# DigestMAX Ultra

ADVANCED Naturals PRODUCT MONOGRAPH

**Product composition**
Medicinal Ingredients:
Each capsule contains:
Protease (Aspergillus oryzae)........100,000 HUT
Lipase (Rhizopus oryzae)........18,750 LU
Cellulase (Trichoderma reesei) ........1500 CU
Glucoamylase (Aspergillus niger)........50 AG
Beta Glucanase (Trichoderma reesei) ........25BGU
Hemicellulase (Aspergillus niger) ........30 HCU
Phytase (Aspergillus niger)........5 U
Amylase (Aspergillus oryzae)........25,000 DU
Lactase (Aspergillus oryzae) ........1200 ALU
Invertase (sucrase) (Saccharomyces cervesiae)........250 SU
Alpha Galactosidase (Aspergillus niger)........500 GAL
Xylanase (Trichoderma reesei) ........550 XU
Pectinase (Aspergillus niger)........45 AJDU
Papain (Carica papaya)........50,000 PU

Non-medicinal ingredients: Hydroxypropyl Methylcellulose, water

Recommended dose: Adults: 1-2 capsules with each meal, to a maximum of 6 capsules per day.

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

Indication:
- Digestive enzyme formula.
- This product will aid in the process of digestion, and support intestinal health.

Contraindications: Do not use if pregnant, breast feeding, or after recent surgery. Do not use if you have gastritis, peptic ulcer, duodenal ulcer or bowel obstruction. Do not exceed recommended dose.

Warnings: Keep out of reach of children.

Precautions: None

Adverse Effects: Discontinue use should abdominal pain, nausea, or vomiting occur.

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

**Protease (*Aspergillus oryzae*) 100,000 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 (*Aspergillus niger*) 18,750 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.

**Cellulase (*Trichoderma reesei*) 1500 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 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.

**Glucoamylase (*Aspergillus niger*) 50 AG**
Glucoamylase is also known as γ-amylase and is present in the brush border of the human gastric mucosa. Physiologically, this enzyme is important for the digestion of glucose chains of intermediate lengths (Lee *et al.* 2004). Structurally, starches are branched or unbranched glucose polymers and digestion of these starches yields glucose monomers. A clinical trial was conducted to assess glucoamylase activity in 214 children. Initially, small bowel biopsies were taken and enzyme activities were measured. Severe inflammation of the gastric mucosa was associated with a glucoamylase deficiency (Lee *et al.* 2004). Furthermore, a decrease in amylase activity would result in a decrease in starch degradation and consequently, glucose absorption. A similar multi-centred study was performed in 511 children suffering from chronic diarrhea. Biopsies and stool samples were collected from the subjects and analyzed for glucoamylase activity. The results suggest that low levels of glucoamylase were associated with severe small intestinal mucosal injury in 9 children. Overall, the study suggests that chronic diarrhea was associated with glucoamylase deficiency (Lebenthal *et al*. 1993). Furthermore, this evidence suggests that daily supplementation with glucoamylase may increase the digestion of glucose-containing starches potentially increasing nutrient absorption.

**Beta Glucanase (*Trichoderma reesei*) 25BGU**
Beta-glucanase is important for the breakdown of fibre, but unfortunately cannot be produced by the human body. Animal studies have been conducted to assess the effects of enzyme supplementation on digestion and nutrient absorption. Pigs were fed a standardized daily diet with or without enzyme supplementation containing 10 000 U/g b-glucanase and 80 000 U/g xylanase daily for 4 weeks. Significant increases in average daily weight gain and decreases in the feed to weight gain ratio were associated with enzyme supplementation when compared to the control group. However, no changes were observed for average daily feed intake. These results suggest that enzyme supplementation was associated with increased digestion and nutrient absorption in pigs (Fan *et al.* 2008). A second study conducted in male turkeys assessed the effects of a combination of xylanase and beta-glucanase on feed efficiency. Turkeys were fed a standardized diet rich in wheat, barley and soybean. Supplementation with 560 and 2800 IU of xylanase and beta-glucanase, respectively, was associated with increased feed efficiency and weight gain (Mathlouthi *et al.* 2003) suggesting that supplementation with a combination of enzymes may enhance digestion and absorption of grain products.

**Hemicellulase (*Aspergillus niger*) 30 HCU**
Hemicellulose is a polymer present in the cell wall of plants and is present in many of the plant materials used for human consumption. Unfortunately, the human digestive system does not synthesize cellulases. Hemicellulase is a type of cellulase which catalyzes the breakdown of hemicellulose. Supplementation with cellulase would allow for the digestion of foods high in cellulose, a type of fibre which when ingested, promotes a laxative effect by increasing gastric motility in the colon (Campbell, 1996). Animal studies have been conducted to assess the effects on combination enzyme treatment on nutrient absorption in chickens. Chickens were supplemented with 0.33, 2, and 2 IU of cellulase, hemicellulase and pectinase, respectively. Results indicate that supplementation with combination enzyme treatment increased both digestion and nutrient absorption (Tahir *et al.* 2008). Moveover, the breakdown of fibres improves their ability to be absorbed into by the body such that daily supplementation with cellulose may help with digestion of foods high in fibre potentially increasing the absorption of nutrients.

**Phytase (*Aspergillus niger*) 5 U**
Phytate is a compound present in plant materials such as grains and oil seeds. Phytase is the enzyme 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.

**Amylase (*Aspergillus oryzae*) 25,000 DU**
Amylase is an enzyme which facilitates the breakdown of complex carbohydrates into maltose and maltriose (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.

**Lactase (*Aspergillus oryzae*) 1200 ALU**
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 and the condition is 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.

**Invertase (Sucrase) (*Saccharomyces cerevisiae*) 250 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 administrated 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.

**Alpha Galactosidase (*Aspergillus niger*) 500 GAL**

Physiologically, alpha Galactosidase is important for the cleavage of galactosyl groups from glycolipids and glycoproteins. A deficiency in alpha galactosidase, known as Fabry disease, occurs in the general population as a rare disease affecting less than 1 in 200 000 individuals (Canadian Fabry Association, 2010). The disease is characterized by the body's inability to break down glycosylated proteins and lipids, resulting in an accumulation of these molecules (Clarke, 2007). High levels of glycolipds/proteins can increase the likelihood of complications and are associated with severe morbidity and/or death. Currently enzyme replacement therapy supplementing beta-galactosidase is occurring in the US. However, studies have been conducted assessing the safety and efficacy of enzyme replacement therapy focussing on alpha-galactosidase. A recent review by Morel and Clark (2009) summarized various findings from previously conducted clinical trials. They state that a recombinant for of alpha galactosidase has potential as a treatment for Fabry disease. Various clinical studies assessed multiple endpoints such as neuropathic pain, renal function and cardiac function. The conclusion of the review indicated that therapy with alpha glacatosidase may reduce the accumulation of glyco-proteins and –lipids and help alleviate symptoms associated with Fabry disease. A reduction in the prevalence of symptoms would indicate that the recombinant form of the protein is active and contributing to the breakdown of the glycosylated proteins and lipids, which may potentially increase the absorption of nutrients.

**Xylanase (*Trichoderma reesei*) 550 XU**

Xylanase is involved in the breakdown of carbohydrate polymers. The enzyme works in accordance with hemicellulase to catalyze the breakdown of fibres in dietary plant materials. Animal studies have been conducted to evaluate the effects of xylanase on the decomposition of fibre-rich diets. In one study, pigs were fed a standardized daily diet for a 4 week period with or without an enzyme supplement containing 10 000 U/g beta-glucanase and 80 000 U/g xylanase. Significant increases in average daily weight gain and corresponding decreases in feed to weight gain ratio were associated with enzyme supplementation. Furthermore, no changes were observed for average daily feed intake. These results suggest that enzyme supplementation was associated with increased digestion and nutrient absorption in pigs (Fan *et al.* 2008). A second study conducted in male turkeys assessed the effects of a combination of xylanase and beta-glucanase on feed efficiency. Turkeys were fed a standardized diet which was rich in wheat, barley and soybean. Supplementation with 560 and 2800 IU of xylanase and beta-glucanase, respectively was associated with increased feed efficiency and weight gain (Mathlouthi *et al.* 2003) suggesting that supplementation with a combination of enzymes may enhance digestion and absorption of grain products. Scientific evidence has suggests that xylanase may be effective in aiding digestion when taken as part of a combination enzyme therapy.

**Pectinase (*Aspergillus niger*) 45 AJDU**

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 ripining. 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 following pectin administration. 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.

**Papain (*Carica papaya*) 50,000 PU**

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 raw (Facciola, 1998). Traditional evidence suggests that the papain is effective as a digestion aid.

Ingredient Summary:

**Protease (*Aspergillus oryzae*) 100,000 HUT**
- Helps with the digestion of proteins

**Lipase (*Aspergillus niger*) 18,750 LU**
- Helps with the digestion of fats

**Cellulase (*Trichoderma reesei*) 1500 CU**
- Helps with the digestion of fibre

**Glucoamylase (*Aspergillus niger*) 50 AG**
- Helps with the digestion of starch

**Beta Glucanase (*Trichoderma reesei*) 25BGU**
- Helps with the digestion of fibre

**Hemicellulase (*Aspergillus niger*) 30 HCU**
- Helps with the digestion of fibre

**Phytase (*Aspergillus niger*) 5 U**
- Helps with the digestion of phytate

**Amylase (*Aspergillus oryzae*) 25,000 DU**
- Helps with the digestion of starch

**Lactase (*Aspergillus oryzae*) 1200 ALU**
- Helps with the digestion of lactose

**Invertase (sucrase) (*Saccharomyces cerevisiae*) 250 SU**
- Helps with the digestion of table sugar

**Alpha Galactosidase (*Aspergillus niger*) 500 GAL**
- Helps with the digestion of glycoproteins and glycolipids

**Xylanase (*Trichoderma reesei*) 550 XU**
- Helps with the digestion of fibre

**Pectinase (*Aspergillus niger*) 45 AJDU**
- Helps with the digestion of pectin

**Papain (*Carica papaya*) 50,000 PU**
- Traditionally used to enhance digestion

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