Reducing Inflammation with Proteolytic Enzymes, Part One: Absorption and Sources

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This month we will continue the theme of naturally reducing inflammation by focusing on proteolytic enzymes. Proteolytic enzymes sever peptide bonds in proteins with varying degrees of specificity. When an injury occurs, the body responds with an inflammatory cascade. Excessive inflammation can retard the healing process. Proteolytic enzyme supplementation reduces inflammation by neutralizing bradykinins and pro-inflammatory eicosanoids to levels where the synthesis, repair and regeneration of injured tissues can begin. Proteolytic enzymes do not completely inhibit all phases of the inflammatory cascade to a point where the body is unable to trigger the normal healing process.

Absorption

In digestive physiology, we learn that proteins are digested in the stomach and small intestines and absorbed as single amino acids, dipeptides and tripeptides. The dipeptides and tripeptides are then further broken down into single amino acids by gut enterocytes, where they then enter portal circulation. Since proteolytic enzymes are proteins, many people feel they have no biological activity other than that of a protein source, and are simply digested as expensive protein fragments with inert properties.

A literature review yielded studies beginning with Brendel, et al., in 1956, who demonstrated that trypsin had an anti-inflammatory action when administered buccally. In 1957, Martin, et al., showed that when trypsin, chymotrypsin and papain were injected into the small intestines, they were not denatured or digested, but absorbed with enough of the molecules intact to exert marked systemic anti-inflammatory effect. They theorized that enterically coating these substances would enable them to be administered orally.

Ambrus, et al., showed that oral administration of enterically coated trypsin and chymotrypsin resulted in increased specific blood activity changes that could occur only if these enzymes were absorbed intact. Vakians demonstrated that enterically coated chymotrypsin was absorbed orally and remained functional in the blood stream for four hours after administration. Miller and Opher showed in 1964 that enterically coated bromelain given orally caused an increase in blood serum proteolytic activity. Innerfield and
Wernick showed that oral administration of papain resulted in a decreased clotting time. Along with increased serum levels and reduced clotting times, other methods used by researchers to prove oral enzymes were absorbed at levels where physiologic effects occurred included enzyme proteolytic activity, antibody identification, radiographic tracing and electrophoretic separation. There were enough studies on the absorption of proteolytic enzymes beginning in the late 1950s and throughout the 1960s that researchers were able to conclude that the classic theory of a protein impermeable intestinal barrier was simply incorrect.

There were two other interesting findings: proteolytic enzymes ingested on an empty stomach can retain up to 40% of their activity, and proteolytic enzymes appear to have an affinity to accumulate at sites of inflammation.

When nonsteroidal anti-inflammatories began to appear on the market in the 1960s, interest in proteolytic enzymes decreased dramatically. There was very little research on enzymes in the 1970s and 1980s. In the 1990s, some scientists began to take another look at proteolytic enzymes. There were some impressive European studies that showed marked reductions in healing times of patients who used proteolytic enzymes.

In 1998, researchers gave bromelain and trypsin at 400 to 800 mg four times a day for four days to 21 people. They found that the plasma levels of both enzymes increased and that these increases correlated with the amount of enzymes supplemented. They concluded that the absorption of large protein molecules of proteolytic enzymes does occur, and they felt this could explain why proteolytic enzymes have been successfully used to treat posttraumatic inflammation, edema and bruising.

This year, in a double-blind, placebo-controlled investigation, researchers gave a seven-enzyme mixture that included 75 mg of trypsin, 50 mg of papain and 50 mg of bromelain four times per day, beginning 24 hours prior to and 48 hours following downhill running. The researchers reported that there was less muscle soreness in the group that supplemented with the enzymes. My extrapolation from this study is as follows:

1. There was less soreness in the muscles because there was less inflammation in the muscles.
2. There was less inflammation in the muscles because the enzyme mixture was obviously not digested and absorbed as inert single amino acids.

**Animal-Based Enzymes**

Animal-based proteolytic enzymes come from the pancreases of pigs and cows. These glands are defatted and dried, yielding a raw pancreatin mixture that includes trypsin, chymotrypsin and other peptidases. Further refinement yields a trypsin-chymotrypsin blend with significantly more trypsin.\textsuperscript{10} Trypsin hydrolyzes peptide bonds at arginine and lysine linkages. Chymotrypsin hydrolyzes peptide bonds at carboxyl groups.\textsuperscript{10} When animal-based enzymes are enterically coated, they are able to resist stomach acidity, thus yielding higher serum levels.

**Vegetable-Based Enzymes**

Bromelain is a group of enzymes derived mostly from pineapple stems. Some scientists categorize bromelain as a member of the bioflavonoid family. Bromelain has a very wide range of activity for severing peptide bonds.\textsuperscript{10}

Papain and chymopapain are derived from papaya fruit. The range of activity from papaya-based enzymes is similar to that of bromelain.\textsuperscript{10}

Fungal proteolytic enzymes are usually derived by fermentation of various strains of aspergillus. They also exhibit a broad range of activity to sever peptide bonds.\textsuperscript{10}

Vegetable-based enzymes also work better when they are enterically coated. Because of its wide range of pH stability, bromelain can be effective even if it is not enterically coated.\textsuperscript{10}

Next month, we will discuss common uses of enzymes along with side effects, dosing protocols and measuring activity.

**References**


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