THE GLANDULAR CORNER: PANCREAS

Linda Isaacs, MD, Discusses Pancreatic Glandular Therapies, Including Their History and Current Clinical Applications

Linda L. Isaacs, M.D., received her Bachelor of Science degree from the University of Kentucky, graduating with High Distinction with a major in biochemistry. She is a graduate of Vanderbilt University School of Medicine and is certified by the American Board of Internal Medicine, completing the recertification process in 2001, in 2011, and in 2019.

In the earliest days of the use of pancreatic proteolytic enzymes, they were referred to as "ferments," since their action was similar to the well-known process of fermentation of food. Scientists in the 19th century figured out that there were differences in the functions of pepsin, trypsin, and enterokinase, and that a precursor form of trypsin existed, well before the nature of protein was understood.[1,2]

An 1898 edition of *Fairchild's Hand-Book of the Digestive Ferments* states:

> "No digestive ferment has been absolutely isolated, consequently the chemical constitution of these principles is yet a matter of conjecture. We do not know how they perform their marvelous work, nor the exact chemical formula of the various derivatives of digestion. These limitations to our knowledge of the digestive ferments do not impose any limitations upon our practical use of them. For we are able to extract them from the digestive juices or secreting glands and to preserve them indefinitely as reliable agents of the materia medica."[3]

Fairchild offered pepsin, trypsin, and amylase, which were taken orally for digestive issues. Enzymes were also applied to the throat membrane that develops in diphtheria, and instilled into abscesses or necrotic tissue.

Pancreatic extracts have primarily been used to treat digestive problems, though at times they were reported helpful for other conditions, such as arthritis and cancer.[4,5,6] Typical processing included the removal of fat with various solvents and the activation of the precursor forms of enzymes, as illustrated by the process patented by Levin.[7] It has long been known that trypsin is inactive in an acid environment and destroyed by pepsin, as carefully documented by Heizer et al. in 1965.[8] Many products have enteric coatings to protect the enzymes from destruction in the stomach, but coatings can dissolve at the wrong times and cause their own problems.[9]

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In my own practice, I recommend a pancreas product that has been minimally processed and lyophilized (freeze-dried) with the fat in the organ intact, without an enteric coating. Why? Well, for one thing, I can still vividly remember the chemical aftertaste when I took enterically coated, highly processed enzymes years ago.

In the experiments about the stability of the proteases when exposed to acid and pepsin, Heizer et al. used purified enzymes and processed, defatted pancreatin. Leaving the fat intact in the product may help to protect the enzymes because fat suppresses pepsin and acid production.[10] No investigations have yet been done with the particular form of processing I prefer; the closest study I have found involves various preparations, including raw pancreas, given to dogs with pancreatic insufficiency.[11] Samples from the jejunum were taken. Westermarck found:

> "The highest lipase activities in the jejunal samples were achieved using raw pig pancreas. Commercial enzyme preparations yielded activities that were only one tenth of those attained with raw pancreas."[11]

Proteases were also measured and were markedly higher with the raw pancreas supplementation. Dogs are reportedly quite enthusiastic about raw pancreas, but most humans prefer a lyophilized product.

Can orally ingested pancreas product work systemically? Many would say no, stating that the molecules are too large to be absorbed, and that proteolytic enzymes only function to destroy proteins. However, recent articles in the medical literature detail a much wider role in physiology for proteases than previously believed, since they can modulate many cellular reactions through protease-activated receptors in cell membranes.[12] Another article suggests that protease-activated receptors help regulate intestinal permeability, and that proteases may interact with those receptors to facilitate their own absorption.[13] Additionally, ingested pancreas, by improving the digestion of food, could cause a shift in the microbiome that would have a systemic effect.[14,15]

Research about the actions of proteolytic enzymes is rapidly moving forward. The use of pancreas glandular product may prove to be of value for much more than improved digestion. ■

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