PROTOCOL FOR LIFE BALANCE®

Dietary Supplement Information
for Physicians with Naturokinetics®
**PRODUCT CODE: P2997**
**CATEGORY: DIGESTIVE SUPPORT***

# GI Guard™ PM

## TECHNICAL SUMMARY

GI Guard™ PM is a nutritional formula with PepZin GI™, melatonin, amino acids, and B vitamins designed to help maintain the strength and integrity of the gastrointestinal mucosal barrier.* GI Guard™ PM features PepZin GI™, which has been shown in clinical studies to promote a healthy stomach lining and to support proper gut repair processes.* Melatonin, a potent free radical scavenger, is known to exist at high levels in the gut, where it exerts its protective effects against oxidative stress throughout the gastrointestinal tract.* Melatonin also helps support healthy gastric pH levels, normal pepsin production in the stomach, and helps to regulate proper intestinal motility.* B vitamins and amino acids, such as tryptophan, are necessary for melatonin synthesis.*

**Structure Formula:**

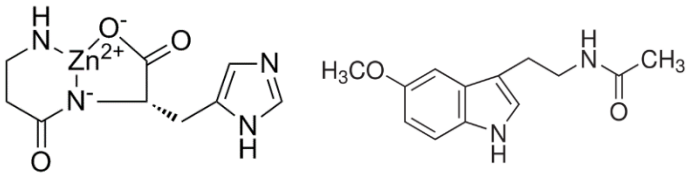

Figure 1: Chemical structure of Zinc-L-Carnosine (left) and Melatonin (right).

**Chemical Name:**

Zinc-L-Carnosine: zinc N-(3-aminopropionyl) histidine

Melatonin: *N*-Acetyl-5-methoxytryptamine

**Allergen and Additive Disclosure:** Not manufactured with wheat, gluten, soy, milk, egg, fish, shellfish, or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

**Delivery Form:** Vegetable Capsules

## ROLE AS NUTRIENT/FUNCTION

Zinc is known for its stabilizing effect on gastric mucosa.* This effect is enhanced by slow dissociation of PepZin GI™ (zinc-L-carnosine), which causes zinc to remain within the GI tract long enough to bind to GI epithelium, while L-carnosine simultaneously helps to neutralize free-radicals in and around the intestinal mucosa.*

Melatonin influences a variety of biological processes including circadian rhythms, neuroendocrine, immune, and cardiovascular functions.* It is also a potent free-radical scavenger.* Melatonin has been shown to be generated locally by neuroendocrine cells in many tissues including the GI tract. The endogenous secretion of melatonin in the GI tract is mainly regulated by the periodicity of food intakes and is especially sensitive to dietary tryptophan (this product has 200 mg tryptophan per serving). It is also subjected to a circadian cycle (the endogenous secretion of melatonin naturally varies over a 24-hour period) with high levels of melatonin produced at night and low levels during the day.* In the gastric mucosa, melatonin acts via specific membrane receptors. It exerts a protective effect on the gastric lining by promoting balanced immune responses, helps support healthy pH levels, as well as normal pepsin and gastrin production.*

## Supplement Facts

Serving Size 2 Veg Capsules — Servings Per Container 30

| | Amount Per Serving | % Daily Value |
|---|---|---|
| Vitamin B-6 (from Pyridoxine HCl) | 25 mg | 1471% |
| Folate | 800 mcg DFE [400 mcg (6S)-5-MTHF**] [from Quatrefolic® (6S)-5-MTHF** Glucosamine Salt] | 200% |
| Vitamin B-12 (as Methylcobalamin) | 50 mcg | 2083% |
| Zinc (from PepZin GI®) | 15 mg | 136% |
| PepZin GI® (Zinc-L-Carnosine Complex) | 75 mg | † |
| L-Carnosine (from PepZin GI®) | 57 mg | † |
| Melatonin | 6 mg | † |
| L-Tryptophan | 200 mg | † |
| L-Methionine | 100 mg | † |
| Trimethylglycine (TMG) | 100 mg | † |
| Taurine | 100 mg | † |

† Daily Value not established.

Other ingredients: Hypromellose (cellulose capsule), Microcrystalline Cellulose, Silicon Dioxide and Magnesium Stearate (vegetable source).

- **Supports Nighttime Gastric Health and Comfort***
- **Use with GI Guard™ AM**

**SUGGESTED USAGE:** Take 1-2 capsules 30 to 60 minutes before bedtime, or take as directed by your healthcare practitioner.

## NATUROKINETICS®

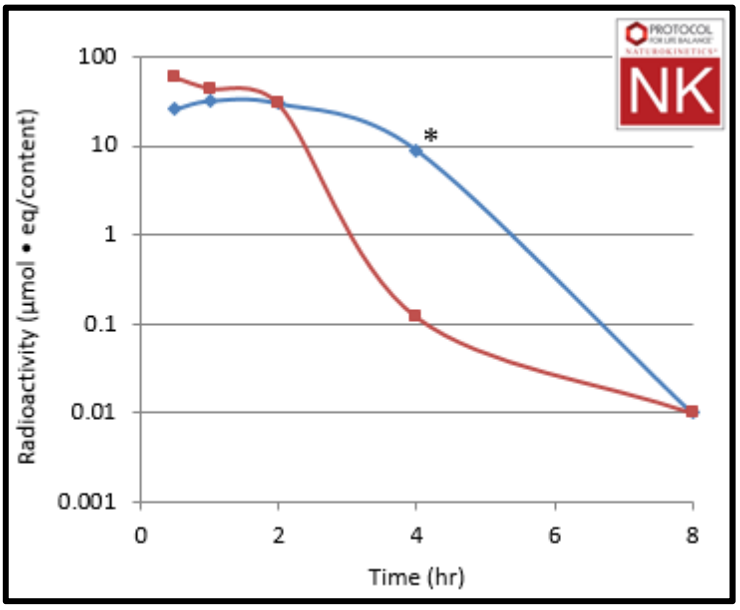


**Fig 1:** Time course of total mean radioactivity in gastric contents after oral administration of zinc in the form of PepZin GI™ or zinc sulfate ( ♦ $^{65}$Zn PepZin GI™; ■ $^{65}ZnSO_4$; *$P < 0.05$).

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

**Liberation:** Disintegration of the vegetable capsule is measured in water using a USP testing method with disintegration between zero and 60 minutes.

**Absorption:** Due to its slow dissociation, absorption of zinc from zinc-L-carnosine is significantly delayed, which allows for adhesion of zinc ions to gastric epithelium. Elevated gastric Zn concentration is maintained for a significantly longer period of time after zinc-L-carnosine compared to zinc sulfate administration (Figure 1). The amount of Zn absorbed from zinc-L-carnosine is estimated to be 11%.

Melatonin plasma levels are elevated with supplementation. Dosages of 1-5 mg melatonin achieved 10-100 times the usual night-time plasma peak levels within 1 hour of administration. In healthy volunteers with normal sleep-wake cycle, a single administration of 2 or 4 mg melatonin tablets results in maximum plasma concentrations in approximately 1 hour ($T_{max}$) with absolute bioavailability of about 15% due to significant first-pass hepatic metabolism.

**Distribution:** Absorbed zinc and L-carnosine are distributed to the liver, kidney, prostate, and to a lesser extent to the testes and brain, where zinc uptake is tightly regulated by the blood-brain barrier.

Melatonin is subject to systemic distribution with levels detected in salivary fluid and used to estimate plasma levels. Melatonin is lipid-soluble and easily crosses blood-brain barrier.

**Metabolism:** L-carnosine is metabolized via hydrolysis to β-alanine and L-histidine by carnosinase in the blood, liver, and kidneys.

Melatonin is metabolized in the liver into 6-sulfatoxymelatonin, which then undergoes conjugation and excretion as a sulfate or glucuronide. In the pineal gland and retina, melatonin is metabolized via deacetylation to 5-methoxytryptamine.

**Elimination:** Following a single administration of radiolabeled Zinc-L-Carnosine, 85% of $^{65}Zn$ was eliminated with feces and 0.3% with urine.

Predominant route of elimination of melatonin and its metabolite 6-sulfatoxymelatonin is via urine.

## CLINICAL VALIDATION

- **Digestive support and zinc L-carnosine:** In a randomized crossover trial with healthy volunteers receiving a compound known to alter gut permeability and 37.5 mg zinc L-carnosine twice daily or a placebo for five days, no alteration of gut permeability was observed in individuals in the zinc L-carnosine group. However, under these experimental conditions, in the placebo group, an increase in gut permeability was observed.* These experimental results suggest that zinc L-carnosine contributes to preserving the integrity of the gut-barrier function when it is subjected to an external aggression.*
- **Digestive support and melatonin.*** In a 11-day randomized, placebo controlled experimental trial including 30 healthy male volunteers, supplementation with 5 mg melatonin or placebo daily 30 minutes before the ingestion of a compound known to trigger stomach lining damage resulted in significantly less visible mucosal injuries when explorative upper-GI endoscopies were performed in the melatonin group than in the placebo group.* These experimental results suggest that zinc L-carnosine contributes to the preservation of the integrity of gut-barrier function.* These experimental results suggest that melatonin contributes to preserving the integrity of stomach lining when it is subjected to an external aggression.*

## SAFETY INFORMATION

**Tolerability:** Zinc, carnosine, and melatonin are generally well tolerated. Zinc may cause gastrointestinal disturbances when taken at high amounts.

**Contraindications:** Do not drive or use machinery for 4 to 5 hours after taking melatonin.

## INTERACTIONS

**Drug Interactions:** Zinc has been shown to decrease the absorption of cisplatin, penicillamine, quinolone, and tetracycline antibiotics due to the formation of insoluble complexes with these medications in the gastrointestinal tract and thus reducing their systemic availability.

Concomitant use of melatonin with alcohol, benzodiazepines, or other similar drugs might cause increased sedation. Melatonin may exhibit interaction with anti-coagulant/anti-platelet medications, anti-depressants, anti-hypertensive, anticonvulsants, and anti-diabetes drugs.

**Supplement Interactions:** Zinc may inhibit function of supplemental enzymes, including bromelain. Large amounts of supplemental zinc can competitively inhibit copper, magnesium, and iron absorption. Zinc may increase manganese absorption when taken together.

Melatonin may potentiate effect of the supplements with sedative component (5-HTP, kava kava, valerian root). Melatonin may increase the effects of herbal supplements that have antiplatelet/anticoagulant properties including angelica, clove, garlic, ginger, ginkgo, *Panax ginseng*, and others.

**Interaction with Lab Tests:**

Melatonin supplementation may interfere with human growth hormone serum levels and serum luteinizing hormone levels

## STORAGE

Store in a cool, dry place.