11 Digestion and Absorption of Carbohydrates, Lipids and Proteins

DIGESTION OF CARBOHYDRATES

Dietary carbohydrates principally consists of the

- ***Polysaccharides:*** starch and glycogen. It also contains • ***disaccharides:*** sucrose (cane sugar), • lactose (milk sugar) and • maltose and in small amounts ***monosaccharides*** like • fructose and • pentoses. Liquid food materials like milk, soup, fruit juice escape digestion in mouth as they are swallowed, but solid foodstuffs are masticated thoroughly before they are swallowed.

1. Digestion in Mouth: Digestion of carbohydrates start at the mouth, where they come in contact with saliva during mastication.

- Saliva contains a carbohydrate splitting enzyme called salivary ***amylase (ptyalin).***
- ***Action of Ptyalin (salivary amylase):*** It is ***α-amylase,*** requires Cl^- ion for activation and optimum pH 6.7 (range 6.6 to 6.8). The enzyme hydrolyzes α-1-4 glycosidic linkages at random deep inside polysaccharide molecule like starch, glycogen and dextrins, producing smaller molecules *maltose, glucose* and trisaccharide *maltotriose*. Ptyalin action stops in stomach when pH falls to 3.0.

$$\text{Starch, Glycogen and Dextrins} \xrightarrow{\alpha\text{-Amylase}} \text{Glucose, Maltose and Maltotriose}$$

hydrolyzed to equimolar amounts of glucose and fructose by HCl.

3. Digestion in Duodenum: Food bolus reaches the duodenum from stomach where it meets the pancreatic juice. Pancreatic juice contains a carbohydrate-splitting enzyme ***pancreatic amylase*** (also called ***amylopsin***) similar to salivary amylase.

Action of Pancreatic Amylase: It is also an ***α-amylase,*** optimum pH 7.1. Like *ptyalin* it also requires Cl^- for activity. The enzyme hydrolyzes α-1→4 glycosidic linkage situated well inside polysaccharide molecule. Other criteria and end products of action are similar to ptyalin.

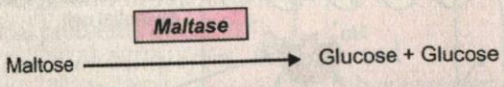
4. Digestion in small Intestine: ***Action of Intestinal Juice:***

- ***Intestinal amylase:*** This hydrolyzes terminal α-1→4, glycosidic linkages in polysaccharides and oligosaccharide molecules liberating free glucose molecule.
- ***Lactase:*** It is a β-galactosidase, its pH range is 5.4 to 6.0. Lactose is hydrolyzed to equimolar amounts of glucose and galactose.

$$\text{Lactose} \xrightarrow{\text{Lactase}} \text{Glucose + Galactose}$$

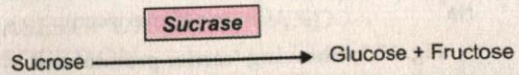
- ***Isomaltase:*** It catalyzes hydrolysis of α-1→6 glycosidic linkage, thus splitting α-limit dextrin at the branching points and producing maltose and glucose.

ties of two glucose molecules. Its pH range is 5 8 to 6.2.



Five maltases have been identified in intestinal epithelial cells.
Maltase V can act as *isomaltase* over and above its action on maltose.

- *Sucrase:* pH range 5.0 to 7.0. It hydrolyzes sucrose molecule to form equimolar quantities of glucose and fructose.
  Maltase III and ***maltase IV*** also **have *sucrase* activity**



ABSORPTION OF CARBOHYDRATES

It is observed from above that carbohydrate digestion is complete when the food materials reach small intestine and all complex dietary carbohydrates like starch and glycogen and the disaccharides are ***ultimately converted to simpler monosaccharides.***

- All monosaccharides, products of digestion of dietary carbohydrates, are practically completely absorbed almost entirely from the small intestine.
- Rate of absorption diminishes from above downwards; proximal jejunum three times greater than that of distal ileum.
- It is also proved that some disaccharides, which escape digestion, may enter the cells lining the intestinal lumen may be by ***"pinocytosis"***; and are hydrolyzed within these cells.

Note: No carbohydrates higher than the monosaccharides can be absorbed directly into the

A portion enters in thoracic lymph, but the majc portion passes into the portal blood, and carrie directly to liver.

- **Cori** studied the rate of absorption of differer sugars from small intestine in rat. Takin glucose absorption as 100, comparative ra of absorption of other sugars were found a follows:

Galactose	Glucose	Fructose	Mannose
110	100	43	19

Xylose	Arabinose
15	9

- The above study proves that ***glucose ar galactose are absorbed very fast;*** fructose ar mannose intermediate rate and the pentos are absorbed slowly. ***Galactose is absorb more rapidly than glucose.***

MECHANISMS OF ABSORPTION

Two mechanisms are involved.

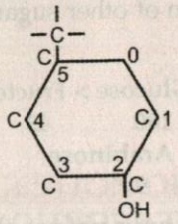
1. Simple Diffusion: This is dependent on sug concentration gradients between the intestin lumen, mucosal cells, and blood plasma. All t monosaccharides are probably absorbed to son extent ***by simple "passive" diffusion.***

2. Active Transport Mechanisms:

- ***Glucose*** and ***galactose*** are absorbed ve rapidly and hence it has been suggested th they are ***absorbed actively*** and ***it requi energy.***
- Fructose absorption is also rapid but not much as compared to glucose and galacto but it is definitely faster than pentoses. Hen fructose is not absorbed by simple diffusi alone and it is suggested that some mecl nism facilitates its transport, called as ***fac tated transport.***

WILSON AND CRAINE'S HYPOTHESIS

- They must have a ***six-membered ring***
- Secondly, they **must have one or more carbon atoms attached to C5,** and
- Thirdly, they must have ***α-OH group at C-2*** with the same stereoconfiguration as occurs in D-glucose.



Note: -OH group on carbon 2 and 5 hydroxymethyl or methyl group on the pyranose ring appear to be essential structural requirements for the active transport mechanism.

Craine and his collaborators explain active transport by envisaging the presence of a ***Carrier protein (transport protein)*** in the brush border of intestinal epithelial cell. The "carrier protein" has the following characteristics:

- It has ***two binding sites one for sodium and another for the glucose***
- The carrier protein is ***specific for sugar.***
- It is ***mobile***
- It is ***sodium-dependent***
- It is ***energy-dependent***

Energy: Energy is provided by ATP.

- It is believed that ***sodium binding by the carrier protein is a prerequisite for glucose binding.*** Sodium binding changes the conformation of the protein molecule, enabling the binding of glucose to take place and thus the absorption to occur. It is presumed that analogous "carrier protein" exists for D-galactose also ***(Fig. 11.1).***

Absorption of Other Sugars

- Sugars like D-fructose and D-mannose are

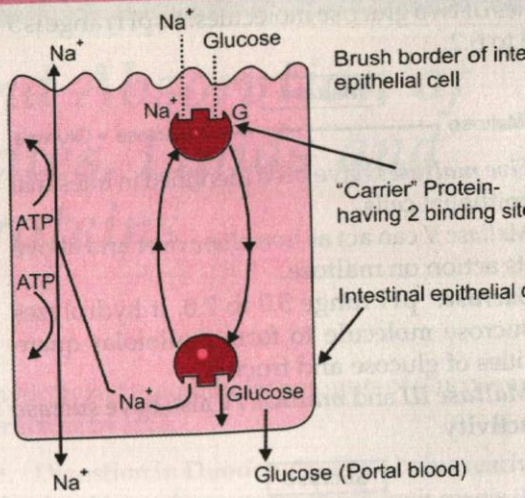


Fig. 11.1: Showing 'carrier protein' and transport of glucose

Factors Influencing Rate of Absorption

1. ***State of mucous membrane and length of of contact:*** If mucous membrane is not hea absorption will suffer. Similarly in hurried bo length of contact is less as such absorption wi less.
2. ***Hormones:***
   - ***Thyroid hormones:*** These increase absorp of hexoses and act directly on intest mucosa.
   - ***Adrenal cortex:*** Absorption decrease adrenocortical deficiency, mainly due to reased concentration of sodium in body fl
   - ***Anterior pituitary:*** This affects absorp mainly through its influence on thyro Hyperpituitarism induces thyroid overacti and *vice versa.*
   - ***Insulin: This has no effect on absorptio glucose.***
3. ***Vitamins:*** Absorption is diminished in st

DIGESTION OF LIPIDS

The digestion of fats and other lipids poses a special problem because of:

- The ***insolubility of fats in water***, and
- Because ***lipolytic enzymes***, like other enzymes, are ***soluble in an aqueous medium.***

The above problem is solved in the ***gut by emulsification of fats, particularly by bile salts, present in bile and PL.*** The breaking of large fat particles or oil globules, into smaller fine particles by emulsification increases the surface exposed to interaction with lipases and, thus, the rate of digestion is proportionally increased.

PHASES OF DIGESTION AND ABSORPTION

The whole process of digestion of dietary lipids and its subsequent absorption may be arbitrarily divided into ***three phases:***

- ***Preparatory phase:*** Which includes the digestion of lipids in the intestine. The large lipid particles are broken down into smaller particles with the help of lipolytic enzymes.
- ***Transport phase:*** Which includes the transport of digested fats across the membrane of intestinal villous layer into intestinal epithelial cells.
- ***Transportation phase:*** Which includes the events of action that take place inside intestinal epithelial cells and its passage through lacteals to Lymph/or in portal blood.

Dietary Sources of Lipids: The chief dietary sources of lipids in human beings:

- ***Animal source:*** Dairy products like milk, butter, ghee, etc. meat and fish, especially pork, eggs.
- ***Vegetable source:*** Various cooking oils from various seeds, viz. sunflower oil, groundnut oil, cotton seed oil, mustard oil, etc. and fats

Lingual Lipase:

- The pH range of activity is 2.0 to 7.5 (optim pH value is 4.0 to 4.5). *Lingual lipase* activi is continued in the stomach also where th pH value is low. Due to retention of foo bolus for 2 to 3 hours, about 30 percent dietary triacyl glycerol (TG) may be digeste
- ***Lingual lipase*** is more active on TG havir shorter FA chains and is found to be mo specific for ester linkage at 3-position rath than position-1.
- Milk fats contain short and medium chain F which tend to be esterified in the 3-positio Hence, ***milk fat appears to be the best substra for this enzyme.*** The released short chain fat acids are relatively more soluble an hydrophilic and can be absorbed directly fro the stomach wall and enter the portal vein.

Gastric Lipase: There is evidence of presence small amounts of *gastric lipase* in gastric secretio The overall digestion of fats, brought about b gastric lipase is negligible because:

- No emulsification of fats takes place i stomach,
- The enzyme secreted in small quantity,
- pH of gastric juice is not conducive which highly acidic, whereas gastric lipase activit is more effective at relatively alkaline pH (average pH 7.8).
- *Gastric lipase* activity requires presence Ca^{++}. Activity of gastric lipase is seen whe intestinal contents are regurgitated into th gastric lumen.
- Recent studies have shown that gastric lipas is not capable of hydrolyzing fats containin long-chain FA. Whatever minimal action gastric lipase is there, it is confined to highl emulsified fats, viz. those of milk fats or fat present in egg-yolk or fats with short chai

f food from the stomach. ***Thus, fats have a high atiety value.***

. Digestion in Small Intestine: The major site f fat digestion is the small intestine. This is due o presence of a powerful lipase, ***steapsin*** in the ancreatic juice and presence of bile salts which cts as an effective emulsifying agent for fats. ancreatic juice and bile enter the upper small ntestine, the duodenum, by way of the pancre- tic and bile ducts respectively. Secretion of pan- reatic juice is stimulated by the

- Passage of an acid gastric contents (acid chyme) into the duodenum, and
- By secretion of the GI hormones, *secretin* and CCK-PZ.

Secretin increases the secretion of electrolytes and fluid components of pancreatic juice, whereas ***pancreozymin of CCK-PZ***, stimulates the secretion of the pancreatic enzymes. ***Cholecystokinin*** of ***CCK-PZ***, in turn, cause contraction of the gall bladder and discharge the bile into the duodenum. Discharge of bile is also stimulated by *secretin* and bile salts themselves.

Hepatocrinin released by the intestinal mucosa stimulates more bile formation which is relatively poor in the bile salt content.

The above sequence of events prepares the small intestine for the digestion of fats.

LIPOLYTIC ENZYMES IN PANCREATIC JUICE

Pancreatic juice has been shown to contain a number of lipolytic enzymes:

- ***Pancreatic lipase (steapsin),***
- ***Phospholipase A_2 (lecithinase),*** and
- ***Cholesterol esterase.***

The pancreatic lipase is the most important which hydrolyzes TG containing short-chain FA as well as long-chain FA. Other two enzymes are required for phospholipids / and cholesterol respectively.

Pancreatic Lipase (Steapsin): It is an *esterase* with

- Bile salts help in combination of *"lipase"* with two molecules of a small protein called as ***colipase*** (mol wt = 10,000) in the intestinal lumen. ***This combination of lipase with colipase has two effects:***
  - enhances the lipase activity of the intestinal pH,
  - also protects the enzyme against inhibitory effects of bile salts and against surface denaturation
- Bile salts also help in emulsification of fats.

2. Role of Ca^{++}: In the presence of Ca^{++} in the intestine, the FFA are immediately precipitated as "soaps" (insoluble Ca-soaps) and are thereby prevented from inhibiting further lipase action. Thus, ***Ca^{++} facilitates lipase action.***

Mode of Action of Pancreatic Lipase: The complete hydrolysis of fats (TG) produces glycerol and FA. ***Pancreatic lipase is virtually specific for the hydrolysis of "primary ester linkage". It cannot readily hydrolyze the ester linkage of position-2(β), if it does so it occurs at a very slow rate.***

- Digestion of TG molecule by pancreatic lipase proceeds:
  - First by removal of a terminal FA to produce an ***"α, β-diglyceride"***, and
  - The other terminal FA is then removed to produce a ***"β-monoglyceride"***.
- Since the last FA at position (Sn-2) is linked by a secondary ester group and as it cannot be hydrolyzed easily by pancreatic lipase, the ***β-monoglyceride is first converted to α-monoglyceride*** by isomerization ***by an isomerase enzyme.*** Then the α-monoglyceride is hydrolyzed by pancreatic *lipase*.
- Sequence of events that occurs in the intestinal lumen is shown schematically in *Fig. 11.*
- As it is seen from above, by the action of ***pancreatic lipase*** and **isomerase** α and

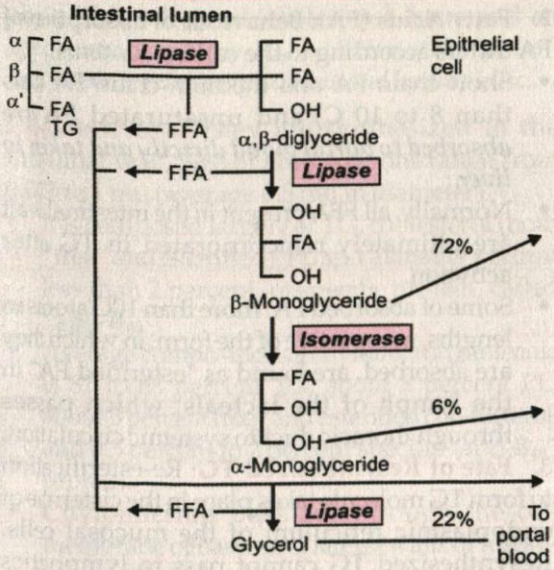


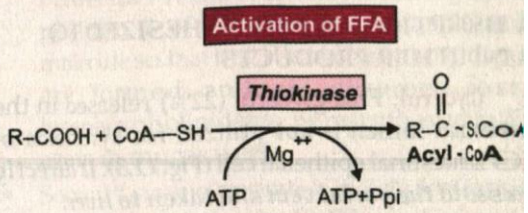
Fig. 11.2: Sequence of events in intestinal lumen

"Micelle" Formation:

- Bile salts and soaps formed in the intestinal lumen and bicarbonates of pancreatic and intestinal juices, collect the molecules of higher FA, mono- and diglycerides, lecithins, cholesterol, etc. in the form of ***water-soluble molecular aggregates*** called ***mixed micelles,*** which are much smaller than the droplets of emulsified fats (size 0.1 to 0.5 μ in diameter) and are absorbed mainly from duodenum and jejunum.
- Bile salts of the "micelles" are not absorbed at this point but are redissolved in other emulsoid particles. ***They are reabsorbed later in the lower part of the small intestine and return to the liver*** via the portal vein for resecretion into the bile. This is known as ***entero-hepatic circulation of bile salts.***

B. TRANSPORT PHASE

- Short and medium chain FA (6 to 10 C) and unsaturated FA are more readily absorbed than the long chain FA (12 to 18 C). Also, the short chain FA appears to enhance the absorption of fats in general, whereas long chain FA tend to impair the process.
- *Pinocytosis* does not appear to play a significant role in fat absorption as was formerly believed; probably less than 5 per cent absorbed in emulsified forms may be absorbed by pinocytosis.
- The products of digestion next appear to be taken up by the smooth endoplasmic reticulum and ***re-synthesized into TG*** again by enzymes present in the membrane and/or cavities of the reticulum.



- There is a merging of the smooth endoplasmic reticulum into rough endoplasmic reticulum, in which probabaly enzymes for TG resynthesis are formed as well as the protein component (apo-B_{48}) of lipoprotein complex ***chylomicron.***

C. TRANSPORTATION PHASE

Sequence of events inside the intestinal mucosal cell is as follows:

- Within the intestinal epithelial cell, α-monoglycerides (6%) are further hydrolyzed by *intestinal lipase* to produce freeFA and glycerol.

Intestinal Lipase: A lipase distinct from that of the pancreatic lipase is present in the intestinal mucosal cell. Principal action of this enzyme is confined within epithelial cell.

- *Note that glycerol released within the intestinal wall cells are reutilized for TG resynthesis.* Glycerol is converted to α-glycerol-(P) by *glycerokinase* in presence of ATP. Some amount of α-glycero-(P) can be contributed from glycolysis operating in intestinal epithelial cell. α-glycero (P) thus formed combines with "acyl-CoA" to form TG molecule.
- β-monoglyceride (72%) which is absorbed from intestinal lumen can combine directly with "acyl CoA" to reform TG. Sequence of events that takes place in resynthesis of TG is shown in *Fig. 11.3.*

ABSORPTION OF LIPIDS

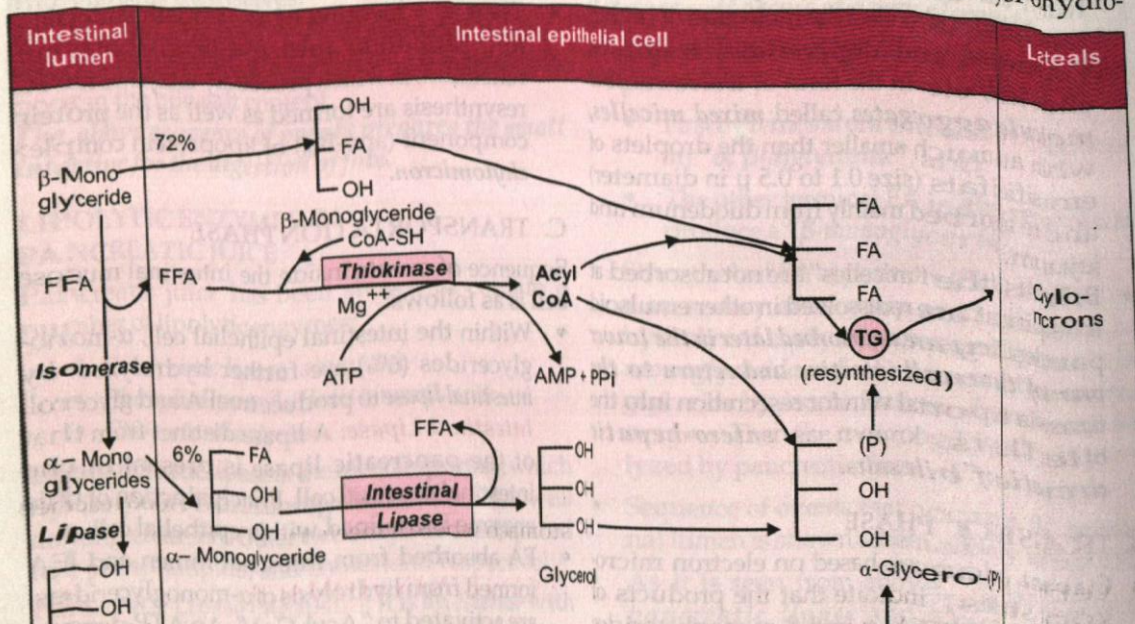
ABSORPTION OF RESYNTHESIZED TG AND OTHER PRODUCTS

1. Glycerol: Free glycerol (22%) released in the intestinal lumen is *not* utilized for synthesis of TG in intestinal epithelial cell *(Fig.11.3). It directly passes to the portal vein and taken to liver.*

2. Fatty Acids (FA): Behaviour of absorpon of FA differs according to the carbon content

- Short-chain FA and medium-chain F (less than 8 to 10 C) and unsaturated FA *are absorbed to portal blood directly and taken to liver.*
- Normally, all FFA present in the intestinal wall are ultimately reincorporated in TG after activtion.
- Some of absorbed FA, more than 10C atoms in lengths, irrespective of the form, in which they are absorbed, are found as "esterified FA" in the lymph of the lacteals, which passes through thoracic duct to systemic circlation.

3. Fate of Resynthesized TG: Re-esterication to form TG molecule takes place in the cisternae of endoplasmic reticulum of the mucosal cells. Resynthesized TG cannot pass to lymphatics (lacteals) nor to portal blood as it is insoluble in water (hydrophobic). ***Hence, it is converted to water soluble lipoprotein complex called chylomicrons.*** Each droplet of hydrophobic and water insoluble TG gets covered with a layer of hydro-



philic PL, cholesterol/cholesterol esters and an apoprotein called ***apo-B_{48}. Addition of the "polar" ions make it relatively soluble and hydrophilic.***

Chylomicrons: They are synthesized in the intestinal wall. Size of chylomicrons range from 0.075 to 1 mμ (average 0.5 mμ in diameter)

- It is composed largely of TG, cholesterol (both "free" and esterified), PL and a smaller percent less than 2 percent, of specific protein, called "**apo-B_{48}**".
- Average composition of chylomicron molecule is 87 to 88 percent TG, about 8 percent PL, about 3 percent free/and esterified cho-lesterol, and 0.5 percent to 2 percent specific "apo-B_{48}" protein.
- Chylomicrons pass out through the cell membrane of bases and lateral walls of intestinal epithelial cells, and moves through extracellular spaces between those cells to enter lymphatic vessels of abdominal region, and later goes to systemic circulation through the thoracic duct.

DIGESTION AND ABSORPTION OF CHOLESTEROL:

- Pancreatic juice contains an enzyme ***cholesterol esterase***, which may either catalyze the esterification of free cholesterol with FA or it may also catalyze the opposite reaction, i.e. hydrolysis of cholesterol esters. In the intestinal lumen, depending on the equilibrium, the "cholesterol-esters" are hydrolyzed by this enzyme. ***Thus, cholesterol appears to be absorbed from the intestine almost entirely in "free" (unesterified) form.*** Nevertheless, 85 to 90 percent of the cholesterol in the lymph is found to be in esterified form, indicating that esterification of cholesterol, like that of FFA, must take place within the

DIGESTION AND ABSORPTION OF PHOSPHOLIPIDS:

- Dietary phospholipids may be absorbed fro intestine without any digestion. Due to polar structure and hydrophilic propertie they are ***absorbed directly to portal blood a taken to liver.***
- Pancreatic juice contains an enzyme call ***phospholipase A_2*** **(or *lecithinase*)**. It is *esterase*, and secreted as an inactive zymog "proenzyme", which is changed to active for by hydrolysis of a peptide molecule with t help of *trypsin*.
- In the presence of bile salts and Ca^{++}, the acti *phospholipase* B_2 hydrolyzes the ester linka between a FA and secondary alcohol group position 2 of glycerol in a phospholip molecule so that free FA and lysophospholip are formed and are absorbed. Son lysophospholipid may be resynthesized to l again in mucosal cell.
- Some PL is incorporated in "chylomicron synthesis and also for VLDL synthesis in i testinal mucosal cell and carried in lympha vessels.

DIGESTION OF PROTEINS

Dietary Proteins: Proteins which we take in o diet are either from animal source or vegetab source.

- ***Animal sources:*** Milk and dairy produc meat,fish, liver, eggs.
- ***Vegetable sources:*** Cereals, pulses, peas a beans, nuts.

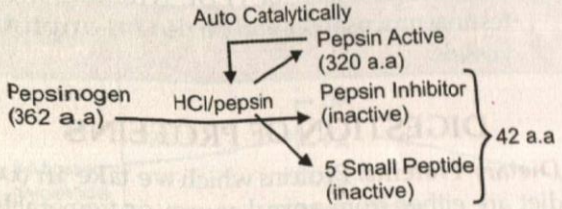
DIGESTION IN MOUTH

There are ***no proteolytic enzymes in mouth***. Af mastication and chewing, the bolus of food reach

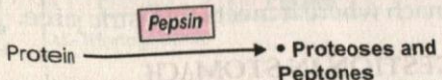
- *Pepsin,*
- *Rennin,*
- *Gastriscin,*
- *Gelatinase.*

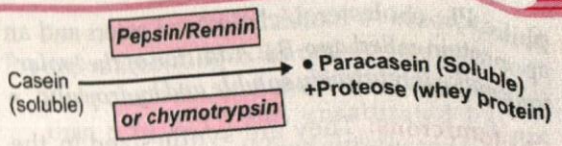
1. Pepsin: It is a potent proteolytic enzyme and is present in gastric juice of different species including the mammals.

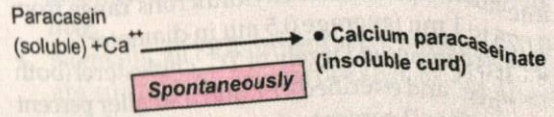
- It is secreted as inactive ***zymogen*** form, ***pepsinogen,*** having a mol wt of 42,500 approx. it is synthesized in **"chief cells"** of stomach, and 99 percent is poured in gastric juice as *pepsinogen*. Remaining 1 percent is secreted in the blood stream from where it is ultimately excreted in the urine. ***Urinary pepsin is known as uropepsin.***
- Pepsinogen is hydrolyzed in the stomach with the help of HCl or pepsin itself ***(autocatalytically)*** to form the **"active"** ***pepsin*** (mol wt = 34,500).
- In the process of activation,
  - An inactive peptide called as ***"pepsin inhibitor"***. (mol wt 3242), and
  - 5 smaller peptides are liberated.



- HCl maintains the gastric pH at about 1 to 2 and ensures maximum pepsin activity. Optimum pH for pepsin is 1.6 to 2.5 and pepsin gets denatured if the pH is greater than 5.
- ***Pepsin is a proteinase,*** a nonspecific endopeptidase, and it hydrolyzes peptide bonds well inside the protein molecule and produces *proteoses* and *peptones*.







Action of Pepsin on Milk: Pepsin can act on milk. It hydrolyzes the soluble phosphoprotein "casein" of milk to produce ***"paracasein"*** and a proteose, the latter is the whey protein. Paracasein is then precipitated as ***"ca-paracaseinate"*** which is further digested by pepsin to peptones.

2. Action of Rennin: ***Rennin is absent in adult humans,*** and many non-ruminants. Certain amount of rennin activity is seen in babies in infancy. In the calf, it is secreted in zymogen form ***prorennin,*** which is activated in the stomach to form ***active rennin*** (mol wt 40,000) and in the process of activation an inactive peptide is split off. Optimum pH for activity is 4.0 and specificity of action is very similar to pepsin, in that it ***hydrolyzes peptide bonds connected with L-aromatic amino acids.*** Like pepsin, it also acts on casein of milk to form paracasein which is immediately precipitated by Ca^{++}. Thus it also coagulates milk like *pepsin* (see above).

3. Gastricin: The enzyme is secreted in the gastric juice of humans as inactive zymogen form, which is activated in presence of HCl. Optimum pH is 3 to 4. It acts as *Proteinase* and requires an acidic medium for its activity.

4. Gelatinase: Gelatin is hydrolyzed by the enzyme *gelatinase* present a gastric juice to form polypeptides. It acts in an acidic medium.

DIGESTION IN DUODENUM

The bolus of blood after leaving stomach reaches

- *Trypsin,*
- *Chymotrypsin,*
- *Carboxy peptidases,*
- *Elastases, and Collagenases.*

1. Trypsin: Trypsin, a ***proteinase***, is secreted as an inactive zymogen form ***trypsinogen***, which is activated to form ***active Trypsin***, which has strong proteolytic activity and an inactive hexapeptide which is produced and liberated during the process of activation ***(Fig. 11.4).***

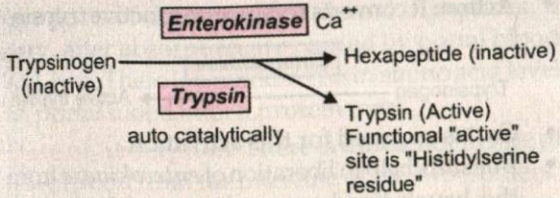


Fig. 11.4: Process of activation of trypsin

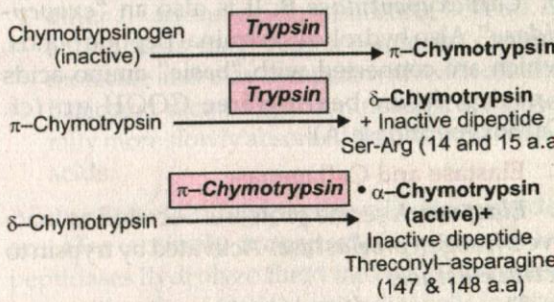
- Activation is brought about by:
  - A glycoprotein enzyme known as ***entero kinase*** of the intestinal juice at a pH of 5.5 and
  - Also by ***trypsin itself*** once it is formed, ***autocatalytically,*** at a pH of 7.9.
  - Ca^{++} also is required for the activation.
- Trypsin acts in an alkaline medium pH 8 to 9 (optimum pH 7.9).

Note:

- Though trypsin is a strong proteolytic enzyme, it cannot hydrolyze any peptide bond with proline residue.
- ***Trypsin-inhibitors:***
  Our food may contain trypsin-inhibitors, for example;
  - Egg-white contains water soluble muco-protein, a very potent trypsin inhibitor,
  - Human and bovine colostrum and raw

2. Chymotrypsin: Chymotrypsin, a ***proteinase*** is secreted as inactive zymogen ***chymotrypsinogen,*** which is activated by trypsin and completed by chymotrypsin which ***acts autocatalytically. Three chymotrypsinogens A, B and C are found in pancreatic juice*** of vertebrates. During its activation two inactive peptides are liberated in two stages:

- Seryl-arginine dipeptide (a.a 14 to 15) and
- Threonyl-asparagine (a.a 147 and 148)



α-Chymotrypsin: Also included under ***serine proteases*** like trypsin.

- Optimum pH = 7 to 8
- α-Chymotrypsin converts the proteose peptones and peptides to smaller peptides and amino acids.

Action of Chymotrypsin on Milk: α-Chymotrypsin can hydrolyze milk protein casein into paracasein and a proteose (whey protein). Paracasein is then precipitated by a spontaneous reaction with Ca^{++} and forms Ca paracaseinate.

3. Carboxypeptides: There are **two types** of carboxy peptidases.

- ***Carboxypeptidase A***
- ***Carboxypeptidase B***

a. ***Carboxy Peptidase A***: It is a metallo-enzyme contains zinc (*Zn-protein*).

- Secreted as inactive zymogen ***Pro-carbo***

procarboxy peptidase A to *active carboxy peptidase A* (see ahead).

- It is an *exopeptidase* and cannot act on peptide bonds well inside the protein molecule. *The enzyme hydrolyzes the terminal peptide bond* connected to an end a.a bearing free α-COOH group, particularly if the end a.a is *Tyr, Phe or Trypt. It liberates the end a.a as "free" form, so that the peptide becomes shorter by one a.a.*

b. *Carboxypeptidase B*: It is also an *"exopeptidase"*. Also hydrolyzes terminal peptide bonds, which are connected with "basic" amino acids e.g. *Arg, lysine* bearing free COOH gr. (cf. Carboxypeptidase A)

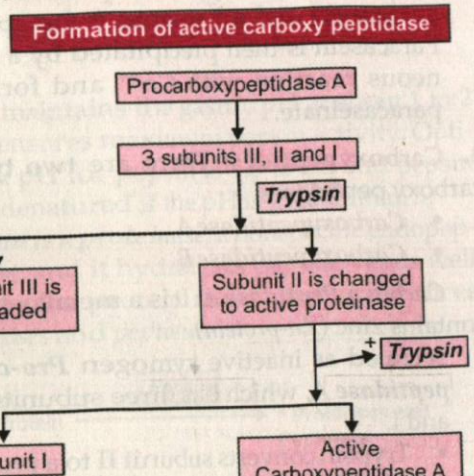
4. Elastase and Collagenase

a. Elastase: A serine protease. Secreted as inactive zymogen *proelastase*. Activated by trypsin to *active elastase*.

- The enzyme has maximum activity on peptide bonds connected to carbonyl groups of neutral aliphatic a.a.

b. Collagenase: An enzyme which can act on proteins present in collagen.

Both the enzymes can digest yellow and white connective tissue fibres respectively to yield peptides.



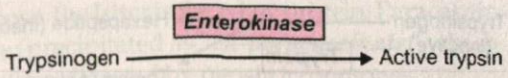
DIGESTION IN SMALL INTESTINE

Proteolytic enzymes present in intestinal juice are

- *Enterokinase*
- *Amino peptidases*
- *Prolidase*
- *and tri and Di-peptidases.*

1. Enterokinase: Also Known as *enteropeptidase*. A glycoprotein enzyme, also present in the epithelial cells of brushborder of duodenal mucosa and secreted in duodenum.

- **Action:** It converts trysinogen to active trypsin.



- Ca^{++} is required for this activation.
- *Bile salts* help in liberation of *enterokinase* from the brush border membrane of intestinal epithelial cells to intestinal lumen.

2. Aminopeptidases: Best example of aminopeptidase is LAP (leucine aminopeptidase)

- Can hydrolyze peptides to tripeptides.
- Cannot hydrolyze a dipeptide
- Requires presence of Zn^{++}, Mn^{++} and Mg^{++} which help in formation of a metal-enz-substrate coordination complex for the catalysis.

3. Prolidase: An *exopeptidase*, can hydrolyze a proline peptide of collagen molecule, acts on terminal peptide bond connected to proline as end a.a, liberating a proline molecule.

4. Tri and Di-peptidases: These enzymes hydrolyze the peptides at either of two places:

- In microvillus membrane of intestinal epithelial cells, or
- Inside the epithelial cells after the peptides have been absorbed inside the cell.

- *Tri-peptidase* acts on a tripeptide and produces a dipeptide and free a.a.
- A *dipeptidase* hydrolyzes a dipeptide to produce two molecules of amino acids.
- They require the presence of Mn^{++}, Co^{++} or

ABSORPTION OF AMINO ACIDS

Under normal circumstances, the dietary proteins are almost completely digested to their constituent amino acids. But some amounts of oligopeptides like tri and dipeptides may remain as such. The above products of digestion are rapidly absorbed.

Site of Absorption: ***Amino acids are absorbed from ileum and distal jejunum.*** Oligopeptides like di and tri peptides are absorbed from duodenum and proximal jejunum.

How they Reach Liver?: Amino acids and other products of digestion like di- and tripeptides, if any, after absorption are carried by portal blood to Liver. There is a marked rise in amino acid level in portal blood after a protein meal.

Rate of Absorption: There is difference in rate of absorption from the intestine of the two isomers.

- ***L-amino acids and L-peptides are absorbed more rapidly than D-isomers*** and they have been shown to be absorbed by ***active transport*** process. *L*-aminoacids are actively transported across the intestine from mucosa to serosal surface. Pyridoxal-(P) (B_6-PO_4) is probably involved in this process.
- *D*-amino acids are absorbed slowly and they are absorbed by ***simple passive diffusion.***

Mechanism of Absorption of L-amino acids-Ion gradient hypothesis:

L-amino acids are absorbed from small intestine by ***sodium (Na^+) dependent, carrier-mediated process.*** This transport is ***energy dependent*** and ***energy is provided by ATP*** (similar to absorption of glucose and galactose).

Note: Different classes of *L*-amino acids viz. diamino acids, small neutral a.a., iminoacids, and large neutral a.a are believed to be absorbed by different "carrier" protein molecules present in the microvillus membrane of intestinal cells.

- High concentration of one *L*- aminoacid sometimes reduces the rate of absorption of some other *L*- amino acids, indicating several *L*-amino acids may share a common "carrier" molecule and may compete with each other.
- Basic and dicarboxylic aminoacids are generally more slowly absorbed than neutral amino acids.

Absorption of *L*-Oligopeptides: *L*- oligopeptides are ***also actively transported.*** Intracellular peptidases hydrolyze them into a.a. This hydrolysis within the intestinal epithelial cells is rapid enough to keep peptide concentration low in these cells. Transport mechanisms for *L*-peptides appear to be independent of *L-amino acids*.

Role of Glutathione in Amino Acid Absorption

Meister has proposed that ***glutathione participates in an "active group translocation" of L-amino acids (except L-proline)*** into the cells of small intestine, kidneys, seminal vesicles, epididymis and brain. He proposed a "cyclic" pathway, in which the glutathione is regenerated again, and it is called ***γ-glutamyl cycle*** (***Fig. 11.5***).