

ParaZYME

ADVANCED Naturals

PRODUCT MONOGRAPH

Product composition

Medicinal Ingredients:

Each capsule contains:

Betaine hydrochloride (sugar beet)	350 mg
L-Glutamine (from Glycine max, soy bean)	250 mg
Amylase (<i>Aspergillus oryzae</i>)	4.2 mg (417 DU)
Protease (<i>Aspergillus oryzae</i>)	4.2 mg (2083 HUT)
Lipase (<i>Rhizopus oryzae</i>)	0.22 mg (17 LU)
Lactase (<i>Aspergillus oryzae</i>)	0.6 mg (58 LaCU)
Cellulase (<i>Trichoderma reesei</i>)	1.1 mg (167 CU)
Invertase (<i>Saccharomyces cerevisiae</i>)	0.5 mg (50 SU)
Malt Diastase (<i>Hordeum vulgare L.</i>)	0.2 mg (2 DP)
Pectinase (<i>Aspergillus niger</i>)	0.4 mg (6 ADJU)
Phytase (<i>Aspergillus niger</i>)	0.1 mg (2 U)
Bromelain (<i>Ananas comosus</i> , stem)	17 mg (40.8 gdu)
Papain (<i>Carica papaya</i> , fruit)	17 mg (1.19 mcu)
Pepsin (Porcine source)	35 mg (1:3000 USP)
Gamma Oryzanol (from rice bran oil)	50 mg
N-Acetyl-Glucosamine (from Shrimp & Crab shell)	50 mg

Non-medicinal ingredients: Hypromellose, water

Recommended dose: Adults: Take 1 capsule 3 times daily with meals.

Duration of use: For prolonged use please consult a health care practitioner.

Indication:

- Digestive aid.
- Aids in the digestion of food.
- This product will aid in digestion.

Contraindications: Do not use if pregnant or breastfeeding or after recent surgery.

Warnings: Keep out of reach of children.

Precautions: Not to be used by children.

Adverse Effects: Discontinue use if abdominal pain, nausea or vomiting occurs, unless otherwise directed by a health care practitioner.

Overdose: For management of suspected product overdose it is recommended to contact your physician.

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

Supporting Research and Traditional Evidence

Betaine hydrochloride (sugar beet)

Betaine is a natural phytochemical present in the sugar beet (Gruenwald *et al.* 2007). The addition of a chloride ion to the molecule yields betaine hydrochloride (betaine HCl) which has been implicated in promoting gastrointestinal health through its delivery of hydrochloric acid (HCl) (Alternate Medicine Review, 2003). Betaine HCl works in accordance with proteases, enzymes also present in this formulation of ParaZYME, to increase the hydrolysis of polypeptides and increase the potential for the absorption of protein moieties. The combination has also been implicated in the treatment of the symptoms associated with dyspepsia and other gastrointestinal disorders (Sweetman, 2007). A clinical trial by Pereira (2006) evaluated the effects of betaine as part of a combination therapy on the suppression of symptoms associated with gastroesophageal reflux disease. In a 40 day randomized, single-blind study, a dietary supplement containing melatonin (6 mg), tryptophan (200 mg), vitamin B12 (50 µg), methionine (100 mg), vitamin B6 (25 mg), betaine (100 mg) and folic acid (10 mg) was administered to 176 patients suffering from moderate to very-severe heartburn. Omeprazole (20 mg) was administered to an additional 175 patients suffering from severe heartburn as a positive control for heart burn relief. Upon comparison, the results suggested that betaine was as effective as omeprazole in reducing the symptoms associated with gastroesophageal reflux disease. Scientific evidence suggests that a daily supplement containing betaine HCl may enhance digestion and potentially stimulate nutrient absorption in the intestine.

L-Glutamine (from Glycine max, soy bean)

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 and Burren, 2001). The primary location for metabolism of Glutamine is 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 *et al.* 1999). Glutamine may play an important role in intestinal mucin synthesis and hence the maintenance of passive barrier to bacterial ingress (Khan *et al.* 1999). 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. Results indicated that at a single oral dose of glutamine the plasma glutamine concentrations rose two-fold after 1 hour and returned to basal levels within 4 hours (Ziegler *et al.* 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). Specific clinical studies by Peng *et al.* (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 *et al.* (1998) on AIDS patients examined abnormal intestinal permeability and showed a trend towards intestinal permeability improvements in this subpopulation at a daily dose of 4 g or 8 g per day. Authors of the study suggested that a dose of 20 g glutamine may be necessary to see significant effects. Yoshida *et al.* (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 *et al.* (1993) showed administration of glutamine via parenteral feeding prevented the deterioration of gut permeability and preserved mucosal structure. Overall, clinical evidence and the NHPPD (2008) support the role of L-glutamine for intestinal health when taken in recommended doses of 5-9 g daily with a good safety profile.

Amylase (*Aspergillus oryzae*) (417 DU)

Amylase is an enzyme which facilitates the breakdown of complex carbohydrates into maltose and maltotriose (Whitcomb and Lowe, 2007; Ganong, 2009). There are various forms of amylase, including α -amylase, β -amylase and γ -amylase. α -amylase is present in the saliva as the first mechanism of carbohydrate catabolism. α -amylase can also be secreted by other organs, such as the pancreas (Whitcomb and Lowe, 2007). A small-scale study by Layer *et al.* (1986) used an amylase inhibitor to assess the effects of digestive enzyme inhibition on gastric motility. Fasting participants were given 50 g of rice starch with either an

α -amylase inhibitor or placebo. The results suggest that amylase inhibition reduced starch digestion and consequently nutrient absorption in the small intestine. Furthermore, in a randomized, placebo-controlled study, a supplement containing lipase, protease and amylase was administered with meals for 14 days. Only patients demonstrating pancreatic insufficiency, as determined by a fat excretion amount of less than 10 g/day, were included in the trial. The results of the study suggest that treatment with the enzyme mixture was associated with increased nutrient absorption when compared with placebo control (O'Keefe *et al.* 2001). Clinical evidence suggests that amylase aids digestion by degrading starch which may potentially facilitate nutrient absorption within the intestine.

Protease (*Aspergillus oryzae*) (2083 HUT)

The function of the gastrointestinal tract is to secrete digestive enzymes to promote the breakdown of food stuffs and facilitate the absorption of nutrients in the upper digestive tract. One type of digestive enzyme, protease, facilitates the breakdown of proteins. There are 6 types of proteases, aspartic, cysteine, glutamic, metallo, serine, and threonine, all which contribute to protein catabolism (Shen and Chou, 2009). Following catabolism, absorption occurs in 3 locations: the intestinal lumen, the brush border and/or the cytoplasm of the mucosa cells. Approximately 50% of digested protein comes from diet (Ganong, 2009). Clinical evidence suggests that a combination enzyme therapy improved digestion and nutrient absorption in patients suffering from chronic pancreatitis. In a parallel-armed, randomized, placebo-controlled study, a supplement containing lipase, protease and amylase was administered with meals for 14 days. Only patients demonstrating pancreatic insufficiency, as determined by a fat excretion amount of less than 10 g/day, were included in the trial. Treatment with the enzyme mixture was associated with increased nutrient absorption when compared with placebo control (O'Keefe *et al.* 2001). Overall, scientific evidence suggests that proteases, as part of a combination enzyme supplement, may enhance digestion and nutrient absorption.

Lipase (*Rhizopus oryzae*) (17 LU)

In the digestive tract, lipase is essential for the breakdown and absorption of fatty acids and triglycerides. *In vivo* studies have been conducted to assess the effects of enzyme supplementation on nutrient absorption rates in broiler chickens. A combination enzyme supplement containing xylanase, amylase and protease was fed to the chickens daily for 3 weeks. Body weights and fecal nutrient levels were recorded weekly. The results indicate that enzymes as a dietary supplement improved nutrient absorption (Cowieson and Ravindran, 2008). Furthermore, clinical evidence suggests that lipase improves the digestive absorption rate in humans. In a double-blind, randomized, crossover pilot study, healthy participants were given 3 capsules containing pancrelipase, or sucrose as a control, and then fed a fatty meal. The researchers recorded the amount of gastrointestinal discomfort associated with the high fat meal, in the form of abdominal symptom scores and methane production. Treatment with digestive enzymes was associated with a significant reduction of abdominal symptoms which suggests that treatment with enzymes improved digestion and absorption of the fatty acids (Suarez *et al.* 1999). A second single-blind analysis was performed to evaluate the use of lipases to increase digestion and absorption of fatty acids. Patients suffering from pancreatic insufficiency were treated with a supplement of lipase, or placebo, and digestive parameters were assessed for an average of 54 weeks. The results of the study suggest that treatment with digestive enzymes, such as lipase, improves the absorption of fatty acids (Valerio *et al.* 1981). Scientific evidence has suggested lipase is effective in improving fat absorption.

Lactase (*Aspergillus oryzae*) (58 LaCU)

Lactase, a β -galactosidase, is responsible for the hydrolysis of lactose into its monomers, galactose and glucose (Ganong, 2009). Lactase is present in the brush border of the upper intestine and indirectly plays a role in the absorption of simple sugars. Inactivity of the enzyme is common in society, a condition generally known as lactose intolerance (as reviewed by Lomer *et al.* 2007). Associated with lactose intolerance is gastrointestinal discomfort which occurs when lactose is not degraded in the intestine. Typical side effects include abdominal pain, bloating, flatus, diarrhea, nausea and vomiting (Lomer *et al.* 2007). Since lactase is an enzyme involved in the digestion of milk sugar, supplementation with the enzyme may increase the digestion of lactose which could potentially increase nutrient absorption in the intestine.

Cellulase (*Trichoderma reesei*) (167 CU)

Cellulase is a plant-derived enzyme involved in the catabolism of cellulose. Cellulose is a key component in plant physiology. The fibrous compound gives structural stability to plant cellular walls. Consequently, cellulase is endogenous to plant cells only. Ingestion of cellulose results in increased gastric motility since there is no natural mechanism for the digestion of fibre within the human digestive tract (Campbell, 1996). Supplementation with dietary cellulase would promote the digestion of foods high in cellulose yielding glucose monomers upon complete breakdown of the polymer. Glucose, in its monomeric form, readily undergoes absorption into the gastric mucosal cell. Subsequently, the simple sugar can diffuse through the cytoplasm to be transported across the baso-lateral membrane into the blood stream (Ganong, 2009). Therefore, supplementation with a daily supplement of cellulase may help to increase digestion of usually indigestible foods, such as cellulase, and facilitate glucose absorption.

Invertase (*Saccharomyces cerevisiae*) (50 SU)

Physiologically, invertase (also known as sucrase) is found in the brush border of the small intestine and facilitates the breakdown of sucrose into glucose and fructose (Ganong, 2009). Sucrose is commonly known as table sugar and is ingested in our daily diets in desserts and sweets. In the intestinal lumen, both glucose and fructose can be transported across the apical cell membrane. Fructose readily passes across the cellular plasma membrane, whereas glucose typically undergoes active diffusion to be absorbed (Gray, 1971). Increased digestion of the sugar would result in increased nutrient absorption within the small intestine. In a double-blind placebo-controlled clinical trial, a yeast-derived sucrase enzyme was administered to patients suffering from sucrase-isomaltase deficiency and the prevalence of digestive disturbances was evaluated. Patients received enzyme replacement therapy at various doses in addition to ingesting sucrose in their daily diets. The findings of the study suggest that supplementation with yeast-derived sucrase replacement therapy improved sucrose digestion as indicated by the reduction of gastrointestinal disturbances (Treem *et al.* 1993). Clinical evidence suggests that daily supplementation with sucrase may help digestion and potentially contribute to the increased absorption of glucose and fructose within the intestine.

Malt Diastase (*Hordeum vulgare L.*) (2 DP)

Complex carbohydrates, such as starches are not readily absorbed in their parent structure. They require digestive enzymes to provide nutritional value following ingestion. Physiologically, diastase is important for digestion of starches in the upper intestinal lumen (Ganong, 2009). Currently, the term diastase means an enzyme mixture consisting of α -amylase, β -amylase and/or γ -amylase which function as hydrolases to mediate the breakdown of starches (Gibbons, 1979). Classically, diastase was isolated from barley and considered to be one of the first discovered enzymes, and a first step towards the development of modern enzyme kinetics (Schultz, 1994). The breakdown of starch yields disaccharides or trisaccharides which may be transported into the intestinal mucosa cells and across the



baso-lateral membrane to be absorbed into the bloodstream. In the human digestive tract, there are various enzymes which work in harmony to catabolise macromolecules and facilitate the absorption of nutrients (Ganong, 2009). Diastase one of these enzyme which when taken as a daily supplement may aid digestion to enhance nutrient absorption.

Pectinase (*Aspergillus niger*) (6 ADJU)

In plant physiology, pectinase is important since it facilitates the extension of plant cell walls and the softening of plant tissues for storage and fruit ripening. Pectinases catalyze the breakdown of various pectic substances, such as pectin, pectinic acids, pectic acids and protopectin (as reviewed by Jayani *et al.* 2005). Pectin itself is soluble, but is not readily absorbed from the intestinal lumen. If unabsorbed, pectin passes into the colon where it is undergoes bacterial fermentation. A small-scale clinical trial was conducted to assess the digestion of pectin healthy subjects. Twenty-two participants were fed a meal containing 5 g of pectin and their fecal matter was collected. The study suggested that approximately 90% of the pectin was not degraded and that only a small amount was fermented. This study suggests that pectin is not naturally cleaved and/or absorbed in the human gastrointestinal tract (Chinda *et al.* 2003), such that supplementation with an enzyme such as pectinase may improve the degradation of pectin and facilitate the absorption of nutrients in the human digestive tract.

Phytase (*Aspergillus niger*) (2 U)

Phytate is a compound present in plant materials such as grains and oil seeds. The enzyme is responsible for the digestion of phytate, but unfortunately is not present in the human digestive system. The breakdown of phytate yields carbohydrate moieties and phosphorus (Schlemmer *et al.* 2009). The effects of dietary phytase on the breakdown of phytate in the human small intestine were assessed in a small scale-clinical study. Nine patients who had previously undergone proctocolectomy for ulcerative colitis were given a low-fibre diet for a week and then supplemented with 16 g of phytase-deactivated grain products, grain products containing active phytase or a low fibre diet the following week. The phytase-active grains and low-fibre diet treatment groups demonstrated increased phytate degradation when compared to the phytase-deactivated treatment groups (Sandberg and Andersson, 1988). Since phytase is not present endogenously in the human gastrointestinal tract, daily supplementation with the enzyme may enhance the natural digestion processes and indirectly increase nutrient absorption.

Bromelain (*Ananas comosus*, stem)

Bromelain is a pharmacologically active phytochemical mixture present in the pineapple stem consisting of a pair of proteolytic enzymes (Blumenthal *et al.* 1998). Proteolysis is an important process linked to protein absorption into the body. The cleavage of protein chains yields peptides which upon digestion produce free amino acids. The lining of the gastric mucosa has the ability to take up both small peptide chains and amino acids. Supplementation with a protease complex would help with digestion and facilitate the uptake of peptides and amino acids (Ganong, 2009). Bromelain has been used in the food industry as a meat tenderizer demonstrating its effectiveness for digesting protein chains (Facciola, 1998). Daily supplementation with bromelain would assist the body's natural proteases in the digestion of protein foodstuffs and contribute to increased nutrient absorption.

Papain (*Carica papaya*, fruit)

Various parts of the papaya plant have been used in traditional Western herbalism. Typically, the leaves and fruit have been used to treat certain gastrointestinal discomforts by enhancing digestion (Blumenthal *et al.* 1998). Papaya contains the active compound papain, an enzyme mixture extracted from the raw fruit comprised of chymopapain A and B as well as papaya peptidase A (Blumenthal *et al.* 1998). Pharmacologically, papain acts by cleaving protein chains into moieties which are more readily absorbed into the body. Upon entry into the stomach, proteins are slowly digested into smaller protein chains, peptides and finally, free amino acids. Physiologically, the final digestion of peptides into free amino acids can occur in 3 locations: the intestinal lumen, at the mucosal brush border or inside the mucosal cells (Ganong, 2009). Supplementation with papaya fruit containing the digestive enzyme complex would facilitate the first step of the protein degradation process to help with overall digestion and enhance nutrient absorption into the mucosal capillaries (Ganong, 2009). While papaya fruit has traditionally been used as a medicine in traditional herbalism, the fruit has been eaten as food in various forms, such as in jams, jellies, desserts or bar (Facciola, 1998). Traditional evidence suggests that the papain is effective as a digestion aid.

Pepsin (*Porcine source*)

Pepsin is a naturally occurring enzyme in the human gastrointestinal tract. It is synthesized endogenously as pepsinogen, the inactive precursor to pepsin. In the stomach, the proenzyme is stimulated by hydrochloric acid to cleave protein chains (Ganong, 2009; Sweetman, 2007). The targets of action for pepsin are protein linkages adjacent to aromatic amino acids, such as phenylalanine or tryptophan. Furthermore, cleavage of these bonds yields polypeptides of varying lengths which are then further degraded by the digestive enzymes located in the small intestine (Ganong, 2009). Since pepsin works in the presence of hydrochloric acid to induce protein cleavage, a dietary supplement containing pepsin and betaine hydrochloride, a source of HCl present in this formulation of ParaZYME (Sweetman, 2007), may help with digestion of proteins and potentially contribute to increased nutrient absorption.

Gamma Oryzanol (from rice bran oil)

Gamma oryzanol is defined as a mixture of ferulic acid esters of sterol and triterpene alcohols. This mixture is present in rice bran oil typically at a level of 1-2% (Scavariello and Arellano, 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 *et al.* (1976), 22 subjects with chronic gastritis were orally administered 300 mg/day gamma oryzanol. After 2 weeks, 5 subjects reported that gamma oryzanol was extremely effective and 12 said it was moderately effective. An average of 87% of subjects experienced some benefit from supplementation. In another study, 18 subjects with varying types of gastritis also received 300 mg/day gamma oryzanol (Kamiji *et al.* 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 *et al.* (1977) recruited approximately two thousand subjects with varying gastrointestinal complaints, including gastritis. Enrolled subjects were given approximately 100 mg gamma oryzanol 3 times daily. Some individuals were required to ingest as much as 600 mg/day before improvements in symptoms were noted. Duration of the study ranged from less than a month up to 275 days for some subjects. Clinical evidence suggests a role for gamma oryzanol in helping with digestion as contributes to gastrointestinal health with a good safety profile when taken at recommended doses.

N-Acetyl-Glucosamine (from Shrimp & Crab shell)

Glucosamine is an amino-monosaccharide naturally produced in humans and various species of animals and is one of the principal substrates used in the biosynthesis of macromolecules comprising articular cartilage, such as glycosaminoglycans, proteoglycans, and hyaluronic acid. Upon oral ingestion glucosamine is absorbed from the small intestine (Setnikar *et al.* 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 and Gracy, 1996). A small scale pilot study conducted by Salvatore *et al.* (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 3-6 g/day N-acetyl glucosamine. Results suggested that 8 children of the 12 demonstrated clear improvements indicating that N-acetyl glucosamine is a strong candidate for reducing inflammatory conditions of the intestinal lining. Overall, clinical evidence suggests that N-Acetyl-D-Glucosamine is an effective ingredient to benefit intestinal health. A healthy gastrointestinal tract is associated with healthy digestion. Evidence suggests that N-acetyl-glucosamine contributes to healthy digestion with a good safety profile when taken at recommended doses.

Ingredient Summary:

Betaine hydrochloride (sugar beet)

- Contributes hydrochloric acid to aid digestion

L-Glutamine (from Glycine max, soy bean)

- Supports a healthy intestinal lining

Amylase (*Aspergillus oryzae*) (417 DU)

- Helps with the digestion of starch

Protease (*Aspergillus oryzae*) (2083 HUT)

- Helps with the digestion of proteins

Lipase (*Rhizopus oryzae*) (17 LU)

- Helps with the digestion of fats

Lactase (*Aspergillus oryzae*) (58 LacU)

- Helps with the digestion of lactose

Cellulase (*Trichoderma reesei*) (167 CU)

- Helps with the digestion of fibre

Invertase (*Saccharomyces cerevisiae*) (50 SU)

- Helps with the digestion of table sugar

Malt Diastase (*Hordeum vulgare L.*) (2 DP)

- Helps with the digestion of starch

Pectinase (*Aspergillus niger*) (6 ADJU)

- Helps with the digestion of pectin

Phytase (*Aspergillus niger*) (2 U)

- Helps with the digestion of phytate

Bromelain (*Ananas comosus*, stem)

- Traditionally used to enhance digestion

Papain (*Carica papaya*, fruit)

- Traditionally used to enhance digestion

Pepsin (*Porcine source*)

- Helps with the digestion of protein

Gamma Oryzanol (from rice bran oil)

- May help reduce the prevalence of gastritis-associated symptoms which contributes to a healthy gastrointestinal tract

N-Acetyl-Glucosamine (from Shrimp & Crab shell)

- May reduce inflammatory conditions of the intestinal lining which contributes to a healthy gastrointestinal tract

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