NON-PRESCRIPTION ENZYME SUPPLEMENTS

The use of over-the-counter enzyme supplements is increasing in the United States due to claims of beneficial effects from manufacturers. This issue of CLIPs briefly summarizes a review regarding current literature for the use of OTC enzymes in a variety of disease states. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Background

- Several enzyme supplements are available over-the-counter (OTC) including bromelain, papain, trypsin, chymotrypsin, and other combination products (see table 1).
- Enzyme supplements are promoted for beneficial effects of a variety of disease states including inflammatory disorders, multiple sclerosis, pancreatic insufficiency, allergies, burns, infections and cancers.
- Although the quality of dietary supplements may be unreliable, some patients still use these as an alternative to prescription medications.
- Enzyme products are derived from several sources. Plant sources appear to remain active over a broader pH range which decreases the degradation in an acidic environment.
- As a result, clinicians should be aware of the potential effects of these supplements in their patients.

Table 1: Over-the-Counter Enzymes: Use, dosage, and potential adverse effects

<table>
<thead>
<tr>
<th>Product</th>
<th>Proposed indication</th>
<th>Dosage</th>
<th>Potential adverse effects</th>
<th>Potential drug interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bromelain (derived from stem and fruit of pineapple)</td>
<td>Acute postoperative and posttraumatic conditions of swelling, burn debridement, anti-inflammatory action, allergic rhinitis</td>
<td>Up to 400 mg/day PO</td>
<td>GI cramping, diarrhea, IgE-mediated allergic reactions</td>
<td>Moderate interaction with amoxicillin and anticoagulant/antiplalet drugs</td>
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<tr>
<td>Papain (derived from papaya fruit)</td>
<td>Posttraumatic/postoperative inflammation, digestive aid, pharyngitis, herpes zoster symptoms, chronic diarrhea</td>
<td>Up to 1500 mg/d PO</td>
<td>Esophageal perforation, gastritis, allergic reactions</td>
<td>None known</td>
</tr>
<tr>
<td>Trypsin (derived from bacterial, fungal, or porcine sources)</td>
<td>Digestive enzyme supplementation, osteoarthritis, topically for wound healing</td>
<td>Up to 50 mg, usually combined with bromelain</td>
<td>Localized pain and transient burning</td>
<td>None known</td>
</tr>
<tr>
<td>Chymotrypsin (derived from bovine or porcine)</td>
<td>Reducing inflammation and edema associated with abscesses, ulcers, surgery, or traumatic injuries</td>
<td>Up to 100,000 U USP 4 times daily PO</td>
<td>Anaphylaxis (rare)</td>
<td>None known</td>
</tr>
</tbody>
</table>

PO-by mouth; GI-gastrointestinal; USP-United States Pharmacopeia

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Mechanism of action

- The mechanism of action of these products is not understood; however, they appear to have some pro-inflammatory and anti-inflammatory effects.
- Bromelain appears to affect the growth of malignant cells and inhibits platelet aggregation.
- Papain may release reactive oxygen species by polymorphonuclear cells.
- Trypsin may have proteolytic activity, especially in wounds.
- Chymotrypsin acts to reduce tissue destruction through its proteolytic, anti-inflammatory, and antioxidant properties.
- Although consumers speculate that enzyme production decreases with age, there is no evidence supporting the theory that this is true.
- In addition, some suggest that gas and bloating may be due to a deficiency in digestive enzymes. A study citing receipt of enzyme supplementation containing lipase, protease, and amylase before and after a fatty meal was associated with less gas, bloating, and fullness compared to controls; however, the product used in the study was a prescription product.

Effects of enzyme supplementation

- Evidence suggests that small amounts of the enzymes reach the systemic circulation.

Osteoarthritis

- Limited evidence suggests that a commercially available product combined with diclofenac compared with diclofenac monotherapy was associated with improved pain control. Similarly, reduced pain and improved joint function was observed in enzyme supplement groups compared to NSAID groups.
- Additional studies need to be performed to confirm these effects in a larger population.

Muscle soreness in athletes

- Evidence in athletes has been conflicting. One study indicated that improved pain was observed after running downhill.
- A double-blind clinical trial with bromelain and placebo indicated no difference in muscle soreness.

Cancer

- Most data related to decreasing complications of therapy instead of decreasing the disease progress.
- Data for the use of enzyme supplementation for cancer did not evaluate statistically significant differences or no significant improvements were observed.

Patient-specific information about enzyme supplementation

- Risks associated with therapy appear to be low; however, products may be contaminated since they do not undergo stringent testing prior to distribution.
- Little is known about significant drug-drug interactions.
- A more complete listing of adverse effects are included in table 1.

Conclusions

- Although little clinical evidence is available supporting the use of these agents, patients should be informed of the potential for adverse drug reactions and drug-drug interactions associated with these products.
- Practitioners should recommend a timed personal approach whereby patients initiate drug therapy for a particular time frame and reassess the beneficial effects of the products. If an improvement is not observed, discontinuation is recommended.

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