General Protein Metabolism

Protein Digestion

Dietary proteins are very large complex molecules that cannot be absorbed from the intestine. To be absorbed, dietary proteins must be digested to small simple molecules (amino acids), which are easily absorbed from the intestine.

I- Digestion in the stomach
  Protein digestion begins in the stomach by gastric juice.

1- Role of gastric HCl
   - It causes denaturation of proteins.
   - It converts proteins to metaproteins, which are easily digested.
   - It activates pepsinogen to pepsin.
   - It makes pH in the stomach suitable for the action of pepsin.

2- Pepsin
   - It is an endopeptidase acting on central peptide bond in which amino group belongs to aromatic amino acids e.g. phenyl alanine, tyrosine and tryptophan.
   - It is secreted in an inactive form called pepsinogen.
   - Its optimum pH: 1.5-2.2
   - It is activated by HCl then by autoactivation.

   ![Pepsinogen to Pepsin Diagram]

3- Rennin
   - It is a milk-clotting enzyme.
   - It is present in stomachs of infants and young animals.
   - Its optimum pH: 4
   - It acts on casein converting it to soluble paracasein, which in turn binds calcium ions forming insoluble calcium paracaseinate. Calcium paracaseinate is then digested by pepsin.

   ![Casein to Calcium Paracaseinate Diagram]

4- Gelatinase
   - It is an enzyme that liquefies gelatin.

The end products of protein digestion in the stomach are proteoses, peptones and large polypeptides.

II- Digestion in the small intestine
  Digestion of proteins is completed in the small intestine by proteolytic enzymes present in pancreatic and intestinal juices.
A. Pancreatic Juice

1- Trypsin
- It is an endopeptidase that hydrolyzes central peptide bond in which the carboxyl group belongs to basic amino acids e.g. arginine, lysine and histidine.
- It is secreted in an inactive form called trypsinogen.
- Its optimum pH: 8
- It is activated by enterokinase enzyme then by autoactivation.

Trypsinogen ➔ Enterokinase ➔ Trypsin

Trypsinogen ➔ Trypsin

2- Chymotrypsin
- It is an endopeptidase that hydrolyzes central peptide bond in which the carboxyl group belongs to aromatic amino acids.
- It is secreted in an inactive form called chymotrypsinogen.
- It is activated by trypsin.
- Its optimum pH: 8

3- Elastase
- It is an endopeptidase acting on peptide bonds formed by glycine, alanine and serine.
- It is secreted in an inactive form called proelastase.
- It is activated by trypsin.
- It digests elastin and collagen.
- Its optimum pH: 8

4- Carboxypeptidase
- It is an exopeptidase that hydrolyzes the terminal (peripheral) peptide bond at the carboxyl terminus (end) of the polypeptide chain.
- It is secreted in an inactive form called procarboxypeptidase.
- It is activated by trypsin.
- Its optimum pH: 7.4

B. Intestinal Juice

1- Aminopeptidase
- It is an exopeptidase that acts on the terminal peptide bond at the amino terminus of the polypeptide chain.
- It releases a single amino acid

2- Tripeptidase
- It acts on tripeptides
• It releases a single amino acid and dipeptide

3- Dipeptidase
• It acts on dipeptides
• It releases 2 amino acids

The end products of protein digestion in the small intestine are amino acids

Protein Absorption

It is an active process that needs energy.
Energy needed is derived from hydrolysis of ATP.
It occurs in small intestine.
Absorption of amino acids is rapid in the duodenum and jejunum, but slow in the ileum.

Mechanisms of amino acids absorption

There are two mechanisms for amino acids absorption.
1- Carrier proteins transport system
2- Glutathione transport system (γ−Glutamyl cycle)

1- Carrier proteins transport system
• It is the main system for amino acid absorption.
• It is an active process that needs energy.
• The energy needed is derived from ATP.
• Absorption of one amino acid molecule needs one ATP molecule.
• There are 7 carrier proteins, one for each group of amino acids.
• Each carrier protein has two sites: one for amino acid and one for Na⁺.
• It co-transport amino acid and Na⁺ from intestinal lumen to cytosol of intestinal mucosa cells.
• The absorbed amino acid passes to the portal circulation, while Na⁺ is extruded out of the cell in exchange with K⁺ by sodium pump.
Cell membrane

Intestinal lumen

Cytosol

Portal circulation

Amino acid

Na$^+$

Carrier protein

Amino acid

Na$^+$

ATPase

K$^+$

ATP

ADP + Pi

Carrier Protein Transport System
2- Glutathione transport system (γ−Glutamyl cycle)

- Glutathione is used to transport amino acids from intestinal lumen to cytosol of intestinal mucosa cells.
- It is an active process that needs energy.
- The energy needed is derived from ATP.
- Absorption of one amino acid molecule needs 3 ATP molecules.
- Glutathione reacts with amino acid in the presence of γ−glutamyl transpeptidase to form γ−glutamyl amino acid.
- γ−glutamyl amino acid releases amino acid in the cytosol of intestinal mucosa cells with formation of 5-oxoproline that is used for regeneration of glutathione to begin another turn of the cycle.

Oxoprolinuria

It is a disease caused by a defect in glutathione synthetase enzyme
It is characterized by accumulation of 5-oxoproline in blood and hence excreted in urine. It is associated with mental retardation.
Glutathione transport system (γ-Glutamyl cycle)

Intestinal lumen

Cell membrane

Amino acid

γ-Glutamyl transpeptidase

γ-Glutamyl Cysteinyglycine

Cytosol

ADP + P\textsubscript{i}

ATP

γ-Glutamyl cysteine

γ-Glutamyl amino acid

Amino acid

5 oxoproline

Glutamic acid

Glycine

Cysteine

Cysteinyglycine

ATP

ADP + P\textsubscript{i}