In considering the use of digestive enzyme supplements, it is not uncommon to question the survivability of unprotected enzymes through the digestive process. Pancreatic enzymes, available as both drugs and dietary supplements, are known to require enteric coating to prevent permanent denaturing by gastric acidity. Fortunately, not all enzymes require these coatings to survive the gastric environment. Certain plant and microbial enzymes are known to be stable under a broad pH range and are capable of acting throughout the digestive tract. This paper will examine the hazards of the digestive tract for enzyme proteins and provide a brief review of some of the research that supports the stability of specific enzymes.

During the digestive process, the gastric environment is primed for the hydrolysis of proteins. Hydrochloric acid is secreted by the parietal cells for two digestive functions: 1) the activation of pepsin, and 2) denaturing, or unfolding, proteins to allow access to the peptide bonds. Enzymes are proteins and may be digested just as any other protein. Enzymes possess no special protective mechanism that shields them from the hydrolytic action of pepsin. However, supplemental enzymes are protected by the laws of probability.

When enzymes are consumed with a meal, the amount of protein contributed by the food is much greater than that consumed as enzymes. The chances are much greater that pepsin will encounter food proteins. As a simple illustration, imagine a game of marbles. There are over one hundred marbles in the ring, 80 have a diameter of 1-inch, 15 have a diameter of ½-inch, and only 5 have a diameter of ¼-inch. The marble you are shooting also has a ¼-inch diameter. What size marbles are you most likely to hit?

In this illustration (Figure One), the 1-inch marbles are undigested food, the ½-inch marbles are partially digested food, and the ¼-inch marbles are supplemental enzymes. The smaller the molecule, the less likely it will be hit early in the game (or early in digestion). As digestion continues (Figure Two), more mid-sized molecules (1/2-inch marbles) are created increasing the total available contacts. In this manner, supplemental enzymes are
assured a high rate of survival despite the action of pepsin due to their relatively small molecular size and smaller contribution to the total protein load. Even pepsin itself faces the same chance of proteolytic digestion, should the protein come in contact with another molecule of pepsin.

Non-enteric coated enzymes are able to interact with ingested foods in the upper region of the stomach before mixing with the gastric secretions. Dr. Edward Howell often referred to this region as the food enzyme stomach; “pre-digestion” of foods can occur in this environment for as long as one hour before the body’s active digestive process begins. Salivary amylase, mixed with food during chewing, continues its digestive action in this region until inactivated by low gastric pH or proteolytic digestion. It is estimated that salivary amylase digests as much as 40 percent of starch before the food reaches the small intestine. Supplemental enzymes may contribute significantly to digestion in the upper stomach through the “pre-digestive” process.

The acidic pH of the gastric region is also a potential challenge for supplemental enzymes. Few enzymes are able to survive the pH of pure gastric acid. However, in the presence of food, the gastric pH is buffered significantly, ranging from 2.5 to 5.0 depending upon the foods consumed. Within this environment, many supplemental enzymes are not permanently denatured or harmed. In fact, many enzymes function optimally under these conditions.

National Enzyme Company selects the enzymes used in dietary supplements based upon their ability to survive and function across a broad pH range. Unlike pancreatic enzymes, many fermented and plant enzymes do not require protective or enteric coatings to maintain activity through the digestive system.

In 2004, NEC sponsored a study investigating the efficacy of an enzyme supplement in a computer-controlled dynamic model of the digestive system known as TIM. TIM was developed by The Netherlands Organization for Applied Scientific Research (TNO) in Zeist, Netherlands. The TIM model has been validated and is widely accepted in drug investigation studies. The study evaluated the effects of the supplement under simulated conditions of healthy human digestion and impaired human digestion. Results for carbohydrate digestion showed increased glucose availability under both healthy and impaired conditions. This supports not only the efficacy of the carbohydrase enzymes but also indicated survivability through the gastric environment. Likewise, the proteolytic enzymes showed similar improvements in the availability of nitrogen in both healthy and impaired digestive scenarios.

The TNO results are further supported by in vitro analysis conducted by NEC exploring the pH profile and simulated gastrointestinal survivability of various enzymes. These tests consistently showed that enzymes selected by NEC for use as digestive supplements are capable of functioning within the pH range found within the gastrointestinal tract. Most of these functioned within their optimum pH range. In addition, these enzymes retain a significant portion of their activity after exposure to gastric acidity when placed into simulated intestinal fluid. It
is theorized that the low-gastric acid may temporarily inactivate certain enzymes, due to pH-induced unfolding, which are able to regain their active conformation under intestinal conditions.

There are also published studies focusing on the ability of certain fungal lipases to survive the gastric environment and contribute to the hydrolysis of dietary fats. Griffin et. al. (1989) reported on the efficacy of non-enteric coated, acid-stable *Aspergillus* lipase in the reduction of steatorrhea in dogs with surgically-induced pancreatic insufficiency. The researchers contrasted the *Aspergillus* lipase with both non-enteric coated and enteric coated pancreatic preparations and concluded that it was effective and offered a viable treatment option. Fieker (2011) reviews the current status of enzyme replacement therapy for pancreatic insufficiency. Within the review, the authors discuss some of the problems with enteric coated pancreatic preparations including the high dosage levels and the incidence of fibrosing colonopathy. Current research indicates that this side effect of pancreatic medicines may be related to the components of the enteric coating along with the high dose requirements. The review also presents alternative sources of lipases including those produced by microbial fermentation including *Rhizopus oryzae* (arrhizus), *Candida rugosa* (cylindacea) and *Aspergillus niger*. Borowitz and colleagues have published several articles reporting on the clinical trials of a novel blend of highly purified fermented enzymes consisting of bacterial lipase along with fungal protease and amylase. This product has shown good tolerance and efficacy without the need for enteric coating or high doses in human clinical trials.

Several studies have been conducted examining the efficacy of various lactase supplements. Gao (2002) specifically reported on the gastric survivability of the enzyme when taken with milk. The study reported that the ingestion of 300mL of milk resulted in a gastric pH of approximately 6.0, which protected the supplemental lactase and allowed lactose digestion to begin in the stomach. Further support is presented in the studies of Lin (1993) and Ramirez (1994).

Properly formulated enzyme supplements have the capacity to support the digestive process throughout the gastrointestinal tract. Their first site of action resides in the upper stomach where they initiate the process of “pre-digestion.” Many remain active within the food bolus during active gastric digestion while others may be temporarily inactivated. A significant portion of inactivated enzymes may then regain functionality in the increased pH of the small intestine to further hydrolyze ingested proteins, fats and carbohydrates. The gastric survivability of supplemental enzymes is a key factor in selecting enzymes for use in non-enteric coated digestive supplements.

REFERENCES:


Ramirez et al. All lactase preparations are not the same: results of a prospective, randomized, placebo-controlled trial. Am J Gastroenterol 1994 Apr; 89(4): 566-70.