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starchlipidproteinamine carbohydratesisomersketone

Biochemistry 2

Doctor 2018 | Medicine | JU

◉ Sheet ○ Slides

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Carbohydrate Metabolism, an introduction:

(you can find this lecture in chapter 7 of Lippincott, 10th edition.)

Carbohydrates, also known as Saccharides, are the most abundant organic molecules in nature. In the next couple of lectures, we'll be discussing topics related to carbohydrates and their metabolism. Some of the objectives we are aiming to cover are:

1) Glucose, which is a monosaccharide, is a source of energy. Glucose degradation produces Acetyl CoA, which is a molecule that enters the TCA cycle and produces energy.

2) Ways to transfer non-carbohydrate sources (i.e. Amino Acids) to Glucose, since Glucose can't be stored in the body for a long period of time.

3) The process of storing Glucose in the form of Glycogen (Glycogenesis).

4) The process of breaking down Glycogen to form Glucose (Glycogenolysis).

5) The production of NADPH and GSH (Glutathione).

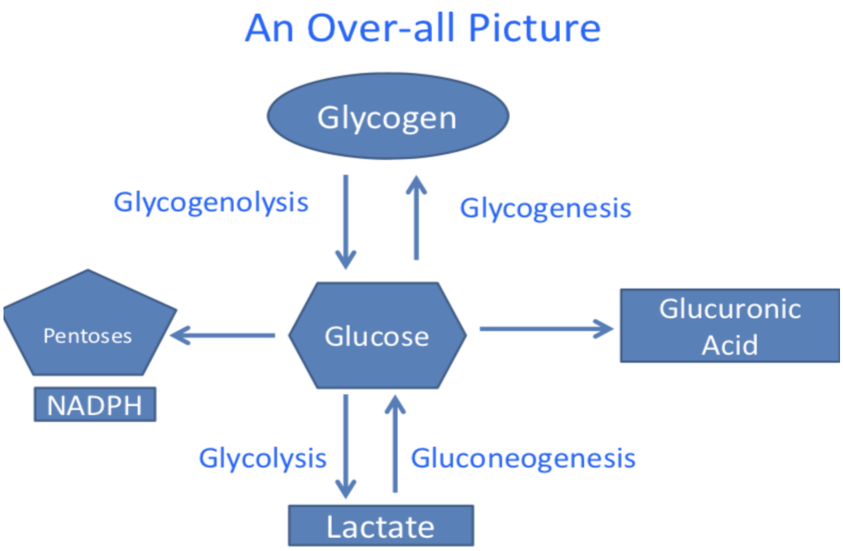
6) The production of Glucuronic Acid, which is used in drug metabolism to convert hydrophobic molecules to hydrophilic ones.

7) Interconversion of sugars, which is the process of turning one sugar to another (i.e. Galactose to Glucose).

An Over-All Picture

Glucose out of the many molecules we are about to discuss, seems to be the most important carbohydrate for humans. It's the form of sugar that runs in our blood and is used mainly as the source of energy in humans.

Glucose is involved in several reactions that happen on a daily basis. The picture below shows an over-all chart of the reactions that glucose takes part of:



1) **Glycolysis**: Glycolysis is the process of turning Glucose to Pyruvate or Lactate to obtain energy. (Glyco: Glucose, lysis: break-down)

2) **Gluconeogenesis**: The conversion of Lactate or Pyruvate to Glucose. This is the opposite of Glycolysis. (Gluco: glucose, neo: new, genesis: production of. Altogether, it's the production of a new glucose molecule)

3) **Glycogenesis**: The production of Glycogen from Glucose. (Glyco: Glycogen, genesis: Production of)

4) **Glycogenolysis**: breaking down Glycogen to Glucose. (Glycogen: self explanatory, lysis: break-down)

5) **Glucuronic Acid**: an acid used to convert hydrophobic drugs to hydrophilic ones.

6) **Pentoses and NADPH:** NADPH is a molecule used in anabolism, unlike NADH which is used is catabolism.

Distinguishing Sugars: Classification and Structure

Monosaccharides can be classified according to:

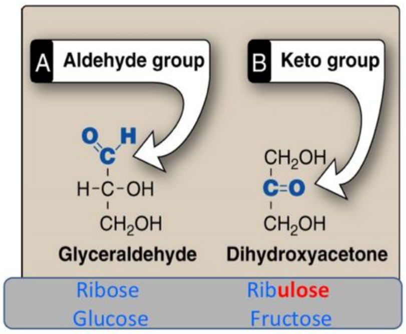
1) Number of carbons:

Monosaccharides can be categorized into different classes based on the number of carbons they have. We have trioses, pentoses, hexoses …etc. The table on the right shows the different classes of sugars depending on the number of carbons they have.

Generic names		Examples
3 carbons:	trioses	Glyceraldehyde
4 carbons:	tetroses	Erythrose
5 carbons:	pentoses	Ribose
6 carbons:	hexoses	Glucose
7 carbons:	heptoses	Sedoheptulose
9 carbons:	nonoses	Neuraminic acid

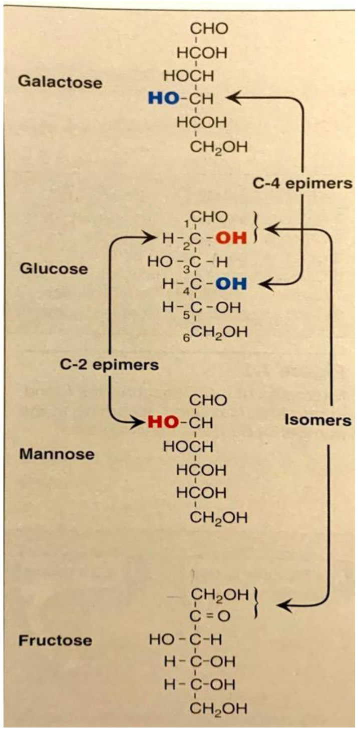
2) Carbonyl Group:

This classification gives us two types of sugars: Aldoses and Ketoses. Aldoses are sugars with an Aldehyde group on carbon number 1. The simplest Aldose is **Glyceraldehyde**, which contains 3 carbons. Ketoses are sugars with a Ketone group on carbon number 2. The simplest Ketose is **Dihydroxyacetone**, and this sugar also has 3 carbons.



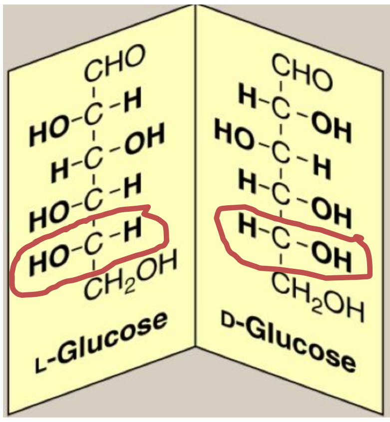
(Note: you should know the structures of the simplest Aldose and Ketose)

3) Isomers and Epimers:



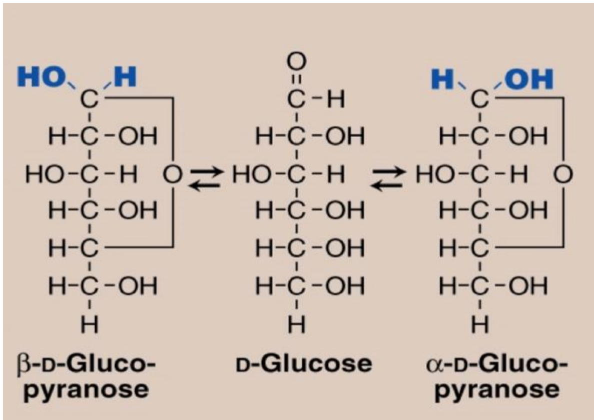
Isomers are compounds that have the same chemical formula, but different structures. For example, Fructose, Glucose, Mannose and Galactose are all isomers of each other, with the chemical formula $C_6H_{12}O_6$. Isomers that differ in the configuration around only one carbon atom, with the exception of the carbonyl carbon, are called epimers of each other. Glucose and Galactose are C4 Epimers, because their structure differs only in the position of the Hydroxyl (-OH) group at Carbon 4. Glucose and Mannose are C2 Epimers. However, Galactose and Mannose are only isomers. (You have to note that isomers or epimers are two different sugars with different characteristics, even if the change is as slight as a hydroxyl group on one carbon).

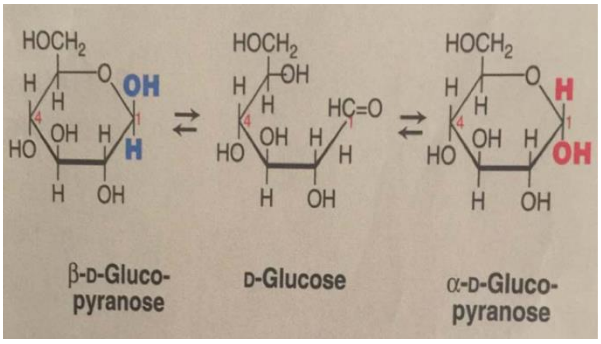
4) Enantiomers:



A special type of isomerism is found in pairs of sugars that are mirror images of each other (not just one carbon is different). These mirror images are called Enantiomers. Enantiomers are described as D-Enantiomers, and L-Enantiomers. The D-Enantiomer has the Hydroxyl Group (-OH) on the chiral carbon that is furthest from the carbonyl carbon to the right, while is L-Enantiomer is to the left. Most sugars in the body are in the D-Isomers

(Easy mnemonic: L is for Left, so D is Right)





5) Cyclic Forms:

The Carbonyl Group (Aldehyde or Ketone) reacts with the hydroxyl group on the same sugar, making the Carbonyl group asymmetric. This asymmetric carbon is referred to as the anomeric carbon. This genetrates a new pair of isomers, Alpha (α) and Beta (β).
Alpha configuration is when the Hydroxyl group on the anomeric carbon is downwards (originally left in the chain form), while Beta configuration is when it's upwards (originally right in the chain form.
Less than 1% of Monosaccharides with 5 or more carbons exist in the chain form. This also makes sugars reducing or non-reducing. If the Hydroxyl group on the Anomeric carbon in a cyclized sugar is not linked to another compound in a glycosidic bond, then this sugar is a reducing sugar, and it gets oxidized.

Monosaccharide Joining

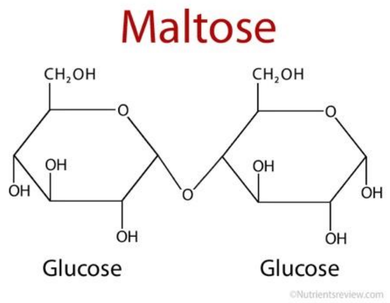
Monosaccharides are joined to form a 2-unit sugar called a Disaccharide, or an Oligosaccharide, which contains 3-10 monosaccharides, or a Polysaccharide which has more than 10 monosaccharide units. This process removes one water molecule per 2 sugars joined, meaning the total number of water molecules removed (= number of sugars -1). The linkage between two monosaccharides is referred to as a Glycosidic Bond.

Glycosidic Bonds are named according to the carbons participating the bond, and the cyclic configuration (α or β) of the sugar participating with the Anomeric carbon.

We will mainly discuss three Disaccharides here, just to get the idea, and the rest follows the same path.

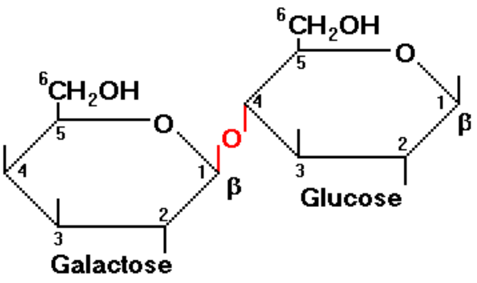
1) **Maltose:**

Also known as the malt sugar, maltose is a Disaccharide made of 2 Glucose molecules, linked together in a glycosidic (α 1-4) linkage. The right glucose molecule in the picture has a free hydroxyl group on the anomeric carbon, meaning that Maltose is a reducing sugar, and can be oxidized.



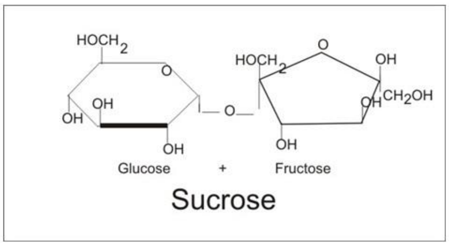
2) **Lactose:**

Also known as the milk sugar, Lactose is a Disaccharide made of a Glucose and a Galactose molecule joined together in a (β 1-4) linkage. The right glucose molecule in the picture has a free hydroxyl group on the anomeric carbon, meaning Lactose is a reducing sugar, and can be oxidized.



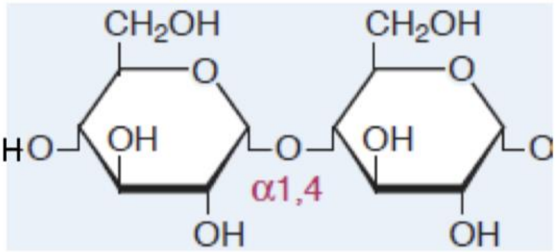
3) Sucrose:

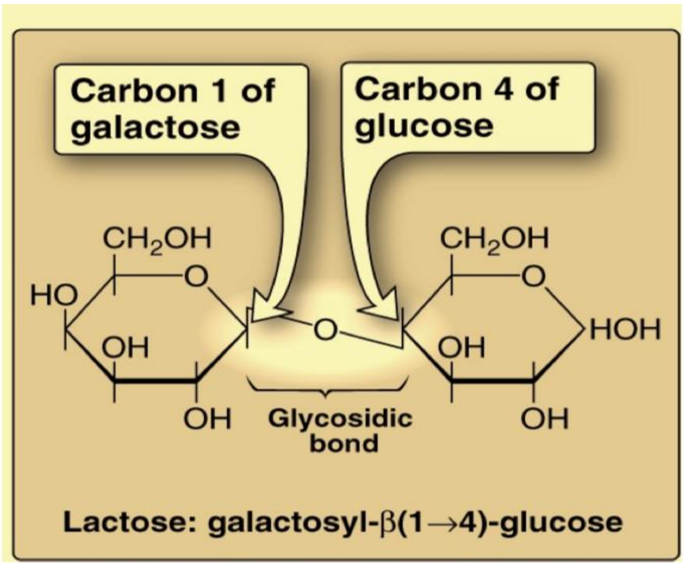
Also known as table sugar, Sucrose is a Disaccharide made of a Glucose and a Fructose molecule joined together in an (α 1-2) linkage. The right Fructose molecule in the picture doesn’t have a free hydroxyl group on the anomeric carbon, meaning that Sucrose is not a reducing sugar, and can’t be oxidized.



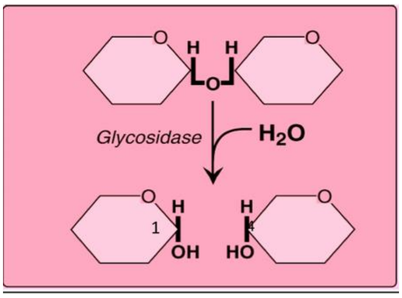
Disaccharide: A sugar made of two sugar units joined by glycosidic bond

Maltose: a disaccharide made from two glucose units





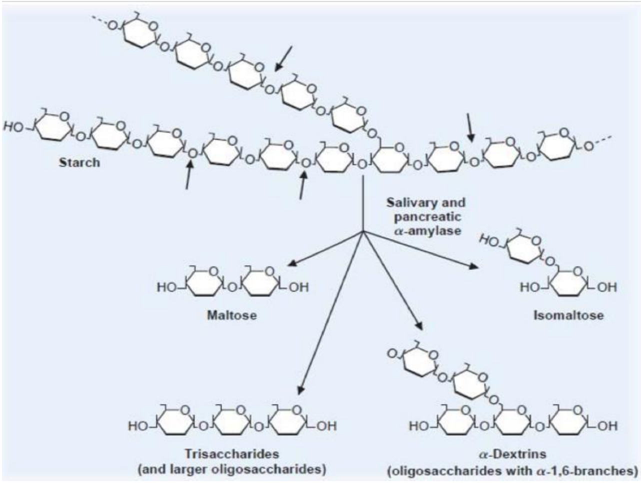
Breakdown of Sugars: Glycosidic Bond Cleavage



This is the exact opposite of monosaccharide joining. It requires the same number of water molecules removed to get the sugar broken down, because it's a hydrolysis process.

Enzymes responsible for the cleavage are called **Glycosidases**, which, as the name implies, hydrolyses and breaks down Glycosidic bonds.

- Here's an example to see how they work:



This picture on the right has part of a starch chain (which is made of Amylose and Amylopectin) that we ingest on daily basis. If this was exposed to Glycosidases (i.e. α- Amylase, which will be discussed later), it will result in 4 types of sugars:

1) **Maltose:** If the cleavage happened in a linear way (no branch included) at the sides of 2 glucose molecules (α 1-4 linkage).

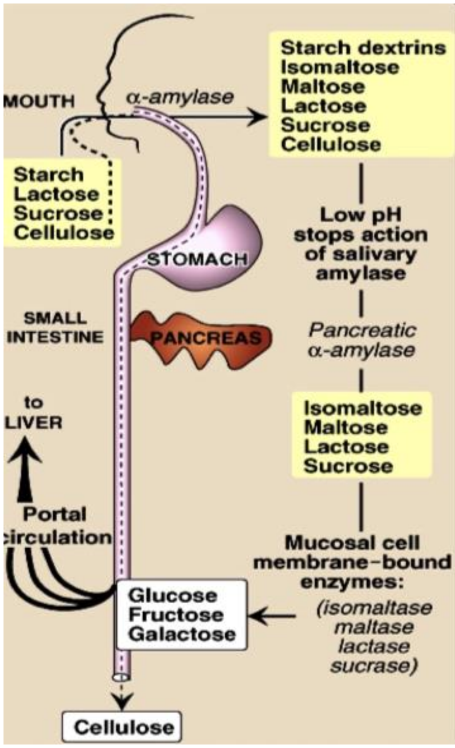
2) **Trisaccharides:** Same concept as Maltose, but at the sides of 3 adjacent Glucose molecules.

3) **Isomaltase:** if the cleavage made a cut around the Glucose that is branched (remember that the α 1-4 is broken and not the α 1-6 at the branch).

4) **α -Dextrins:** Oligosaccharides with (α 1-6) branches. (smaller than starch).

Dietary Carbohydrate Metabolism

Since we take very little Monosaccharides in our diet, as the majority is Polysaccharides, the body uses breakdown methods to convert these Polysaccharides to Monosaccharides. This happens mainly in the mouth (using salivary α- Amylase) or in the intestinal lumen (using pancreatic α-Amylase and other specific enzymes, such as Maltase). α – Amylase in all its kinds works on hydrolyzing (α 1-4) bonds only, and that's how it gets its name. The process is summarized as follows:



Mucosal cell membrane-bound enzymes

ENZYME	Bond Cleaved	Substrates
Isomaltase	α 1→ 6	Isomaltose
Maltase	α 1→ 4	Maltose
Sucrase	α 1→ 2	Sucrose
Lactase	β 1→ 4	Lactose
Trehalase	α 1→ 1	Trehalose
Exoglucosidase	α 1→ 4	Glucoamylose

- the food enters the mouth as Polysaccharides and the break-down starts by **Salivary α-Amylase**. Examples on sugars that enter are starch, lactose, sucrose and cellulose, which this example is shows.

- α -Amylase breaks down starch to the parts in the previous page but can't break down the other sugars mentioned because they don't have (α 1-4) Glycosidic bonds.

- Salivary α -Amylase gets inactivated in the stomach, because of the high acidity.

- The Pancreas then releases pancreatic α-Amylase that works just the salivary α-Amylase, and the break down continues.

- Remember the other sugars that don't have (α 1-4) linkages? The mucosal membrane of the intestines has a specific set of proteins for breaking down specific sugars, such as Lactose, Sucrose and etc… Cellulose can't be broken down, since humans don't have the enzymes to do so.

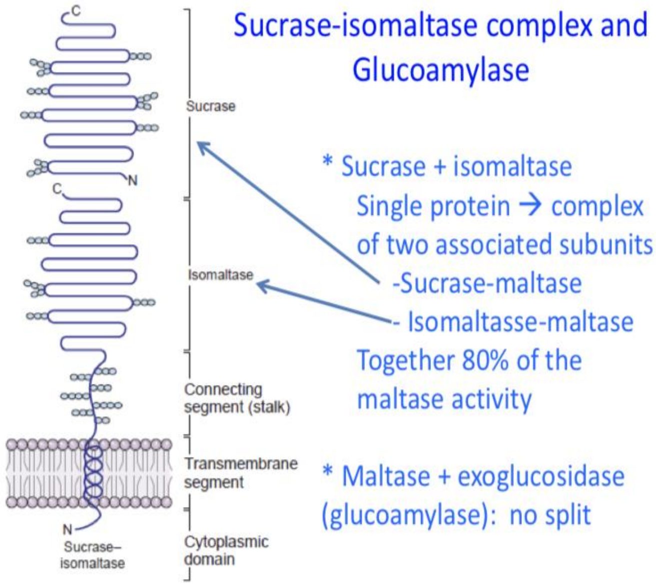
- Then we end up with the basic units (Glucose, Fructose and Galactose) which get absorbed and enter the circulation.

Sucrase- Isomaltase Complex and Glucoamylase

Sucrase- Isomaltase is a transmembrane protein, that is formed from 2 subunits (2 Polypeptides). After synthesis, these 2 Polypeptides go through modifications and get cleaved giving 2 enzymes:

- Sucrase-Maltase: Breaks-down Sucrose and Maltose.
- Isomaltase-Maltase: Breaks-down Isomaltase and Maltase.

Together, they form 80% of the total maltase activity.



Glucoamylase is a specific type of Amylase that is produces when these 2 subunits don't break.

FIG. 27.5. The major portion of the sucrase–isomaltase complex, containing the catalytic sites, protrudes from the absorptive cells into the lumen of the intestine. Other domains of the protein form a connecting segment (stalk) and an anchoring segment that extends through the membrane into the cell. The complex is synthesized as a single polypeptide chain that is split into its two enzyme subunits extracellularly. Each subunit is a domain with a catalytic site (distinct sucrase–maltase and isomaltase–maltase sites). In spite of their maltase activity, these catalytic sites are often called just *sucrase* and *isomaltase*.

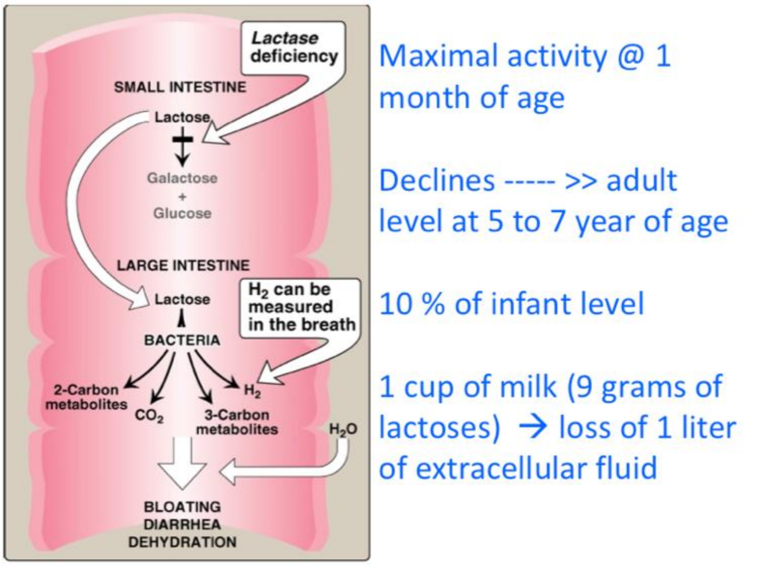
Abnormal Degradation of Disaccharides

A lot of people have problems in digesting Disaccharides, such as Lactose. Here we discuss some problems that are related to the degradation of Disaccharides and their causes:

1) Lactose Intolerance (Lactase deficiency):

Over 50% of the world's population suffers from this problem. This could be due to a problem in the existing Lactase, or a deficiency in synthesizing it.

- The maximum activity of Lactase is at one month of age, and it starts to decline afterwards.
- When someone is 5-7 years old, the level of activity reaches its adult or normal level, which is around 10% of the maximum level.



- If someone is intolerant to Lactose, and they end up ingesting it in some way, their bodies wouldn't be able to handle the Lactose ingested. Instead, it will be metabolized by intestinal bacteria, giving off 2 and 3 carbon metabolites, which stay in the stomach until the extracellular fluid comes and washes them out from the intestines. Each cup of milk (9 g of lactose) needs 1 liter of extracellular fluid to wash it out. This causes diarrhea.

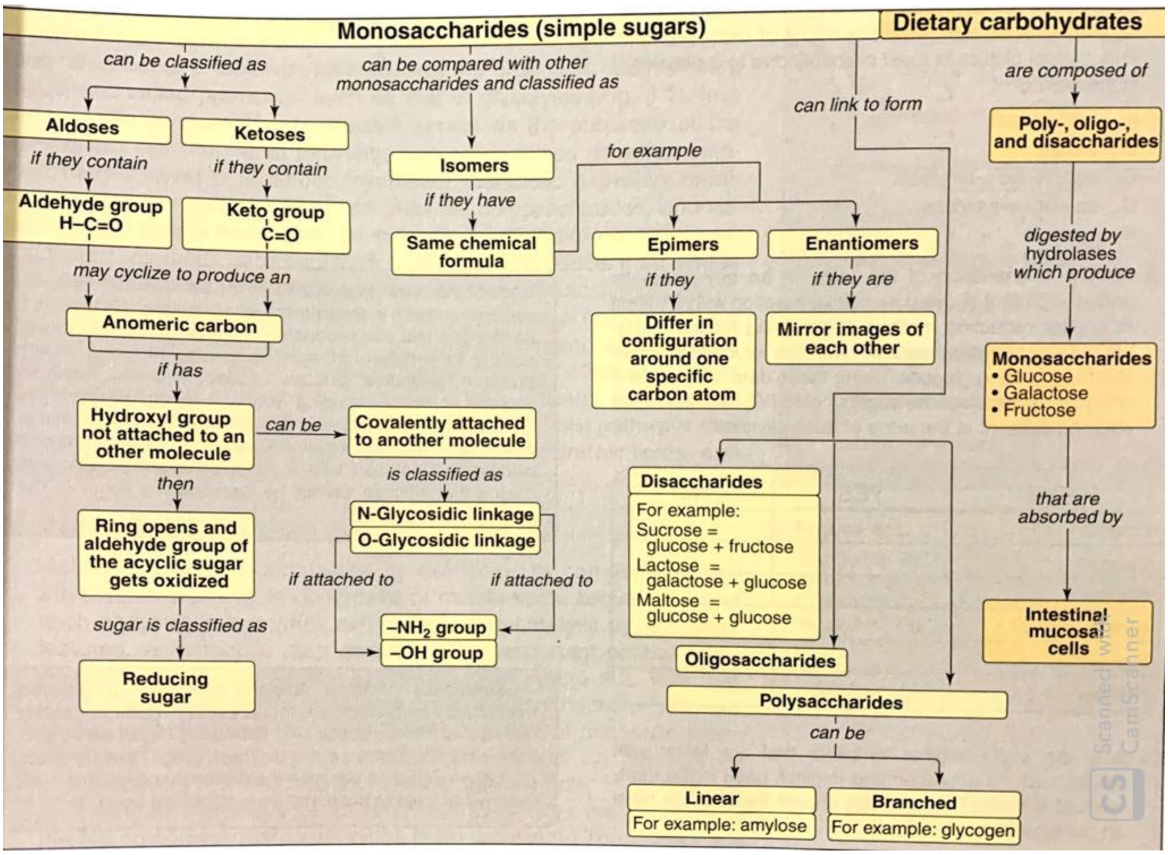
- Another metabolite that comes out gases, such as CO_2 and H_2. These cause bloating.

- The net result is bloating, diarrhea and loss of fluids.

Prevalence of Late-onset Lactase Deficiency

Group	Prevalence (%)
US population	
Asians	100
American Indians (Oklahc	95
Black Americans	81
Mexican Americans	56
White Americans	24
Other populations	
Ibo, Yoruba (Nigeria)	89
Italians	71
Aborigines (Australia)	67
Greeks	53
Danes	3
Dutch	0

To summarize



Thank you so much for bearing!