Advanced Clinical 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.
Trypsin cleaves peptide bonds in which the carboxyl group is contributed by arginine or lysine.

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.

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.
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.

Carboxypeptidase A cleaves aromatic amino acids from the C terminus.

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

\[ \text{pepsinogen} \xrightarrow{H^+} \text{pepsin} \]
- general protease with preference for acidic & aromatic amino acids

Exocrine Pancreas secretion into the Small Intestine:
- trypsinogen \xrightarrow{\text{enteropeptidase}} \text{trypsin} \quad \{ \text{arginine, lysine} \}
- chymotrypsinogen \xrightarrow{\text{trypsin}} \text{chymotrypsin} \quad \{ \text{tryptophane, phenylalanine, tyrosine, leucine} \}
- proelastase \xrightarrow{\text{trypsin}} \text{elastase} \quad \{ \text{alanine, glycine, serine} \}
- procarboxypeptidases \xrightarrow{\text{trypsin}} \text{carboxypeptidases} \quad \{ \text{hydrophobic amino acids} \}
  \begin{align*}
  & \text{A} \quad \{ \text{basic amino acids} \\
  & \quad \{ \text{arginine, lysine} \}
  \end{align*}

Secretion by the Brush Border of the Small Intestine:
- aminopeptidases \{ many \}
Proenzymes (zymogens) → Active enzymes

Pepsinogen → Pepsin

Trypsinogen → Trypsin

Chymotrypsinogen → Chymotrypsin

Proelastase → Elastase

Procarboxypeptidases → Carboxypeptidases

HCL

enteropeptidase

trypsin

trypsin
Thank you