بسم الله الرحمـٰـن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Metabolism | Lecture 9

Carbohydrates Metabolism pt.1

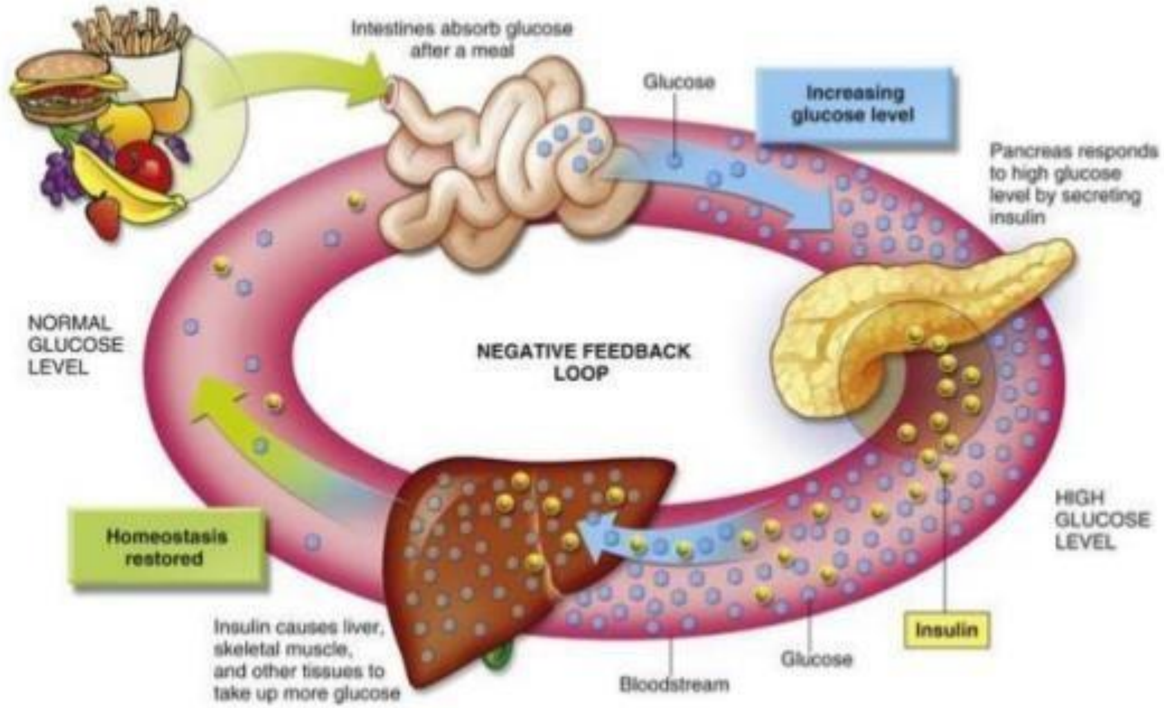
Written by : DST

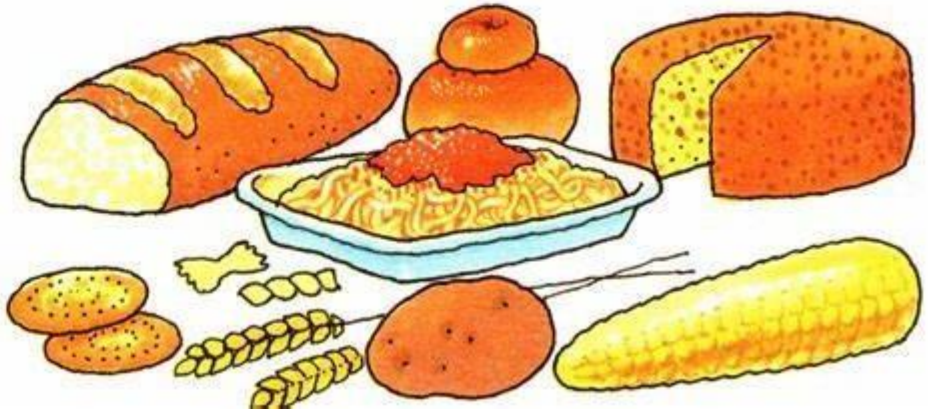
Reviewed by : NST

Carbohydrates Metabolism

Review of Carbohydrates
Digestion and absorption of carbohydrates

Dr. Diala Abu-Hassan





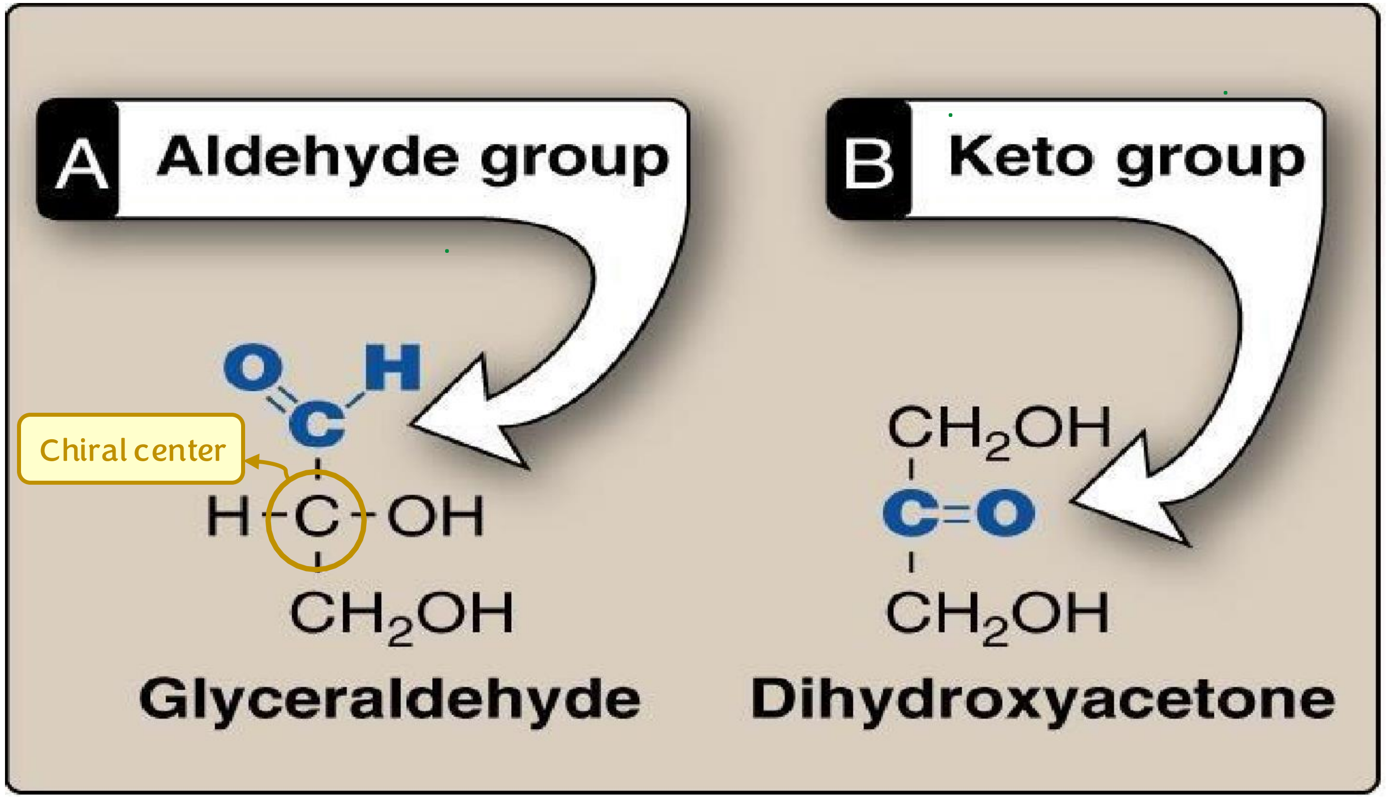
- Sugars (Carbohydrates) are either classified into:

1. polyhydroxy aldehydes (aldoses) (more common)
2. polyhydroxy ketones (ketoses).

- The simplest aldehyde sugar (Glyceraldehyde) has one chiral center and 2 stereoisomers (L & D enantiomers)

- The simplest ketone sugar (Dihydroxyacetone) doesn't have any chiral center, thus no enantiomers

The suffix "...ulose" refers to the sugar being ketoses



Ribose	Ribulose
Glucose	Fructose

Fructose is the most abundant naturally occurring monosaccharide.

- Recall from Biochemistry course:

- Carbohydrates are classified based on:
  - Their functional group (Aldoses/Ketoses).
  - The number of carbons they contain.

- The number of chiral centers in:
  - Aldoses = n-2
  - Ketoses = n-3

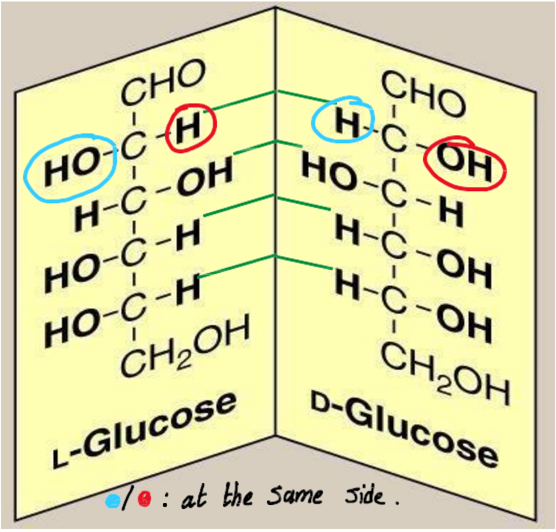
(Where n is the number of carbons.)

Examples of monosaccharides found in humans

- The most common monosaccharides are the ones containing 5 and 6 carbons

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

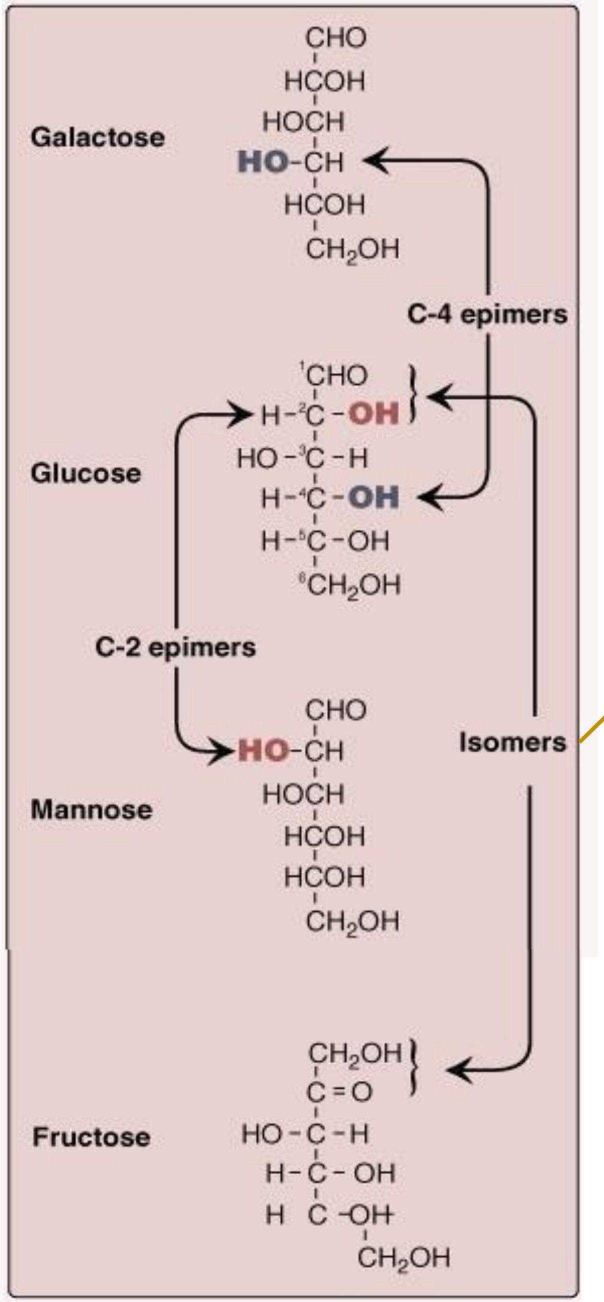
Enantiomers



- Each group or atom surrounding the chiral center is reverted in the opposite direction in its mirror image.
- **Chiral center**: A carbon atom that is bonded to four different groups.
- **Enantiomers**: Stereoisomers that are non-superimposable, mirror images of each other.

D- and L- classification: Determined by the orientation/position of the hydroxyl (-OH) group on the last chiral carbon (the chiral center farthest from the carbonyl group).
- If the -OH group is on the right, it is a D-sugar.
- If the -OH group is on the left, it is an L-sugar.

We utilize D sugars in metabolic pathways.



Sugars have Isomers

- Epimers are isomers that differ at only one –OH position, producing a different sugar.

- Changing the orientation of **one** hydroxyl group will produce a different sugar

Glucose and Fructose are isomers

Why we study these details ?

- These minor differences between sugar molecules are important to expect the function of the enzyme that can interconvert them.

- Most of the metabolic pathways are designed from glucose.

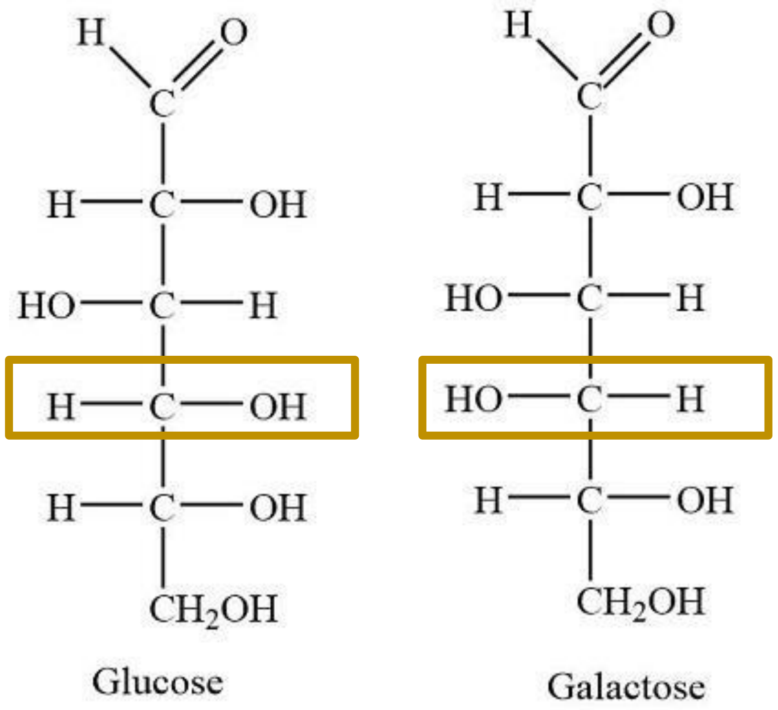
- Our metabolic pathways recognize only glucose, so we must convert other sugars into glucose through isomerization reactions.

1. Diastereomers and Epimers:

- **Diastereomers:** they are compounds that have similar configuration at some carbons and different configuration at some carbons.
- **Epimers:** compounds that differ in configuration at only one chiral carbon.

A) Glucose and Galactose: They differ in orientation of -OH at carbon number four.

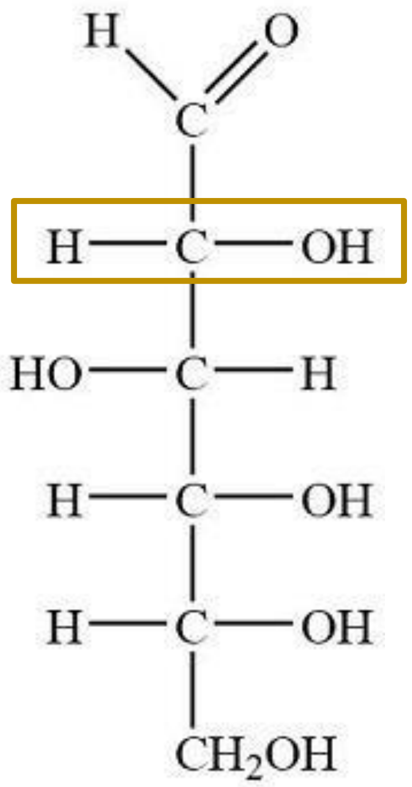
In glucose, the hydroxyl group is on the right of the fourth carbon in the open-chain form . And it is oriented downward in the ring structure.

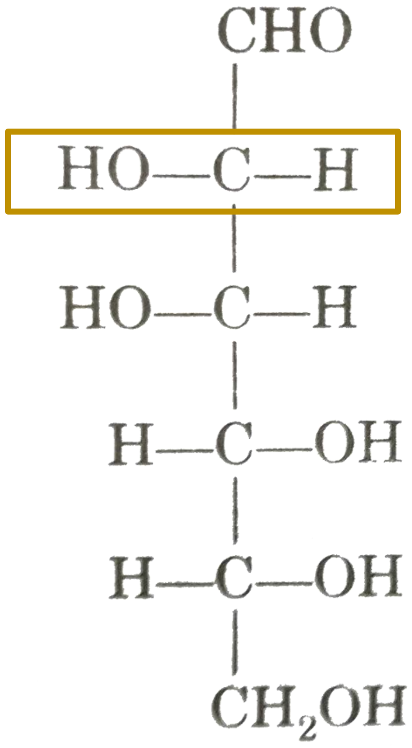


In galactose, the hydroxyl group on the left of the fourth carbon in the open- chain form . And it is oriented upward in the ring structure.

B) Glucose and Mannose:

They differ in orientation of -OH at carbon number two.



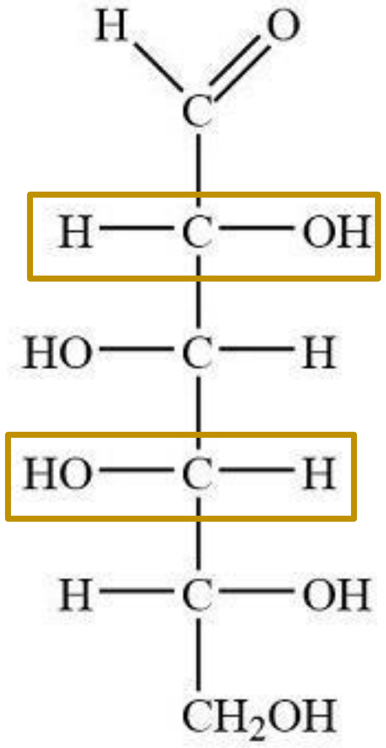


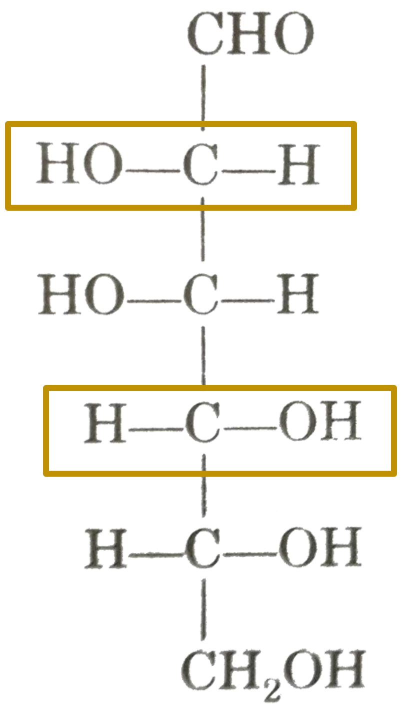
Glucose Mannose

Epimers and Diastereomers

C) Glucose and Mannose:

They differ in orientation of -OH at carbon number two and four.



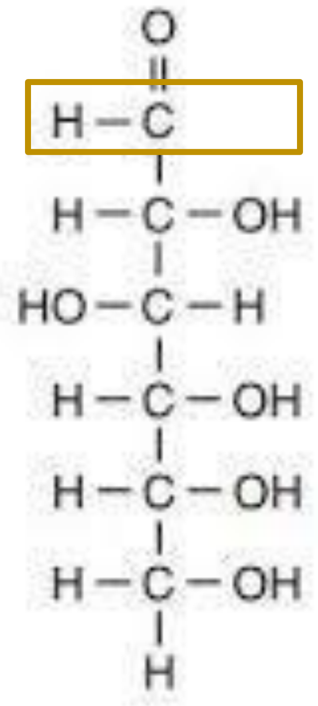


Galactose Mannose

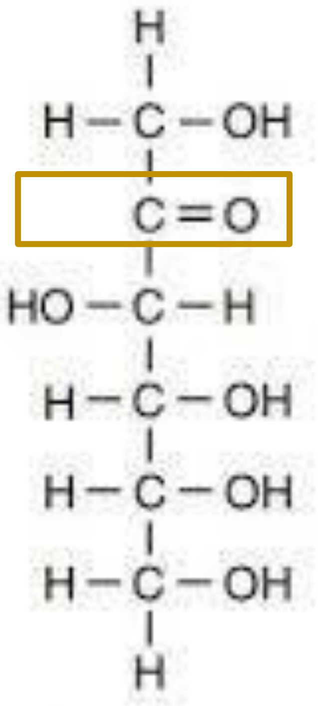
Diastereomers but not Epimers

2. Constitutional Isomers:

- **Constitutional isomers :** they are compounds that have the same molecular formulas, but they have different connectivities. (They differ in their functional groups.)



Glucose



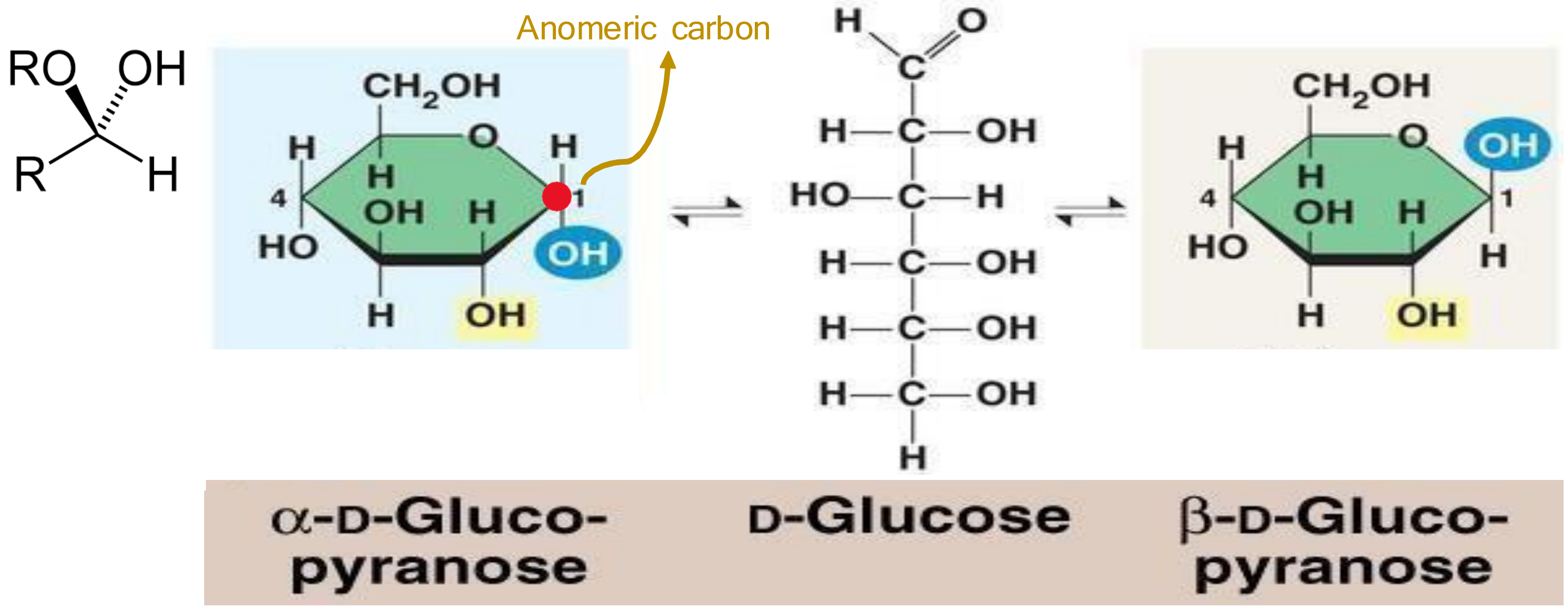
Fructose

➢ Constitutional isomers but not stereoisomers

Both have the formula C6H12O6 but one is and aldose and the other is a ketose

3. Anomers (Alpha and Beta Sugars)

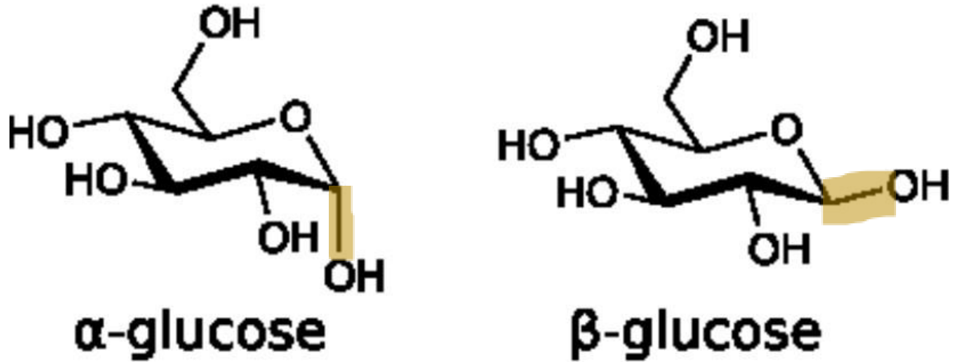
- They form when the open-chain (linear) sugars cyclize to form a ring structure.
- When an aldehyde sugar forms a ring, it becomes a hemiacetal. (ketone -> hemiketal)
- Both α and β anomers can exist in equilibrium in the same solution.



- Each glucose molecule can alternate between three states (liner structure “open chain form” , α-D-Gluco- pyranose , β-D-Gluco-pyranose).
- The interconversion between α and β anomers occurs spontaneously – unlike the conversions between L and D forms – (this process is called mutarotation).

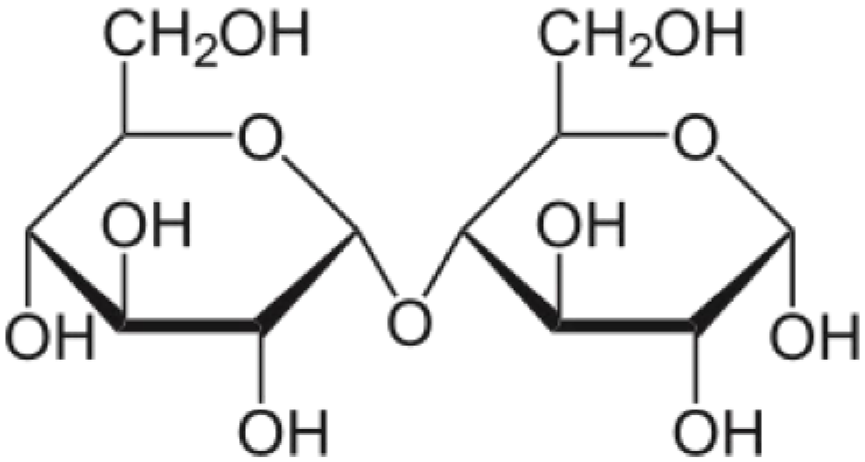
https://mysciencesquad.weebly.com/ib-hl-23a1--s1-cellulose--starch-v-glycogen.html

- In solutions, glucose mainly exists in cyclic forms — about 64% as the β-anomer and 36% as the α-anomer, with only a trace in the open-chain form.
- The β-anomer is the most stable, so glucose predominantly remains in this form, It can, however, interconvert with the α-anomer through the open-chain form during reactions.
- The stability order of glucose forms is: β > α > open-chain, since ring structures are more stable than the linear form.
- Although the open-chain form is the least stable, it plays an essential role in chemical reactions such as oxidation and mutarotation.
- The position of the hydroxyl group at the anomeric carbon affects stability: if it is above the ring (β), it is in the equatorial position, which is more stable; if it is below the ring (α), it is in the axial position, which is less stable (Look at the picture below).
- Additionally, the OH groups on carbons 1 and 2 in the β anomer are farther apart and have more space.
- Your body's enzymes are capable of distinguishing anomers depending on the reaction.



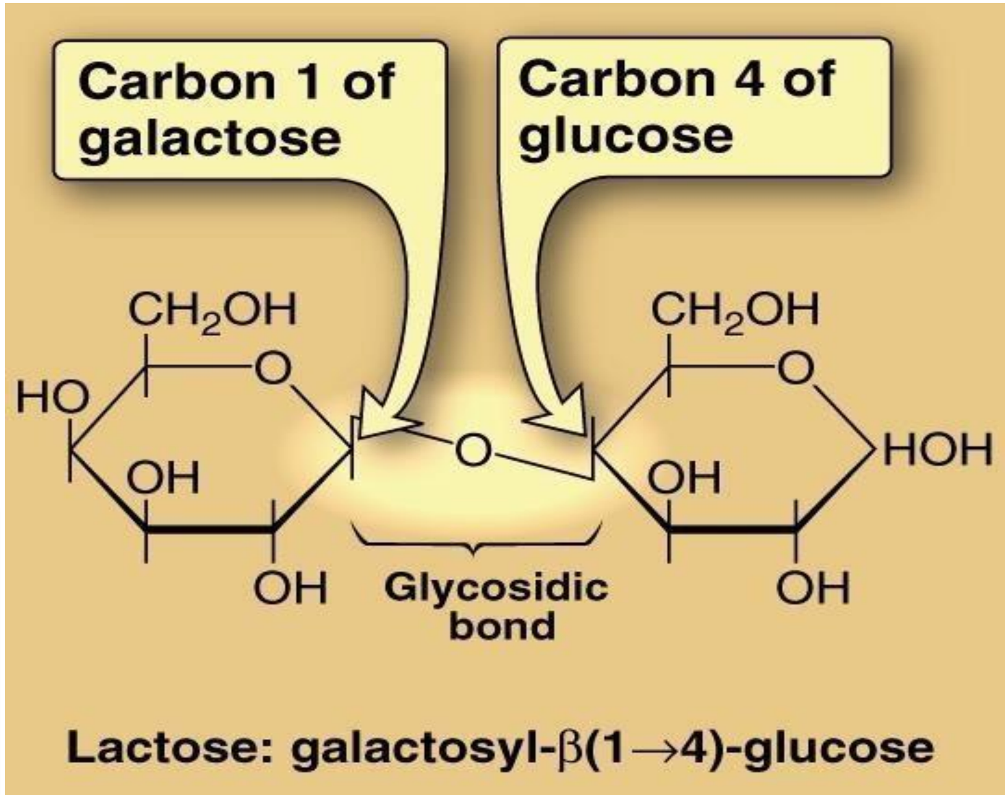
Disaccharides

Sugars made of two monosaccharide units joined by a glycosidic bond



Maltose: a disaccharide made from <u>two glucose units</u>

(thus considered a homo-disaccharide)



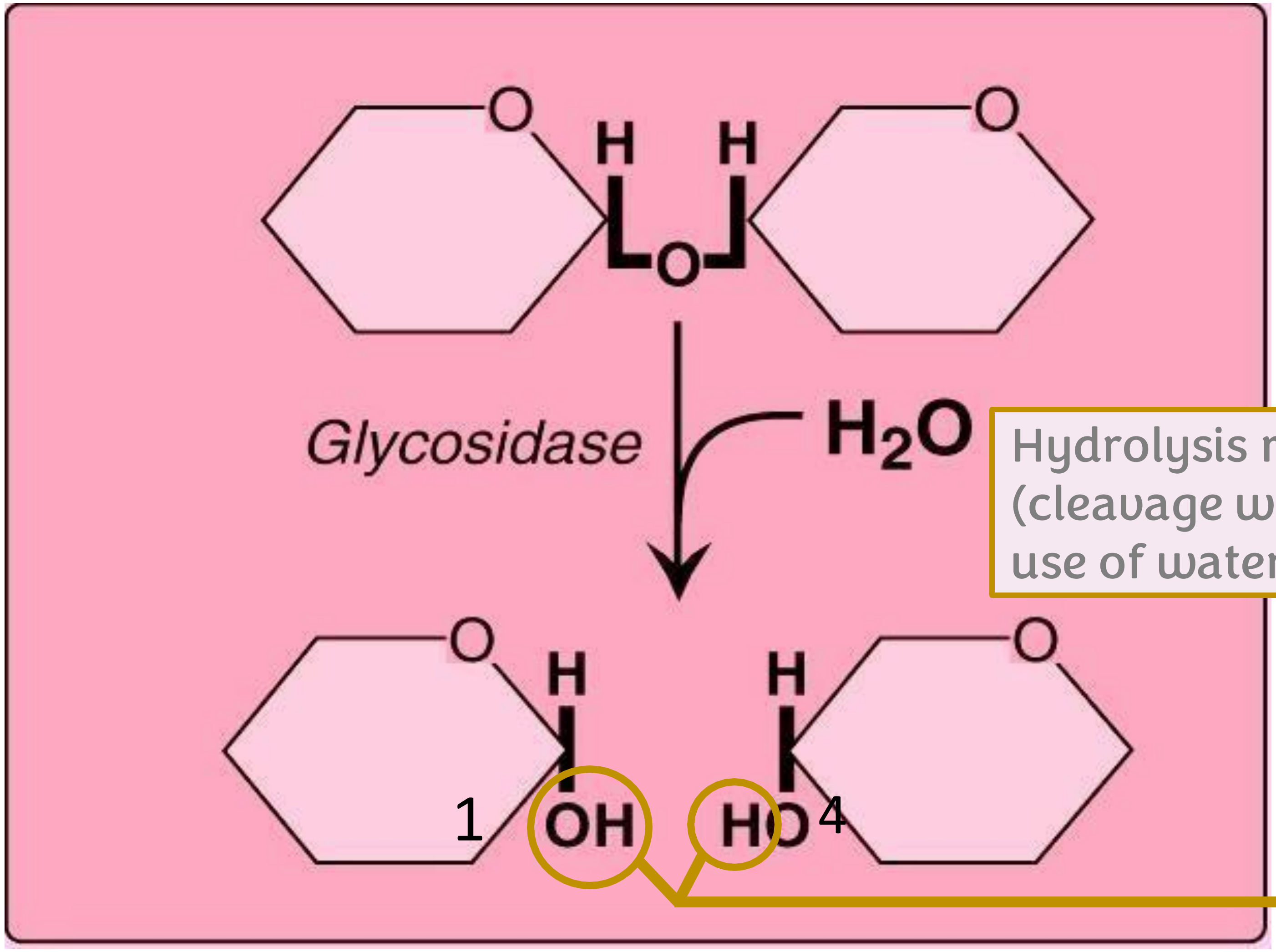
Let’s talk about the formation of disaccharides:

- Linking sugar monomers together produces water via a dehydration reaction, which is responsible for forming a glycosidic bond.
- Different disaccharides can be formed either from two of the same type of monosaccharide (such as maltose, which is made from two glucose residues linked by a α-1,4 glycosidic linkage) or from two different monosaccharides (such as lactose, which is made from glucose and galactose linked by a β-1,4 glycosidic linkage). Sucrose is another disaccharide, composed of glucose and fructose linked by an α-1,2 glycosidic linkage.

قال إبراهيم الخليل مخاطبًا الرسول عليه الصلاة و السلام « يا محمد , أقرئ أمتك مني السلام , وأخبرهم أن الجنة
طيبة التربة، عذبة الماء، وأنها قيعان , وأن غراسها: سبحان الله، والحمد لله، ولا إله إلا الله , والله أكبر»

Glycosidic bond is cleaved by glycosidase enzyme

- Glycosidases enzymes are a group of enzymes (since there are many types of glycosidic bonds).



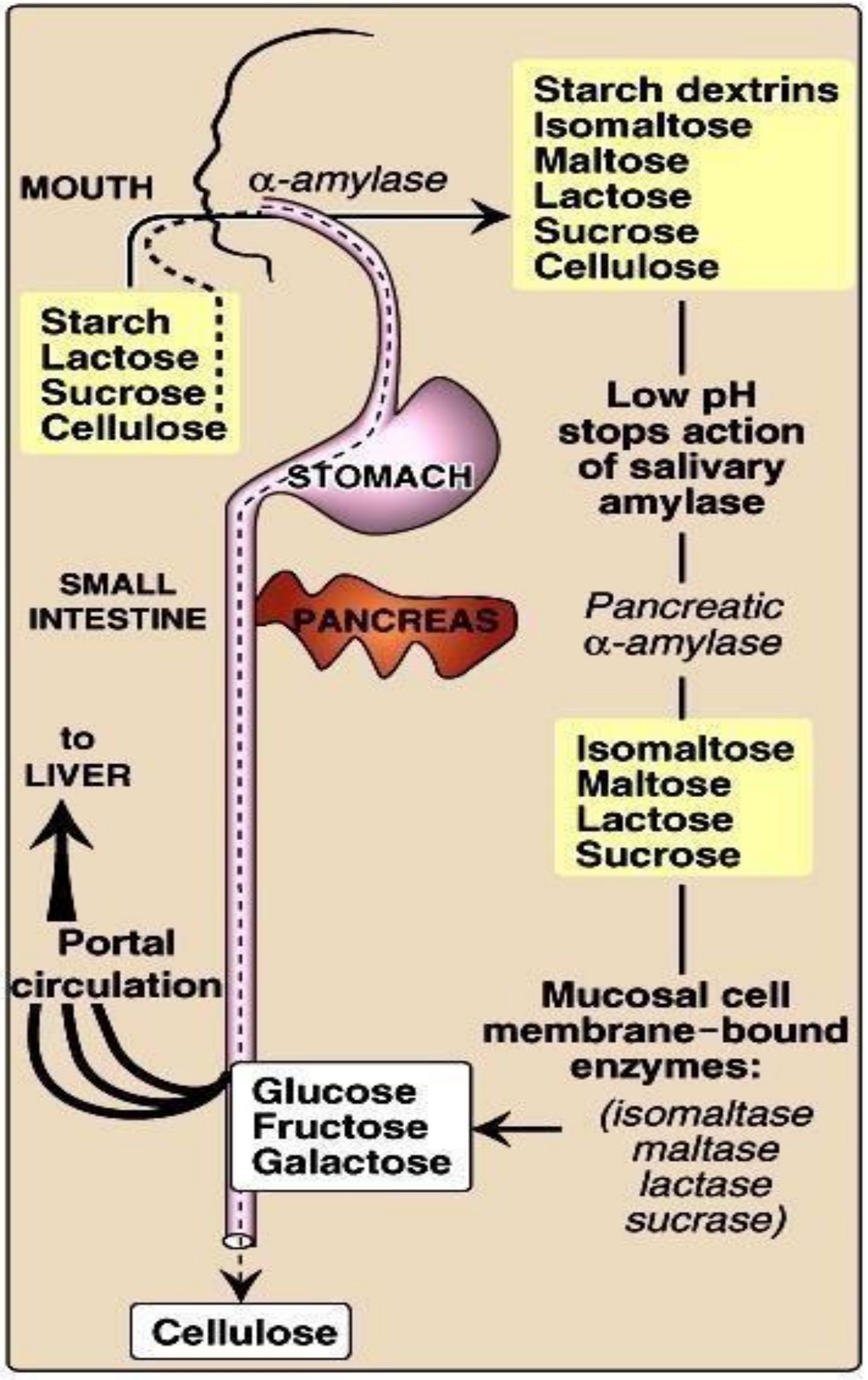
- A disaccharide is broken down to 2 monosaccharides (using glycosidases enzyme and a water molecule) which will then be absorbed (Disaccharides cannot be absorbed directly, even though they are only slightly larger than monosaccharides).

Absorption = Transfer of molecules from intestinal lumen → intestinal cells → bloodstream.

Hydrolysis reaction (cleavage with the use of water).

That's what happens during digestion using specialized enzymes.

Bond formation requires removing the hydroxyl group from carbon 1 and the hydrogen atom from carbon 4.



Oral digestion

Stomach

Digestion of Carbohydrates

Go to the next slides for explanation… Pages (16+17)

Pancreatic enzymes

Of course, these enzymes perform their function in the intestines, but here we have organized the information based on enzyme groups rather than their site of action.

Intestinal enzymes

How does digestion occur, and where does it take place?

- Digestion of carbohydrates starts very early on the oral cavity.
- Salivary glands secrete salivary enzyme "α amylase", which can recognize the α-1,4 linkages of starch (amylose and amylopectin).
- No things happen to lactose, sucrose, cellulose…
- It will randomly start hydrolysis different bonds, resulting in fragmentation of starch. (The doctor then began explaining page 18).
- Chewing typically lasts about 10 seconds. However, because time is a crucial factor for enzyme activity, this brief period often limits the complete digestion of starch molecules, resulting in only partial digestion.

- The dietary components move to the stomach (no things happen to the Carbs in the stomach, because there is no carbs digestion enzymes in the stomach). It involves the digestion of proteins by pepsin in a low pH environment.

How does digestion occur, and where does it take place?

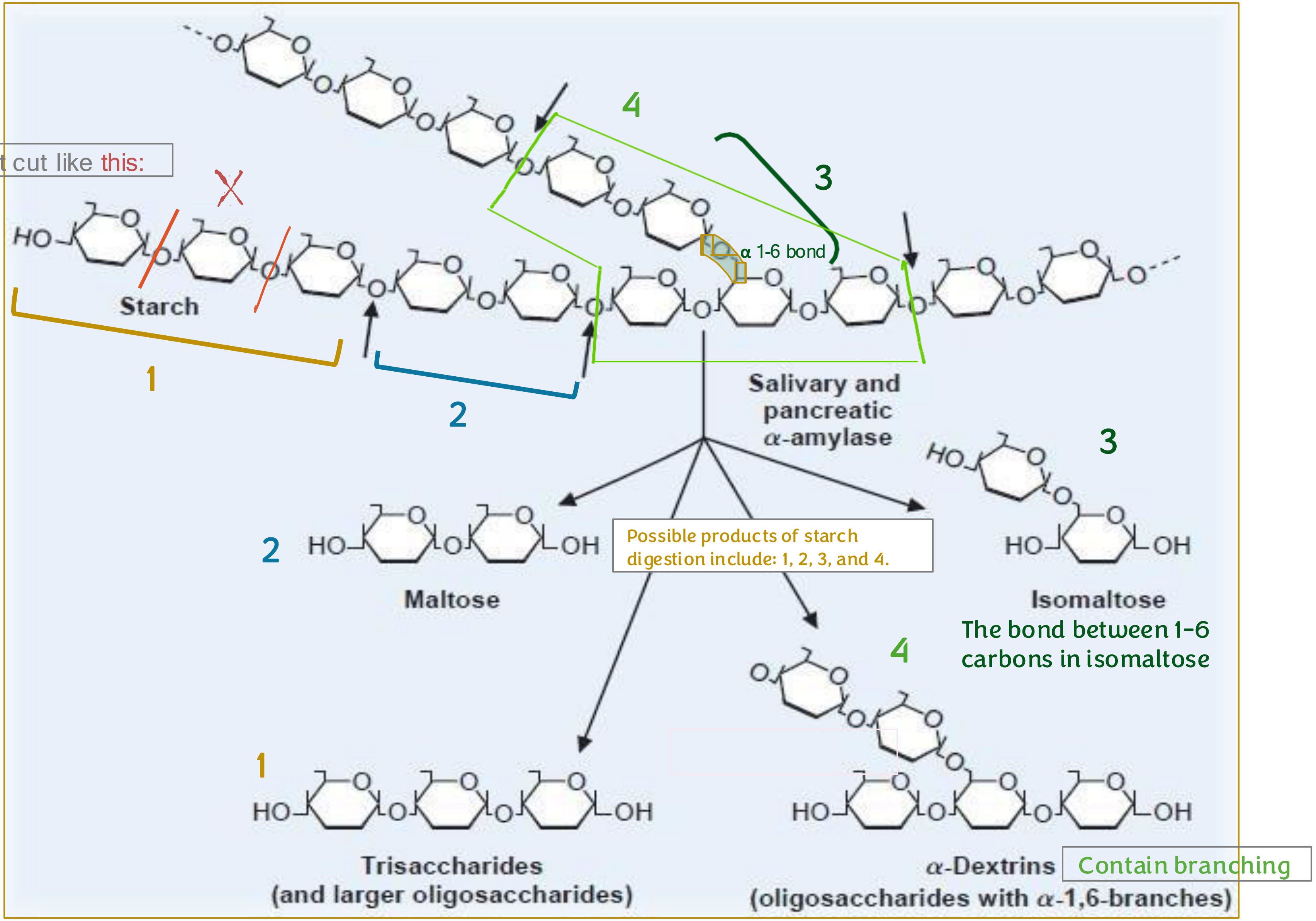
- Then they continue to the small intestine (especially duodenum).
- The pancreatic duct delivers digestive enzymes (for lipids, proteins, and carbohydrates) into the duodenum. (endocrinal gland produces insulin and glucagon, exocrine produces pancreatic juice)
- Regarding the carbs digestive enzyme, it is pancreatic α-amylase. It digests the α-1,4 linkages in starch but does not affect the branching (α-1,6 linkages). Digestion is more efficient because dietary components remain in the small intestine for a longer duration, allowing for complete digestion into disaccharides such as maltose and isomaltose (too small).

- Small intestinal cells protrude some digestive enzymes (membrane-bound enzymes) . These enzymes are specific in targeting different types of disaccharides (e.g, lactase, maltase, isomaltase, and sucrase). They digest disaccharides into monosaccharides, which can be absorbed.

Starch Digestion

See the next slide for explanation...

Doesn't cut like this:



Explaining of the previous slide:

- Before we begin, here is some basic information:
- Starch can exist as either **amylose** (an unbranched polymer of glucose) or **amylopectin** (a branched polymer, with branches occurring at carbon number 6 via **alpha-1,6 bonds**).
- The digestion of starch is carried out by the enzyme **amylase** (either **pancreatic amylase** or **salivary amylase**). Amylase can only hydrolyze **alpha- 1,4 glycosidic bonds.**

➢ Now, let's discuss the possible products of starch digestion:

1. **Trisaccharides or Larger Oligosaccharides:** unbalanced products that contain only glucose residues linked by **alpha-1,4 bonds**.
2. **Maltose:** A disaccharide made up of **two glucose residues** connected by an **alpha-1,4 bond**.
3. **Isomaltose:** A disaccharide composed of two glucose residues linked by an **alpha-1,6 bond.**
4. **Dextrins:** A broad category of molecules produced from the partial degradation of starch. Dextrins contain both **α-1,4** and **α-1,6 linkages** and often retain branch points.

- It doesn't break the ends monomer by monomer (it is not as meticulous as that).
- It is a random process.

Is it clear now?

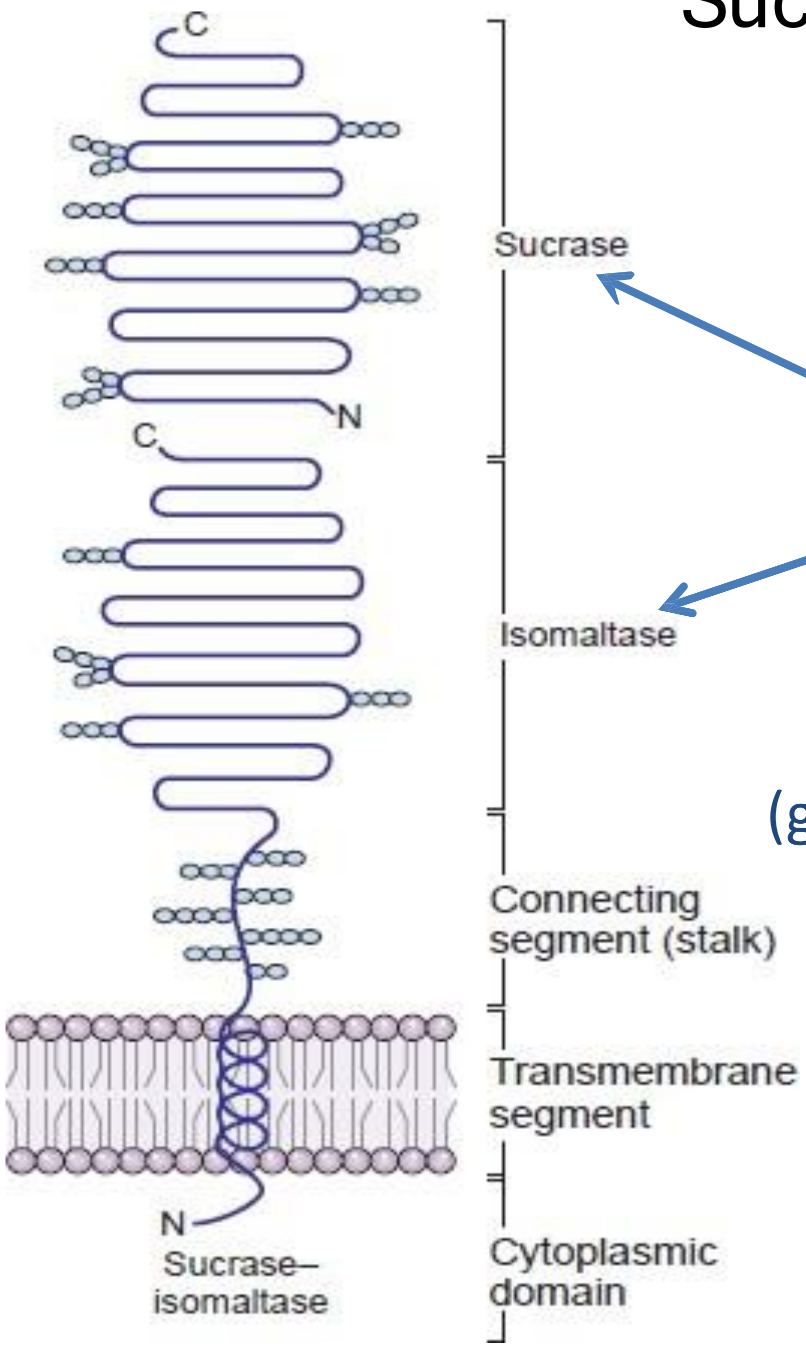
Mucosal cell membrane-bound enzymes

ENZYME	Bond Cleaved	Substrates
Isomaltase	α 1→ 6	Isomaltose
Maltase	α 1→ 4	Maltose
Sucrase	α 1→ 2 Anomeric	Sucrose
Lactase	β 1→ 4	Lactose
Trehalase	α 1→ 1	Trehalose 2 glucose residues connected to each other by α 1-1
Exoglycosidase (Glucoamylase) Acts on the termini	α 1→ 4 and α 1→ 6	Starch

Found in mushroom, honey, and sea food

اللهم أصلح أحوال المسلمين، وأنجِ المستضعفين منهم برحمتك، اللهمَّ عليك باليهود و أوليائهم، دمرهم اللهمَّ واطمس على أموالهم و عدتهم وأرِنا بهم يومًا أسودَ كيوم عادٍ وثمود

Sucrase-isomaltase complex and Glucoamylase



* Sucrase + isomaltase
Single protein → complex of two associated subunits
-Sucrase-maltase
- Isomaltase-maltase
Together 80% of the maltase activity

* Maltase + exoglycosidase (glucoamylase): no split

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*.

Sucrase-Isomaltase complex, which is a single polypeptide chain **encoded by the same gene**. This chain is later **cleaved** into enzymatic sites, with each having distinct but overlapping activities.

Enzymatic Activities:

Sucrase primarily hydrolyzes sucrose.

Isomaltase hydrolyzes isomaltose and maltose.

Combined Activity: Both enzymes have maltase activity greater than 80% when combined.

Post-translational Modification: The polypeptide chain undergoes cleavage after translation to become functional.

Structural Overview: The majority of the molecule is located on the luminal site, while a small helical transmembrane domain anchors it to the membrane.

Structural Functions:

The membrane-bound part functions as a connecting segment to stabilize the enzyme on the membrane.

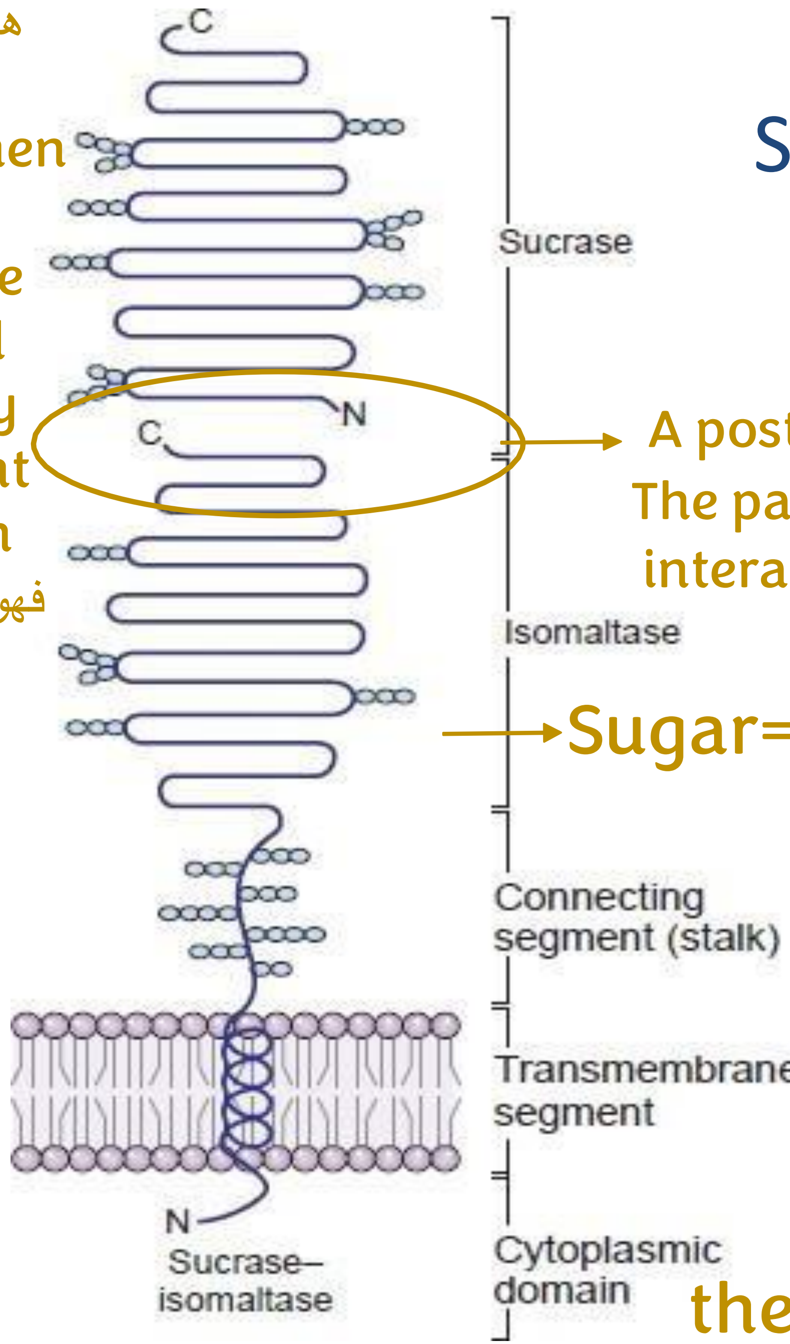
The transmembrane segment is a small helical domain.

The N-terminus of the enzyme is intracellular.

هل بنقطع وبصير
يسبح بال
Intestine lumen
لحاله ؟

No they are connected together by noncovalent interaction
فهو ماسك فعليا مش
انهfloating

Sucrase-isomaltase complex



A post transitional modification (cleavage of the chain)
The part that acts as a sucrase attached by non-covalent interactions to membrane-bound part.

Sugar= glycoprotein

The majority of molecule is located on the luminal site
(طالع لبرا)

A small/ single helical transmembrane domain.

their N-terminus is intracellular.

Maltase-exoglycoidase (Glucoamylase) complex

exoglycosidases, these are enzymes that hydrolyze the terminal sugar residues of oligosaccharides or glycoproteins.

This complex is embedded in the intestinal cell membrane by a helical transmembrane domain, with the majority of the chain located in the intestinal lumen.

The Maltase-exoglucosidase complex has two enzymatic activities: Maltase activity and Glucoamylase activity. It accounts for 20% of maltase activity.

Maltase-exoglycoidase (Glucoamylase) complex

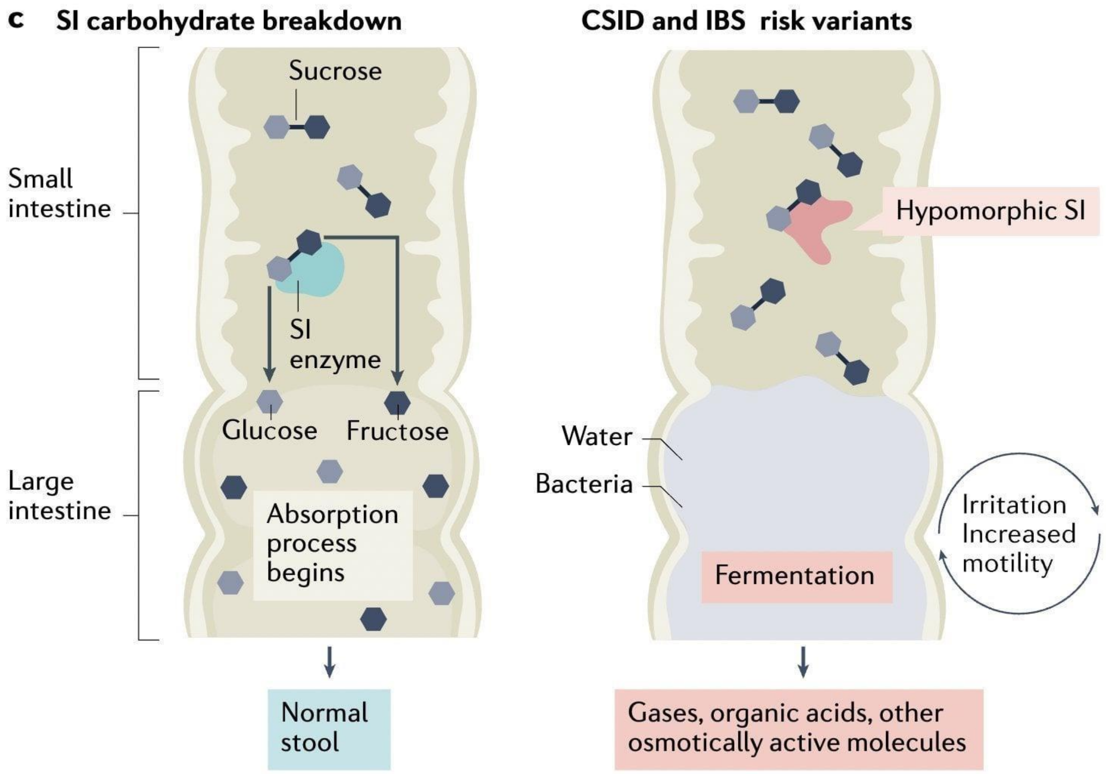
Comparison with Sucrase-Isomaltase Complex:
The Sucrase-Isomaltase (SI) complex is cleaved into two functional subunits, which remain associated with the cell membrane and perform two enzymatic activities.
In contrast, the Maltase-exoglucosidase complex (MGA) **does not get cleaved** and has two enzymatic activities: maltose digestion and glucoamylase activity (cleaving ($\alpha 1 \rightarrow 4$) glycosidic bonds in dextrins).
Maltase targets the 1-4 glycosidic bond between glucose units in maltose.
Sucrase targets the 1-2 glycosidic bond between glucose and fructose in sucrose.

Clinical Hint: Abnormal Degradation of disaccharides

1. Sucrase-isomaltase deficiency:

Causes:

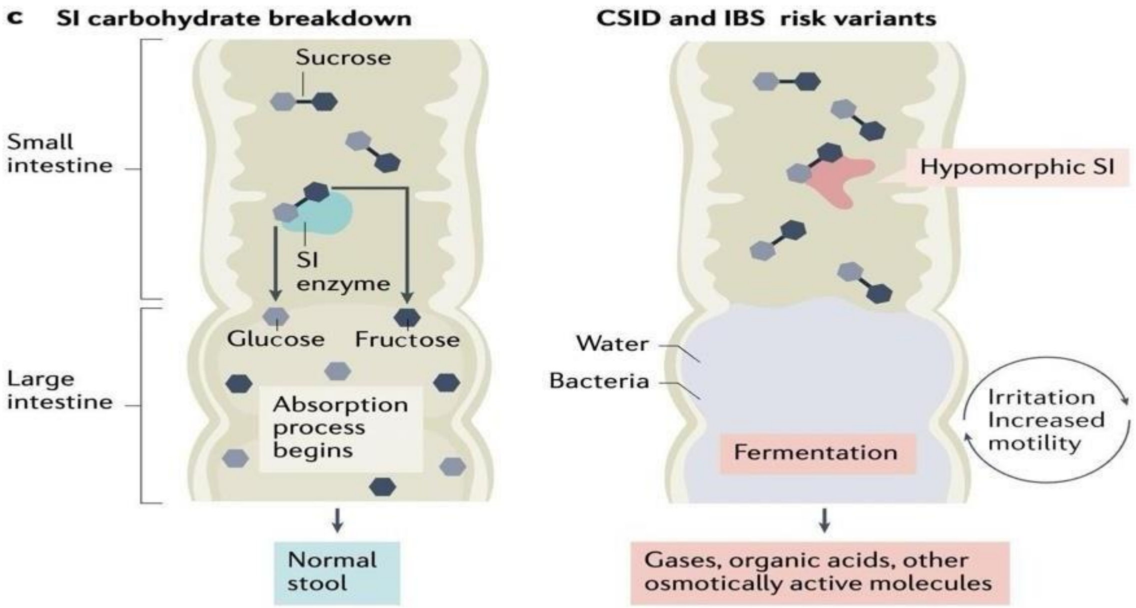
- Genetics
- Variety of intestinal diseases
- Malnutrition
- Injury of mucosa i.e by drugs
- Severe diarrhea



اللَّهُمَّ إِنِّي تَبَرَّأْتُ
مِنْ حَوْلِي وَقُوَّتِي،
وَاعْتَصَمْتُ بِحَوْلِكَ
وَقُوَّتِكَ، فَلَا حَوْلَ
وَلَا قُوَّةَ إِلَّا بِكَ.

Clinical Hint: Abnormal Degradation of disaccharides

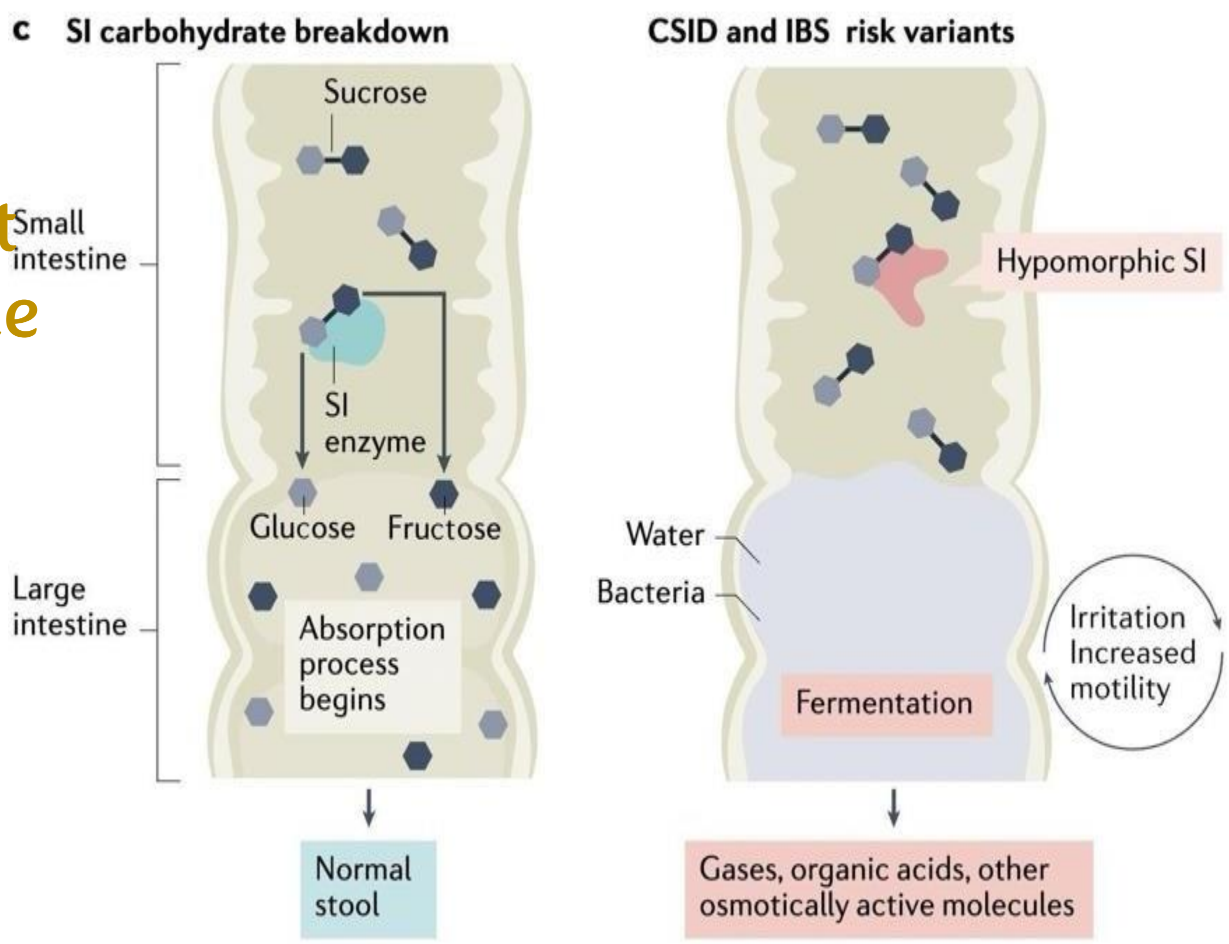
- The cells of the small intestine regenerate rapidly, every 3 days. However, if there is an underlying disease or medication involved, cell death will exceed regeneration, leading to a decrease in the number of cells. This results in a deficiency in digestion and absorption.



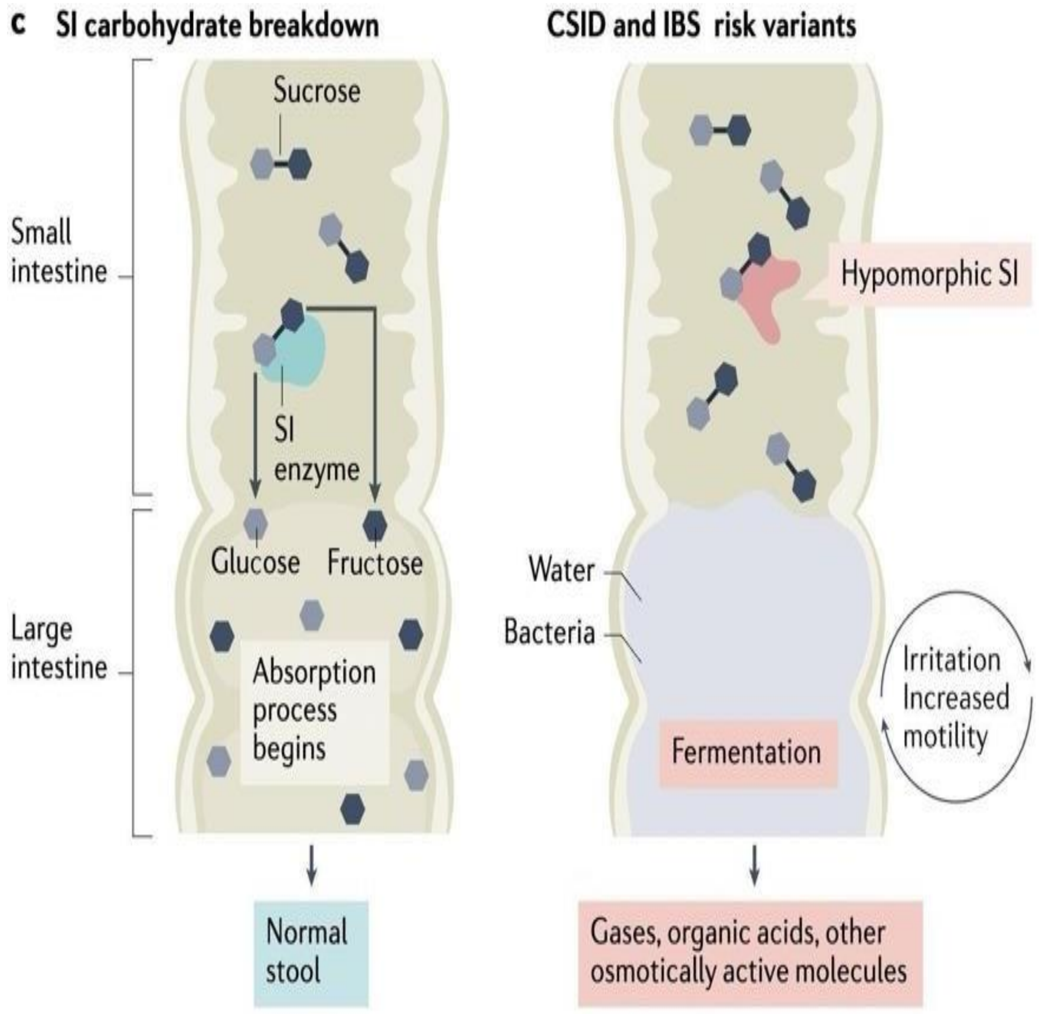
- People with malnutrition may have enzymes present, but there is no food available for absorption. Due to a prolonged lack of nutrition, the body loses its ability to produce proteins. Protein production (including enzymes) requires high amounts of energy.

- Diarrhea can sometimes be a result, and other times it can be a cause. For example, in chronic diseases, diarrhea is often a result of the condition. It affects the time factor, which in turn impacts digestion and absorption.

كل هذول يعتبروا عندهم
deficiency



When substances are not properly digested, they accumulate in the small intestine, increasing osmotic pressure. This causes water to enter the intestine, leading to diarrhea. Subsequently, the bacteria present in the intestine begin to use this undigested food, producing by-products such as methane gas and carbon dioxide. هذا الي بفسر لما واحد يحكيلك معي نفخه



رسالة من الفريق العلمي:

قال عمر بن الخطاب: "حَاسِبُوا أَنْفُسَكُمْ قَبْلَ أَنْ تُحَاسَبُوا ، وَزِنُوا أَنْفُسَكُمْ قَبْلَ أَنْ تُوزَنُوا ، فَإِنَّهُ أَهْوَنُ عَلَيْكُمْ فِي الْحِسَابِ غَدًا ، أَنْ تُحَاسِبُوا أَنْفُسَكُمُ الْيَوْمَ، وَتَزَيَّنُوا لِلْعَرْضِ الأَكْبَرِ، يَوْمَئِذٍ تُعْرَضُونَ لا تَخْفَى مِنْكُمْ خَافِيَةٌ".

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			