

# Intestinal Therapy

(NPN 80002822)

ADVANCED  
Naturals

PRODUCT MONOGRAPH

## Product composition

### Medicinal Ingredients:

Each scoop (5.4g) contains:

Glutamine .....	5,000 mg
N-Acetyl-Glucosamine .....	200 mg
Gamma oryzanol .....	125 mg
Cranesbill root (Geranium maculatum) .....	18.75 mg
Ginger root, Rhizome (Zingiber officinale) .....	18.75 mg
Marigold flower (Calendula officinalis) .....	18.75 mg
Marshmallow root (Althaea officinalis) .....	18.75 mg

Non-medicinal ingredients: None

Recommended dose: Adults: 1 scoop per day, mixed in water, in the morning on an empty stomach.

Duration of use: Consult a health care practitioner for use beyond 6 weeks.

Indication: Supports a healthy intestinal lining.

Contraindications: Do not use if pregnant, breastfeeding, or are sensitive to the Asteraceae/Compositae family of plants (i.e. Marigold). Do not exceed recommended dose.

Warnings: Keep out of reach of children.

Precautions: Discontinue use if abdominal pain, nausea, or vomiting occurs unless otherwise directed by a physician. Consult your physician prior to use if you have a serious medical condition, kidney disease, or are following a low protein diet.

Adverse Effects: None.

Overdose: For management of suspected product overdose it is recommended to contact your physician. If unavailable, seek emergency assistance.

Symptoms of Overdose: Has not been investigated nor any reports have been filed.

### Supporting Research and Traditional Evidence

#### **Glutamine (L-Glutamine)**

L-Glutamine is a dispensable amino acid and following ingestion it is metabolized mainly in the splanchnic tissues. Following absorption it is metabolized to citrulline, arginine, glutamate, and proline. (Reeds, 2001). Glutamine is quantitatively the most important fuel for intestinal tissue. It is metabolized to L-alanine by a route involving conversion to glutamate, then 2-oxoglutarate via glutaminase and glutamate dehydrogenase respectively, then tricarboxylic acid cycle conversion to malate (2-oxoglutarate, succinate, fumarate and finally malate) followed by the action of NADP+- dependent malic enzyme to create pyruvate which undergoes amination to produce L-alanine via the action of alanine transaminase (Newsholme, 2003). Other areas of metabolism of Glutamine also occur in the liver, kidneys and lymphocytes. Endogenous metabolism of Glutamine synthesis also occurs in muscle, intestine and brain (LSRO, 1992). Endogenous production in an adult is estimated to be 60-100 g per day (van Acker, 1999). Glutaminase and glutamine synthetase are the two primary enzymes responsible for glutamine metabolism.

Numerous studies evaluated safety of orally ingested glutamine at doses of 0.3g/kg of body weight and intravenous infusions of glutamine at doses up to 0.025 g/kg body weight/hour. Effects of total parenteral nutrition were also conducted at doses of 0.57g/kg body weight per day over duration of 5 days. Results indicated that at a single oral dose of glutamine the plasma glutamine concentrations rose twofold after 1 hour and returned to basal levels within 4 hours. In the total parenteral nutrition there was no evidence of neurotoxicity and none of the other studies revealed any adverse effects at any dose via oral or intravenous administration (Ziegler, 1990).

A number of other studies have also been performed using high doses of glutamine and similarly no notable significant adverse effects have been reported (IOM, 2002).

The intestines primary role is of digestion, nutrient absorption and fermentation. In addition new evidence is pointing to it's role in more complex roles of such as immune surveillance and in generating

endocrine responses to the luminal environment (Burrin,2000). Supplemental glutamine administration has two primary potential implications on intestinal health. First, by influencing the synthesis of components of the extracellular matrix, glutamine may be one important factor in the mucosal structure and in particular the maintenance of tight junctions (Panigrahi, 1997). Secondly, glutamine may be a potential precursor for N-acetyl glucosamine and N-acetylgalactosamine synthesis. Glutamine may play an important role in intestinal mucin synthesis and hence the maintenance of passive barrier to bacterial ingress (Khan, 1999).

Specific clinical studies by Peng, 2004 have shown that 0.5 g/kg of glutamine granules administered to severe burn patients abated the degree of intestinal injury, reduced intestinal mucosal permeability, ameliorated wound healing and reduced hospital stay. A study performed by Noyer, 1998 on AIDS patients examined abnormal intestinal permeability and showed a trend towards intestinal permeability improvements in this subpopulation at a daily dose of 4g or 8g per day. Authors of the study suggested that a dose of 20g glutamine may be necessary to see significant effects. Yoshida, 1998 evaluated the use of glutamine supplementation in 13 patients with esophageal cancer undergoing radiochemotherapy. Glutamine was administered orally at a dose of 30 g/day at the start of radiochemotherapy and for the subsequent 28 days. Results indicated that oral glutamine supplementation protects lymphocytes and attenuates gut permeability in patients with esophageal cancer during radiochemotherapy. Lastly, a study performed by van der Hulst, 1993 showed administration of glutamine via parenteral feeding prevented the deterioration of gut permeability and preserved mucosal structure.

#### **N-acetyl glucosamine**

##### **(2-Acetamido-2-deoxy-alpha-glucopyranose)**

Glucosamine is an amino-monosaccharide naturally produced in humans. N-acetyl glucosamine is an amide of glucosamine and acetic acid and is one of the principal substrates used in the biosynthesis of macromolecules that comprise articular cartilage, such as glycosaminoglycans, proteoglycans, and hyaluronic acid. Upon oral ingestion glucosamine is absorbed from the small intestine (Setnikar, 1993). A small scale evaluation of N-acetyl glucosamine and polymeric form of N-acetyl glucosamine suggests that it is readily absorbed with the polymeric form, producing sustained levels (Talent, 1996).

A small scale pilot study conducted by Salvatore, 2000 in 12 children evaluated the effects of N-acetyl glucosamine as an adjunct therapy in treating inflammatory bowel disease. Enrolled subjects were diagnosed with refractory inflammatory bowel disease, Crohn's disease and/or ulcerative colitis. Every subject was administered 3-6g/day N-acetyl glucosamine. Results showed that eight children of the twelve demonstrated clear improvements indicating that N-acetyl glucosamine is a strong candidate for reducing inflammatory conditions of the intestinal lining.

#### **Gamma oryzanol**

Gamma oryzanol is defined as a mixture of ferulic acid esters of sterol and triterpene alcohols. This mixture occurs in rice bran oil typically at a level of 1-2% (Scavariello, 1998).

A number of clinical trials suggest that gamma oryzanol may be helpful for people with gastritis and other gastrointestinal complaints. In a study by Maruyama, 1976, twenty two subjects with chronic gastritis were orally administered 300mg/day gamma oryzanol. After two weeks, five subjects reported that gamma oryzanol was extremely effective and twelve said it was moderately effective. An average of 87% of subjects experienced some benefit from supplementation. In another study, eighteen subjects with varying types of gastritis also received 300mg/day gamma oryzanol (Kamiji, 1976). Following two week supplementation more than 62% of those with superficial gastritis and over 87% with atrophic gastritis benefited. A large scale hospital study conducted by Takemoto, 1977 recruited approximately two thousand subjects with varying gastrointestinal complaints, including gastritis. Enrolled subjects were given approximately 100mg gamma oryzanol three times daily. Some individuals were required to ingest as much as



600mg/day before improvements in symptoms were noted. Duration of the study ranged from less than a month up to 275 days for some subjects.

### Cranesbill root (*Geranium maculatum*)

Geranium root chemically contains a large proportion of tannins (10%-28%) of the hydrolysable type most likely including geraniin (Hajkova, 1964). Traditionally *Geranium maculatum* has been used internally for peptic and duodenal ulcers (Bradley, 2006). It has been reported that when duodenal or gastric ulceration is associated with bleeding, this herb may be used in combination with other relevant herbs to combat the condition. Additionally, geranium provides astringent, anti-inflammatory and vulnerary properties (Hoffmann, 2003).

### Ginger root, Rhizome (*Zingiber officinale*)

Constituents of ginger known for its "pungent principles" or non-volatile constituents are considered responsible for its pharmacological activity. These include: gingerols including (6)-gingerol (usually <1% of the root's weight) (Wang, 2005), (6)-shogaol (a dehydroxylated analog of (6)-gingerol), (6)- and (10)-dehydro-gingerdione, (6)- and (10)-gingerdione, (6)-paradol, vallinoids, galanals A and B, and zingerone (Surh, 1999). Ginger finds wide spread use in many of the world's traditional medicinal systems. Traditionally, this use has been for disorders of the gastrointestinal tract, as a stomachic, laxative, sialogogue, gastric emptying enhancer, appetizer, antiemetic, and antidiarrheal and, at the same time, as an antidiarrheal and anticolic agent (Ghayur, 2005; Nadkarni, 1976). Specifically in Western Traditional Herbal Medicine ginger has been well documented to help relieve digestive upset and disturbances including lack of appetite, nausea, digestive spasms, indigestion, dyspepsia and flatulent colic (NHPD, 2009).

Clinical research has shown ginger to be effective in accelerating gastric emptying and stimulation of antral contractions in healthy volunteers when subjects were administered 1200mg/day ginger (Wu, 2008). A study by Micklefield, 1999 confirmed these results by showing that two doses of 100mg ginger rhizome extract also improved gastroduodenal motility after a test meal in twelve healthy volunteers. The pharmacological basis for the medicinal use of ginger in gastrointestinal disorders has been studied in animal models (Ghayur, 2005). Prokinetic activity of ginger extract was confirmed in an *in vitro* test when it enhanced the intestinal travel of charcoal meal in mice. Ginger extract also showed an atropine-sensitive dose-dependent spasmogenic effect *in vitro* as well as in isolated rat and mouse stomach fundus tissues. In atropinized tissue, it showed spasmolytic activity as shown by the inhibition of 5-HT- and K<sup>+</sup>-induced contractions. The results of the study showed that ginger extract contains cholinergic, spasmogenic component evident in stomach fundus preparations which support a mechanistic explanation for the prokinetic action of ginger.

### Marigold flower (*Calendula officinalis*)

The primary identified constituents of marigold are triterpenoids and flavonoids (Yoshikawa, 2001; Vidal-Ollivier, 1989). At least eight bioactive triterpenoid monoesters have been found in Marigold flowers: faradiol-3-O-palmitate, faradiol-3-O-myristate, faradiol-3-O-laurate, arnidiol-3-O-palmitate, arnidiol-3-O-myristate, arnidiol-3-O-laurate, calenduladiol-3-O-palmitate, and calenduladiol-3-O-myristate (Neukirch, 2004). Triterpenoids and in particular faradiol monoesters are suspected to be responsible for marigold's anti-inflammatory effects (Della, 1990; Della, 1994).

Experiments in cell-free systems with marigold extracts showed inhibitory activity of 5-lipoxygenase (5-LO) and cyclooxygenase-2 (COX-2) which are key enzymes involved in inflammatory pathways further suggesting the possible mechanisms of action (Bojadjev, 1964). Based on traditional medicines, marigold flower has been stated to possess anti-inflammatory and gastroprotective properties. Traditionally it has been used internally for inflammatory complaints of the digestive system such as gastric and duodenal ulcer, gastritis and colitis (Bradley, 2006).

### Marshmallow root (*Althaea officinalis*)

Marshmallow root contains mucilage polysaccharides typically found at 6.2%-11.6% concentration. These polysaccharides are composed of galacturonorhammans, arabinans, glucarins and arabinogalactans. Other constituents typically found are carbohydrates, flavanoids, glycosides, sugars, amines, fat, calcium oxalate, coumarins, phenolic acid and sterols (Gudej, 1991). Traditionally, marshmallow root has been effectively used for gastro-enteritis, peptic and duodenal

ulceration, common and ulcerative colitis and enteritis and is stated to possess demulcent, emollient and anti-inflammatory properties (Bradley, 1992).

### Ingredient Summary

#### Glutamine

- Supports a healthy intestinal lining.

#### N-acetyl glucosamine

- May reduce inflammatory conditions of the intestinal lining.

#### Gamma oryzanol

- May help with reductions of complaints associated with gastritis.

#### Cranesbill root (*Geranium maculatum*)

- Traditionally used for peptic and duodenal ulcers.

#### Ginger root, Rhizome (*Zingiber officinale*)

- Traditionally used to relieve digestive upset and disturbances including lack of appetite, nausea, digestive spasms, indigestion, dyspepsia and flatulent colic.

#### Marigold flower (*Calendula officinalis*)

- Traditionally used for complaints of the digestive system such as gastric and duodenal ulcer, gastritis and colitis.

#### Marshmallow root (*Althaea officinalis*)

- Traditionally used for gastro-enteritis, peptic and duodenal ulceration, common and ulcerative colitis and enteritis.

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