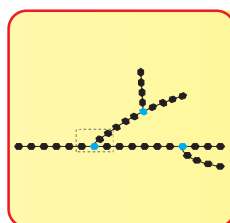


## Carbohydrates

**The carbohydrates speak :**

*“We are polyhydroxyaldehydes or ketones;  
Classified into mono-, oligo- and polysaccharides;  
Held together by glycosidic bonds;  
Supply energy and serve as structural constituents.”*

Carbohydrates are the most abundant organic molecules in nature. They are primarily composed of the elements **carbon, hydrogen and oxygen**. The name carbohydrate literally means ‘**hydrates of carbon**’. Some of the carbohydrates possess the empirical formula  $(C.H_2O)_n$  where  $n \leq 3$ , satisfying that these carbohydrates are in fact carbon hydrates. However, there are several non-carbohydrate compounds (e.g. acetic acid,  $C_2H_4O_2$ ; lactic acid,  $C_3H_6O_3$ ) which also appear as hydrates of carbon. Further, some of the genuine carbohydrates (e.g. rhamnohexose,  $C_6H_{12}O_5$ ; deoxyribose,  $C_5H_{10}O_4$ ) do not satisfy the general formula. Hence carbohydrates cannot be always considered as hydrates of carbon.

**Carbohydrates may be defined as polyhydroxyaldehydes or ketones or compounds which produce them on hydrolysis.** The term ‘sugar’ is applied to carbohydrates soluble in water and sweet to taste.

**Functions of carbohydrates**

Carbohydrates participate in a wide range of functions

1. They are the most abundant dietary **source of energy** (4 Cal/g) for all organisms.
2. Carbohydrates are precursors for many organic compounds (fats, amino acids).
3. Carbohydrates (as glycoproteins and glycolipids) participate in the structure of cell membrane and cellular functions such as cell growth, adhesion and fertilization.
4. They are structural components of many organisms. These include the fiber (cellulose) of plants, exoskeleton of some insects and the cell wall of microorganisms.
5. Carbohydrates also serve as the storage form of energy (glycogen) to meet the immediate energy demands of the body.

**CLASSIFICATION OF CARBOHYDRATES**

Carbohydrates are often referred to as saccharides (*Greek*: sakcharon–sugar). They are broadly classified into three major groups—**monosaccharides, oligosaccharides and polysaccharides**. This categorization is based on the

TABLE 2.1 Classification of monosaccharides with selected examples

<i>Monosaccharides (empirical formula)</i>	<i>Aldose</i>	<i>Ketose</i>
Trioses (C <sub>3</sub> H <sub>6</sub> O <sub>3</sub> )	Glyceraldehyde	Dihydroxyacetone
Tetroses (C <sub>4</sub> H <sub>8</sub> O <sub>4</sub> )	Erythrose	Erythrulose
Pentoses (C <sub>5</sub> H <sub>10</sub> O <sub>5</sub> )	Ribose	Ribulose
Hexoses (C <sub>6</sub> H <sub>12</sub> O <sub>6</sub> )	Glucose	Fructose
Heptoses (C <sub>7</sub> H <sub>14</sub> O <sub>7</sub> )	Glucoheptose	Sedoheptulose

number of sugar units. **Mono- and oligosaccharides** are sweet to taste, crystalline in character and soluble in water, hence they are commonly known as **sugars**.

### Monosaccharides

Monosaccharides (*Greek*: mono-one) are the simplest group of carbohydrates and are often referred to as simple sugars. They have the general formula C<sub>n</sub>(H<sub>2</sub>O)<sub>n</sub>, and they cannot be further hydrolysed. The monosaccharides are divided into different categories, based on the functional group and the number of carbon atoms

**Aldoses** : When the functional group in

monosaccharides is an aldehyde ( $\begin{matrix} \text{H} \\ | \\ \text{---C=O} \end{matrix}$ ), they are known as aldoses e.g. glyceraldehyde, glucose.

**Ketoses** : When the functional group is a keto ( $\begin{matrix} \text{---C=O} \\ | \end{matrix}$ ) group, they are referred to as ketoses e.g. dihydroxyacetone, fructose.

Based on the number of carbon atoms, the monosaccharides are regarded as **trioses (3C)**, **tetroses (4C)**, **pentoses (5C)**, **hexoses (6C)** and **heptoses (7C)**. These terms along with functional groups are used while naming monosaccharides. For instance, **glucose is an aldohexose while fructose is a ketohexose (Table 2.1)**.

The common monosaccharides and disaccharides of biological importance are given in the **Table 2.2**.

### Oligosaccharides

Oligosaccharides (*Greek*: oligo-few) contain **2-10 monosaccharide** molecules which are

liberated on hydrolysis. Based on the number of monosaccharide units present, the oligosaccharides are further subdivided to **disaccharides**, **trisaccharides** etc.

### Polysaccharides

Polysaccharides (*Greek*: poly-many) are polymers of monosaccharide units with high molecular weight (up to a million). They are usually tasteless (non-sugars) and form colloids with water. The polysaccharides are of two types – **homopolysaccharides** and **heteropolysaccharides**.

## MONOSACCHARIDES— STRUCTURAL ASPECTS

**Stereoisomerism** is an important character of monosaccharides. Stereoisomers are the compounds that have the same structural formulae but differ in their spatial configuration.

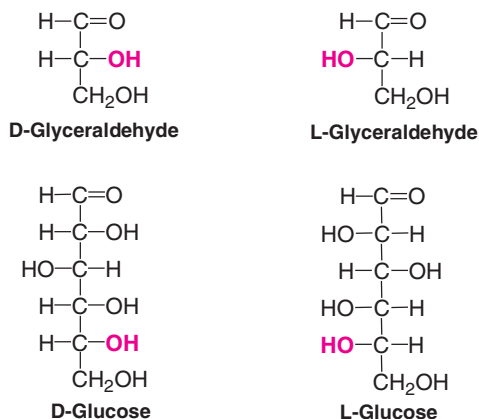
A carbon is said to be **asymmetric when** it is **attached to four different atoms or groups**. The number of asymmetric carbon atoms (n) determines the possible **isomers** of a given compound which is equal to **2<sup>n</sup>**. Glucose contains 4 asymmetric carbons, and thus has 16 isomers.

### Glyceraldehyde —the reference carbohydrate

Glyceraldehyde (triose) is the simplest monosaccharide with one asymmetric carbon atom. It exists as two stereoisomers and has been chosen as the reference carbohydrate to represent the structure of all other carbohydrates.

TABLE 2.2 Monosaccharides and disaccharides of biological importance

<i>Monosaccharides</i>	<i>Occurrence</i>	<i>Biochemical importance</i>
<b>Trioses</b>		
Glyceraldehyde	Found in cells as phosphate	Glyceraldehyde 3-phosphate is an intermediate in glycolysis
Dihydroxyacetone	Found in cells as phosphate	Its 1-phosphate is an intermediate in glycolysis
<b>Tetroses</b>		
D-Erythrose	Widespread	Its 4-phosphate is an intermediate in carbohydrate metabolism
<b>Pentoses</b>		
D-Ribose	Widespread as a constituent of RNA and nucleotides	For the structure of RNA and nucleotide coenzymes (ATP, NAD <sup>+</sup> , NADP <sup>+</sup> )
D-Deoxyribose	As a constituent of DNA	For the structure of DNA
D-Ribulose	Produced during metabolism	It is an important metabolite in hexose monophosphate shunt
D-Xylose	As a constituent of glycoproteins and gums	Involved in the function of glycoproteins
L-Xylulose	As an intermediate in uronic acid pathway	Excreted in urine in essential pentosuria
D-Lyxose	Heart muscle	As a constituent of lyxoflavin of heart muscle
<b>Hexoses</b>		
D-Glucose	As a constituent of polysaccharides (starch, glycogen, cellulose) and disaccharides (maltose, lactose, sucrose). Also found in fruits	The 'sugar fuel' of life; excreted in urine in diabetes. Structural unit of cellulose in plants
D-Galactose	As a constituent of lactose (milk sugar)	Converted to glucose, failure leads to galactosemia
D-Mannose	Found in plant polysaccharides and animal glycoproteins	For the structure of polysaccharides
D-Fructose	Fruits and honey, as a constituent of sucrose and inulin	Its phosphates are intermediates of glycolysis
<b>Heptoses</b>		
D-Sedoheptulose	Found in plants	Its 7-phosphate is an intermediate in hexose monophosphate shunt, and in photosynthesis
<i>Disaccharides</i>	<i>Occurrence</i>	<i>Biochemical importance</i>
Sucrose	As a constituent of cane sugar and beet sugar, pineapple	Most commonly used table sugar supplying calories
Lactose	Milk sugar	Exclusive carbohydrate source to breast fed infants. Lactase deficiency (lactose intolerance) leads to diarrhea and flatulence
Maltose	Product of starch hydrolysis, occurs in germinating seeds	An important intermediate in the digestion of starch



**Fig. 2.1 :** D-and-L- forms of glucose compared with D- and L- glyceraldehydes (the reference carbohydrate).

### D- and L-isomers

The D and L isomers are mirror images of each other. The spatial orientation of  $-\text{H}$  and  $-\text{OH}$  groups on the carbon atom ( $\text{C}_5$  for glucose) that is adjacent to the terminal primary alcohol carbon determines whether the sugar is D- or L-isomer. If the  $-\text{OH}$  group is on the right side, the sugar is of D-series, and if on the left side, it belongs to L-series. The structures of D- and L-glucose based on the **reference monosaccharide, D- and L-glyceraldehyde** (glycerose) are depicted in **Fig.2.1**.

It may be noted that the naturally occurring monosaccharides in the mammalian tissues are mostly of D-configuration. The enzyme machinery of cells is specific to metabolise D-series of monosaccharides.

### Optical activity of sugars

Optical activity is a characteristic feature of compounds with **asymmetric carbon** atom. When a beam of polarized light is passed through a solution of an optical isomer, it will be rotated either to the right or left. The term **dextrorotatory (d+)** and **levorotatory (l-)** are used to compounds that respectively rotate the plane of polarized light to the right or to the left.

An optical isomer may be designated as D(+), D(-), L(+) and L(-) based on its structural

relation with glyceraldehyde. It may be noted that the D- and L-configurations of sugars are primarily based on the structure of glyceraldehyde, the optical activities however, may be different.

**Racemic mixture :** If **d-** and **l-isomers** are present in **equal** concentration, it is known as racemic mixture or **dl mixture**. Racemic mixture **does not exhibit any optical activity**, since the dextro- and levorotatory activities cancel each other.

In the medical practice, the term **dextrose** is used for **glucose in solution**. This is because of the dextrorotatory nature of glucose.

### Configuration of D-aldoses

The configuration of possible D-aldoses starting from D-glyceraldehyde is depicted in **Fig.2.2**. This is a representation of **Killiani-Fischer synthesis**, by increasing the chain length of an aldose, by one carbon at a time. Thus, starting with an aldotriose (3C), aldotetroses (4C), aldopentoses (5C) and aldohexoses (6C) are formed. Of the 8 aldohexoses, glucose, mannose and galactose are the most familiar. Among these, D-glucose is the only aldose monosaccharide that predominantly occurs in nature.

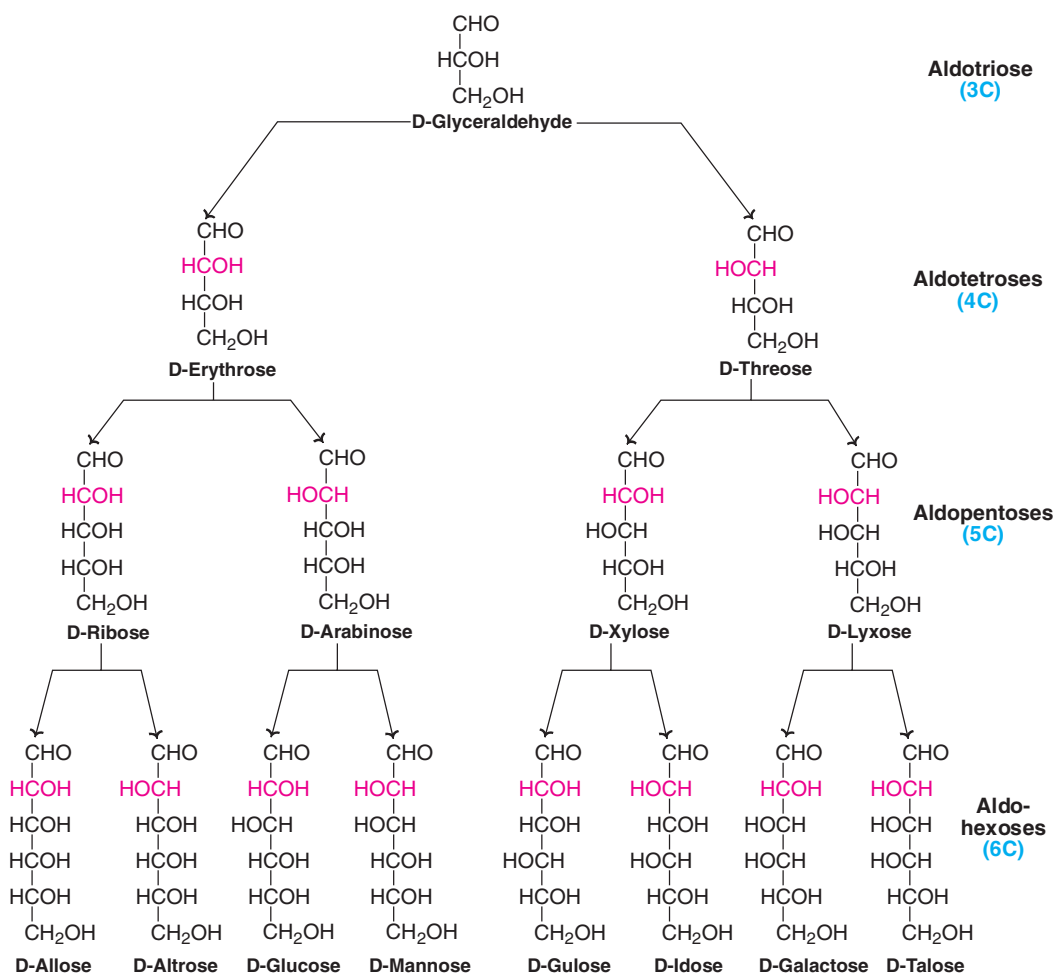
### Configuration of D-ketoses

Starting from dihydroxyacetone (triose), there are five keto-sugars which are physiologically important. Their structures are given in **Fig.2.3**.

### Epimers

If two monosaccharides **differ** from each other in their **configuration around a single specific carbon** (other than anomeric) atom, they are referred to as **epimers** to each other (**Fig.2.4**). For instance, **glucose and galactose are epimers** with regard to carbon 4 ( $\text{C}_4$ -epimers). That is, they differ in the arrangement of  $-\text{OH}$  group at  $\text{C}_4$ . Glucose and mannose are epimers with regard to carbon 2 ( $\text{C}_2$ -epimers).

The interconversion of epimers (e.g. glucose to galactose and vice versa) is known as



**Fig. 2.2 :** The structural relationship between D-aldoses shown in Fischer projection. (The configuration around C<sub>2</sub> (red) distinguishes the members of each pair).

epimerization, and a group of enzymes—namely—**epimerases** catalyse this reaction.

### Enantiomers

Enantiomers are a special type of stereoisomers that are **mirror images of each other**. The two members are designated as D- and L-sugars. Enantiomers of glucose are depicted in **Fig.2.5**.

Majority of the sugars in the higher animals (including man) are of D-type (**Fig.2.5**).

The term **diastereomers** is used to represent the **stereoisomers** that are **not mirror images of one another**.

### STRUCTURE OF GLUCOSE

For a better understanding of glucose structure, let us consider the formation of hemiacetals and hemiketals, respectively produced when an aldehyde or a ketone reacts with alcohol.

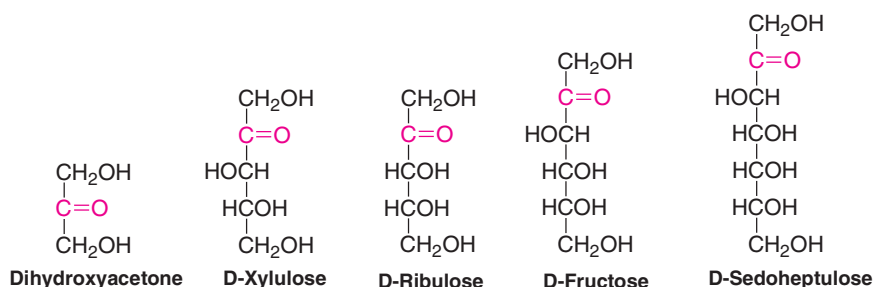
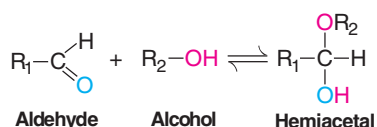


Fig. 2.3 : Structures of ketoses of physiological importance.



The hydroxyl group of monosaccharides can react with its own aldehyde or keto functional group to form hemiacetal and hemiketal. Thus, the aldehyde group of glucose at C<sub>1</sub> reacts with alcohol group at C<sub>5</sub> to form two types of cyclic hemiacetals namely  $\alpha$  and  $\beta$ , as depicted in Fig.2.6. The configuration of glucose is conveniently represented either by Fischer formulae or by Haworth projection formulae.

### Pyranose and furanose structures

Haworth projection formulae are depicted by a six-membered ring pyranose (based on pyran) or a five-membered ring furanose (based on furan). The cyclic forms of glucose are known as  $\alpha$ -D-glucopyranose and  $\alpha$ -D-glucofuranose (Fig.2.7).

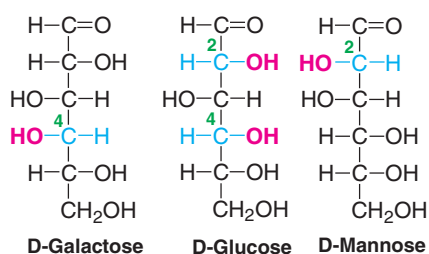


Fig. 2.4 : Structures of epimers (glucose and galactose are C<sub>4</sub>-epimers while glucose and mannose are C<sub>2</sub>-epimers).

### Anomers—mutarotation

The  $\alpha$  and  $\beta$  cyclic forms of D-glucose are known as *anomers*. They differ from each other in the configuration only around C<sub>1</sub> known as *anomeric carbon* (hemiacetal carbon). In case of  $\alpha$  anomer, the -OH group held by anomeric carbon is on the opposite side of the group -CH<sub>2</sub>OH of sugar ring. The reverse is true for  $\beta$ -anomer. The anomers differ in certain physical and chemical properties.

**Mutarotation :** The  $\alpha$  and  $\beta$  anomers of glucose have different optical rotations. The specific optical rotation of a freshly prepared glucose ( $\alpha$  anomer) solution in water is +112.2° which gradually changes and attains an equilibrium with a constant value of +52.7°. In the presence of alkali, the decrease in optical rotation is rapid. The optical rotation of  $\beta$ -glucose is +18.7°. **Mutarotation is defined as the change in the specific optical rotation representing the interconversion of  $\alpha$  and  $\beta$**

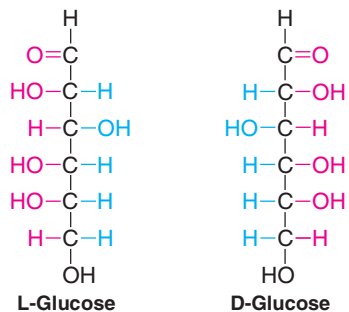
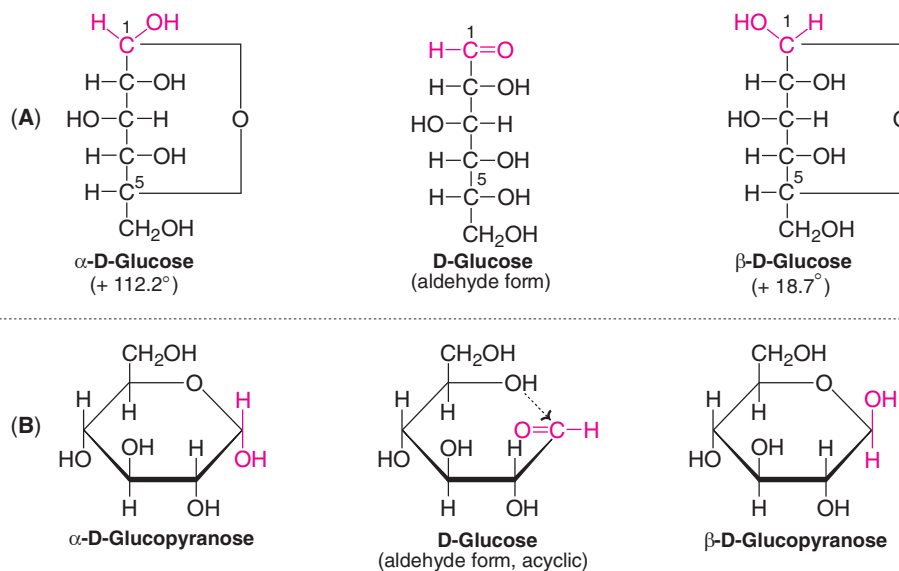
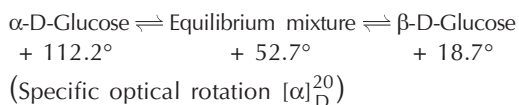


Fig. 2.5 : Enantiomers (mirror images) of glucose.



**Fig. 2.6 :** Mutarotation of glucose representing  $\alpha$  and  $\beta$  anomers (A) Fischer projections (B) Haworth projections.

**forms of D-glucose to an equilibrium mixture.** Mutarotation depicted in Fig. 2.6, is summarized below.

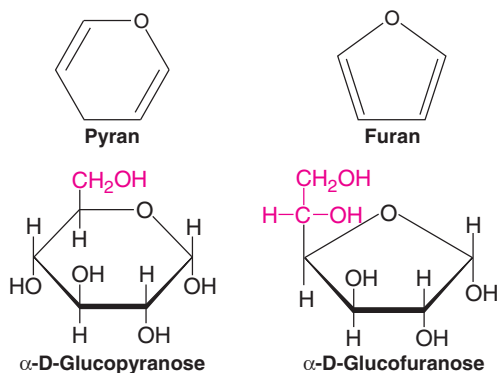


The equilibrium mixture contains 63%  $\beta$ -anomer and 36%  $\alpha$ -anomer of glucose with

1% open chain form. In aqueous solution, the  $\beta$  form is more predominant due to its stable conformation. The  $\alpha$  and  $\beta$  forms of glucose are interconvertible which occurs through a linear form. The latter, as such, is present in an insignificant quantity.

**Mutarotation of fructose :** Fructose also exhibits mutarotation. In case of fructose, the pyranose ring (six-membered) is converted to furanose (five-membered) ring, till an equilibrium is attained. And fructose has a specific optical rotation of  $-92^\circ$  at equilibrium.

The conversion of dextrorotatory (+) sucrose to levorotatory fructose is explained under inversion of sucrose (see later in this chapter).



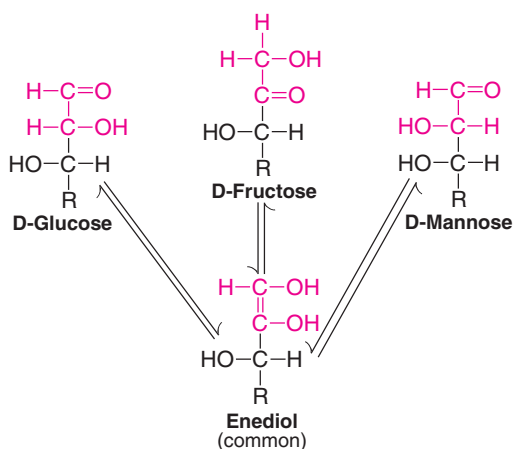
**Fig. 2.7 :** Structure of glucose-pyranose and furanose forms.

## REACTIONS OF MONOSACCHARIDES

### Tautomerization or enolization

The process of shifting a hydrogen atom from one carbon atom to another to produce **enediols** is known as **tautomerization**. Sugars possessing anomeric carbon atom undergo tautomerization in alkaline solutions.

When glucose is kept in alkaline solution for several hours, it undergoes isomerization to form



**Fig. 2.8 :** Formation of a common enediol from glucose, fructose and mannose (*R* corresponds to the end 3 carbon common structure).

D-fructose and D-mannose. This reaction—known as the **Lobry de Bruyn-von Ekenstein transformation**—results in the formation of a common intermediate—namely **enediol**—for all the three sugars, as depicted in **Fig.2.8**.

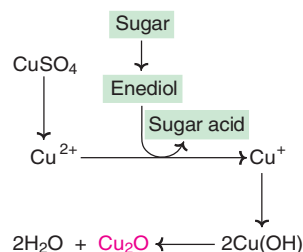
The enediols are highly reactive, hence sugars in alkaline solution are powerful reducing agents.

### Reducing properties

The sugars are classified as reducing or non-reducing. The reducing property is attributed to the **free aldehyde** or **keto group** of anomeric carbon.

In the laboratory, many tests are employed to identify the reducing action of sugars. These include **Benedict's test**, **Fehling's test**, **Barfoed's test** etc. The reduction is much more efficient in the alkaline medium than in the acid medium.

The **enediol forms** (explained above) or sugars reduce cupric ions ( $\text{Cu}^{2+}$ ) of copper sulphate to cuprous ions ( $\text{Cu}^+$ ), which form a yellow precipitate of cuprous hydroxide or a red precipitate of cuprous oxide as shown next.



It may be noted that the reducing property of sugars cannot help for a specific identification of any one sugar, since it is a general reaction.

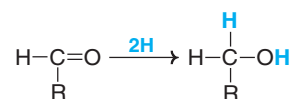
### Oxidation

Depending on the oxidizing agent used, the terminal aldehyde (or keto) or the terminal alcohol or both the groups may be oxidized. For instance, consider glucose :

1. Oxidation of aldehyde group ( $\text{CHO} \longrightarrow \text{COOH}$ ) results in the formation of gluconic acid.
2. Oxidation of terminal alcohol group ( $\text{CH}_2\text{OH} \longrightarrow \text{COOH}$ ) leads to the production of glucuronic acid.

### Reduction

When treated with reducing agents such as sodium amalgam, the aldehyde or keto group of monosaccharide is reduced to corresponding alcohol, as indicated by the general formula :



The important monosaccharides and their corresponding alcohols are given below.

D-Glucose	$\longrightarrow$	D-Sorbitol
D-Galactose	$\longrightarrow$	D-Dulcitol
D-Mannose	$\longrightarrow$	D-Mannitol
D-Fructose	$\longrightarrow$	D-Mannitol + D-Sorbitol
D-Ribose	$\longrightarrow$	D-Ribitol

**Sorbitol** and **dulcitol** when accumulate in tissues in large amounts cause strong osmotic effects leading to swelling of **cells**, and certain pathological conditions. e.g. **cataract**, peripheral neuropathy, nephropathy. Mannitol is useful to reduce intracranial tension by forced diuresis.



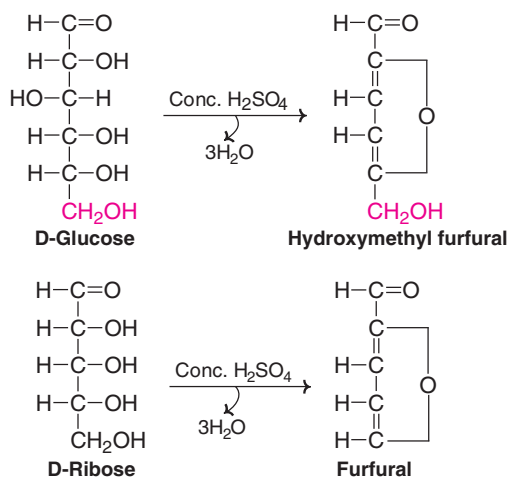


Fig. 2.9 : Dehydration of monosaccharides with concentrated H<sub>2</sub>SO<sub>4</sub>.

### Dehydration

When treated with concentrated sulfuric acid, monosaccharides undergo dehydration with an elimination of 3 water molecules. Thus hexoses give hydroxymethyl furfural while pentoses give furfural on dehydration (Fig.2.9). These **furfurals** can condense with phenolic compounds ( $\alpha$ -naphthol) to form coloured products. This is the chemical basis of the popular **Molisch test**. In case of oligo- and polysaccharides, they are first hydrolysed to monosaccharides by acid, and this is followed by dehydration.

**Bial's test** : Pentoses react with strong HCl to form furfural derivatives which in turn react with orcinol to form green coloured complex. Bial's test is useful for detection of xylose in urine in essential pentosuria.

**Mucic acid test** : Galactose when treated with nitric acid forms insoluble mucic acid crystals.

### Osazone formation

**Phenylhydrazine** in acetic acid, when boiled with reducing sugars, forms osazones in a reaction summarized in Fig.2.10.

As is evident from the reaction, the **first two carbons** (C<sub>1</sub> and C<sub>2</sub>) are **involved** in osazone formation. The sugars that differ in their

configuration on these two carbons give the same type of osazones, since the difference is masked by binding with phenylhydrazine. Thus **glucose, fructose** and mannose give the same type (**needle-shaped**) osazones.

Reducing disaccharides also give osazones—maltose sunflower-shaped, and lactose powder-puff shaped.

### Formation of esters

The alcoholic groups of monosaccharides may be esterified by non-enzymatic or enzymatic reactions. Esterification of carbohydrate with phosphoric acid is a common reaction in metabolism. Glucose 6-phosphate and glucose 1-phosphate are good examples. ATP donates the phosphate moiety in ester formation.

### GLYCOSIDES

Glycosides are formed when the hemiacetal or hemiketal hydroxyl group (of anomeric carbon) of a carbohydrate reacts with a hydroxyl group of another carbohydrate or a non-carbohydrate (e.g. methyl alcohol, phenol, glycerol). The bond so formed is known as **glycosidic bond** and the **non-carbohydrate moiety** (when present) is referred to as **aglycone**.

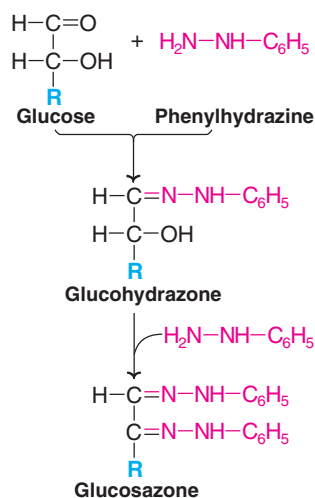


Fig. 2.10 : A summary of osazone formation (R represents C<sub>3</sub> to C<sub>6</sub> of glucose).

The monosaccharides are held together by glycosidic bonds to result in di-, oligo- or polysaccharides (see later for structures).

**Naming of glycosidic bond :** The nomenclature of glycosidic bonds is based on the linkages between the carbon atoms and the status of the anomeric carbon ( $\alpha$  or  $\beta$ ). For instance, lactose—which is formed by a bond between C<sub>1</sub> of  $\beta$ -galactose and C<sub>4</sub> of glucose—is named as  $\beta(1 \rightarrow 4)$  glycosidic bond. The other glycosidic bonds are described in the structure of di- and polysaccharides.

### Physiologically important glycosides

1. **Glucovanillin** (vanillin-D-glucoside) is a natural substance that imparts vanilla flavour.
2. **Cardiac glycosides** (steroidal glycosides) : Digoxin and digitoxin contain the aglycone steroid and they stimulate muscle contraction.
3. **Streptomycin**, an antibiotic used in the treatment of tuberculosis is a glycoside.
4. **Ouabain** inhibits Na<sup>+</sup> – K<sup>+</sup> ATPase and blocks the active transport of Na<sup>+</sup>.
5. **Phlorhizin** produces renal damage in experimental animals.

### DERIVATIVES OF MONOSACCHARIDES

There are several derivatives of monosaccharides, some of which are physiologically important (**Fig.2.11**)

1. **Sugar acids** : Oxidation of aldehyde or primary alcohol group in monosaccharide results in sugar acids. Gluconic acid is produced from glucose by oxidation of aldehyde (C<sub>1</sub> group) whereas glucuronic acid is formed when primary alcohol group (C<sub>6</sub>) is oxidized.
2. **Sugar alcohols** (polyols) : They are produced by reduction of aldoses or ketoses. For instance, sorbitol is formed from glucose and mannitol from mannose.
3. **Alditols** : The monosaccharides, on reduction, yield polyhydroxy alcohols, known as alditols. Ribitol is a constituent of flavin coenzymes; glycerol and *myo*-inositol are components of lipids. Xylitol is a sweetener used in sugarless gums and candies.
4. **Amino sugars** : When one or more hydroxyl groups of the monosaccharides are replaced by amino groups, the products

formed are amino sugars e.g. D-glucosamine, D-galactosamine. They are present as constituents of heteropolysaccharides.

N-Acetylneuraminic acid (NANA) is a derivative of N-acetylmannose and pyruvic acid. It is an important constituent of glycoproteins and glycolipids. The term **sialic acid** is used to include NANA and its other derivatives.

Certain antibiotics contain amino sugars which may be involved in the antibiotic activity e.g. erythromycin.

5. **Deoxysugars** : These are the sugars that contain **one oxygen less** than that present in the parent molecule. The groups –CHOH and –CH<sub>2</sub>OH become –CH<sub>2</sub> and –CH<sub>3</sub> due to the absence of oxygen. D-2-Deoxyribose is the most important deoxysugar since it is a structural constituent of DNA (in contrast to D-ribose in RNA). **Feulgen staining** can specifically detect deoxyribose, and thus DNA in tissues. Fucose is a deoxy L-galactose found in blood group antigens, and certain glycoproteins.

6. **L-Ascorbic acid** (vitamin C) : This is a water-soluble vitamin, the structure of which closely resembles that of a monosaccharide.

### DISACCHARIDES

Among the oligosaccharides, disaccharides are the most common (**Fig.2.12**). 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.

### Maltose

Maltose is composed of **two  $\alpha$ -D-glucose** units held together by  $\alpha(1 \rightarrow 4)$  glycosidic bond. The free aldehyde group present on C<sub>1</sub> of second glucose answers the reducing reactions, besides

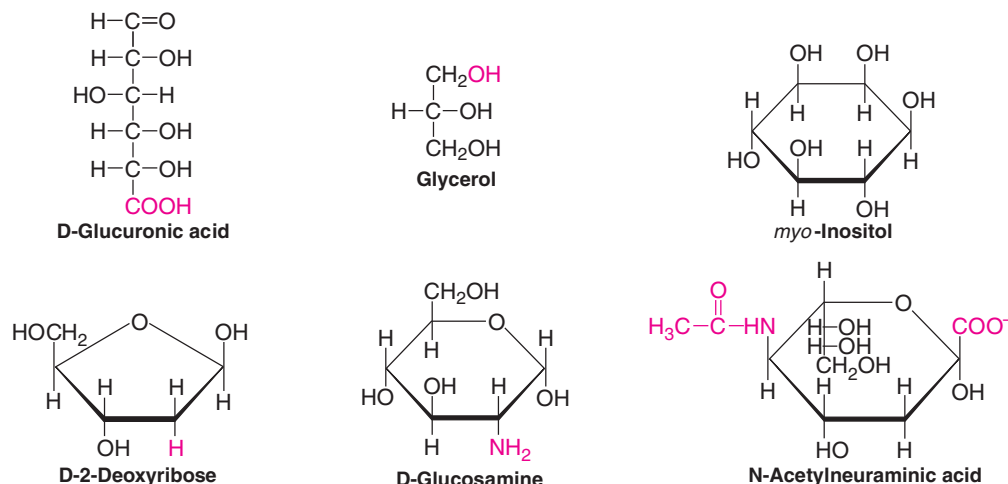


Fig. 2.11 : Structures of monosaccharide derivatives (selected examples).

the osazone formations (sunflower-shaped). Maltose can be hydrolysed by dilute acid or the enzyme maltase to liberate two molecules of  $\alpha$ -D-glucose.

In **isomaltose**, the glucose units are held together by  $\alpha$  (1  $\rightarrow$  6) glycosidic linkage.

**Cellobiose** is another disaccharide, identical in structure with maltose, except that the former has  $\beta$  (1  $\rightarrow$  4) glycosidic linkage. Cellobiose is formed during the hydrolysis of cellulose.

### Sucrose

Sucrose (**cane sugar**) is the sugar of commerce, mostly produced by sugar cane and sugar beets. Sucrose is made up of  **$\alpha$ -D-glucose and  $\beta$ -D-fructose**. The two monosaccharides are held together by a glycosidic bond ( $\alpha_1 \rightarrow \beta_2$ ), between C<sub>1</sub> of  $\alpha$ -glucose and C<sub>2</sub> of  $\beta$ -fructose. The reducing groups of glucose and fructose are involved in glycosidic bond, hence sucrose is a **non-reducing sugar, and it cannot form osazones**.

Sucrose is an important source of dietary carbohydrate. It is sweeter than most other common sugars (except fructose) namely glucose, lactose and maltose. Sucrose is employed as a sweetening agent in food industry. The intestinal enzyme—sucrase—hydrolyses sucrose to glucose and fructose which are absorbed.

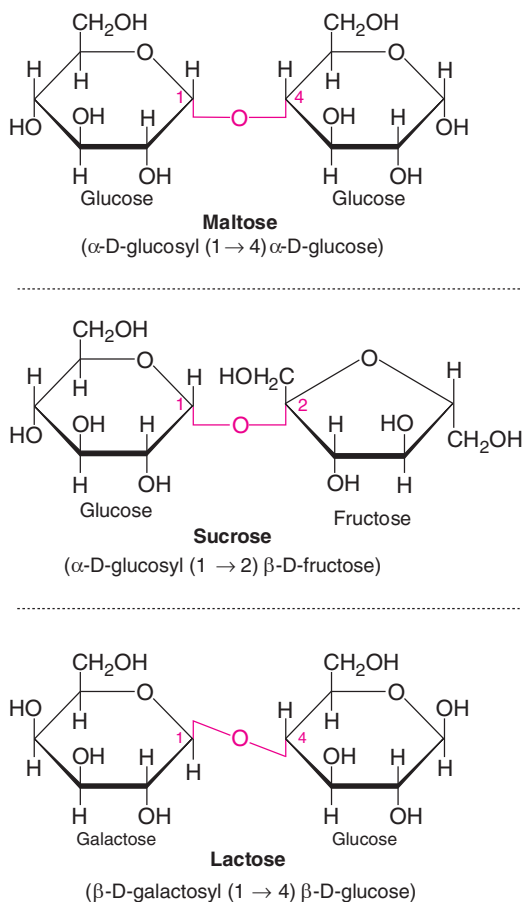
### Inversion of sucrose

Sucrose, as such is dextrorotatory (+66.5°). But, when hydrolysed, sucrose becomes levorotatory (−28.2°). 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**. The process of inversion is explained below.

Hydrolysis of sucrose by the enzyme **sucrase** (**invertase**) or dilute acid liberates one molecule each of glucose and fructose. It is postulated that sucrose (dextro) is first split into  $\alpha$ -D-glucopyranose (+52.5°) and  $\beta$ -D-fructofuranose, both being dextrorotatory. However,  $\beta$ -D-fructofuranose is less stable and immediately gets converted to  $\beta$ -D-fructopyranose which is strongly levorotatory (−92°). The overall effect is that dextro sucrose (+66.5°) on inversion is converted to levo form (−28.2°).

### Lactose

Lactose is more commonly known as **milk sugar** since it is the disaccharide found in milk. Lactose is composed of  **$\beta$ -D-galactose and  $\beta$ -D-glucose** held together by  $\beta$  (1  $\rightarrow$  4) glycosidic bond. The anomeric carbon of C<sub>1</sub> glucose is free, hence lactose exhibits reducing properties and forms osazones (powder-puff or hedgehog shape).



**Fig. 2.12 :** Structures of disaccharides  
—maltose, sucrose and lactose.

Lactose of milk is the most important carbohydrate in the nutrition of young mammals. It is hydrolysed by the intestinal enzyme lactase to glucose and galactose.

### Lactulose

Lactulose is a synthetic disaccharide containing **galactose** and **fructose**. It is neither digested nor absorbed in the intestine. Lactulose is useful for the treatment of **hepatic encephalopathy**, a disorder characterized by elevated plasma ammonium levels. Lactulose converts ammonia ( $\text{NH}_3$ ) in the lumen to ammonium ion ( $\text{NH}_4^+$ ). This results in a reduction in the plasma  $\text{NH}_3$ , since  $\text{NH}_4^+$  ions are not easily absorbed.

## POLYSACCHARIDES

Polysaccharides (or simply **glycans**) consist of repeat units of monosaccharides or their derivatives, held together by glycosidic bonds. They are primarily concerned with two important functions—structural, and storage of energy.

**Polysaccharides are linear as well as branched polymers.** This is in contrast to structure of proteins and nucleic acids which are only linear polymers. The occurrence of branches in polysaccharides is due to the fact that glycosidic linkages can be formed at any one of the hydroxyl groups of a monosaccharide.

Polysaccharides are of two types

1. **Homopolysaccharides** on hydrolysis yield only a **single type of monosaccharide**. They are named based on the nature of the monosaccharide. Thus, **glucans** are polymers of glucose whereas **fructosans** are polymers of fructose.

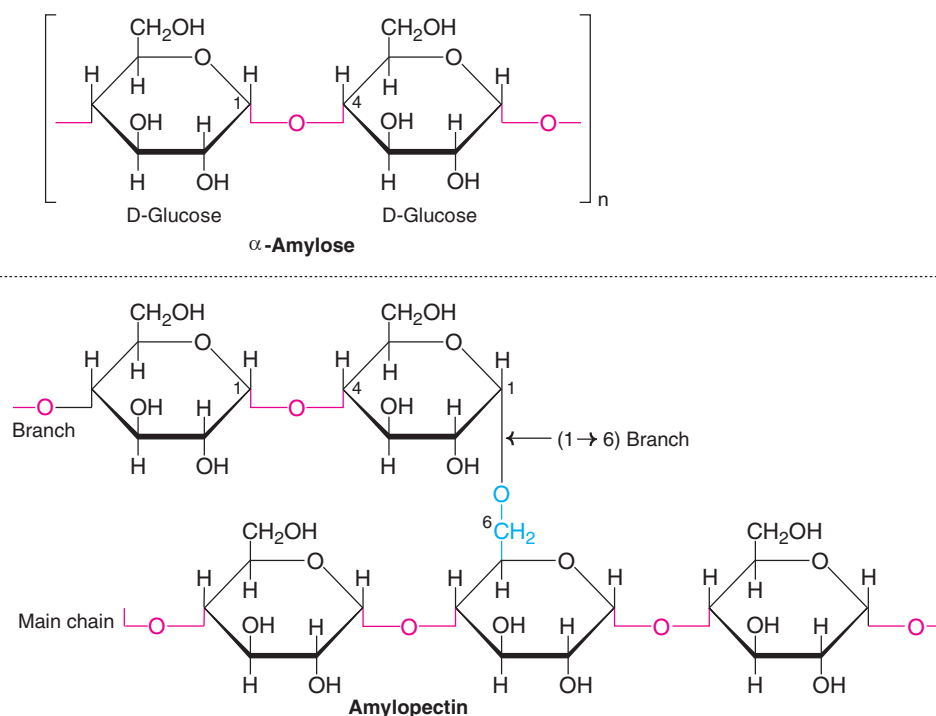
2. **Heteropolysaccharides** on hydrolysis yield a **mixture** of a few monosaccharides or their derivatives.

## HOMOPOLYSACCHARIDES

### Starch

Starch is the carbohydrate reserve of plants which is the most important dietary source for higher animals, including man. High content of starch is found in cereals, roots, tubers, vegetables etc. Starch is a homopolymer composed of D-glucose units held by  $\alpha$ -glycosidic bonds. It is known as **glucosan or glucan**.

Starch consists of two polysaccharide components—water soluble **amylose** (15-20%) and a water insoluble **amylopectin** (80-85%). Chemically, amylose is a long unbranched chain with 200–1,000 D-glucose units held by  $\alpha$  (1  $\rightarrow$  4) glycosidic linkages. Amylopectin, on the other hand, is a branched chain with  $\alpha$  (1  $\rightarrow$  6) glycosidic bonds at the branching points and  $\alpha$  (1  $\rightarrow$  4) linkages everywhere else (**Fig. 2.13**). Amylopectin molecule containing a few thousand glucose units looks like a branched tree (20–30 glucose units per branch).



**Fig. 2.13 :** Structure of starch ( $\alpha$ -amylose and amylopectin).

Starches are hydrolysed by **amylase** (pancreatic or salivary) to liberate dextrans, and finally maltose and glucose units. Amylase acts specifically on  $\alpha$  (1  $\rightarrow$  4) glycosidic bonds.

### Dextrans

Dextrans are the **breakdown products of starch** by the enzyme amylase or dilute acids. Starch is sequentially hydrolysed through different dextrans and, finally, to maltose and glucose. The various intermediates (identified by iodine colouration) are soluble starch (blue), **amyloextrin** (violet), **erythroextrin** (red) and **achroextrin** (no colour).

### Dextrans

Dextrans are polymers of glucose, produced by microorganisms. They are used as plasma volume expanders in transfusion, and chromatography (e.g. gel filtration).

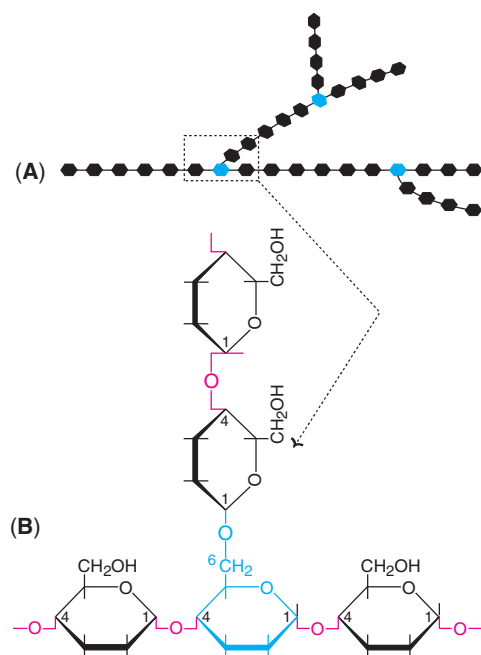
### Inulin

Inulin is a polymer of fructose i.e., **fructosan**. It occurs in dahlia bulbs, garlic, onion etc. It is a low molecular weight (around 5,000) poly-saccharide easily soluble in water. Inulin is not utilized by the body. It is used for assessing kidney function through measurement of **glomerular filtration rate (GFR)**.

### Glycogen

Glycogen is the carbohydrate reserve in animals, hence often referred to as **animal starch**. It is present in high concentration in liver, followed by muscle, brain etc. Glycogen is also found in plants that do not possess chlorophyll (e.g. yeast, fungi).

The structure of glycogen is similar to that of amylopectin with more number of branches. **Glucose** is the repeating unit in glycogen joined together by  $\alpha$  (1  $\rightarrow$  4) glycosidic bonds, and



**Fig. 2.14 :** Structure of glycogen (A) General structure (B) Enlarged at a branch point.

$\alpha(1 \rightarrow 6)$  glycosidic bonds at branching points (Fig.2.14). The molecular weight (up to  $1 \times 10^8$ ) and the number of glucose units (up to 25,000) vary in glycogen depending on the source from which glycogen is obtained.

### Cellulose

Cellulose occurs exclusively in plants and it is the most abundant organic substance in plant kingdom. It is a predominant constituent of plant cell wall. Cellulose is totally absent in animal body.

Cellulose is composed of  $\beta$ -D-glucose units linked by  $\beta(1 \rightarrow 4)$  glycosidic bonds (Fig.2.15). Cellulose cannot be digested by mammals—including man—due to lack of the enzyme that cleaves  $\beta$ -glycosidic bonds ( $\alpha$  amylase breaks  $\alpha$  bonds only). Certain ruminants and herbivorous animals contain microorganisms in the gut which produce enzymes that can cleave  $\beta$ -glycosidic bonds. Hydrolysis of cellulose yields a disaccharide **cellobiose**, followed by  $\beta$ -D-glucose.

Cellulose, though not digested, has great importance in human nutrition. It is a major constituent of **fiber**, the non-digestible carbohydrate. The functions of dietary fiber include decreasing the absorption of glucose and cholesterol from the intestine, besides increasing the bulk of feces. (For details, Chapter 23)

### Chitin

Chitin is composed of N-acetyl D-glucosamine units held together by  $\beta(1 \rightarrow 4)$  glycosidic bonds. It is a structural polysaccharide found in the exoskeleton of some invertebrates e.g. insects, crustaceans.

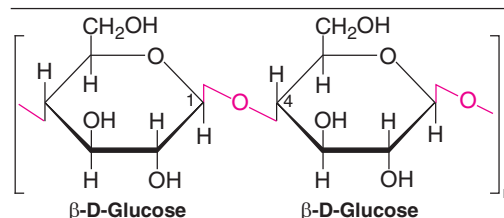
## HETEROPOLYSACCHARIDES

When the polysaccharides are composed of different types of sugars or their derivatives, they are referred to as heteropolysaccharides or **heteroglycans**.

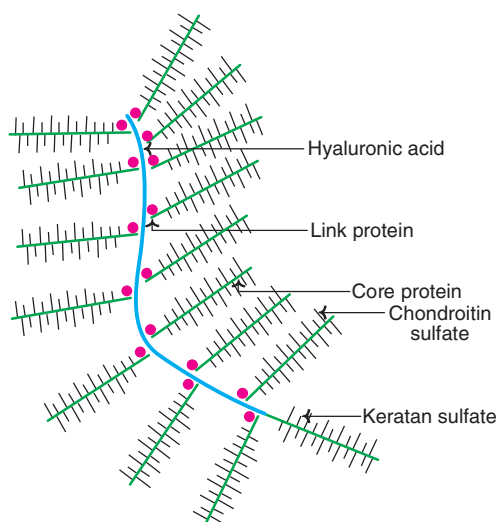
## MUCOPOLYSACCHARIDES

Mucopolysaccharides are heteroglycans made up of repeating units of sugar derivatives, namely amino sugars and uronic acids. These are more commonly known as **glycosaminoglycans (GAG)**. Acetylated amino groups, besides sulfate and carboxyl groups are generally present in GAG structure. The presence of sulfate and carboxyl groups contributes to acidity of the molecules, making them **acid mucopolysaccharides**.

Some of the mucopolysaccharides are found in combination with proteins to form **mucoproteins** or **mucoïds** or **proteoglycans** (Fig.2.16). Mucoproteins may contain up to 95% carbohydrate and 5% protein.



**Fig. 2.15 :** Structure of cellulose (The repeating unit 'n' may be several thousands).



**Fig. 2.16 :** Diagrammatic representation of a proteoglycan complex.

Mucopolysaccharides are essential components of tissue structure. The extracellular spaces of tissue (particularly connective tissue-cartilage, skin, blood vessels, tendons) consist of collagen and elastin fibers embedded in a matrix or ground substance. The ground substance is predominantly composed of GAG.

The important mucopolysaccharides include hyaluronic acid, chondroitin 4-sulfate, heparin, dermatan sulfate and keratan sulfate (**Fig.2.17**).

### Hyaluronic acid

Hyaluronic acid is an important GAG found in the ground substance of synovial fluid of joints and vitreous humor of eyes. It is also present as a ground substance in connective tissues, and forms a gel around the ovum. Hyaluronic acid serves as a **lubricant and shock absorbant in joints**.

## BIOMEDICAL / CLINICAL CONCEPTS



- ☞ Glucose is the most important energy source of carbohydrates to the mammals (except ruminants). The bulk of dietary carbohydrate (starch) is digested and finally absorbed as glucose into the body.
- ☞ Dextrose (glucose in solution in dextrorotatory form) is frequently used in medical practice.
- ☞ Fructose is abundantly found in the semen which is utilized by the sperms for energy.
- ☞ Several diseases are associated with carbohydrates e.g., diabetes mellitus, glycogen storage diseases, galactosemia.
- ☞ Accumulation of sorbitol and dulcitol in the tissues may cause certain pathological conditions e.g. cataract, nephropathy.
- ☞ Inulin, a polymer of fructose, is used to assess renal function by measuring glomerular filtration rate (GFR).
- ☞ The non-digestible carbohydrate cellulose plays a significant role in human nutrition. These include decreasing the intestinal absorption of glucose and cholesterol, and increasing bulk of feces to avoid constipation.
- ☞ The mucopolysaccharide hyaluronic acid serves as a lubricant and shock absorbant in joints.
- ☞ The enzyme hyaluronidase of semen degrades the gel (contains hyaluronic acid) around the ovum. This allows effective penetration of sperm into the ovum.
- ☞ The mucopolysaccharide heparin is an anticoagulant (prevents blood clotting).
- ☞ The survival of Antarctic fish below  $-2^{\circ}\text{C}$  is attributed to the antifreeze glycoproteins.
- ☞ Streptomycin is a glycoside employed in the treatment of tuberculosis.

Hyaluronic acid is composed of alternate units of D-glucuronic acid and N-acetyl D-glucosamine. These two molecules form disaccharide units held together by  $\beta$  (1  $\rightarrow$  3) glycosidic bond (**Fig.2.16**). Hyaluronic acid contains about 250–25,000 disaccharide units (held by  $\beta$  1  $\rightarrow$  4 bonds) with a molecular weight up to 4 million.

**Hyaluronidase** is an enzyme that breaks ( $\beta$  1  $\rightarrow$  4 linkages) hyaluronic acid and other GAG. This enzyme is present in high concentration in testes, seminal fluid, and in certain snake and insect venoms. Hyaluronidase of semen is assigned an important role in fertilization as this enzyme clears the gel (hyaluronic acid) around the ovum allowing a better penetration of sperm into the ovum. Hyaluronidase of bacteria helps their invasion into the animal tissues.

### Chondroitin sulfates

**Chondroitin 4-sulfate** (*Greek*: chondros-cartilage) is a major constituent of various mammalian tissues (bone, cartilage, tendons, heart, valves, skin, cornea etc.). Structurally, it is comparable with hyaluronic acid. Chondroitin 4-sulfate consists of repeating disaccharide units composed of D-glucuronic acid and N-acetyl D-galactosamine 4-sulfate (**Fig.2.17**).

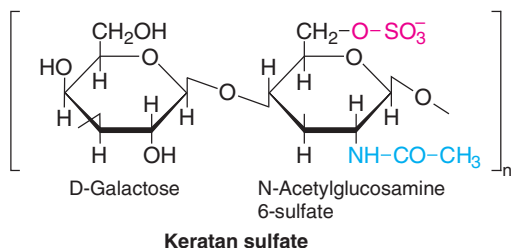
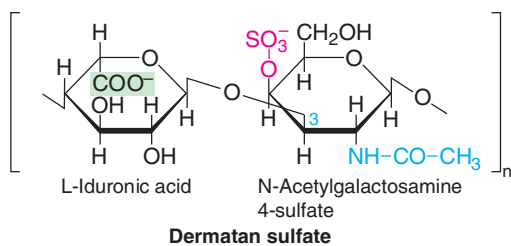
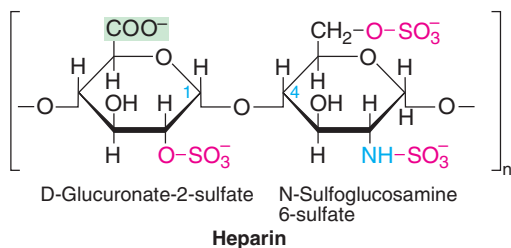
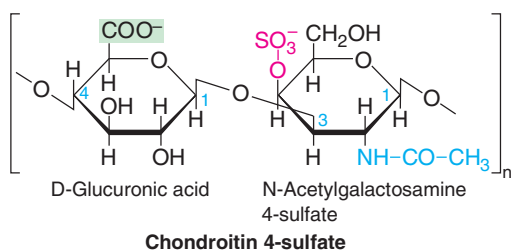
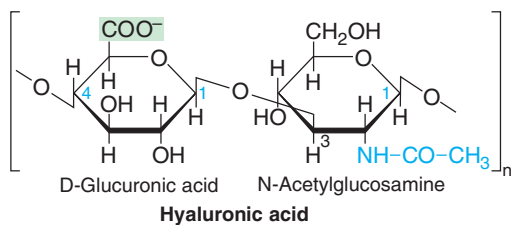
### Heparin

Heparin is **an anticoagulant** (prevents blood clotting) that occurs in blood, lung, liver, kidney, spleen etc. Heparin helps in the release of the enzyme lipoprotein lipase which helps in clearing the turbidity of lipemic plasma.

Heparin is composed of alternating units of N-sulfo D-glucosamine 6-sulfate and glucuronate 2-sulfate (**Fig.2.17**).

### Dermatan sulfate

Mostly found in skin, dermatan sulfate is structurally related to chondroitin 4-sulfate. The only difference is that there is an inversion in the configuration around  $C_5$  of D-glucuronic acid to form L-iduronic acid (**Fig.2.17**).



**Fig. 2.17** : Structures of common glycosaminoglycans – the disaccharides as repeating units.



TABLE 2.3 A summary of glycosaminoglycans – composition, distribution and functions

<i>Glycosaminoglycan</i>	<i>Composition</i>	<i>Tissue distribution</i>	<i>Function(s)</i>
Hyaluronic acid	D-Glucuronic acid, N-acetylglucosamine	Connective tissue, synovial fluid, vitreous humor	Serves as a lubricant, and shock absorber. Promotes wound healing
Chondroitin sulfate	D-Glucuronic acid, N-acetylgalactosamine 4-sulfate	Cartilage, bone, skin, blood vessel walls	Helps to maintain the structure and shapes of tissues
Heparin	D-Glucuronate 2-sulfate, N-sulfoglucosamine 6-sulfate	Blood, lung, liver, kidney, spleen	Acts as an anticoagulant
Dermatan sulfate	L-Iduronic acid, N-acetyl-galactosamine 4-sulfate	Blood vessel valves, heart valves, skin	Maintains the shapes of tissues
Keratan sulfate	D-Galactose, N-acetyl-glucosamine 6-sulfate	Cartilage, cornea, connective tissues	Keeps cornea transparent

### Keratan sulfate

It is a heterogeneous GAG with a variable sulfate content, besides small amounts of mannose, fructose, sialic acid etc. Keratan sulfate essentially consists of alternating units of D-galactosamine and N-acetylglucosamine 6-sulfate.

### AGAR AND PECTINS

**Agar**, mostly found in sea weeds, is a polymer of galactose sulfate and glucose. Since agar is not digested, it serves as a dietary fiber (**Refer Chapter 23**). **Agarose** (with galactose and anhydrogalactose) is useful in the laboratory as a major component of microbial culture media, and in electrophoresis.

**Pectins**, found in apples and citrus fruits, contain galactouronate and rhamnose. Pectins, being non-digestible, are useful as dietary fiber. They are also employed in the preparation of jellies.

### GLYCOPROTEINS

Several proteins are covalently bound to carbohydrates which are referred to as glycoproteins. The carbohydrate content of glycoprotein varies from 1% to 90% by weight.

Sometimes the term **mucoprotein** is used for glycoprotein with carbohydrate concentration more than 4%. Glycoproteins are very widely distributed in the cells and perform variety of functions. These include their role as enzymes, hormones, transport proteins, structural proteins and receptors. A selected list of glycoproteins and their major functions is given in **Table 2.4**.

The carbohydrates found in glycoproteins include mannose, galactose, N-acetylglucosamine, N-acetylgalactosamine, xylose,

TABLE 2.4 A selected list of glycoproteins and their major functions

<i>Glycoprotein(s)</i>	<i>Major function(s)</i>
Collagen	Structure
Hydrolases, proteases, glycosidases	Enzymes
Ceruloplasmin	Transport
Immunoglobulins	Defense against infection
Synovial glycoproteins	Lubrication
Thyrotropin, erythropoietin	Hormones
Blood group substances	Antigens
Fibronectin, laminin	Cell-cell recognition and adhesion
Intrinsic factor	Absorption of vitamin B <sub>12</sub>
Fibrinogen	Blood clotting

L-fucose and N-acetylneuraminic acid (NANA). NANA is an important sialic acid (See Fig.2.11).

**Antifreeze glycoproteins :** The Antarctic fish live below  $-2^{\circ}\text{C}$ , a temperature at which the blood would freeze. It is now known that these fish contain **antifreeze glycoprotein** which lower the freezing point of water and interfere with the crystal formation of ice. Antifreeze glycoproteins consist of 50 repeating units of the tripeptide, **alanine-alanine-threonine**. Each threonine

residue is bound to  $\beta$ -galactosyl (1  $\rightarrow$  3)  $\alpha$  N-acetylgalactosamine.

### Blood group substances

The blood group **antigens** (of erythrocyte membrane) contain carbohydrates as glycoproteins or glycolipids. N-Acetylgalactosamine, galactose, fucose, sialic acid etc. are found in the blood group substances. The carbohydrate content also plays a determinant role in blood grouping.

## SUMMARY



1. Carbohydrates are the polyhydroxyaldehydes or ketones, or compounds which produce them on hydrolysis. The term sugar is applied to carbohydrates soluble in water and sweet to taste. Carbohydrates are the major dietary energy sources, besides their involvement in cell structure and various other functions.
2. Carbohydrates are broadly classified into 3 groups—monosaccharides, oligosaccharides and polysaccharides. The monosaccharides are further divided into different categories based on the presence of functional groups (aldoses or ketoses) and the number of carbon atoms (trioses, tetroses, pentoses, hexoses and heptoses).
3. Glyceraldehyde (triose) is the simplest carbohydrate and is chosen as a reference to write the configuration of all other monosaccharides (D- and L- forms). If two monosaccharides differ in their structure around a single carbon atom, they are known as epimers. Glucose and galactose are  $C_4$ -epimers.
4. D-Glucose is the most important naturally occurring aldose/monosaccharide. Glucose exists as  $\alpha$  and  $\beta$  anomers with different optical rotations. The interconversion of  $\alpha$  and  $\beta$  anomeric forms with change in the optical rotation is known as mutarotation.
5. Monosaccharides participate in several reactions. These include oxidation, reduction, dehydration, osazone formation etc. Formation of esters and glycosides by monosaccharides is of special significance in biochemical reactions.
6. Among the oligosaccharides, disaccharides are the most common. These include the reducing disaccharides namely lactose (milk sugar) and maltose (malt sugar) and the non-reducing sucrose (cane sugar).
7. Polysaccharides are the polymers of monosaccharides or their derivatives, held together by glycosidic bonds. Homopolysaccharides are composed of a single monosaccharide (e.g., starch, glycogen, cellulose, inulin). Heteropolysaccharides contain a mixture of few monosaccharides or their derivatives (e.g., mucopolysaccharides).
8. Starch and glycogen are the carbohydrate reserves of plants and animals respectively. Cellulose, exclusively found in plants, is the structural constituent. Inulin is utilized to assess kidney function by measuring glomerular filtration rate (GFR).
9. Mucopolysaccharides (glycosaminoglycans) are the essential components of tissue structure. They provide the matrix or ground substance of extracellular tissue spaces in which collagen and elastin fibers are embedded. Hyaluronic acid, chondroitin 4-sulfate, heparin, are among the important glycosaminoglycans.
10. Glycoproteins are a group of biochemically important compounds with a variable composition of carbohydrate (1-90%), covalently bound to protein. Several enzymes, hormones, structural proteins and cellular receptors are in fact glycoproteins.