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Zinc-Carnosine: An Exciting Approach to Gastric Mucosal Health and Dyspeptic Symptom Relief

BY HILDA MALDONADO, M.D.

Approximately 25% to 40% of Americans suffer from dyspepsia, commonly known as indigestion, which results in symptoms such as heartburn, upset stomach, nausea, or bloating.¹ While the majority of individuals with indigestion do not have an underlying medical condition, some may suffer from conditions such as gastritis or peptic ulcer.¹ Each year, gastritis accounts for approximately 2 million doctor visits, and as many as 4 million Americans are diagnosed with peptic ulcer disease.^{2,3}

Gastritis, or inflammation of the stomach, is generally classified as acute or chronic. Acute gastritis has a rapid onset with signs of erosion, excess fluid, or bleeding in the stomach. Chronic gastritis also includes wasting away of stomach tissue. Similar in pathology, peptic ulcer is characterized by erosion of the gastric (stomach) or intestinal wall. What many people may not know is that these conditions and the resulting symptoms may be related to *Helicobacter pylori* infection.

***Helicobacter pylori*: Role in Indigestion**

An estimated two-thirds of people worldwide are infected with *H. pylori* bacteria.³ While the majority of infected individuals do not have symptoms, *H. pylori* can increase risk of developing conditions such as indigestion, gastritis, peptic ulcer, and stomach cancer.^{4,6}

To date, the method of *H. pylori* transmission remains unclear. It is thought to either be passed down from generation to generation, transmitted orally, or caused by contaminated food or water consumption.⁷⁻⁹

What is clear is that *H. Pylori* has an extraordinary ability to infect human stomachs. It is able to survive in the stomach environment, where many other bacteria cannot.¹⁰ *H. pylori* produces substances that weaken the stomach lining and make it susceptible to the digestive action of stomach acid. In some cases, this can result in wasting away or ulceration of the stomach lining.

Relieving Indigestion with Antacids

Many individuals use over-the-counter antacids to relieve indigestion. Unfortunately, long-term antacid use may negatively impact digestion and make the environment more susceptible to bacterial overgrowth, such as *H. pylori* infection.^{12,13}

Antibiotic Therapy for *H. pylori* Infection

Antibiotics are usually prescribed to eradicate *H. pylori* when it is detected. Unfortunately, with the upsurge in antibiotic usage, there is increasing concern about the development of antibiotic-resistant *H. pylori* strains.¹⁶⁻¹⁸ This has led researchers to investigate alternative therapies that can also be used to enhance the effectiveness of antibiotic therapy for *H. pylori* eradication.

Zinc-Carnosine in Supporting Stomach Health

Zinc-carnosine is a specific form of zinc that has been recommended by healthcare practitioners in Japan since 1994 to relieve indigestion and promote healing of the stomach lining. Over 20 published studies support the use of zinc-carnosine in promoting stomach health. In addition, when combined with antibiotic ther-

apy, it has been found to significantly increase the cure rate of *H. pylori* infection. In fact, when combined with a 7-day triple antibiotic therapy, zinc-carnosine significantly improved the eradication rate of *H. pylori* infection over the antibiotic therapy alone (from 90% to 100%).²³ It has also been clinically demonstrated to reduce symptoms of indigestion, such as heartburn, nausea, upset stomach, belching, and bloating.²⁰⁻²⁵

It has also demonstrated positive results in individuals with gastritis. In a clinical study of 173 subjects with acute or chronic gastritis, supplementation with zinc-carnosine, at 75 mg twice daily, was shown to inhibit stomach erosion and bleeding (74.5% and 82.5%, respectively), as well as relieve symptoms such as abdominal pain, heartburn, nausea, and vomiting.²⁶

In another clinical study, 44 patients with gastric ulcers were given 75 mg of zinc-carnosine twice daily. Patients were assessed by endoscopic examination and self-reported symptoms of abdominal pain, bloating, heartburn, belching, nausea, and other symptoms of indigestion. Patients demonstrated a 75.7% improvement in symptoms at 4 weeks and 89.3% at 8 weeks.²¹

The Preferred Form of Zinc for Stomach Health

In an animal study, zinc-carnosine was shown to be three times more effective than zinc sulfate or L-carnosine alone in healing stomach lesions. Researchers concluded that whereas zinc plays a role in tissue healing, the overall beneficial effects are dependent upon the combined action of the zinc-carnosine complex, suggesting it is a superior form of zinc for promoting stomach and intestinal health.²⁷

Zinc not only plays a role in tissue repair, but it also supports healthy immunity, helps prevent inflammation, and protects against bacterial overgrowth.^{28,29} Zinc deficiency has been associated with frequent bacterial infections, intestinal inflammation, delayed wound healing, and impaired immune system function.^{28,30}

L-carnosine, an amino acid naturally found in muscle and brain tissue, contributes to the tissue-healing effects of zinc through its antioxidant properties and apparent synergistic action.³¹ In addition, L-carnosine appears to help transport the zinc-carnosine compound directly to the site of ulceration, where it adheres to and exerts its tissue-healing action.³²

Conclusion

Zinc-carnosine complex is a unique dietary supplement that provides targeted support for stomach health, and relieves a number of symptoms associated with indigestion. This remarkable supplement is now available through healthcare professionals in the United States.

Zinc-Carnosine: An Exciting Approach to Gastric Mucosal Health and Dyspeptic Symptom Relief

BY HILDA MALDONADO, M.D.

ABSTRACT: *Approximately 25% to 40% of Americans suffer from dyspepsia, commonly known as indigestion, resulting in symptoms such as heartburn or upset stomach. Although the majority of individuals with dyspepsia do not have underlying pathology, some may suffer from gastritis or peptic ulcer disease. Helicobacter pylori infection is thought to be responsible for the majority of peptic ulcers, and has also been associated with gastritis, gastric cancer, and non-ulcer dyspepsia. Eradication of H. pylori with antibiotics has been shown to improve dyspeptic symptoms. However, there is increasing con-*

cern about the development of antibiotic-resistant H. pylori strains. This has led researchers to investigate alternative and complementary therapies to be used in H. pylori eradication and dyspeptic symptom relief. Zinc-carnosine, a gastro-supportive complex recommended in Japan since 1994, has been found to yield promising results in enhancing gastric mucosal defenses and modulating H. pylori growth. It also has been shown to relieve a number of dyspeptic symptoms, including heartburn, nausea, upset stomach, and abdominal distention. This exciting compound has recently become available in the United States.

In the United States, an estimated 25% to 40% of Americans suffer from upper abdominal complaints, or dyspepsia.¹ Dyspepsia has been defined as indigestion, resulting in symptoms such as heartburn, upset stomach, nausea, or abdominal distention. While the majority of individuals suffering from these symptoms will not have visible mucosal abnormalities if they undergo endoscopic examination, some will have underlying pathology of the gastric or duodenal mucosa, such as gastritis or peptic ulcer.¹ Each year, gastritis accounts for approximately 2 million doctor visits, and as many as 4 million Americans are diagnosed with peptic ulcer disease.^{2,3}

Gastritis, or inflammation of the gastric mucosa, is generally classified as acute or chronic. Acute gastritis has a rapid onset with indications of erosion, hemorrhage, or mucosal edema. Chronic gastritis includes atrophy of the endemic gastric gland and mucosa. The etiology of gastritis is said to be similar in pathology to that of peptic ulcer disease, which is characterized by erosion of the gastric or duodenal mucosal lining when it has been rendered susceptible to the digestive action of gastric juice.

Helicobacter pylori: Role in Dyspepsia and Related Disorders

An estimated two-thirds of people worldwide are infected with *H. pylori*.³ Although asymptomatic infection is very common for reasons yet to be determined, it has been reported that infected individuals are at an increased risk of developing non-ulcer dyspepsia, peptic ulcers, or gastritis. Whereas *H. pylori* and non-ulcer dyspepsia have been shown to have a small but statistically significant association, a more notable association has been found between *H. pylori* and gastritis. That is, immediately following infection, *H. pylori* infection can cause acute gastritis;

whereas long-term *H. pylori* infection can result in chronic gastritis in some individuals.⁴ Moreover, according to the Center for Disease Control, *H. pylori* infection is the leading cause of peptic ulcers, attributing to approximately 80% of gastric and 90% of duodenal ulcers.⁵ *H. pylori* infection has also been associated with an increased risk of gastric adenocarcinoma and mucosal-associated-lymphoid-type (MALT) lymphoma.⁶

To date, the mechanism for *H. pylori* transmission remains unclear. However, similarities in *H. pylori* genotypes have been identified in isolates among families, leading some researchers to theorize it may be passed down from generation to generation.⁷ Other researchers postulate that oral-to-oral transmission is the primary mechanism, due to the fact that *H. pylori* has been detected in the oral cavities of gastritis patients.⁸ Research on DNA motifs (specific genome characteristics) of more than 500 *H. pylori* strains from 5 continents suggests there are common *H. pylori* genotypes among native populations, providing more insight into the evolving nature of *H. pylori* as it has become such a widespread problem.⁹ These findings have led some researchers to believe that *H. pylori* has survived for hundreds of years in human evolution. It is also possible that the high prevalence of *H. pylori* in developing countries is attributed to contaminated food and water, although environmental reservoirs harboring *H. pylori* have not been identified.⁷

H. pylori is a bacterium that has an extraordinary ability to infect human stomachs. It can survive in the gastric environment by producing urease—an enzyme that neutralizes gastric acid.¹⁰ Because of its spiral shape and the way it moves, *H. pylori* can penetrate the protective mucus and enter the gastric or duodenal epithelium—more hospitable environments. Thus, urease pro-

duction is necessary for initial colonization of *H. pylori*, but not for continued propagation. Once imbedded in the epithelium, *H. pylori* produces substances that weaken gastric and duodenal cells, rendering them more susceptible to the corrosive action of gastric acid and pepsin. *H. pylori* can also adhere to gastric cells and stimulate gastric acid secretion, further weakening defense mechanisms and causing local inflammation in the less protected gastrointestinal (GI) epithelium. In some cases, the corrosive action of gastric acid and pepsin can lead to atrophy or ulceration.

Methods of Diagnosing *H. pylori* Infection

Currently, there are several methods used to diagnose *H. pylori* infection. These include:

1. Blood tests that measure specific *H. pylori* IgG antibodies.
2. Breath tests that measure exhaled carbon dioxide. Prior to the test, patients are given a drink containing either ¹³C- or ¹⁴C-labeled urea. *H. pylori* quickly metabolizes urea, and the labeled carbon is present in expired breath, then *H. pylori* infection is diagnosed.
3. Tissue tests (such as upper esophagogastroduodenal endoscopy), that may include analyzing affected tissue for the bacteria's enzyme urease, processing the tissue and watching for *H. pylori* growth, or examining the tissue under a microscope.
4. *H. pylori* stool antigen tests, which are noninvasive and useful for detecting the presence of *H. pylori*.

Conventional Management of Dyspeptic Symptoms

Conventional approaches to managing dyspeptic symptoms often include acid-suppressing drugs, but unfortunately, continual suppression of gastric acid may negatively impact digestion and make the environment more susceptible to bacterial overgrowth.¹¹⁻¹³ For example, gastric acid plays a role in triggering bile and exocrine enzyme production, which promote digestion in the duodenum. It also stimulates bicarbonate, which provides a healthy alkaline pH in the small bowel to control bacterial growth in this area.¹⁴ With the high prevalence of individuals who regularly self-medicate with over-the-counter antacids, maintaining these functions may be of concern to some experts in the field. In fact, a number of healthcare practitioners postulate that when individuals regularly use antacids to relieve digestive symptoms (that may be associated with various health conditions), they may not only further impair digestive function, but also compromise gut immunity against bacterial growth such as *H. pylori*.¹³

Table 1. Symptoms that may lead individuals to regularly use antacids¹⁵

| Symptoms | Functional Dyspepsia | Ulcer | Gastritis |
|---|----------------------|-------|-----------|
| Heartburn | ● | ● | |
| Epigastric tenderness | ● | ● | ● |
| Food repeating (regurgitation of gastric contents into mouth) | ● | | |
| Abdominal fullness | ● | | |
| Abdominal distention | ● | ● | ● |
| Belching | ● | | |
| Nausea | ● | ● | ● |

Antibiotic Therapy for *H. pylori* Infection: Cause for Concern

Antibiotics such as clarithromycin, amoxicillin, metronidazole, tetracycline, or a combination thereof are often prescribed to eradicate *H. pylori* when it is detected. Unfortunately, with the upsurge in antibiotic usage, there is increasing concern regarding the development of more resistant *H. pylori* strains. This is particularly apparent in Japan and Eastern Europe, where a high rate of clarithromycin and metronidazole resistance exists, suggesting these therapies may be less effective in the near future.^{16,17}

In an analysis of clinical trials performed in the U.S. between 1993 and 1999, the frequency of *H. pylori* resistance to clarithromycin and metronidazole was 39% by Etest and 21.6% by agar dilution. Antibiotic resistance in individuals gradually increased up to age 70, followed by a gradual decrease with advancing age. Researchers hypothesized that the high prevalence of antibiotic resistance may soon require testing of *H. pylori* isolates prior to initiating treatment.¹⁸ Furthermore, although *H. pylori* is seldom resistant to amoxicillin, this treatment has been reported to be successful in only 60% of *H. pylori* infection cases.¹⁹ Combination antibiotic therapy appears to be more effective, but may not eradicate *H. pylori* in every case. Taking these factors into consideration, it is no wonder why researchers continue to search for alternative therapies that may also enhance the effectiveness of antibiotics in *H. pylori* eradication.

The Emerging Role of Zinc-Carnosine in Supporting Gastric Health

Zinc-carnosine is a specific chelate of zinc that has been recommended by healthcare practitioners in Japan since 1994 to promote healing of the gastric mucosal lining and relieve dyspeptic symptoms. Over 20 published studies, including at least 6 human clinical trials, support the use of zinc-carnosine in promoting a healthy gastric environment. In addition, when combined with

conventional antibiotic therapy, it has been found to significantly increase the cure rate of *H. pylori* infection. It also has been clinically demonstrated to reduce a number of symptoms associated with ulcer development (Table 2).²⁰⁻²⁵

Table 2. Improved subjective and objective symptoms using zinc-carnosine

| | |
|------------------------|------------------------|
| • Heartburn | • Belching |
| • Nausea/vomiting | • Abdominal distension |
| • Anorexia | • Constipation |
| • Tender epigastralgia | |

Zinc-carnosine has been clinically demonstrated to be an effective adjunct to antibiotic therapy in *H. pylori* eradication.^{19,23} When combined with a 7-day triple therapy containing lansoprazole, amoxicillin, and clarithromycin, zinc-carnosine significantly improved the eradication rate of *H. pylori* infection over triple therapy alone (from 90% to 100%) without an increase in side effects.²³

It has also demonstrated positive results in individuals with gastritis. In a double-blind study of 173 subjects with acute or chronic gastritis, supplementation of zinc-carnosine 75 mg twice daily was shown to help improve erosion and hemorrhaging, 74.5% and 82.5%, respectively. Subjective and objective symptoms, such as epigastric pain, bloody stools, heartburn, nausea, and vomiting, were also improved. No serious side effects were reported. Researchers concluded that zinc-carnosine was beneficial in subjects with gastritis.²⁶

In another study, 44 patients with gastric ulcers were given 75 mg of zinc-carnosine twice daily (after breakfast and before bed). Patients were assessed by endoscopic judgement and self-reported symptoms of epigastric pain, abdominal distention, heartburn, belching, nausea, and other GI disturbances. Overall, patients demonstrated favorable improvements in both objective and subjective symptoms: 75.7% at 4 weeks and 89.3% at 8 weeks. No significant side effects were reported.²¹

These findings were confirmed in a subsequent clinical study, wherein 25 patients diagnosed with gastric ulcer given 75 mg of zinc-carnosine twice daily demonstrated significant improvements in epigastric pain (53.3% after meals, 76.9% fasting, and 90.9% at night) and endoscopic healing rate (65.0%) after 8 weeks of use.²⁰

Zinc-Carnosine is the Preferred Molecular Form of Zinc for the GI Tract

The superiority of this unique zinc chelate was demonstrated in an animal study, wherein researchers compared the effects of zinc-carnosine, zinc sulfate, or L-carnosine alone on acute gastric lesions in rats. Results showed that zinc sulfate and L-carnosine alone were three times less effective than zinc-carnosine complex alone. Researchers concluded that whereas zinc ions

play a role in tissue healing, the overall beneficial effects of zinc-carnosine are dependent upon the action of the chelate as a whole rather than the action of each individual ingredient.²⁷

Mechanisms of Action

Zinc is an essential trace element that is a cofactor in over 300 biochemical reactions. Discovery of zinc-finger proteins, which bind directly to the DNA helix, has resulted in exciting, ongoing research on the role of zinc in genetic expression and regulation. This role in DNA and RNA synthesis is crucial for tissue repair as well as lymphocyte proliferation and cytokine production. Zinc has also been shown to have an antibacterial effect against some aerobic and anaerobic bacteria in vitro, and a deficiency can lead to frequent microbial infections in humans.^{28,29} Zinc deficiency has also been associated with altered cytokine production, resulting in intestinal inflammation; delayed wound healing; impaired immune system function; and destabilization of cell membranes.^{28,30}

L-carnosine, a dipeptide (beta-alanine and L-histidine) naturally found in muscle and brain tissue, contributes to the tissue supportive effects of zinc through its ability to scavenge free radicals.³¹ Moreover, L-carnosine appears to help transport the zinc-carnosine compound directly to the site of ulceration, where it adheres to gastric mucosal cells and helps to protect against noxious agents.³² It is postulated that specific adherence to the ulceration is due to the formation of a chemical bond between zinc and proteins, such as albumin, forming mixed ligand complexes.³³ Zinc-carnosine's unique transport capabilities are thought to be dependent upon its ability to remain in the gastric juice without immediately being destroyed. By prolonging its existence, zinc-carnosine is able to maintain tissue-supportive effects for a long period of time.

Zinc-carnosine is also thought to promote gastric mucosal defenses. Animal and in vitro studies suggest its beneficial effects are attributed to a number of mechanisms (Table 3).

Table 3. Activities of Zinc-Carnosine

| Beneficial Effect | Proposed Mechanism |
|---------------------------------|---|
| Inhibits <i>H. pylori</i> | Anti-urease activity ³¹ |
| Attenuates gastric inflammation | Inhibits expression of TNF- α and IL-8 cytokines, without affecting PGE ₂ production ³⁴⁻³⁶ |
| Protects cellular integrity | Antioxidant activity ^{32,37} |
| Protects gastric epithelium | Stimulates mucus secretion ³⁸ |
| Adheres to wound site | L-carnosine transports zinc to wound site; zinc is an important cofactor for many proteins. |

Conclusion

The high prevalence of *H. pylori* infection, chronic symptom self-treatment with acid-suppressing agents, and increased resistance to antibiotic therapy contribute to the need for agents that promote a healthy gastric environment. Zinc-carnosine has well-documented gastro-supportive benefits and has been recommended by healthcare professionals in Japan since 1994. It has not only been shown to help modulate *H. pylori* growth, particularly when combined with antibiotic therapy, but also to relieve dyspeptic symptoms. The benefits of this exciting compound can now be obtained in dietary supplement form in the United States.

For more information on complementary nutritional protocols for GI dysfunction, please refer to the following Applied Nutritional Science Reports:

- 1) *Gut Dysfunction and Chronic Disease: The Benefits of Applying the 4R GI Restoration Program*, by DeAnn J. Liska, Ph.D. and Dan Lukaczer, ND.
- 2) *Herbal Antimicrobials for Intestinal Infections*, by Myron Lezak, M.D.
- 3) *Proven Therapeutic Benefits of High Quality Probiotics*, by Robert Roundtree, M.D.
- 4) *The Role of Standardized Herbal Formulas in Contemporary Healthcare Delivery*, by Margaret Jordan Parker, L.Ac, OMD.