

ZINC-CARNOSINE PEPZINGI® BRAND

Integrative Therapeutics™ delivers the clinically studied PepZinGI brand Zinc-Carnosine to protect and stabilize the gastric and intestinal mucosal lining, support a healthy gastric microbial balance, and help relieve mild gastric discomforts, such as occasional heartburn, nausea, bloating, and upset stomach.* Its gastro-supportive benefits have been demonstrated in over 20 published studies.*

This unique ingredient combines L-carnosine, a naturally occurring combination of the amino acids beta-alanine and L-histidine, with elemental zinc. Zinc-Carnosine is unique in that it supports the natural protective mechanisms in the gastrointestinal tract without suppressing stomach acid or otherwise interfering in the normal digestive process.* The efficacy and safety of Zinc-Carnosine have been demonstrated in numerous published, controlled clinical trials in humans.

- Fully established and consistent molecular profile
- Hypoallergenic formula with no undesirable excipients
- Clinically validated dose at an affordable price

Zinc-Carnosine is a part of our Digestive Restoration Program which offers you a flexible approach to individualized patient care. Learn more at integrativepro.com/digestion.



PepZinGI® brand is a registered trademark of Hamari Chemicals, Ltd.

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ZINC-CARNOSINE

Zinc-Carnosine: Supporting the Natural Defense Mechanism of the Stomach

Zinc-Carnosine is a novel dietary ingredient that supports gastrointestinal tissue health.* It has been successfully used in Japan since the early 1990s to support mucosal integrity, gastrointestinal immune defense, and occasional indigestion.*

Zinc-Carnosine is a unique combination of the essential mineral zinc, which is well known for its antioxidant properties. Zinc is a component of more than 300 enzymes needed for tissue repair; for morphologic, physiologic, and metabolic functions in the reproductive system; to synthesize protein; to preserve vision; and to boost immunity, among other functions.*¹ L-carnosine is a dipeptide consisting of beta-alanine and L-histidine. It is an antioxidant, occurring in all mammalian cells, with the highest concentrations found in muscle and brain tissue.²

Animal studies have shown that Zinc-Carnosine has biological activity surpassing that of the individual constituents or the same ingredients physically mixed together. Clinical trials have demonstrated significant improvements in both objective outcomes and subjective measures during intervention periods with Zinc-Carnosine (ZnC). More importantly, clinical trials have shown endoscopically demonstrable effects within 4 to 8 weeks. Dozens of research studies on PepZinGI® brand Zinc-Carnosine have been conducted, with a strong track record of safety and clinical efficacy.^{3,4}

Mechanisms of Action

While most digestive aids focus either on suppressing or neutralizing stomach acid, Zinc-Carnosine is unique in that it supports the natural cytoprotective mechanisms without interfering in the normal digestive process (i.e., it does not suppress stomach acid production or neutralize HCl, which is required for mineral absorption).* Instead, Zinc-Carnosine bolsters the stomach's inherent mucosal defenses,^{5,6} stabilizing integrity of tissues not only of the stomach, but throughout the GI tract: in the mouth,⁷ small intestine,^{8,9} colon,^{10,11} and liver.*¹² Zinc-Carnosine supports the body's natural mechanisms for rapidly regenerating epithelia in the presence of various stressors.^{5,6,10,11,13-17} It also supports healthy gastric balance of microflora in animals¹⁸ and humans.*¹⁹

In animal studies, Zinc-Carnosine has been shown to modulate the immunological cascade that can follow local tissue challenge to the stomach lining.* This includes effects on the release of cytokines,²⁰ NF kappa-B activation,^{20,21} modulation of IGF-1,²² TNF-alpha,¹⁵ and induction of heme oxygenase (HO)-1.²³ The slow release of free zinc and L-carnosine in the stomach cellular space provides antioxidant and membrane-stabilizing effects, while at the same time providing a highly bioavailable source of elemental zinc.

When the ingredient is released in the stomach, it is thought to adhere to needful areas of the gastric lining, supporting the inherent protective and regenerative functions of gastric mucosal cells.* A study by Furuta, et al showed via radioisotope identification that chelated Zinc-Carnosine stayed in the stomach twice as long (2 hours) as a physical mixture of zinc and L-carnosine similarly tagged.²⁴

Clinical Efficacy Studies

The efficacy and safety of PepZinGI brand Zinc-Carnosine for supporting gastrointestinal mucosal health has been demonstrated in humans in numerous published double-blind²⁵⁻³⁰ and open-label^{19, 38-39} clinical trials.* Zinc-Carnosine is also referred to in the medical literature as Zinc-L-Carnosine, Polaprezinc, Z-103, L-CAZ, and N-(3 aminopropionyl)-L-



Zinc-Carnosine Double-Blind Studies

Author	Design	N	Duration	Dose	Outcome
Miyoshi et al, 1992a. ²⁵	Multicenter double-blind dose-finding study	229	8 weeks	50 mg BID, 75 mg BID, or 100 mg BID	Markedly improved in 75.4% for the 100 mg group, 71.6% for the 150 mg group and 78.5% for the 200 mg group. "Moderately improved" in 86.9%, 91.0%, and 87.7%, respectively.
Miyoshi et al, 1997. ²⁶	Multicenter double-blind dose-finding study for acute exacerbations	173	2 weeks	37.5 mg BID or 75 mg BID	"Significantly improved" and "Moderately improved" combined was 46.4% in 75 mg group and 40.4% in the 150 mg group after three days, 74.0% and 78.1% after one week in 75 mg group and 150 mg group, respectively, and 85.5% and 88.6% after two weeks in 75 mg group and 150 mg group, respectively.
Miyoshi et al, 1992b. ²⁷	Multicenter double-blind comparison study	299	8 weeks	75 mg BID ZnC (N=148) or 400 mg BID of standard treatment (N=151), both vs placebo.	Endoscopically normal at 4 weeks: 26.3% on ZnC vs. 16.2% on standard treatment; at 8 weeks: 60.4% in ZnC group vs. 46.2% on standard therapy (p<0.05). "Markedly improved" symptoms at 8 weeks: 50.4% in ZnC group, 37.0% in standard group (p<0.05). Moderately improved or better: 74% in ZnC group, 67.7% in standard group.
Hayakawa et al, 1992. ²⁸	Double-blind clinical trial	44	8 weeks	75 mg BID	Significant improvement: 51.4% at 4 weeks; 60.7% at 8 weeks. Moderate or better improvement: 75.7% at 4 weeks; 89.3% at 8 weeks. Endoscopic normal and nearly normal rate: 37.8% at 4 weeks; 80.0% at 8 weeks.
Suzuki Y et al, 1992. ²⁹	Multicenter, phase III, double-blind clinical trial	28	8 weeks	75 mg BID	Improvement rate of subjective and objective symptoms was as high as 83.3% at 4 weeks and 90.9% at 8 weeks. Endoscopic normal rate was as high as 41.7% at 4 weeks and 70.0% at 8 weeks. Final global improvement (moderately improved or better) was 72.0%.
Nakajima M, 1997. ³⁰	Multicenter, double-blind comparison study	348	2 weeks	75 mg BID versus comparison substance, placebo.	Overall improvement was 81.2% in the ZnC and 78.4% in the standard therapy group. Endoscopic improvement was 75.5% in the ZnC group and 71.3% in the standard group.

Zinc-Carnosine Open-Label Studies

Author	Design	N	Duration	Dose	Outcome
Mori et al, 1992. ³⁴	Multicenter clinical trial	38	8 weeks	75 mg BID	Disappearance of subjective and objective symptoms at 8 weeks was 100% after meals, 82.6% fasting, 94.4% at night, 92.3% for occasional heartburn, 91.7% for belching, 88.9% for nausea, and 100% for abdominal distention. For improvement in subjective and objective symptoms, 72% were markedly improved and 80% were moderately improved or better at final assessment.
Miyoshi et al, 1992c. ³⁵	Preliminary dose evaluation	156	8 weeks	Group A: 50 or 75 mg TID; Group B: 75 mg BID	Group A: Moderately improved or better for Group A in 85.7% for the 150 mg and 72.7% for the 225 mg, respectively. Group B: "Moderately improved or greater" in 83.3% for the 150 mg (before breakfast and before bed) and 93.5% (after breakfast and before bed), respectively.
Kashimura et al, 1999. ¹⁹	Randomized comparison trial	66	7 days	Group A received triple therapy; Group B received triple therapy plus ZnC 150 mg BID	By per protocol analysis, success was achieved in 86% after triple therapy, and in 100% after triple therapy plus ZnC (P < 0.05).
Misawa et al, 1992. ³⁶	Clinical trial	28	8 weeks	75 mg BID	"Significant improvement" was 68.4% after 4 weeks and 68.8% after 8 weeks. "Moderate improvement" or more was 78.9% after 4 weeks and 87.5% after 8 weeks.
Shibata et al. ³⁷	Tolerability and pharmacokinetic study	6	Single dose or 7 days	Single-dose of 150 mg, 300 mg or 600 mg; 7-day continuous administration of 150 mg TID	Oral administration of ZnC in healthy males was well tolerated. Mild, transient heartburn occurred in 2/6 subjects receiving 300 mg. No ZnC accumulated in the plasma. No significant increase in urinary zinc excretion. Safety of single doses up to 600 mg was confirmed.
Morise et al, 1992. ³⁸	Clinical trial	64	8 weeks	75 mg BID	Improvement in subjective and objective measures defined as "significantly improved" was 69.8% and the combined "moderately improved" and "significantly improved" was 84.9%. The percentage of endoscopic normal was 31.6% after 4 weeks and 67.4% after 8 weeks.
Amakawa et al, 1992. ³⁹	Phase III clinical trial	25	8 weeks	75 mg BID	Disappearance rate for subjective and objective symptoms at 8 weeks was 53.3% after meals, 76.9% fasting, and 90.9% at night for epigastric symptoms; and 63.6% for occasional heartburn, 80.0% for belching, and 76.9% for abdominal distention. The endoscopic normal rate was 65.0% at 8 weeks.

histidine. PepZinGI brand Zinc-Carnosine is far and away the best-studied form of Zinc-Carnosine. Double-blind studies are summarized in the table above. In addition to these studies, Zinc-Carnosine has also demonstrated clinical efficacy for support of the liver,^{31,32} taste sense,³³ and integrity of the oral mucosa.^{*7} In a randomized crossover trial (N=10), co-administration of Zinc-Carnosine (37.5 mg BID) supported healthy intestinal permeability as compared with controls receiving no Zinc-Carnosine.^{*8}

Dosing

Most clinical trials of Zinc-Carnosine used 37.5 to 75 mg twice daily (before breakfast and at bedtime) for 8 weeks. This amount provides 8 mg to 16 mg of elemental zinc per dose.

Zinc-Carnosine has not been evaluated for long-term use. Because zinc inhibits copper absorption, copper intake should be increased if zinc supplementation continues long-term (except for people with Wilson's disease).⁴⁰ Typically, a 10:1 ratio of zinc to copper is recommended. Evidence suggests that 2 mg of copper per day is sufficient to prevent zinc-induced copper deficiency.⁴¹

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Supplement Facts

Serving Size 1 capsule

Amount per capsule	%DV
Zinc	16 mg 107%
Zinc-Carnosine (PepZin GI® brand)	75 mg **

**Daily Value (DV) not established.

Other ingredients: cellulose, vegetable capsule (modified cellulose), calcium laurate, and silicon dioxide.

Recommendations: Take 1 capsule twice daily, or as recommended by your healthcare professional.

If pregnant, nursing, or taking prescription drugs, consult your healthcare professional prior to use.

PepZin GI® is a registered trademark of Hamari Chemicals, LTD.

Contains no: sugar, salt, yeast, wheat, gluten, corn, soy, dairy products, artificial coloring, artificial flavoring, preservatives, or ingredients of animal origin. This product contains natural ingredients; color variations are normal.

Integrative Therapeutics	Natural Partners	Emerson Ecologics
60 CT - 10033	60 CT - IT10033	60 CT -IT0091

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