Badji Mokhtar University of Annaba
Faculty of Medicine
1st year of Medicine.
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MODULE: BIOCHEMISTRY

CHAPTRE 1: Carbohydrates

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I- Introduction

- Carbohydrates are the most abundant organic molecules in nature and represent the primary source of energy for living organisms.

- Carbohydrates may be defined as polyhydroxy-aldehydes or ketones or compounds which produce them on hydrolysis.

- The term ***"sugar"*** is applied to carbohydrates soluble in water and sweet to taste.

- The empirical formula of many carbohydrates can be expressed as $(CH_2O)n$, hence the term **" hydrates of carbon".**

- Further, some of the genuine carbohydrates (e.g. deoxyribose, $C_5H_{10}O_4$) do not satisfy the general formula. Hence carbohydrates cannot be always considered as hydrates of carbon.

II- Biological Roles of Carbohydrates

Carbohydrates are indispensable to life. The major functions can be summarized as follows:

- **Source of energy:** Glucose is the principal fuel of the body, particularly for the brain and red blood cells. Each gram of carbohydrate provides approximately 4 kcal of energy.

- **Storage form of energy:** Carbohydrates are stored as glycogen in animals (mainly in the liver and muscles) and as starch in plants.
These reserves can be mobilized rapidly to meet energy demands during fasting or intense activity.

- **Structural role** In plants, cellulose (a linear polymer of β-D-glucose) provides rigidity to cell walls.

• In animals, structural carbohydrates include glycosaminoglycans (e.g., hyaluronic acid, chondroitin sulfate), which contribute to the extracellular matrix and connective tissue.

• Chitin, a polymer of N-acetylglucosamine, is an essential structural component of the **exoskeleton** of **insects** and **crustaceans**.

II- Biological Roles of Carbohydrates

➢ **Components of nucleic acids** Ribose and deoxyribose, both pentoses, are integral to the structure of RNA and DNA, respectively. Without these sugars, genetic material and information storage would not be possible.

➢ **Cell-cell recognition and communication** Carbohydrates attached to proteins and lipids (glycoproteins and glycolipids) are located on the outer surface of cell membranes. These glycoconjugates play critical roles in intercellular recognition, immune response, and receptor-ligand interactions.
Blood group antigens (ABO system) are determined by specific carbohydrate structures present on the surface of red blood cells.

➢ **Protective and lubricating functions** Mucopolysaccharides (glycosaminoglycans) are components of mucus and synovial fluid, providing lubrication and protection in tissues and joints.

Note: ***Clinical relevance Abnormalities*** *in carbohydrate metabolism or structure are associated with several diseases. Examples include diabetes mellitus (altered glucose homeostasis), lactose intolerance (enzyme deficiency), and glycogen storage disorders.*

III- Classification of Carbohydrates

Carbohydrates

1- Holosides (only sugars)

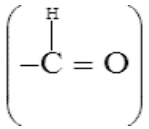
2- Heterosides (Glycosides) Sugars + Non-Sugar (Aglycone)

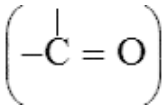
e.g. Nucleosides (Ribose + Base)
Cardiac glycosides (Digitoxin, Ouabain)
Saponins, Flavonoids

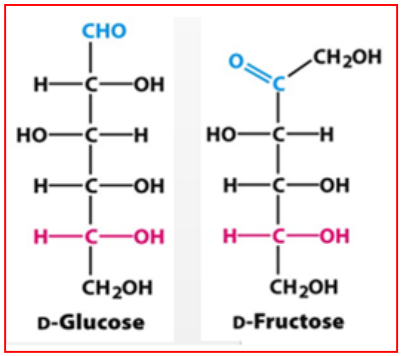
Monosaccharides

(Greek : mono-one)

Aldoses ***Ketoses***







Oligosaccharides

(Greek: oligo-few)

(2- 10 units)

Disacharides: (Lactose, maltose, sucrose...)
Others: (Raffinose, stachyoses...)

Polysaccharides

(Greek: poly-many)
(> 10 units)
(High molecular weight)

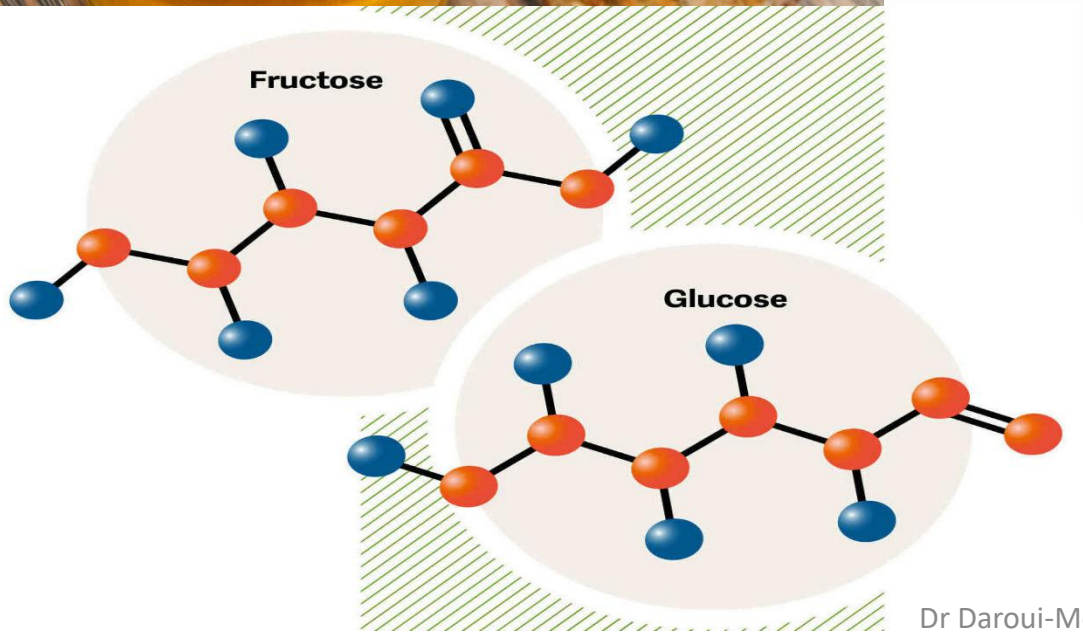
Heteropolysaccharides.

Mixture of few monosaccharides or their derivatives (mucopolysaccharides: Hyaloronic acide, hyparin...).

Homopolysaccharides

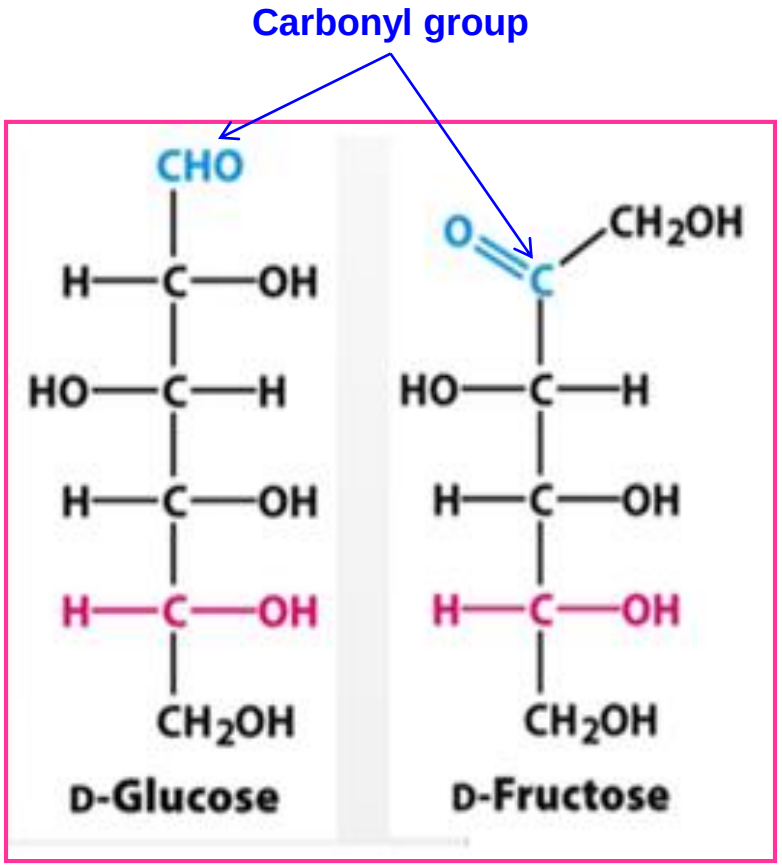
(Single monosaccharide: e.g.: Glucose)
(starch, glycogen, cellulose, chitin, inulin)

IV- Monosaccharides



IV- Monosaccharides

- Monosaccharides are the simplest form of carbohydrates, consisting of a single polyhydroxy aldehyde or ketone unit.
- They represent the fundamental building blocks of all other classes of carbohydrates.
- They are colorless, crystalline, water-soluble, and sweet-tasting (commonly known as simple sugars).
- They cannot be hydrolyzed into simpler carbohydrates.
- They generally conform to the formula $(CH_2O)n$, where n = 3–7.



Glucose** is an **aldohexose** while **fructose** is a **ketohexose

CH2OH: Primary alcohol function
CHOH: Secondary alcohol function

Classification of monosaccharides with selected examples

- When the **functional group** in monosaccharides is an aldehyde , they are known as aldoses.
- When the functional group is a keto group, they are referred to as Ketoses.
- Based on the **number of carbon atoms**, the monosaccharides are regarded *as trioses (3C), tetroses (4C), pentoses (5C), hexoses (6C) and heptoses (7C).*

Monosaccharides (empirical formula)	**Aldoses**	**Ketoses**
Trioses ($C_3H_6O_3$)	Glyceraldehyde	Dihydroxyacetone
Tetroses ($C_4H_8O_4$)	Erythrose	Erythrulose
Pentoses ($C_5H_{10}O_5$)	Ribose	Ribulose
Hexoses ($C_6H_{12}O_6$)	Glucose	Fructose
Heptoses ($C_7H_{14}O_7$)	Glucoheptose	Sedoheptulose

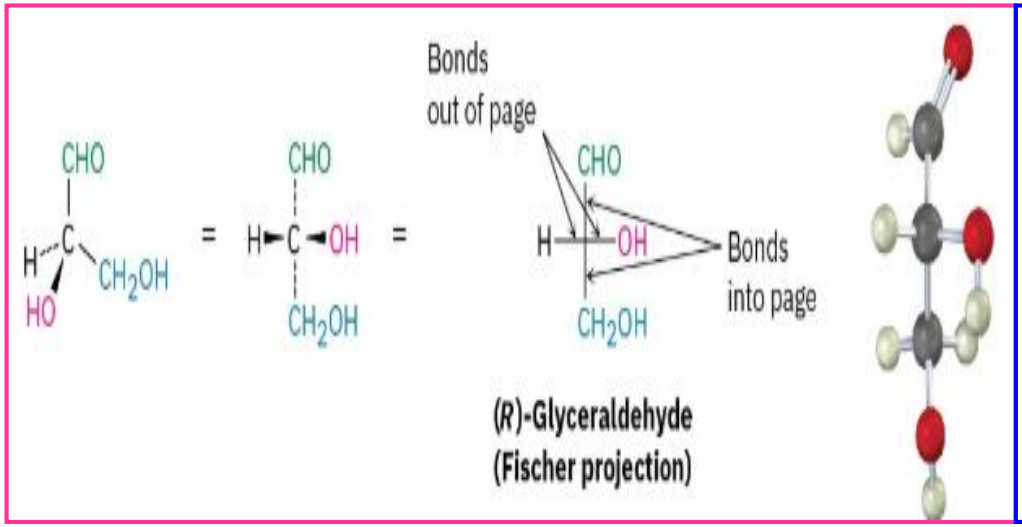
Structural Representation

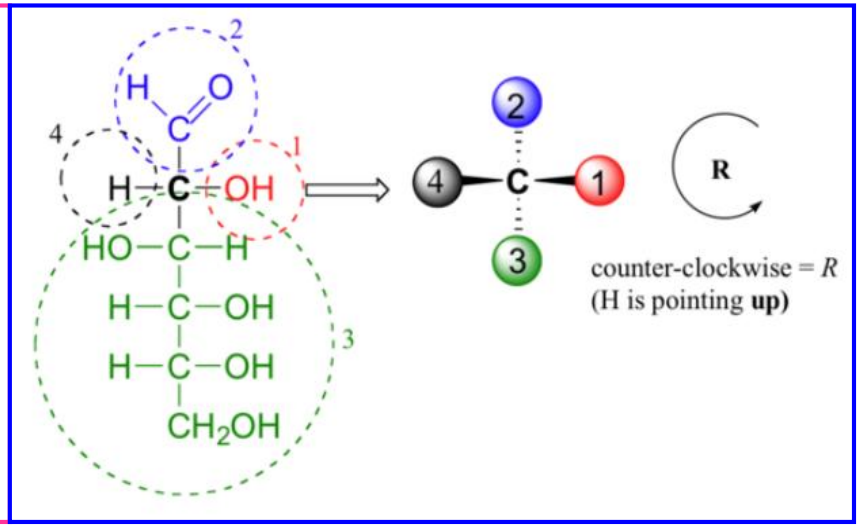
Fischer Projection

- The most oxidized group (aldehyde or ketone) is placed at the **top**.

Example: **D-Glyceraldehyde** and **D-Glucose.**

- A two-dimensional representation showing the arrangement of hydroxyl groups (-OH) around each carbon atom.





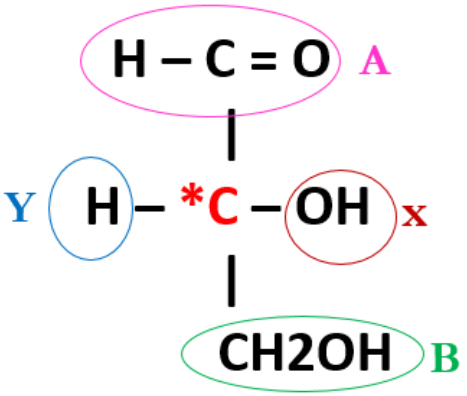
- **Fischer projections** are useful when looking at many different diastereomeric sugar structures, because the **eye** can quickly pick out stereochemical differences according to whether a **hydroxyl group** is on the **left** or **right** side of the structure.

Stereoisomerism – Chirality

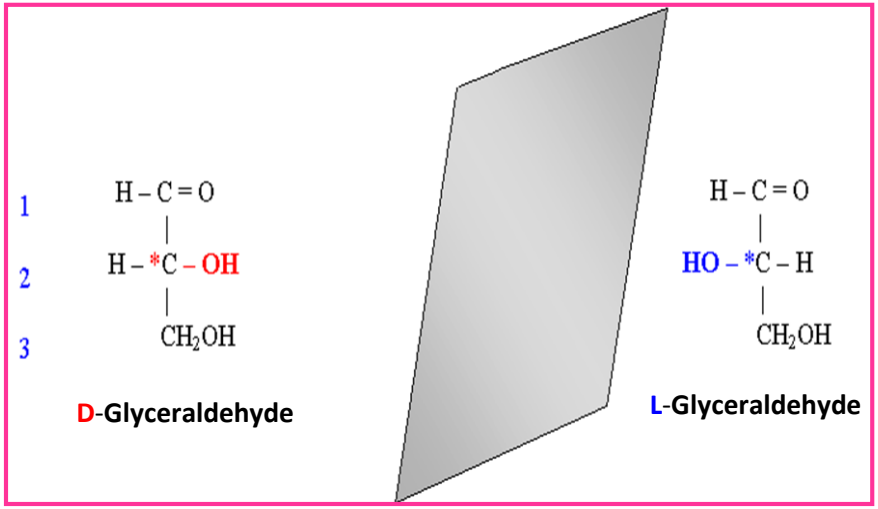
- ***Stereoisomerism is an important character of monosaccharides.***

- *Stereoisomers:* are the compounds that have the same structural formulae but differ in their spatial configuration.

A carbon is said to be ***asymmetric*** **(C*)** *when it is attached to four different atoms or groups* (**A , B, X, Y**).

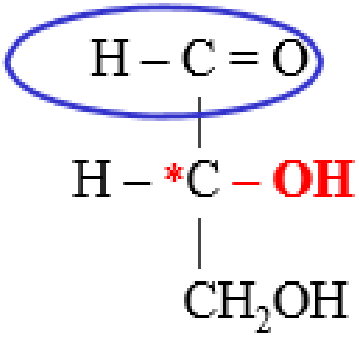


D-Glyceraldehyde

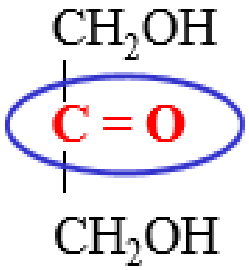


- It exists as two stereoisomers (**D-Glyceraldehyde and L-Glyceraldehyde)** and has been chosen as the reference Carbohydrate to represent the structure of all other carbohydrates.

Stereoisomerism – Chirality

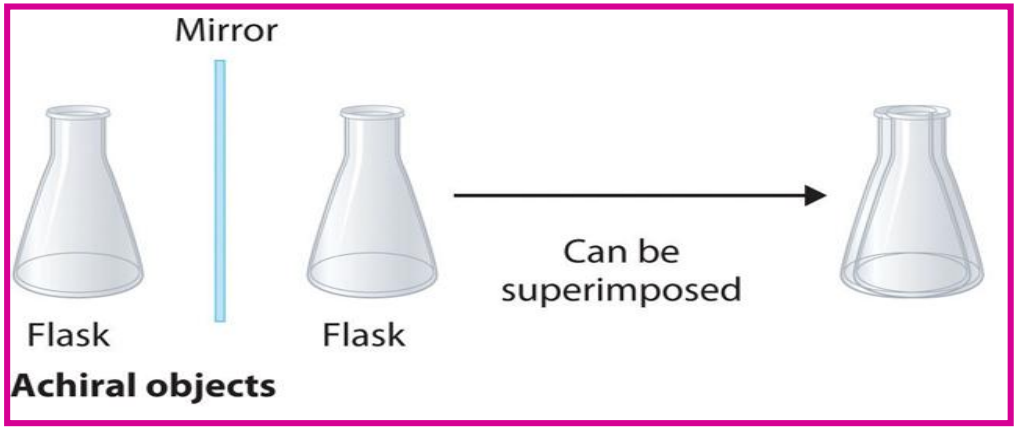


D-Glyceraldehyde



Dihydroxyacetone

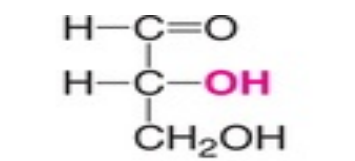
Dihydroxyacetone (Ketose) is an achiral molecule, it has no asymmetric carbon atom.



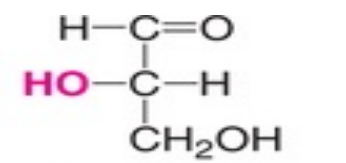
Stereoisomerism – Chirality

D- and L- isomers

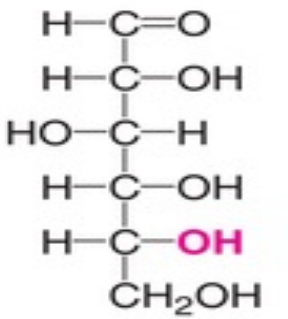
➢ The structures of D-and L-glucose based on the ***reference monosaccharide, D- and L-glyceraldehyde (glycerose).***



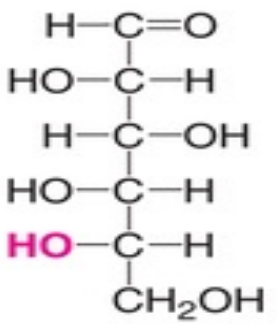
D-Glyceraldehyde



L-Glyceraldehyde



D-Glucose



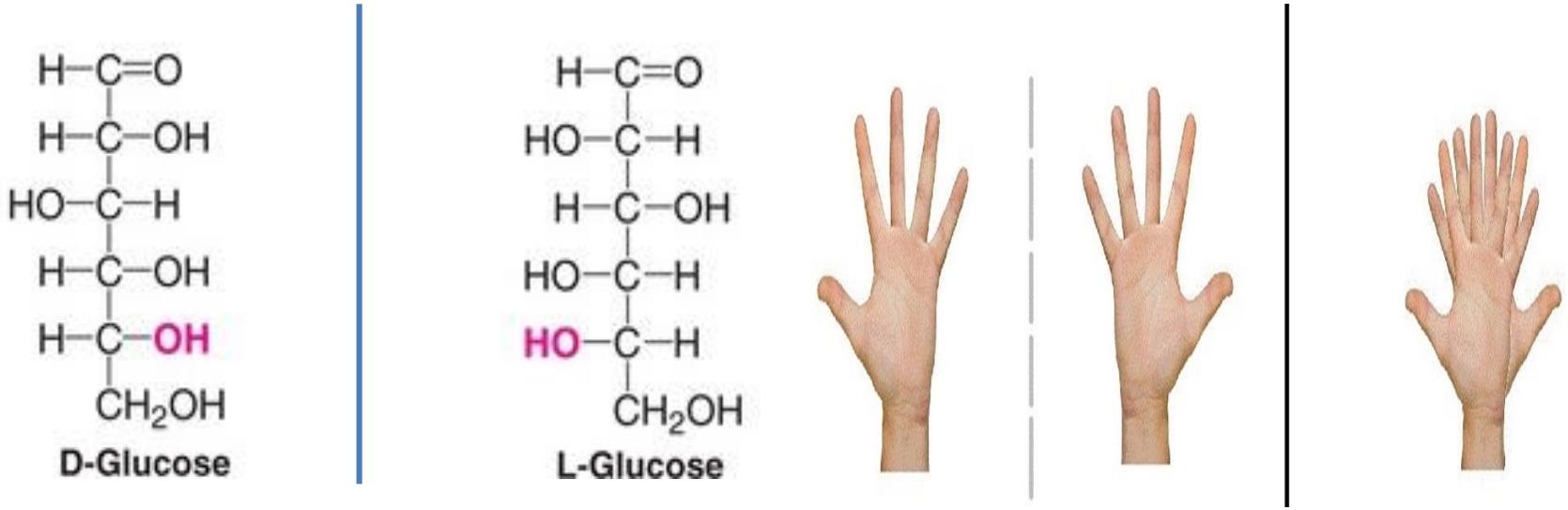
L-Glucose

➢ The spatial orientation of **-H and -OH groups** on the carbon atom (C5 for glucose) that is **adjacent** to the terminal primary alcohol carbon determines whether the sugar is **D- or L-isomer.**

➢ If the -OH group is on the **right** side, the sugar is of **D-series**, and if on the **left** side, it belongs to **L-series.**

Stereoisomerism – Chirality

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



Mirror images = chiral molecules, stereoisomers (enantiomers)

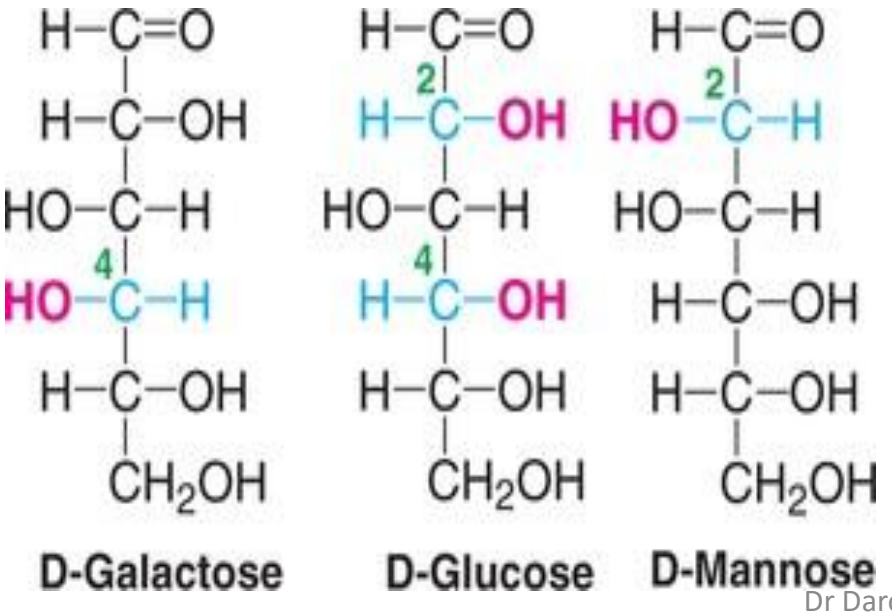
Note : *Majority of the sugars in the higher animals (including man) are of D-configuration. The enzyme machinery of cells is specific to metabolise D-series of monosaccharides.*

Stereoisomerism – Chirality

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**.**

➢ **For instance, glucose and galactose** are (C4 epimers). That is, they differ in the arrangement of-OH group at C4.
Glucose and **mannose** are epimers with regard to carbon 2 (C2 epimers).

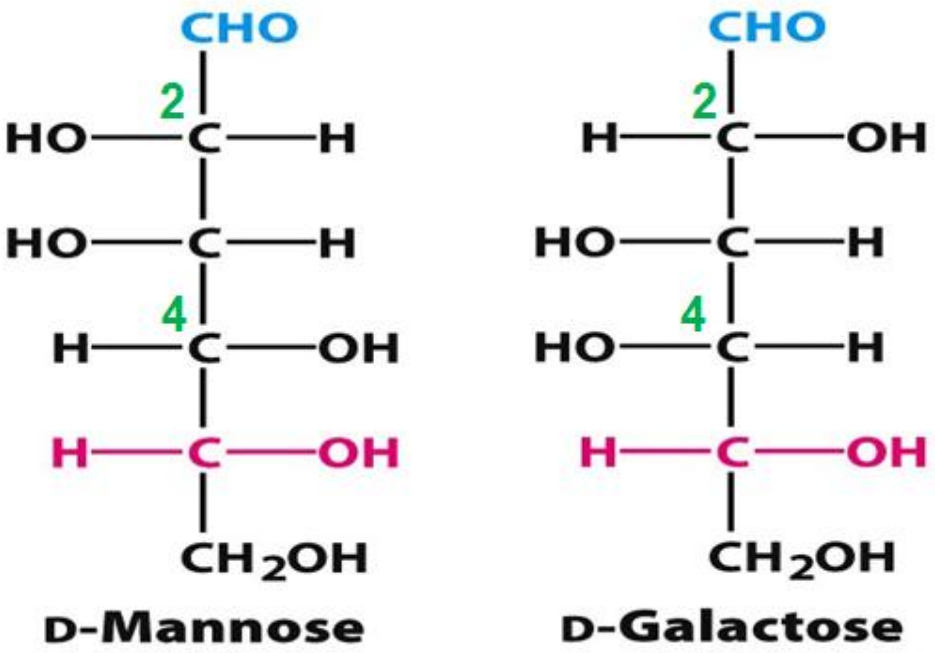


The interconversion of epimers (e.g. glucose to galactose and vice versa) Is known as epimerization, and a group of enzymes namely *epimerases* Catalyse this reaction.

Stereoisomerism – Chirality

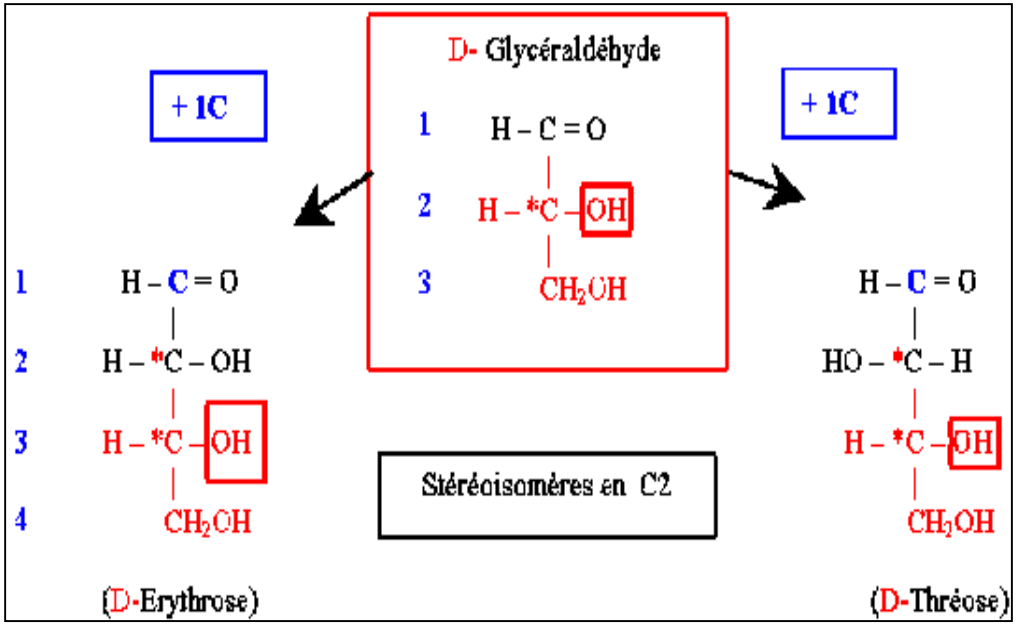
Diastereomers: is used to represent the stereoisomers that are not **mirror images** of one another.

For instance Mannose and Galactose are diastereomers



Configuration of D-aldoses

Representation of ***Killiani-Fischer synthesis, by*** increasing the chain length of an aldose, by one carbon at a time.



*The number of **asymmetric carbon** atoms **(n)** determines the possible isomers **N** of a given compound which is equal to 2.*

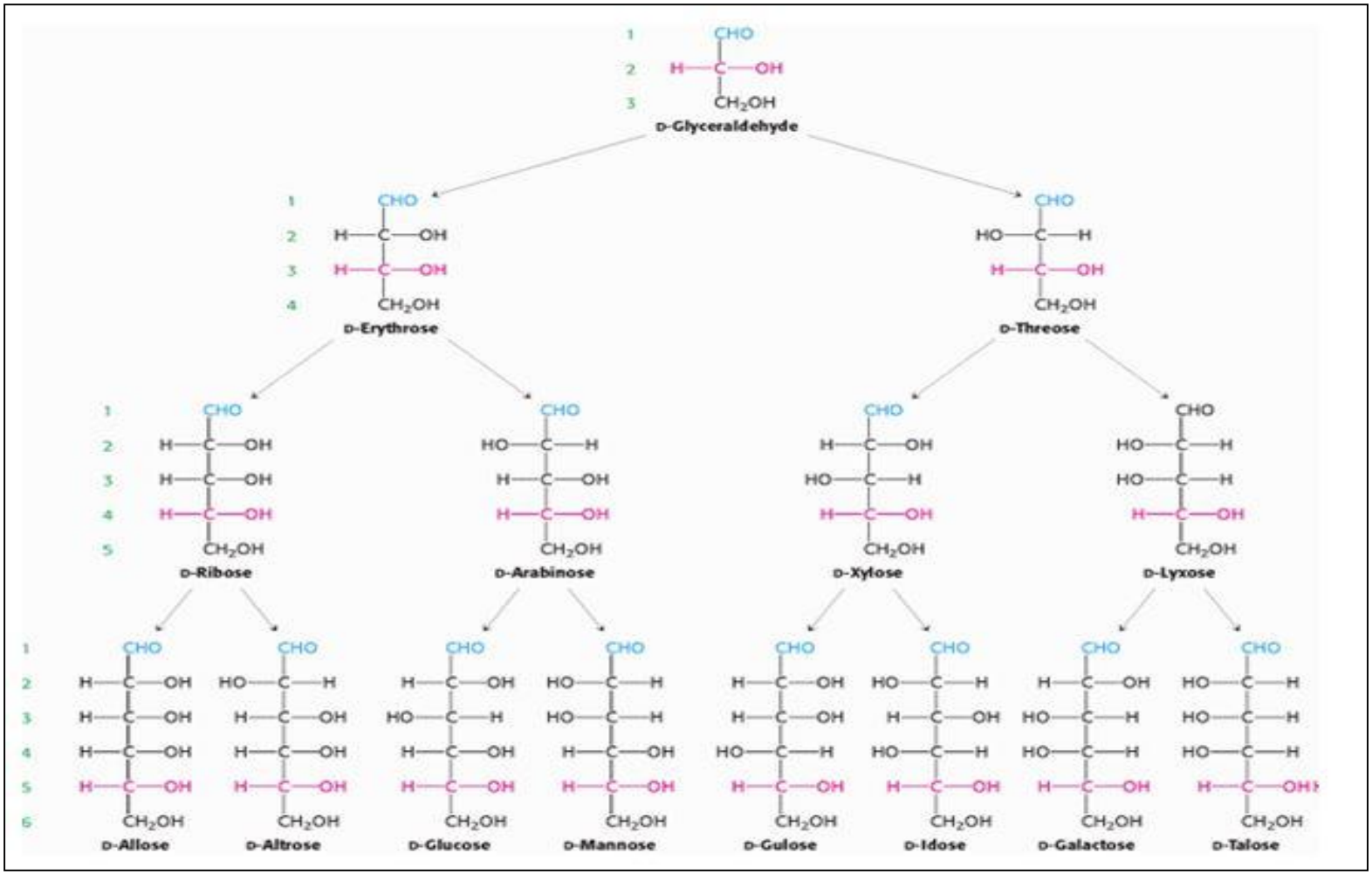
$N = 2^n$

N: Nombre d'isomères

n: Nombre de C*

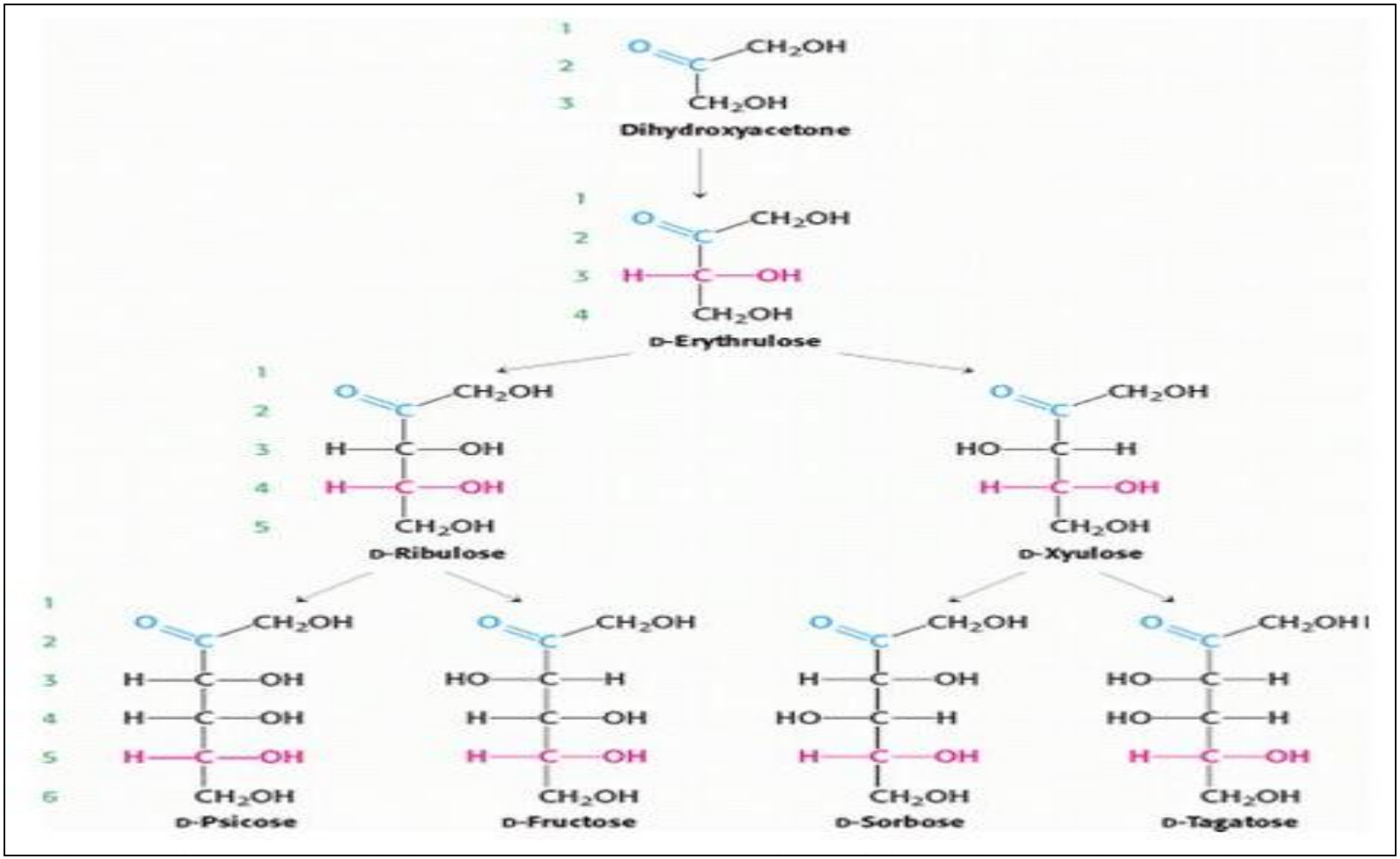
e.g. D-Erythrose contains 2 asymmetric carbons, and thus has 4 isomers (2 D and 2 L).

The structural relationship between D-aldoses shown in Fischer projection



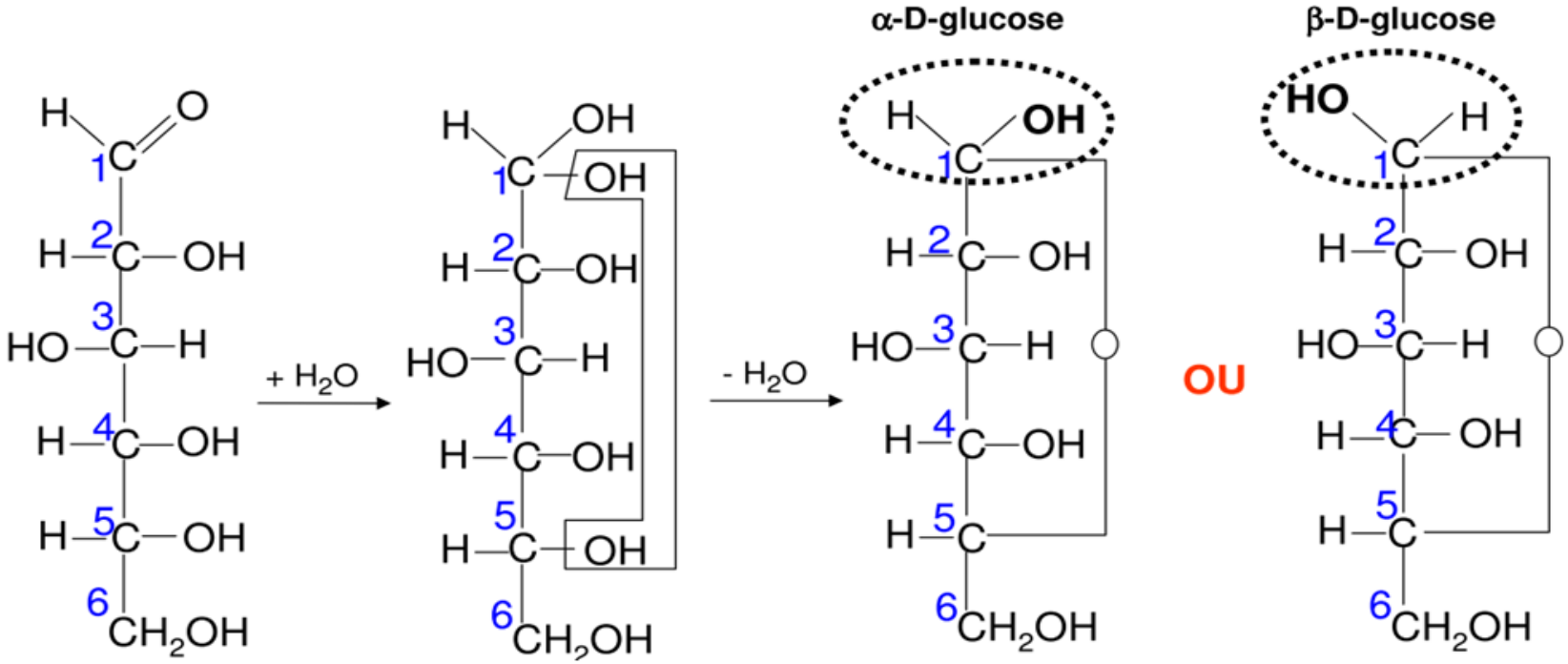
- This figure represents D-aldoses containing three, four, five and six carbon atoms.
- Of the 8 aldohexoses, glucose, mannose and galactose are the most familiar among these.
- D-glucose is the only aldose monosaccharide that predominantly occurs innature.

The structural relationship between D-ketoses shown in Fischer projection



- The figure illustrates D-ketoses containing three, four, five and six carbon atoms.
- Starting from dihydroxyacetone (triose), there are **five** keto-sugars which are **physiologically** important: Dihydroxyacetone **(3 C),** D-Xylulose **(5 C),** D-Ribulose **(5 C),** D-Fructose **(6 C) and** D-Sedoheptulose **(7 C).**

Cyclic Representation



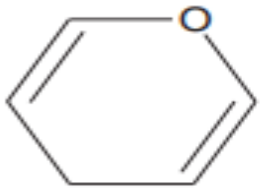
Fischer Linear form — Hydrate aldehyde — Hemiacetal

Tollens cyclic form (C1-C5)

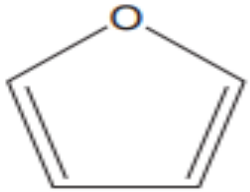
Cyclic Representation

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).

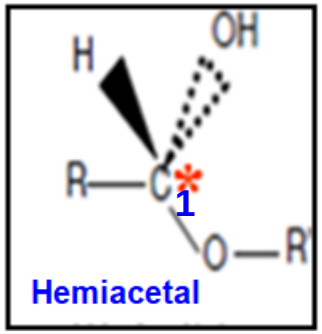


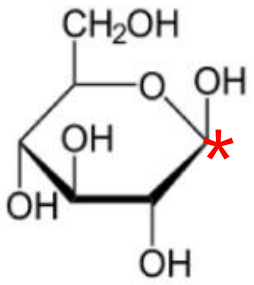
Pyran



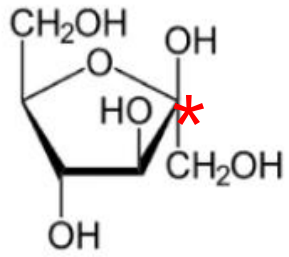
Furan

These cyclic forms are known as β-D-glucopyranose and β-D-fructofuranose

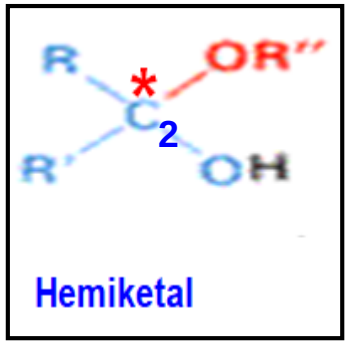




β D glucopyranose



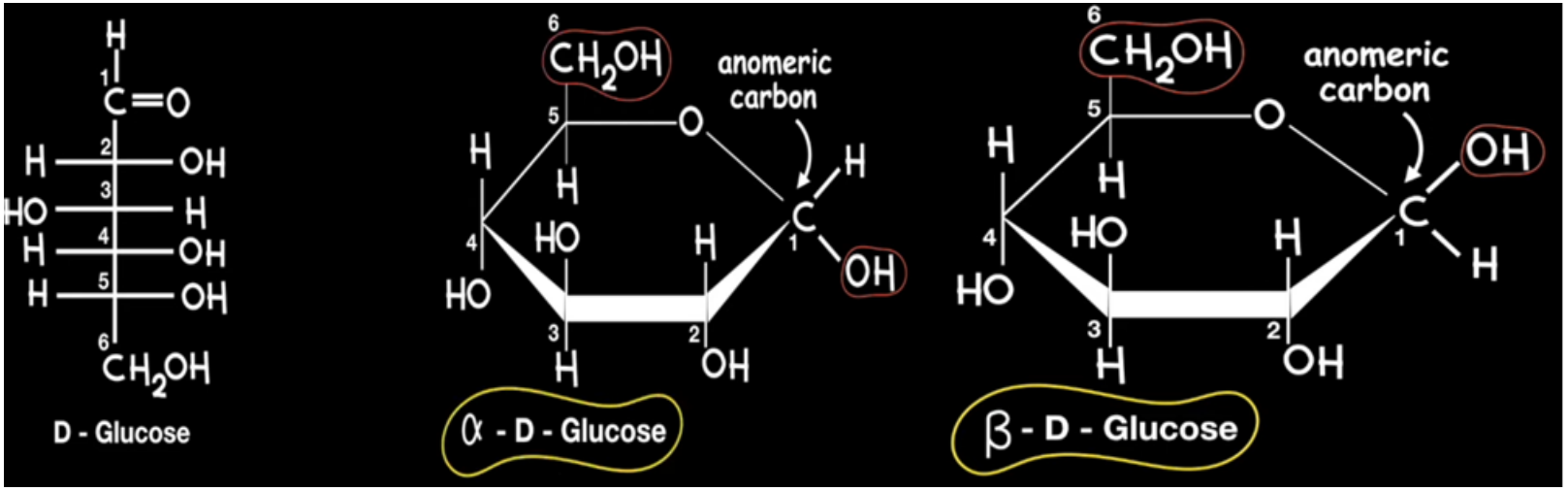
β D fructofuranose



Haworth projection formulae or pyranose structures of D-Glucose

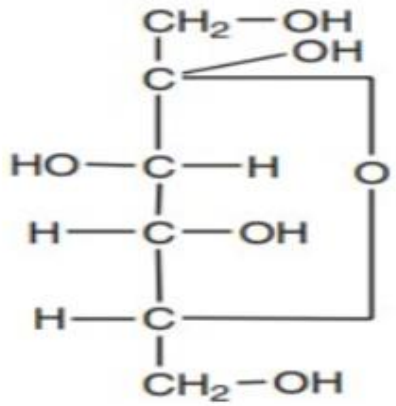
➢ In **Haworth** structures drawn with the heterocyclic oxygen in the upper right corner, the α-form has the **–OH** group on **C1** pointing "down". The β-form has the same group pointing "up".

➢ For **D-sugars**, the free –**CH2OH** group of an aldohexose is drawn above the plane of ring when ring oxygen is in the upper right. The rest is the simple, the groups on the **left** of the **Fisher** projection are **up** and those on the **right** are **down** in the Haworth structure.

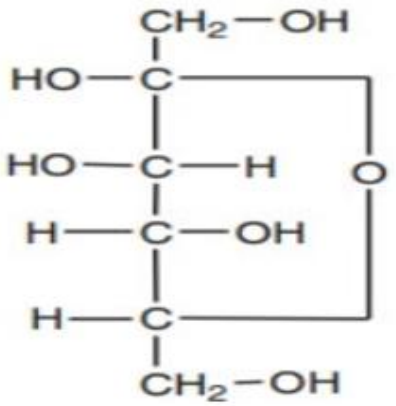


➢ The **α-D-glucopyranose** and **β-D-glucopyranose** are known as anomers. They differ from each other in the configuration only around **C1** known as anomeric carbon (hemiacetal **carbon**).

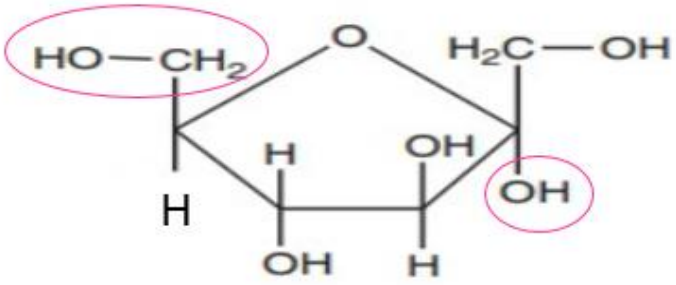
Haworth projection formulae or furanose structures of D-Fructose



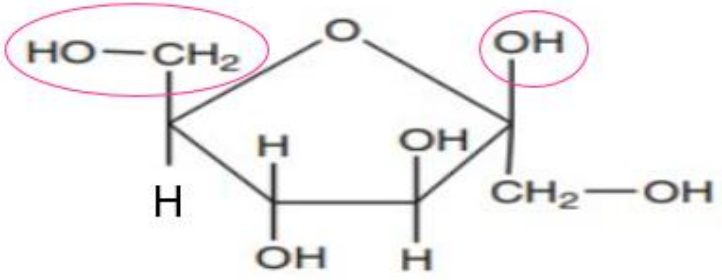
α D - Fructose



β D - Fructose



α D - Fructofuranose



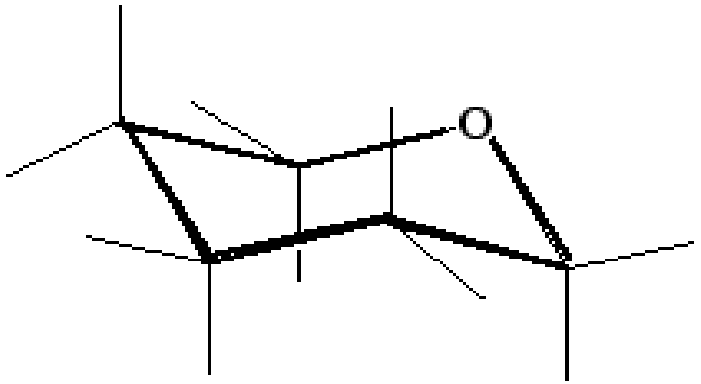
β D - Fructofuranose

The **α-D-fructofuranose** and **β-D-fructofuranose** are known as anomers. They differ from each other in the configuration only around **C2** known as anomeric carbon (hemiketal **carbon**).

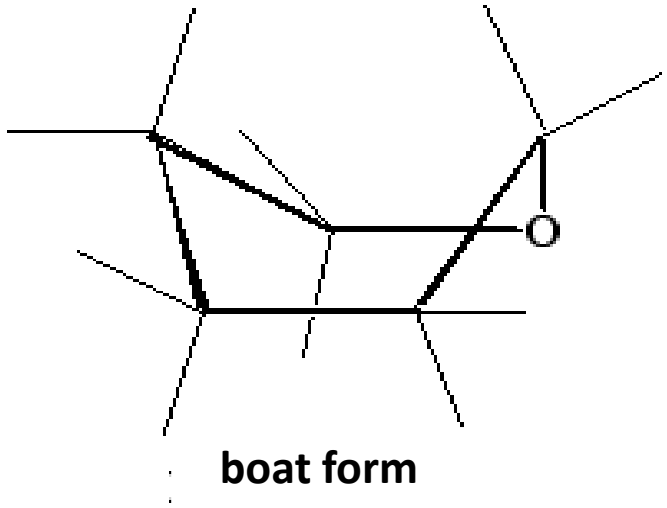
Cyclisation

Form	Aldoses	Ketoses
Pyran	C1 – C5	C2 –C6
Furan	C1 – C4	C2 – C5

Cyclic forms conformation

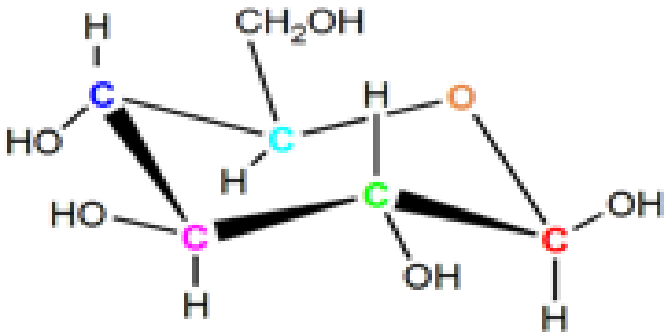


chair form



boat form

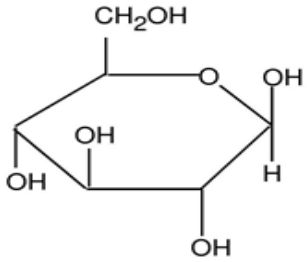
E. Jaspard (2008)



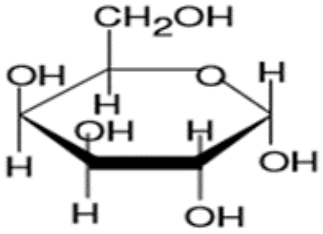
β- D- Glucopyranose

The **chair form** of glucose is the most **stable** conformation.

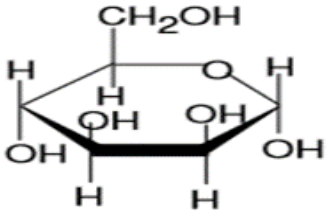
Some Monosaccharides of Biological Interest



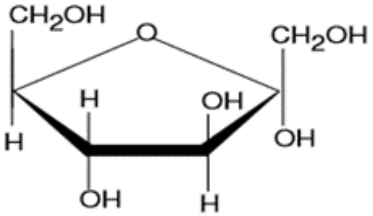
D-Glucose



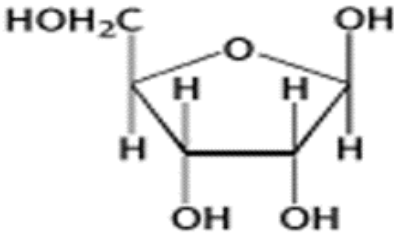
D-Galactose



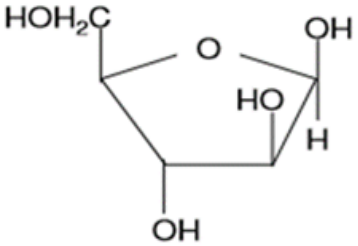
D-Mannose



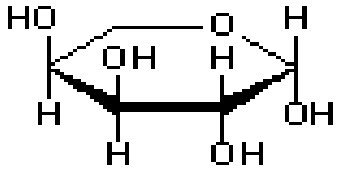
D-Fructose



D-Ribose



D-Arabinose



L-Arabinose

Some Monosaccharides of Biological Interest

D-Glucose	It is the most important energy source of carbohydrates to the mammals (except ruminants). The concentration of glucose in blood (glycemia) is approximately 0.80 g/L. Any imbalance is related to diabetes.
D-Galactose	It is transformed into glucose in the liver and metabolized. It is a constituent of lactose in mammalian milk. It also forms part of oligosaccharides and glycolipids.
D-Mannose	It is a constituent of several glycoproteins.
D-Fructose	Sugar present in fruits, honey, and seminal fluid (as an energy substrate for spermatozoa). It is absorbed and metabolized in the liver. However, in humans, it is only partially utilized.
D-Ribose	The β-D-ribose is part of β-D-2-deoxyribose, a constituent of nucleic acids (RNA and DNA). It is linked to purine and pyrimidine bases through N-glycosidic bonds (nucleosides, nucleotides).
D-Arabinose	A component of arabic gum, prune gum, and certain cereals. It is a precursor of D-ribose and D-mannose. It is not metabolized by humans and is excreted directly in the urine.
L-Arabinose	One of the rare naturally occurring sugars in the L-series. It is present in many plants. It is not metabolized by humans and is excreted in the urine without pathological consequences

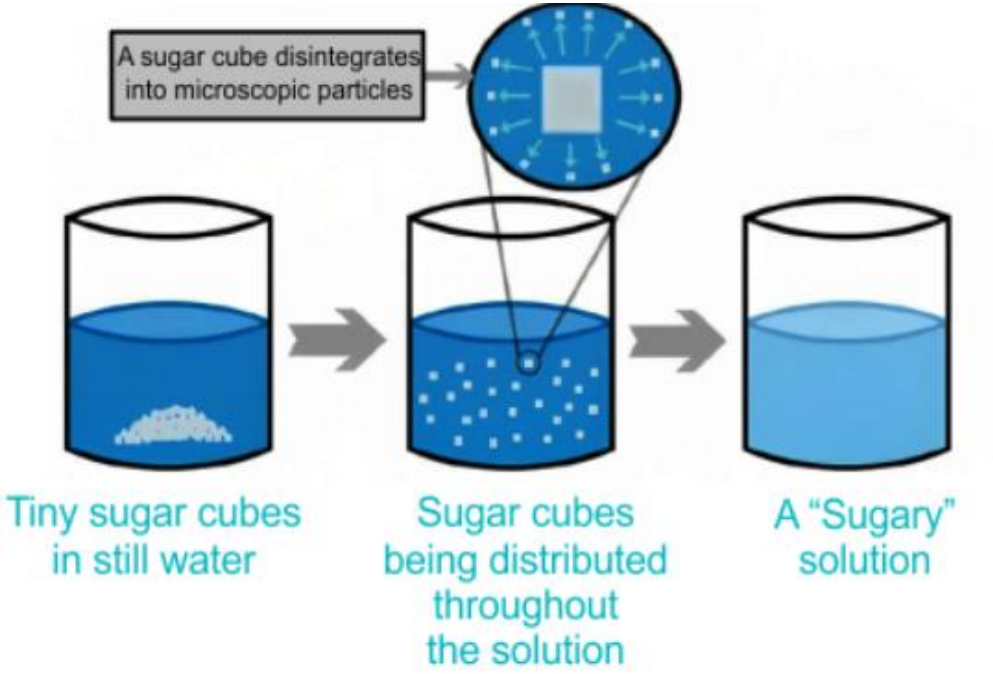
Physical Properties of Monosaccharides

Physical Properties

Solubility

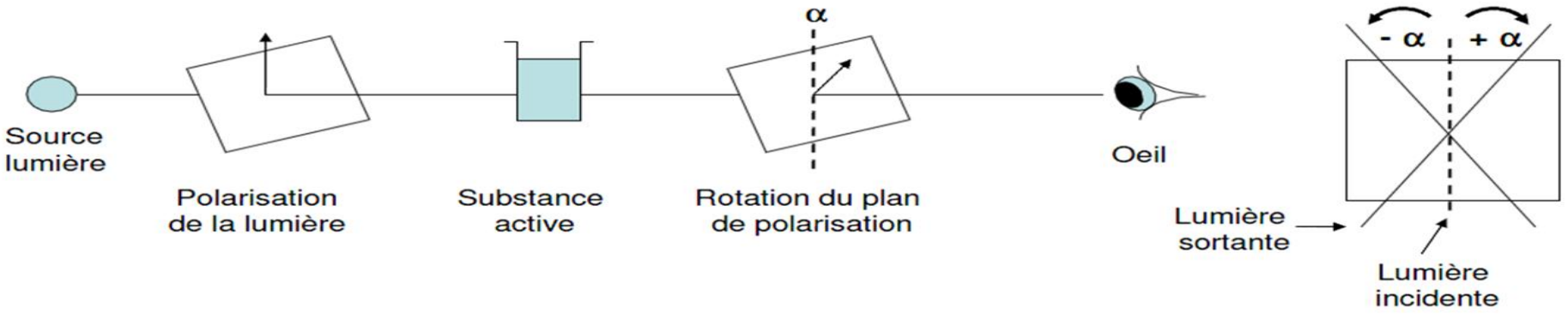
- Monosaccharides are highly soluble in water but only slightly or not soluble in organic solvents.

- Fructose exhibits greater solubility than glucose.



Optical activity

➢ Monosaccharides possess optical activity due to the presence of one or more **asymmetric carbon atoms.**



➢ If a beam of light passes through a **substance in solution**, the plane of polarization is rotated by an angle that depends on the **nature** of the **solute**. The substance is said to be ***optically active***; it therefore exhibits ***optical rotation*.**

➢ Optical rotation is measured using a polarimeter at 20 °C, and the monochromatic light employed corresponds to the sodium D-line (589 nm).

Optical activity

Optical rotation is expressed according to Biot's law.

$$[\alpha]_D^{20^\circ} = \frac{\alpha}{c \times l}$$

$[\alpha]^{D20°}$: Specific optical rotation (in degrees)

α : Observed angle of rotation (in degrees)

C : Concentration of the substance (in g/mL)

L : Length of the polarimeter tube (in decimeters)

- Dextrorotatory (+): If the sugar solution turns the plane of polarized light to right.
- Levorotatory (-) : If the sugar solution turns the plane of polarized light to left.
- In the medical practice, the term *dextrose* is used for glucose in solution. This is because of the dextrorotatory nature of ***glucose***.

Relationship between Optical Rotation and Molecular Asymmetry

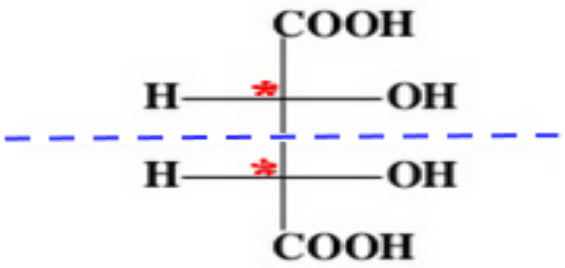
A molecule is said to exhibit **optical activity** if:

- It contains at least one **asymmetric carbon** atom.

- It does not possess a **plane of symmetry** (a plane dividing the molecule into two superimposable halves).

Example:

Tartaric acid contains **two asymmetric carbon** atoms but does not exhibit optical activity because it has a plane of symmetry.



Tartaric acid

Relationship between Optical Rotation and Molecular Asymmetry

- Enantiomers, also called **optical isomers**, are mirror images of each other. Their optical rotations are equal in magnitude but opposite in direction. One is **dextrorotatory** and the other **levorotatory**.

Example:

D-Glucose (+) = + 52° L-Glucose = – 52°

D-Fructose (–) = – 92.2° L-Fructose = + 92.2°

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

- The fact that a molecule is **levorotatory (–)** or **dextrorotatory (+)** has no relationship with its **D or L configuration** in the **Fischer projection**.

- The **optical rotations** of molecules in a solution are **additive**.

Mutarotation

- The formation of equilibrium mixture can be explained as:

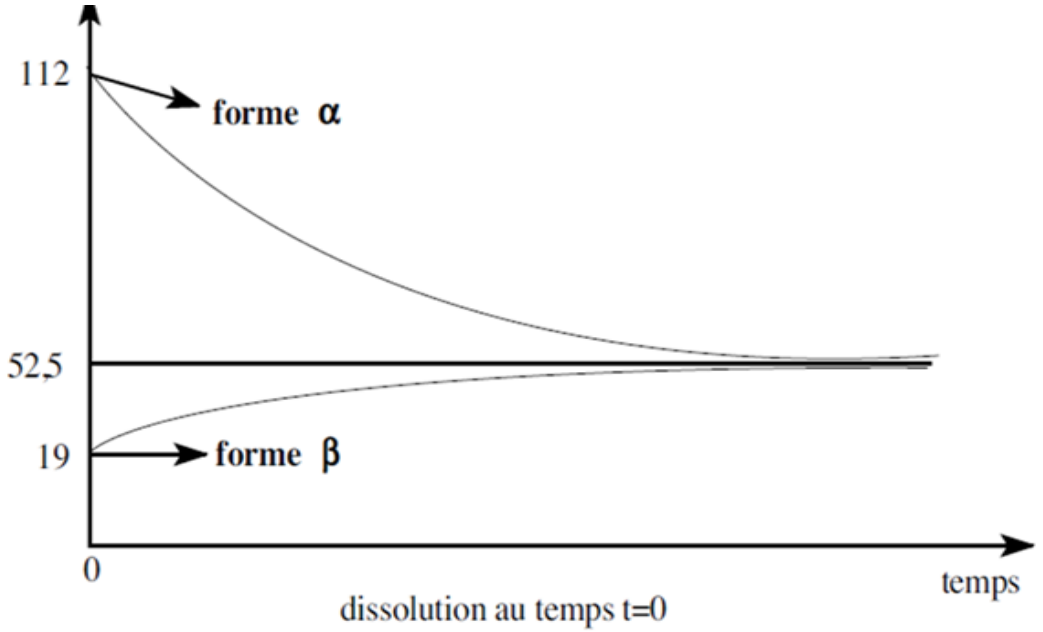
- The α- D-glucose has a specific rotation of +111° , while β- D-glucose has a specific rotation of +19.2°.

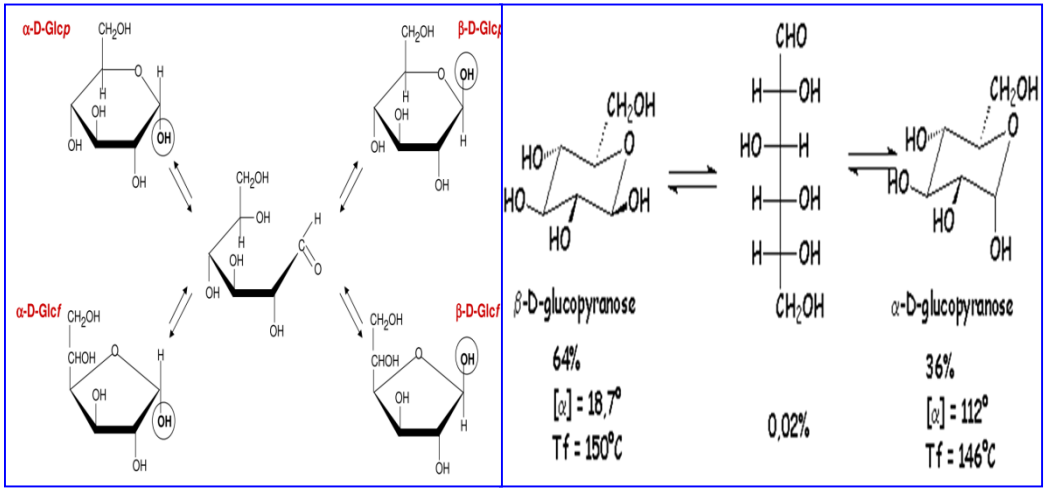
- When α-form is dissolved in water, its specific rotation falls until a constant value of +52.5° is reached.

- On the other hand, when β-form is dissolved in water, its specific rotation increases and becomes constant at 52.5°.

- This spontaneous change in specific rotation of an optically active compound with time to an equilibrium value is called mutarotation (Latin, muto means to change).

- Thus, there is an equilibrium mixture of α- and β-forms in the solution.





Chemical Properties of Monosaccharides

Chemical Properties

➢ **Monosaccharides** exhibit several important chemical properties due to the presence of multiple **hydroxyl** (–OH) groups and a **carbonyl group** (aldehyde or ketone).

➢ Their main chemical reactions include:

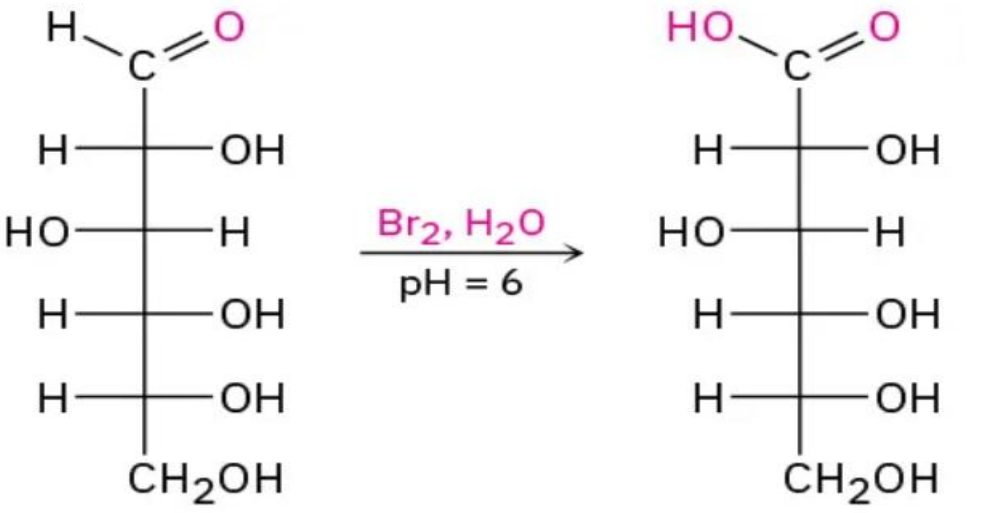
a- Oxidation
b- Reduction
c- Enolization
d- Dehydration
e- Esterification
f- Methylation

a- Oxidation reactions

Mild oxidation ⟶ *aldonic acids*

Aldoses can be oxidized to yield ***aldonic acids*** (oxidation of the aldehyde group)

Example: ***D-glucose*** ⟶ *D-gluconic acid.*

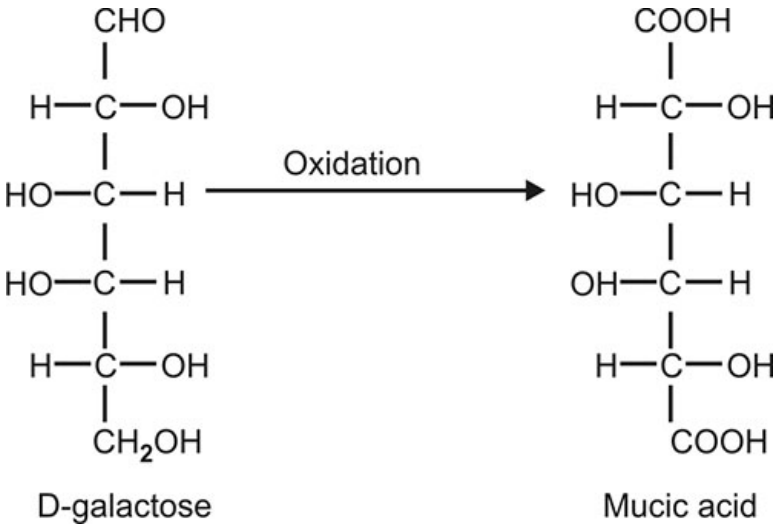


D-Glucose D-Gluconic acid

Note: *Ketoses do not undergo oxidation under these conditions.*

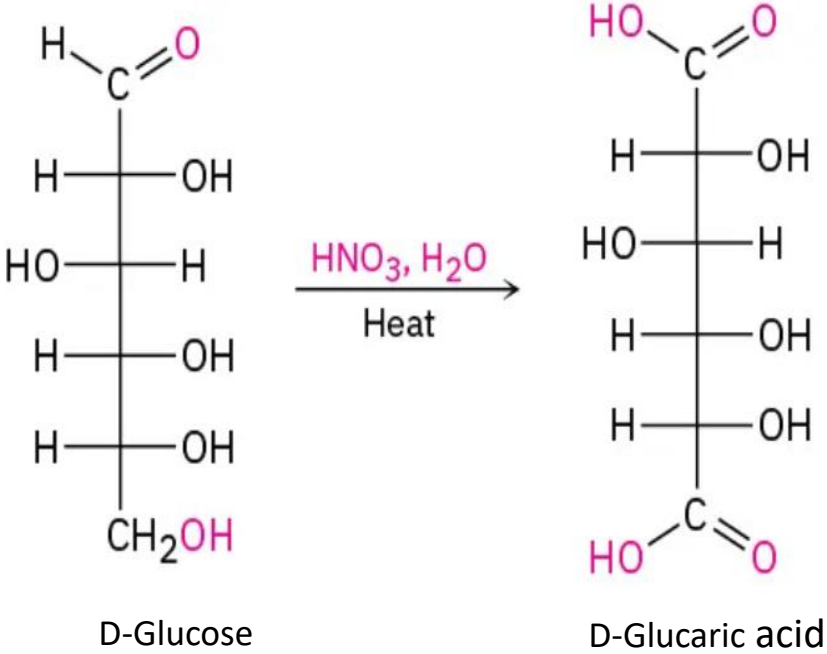
Strong oxidation ⟶ Aldaric acids

Oxidation of both the **aldehyde** and the **primary alcohol groups**.



D-galactose

Mucic acid



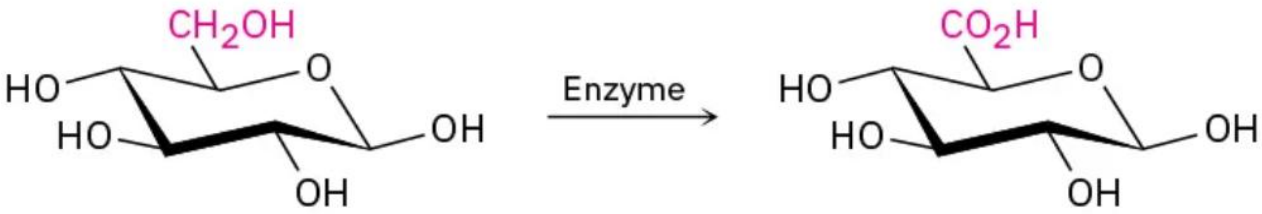
D-Glucose

D-Glucaric acid

***Note**: **Mucic acid test, galactose** when treated with **nitric acid** forms **insoluble** mucic acid crystals. Mucic acid is optically inactive because it possesses a plane of symmetry in its structure.*

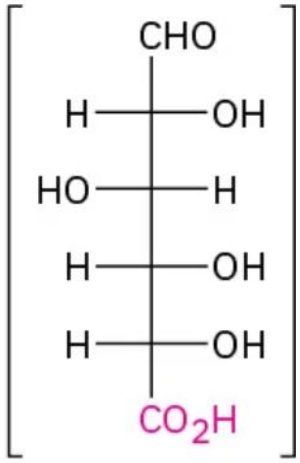
Strong oxidation ⟶ *Uronic acids*

Oxidation of ***terminal alcohol group*** (CH2OH ⟶ COOH) leads to the production of glucuronic acid.



D- Glucose

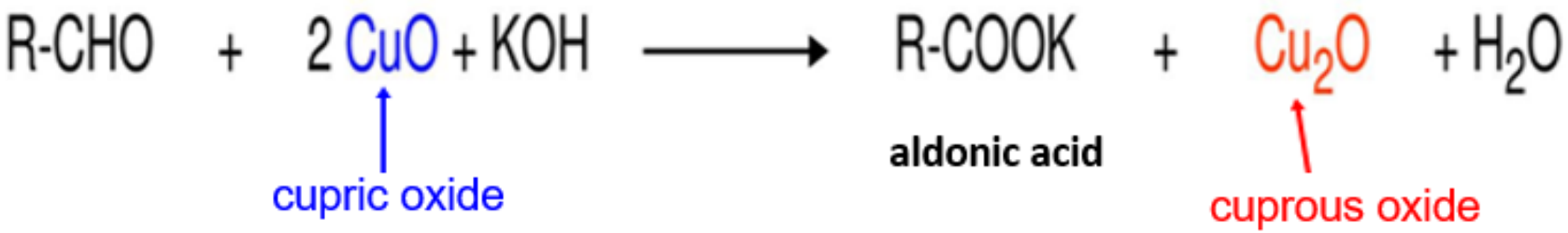
D-Glucuronic acid



Note: *Uronic acids play an essential biological role. They are involved in* ***hepatic detoxification*** *by conjugating with various substances (bilirubin, hormones, drugs) to form soluble* ***glucuronides****, thereby facilitating their elimination through urinary or biliary pathways.*

In addition, they are components of many ***structural polysaccharides*** *such as* ***glycosaminoglycans*** *(hyaluronic acid, heparin), contributing to the mechanical strength and hydration of connective tissues. (see later for structures).*

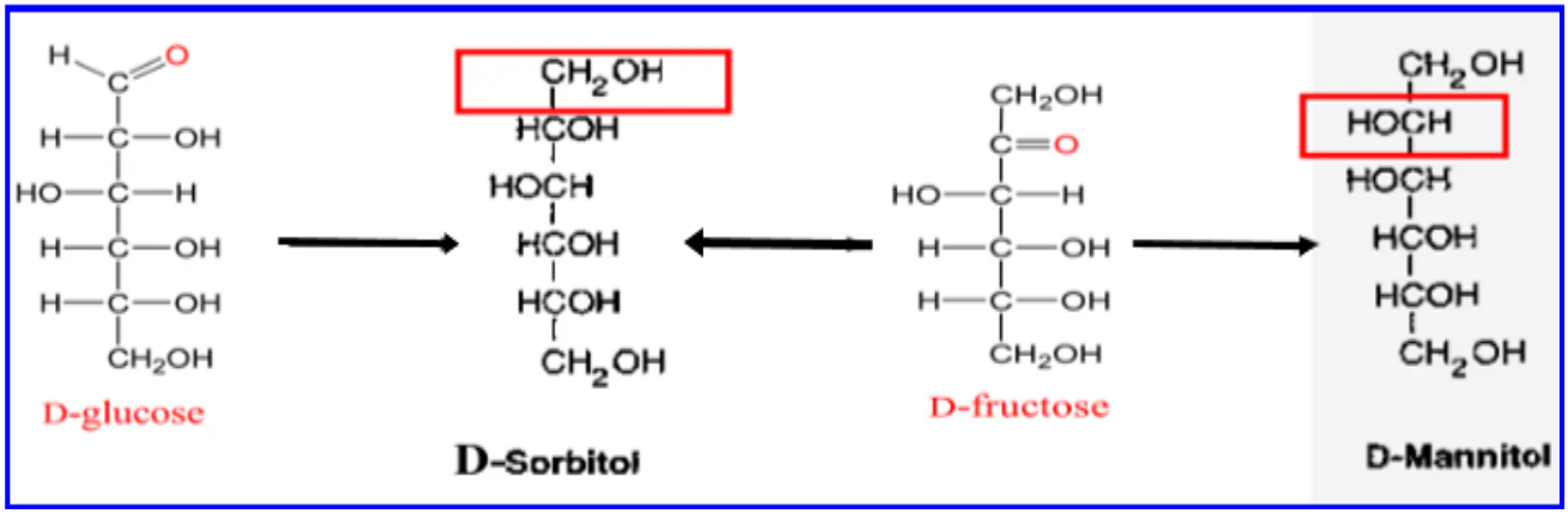
Oxydation par les sels des métaux



In an alkaline and heated medium, cupric oxide oxidizes **aldoses** into **aldonic acids**, while it is itself reduced to cuprous oxide, which precipitates as a red solid and is quantified using Fehling's solution. The sugar is therefore referred to as a reducing sugar.

b- Reduction reactions

When treated with reducing agents such as sodium amalgam, the ***aldehyde*** or ***keto*** group of monosaccharide is reduced to corresponding alcohol.



b- Reduction reactions

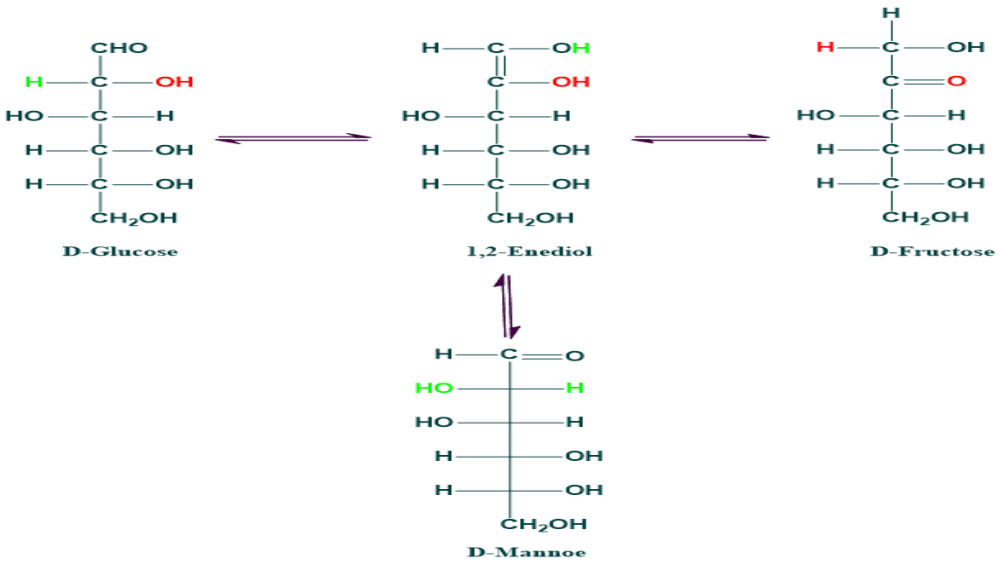
The important monosaccharides and their corresponding alcohols are given below:

D-Glucose ⟶ D-Sorbitol
D-Galactose ⟶ D-Dulcitol
D-Mannose ⟶ D-Mannitol
D-Fructose ⟶ D-Mannitol + D-Sorbitol
D-Ribose ⟶ D-Ribitol
D-Glyceraldehyde ⟶ D-Glycerol

Note: *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.*

c- Enolization

- The process of shifting a hydrogen atom from one carbon atom to another to produce **enediols** is known as **tautomerization** or **enolization**.
- Applying diluted aqueous alkalies causes aldoses and ketoses to convert into enediols. Enediol is the **enol form** of sugar because two OH groups are attached to the **double-bond carbon**.
- Through the formation of common **1,2-enediol**, glucose, fructose, and mannose may **isomerize** into each other in a dilute alkaline solution.

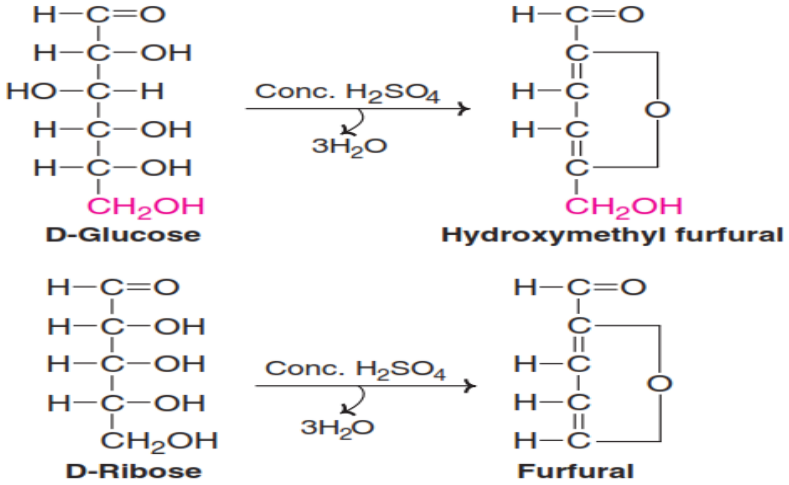


Note: *Enolization, the conversion of keto or aldehyde groups into enol forms, plays a key* ***medical*** *role by influencing* ***drug activation***, ***metabolism***, ***antioxidant activity***, *and* ***enzyme interactions.*** *This tautomerism can modulate* ***bioactivity***, ***solubility***, *and* ***pharmacological effects*** *of therapeutic compounds.*

d- Dehydration

- Pentoses ($C_5H_{10}O_5$) lose three molecules of water under the action of a concentrated acid to form furfural.

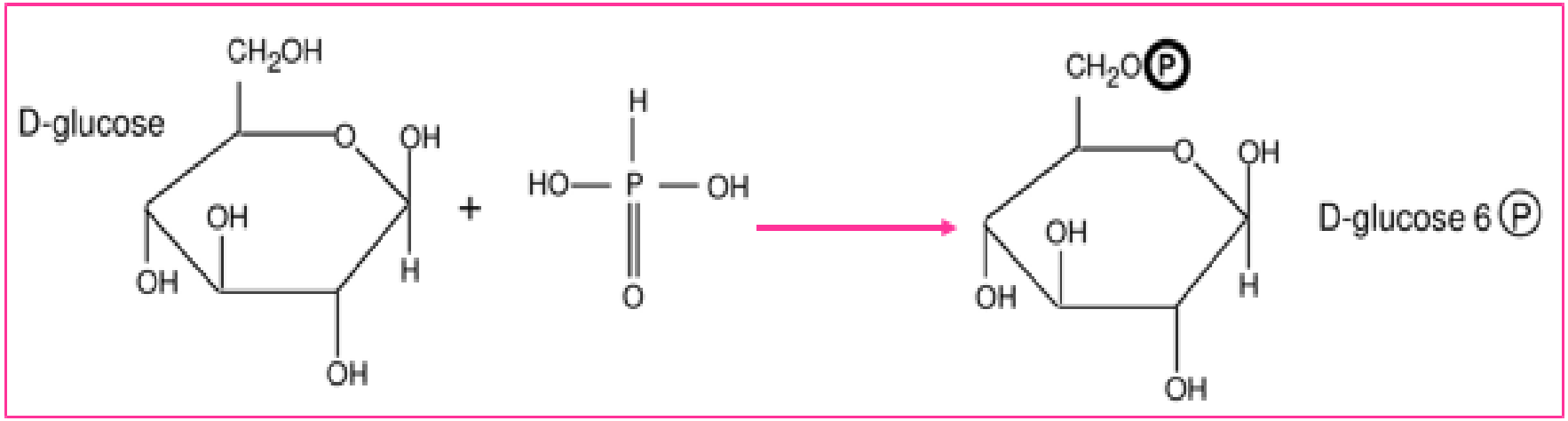
- Hexoses ($C_6H_{12}O_6$) also lose three molecules of water to yield **5-hydroxymethylfurfural** (HMF).



Note: *Furfural is a volatile compound with an almond-like odor, used as a* ***chemical intermediate*** *and in the* ***Bial's test*** *(orcinol reaction). This test is useful for detection of* ***xylose*** *in* ***urine*** *in* ***essential pentosuria****.*
(HMF) is a key compound formed by the dehydration of hexoses (such as glucose or fructose) under acidic conditions. Its significance is biochemical, analytical, and industrial. It serves as a marker of sugar dehydration and an indicator of ***Maillard reactions*** *(non-enzymatic browning) in food.*

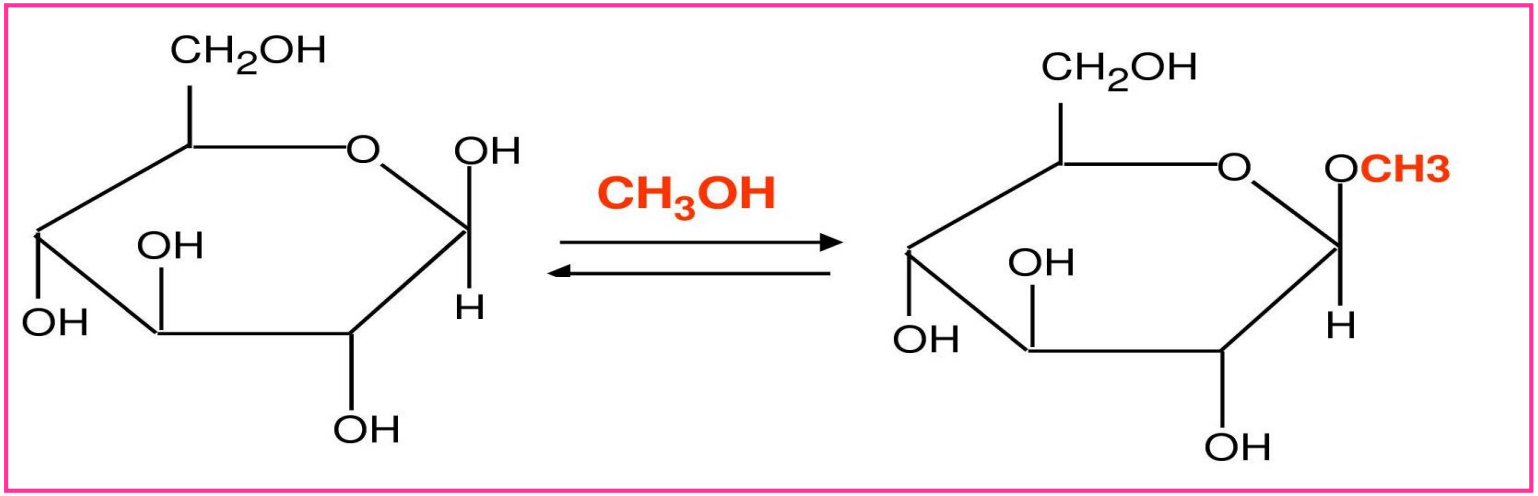
e- Esterification

- 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**.
- Examples: *Glucose 6-phosphate* and *glucose 1-phosphate* are good examples. **ATP** donates the phosphate moiety in ester formation.



Note: *Phosphorylated sugars are key intermediates in **cellular metabolism**, **regulating energy production**, **glycogen synthesis**, and **signaling pathways**. Alterations in their metabolism can lead to metabolic diseases (e.g., **diabetes**, **glycogen storage disorders**) and enzymes that process them serve as therapeutic targets.*

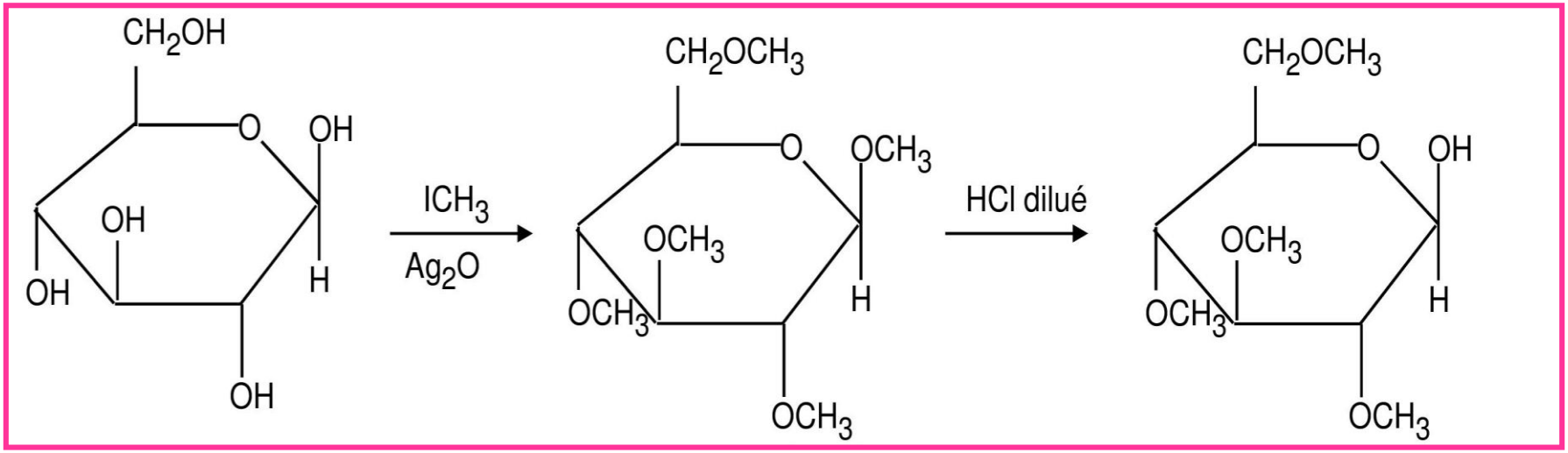
f- Methylation



The **anomeric hydroxyl** group is **blocked**, therefore, the sugar behaves as a non-reducing sugar.

Note: *Some* ***glycolipids*** *and* ***glycoproteins*** *contain methylated sugars involved in cell* ***recognition*** *mechanisms (adhesion, immunity, signaling).*
Examples*: certain methyl-hexoses present in* ***bacterial polysaccharides*** *play a role in virulence or resistance to immune defenses.*

Complete methylation



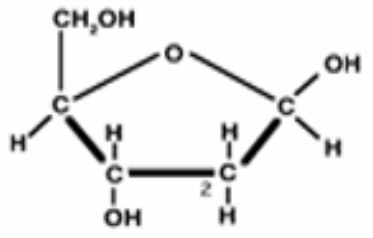
This reaction is mainly used to:

- Determine the **position** of **glycosidic linkages** in polysaccharides, by identifying which hydroxyl groups are involved in **bonding**.

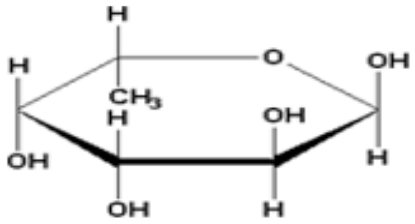
- **Protect** hydroxyl groups during complex synthetic procedures.

Derivatives of monosaccharides

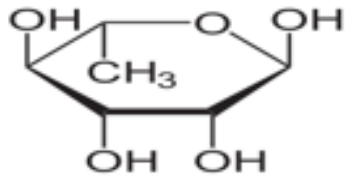
2-β D-Deoxyribose



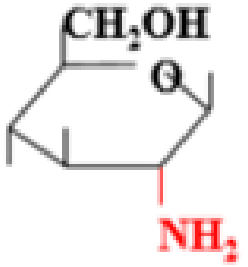
L-Fucose



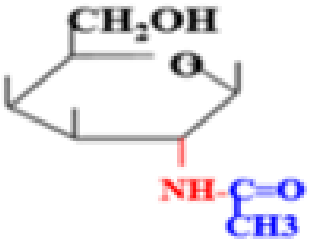
L- Rhamnose



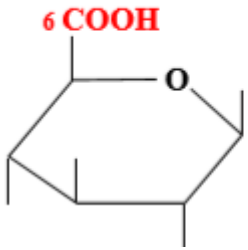
2-βD-Glucosamine



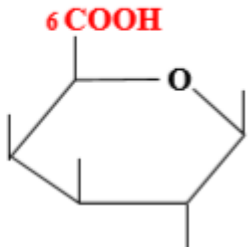
2-N-Acetyl-D Galactosamine



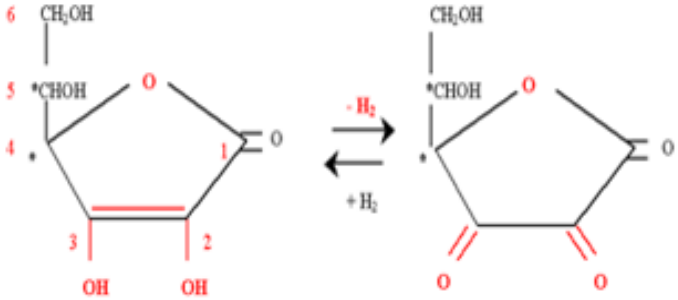
βD-Glucuronic Acid



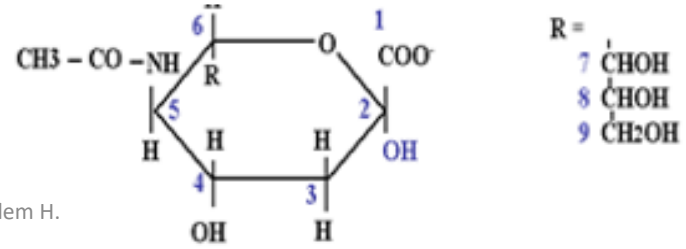
βD-Galacturonic Acid



Ascorbic Acid



Sialic acid :
N-Acetyl-Neuraminic Acid
(NANA)



Derivatives of monosaccharides

➢ Deoxy Sugars: **Deoxyribose**, a constituent of deoxyribonucleic acid (DNA), carries a CH_2 group on carbon 2 and occurs in the furanose ring form.
Fucose is 6-deoxy-L-galactose, found in blood group antigens and certain glycoproteins.
Rhamnose is 6-deoxy-L-mannose, found notably in hemicelluloses of plant cell walls.

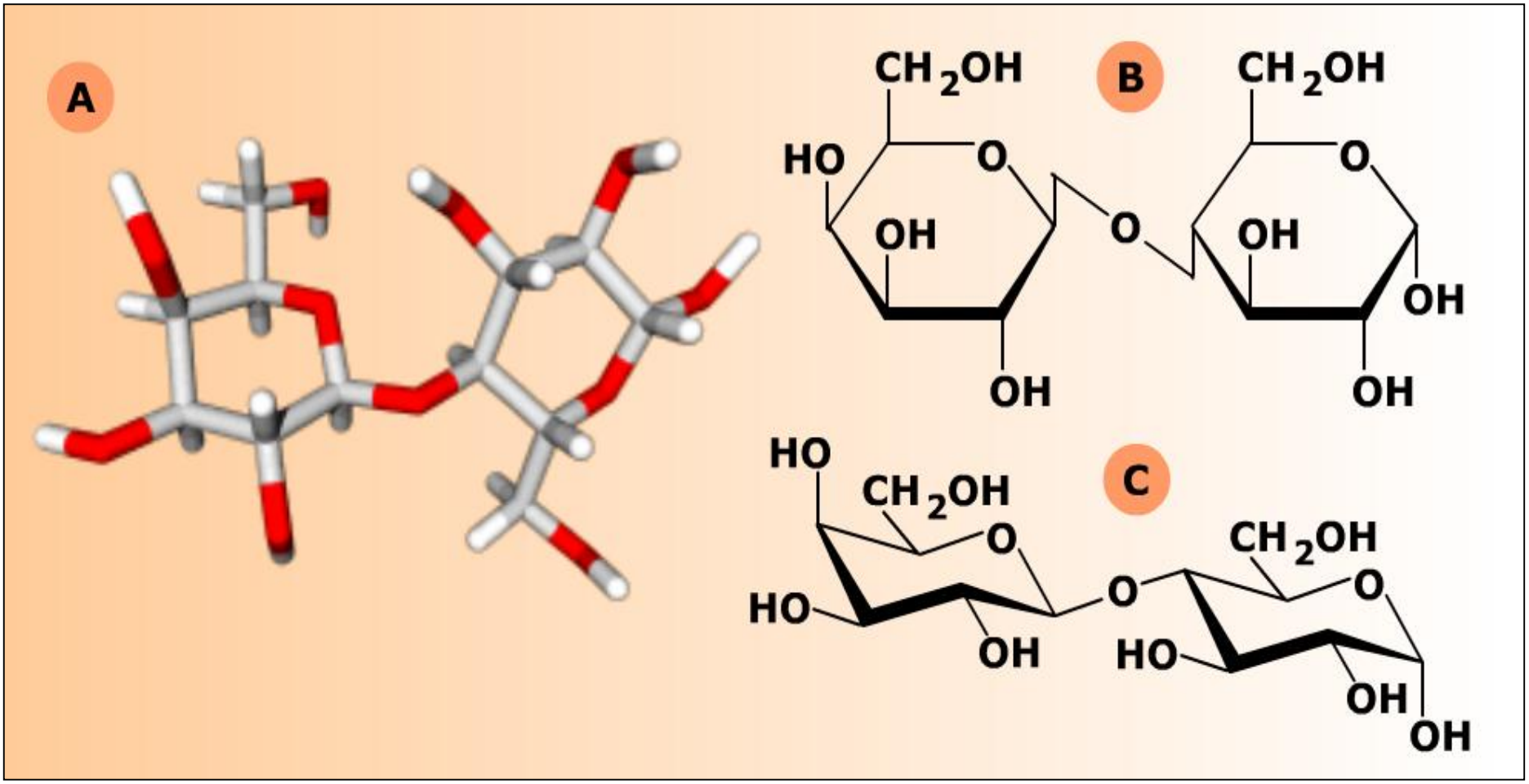
➢ Amino Sugars (Osamines): They occur in polymerized form in chitin (the exoskeleton of arthropods), murein (bacterial cell walls), and glycoproteins. Examples include D-glucosamine, D-galactosamine, and D-mannosamine. The hydroxyl group at **carbon 2** (C2) is replaced by an **amino group ($-NH_2$)**, which is often acetylated to yield N-acetylglucosamine, N-acetylgalactosamine, or N-acetylmannosamine. Certain antibiotics contain amino sugars which may be involved in the antibiotic activity e.g. erythromycin.

➢ Uronic Acids: These are components of glycosaminoglycans, playing an essential biological role in hepatic detoxification.

➢ Vitamin C (L-Ascorbic Acid): Only the L-form is biologically active. It is characterized by its **ene-diol function**. Humans are unable to synthesize this compound, which is why it is considered a water-soluble vitamin. Deficiency leads to abnormal collagen synthesis and fragility of blood vessel walls, resulting in **scurvy**.

➢ Sialic Acid (9 Carbons): or **N-Acetyl-Neuraminic Acid (NANA),** is formed by the condensation of **pyruvic acid (3C)** and **D-mannosamine (6C).** In eukaryotic cell membranes, sialic acids are components of **glycolipids** and **glycoproteins**, arranged at regular intervals along the chain. They create an electron-dense, negatively charged cloud that, through electrostatic repulsion, maintains the molecule in an extended, rod-like conformation.

V-Oligosaccharides

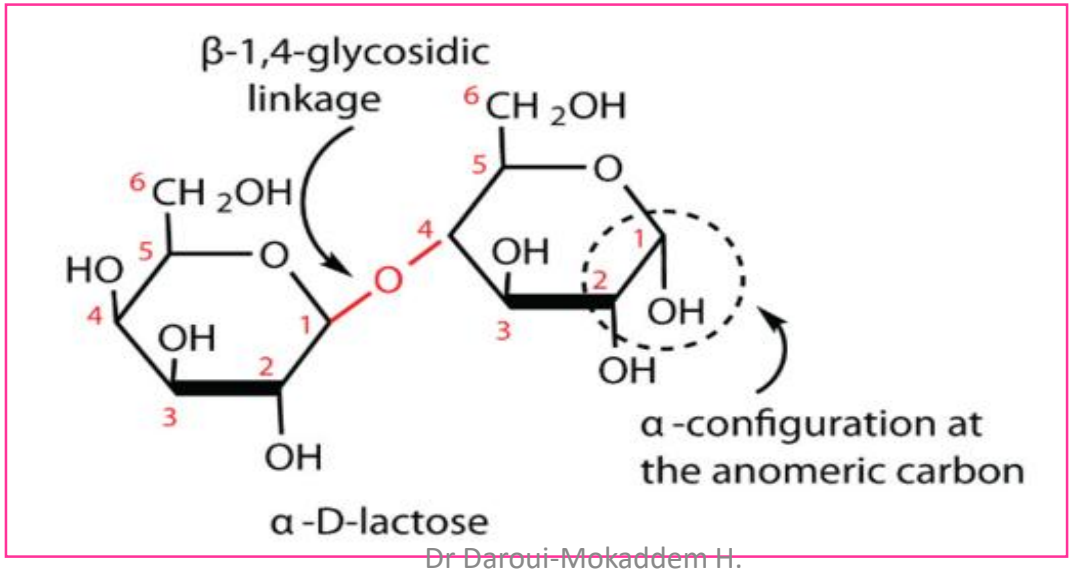


Glycosidic bonds

- The monosaccharides are held together by glycosidic bonds to result in **di-**, **oligo-** or **polysaccharides**.

- 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 (α or β).

- For instance, lactose which is formed by a bond between **C1 of β-galactose** and **C4 of glucose** is named as β (1- 4) glycosidic bond. The other glycosidic bonds are described in the structure of di- and polysaccharides.



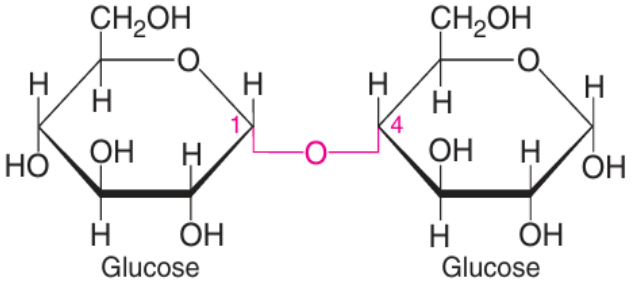
Disaccharides

- 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:

- Reducing disaccharides with free aldehyde group e.g. *maltose*, *cellobiose*, *lactose* (milk sugar).
- Non-reducing disaccharides with no free aldehyde or keto group e.g. *sucrose* (cane sugar) , *trehalose*.

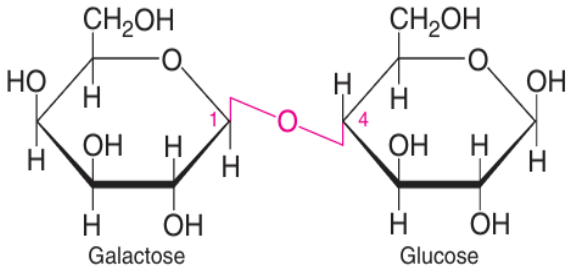
Note: *Lactulose is a synthetic* ***disscharide*** *containing* ***galactose*** *and* ***fructose****. It is neither digested nor absorbed in the intestine. Lactulose is useful for the treatment of* ***hepatic encephalopathy****, a* ***disorder*** *characterized by elevated plasma* ***ammonium*** *levels. Lactulose converts ammonia (****NH3****) in the lumen to ammonium ion (****NH4 +****). This results in a reduction in the plasma NH3, since NH4 + ions are not easily absorbed.*

Structures of oligosaccharides



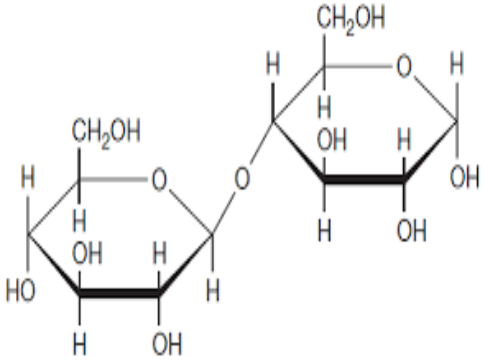
α-Maltose

α-D-glucopyranosyl (1-4) α D-glucopyranose



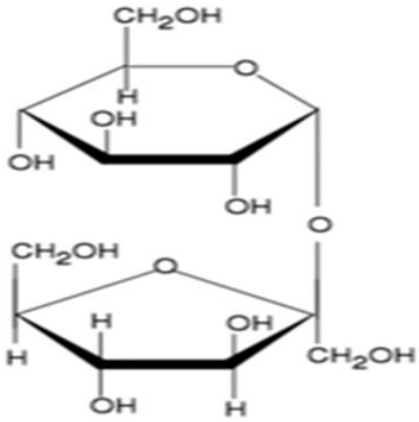
β-Lactose

β-D-galactopyranosyl (1-4) β-D-glucopyranose



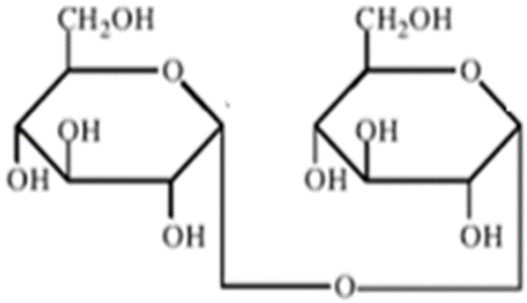
α-Cellobiose

β-D-glucopyranosyl (1-4) α-D-glucopyranose



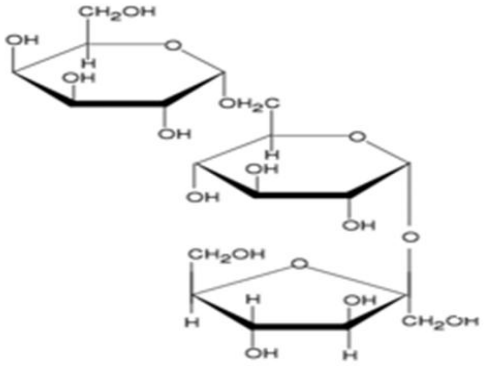
Sucrose

α-D-glucopyranosyl (1-2) β-D-fructofuranoside



Trehalose

α-D-glucopyranosyl (1-1) α-D-glucopyranoside



Raffinose

α-D-galactopyranosyl(1-6) glucopyranosyl (1-2) β-D-fructopyranoside

Reducing oligosaccharides

Maltose: It is produced from the digestion of polysaccharides such as starch or glycogen. Glucose residues are released through chemical hydrolysis or by the action of the enzyme **α-glucosidase**.

Lactose: This is the carbohydrate found in milk and nowhere else. Its concentration ranges from 10 to 80 g/L: about 75 g/L in human milk and 48 g/L in cow's milk. Its taste is only mildly sweet. It is the **only naturally occurring reducing disaccharide**.

Cellobiose: A reducing disaccharide resulting from the degradation of cellulose; it is similar to maltose, but the type of glycosidic linkage is **β(1→4)**.

Non-Reducing oligosaccharides

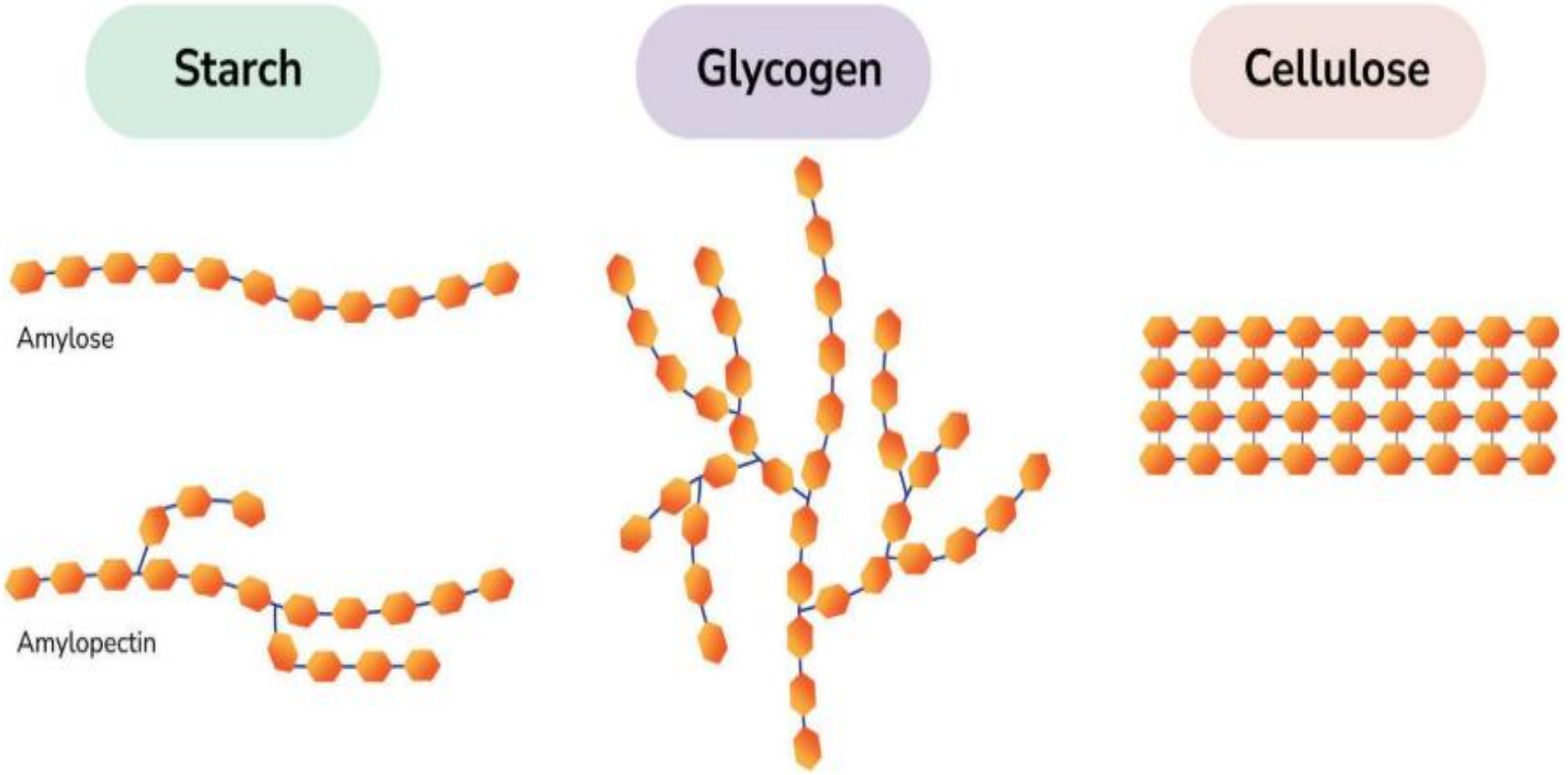
Sucrose: This is the most widespread disaccharide; it is the sugar obtained from sugar cane and sugar beet. Sucrose is **dextrorotatory** (+66.5°), while its hydrolysis products are **levorotatory** (–28.2°), a property known as **sucrose inversion**. Hydrolysis occurs through the action of **α-D-glucosidase** or **β-D-fructosidase (invertase)**.

Trehalose: Its sweetening power is about **40– 45% that of sucrose**. Many organisms (such as fungi and bacteria) accumulate it in response to **thermal stress (cold)** or **desiccation**.

Raffinose: Is the most common **triholoside** after sucrose and is found in **sugar beet**, from which it is removed during refining (hence its name).

***Note**: Trehalose has significant applications in cosmetics. Due to its **high water-retention** capacity and its ability to stabilize **proteins** and **cellular membranes**, it is incorporated into hydrating, soothing, and anti-aging formulations.*

VI-Polysaccharides



Polysaccharides

Polysaccharides are of two types:

- *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.

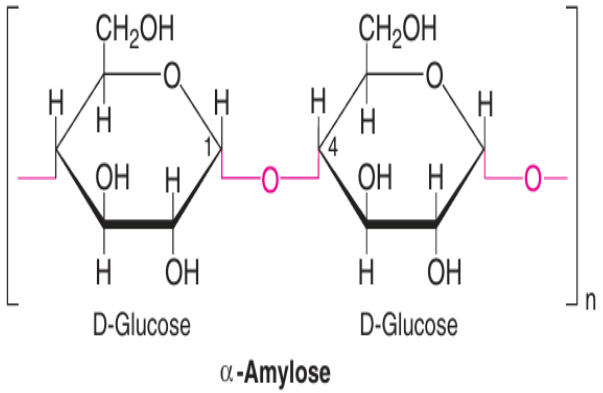
- *Heteropolysaccharides* on hydrolysis yield a **mixture** of a **few monosaccharides** or their **derivatives.**

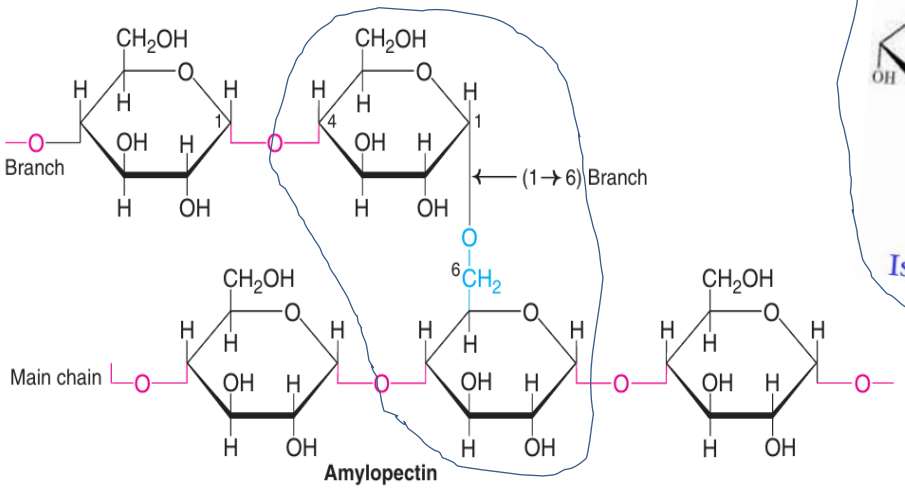
Note: *Monosaccharides and disaccharides* ***dissolve*** *easily in water because water is a polar solvent. In contrast, polysaccharides* ***do not dissolve*** *readily due to their* ***high molecular weight****; instead, they form colloidal solutions in water.*

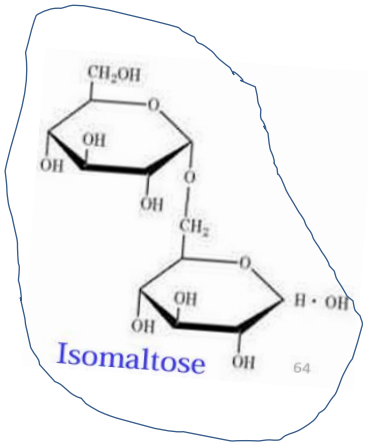
Homopolysaccharides

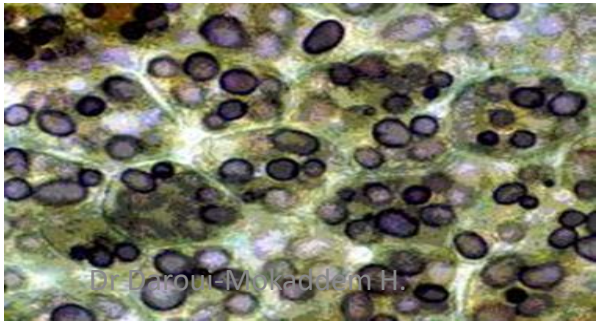
Starch

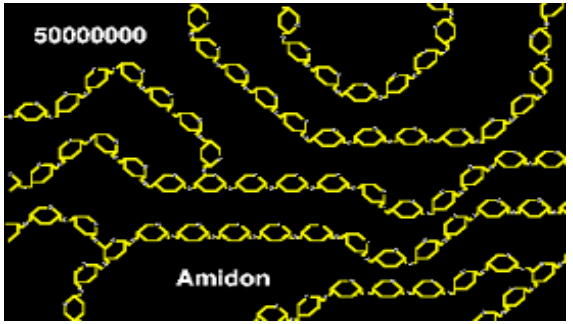
- Starch is the carbohydrate reserve of plants which is the most important dietary source for higher animals, including man.
- Starch is a homopolymer composed of D-glucose units held by α-glycosidic bonds. Both humans and other animals have amylases to digest starches.
- Starch consists of two polysaccharide components-water soluble ***amylose*** (15-20%) and a water insoluble ***amylopectin*** (80-85%).







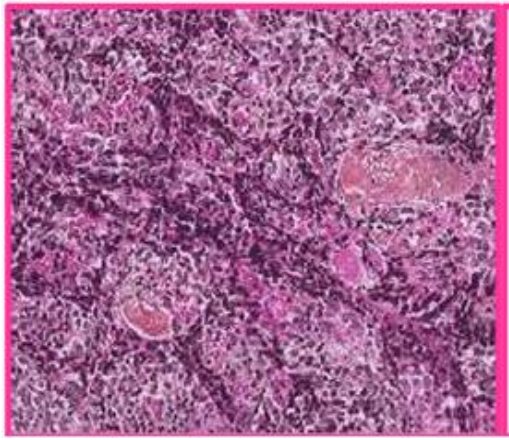


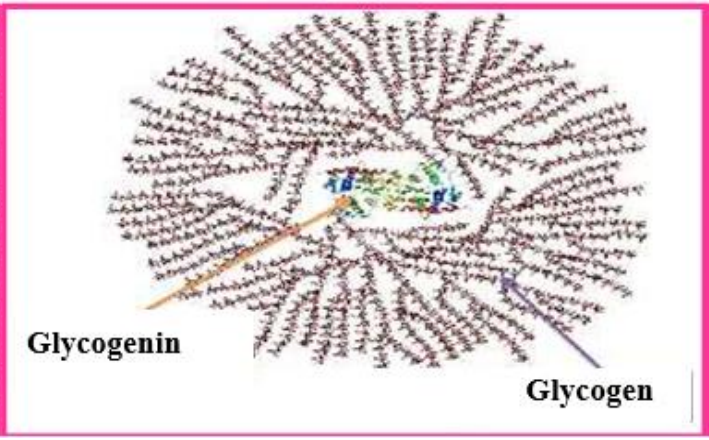


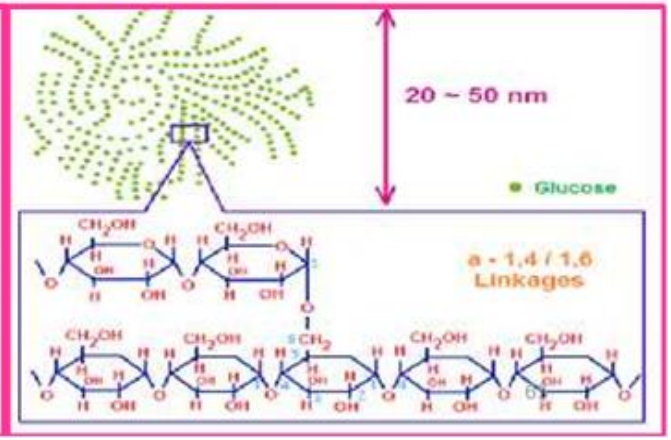
Homopolysaccharides

Glycogen

- Glycogen is the carbohydrate reserve in animals, hence often referred to as animal starch.
- It is present in high concentration in **liver** and **muscles**.
- 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 **α (1- 4)** glycosidic bonds, and **α (1- 6)** glycosidic bonds at branching points.







Note: ***Glycogen*** *contains at its core a small* ***protein*** *called glycogenin.*

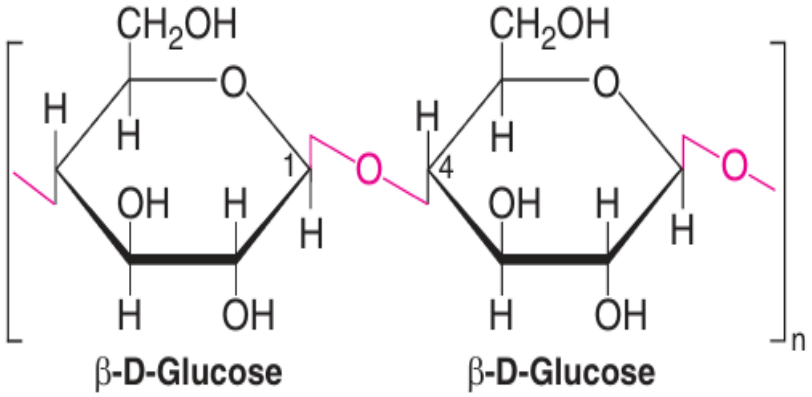
Glycogenin has significant ***biomedical importance****, as it plays an essential role in the biosynthesis of glycogen by initiating the* ***polymerization*** *of glucose residues.*

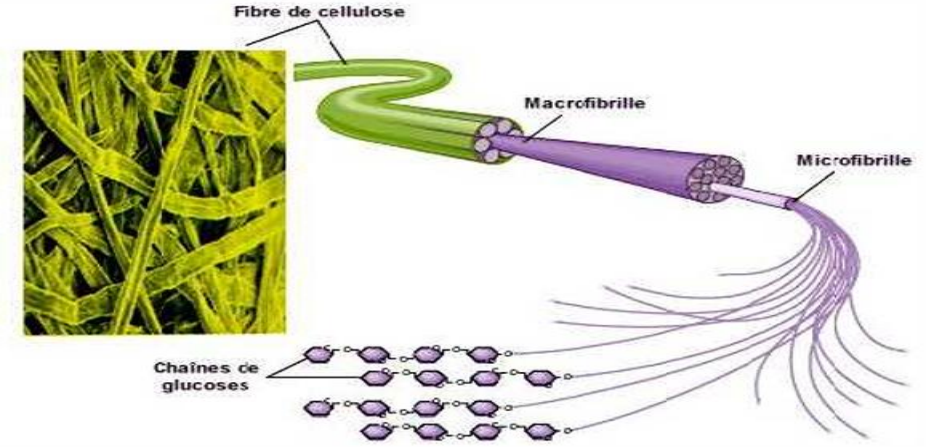
Mutations *in the* ***GYG1 gene****, which encodes* ***glycogenin-1****, are associated with certain* ***glycogen storage diseases*** *and specific forms of* ***muscle myopathies.***

Homopolysaccharides

Cellulose

- ***Cellulose*** occurs exclusively in plants and it is the most abundant organic substance in plant kingdom.
- Cellulose is composed of **β-D-glucose** units linked by **β- (1-4)** glycosidic bonds.
- Cellulose cannot be digested by mammals, including man, due to lack of the enzyme that cleaves β-glycosidic bonds.
- Certain ruminants and herbivorous animals contain microorganisms in the gut which produce enzymes that can cleave β-glycosidic bonds. Hydrolysis of cellulose yields a disaccharide c**ellobiose,** followed by β-**D-glucose.**





Note: *It is a major constituent of fiber, the non-digestable carbohydrate. The functions of dietary fiber include* ***decreasing*** *the absorption of* ***glucose*** *and* ***cholesterol*** *from the intestine, besides increasing the bulk of feces.*

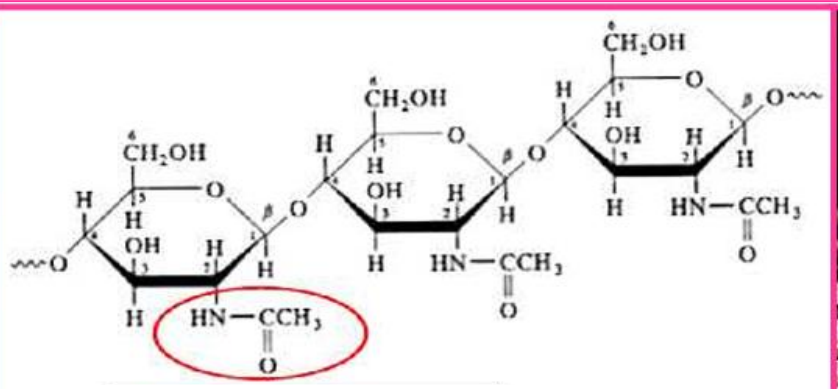
Homopolysaccharides

Chitin

- **Chitin** is composed of N-acetyl D-glucosamine units held together by β-(1-4) glycosidic bonds.

- It is a **structural** polysaccharide found in the **exoskeleton** of some **invertebrates** e.g. insects, crustaceans...

- *It plays a **protective and structural role**, providing **rigidity and mechanical strength**.*



N-acetylamine group

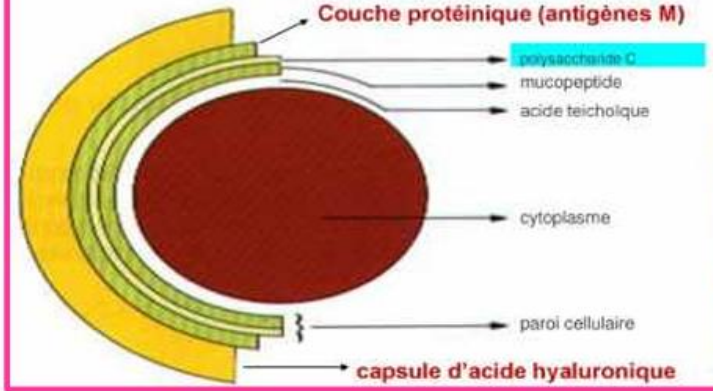
Note: *Chitin is also a source of chitosan, obtained by deacetylation, which is used in **pharmacy, cosmetics, agriculture,** and **water treatment**.*
*Both **chitosan** and **chitin** exhibit **biocompatible, biodegradable,** and **non-toxic** properties, making them promising biomaterials for applications such as **wound dressings, controlled drug delivery,** and **membrane production**.* Dr Daroui-Mokaddem H.

Heteropolysaccharides

Polymers composed of two or more types of monosaccharides arranged in a **repetitive sequence** pattern contribute to the structural organization of cellular envelopes.

- In **plants**, such polymers include gums, which consist of repeating units of (**D-galactose + L-arabinose + L-rhamnose + D-glucuronate)$_n$**.
- Agar-agar polysaccharide, extracted from **red algae**, is widely used as a solidifying agent in microbial culture media due to its gel-forming properties.
- Capsular polysaccharides of pneumococcal and streptococcal bacteria are other examples. These polysaccharides confer antigenic specificity to the bacteria, playing a key role in their pathogenicity and immune recognition.

Agar-agar gel

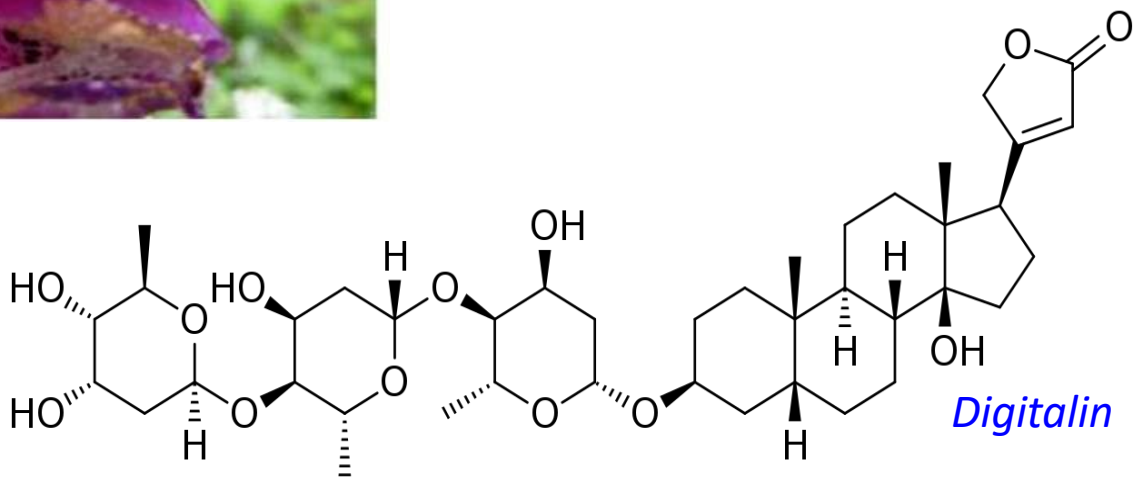


Streptococcus

Pneumococcus

VII-Heterosides (Glycosides)
Sugars + Non-Sugar (Aglycone)

Digitalis purpurea



Digitalin

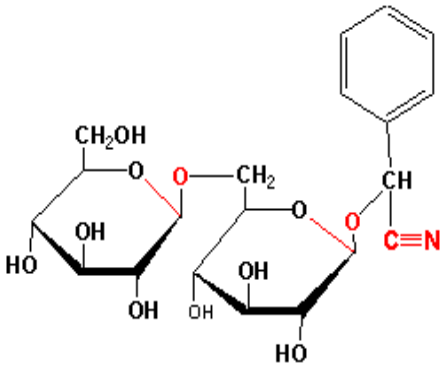
Heterosides (glycosides)

Heterosides: These are compounds formed by the condensation of monosaccharides with non-carbohydrate substances, known as aglycones. They are widely distributed in both the plant and animal kingdoms. Depending on the type of **glycosidic linkage**, several classes are distinguished:

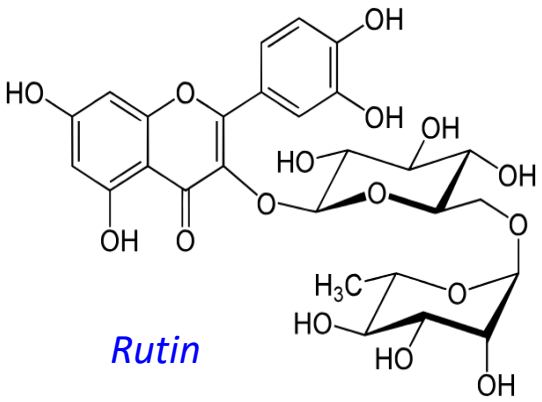
- O-heterosides: The aglycone is linked to the sugar through an oxygen atom. **Examples: Amygdalin** extracted from bitter almonds, **Digitalin** found in *Digitalis purpurea,* **Sennoside** *derived from senna,* **Rutin** found in buckwheat and citrus fruits.
- N-heterosides: The aglycone is linked to the sugar through a nitrogen atom. The amine group is most often part of a purine or pyrimidine base, as in **nucleosides**.
- S-heterosides: The aglycone is linked to the sugar through a thiol (-SH) group. Example: **Sinigrin** (found in black mustard seeds).

Note: *Amygdalin is a **cyanogenic glycoside**, can release hydrocyanic acid (HCN) through enzymatic hydrolysis. At low doses, it has been studied for its **potential analgesic** or **anticancer** effects, but it is **toxic** at high doses.*
*Digitalin is a **cardiotonic glycoside** composed of a sugar moiety and a **steroidal** aglycone.*
*Sennoside is an **anthraquinone glycoside** that has a **laxative** effect by stimulating intestinal motility.*
*Rutin is a **flavonoid glycoside** exhibits antioxidant, anti-inflammatory, and vasoprotective properties, and is used therapeutically to strengthen blood vessels and improve circulation.*

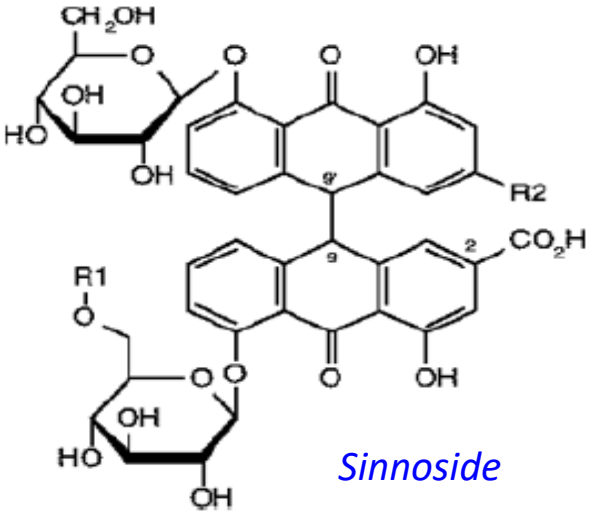
Heterosides



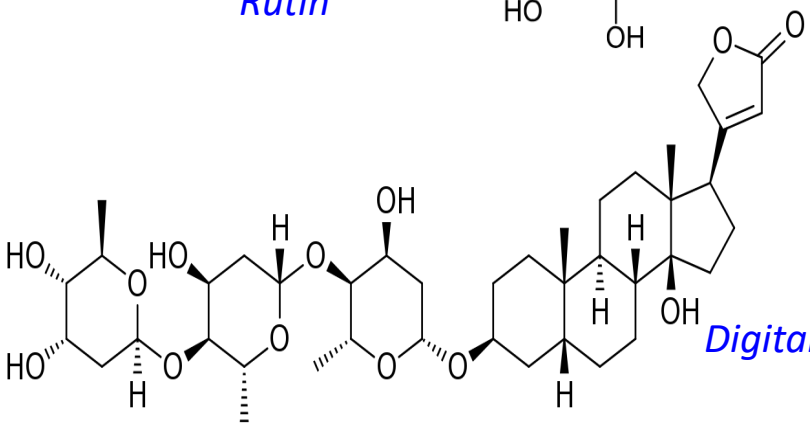
Amygdalin



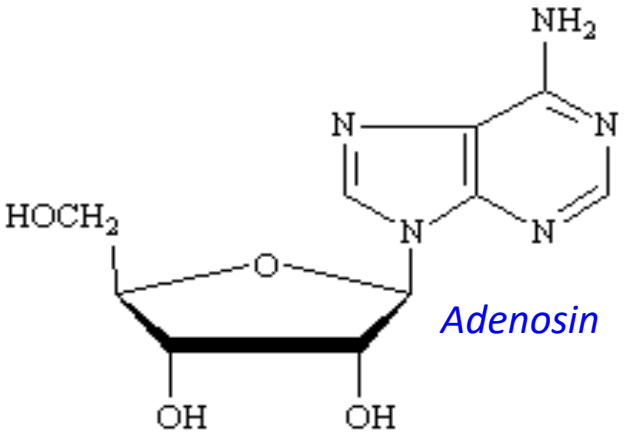
Rutin



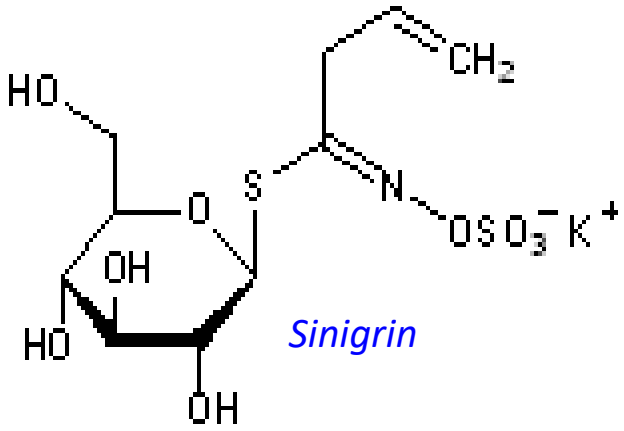
Sinnoside



Digitalin



Adenosin



Sinigrin

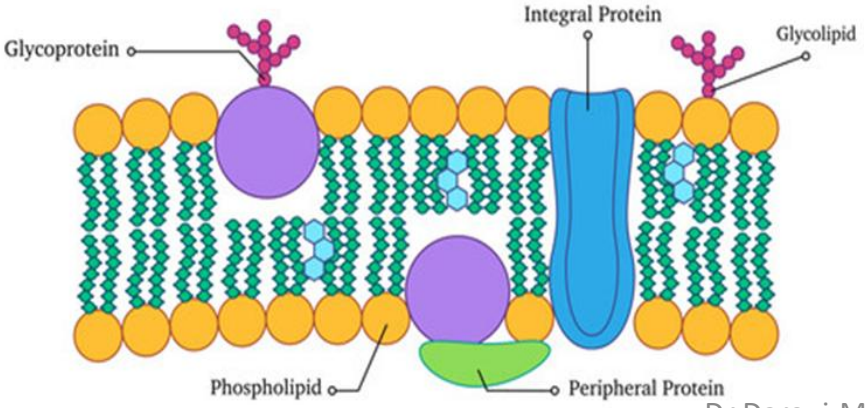
Heterosides

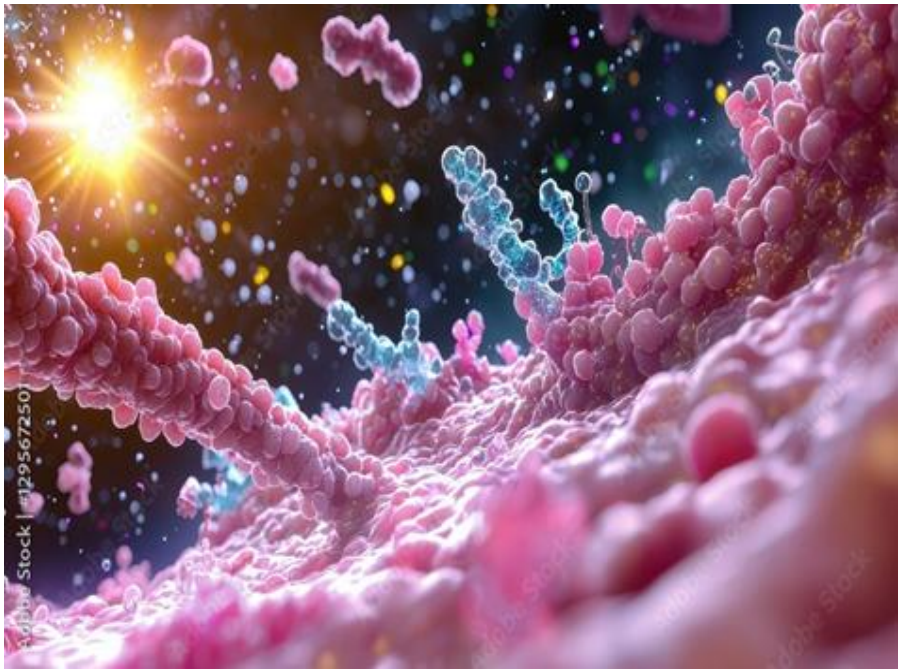
- *Peptidoglycans*: These are polysaccharides linked by numerous short peptide chains; the typical example is **murein**, which forms the **bacterial cell wall**.
- *Glycated proteins:* A glucose unit becomes covalently attached to a protein. In **insulin-dependent diabetes**, **hyperglycemia** promotes the attachment of this sugar to **hemoglobin**, serving as a **biochemical marker of diabetes**.
- *Glycoproteins (GP):* 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.

Specific linkages:

O-glycosidic linkages: The protein is bound to the carbohydrate chain via the hydroxyl group of a serine or threonine residue.

N-glycosidic linkages: The protein is attached to the carbohydrate chain through the amide nitrogen of a basic amino acid, typically asparagine.





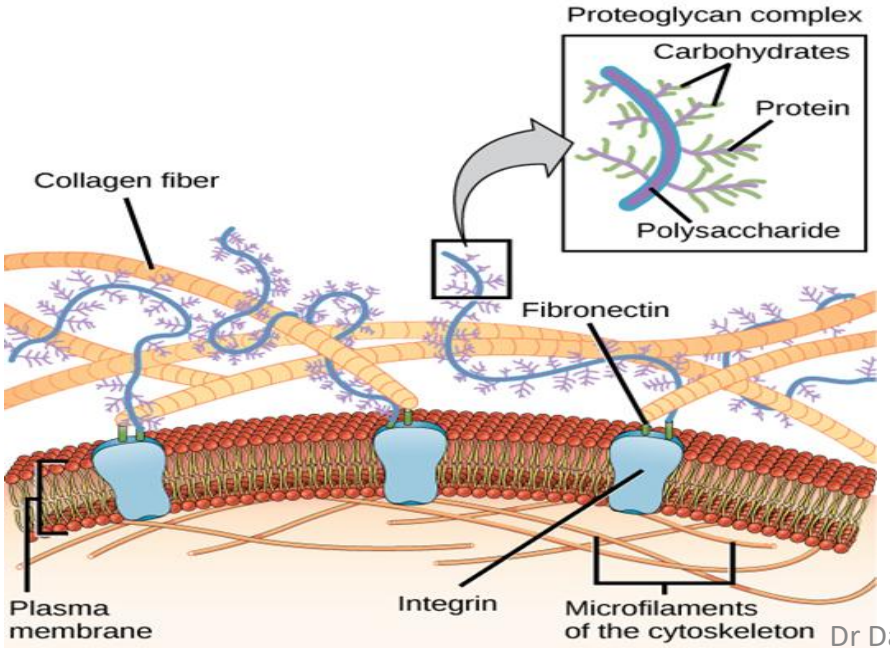
*A 3D rendering unveils the intricate structure of a cell membrane, revealing its diverse components: **glycoproteins** and **glycolipids**, cholesterol, peripheral proteins…*

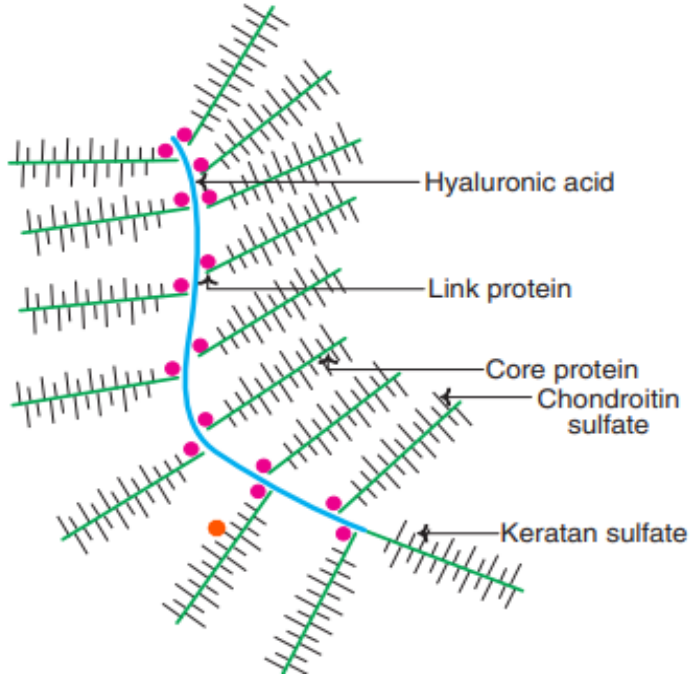
Heterosides

➢ *Proteoglycans (PG):* are macromolecules composed of **very long polysaccharide chains** (known as **glycosaminoglycans** or **GAGs**) covalently linked to a **protein core**, with the polysaccharide component being predominant (**> 90%**).

➢ The GAGs possess an acidic character due to their sulfate and carboxyl groups. Two main types are distinguished:

- **Structural GAGs**: such as hyaluronic acid, chondroitin sulfates, Dermatan sulfate and Keratan sulfate.
- **Secretory GAGs**: such as heparin.





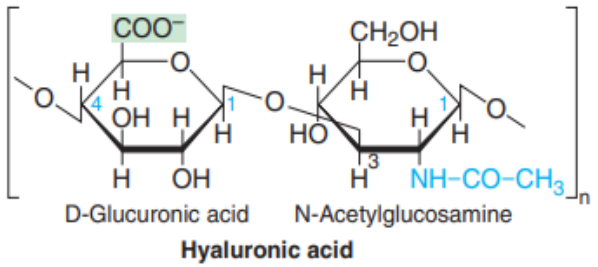
Diagrammatic representation of a proteoglycan complex.

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. Hyaluronidase is an enzyme that breaks the (β1→4) linkages in hyaluronic acid surrounding the ovum, thereby facilitating sperm penetration.

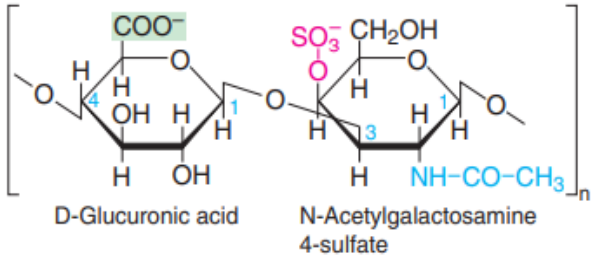
Chondroitin 4-sulfate: is a major constituent of various mammalian tissues (bone, cartilage, tendons, heart, valves, skin, cornea etc.). Structurally, it is comparable with hyaluronic acid.

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 C5 of D-glucuronic acid to form L-iduronic acid,

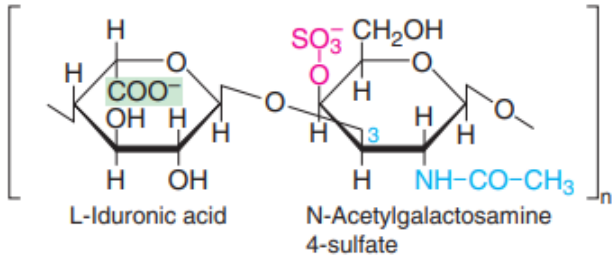
Keratan sulfate: It is a heterogeneous GAG with a variable sulfate content, besides small amounts of mannose, fructose, sialic acid etc. Keratan sulfate essentially consists of alternating units of D-galactosamine and N-acetylglucosamine 6-sulfate.



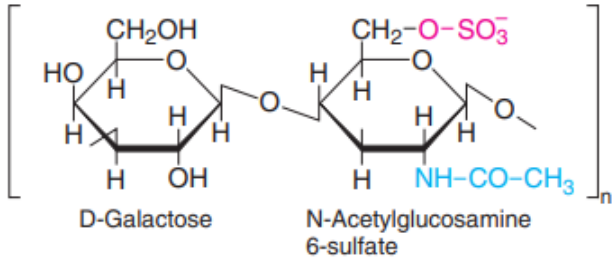
Hyaluronic acid



Chondroitin 4-sulfate



Dermatan sulfate



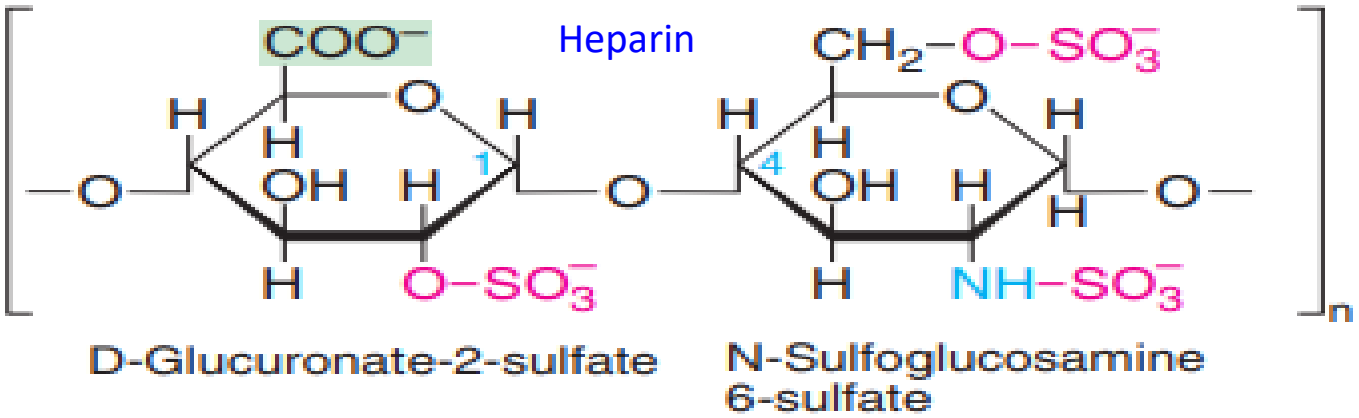
Keratan sulfate

Heparin

➢ It is a **physiological anticoagulant** (prevents blood clotting) present in many tissues, including the **liver, lungs, kidneys, and heart**. Heparin helps in the release of the enzyme lipoprotein lipase which helps in clearing the turbidity of lipemic plasma.

➢ The **glycosidic linkages** within and between the repeating units are of the **(α 1→4)** type.

➢ **Sulfate groups** are essential for its **biological activity**; they are attached to the **nitrogen atom** and to the **primary hydroxyl group at carbon 6** of glucosamine.



A summary of glycosaminoglycans – composition, distribution and functions

Glycosaminoglycan	Composition	Tissue Distribution	Function(s)
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 maintain the structure and shape of tissues
Heparin	D-Glucuronate-2-sulfate, N-sulfoglucosamine-6-sulfate	Blood, lungs, liver, kidneys, spleen	Acts as an anticoagulant
Dermatan sulfate	L-Iduronic acid, N-acetylgalactosamine-4-sulfate	Blood vessel valves, heart valves, skin	Maintains the shape of tissues
Keratan sulfate	D-Galactose, N-acetylglucosamine-6-sulfate	Cartilage, cornea, connective tissues	Keeps the cornea transparent