Tishk International University
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ADVANCED CLNICAL BIOCHEMISTRY

Gastrointestinal tract

Digestion of proteins

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Digestion In the stomach

- pepsin is the major proteolytic enzyme. It cleaves proteins to smaller polypeptides
- **A Pepsin** is produced and secreted by the chief cells of the stomach as the inactive zymogen pepsinogen.
- Hydrochloric acid (HCl) produced by the parietal cells of the stomach causes a conformational change in pepsinogen, forming active pepsin.
- **Pepsin** cleaves peptide bonds in which the carboxyl group is contributed by the acidic amino acids, **aromatic amino** acids, or **leucine**.

Digestion In the intestine

The partially digested material from the stomach encounters pancreatic secretions, which include bicarbonate and a group of proteolytic enzymes.

a. Bicarbonate neutralizes the stomach acid, raising the pH of the contents of the intestinal lumen into the optimal range for the digestive enzymes to act.

b. Endopeptidases from the pancreas cleave peptide bonds within protein chains.

(1) **Trypsin** cleaves peptide bonds in which the carboxyl group is contributed by arginine or lysine.

(2) **Chymotrypsin** usually cleaves peptide bonds at the carboxyl group of **aromatic amino** acids or **leucine**. Chymotrypsinogen, the inactive zymogen, is cleaved to form active chymotrypsin by trypsin.

(3) **Elastase** cleaves at the carboxyl end of amino acid residues with small, uncharged side chains such as **alanine**, **glycine**, or **serine**. Proelastase, the inactive zymogen, is cleaved to active elastase by trypsin.

(4) **Exopeptidases** in the pancreas (**carboxypeptidases A and B**) cleave one amino acid progressively from the C-terminal end of the peptide. The carboxypeptidases are produced as inactive procarboxypeptidases, which are cleaved to their active form by trypsin.

(1) Carboxypeptidase A cleaves **aromatic amino** acids from the C terminus.

(2) Carboxypeptidase B cleaves the basic amino acids, **lysine** and **arginine**, from the C terminus.

Proteases produced by intestinal epithelial cells complete the conversion of dietary proteins to peptides and finally to amino acids.

(1) Aminopeptidases are exopeptidases produced by intestinal cells, cleaving one amino acid at a time from the N terminus of peptides.

(2) **Dipeptidases** and **tripeptidases** associated with the intestinal cells produce amino acids from dipeptides and tripeptides.

The proteolytic enzymes include:

- **Endopeptidases:** They act on peptide bonds inside the protein molecule, so that the protein becomes successively smaller and smaller units. This group includes pepsin, trypsin, chymotrypsin, and elastase.
- **Exopeptidases:** This group acts at the peptide bond only at the end region of the chain. This includes carboxypeptidase acting on the peptide only at the carboxyl terminal end on the chain and aminopeptidase, which acts on the peptide bond only at the amino terminal end of the chain.

In the Stomach:

parietal cells secrete HCl
chief cells secrete pepsinogen

endopeptidases

pepsinogen $\xrightarrow{H^+}$ pepsin { general protease with preference for acidic & aromatic amino acids

Exocrine Pancreas secretion into the Small Intestine:

endopeptidases

trypsinogen $\xrightarrow{\text{enteropeptidase}}$ trypsin { arginine, lysine

chymotrypsinogen $\xrightarrow{\text{trypsin}}$ chymotrypsin { tryptophane, phenylalanine, tyrosine, leucine

proelastase $\xrightarrow{\text{trypsin}}$ elastase { alanine, glycine, serine

exopeptidases

procarboxypeptidases $\xrightarrow{\text{trypsin}}$ carboxypeptidases

A { hydrophobic amino acids

B { basic amino acids
arginine
lysine

Secretion by the Brush Border of the Small Intestine:

exopeptidases

aminopeptidases { many

Proenzymes (zymogens) → Active enzymes

Pepsinogen —*HCL*→ **Pepsin**

Trypsinogen —*enteropeptidase*→ Trypsin

Chymotrypsinogen —*trypsin*→ Chymotrypsin

Proelastase —*trypsin*→ Elastase

Procarboxypeptidases —*trypsin*→ Carboxypeptidases

Thank you