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39 percent: acid reflux (heartburn)
23 percent: dyspepsia (indigestion)
9 percent: gastritis
18 percent: irritable bowel
syndrome (IBS)

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<p>inflammatory bowel diseases such as CD and ulcerative colitis, according to a review from the same institution.⁷</p> <p>Two types of fiber consumed for their broad range of digestive benefits are oat bran and wheat bran. In particular, both compounds are valued for their ability to increase stool weight. A clinical trial from the University of Wisconsin-Madison tested the different mechanisms by which oat and wheat brans produce these effects and found bacteria and lipids are major contributors to the increase in stool weight seen with oat bran consumption, whereas undigested plant fiber is responsible for much of the increase in stool weight produced by wheat bran consumption.⁸</p>	<p>16 percent: lactose intolerance</p> <p>Percent Willing to Use Natural Products for Treatment</p> <p>54 percent would use supplements for acid reflux 44 percent would use functional foods/beverages for acid reflux 44 percent would use supplements for constipation 62 percent would use functional foods/beverages for constipation</p> <p>Source: The Natural Marketing Institute's (NMI) 2004 Health and Wellness Trends Database (HWTD)</p>
<p>Another variety of fiber valued for its positive influence on elimination is psyllium (<i>Plantago ovata</i> Forsk). According to the <i>PDR</i>, the bulk of psyllium's digestive benefits are derived from the refined xylan-rich seed husk of the plant, the component principally used as a soluble fiber source for laxatives, ready-to-eat cereals and nutritional supplements. Researchers from the University of Illinois, Urbana, used a digestion simulation model to test effects of various soluble and insoluble fibers, and speculated psyllium, due to its particularly viscous characteristics throughout small intestinal simulation, should be particularly effective in modulating blood glucose and lipids.⁹ Other studies on psyllium have shown the compound is particularly adept in lowering intestinal inflammation. A Spanish, open label, parallel-group, multicenter, randomized clinical trial on 105 patients with ulcerative colitis in remission found <i>Plantago ovata</i> seeds (dietary fiber) might be as effective as mesalamine to maintain remission of the disease.¹⁰</p> <p>Insoluble fiber from flax and pea, as well as the soluble fiber glucomannan are newer fiber ingredients gaining in popularity as treatments for constipation. Supplemental flax intake of 9.0 g/d produced fecal bulking capacity of about 2.9 g of fecal weight/g of fiber, according to a University of Saskatchewan study.¹¹ The same researchers found the addition of pea fiber to the usual diet of elderly residents in long-term care resulted in increased stool frequency.¹² And glucomannan reduced abdominal pain and improved constipation in a study conducted on children by scientists from the University of Iowa.¹³</p> <p>Certain insoluble fibers act as prebiotics, non-digestible oligosaccharides including fructooligosaccharides (FOS), a mixture of glucose-terminated fructose chains with a maximum length of five units, and inulin, a long-chain, glucose-terminated polysaccharide mixture with a partially hydrolyzed form known as oligofructose. Prebiotics encourage proliferation of probiotics, beneficial bacteria that form complex ecosystems in the GI tract.</p> <p>In addition to boosting the population of probiotics, prebiotics have been shown to independently generate or collaborate with probiotics to provide many of the same effects on the digestive system as probiotics. For example, prebiotics have been shown to prevent the symptoms of IBD,^{14,15} improve bowel function by increasing stool frequency and stool weight, and reduce the risk of certain diseases such as colon cancer. In addition, prebiotics may support healthy digestive function by preventing intestinal attachment of enteropathogens by acting as receptor homologues, resulting in the suppression of harmful microorganisms, the stimulation of probiotic growth, or both.¹⁶</p>	
<p>Boosting Immunity Through GI Function</p> <p>Beyond its core functions of extracting nutrients necessary for life from foods and eliminating wastes, the gastrointestinal (GI) system plays a role in immunity. Saliva and bile have antimicrobial properties, and the pH of the stomach is fatal to most pathogens. Further, intestinal mucosa eliminate invading pathogens and other threats by working with lymphocytes and their products, excreting immunoglobulins and providing a home for billions of beneficial antipathogenic bacteria, which co-evolved with the human host.¹ Disruption of the homeostasis of these bacteria interferes with signal transduction at the epithelial cell level and may lead to inflammation of intestinal mucosa,² which promotes development of diseases such as GI cancers,³ and autoimmune disorders such as Crohn's disease.⁴</p> <p>Supplementation with probiotics may be one way to optimize immunity through the GI tract. According to a study presented by university researchers at the 2006 North American Research Conference on Complementary and Integrative Medicine, ingestion of delayed release, four-species probiotic supplement (as</p>	<p>Since the human digestive system has co-evolved with probiotics, it cannot sustain proper function without these symbionts. S.K. Dash, Ph.D., founder of UAS Laboratories, addressed the many benefits of probiotics in <i>A Consumer's Guide to Probiotics</i>: "Healthpromoting effects of beneficial bacterial include stimulation of the immune system, reducing gas problems, improved absorption of essential nutrients, even synthesis of vitamins. We should also note that beneficial bacteria help us to maintain healthy cholesterol levels, fight cancer and even promote resistance to food-borne pathogens."</p> <p>According to numerous clinical trials, probiotics benefit digestive function by breaking down lactose and producing lactic acid to help acidify the intestinal tract; deconstructing protein to free amino acids; and regulating peristalsis and bowel movements; thus improving nutrient absorption.¹⁷ They also perform metabolic activities to salvage nutrients, thus increasing absorption of calcium, copper, iron and magnesium,¹⁸ preventing diarrhea¹⁹ and constipation.²⁰ In the upper digestive tract, probiotics balance bacteria levels to combat gut-caused</p>

Immunobiotix®, from Nutraceutix) over eight weeks produced a statistically significant increase in percent of phagocytic peripheral blood monocytes and polymorphonucleocytes (PMN) in healthy, non-elderly adults. Each tablet contained a minimum of 2 x 10⁹ organisms from four species of probiotics, including *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Lactobacillus salivarius* and *Bifidobacterium bifidum*. Volunteers, who had avoided use of antibiotics, probiotics or fermented foods six months prior to the study, ingested three tablets daily for eight weeks. Researchers monitored natural killer (NK) cell and phagocytic activity, and levels of salivary secretory IgA at baseline and at three, five and eight weeks. Although treatment did not significantly increase salivary secretory IgA or NK cell activity, Increases in percent phagocytosing cells occurred in both monocytes and PMN. The researchers concluded ingestion of a four-species probiotic formulation induces changes in immune function in healthy individuals.

halitosis²¹ and thwart peptic ulcers through the elimination of *Helicobacter pylori* bacteria in the stomach.²²

Probiotics also benefit the digestive tract by helping to control inflammatory bowel diseases, according to numerous clinical trials. In a study conducted at the S. Raffaele University Hospital, Milan, Italy, a cohort of 25 patients with a mild to moderate clinical flare-up of ulcerative colitis received 250 mg of the probiotic *Saccharomyces boulardii* (S. boulardii) three times per day for four weeks during maintenance treatment with the drug mesalazine.²³ Of the 24 patients who completed the study, 17 attained endoscopically-confirmed clinical remission of colitis.

Another branch of inflammatory bowel disease where probiotic therapy has been established as effective is IBS. In a study conducted at the Mayo Clinic and

Mayo Foundation, Rochester, Minn., 25 patients with Rome II IBS with predominant diarrhea were randomly assigned to receive 450 billion lyophilized probiotic bacteria or matching placebo twice daily for eight weeks after a two-week run-in period.²⁴ Patients were assessed for pre- and post-treatment GI transit as well as daily bowel function and symptoms. The scientists concluded the probiotic supplement appeared to be promising in the relief of abdominal bloating in patients with diarrheapredominant IBS.

Probiotics have also been shown effective in controlling the inflammatory bowel condition pouchitis. In a study conducted at St Mark's Hospital, London, England, 36 patients who had experienced episodes of pouchitis at least twice in the previous year or needed continuous antibiotics to control pouchitis, and in whom remission was induced by four weeks of combined antibiotics therapy, were randomized to receive probiotics (20 subjects) or placebo (16 subjects) once daily for one year or until relapse.²⁵ Remission was maintained for one year in 17 patients receiving probiotics and in one patient on placebo, while the quality of life score remained high in the probiotics group but deteriorated in the placebo group.

Other bowel ailments where probiotics have been found helpful include diarrhea and constipation. In a double blind study conducted on children at the University of Buenos Aires, Argentina, 89 children with diarrhea (caused by enteric pathogens in 40 percent of the patients) were randomized to receive 175 g of pasteurized dairy milk containing two viable lyophilized probiotics strains of lactobacilli and lyophilized S. boulardii, or non-probiotic pasteurized cow milk as placebo twice daily for a five-day period.²⁶ Stool frequency, duration of illness and frequency of vomiting were monitored. Lactobacilli and S. boulardii significantly reduced stool frequency, duration of the illness and vomiting as compared with placebo.

Similarly, at the German Institute of Human Nutrition, a double blind, placebo-controlled, randomized study was conducted over a four-week period in patients with chronic constipation.²⁷ Study subjects received 65 mL/day of a beverage containing *Lactobacillus casei* Shirota (LcS) or placebo. The study subjects were monitored for gastrointestinal symptoms, well-being and stool habits and underwent a medical examination weekly. Patients consuming LcS experienced significant improvement in severity of constipation and stool consistency, starting in the second week of treatment. In the final examination, 89 percent of the LcS group and 56 percent of the placebo group reported a positive effect of their beverage on constipation. The researchers concluded the results of the study indicated a beneficial effect of probiotics on gastrointestinal symptoms of patients with chronic constipation, and the administration of probiotics may be recommended as an adjunctive therapy for this condition.

Probiotics may also inhibit overgrowth of yeast (*Candida albicans*) in the digestive tract, a condition often caused by use of antibiotics. A pilot clinical study from Wakunaga, manufacturers of the Kyo-Dophilus® line of probiotics, showed 89 percent of 36 patients infected with *Candida* had lower symptom scores after taking *Lactobacillus acidophilus* and *Bifidobacterium bifidum* (from Wakunaga). In addition, of those supplemented, 72 percent had a greater than 25-percent improvement in symptom scores, 33 percent had a more than 50-percent improvement in scores, and two patients became completely symptom free after one month without undergoing any changes in diet or other treatments.

According to research from Nebraska Cultures, L. acidophilus DDS-1 is a particularly valuable strain as its acid, bile and alkaline stability allow it to survive the harsh environment in the stomach and proliferate in the intestines. The study also found L. acidophilus DDS-1 has excellent capacity to bind to intestinal cell lines, with a capability to displace the harmful bacterium *Escherichia coli* (E. coli); the researchers noted the strain's antimicrobial activity might help to alleviate diarrhea and other intestinal infections.

In his book, Dash suggested companies select cultures that are GRAS (generally recognized as safe) or have been subjected to toxicological studies prior to incorporation into products. He further noted the culture should adhere to the intestinal walls, be proven to survive stomach acids, and produce beneficial compounds including lactic acid, hydrogen peroxide and natural antibiotics.

Another category of ingredients marketed for digestive health is digestive enzymes, which combat dyspepsia and aid digestion by breaking down food in the digestive tract. Proteases digest protein, amylases digest carbohydrate and lipases digest fat. According to Edward Howell, M.D., founder of National Enzyme Company (NEC), the human body relies on food enzymes to help with digestion and cannot carry the entire load alone; intake of exogenous enzymes from foods or supplements allows the body to concentrate more of its energy on the activity of metabolic enzymes.²⁸

Digestive enzymes are often derived from porcine and bovine pancreas. These types of enzymes, pancreatins, are of particular benefit to patients with malabsorption syndrome due to pancreatic insufficiency.²⁹ Animals also provide pepsin, a proteolytic enzyme produced by the stomach.

Enzymes are also derived from plant sources. Various fruits contain proteolytic enzymes, which are capable of digesting protein in acid, alkaline or neutral media. Papaya contains the proteinases papain, caricain, chymopapain and glycine endopeptidase,³⁰ and pineapple, used for centuries by South and Central Americans to improve digestion,³¹ is a source of the enzyme bromelain. Papaya and pineapple enzymes are thought to be particularly effective in lowering intestinal inflammation, as they become active in higher temperatures associated with the inflammatory response.

Certain enzymes are vulnerable to denaturation in the upper GI tract before they can deliver benefits. A March 2006 study published in *Biochemical and Biophysical Research Communications* found the four papaya proteinases undergo, at low pH, a conformational transition that instantaneously converts their native forms into unstable globules that are rapidly and irreversibly degraded by pepsin; the researchers concluded plant proteinases may require protection against both acid denaturation and proteolysis to be effective in the gut after oral administration.³²

NEC offers Biocore™, a line of enzymes including lipases designed to target digestive problems associated with the high fat content of a fast food diet, enzymes designed to improve assimilation of carbohydrates, and products geared toward specific GI and digestive conditions such as lactose intolerance. According to a proprietary study from NEC and The Netherlands Organization for Applied Scientific Research (TNO), a blend of fungal proteases, carbohydrases and lipases improved digestibility and bioaccessibility of proteins and carbohydrates in the lumen of the small intestine in computer-controlled dynamic gastrointestinal models (TIM) of healthy and impaired human digestion. According to the company, the study demonstrates the value of enzyme supplementation in both healthy individuals and those with digestive problems.

Beyond papaya and pineapple enzymes, several other botanical therapies have been shown to support digestive health. The antioxidant bioflavonoid quercitrin, a glycosylated form of quercetin, may protect the GI tract from injury by stabilizing GI mast cells, which are involved in many pathologic effects in the GI system, such as food hypersensitivity.³³ A study from Granada University in Spain showed concurrent administration of a fish oil-, olive-oil and quercitrin-rich diet to rats with induced colitis produced an intestinal anti-inflammatory effect, as evidenced by a significant improvement of all biochemical parameters of colonic inflammation assayed in comparison with control rats.³⁴

Another botanical thought to lower intestinal inflammation by stabilizing mast cells is aloe vera.³⁵ The plant's neutral polysaccharides, aloemmannan and acemannan, are responsible for some of its anti-inflammatory effects.³⁶ Another anti-inflammatory compound in aloe is alprogen, which Korean research suggests inhibits histamine and leukotriene release in mast cells activated with specific antigen-antibody reactions.³⁷ Aloe vera treatment can reduce leukocyte adherence and TNF-alpha level, elevate IL-10 level and promote gastric ulcer healing, according to a rodent study from Chulalongkorn University, Bangkok, Thailand.³⁸ Further, an antioxidant preparation based on aloe vera and ubiquinol reduced intestinal inflammation, lesions, and pathological alterations of the intestinal electrophysiological activity and motility, in a rat model of DSS-induced colitis.

Peppermint is another herbaceous compound known to facilitate good digestion. Rapidly absorbed after oral administration and eliminated mainly via the bile, menthol from the plant has a dose-dependent antispasmodic effect on the smooth musculature of the GI tract, interfering with the movement of calcium across cell membranes.^{39,40} The anti-spasmodic quality of the botanical is so effective, in fact, that it was successfully used as a replacement for hyoscine-N-butylbromide during upper endoscopy in a study conducted by scientists from the University of Tokyo Graduate School of Medicine.⁴¹ According to a review from the University of Exeter in the United Kingdom, nine randomized clinical trials involving peppermint and dyspepsia found symptoms were reduced by peppermint in 60 to 95 percent of patients.⁴²

As anyone who turned to ginger ale as a child with a stomach ache knows, there is something beneficial about ginger for the digestive tract. A meta-analysis from Naresuan University in Phitsanulok, Thailand, reviewed five randomized trials including 363 patients and found a fixed dose of 1 g of ginger was more effective than placebo for preventing postoperative nausea and vomiting.⁴³ Similar findings on ginger's antinausea effects were reported by Australian researchers, who administered 1 g of ginger daily for three weeks to women (n=291) less than 16

weeks pregnant, and found the herb reduced nausea and vomiting.⁴⁴ Taiwanese researchers speculated ginger may ameliorate nausea by preventing development of gastric dysrhythmias and elevation of plasma vasopressin; their theory was supported in a study of 13 volunteers with motion sickness, for whom preadministration of ginger reduced symptoms and improved recovery after circularvection.⁴⁵

In addition, basic nutrients also offer benefits in the GI field. Zinc, for example, has proven beneficial in helping mitigate the impact of diarrhea, particularly in children. A review from All India Institute of Medical Sciences, New Delhi, noted zinc deficiency is common in children from developing countries, and supplementation has been shown to have significant benefits in preventing and treating diarrhea.⁴⁶ For example, a randomized, double blind trial in Peru involved co-supplementation with ferrous sulfate for anemia with or without zinc sulfate.⁴⁷ Adding zinc to the iron treatment increased the hemoglobin response and reduced diarrheal incidence compared to iron alone. Another study conducted in two hospitals in New Delhi found administration of zinc with rehydration therapy to children with acute diarrhea reduced stool output and duration of illness.⁴⁸ The benefits of zinc in diarrheal treatment led researchers from the Centre for International Health at the University of Bergen, Norway, to conclude zinc should be included in standard case management of acute diarrhea in developing countries as a cost-effective means of enhancing standard management of the illness.⁴⁹

Zinc may also prove beneficial for Crohn's patients, who often have low antioxidant defenses. Low serum zinc concentrations in Crohn's sufferers are related to significantly reduced zinc absorption, even with supplementation.⁵⁰ But Italian researchers found in a study of 12 patients with Crohn's disease that supplementation with zinc sulfate (110 mg tid) improved intestinal barrier function and helped reduce the risk of relapse.⁵¹

Whether consumers are turning to beneficial bacteria to boost their natural defenses, or fighting disease states with specially-formulated nutritional products, the market for options to support gastrointestinal health continues to grow. Examining relevant research and determining optimal formulation and delivery options will ensure those consumers are getting the high quality products they expect.

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Protecting the Stomach

Given the strong enzymes and acids that work in the digestive system, it is not surprising that one in 10 Americans develops an ulcer at some time in his lifetime. Common causes include long-term use of non-steroidal anti-inflammatories (NSAIDs) or bacterial infection, generally with *Helicobacter pylori* (H. pylori). It is estimated that approximately 20 percent of Americans under the age of 40 are infected with H. pylori, and up to half of those over 60. Treatment for H. pylori generally involves a combination of antibiotics, acid suppressors and stomach protectors; however, a growing body of research suggests nutritional adjuncts may prevent infection or help in the eradication process.

Antioxidants, including vitamins A, C and E, plus carotenoids and flavonoids, have been the focus of many studies in this area. Swedish researchers conducted a study on dietary antioxidant levels in guinea pigs infected with H. pylori, and found supplementation with vitamins A, C and E and selenium reduced H. pylori infection rates and gastritis incidence.¹ Follow-up work from the group also found supplementation with only vitamin C or astaxanthin also had an effect on infection and gastritis, but not to the same degree. An astaxanthin-rich extract of *Haematococcus* algae has proven effective at reducing gastric inflammation associated with H. pylori infection in mice, apparently by inhibiting lipid peroxidation and H. pylori growth.² In vitro work has further shown the ability of astaxanthin to protect against NSAID-induced gastric ulcer and prevent associated increases in oxidative damage in the gut.³ Astaxanthin also appears to work well in combination with vitamin C, showing complementary free radical scavenging ability as well as antimicrobial action.⁴

Vitamin C has been one of the primary compounds investigated for its interaction with H. pylori. Data from 6,746 adults enrolled in the Third National Health and Nutrition Examination Study (NHANES III) was analyzed to determine the relationship between serum ascorbic acid and H. pylori expression.⁵ The researchers found higher serum levels of ascorbic acid were associated with a decreased incidence of H. pylori infection, leading them to conclude ascorbic acid may positively impact infection rate and the risk for peptic ulcer and gastric cancer.

L-carnitine, a derivative of the amino acid lysine, is more widely known for applications in cardiovascular wellness, performance nutrition and cognitive health. However, the compound has also been shown to protect intestinal mucosa. Possibly due to its antiperoxidative effects, L-carnitine significantly prevented gastric ulcerogenesis and decreased the ulcer index in rats with ethanol-induced mucosal injury, according to research from Trakya University in Turkey.⁶ Further, a study from Sutcu Imam University determined L-carnitine may be beneficial for patients with ulcerative colitis.⁷ Treatment of rats with acetic acid caused severe damage macroscopic and histopathological damage in the colon and significantly increased markers of oxidative stress in

colonic tissue. The researchers observed administration of L-carnitine to the animals improved histopathologic scores, significantly decreased malondialdehyde and myeloperoxidase levels, prevented the depletion of reduced glutathione levels and significantly increased superoxide dismutase levels. Another study on L-carnitine and gastric mucosa, conducted by scientists from Akdeniz University, found administration of L-carnitine protected the gastric mucosa of rats with intestinal injury induced by cold-restraint stress (CRS).⁸ In rats exposed to CRS, ulcer index was higher, gastric acid production was lower, hemoglobin leakage into the gastric lumen was increased, and gastric mucosal mucin and PGE content were reduced, in comparison with control rats. L-carnitine treatment prior to CRS led to attenuation of changes in ulcer index, gastric acid secretion, hemoglobin leakage into the gastric lumen and gastric PGE2 content.

Chelating the amino acid L-carnosine with zinc is another patented treatment for its ability to support mucous secretion and exert antioxidant effects. Research studies have referenced it by several names, including Polaprezinc, Z-103, and Zinc L-carnosine; it is sold in the United States by Lonza Inc. as PepZin GI®.

Research conducted at the Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan, investigated the impact of Polaprezinc on H. pylori-induced gastritis in gerbils.⁹ After 12 weeks, the researchers found supplementation had no influence on the H. pylori density; however it attenuated the development of gastritis by scavenging monochloramine, an important compound in the development of gastric mucosal injury. Further research in H. pylori-inoculated gerbils found Polaprezinc has the ability to inhibit gastric lesion formation and reduce mucosal oxidative inflammation.¹⁰ Additional in vitro studies suggest Polaprezinc enhanced mucosal growth factor expression to heal lesions;¹¹ and further protected the stomach against NSAID-induced mucosal injury, probably through its antioxidative and anti-inflammatory properties.¹²

In addition to nutrients and amino acids, several botanical compounds may have antiulcer activity, including flavonoids, aloe and licorice.¹³ In vitro work has found aloe has anti-secretory activity on gastric acid, and could thereby protect the gastric mucosa against infectious agents.¹⁴ Another review on botanical compounds and gastric health reported studies on garlic have found the plant to be effective against common pathogenic bacteria, including H. pylori.¹⁵ And researchers from the University of Illinois, Chicago, focused their attention on the ability of gingerols, polyphenolic compounds isolated from ginger root (*Zingiber officinale*), to inhibit the growth of H. pylori in vitro.¹⁶ They found a methanol extract of ginger rhizome inhibited the growth of all 19 strains of H. pylori tested, concluding its activity against H. pylori could also prevent development of gastric cancer.

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