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Systemic Enzyme Support: An Overview

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Introduction

A large number of conditions are primarily inflammatory in nature and may be significantly complicated by the presence of secondary forms of inflammation. Regardless of whether the cause of the problem is due to bacterial, viral or auto-immune influences, the result may be an ongoing situation with significant clinical and laboratory manifestations of the inflammatory process.

Dietary supplements designed to provide Systemic Enzyme Support (SES) can play an important role in helping to maintain normal inflammatory processes within the body and thereby help support and speed healing. This is not only beneficial for the patient, but for healthcare in general as ultimately it may help to reduce the costs associated with maintaining health.

Most healthcare professionals select treatments based on what they believe will be effective over a long period of time as well as what will bring a specific patient the fewest risks in connection with treatment. One of the major benefits of using systemic enzyme support is the relatively small amount of undesirable effects combined with good tolerance and efficacy.

Systemic enzyme support was for a long time regarded as a purely empirical treatment method. Due to the rapid development of immunology, biochemistry and molecular biology in the last few decades, systemic enzyme support has undergone significant development, as it has been shown that behind the empirically supported clinical results are a complex set of regulatory processes, which previously were unknown. Today, scientists have a better understanding with respect to the mechanisms by which Systemic Enzyme Support may be exerting it's desired effects. Specifically, the effect of proteolytic enzymes (proteases) on the cytokine network and their action at the level of the cell membrane both in terms of cellular adhesion as well as modulation of cellular receptors has been described. One of the main pioneers in the clinical use of the systemic proteases was Professor Max Wolf, who worked in New York in the 1930s not only as a sought-after physician but also as a

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The Importance of Good Digestion

by Rodger H. Murphree II, D.C., C.N.S.

It's often been said "you are what you eat." However a more accurate statement might be you are what you eat, digest, absorb, and assimilate. Food, carbohydrates, fats, and proteins are the body's building blocks. We need them for our very survival. Carbohydrates are the body's main source of fuel. Protein is needed for making the essential hormones and enzymes, preserving lean muscle mass, and for tissue repair. Dietary fat provides energy, maintains cell membranes, and helps absorb vitamins A, D, E, K, and carotenoids. The digestion, absorption, and assimilation of the macronutrients, ensures we get adequate amounts of essential micronutrients-enzymes, vitamins, minerals, amino acids, and fatty acids which affect every cell in the body. The health of the digestive system not only determines how well we absorb these essential nutrients, it also functions as the immune system's first line of defense. Stomach acid provides an important barrier to unwanted bacteria, yeasts, viruses, and parasites that may enter our bodies along with our food. By absorbing and

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researcher at Fordham University. At the present time, with regard to the historically best known pharmacological and clinical effects, proteases are placed in the international ATC classification in the M09AB group – anti-inflammatory enzymes.

Systemic Enzyme Support – definition

Hydrolytic enzymes have been used widely for decades and a range of scientific publications have recently demonstrated their importance in supporting numerous areas of health. At the present time proteases are indicated for parenteral application in malfunctions of blood coagulation (urokinase), to affect fibrotic processes (hyaluronidase) or in treatment of malignant hemotological conditions (asparaginase). The aim of oral application of enzymes may be either substitution of digestive enzymes in external secretory insufficiency of the pancreas (see accompanying article: "The Importance of Good Digestion") or use of their systemic effects (proteases). So, Systemic Enzyme Support can be defined as a modality which uses oral administration of exogenous hydrolytic (mainly proteolytic) enzymes of animal origin (trypsin, chymotrypsin) and plant origin (bromelain, papain) in the form of enteric-coated tablets for supporting healthy and normal inflammatory processes in the body. As a result, systemic enzyme support can help maintain a healthy immune system, healthy blood flow and circulation, healthy joint function, as well as help to reduce muscles pain after exercising. Systemic enzymes can exert a positive effect on rheological properties of blood as a result of their fibrinolytic properties. Data have also shown that administering systemic enzymes together with certain antibiotics is able to improve the tissue availability of the antibiotics.

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Proteases

The main component of products designed for systemic enzyme support are proteolytic (i.e. protein splitting) enzymes of animal or plant origin. These are endopeptidases which hydrolyze peptide bonds in certain protein (peptide) chain locations on the basis of a more or less specific affinity to particular amino acid elements of these chains.

Trypsin is a pancreatic endopeptidase, which splits peptide bonds formed by the carboxylic group of the amino acids such as lysine or arginine. It is obtained from the pancreas of pigs by repeated refining and subsequent activation of the proenzyme trypsinogen.

Chymotrypsin is a pancreatic endopeptidase, which hydrolytically splits peptide bonds formed by carboxylic groups of the amino acids tyrosine, phenylalanine and tryptophan. Chymotrypsin is obtained by extraction and chromatographic purification from the pancreas of cattle and subsequent activation of the proenzyme chymotrypsinogen.

Bromelain is an endopeptidase obtained from pineapples. Bromelain hydrolytically splits peptide bonds formed by the amino acids lysine, alanine, tyrosine and glycine. Bromelain is a family of individual macromolecules and is not a single enzyme.

Papain is a mixture of proteolytic enzymes separated from the fruit of the tropical *Carica papaya*, which is a member of the melon family. Papain splits polypeptides, particularly between the bonds of arginine, phenylalanine and lysine.

These proteases are typically combined in preparations for oral administration. The reason for these combinations is an assumption that the effects of individual enzymes will complement each other resulting in the multiplication of the final therapeutic efficacy. Another reason for these combinations is the assumption of an increase in the resorption of individual proteases by the intestinal mucous membrane when administered together with other proteases.

Most of the combined systemic enzyme support preparations currently used usually contain rutin (rutoside) in addition to two or more proteases. Rutin belongs to the group of bioflavonoids and can help to reduce the permeability of veins and capillaries.

Resorption of enzymatically active macromolecules and their pharmacokinetics

The basic condition of the systemic effect of proteases administered orally is their absorption in an enzymatically active form. The coated tablet ensures that the content will resist the acid gastric juices and not break down until it has reached the mucosa of the small intestine with a pH of about 7. After absorption, certain parts of the proteolytic enzymes pass into the blood stream and the lymph where their enzymatic activity allows them to bind to natural antiproteases of which the most important are alpha-2-macroglobulin (α-2-M) and alpha-1-antitrypsin (α-1-AT).

Many effects of SES are based on α-2-M-protease complex. The complex formation starts with the hydrolysis of the specific peptide

bond in α-2-M by a protease. It causes a very deep conformational change of the entire α-2-M molecule. The protease becomes trapped in the α-2-M molecule in a way that prohibits many of its potential proteolytic abilities, however, some smaller or less protected substrates can still reach the reaction center and thus it does retain some catalytic activity. In the complex, α-2-M masks the protease macromolecule's antigenic determinants, so the enzyme has no allergenic effect on the organism. By its interaction with a protease, α-2-M is transformed into an "active" form (so called "fast form") which has new properties in relation to many physiologically active molecules, especially, to a broad spectrum of substances which participate in the immune response.

Protease-antiprotease complexes are transported into tissues, where the proteases can be released (from α-1-AT, but not from α-2-M) and operate for a short time as free enzymes or have a relatively long-term effect as entire complexes. In these complexes, the proteases are captured by the liver and the pancreas where 90 % of them are eliminated in bile and excreted in stools. The biological half-life for elimination of enzymes after their resorption is relatively long (6 hours for bromelain and 12-20 hours for trypsin). The biological availability of enzymes in terms of systemic effects is relatively low after oral administration, i.e. around 1% of the total dose administered. This explains the necessity to administer proteolytic enzymes in large doses.

Bromelain and trypsin and similarly other proteases that are administered for systemic effects are resorbed from the intestine as active molecules. Penetration by the enzyme through the wall of the intestine in an active state has also been demonstrated for other enzymes (horse-radish peroxydase, 40 kDa; botulotoxin, 150 kDa). At the present time the generally accepted opinion is that even molecules with a weight of more than 1000 kDa can also penetrate the intestinal barrier to a limited extent.

Currently a number of mechanisms for the transfer of macromolecules through the intestine wall are described. In the upper part of the small intestine, persorption is regarded as the main mechanism. This is linked with continuous desquamation of dying enterocytes, which causes the short-term increase in permeability of the intestinal barrier. In addition, absorption by M-cells (microfold cells) accumulated in the intestinal mucosa over the Payer's plaques takes part in the transfer in the ileum. Another mechanism is the receptor-mediated endocytosis linked with internalisation and recycling of the receptor. In addition to transcellular paths, paracellular transfer through tight junctions also appears to be another possibility.[18]

Mechanisms of the effect of proteases after oral application

The systemic effect of proteases is realized in the organism either by way of direct proteolysis of physiologically important molecules of a protein nature or indirectly by affecting the properties of important regulatory molecules (e.g. α-2-M or proteinase-activated receptors, PARs).

1. Direct proteolytic effects

In blood plasma, equilibrium is established under physiological conditions between the body's own free proteases and those bound to antiproteases (α-2-M, α-1-AT). After oral application of exogenous proteases and their absorption in the intestine, there is a shift in this equilibrium state in terms of an increase in what is termed proteolytic activity of the blood. Proteases bound to α-2-M, which preserve part of their proteolytic activity ("limited proteolysis"), also take part in this.

Proteases take part in specific activation, regulation and degradation of a whole range of factors connected with an inflammatory response. For example, by means of revealing antigenous epitopes, specific proteolysis of a range of cytokines, degradation of regulatory factors of a protein nature or activation of receptors. In addition to this, proteases degrade proteins and peptides damaged by inflammation and thereby allow for easier phagocytosis and removal by means of the venous and lymphatic systems.

2. Effect on adhesion molecules

Adhesion molecules (AM) – are structures on the surface of cells which play an important role in intercellular communication, particularly in the case of immune cells. The degree of their expression is determined by the state of activation of the cell and has an important influence on its properties. For example, increased expression of certain AMs on endothelial cells and thrombocytes and also leukocytes, accompanies an inflammatory response of the organism in all phases. In vitro and in vivo experiments show that enzymes contained in systemic enzyme support products selectively reduce the density of certain adhesion molecules on endothelial cells, in damaged tissues and also on cell membranes of certain inflammatory cells. By reducing the density of these molecules, there occurs an increase in the activation threshold of elements which take part in an inflammatory reaction.

In terms of immunomodulation, the ability of trypsin to increase the activation threshold of T-lymphocytes, owing to reduction in the number of CD4, CD44 and B7-1 adhesion molecules on their surface, appears to be very important. Increased expression of CD4, CD44 and B7-1 and the reduction of the activation threshold of T-lymphocytes connected with this is regularly observed in the focus of inflammation. This is produced by stimulation of INFγ and targeted to increasing the reaction capability of T-lymphocytes. In view of the fact that an activated T-lymphocyte produces additional INFγ, the whole process is amplified. The action of trypsin on the above mentioned adhesion molecules (also with increased elimination of INFγ through the binding to the complex protease – α-2-M, see below) returns T-lymphocytes to an inactive state and thereby helps to maintain normal inflammatory processes.

3. Effect on cytokines operating locally and systemically

In normal inflammatory processes, a whole range of cytokines come into play (e.g. TNF-α, TGF-β, IFNγ, IL-1, IL-6). Some of these cytokines can contribute to the development of imbalances in the inflammatory process. Lately, attention has been focused mainly on the autocrine cytokine TGF-β, whose excessive formation plays a part in various immuno-pathological processes. Cytokines in plasma are bound (like proteases) to antiproteases, particularly to α-2-M. The bond of a cytokine to the antiprotease itself is reversible and a cytokine may manifest its own activity again after being liberated. However, when a cytokine is bound to α-2-M that contains a linked protease, a stable bond is formed, which in turn inactivates the cytokine. Consequently, the whole complex (protease-antiprotease-cytokine) is quickly eliminated by phagocytosis in the liver and the spleen. Therefore, systemic proteases can help to accelerate the clearance of increased levels of certain cytokines.

A similar elimination mechanism has also been demonstrated for immune complexes and even for amyloid polymer which play a

part in the development of certain chronic conditions.

4. Effect by means of protease-activated receptors

Protease-activated receptors – PARs (e.g. PAR-2 is a trypsin-activated receptor) - present on the surface of most of the body cells. They have a physiological importance, for instance in regulating the exchange of substances between the lumen of the blood vessels and the interstitial space. Through the protease-PAR interaction, proteases are considered as key modulators of immune and inflammatory responses. PAR activation by systemic enzymes can contribute to changes in hydrodynamics, and oncotic pressure and thereby can help to maintain normal inflammatory processes and blood flow. Overall, this can help to improve microcirculation and to remove cellular detritus.

5. Effect on AGEs by exogenous proteases

Advance glycation end-products (AGEs), which are formed by non-enzymatic reaction of sugars, ketones or aldehyde groups with a free amino group of proteins, lipids or amino acids, induce chemical modification of proteins and lipids, including LDL particles. This modification is the basis for changes of the structural and functional properties of plasma proteins and extracellular matrices. There is, for example, cross-linking and thickening of basal membranes. The result of AGE-induced modification of lipoproteins (apoprotein-B, LDL) is their delayed clearance through LDL receptors. The interaction of AGEs with their receptors (RAGEs) and/or binding proteins on the surface of cells may induce cell activation and increased formation of oxygen radicals with subsequent activation of the nuclear factor κB (NF-κB) and increased synthesis of cytokines, growth factors and adhesion molecules. Similarly, depending on what type of cell that AGEs are interacting with, they may impact cell proliferation as well as programmed cell death. These effects of AGEs explain the critical role they may play in the pathogenesis of vascular complications of certain chronic conditions. Additionally, aging in general is also thought to be associated with increased AGEs.

The effects of AGEs on the endothelial function have also been well characterized. In in vitro and in vivo experiments, AGEs alter the effect of nitric oxide, which results in changes in vasodilatation. Transendothelial chemotaxis of monocytes and PDGF (platelet derived growth factor) secretion are increased, as is the expression of certain adhesion molecules, such as VCAM-1 (vascular cell adhesion molecule-1) and ICAM-1 (intercellular adhesion molecule-1). When extracellular matrix glycation and inflammatory stimuli are combined, the intensity of the endothelial adhesion can be amplified.

Proteases (trypsin and bromelain) significantly reduce the concentration of AGEs and lipid oxidation products, both in vitro and and in vivo. After application of proteases, reduction in the number of over-expressed RAGEs on the surface of cells accompanied by an increase of their concentration in the intercellular area was observed. This both reduces the probability of interaction of AGEs with their receptors and also enables "inactivation" of AGEs through AGE-soluble RAGE complexes. In connection with a reduction of AGE level, a reduction in the concentration of TGF-β and a lower occurrence of DNA "damage" has also been observed.

These findings also corroborate the idea that AGEs-induced genotoxicity is mediated via the binding of receptors and that trypsin and bromelain may inactivate the extracellular domain of this receptor.

6. Immunomodulation by means of intestinal bacteria

The effect of systemic enzymes on immune function may also be mediated at the level of the intestine. While only a hypothesis, the thought that systemic effects may in part be related to local actions at the level of the gut arises from the observation that certain proteases (e.g. trypsin) can strengthen the bacteriocidal effect of intraluminal intestinal enzymes (e.g. lysozyme). This may result in the induction of immunocompetent cells occurring directly or in immediate contact with the intestinal epithelium.[1]

Pharmacodynamic effects of SES

The effects of proteases administered orally are highly interconnected and can be derived from the mechanisms stated above.

The ability of systemic enzymes to support normal inflammatory processes is a crucial and a highly complex one. The action of proteases on normal inflammatory processes works in a number of ways,[46] which helps to explain the wide spectrum of potential health issues for which systemic enzymes can help to support.

In instances involving occurrences such trauma, burns, haematoma, etc., a combination of proteolytic enzymes works mainly by improving blood rheology and by breakdown of tissue detritus. Specifically, deposits of proteins escaped from the arterial or venous lumen are cleaved and degraded by proteolytic enzymes. Small thrombi created in the periphery of the "vascular bed" can be reduced which promotes the supply of immunocompetent cells and oxygen necessary to rebalance normal inflammatory processes.

In addition to the aforementioned, in situations of ongoing imbalances of the inflammatory system, proteases can help to eliminate immunocomplexes, alter the expression of adhesion molecules, and normalize the cytokine network, and overall haemostasis.

The extent of interaction of proteolytic enzymes with key inflammation reaction mechanisms ranges from supporting the bodies normal inflammatory reaction to helping decrease on overactive system. In contrast to conventional medical products, proteases therefore optimize the physiological course of inflammation and help maintain a balanced process.

The effect on rheological blood and lymph properties, which leads to their decreased viscosity and improved fluidity, is caused by interactions with the fibrinogen/fibrin system and the ability to activate plasminogen into plasmin and increase the levels of anti-thrombine III. Restriction of aggregation and adhesion of thrombocytes and reduction in aggregation and improvement of the flexibility of erythrocytes has also been described.

Improvement of microcirculation by affecting the rheological properties of body fluids is also regarded as one of the factors contributing to the beneficial effects of systemic enzymes. Other important factors which play a part in this effect are all the mechanisms which lead to normalizing an immune response reaction and minimizing secondary damage.

The immunomodulatory effect of systemic enzymes is mediated through affecting the expression of adhesion molecules, interventions in the cytokine network and impact on protease-activated receptors. The effect on various cellular components of the immune system (macrophages, granulocytes, NK cells, T lymphocytes) and the impact on production and elimination of immunocomplexes have also been demonstrated.

It has been shown that some individual proteases and also combined preparations increase the concentration of antibiotics, chemotherapeutic drugs and certain other medical products in the blood and tissues.

Certain relatively recent papers refer to the ability of proteases to reduce the level of LDL–cholesterol. The mechanism underlying the increased elimination of LDL-cholesterol may be the ability of α-2-M-protease complexes to activate common receptors specific for LDL and α-2-M on the membranes of phagocytic cells, in particular the phagocyte system of the liver and the spleen.

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Dr. Wald is a 1981 graduate of the Medical School at Charles University in Prague. In 1991, he accepted a position of house surgeon at the Department of Surgery, 2nd Medical School at Charles University in Prague-Motol. The following year, he became a postgraduate fellow at the same department. Since 1990 Dr. Wald's interests, beyond surgery, have included the systemic effects of proteases on organisms, both in humans and animals. His research, lecture and publication activities primarily involve this field from the point of view of theoretical aspects, experimental works and clinical application of proteases in surgery. For many years he has also been engaged in breast health, related to both diagnostic and surgical therapy. His work has been published in Czech and international journals as well as being presented at congresses in the Czech Republic and abroad.

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Dr. Masinovský was a member of the faculty with the Department of Biophysics at Moscow State University and received his Ph.D. at the Institute of Microbiology, Czechoslovak Academy of Sciences. His work includes work at the Department of Evolutionary Biology at the Institute of Microbiology as and the Laboratory of Evolutionary Biology (LEB) of the Czechoslovak Academy of Sciences as a researcher in the field of biochemistry and biophysics focused on early evolution and enzymes and photobiological mechanisms. Dr. Masinovský is a former councilor at the International Society for the Study of the Origin of Life, author of 65 scientific articles and a member of the J.E.Purkyne Czech Medical Association.

utilizing essential nutrients, removing toxic waste products, and protecting us from harmful pathogens, the health of our digestive system largely determines our overall health.

Digestion

Just thinking about or smelling food can trigger certain chemicals including the hormone gastrin that stimulates the stomach cells. The process of chewing also initiates chemical reactions that prepare the stomach, gallbladder, and pancreas for proper digestion. The esophageal sphincter opens to receive food and then closes to prevent stomach acid or food-stuff from returning back up into the throat.

The Stomach

Food is released into the stomach where the digestive enzymes and gastric juices turn it into a chopped up, liquid mush. The gastric juices contain hydrochloric acid and the enzyme pepsinogen. The hydrochloric acid breaks down the predigested food-stuff and helps turn the enzyme pepsinogen into pepsin, a proteolytic (protein-breaking) enzyme.

The Small Intestine

The small intestine needs an alkaline environment to further breakdown the chyme. Stimulated by the gastric juices, the pancreas releases sodium bicarbonate along with some 22 different digestive enzymes. So far only a few of the proteins and carbohydrates have been broken down, and none of the fats. This is where pancreatic enzymes go to work. The pancreatic enzymes trypsin and chymotrypsin continue to breakdown protein molecules. Amylase further breaks down starches into maltose. And the fat dissolving enzyme lipase begins to digest fats into glycerol and fatty acids.

Peristalsis keeps chyme moving into a part of the small intestine known as the jejunum. This is where most of the absorption takes place. Enzymes embedded in the lining of the small intestine complete the digestion of peptides and maltose into absorbable amino acids and simple sugars, respectively.

The Large Intestine

The remaining food-stuff then moves into the large intestine. Once in the colon several important functions take place including the absorption of water and sodium and with the help of the intestinal flora, the creation and absorption of micronutrients. What's left of the broken down food particles is formed into stool, which is then voided out during a bowel movement.

So What Can Go Wrong? Achlorhydria

Numerous studies have shown stomach acid secretion declines with advancing age. Some studies have shown that, on average, acid production is significantly decreased in up to 50% of those over the age of 60.

An acidic pH ensures proper absorption of selected micronutrients. Folic acid, vitamin C, beta-carotene, calcium, and the B vitamins, are dependant on ample amounts of hydrochloric acid.

Without adequate gastric secretions, foods (macromolecules – carbohydrates, fats and proteins) may be incompletely digested creating mild to moderate nutritional deficiencies.

Mild, sometimes significant signs of malnourishment may reveal themselves as general fatigue, poor mental clarity, low moods, dry skin, unhealthy nails, poor immune function, and general malaise. And once again, one of the major functions of stomach acid is to initiate the conversion of pepsinogen to the enzyme pepsin. Pepsin is responsible for digesting protein and releasing the all-important amino acids. Without pepsin, large incompletely digested protein fragments may be absorbed into the bloodstream. The absorption of these large molecules may contribute to the development of intestinal permeability.

Intestinal permeability or leaky gut is associated with:

- Ankylosing spondylitis
- Rheumatoid arthritis
- Food allergies
- Crohn's disease
- Eczema
- CFS
- IBS
- Cystic fibrosis
- Chronic hepatitis
- Autoimmune diseases

Symptoms associated with low gastric acidity (achlorhydria) include bloating, gas, indigestion, heartburn, and distention after eating, diarrhea, and constipation, hair loss in women, parasitic infections, rectal itching, and malaise, multiple food allergies, nausea, or nausea after taking supplements, restless legs, sore or burning tongue, a dry mouth, and believe it or not heartburn or reflux. In fact heartburn may actually be caused by too little stomach acid, instead of too much, at least initially.

Heartburn and Reflux

Estimates report that 40% of the US population has some degree of esophageal reflux, with 20% of adults complaining of weekly episodes of heartburn and 7–10% complaining of daily symptoms. Esophageal reflux occurs when the lower esophageal sphincter malfunctions, allowing the backward flow of acid, bile, and other contents from the stomach into the esophagus.

Conventional treatment of gastroesophageal reflux disease (GERD) relies on H2 antagonists (Tagament, Pepcid, Zantac, and Axid) and antacids (Tums, Maalox, etc.) as the first line of treatment. If these fail to work, then proton-pump inhibitor drugs (Nexium, Prevacid, or Prilosec) are initiated. Antacids do relieve the symptoms of heartburn and reflux but may not be appropriate. Acid blocking drugs prevent the stomachs hydrochloric acid from turning the enzyme pepsinogen into pepsin. Stomach acid also helps stimulate the pancreas to release sodium bicarbonate into the small intestine. As you may remember pancreatic enzymes need an alkaline environment to function properly.

Without enough stomach acid to stimulate proper pancreatic enzyme production, further digestion and absorption in the small intestine is compromised and poor health follows.

Some doctors believe that when there's not enough stomach acid present the esophageal sphincter may not close properly. Increasing, instead of decreasing stomach acid, may be the best way to treat reflux symptoms.

Betaine HCL

Many of my patients with recent onset of heartburn or GERD respond quite favorably after they begin taking betaine HCL with pepsin supplements.

Betaine HCl supplements are a combination of betaine, a vitamin-like substance typically derived from beets, and hydrochloric acid. The digestive enzyme pepsin is usually included in betaine HCl supplements. Some patients may find that taking betaine HCl will actually cause their GERD to become worse. This is especially true of those who've been taking acid blocking medications for prolonged periods of time. For patients who have advanced GERD, esophageal erosion or who simply can't tolerate betaine HCl, pancreatic enzymes are the next best option. In spite of low or no stomach acid (no pepsin), using pancreatic enzyme therapy (note: this is different from the use of pancreatic enzymes being discussed in the accompanying article) helps ensure proper digestion occurs within the small intestine.

Pancreatic Enzymes non-Systemic uses

The two main digestive enzyme supplement products are either plant based or animal based.

Plant based enzymes may be the most active and are probably the most popular enzymes found in natural food supplements. The four most common are protease, lipase, amylase and cellulase. They are usually sourced from *Aspergillus oryzae* and grown in a laboratory setting.

Plant enzymes work in a very broad pH range, 3.0 to 9.0, offering an advantage over animal derived enzymes (pancreatin).

Plant enzymes work in both the stomach and intestines. Pancreatic enzymes, whether produced by the body or provided as a dietary supplement, work in the small intestine only. Taken with a meal plant based digestive enzymes begin to work rather quickly within the stomach. By breaking down food within the stomach, they save the body from having to release as many of its own enzymes. This energy saving step allows the body to devote more of its attention to supplying metabolic enzymes, required by numerous bodily processes.

Animal based pancreatic enzymes are primarily derived from bovine or porcine pancreatic extracts. Lipase may be obtained from microbial sources including Aspergillus niger and Asperillus oryzae. Chymotrypsin and trypsin are crystallized from either bovine or porcine pancreas extract. Pancrelipase, similar to pancreatin but containing more lipase, is obtained from porcine pancreas extracts. Pancreatin may be obtained from either porcine or bovine pancreas sources.

Accodring to the US Pharmacopia guidelines pancreatic digestive enzyme supplements typically contain chymotrypsin, rypsin, pancrelipase, and pancreatin (containing proteolytic, amylolytic, lipolytic properties).

Digestive enzyme supplements help digest our food, reducing pancreatic stress.

Pancreatic enzymes may become deficient for a variety of reasons including age and poor dietary habits, (excess sugar, deficient essential fatty acids, trans-fatty acids, overeating, etc.).

Normally the enzymes in raw foods, fruits, vegetables, raw sprouted grains, seeds, nuts, and unpasteurized dairy products, help start the process of digestion and reduce the body's need to produce digestive enzymes. However today's diet relies more on processed foods and is largely devoid of enzyme rich fruits and vegetables. In today's fast paced, fast food society, our diets can actually deplete our own natural digestive enzymes. And the more pancreatic digestive enzymes required for digestion, the fewer enzymes it can create for vital metabolic functions.

And cooking our foods doesn't help either - all enzymes are deactivated at a liquid temperature of 118 degrees Fahrenheit, and a dry-heat temperature of about 150 degrees.

It's no wonder estimates now show that after the age of 40 our body's ability to produce enzymes drops by a minimum of 20-30%.

This is why I recommend patients hedge their bets (even if they're not having digestive problems) and take digestive enzymes on a daily basis.

Supplementing with digestive enzymes may provide positive results for anyone suffering with digestive disorders. And for those with chronic health problems or over 40 years of age, adding one or more of the digestive enzyme supplements mentioned above may yield an assortment of health enhancing benefits.

The intricate steps of the digestive system can be compared to a jigsaw puzzle - each piece of the puzzle needs to fit precisely within

Digestive Enzymes: A Glossary

- **alpha-chymotrypsin** – an animal-derived enzyme, breaks down proteins.
- **alpha-glactosidase** – facilitates digestion of beans, legumes, seeds, roots, and soy products.
- **amylase** – breaks down carbohydrates, starches, and sugars which are prevalent in potatoes, fruits, and vegetables.
- **betaine HCL** – increases the hydrochloric acid content of the upper digestive system; activates the protein digesting enzyme pepsin in the stomach.
- **bromelain** – derived from pineapple, breaks down a broad spectrum of proteins, has anti-inflammatory properties, effective over very wide pH range.
- **glucoamylase** – breaks down starch to glucose.
- **invertase** – breaks down sucrose (table sugar).
- **lactase** – breaks down lactose (milk sugars).
- **lipase** – breaks down fats found in most dairy products, nuts, oils, and meat.
- **maltase** – digests disaccharides to monosaccharides (malt sugars).
- **pancreatin** – an animal-derived enzyme, breaks down protein and fats.
- **pancrelipase** – an animal-derived enzyme, breaks down protein, fats, and carbohydrates.
- **papain** – derived from raw papaya, broad range of substrates and pH, works well breaking down small and large proteins.
- **pepsin** – breaks down proteins into peptides.
- **peptidase** – breaks down small peptide proteins to amino acids.
- **protease** – breaks down proteins found in meats, nuts, eggs, and cheese.
- **sucrase** – digests complex sugars and starches.
- **trypsin** – derived from animal pancreas, breaks down proteins.

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The Importance of Good Digestion

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the next piece to create a whole. One missing piece and the whole system is affected.

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Dr. Murphree is a board certified nutritional specialist and chiropractic physician who has been in private practice since 1990. He is the founder and past clinic director for a large integrated medical practice located on the campus of Brookwood Hospital in Birmingham Alabama. The clinic was staffed with medical doctors, chiropractors, acupuncturists, nutritionists, and massage therapists. The clinic combined prescription and natural medicines for acute and chronic illnesses. He is the author of 5 books for patients and doctors, "Treating and Beating Fibromyalgia and Chronic Fatigue Syndrome," "The Patient's Self-Help Manual for Treating and Beating Fibromyalgia and Chronic Fatigue Syndrome," "Treating and Beating Fibromyalgia and Chronic Fatigue The Manual for Non-Allopathic Doctors," "Heart Disease What Your Doctor Won't Tell You'" and "Treating and Beating Anxiety and Depression with Orthomolecular Medicine."

In 2002 Dr. Murphree sold his medical practice and now maintains a busy solo practice specializing in fibromyalgia, chronic fatigue syndrome, heart disease, mood disorders, and other chronic illnesses. He also consults with other physicians, lectures throughout North America, and conducts 2-day doctor continuing education seminars.

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