Arthritis (polyarthritis)	1935
2. Gastric and duodenal ulcers	1936
3. Wound healing	1940
4. Hypertension (blood pressure)	1941
5. Antibiotic effect	1969
6. Adrenal cortex effect	1976
7. Alleviation of sleep apnea	1977
8. Treatment of trauma	1980
9. Prevention of seizures	1989
10. Coronary heart disease	1989
11. Anti-inflammatory effect	1971, 1986
12. Cataracts	1989
13. Anti-carcinogenic effect	1989
14. Immunologic effects	1986,1989
15. Prevention of radiation damage	1990
16. ADHD, Autistic Spectrum Disorder, epilepsy, other neurological & psychiatric	2001

### Summary of Benefits

- safe, naturally present in food and in the body
- versatile antioxidant and aldehyde scavenger
- quenches hydroxyl, superoxide and peroxy radicals
- superior protection of chromosomes from oxygen damage
- suppresses lipid peroxidation
- most effective natural glycation fighter
- inhibits formation of AGEs
- protects proteins from AGE toxicity
- protects proteins from cross-linking
- multifunctional protein and phospholipid protector
- protects against formation of protein carbonyls, the hallmark of protein damage
- inhibits damaged proteins from damaging healthy proteins
- aids recycling of damaged proteins by protecting the proteasomes
- helps preserve normal protein turnover
- extends lifespan 20 % in senescence-accelerated mice
- dramatically improves behavior and appearance of old mice
- dramatic effect in Autistic Spectrum Disorders
- protects brain cells from excitotoxicity
- protects brain proteins and biochemistry
- preserves brain biochemical functions
- safeguards brain chemistry in disorders overproducing free radicals

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- rejuvenates senescent human cells in culture
- increases cell life span
- restores youthful appearance and growth patterns to cells approaching senescence
- protects against metal toxicity
- chelates copper and zinc
- naturally protects against copper-zinc toxicity in the brain
- copper-zinc chelators dissolve Alzheimer's disease plaques
- inhibits cross-linking of amyloid-beta into Alzheimer's disease plaques

## How Carnosine Works

### L-Carnosine - "The Super Peptide"

L-Carnosine (kahr'no-sën), is a well-known neuropeptide consisting of alanine and histidine (beta-alanyl-L-histidine). It is normally made in the human body and is found at high levels in brain, innervated tissues, the lens of the eye, and skeletal muscle tissue.

In laboratory studies, it has been demonstrated that carnosine has the ability to protect cells against oxidative stress as well as to increase their resistance toward functional exhaustion and accumulation of senile features. Mechanisms of such protection are explained in terms of:

- proton buffering (maintaining pH balance in the muscles in heavy exercise)
- heavy metal chelating (especially copper and zinc)
- free-radical and active sugar molecule scavenging (prevents glycation and carbonylation of proteins)
- preventing the modification of biomacromolecules thereby keeping their native functionality under oxidative stress

Physiological concentrations (20-30 micromoles, or mM) in standard media prolong the in-vitro life span of human fibroblast cells and strongly reduce the normal features of senescence (ageing). In laboratory animals, carnosine clearly improved the external appearance of experimental animals and produced apparent beneficial effects on behavioral parameters and average life span.

### Age-related conditions that carnosine may be useful for include:

- neurological degeneration (Alzheimer's, Parkinson's, epilepsy depression, schizophrenia, mild cognitive impairment, dementia and stroke)
- Autistic Spectrum Disorders, Asperger's syndrome, ADHD, dyslexia
- cellular senescence (ageing) in general
- cross-linking of the eye lens (cataracts)
- cross-linking of skin collagen (skin ageing)
- formation of advanced glycation end products (AGES)
- accumulation of damaged proteins
- muscle atrophy

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- brain circulation deficit (stroke)
- cardiovascular conditions
- diabetes and its complications.

Carnosine as a multifunctional dietary supplement is a relatively new discovery. It is an amazing physiological and 100 % natural super-antioxidant with numerous biological roles including (in addition to the above mentioned):

- universal and versatile antioxidant activity
- supporting muscle vitality
- increasing muscle strength and endurance
- speeding up recovery after sprints
- inhibiting cellular damage caused by alcohol

## Side-effects:

- None reported. Carnosine is nontoxic.

## Carnosine - A Multi-Potent Super-Antioxidant

Carnosine is an antioxidant which stabilizes and protects the cell membrane. Specifically, as a water-soluble free radical scavenger it prevents lipid peroxidation within the cell membrane. Many antioxidants (like vitamins E and C) are aimed at preventing free radicals from entering the tissues, but have no effect after this first line of defense is broken. Free radicals cause oxidative stress in the body.

Carnosine is not only effective in prevention, but it is also active after free radicals react to form other dangerous compounds, like lipid peroxides and secondary products. So, it protects the tissues from these damaging 'second-wave' chemicals. For example, a highly reactive lipid peroxidation end-product called malondialdehyde or MDA, a dangerous product of free radical reactions, is blocked by carnosine. MDA, if left uncontrolled, can cause damage to lipids, enzymes and DNA, and plays a part in the process of atherosclerosis, joint inflammation, cataract formation, and aging in general. Carnosine, by reacting

**Table 1. Mediators of Oxidative Stress**

### Reactive Oxygen Species

#### Free radicals

Hydroxyl radical (HO·)

Superoxide radical (O<sub>2</sub><sup>·-</sup>)

#### Nonradicals

Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>)

Singlet oxygen (<sup>1</sup>O<sub>2</sub>)

#### Lipid Peroxidation Products

Peroxyl radical (ROO·)

Alkoxy radical (RO·)

#### Secondary Products

Malondialdehyde

4-Hydroxyalkenals

*Carnosine reacts chemically all reactive oxygen species thus preventing oxidative stress.*

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and inactivating MDA, sacrifices itself in order to protect the amino acids on the protein molecule.

A rather unusual antioxidant property of carnosine is its ability to reduce concentrations of thiobarbituric acid reactive substances (TBARS).

Carnosine is a substance that protects and extends the functional life of the body's key building blocks-cells, proteins, DNA, and lipids and can be fairly called an agent of longevity.

Interacting with aldehydic lipid oxidation products, carnosine protects biological tissues from oxidation, since aldehydes can form adducts with DNA, proteins, enzymes, and lipoproteins, causing harmful alterations in their biological activity (Burcham et al. 2002).

Oxidative stress and trauma cause a reduction in carnosine levels, which may help explain the increased mortality in the elderly following stressful events. That is why proper antioxidant defense is crucial for good health, in particular for elderly individuals. Carnosine in an all-in-one super antioxidant pill for those, who do not wish to swallow a handful of tablets every day.

The anti-ageing properties of carnosine go far beyond its antioxidant properties, as you will soon learn.

## Carnosine - Metal Chelation Therapy

Many investigators believe that carnosine exerts - at least partly - its beneficial health effect due to its ability to chelate metals (Miller and O'Dowd 2000, Chez 2003).

### What does it mean in plain English?

The term chelate, from the Greek 'chele' for 'claw', refers to the ability of a material to combine with excess metals in the cells and blood stream, so the liver and kidney can excrete them. Chelation therapy, is normally given as a series of intravenous infusions containing di-sodium EDTA and various other substances like penicillin.

Chelation therapy has been traditionally applied in Occupational Medicine, as it effectively removes toxic heavy metals (such as lead) from the body. In occupational health chelation therapy is strictly conventional medicine, not alternative medicine. However, chelation therapy is also used, at private clinics, as a complementary treatment for a number of other conditions than heavy metal intoxications, as it may provide the following benefits:

- Dilates constricted arteries
- Reduces high blood pressure
- Diminishes free radical activity
- Improves uptake of oxygen to the cells
- Removes toxic heavy metals from the body
- Improves memory
- Relieves pain in the extremities
- Increases elasticity of blood vessels
- Improves blood flow to the heart, brain, body organs, and legs
- Improves enzyme activity.

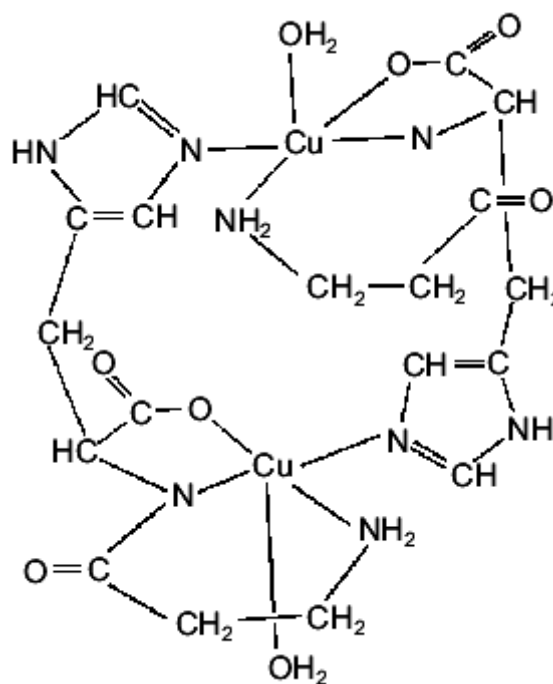


Fig 1. Carnosine-Copper chelate

## Vaccinations & Mercury

In the context of vaccination chelation with carnosine may be crucial, as it removes organic mercury (thiomersal or thimerosal) from a child. Organic mercury is present in most vaccines as an antimicrobial preservative, although it

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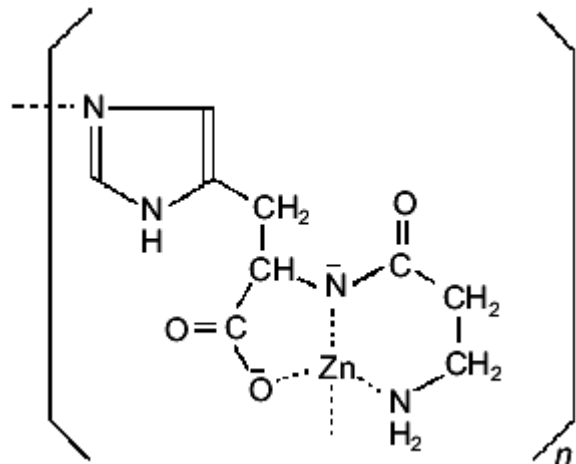
since the 1930's has been recognised as a toxic substance affecting the central nervous system. In my opinion every vaccinated child and adult should take carnosine as a precaution in order to remove thiomersal from the body as soon as possible.

## EDTA Chelation Therapy & Atherosclerosis

Chelation therapy became a popular "alternative" treatment after EDTA was found effective in chelating and removing toxic metals from the blood, and some scientists postulated that hardened arteries could be softened if the calcium in their walls was removed. The first indication that EDTA treatment might benefit patients with arteriosclerosis came from Clarke, Clarke, and Mosher, who, in 1956, reported that patients with occlusive peripheral vascular disease said they felt better after treatment with EDTA.

### Personal Experience

Some elderly people, who on a regular basis take EDTA chelation therapy on the Costa del Sol, Spain, and they claim it has kept them alive and healthy well into their golden years. The EDTA therapy is, however, expensive and cumbersome, as it is given intravenously as a slow infusion at a clinic.



*Fig 2. Carnosine-Zinc chelate*

### In Summary

Carnosine, as a dietary supplement, seems to have all the same chelating properties as EDTA, and it offers a possibility for an inexpensive oral chelation therapy. Carnosine has an ability to chelate prooxidative metals, such as copper, zinc and toxic heavy metals (lead, mercury, cadmium, nickel).

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## Carnosine - Protection from Age Related Diseases (Prevention of Glycation)

"...Because of its anti-glycation actions, carnosine may be useful in preventing and treating diabetic complications such as cataract, neuropathy, arteriosclerosis and kidney failure. It can also be helpful to all of us since AGES age us all, although not as rapidly as diabetics..."

Most recent research suggests that the most important action of carnosine is its anti-glycation effect (*Aldini et al 2002a, 2002b, Yeargans and Seidler 2003*).

### Then what is this glycation?

Let me try to explain it to you in a simple way.

Every second, a destructive process called "glycation" occurs throughout the body. Glycation can be described as the binding of a protein molecule to a glucose molecule resulting in the formation of damaged, nonfunctioning structures. Glycation alters protein structure and decreases biological activity. Glycated proteins, which accumulate in affected tissue, are reliable markers of disease. Many age-related diseases such as arterial stiffening, cataract and neurological impairment are at least partially attributable to glycation.

Carnosine, which prevents glycation, may also play a role in the disposal of glycated protein. Carnosinylation (the process where carnosine combines with denaturated molecules) tags glycated proteins for cell removal.

Glycation, also known in biochemistry as the Maillard reaction, occurring between proteins and glucose, is recognized as a major contributor to aging and perhaps cancer, as well as the complications arising from diabetes. Glucose provides the fuel for glycation, the insidious protein/glucose combination that (following several steps including the oxidation process) results in the formation of an advanced glycation end product or AGEs.

Once AGEs are formed, they interact with neighboring proteins to produce pathological cross linkages that toughen tissues. It has been speculated that no other molecule has the potential toxic effects on proteins as advanced glycation end products. Diabetic individuals form excessive amounts of Ages earlier in life than non-diabetics, a process that disrupts the normality of organs that depend on flexibility for function. It has been shown that it is glycation hardens the arteries of a diabetic individual.

Ages trigger a cascade of destructive events as Ages cling to cellular binding sites. One of the consequences of Ages is a 50-fold increase in free radical

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formation. As diabetes, a condition of accelerated aging, spawns a harvest of Ages, the arteries, the lens and the retina of the eye, peripheral nerves and the kidneys are under specific attack. By opposing glycation, glomerular damage and the resulting inflammation and renal degeneration is reduced. Diabetic rats, not treated with glycation inhibitors, show a twofold increase in glomerular staining for advanced-glycation end products compared with a similar group of diabetic rats receiving treatment (Forbes et al., 2001).

Cataracts (another complication common to diabetics) are also likely to form as a result of glycation, while glycation inhibitors, like carnosine and calcium pyruvate protect against the damage. Supplementation with glycation inhibitors enable humans to prevent many of the adversities that accompany aging. Because carnosine structurally resembles the sites that glycating agents attack, it appears to sacrifice itself to spare the target. Carnosine also bolsters proteolytic pathways, i.e., the disposal of damaged and unneeded proteins.

Because of its anti-glycation actions, carnosine may be useful in preventing and treating diabetic complications such as cataract, neuropathy, arteriosclerosis and kidney failure. It can also be helpful to all of us since Ages age us all, although not as rapidly as diabetics.

## **Carnosine - Carbonylation - Beyond antioxidants**

Why do older people, and animals, look different than younger ones? This has to do with changes in the proteins of the body. Proteins are the substances most responsible for the daily functioning of living organisms, which gives protein deterioration its dramatic impact on the body's function and appearance. Many lines of research over the last decade converge on protein modification as a major pathway for aging and degenerative disease. These modifications result from oxidation (as by free radicals) and interrelated processes such as glycation.

Our body is made up largely of proteins. Because the body's antioxidant system and other lines of defense cannot completely protect proteins, they tend to undergo destructive changes as we age, due largely to oxidation, glycation and another process called carbonylation. In other words carbonyl groups ( $>C=O$ ) adhere to the protein molecules (and phospholipids as well). As a result the proteins break up in a process called proteolysis. Since protein carbonylation clearly preceded the loss of membrane integrity, it may be associated with the toxic process leading to cell senescence and death. In order to understand the implications of the proteolytic decline and buildup of aberrant proteins, it is necessary to revise the picture.

These interrelated protein denaturation and proteolysis include oxidation, carbonylation, cross-linking, glycation and advanced glycation endproduct (AGE) formation, as explained above. They figure prominently not only in the processes

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of ageing but also in its familiar signs such as skin aging, cataracts and neurodegeneration (i.e., loss of memory and dementia). A vast number of scientific studies, published by investigators in the east and west, show that carnosine is effective against all these forms of protein denaturation. Carnosine reacts with the carbonyl group and form an inert protein-carbonyl-carnosine adduct, thus protecting the proteins and reversing the denaturation.

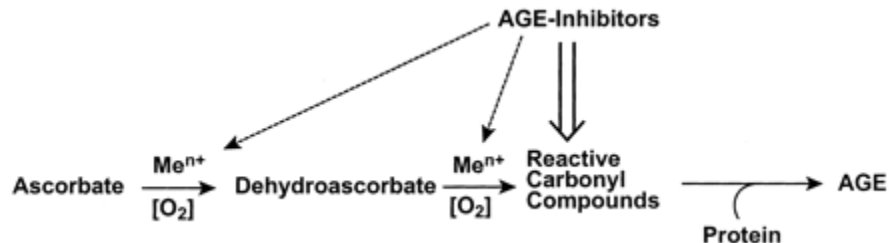


Figure 4. This is how AGE-inhibitors act. Quenching of the carbonyl (bold arrow) is the main way of action. Carnosine and other AGE-inhibitors chelate metals, and hence they prevent the metals from catalyzing oxidation and producing AGE's (Price et al. 2001)

## How does carnosine do this?

Carnosine simply restores the normal cell cycle control. To understand how this can happen, consider an engine whose oil isn't changed regularly. When the detergent in the oil is used up, contaminants precipitate and sludge forms on vital engine parts. The sludge accumulates, impairing engine performance, until finally the engine dies. The body too needs an efficient sludge removal system. When protein "sludge" accumulates, the gears of the cell cycle can get clogged up. This could impair the efficiency of cell division, and perhaps more importantly, enable damaged cells to reproduce. The result is increasing chromosomal instability, leading to degeneration and cancer. Another possible outcome is cellular senescence, when the cell cycle grinds to a halt. Protein carbonylation thus becomes a potentially terminal condition. Carnosine behaves us to maintain healthy intact proteins and to ensure their timely turnover.

Carnosine seems to be far superior to traditional antioxidants, e.g., vitamin E and selenium, that are not as effective as we hoped in the past. They do suppress some of the many pathways involved, while having no effect upon the others, like glycation and carbonylation. It has been established beyond question that antioxidants perform a crucial biochemical function in preventing reactive oxygen damage. However expecting an antioxidant to protect proteins against every form of glycation and carbonylation is like attempting to build a house with only a screwdriver - an essential tool, but incapable of replacing the rest of the toolbox.

Carnosine, nature's multipurpose tool for protein protection, was designed by evolution to control the many factors that cooperate in degrading the body's proteins. The chemical side-reactions that erode biological structure and function in the course of ageing result from toxic effects of the most basic elements in the

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body's chemistry-oxygen, sugars, lipids and essential metals. We cannot do without these biochemical elements, but nutritional science is now giving us the understanding to better control their side effects.

Proteins are not the only molecules denatured by carbonylation - phospholipids are carbonylated as well. And the carbonylation of phospholipids cause damage particularly in the central and peripheral nervous system, resulting in memory impairment and other deterioration of cognitive skills. As carnosine fights carbonylation of the phospholipids as well, it is now wonder that this dipeptide is a marvelous neuroprotectant, as we will see further on.

In sports and body building carnosine is involved in the detoxification pathway of reactive aldehydes from lipid peroxidation generated in skeletal muscle during physical endurance (Aldini et al. 2002a,b). Hence carnosine protects the skeletal muscles from injury, increases muscle strength and endurance and speed up recovery after strenuous exercise, as I will explain in detail later on in this review.

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