Science Brief: Improved Digestion Supplementing with Oral Digestive Enzymes

Consider the following review of clinical research and observations regarding improved supplementation with Transformation's Professional Protocol™ Digest.

Transformation Enzyme Corporation (TEC) is a nutritional supplement company specializing in the development of quality enzyme-based products for the health care professional. Through clinical and observational research, TEC's efforts focus on teaching the importance of nutrient acquisition as the foundation of wellness and healthy living.

A poor diet and a digestive system that fails to process food for bioavailability and absorption will undermine the body's coping ability and create conditions favorable for disease and metabolic disorders. Based on this fact, TEC strives to educate health care professionals worldwide on the benefits of a balanced diet and proper digestion. The primary benefits are:

1. maintaining a strong digestive system
2. enhancing bioavailability of nutrients to the cells
3. supporting immune health and cellular vitality
4. promoting efficient and timely removal of metabolic byproducts and environmental toxins

The only thing that any biological system ultimately requires is an ensured way of delivering nutrients to the cells.

Historically, supplemental digestive enzymes were obtained from the pancreatic juice of animals, commonly bovine and porcine. However, in the past several decades, enzymes derived from non-animal sources have gained recognition. Plant enzymes such as bromelain and papain are commonly used. More current research suggests mycelial enzymes from *Aspergillus oryzae* and *niger* as well as other microorganisms have been proven safe, effective, and in many cases superior to traditional "animal" and "plant" enzymes for digestion.

Contrary to the long held belief that enzymes do not survive the gastrointestinal environment, several studies have demonstrated that some orally ingested enzymes remain active in the GI tract. Furthermore, some enzymes are absorbed into the blood stream where they remain active and impart systemic benefit.

TEC's scientific staff with decades of combined experience in biochemistry, nutrition, and cellular and molecular biology has formulated a highly specific digestive enzyme product to facilitate digestion and support the body to maintain health and wellness. This science brief will review the effects of supplemental digestive enzymes on preventive health and wellness as well as their safety and efficacy for human consumption. Additionally, this science brief will highlight Transformation's Professional Protocol™ (TPP) Digest formula.

The Importance of Good Nutrition and, More Importantly, Optimal Digestion

The number of reported digestive disorders is on the rise. It is estimated that over 80 million Americans are affected by various forms of digestive diseases. According to the NIH, the related health care cost is estimated at over $107 billion. TEC believes this increase can be attributed to poor diet, improper digestion, stressful lifestyles, and the prevalence of toxins in the environment. While genetics may play a part, scientists continue to find more and more evidence that points to the fact that the vast majority of *all* disease can be traced back to poor diet, mal-digestion and the inability of the gut to function properly.

TEC suggests practitioners look at two variables: food choices and digestion. These can be addressed immediately simply by paying attention to what one eats and by supplementing with digestive enzymes. The benefits to overall health are extensive:

- Bioavailability of nutrients to the cell improves cellular vitality and function
  - Proteins supply amino acids, the structural components for every cell, tissue, muscle, and organ
  - Carbohydrates are the body's main energy source
  - Fats supply fatty acids for energy and structural

components of cell walls, cholesterol, and hormones
  - Vitamins and minerals are key to all the processes that take place in the body and serve as cofactors for many biochemical reactions
- Efficient, appropriate, and precise immune function
- Reduced digestive distress (inflammatory bowel disorders, GERD, food intolerances, and allergies)
- Improved elimination of waste / decreased toxic load
- Reduced oxidative stress and free radical damage

When the body receives good nutrition along with optimal digestion, the opportunity for health and wellness is multiplied.

The Safety of Enzymes Derived from *Aspergillus oryzae* and *Aspergillus niger*

Before a fungal organism is used in fermentation, the specific strain is extensively screened to determine if the organism is capable of producing mycotoxins under the conditions of fermentation. Only those organisms that do not produce any toxins are selected for use in the fermentation process. Even after an organism is determined to be "safe" and is used in fermentation, every second generation is again checked to verify that mutations have not occurred which might enable the organism to produce mycotoxins. Enzymes derived from *Aspergillus* fermentation were first used in food production at the turn of the century. Since their introduction, there has never been a documented case of illness from mycotoxins associated with fermented enzymes, which is testament to the effectiveness of the screening process employed by the enzyme manufacturing industry.

The system that ensures and controls health and whose effective performance ultimately guarantees wellness is the digestive system.

Once fermentation by the *Aspergillus* organism is complete, the enzymes are extracted by a complex process that isolates protein compounds from the surrounding material. No living *Aspergillus* cells remain in the isolated enzyme after the extraction process is complete. Mycotoxins are not protein-based substances; therefore, in the extremely unlikely event that mycotoxins were produced during fermentation, they would not be extracted with the enzymes. Instead, any mycotoxins present would remain in the discarded portion of the fermentation. Even so, the final enzyme product is routinely checked for the presence of mycotoxins and aflatoxins.

Enzymes derived from the fermentation of *Aspergillus* are purified compounds which do not contain any living *Aspergillus* cells and therefore cannot initiate infection or colonization. *Aspergillus*, like any other fungus, can act as an opportunistic pathogen; however, the relative rarity of *Aspergillus* infections indicates the low degree of innate virulence of these organisms. Infectious diseases associated with *Aspergillus* involve growth of fungal mycelia within body tissue, most commonly within the pulmonary system. In order for mycelial colonization to occur, the *Aspergillus* must be introduced to the body in a living form. It is important to note that no cases of *Aspergillus* infections have ever been documented in association with the consumption of purified fermented fungal enzymes.

Allergic responses to *Aspergillus* organisms and the products of their fermentation rarely occur, and their occurrence is largely isolated to regular air-borne "dust" exposure by workers in the food industry. If an allergic reaction is to occur, it is generally the protein faction of a substance that will illicit such a reaction. Although enzymes derived from *Aspergillus* fermentation are free of any living *Aspergillus* cells, the fact remains that these enzymes are a purified protein faction of the Aspergillus organism.

TPP Digest – product highlights

Enzyme blends and enzyme sources have been carefully researched and selected to provide you with a highly effective, stable and functional digestive enzyme formula. TPP Digest is a comprehensive digestive enzyme formula designed to optimize complete digestion of all foods. TPP Digest includs proteolytic, lipolytic, and polysaccharolytic enzyme blends from microbial fungal sources, making them safe, effective, and GI tract stable and functional. This means the enzyme blends in TPP Digest do not require an enteric coating to survive the harsh environment of the stomach but rather initiate digestion in the stomach and continue the digestive process in the small intestines. This is important when you consider that as much as 80% of the body's energy is required during the digestive process. TPP Digest will work with the body, making it more efficient in liberating nutrients while lessening the overall burden. In the long term, this can improve health, vitality, and longevity.

Proteases

This formula contains a proprietary blend of proteases that are active throughout the gastrointestinal tract. The proteolytic enzyme blend in TPP Digest includes proteases and peptidase that maintain activity in a broad pH range of 2.0-8.0. Peak activities are demonstrated at pH of 3.0 and 6-7. This is important because it is consistent with that of the human GI tract. Working with the body's own digestive enzymes these supplemental enzymes ensure optimal digestion of proteins beginning in the stomach and continuing in the small intestines. The proteases in TPP Digest are standardized using the FCC (Food Chemical Codex) activities HUT and SAPU.

Clinical Application

Undigested protein can lead to many digestive and systemic disorders ranging from heartburn, acid reflux, gas, and bloating to allergies, inflammation, and autoimmune disorders. Intact protein in the large intestine may be fermented by intestinal flora, resulting in the formation of various metabolites that may be absorbed into the blood circulation. These toxins include ammonia, branch chained fatty acids, phenols, and hydrogen sulfides, all of which under certain conditions can trigger systemic diseases. TPP Digest may also reduce the signs and symptoms associated with autism. Additionally, the trend of high protein diets necessitates a greater need for supplementing with proteolytic enzymes.

Lipases

TPP Digest features a highly concentrated blend of acid-resistant lipases produced from the controlled fermentation of *Rhizopus oryzae* and *Candida rigosa*. These lipolytic enzymes catalyze the hydrolysis of tryglycerides, yielding mono- and diglycerides, glycerol, and free fatty acids. They are an effective digestive aid because of their broad substrate specificity on fats and oils from vegetable and animal origin. Additionally, they demonstrate an effective 3.0-8.0 pH range, making them highly stable and functional in the gastrointestinal tract. The lipases in TPP Digest are measured in FCC (Food Chemical Codex) activities LU and FIP (Federation International Pharmacopia) lipase units. The conversion for FCCLU to FCCFIP is 1:2.5. TPP Digest is formulated with 7,518 FCC FIP (3,007 FCCLU) of Lipase to continue to support maximum digestion of dietary fats and reduce digestive stress.

Clinical Application

Over-consumption of fat and difficulty digesting fat can lead to gall bladder stress, gall stones, diabetes, obesity, high cholesterol, and other cardiovascular diseases. Given the fact that diabetes (type II), obesity, and cardiovascular disease are among the top 10 most prevalent health challenges facing Americans today, a closer look at prevention deserves attention. TPP Digest addresses prevention by promoting absorption of essential fatty acids, which are known to help reduce the risk of cardiovascular disease.

Did you know?

- Digestive diseases are the third largest category of illness in the US with as many as 70 million reported cases, second only to the common cold as the most frequent reason to seek medical advice.
- The digestive system has more nerve endings than the spine and manufacturers more neurotransmitters than the brain. 90% of all serotonin is made in the gut and a full 70% of the immune system is located in or around the digestive system.
- TPP Digest is used by surgeons, medical doctors, naturopaths, chiropractors, acupuncturists, psychologists, colon hydrotherapists, massage therapists, dieticians, nutritional counselors, and more!

Professional Protocol™ Digest: Transformation's Comprehensive, Therapeutic Digestive Formula

Supplement Facts

Serving Size: 1 Capsule
Servings Per Container: 60/90/120

Amount Per Serving		% Daily Value
Tzyme™ Protease Blend (Protease and peptidase) (55,131 HUT + 11 SAPU)	67 mg	†
Lipase (7,518 FIP)	24 mg	†
Tzyme™ Polysaccharolytic Blend	301 mg	†
Amylase	20,000 DU	†
Phytase	42 FTU	†
Glucoamylase	25 AGU	†
Alpha-galactosidase	438 Gal U	†
Macerase	400 CU	†
Beta-glucanase	25 BGU	†
Lactase	610 ALU	†
Pectinase	14 endo-PGU	†
Cellulase	295 CU	†
Diastase	168 DP°	†
Invertase	56 SU	†
Hemicellulase	28 HCU	†

† Daily Value not established

OTHER INGREDIENTS: HYPROMELLOSE, WATER, CALCIUM CITRATE

Carbohydrases

TPP Digest contains one of the most extensive blends of carbohydrases for maximum digestion of starches and sugars. This proprietary carbohydrase blend is acid stable and works in a wide pH range, therefore functioning throughout the gastrointestinal tract. TPP Digest contains amylase, glucoamylase, and malt diastase for assistance in breaking down starchy foods. Invertase, lactase, macerase, alpha galactosidase, and xylanase are for optimal digestion of sugars. Additionally, this comprehensive blend includes beta-glucanase, phytase, pectinase, cellulase, and hemicellulase to help with the breakdown of fiber, promoting the release of vital nutrients often "locked" within these chemical structures. This does not, however, negatively impact or diminish the presence of fiber necessary for proper elimination of wastes. This unique formula with over a dozen specifically selected enzymes is perfect for everyone. The carbohydrases in TPP Digest are standardized using the appropriate FCC activities DU, GalU, FFU, AGU, CU, PGU, BGU, ALU, DP°, SU, and HCU.

Clinical Application

Assisting with the proper digestion of various carbohydrates can alleviate and control many digestive disorders. TPP Digest can reduce the discomfort associated with gas, bloating, cramping, diarrhea, and constipation. TPP Digest may also reduce the signs and symptoms associated with Crohn's disease, Celiac disease, milk intolerance, and many other food intolerances or allergies.

Beta-Glucanase

In addition to the presence of a highly effective amylase and other carbohydrases, the TPP Digest formula contains beta-glucanase, an enzyme that acts on the 1,4-beta-glucosidic bonds of beta glucans containing mixed 1,3 and 1,4 bonds. Under normal conditions, the beta glucans are not readily hydrolyzed in the digestive system. Although their presence in the gut provides some benefits, it is good to induce limited hydrolysis of beta glucans.

As conceived in the TPP Digest formulation, this limited digestion of the fibrous constituents found in the cell walls of grains caused by beta-glucanase will help render many grain food products more amenable to further digestion by other enzymes. This supplemental enzyme is GI tract stable and functional, showing activity in a broad pH range of 2-7 with optimal activity in a pH of 3.5-6.

Clinical Application

This enzyme will further enhance the digestion of grains, liberating vital nutrients as well as reducing digestive stress. Specifically, the presence of beta-glucanase in the TPP Digest formula:

- ensures the breakdown of complex carbohydrates for the release of various nutrients from grains
- enhances the action of enzymes such as proteases to reach their substrates, hydrolyze the proteins, and avoid nutritional / neurobiological complications
- facilitates good water binding in the colon for adequate bowel movement
- ensures removal of various undesirable metabolites such as excess cholesterol
- helps provide many health benefits linked to cardiac health, sugar tolerance, and cholesterol control

Vegetarian Formula

TPP Digest is a vegetarian product that contains absolutely no fillers or binders. It is dairy free and gluten free. As with the majority of Transformation's products, this product is presented in a capsule made of celluose and water. TPP Digest includes no fillers and is non-allergenic.

Recommended Usage

Healthy food choices are a great start to promoting health. However, this represents just the first step. To benefit from all the nutritious components of our food a healthy digestive system is needed. Dozens of factors including genetics, stressful lifestyles, poor diet, processed foods, and the environment all influence digestion. Supplementing a healthy diet and lifestyle with digestive enzymes is the next step in health.

Our most comprehensive digestive enzyme formula includes highly active enzymes with a broad range of specificities needed to digest the foods most commonly found in the human diet. Once the food is broken down into simple nutrients, the body can then assimilate these for energy, growth, and repair.

TPP Digest is available in bottles of 60, 90, and 120 capsules. To help promote availability and absorption of nutrients, health and vitality of cells, and improved overall digestive and immune system health, take one (1) capsule with every meal or snack with at least 8 oz. of liquid or as directed by a health care practitioner. If swallowing capsules is difficult, the vegetarian two-piece capsules can be pulled apart and the contents may be taken by spoon immediately after mixing with a small amount of tepid water.

Questions? 1-800-777-1474
email moreinfo@tecenzymes.com
www.transformationenzymes.com

TRANSFORMATION
THE GENESIS OF GOOD HEALTH™

***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.**

Appendix - The Efficacy of GI Stable and Functional Enzymes

Enzymes, as proteins, are normally susceptible to pH change as well as hydrolysis and denaturation by various factors. A common argument against the oral administration of supplemental digestive enzymes has been their susceptibility to denaturation and hydrolysis by the gastric secretions. Thus, there has been a need to determine the efficacy as well as the stability of some of these supplemental enzymes in the gastric environment. Several enzymes are on the market, yet few of these products have been shown to sustain the harsh gastric environment.

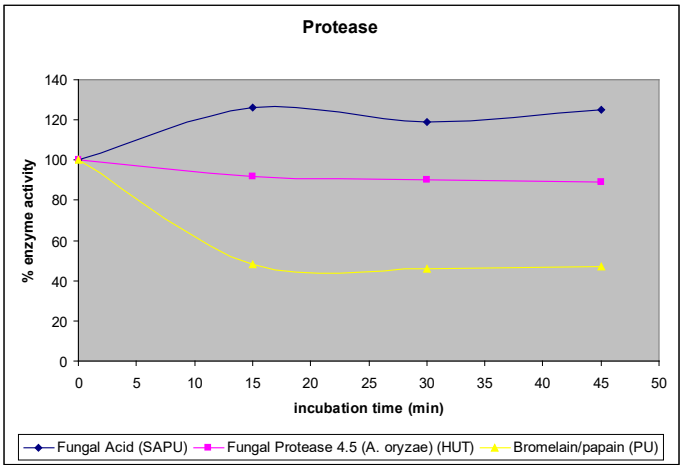
Therefore, TEC participated in a study to determine the level of stability of specific supplemental enzymes and their effectiveness in hydrolyzing food macromolecules. The specific enzymes that were tested include fungal protease 4.5 (*A. oryzae*), fungal acid stable protease (*A. niger*), bromelain and papain, amylase (*A. oryzae*), lactase (*A. oryzae*), glucoamylase (*A. niger*), lipase (*A. niger* and *Rhizopeus oryzae*), and cellulase (*Trichoderma longibrachiatum*).

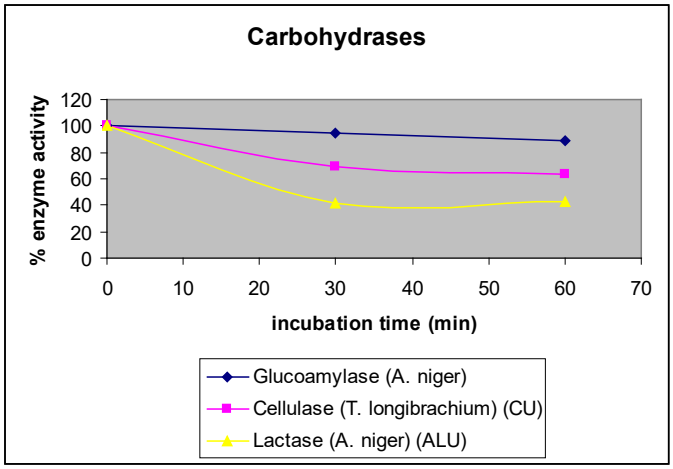
In all cases, the enzymes assayed proved to sustain the simulated gastric fluid, albeit with varying degrees of stability. Some enzymes appeared to have considerably lower activity, so a sample was further incubated in a simulated intestinal fluid that was void of any pancreatic enzymes. Upon assay, the sample incubated in gastric fluid and then in intestinal fluid recovered its activity and moreover had a higher enzyme activity than even the control that was not subjected to any gastric fluid treatment. This indicated that the gastric fluid did not irreversibly denature that enzyme and, interestingly, there appeared to be some activity enhancement resulting from the treatment(s) as seen in the following graphs.

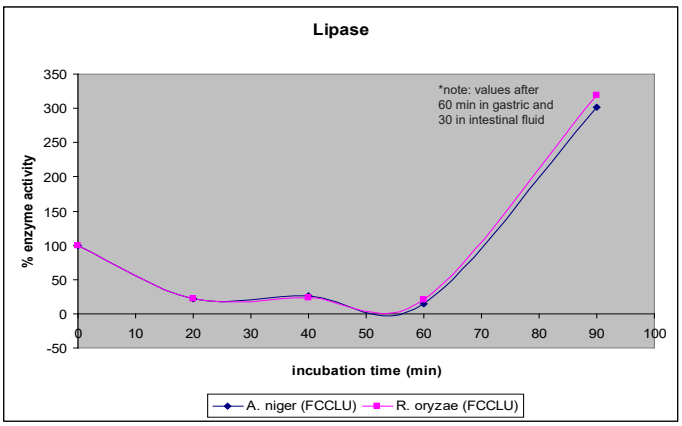
Furthermore, the conditions of these experiments (i.e., direct contact of the enzymes with the harsh simulated gastric fluid) do not occur under normal conditions. Upon taking supplemental digestive enzymes with meals, various macromolecules act as a “protective shield” protecting the direct exposure of the enzymes to the low pH. Some foods actually contribute some buffering of the gastric content during the initial phases of eating. During that initial time, supplemental enzymes within the food bolus are able to continue their hydrolytic action.

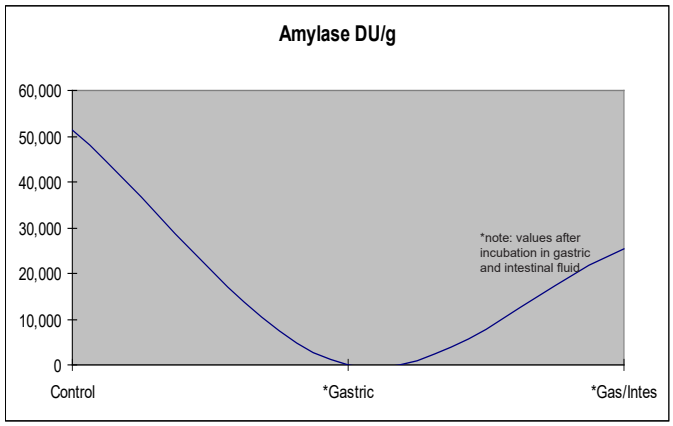
The data here indicates that even without the benefits therein mentioned of the ingested foods, the supplemental enzymes used in this study could sustain the stomach environment, as can be deduced from the simulated gastric fluid exposure, and help in enhancing the digestion of the food macromolecules. Additionally, under some conditions, the enzymes appeared to temporarily lose their activity until they reached a more favorable environment in the small intestine.

This study indicates that the enzymes in TPP Digest maintained enzyme activity after exposure to simulated gastric fluid as used in pharmaceutical studies. This proves our digestive enzymes are stable to low pH conditions thereby enhancing the digestive process and promoting health.









For a copy of the complete study, please contact TEC at 1-800-777-1474 or email moreinfo@tecenzymes.com

References

Arai K, Lee F, et al. “Cytokines: coordinators of immune and inflammatory responses.” Annu Rev Biochem. 1990;59:783-836.

Barbesgaard P, Heldt-Hansen HP, Diderichsen B. “On the safety of Aspergillus oryzae: a review.” Appl Microbiol Biotechnol. 1992 Feb;36(5):569-72.

Bashaw E. Digestion, Assimilation, Elimination, and You. Woodland Pub: 1984.

Baur X, Chen Z, Sander I. “Isolation and denomination of an important allergen in baking additives: α-amylase from Aspergillus oryzae (Asp o II).” Clin Exp Allergy. 1994 May;24(5):465-70.

Beazell JJ. “A re-examination of the role of the stomach in the digestion of carbohydrate and protein.” Am J Physiol. 1941;132:42-50.

Bland J. Natural Foods Network Newsletter. August, 1985.

Blitz JJ, Smith JW, Gerard JR. “Aloe vera gel in peptic ulcer therapy: preliminary report.” J Am Osteopath Assoc. 1963 Apr;62:731-5.

Blumenthal M. The Complete German Commision E Monographs. American Botanical Council: Austin, TX; 1998, p129.

Burton AF, Anderson FH. “Decreased incorporation of 14C glucosamine relative to 3H-N-acetyl glucosamine in the intestinal mucosa of patients with inflammatory bowel disease.” Am J Gastroenterol. 1983 Jan;78(1):19-22.

Castell JV. “Intestinal absorption of undegraded bromelain in humans.” in Absorption of Orally Administered Enzymes. Gardner MLG, Steffens KJ, eds. Springer-Verlag, 1995.

Castell JV, Friedrich G, Kuhn CS, Poppe GE. “Intestinal absorption of undegraded proteins in men: presence of bromelain in plasma after oral intake.” Am J Physiol. 1997 Jul;273(1 Pt 1):G139-46.

Chainani-Wu N. “Safety and anti-inflammatory activity of curcumin: a component of tumeric (Curcuma longa).” JJ Altern Complement Med. 2003 Feb;9(1):161-8.

Chevallier A, The Encyclopedia of Medicinal Plants. DK Publishing: New York, NY; 1996, p163.

Desser L, Rehberger A, et al. “Cytokine synthesis in human peripheral blood mononuclear cells after oral administration of polyenzyme preparations.” Oncology. Nov-Dec 1993;50(6):403-7.

Desser L, Rehberger A, Paukovits W. “Proteolytic enzymes and amylase induce cytokine production in human peripheral blood mononuclear cells in vitro.” Cancer Biother. Fall 1994;9(3):253-63.

Dixon DM, Walsh TJ. “Human Pathogenesis.” in Aspergillus: Biology and Industrial Applications. Bennet JW, Klich MA, eds. Butterworth-Heinemann: Boston, MA; 1992, p249-65.

Dutta S, Rubin J, Harvey J. “Comparative evaluation of the therapeutic efficacy of a pH-sensitive enteric coated pancreatic enzyme preparation with conventional pancreatic enzyme therapy in the treatment of exocrine pancreatic insufficiency.” Gastroenterology. 1983 Mar;84(3):476-82.

Emele JF, Shanaman J, Winbury MM. “The Analgesic Anti-Inflammatory Activity of Papain.” Warner Lambert Research Institute, Department of Pharmacology; Morris Plains, NJ.

Fuller D. The Healing Power of Enzymes. Forbes Publishing Co: New York, NY; 1998.

Gardner MLG, Steffens KJ, eds. Absorption of Orally Administered Enzymes. Springer-Verlag: Berlin, Germany; 1995.

Gerard G. “Anticancer treatment and bromelains.” Agressologie. 1972;13(4):261-74.

Gesualdo L, Ricanati S, Hassa MO, Emancipator SN, Lamm ME. “Enzymolysis of glomerular immune deposits in vivo with dextranase/protease ameliorates proteinuria, hematuria, and mesangial proliferation in murine experimental IgA nephropathy.” J Clin Invest. 1990 Sep;86(3):715-22.

Godfrey T, Reichelt J. Industrial Enzymology: The Application of Enzymes in Industry. The Nature Press: New York, NY; 1983.

Graham DY. “Ins and outs of pancreatic enzymes and adjuvant therapies.” JJ Pediatr Gastroenterol Nutr. 1984;3 Suppl 1:S120-6.

Grossman MI, Greengard H, Ivy AC. “The effect of dietary composition on pancreatic enzymes.” Am J Physiol. 1942;139:676-82.

Grossman MI, Greengard H, Ivy AC. “On the mechanism of the adaptation of pancreatic enzymes to dietary composition.” Am J of Physiol. 1944;141:38-41.

Guyton AC. Textbook of Medical Physiology, 8th ed. WB Saunders Company: Philadelphia, PA; 1991.

Hale LP, Haynes BF. “Bromelain treatment of human T cells removes CD44, CD45RA, E2/MIC2, CD6, CD7, CD8, and Leu 8/LAM1 surface molecules and markedly enhances CD2-mediated T cell activation.” J Immunol. 1992 Dec 15;149(12):3809-16.

Harrach T, Gebauer F, et al. “Bromelain proteinases modulate the cd44 expression on human molt-4/8 leukemia and sk-mel-28 melanoma-cells in-vitro.” Int J Oncol. 1994 Sep;5(3):485-8.

Hills JM, Aaronson PI. “The mechanism of action of peppermint oil on gastrointestinal smooth muscle. An analysis using patch clamp electrophysiology and isolated tissue pharmacology in rabbit and guinea pig.” Gastroenterology. 1991 Jul;101(1):55-65.

Howell E. The Status of Food Enzymes in Digestion and Metabolism. Avery Publications, 1946.

Howell E. Food Enzymes for Health and Longevity. Omangod Press: Woodstock Valley, CN; 1980.

Howell E. Enzyme Nutrition: The Food Enzyme Concept. Avery Publishing Group, Inc: Wayne, NJ; 1985.

Ivy AC, Schmidt CR, Beazell JM. “On the effectiveness of malt amylase on the gastric digestion of starches.” J Nutrition. 1936;12:59-83.

Kiessling LL, Gordon EJ. “Transforming the cell surface through proteolysis.” Chem Biol. 1998 Mar;5(3):R49-62.

LaMarre J, Wollenberg GK, Gonias SL, Hayes MA. “Biology of Disease: Cytokine binding and clearance properties of proteinase-activated a2 -macroglobulins” Lab Inv 1991;65:3-14.

Larsson LJ, Frisch EP, Törneke K, Lindblom T, Björk I. “Properties of the complex between alpha 2-macroglobulin and brinase, a proteinase from Aspergillus oryzae with thrombolytic effect.” Thromb Res. 1988 Jan 1;49(1):55-68.

Lietti A. “Choleretic and cholesterol lowering properties of two artichoke extracts.” Fitoterapia. 1977;48:153-8.

Losada E, Hinojosa M, Quirce S, Sánchez-Cano M, Moneo I. “Occupational asthma caused by alpha-amylase inhalation: clinical and immunologic findings and bronchial response patterns.” J Allergy Clin Immunol. 1992 Jan;89(1 Pt 1):118-25.

Mamadou M, Marr S, Paydon K, Medhektar R. “Stability and Activity of Supplemental Digestive Enzymes in Simulated Gastric Fluid.” presented at the Scripps Conference in San Diego, January 7-9, 2005.

Meagher MM, Reilly PJ. “Kinetics of the hydrolysis of di- and trisaccharides with Aspergillus niger glucoamylases I and II.” Biotechnol Bioeng. 1989 Aug 20;34(5):689-93.

Mills S, Bone K. Principles and Practice of Phytotherapy. Modern Herbal Medicine: Churchill Livingstone, Edinburgh; 2000, p574-5.

Nouza K. “Outlooks of systemic enzyme therapy in rheumatoid arthritis and other immunopathological diseases.” Acta Univ Carol Med (Praha). 1994;40(1-4):101-4.

Quirce S, Cuevas M, Díez-Gómez M, Fernández-Rivas M, Hinojosa M, González R, Losada E. “Respiratory allergy to Aspergillus-derived enzymes in bakers’ asthma.” J Allergy Clin Immunol. 1992 Dec;90(6 Pt 1):970-8.

Reed G. Enzymes in Food Processing. 2nd ed. Academic Press: New York, NY; 1975.

Schechtman MG. “United States Government Regulations Affecting Aspergilli and their Products.” in Aspergillus: Biology and Industrial Applications. Bennet JW, Klich MA, eds. Butterworth-Heinemann: Boston, MA; 1992, p233-47.

Schwimmer S. Source Book of Food Enzymology. The AVI Publishing Company, Inc: Westport, CT; 1981.

Seifert KJ, et al. “The quantitative absorption of orally administered proteins and histological evidence of enzymes in the wound.” in Absorption of orally Administered Enzymes. Gardner MLG, Steffens KJ, eds. Springer Verlag: Stuttgart, Germany; 1995.

Smyth RD, Brennan R, Martin GJ. “Systemic biochemical changes following oral administration of the proteolytic enzyme bromelain.” Archives of International Pharmacodynamics. 1962;136:230-6.

Targoni OS, Tary-Lehmann M, Lehmann PV. “Prevention of murine EAE by oral hydrolytic enzyme treatment.” J Autoimmun. 1999 May;12(3):191-8.

Taussig SJ, Batkin S. “Bromelain, the enzyme complex of pineapple (Ananas comosus) and its clinical application. An update.” J Ethnopharmacol. Feb-Mar 1988;22(2):191-203.

Wald M, Závadová E, et al. “Polyenzyme preparation Wobe-Mugos inhibits growth of solid tumors and development of experimental metastases in mice.” Life Sci. 1998;62(3):PL43-8.

Wolf M, Ransberger K. Enzyme Therapy. Regent House, New York, NY; 1972.

Wren RW. Potters New Cyclopedia of Botanical Drugs and Preperations. 7th ed. Health Science Press: Rustington, Gland; 1970.

Zavadova E, Desser L, Mohr T. “Stimulation of reactive oxygen species production and cytotoxicity in human neutrophils in vitro and after oral administration of a polyenzyme preparation.” Cancer Biother. Summer 1995;10(2):147-52.