

The Use of Enzymes in Dietary Supplements

USP Enzyme Workshop

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Introduction and History of Use

Commercial production of enzymes for use as digestive aids has an extensive history extending back for well over 60 years

- Whole food sources
- Fermented foods
- Animal tissue

Introduction and History of Use

Commercial Production of Enzyme Digestive Aids

- **Treatment of digestive diseases**
 - Pancreatic insufficiency and cystic fibrosis
 - General nutritional deficiencies
 - OTC pancreatic digestive aids
 - Challenges with variability in activity
 - Nutritional enzyme supplements
- **Known enzyme deficiencies**
 - Lactose intolerance
 - Pharmaceutical applications
- **Wobenzym**

Sources for Enzymes in Nutritional Supplements

- **Animal sourced enzymes**
 - Pepsin, Trypsin, Chymotrypsin, Pancreatin
 - Low gastric survivability/enteric coated
 - Function in small intestine
- **Plant Sourced enzymes**
 - Fruits (Proteolytics) – bromelain, papain, ficin, actinidin
 - Barley – malt diastase
- **Microbial sourced enzymes**
 - Fungi (including yeasts) and bacterial sources
 - Improved gastric survivability
 - Increased variability in enzymatic activity
 - Amylase, glucoamylase, multiple proteases, lipase, multiple saccharidases

Enzymes in Nutritional Supplements

Industry preferences

- Non-GMO production organisms
- Preservative-free
- No sterilization
- Physical consistency; i.e. color, texture

Enzyme Supplement Applications

- **Digestive aids**
 - General digestive support
 - Compensate for poor eating habits
 - Indigestion
 - Enzyme deficiencies
- **Systemic uses**
 - Anticoagulant (Fibrinolytic) properties of proteolytic enzymes
 - “Anti-inflammatories”

Enzyme Supplement Applications

- **Most are mixtures of several enzymatic activities and may be combined with botanicals or other dietary ingredients**
- **Often listed as proprietary blends targeted to a specific type of activity**
- **Digestive aid supplements dosed to accommodate 1-2 capsules, up to 3 times per day with meals**
- **Systemic formulas display dosing instructions recommending multiple tablet/capsule dosing between meals**

Regulation of Enzymes in Dietary Supplements

- **DSHEA (Dietary Supplement Health and Education Act of 1994)**
- **“Pre-94” list of enzymes**
 - ETA compiled list
 - Food Grade – Processing aid enzymes
 - GRAS
- **Pre-Market Notification**
 - Serratiopeptidase
 - Nattokinase
 - Levansucrase

Manufacturing Issues Unique to Dietary Supplements

- **Physical considerations for blending and encapsulation**
 - Flow
 - Particle Size
 - Density
- **Tableting**
 - Compactability issues necessitating use of processing aids
- **Safety of manufacturing personnel**

Manufacturing Issues Unique to Dietary Supplements - Assays

- **High variability in assay methods for same enzymes**
- **Advantage of FCC or compendia based assays**
 - Generally accepted by regulatory bodies such as TGA and NSF
 - Consistency of activity units
- **Assay significance**
 - Basic laboratory assays or functional assays
 - Customer understanding of activity units
 - Does the customer or end consumer care?

Dosing

- **History of use**
- **Weight versus activity**
- **“More is better” or is it?**
- **Digestive system variability**
- **Changes in digestive efficiency**
 - Increase in number of individuals with digestive disorders
 - Pharmaceutical trends (acid reducers)

Product Safety Issues

- **Allergenicity**
 - Sensitivity to enzyme protein
 - Allergy to co-ingredients
- **Adverse events**
 - Very low risk
 - Gastrointestinal discomfort
- **Toxicity**
- **Overdosing**

FDA Regulatory Issues

- **GMPs**
 - Developing appropriate specs for “purity, strength, composition and contamination”
 - Methods/manufacturing validation
 - Finished product testing challenges
- **Claims issues**
 - Structure/Function claims
 - Lack of general safety and efficacy studies

FDA Regulatory Issues

Labeling

- **Blends of enzymes**
- **Order of predominance**
 - Order by weight, not activity
 - Varying concentrations of same enzyme
 - Tolerance in supplier concentrations compared to 100% mandate in DS labeling
- **Proprietary blends**
 - Marketing protection
 - Labeling order of predominance

Issues for the Future

- **Still relatively small segment of dietary supplement industry**
- **But, one of the fastest growing - \$40-50 million.**
- **Increased education needed**
 - Supplier and manufacturer responsibilities
 - Assay methodology
 - Distributor knowledge
 - End consumer understanding of physiological functioning

Thank you