tolerated by those with lactase-deficiency than nonfermented milk.

ADVERSE REACTIONS

There are some reports of flatulence and diarrhea in some with lactase-deficiency.

OVERDOSAGE

None known.

DOSAGE AND ADMINISTRATION

Yogurt is available in many different preparations. Yogurt may be considered a functional food. In some yogurt preparations, the lactic acid bacteria have been killed during the processing of the product via pasteurization. Yogurt preparations in which the lactic acid bacteria have been killed may still confer some, but probably not all, of the possible health benefits.

Intake of yogurt is variable. One study showing a possible anti-allergy effect of yogurt used 200 grams daily for one year. Unpasteurized yogurt was found to be more effective than pasteurized yogurt in this study.

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Zinc

DESCRIPTION

Zinc is an essential element in human and animal nutrition with a wide range of biological roles. Zinc plays catalytic, structural or regulatory roles in the more than 200 zinc metalloenzymes that have been identified in biological systems. These enzymes are involved in nucleic acid and protein metabolism and the production of energy, among other things. Zinc plays a structural role in the formation of the so-called zinc fingers. Zinc fingers are exploited by transcription factors for interacting with DNA and regulating the activity of genes. Another structural role of zinc is in the maintenance of the integrity of biological membranes resulting in their protection against oxidative injury, among other things.

Zinc is a metallic element with atomic number 30 and an atomic weight of 65.37 daltons. Its atomic symbol is Zn. Zinc exists under physiological conditions in the divalent state. The adult body contains about 1.5 to 2.5 grams of zinc. It is present in all organs, tissues, fluids and secretions. Approximately 90% of total body zinc is found in skeletal muscle and bone. Over 95% of total body zinc is bound to proteins within cells and cell membranes. Plasma contains only 0.1% of total body zinc. Most of the zinc (75% to 88%) in blood is found in the red blood cell zinc metalloenzyme carbonic anhydrase. In the plasma, approximately 18% of zinc is bound to alpha-2-macroglobulin, 80% to albumin and 2% to such proteins as transferrin and ceruloplasmin.

Physiologically, zinc is vital for growth and development, sexual maturation and reproduction, dark vision adaptation, olfactory and gustatory activity, insulin storage and release and for a variety of host immune defenses, among other things. Zinc deficiency can result in growth retardation, immune dysfunction, increased incidence of infections, hypogonadism, oligospermia, anorexia, diarrhea, weight loss, delayed wound healing, neural tube defects of the fetus, increased risk for abortion, alopecia, mental lethargy and skin changes.

Moderate to severe zinc deficiency is rare in industrialized countries. However, it is highly prevalent in developing countries. Many, however, are at risk for mild zinc deficiency in industrialized countries. Several diseases and situations predispose to zinc deficiency, including the autosomal recessive disease acrodermatitis enteropathica, alcoholism, malabsorption, thermal burns, total parenteral nutrition (TPN) without zinc supplementation and certain drugs, such as diuretics, penicillamine, sodium valproate and ethambutol. Zinc intake in many of the elderly may be suboptimal and, if compounded with certain drugs and diseases, can lead to mild or even moderate zinc deficiency.

Zinc acetate is an FDA-approved orphan drug for the treatment of the copper-overload disorder Wilson's disease.

ACTIONS AND PHARMACOLOGY

ACTIONS

Zinc may have immunomodulatory activity. It may also have antioxidant activity. Zinc has putative antiviral, fertility-enhancing and retinoprotective activities.

MECHANISM OF ACTION

Zinc is required for a number of immune functions, including T-lymphocyte activity. Zinc deficiency results in thymic involution, depressed delayed hypersensitivity, decreased peripheral T-lymphocyte count, decreased proliferative T-lymphocyte response to phytohemagglutinin (PHA), decreased cytotoxic T-lymphocyte activity, depressed T helper lymphocyte function, depressed natural killer cell activity, depressed macrophage function (phagocytosis), depressed neutrophil functions (respiratory burst, chemotaxis) and depressed antibody production. Zinc supplementation can restore impaired immune function in those with zinc deficiency, as found in malabsorption syndromes and acrodermatitis enteropathica.

There is little evidence that zinc supplementation will enhance immune responses in those who are not zinc deficient. High doses of zinc may even be immunosuppressive. Zinc supplementation may improve immune function in healthy elderly individuals who are marginally zinc deficient.

The mechanism underlying the immune effects of zinc is not fully understood. Some of these effects may be accounted for by zinc's membrane-stabilization effect. This could affect signaling processes involved in cell-mediated immunity. Zinc is known to be involved in such signaling processes. Zinc may also influence gene expression by structural stabilization of different immunological transcription factors. Zinc ions can induce blast formation of human peripheral blood monocytes (PBMCs). In PBMCs, zinc induces cytokines, including interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)-alpha. Cytokine induction by zinc is caused by a direct interaction of zinc with monocytes. The stimulation by zinc of T-lymphocytes appears to occur via monocyte released IL-1 and cell-cell contact. High zinc concentrations inhibit T-lymphocyte proliferation by blocking the IL-1 type 1 receptor-associated kinase. T-lymphocyte activation appears to be delicately regulated by zinc concentrations.

Zinc may have secondary antioxidant activity. Zinc does not have redox activity under physiological conditions. Zinc may influence membrane structure by its ability to stabilize thiol groups and phospholipids. It may also occupy sites that might otherwise contain redox active metals such as iron. These effects may protect membranes against oxidative damage. Zinc also comprises the structure of copper/zinc-superoxide dismutase (Cu/Zn-SOD). Zinc plays a structural role in Cu/Zn-SOD. Zinc may also have antioxidant activity via its association with the copper-binding protein metallothionein.

The role of zinc gluconate in the management of the common cold remains controversial (see Research Summary). The mechanisms proposed for zinc's effects on the duration of colds are inhibition by zinc of the replication of rhinoviruses and/or inhibition of virus entry into cells. Zinc ions, however, have only modest nonselective inhibitory effects for rhinoviruses *in vitro*.

Zinc is involved in sperm formation and testosterone metabolism. Zinc deficiency results in oligospermia. There is little evidence that zinc supplementation affects sperm production in those who are not zinc deficient.

The mechanism of the putative effect of zinc in age-related macular degeneration (ARMD) is unknown.

PHARMACOKINETICS

The efficiency of absorption (fractional absorption) of a zinc salt on an empty stomach ranges from 40% to 90%. The fractional absorption of zinc with food appears to be lower. Zinc-histidine, zinc-methionine and zinc-cysteine complexes appear to be more efficiently absorbed than other zinc supplementary forms. Zinc is absorbed all along the small intestine. Most ingested zinc appears to be absorbed from the jejunum. Zinc uptake across the brush border appears to occur by both a saturable barrier-mediated mechanism and a nonsaturable nonmediated mechanism. The exact mechanism of zinc transport into the enterocytes remains unclear. Zinc transporters have been identified in animal models. Once zinc is within the enterocyte, it can be used for zinc-dependent processes, become bound to metallothionein and held within the enterocyte or pass through the cell. Transport of zinc across the serosal membrane is carrier mediated and energy dependent.

Zinc is transported to the liver via the portal circulation. A fraction of zinc is extracted by the hepatocytes, and the remaining zinc is transported to the various cells of the body via the systemic circulation. Zinc is transported in the plasma bound to albumin (about 80%), alpha-2-macroglobulin (about 18%) and to such proteins as transferrin and ceruloplasmin (about 2%). The major route of zinc excretion is via the gastrointestinal tract. Fecal zinc excretion is comprised of unabsorbed zinc and zinc derived from biliary, pancreatic, and gastrointestinal secretions and zinc from sloughing of mucosal cells.

Much of the pharmacokinetics of zinc in humans is unknown. Research is ongoing.

INDICATIONS AND USAGE

Even borderline zinc deficiency or disturbances in zinc metabolism can have profound adverse health effects. Those at greatest risk of such deficiencies and disturbances include infants, children, the elderly and pregnant women. Due to conditions that can limit the bioavailability of zinc, even when there is adequate zinc intake, zinc deficiency may affect still larger populations.

Among diseases and conditions associated with zinc deficiency are alcoholism, malabsorption syndromes, acrodermatitis enteropathica, anorexia nervosa, thermal burns and total parenteral nutrition (TPN) without zinc supplementation. Supplemental zinc may be helpful in some of the foregoing, in some conditions of immune impairment, in some complications of pregnancy, in the prevention of some cases of fetal neural tube defects, diarrhea, oligospermia, delayed wound healing and some cognitive disorders. It may also help protect against some inflammatory conditions.

Some claim that zinc is neuroprotective, others that it is neurotoxic in some circumstances. Some have suggested it might be useful in depression, and some others have proposed that it might be used as an antiaging substance. Mixed results are reported in the use of zinc in childhood pneumonia.

Widely publicized claims that zinc is efficacious in preventing and ameliorating symptoms of the common cold are supported by some studies but not by others. There is the suggestion in some experimental research that zinc might have some anticarcinogenic effects. There is little evidence that zinc is helpful in diabetes. Topical zinc is useful in treating some skin conditions. Claims that it can prevent or reverse baldness are unsubstantiated except in some cases of severe zinc deficiency. It has no effect on typical male pattern baldness. It may be useful in dysgeusia (taste disorder) in those who are zinc deficient. There is growing evidence that zinc might be helpful in preventing age-related macular degeneration.

RESEARCH SUMMARY

Zinc deficiency has been shown to impair immunity in many ways. It decreases T- and B-lymphocyte function and diminishes proliferative responses to mitogens. It also reduces the biological activity of many cytokines. Zinc deficiency has been shown to impair placental transport of antibodies from mother to fetus. Even mild zinc deficiency has been shown to produce an imbalance between cell-mediated and humoral immunity. Zinc supplementation has reversed many of these and other immune deficits in several *in vitro*, animal and human studies.

Supplementation with zinc reduced the incidence of childhood pneumonia by 41% and incidence of diarrhea in children by 25%, according to the findings of a review of ten randomized, controlled studies in the developing world. Zinc was found, in this review analysis, to be more effective than any other treatment for childhood pneumonia and was said to equal most other effective interventives for diarrhea in these populations. The diarrheas studied were related to diminished immune competence and high rates of exposure to infectious diseases. The significance of these findings is underscored by the fact that respiratory infections, and pneumonia in particular, are the cause of approximately one-third of all deaths among children in developing countries.

Many healthy elderly individuals and even more unhealthy elderly have marginal zinc deficiencies. There is both clinical and experimental evidence of impaired T-lymphocyte function, with associated increases in morbidity and mortality due to infectious diseases, among the elderly. Zinc deficiency has been shown to play a key role in this situation. Zinc supplementation in the elderly has produced mixed results with respect to immune restoration. Many researchers agree, however, that some of the negative results are probably due to the heterogeneity of elderly populations with respect to immune response, and most call for better-designed studies to bring hitherto ambiguous data into sharper focus.

Disturbances in metabolism, as well as zinc deficiency, have been associated with some inflammatory conditions, including some inflammatory bowel diseases and rheumatoid arthritis. The use of supplemental zinc in gastrointestinal inflammation, however, is highly experimental and is not without peril since inappropriate or uncontrolled administration can exacerbate, rather than ameliorate, some of these conditions. In some circumstances, however, supplemental zinc has enhanced the mucosal capacity of the small bowel to absorb water and electrolytes, thus easing inflammation. There is also some experimental evidence that zinc can stimulate tissue repair in some ulcer conditions.

There is some preliminary clinical evidence that supplemental zinc can produce benefit in some with rheumatoid arthritis. Diminished plasma zinc has been reported in some with this disease. Zinc has demonstrated an ability to inhibit mixed lymphocyte reaction in some of these subjects. Some researchers have suggested that further research is warranted to see if zinc might be a useful new therapy in T-cell-mediated auto-immune and graft-versus-host diseases.

One review author has presented evidence that zinc can be neurotoxic in some experimental circumstances and neuroprotective in others. The author warned that "there is a large and growing body of evidence showing that after CNS injury, large quantities of free zinc can be released, not just from pre-synaptic vesicles but also from metalloproteins and

from mitochondrial zinc pools, resulting in neuronal damage and death." Some *in vitro* work has shown neurotoxic zinc effects, and some *in vivo* studies have shown free zinc accumulation reportedly leading directly to neuronal death after ischemia, traumatic brain injury and seizure. And there is some, albeit inconsistent, data suggesting that zinc chelators may protect neurons after injury. At the same time, there is data indicating that following traumatic brain injury, the risk for moderate-to-severe zinc deficiency increases significantly in humans. Hence the reviewer stated that "while these data make it clear that systemic zinc deficiency after CNS injury should be avoided, our understanding of the role of free zinc in neuronal death raises the question of whether clinicians should be treating brain-injured patients with supplemental zinc."

This issue was tested in a rat model of traumatic brain injury. Dietary supplementation with zinc subsequent to the induced brain trauma did not have deleterious effects, but the researchers cautioned that in patients with severe traumatic brain injury zinc supplementation would necessarily be administered parenterally with, potentially, significantly different effects. Another study provided at least some reassurance in this context: brain injured human adults received intravenous zinc for 15 days beginning within 72 hours of injury; three weeks after treatment began no adverse effects were observed, and, in fact, within two weeks after injury, those receiving zinc compared to those who did not receive it had improved recovery scores on the Glasgow Coma Scale. In another study, however, zinc chloride administered intraperitoneally 30 minutes prior to embolization of the middle cerebral artery in adult male rats resulted in increased infarct size and diminished behavioral outcomes, compared with other agents tested. Both studies used the same zinc form and dose. But the methods used to induce transient ischemia and reperfusion were different. Clearly more research needs to be done to try to further clarify the issues raised in these conflicting studies.

A group of reviewers examined data they said might indicate a role for zinc in treating depression. They presented evidence indicating that zinc deprivation influences brain homeostasis, mental function and susceptibility to epileptic convulsions. They also pointed to recent rat studies showing that chronic treatment with antidepressants and electroconvulsive shock therapy induces increased brain concentrations of zinc. Zinc supplementation has produced antidepressant-like effects in various animal depression models. The activity of some antidepressants was said to be enhanced when used in combination with zinc. There have been some reports that depression in humans is associated with lower serum zinc concentrations. At least one such inquiry, however, failed to find such an association. A preliminary clinical trial found some benefit from zinc supplementation in depressed individuals. More research is needed and warranted.

Another group of researchers, surveying a broad range of zinc data, recently concluded that zinc may have general antiaging properties: "An overall estimation of all experimental and clinical observations on the biological role of zinc seems to lead us to the conclusion that zinc supply may be useful in reducing infection relapse and in restoring immune efficiency in ageing and in preventing age-related degenerative disease." However, they cautioned that it is far from being the ideal antiaging substance since there is also the potential for "acute and chronic zinc poisoning."

Diminished zinc status has been associated with HIV disease and higher incidence of opportunistic infections. Zinc supplementation has produced higher CD4+ lymphocyte cell counts and reduced incidence of bacterial infections among patients with HIV disease in one study.

In a double-blind study, subjects were randomized to receive zinc lozenges containing 13.3 milligrams of zinc every two hours while awake for as long as they had symptoms of the common cold. Subjects were enrolled within 24 hours of first reporting cold symptoms. Median time to complete resolution of cold symptoms was 4.4 days in those supplemented with zinc, compared with 7.6 days in those receiving placebo. Patients dissolved the lozenges in their mouths, rather than immediately swallowing them.

A recent review of studies found findings similar to those reported above in three additional studies. Four other studies, however, found no benefit from zinc in shortening duration of cold symptoms. In one of the other positive studies, zinc supplementation reduced duration of symptoms by 42%, compared with placebo, when initiated on the first day of symptoms. When withheld until the second day, zinc reduced cold duration by 26%, compared with placebo.

Some have challenged the validity of the four studies that found no zinc effect on the basis of poor bioavailability of the zinc lozenge preparations, either due to a proposed failure of the lozenge formulations to provide adequate amounts of free zinc ions to the saliva and oral tissues or due to doses of zinc in the lozenge that were below a possible therapeutic threshold. On the other hand, some have also argued that there were significant methodological flaws in some of the positive studies. A recent review of the zinc/cold data evaluated 14 randomized, placebo-controlled studies. Half reported positive effects; half reported no effect. Of the four studies the review authors considered the most rigorous and best-designed, three found no effect, and one reported a positive effect—but it used a nasal gel as the delivery form. Whether zinc is truly effective against colds remains an unresolved issue.

A group of researchers has recently concluded that supplemental zinc has been shown to reduce the incidence of childhood pneumonia. Some studies in which it has been used as an adjunct to antibiotic therapy have yielded mixed results. A recent trial suggested that supplemental zinc might actually be detrimental in some cases of childhood pneumonia. Again, the picture is unclear, and more research is required.

Zinc supplementation has reversed some of the signs of anorexia nervosa, including weight loss, in some women. Weight has increased in some zinc-supplemented women with this condition, and menstruation has been restored in some supplemented with zinc.

Zinc supplementation has overcome some forms of both female and male infertility in those who are zinc deficient. Zinc is essential for proper formation and maturation of spermatozoa.

Zinc plays many roles in pregnancy, and disturbances in zinc metabolism, as well as zinc deficiency, can have serious adverse effects on the course of pregnancy and upon the growth of the fetus and newborn. Zinc deficiency can be teratogenic, producing neural tube defects. Zinc is also very important to the newborn when breast milk may be its only source of zinc (during the first few months of life). Premature infants may be at even greater risk of zinc deficiency. Impaired disease resistance and diminished vaccine efficacy in infants may result from zinc deficiency at this stage. Some studies have shown that giving 15 milligrams of zinc daily to breast-feeding mothers produced more weight gain in their babies than in the babies of unsupplemented mothers. Zinc supplementation in infants not breast fed has also shown benefits. Zinc supplementation has also shown benefit in regulating and promoting proper growth in some groups of young children with non-organic failure to thrive.

There is some evidence that zinc can promote and accelerate wound healing in some circumstances. There is very preliminary experimental evidence that it may have some protective effects against prostate cancer and some equally preliminary data suggesting that it might enhance neuropsychological performance in children, most likely those with zinc deficiencies.

There was an early report that 100 milligrams of zinc twice a day with meals significantly reduced visual loss in subjects with macular degeneration. Subsequently, in a much larger study organized by the National Eye Institute, a combination of zinc, vitamin E, beta-carotene and vitamin C reportedly reduced the risk of developing age-related macular degeneration and prevented blindness in a high-risk group of elderly subjects. Mortality was also increased in the supplemented group.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Zinc is contraindicated in those who are hypersensitive to any component of a zinc-containing supplement.

PRECAUTIONS

Pregnant women and nursing mothers should avoid zinc doses higher than RDA amounts (15 milligrams/day for pregnant women, 19 mg/day for lactating women during the first six months and 16 mg/day for lactating women during the second six months).

ADVERSE REACTIONS

Doses of zinc up to 30 milligrams daily are generally well tolerated. Higher doses may cause adverse reactions. The most common adverse reactions are gastrointestinal and include nausea, vomiting and gastrointestinal discomfort. Other adverse reactions include a metallic taste, headache and drowsiness. There are some reports of decreased HDL-cholesterol in those taking high doses of zinc. Chronic intake of high doses of zinc can lead to copper deficiency and hypochromic, microcytic anemia secondary to zinc-induced copper deficiency.

High doses of zinc may be immunosuppressive.

INTERACTIONS

DRUGS

Bisphosphonates (alendronate, etidronate, risedronate): Concomitant intake of a bisphosphonate and zinc may decrease the absorption of both the bisphosphonate and zinc.

Quinolones (ciprofloxacin, gatifloxacin, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, sparfloxacin, trovafloxacin): Concomitant intake of a quinolone and zinc may decrease the absorption of both the quinolone and zinc.

Penicillamine: Concomitant intake of penicillamine and zinc may depress absorption of zinc.

Tetracyclines (doxycycline, monocycline, tetracycline): Concomitant intake of a tetracycline and zinc may decrease the absorption of both the tetracycline and zinc.

NUTRITIONAL SUPPLEMENTS

Calcium: Concomitant intake of calcium and zinc may depress zinc absorption in postmenopausal women.

Copper: Concomitant intake of copper and zinc may depress the absorption of copper. Intake of large doses of zinc can negatively affect the copper status of the body. This is the basis for the use of high doses of zinc for the treatment of Wilson's disease. It is thought that high intakes of zinc induce synthesis of the copper-binding protein metallothio-

nine in the gastrointestinal mucosal cells. Metallothionine can sequester copper. This makes copper unavailable for copper absorption.

L-cysteine: Concomitant intake of L-cysteine and zinc may enhance the absorption of zinc.

L-histidine: Concomitant intake of L-histidine and zinc may enhance the absorption of zinc.

Inositol Hexaphosphate: Concomitant intake of inositol hexaphosphate and zinc may depress the absorption of zinc.

Iron: Concomitant intake of iron and zinc may depress the absorption of both iron and zinc.

L-methionine: Concomitant intake of L-methionine and zinc may enhance the absorption of zinc.

N-acetyl-L-cysteine (NAC): Concomitant intake of NAC and zinc may enhance the absorption of zinc.

Phosphate Salts: Concomitant administration of zinc and phosphate salts may decrease the absorption of zinc.

FOODS

Caffeine: Concomitant intake of coffee, caffeinated beverages or caffeine and zinc may depress the absorption of zinc.

Cysteine-containing Proteins: Foods rich in cysteine-containing proteins (e.g., animal muscle tissue) may increase the absorption of zinc if ingested concomitantly.

Oxalic Acid: Concomitant intake of zinc with foods rich in oxalic acid (spinach, sweet potatoes, rhubarb and beans) may depress the absorption of zinc.

Phytic Acid: Concomitant intake of zinc with foods rich in phytic acid (unleavened bread, raw beans, seeds, nuts and grains and soy isolates) may depress the absorption of zinc.

Tea: Concomitant intake of tea (tannins) and zinc may cause decreased absorption of zinc.

OVERDOSAGE

There are no reports of overdosage from use of zinc supplements.

DOSAGE AND ADMINISTRATION

There are several zinc supplementary forms. These include zinc gluconate, zinc oxide, zinc aspartate, zinc picolinate, zinc citrate, zinc monomethionine and zinc histidine. Zinc supplements are available in stand-alone or in combination products. A typical dose of zinc is about 15 milligrams (as elemental zinc) daily.

The Food and Nutrition Board of the Institute of Medicine of the National Academy of Sciences has recommended the following Dietary Reference Intakes (DRI) for zinc:

	Recommended Daily Allowance (RDA)
0-6 months	2 mg/day (AI, adequate intake)
7-12 months	3 mg/day
Children	**Recommended Daily Allowance (RDA)**
1-3 years	3 mg/day
4-8 years	5 mg/day
Boys	
9-13 years	8 mg/day
14-18 years	11 mg/day
Girls	
9-13 years	8 mg/day
14-18 years	9 mg/day
Men	
19-30 years	11 mg/day
31-50 years	11 mg/day
51-70 years	11 mg/day
Older than 70 years	11 mg/day
Women	
19-30 years	8 mg/day
31-50 years	8 mg/day
51-70 years	8 mg/day
Older than 70 years	8 mg/day
Pregnancy	
14-18 years	12 mg/day
19-30 years	11 mg/day
31-50 years	11 mg/day
Lactation	
14-18 years	13 mg/day
19-30 years	12 mg/day
31-50 years	12 mg/day

The following summarizes the Tolerable Upper Intake Level (UL) for various age groups and conditions:

Infants	
0-6 months	4 mg/day
7-12 months	5 mg/day
Children	**(UL)**
1-3 years	7 mg/day
4-8 years	12 mg/day
9-13 years	23 mg/day
Adolescents	
14-18 years	34 mg/day

Adults	
19 years and older	40 mg/day
Pregnancy	
14-18 years	34 mg/day
19 years and older	40 mg/day
Lactation	
14-18 years	34 mg/day
19 years and older	40 mg/day

The DV (Daily Value) for zinc, which is used for determining percentage of nutrient daily values on nutritional supplement and food labels, is 15 mg. The basis for the DV for zinc is the 1973 U.S. RDA.

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Zinc L-Carnosine

DESCRIPTION

Zinc L-carnosine is a chelate of divalent zinc and the dipeptide L-carnosine. L-carnosine (see Carnosine) is comprised of the nonprotein amino acid beta-alanine (see Beta-alanine) and the protein amino acid L-histidine.

Zinc L-carnosine was synthesized by the Japanese in the late 1980s. It was first known as Z-103 and later on as polaprezinc. The idea for the synthesis of zinc L-carnosine came from the knowledge that L-carnosine was reported to increase granulation tissue and accelerate gastric healing in rats, and that zinc had been reported to have protective action against various experimental gastric lesions and also had been reported to possess antiulcer action in clinical studies. The thinking was that the combination of the beneficial effects of zinc and L-carnosine under the chemical roof of one molecule would make for a novel and potent antiulcer agent. Japanese researchers found that the zinc L-carnosine complex did exhibit marked antiulcer activity against various experimental models of gastric ulcers and duodenal ulcers by acting directly on the gastric and intestinal mucosa. However, even during the early days of zinc L-carnosine research, it was already demonstrated to have other activities, such as inhibition of bone resorption in experimental animals. Recently, zinc L-carnosine entered the dietary supplement marketplace in the United States.

Zinc L-carnosine is described chemically as 2-[(3-azanidyl-1-oxidopropylidene)amino]-3-(3*H*-imidazol-4-yl)propanoate. It is also known as polaprezinc, zinc carnosine, β-alanyl-L-histidinato zinc, *N*-(3-aminopropionyl)-L-histidinato zinc, [*N*-β-alanyl-L-histidinato(2-)-*N,N*^{N}, O$^{\alpha}$]zinc, and catena-(*S*)-[lm-[*N*$^{\alpha}$-(3-aminopropionyl)-L-histidinato (2-)-*N*^{1},N^{2},O:*N*$^{\tau}$]-zinc]. Originally known as Z-103, zinc L-carnosine was demonstrated to be much more active against gastric ulceration in rats than various other Zn(II) complexes. Zinc D-carnosine was found to have little or no activity. Spectroscopic data indicated that the zinc ions coordinate with L-carnosine to form a quadridentate 1:1 complex of