Unit-1 (Carbohydrates)

Lecture-I

Title : CARBOHYDRATES- an Introduction

Biomolecule, also called **biological molecule**, any of numerous substances that are produced by cells and living organisms. Biomolecules have a wide range of sizes and structures and perform a vast array of functions. The four major types of biomolecules are carbohydrates, lipids, nucleic acids, and proteins.

CARBOHYDRATES- an Introduction

Carbohydrates are the most abundant biomolecules on Earth. Each year, photosynthesis converts more than 100 billion metric tons of CO_2 and H_2O into cellulose and other plant products. Carbohydrates like (sugar and starch) are a dietary staple in most parts of the world, and the oxidation of carbohydrates is the principal energy-yielding pathway in most non-photosynthetic cells. Insoluble carbohydrate polymers serve as structural and protective elements in the cell walls of bacteria and plants and in the connective tissues of animals. Other carbohydrate polymers lubricate skeletal joints and participate in recognition and adhesion between cells. More complex carbohydrate polymers covalently attached to proteins or lipids act as signals that determine the intracellular location or metabolic fate of these hybrid molecules, called **glycoconjugates.**

In this unit we will get familiar with the major classes of carbohydrates and glycoconjugates and provides a few examples of their many structural and functional roles.

Definition: Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis.

Many, but not all, carbohydrates have the empirical formula (CH2O)*n*; some also contain nitrogen, phosphorus, or sulfur.

There are three major classes of carbohydrates: monosaccharides, oligosaccharides, and polysaccharides (the word “saccharide” is derived from the Greek *sakcharon*, meaning “sugar”).

- **Monosaccharides,** or simple sugars, consist of a single polyhydroxy aldehyde or ketone unit cannot be hydrolyzed to smaller carbohydrates. The most abundant monosaccharide in nature is the six-carbon sugar D-glucose, sometimes referred to as dextrose. Monosaccharides of more than four carbons tend to have cyclic structures. The general chemical formula of an unmodified monosaccharide is $(C_nH_2O)_n$. **n=no. of carbon atoms**

- **Oligosaccharides** consist of short chains of monosaccharide units, or residues, joined by characteristic linkages called glycosidic bonds. The most abundant are the **disaccharides,** with two monosaccharide units.Typical is sucrose (cane sugar), which consists of the six-carbon sugars D-glucose and D-fructose. All commonmonosaccharides and disaccharides have names ending with the suffix “-ose.” In cells, most oligosaccharides consisting of three or more units do not occur as free entities but are joined to non-sugar molecules (lipids or proteins) in glycoconjugates.
- The **polysaccharides** are sugar polymers containing more than 20 or so monosaccharide units, and some have hundreds or thousands of units. Some polysaccharides, such as cellulose, are linear chains; others such as glycogen, are branched. Both glycogen and cellulose consist of recurring units of D-glucose, but they differ in the type of glycosidic linkage and consequently have strikingly different properties and biological roles.

Organic vs Inorganic

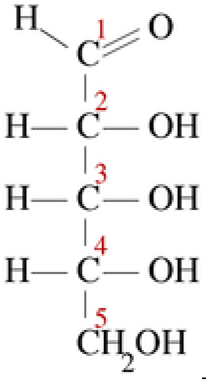
*Living organisms contain **inorganic compounds** (mainly water and salts) and organic molecules. Organic molecules contain carbon; inorganic compounds do not. **Organic compound**, any of a large class of chemical **compounds** in which one or more atoms of carbon are covalently linked to atoms of other elements, most commonly hydrogen, oxygen, or nitrogen. Carbon oxides and carbonates are exceptions; they contain carbon but are considered inorganic because they do not contain hydrogen. The atoms of an **organic molecule** are typically organized around chains of carbon atoms. The modern meaning of organic compound is any compound that contains a significant amount of carbon—even though many of the organic compounds known today have no connection to any substance found in living organisms*. Four major classes of Organic compounds in living organism include **carbohydrates**, **proteins**, **carbohydrates**, **lipids**, and **nucleic acids**.

Sem-I

Unit_- I (Carbohydrates)
Lecture -2 (Classification)

Carbohydrates

Definition: Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis



RIBOSE

They are primarily produced by plants and form a very large group of naturally occurring organic substances. Some common examples are cane sugar, glucose, starch, etc. They have general molecular formulas that make them appear to be hydrates of carbon, Cn(H2O)n, from where the name carbohydrate was derived. Carbohydrates are formed in the plants by photosynthesis from carbon dioxide and water in the presence of sunlight.

Classification of Carbohydrates

- Monosaccharides contain a single polyhydroxy aldehyde or ketone unit (saccharo is Greek for "sugar") (e.g., glucose, fructose).

- Disaccharides consist of two monosaccharide units linked together by a covalent bond (e.g., sucrose).

- Oligosaccharides contain from 3 to 10 monosaccharide units (e.g., raffinose).

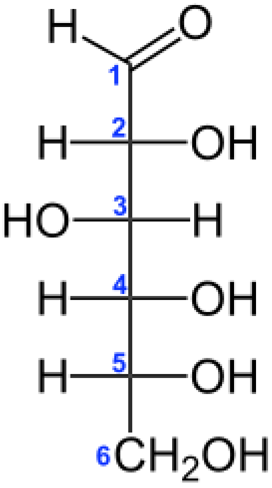
- Polysaccharides contain very long chains of hundreds or thousands of monosaccharide units, which may be either in straight or branched chains (e.g., cellulose, glycogen, starch).

<u>Monosaccharides</u>

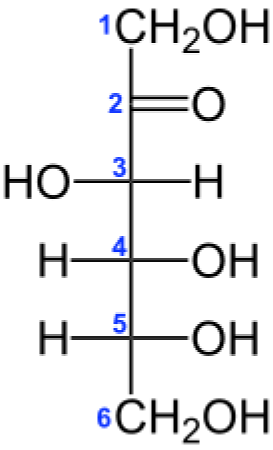
The simplest form of carbohydrates is the monosaccharide. 'Mono' means 'one' and 'saccharide' means 'sugar'. Monosaccharides are polyhydroxy aldehyde or ketone that cannot be hydrolyzed further to give simpler sugar. They may again be classified on the basis of the nature of carbonyl group.

- Polyhydroxy aldehydes are called aldoses. Example: Glucose

- Polyhydroxy ketones are called ketoses. Example: Fructose



Glucose (Aldose)



Fructose (Ketose)

The carbons of a sugar are numbered beginning at the end of the chain nearest the carbonyl group.

Monosaccharides are colorless, crystalline solids that are freely soluble in water but insoluble in nonpolar solvents. Most have a sweet taste. The backbones of common monosaccharide molecules are unbranched carbon chains in which all the carbon atoms are linked by single bonds. In the open-chain form, one of the carbon atoms is double-bonded to an oxygen atom to form a carbonyl group; each of the other carbon atoms has a hydroxyl group. If the carbonyl group is at an end of thecarbon chain (that is, in an aldehyde group) the monosaccharide is an **aldose;** if the carbonyl group is at any other position (in a ketone group) the monosaccharide is a **ketose.** The aldoses and ketoses are further divided based on the number of carbons present in their molecules, as trioses, tetroses, pentoses, hexoses etc. They are referred to as aldotrioses, aldotetroses, aldopentoses, aldohexoses,ketopentoses, ketohexoses etc. The simplest monosaccharides are the two three-carbon trioses: glyceraldehyde, an aldotriose, and dihydroxyacetone, a ketotriose . The hexoses, which include the aldohexose D-glucose and the ketohexose D-fructose are the most common monosaccharides in nature. The aldopentoses D-ribose and 2-deoxy-D-ribose are components of nucleotides and nucleic Acids.

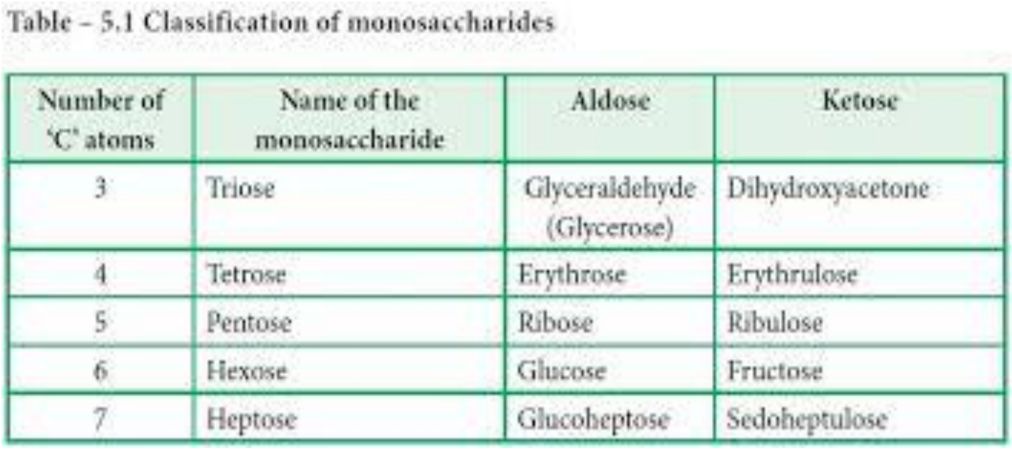
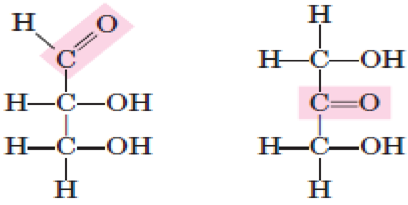


Table – 5.1 Classification of monosaccharides

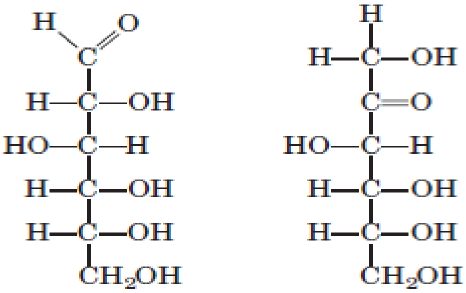
Number of 'C' atoms	Name of the monosaccharide	Aldose	Ketose
3	Triose	Glyceraldehyde (Glycerose)	Dihydroxyacetone
4	Tetrose	Erythrose	Erythrulose
5	Pentose	Ribose	Ribulose
6	Hexose	Glucose	Fructose
7	Heptose	Glucoheptose	Sedoheptulose



Glyceraldehyde, an aldotriose

Dihydroxyacetone, a ketotriose

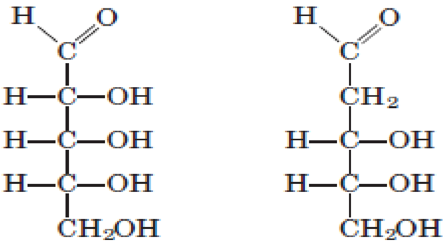
(a)



D-Glucose, an aldohexose

D-Fructose, a ketohexose

(b)

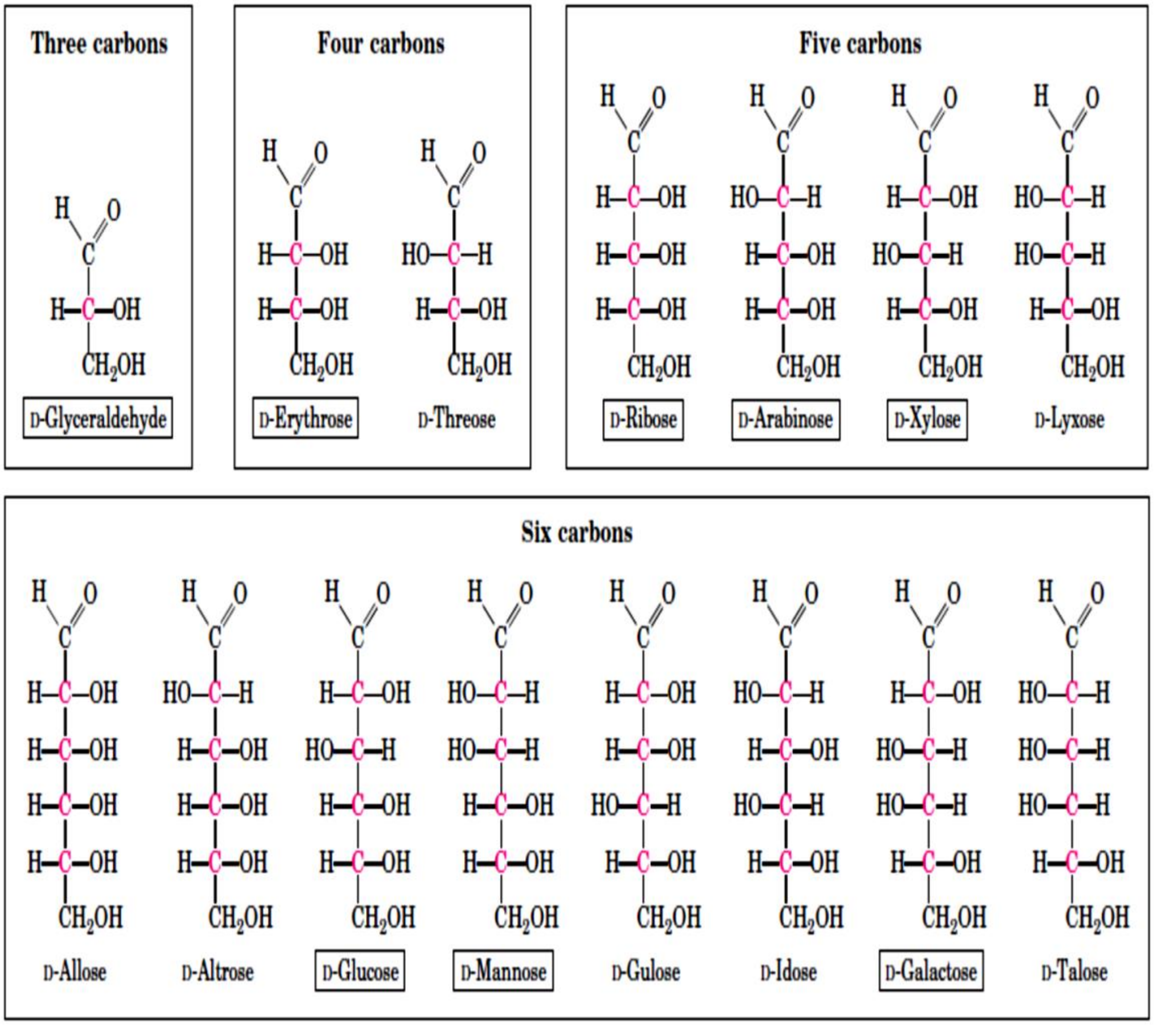


D-Ribose, an aldopentose

2-Deoxy-D-ribose, an aldopentose

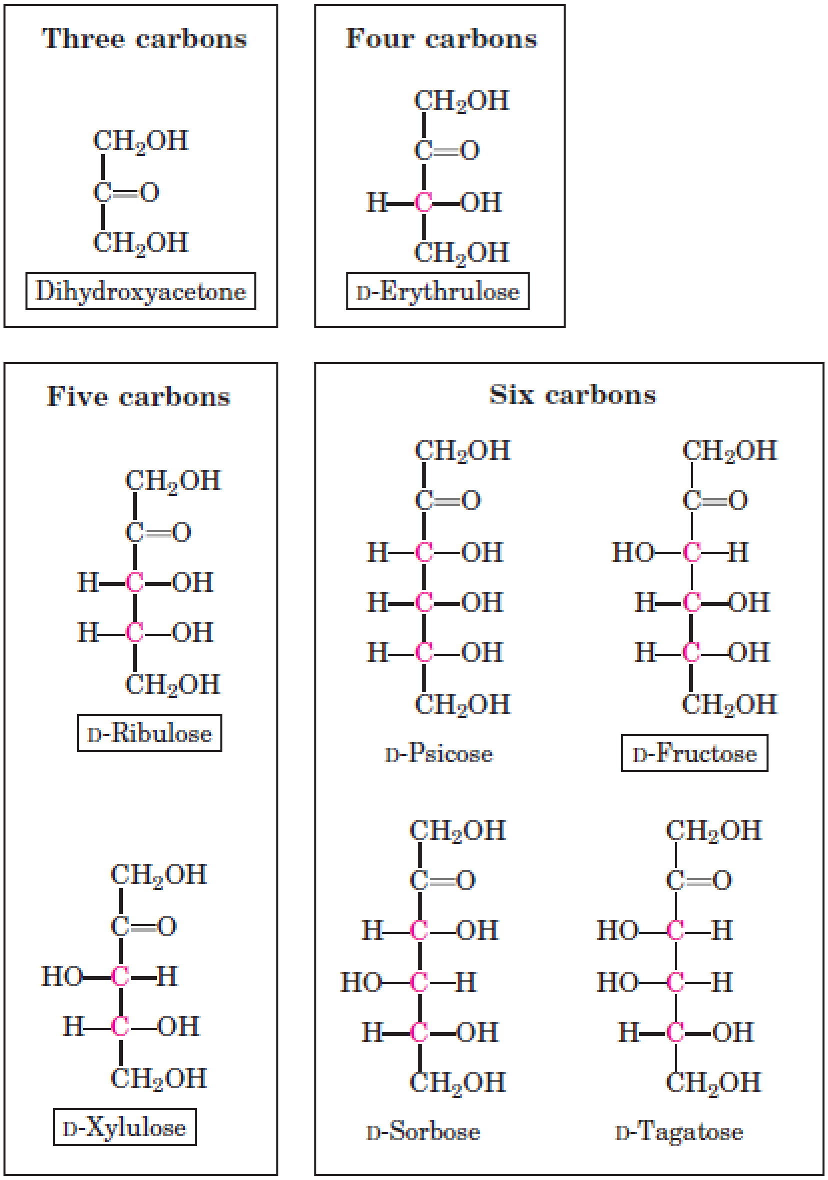
(c)

Representative monosaccharides. (a) Two trioses, analdose and a ketose. The carbonyl group in each is shaded. **(b)** Two common hexoses. **(c)** The pentose components of nucleic acids. D-Ribose is a component of ribonucleic acid (RNA), and 2-deoxy-Dribose is a component of deoxyribonucleic acid (DNA).


Three carbons
D-Glyceraldehyde
Four carbons
D-Erythrose
D-Threose
Five carbons
D-Ribose
D-Arabinose
D-Xylose
D-Lyxose
Six carbons
D-Allose
D-Altrose
D-Glucose
D-Mannose
D-Gulose
D-Idose
D-Galactose
D-Talose

D-Aldoses

(a)



D-Ketoses
(b)

For students: What is the difference between an aldehyde and a Ketone?.

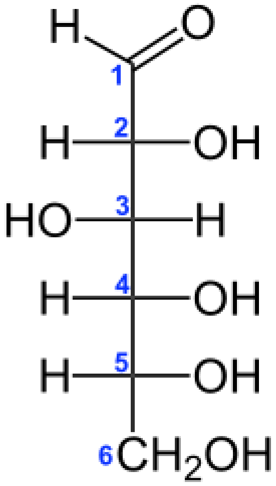
ISOMERISM OF CARBOHYDRATES

Isomers are compounds having same molecular formulae but different molecular structures. Monosaccharides show isomerism

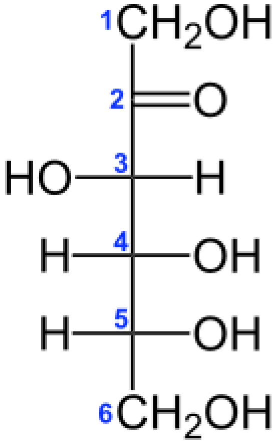
The isomers are of two types: structural isomers and sterioisomers.

Structural isomers

1.**Structural isomers** have same molecular formula but different structures due to difference in chain length (chain isomers), position of substituent groups (positional isomers) or different functional groups. Glucose and fructose are structural (functional) isomers as both have same molecular formula (C6H1206) but have different functional groups, aldehyde and ketone respectively.



Glucose (Aldose)



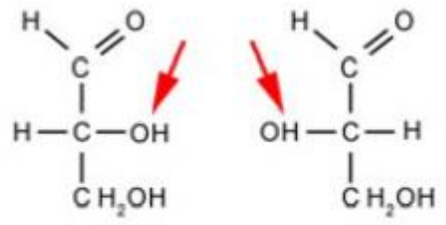
Fructose (Ketose)

2.**Stereoisomers** have the same molecular formula and sequence of bonded atoms (constitution), but differ only in the three-dimensional orientations of their atoms in space. The monosaccharides having asymmetric (chiral) carbon atoms exhibit steriosomerism. ***Asymmetric carbon atom is the carbon atom that is attached to four different groups***. All monosaccharides except- Dihydroxy acetone, have asymmetric carbon atoms and show stereoisomerism. The number of possible stereoisomers depends upon the number of chiral centers in the molecule. Van't Hoffs rule states: number of stereoisomers = 2^n , where n = number of chiral centers. For example, a molecule with 2 chiral centers can have 4 stereoisomers..

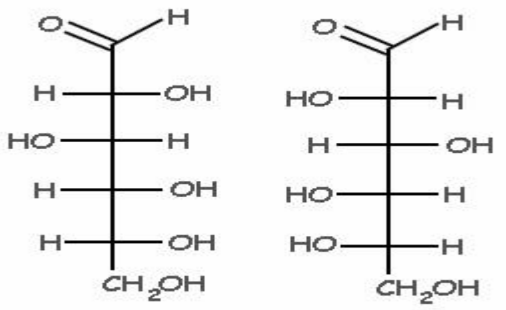
Because of the presence of the chiral carbon the following types of isomerism are observed in monosaccharides

i. Enantiomers /D-L isomers: Enantiomers are the stereoisomers that are mirror images of each other and are "non-super imposable" (not identical) on each other . non-super imposable" mirror images differ in configuration around every chiral centre.The two enantiomers are designated as D & L isomers based on the orientation of H and OH groups attached to the carbon atom adjacent to the terminal primary alcohol carbon (carbon 5 in glucose). When the —OH group on this carbon is on the right the sugar is the D isomer; when it is on the left, it is the L isomer. The simplest aldose, glyceraldehyde, contains one chiral center (the middle carbon atom) and therefore has two different enantiomers.

   Glyceraldehyde has only one asymmetric carbon atom so it can exist in 2 isomeric forms as D and L- forms. One for in which H-atom at carbon 2 is projected to the left and OH-group to the right is designated as D-form and the other form where H-atom is projected to the right side and OH-group to the left is called as L-form.



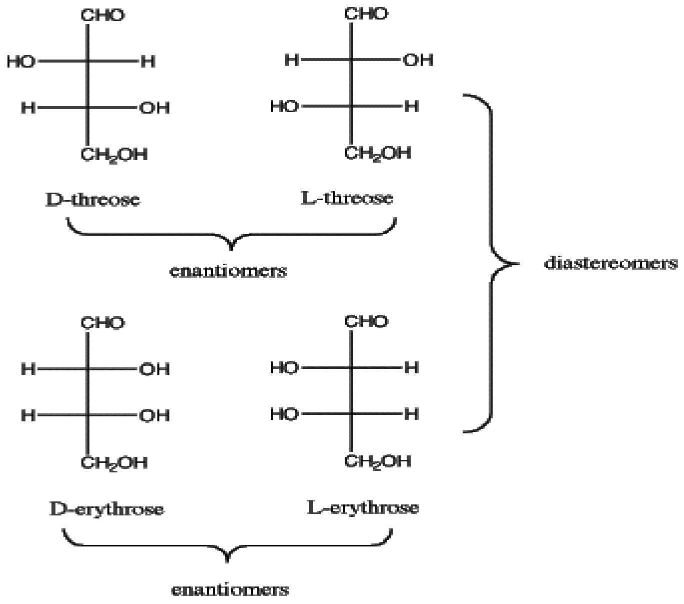
D-Glyceraldehyde L-Glyceraldehyde



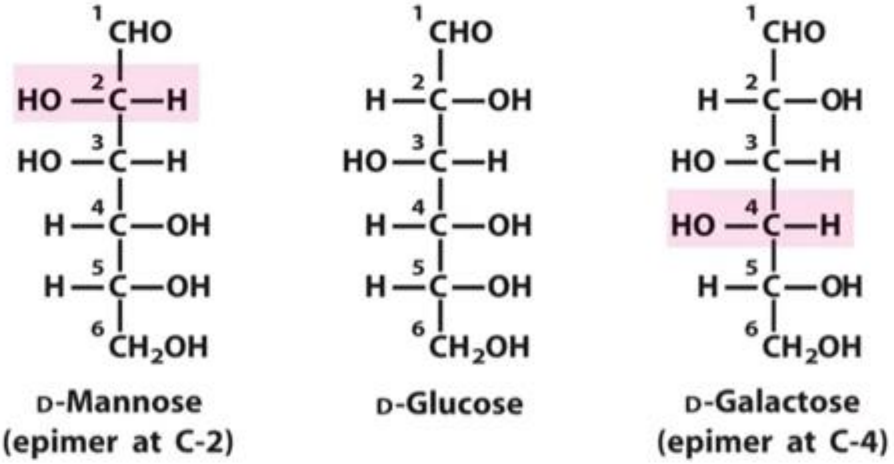
D-Glucose L-Glucose

ii. Optical Isomerism- The presence of asymmetric carbon atoms also confers optical activity on the compound. When a beam of plane-polarized light is passed through a solution of an optical isomer, it rotates either to the right, dextrorotatory (+), or to the left, levorotatory (–). The direction of rotation of polarized light is independent of the stereochemistry of the sugar, so it may be designated D (–), D (+), L (–), or L (+) .For example, the naturally occurring form of fructose is the D (–) isomer. In solution, glucose is dextrorotatory, and glucose solutions are sometimes known as dextrose. Measurement of optical activity in chiral or asymmetric molecules using plane polarized light is called Polarimetry. The measurement of optical activity is done by an instrument called Polarimeter.

iii. Diastereomers are the stereoisomers that have different configurations at one or more (but not all) of the stereocenters and are not mirror images of each other. Diastereomers occur in compounds containing more than one chiral center. In a pair of diastereomers, some chiral centers are the same and some are opposite. The molecule is neither identical to nor the mirror image of its diastereomer. D-threose is the enantiomer of L-threose. The two are non-identical, but they are mirror images of each other. Diastereoisomers of a compound have different configurations at one or more (but not all) of the equivalent (related) stereocenters and are not mirror images of each other. When two diastereoisomers differ from each other at only one stereocenter they are called epimers

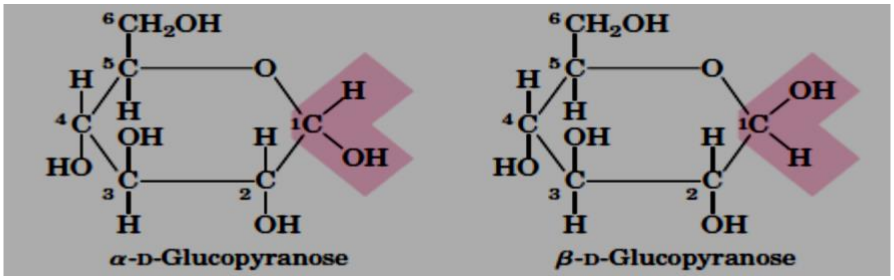


iv. Epimers are the diastereomers that differ in only at one stereocenter. As shown in the figure below, D-Glucose and D-Mannose are an example of an C-2 epimers. , D-Glucose and D-Galctose are an example of an C-4 epimers



Mannose and Galactose are not epimers of each other as they differ in configuration around two carbon atoms. They are diastereoisomers.

I. Anomers: Monosaccharides that contain five or more carbons atoms form cyclic structures in aqueous solution. The cyclization process creates a new stereogenic center, C-1, which is referred to as the anomeric carbon. Two cyclic stereoisomers can form from each straight-chain monosaccharide that differ in configuration around the anomeric carbon, these are known as anomers Glucose can exist as an α or a β isomer, depending on whether the OH group attached to the anomeric carbon (C-1) is on the same side as the CH2OH group or is on the opposite side. Anomers are a special case of epimers. The main difference between them is that epimers differ in configuration at any one chiral (stereogenic) center, but anomers differ in configuration, especially at the acetal or hemiacetal carbon i-e anomeric carbon.

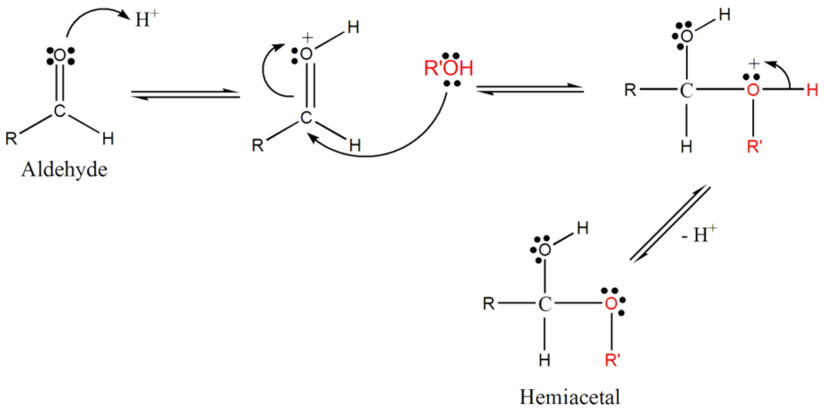


Question of the day: what is the difference between enantiomers and Diasterioisomers?

Lecture# 04

Cyclisation of Monosaccharides

So far we have represented monosaccharides as linear molecules, but many of them also adopt cyclic structures. This conversion occurs because of the ability of aldehydes and ketones to react with alcohols: When an alcohol adds to an aldehyde, **hemiacetal is formed** & when an alcohol adds to a ketone the resulting product is a **hemiketal**..This happens through the nucleophilic attack of the hydroxyl group at the electrophilic carbonyl group. Since alcohols are weak nucleophiles, the attack on the carbonyl carbon is usually promoted by protonation of the carbonyl oxygen. When this reaction takes place with an aldehyde, the product is called a 'hemiacetal'; and when this reaction takes place with a ketone, the product is referred to as a 'hemiketal'.

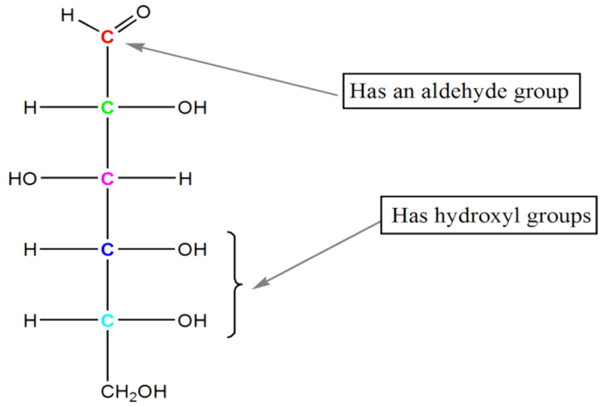


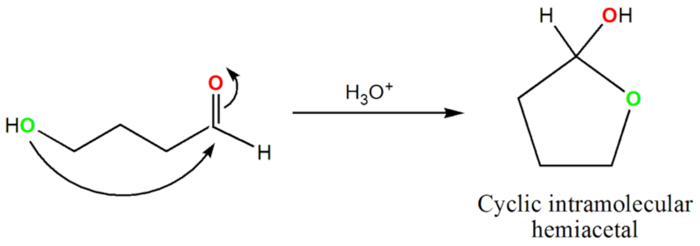
Reaction creating hemiacetal

The above reaction exemplifies the formation of an intermolecular hemiacetal. These are intrinsically unstable and tend to favor the parent aldehyde.

I. Molecules (aldehyde or ketone), which contain both an alcohol and a carbonyl group, can instead undergo an intramolecular reaction to form a cyclic hemiacetal/ hemiketal. These, on the contrary, are more stable as compared to the intermolecular hemiacetals/hemiketals.

Stability of cyclic hemiacetals/hemiketals is highly dependent on the size of the ring, where 5 & 6 membered rings are generally favored.



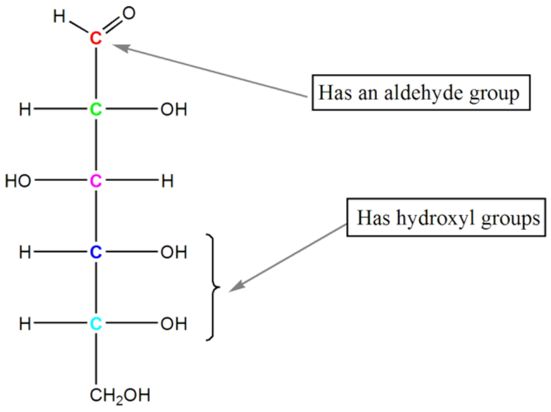


Reaction creating cyclic intramolecular hemiacetal

II. Intramolecular hemiacetal and hemiketal formation is commonly encountered in sugar chemistry. Just to give you an example: in solution, ~ 99% of glucose exists in the cyclic hemiacetal form and only 1% of glucose exists in the open form.

Cyclization of glucose to its hemiacetal form

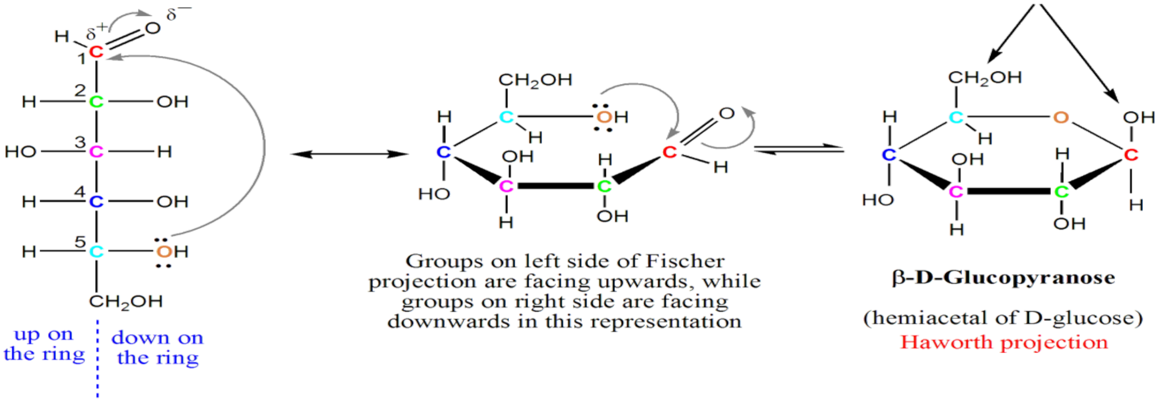
Let's first draw a molecule of glucose (C6H$_{12}$O$_6$) The simplest way to do so is by using the Fischer Projection as shown below



Has an aldehyde group

Has hydroxyl groups

Glucose has an aldehyde group and five hydroxyl groups and can form an intramolecular cyclic hemiacetal. Let’s now show the formation of hemiacetal of glucose starting from its open structure (Fischer projection).



It's **beta-anomer** when CH_2OH and OH are on the same side

up on the ring

down on the ring

D-Glucose

Fischer projection

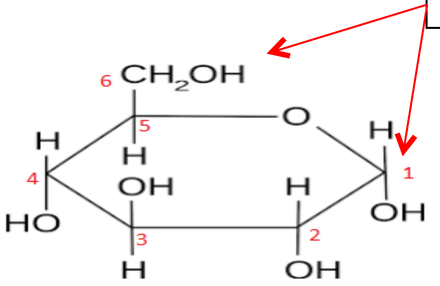
Groups on left side of Fischer projection are facing upwards, while groups on right side are facing downwards in this representation

β-D-Glucopyranose

(hemiacetal of D-glucose)

Haworth projection

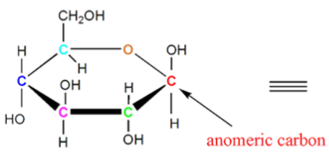
It is α-anomer when CH_2OH and OH are on Opposite Side



α- D Glucopyranose

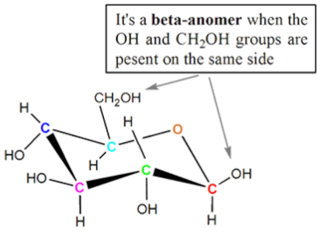
(So why doesn't the hydroxyl attached to C-4 react with the carbonyl group? Why does the carbonyl group react with the hydroxyl attached to C-5? C-4 hydroxyl attacking the carbonyl group will lead to the formation of a 5-membered ring, while the attack of C-5 hydroxyl at the carbonyl group will generate a 6-membered ring (as shown in the above figure). In the case of glucose, a 6-membered ring is thermodynamically more stable than a 5-membered ring, thus favoring the formation of a 6-membered ring over a 5-membered ring.)

This cyclization process creates a new stereogenic center, C-1, which is referred to as the anomeric carbon. Glucose can exist as an α or a β isomer, depending on whether the OH group attached to the anomeric carbon (C-1) is on the same side as the CH2OH group or is on the opposite side. These two forms are referred to as anomers of glucose.



β-D-Glucopyranose

(hemiacetal of D-glucose)
Haworth projection


It's a **beta-anomer** when the OH and CH$_2$OH groups are pesent on the same side

β-D-Glucopyranose

(hemiacetal of D-glucose)
Chair conformation

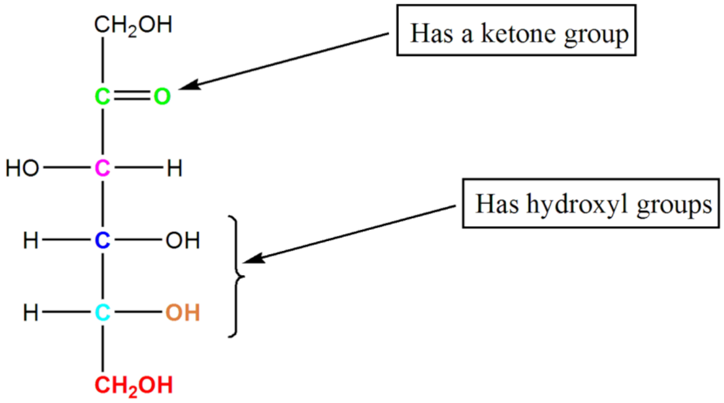
PS: when you move from a Haworth projection to a chair conformation, the groups pointing upwards in the former become equatorial and the groups pointing downwards become axial respectively in the latter.

Question of the day: How does α-D Glucose differ from β D-Glucose?

Lecture# 05

Cyclization of fructose to its hemiketal form

Now let’s apply the same principles (as applied to glucose) to a molecule of fructose. Fructose has a ketone group and five hydroxyl groups. So, fructose should also be able to cyclize to form an intramolecular hemiketal.



D-Fructose

Diagram of D-fructose

There are in fact two ways in which a molecule of fructose can cyclize. The first is as illustrated below

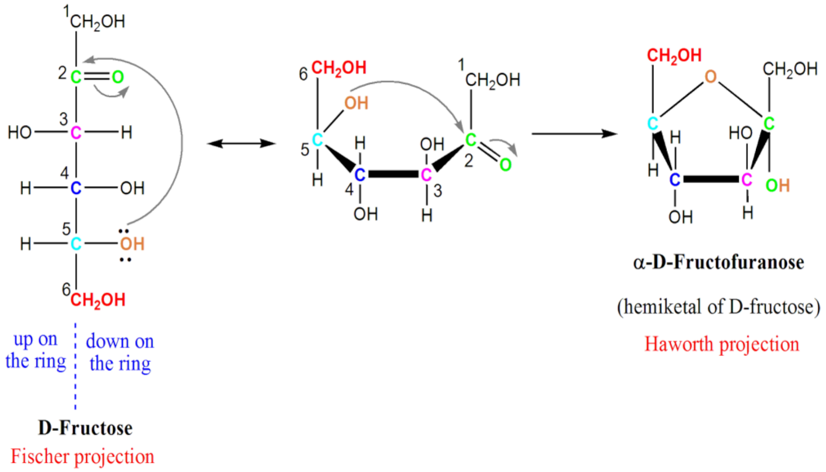
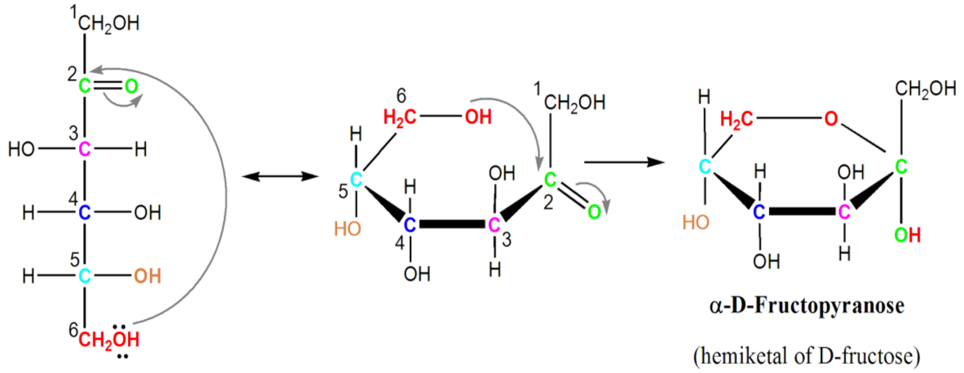


Diagram of fructose cyclizing

Here, as you can see, the hydroxyl attached to C-5 attacks the carbonyl group, yielding a 5-membered ring (furanose form).

In the second scenario (as shown below), the hydroxyl attached to C-6 attacks the carbonyl group, resulting in a 6-membered ring (pyranose form).



α-D-Fructopyranose

(hemiketal of D-fructose)

Haworth projection

Mutarotation

The α and β anomers of D-glucose interconvert in aqueous solution by a process called **mutarotation.** Thus, a solution of _ α -D-glucose and a solution of β -D-glucose eventually form identical equilibrium mixtures having identical optical properties. This mixture consists of about one-third (α) D-glucose, two-thirds β -D-glucose, and very small amounts of the linear and five-membered ring (glucofuranose) forms. Each of these two forms can be synthesized and isolated as pure compounds.

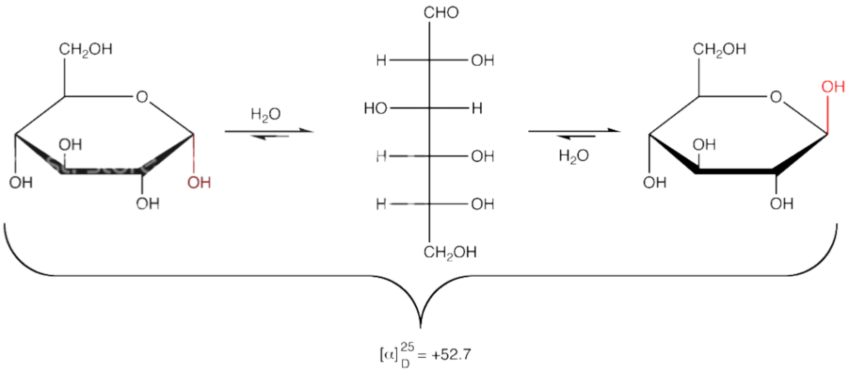
- The alpha (α) anomer of D-glucose has a specific rotation of +112 degrees in water.
- The beta (β) anomer of D-glucose has a specific rotation of +19 degrees. (18.7 actually, but rounding up to 19).

Here's the interesting thing. When either anomer is dissolved in water, **the value of the specific rotation changes over time, eventually reaching the same value of +52.5°.**

- The specific rotation of α-D-glucopyranose decreases from +112° to +52.5°.
- The specific rotation of β-D-glucopyranose increases from +19° to +52.5°.

This behaviour is called **mutarotation** (literally, "change in rotation").

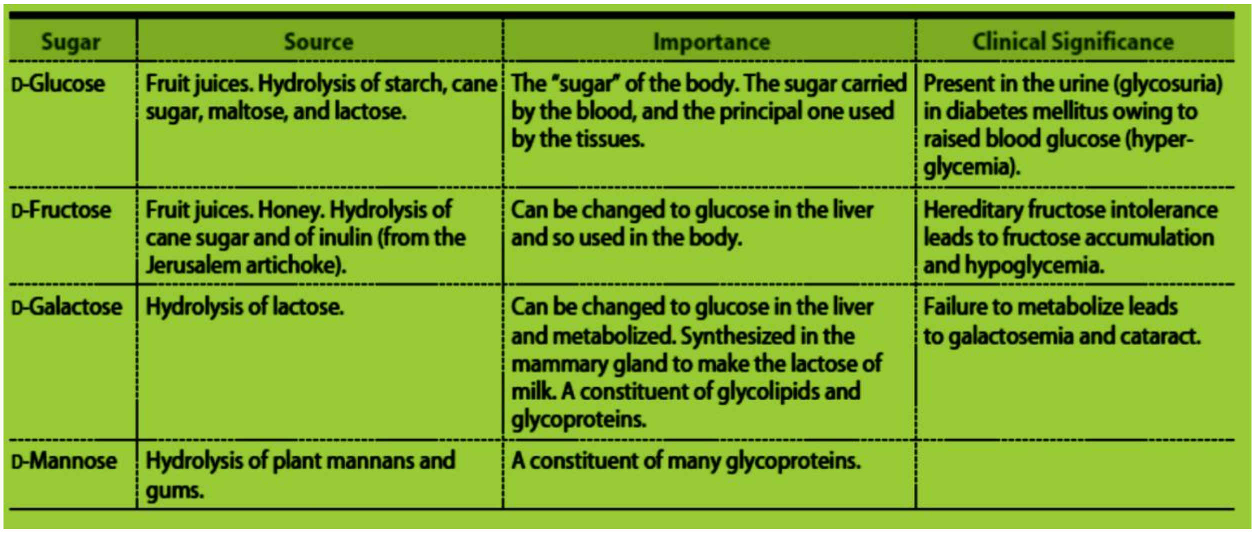
***Mutarotation** is the change in the optical rotation because of the change in the equilibrium between two anomers, when the corresponding stereocenters interconvert. Cyclic sugars show **mutarotation** as α and β anomeric forms interconvert.*



Question of the day: What is mutarotation?

Lecture #6 Disaccharides

Hexoses of physiological Importance



Sugar	Source	Importance	Clinical Significance
D-Glucose	Fruit juices. Hydrolysis of starch, cane sugar, maltose, and lactose.	The "sugar" of the body. The sugar carried by the blood, and the principal one used by the tissues.	Present in the urine (glycosuria) in diabetes mellitus owing to raised blood glucose (hyperglycemia).
D-Fructose	Fruit juices. Honey. Hydrolysis of cane sugar and of inulin (from the Jerusalem artichoke).	Can be changed to glucose in the liver and so used in the body.	Hereditary fructose intolerance leads to fructose accumulation and hypoglycemia.
D-Galactose	Hydrolysis of lactose.	Can be changed to glucose in the liver and metabolized. Synthesized in the mammary gland to make the lactose of milk. A constituent of glycolipids and glycoproteins.	Failure to metabolize leads to galactosemia and cataract.
D-Mannose	Hydrolysis of plant mannans and gums.	A constituent of many glycoproteins.	

Monosaccharides Are Reducing Agents

Monosaccharides can be oxidized by relatively mild oxidizing agents such as ferric (Fe3———
) or

cupric (Cu2———————————————————————————
) ion (Fig. 7–10a). The carbonyl carbon is oxidized to a carboxyl group. Glucose and other sugars capable of reducing ferric or cupric ion are called reducing sugars. This property is the basis of Fehling’s reaction, a qualitative test for the presence of reducing

sugar. By measuring the amount of oxidizing agent reduced by a solution of a sugar, it is also possible to estimate this test was used to detect and measure elevated glucose levels in blood and urine in the diagnosis of diabetes mellitus. Now, more sensitive methods for measuring blood glucose employ an enzyme, glucose oxidase-

GLYCOSIDES

Glycosides are formed by condensation between the hydroxyl group of the anomeric carbon of a monosaccharide, or monosaccharide residue, and a second compound that may—or may not (in the case of an **aglycone**)—be another monosaccharide. If the second group is a hydroxyl,the O-glycosidic bond is an **acetal** link because it results from a reaction between a hemiacetal group (formed from an aldehyde and an -OH group) and another-OH group. If the hemiacetal portion is glucose, the resulting compound is a **glucoside;** if galactose, a **galactoside;** and so on. If the second group is an amine, an N-glycosidic bond is formed, eg, between adenine and ribose in nucleotides such as ATP. Glycosides are widely distributed in nature; the aglycone may be methanol, glycerol, a sterol, a phenol, or a base such as adenine. The glycosides that are important in medicine because of their action on the heart **(cardiacglycosides)** all contain steroids as the aglycone. The monosaccharides are held together by o-glycosidic bonds to result in di-, oligo- or polysaccharides.

Oligosaccharides/disaccharides

Oligosaccharides are carbohydrate chains containing 3–10 sugar units. However, some authors also include carbohydrates with up to 20 residues or even **disaccharides**

We generally associate sugar with glucose. But did you know the table sugar we use every day is not glucose? It is, in fact, a disaccharide known as sucrose.

Disaccharides

As is evident from the name, a disaccharide consists of two monosaccharide units(similar or dissimilar held together by a glycosidic bond. They are crystalline, water-soluble and sweet to taste. The disaccharides are of two types

'1. Reducing disaccharides with free aldehyde or keto group e.g. maltose, lactose.

2. Non-reducing disaccharides with no free aldehyde or keto group e.g. sucrose, trehalose.

The oxidation of a sugar’s anomeric carbon by cupric or ferric ion (the reaction that defines a reducing sugar) occurs only with the linear form, which exists in equilibrium with the cyclic form(s). When the anomeric carbon is involved in a glycosidic bond, that sugar residue cannot take the linear form and therefore becomes a non-reducing sugar. In describing disaccharides or polysaccharides, the end of a chain with a free anomeric carbon (one not involved in a glycosidic bond) is commonly called the **reducing end. Common disaccharides are maltose, lactose, and sucrose**

1.Maltose

The disaccharide maltose contains two D-glucose residues joined by a glycosidic linkage between C-1 (the anomeric carbon) of one glucose residue and C-4 of the other. Because the disaccharide retains a free anomeric carbon (C-1 of the glucose residue on the right in Fig. 7–11), maltose is a reducing sugar. The configuration of the anomeric carbon atom in the glycosidic linkage is . The glucose residue with the free anomeric carbon is capable of existing in α- and β pyranose forms.

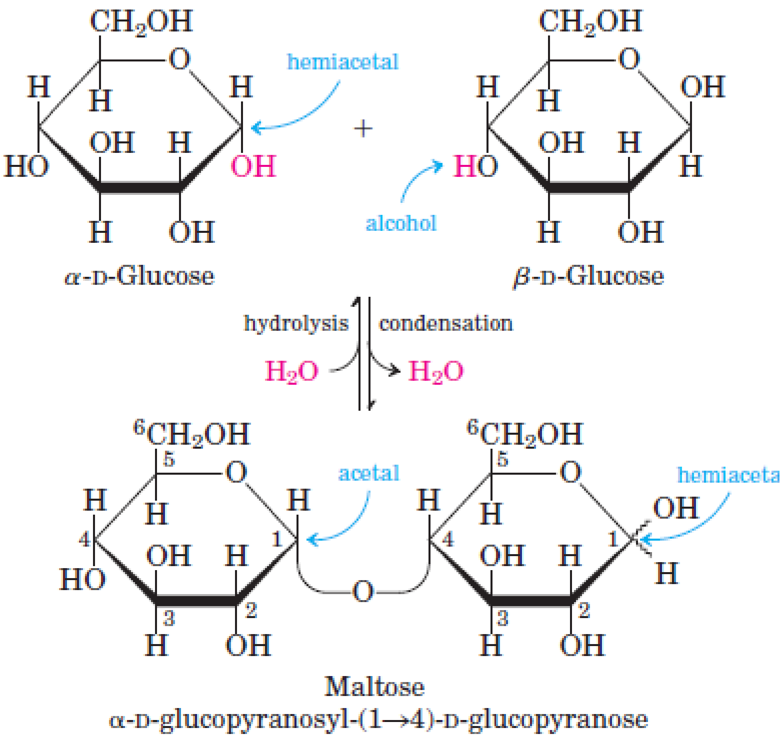


FIGURE 7–11 **Formation of maltose.** *A disaccharide is formed from two monosaccharides (here, two molecules of D-glucose) when an -OH (alcohol) of one glucose molecule (right) condenses with the intramolecular hemiacetal of the other glucose molecule (left), with elimination of H2O and formation of an O-glycosidic bond. The reversal of this reaction is hydrolysis—attack by H2O on the glycosidic bond. The maltose molecule retains a reducing hemiacetal at the C-1 not involved in the glycosidic bond. Because mutarotation interconverts the α and β forms of the hemiacetal, the bonds at this position are sometimes depicted with wavy lines, as shown here, to indicate that the structure may be either α .or β*

To name reducing disaccharides such as maltose unambiguously, and especially to name more complex oligosaccharides, several rules are followed. By convention, the name describes the compound with its nonreducing end to the left, and we can “build up” the name in the following order. (1) Give the configuration (*α* or β) at the anomeric carbon joining the first monosaccharide unit (on the left) → to the second. (2) Name the nonreducing residue; to distinguish five- and six-membered ring structures, insert “furano” or “pyrano” into the name. (3) Indicate in parentheses the two carbon atoms joined by the glycosidic bond, with an arrow connecting the two numbers; for example, (1 4) → shows that C-1 of the first-named sugar residue is joined to C-4 of the second. (4) Name the second residue. If there is a third residue, describe the second glycosidic bondby the same conventions. Following this convention for naming oligosaccharides, maltose is *α*-D-glucopyranosyl (1→ 4) D glucopyranose.

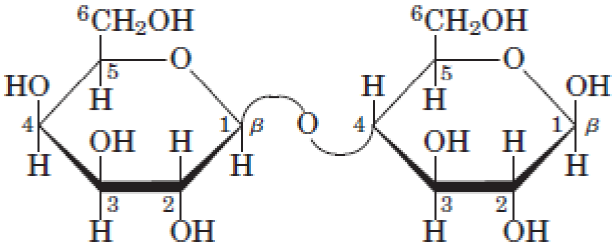
Lactose

Lactose is more commonlv known as milk sugars ince i t is the disacchar idefo und in milk. Lactose composes about 2–8% of milk by weight.Lactose is composed of β-D-galactose and α-D-glucose held together by β (1→ 4)glycosidic bond. The anomeric carbon of C1 glucose is free, hence lactose exhibits reducing properties and formso sazones(powder-puff or hedgehog shape). Its abbreviated name is Gal (β*1→4)*Glc. In humans, lactase (beta-galactosidase) breaks down lactose at the brush border of the small intestine.. This enzyme cleaves the lactose molecule into its two subunits, the simple sugars glucose and galactose, which can be absorbed.

The sweetness of lactose is 0.2 to 0.4, relative to 1.0 for sucrose.[15] For comparison, the sweetness of glucose is 0.6 to 0.7, of fructose is 1.3, of galactose is 0.5 to 0.7, of maltose is 0.4 to 0.5

Its mild flavor and easy handling properties have led to its use as a carrier and stabiliser of aromas and pharmaceutical products. Lactose is not added directly to many foods, because its solubility is less than that of other sugars commonly used in food. Infant formula is a notable exception, where the addition of lactose is necessary to match the composition of human milk.

Lactose intolerance is a digestive disorder caused by the inability to digest lactose, the main carbohydrate in dairy products.It can cause various symptoms, including bloating, diarrhea and abdominal cramps.People with lactose intolerance don't make enough of the enzyme lactase, which is needed to digest lactose.

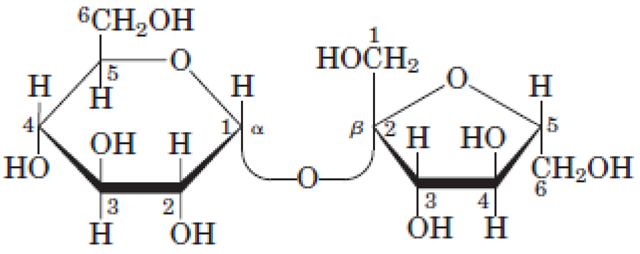


Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc

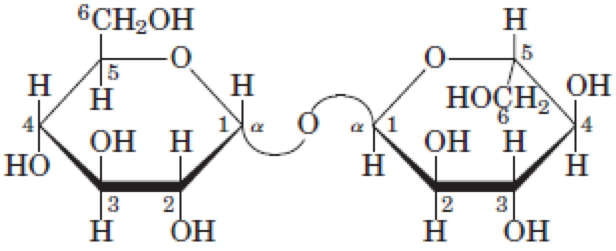
Sucrose

Sucrose (table sugar) is a disaccharide of glucose and fructose. It has the molecular formula $C_{12}H_{22}O_{11}$.It is formed by plants but not by animals. For human consumption, sucrose is extracted and refined from either sugarcane or sugar beet In contrast to maltose and lactose, sucrose contains no free anomeric carbon atom; the anomeric carbons of both monosaccharide units are involved in the glycosidic bond . Sucrose is therefore a nonreducing sugar. Nonreducing disaccharides are named as glycosides; in this case, the positions joined are the anomeric carbons. In the abbreviated nomenclature, a double-headed arrow connects the symbols specifying the anomeric carbons and their configurations. For example, the abbreviated name of sucrose is either Glc(α1↔2β)Fru or Fru(β2↔1α)Glc. Sucrose is a major intermediate product of photosynthesis; in many plants it is the principal form in which sugar is transported from the leaves to other parts of the plant body. Trehalose, Glc(α1↔1α)Glc —a disaccharide of D-glucose that, like sucrose, is a non-reducing sugar—is a major constituent of the circulating fluid (hemolymph) of insects, serving as an energy-storage compound.

Hydrolysis breaks the glycosidic bond converting sucrose into glucose and fructose. Hydrolysis is, however, so slow that solutions of sucrose can sit for years with negligible change. If the enzyme sucrase is added, however, the reaction will proceed rapidly. Hydrolysis can also be accelerated with acids, such as cream of tartar or lemon juice, both weak acids. Likewise, gastric acidity converts sucrose to glucose and fructose during digestion, the bond between them being an acetal bond which can be broken by an acid.



Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru



Trehalose
α-D-glucopyranosyl α-D-glucopyranoside
Glc(α1↔1α)Glc

Inversion of sucrose

Sucrose, as such is dextrorotatory (+66.5 ^{o}). But, when hydrolysed, sucrose becomes levorotatory (-28.2 ^{o}). The process of change in optical rotation from dextrorotatory (+) to levorotatory (-) is referred to as inversion. The hydrolysed mixture of sucrose, containing glucose and fructose, is known as ***invert sugar***. Hydrolysis of sucrose by the enzyme sucrose (invertase) or dilute acid liberates one molecule each of glucose and fructose. it is postulated that sucrose (dextro) is first split into a-Dglucopyranose(+52.5^{o}) and p-D-fructofuranose, both being dextrorotatory. However, β-D fructofuranose is lesss table and immediately gets converted to β-D fructopyranose which is strongly levorotatory(-92 ^{o}). The overall effect is that dextro sucrose (+66.5 ^{o}) on inversion is converted to levo form (-28.2 ^{o}).

Question of the day: What is Invert sugar

Polysaccharides

Most carbohydrates found in nature occur as polysaccharides, polymers of medium to high molecular weight. Polysaccharides are complex biomacromolecules that are made up chains of monosaccharides that are joined by glycosidic linkages as in disaccharides. By convention, a polysaccharide consists of more than ten monosaccharide units, while an oligosaccharide consists of three to ten linked monosaccharides. Polysaccharides, also called glycans, differ from each other in the identity of their recurring monosaccharide units, in the length of their chains, in the types of bonds linking the units, and in the degree of branching. Polysaccharides may be classified according to their composition as either homopolysaccharides or heteropolysaccharides.

A **homopolysaccharide** or homoglycan consists of single type of monosaccharide or sugar derivative. For example, cellulose, starch, and glycogen are all composed of glucose subunits. Chitin consists of repeating subunits of *N*-acetyl-*D*-glucosamine, which is a glucose derivative.

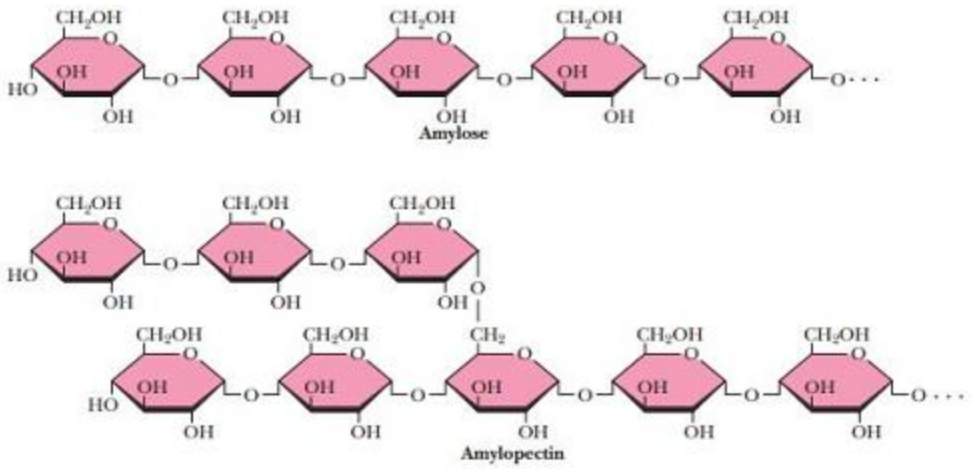
A **heteropolysaccharide** or heteroglycan contains more than one type sugar or sugar derivative. In practice, most heteropolysaccharides consist of two monosaccharides (disaccharides). They are often associated with proteins. A good example of a heteropolysaccharide is hyaluronic acid, which consists of *N*-acetyl-*D*-glucosamine linked to glucuronic acid (two different glucose derivatives).

Some homopolysaccharides serve as storage forms of monosaccharides that are used as fuels; starch and glycogen are homopolysaccharides of this type. Other homopolysaccharides (cellulose and chitin, for example) serve as structural elements in plant cell walls and animal exoskeletons. Heteropolysaccharides provide extracellular support for organisms of all kingdoms. For example, the rigid layer of the bacterial cell envelope (the peptidoglycan) is composed in part of a heteropolysaccharide built from two alternating monosaccharide units. In animal tissues, the extracellular space is occupied by several types of heteropolysaccharides, which form a matrix that holds individual cells together and provides protection, shape, and support to cells, tissues, and organs.

Starch & Glycogen – The Storage Polysaccharides

The most important storage polysaccharides are starch in plant cells and glycogen in animal cells. Both polysaccharides occur intracellularly as large clusters or granules (Fig. 7–14). Starch and glycogen molecules are heavily hydrated, because they have many exposed hydroxyl groups available to hydrogen-bond with water. Most plant cells have the ability to form starch, but it is especially abundant in tubers, such as potatoes, and in seeds.

Starch contains two types of glucose polymer, amylose and amylopectin. The former consists of long, unbranched chains of D-glucose residues connected by α(1 - > 4) linkages. Such chains vary in molecular weight from a few thousand to more than a million. Amylopectin also has a high molecular weight (up to 100 million) but unlike amylose is highly branched. The glycosidic linkages joining successive glucose residues in amylopectin chains are α(1 - > 4) the branch points (occurring every 24 to 30 residues) are α(1 - > 6) linkages.The most usual conformation of amylose is a helix with six residues per turn. Iodine molecules can fit inside the helix to form a starch–iodine complex, which has a characteristic dark-blue color. The formation of this complex is a well-known test for the presence of starch. If there is a preferred conformation for amylopectin, it is not yet known. (It *is* known that the color of the product obtained when amylopectin and glycogen react with iodine is red-brown, not blue.)



ANIMATED FIGURE 16.23 Amylose and amylopectin are the two forms of starch. Note that the linear linkages are α(1 → 4), but the branches in amylopectin are α(1 → 6). Branches in polysaccharides can involve any of the hydroxyl groups on the monosaccharid components. Amylopectin is a highly branched structure, with branches occurring at every 12

Because starches are storage molecules, there must be a mechanism for releasing glucose from starch when the organism needs energy. Both plants and animals contain enzymes that hydrolyze starches. Two of these enzymes, known as α- and β-*amylase* (the α and β do not signify anomeric forms in this case), attack α(1 - > 4) linkages. β-amylase is an *exoglycosidase* that cleaves from the nonreducing end of the polymer. Maltose, a dimer of glucose, is the prod-uct of reaction. The other enzyme, α-amylase, is an *endoglycosidase*, which can hydrolyze a glycosidic linkage anywhere along the chain to produce glucose and maltose. Amylose can be completely degraded to glucose and maltose by the two amylases, but amylopectin is not completely degraded because the branching linkages are not attacked.

However, *debranching enzymes* occur in both plants and animals; they degrade the α(1 - > 6) linkages. When these enzymes are combined with the amylases, they contribute to the complete deg-radation of both forms of starch.

Glycogen is the main storage polysaccharide of animal cells. Like amylopectin, glycogen is a polymer of α(1 - > 4) linked subunits of glucose, with α(1 - > 6) linked branches, but glycogen is more extensively branched (on average, every 8 to 12 residues) and more compact than starch. Glycogen is especially abundant in the liver, where it may constitute as much as 7% of the wet weight; it is also present in skeletal muscle. In hepatocytes glycogen is found in large granules which are themselves clusters of smaller granules composed of single, highly branched glycogen molecules with an average molecular weight of several million. Such glycogen granules also contain, in tightly bound form, the enzymes responsible for the synthesis and degradation of glycogen. Because each branch in glycogen ends with a non-reducing sugar unit, a glycogen molecule has as many non-reducing ends as it has branches, but only one reducing end. When glycogen is used as an energy source, glucose units are removed one at a time from the nonreducing ends. Degradative enzymes that act only at non-reducing ends can work simultaneously on the many branches, speeding the conversion of the polymer to monosaccharides.

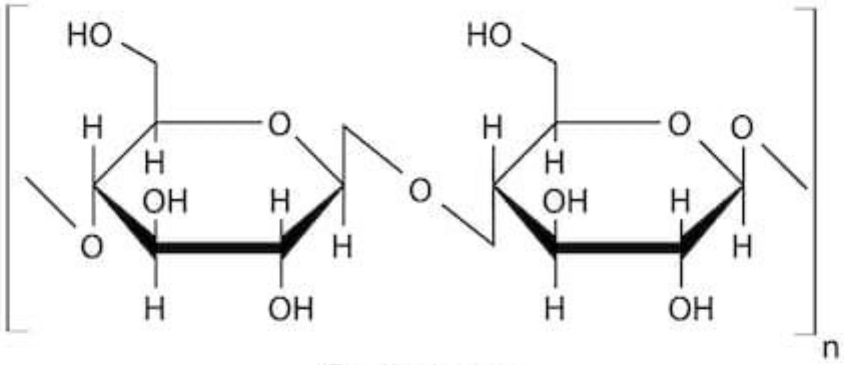
***Dextrans** are bacterial and yeast polysaccharides made up of (α1 - > 4) linked poly-D-glucose; all have (α1 - > 3) branches, and some also have α(1 - > 2) or α(1 - > 4) branches. Dental plaque, formed by bacteria growing on the surface of teeth, is rich in dextrans.*

Q.Why Glucose is not stored in its monomeric form?

Cellulose – the structural Polysaccharides

Cellulose, a fibrous, tough, water-insoluble substance, is found in the cell walls of plants, particularly in stalks, stems, trunks, and all the woody portions of the plant body. Cellulose constitutes much of the mass of wood, and cotton is almost pure cellulose. Like amylose and the main chains of amylopectin and glycogen, the cellulose molecule is a linear, unbranched homopolysaccharide, consisting of 10,000 to 15,000 D-glucose units. But there is a very important difference: in cellulose the glucose residues have the β-configuration. whereas in amylose, amylopectin, and glycogen the glucose is in the α-configuration. The glucose residues in cellulose are linked by (β1→4) glycosidic bonds, in contrast to the (α1→4) bonds of amylose, starch, and glycogen. This difference gives cellulose and amylose very different structures and physical properties.

Glycogen and starch ingested in the diet are hydrolyzed by α-amylases, enzymes in saliva and intestinal secretions that break (α1→4) glycosidic bonds between glucose units. Most animals cannot use cellulose as a fuel source, because they lack an enzyme to hydrolyze the (β1→4) linkages. Termites readily digest cellulose (and therefore wood), but only because their intestinal tract harbors a symbiotic microorganism, *Trichonympha*, that secretes cellulase, which hydrolyzes the (_β1→4) linkages. Wood-rot fungi and bacteria also produce Cellulase.



Cellulose

Chitin

Chitin is a linear homopolysaccharide composed of *N*-acetylglucosamine residues inβ linkage. The only chemical difference from cellulose is the replacement of the hydroxyl group at C-2 with an acetylated amino group. Chitin forms extended fibers similar to those of cellulose, and like cellulose cannot be digested by vertebrates. Chitin is the principal component of the hard exoskeletons of nearly a million species of arthropods—insects, lobsters, and crabs, for example— and is probably the second most abundant polysaccharide, next to cellulose, in nature.

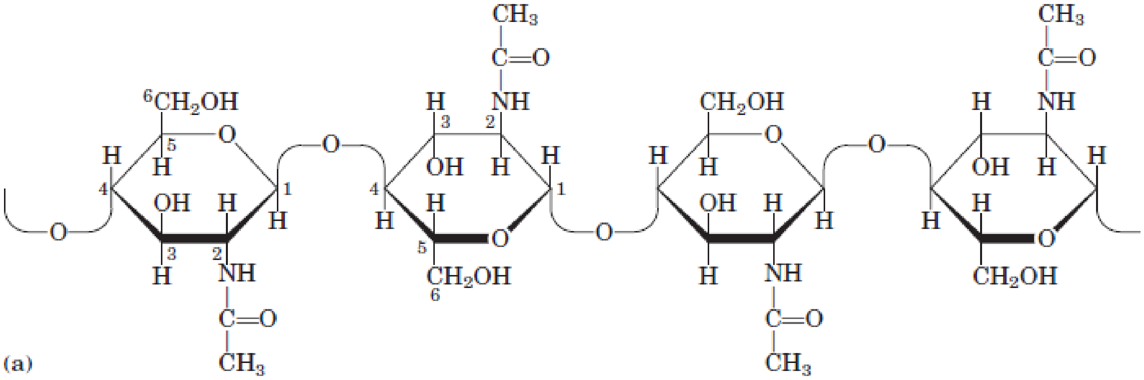


Fig Chitin. (a) A short segment of chitin, a homopolymer of *N*-acetyl-D-glucosamine units in

(β1→4) linkage. **(b)** A spotted June beetle (*Pellidnota punetatia*), showing its surface armor (exoskeleton) of chitin.

Heteropolysaccharide -Glycosaminoglycans (Mucopolysaccharides)

Glycosaminoglycans are linear, usually sulphated, negatively charged polysaccharides that have molecular weights of roughly 10–100 kDa. There are two main types of GAGs. Non-sulphated GAGs include hyaluronic acid (HA), whereas sulphated GAGs include chondroitin sulphate (CS), dermatan sulphate (DS), keratan sulphate (KS), heparin and heparan sulphate (HS). Glycosaminoglycans chains are composed of disaccharide repeating units called disaccharide repeating regions . The repeating units are composed of uronic acid : D-glucoronic acid or L-iduronic acid (except in the case of keratan, where, in place of the uronic sugar there is a galactose unit) and amino sugar (D-galactosamine or D-glucosamine). Hence, GAGs differ according to the type of hexosamine, hexose or hexuronic acid unit that they contain, as well as the geometry of the glycosidic linkage between these units. Chondroitin sulphate and DS, which contain galactosamine, are called galactosaminoglycans, whereas heparin and HS, which contain glucosamine, are called glucosaminoglycans. The amino sugar may be sulphated on carbons 4 or 6 or on the non-acetylated nitrogen; however, the sugar backbone of GAGs can be sulphated at various positions.. At physiological pH, all carboxylic acid and sulphate groups are deprotonated, giving GAGs very high negative charge densities (heparin has the highest negative charge density of any known biomolecule). **The combination of sulfate groups and the carboxylate groups of the uronic acids gives glycosaminoglycans a very high density of negative charge, and an extended rod-like structure in solution.** Because GAGs are highly polar molecules and attract water; the body uses them as lubricants or shock absorbers.

- Glycosaminoglycans are heteropolysaccharides that are only present in animals and bacteria and not in plants.
- Glycosaminoglycans are sometimes known as mucopolysaccharides because of their viscous, lubricating properties, as found in mucous secretions. These molecules are present on all animal cell surfaces in the extracellular matrix (ECM), and some are known to bind and regulate a number of distinct proteins, including chemokines, cytokines, growth factors, morphogens, enzymes and adhesion molecules
- Historically, the function of GAGs was thought to be limited to cell hydration and structural scaffolding. However, evidence now suggests that GAGs play a key role in cell signaling, which serves to modulate a vast amount of biochemical processes. The four primary groups of GAGs are classified based on their core disaccharide units and include heparin/heparan sulfate, chondroitin sulfate/dermatan sulfate, keratan sulfate, and hyaluronic acid.

Hyaluronic acid

Hyaluronic acid is a linear heteropolysaccharide (glucosaminoglycan, mucopolysaccharide) with high molecular weight formed by regularly repeating residues of N-acetyl-D-glucosamine and D-glucuronic acid [1,29]. In a hyaluronic acid molecule, the D-glucuronic acid is associated with amino-sugar by β-(1 → 3)-glycosidic linking, and amino-sugar is connected with the D-glucuronic acid by a β-(1 → 4)-glycoside tieup.

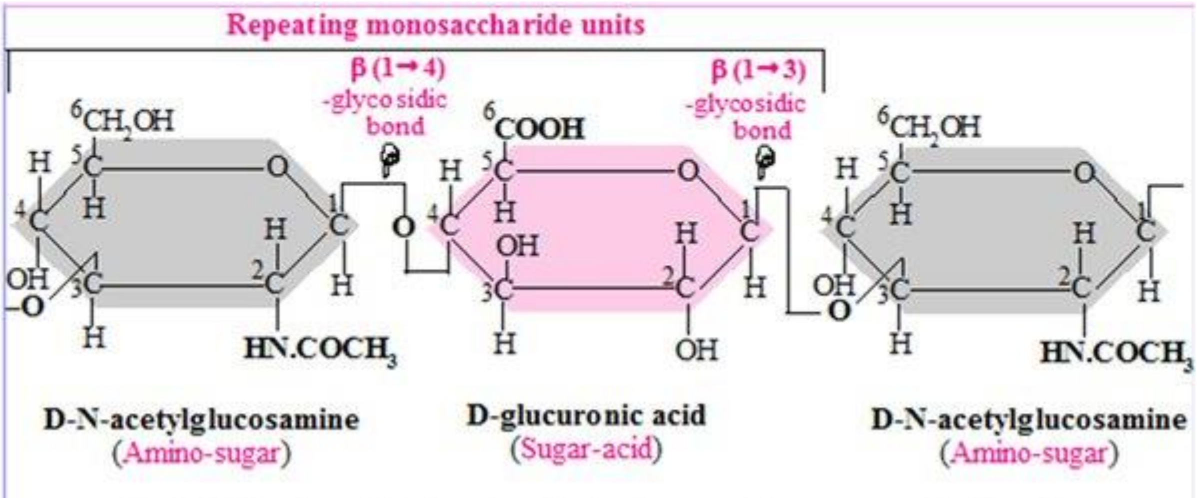


Fig. 4.20: Structure of hyaluronic acid showing repeating monosaccharide units

In nature, all GAG chains with the exception of HA are covalently linked to a core protein to give a PG.

Functions of HA include the following: hydration, lubrication of joints, a space filling capacity, and the framework through which cells migrate. The synthesis of HA increases during tissue injury and wound healing.

Taking hyaluronic acid or using cosmetic products that contain it may improve skin hydration and reduce signs of aging.

Heparan sulfate (HS) and heparin (Hp)

Native heparin is a polymer with a molecular weight ranging from 3 to 30 kDa, although the average molecular weight of most commercial heparin preparations is in the range of 12 to 15 kDa.[58] Heparin is a member of the glycosaminoglycan family of carbohydrates (which includes the closely related molecule heparan sulfate) and consists of a variably sulfated repeating disaccharide unit. The main disaccharide units that occur in heparin are shown below. The most common disaccharide unit* (see below) is composed of a 2-O-sulfated iduronic acid and 6-O-sulfated, N-sulfated glucosamine, IdoA(2S)-GlcNS(6S).

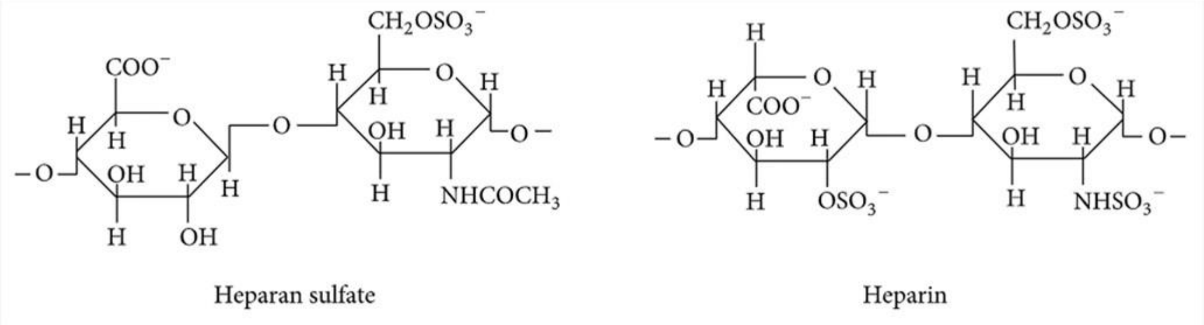
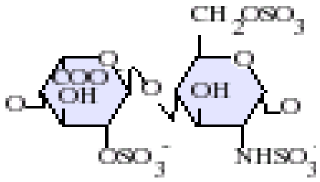
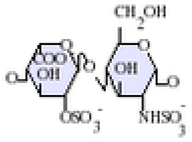


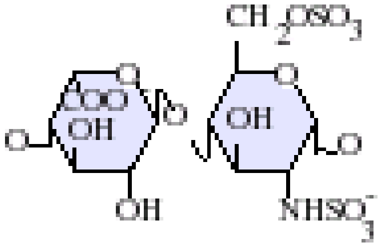
Fig: Most Predominant Disacharide units found in HS/HP

<u>Different Disaccharide units found in Heparin/Heparin Sulfate</u>

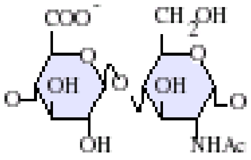




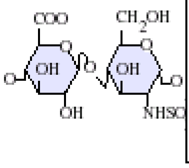
IdoA(2S)-GlcNS

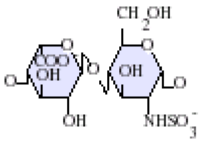


IdoA-GlcNS(6S)



GlcA-GlcNAc





IdoA-GlcNS

Heparan sulfate (HS) and heparin (Hp) are the glycosaminoglycans (GAGs) of the most complex structure among all GAGs. They are made of recurring, disaccharide units consisting of glucuronic acid and N-acetylglucosamine residues , in which the glycosidic bond between the hexuronic acid and N-acetylglucosamine assumes the configuration of β1--4 while the bond between N-acetylglucosamine and hexuronic acid assumes the configuration α1—4. The amino group of the glucosamine residue may be substituted with an acetyl or sulphate group, or remain unsubstituted. The 3- and 6-positions of the glucosamine residues can either be substituted with an *O*-sulphate group or remain unsubstituted. The uronic acid, which can either be L-iduronic or D-glucuronic acid, may also contain a 2-*O*-sulphate group.

Despite the fact that heparin is often considered an analogue of heparin sulfate, as both GAGs are made of the same, monomeric subunits, postsynthetic modifications, the range of which is significantly different in both glycosaminoglycans, definitely differentiate these biopolymers Namely,

- monomeric heparin subunits are sulfated to a greater degree than the subunits of HS. On average, one disaccharide unit of heparin contains 3 sulfate groups, while one disaccharide unit of heparan sulfate contains only one sulphate group . The negative charge density, which is displayed by heparin, is the highest among biologic macromolecules and is responsible for the fact that this GAG is the most acidic macromolecule of human body.
- Iduronic acid dominates in heparin structure constituting 90% of all acid residues, while in the heparan sulfate, glucuronic acid, being the C5 epimer of the iduronic acid occurs in greater amounts.
- The molecular mass of the heparin molecule on average equals 15 kDa, while in the case of heparin sulfate about 30 kDa. Moreover, the chains of the latter one are longer than in the case of heparin.

Heparin and heparan sulfates are initially composed of GlcNAc and glucuronic acid (GlcA) disaccharide units. Following formation of the disaccharide unit it undergoes extensive modifications. Both disaccharide units are sulfated with heparins being more highly sulfated than heparan sulfates. Heparin is produced solely as serglycin proteoglycan by connective-tissue associated mast cells, whereas heparan sulfates are made by virtually all cells of the body. As this family of GAG chains polymerizes, the sugars undergo a series of modification reactions. These modifications are carried out by an epimerase and at least four families of sulfotransferases.During synthesis heparin becomes more sulfated than heparan sulfates and also there is a higher degree of GlcA epimerization to IdoA in heparins than in heparan sulfates. In heparin, more than 80% of the GlcNAc residues are first N-deacetylated and then the resultant glucosamine (GlcN) is N-sulfated and more than 70% of the GlcA is epimerized to IdoA.

The major and best known function of heparin is anticoagulation. Heparin binds to serine protease inhibitor antithrombin III (AT) which results in activation of AT. The activated AT blocks thrombin and inactivates factors Xa and IIa which are responsible for blood coagulation.

Sem-I

Lecture#

Unit-I

Glycoproteins

A glycoprotein is a type of protein molecule that has had a carbohydrate attached to it. The process either occurs during protein translation or as a posttranslational modification in a process called glycosylation.

The carbohydrate is an oligosaccharide chain (glycan) that is covalently bonded to the polypeptide side chains of the protein. Because of the -OH groups of sugars, glycoproteins are more hydrophilic than simple proteins. This means glycoproteins are more attracted to water than ordinary proteins. The hydrophilic nature of the molecule also leads to the characteristic folding of the protein's tertiary structure.

The carbohydrate is a short molecule, often branched, and may consist of:

- simple sugars (e.g., glucose, galactose, mannose, xylose)
- amino sugars (sugars that have an amino group, such as N-acetylglucosamine or N-acetylgalactosamine)
- acidic sugars (sugars that have a carboxyl group, such as sialic acid or N-acetylneuraminic acid).

  Some glycoproteins have a single oligosaccharide chain, but many have more than one; the carbohydrate may constitute from 1% to 70% or more of the glycoprotein.

O-Linked and N-Linked Glycoproteins

Glycoproteins are categorized according to the attachment site of the carbohydrate to an amino acid in the protein.

- O-linked glycoproteins are ones in which the carbohydrate bonds to the oxygen atom (O) of the hydroxyl group (-OH) of the R group of either the amino acid threonine or serine. O-linked carbohydrates may also bond to hydroxylysine or hydroxyproline. The process is termed O-glycosylation. O-linked glycoproteins are bound to sugar within the Golgi complex.
- N-linked glycoproteins have a carbohydrate bonded to the nitrogen (N) of the amino group ($-NH_2$) of the R group of the amino acid asparagine. The R group is usually the amide side chain of asparagine. The bonding process is called N-glycosylation. N-linked glycoproteins gain their sugar from the endoplasmic reticulum membrane and then are transported to the Golgi complex for modification.

While O-linked and N-linked glycoproteins are the most common forms, other connections are also possible:

- P-glycosylation occurs when the sugar attaches to the phosphorus of phosphoserine.
- C-glycosylation is when the sugar attaches to the carbon atom of amino acid. An example is when the sugar mannose bonds to the carbon in tryptophan.
- Glypiation is when a glycophosphatidylinositol (GPI) glycolipid attaches to the carbon terminus of a polypeptide.

Glycoprotein Examples and Functions

Glycoproteins function in the structure, reproduction, immune system, hormones, and protection of cells and organisms.

- Glycoproteins are found on the surface of the lipid bilayer of cell membranes. Their hydrophilic nature allows them to function in the aqueous environment, where they act in cell-cell recognition and binding of other molecules. Cell surface glycoproteins are also important for cross-linking cells and proteins (e.g., collagen) to add strength and stability to a tissue. Glycoproteins in plant cells are what allows plants to stand upright against the force of gravity. One of the best-characterized membrane glycoproteins is glycophorin A of the erythrocyte membrane (see Fig. 11–8). It contains 60% carbohydrate by mass, in the form of 16 oligosaccharide chains (totaling 60 to 70 monosaccharide residues) covalently attached to amino acid residues near the amino terminus of the polypeptide chain. Fifteen of the oligosaccharide chains are *O*-linked to Ser or Thr residues, andone is *N*-linked to an Asn residue.
- Glycosylated proteins are not just critical for intercellular communication. They also help organ systems communicate with each other. Glycoproteins are found in brain gray matter, where they work together with axons and synaptosomes.
- Hormones may be glycoproteins. Examples include human chorionic gonadotropin (HCG) and erythropoietin (EPO).
- Blood clotting depends on the glycoproteins prothrombin, thrombin, and fibrinogen.
- Glycoproteins are important for reproduction because they allow for the binding of the sperm cell to the surface of the egg.
- Mucins are glycoproteins found in mucus. The molecules protect sensitive epithelial surfaces, including the respiratory, urinary, digestive, and reproductive tracts.
- The immune response relies on glycoproteins. The carbohydrate of antibodies (which are glycoproteins) determines the specific antigen it can bind. B cells and T cells have surface glycoproteins which bind antigens, as well.

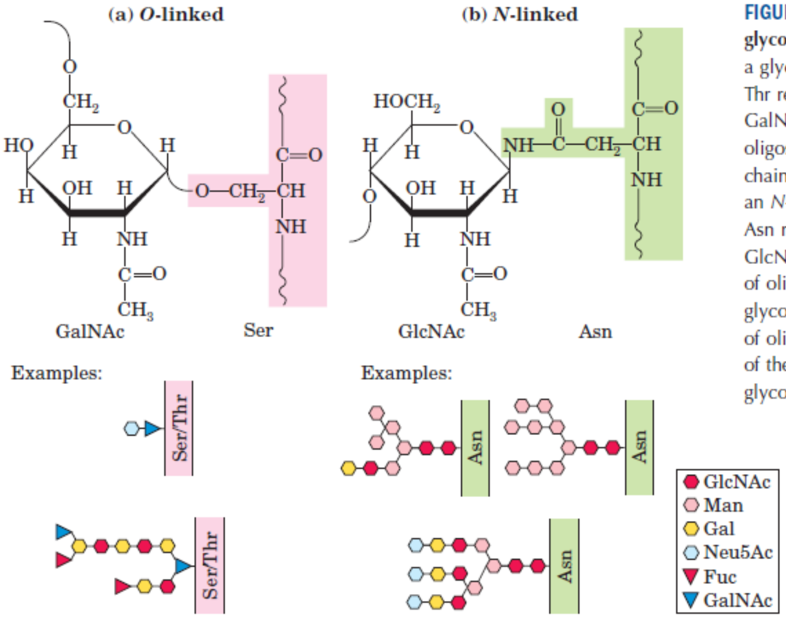


FIGURE 7–31 Oligosaccharide linkages in glycoproteins. **(a)** *O*-linked oligosaccharides have a glycosidic bond to the hydroxyl group of Ser or Thr residues (shaded pink), illustrated here with GalNAc as the sugar at the reducing end of the oligosaccharide. One simple chain and one complex chain are shown. **(b)** *N*-linked oligosaccharides have an *N*-glycosyl bond to the amide nitrogen of an Asn residue (shaded green), illustrated here with GlcNAc as the terminal sugar. Three common types of oligosaccharide chains that are *N*-linked in glycoproteins are shown. A complete description of oligosaccharide structure requires specification of the position and stereochemistry (α or β) of each glycosidic linkage.

Q. What is the difference between glycoproteins and proteoglycans?