

CC7 Unit 2.1: Monosaccharides and Disaccharides, Types and Properties

There are four major classes of biomolecules present in the biosphere, a) Proteins, b) Lipids, c) Nucleic acids and d) Carbohydrates. Carbohydrates are the most abundant biomolecules on earth. Carbohydrates serve various functions including,

i) It acts as reservoir of energy stores, fuels and metabolic intermediates. The oxidation of carbohydrates plays the central role in energy metabolism in most of the non-photosynthetic cells.

ii) The polymers of carbohydrates are the main ingredients in the bacterial cell wall and plants and serve as structural framework to maintain shape and size of these cells.

iii) The ribose and deoxyribose sugars form part of the structural framework of genome that includes DNA and RNA.

iv) Carbohydrates are also attached to many proteins and lipids and these linked carbohydrates play a key role in cell to cell communication such as its interaction between the cells and with the cellular environments.

v) Carbohydrates also show huge structural diversity that makes carbohydrate an important mediator of various biological processes.

- Chemically, carbohydrates are aldehyde or ketones with multiple hydroxyl groups. Many, but not all, carbohydrates have empirical formula $(\text{CH}_2\text{O})_n$, some carbohydrates also contain nitrogen, sulphur and phosphorus.

Carbon-hydrate

Based on its size, the carbohydrates have been characterized into three major classes

1) Monosaccharides: contains single polyhydroxy aldehyde or ketones such as glucose

2) Oligosaccharides: contains short chain of monosaccharide units joined by glycosidic linkage. It contains 2 to 10 monosaccharide units.

3) Polysaccharides: they are sugar polymers having more than 20 monosaccharide units joined by glycosidic linkage and might contain tens of thousands of monosaccharide units.

Monosaccharides

The simplest of the carbohydrates, the monosaccharides, are either ketones or aldehydes with two or more hydroxyl groups. The number of carbon atoms in monosaccharides can be

from three to eight but the most common is five (e.g., pentoses, $C_5H_{10}O_5$) or six (e.g., hexoses, $C_6H_{12}O_6$). They are termed as follows:

3 carbon: Trioses

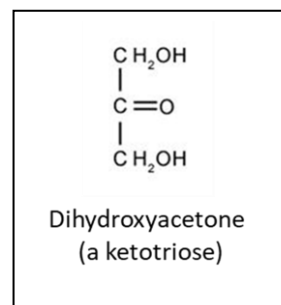
4 Carbon: Tetroses

5 Carbon: Pentoses

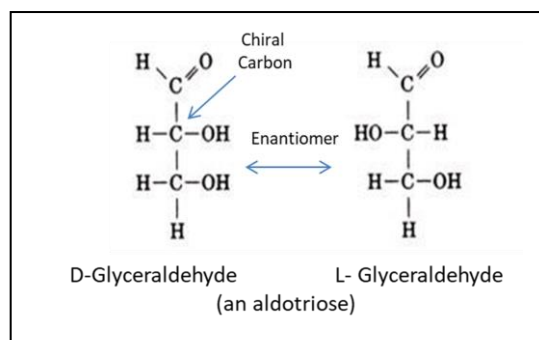
6 Carbon: Hexoses

7 Carbon: Heptoses

- The simplest monosaccharide are trioses ($n=3$), named as dihydroxyacetone and glyceraldehyde. Except dihydroxyacetone, all monosaccharides have one or more chiral carbon atoms and thus they occur in optically active isomeric forms.

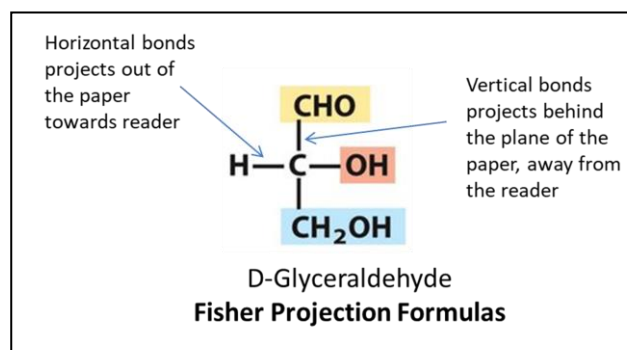


- The simplest aldose, glyceraldehyde, contains one chiral centre and therefore has two different optical isomers or enantiomers.
- The D and L designate the absolute configuration of the asymmetric carbon atoms farthest from the aldehyde or ketone groups.

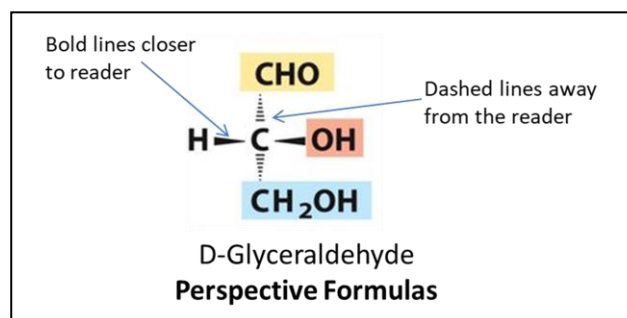


- It is referred to as **D-** if the OH on the farthest chiral centre points to the right and it is referred to as **L-** if the OH on the farthest chiral centre points to the left.

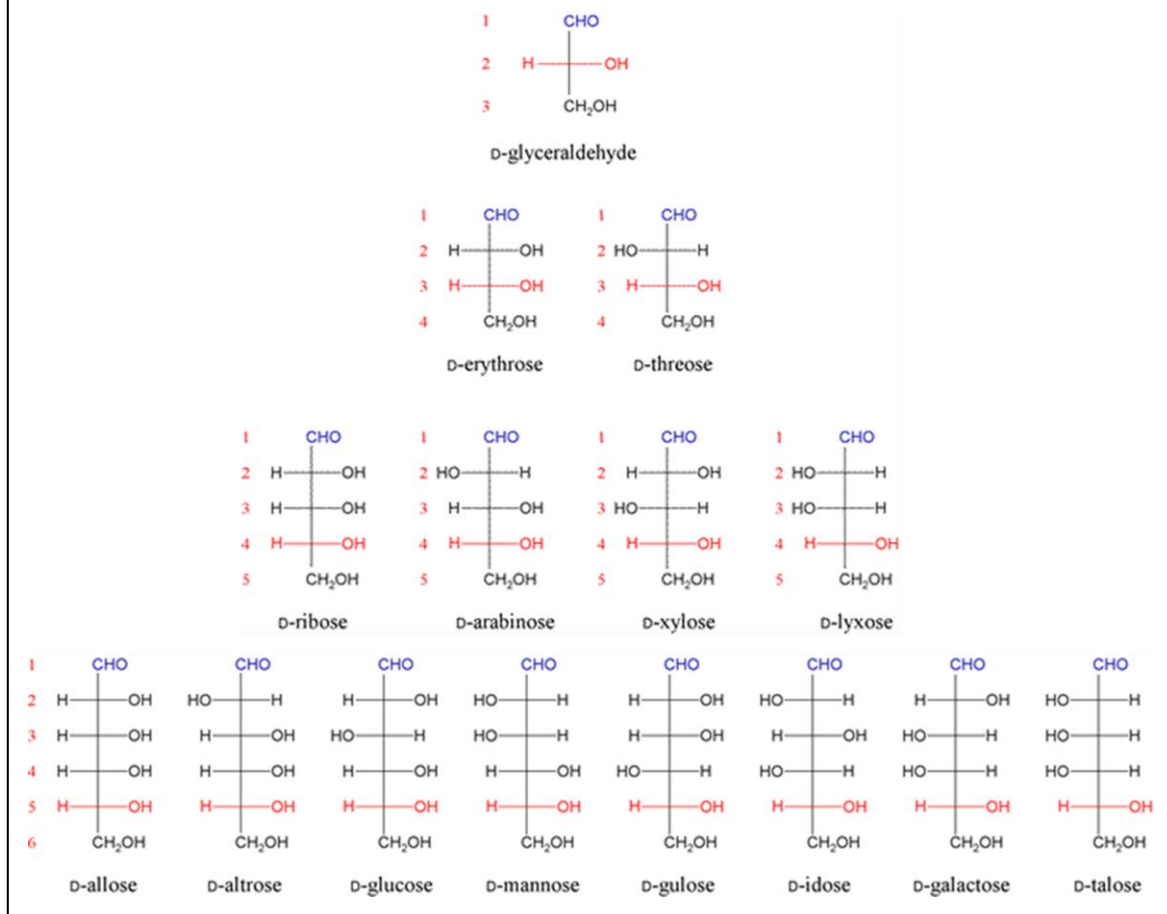
- To represent 3D structure of carbohydrates on paper, we often use Fischer projection formulas. According to Fischer projection the horizontal bonds projects out of the paper towards reader; vertical bonds projects behind the plane of the paper, away from the reader.



- The 3D structure of molecules can also be drawn by Perspective formula in which the bold lines projects being closer to us and the dashed lines fading away in the background.



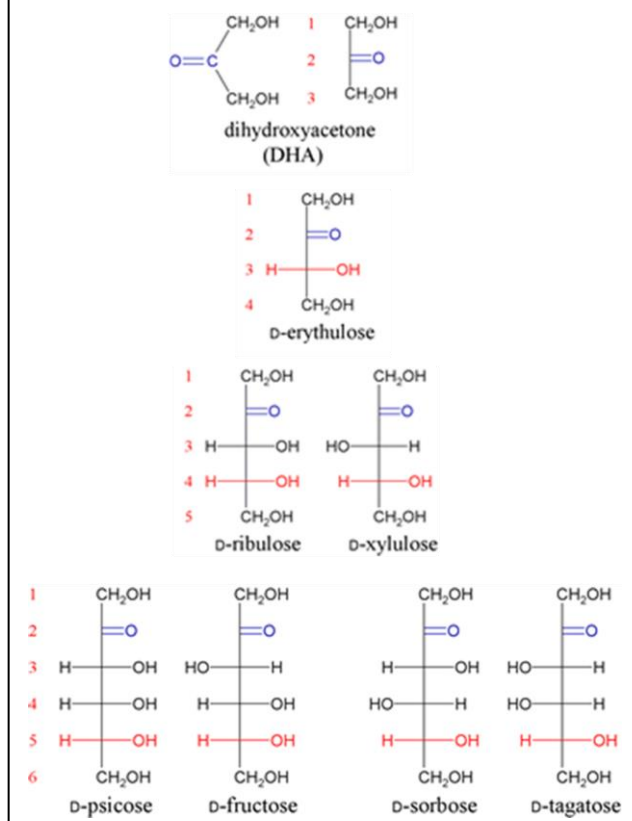
Diagrammatic representation of aldoses from three to six carbon atoms.



Sugars differing in configuration at a single asymmetric center are called epimers. Therefore, D-glucose and D-mannose are epimeric at C-2 position and D-glucose and D-galactose are epimeric at C-4 position.

The ketoses have one fewer asymmetric center than aldoses with the same number of carbon atoms. D-fructose is most abundant ketohexose. Almost all sugars exist in the D-form However, some sugar occurs naturally in their L-form such as L-arabinose.

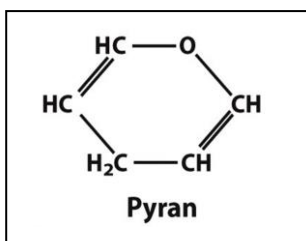
Diagrammatic representation of Ketoses from three to six carbon atoms.



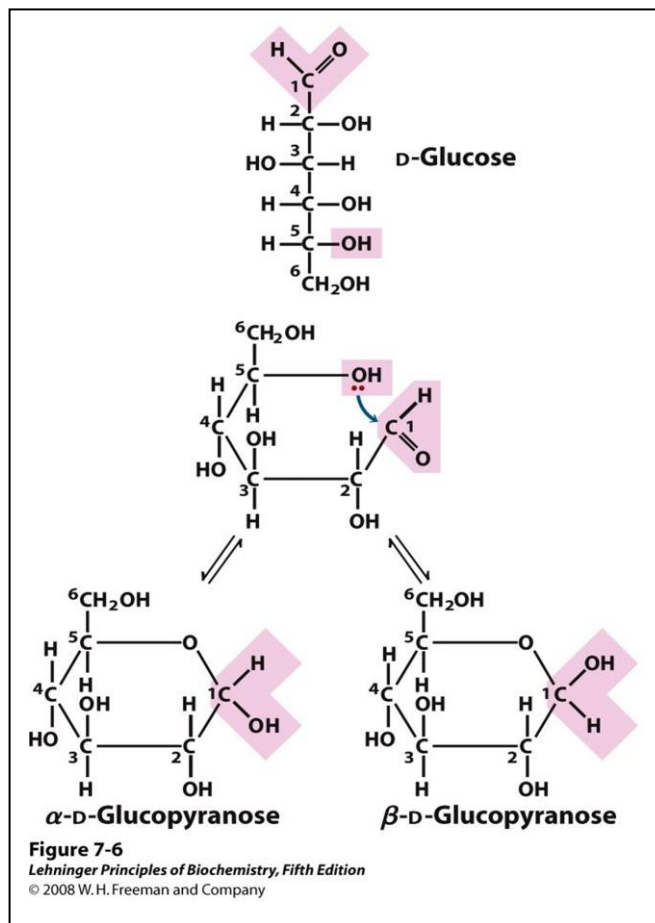
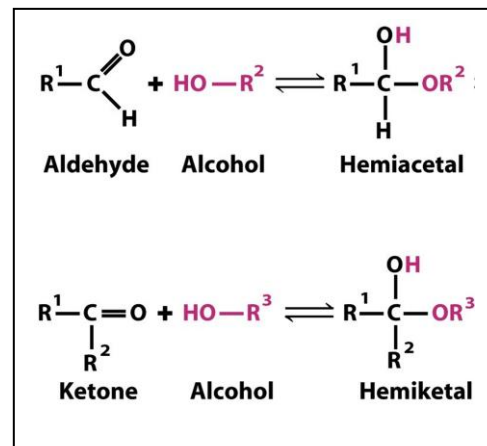
The common Monosaccharides have cyclic structures

In aqueous solutions, aldotetrose and all monosaccharides with 5 or more carbon atoms in the backbone occurs predominantly as cyclic (ring) structures.

- The ring structure is energetically more stable than their linear form. The formation of these ring structures is the result of a general reaction between alcohol and aldehydes or ketones to form derivative called hemiacetals or hemiketals.
- For aldohexoses (glucose) C1 aldehyde (open chain) reacts with C5 hydroxyl group to form an intramolecular hemiacetal. The resulting 6-membered ring is called Pyranose because of its similarity with Pyran.

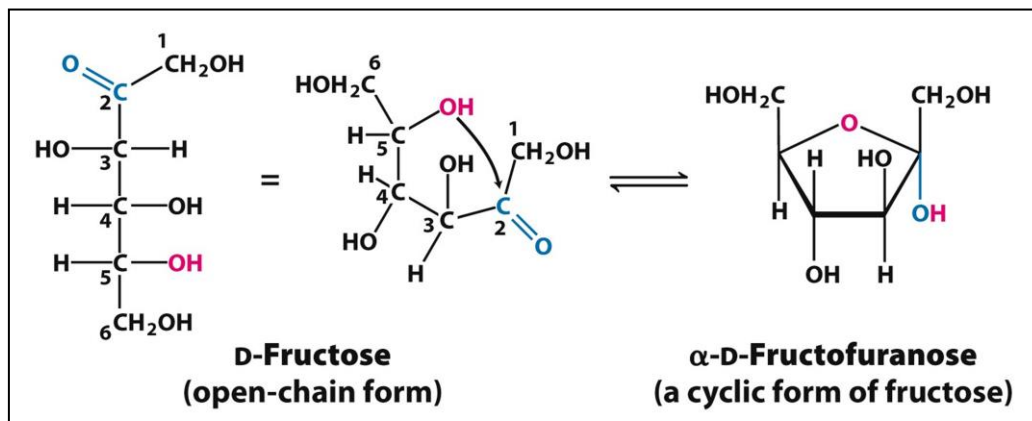
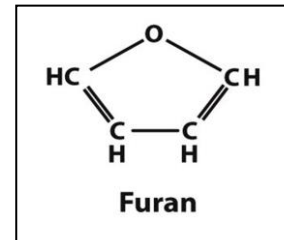


- The hemiacetals contains an additional asymmetric carbon atom and thus can exist in two stereoisomeric forms. Such as, D-glucose exists in solution as an

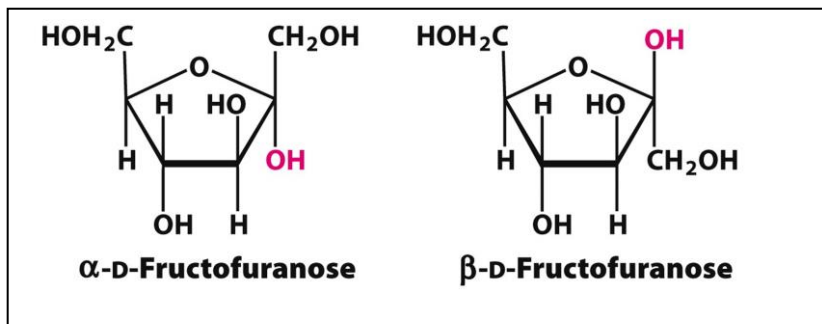


intramolecular hemiacetals in which free hydroxyl group at C5 has reacted with the aldehydic C1, causing the C1 to become asymmetric and producing two stereoisomers, denoted by α and β isomers. The C1 carbon atom is called anomeric carbon atom and the α and β forms are called anomers. The equilibrium mixture of glucose is approximately 1/3 α -anomer, 2/3 β -anomer and < 1% open chain form.

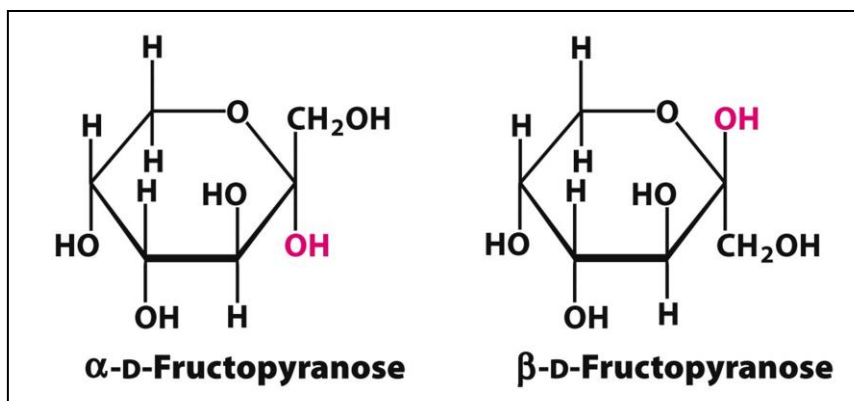
- Similarly ketohexose (fructose), the C2 keto group (open chain) reacts with a hydroxyl group within the same molecule to form an intramolecular hemiketal. The C2 keto group can react with either C6 hydroxyl group to form 6 membered ring or the C5 hydroxyl group to form 5-membered ring. The 5-membered ring is called Furanose because of its similarity with Furan.



D-Fructofuranose can also exist in two stereo-isomeric forms (α and β isomers).



Fructose forms both pyranose and furanose rings. The pyranose form predominates in fructose solution and the furanose form predominates in many fructose derivatives. The α and β forms interconvert in the aqueous solution by the process called mutarotation.

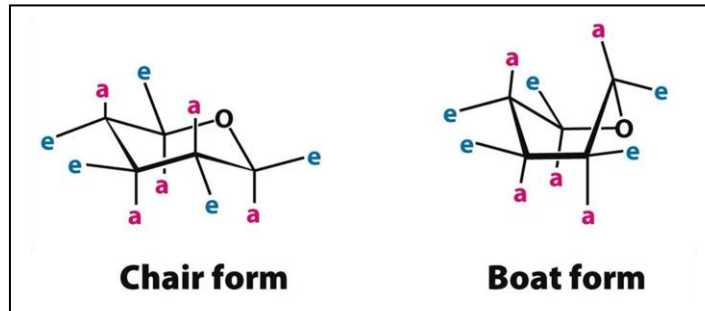


Pyranose and Furanose rings can assume different conformations

The six membered pyranose rings are not planar; similarly the five membered furanose rings are also not a planar structure.

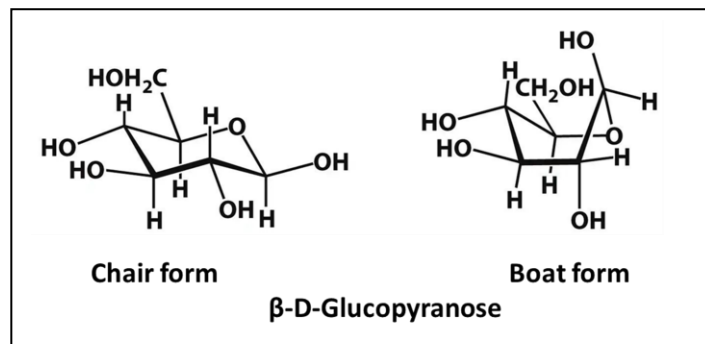
The specific 3D structures of the monosaccharides units are important for determining the biological properties and functions of various polysaccharides.

- The pyranose ring can attain either chair and boat form. In the chair form, the substituents on the ring carbon atoms have two orientations; axial (a) and equatorial (e).



- The axial bonds are nearly perpendicular to the average plane of the ring; whereas, equatorial bonds are nearly parallel to this plane. Axial substitution sterically hinders each other if they emerge on same side of the ring. In contrast, equatorial substituents are less crowded.

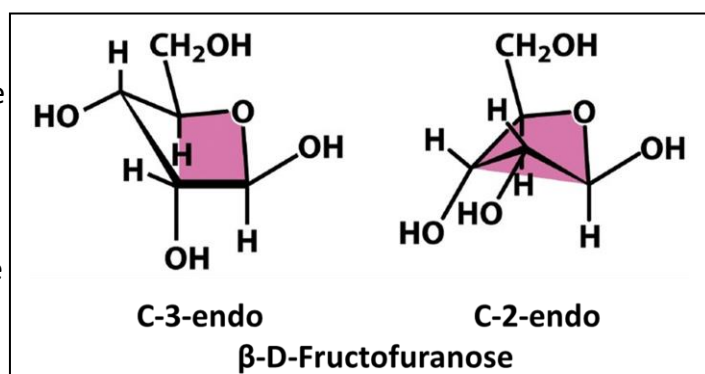
- The chair form of β -D-glucopyranose predominates because all axial positions are occupied by hydrogen atoms. The bulkier -OH and -CH₂OH groups



-OH and -CH₂OH groups emerge at less hindered periphery. The boat form of D-glucopyranose is disfavoured because it causes steric hindrance.

- Similar to pyranose rings the furanose rings are not planar. The four atoms of the ring structure are planar while the fifth atom is 0.5 angstrom away from this plane.

- The conformation of furanose is called envelope form because the structure resembles an opened envelope with the flap raised. Either C2 or C3 is out of the plane on the same side as C5. These



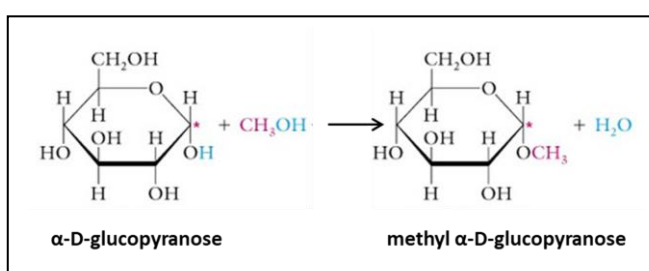
conformations are called C2-endo and C3-endo, respectively.

- The two conformation chair/boat or C3-endo/C2-endo is inter-convertible without breaking the covalent bonds. However, the conformation of α/β can be interconverted only after breakage of the covalent bond.

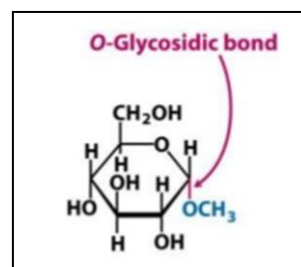
Derivatives of Monosaccharides

There are various derivatives of monosaccharides observed in nature. These derivatives are formed by addition of specific chemical groups to the backbone of monosaccharides. Such as monosaccharides may react with hydroxyl and amine groups to form modified monosaccharides.

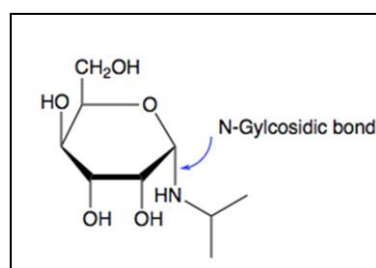
- For example, α -D-glucopyranose reacts with methanol to form sugar acetal also known as glycosides. The anomeric carbon of D-glucopyranose (C1) reacts with hydroxyl group of methanol.



- The bond formed between the anomeric carbon atom of sugar and the hydroxyl oxygen atom of alcohol is called 'glycosidic bond' or more specifically termed as 'O-glycosidic bond'.

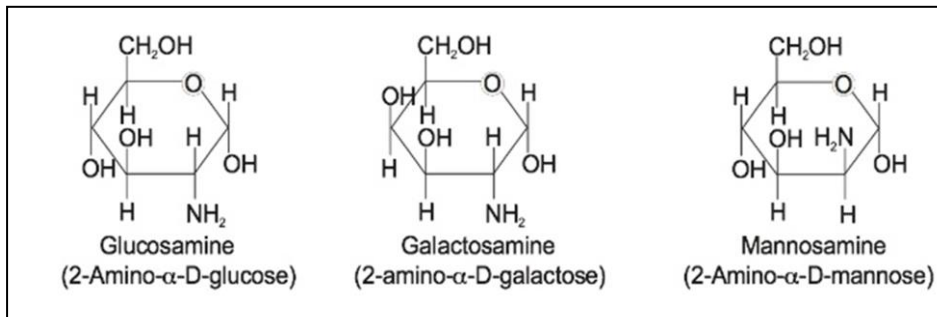


- Alternatively, the anomeric carbon atom of sugar can be linked to the nitrogen atom of an amine to form the 'N-glycosidic bond'.

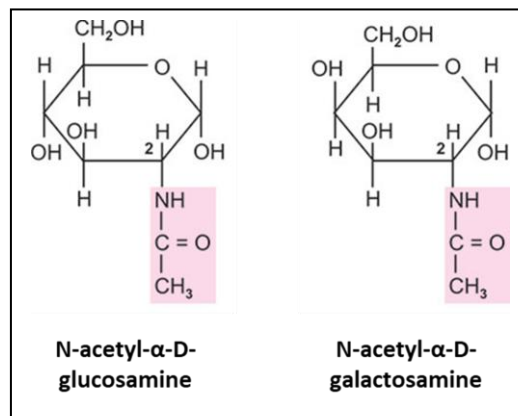


Simple hexoses such as glucose, galactose and mannose are modified to form various derivatives in which the hydroxyl group in parent molecule is replaced with another substituent, or a carbon atom is oxidised to carboxylic group.

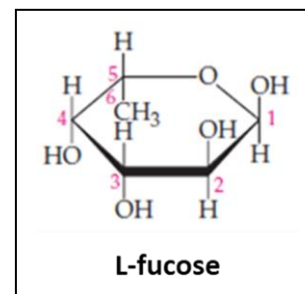
- In glucosamine, galactosamine and mannosamine, the hydroxyl group in parent molecule (C2 position) is replaced with amino group.



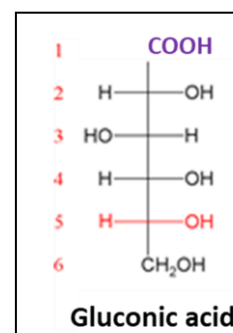
- The amino group is often associated with acetic acids to form N-acetyl glucosamine or N-acetyl- α -D-glucosamine. All of these derivatives are often expressed on the cell surface including the bacterial cell wall.



- The substitution of hydrogen for the hydroxyl group at C6 of L-galactose produces L-fucose. It is found in the complex oligosaccharide components of glycoproteins and glycolipids.

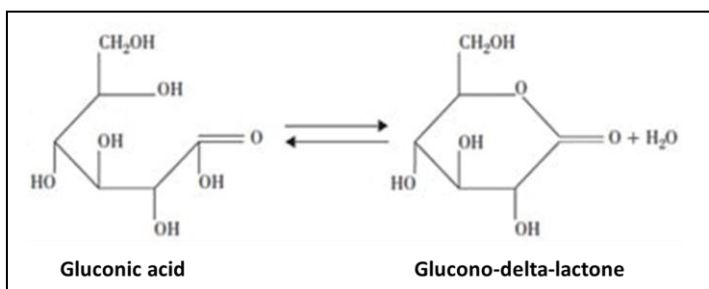


- The oxidation of carbonyl (aldehyde) carbon (C1) of glucose to carboxylic group is termed as gluconic acid (other aldoses yield aldonic acid).

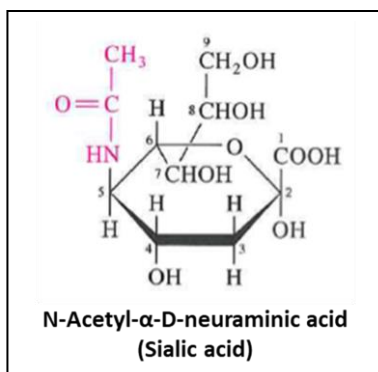


- The oxidation of carbon at the other end of the carbon chain such as C6 of glucose, galactose or mannose forms uronic acid and termed as glucuronic acid, galacturonic acid, mannuronic acid respectively.

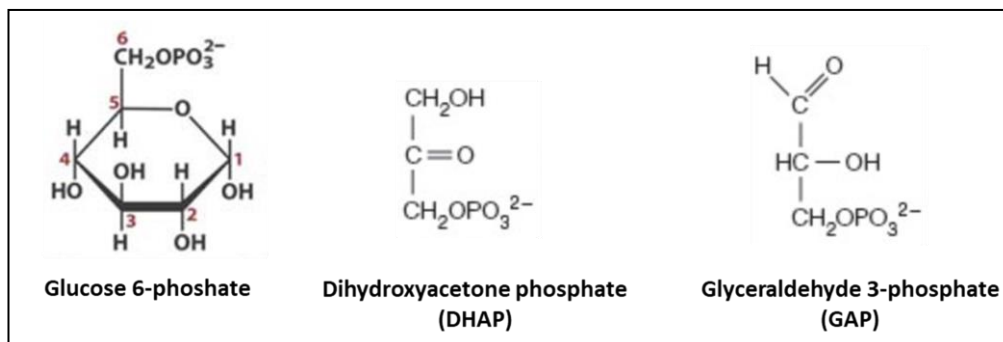
- Both aldonic and uronic acids form stable intramolecular esters called lactones.



- Another important derivative of hexose sugar is sialic acid also known as N-acetylneuraminic acid which is a component of various glycoprotein and glycolipids in animals.



- Phosphorylated sugars are key intermediates in energy metabolism. Phosphorylation makes sugar ionic thereby the negative charge prevents these sugar derivatives from spontaneously leaving the cells by crossing lipid bilayer membrane. Phosphorylation also creates a reactive intermediate that forms linkage with other biomolecules such as in the biosynthesis of purine and pyrimidine.



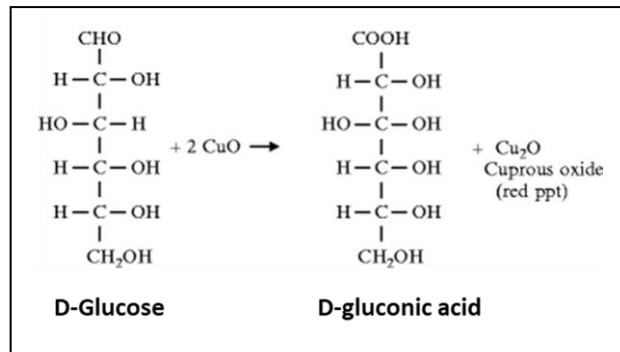
Some of the common phosphorylated monosaccharides are glucose 6-phosphate, dihydroxyacetone phosphate and glyceraldehyde 3-phosphate.

Monosaccharides are reducing sugar

Monosaccharides can be oxidised by relatively mild oxidising agents such as cupric (Cu²⁺) ions and during this reaction the carbonyl carbon is oxidised to carboxyl group. The oxidation of sugar by cupric ion occurs only with the linear form, which exists in equilibrium

with cyclic form. The reaction of reducing sugar with cupric ions forms enediols which are converted to aldonic acid and then to a mixture of 2, 3, 4 and 6-carbon acids.

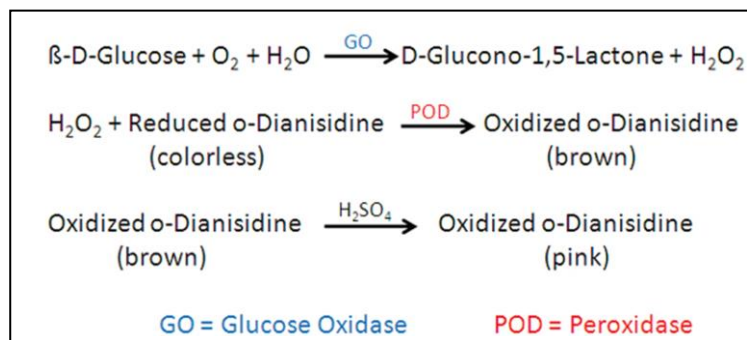
This is the working principle of Fehling reaction (a qualitative test for the presence of reducing sugars). The glucose and other sugars capable of reducing cupric ions are called reducing sugars.



Blood glucose measurements

- By measuring the amount of oxidising agents reduced by the solution of a sugar, it is possible to estimate the concentration of sugar present in the solution. This principle is used to measure glucose levels in the blood and more specifically to determine the alteration of glucose levels in metabolic disorders such as diabetes mellitus.

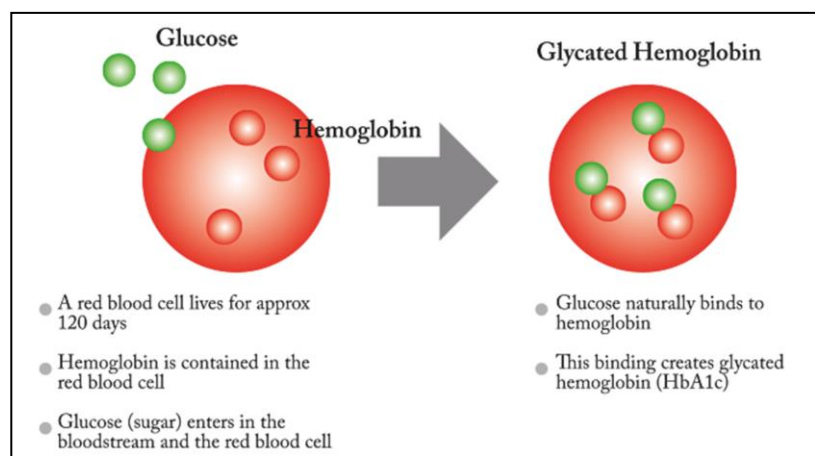
- By using traditional methods (glucose oxidases and peroxidase are used) the glucose levels is measured multiple times to calculate the average glucose levels in an individual.



- The average glucose levels can also be measured by assessing haemoglobin. Normally a non-enzymatic reaction occurs between the glucose and primary amino groups of

hemoglobin (valine or lysine) and termed as glycated haemoglobin (GHB). The rate of GHB formation is proportional to the amount of glucose present in the blood.

Therefore, this reaction



can be used as the basis for estimating average glucose levels for weeks because GHB is stable for weeks. The amount of GHB present at any time reflects the average blood

glucose concentration over two week range. For measuring glucose concentration the GHB is extracted from RBC and measured. The 5% GHB is considered normal (120mg/100ml) and in diabetic individuals it is around 13%.

Disaccharides

Disaccharides contain two monosaccharides units joined together by O-glycosidic bond. The O-glycosidic bond is formed when a hydroxyl group of one sugar reacts with anomeric carbon of other monosaccharide unit. When the anomeric carbon is involved in glycosidic bond, that sugar residue loses its ability to convert to linear form and therefore becomes non-reducing sugar. In disaccharides or polysaccharides, the end of the chain with free anomeric carbon (the one which is not involved in glycosidic bond) is commonly termed as reducing end.

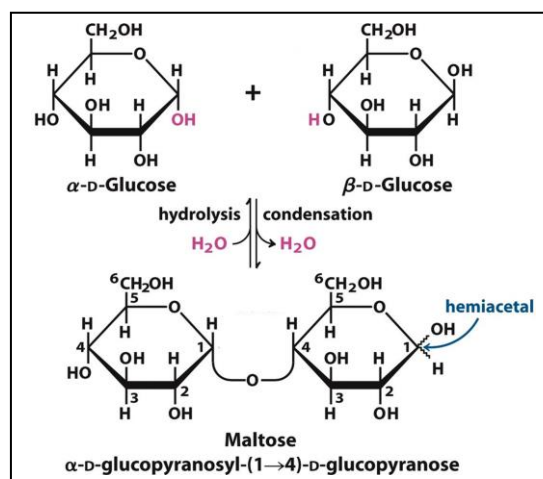
Convention for naming disaccharides

The nomenclature of compound is started with its non-reducing end to the left. The name is written as follows:

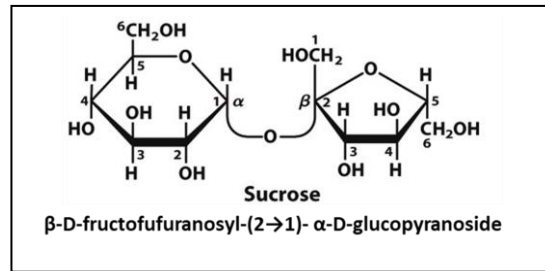
- i) Provide the configuration (α or β) at the anomeric carbon joining the first monosaccharide unit (on the left) to the second unit.
- ii) name the non-reducing residue; to distinguish insert 'furano' or 'pyrano' to the name.
- iii) indicate in the parentheses the two carbon atoms joined by glycosidic bond, with an arrow connecting the two numbers such as (1 \rightarrow 4)
- iv) name the second residue.
- v) if the third residue is present then describe the second glycosidic bond with the same convention as mentioned above.

Some common disaccharides are:

a) Maltose: It is comprised of two glucose residues that are linked by O-glycosidic linkage. The maltose has one anomeric carbon (right ring) free, therefore, it is a reducing sugar. The glucose residue (in maltose) with free anomeric carbon can exist as both α and β pyranose form.

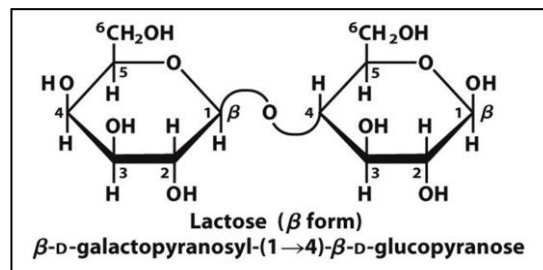


b) Sucrose: It is comprised of one glucose and one fructose residues that are linked by O-glycosidic linkage. Sucrose can be written with both sugar residues because both of them have anomeric carbon that is used for O-glycosidic linkage. Sucrose is a non-reducing sugar because none of the monosaccharide



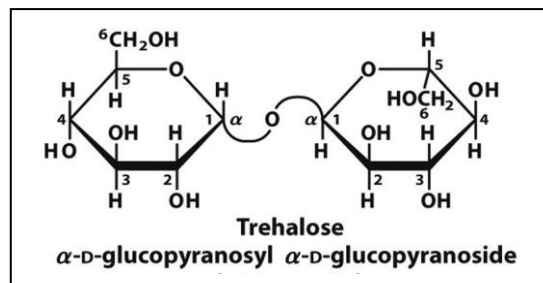
units can be converted into aldehyde or ketone functional groups or it lacks free anomeric carbon atom. Sucrose is table sugar and formed by the plants (not animals).

c) Lactose: It is comprised of one galactose and one glucose residues that are linked by O-glycosidic linkage. The sugar residues of lactose can be α or β or both can be β. Lactose have free anomeric carbon therefore it is reducing sugar. Lactose is disaccharide found in milk. Lactose is hydrolysed to monosaccharides by



lactase enzyme in humans and β-galactosidase enzyme in bacteria.

d) Trehalose: It is comprised of two residues of glucose but the glycosidic linkage (α-1→1) is between the anomeric carbon atoms therefore, it is a non-reducing sugar. Trehalose is a major constituent of circulating fluid (hemolymph) of insects, serves as an energy storage compound.



Some common oligosaccharides

Raffinose (Trisaccharide): comprised of galactose+glucose+fructose.

Maltotriose (Trisaccharide): comprised of glucose+glucose+glucose

Melezitose (Trisaccharide): glucose+fructose+glucose

Maltotetraose (Tetrasaccharide): glucose+glucose+glucose+glucose

Stachyose (Tetrasaccharide): galactose+galactose+glucose+fructose

References:

¹*Lehninger Principles of biochemistry*

²*Lubert Stryer Biochemistry*