First Lecture

Digestion of Carbohydrate

Dietary carbohydrates principally consist 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 foodstuffs 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 starts at the mouth, where they come in contact with saliva during mastication. Saliva contains a carbohydrate splitting enzyme called *salivary amylase (ptyalin)*.



- **2. Digestion in stomach:** Practically no action. *No carbohydrate splitting enzymes available in gastric juice*. Some dietary sucrose may be hydrolysed 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.

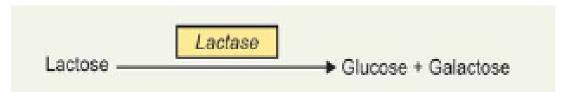
Action of Pancreatic Amylase

It is also an α -amylase, optimum pH 7.1 Like ptyalin it also requires Cl for activity. The enzyme hydrolyses α - 1 \rightarrow 4 glycosidic linkage situated well inside polysaccharide molecule. Other criteria and end products of action similar to ptyalin.

4. Digestion in Small Intestine

Action of Intestinal Juice

- *Intestinal amylase:* This hydrolyses terminal α -1 \rightarrow 4, glycosidic linkage 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 hydrolysed to equimolar amounts of glucose and galactose.



- Isomaltase: It catalyses hydrolysis of α -1 \rightarrow 6 glycosidic linkage, thus splitting α -limit dextrin at the branching points and producing maltose and glucose.
- *Maltase:* The enzyme hydrolyses the α -1 \rightarrow 4 glycosidic linkage between glucose units in maltose molecule liberating equimolar quantities 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 hydrolyses sucrose molecule to form equimolar quantities of glucose and fructose. Maltase III and maltase IV also have sucrase activity



Absorption of Carbohydrate

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 hydrolysed within these cells. No carbohydrates higher than the monosaccharides can be absorbed directly into the bloodstream in normal health and if administered

parenterally, they are eliminated as foreign bodies.

• **Cori** studied the rate of absorption of different sugars from small intestine in rat. Taking glucose absorption as 100, comparative rate of absorption of other sugars were found as follows.

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

Mechanism of Absorption

Two mechanisms are suggested:

1. Simple diffusion: This is dependent on sugar concentration gradients between the intestinal lumen, mucosal cells and blood plasma. All the monosaccharides are probably absorbed to some extent by simple 'passive' diffusion.

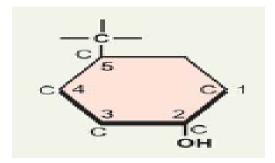
2. "Active" Transport Mechanisms

- Glucose and galactose are absorbed very rapidly and hence it has been suggested that they are *absorbed actively and it requires energy*.
- Fructose absorption is also rapid but not so much as compared to glucose and galactose, but it is definitely faster than pentoses. Hence fructose is not absorbed by simple diffusion alone and it is suggested that some mechanism facilitates its transport, called as *facilitated transport*.

Wilson and Crane's Hypothesis of Active Transport

Wilson and Crane have shown that sugars which are 'actively' transported have several chemical features in common. They suggested that to be actively transported sugar must have the following:

- They must have a six-membered ring,
- Secondly, they must have one or more carbon atoms attached to C 5, and
- Thirdly, they must have a -OH group at C-2 with the same stereo-configuration as occurs in D-glucose. -OH group and 5 hydroxymethyl or methyl group on the pyranose ring appear to be essential structural requirements for the active transport mechanism.

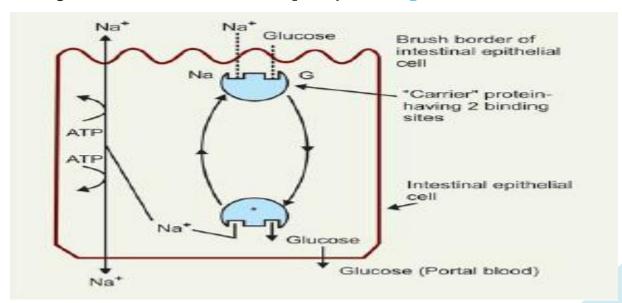


• Crane and his collaborators explain active transport by envisaging the presence of a Carrier protein (transport protein) in the brush border of

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: It is provided by ATP, by the interaction of the sodium dependent sugar carrier and the sodium pumps, actively transported sugars are concentrated within the cell without any back leakage of the sugar into the lumen. It is believed that sodium binding by the carrier-protein is pre-requisite 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. This is a cotransport system (Fig. below).



Absorption of Other Sugars

- Sugars like D-fructose and D-mannose are probably absorbed by facilitated transport which requires the presence of carrier protein but does not require energy.
- Other sugars like *pentoses* and *L-isomers* of glucose and galactose are absorbed passively by simple diffusion.

Factors Influencing Rate of Absorption

1. State of mucous membrane and length of time of contact: If mucous membrane is not healthy, absorption will suffer. Similarly in hurried bowel, length of contact is less and as such absorption will be less.

2. Hormones

- *Thyroid hormones:* These increase absorption of hexoses and act directly on intestinal mucosa.
- Adrenal cortex: Absorption decreases in adrenocortical deficiency, mainly due to decreased concentration of sodium in body fluids.
- *Anterior pituitary:* This affects absorption mainly through its influence on thyroids. Hyperpituitarism induces thyroid over activity and *vice versa*.
- Insulin: This has no effect on absorption of glucose.
- **3.** *Vitamins:* Absorption is diminished in states of deficiency of B-vitamins, viz, thiamine, pyridoxine and pantothenic acid.
- **4.** *Inherited enzyme deficiencies:* Inherited enzyme deficiencies like sucrase and lactase can interfere with hydrolysis of corresponding disaccharides and their absorption.

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Clinical Aspect

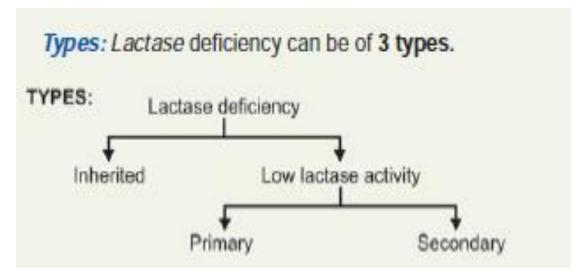
Defects in digestion and Absorption of Carbohydrates(including inherited disorders)

1. Lactase Deficiency

Some infants may have deficiency of the enzyme lactase and they show intolerance to lactose, the sugar of milk.

Symptoms and signs seen in affected infants include:

- Diarrhoea and flatulence
- Abdominal cramps
- Distension.



Inherited Lactase Deficiency

- Rare disorder
- Symptoms of intolerance to milk such as diarrhoea and wasting incident to fluid and electrolyte disturbances as well as inadequate nutrition, all develop very soon after birth

- Urine: Presence of lactose in urine is a prominent feature (lactosuria)
- **Treatment:** Feeding of lactose-free diet results in disappearance of the symptoms and marked improvement.

Low Lactase Activity

- **a. Primary low lactase activity:** It is relatively a common syndrome. It is seen particularly among non-white population in USA as well as other parts of the world specially South East Asia including India. Intolerance to lactose is not a feature in early life and appears later in life. It is presumed to represent a gradual decline in the activity of the enzyme lactase in susceptible individuals.
- **b. Secondary low lactase deficiency:** This is secondary to many GI conditions prevalent in tropics and non-tropical countries like:
- Tropical and nontropical sprue (Celiac disease)
- Kwashiorkor
- Colitis and chronic gastroenteritis Also can occur after surgery of peptic ulcer.

2. Sucrase Deficiency

Inherited deficiency of **sucrase** and **isomaltase** have been reported. Symptoms occur in early childhood with ingestion of sugars (cane sugar and table sugar) sucrose, a disaccharide. Symptoms and signs as in lactase deficiency.

3. Disacchariduria

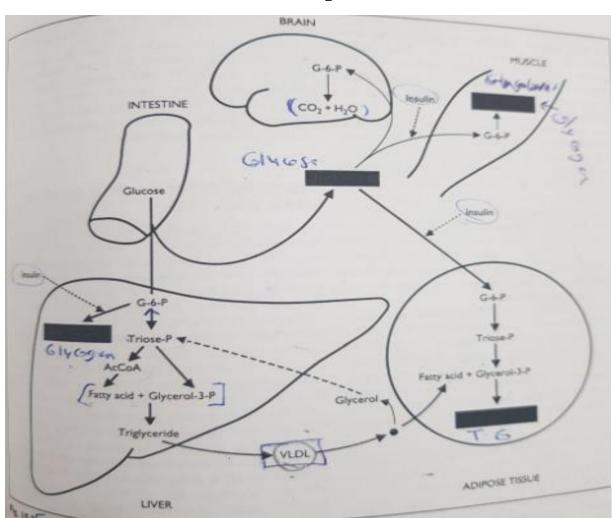
An increase in the excretion of disaccharides may be observed in some patients with **disaccharidase** deficiency. As much as 300 mg or more of

disaccharides may be excreted in those people and in patients with intestinal damage (e.g. sprue and celiac disease).

4. Monosaccharide Malabsorption

Inherited disorders in which glucose and/or galactose are absorbed very slowly have been reported. The reason probably is absence of "carrier protein" necessary for absorption of glucose/galactose.

Insulin effect on different transports.



Metabolism, Anabolism and catabolism

Anabolism and catabolism are the two broad types of biochemical reactions that make up metabolism. Anabolism builds complex molecules from simpler ones, while catabolism breaks large molecules into smaller ones.

Most people think of metabolism in the context of weight loss and bodybuilding, but metabolic pathways are important for every cell and tissue in an organism. Metabolism is how a cell gets energy and removes waste. Vitamins, minerals, and cofactors aid the reactions.

Anabolism Examples

Anabolic reactions are those which build complex molecules from simple ones. Cells used these processes to make polymers, grow tissues, and repair damage. For example:

- Glycerol reacts with fatty acids to make lipids: $CH_2OHCH(OH)CH_2OH + C_{17}H_{35}COOH \rightarrow CH_2OHCH(OH)CH_2OOCC_{17}H_{35}$
- Simple sugars combine to form disaccharides and water: $C_6H_{12}O_6+C_6H_{12}O_6 \ \to \ C_{12}H_{22}O_{11}+H_2O$
- Amino acids join together to form dipeptides: $NH_2CHRCOOH + NH_2CHRCOOH \rightarrow NH_2CHRCOOH + H_2O$
- Carbon dioxide and water react to form glucose and oxygen in photosynthesis:

$$6CO_2 + 6H_2O \rightarrow C_6H_{12}O_6 + 6O_2$$

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Catabolism Definition

Catabolism is the set of biochemical reactions that break down complex molecules into simpler ones. Catabolic processes are thermodynamically favorable and spontaneous, so cells use them to generate energy or to fuel anabolism. Catabolism is exergonic, meaning it releases heat and works via hydrolysis and oxidation.

Cells can store useful raw materials in complex molecules, use catabolism to break them down, and recover the smaller molecules to build new products. For example, catabolism of proteins, lipids, nucleic acids, and polysaccharides generates amino acids, fatty acids, nucleotides, and monosaccharides, respectively. Sometimes waste products are generated, including carbon dioxide, urea, ammonia, acetic acid, and lactic acid.

Catabolism Examples

Catabolic processes are the reverse of anabolic processes. They are used to generate energy for anabolism, release small molecules for other purposes, detoxify chemicals, and regulate metabolic pathways. For example:

 During cellular respiration, glucose and oxygen react to yield carbon dioxide and water

$$C_6 H_{12} O_6 + 6 O_2 \ \to \ 6 C O_2 + 6 H_2 O$$

• In cells, hydroxide peroxide decomposes into water and oxygen:

$$2H_2O_2 \ \rightarrow \ 2H_2O + O_2$$

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Amphibolic Pathways

A metabolic pathway that can be either catabolic or anabolic, depending on energy availability, is called an amphibolic pathway. The glyoxylate cycle and the citric acid cycle are examples of amphibolic pathways. These cycles can either produce energy or use it, depending on cellular needs.