

GastroThera™

Nutritional and Herbal Support for the Gastrointestinal Tract

DESCRIPTION

GastroThera™ provides intensive nutritional and herbal support for the entire gastrointestinal tract by addressing four key areas of intestinal function: energy requirements of intestinal cells, structural integrity of the intestinal mucosa, microorganism balance, and cellular protection against chemical and oxidative damage. GastroThera™ includes large amounts of the amino acid glutamine, the primary fuel for intestinal cells, to meet the high energy demands of the GI tract and the immune system during periods of physiological stress. Glutamine also transports potentially toxic ammonia to the kidneys for excretion. *Acacia senegal* contributes soluble, non-bulking fiber that is readily fermentable to acetic, butyric and propionic acids, which create a supportive environment for the growth of beneficial probiotic organisms, assist in water absorption, and support intestinal cell function. Inulin supplies non-digestible oligosaccharides to further encourage the growth of beneficial microorganisms. N-Acetyl-D-Glucosamine is a structural component of the intestinal mucosa and can be used to help protect and repair intestinal tissues. GastroThera™ vegetarian capsules can be taken regularly or periodically whenever nutritive support of GI function and associated immune modulation is warranted.

OVERVIEW

The gastrointestinal tract has long been thought of simply as a site of food digestion, nutrient absorption and water homeostasis. Recently, a much deeper understanding of this organ's complex physiology and functioning has given rise to the view of the intestinal tract as an "intelligent" barrier, a critical interface between host and environment, responsible for discriminating between self and non-self, and selectively absorbing substances beneficial to the host while barring entry to harmful entities. This newer view highlights the importance of maintaining the integrity of the intestinal lining and understanding that dysregulation of its essential barrier function can lead to both intestinal and extraintestinal disorders.

Many environmental stressors and disease states are thought to be involved in impairing intestinal barrier function and leading to what has been called "leaky gut." These include psychological stress, trauma, burns, surgery, intestinal infections, dietary influences, overuse of alcohol, free radical damage, disruption of intestinal flora, medications (e.g. NSAIDs), chemotherapy and radiation, gastrointestinal disorders (e.g. inflammatory bowel disease, gluten enteropathy), hepatobiliary disorders and aging. These factors appear to alter gut permeability primarily by disrupting normal absorption pathways through either intestinal epithelial cells (i.e. transcellular pathways) or the tight junctions between epithelial cells (i.e. paracellular pathways).

Once intestinal hyperpermeability is established, continuous entry of harmful substances from the intestinal lumen into the mucosa and beyond can lead to a variety of health conditions. For example, translocation of proinflammatory substances can either cause or exacerbate intestinal or systemic inflammatory disorders; translocation of antigenic material may give rise to allergic or autoimmune reactions; translocation of microorganisms may increase the risk of sepsis, etc. Therefore, reduction of intestinal permeability could favorably affect the course of many clinical conditions.

Glutamine

L-Glutamine is the most abundant amino acid in the body. It is essential to the production of glucose, nucleic acids, peptides and proteins. Glutamine plays a role in the maintenance of normal body acid-base (pH) balance and helps protect the body from high ammonia levels by transporting ammonia (as amino groups) to the liver for conversion to urea or to the kidneys for direct excretion in the urine. Glutamine is considered non-essential in normal physiology, but may become conditionally-essential under conditions such as trauma, burns or major surgery. The intestinal tract is an avid user of glutamine and may deplete body stores to effect mucosal repairs when necessary. Under adverse conditions, the body may thus require more glutamine than can be obtained from the diet, or produced endogenously, and a deficiency may develop. Inadequate glutamine can lead to impairment of multiple body systems including the gastrointestinal, immune and musculoskeletal systems.

One of glutamine's primary benefits is in the nutritional support and recovery of critically-ill patients. Persons who experience trauma, serious infection, burns or gastrointestinal surgery often experience damage to intestinal barrier function which can lead to bacterial or endotoxin translocation and sometimes sepsis. Glutamine has been used both parenterally and enterally to help maintain mucosal barrier function, but enteral feeding, where possible, is becoming the preferred standard of nutritional support in intensive care settings as parenteral feeding has been associated with atrophy of the mucosal lining as well as increased risk for both infectious and non-infectious complications.

Glutamine is a primary fuel for enterocytes and has been shown to limit mucosal barrier damage by inhibiting production of proinflammatory cytokines and enhancing the expression of heat-shock protein. Glutamine is also a precursor for glutathione, the body's primary intracellular antioxidant and an important agent of cellular protection and survival. Other evidence suggests that glutamine has an anti-apoptotic effect in intestinal cells and may enhance mucosal repair by increasing collagen synthesis in fibroblasts.

Studies undertaken in hospital settings have demonstrated the benefits of glutamine in preserving the integrity of the intestinal lining. In one study of severely burned patients, oral glutamine supplied at 0.5 gm/kg/d for fourteen days was found to significantly reduce intestinal permeability and plasma endotoxin levels and decrease the length of hospital stays compared to placebo. Similar results were obtained in a group of abdominal surgery patients using 30 gm/day of glutamine for seven days. While these doses were at the higher end of the therapeutic dose range, they were administered for short periods of time, suggesting that lower doses given for longer periods may provide similar benefits in less acute situations.

Interestingly, while glutamine tends to decrease intestinal permeability to microorganisms and endotoxins, it may enhance intestinal absorption of certain nutrients. In one study on HIV patients with abnormal intestinal permeability, a trend towards improved absorptive function was demonstrated with as little as 4 gm/d of glutamine. Correction of malabsorption could potentially enhance the health status of a number of populations, including those with HIV, the chronically ill and the elderly.

Glutamine may also be useful in reducing the adverse effects associated with systemic chemotherapy and radiation. The intestinal damage caused by chemotherapeutic agents and radiation often leads to increased intestinal permeability, reduced intestinal absorption of nutrients, and diarrhea. One study reported in the journal, *Cut*, found that 18 gm/day of oral glutamine, administered concurrently with 5-Fluorouracil, reduced intestinal permeability by approximately 32 percent, attenuated the reduction in intestinal absorption by over 50 percent and diminished the incidence, duration and severity of diarrheal episodes compared to placebo.

Altered permeability of the intestinal lining is associated with other types of gastrointestinal pathology such as irritable bowel syndrome (IBS). IBS is a chronic disorder which can significantly impact one's quality of life and is not easily treatable. Impaired barrier function in IBS patients has been associated with passage of luminal antigens (e.g. food, bacterial) into mucosal cells which promote mucosal inflammation. Treatments aimed at reducing gut permeability may thus improve the course of this disorder. While glutamine has not been directly studied in persons with IBS, its ability to reduce intestinal permeability in the critically-ill and those undergoing chemotherapy suggest it may improve clinical outcomes for IBS patients as well.

Insults to the gastrointestinal tract from trauma, surgery, chemotherapy, etc. cause a marked increase in the utilization of glutamine for intestinal repair. This can result in reduced body stores of glutamine and an attendant reduction in essential functions, such as immune function. Immune cells, like enterocytes and other rapidly-dividing cells, are particularly dependent upon glutamine for their growth, metabolic function and survival.

Enhancement of immune function is an important component of recovery in the critically-ill. A recent meta-analysis of studies undertaken between 1998 and 2003 in which critically-ill patients were supplemented with enteral glutamine found an overall significant reduction in infection in the study participants (RR 0.76). In one of these studies in which burn victims were supplemented with glutamine, the incidence of positive blood cultures (in terms of days per patient) was more than three times lower in the glutamine group than in the control group. In another study, enteral glutamine supplied to a group of critically-ill patients reduced the incidence of nosocomial pneumonia from 33 percent to 14 percent compared to a control diet. In these settings, glutamine appears to significantly reduce infectious morbidity by enhancing systemic immunity, intestinal immunity, or both.

Acacia senegal

Acacia senegal is one of several species of Acacia tree from which the soluble fiber, gum arabic (GA), can be derived. GA consists of branching polysaccharide chains containing the sugars galactose, rhamnose, arabinose and glucuronic acid. Soluble fibers like GA form slippery, gel-like substances when hydrated and have traditionally been used to soothe inflamed and irritated mucous membranes.

The polysaccharide chains in GA can be used as a fuel source for intestinal bacteria which metabolize them to the short chain fatty acids (SCFAs) acetic, butyric and propionic acids. SCFAs are, in turn, a fuel source for enterocytes and also enhance mineral absorption and resistance to pathogenic microorganisms by lowering the pH of the intestinal lumen. The ability of a substance to be selectively utilized as an energy source by healthy intestinal flora is known as the prebiotic effect. The prebiotic nature of GA has been observed in a human study where GA feeding led to increases in the concentration of the beneficial probiotic organism *Bifidobacterium longum*. Animal studies suggest GA exerts a protective effect against toxic damage to the gastrointestinal lining and can help correct disrupted water and nutrient absorption. A controlled study on a group of persons with diarrhea demonstrated that GA was able to significantly decrease the number of loose and watery stools compared to placebo.

Inulin

Inulin is a fiber-like carbohydrate consisting of fructose sugar molecules linked together by beta-2,1 glycosidic bonds. Found naturally in foods like bananas, garlic, leeks and onions, inulin is a dietary substance and should not be confused with insulin, a hormone secreted by the pancreas that is used to regulate blood glucose levels. Like fibers, inulin cannot be broken down by human digestive enzymes, but can be metabolized by microorganisms in the intestinal tract to SCFAs. Inulin has been shown to be a preferred energy source for the bifidobacteria and to selectively support the growth of these beneficial probiotic organisms in the human colon. Animal and *in vitro* studies suggest inulin may support the growth of probiotic lactobacilli in the intestinal tract as well.

Inulin has demonstrated benefits for gastrointestinal disorders in several human studies. In one trial, inulin significantly increased fecal bifidobacteria counts and reduced constipation in a group of elderly participants. In another study, supplementation with inulin-like fructooligosaccharides helped reduce the incidence of diarrhea in travelers. Preliminary data also suggest dietary inulin, and inulin-type fructans, may play a role in reducing the risk of colon carcinogenesis.

Inulin also appears to have extraintestinal benefits including enhancement of systemic immune function and regulation of blood lipids. In animals, inulin feeding reduced mortality from the food-borne pathogen *Listeria monocytogenes* from nearly 30 percent in control mice to zero. In humans, supplementation with inulin has been shown to significantly lower serum triglycerides.

NAG

N-acetyl-D-glucosamine (NAG) is the acetylated form of the amino sugar glucosamine. Glucosamine is well known for its role as a substrate for endogenous glycosaminoglycan (aka mucopolysaccharide) synthesis and its protective effects in joint tissue. Less well known is the fact that extensive breakdown of glycosaminoglycans also occurs in certain gastrointestinal diseases like IBD. NAG can help with the repair of damaged intestinal tissues by acting as a building block for structural complexes such as glycosaminoglycans and proteoglycans. NAG may be of particular benefit for intestinal tissues as it has been shown to be better taken up than glucosamine by tissue samples from IBD patients. This suggests that n-acetylation of glucosamine, a necessary step in tissue repair, may be deficient in IBD patients. A pilot study using 3-6 gm/d of NAG in a group of drug-resistant children with IBD (10 Crohn's, 2 ulcerative colitis) led to clinical improvement in 66 percent of the cases.

INDICATIONS

GastroThera™ is designed for persons who want to provide direct nutritional support and protection for the intestinal mucosa as well as favorably affect the intestinal flora and immune function. GastroThera™ may be suitable for those undergoing heightened stress, trauma, surgery, chemotherapy or radiation who wish to prevent or reduce intestinal permeability and normalize gastrointestinal function.

FORMULA

Supplement Facts

Serving Size 6 Capsules • Servings Per Container 30

Amount Per 6 Capsules

Calories	15
Glutamine (as L-glutamine USP)	3,750 mg*
Gum arabic (<i>Acacia senegal</i>)	375 mg*
Inulin	187 mg*
N-Acetyl-D-Glucosamine (from crab and/or shrimp shells)	187 mg*

*Daily Value not established.

Other ingredients: Vegetarian capsule (hydroxypropyl methylcellulose, water), cellulose, silicon dioxide, and L-leucine.

Supplement Facts

Serving Size 1 Scoop (6 grams) Servings Per Container 60

Amount Per Scoop

Calories	20
Glutamine (as L-glutamine USP)	5,000 mg*
Gum arabic (<i>Acacia senegal</i>)	500 mg*
Inulin	250 mg*
N-Acetyl-D-Glucosamine (from crab and/or shrimp shells)	250 mg*

*Daily Value not established.

Other ingredients: None.

SUGGESTED USE

For daily maintenance, take 2 GastroThera™ capsules three times daily, with or between meals. For more intensive therapy, take 1 scoop (approximately 6 grams) of GastroThera™ powder one to three times daily. Powder should be mixed in cold or room-temperature water or a non-acidic juice and taken between meals. Best results may be obtained when used in conjunction with a probiotic supplement such as Ther-Biotic® Complete or Vital-10®.

ADVERSE REACTIONS

Supplemental glutamine has been shown to be exceptionally safe in the vast majority of studies, but has been reported to increase blood ammonia levels in cirrhotic patients and to reduce the lymphocyte mitotic index in persons with Alzheimer's disease. Two case reports have also been published of supplemental glutamine causing manic and hypomanic symptoms in persons without a history of manic behavior. While very rare, allergic reactions to gum arabic and inulin can occur. One case report exists of an anaphylactic response to a gum arabic coating on coffee beans, but this reaction was potentiated by the use of a beta-blocking ophthalmic agent. Two case reports of anaphylaxis upon exposure to inulin have been published, one of which involved an inulin-dairy-protein complex formed during food processing.

DRUG INTERACTIONS

In a small, open study, an unspecified amount of gum arabic was shown to significantly reduce the absorption of the drug amoxicillin. Persons taking amoxicillin, and perhaps other medications, should take it separately from GastroThera™ by at least four hours. In an animal study, glutamine significantly reduced systemic clearance of the chemo-therapeutic agent methotrexate. Persons taking chemotherapeutic drugs, especially methotrexate, should consult with their physician before using this product.

CONTRA-INDICATIONS

GastroThera™ should not be used by persons with cirrhosis of the liver, Alzheimer's disease or manic symptoms except under the care of a qualified physician. Do not use if you have a history of allergy to gum arabic, inulin or high-inulin foods such as artichoke, asparagus, bananas, burdock root, chicory root, endive, garlic, Jerusalem artichoke, leeks, onions or salsify. Pregnant or nursing women should consult with a healthcare provider before using this product.

HOW SUPPLIED

Capsules: 180 vegetarian capsules per bottle with full-bottle shrinkwrap. Packaged 12 bottles per case.

Powder: 12.6 ounces (360 grams) powder per bottle with full-bottle shrinkwrap. Packaged 12 per bottles per case.

STORAGE

Store in a cool, dry place (59°F-85°F) away from direct light. Keep out of reach of children.

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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.

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