Carnosine - The New Anti-Aging Supplement

by Marios Kyriazis MD

*Please don't confuse this for the common amino acid CARNITINE (L-Carnitine). Although carnosine (also known as L-carnosine) has been known for about a century, its antiaging properties have only been extensively studied during the past few years. A recent literature review revealed over 780 published studies on carnosine, mainly by Russian and Japanese researchers. However, more widespread interest in this natural non-toxic product has only recently been increased, fuelled by dramatic Australian and British discoveries about its antiaging actions (1).

Carnosine (B-alanyl-L-histidine) is a naturally-occurring di-peptide (a combination of two aminoacids), found in muscle, brain and other innervated animal and human tissues. It is formed by a process involving the enzyme carnosine-synthetase which bonds the aminoacids alinine and histidine. This process occurs mainly in muscles and brain. It is kept in equilibrium by the carnisinases which are enzymes specifically aimed at inactivating carnosine in the tissues or in the blood.

There are several other related dipeptides such as carcinine, anserrine, homocarnosine and ophidine, all of which are naturally-occurring. These are believed to be buffering agents, helping to maintain the homeostatic equilebrium (2).

High concentrations of carnosine are present in long-lived cells (such as in neuronal tissues). The concentration of carnosine in muscles correlates with maximum lifespan, a fact that makes it a promising bio-marker of aging. It is high in actively contracting muscles and low in cases of muscular disease such as Duchennes's muscular dystrophy. Its concentration in mammalian muscles possibly decreases with age, a fact which strengthens the case for supplementation.

In cases of cataract in animals, carnosine concentration in the lens was found to be low. The lower the concentration of carnosine, the higher the severity of cataract. Rabbits fed on a high cholesterol diet, were found to be well protected against atherosclerosis and cataract, if given carnosine supplements. In another experiment, dogs were also found to be protected against cataract if given carnosine supplements (2).

Antioxidant Properties

Carnosine is widely believed to be 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 (3). It is thought to be a natural counterpart to lipid-soluble antioxidants such as vitamin E. Maybe it is not a coincidence that carnosine increases vitamin E levels in rats.

Many antioxidants are aimed at preventing free radicals (FR) from entering the tissues, but have no effect after this first line of defence is broken. Carnosine is not only effective in prevention, but it is also active after FR react to form other dangerous compounds. So, it protects the tissues from these damaging 'second-wave' chemicals. For example, a

highly reactive lipid persoxidation end-product called malondialdegyde (MDA)- a deliterious product of a free radical reaction- is blocked by carnosine (4,5). 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 and inactivating MDA, sacrifices itself in order to protet the aminoacids on the protein molecule.

Other Benefits:
Carnosine plays a part in neurotransmission, it is a heavy metal binder (chelates ionic metals) and modulates enzymatic activities. Other actions, some of which are not extensively studies, include:

- anti-neoplastic properties, which make it a potentially beneficial agent for use in cancer prevention.
- immune booster (it stimulates maturation of immunocompetent cells), and reduces inflammation.
- wound healing properties and protection against radiation damage (both preventing damage and reversing the post-radiation syndrome). Laboratory animals treated with carnosine were found to have faster and better wound healing rates compared to controls. This has potential applications to treating burns, wounds following surgery, or during nutritional preparation for surgery (6).
- a reduction of gastric ulceration (particularly when the ulcer is related to stress), both by preventing the formation of the ulcer and by healing it (carnosine increases the formation of granulation tissue). It does not affect acid secretion.

Glycosylation:
Perhaps, the most important action of carnosine is its anti-glycosylation effect (8). One of the cardinal processes of aging, apart from free-radical damage, is the process of glycosylation (or glycation). During normal, everyday metabolism, sugar aldehydes may react with the aminoacids on the protein molecule. The result is the formation of AGEs (Advance Glycosylation End-products). These are abnormal, cross-linked, oxidised products which are thought to cause extensive damage to the organism. Carnosine blocks this deleterious reaction, protecting against cross-linking of proteins, cross-linking of proteins to DNA molecules, and formation of other abnormal proteins, all of which are fundamental features of the aging process.

Other anti-glycators such as aminoguanidne may also protect against glycosylation but not as effectively as carnosine. Some aminoacids (arginine or lysine) are also able to combine with glucose in order to eliminate dangerous AGEs, but the end-product of this reaction is mutagenic (i.e. it may cause cancer). The combination of carnosine with glucose however is not mutagenic.

Specifically, carnosine reacts with and inactivates aldehydes and ketones, reducing protein glycosylation and the formation of AGEs. It also binds to already formed AGEs and inactivates them. Normally, AGEs are removed by scavenging macrophages (immune system cells) which carry special receptors called RAGEs. Carnosine facilitates

this process of elimination, by helping macrophages to better recognise the AGE molecule. Because of its anti-glycosylation actions, carnosine may be useful in treating or preventing diabetic complications such as cataract, neuropathy and kidney failure.

Amyloid Protection:
In experiments, treatment with carnosine was found to reduce or completely prevent cell damage caused by beta amyloid (9), the substance found in the brain of Alzheimer's disease patients. Beta amyloid can interact with certain RAGE receptors causing damage to the nerves and arteries of the brain. Carnosine blocks and inactivates beta amyloid, so it protects neural tissues against diseases such as dementia.

There have been some concerns regarding carnosine's ability to form lipofuscin (the age pigment commonly found in the aging brain and in other tissues). Lipofuscin is merely a sign that other deleterious reactions have already taken place. For example, free radicals and toxic aldehydes may react with valuable proteins as described above, and cause damage, leaving lipofuscin as a left-over product. (Ed.-It may be advisable to take a lipofuscin supplement such as Centrophenoxine or acetyl-L-carnitine whilst on a carnosine program). One way to save the protein molecule is to use carnosine instead. Carnosine actively and swiftly binds to aldehydes before these are able to cause any damage. The end-result of this reaction may also be inactive lipofuscin compounds.

In this case, lipofuscin is formed not by wasting valuable protein material but by using sacrificial carnosine, leaving the proteins free to function properly. Lipofuscin, however formed, is thought to be generally inactive to normally everyday situations. High amounts of free radicals and toxin in the organism are best inactivated by using supplementary carnosine than tissue protein. Of course, it would be best to reduce the exposure to too many free radicals in the first place. This can be achieved for example, by avoiding pollution, cigarette smoking, sedentary life, and unsuitable nutrition.

Use on Humans:
After dozens of reports about carnosine's antiaging actions in laboratory experiments, the next logical step was to start using it on humans, specifically for antiaging purposes. Carnosine supplements have been used in the past by body-builders, atheletes and others, but its use has been confined mainly for improving muscular fatigue, and not for longevity.

Recently, eye drops containing carnosine have been developed and used by Russian researchers (10). The drops were found to be effective in treating human corneal erosions and other corneal diseases. For example, carnosine drops accelerate the healing of ulcers in herpes and bacterial infections of the eye.

During a preliminary experiment designed specifically for antiaging (11), I used L-carnosine supplements (50 mg daily) on 20 healthy human volunteers, aged 40 - 75 years, for a period of 1-4 months. No side affects were reported. Five users noticed significant improvements in their facial appearance (firmer facial muscles), muscular stamina and general well-being. Five others reported possible benefits, for example better sleep

patterns, improved clarity of thought and increased libido. The rest did not report any noticeable effects. This is not surprising because supplementation with carnosine is not expected to show any significant noticeable benefits in a short time, but it should be used as an insurance against deleterious effects of the aging process. If any benefits are noted, these should be considered as an added extra bonus. It is worthwhile persevering with the supplementation long term, even if you do not experience any obvious benefits, as you will still be well protected against aging.

Carnosine can be used together with vitamin E and/or Co-enzyme Q10 for full antioxidant protection, but even if it is used on its own it should still confer significant protection both against free radicals and against glycosylation. Indeed, the carnosine preparation I used in my experiments contains also 30 iu of vitamin E as standard. Other nutritional products such as GH (growth hormone)-releasers are fine to use with carnosine, if required. Some people prefer to use 100 mg of carnosine a day (i.e. double the initial standard dose) and they find that there are still no side effects. It may be preferable however to only start with 50 mg a day under advice from your physician or nutritionist, and only increase the dose if recommended so following professional advice. Foodstuffs containing dietary carnosine are lean red meat, and chicken.

Conclusion:
Where do we go from here? Further experiments are in progress, aimed at examining more widely the effects of carnosine on human aging. Those who want to be at the forefront of innovative antiaging medicine should be taking carnosine now. It is expected that carnosine supplementation will become much more widespread during the next five years, making carnosine as popular as vitamin E is today.

Footnote:
Anyone interested in joining the British Longevity Society can contact its founder, Dr. Marios Kyriazis at:
British Longevity Society
PO Box 71, Dept I,
Northampton NN1 5HJ
England
or email: kyriazis@antiageing.freeserve.co.uk or take a look at their website at www.antiageing.freeserve.co.uk

References
1) Hipkiss A. Carnosine, a protective, anti-ageing peptide? Int J Biochem Cell Biol, 1998, 30; 863-868.
2) Quinn PJ, Boldyrev AA, Formaziuk VE. Carnosine: its properties, functions and potential therapeutic applications. Mol Aspects Med, 1992, 13(5);379-444.
3) Tamba M, et al. Hydroxyl radical scavenging by carnosine and Cu(ii)-carnosine complexes. Int J Radiat Biol, 1999 75(9);1177-1188.
4) Hipkiss A, et al. Protective effects of carnosine against MDA-induced toxicity towards cultured rat brain endothelial cells. Neuroscience Letters, 1997, 135-138.

5) Hipkiss A et al. Protective effects of carnosine against protein modification mediated by malondialdehyde and hypochlorite. Bioch Biophys Acta 1998, 1380;46-54.
6) Roberts PR, Black KW, Santamauro JT. Dietary peptides improve wound healing following surgery. Nutrition, 1998, 14(3);266-269.
7) McFarland GA, Holliday R. Further evidence for the rejuvenating effects of the dipetide L-carnosine on cultured human diploid fibroblast. Exp Gerontol 1999 34(1);35-45.
8) Hipkiss A, Chana H. Carnosine protects proteins against methylglyoxal-mediated modicatiations. Biochem Biophys Res Comm 1998, 248 (1); 28-32.
9) Preston J et al. Toxic effects of B-amyloid on immortalised rat brain endothelial cell: protection by carnosine, homocarnosine and B-alanine. Neuroscience letters 1998, 242; 105-108.
10) Maichuk IuF, Formaziuk VE, Sergienko VI. Development of carnosine eye drops and assessing their efficiency in corneal diseases. Vestn Oftalmol 1997,113(6);27-31. 11) Kyriazis M, 1999, Data on file.

Last Updated: Wednesday, March 21, 2001

5083 S. McCarran Blvd. Reno, NV 89502
Phone: (775) 824-0704 Fax: (775) 824-0217 Email