A Functional Approach to Upper GI Health

The upper gastrointestinal tract is comprised of several organs, each with its own specific function. Food moves through the digestive system via peristalsis, a series of involuntary muscle contractions that move food down the digestive tract. At each site along this path, digestive organs act uniquely to dissolve ingested materials. The highly acidic environment of the stomach is designed to kill off pathogenic microbes and break down food. The upper digestive tract also includes the esophagus, liver, gallbladder, and pancreas. These organs have important functions in regards to metabolism, such as the production and storage of digestive enzymes. Imbalances in the upper GI organs may result in *Helicobacter pylori* infection, acid reflux, functional dyspepsia, and altered bile production, which can lead to significant downstream effects. For example, acid reflux degrades the lining of the esophagus and uncontrolled *H. pylori* growth can cause ulcers and stomach cancer. Furthermore, inadequate bile production disturbs fat digestion, interferes with the body's natural detoxification pathways, and may cause gallstones.

THE HEALTH RISKS OF ACID-REDUCING DRUGS

Proton pump inhibitors (PPIs) block the production of stomach acid by binding to the enzymes in the stomach responsible for acid production, also known as the gastric proton pumps.[2] Histamine antagonists, also known as H2 blockers, reduce gastric acid secretion by binding to histamine H2 receptors located on gastric parietal cells. This inhibits the binding and action of endogenous histamine.[3] While this may offer relief of burning sensations, it can cause detrimental effects on the rest of the gastrointestinal tract, particularly on the gut microbiome.

PPIs and H2 blockers are intended for short-term use; however, in the absence of effective education and communication with physicians, patients may remain on this medication for longer than its intended use. In fact, a recent study showed that 70% of patients prescribed PPI medications in a hospital setting did not actually require this treatment.[4] Furthermore, 19% were discharged from the hospital with PPIs, many of them believing they would need to remain on this medication indefinitely.[4] Long-term use of this medication decreases the acidity of the stomach, disrupting one its primary protective functions: to kill pathogens with the highly acidic gastric juices. Research shows that inappropriate use of PPIs increases susceptibility to the bacterial enteropathogens *Salmonella, Campylobacter jejuni*, invasive strains of *Escherichia coli, Clostridium difficile, Vibrio cholerae,* and *Listeria*.[5] Additional research supports this conclusion, finding that not only do PPIs increase the abundance of *Escherichia coli* and *Clostridium difficile* in the gut microbiome, but they also reduce the overall diversity and abundance of healthy gut bacteria.[6] Keystone bacterial strains such as *Bifidobacterium spp., Lactobacillus spp., Faecalibacterium prausnitzii*, and *Akkermansia muciniphila* aid the human immune system, resist colonization of inflammatory/infectious bacterial strains, protect the intestinal epithelium, and promote healthy metabolism.[6] When these populations are compromised, the immune, endocrine, and digestive systems are negatively impacted.

H2 blockers are commonly used in conjunction with PPIs to control *H. pylori*, a bacterium linked to stomach cancer. Ironically, long term use of this practice is actually associated with increased rates of stomach cancer, as well as short-term effects such as headaches, constipation, diarrhea, and difficulty sleeping.[7] Physicians and researchers in both functional and conventional medicine agree that alternative approaches to functional dyspepsia and acid reflux must be taken to ensure optimal health for all patients.

GUTGARD®

A recent, thorough review of current research found that of all the herbal supplements available, ginger and artichoke leaf extracts are among the most effective to combat functional dyspepsia.[1] Additionally, there is abundant evidence highlighting the potent healing qualities of an ingredient known as GutGard®.[8-13] This is a standardized extract of licorice polyphenols (*Glycyrrhiza glabra*) formulated to have high potency of the highly bioactive phytonutrient known as glabridin. Other components of the plant, such as glycyrrhizin, have been removed. Research states that, in vitro, glabridin inhibited *H. pylori* growth at 100 mg/ml concentration, whereas glycyrrhizin had no effect of *H. pylori* growth, even at 250 mg/ml concentrations.[9] Researchers attribute GutGard®'s effectiveness to its ability to inhibit protein synthesis by reducing methionine incorporation into the bacteria, and also obstruct an important enzyme, DNA gyrase.[9] Further studies have found that administering 25 mg/kg of GutGard® once daily, 6 times per week for 8 weeks significantly reduced *H. pylori* proliferation in the gastric mucosa of murine models.[10] Glabridin has also been shown to attenuate gastric inflammation of the mucosa as well.[11] By relieving the stomach of damaging inflammatory cytokines, such as IL-1 and IL-6, and blocking inflammatory pathways, GutGard® gives the stomach a chance to heal, resulting in reduced stomach pain, bloating, and discomfort.[11,12] Furthermore, studies show that GutGard® can mimic

pharmaceutical prokinetic agents, such as metoclopramide, domperidone, and levosulpiride, while also aiding in the repair of gastric mucosa.[13] This improves gastric emptying rate and transit times, thereby reducing symptoms of dyspepsia.[13,14]

ARTICHOKE LEAF EXTRACT

Artichoke leaf extracts have been used to treat dyspepsia for generations. This is due to its bitter compounds, such as cynaropicrin, which increase bile flow, protect the liver from free radical damage, and reduce blood lipids.[15] In a six-week, double-blind, placebo-controlled study, researchers tested the effectiveness of artichoke leaf extract on patients with functional dyspepsia.[16] Two hundred forty-seven patients, ages 18-75 years, were randomly divided into 2 groups and asked to take 2 capsules, three times daily for six-weeks. The control group received placebo capsules, while the experiment group received 320 mg of artichoke leaf extract in each capsule. At the end of the study, the experiment group experienced significantly greater reduction in dyspeptic symptoms, as well as an increase in quality of life.[16] This is consistent with other studies that found that artichoke leaf extract improves symptoms related to acute gastritis and increases mucus and gastric juice production.[17] Researchers attribute this effect to the phytonutrient cynaropicrin, present in artichoke leaves.

GINGER

Experimental studies have aimed to elucidate the effects of supplements containing both artichoke leaf extract and ginger on symptoms of dyspepsia.[18] Using 126 patients with dyspepsia, researchers randomly divided 126 patients with dyspepsia into two groups and used multiple centers for the study. One group received a placebo capsule, while the other

received capsules containing 100mg of artichoke and 20mg of ginger. Participants took 2 capsules per day, before lunch and dinner, for a total of 14 days. By the end of the study, the treatment group experienced significant reduction in nausea, epigastric pain, and epigastric fullness.[18]

Further randomized, experimental studies, using only ginger, revealed that such supplements can aid gastric emptying, thereby assisting the natural peristalsis motion.[19] Indigestion, belching, and small intestine bacterial overgrowth are symptoms of delayed gastric emptying. Therefore, ginger has beneficial effects on the entire upper GI, as well as portions of the lower GI.[20] Interestingly, researchers point to the fact that ginger and artichoke complement each other in their action. Ginger can evoke positive outcomes to the stomach, while artichoke is active in the small bowel.[20]

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