

## Key Features:

- Act on the 5-HT receptors to **promote gastrointestinal MMC function**
- Promote **digestive enzyme & bile secretions.**
- Contains cofactors to **support neurotransmitter synthesis & restore MMC**

## Indications:

- Small intestine bacterial overgrowth (SIBO)
- Dyspepsia, Gastroparesis, Indigestion, Nausea & Vomiting
- Gastroesophageal Reflux Disease (GERD)
- Irritable Bowel Syndrome (IBS)

## Description:

Prokinetic agents are a type of medication that enhances gastrointestinal (GI) motility by increasing the frequency of contractions in the small intestine without disrupting the rhythm. They are often used to treat GI symptoms, such as GERD, bloating, dyspepsia, nausea and vomiting, and constipation. **Common mechanism of actions of prokinetics involves the stimulation of the migrating motor complex (MMC) via the bindings of 5-HT (5-hydroxytryptamine) and M (muscarinic) receptors.**

### What is MMC?

MMC is a cyclic, recurring motility pattern that occurs in the stomach and small bowel during fasting. It can be subdivided into four phases; phase III is the most active, induced by 5-HT and dopamine (DA) receptors, with a burst of contractions originating from the duodenum and migrating distally.

**MMC is responsible for intestinal clearance and plays an important role in prevention of bacterial overgrowth and translocation in the gut.**

The role of the vagus nerve in control of the MMC seems to be restricted to the stomach, as vagotomy abolishes the motor activity in the stomach, but leaves the periodic activity in the small bowel intact.

The physiological role of the MMC is incompletely understood, but its absence has been associated with gastroparesis, intestinal pseudo-obstruction and small intestinal bacterial overgrowth.

### 5-L-Hydroxytryptophan (5-HTP)

5-HTP itself is able to stimulate enteric neurons (MMC)

### Quantity: 126 Vegetarian Capsules

#### Ingredients (per 3 capsules):

L-5-Hydroxytryptophan (from <i>Griffonia simplicifolia</i> ).....	225 mg
Ginger Extract ( <i>Zingiber officinalis</i> ).....	600 mg (6% gingerols) (rhizome)
Chamomile Extract ( <i>Maticaria chamomilla</i> ).....	150 mg (10:1) (flower) (equivalent to 1500 mg of dried herb)
Cinnamon Extract ( <i>Cinnamomum aromaticum</i> ).....	90 mg (10:1) (bark) (equivalent to 900 mg of dried herb)
Peppermint Extract ( <i>Mentha x piperita</i> ).....	120 mg (20:1) (herb) (equivalent to 2400 mg of dried herb)
Gentian Extract ( <i>Gentiana lutea</i> ).....	90 mg (10:1) (root) (equivalent to 900 mg of dried herb)
Benfotiamine.....	30 mg
Vitamin B6 (from calcium pyridoxal-5-phosphate).....	15 mg
5-MTHF (from 5-methyltetrahydrofolate, calcium salt).....	300 mcg
Vitamin B12 (methylcobalamin).....	300 mcg

**Non-medicinal Ingredients:** Silicon dioxide, L-leucine, pullulan/hypromellose (capsule)

**Suggested Use:** Adults - Take 1 capsule between each meal and 2 capsules at bedtime, on an empty stomach; or as directed by your health care practitioner.

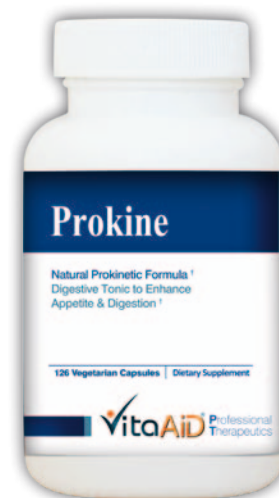
through activation of 5-HT<sub>4</sub> receptors. Moreover, 5-HTP is readily absorbed by enterochromaffin cells in the small intestine, in which it is decarboxylated to serotonin to help support the motility of the gut.

### Ginger Extract – Herbal Prokinetic Agent

Ginger is well-known for its prokinetic action as it is commonly used to treat nausea, vomiting, and constipation. It has been shown to modulate serotonin signaling by binding 5-HT<sub>3</sub> (antagonist) and 5-HT<sub>4</sub> (agonist) receptors in the enteric nervous system on top of its cholinergic action on M<sub>3</sub> receptors, <sup>1,2,3</sup> supporting gastric emptying, intestinal transit, healthy visceral sensation and upper GI comfort.

### Chamomile & Peppermint - Carminative & Calmative

Our gut motility is greatly affected (ie. inhibited) by the stimulation of sympathetic nervous system, which is why chronic stress often causes various types of GI disorders, including IBS and dyspepsia. While SIBO has been identified as one of the major causes of IBS, IBS has long been recognized as a “psychosomatic”



disorder where its physical symptoms are closely associated with mental and emotional wellness.<sup>4</sup>

Chamomile and peppermint are both well-known for their carminative & antispastic actions to help relieve spasms, flatulence, and bloating of the GI tract.<sup>5,6,7</sup> They also exert great calming action on the central nervous system to help relieve tension-headache, anxiety and insomnia.<sup>6,7</sup>

### **Gentian & Cinnamon – Restoring Yin-Yang Balance of the Gut**

Gentian root is often used as a bitter agent, which stimulates appetite, digestion and gut motility by increasing the secretions of digestive enzymes and bile (ie. cholagogue).<sup>5</sup>

Cinnamon is also commonly used to stimulate appetite while exerting an anti-spasmodic (ie. carminative) action on the gut.<sup>5</sup>

In the Traditional Chinese Medicine (TCM) paradigm, Gentian is a very “cooling” herb and exerts draining action to get rid of heat toxins (ie. infections, inflammation). Cinnamon, on the other hand, is quite warming in TCM and tonifies Spleen (ie. digestion). Hand-in-hand, they create a Yin-Yang balance in the GI tract while exerting their respective effects.

### **Support Neurotransmitter Synthesis & Nervous System**

**Pyridoxal-5-phosphate (vitamin B6)** is an important cofactor in many biochemical reactions including the synthesis of serotonin and dopamine – two major neurotransmitters in our gut.

**5-MTHF and methylcobalamin** support the methylation reaction, which is imperative in nerve cell development and integrity.

**Benfotiamine** is a lipid-soluble derivative of thiamine (vitamin B1) that is absorbed much faster than water-soluble thiamine salt. It quickly metabolizes into the active form, thiamine pyrophosphate (TPP) to exert physiological effects in the body. Benfotiamine has been shown to be effective in the treatment of neuropathy by blocking multiple destructive biochemical pathways, such as reactive oxygen species and the production of advanced glycation end-products (AGEs).<sup>8</sup>

### **Reference:**

1. Ghayur MN, Gilani AH. Pharmacological basis for the medicinal use of ginger in gastrointestinal disorders. *Dig Dis Sci.* (2005). 50(10): 1889-97.
2. Giacosa A, Morazzoni P, Bombardelli E, Riva A, Bianchianchi Porro G, Rondanelli M. Can nausea and vomiting be treated with ginger extract? *Eur Rev Med Pharmacol Sci* (2015). 19: 1291-1296.
3. Giacosa A, Guido D, Grassi M, Riva A, Morazzoni P, Bombardelli E, Perna S, Faliva MA, Rondanelli M. The effect of ginger (*Zingiber officinalis*) and artichoke (*Cynara cardunculus*) extract supplementation on functional dyspepsia: a randomised, double-blind, and placebo-controlled clinical trial. *Evid Based Complement Alternat Med* 2015; 2015: 915087
4. Asahina S, Hasegawa K, Tsuboi K. Depression in patients of irritable bowel syndrome. *Nihon Rinsho* (2006). 64(8):1527-31.
5. Hoffmann D. 2003. *Medical Herbalism: The Science and Practice of Herbal Medicine.* Rochester (VT): Healing Arts Press.
6. Blumenthal M, Goldberg A, Brinckmann J, editors. *Herbal Medicine: Expanded Commission E Monographs.* Boston (MA): Integrative Medicine Communications; 2000.
7. Schilcher H. *Phytotherapy in Paediatrics: Handbook for Physicians and Pharmacists.* Stuttgart (D): Medpharm Scientific Publishers; 1997.
8. Balakumar, P., Rohilla, A., Krishan, P., Solairaj, P., & Thangathirupathi, A. The multi-faceted therapeutic potential of benfotiamine. *Pharmacological Research* (2010). 61(6), 482-488.
9. Husebye E, Hellstrom PM, Sundler F, Chen J, Midtvedt T. Influence of microbial species on small intestinal myoelectric activity and transit in germ-free rats. *Am J Physiol Gastrointest Liver Physiol* (2001). 280(3): G368-80.
10. Lesniewska V, Rowland I, Laerke HN, Grant G, Naughton PJ. Relationship between dietary-induced changes in intestinal commensal microflora and duodenojejunal myoelectric activity monitored by radiotelemetry in the rat in vivo. *Experimental Physiology* (2006). 91(1): 229-237.
11. Metugriachuk Y, Marotta F, Pavasuthipaisit K, Juroi O, Tsuchiya J, Lorenzetti A, Fesce E, Minelli E. The aging gut motility decay: may symbiotics be acting as “implantable” biologic pace-makers? *Rejuvenation Res.* (2006). 9(2): 342-5.
12. Quigley EM, Quera R. Small intestinal bacterial overgrowth: roles of antibiotics, prebiotics, and probiotics. *Gastroenterology* (2006). 130(2 Suppl 1):S78-90.

**For Education Purpose Only:** The entire contents are not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because of something you have read in this presentation. All statements in this article have not been evaluated by the Food and Drug Administration and are not intended to be used to diagnose, treat, or prevent any diseases.