



Al-Razi Node

Doctor 022

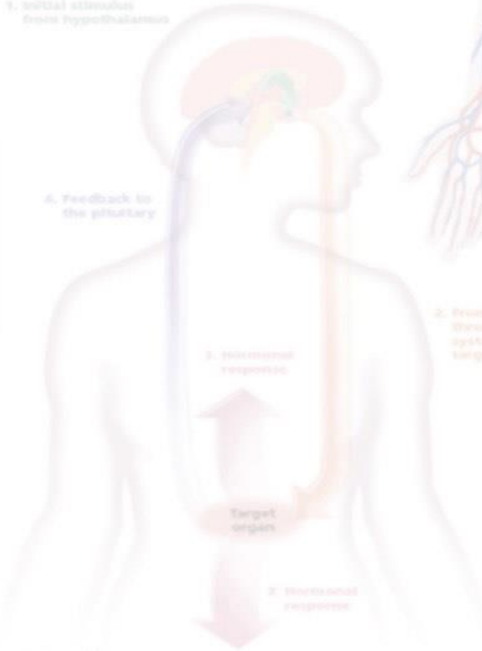


Biochemistry

Sheet no. 6

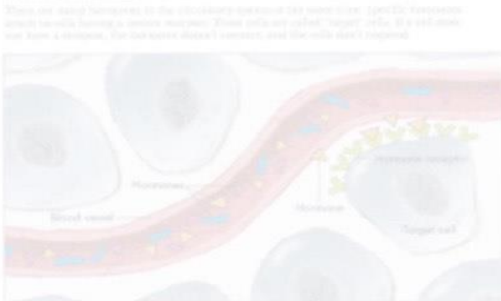
V2

1. Initial stimulus from hypothalamus



4. Feedback to the pituitary

Action of hormones



Pineal gland

The pineal gland secretes the hormones melatonin, prolactin, and growth hormone-inhibiting hormone.

The hypothalamic pituitary gland

The hypothalamus secretes hormones that regulate the anterior pituitary gland. The anterior pituitary gland secretes growth hormone, prolactin, and thyroid-stimulating hormone.

Digestive system

The digestive system of digestion is regulated by hormones including gastrin, cholecystokinin, secretin, and gastric acid.

Adrenal gland

The adrenal gland secretes hormones that regulate the metabolism, electrolyte balance, and blood pressure.

Kidney

The kidney secretes hormones that regulate the metabolism, electrolyte balance, and blood pressure.

Pancreas

The pancreas secretes hormones that regulate the metabolism, electrolyte balance, and blood pressure.

Function of insulin

During digestion, insulin is secreted into the bloodstream and stimulates the production of glucose in the liver. Insulin also stimulates the uptake of glucose by cells in the body.

Diabetes

Diabetes is a condition in which the body does not produce enough insulin or the body's cells do not respond properly to the insulin that is produced.

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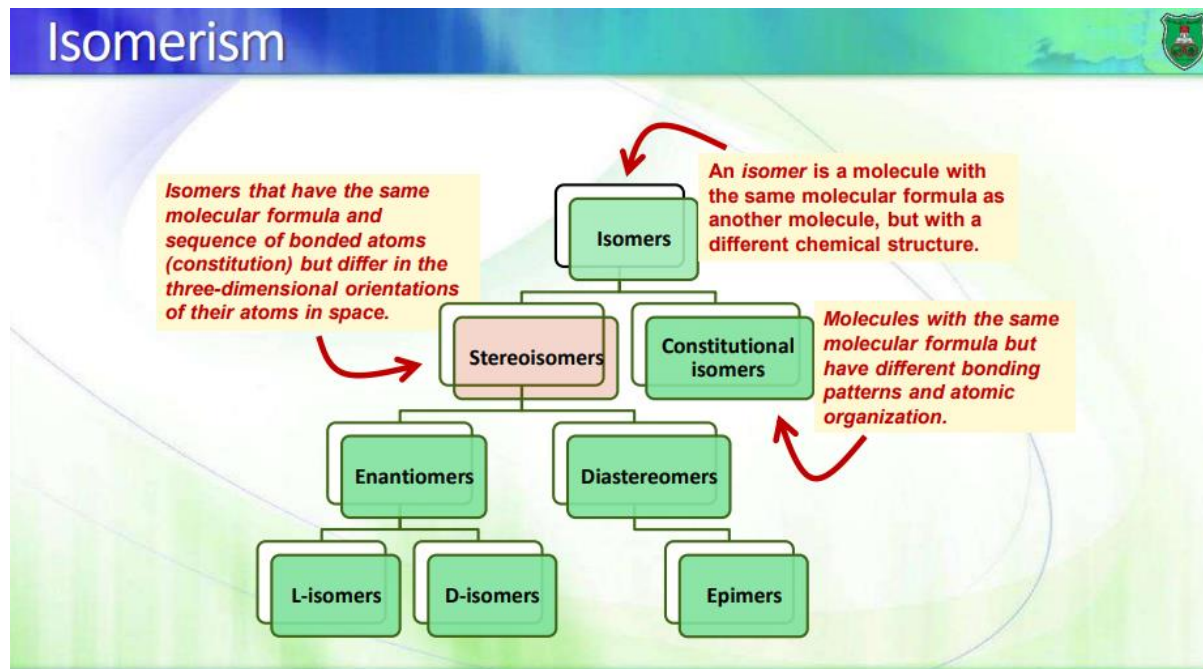
Dr.Diala, Dr.Mamoun

Quick revision :

- Carbohydrates are **Polyhydroxy Aldehydes or Ketones**.
- Aldehyde sugars are called **Aldoses**. Ketone sugars are called **Ketoses**.
- The simplest Aldose has **three** carbons and is called **Glyceraldehyde**. The simplest Ketose also has three carbons and is called **Dihydroxyacetone**.
- The Glyceraldehyde's **chiral center** causes the sugar to have different **stereoisomers** called **Enantiomers, which are non-superimposable mirror images (D or L)**. Note that dihydroxyacetone does not have **any chiral center** therefore **it has neither D nor L forms**.

We will discuss these forms later.

Now we'll revise different kinds of isomers that we'll need to understand for the future of this course.



-Isomers

They, as a whole, have **two** major types:

- 1- **Constitutional isomers.**
- 2- **Stereoisomers.**

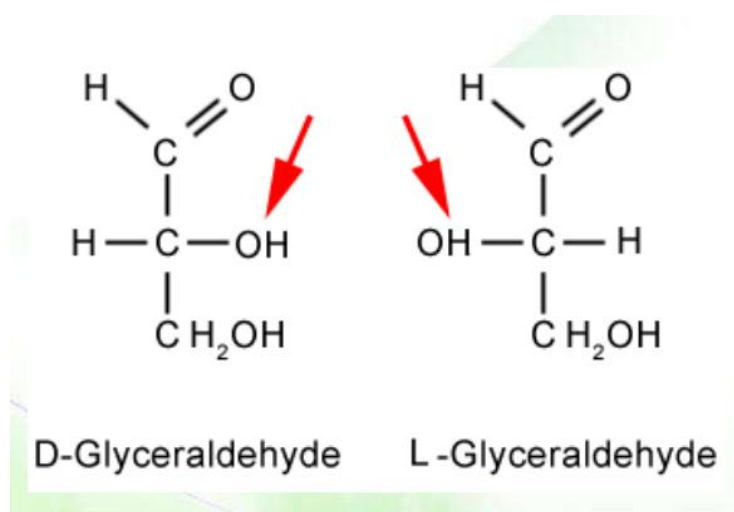
The main difference between the two is that **Stereoisomers differ in the spatial arrangement (الترتيب المكاني) of atoms**, causing the 3D shape of each isomer to be different from the other. **While Constitutional isomers have different bonding patterns (ترتيب الذرات بذرات مختلفة).** We won't be focusing on constitutional isomers for now. We'll be focusing more on Stereoisomers.

Stereoisomers

- 1- **Enantiomers**
- 2- **Diastereomers**

1- Enantiomers:

They are of two forms, 'D' and 'L' (D (dexter, which means 'right'), L (laevus, which means 'left')) the point of difference that decides whether the molecule is 'D' or 'L' is the **OH group's position at the Chiral Center farthest from the carbonyl group (the chiral center with the highest number).** Let's use the example of Glyceraldehyde to explain:

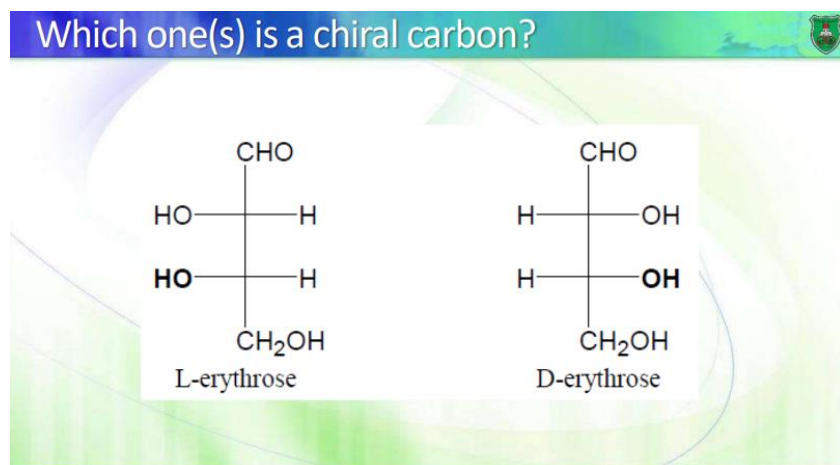


If the OH group at the last chiral center is on the **Right**, the molecule is considered a **'D' enantiomer.**

If the OH group at the last chiral center is on the **Left**, the molecule is considered an '**L**' enantiomer.

Notice how in both cases, the naming of the compound remains "Glyceraldehyde", the only difference being the L/D configuration.

But in case we have a **larger** number of carbons, like in this example :

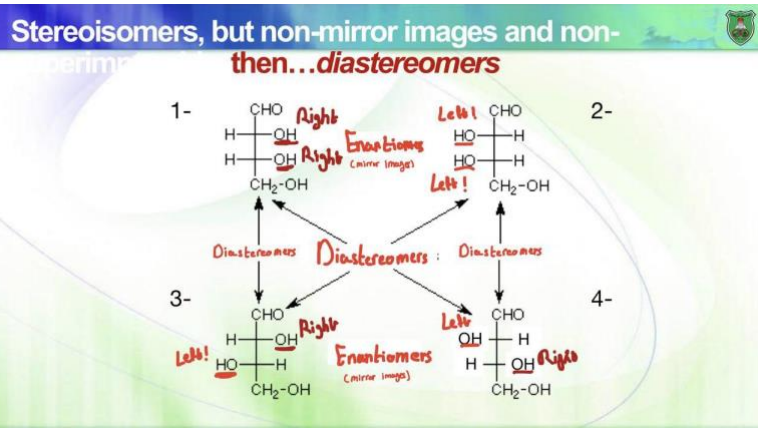


Which chiral center should we use for classification of the sugar into 'D' and 'L'? **The last Chiral Center.**

Enantiomers also have the characteristic of being **Non-superimposable Mirror images** of one another, meaning that **all groups** around a chiral center found on the **right** in one molecule will be on the **left** in its enantiomer. And all those on the left will be on the right. The image in the next page will help in understanding.

2- Diastereomers:

The other type of Stereoisomers is called **Diastereomers**, they are defined as **two molecules with the same formula, same bonding, and the same Orientation *except* for some groups(not mirror images)**. An example to explain this:

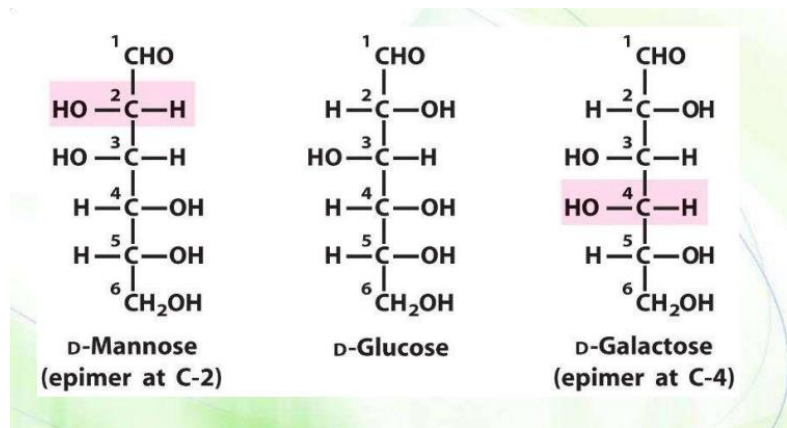


The sugars represented in number 1 and number 3 are **Diastereomers**, because one **OH group** stayed on the right while the other inverted from right to left.

Numbers 2 and 4 are also **Diastereomers** because one **OH group** stayed on the left while the other inverted from left to right.

Now the sugars represented in number 1 and number 2 are **Enantiomers**, because all **OH groups** that were on **the right** of the chiral centers inverted to be on their **left**. Which creates the complete non-superimposable mirror image characteristic of Enantiomers.

So we can understand that Enantiomers differ in the spatial arrangement of **all** groups around the chiral centers, but Diastereomers differ in **some groups** while the **others stay as they are**.



Notice that in different **Diastereomers**, the names of the compounds **change** (unlike enantiomers, where the difference is only in the L and D), such as the Diastereomers Glucose, Galactose and Mannose. The change between the spatial arrangement in these molecules causes them to

have **significantly different** characteristics and reactions where **one is not able to substitute for the other**. Note that the same effect is found in enantiomers, just on a lesser scale. An example would be enzymes not working with L-Glucose but working on D-Glucose.

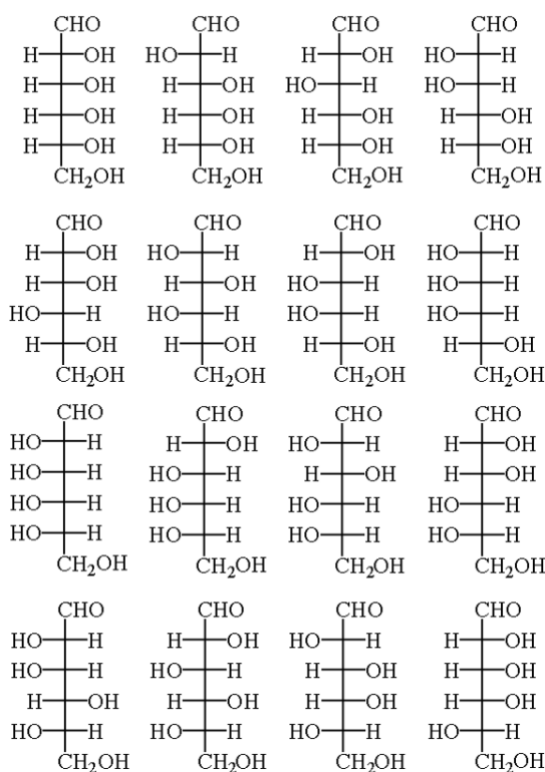
A special case of Diastereomers are **Epimers** where only **one** group changes its spatial arrangement. Such as the example above, **Glucose** differs from **Galactose** only in **carbon 4** having an OH group on the **right in Glucose**, and on the **left in Galactose**. As we can see, only One group has changed, we call these Epimers. Same way between Glucose and Mannose, **carbon 2 in Glucose** has the OH group on the **right**, while **Mannose's** is on the **left**.

However, Mannose and Galactose are not Epimers; because they differ in the configuration at **more than one chiral center** (carbons number 4 and 2).

Note that all Epimers are considered Diastereomers, while not all Diastereomers are Epimers.

Depending on the image below, answer the following questions:

16 Aldohehexoses



-Which structure represents these monosaccharides?(key: we start numbering the columns from left to right)

- 1) D-Glucose(answer: 1st row 3rd column)
- 2) D-Mannose(answer: 1st row 4th column)
- 3)D-Galactose(answer: 2nd row 3rd column)
- 4) L-Glucose(answer: 3rd row 3rd column)
- 5)L-Mannose(answer: 3rd row 4th column)
- 6)L-Galactose(answer: 4th row 3rd column)

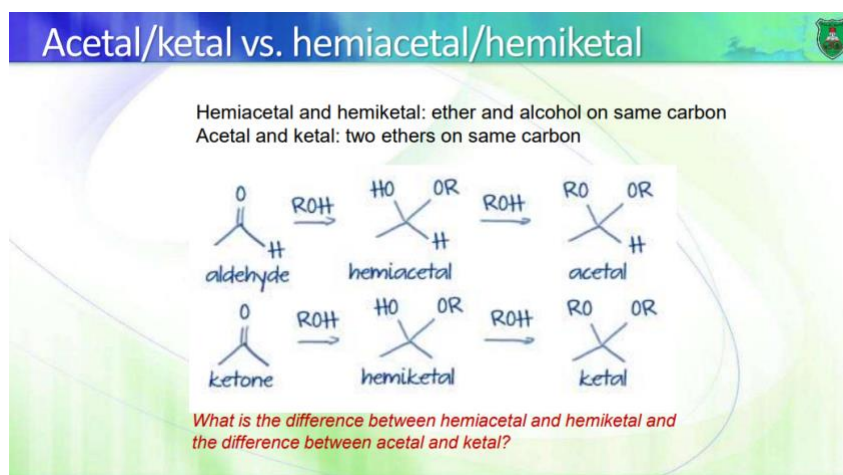
-How many epimers does D-Glucose have? **Answer:4**

Explanation: D-Glucose has 4 chiral centers, an epimer differs in the configuration at only one chiral center, therefore for every chiral center that we change its configuration we obtain an epimer.

-How many diastereomers does D-Glucose have? **Answer:14**

Explanation: we have 16 stereoisomers for an aldohexose, D-glucose and L-Glucose are a pair of enantiomers, the remaining stereoisomers (14) are diastereomers.

Acetal/Ketal, Hemiacetal/Hemiketal, and Sugar Ring Formation :



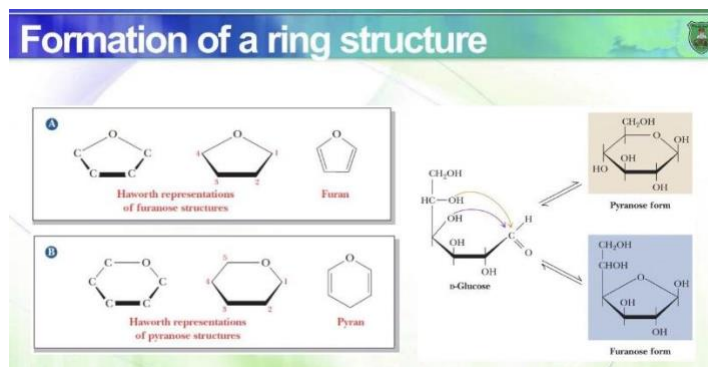
Hemiacetals: are molecules where a carbon is attached to **both an OR group and an OH group.**

Acetals: are molecules where the carbon is attached to **two OR groups.**

Hemiketals and hemiacetals have the same definition, it's just that the **hemiacetals** originate from **Aldehydes**, while **hemiketals** take origin from **Ketones.**

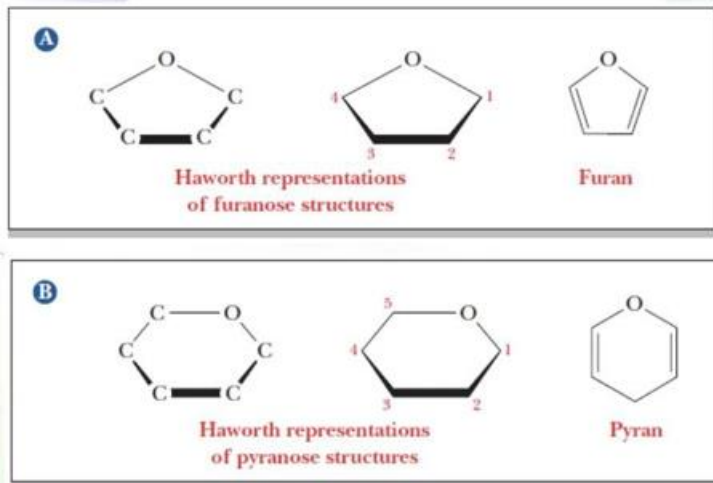
They result from the reaction of **Aldehydes or Ketones** with **Alcohols**. When they react with alcohols the double bond between carbon and oxygen turns into a single bond with a hydrogen atom binds to the oxygen and an OR group binds to the carbon. **when increasing the concentration of the Alcohol or adding a different alcohol**, the OH group that the Hemiacetal or hemiketal has turns into an OR group, which transforms the molecule into an Acetal or a Ketal, respectively.

This is important in the **formation of the Sugar Rings:**



The ring structure of the sugar forms when the **Anomeric** carbon (the carbonyl carbon, in aldoses it's C1, in ketoses it's C2) binds to the oxygen atom of the **last chiral center** of the sugar. When this ring structure forms, the Anomeric carbon would have an **OH group** attached to it, and an **Oxygen atom** which is connected to the rest of the sugar structure, making it an OR group.

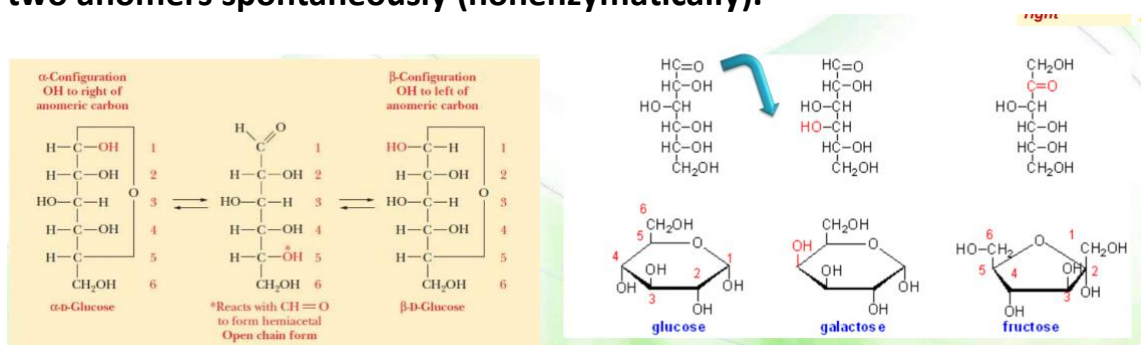
This all would mean that the Anomeric carbon's bonding causes the transformation of **Aldoses** into **Hemiacetals** or **Ketoses** into **Hemiketals**. It's important to know this because that **directs the reactions** that sugars undergo. For example, when **Disaccharides are formed**, one sugar reacts with its **Anomeric carbon** as a **hemiacetal**, and the other reacts as an **alcohol**. This reaction, Hemiacetal and Alcohol, would go on to give us an Acetal, which is a Disaccharide.



Another small note is the **naming** of these ring structures, many books would often refer to certain ring structures with different names depending on **the kind of ring structure** it forms. **Five-membered rings**, which consist of **4 carbons** and **1 oxygen** are called **Furans**. **Six-membered rings** (5 carbon, 1 oxygen) are named **Pyrans**. So Instead of referring to the five-membered ring Ribose as “Ribose”, they’d call it “Ribofuranose” and fructose would be referred to as “fructofuranose”.for glucose (which is a six-membered ring) it would be referred to as “glucopyranose”.

Anomers:

After the Anomeric carbon forms a bond with the oxygen of the last chiral center of a sugar, which makes the ring structure, that carbon obtains an OH group that it didn’t have before. Anomers, specifically, **are derived from the spatial changes in that one OH group**. Sugars can alternate between the two anomers spontaneously (nonenzymatically).



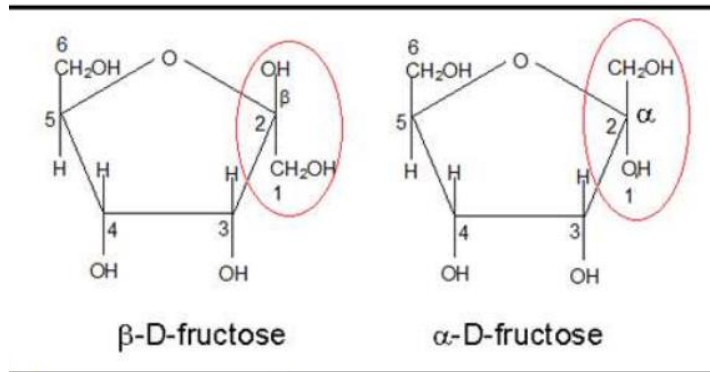
A note before I explain, in the sugar's ring formation, each group that is found on the **right** of each carbon becomes **down/below the sugar ring's plane**, and the ones on the **left** become **above the plane**. Now when the ring was formed, the Anomeric carbon did not have an OH group, but in the final ring structure, it does. This leaves **two** possibilities for the OH group's position, either being **above the plane or below it**. And that's how Anomers are derived. And both those states (OH being below and above) and the linear structure are found **in equilibrium with one another**.

The Anomers in '**D**' form are of two types, either **Alpha** or **Beta**. **Alpha anomer** has the OH group placed **below the plane of the ring**, while **Beta anomer** has the OH group **above the plane of the ring**. The Anomers derived from '**L**' form sugars have opposite definitions to those of "**D**" 's; meaning that **Alpha anomer's OH group in the 'L' form** is found **Above the plane**, while **Beta anomer's OH group** is below the plane.

A note to take is that **Anomers and Enantiomers differ in the point of transformation; 'D' and 'L' sugars don't spontaneously change into one another, while Alpha and Beta (and the linear structure, but it tends to stay more as ring because it's more stable) sugars can and do so occasionally because they are found in equilibrium with one another**.

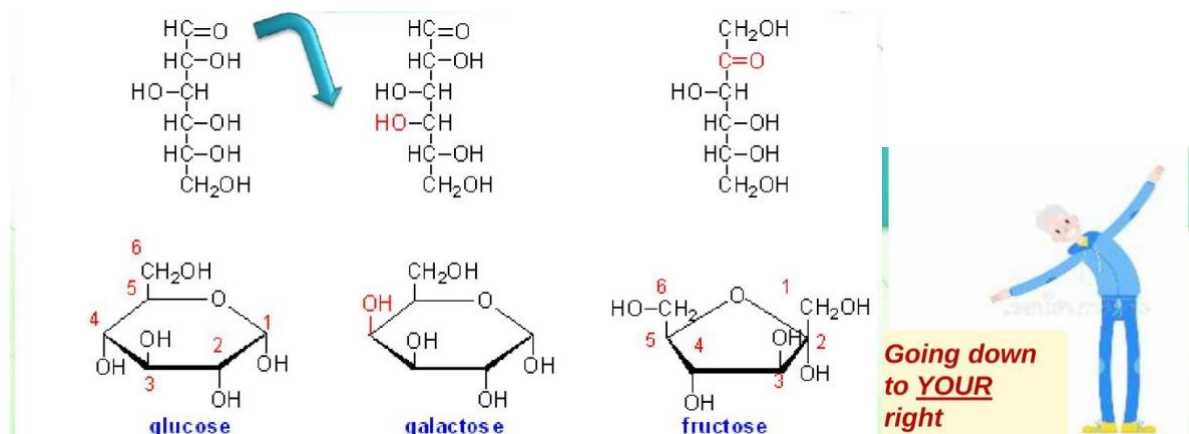
Beta structures for D-glucose are more stable than Alpha structures because they possess less steric hindrance (there is more space between hydroxyl groups when there is one above the plane of the ring and one below it and this is the case in the beta anomer)
64% of the time, a molecule of D-Glucose stays as the Beta Anomer.
36% of the time, D-glucose stays as the Alpha Anomer.
<0.1% of the time, it becomes linear. The low percentage is purely due to its instability, but it's important because it allows for certain reaction of the sugar's to occur.

But, It's good to note that the **Beta** structure **isn't always the most stable** structure for different sugars.



In Fructose, the Beta structure forces the CH₂OH group (which is significantly larger than the OH group) to be in a tighter space due to C3's OH group; causing more steric strain, which makes it less stable. While in the Alpha structure, the smaller group (OH) is placed below where it fits better and the larger group (CH₂OH) is placed with more space, causing less steric strain, making the Alpha structure more stable in the case of Fructose.

Note about formation of anomers: Once the ring structure forms every OH group on the right side moves like this: (below the plane of the ring)

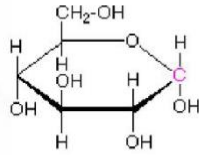


Except the carbonyl group because it did not have an OH group so it could be up or down making different anomers.

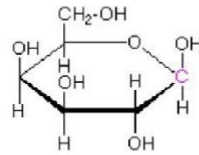
- look at the picture now: the OH attached to carbon number 4 in glucose is directed downward while in galactose it is directed upward.
- How can I determine if this sugar is D or L because the carbon number 5 doesn't have an OH group? If the last carbon (number six in this example) is above the plane of the ring it is a D sugar and if it is below the plane of the ring it is an L sugar.

- We can distinguish between carbons number 2 and 5 in fructose ring structure by knowing that carbon number 2 (the anomeric carbon) has an OH group while carbon number 5 doesn't (it has an H instead).

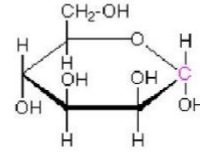
Examples of Some Pyranose Forms of Hexoses



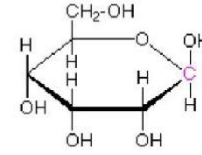
α -D-glucopyranose



β -D-galactopyranose

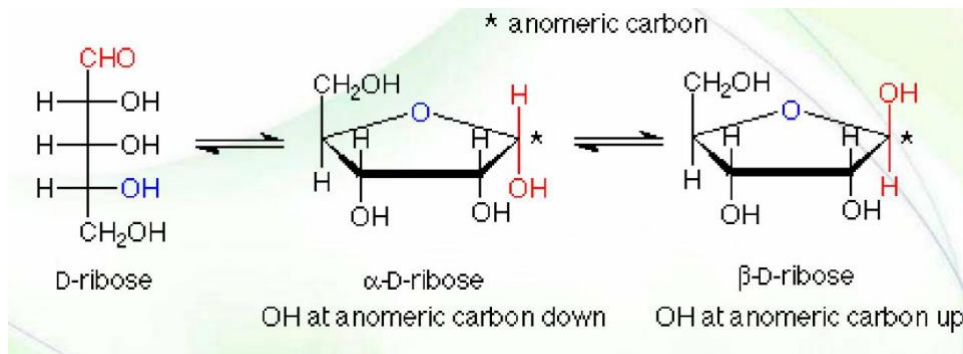


α -D-mannopyranose



β -D-allopyranose

هون بحكيك
امثلة وانه ممكن
الاسم يختلف لكن
هو نفسه يعني
زي الأول هو
glucose



This is ribofuranose. Note that the same sugar can alternate between alpha and beta anomers spontaneously. Beta ribose is more stable than alpha ribose (because of the larger space between hydroxyl groups)

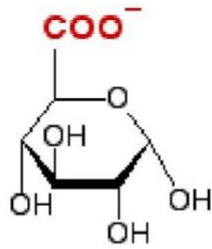
Modified sugars:

Modification of sugars includes reactions or addition of some groups to them To create certain properties such as making them more polar or to incorporate them into different structures.

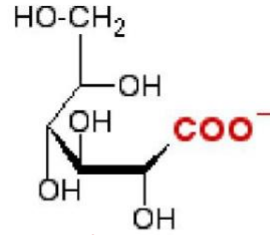
One of these modifications is **Oxidation**.

Oxidation of an aldehyde results in a carboxylic acid, and oxidation of an alcohol results in an aldehyde or a ketone depending on whether the alcohol is 1° or 2°.

(Note that 3° alcohols and ketones don't undergo Oxidation) **look at the picture!**



α -D-glucuronate ال بتميزه ur
(D-glucuronic acid, **GlcUA**)
from **oxidation of glucose C6 OH**

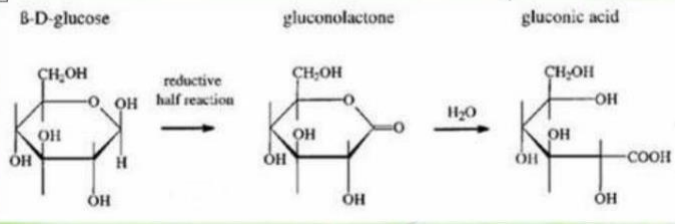
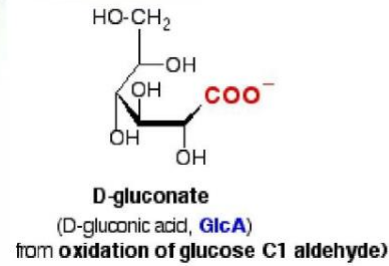
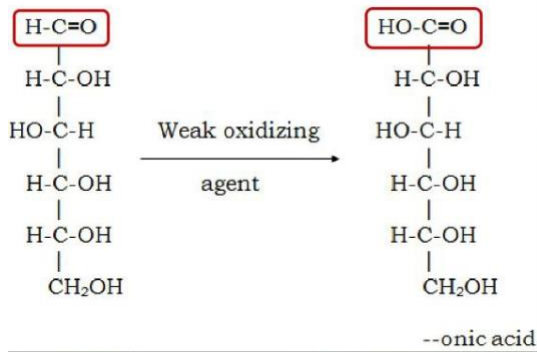


we call it gluconate if only the anomeric carbon is oxidized.
D-gluconate
(D-gluconic acid, **GlcA**)
from **oxidation of glucose C1 aldehyde**

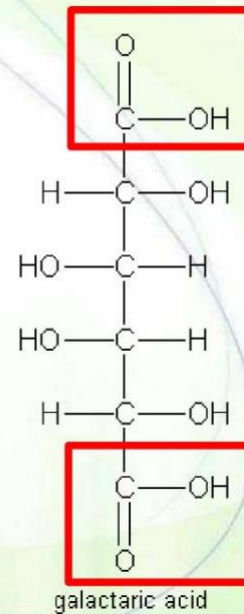
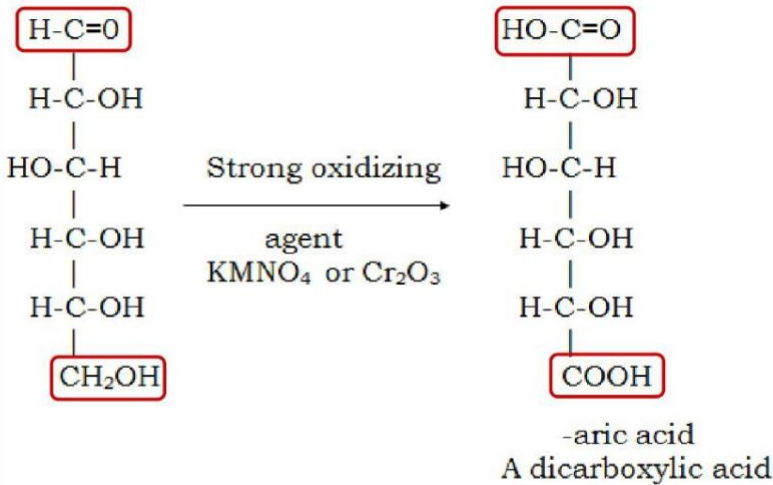
If we look at this picture, we will observe that the Oxidation of an aldehyde is easier than the oxidation of an alcohol (in the presence of weak oxidizing agent) because it happens in one step.

- When we oxidize a 1° alcohol, it will become an aldehyde then a carboxylic acid, undergoing 2 oxidation steps.
- Weak oxidizing agents will oxidize the **anomeric carbon**.
- In the oxidation of the anomeric carbon, the ring opens first, then the reaction occurs, and finally, the ring closes again.
- In the presence of strong oxidizing agent both could happen (oxidation of the aldehyde and alcohol).
- When we oxidize glucose, we will not get glucuronate or gluconate directly. Instead, we will get their acids (glucuronic or gluconic acids).

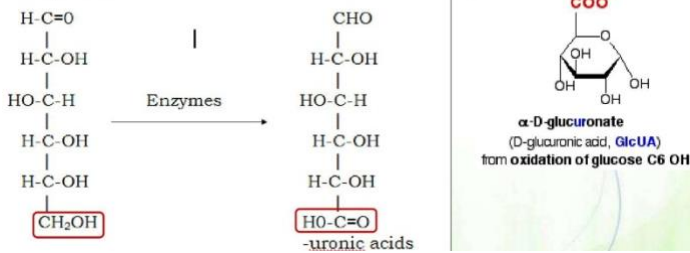
a. Weak oxidizing agent



b. Strong oxidizing agents



c. Oxidation of primary alcohol end in biological systems



If I need GLUCURONATE, how can I get it?

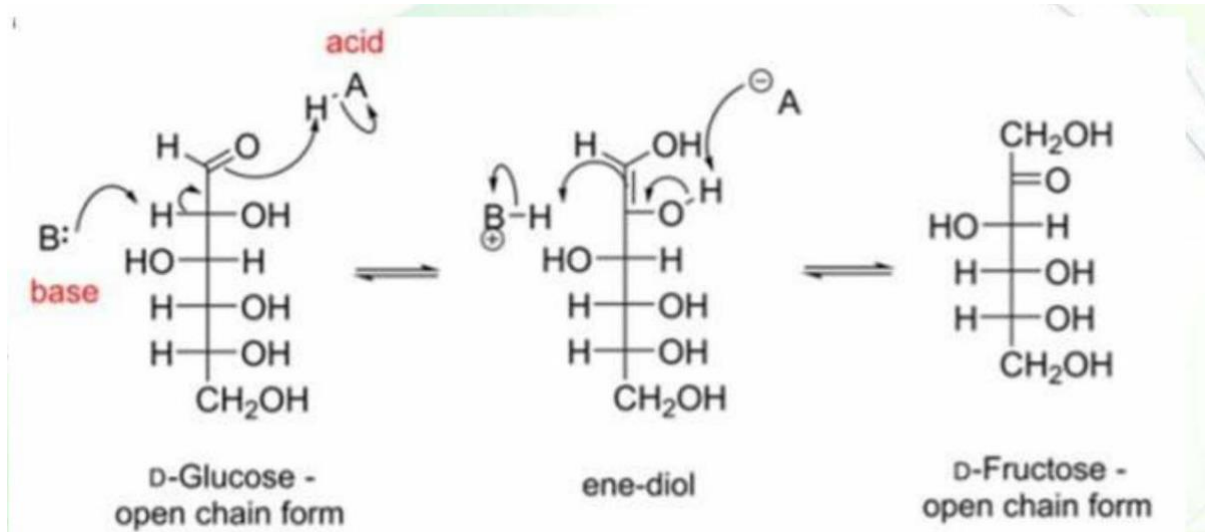
There is an enzyme that can distinguish between carbon number 6 and can oxidize it without oxidizing the anomeric carbon.

So to avoid getting strong and weak oxidizing agents involved I have an enzyme that can do what I have just mentioned.

That doesn't mean that I don't have or don't need gluconate but I need different forms so I must have a way to produce them (like gluconate) which is by using enzymes.

All these oxidations are for aldoses, what about ketoses????

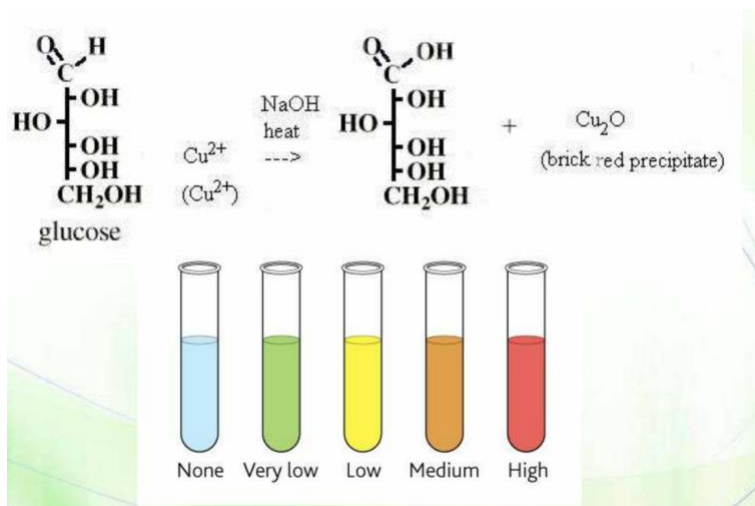
- Ketones don't undergo oxidation, but ketoses can transform into aldoses, which can then undergo oxidation.
- It can transform into aldoses by electron rearrangement (rearrangement of bonds)



Electrons move from the carbon-oxygen double bond to form a carbon-carbon double bond between carbons number 2 and 1, carbon 1 loses a H that becomes bonded to the oxygen (it becomes an OH) forming an ene-diol then the oxygen atom forms a double bond with carbon number 1 and hydrogen becomes bonded with carbon number 2 forming the aldose.

One of the most important biochemical tests that we can use to distinguish the presence of any aldehyde or ketone is **Benedict's test**. (No matter if it was an aldose or a ketose).

- If I have a solution and want to know if it contains a ketone or an aldehyde I add **Benedict's reagent** then I will have a colour change and based on that I can determine the presence of the aldehyde or the lack thereof.



This **Benedict's reagent** at first has Cu^{2+} (**blue**)

If I add glucose (or the aldehyde that I want to test for), it will be oxidized and the Cu^{2+} will be reduced into Cu_2O , this compound is a precipitate and its color is brick red.

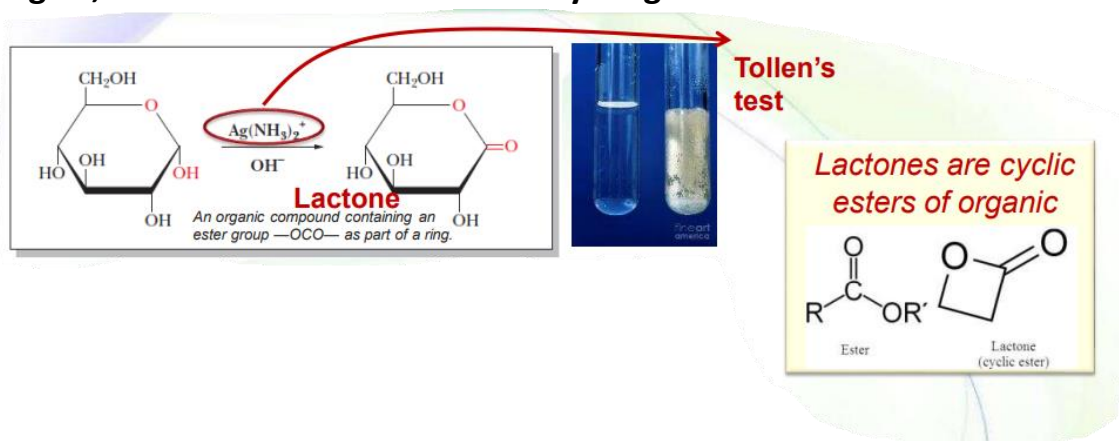
- Oxidation of cyclic sugars (Lactone)

Tollen's test

Another way of oxidizing sugars is using Tollen's reagent ($\text{Ag}(\text{NH}_3)_2^+$), which follows the principle of Benedict's test. Oxidizing reaction using Tollen's reagent precipitates silver (Ag) on the walls of the test tube making a mirror that indicates the oxidization of the sugar (or aldehyde) and reduction of Ag.

Oxidizing a sugar either in open form or ring form, produces a class of organic compounds called Lactones.

A more recent method for the detection of glucose, but not other reducing sugars, is based on the use of the enzyme glucose oxidase.



Oxidation reactions on other organic compounds :

Vitamin C: Also known as (Ascorbic acid), is an unsaturated lactone highly present in citrus (الحمضيات) and has an important role in the human immune system (by attacking AOS and free radical) and it resists oxidizing agents. Vitamin C's oxidation by air, followed the hydrolysis of the ester bond, leads to the loss of its activity as a vitamin.

Therefore, the lack of fresh foods can cause vitamin C deficiencies which, in turn, can lead to scurvy, a disease affecting collagen production (remember that collagen is the most abundant protein in our bodies)

Scurvy is a disease caused by a serious vitamin C deficiency. Left untreated, scurvy can lead to bleeding gums, loosened teeth and bleeding under your skin, it might lead to death.

Reduction reactions

Polyhydroxy aldehydes or ketones —(Reduction)—>Poly atom (primary and secondary alcohol).

Adding (H₂) :

Reducing sugars by adding H₂ returns them into their original form which is Alcohols, by converting the oxo group (=O) into hydroxyl group (-OH).

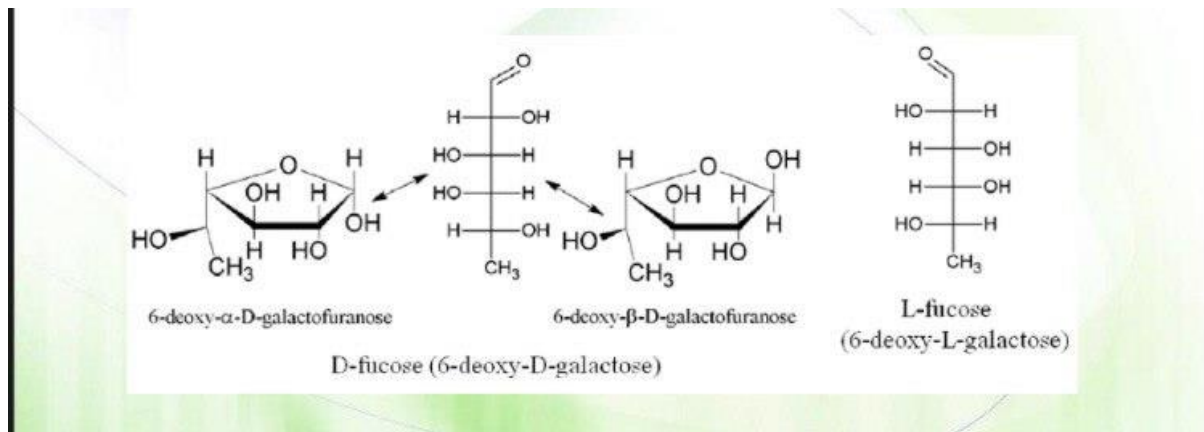
Examples of reduced sugars are : Glycerol (the backbone of fatty acids) , Sorbitol (artificial sweetener) , Mannitol, Inositol and Xylitol

Removing (O) :

Reducing sugars by removing (O) turn sugars into deoxy sugars. It happens by removing the hydroxyl group (-OH) and replacing it with a hydrogen atom (-H). An important example is 2-deoxyribose, which is a constituent of DNA.

Deoxyribose= Ribose – oxygen atom at C2

Another form of reduction reactions is the production of L-fucose (L-6-deoxygalactose), which is found in the carbohydrate portions of some glycoproteins. Here is a clarification :

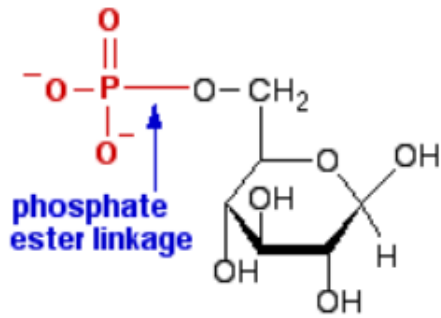


-In the image above hydroxide group is removed so fucose is composed.

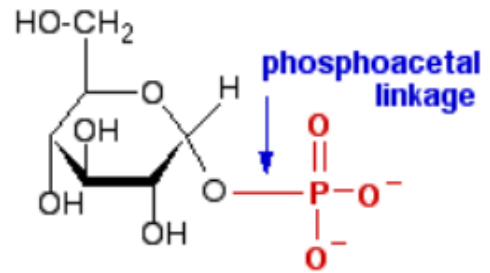
Esterification Reactions

***Reminder: the general formula of esters is (RCOOR).**

The esterification of sugars is not converting sugars into conventional ester, but into a different type of esters called Phosphate Esters, and what used to be (-OH) on the sugar is turned into (-OPO₃).



β -D-glucose-6-phosphate
(an ordinary **phosphate ester**)



α -D-glucose-1-phosphate
(a **phosphoacetal**)

When carbon no 1 (anomeric carbon) is esterified, it turns into phosphoacetal

When carbon no 6 is esterified , it is turns into phosphate ester.

تجري الرِّياحُ بِما يَشاءُ اللهُ لها
للهِ نَحْنُ، وَمَوْجُ البَحْرِ والسُّفُنِ

V2:

1-page 5: replaced “carbon(s)” with “OH group(s)”.

2-rearranged some sentences for a better sequence of information.

3-fixed grammatical and spelling mistakes.