

# Carnosine



**Carnosine** is a dipeptide composed of Alanine and Histidine which occurs naturally in meats and accumulates preferentially in muscle, brain, eyes and nervous tissue.

Benefits proven in studies with a dose of Carnosine ranging from 800 mg/day to 25 mg/lb. body weight:

- a. Reduces glycosylation<sup>1</sup>, has antioxidant action<sup>2</sup>, protects against metal induced toxicity, reduces diabetes complications<sup>8</sup>
- b. Protective effects on brain or heart, especially during injuries such as stroke or ischemic perfusion.<sup>4</sup> Possibly helpful with neuromuscular disease<sup>9</sup>
- c. Speeds up wound healing by stimulating collagen production<sup>6</sup>
- d. Protective on eyesight, specifically cataract and other aging related impairment<sup>7</sup>
- e. Proposed as anti-aging factor with tissue rejuvenative effects as evidenced by in vitro experiments on fibroblasts.<sup>3</sup> Has shown increased life span in animal models.<sup>7</sup>
- f. Protective effect on the brain aging, against amyloid plaque (Alzheimer's)<sup>7</sup> and potentially helpful with autistic disorder (800 mg/day).<sup>5</sup>
- g. Protective on stomach lining in conditions such as ulcer.<sup>7</sup>

THIS INFORMATION IS PROVIDED FOR THE USE OF PHYSICIANS AND OTHER LICENSED HEALTH CARE PRACTITIONERS ONLY. THIS INFORMATION IS INTENDED FOR PHYSICIANS AND OTHER LICENSED HEALTH CARE PROVIDERS TO USE AS A BASIS FOR DETERMINING WHETHER OR NOT TO RECOMMEND THESE PRODUCTS TO THEIR PATIENTS. THIS MEDICAL AND SCIENTIFIC INFORMATION IS NOT FOR USE BY CONSUMERS. THE DIETARY SUPPLEMENT PRODUCTS OFFERED BY DESIGNS FOR HEALTH ARE NOT INTENDED FOR USE BY CONSUMERS AS A MEANS TO CURE, TREAT, PREVENT, DIAGNOSE, OR MITIGATE ANY DISEASE OR OTHER MEDICAL CONDITION.

a. “Carnosine has been shown to react with low-molecular-weight aldehydes and ketones and has been proposed as a **naturally occurring anti-glycating agent**. It is suggested here that carnosine can also react with (“carnosinylate”) proteins bearing carbonyl groups.... Accumulation of protein carbonyl groups is associated with cellular ageing resulting from the effects of reactive oxygen species, reducing sugars, and other reactive aldehydes and ketones.”<sup>1</sup>

“Carnosine and related dipeptides have been shown to **prevent peroxidation** of model membrane systems leading to the suggestion that they represent water-soluble counterparts to lipid-soluble antioxidants such as alpha-tocopherol in **protecting cell membranes from oxidative damage**.”<sup>2</sup>

b. “**pronounced anti-ischemic effects of carnosine in the brain and heart** are due to the combination of antioxidant and membrane-protecting activity, proton buffering capacity, **formation of complexes with transition metals**, and regulation of macrophage function. In experimental cerebral ischemia, carnosine decreases mortality and is beneficial for neurological conditions of the animals. In cardiac ischemia, carnosine protects cardiomyocytes from damage and improves contractility of the heart. The data indicate that **carnosine can be used as an anti-ischemic drug**.”<sup>4</sup>

c. “**Thus, the enhancement by carnosine of wound healing may be ascribed to stimulation of early effusion by histamine and of collagen biosynthesis by beta-alanine**. The wound-healing effects of carnosine were

further demonstrated by the observation that carnosine significantly increased granulation suppressed by cortisone, mitomycin C, 5-fluorouracil, and bleomycin.”<sup>6</sup>

d., e. “It is proposed that the **anti-ageing and rejuvenating effects of carnosine are more readily explainable by its ability to react with protein carbonyls than its well-documented antioxidant activity**.”<sup>2</sup>

“Carnosine is an endogenous free-radical scavenger. The latest research has indicated that apart from the function of protecting cells from oxidation-induced stress damage, carnosine appears to be able to extend the lifespan of cultured cells, rejuvenate senescent cells, inhibit the toxic effects of amyloid peptide (A beta), malondialdehyde, and hypochlorite to cells, **inhibit glycosylation of proteins and protein-DNA and protein-protein cross-linking, and maintain cellular homeostasis**. Also, carnosine seems to **delay the impairment of eyesight with aging, effectively preventing and treating senile cataract and other age-related diseases**. Therefore, carnosine may be applied to human beings as a drug against aging.”<sup>7</sup>

e. “**Carnosine can delay senescence in cultured human fibroblasts and reverse the senescent phenotype**, restoring a more juvenile appearance. As better antioxidants/free-radical scavengers than carnosine do not demonstrate these antisenescent effects, additional properties of carnosine must contribute to its antisenescent activity.”<sup>3</sup>

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# Benfothiamine



**Benfothiamine** (S-benzoylthiamin-o-monophosphate) is a highly efficient fat soluble form of Thiamin (vitamin B1) and occurs naturally in small amounts in crushed garlic, shallots and leeks.

## Benefits proven in studies with a dose of Benfothiamine ranging from 50-350 mg/per day:

- a. Reduces glycation products caused by excessively high glucose/fructose levels, especially inside endothelial, retinal, kidney and nerve cells.<sup>1,3,6</sup>
- b. Prevents the formation of inflammatory signals caused by excessive glycation such as NF-kappaB and PAI-1<sup>1</sup>
- c. Prevents or reduces diabetic neuropathy and retinopathy by as much as 30%-50% as well as nephropathy and hyperfiltration.<sup>4,5,7</sup> Benefits occur as early as 3 weeks<sup>5</sup>
- d. Reduces myocardial dysfunction stemming from damage to the nerves that control the heart beat.<sup>8</sup>
- e. Benfothiamine has a higher bioavailability than Thiamine or TTP (Thiamin Pyrophosphate-the activated coenzyme form of Thiamine) due to the following properties:
  1. Achieves 5 times higher plasma levels due to better intestinal absorption<sup>2</sup>
  2. Better uptake and retention inside the cells due to its lipophilic nature<sup>2</sup>
  3. It has the ability of upregulating the protective transketolase enzyme significantly more than plain thiamin. This enzyme diverts potentially damaging sugar metabolites on a safer metabolic pathway, the pentose phosphate shunt<sup>1</sup>
- f. Enhances heavy metal detoxification<sup>9,10</sup>
- g. Useful in correcting genetic or alcohol induced thiamin deficiency and polyneuropathy<sup>11,12</sup>

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a, b. "Three of the major biochemical pathways implicated in the pathogenesis of hyperglycemia induced vascular damage (the hexosamine pathway, the advanced glycation end product (AGE) formation pathway and the diacylglycerol (DAG)-protein kinase C (PKC) pathway) are activated by increased availability of the glycolytic metabolites glyceraldehyde-3-phosphate and fructose-6-phosphate. We have discovered that the lipid-soluble thiamine derivative **benfothiamine can inhibit these three pathways, as well as hyperglycemia-associated NF-kappaB activation**, by activating the pentose phosphate pathway enzyme transketolase."<sup>1</sup>

c. "benfothiamine, a lipid-soluble form of vitamin B1, can **prevent diabetic retinopathy** and all three forms of metabolic damage by stimulating transketolase activity and thus diverting excess metabolites toward the pentose pathway."<sup>6</sup> "Benfotiamine strongly **inhibited the development of microalbuminuria ...and diabetes-induced hyperfiltration**. This was achieved without change in elevated plasma glucose concentration and glycated hemoglobin in the diabetic state. High-dose thiamine and benfotiamine therapy is a potential novel strategy for the **prevention of clinical diabetic nephropathy**."<sup>7</sup>

d. "Clinical improvement resulting from the use of the above complex (benfotiamine) showed good correlation with a positive course of echocardiographic values of myocardial contractility and pumping function. Elimination of myocardial insufficiency was accompanied by an **increase in the stroke volume, ejection fraction, the rate of circulatory shortening of myocardial fibers, left ventricular mass, and a decrease in end diastolic and systolic volumes**."

f. Some studies have suggested that benfothiamine<sup>9</sup> or thiamine<sup>10</sup> **can increase the effectiveness of chelators such as DMSA or thiol compounds**, specifically reducing liver and kidney toxic metal loads. Heavy metals are known to be a catalyst for non-enzymatic glycation, so this is another mechanism by which benfotiamine reduces glycation.

## References

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