PROTEIN DIGESTION AND ABSORPTION

Dr. Bushra Mahmood Hussein
Chemical Pathologist

- Dietary proteins and endogenous proteins
- The intake of dietary protein is in the range of 50-100 g/day
- About 30-100 g/day of endogenous protein is derived form the digestive enzyme
- Dietary proteins are denatured on cooking & easily digested

- **Proteolytic enzymes are secreted as inactive zymogens & are converted to active form in the intestinal lumen**
- **Proteolytic enzymes include:**
- **Endopeptidases & Exopeptidases**
- **Endopeptidases:**
- **Act on peptide bonds inside the protein molecule, the protein becomes successively smaller & smaller units**
- **Ex. Trypsin, Chymotrypsin, and Elastase**

- **Exopeptidases:**
- **Act at the peptide bond, at the end region of the chain**
- **Ex. Carboxypeptidase acts on the peptide bond only at the carboxy terminal end**
- **Aminopeptidase, which acts on the peptide bond only at amino terminal end**

Digestion of proteins by gastric secretion

- Gastric juice contains HCL & a protease proenzyme namely pepsinogen
- Hydrochloric acid:
- Parietal (oxyntic) cells of gastric gland secrete HCL & pH of the stomach is <2
- HCL causes denaturation of proteins and killing of certain microorganisms
- The denatured proteins are more easily digested

Pepsin

- Secreted by the chief cells of stomach as inactive pepsinogen
- Pepsinogen is converted to pepsin by removal of 44 amino acids from the N-terminal end, by the HCL
- Pepsin is an endopeptidase & its optimum pH is around 2
- It catalyses hydrolysis of the bonds formed by carboxyl groups of Phe, Tyr, Trp and Met
- By the action of pepsin, proteins are broken into proteoses & peptones

Conversion of pepsinogen to pepsin

Pepsinogen $\xrightarrow{HCL}$ pepsin

Proteins $\xrightarrow{Pepsin}$ Proteoses & Peptones

Rennin

- Also called chymosin, is found in the stomach of infants & children
- Rennin is involved in the curdling of milk
- It converts milk protein casein to calcium paracaseinate which can be effectively digested by pepsin
- Rennin is absent in adults

Pancreatic Digestion of Proteins

- The optimum pH for the activity of pancreatic enzymes (pH 8) is provided by the alkaline bile & pancreatic juice
- The secretion of pancreatic juice is stimulated by the peptide hormones, Cholecystokinin and Pancreozymin
- Pancreatic juice contains endopeptidases, namely Trypsin, Chymotrypsin, Elastase & Carboxypeptidase & also secreted as zymogens (trypsinogen, chymotrypsinogen & pro-elastase)

Release and activation of zymogens

- The key enzyme for activation of zymogen is enteropeptidase produced by intestinal (mostly duodenal) mucosal epithelial cells
- Enteropeptidase cleaves off a hexapeptide (6 amino acid fragment) from the N-terminal end of trypsinogen to produce trypsin, the active enzyme
- Trypsin is the common activator of all other pancreatic zymogens to produce the active proteases, namely chymotrypsin, elastase and carboxypeptidase (A & B)

- Trypsin, chymotrypsin and elastase are endopeptidases active at neutral pH
- Gastric HCl is neutralized by pancreatic $NaHCO_3$ in the intestine & creates favourable pH for the action of proteases
- The amino acid serine is essential at the active centre to bring about the catalysis of all the three pancreatic proteases, hence these enzymes are referred to as serine proteases

Activation of inactive zymogens to active enzymes

Trypsinogen —Enteropeptidase→ Trypsin (active)

Chymotrypsinogen —Trypsin→ Chymotrypsin (active)

Proelastase —Trypsin→ Elastase (active)

Carboxypeptidases

- Trypsin & chymotrypsin degrade the proteins into small peptides; further hydrolysed into dipeptides & tripeptides by carboxypeptidases present in the pancreatic juice
- The procarboxypeptidase is activated by trypsin
- They are metalloenzymes requiring zinc
- The pancreatic proteases results in formation of free amino acids & small peptides (2-8 amino acids)

- **Carboxypeptidase A:**
- It is a metallo-enzyme (Zn protein)
- Secreted as procarboxypeptidase & activated by trypsin
- Exopeptidase, cannot act on peptide bond inside the protein
- Hydrolyses carboxyterminal end & liberates free amino acids
- **Carboxypeptidase B:**
- It is also an exopeptidase
- It hydrolyses carboxy terminal end of peptide bonds, connected with basic amino acids

Intestinal Digestion of Proteins

- The luminal surface of intestinal epithelial cells contains aminopeptidases and dipeptidases
- Aminopeptidase is a non-specific exopeptidase, cleaves N-terminal amino acids one by one to produce free amino acids & smaller peptides
- Dipeptidases act on different dipeptides to liberate amino acids

- Amino peptidases includes:
- Leucine aminopeptidase (LAP)
- It releases the N-terminal basic amino acids and glycine
- Proline amino peptidase or Prolidase
- It removes proline from the end of polypeptides
- Dipeptidases and tripeptidases
- They will bring about the complete digestion of proteins

Absorption of amino acids

- The absorption occurs mainly in the small intestine
- It is an energy requiring process
- The di- and tripeptides, after being absorbed are hydrolysed into free amino acids in the cytosol of epithelial cells
- The activities of dipeptidases are high in these cells
- After a protein meal, only the free amino acids are found in the portal vein

- L-Amino acids are more rapidly absorbed than D-amino acids
- The transport of L-amino acids occurs by an active process
- D-amino acids by a simple diffusion

Mechanism of absorption of amino acids

- Na^+ dependent active process & requires ATP
- Na^+ diffuses along the concentration gradient, the amino acid also enters the intestinal cell
- Na^+ & amino acids share a common carrier & transported together
- The compound cytochalasin Inhibits Na^+ independent transport system

Meister Cycle (Gamma Glutamyl Cycle)

- In intestines, kidney tubules and brain, the absorption of neutral amino acids is effected by the gamma glutamyl cycle
- Tripeptide glutathione (GSH) (gamma glutamyl cysteinyl glycine) is essential for Meister cycle
- It reacts with the amino acid to form gamma glutamyl amino acid
- This is catalyzed by gamma glutamyl transferase

- The glutamyl amino acid is then cleaved to give the free amino acid
- The net result is the transfer of an amino acid across the membrane
- The transport of one molecule of amino acid and regeneration of GSH requires 3 molecules of ATP

Absorption of intact proteins and polypeptides

- Immediately after birth, the small intestine of infants can absorb intact proteins and polypeptides
- The uptake of proteins occurs by a process known as endocytosis or pinocytosis
- The direct absorption of intact proteins is very important for the transfer of maternal immunoglobulin's (γ-globulins) to the offspring

- The intact proteins and polypeptides are not absorbed by the adult intestine
- The macromolecular absorption in certain individuals appears to be responsible for antibody formation that often causes food allergy

Abnormalities of protein digestion

- Defect in the pancreatic secretion impairs protein & fat digestion
- Loss of undigested protein in the feces along with the abnormal appearance of lipids
- Hartnup's disease:
- Characterized by the inability of intestinal & renal epithelial cells to absorb neutral amino acids
- Tryptophan absorption is most severely affected, results in symptoms of pellagra
- Impairment in the conversion of tryptophan to NAD^+ & $NADP^+$