Sheet ○Slides

Subject :	Carbohydrate Metabolism
Done by :	Farah Abu Ableeleh
Corrected by :	Rossul Al_Bahadili
Number :	9

I know this sheet may appear long, but it is mostly a revision of what we have already taken at the summer semester, and a lot of it doesn't require memorizing much, instead understanding the concept is enough.

Carbohydrate Metabolism

Metabolism in general is: all the chemical reactions that occur in the cell. So, carbohydrate metabolism is the chemical reactions that occur in the living cells and involves carbohydrates.

What is the purpose of carbohydrate metabolism?

1- The main purpose is to produce energy, which is absolutely required for life, by utilizing glucose and producing ATP.
2- Storage of glucose; because we take glucose irregularly, we have to store it in order to keep making energy continuously. Glycogen is the temporary storage form of glucose for short periods of time (within a day or so).
3- Converting non-carbohydrates to carbohydrates which is eventually converted to glucose.
4- Production of NADPH; which is used in biosynthesis, reduction of molecules such as Glutathione and Glucuronic acid (which is used for synthesis, and metabolism of drugs).
5- Interconversion of sugars, like fructose, galactose and ribose, to glucose.

There are a lot of reactions and pathways that occur in the metabolism of carbohydrates, such as:

1- Glycogenesis: production of glycogen.
2- Glycogenolysis: breaking down of glycogen.
3- Glycolysis: conversion of glucose to pyruvate.
4- Gluconeogenesis: a pathway that results in production of glucose from non-carbohydrate molecules.
5- Pentose phosphate pathway: generates NADPH which is a source of electrons for reductive biosynthetic pathways and neutralization of oxidants, this pathway also generates pentoses (5 carbon sugars).
6- Glucuronic acid synthesis, glucuronic acid is important in detoxification.

Now we will revise the carbohydrates that we have taken at the summer semester.

Note: the food we ingest mainly contains polysaccharides and disaccharides such as: starch and sucrose, these are later broken down into monosaccharides. However, some monosaccharides are used as sweeteners, such as: fructose.

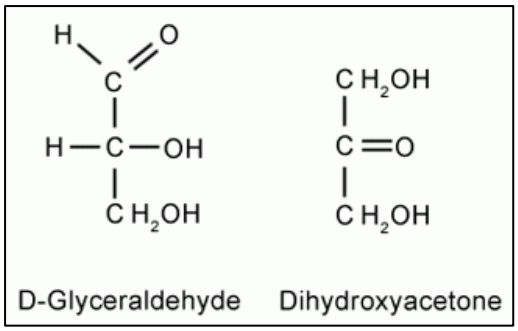
1- Monosaccharides

They have either aldehyde group (terminal carbonyl), and in this case the sugar is called **aldose**. Or they have ketone group (non-terminal carbonyl) and in this case the sugar is called **ketose**. Sugars must have two or more hydroxyl groups.

*The simplest sugar is glyceraldehyde.

*The simplest keto sugar is dihydroxyacetone

Ribulose sugar, for example, is a keto sugar, and it is an isomer of ribose. (Mostly when there is 'ul' in the name it is a ketose)



Monosaccharides can also be classified according to the number of carbon atoms as follows:

Triose (glyceraldehyde), tetrose (erythrose), pentose (ribose), hexose (glucose)…etc.

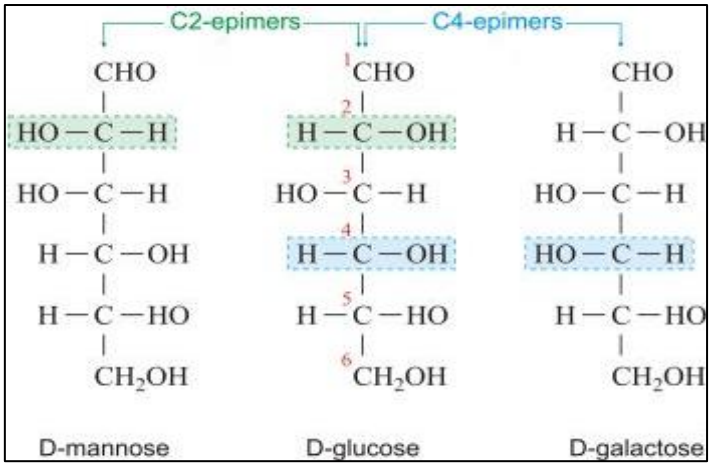
Isomers:

Carbons that carry hydroxyl groups in sugars are mostly asymmetric, changing the orientation of one hydroxyl group produces a new different sugar and it is called epimer.

*Glucose and galactose differ in C-4, therefore, glucose and galactose are epimers)

*Glucose and mannose differ in C-2, glucose and mannose are epimers.

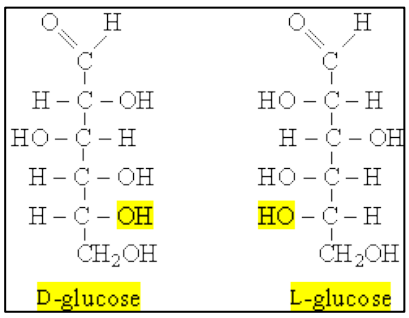
*Notice that



mannose and galactose are not epimers

because they differ in the orientation of two hydroxyl groups; not only one hydroxyl group.

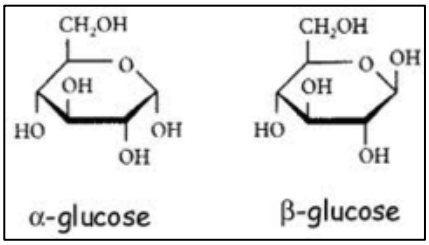
Now if we change the orientation of all of the –OH groups we produce L- and D- stereoisomers, such as L-glucose and D-glucose. L and D glucose are mirror images.



Look at the last asymmetric carbon (carbon number 5) if the –OH group was on the right it is a D-sugar, and if it was on the left it is an L-sugar.

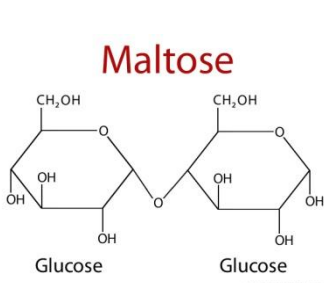
Monosaccharides in real life don not exist as straight chains, but the hydroxyl group of the C-5 reacts with the carbonyl on C-1 to form a hemiacetal bond and the ring structure of monosaccharides. The ring structure is the common structure in nature.

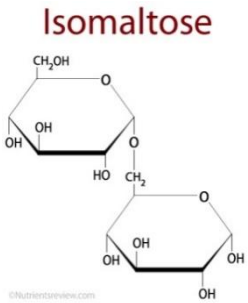
*α-glucose and β-glucose only differ in the orientation of the –OH group on C-1 in the ring structure; in α-glucose hydroxyl group is below the ring, in β-glucose hydroxyl group is above the ring. They are not mirror images.

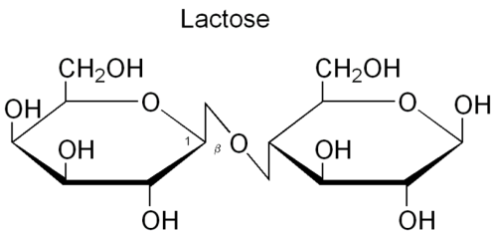


2- Disaccharides:

They are carbohydrates made of two sugar units joined by a glycosidic bond.







Maltose, for example, is composed of two glucose units joined by α(1→4) glycosidic bond.

Isomaltose is: two glucose molecules joined by α(1→6) glycosidic bond.

Lactose is composed of glucose and galactose joined by β(1→4) glycosidic bond.

Note: A glycosidic bond doesn't only join carbohydrates together, it may connect a carbohydrate with a non-carbohydrate molecule. These bonds are cleaved by enzymes called glycosidases that act by adding a water molecule (hydrolysis reaction) to every bond they cleave.

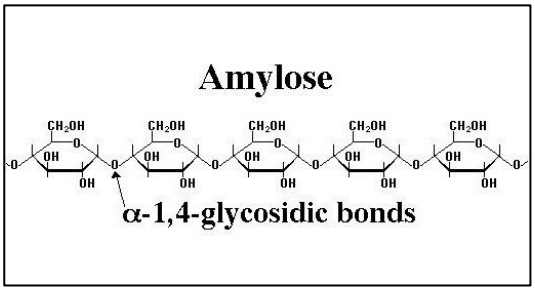
3- Polysaccharides:

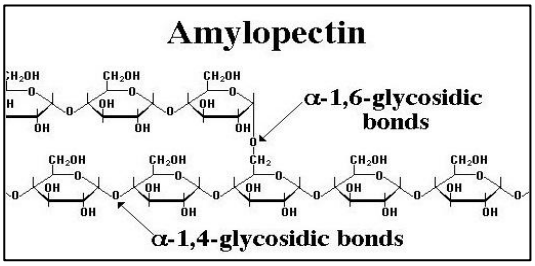
The main polysaccharide is starch which includes amylose and amylopectin.

a- Amylose: repeated glucose units joined by α(1→4) glycosidic bond.

b- Amylopectin: similar to amylose but has branches, and the glycosidic bond at the branches is α(1→6).

c- Glycogen: It is known as the animal starch. It is very similar to amylopectin but has more branches, and it is more complex.

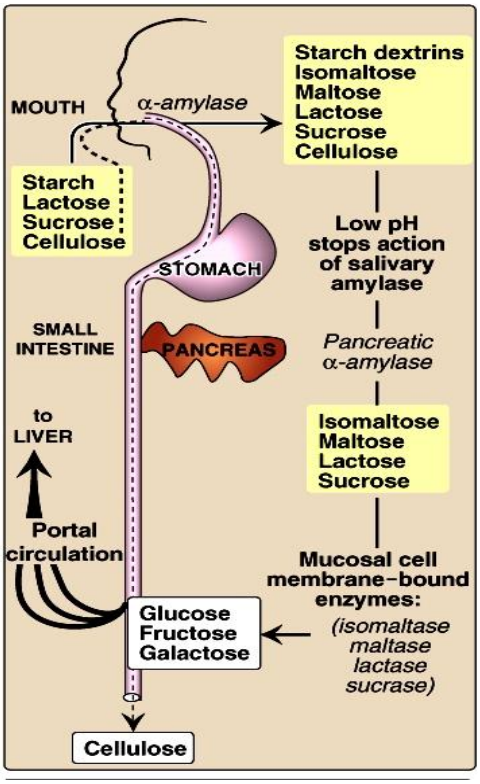




Digestion of Carbohydrates

Amylose is broken down by the amylase enzyme which is present in saliva, that's why once you start eating bread saliva starts digesting it. It breaks down starch to produce what is called starch dextrins, but not for so long. After that the food will go to the stomach. Once it is in the stomach the salivary α-amylase is no longer active. Why? Because of the low pH.

When food reaches the small intestine, the pancreas secretes bicarbonate that neutralizes the acidity of food that came from the stomach. The pH reaches approximately 7.5-8, which is suitable for pancreatic α-amylase to be active.



Note: Salivary α-amylase and pancreatic α-amylase are not exactly the same (isoenzymes).

Once the pancreatic α-amylase is activated all dextrins (partly degraded starch) are converted to maltose and isomaltose. But still the sucrose and lactose are not digested.

The last step of the digestion occurs in the small intestine where disaccharides are digested by disaccharidases. These disaccharidases are produced from intestinal mucosal cells, then they are secreted to cells' surfaces and stay attached and anchored to the membrane, not released in the lumen of the small intestine.

Each disaccharide is digested by its own disaccharidase. Maltose is broken down by maltase, isomaltose is digested by isomaltase, sucrose by sucrase…etc.

Trehalose is broken down by trehalase. Trehalose is a disaccharide present in mushrooms. Some people have problems concerning the trehalase enzyme (rare disease). So they have some troubles when they eat mushrooms because they can't digest the trehalose.

Exoglycosidases: Exo- means outside. These enzymes cleave the glycosidic bond at the terminal end of the polysaccharide chain. One example is glucoamylase that is in the maltose-glucoamylase complex.

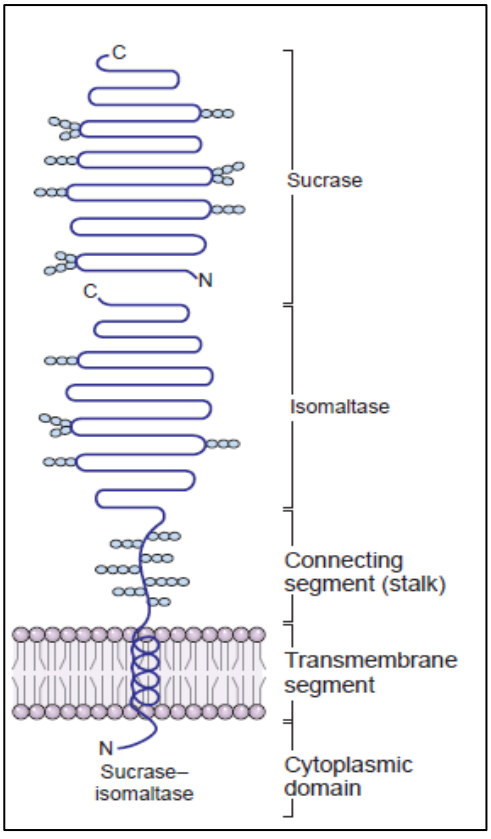
Some glycosidases exist as complexes, these complexes include:

Sucrase-Isomaltase Complex

It is an enzyme that acts on sucrose, isomaltose, and maltose. It is called complex because it is composed of more than one unit.

The sucrase-isomaltase complex has a transmembrane segment which anchors this complex to the membrane of the intestinal mucosal cells.

It has two subunits; sucrase and isomaltase. They may seem like two peptides or two proteins but they are synthesized as a single protein, then it is cleaved to form two subunits joined together as one protein.



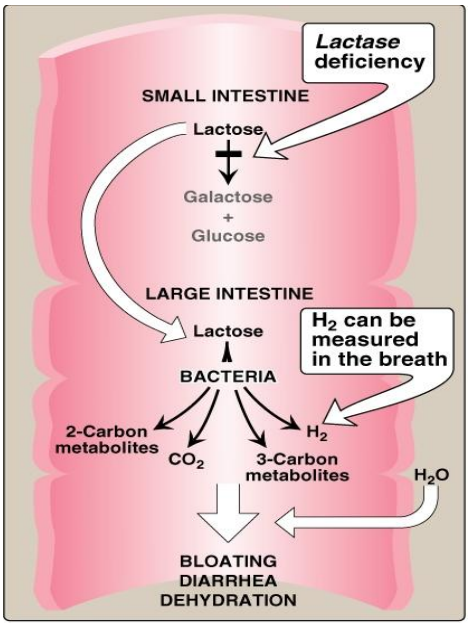
Sucrose is only digested by the sucrase subunit, and the isomaltose is only digested by the isomaltase unit, but both subunits can break down the maltose sugar. These two subunits together account for the digestion of 80% of maltase activity.

Maltase-Glucoamylase Complex

It is very similar to the sucrase-isomaltase complex, but it is not split. One subunit breaks down maltase, and the other breaks down amylose by cleaving one terminal glucose at a time. This complex is attached to mucosal cells membranes.

- ## Abnormal Degradation of Disaccharides

1- Lactase deficiency (also called, adult hypolactasia): not being able to digest and absorb lactose. It is present in 50% of the world's population.



In normal conditions, lactose is broken down in the small intestine to produce glucose and galactose, but if someone has lactase deficiency, the lactose will start to accumulate in the large intestine which is full of bacteria that will start metabolizing the lactose (as a source of energy), and will form products such as 2-carbon metabolites, 3-carbon metabolites, acetic acid, lactic acid and molecular hydrogen. All of these products together in the large intestine will increase the osmotic pressure so water will enter lumen of the large intestine, resulting in diarrhea and bloating.

It is estimated that one cup of milk (containing 9g of lactose) will result in the loss of one liter of extracellular fluid (4-5 cups of water) because of diarrhea.

Lactase enzyme reaches its maximal activity at the age of one month, that's why babies have high tolerance for lactose. And that is very good because milk is the only food babies get at that age. But as they get older the lactase won't be the only sugar they get from their diet. And lactase's activity reaches to 10% of the infants' level.

Lactase deficiency differs between populations. In Jordan, for example, 80% of adults have lactase deficiency. But in Denmark or in Holland, the lactase deficiency percentages are very low.

In case the deficiency was caused by genetic defect, patients are given lactase tablets and lactose-free milk and dairy.

2- Sucrase-Isomaltase Deficiency has many causes such as:
   a- Genetics
   b- Variety of intestinal diseases (the most common cause)
   c- Malnutrition
   d- Injury of mucosa, (i.e. by drugs) in this case, mucosal cells that hold these enzymes are lost.
   e- Severe diarrhea: results in loss of enzymes and loss of cells (also causes lactase deficiency, that's why we don't give anyone that has diarrhea milk to make up for the loss of water).

"Success is simple, do what's right, the right way, at the right time." Sorry if there were any mistakes.