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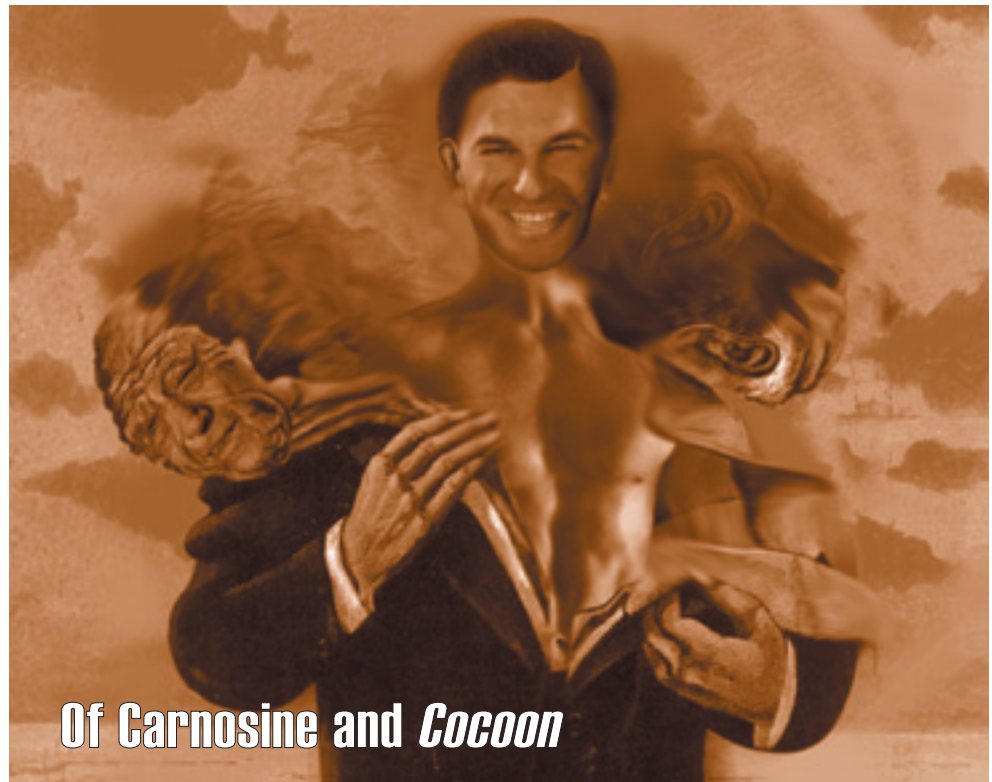
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The Holistic Lifestyle

Volume 1

Issue 5

March 2001



Of Carnosine and Cocoon

Ever see the movie *Cocoon*?

Interesting story. Three old men stumble across a swimming pool at an estate near their nursing home. Since the estate appears to be deserted, but the pool is in good working condition, the men start sneaking the occasional dip. Almost immediately, they notice that something's different: they feel better. Livelier. More energetic. More *youthful*.

And then things begin to happen. A man who spent the early part of the film shuffling around winds up breakdancing at a local club. Sight which had nearly vanished returns to youthful sharpness.

And cancers regress. The men don't just feel younger, miraculous as youthful sparkle can be: they are younger.

The bad news: there's no *proven* "swimming pool of youth" for whole, grown people — yet.

The good news: there *is* such a swimming pool for human cells in culture. For human (and other) cells, a prototype of the pool was made by Australian scientists in 1994, and has since been built and successfully tested in labs around the world. The pool does everything the movie says it will: it restores youthfulness, extends life, fights cancer. It literally makes the cells young

The Holistic Lifestyle

Volume 1, number 5
March 2001

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Holistic International, manufacturers and distributors of the most exciting lines of envelope-pushing nutritional supplements in Canada, welcomes you to this issue of *The Holistic Lifestyle*, published bimonthly. *The Holistic Lifestyle* is designed to provide our customers with essential information and news of breakthrough research to help you make the best decisions to meet your health goals through supplements and lifestyle choices.

The Holistic Lifestyle also provides news about Holistic International and its products, along with trade shows, retailer information, and government regulations and their impact on your health freedom.

Comments? Questions?
We want to hear from you!

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again.

Animal experiments suggest it does something similar in whole organisms. And clinical experience shows that it restores more youthful vision in living, breathing humans.

It has a name. Carnosine. And it may be the most exciting anti-aging nutrient ever discovered.

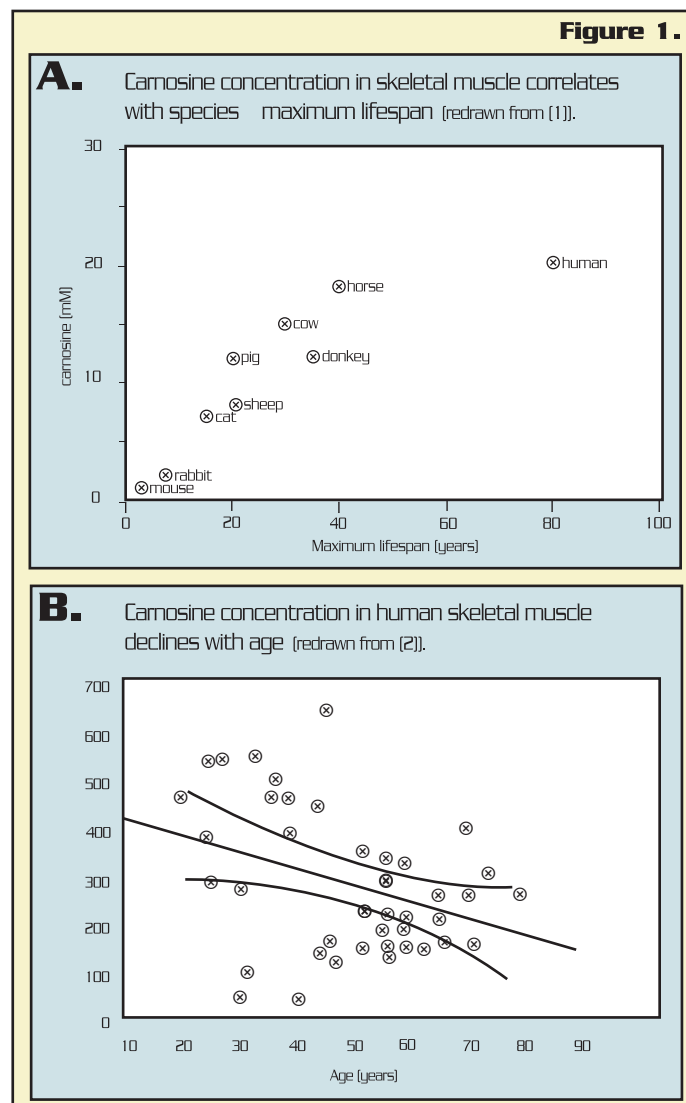
What is This Stuff?

You wouldn't think much of **Carnosine** just to hear about it. It's a simple *dipeptide* (that is, two amino acids joined together — in this case, *beta-alanine* and *histidine*). It's not found in a rare herb from the Caucasus, or the horns of an endangered species in Africa: instead, it's already made by many cells in your body — and especially in muscle, heart, and brain cells. Interestingly, however, longer-lived animals tend to have more **Carnosine** in their cells than do shorter-lived species,¹ and levels of **Carnosine** appear to decline with aging: in preliminary studies, **Carnosine** levels in human skeletal muscle have been found to decrease by 63% between the ages of 10 and 70² (see **Figure 1**). **Carnosine's** biological role is a bit of a mystery.³ No one's quite sure why it's there: it seems as if different cells need it for different purposes — yet its role in each cell type seems vital, even as it is distinct.

Despite an explosion of research on **Carnosine** in the last five years, we only know a little about its role in the body. Or rather, we know *many of the things it can do,*

but each of these things is like a piece in a massive jigsaw puzzle, with so many scattered pieces that we can only guess at the complete image, or where to begin piecing the many segments together.

In muscle cells, for instance, **Carnosine plays a central part in keeping muscle cells contracting and preventing fatigue**, fending off lactic acidosis that leads to muscle exhaustion, restoring the muscle's sensitivity to the flow of calcium



ions that triggers muscular contraction, and allowing isolated muscle cells which have been pushed beyond their workload limits

Of Carnosine and Cocoon

to contract again.⁴ In nerves, its concentration is so targeted, and its release so regular, that it was once thought to be a neurotransmitter; while it now looks as if that's unlikely, **Carnosine does play an important role in modulating brain cell function**, simultaneously making neurons more sensitive to certain signals⁵ and protecting neurons from toxicity from overstimulation.^{6,7} In heart cells, **Carnosine appears to be a central player in regulating the heartbeat** through its role in regulating calcium ions.⁸ But none of that explains its ability to *make old cells young*.

“The Anti-Aging Peptide”

Scientists are of necessity very cautious people. After all, they've been trained in scientific method, which proceeds in baby steps even though history remembers only the paradigm shifts. They've learned to be careful, methodical, precise; to generate solid results, and not to speculate beyond the data. And they have academic reputations to defend.

So it's surprising to see even the *titles* of many of the scientific papers on **Carnosine**. Some of them sound like they could come from supermarket tabloids — not respected biomedical journals. “**Carnosine**, the protective, anti-aging peptide.”⁹ “Use of **carnosine** as a natural anti-senescence drug for human beings.”¹⁰ “A possible new role for the anti-ageing peptide **carnosine**.”¹¹ “Further evidence for the rejuvenating effects of the dipeptide **L-carnosine** on cultured human diploid fibroblasts.”¹² And yet the scientific literature on **Carnosine** is soaked with this kind of language. Why?

It all began with the work of doctors Gail McFarland and Robin Holliday at Australia's Commonwealth Scientific and Industrial Research Organization (CSIRO), a research institute with an astonishingly wide range of research interests. Curious about **Carnosine's** wide range of functions in the body and its unusually high

concentrations in critical tissues like the heart, kidney, muscles, and brain, and looking to clarify its cryptic biological purpose, Holliday and McFarland decided to see what effects **Carnosine** would have on cultured human cells.

Decades of research on such cells had established a well-defined pattern in the growth, development, and aging of such cells: the so-called “**Hayflick phenomenon**.” Placed in a growth vat with a fluid (“**medium**”) rich in essential nutrients, cells from young donors will quickly begin to reproduce, forming colonies which fill the vat — and then stop reproducing, to prevent starving themselves out. If half of these cells are removed from the container, the remaining cells will begin growing again to fill their environment.

But this process can only be carried so far. At each round of division, the cells are *aging* — becoming “**senescent**,” in scientific terms. The process is subtle at first, but as time goes by it becomes more and more obvious that something is very wrong with the cells. They lose their shape and begin to vary wildly in size; they fill up with granular material; they stop

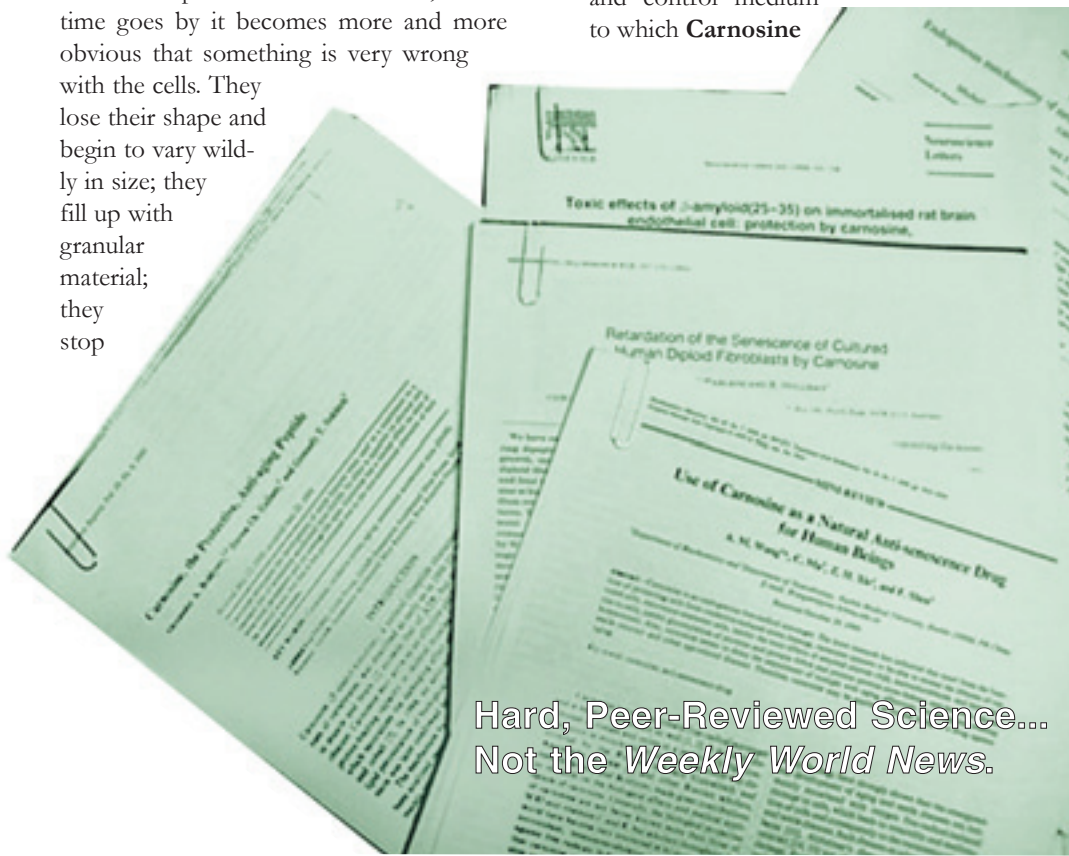
forming continuous colonies, losing their even, patterned, regular spacing, and begin breaking apart, with individual cells drifting off on their own. Senescent cells stop producing the right proteins from their DNA, losing the functions for which they were designed. All of this gives the whole cell culture an unhealthy texture and appearance. Finally, after about 60 divisions, the cells will stop reproducing and slide into a sort of twilight zone, alive but inactive, just waiting for death.

“Retardation of Senescence”

The experiment¹³ was simple. First, raise lung and skin cells in one of two standard cell culture mediums. Then keep half of the cells in the original medium, but transfer the other half into the same medium supplemented with **Carnosine**.

And the results were also simple.

Of course, they were also astonishing. The exact results depended on the cell type and control medium to which **Carnosine**



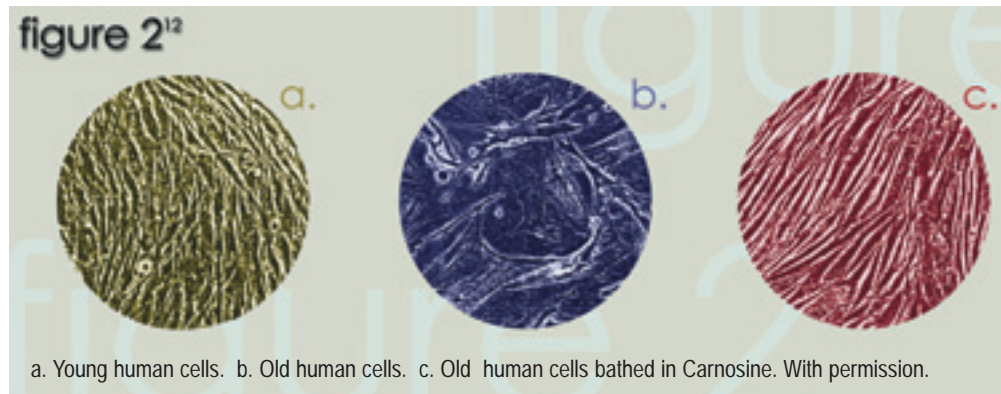
Hard, Peer-Reviewed Science...
Not the *Weekly World News*.

was added, but the general pattern was the same. The cells were able to keep reproducing longer: **Carnosine-supplemented colonies** achieved anywhere from one to seven more population-doublings. And they *lived* longer: in fact, the longest-lived cells lines receiving the **Carnosine** bath survived up to *two-thirds longer* than the cells in the standard mediums. **Carnosine-treated cells had broken the Hayflick limit — and left it in their dust.** In a whole person, this would be like having one Jean Calmet finally passing away at 122 years of age in the control group, while her sister in the **Carnosine** group survives *be two hundred years old.*

But most excitingly, **adding Carnosine to the cell medium made the cells younger.** McFarland and Holliday described the results as “Striking effects on the cell morphology [shape and structure],” saying that “**carnosine** preserved a nonsenescent [youthful] morphology.” Looking at the pictures in their scientific report (see **Figure 2**), it doesn't take a specialist to see why. The cells raised in the usual medium get old, blotchy, and irregular, and are broken apart into scattered islands of twisted debris. Yet clearly, the cells raised in **Carnosine** still have the same appearance they had when they were young: the colonies are flat, still maintaining their youthful whirling patterns; they're still smooth, regular, and even. And, remarkably, **cells bathed in Carnosine stayed youthful almost until the very end of their lives.** It's as if that 200-year-old wonderwoman was still in early middle age until she hit 190, and only then suddenly started to “let herself go.”

“A Remarkable Rejuvenation”

Fascinated, the scientists took cells from the very old cell populations in each group, and switched them from one medium to the other. Perhaps it was not surprising that cells taken away from their nourishing **Carnosine** baths quickly began to go



downhill, returning to “normal” aging sharply and suddenly. But what was surprising was that **cells that were already senescent were made young again by the Carnosine bath.** “These cells showed a remarkable rejuvenation, with regard to their morphology ... and finally reached [ages] significantly greater than the control culture from which they were derived.” Other researchers have confirmed these results.^{14,15}

Other, closely-related compounds — including **Carnosine's** “mirror image,” D-carnosine — fail to accomplish these amazing effects.

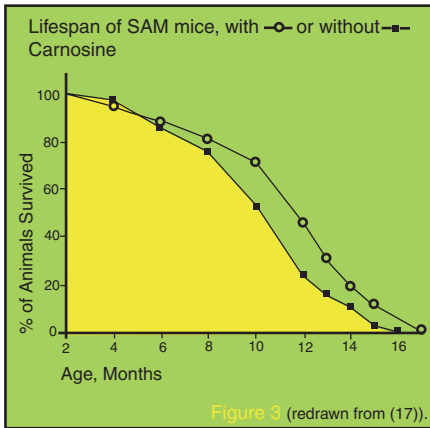
McFarland and Holliday subsequently repeated, confirmed, and expanded on their original results.¹² They showed that they could take cells from the **Carnosine** medium, move them into the standard culture, and see them grow old — but then move them back into the **Carnosine** bath, and have them spring back into youth again. “**Switching cells between media with and without carnosine also switches their phenotype [visibly observable properties] from senescent to juvenile, and the reverse.**” They “propose that **carnosine** is an important component of cellular maintenance mechanisms,” and “favor the view that it may have a very important role in controlling cellular **homeostasis**” — that is, in keeping cells in the tightly-regulated condition that optimizes their function.

“Potential Anti-Senescence Drug”

These effects are very exciting — but clearly **Carnosine** is not likely to double human lifespan. And many compounds look promising in cell cultures that don't seem to do much in the real world of living things. So it's natural to be skeptical of such claims until they've been reproduced in living, breathing organisms. Such experiments have now been done, and while very preliminary, they again hold forth an exciting vision of **Carnosine's** potential.

An international team of scientists has published two papers on the effects of aging in the SAM mouse¹⁶ and the impact of **Carnosine** on aging in this strain.¹⁷ The choice of the SAM mouse for research was an unfortunate one, because SAM mice are unusually short-lived. The advantage to using such short-lived animals is that it allows researchers to generate results quickly. The problem is that, when the results do come in, it's hard to ever be sure what a given result *means*, because there's no sure way to tell what parts of the results are due to a therapy's effects of *aging*, and the therapy's effects on the *disease* which makes them so short-lived to begin with.

For instance: suppose we work with a strain of animal that inevitably develops advanced kidney failure when they're still fairly young. Then suppose we come up with an intervention (a drug, a nutrient, an exercise or diet plan) that we think might



slow down aging. If we give it to short-lived animals like SAM mice, *any* result we get will be ambiguous. If lifespan is extended, we can't be sure if we've got a therapy which slows down aging in the animal in question, or a if we have instead a cure for their unique form of kidney disease. And on the other hand, if we try the therapy, and nothing happens, we *still* won't know what to make of the result, since the therapy might have a true anti-aging effect, but not prevent the animals from dying early of their kidney disease.

But with those preliminary cautions, let's have a look at the SAM data.

Scientists took a group of SAM mice and added **Carnosine** to their drinking water (the human equivalent of about one gram each day, adjusting for metabolic considerations). Right away, the data are frustratingly suggestive, because **animals receiving Carnosine lived 20% longer, on average**, than their non-Carnosine littermates — and more excitingly, **the maximum survivorship was 6% longer, too** (see **Figure 3**).

Since the animals' weights were held constant between the two groups, we can rule out the effects of **caloric restriction (CR)** in these results. This is important, because it sometimes happens that the supplemented food is so distasteful that animals eat less of it. Because CR is known to slow aging in mammals — indeed, it is

the *only* way of doing so which has proven beyond a shadow of a doubt — such “hidden” CR can sometimes create “false positives,” where the animals eat less food, the resulting CR slows aging, and the anti-aging effect is misattributed to the therapy. So it's important to know that the **Carnosine** results had nothing to do with CR. Again, though, *all* SAM mice — **Carnosine** or no **Carnosine** — were still quite dead by the age of 17 months, or about the human equivalent of 56 years of age. So it's hard to say just what this really tells us.

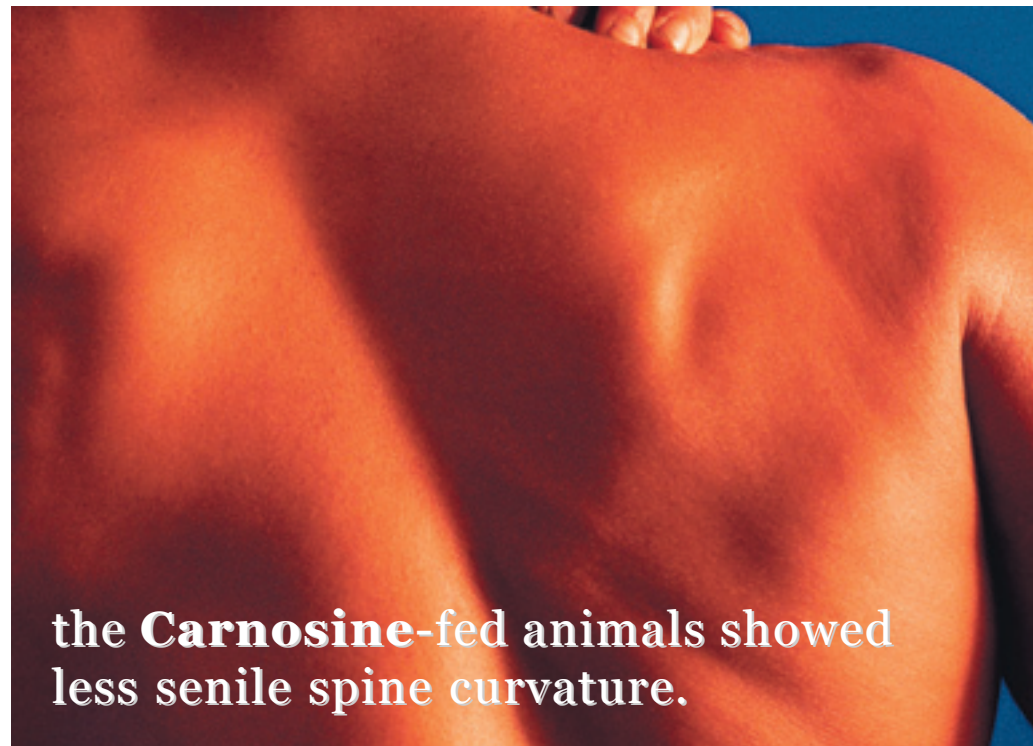
“Resistant to Features of Aging”

When it comes to age-related diseases, however, we're on much more solid ground. **Carnosine-fed animals looked and acted younger throughout their lives** when held up against animals not fed **Carnosine**. Examined at midlife, some age-related damage was not found to be significantly different between the two groups; however, the **Carnosine-fed** animals showed over **40% less loss of hair fullness and color, and suffered 61% fewer skin ulcers**, than the control

animals. The **Carnosine**-fed animals also showed **significantly less of the sores around the eyes** which developed in animals not given **Carnosine**, and **13% less senile spinal curvature**(**Figure 4**).

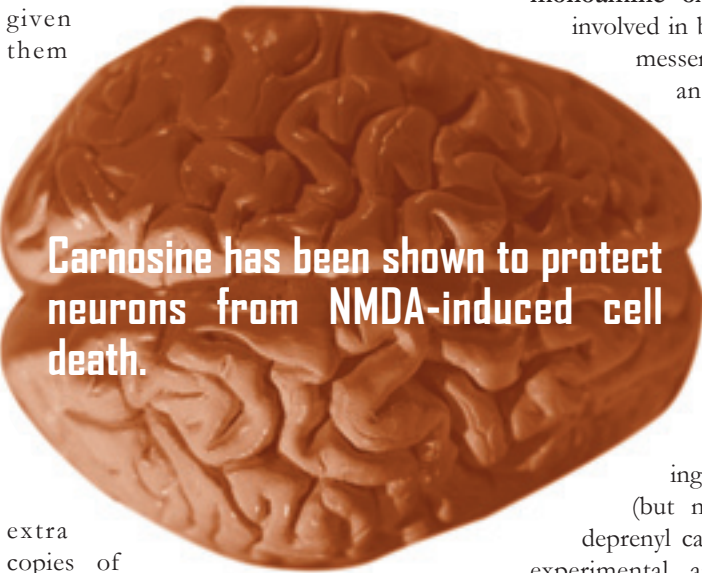
Perhaps most excitingly, **Carnosine-fed animals kept their mental faculties sharper, longer** than their unsupplemented littermates. Animals fed **Carnosine** performed **29% better on tests of passive avoidance** (a measure of how well the animals learned to avoid entering an attractive-looking shock chamber) and **nearly six and a half times better on tests of “reactivity”** (which examine how actively the animals will respond to new phenomena in their environment — a measure of youthful exploratory curiosity). In short, the scientists concluded that, in these short-lived mice, those administered **Carnosine** were “more resistant to features of aging.”

When the researchers looked at the brains of the SAM animals, they discovered some of the biochemical changes which underlay



these results. First, the scientists examined the binding of the brain messenger **glutamate** to the **NMDA (N-methyl-D-aspartate) receptor**, which is recognized as the most important receptor for excitatory signals in the brain. The scientists found that **Carnosine therapy increased the binding of glutamate to this receptor.**

The binding of glutamate to the NMDA receptor is a crucial mechanism involved in forming memories. Indeed, the “Doogie” mice created by Princeton researchers led by Dr. Joe Tsien, whose astoundingly extended youthful brain function¹⁸ put them on the cover of *Time*¹⁹ and earned them a feature story in *Scientific American*,²⁰ got their improved memories because Tsien's team had given them



Carnosine has been shown to protect neurons from NMDA-induced cell death.

extra copies of a subunit of the NMDA receptor, allowing glutamate signals to more easily activate this crucial memory-forming gateway. Interestingly, a key feature of “Doogie” mice, like SAM mice treated with **Carnosine**, is an increase in “reactivity.”

At the same time, the activation of the NMDA receptor can be a lot like opening floodgates. *Excessive* stimulation by NMDA can damage, or even kill, brain cells. In fact, this “**excitotoxicity**” is thought to play a

major role in the degeneration seen in Parkinson's disease. So it's all the more remarkable that, even as it enhances the activation of this crucial memory pathway, **Carnosine has been shown to protect neurons from NMDA-induced cell death,⁷ and to prevent both the overactivation of the NMDA receptor, and the resulting brain damage and loss of mental function,** which occurs when the brain is starved for oxygen (“**ischemic**”).²¹ Such oxygen starvation is what causes the mental impairments which are common in both animals and people who have suffered a **stroke.**

The scientists also reported that **Carnosine inhibits the activity of MAO B in the brain.** MAO B, short for **monoamine oxidase B**, is an enzyme involved in breaking down some brain messengers (such as **dopamine** and **serotonin**). MAO B activity is known to increase production of the free radical (ROS) precursor **hydrogen peroxide**, and the enzyme becomes more active as a person gets older. **Deprenyl**, a drug used to treat people with Parkinson's disease, works by inhibiting MAO B, and some studies (but not all) have found that deprenyl can increase the lifespan of experimental animals.²² The fact that **Carnosine** reduces MAO B activity may thus be another factor involved in both **Carnosine's** enhancement of brain function, and its reduction in free radical damage during brain oxygen deprivation.²¹

Of Cancer and Cataracts

Back to the swimming pool in *Cocoon*. In addition to restoring the men's youth, bathing in the pool wrought miracles in two of the men, restoring the sight of one and curing another of cancer. Again, it is as if the movie were advance publicity for the

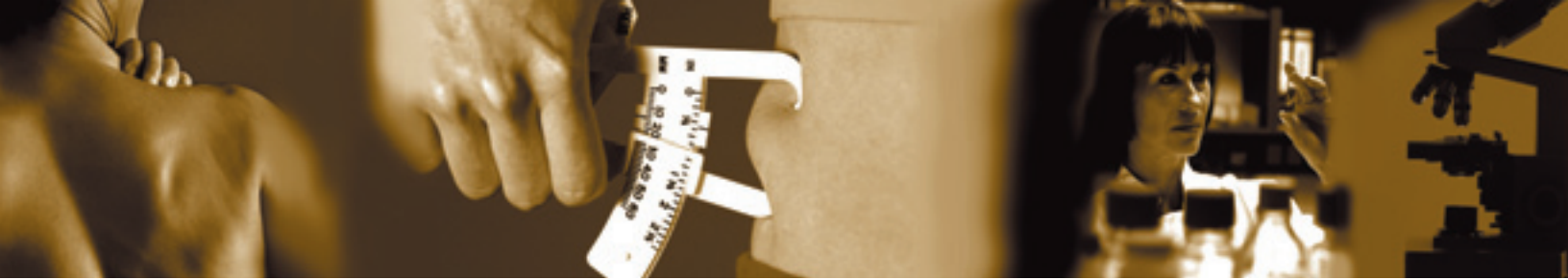
promise of **Carnosine.**

Investigators at the Harbin Medical University have published an English-language review of their uncontrolled work using **Carnosine** in treating patients with vision problems.¹⁰ In an open investigation, 96 senior citizens who had suffered with senile cataracts for 2 to 21 years were treated with **Carnosine** eye drops 3 to 4 times daily for 3 to 6 months, literally *bathing* the eyes in **Carnosine** solution. **The researchers found improvements in eyesight and lens transparency** in the great majority of patients. “The result shows that **carnosine** gives a pronounced effect on primary senile cataract ... **For mature senile cataract, the effect rate is 80%** [emphasis added!], and positive effects were observed in other types of cataract.” The investigators have since expanded these preliminary results through the sequential treatment of nearly 1000 senile cataract patients, with similar results. Side effects have yet to be observed.

Further, the same team has also treated patients in late middle age with *non-cataract* visual impairment, using a similar protocol. They have found that **Carnosine** “appears to alleviate eye tiredness and ... **obviously improve eyesight**, giving more clear vision.”¹⁰ Other investigators have reported **success using Carnosine eyedrops against a variety of disorders of the cornea** (the transparent coating of the pupil), including erosion of the cornea and corneal ulcers created by viral and bacterial infections.²³ It will be exciting to see a double-blind trial to confirm these preliminary results.

The other wonder in *Cocoon* was the regression of cancer. Again, the preliminary evidence suggests that **Carnosine** may fulfill the vision of the film.

While performing their astounding cell-rejuvenation experiments, Holliday and MacFarland happened to find that one of

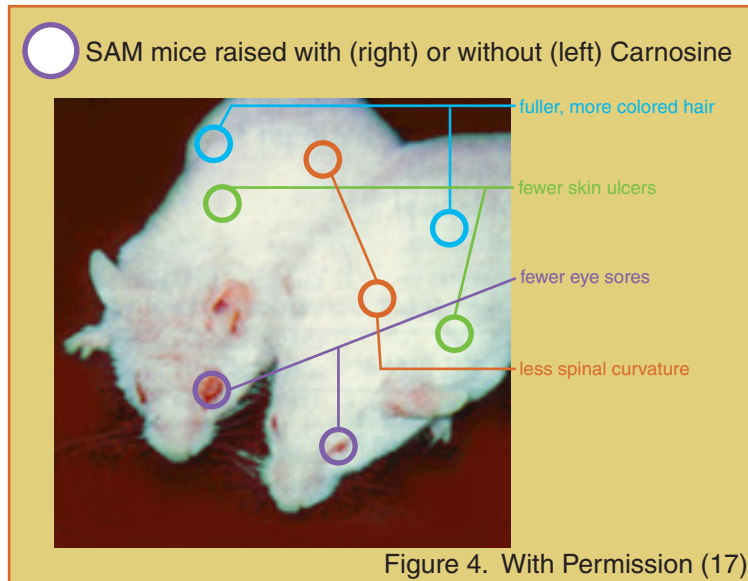


their cell cultures had become contaminated with cancer cells, which quickly began to choke out the healthy ones. But when **Carnosine** was added to samples of this contaminated population, it was found that the cell cultures became free of cancer cells.²⁴ In contrast to healthy cells, **cancerous cells' growth was inhibited by Carnosine**. Curious, the researchers tested **Carnosine** against seven human cancer cell lines: same result. Despite its beneficial properties in normal, healthy cells, **Carnosine was found to be selectively toxic to human cancer cells!** The effect was so distinct that the researchers found that they could add cancerous cells to a culture of healthy ones, bathe the warring tribes in **Carnosine** — and sit back and watch as the cancer cells slowly disappeared from the pool, even as the healthy cells thrived.

In a recent review,²⁵ Holliday and McFarland asserted that these “extremely striking” results are suggest that “It is possible that **carnosine** has anti-cancer activity in vivo [that is, in a whole animal, rather than a cell culture].” Unbeknownst to the Australian researchers, Japanese scientists had already published results suggesting that **Carnosine inhibits tumor growth in living organisms**. Nagai and Suda²⁶ implanted cancer cells into laboratory mice, and then administered a daily injection of **Carnosine** two centimeters away from the implant site. **Carnosine-treated animals showed reduced tumor growth and mortality** compared to animals not receiving the dipeptide. **In some cases, tumors regressed**. The effects were further enhanced when **Carnosine** was combined with an immune-enhancing drug.

How can **Carnosine** be selectively toxic to cancerous cells, while regenerating and extending the life of healthy ones? It would appear that **Carnosine's** cancer-fighting powers derive from a deceptively simple property: namely, its ability to bind up **pyruvate**, a substance used in the cell's

energy cycle. Compared to healthy cells, cancer cells have long been known to be much more dependent on pyruvate: they



have a harder time making it from glucose, and show much higher rates of fermentation of pyruvate to lactic acid.²⁷ Holliday and MacFarland found that adding extra pyruvate to the growth medium could cancel out **Carnosine's** cancer-fighting properties.^{24,28}

Because the fluid bathing cells in the body (the **extracellular fluid**) naturally contains very little pyruvate, the neutralization of **Carnosine's** cancer-fighting properties would not be expected to be an issue in a living organism. This conclusion is reinforced by Nagai and Suda's results. The exception would be if a person were taking supplemental pyruvate, as some athletes presently do. Based on these facts, **it would seem wise to discontinue pyruvate supplements**, whether or not one is supplementing with **Carnosine**.

“Pluripotent Protective Effects”

But if we try to pin down just how it is that **Carnosine** can exert its other, wide-ranging anti-aging effects, we'll have a hard time choosing among all the options. The protective properties of **Carnosine** have

been described as “**pluripotent**”²⁹ — that is, “many-powered.” For starters, **Carnosine is a highly versatile antioxidant**, uniquely capable of quenching a broad range of free radicals (superoxide,³⁰ singlet oxygen, hydrogen peroxide, and both peroxy and hydroxyl radicals³¹) where most antioxidants are “specialists.” Further, **Carnosine** has indirect antioxidant powers through **chelation of pro-oxidant metals** and the **prevention of the destruction of the antioxidant enzyme superoxide dismutase (SOD)**³² normally seen in cells exposed to hydrogen peroxide.

The power of these combined antioxidant actions was shown in experiments in which cells were exposed to toxic levels of oxygen, with¹⁴ or without³³ accompanying nutritional deprivation. **Carnosine** treatment preserved healthy cell structure and reduced damage to the cells' DNA. What makes these results is so impressive is that **Carnosine could protect to DNA when no other tested antioxidant — not vitamin C, not vitamin E, not N-acetylcysteine (NAC), and not the potent synthetic antioxidant ethoxyquin — could do so.**³³

Even a quick survey of the review papers on **Carnosine**^{29,34-36} shows, however, that antioxidant functions are only the beginning of **Carnosine's** sweeping protective and homeostatic properties. **Carnosine also protects against the formation of Advanced Glycation Endproducts (AGEs)**, proteins warped (“glycated”) by sugar. Glycation of proteins leads to the loss of that protein's function, loss of flexibility, atherosclerosis, abnormal cellular signaling, inflammation, the complications of diabetes, and aspects

of the aging process. **Carnosine's** anti-glycating powers are a suicide mission: **Carnosine** allows itself to be glycated, defending other vital proteins from damage. And while the reaction of sugar with some peptides and amino acids also creates cancer-causing substances,³⁷ this is not so with **Carnosine**.³⁸

As people age, their rate of tearing down old, defective cellular proteins (**proteolysis**) slows down, which interferes with cellular function. **Carnosine maintains proteolysis at more youthful levels** in old cells.¹⁵ Further, **Carnosine** has been shown to react with certain abnormal proteins, a process which may make it easier for the body to inactivate and dispose of them.^{29,39}

Carnosine changes gene expression in cells exposed to it, including increasing the expression of **vimentin**, a protein involved in maintaining the integrity and complex internal structure of the cell.⁴⁰ **Carnosine enhances various aspects of immunity**^{41,42} and **protects cells against**

damage from a variety of toxins produced in the body as a part of normal metabolism, including the lipid peroxidation product **malondialdehyde**; the cancer-causing glycation product **methylglyoxal**; **hypochlorite**, a deadly substance made by cells of the immune system to kill off invading pathogens, but also toxic to the body's own cells; **formaldehyde**; and the **amyloid beta-peptide**, which forms the seed of the plaques associated with **Alzheimer's disease**.⁴³ **Carnosine** also prevents the development of amyloid into full-fledged plaques.⁴⁴ The list of protective functions goes on and on.

The Key to Aging?

We now move briefly out of the laboratory and into the theoretician's ivory tower. Cambridge gerontologist Dr. Aubrey de Grey has for some time been developing a theory to explain just how aging happens in the body. While an article of this length and nature can't hope to even scratch the surface of this highly complex theory,⁴⁵⁻⁴⁷ the key point is that cells which have been

taken over by defective cellular “power plants” (**mitochondria**) become “hotspots” for free radical production. The existence of such “hotspot” activity has recently been confirmed experimentally.^{47a} These cells — which de Grey believes actually drive the aging process — survive using a very inefficient, highly abnormal method of harvesting energy. Interestingly, a key part of this abnormal energy processing is a higher dependence on pyruvate for energy production — just as is seen in cancer cells.

A tantalizing possibility is thus raised: if aging is actually driven by a cell type which also depends heavily on pyruvate for survival, and if **Carnosine** can weed out cancer cells precisely by blocking their use of pyruvate, then **might not Carnosine have the same selectively toxic effect on the cells that drive aging?** We have now moved to the far reaches of speculation — but the excitement these speculations generate is very real.

Carnosinase & Effective Dosing

A few years ago, **Carnosine** enjoyed a brief stint of publicity in the nutritional field — not because of its anti-aging properties, but because of the preliminary evidence that it may have great potential as a **sports nutrition supplement**. Because, as noted above, **Carnosine** is an effective buffering agent against lactic acidosis and is depleted by hard workouts, and because exhausted muscle cells can be made to begin contracting again when exposed to **Carnosine**, athletes began supplementing with this vital peptide as the “next creatine,” which would allow them to squeeze out those last two reps and break their gains plateaus.

To cut a long story short, these supplements didn't work. But the lack of effectiveness of these formulas doesn't actually tell us anything about the sports nutrition potential of **Carnosine**, because **the dosages used were literally twenty**



Carnosine changes gene expression in cells exposed to it.



"Vitamin E."
 Alpha-tocopherol."
 Potayto, potahto.
 Tomayto, tomahto.
 Right?"

times lower than they have to be in order for the body to make effective use of **Carnosine** supplements.

The body has a family of enzymes called **carnosinases**, which break **Carnosine** down into its component amino acids. Because of these enzymes, **Carnosine** doses below a certain threshold are rapidly destroyed by the body. Experiments clearly show that feeding laboratory animals **Carnosine** in dosages equivalent to a human taking over five hundred milligrams of **Carnosine** a day (the amount in a 20% beef diet) have no effect on **Carnosine** levels in muscles,^{48,49,58} heart,⁴⁸ or liver,⁴⁸ while higher dosages increase muscle **Carnosine** levels^{49,58} and (as we have seen) have clear therapeutic benefits to the brain^{7,21} and body.^{16,17,50}

While the exact cutoff point is uncertain, and indeed may vary from one individual to another, **benefits clearly and consistently emerge at dosages equivalent to 945 mg/day** and up for a person of average weight (70 kg). Some **Carnosine** products currently on the market contain as little as 50 mg per capsule!

Jump In — The Water's Fine

We still haven't explored many possible roles of **Carnosine** in human health, including studies suggesting that forms of **Carnosine** may prove to be a useful treatment for ulcers^{51,52} and that **Carnosine** is a remarkable heart-protective nutrient which increases the heart's ability to contract⁵³ and helps blood vessels to relax.⁵⁴ But enough for now! From the evidence presented here, it seems plain that, for those hoping for a dip in the *Cocoon* swimming pool, the promise of **Carnosine** sparkles like sunshine from the Fountain of Youth.

WHO SHOULD NOT TAKE CARNOSINE

Serum carnosinase deficiency (SCD) is a neurological disease which is accompanied by low activity of the carnosinase enzyme. The degree of carnosinase deficiency does not seem to be related to the degree of debility,⁵⁵ in particular, families have been located in which, while some members have the disease, others have the characteristic reduced carnosinase activity — but have no impairment of mental function.⁵⁷ Thus, it is now believed by many investigators that the low activity of the enzyme is not the cause of the associated neurological disease. None the less, it seems prudent to suggest that patients with SCD should not take **Carnosine** supplements.

There is also one report⁵⁶ of low carnosinase activity in persons with some other neurological disorders (Parkinson's disease, multiple sclerosis, and stroke complications), though not others (idiopathic epilepsy and motor neuron disease). While unconfirmed, this suggests that persons with neurological disorders should consult their physicians before considering a **Carnosine** supplement.



Wrong.

The fact is, *vitamin E is more than alpha-tocopherol*. It's more than "mixed tocopherols," too. Vitamin E isn't *one* vitamin, but *eight*. Four tocopherols, *plus* the four *tocotrienols*, make up the vitamin E team.

Like the different B-complex vitamins, E vitamins work together, yet different E molecules have different functions. No amount of alpha-tocopherol can fully substitute for gamma-tocopherol -- and no amount of "mixed tocopherols" can make up for getting no tocotrienols in your supplement. The fact is, if you're just getting alpha-tocopherol -- or alpha with a smidgen of "mixed tocopherols" thrown in as an afterthought -- you're not getting "vitamin E." You're getting a lopsided *vitamin E fraction*.

Total E is Canada's first complete, balanced E-complex vitamin. Providing all eight vitamin E molecules, just two **Total E** softgels a day balances out the top-heavy alpha-tocopherol dosing in most "vitamin E" supplements or premium multivitamins.



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Did you know?

In articles in *The Holistic Lifestyle*, we often talk about *clinical trials*: studies in which a vitamin, mineral, herb, or other nutrient was tested in people. Clinical trials are a good way to test supplements: if you want to know what something does, give it to people and see what happens!

But there are different kinds of clinical trials. An *open trial* is one in which the nutrient is given "openly:" everyone knows what the pill is, and who's getting it. Such trials are useful, but they always leave open the possibility that people's expectations influenced the outcome. The mind is the greatest healer in the world, after all: how do you know where the effect of the pill leaves off, and the power of hope begins?

A *double-blind, placebo-controlled trial* helps scientists solve this problem. In these trials, some of the subjects get the nutrient that's being tested — and some get a dummy pill called a *placebo*. Because the trial is set up so that no one — not the scientists, and not the subjects — knows who gets what, expectations are left behind. Everyone wonders: am I taking the real thing, or am I taking a sugar pill?

Because the healing power of the mind is kept equal, this kind of trial gives us the best idea of how well the pill *itself* works. That makes it the best kind of evidence — the *gold standard* for evidence.

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