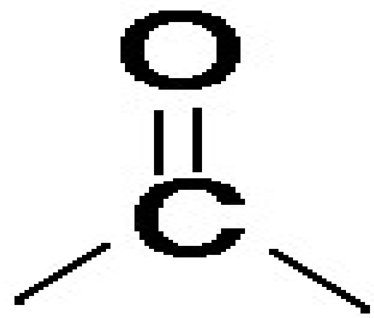
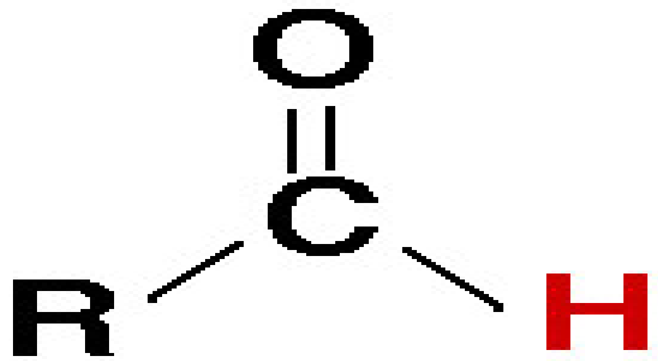
Carbohydrates of biological importance

By

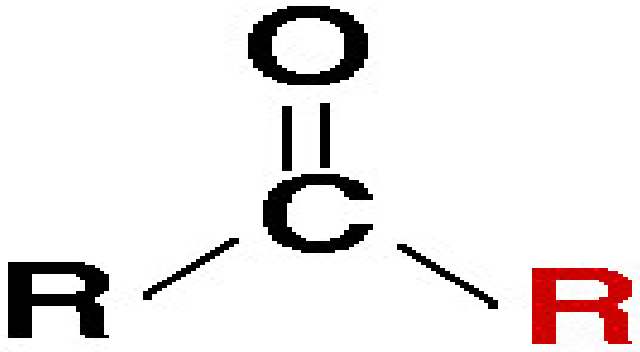
Dr. Walaa Bayoumie El Gazzar



Carbonyl group



Aldehyde



Ketone

where R can be a carbon-containing substituent.

- Carbohydrates are organic compounds composed of carbon, hydrogen, and oxygen.
- Carbo=carbon, hydrates=hydrogen and oxygen in their proportion in water H_2O
- They generally have the common formula **$(CH_2O)_n$** where the least number of n=3
- They are considered as **polyhydroxyketones** or **polyhydroxyaldehydes**

Classification of Carbohydrates:

- **Monosaccharides**: contain one sugar unit.
- **Disaccharides**: contain two sugar units.
- **Oligosaccharides**: contain 3-10 sugar units.
- **Polysaccharides**: contain more than 10 sugar units.

I. Monosaccharides

- **Definition:** They are simple sugars that cannot be hydrolyzed into smaller one.
- **Classification of monosaccharides:**
  - **According to the number of carbon atoms: e.g.**

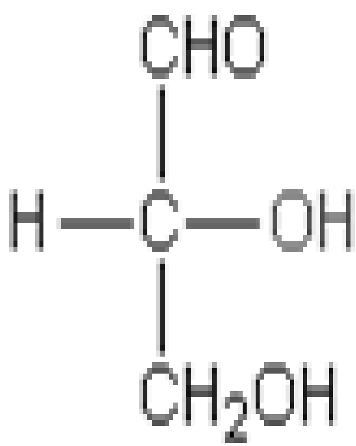
1) **Trioses:** contain three carbon atoms.

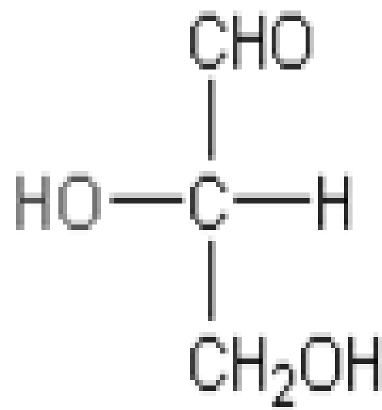
2) **Tetroses:** contain four carbon atoms.

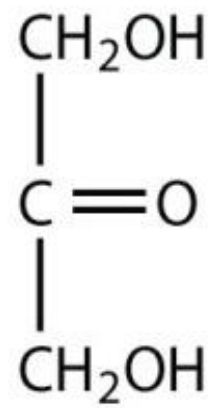
3) **Pentoses:**contain five carbon atoms.

4) **Hexoses**: contain six carbon atoms.

- **Examples of trioses are:** glyceraldehyde and dihydroxyacetone.(They are intermediates in the break down of glucose).







D-Glyceraldehyde

L- Glyceraldehyde

Dihydroxyacetone

D & L denote the absolute configuration. i.e. D means that OH group on the subterminal carbon atom is at the right but L means OH group on the subterminal carbon atom is at the left.

- **According to the active sugar group and number of carbon atoms:**

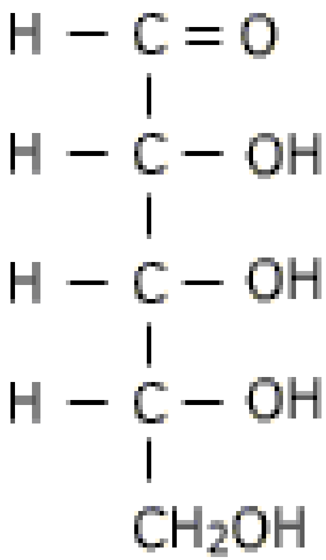
Number of carbons	Aldo-sugars (e.g.)	Keto-sugars (e.g.)
3C	Glycerose	Dihydroxy acetone
4C	Erythrose	Erythrulose
5C	Ribose	Ribulose
6C	Glucose	Fructose

- Most physiologically important isomers that can be utilized in the body are the D form

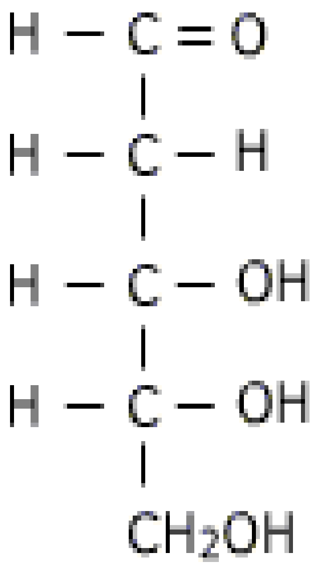
- Some sugars occur naturally in their L-forms:

- L- arabinos and L-fucose which are components of glycoprotein.
- L-xylulose is an intermediate in metabolism and can be utilized by isomerization into D-form.
- L- arabinos is an aldopentose present in some fruits such as cherries, grapes, plums, and prunes. Ingestion of large quantaties of these fruits leads to the appearance of L-arabinose in the urine, a condition called **alimentary pentosuria**.

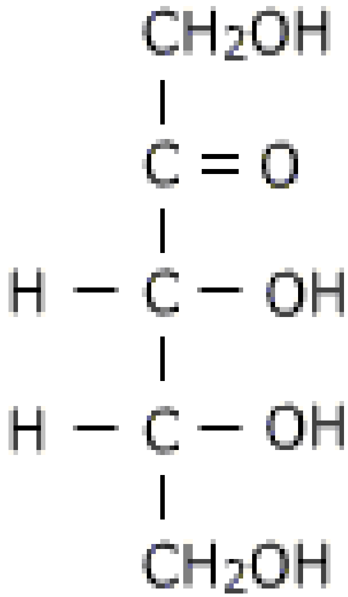
- **Examples of pentoses are:**
- aldopentoses: ribose and deoxyribose, ketopentose: ribulose



D-Ribose



D- deoxyribose

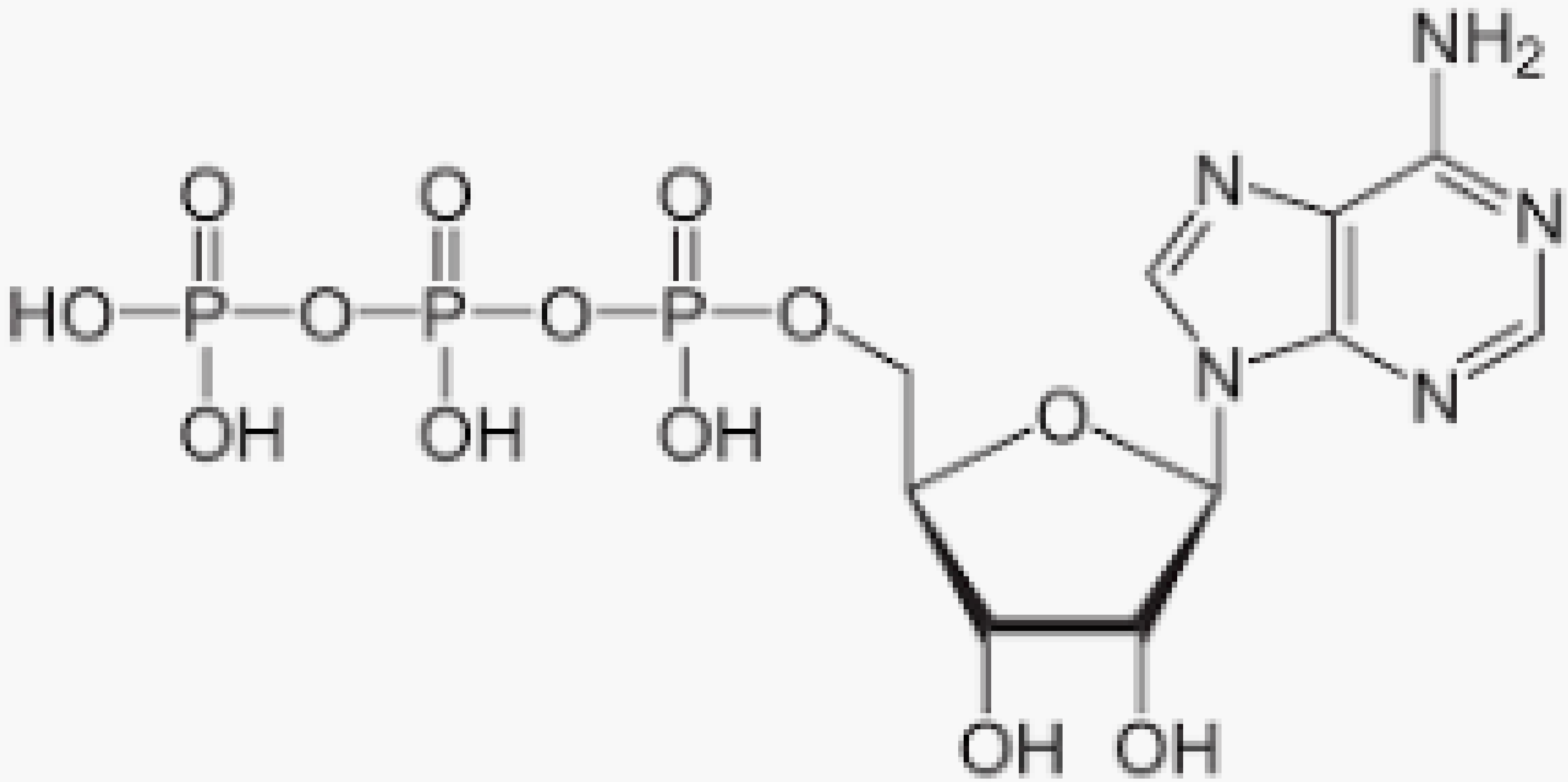


D-Ribulose

Functions of pentoses:

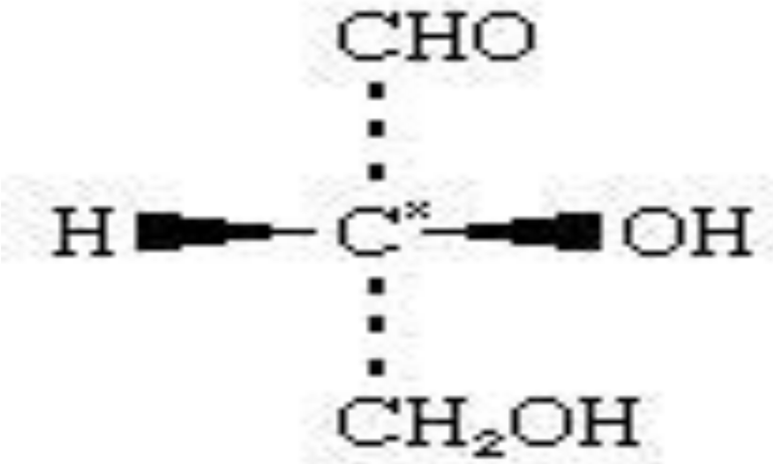
- Ribose and deoxyribose enter in the structure of nucleic acids RNA and DNA.
- Ribose enters in the structure of ATP, GTP and other high energy phosphate compounds.
- Ribose enters in the structure of coenzymes NAD,NADP and flavoproteins.
- Ribose phosphate and ribulose phosphate are intermediates in pentose phosphate pathway (a minor pathway for glucose oxidation).
- They are components of some vitamins (ribitol in vitamin **B2)**

ATP

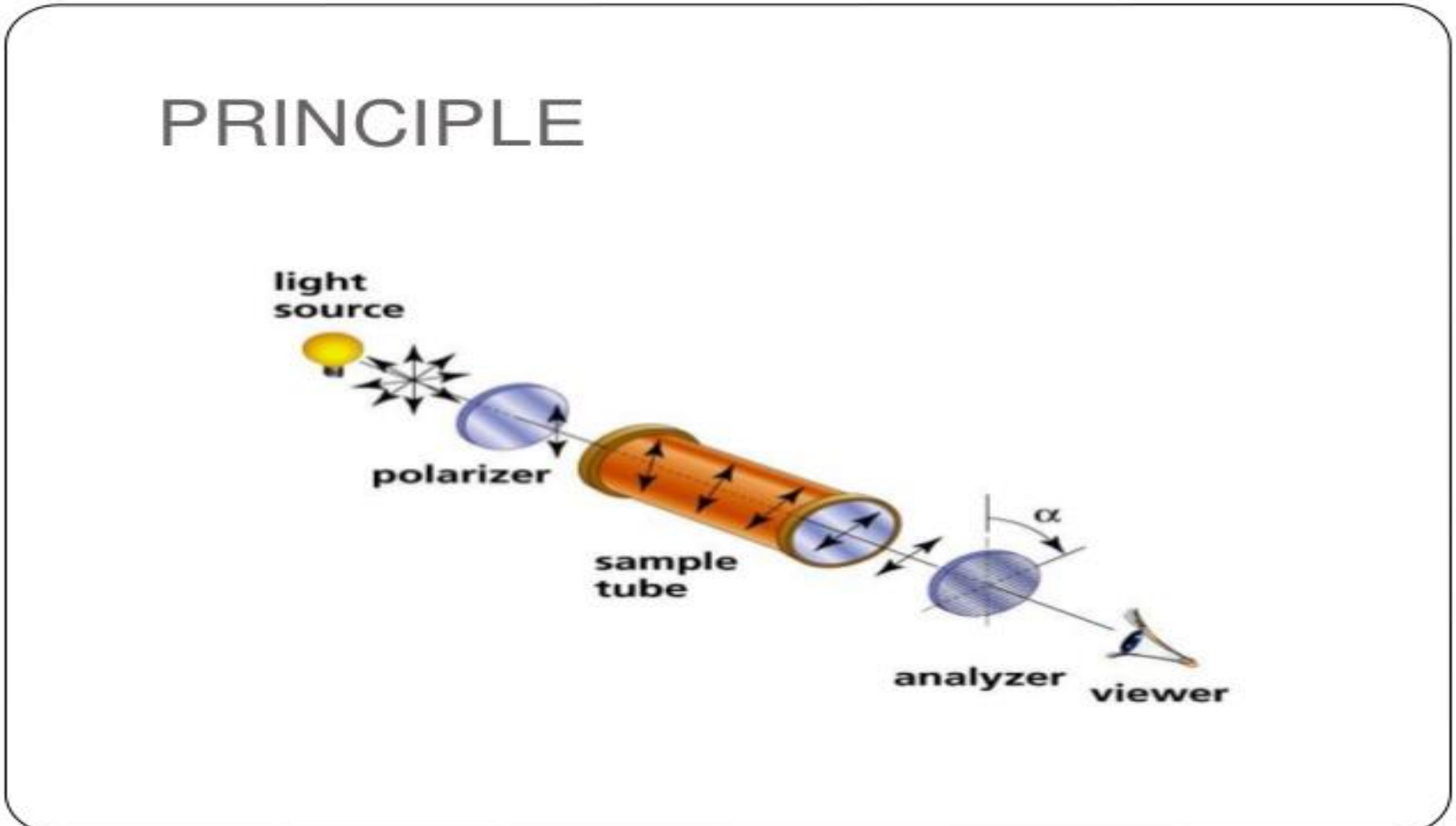


Asymmetric carbon atom:

- It is the carbon atom to which four different groups or atoms are attached. Any substance containing asymmetric carbon atom has optical activity & optical isomerism

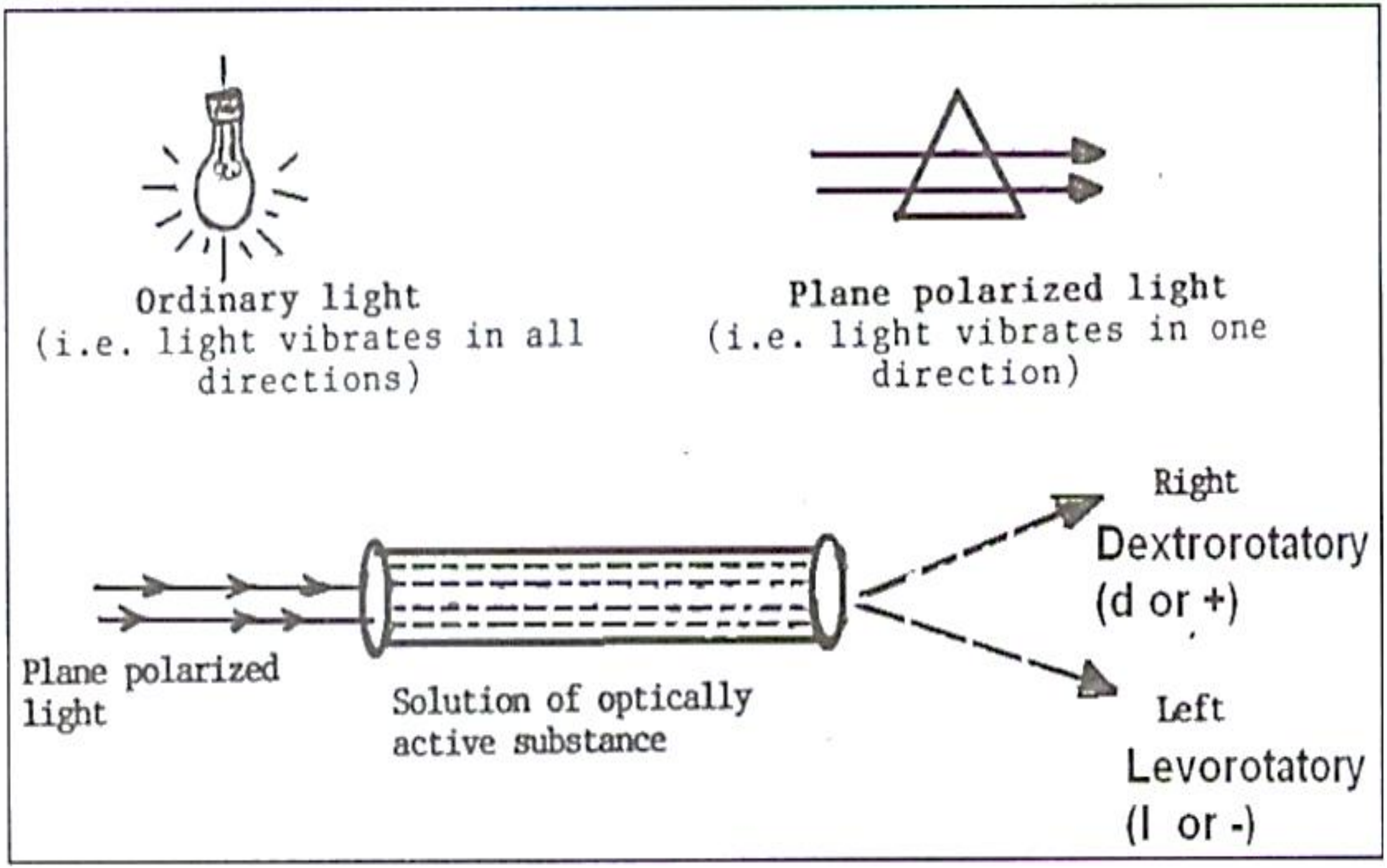


- A **polarimeter** is a scientific instrument used to measure the angle of rotation caused by passing polarized light through an optically active substance.



Optical activity

- It is the ability of substance to rotate plane polarized light (P.P.L) either to the right or to the left.
- If the substance rotates plane polarized light (light vibrate in one direction) to the right it is called: **dextrorotatory** or d or **(+)**.
- If it rotates plane polarized light to the left it is called **levorotatory** or **l** or **(-)**.
- Glucose contains 4 asymmetric carbon atoms. It is dextrorotatory so it is named **dextrose**. Fructose contains 3 asymmetric carbon atoms. It is levorotatory so it is called **levulose**.



Ordinary light
(i.e. light vibrates in all directions)
Plane polarized light
(i.e. light vibrates in one direction)
Right
Dextrorotatory
(d or +)
Plane polarized light
Solution of optically active substance
Left
Levorotatory
(l or -)

- The optical rotation is proportional to the concentration of the optically active substances in solution. Polarimetry may therefore be applied for concentration measurements
- Concentration and purity measurements are especially important to determine product or ingredient quality in the food & beverage and pharmaceutical industries.

Optical isomerism

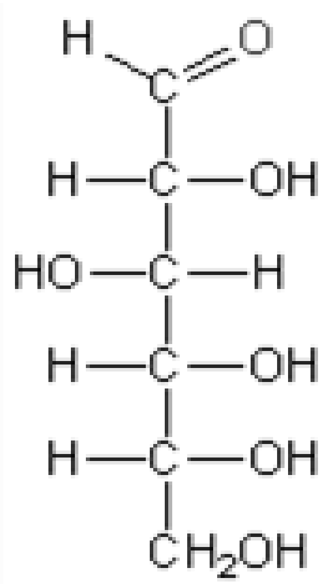
- It is the ability of substance to present in more than one form (isomer).
- A substance containing one asymmetric carbon atom has 2 isomers.
- A substance containing 2 or more asymmetric carbon atoms can exist in a number of isomers = 2^n where n is the number of asymmetric carbon atoms. e.g. glucose has 4 asymmetric carbon atoms so the number of its isomers equal 2^4= 16 isomers.

Epimeric carbon &epimers:

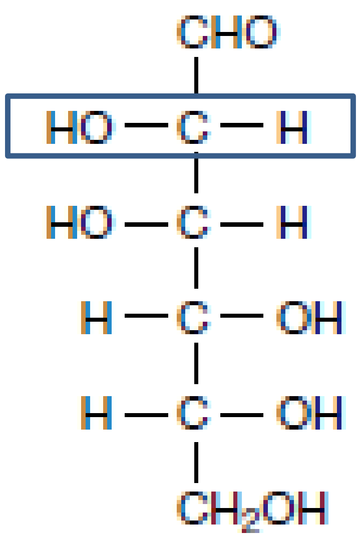
- **Epimers:** These are sugars which differ only in the configuration around a single carbon atom. e.g. Glucose & mannose with respect to C_2. Also, glucose & galactose with respect to C_{4}.
- Or they are optical isomers containing more than one asymmetric carbon atom, all of which identical but only one is different.
- **Epimeric carbon:** is asymmetric carbon atom other than carbon of aldehyde or ketone group, e.g. carbon number 2 in glucose & mannose & carbon number 4 in glucose and galactose.

Examples of hexoses are:

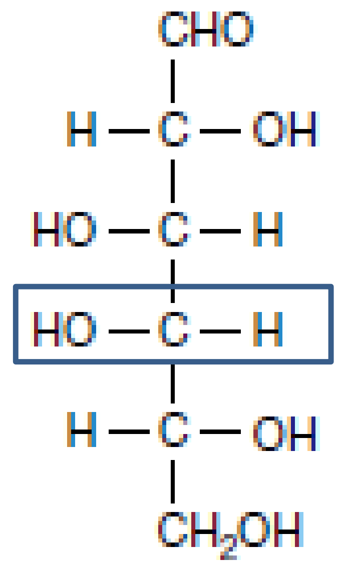
- aldohexoses: glucose, mannose and galactose,
- ketohexoses: fructose



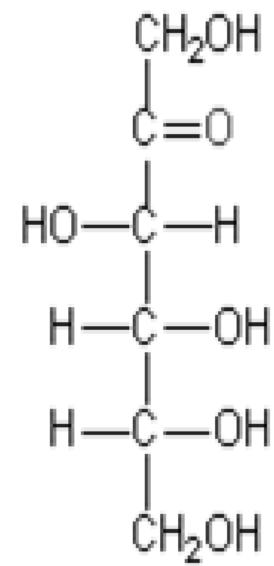
D-Glucose



D-Mannose



D-Galactose



D-Fructose

- **Importance of hexoses:**

D-glucose "grape sugar":

- It is called dextrose (dextro-rotatory).
- It is the most important sugar of carbohydrates.
- It is the main sugar in blood, ranging from 70-110 mg/dl.
- It is one of major sources of energy in the body.
- It is the principle sugar used by the tissues.
- It is widely present in fruits & vegetables associated with fructose.
- It enters in the formation of disaccharides & polysaccharides.
- In the liver & other tissues, it is converted to all carbohydrates in the body e.g. glycogen, galactose, ribose &fructose.
-

D-fructose "fruit sugar":

- It is called Levulose (levo-rotatory).
- It is the main sugar of semen (Source of energy for the sperms).
- It is much reactive & sweeter than glucose.
- It is present in honey & fruits.
- It enters in the formation of sucrose.
- In the liver, it is converted into glucose.

D-galactose"milk sugar":

- It is synthesized in mammary gland to make the lactose of milk.
- In the liver, it can be converted into glucose.
- It enters in the structure of **glycolipids** which are found in many tissues especially in C.N.S.

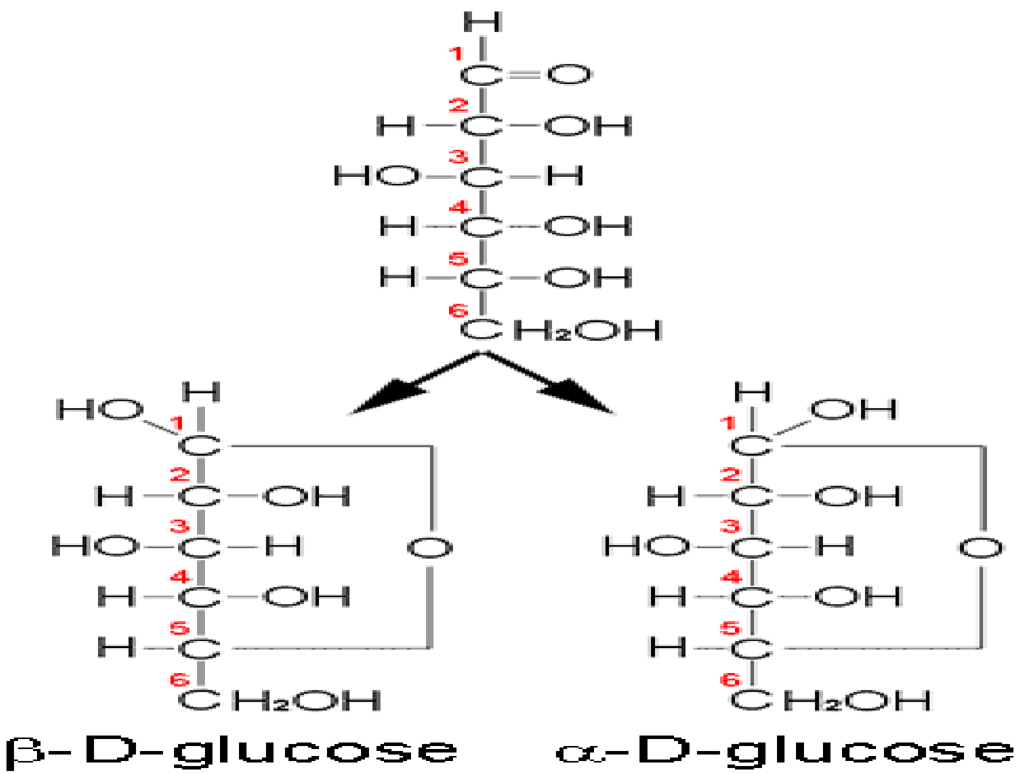
D- mannose:

- It is a constituent of many glycoproteins.

Monosaccharides occur in cyclic form:

- Monosaccharides having five or more carbon atoms usually occur in aqueous solution as **cyclic ring structures** in which the carbonyl group (C1 in aldehyde or C2 in ketone) forms a covalent bond with the oxygen of a hydroxyl group along the chain.
- Therefore C_1 becomes asymmetric carbon atom.
- If the OH group is on the right side it is **(α)** sugar while if the OH group is on the left side it is **(β)** sugar.

- The first carbon is called **anomeric carbon atom** &the α and β sugars are called anomers.
- **Anomers:** These are sugars which have the same configuration but differ only in the arrangement of groups or atoms **around the carbon atom of active sugar group.**

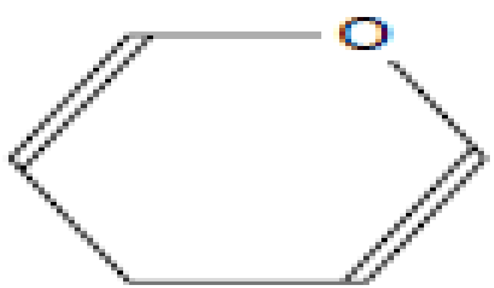


- **Anomeric carbon:** is asymmetric carbon atom obtained from active carbonyl sugar group: carbon number 1 in aldoses & carbon number 2 in ketoses.

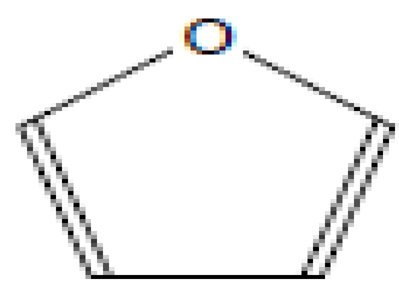
- Two types of cyclic ring structure can be formed:

Pyran ring: a 6 membered ring having 5 carbons.

Furan ring: a 5 membered ring with only 4 carbons.

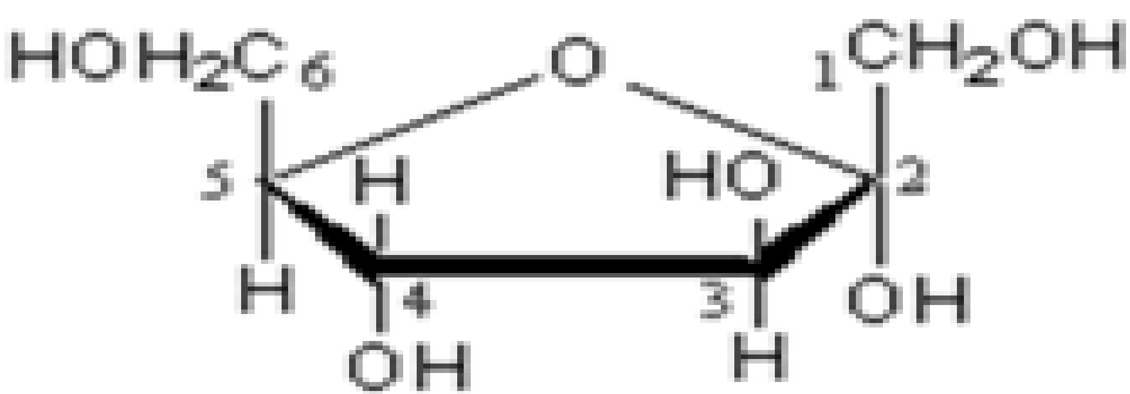


Pyran Form



Furan Form

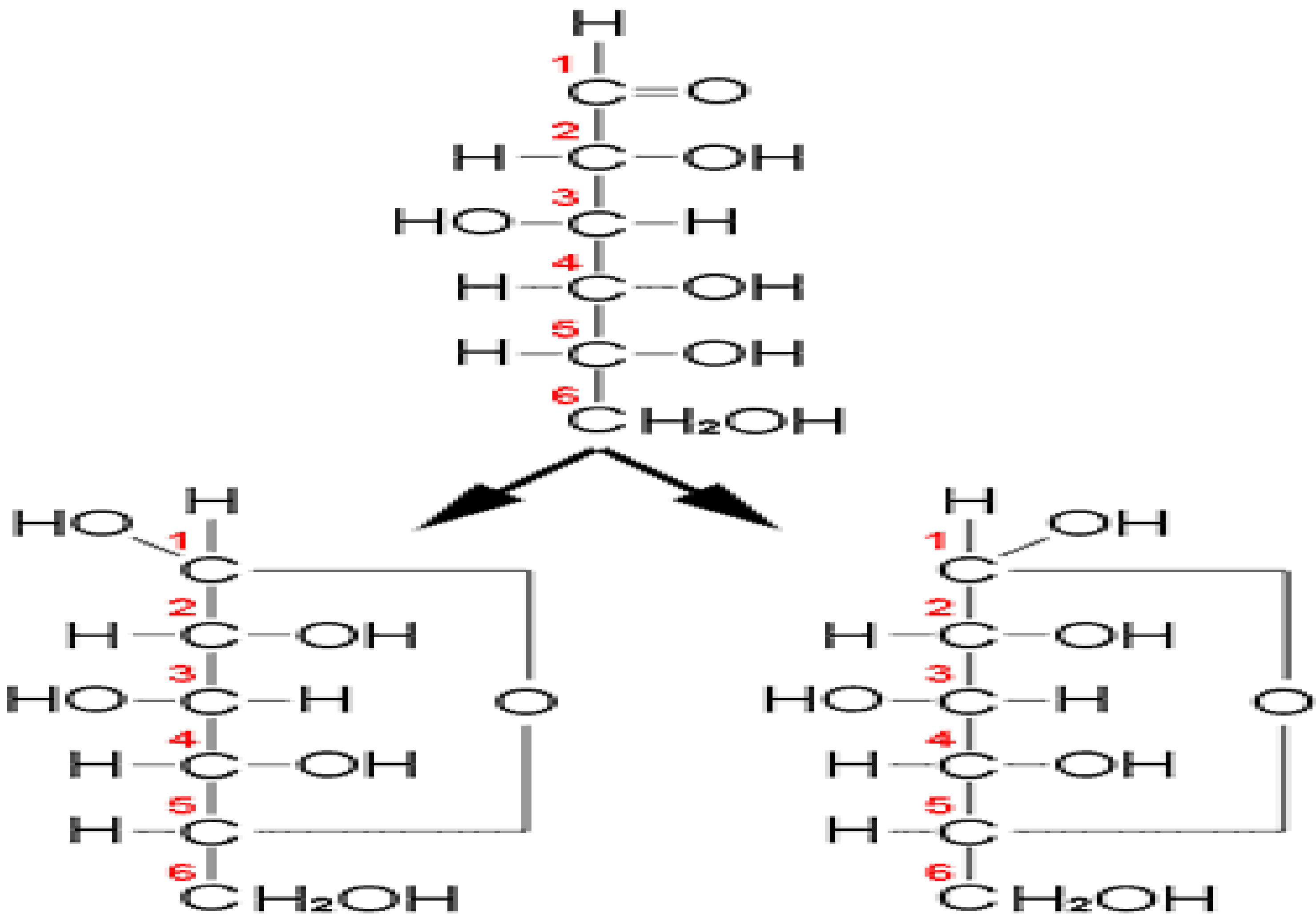
- **Aldohexoses** exist mainly in the six membered pyranose ring which is thermodynamically more stable than the furan ring.
- When fructose is linked to other sugars or when it is phosphorylated it assumes the furanose form. When it is free in solution, it is present in the pyranose form.



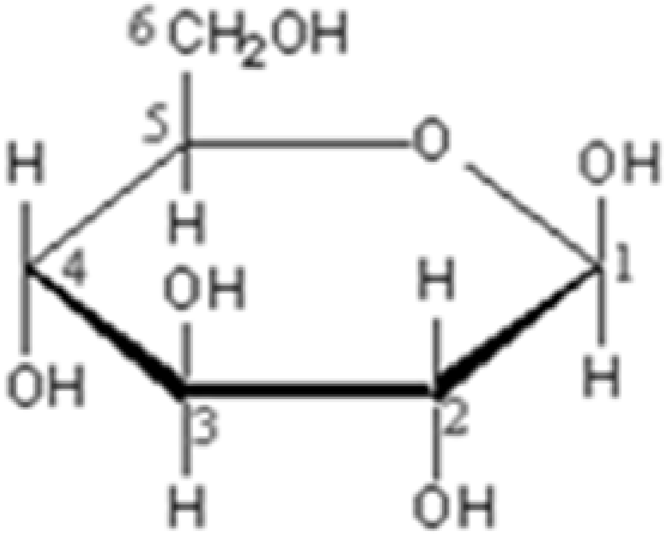
Haworth configuration of cyclic sugars

Cyclic structure of sugars may be present in the form of Haworth formula, the arrangement of H & OH groups around carbon atoms is as follows :

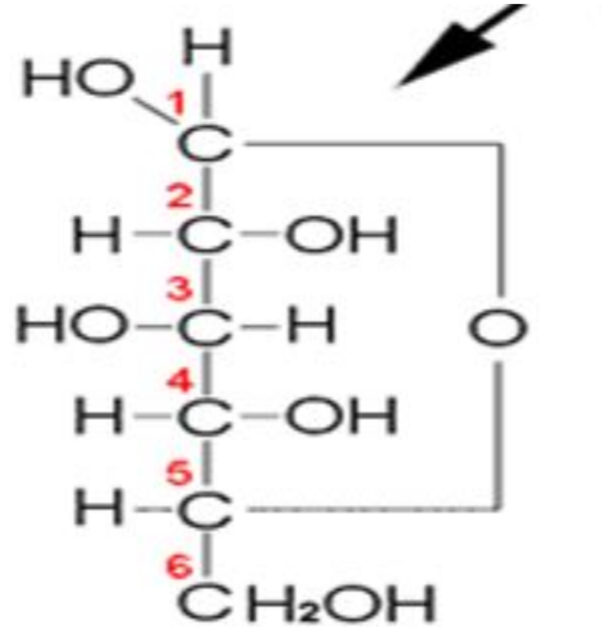
- All the OH groups on the right side in old ring structure are written downwards in Haworth formula.
- All the OH groups on the left side in old ring structure are written upwards in Haworth formula.
- C_6 is outside the ring.



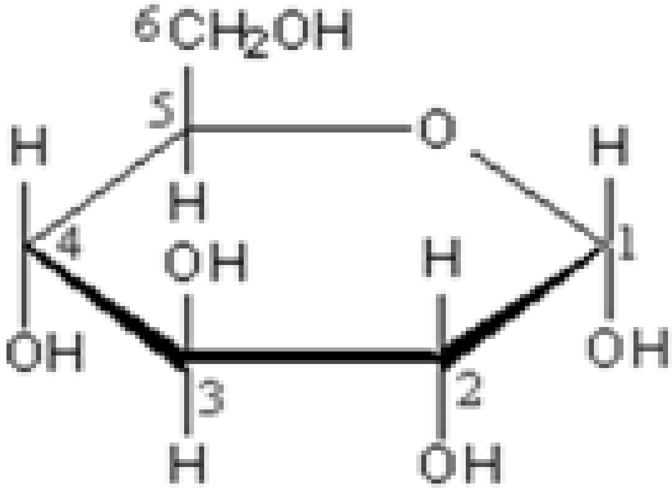
β-D-glucose α-D-glucose



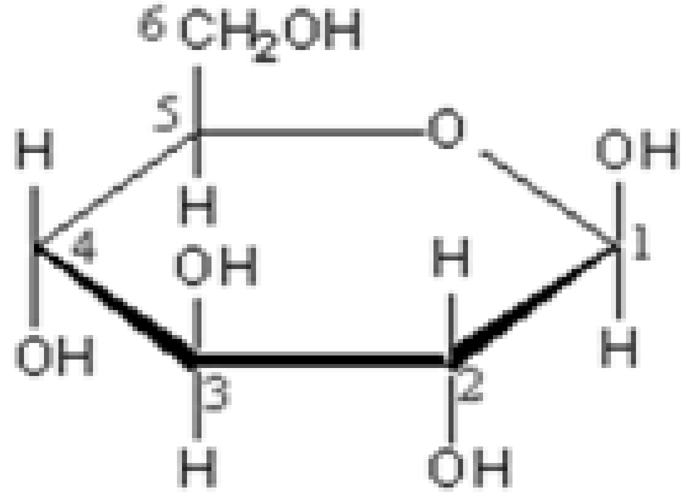
β-D-Glucopyranose



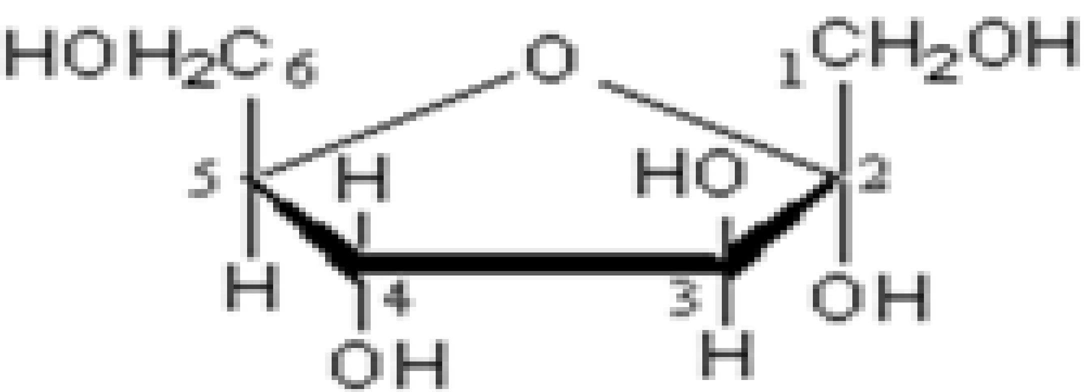
β-D-glucose



α-D-Glucopyranose

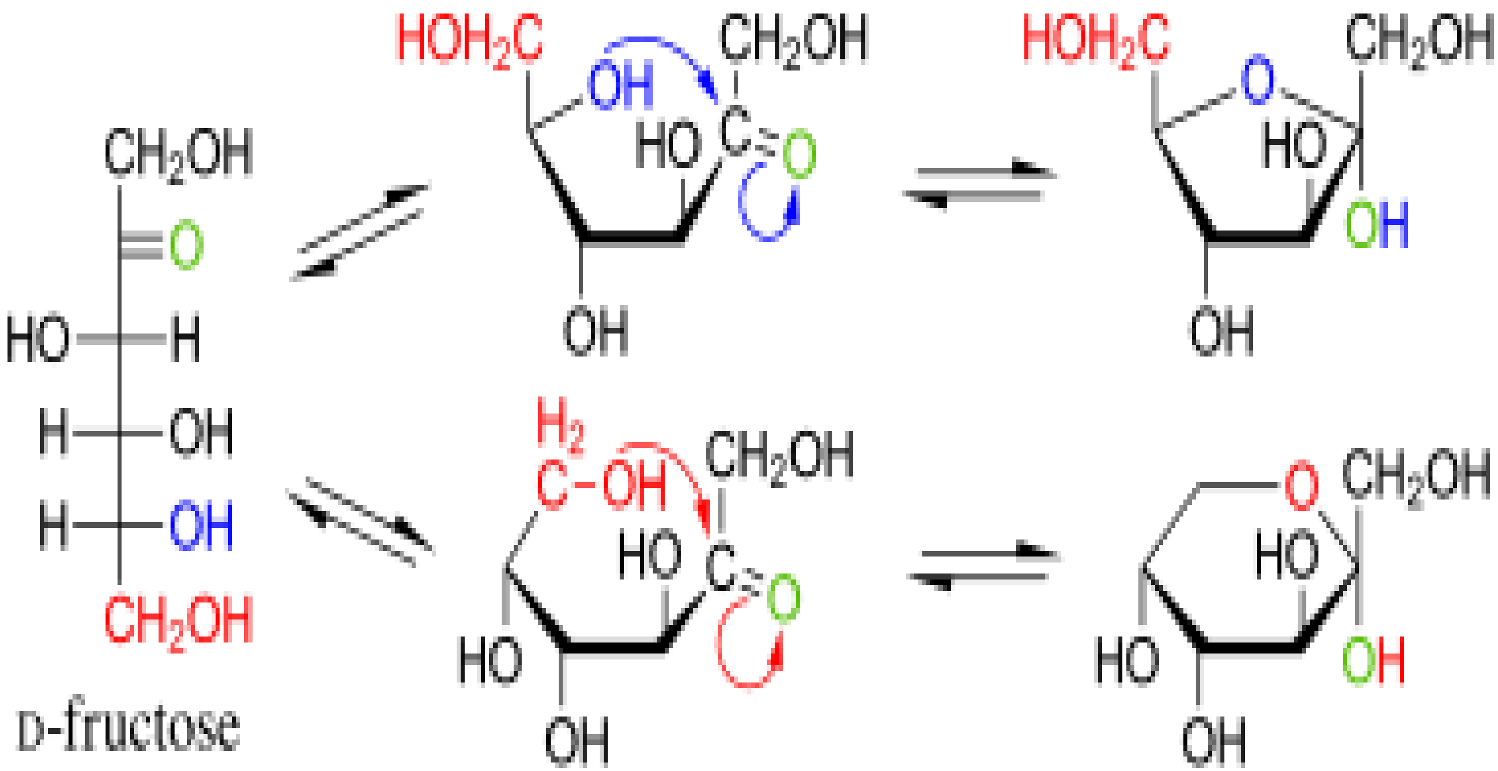


β-D-Glucopyranose



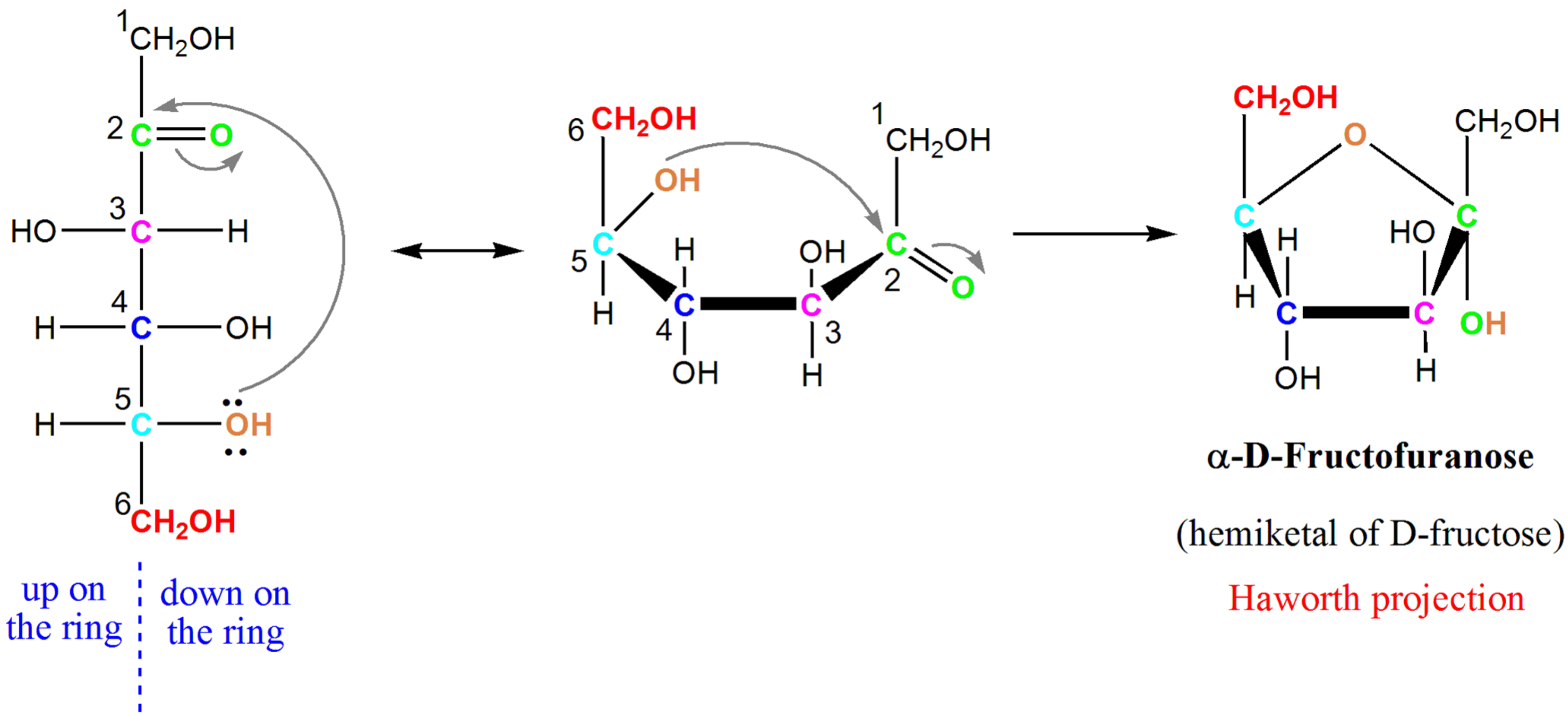
α-D-Fructofuranose

α-D-fructofuranose



D-fructose

α-D-fructopyranose



D-Fructose

Fischer projection

α-D-Fructofuranose

(hemiketal of D-fructose)

Haworth projection

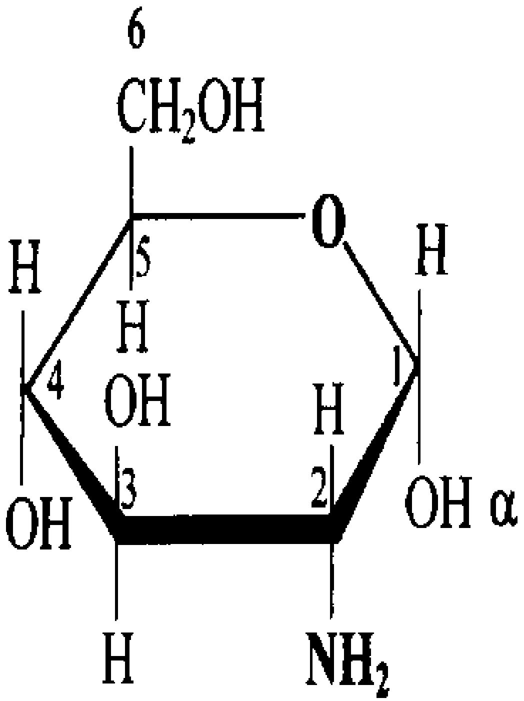
Physiologically important derivatives of monosaccharides

1-Amino sugars:

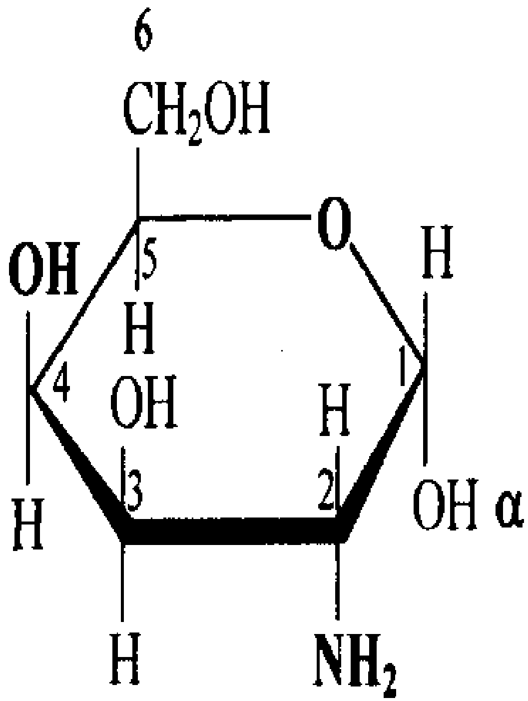
In these sugars, the hydroxyl group attached to carbon number 2 is replaced by an amino group.

Amino sugars are constituents of glycoproteins & glycosaminoglycan.

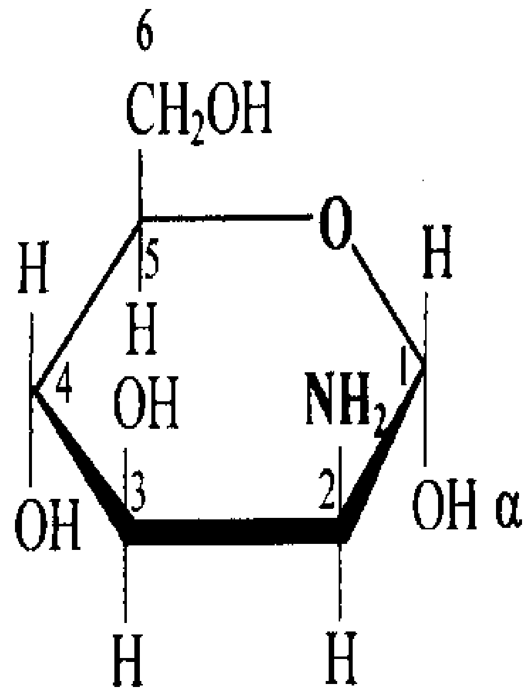
Examples:
glucosamine,galactosamine&mannosamine.



α,D-Glucosamine



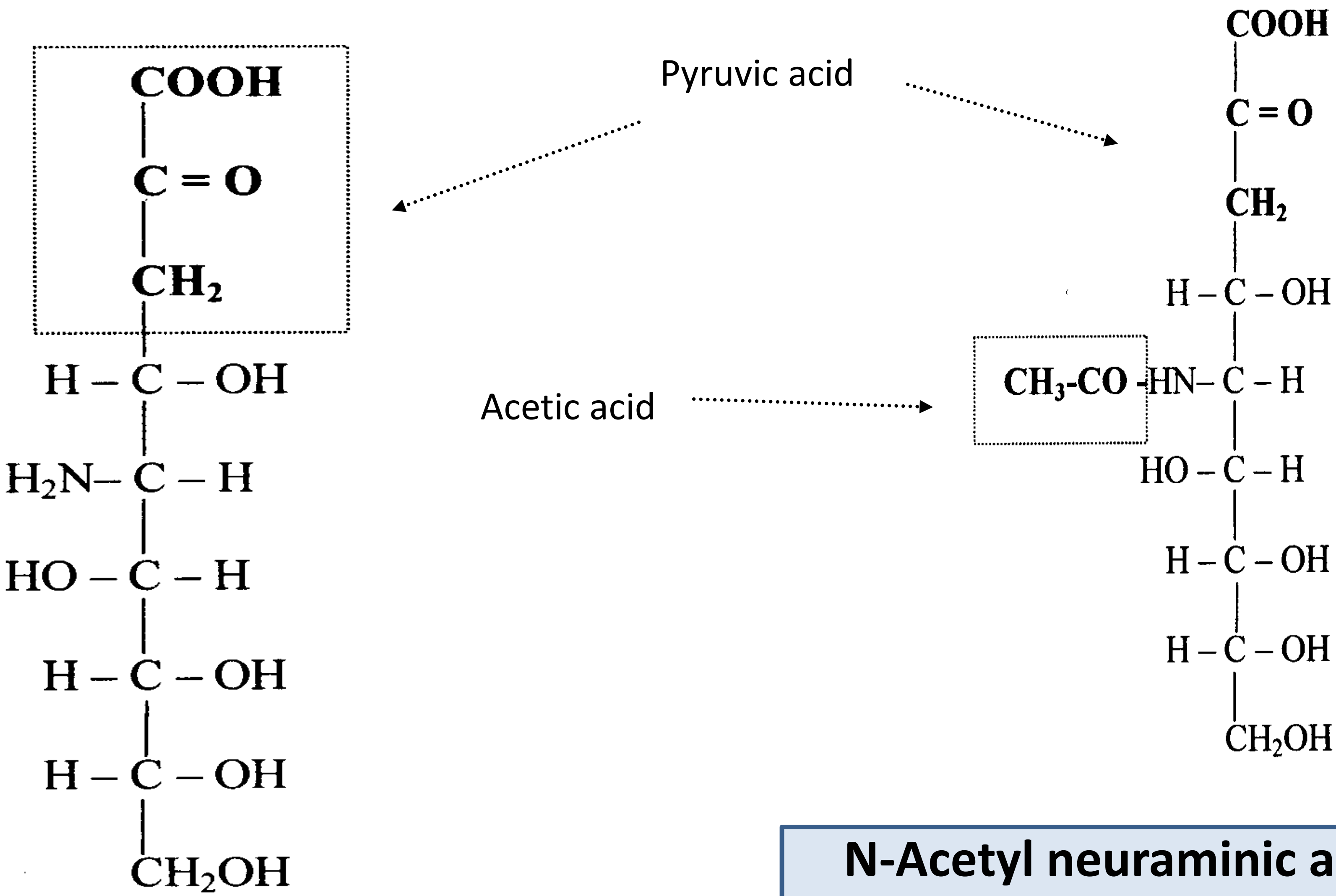
α, D-Galactosamine



α, D-Mannosamine

2-Amino sugar acids

- They are a condensation of amino sugars & some acids. They are occurring in glycoproteins.
- Examples include **neuraminic acid** & **sialic acid** (NANA).
- Neuraminic acid produced as a result of condensation of pyruvic acid and mannosamine.
- Neuraminic acid is unstable and so, it is present in an acetylated form called sialic acid.



Neuraminic acid

N-Acetyl neuraminic acid (NANA) (Sialic acid)

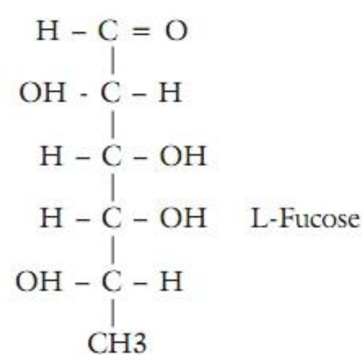
- Lactic acid added to glucosamine gives muramic acid which is a component of the cell wall of some bacteria.

3-Deoxysugars

- These are sugars in which an –OH group is replaced by a hydrogen atom.
- The only important examples are:

-D-2-deoxyribose, which is found in DNA .

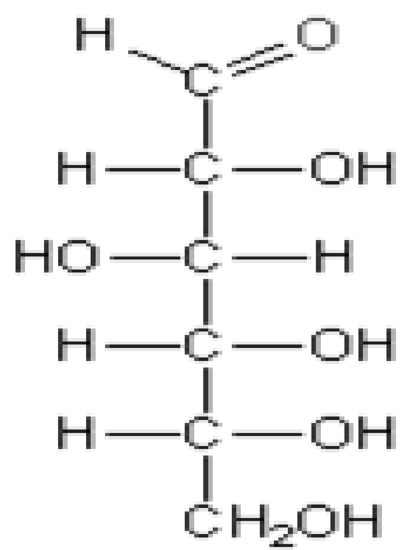
-L- fucose (6-deoxy-L-galactose) is a constituent of cell membrane glycoproteins and glcolipids and is one of the few monosaccharides that exists in the L- configuration.

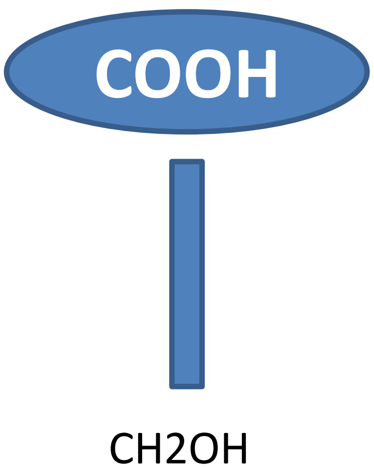


4-Sugar acids

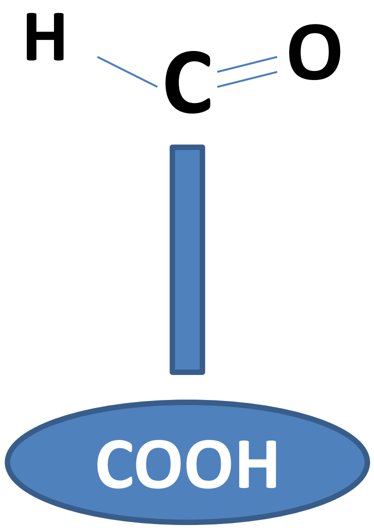
- They are obtained by oxidation of monosaccharides.

- Only the aldehyde carbon (C1) and the terminal hydroxyl group at carbon 6 of aldosugars can be oxidized to form carboxylic group.

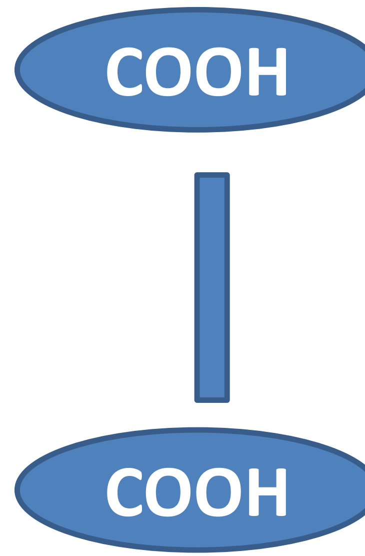




Gluconic acid
(aldonic acid)



Glucuronic acid
(uronic acid)



Glucaric acid
(Saccharic acid)

- The physiologically important sugar acids are aldonic and uronic acids.
- Aldonic acids are formed by oxidation of the aldehyde group of an aldosugars as gluconic acid.
- Uronic acids are formed by oxidation of C6 (the primary alcohol group) as glucuronic acid.
- Aldaric acids these are dicarboxylic acids produced by oxidation of both active carbonyl group & last carbon (saccharic acid).

Importance of sugar acids

- L-ascorbic acid (vitamin C) is a derivative of aldonic acid.
- Glucuronic acid, the uronic acid of glucose, is a component of **glycosaminoglycans**, and is used by the liver for the **detoxification** of aromatic acids and phenols and also involved in the **metabolism of bilirubin.**
- L-iduronic acid (IdUA) is the 5-epimer of D-glucuronic acid and it is a component of glycosaminoglycans.

5-Sugar alcohols

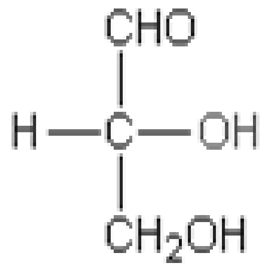
- Reduction of monosaccharides produce the corresponding alcohols.
- They are produced by hydrogenation of aldoses and ketoses.

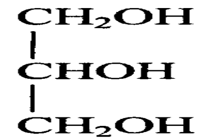
$$-CHO \xrightarrow{2H} -CH_2OH$$

$$C{=}O \xrightarrow{2H} -CHOH$$

<u>There are some sugar alcohols of biochemical important as:</u>

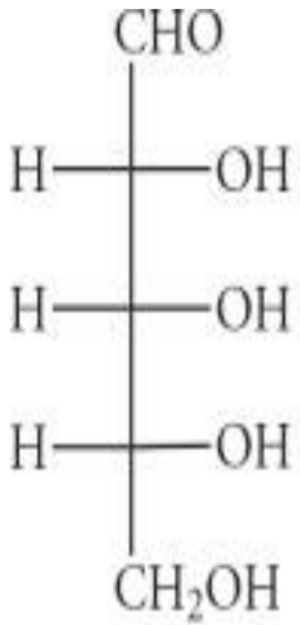
- **Glycerol**:



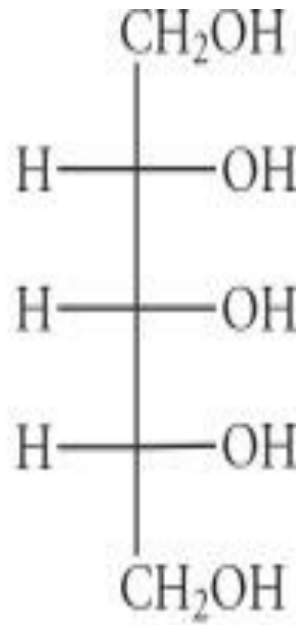


  The alcohol of glyceraldehyde and it is a component of triacylglycerols as well as most phospholipids. (see lipid chemistry).

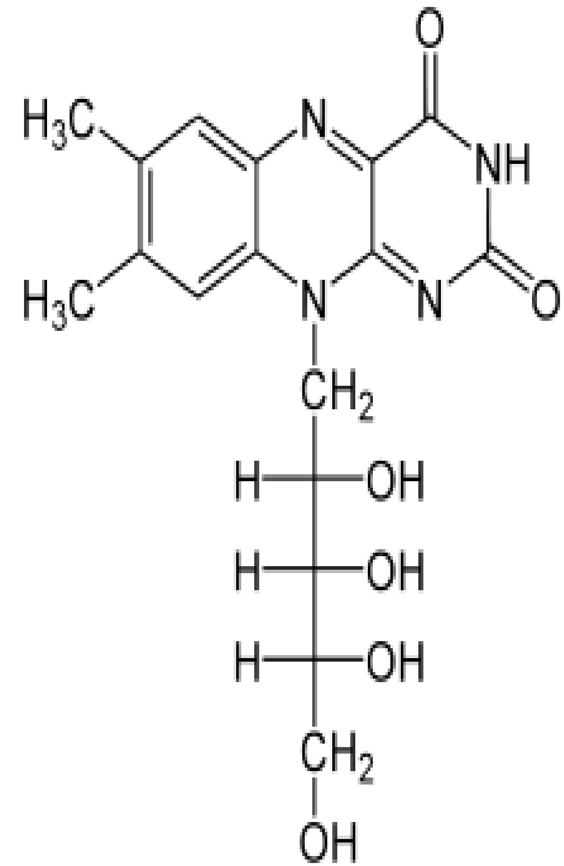
- **Ribitol:** The alcohol of ribose and it is a component of riboflavin (vitamin B2).



ribose



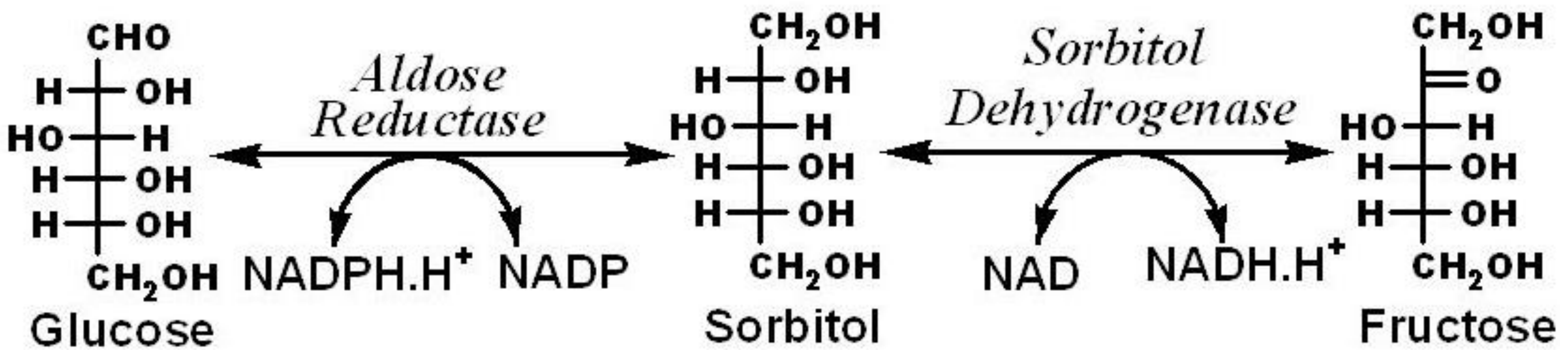
ribitol



riboflavin

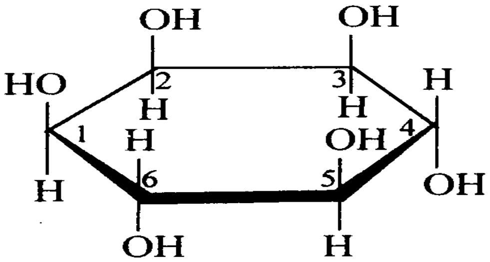
- **Mannitol:** The alcohol of mannose, is given intravenously to produce diuresis and to reduce brain edema after brain operations.

- **Sorbitol:** The alcohol of glucose and it is an intermediate in the conversion of glucose to fructose in the seminal vesicles.



- Conversion of glucose to sorbitol is increased in diabetic subjects. Sorbitol produces osmotic damage of cells which may account for production of diabetic cataract, retinopathy, nephropathy and neuropathy.

- **Myo -Inositol:**



-Sugar alcohol synthesized from glucose-6-phosphate (G-6-P). It is abundant in brain and other mammalian tissues (in humans most inositol is synthesized in the kidneys)

-it is found in animal tissues in the free state as well as in the form of the phospholipid

-It is a constituent of certain phospholipids and hence its role in the mobilization of fats from the liver (lipotropic action i.e. encourages the export of fat from the liver)

-It forms phosphatidyl inositol that enters in structure of plasma membranes and **can serve as a second messenger in action of some hormones i.e. mediates cell signal transduction in response to a variety of hormones)**

❖ ***Second messengers*** *are intracellular signaling molecules released by the cell in response to exposure to extracellular signaling molecules—the* ***first messengers****.*

In plants myoinositol is hexaphosphate (hexaphosphoinositol or **phytic acid**) it inhibits absorption of Ca^{+2}, Mg^{+2}, Mn^{+2}& Fe^{+2} from intestine forming phytate salts and contributes to mineral deficiencies in people whose diets rely highly on bran and seeds, such as occurs in developing countries.

6- sugars phosphates

- They are phosphoric esters of monosaccharides and occur as intermediates in carbohydrate metabolism.
- Sugars are phosphorylated by **kinase enzymes**. The phosphate group can be added to the terminal carbon (glucose-6- phosphate) or to C1 hydroxyl(glucose-1-phosphate) as well as to other carbons (fructose 2,6 bisphosphate).
- Sugar phosphates are negatively charged which results in their intracellular trapping and prevents their diffusion out of the cell.

7- glycosides

- **Glycosidic bond:** It is the bond between a carbohydrate & another compound to form a complex carbohydrate.
- This bond is between **the hydroxyl group of anomeric carbon** of monosaccharide & another compound which may be another monosaccharide to form disaccharide e.g. Maltose, Lactose& Sucrose or **aglycone** i.e. non-carbohydrate to form **glycoside**.

- Digitalis, nucleosides, glycolipids are examples of glycosides composed of a sugar and a non-sugar radical (aglycone).

- Digitalis, a cardiac stimulant, is composed of galactose and a steroid alcohol. They are used in treatment of heart failure.(Stimulate cardiac muscle contraction)

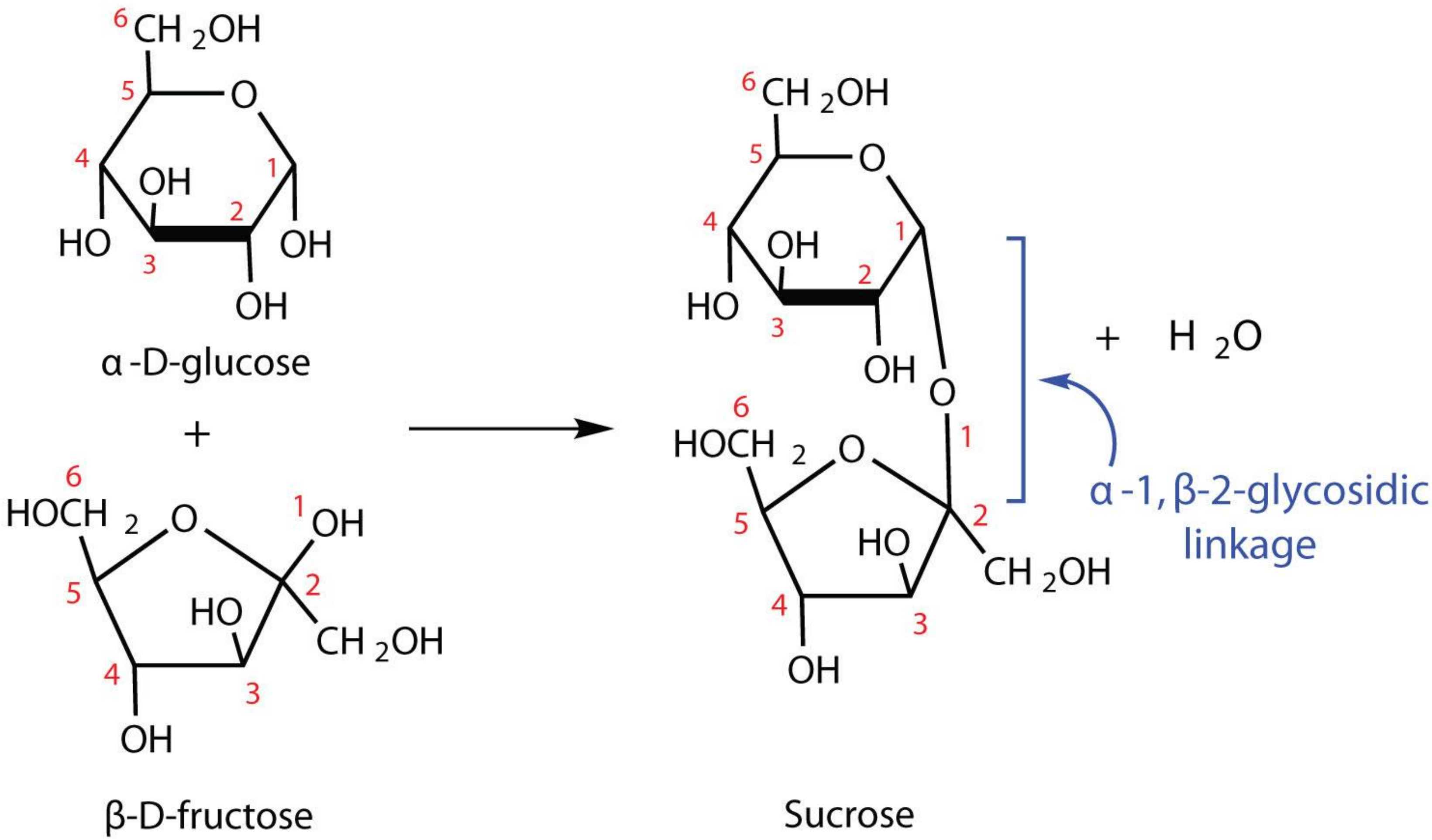
Disaccharides

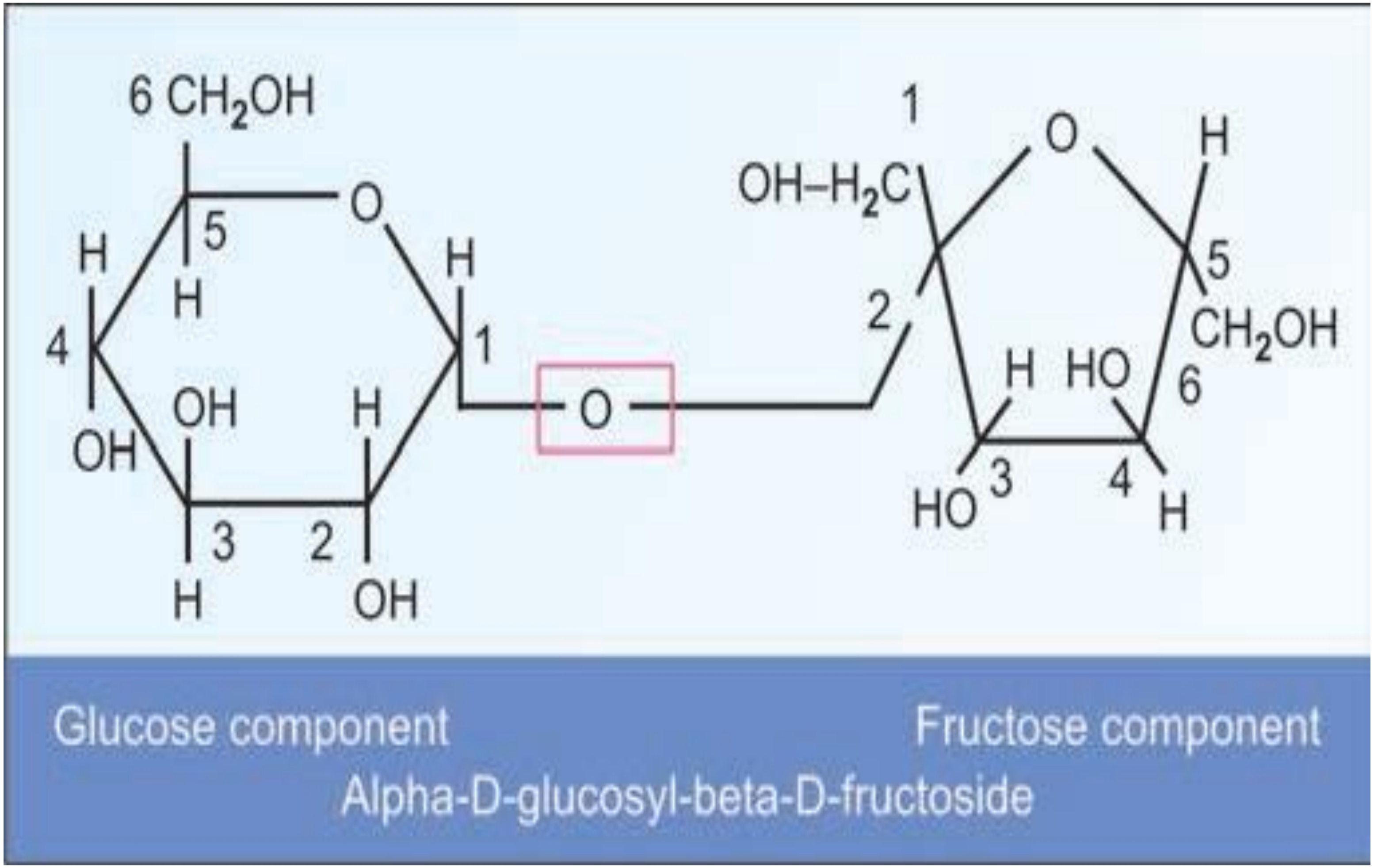
- Disaccharides are sugars which contain two molecules of monosaccharide bound together by **glycosidic bond**.
- The glycosidic bond always involves the anomeric carbon of one participating sugar. The 2nd sugar participates in this bond by using either:
- Its anomeric carbon: in this case, the disaccharide (as sucrose) has no free reactive group.
- A carbon other than the anomeric one. In this case the disaccharide will have a free reactive group and shows reducing character.(Sugars containing free aldehyde or ketone group can reduce other reagents)

- They can be present either in α– or β-form. This occurs if the second monosaccharide residue of the disaccharide contains a free anomeric carbon atom which has the ability to be present in α or β-form.

- The most important disaccharides widely distributed in nature are:

1. **Sucrose.**
2. **Lactose.**
3. **Maltose.**
4. **Isomaltose.**
5. **Cellobiose (formed of two β glucose).**


α -D-glucose
β-D-fructose
Sucrose
+ H 2O
α -1, β-2-glycosidic linkage

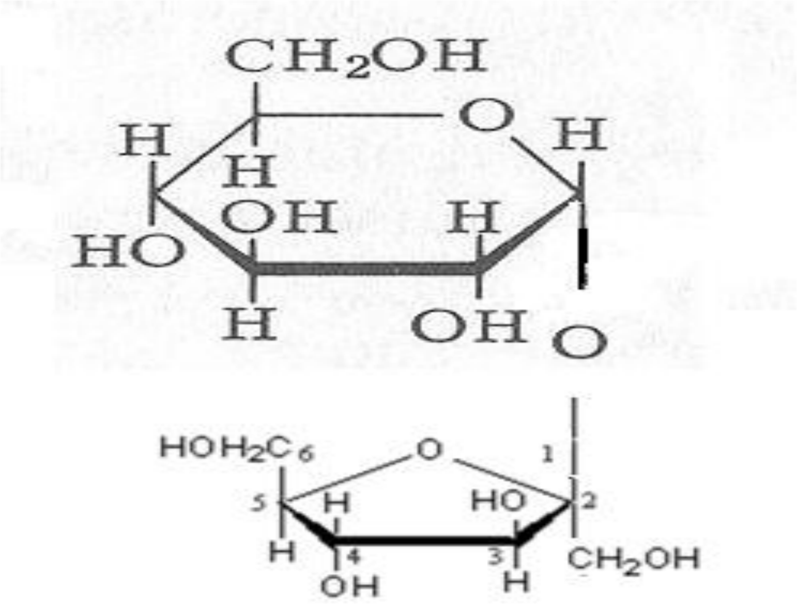


Structure of sucrose (1-2 linkage)

- **1. Sucrose:**
- It is called cane or beet sugar
- It is the common sugar of the table & the kitchen so, it is called table sugar.
- It is formed of α-glucose &β-fructose linked together by <u>**α-1, β-2 glucosidic linkage**</u>

α-D-Glucopyranose

β-D-Fructofuranose



- Sucrose is a **Non-reducing sugar**: because the reducing groups of both glucose & fructose are involved in the linkage between the two sugars. **So,** They cancel the action of each other.

- **Invert sugar:**

* Sucrose before hydrolysis is dextrorotatory and its specific rotation = 66.5°

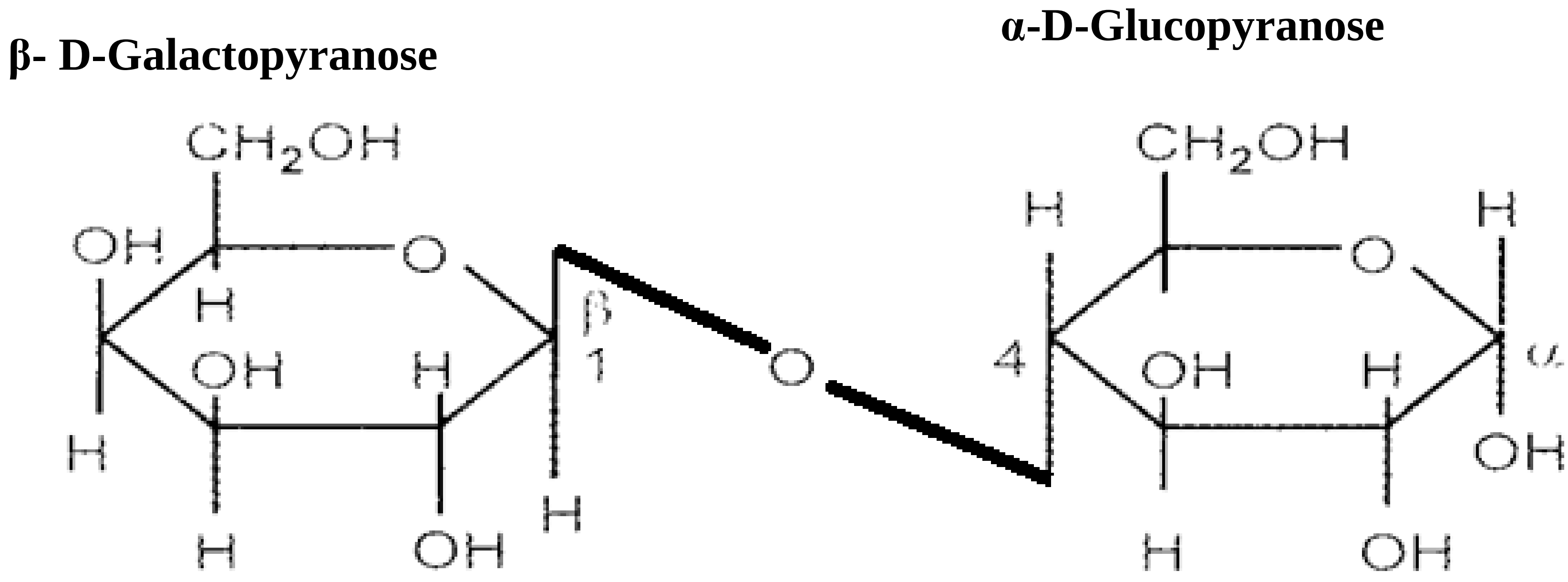
* After hydrolysis by ***sucrase or invertase***, It gives a mixture of D-glucose (α = + 52.5°) and D-fructose (α = - 92°) which is levorotatory.

* This change from dextro (before hydrolysis) to levo- (after hydrolysis) called inversion and the sugar is called invert sugar.(equimolecular mixture of glucose and fructose is called invert sugar)

* Invert sugar is sweeter than sucrose e.g. honey is a chiefly invert sugar.

2. Lactose:

- It is also called milk sugar.
- It is formed of one glucose unit & another one galactose unit.
- Lactose is a **reducing sugar.**
- Usually appear in urine of pregnant female.
- Less sweaty → not block the appetite
- Not fermented → no distension.
- It can be digested by ***lactase enzyme.***
- Deficiency of this enzyme in adults leading to **lactose intolerance** which cause distension & diarrhea.



B-1,4 galactosidic linkage

3. Maltose:

-It is called malt sugar

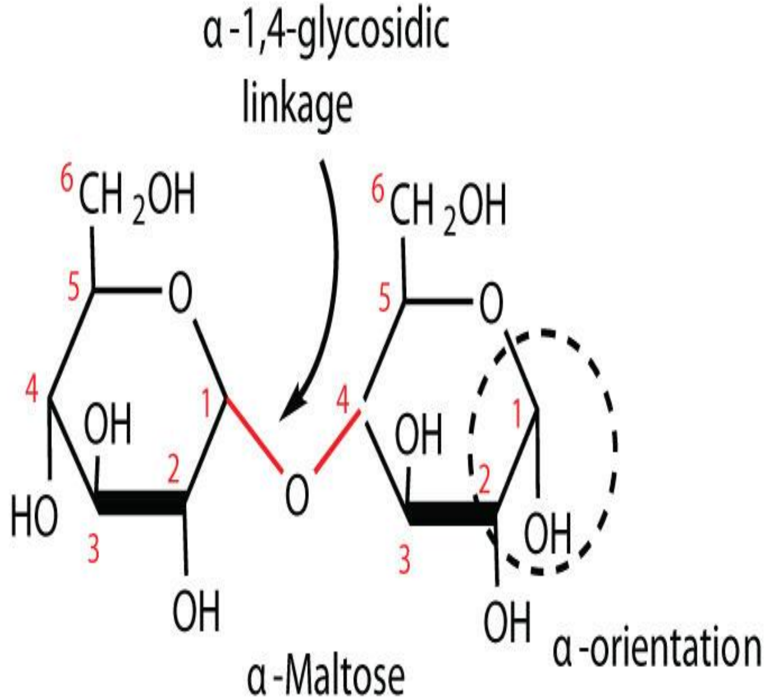
-The main product of digestion of starch by amylase.

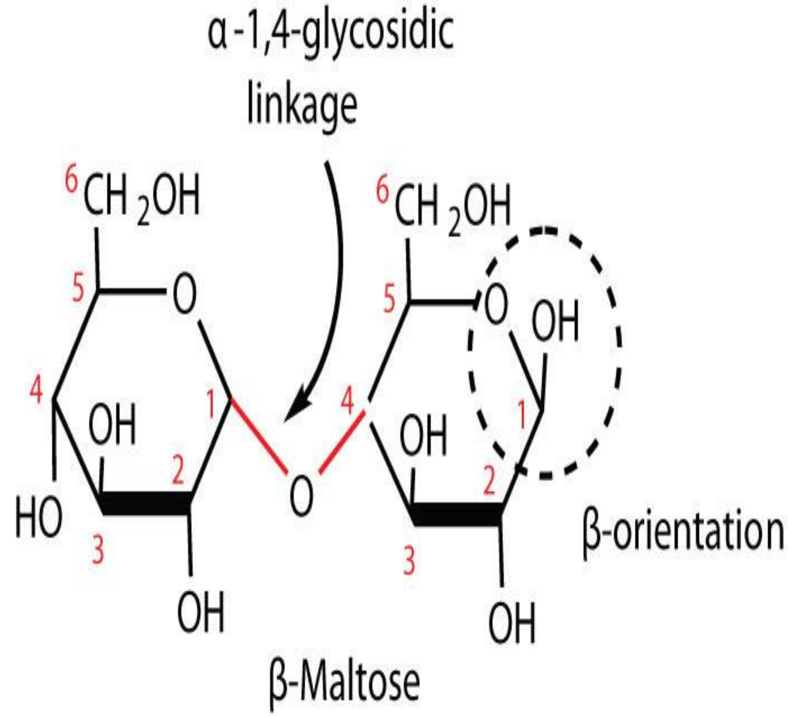
-It is present in 2 forms :

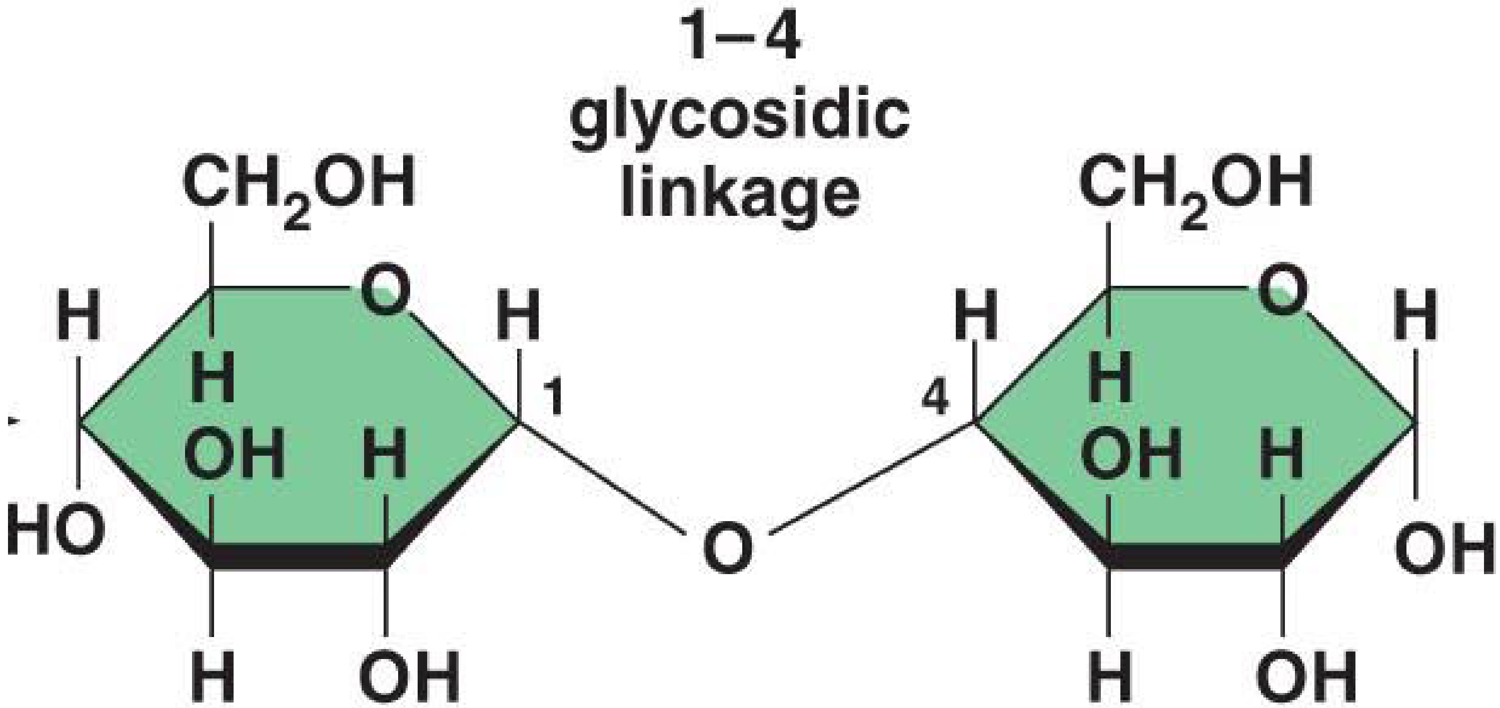
(α- maltose form) = α-glucose + α-glucose

(B-maltose form) = α-glucose + B-glucose

-It is a reducing sugar

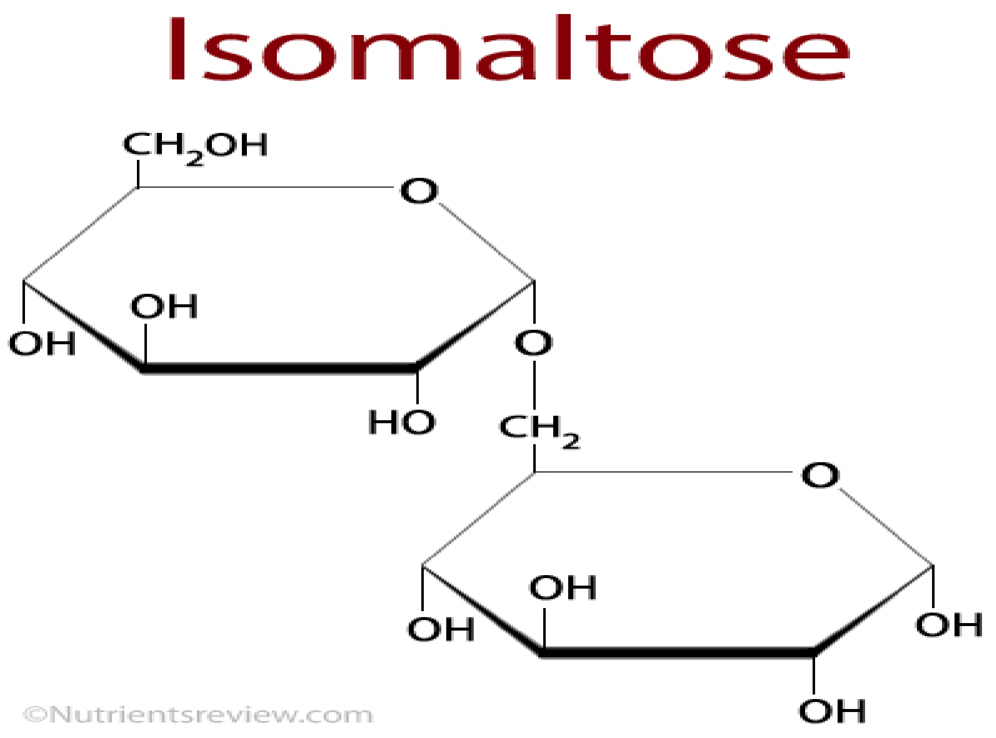

α -1,4-glycosidic linkage
6
CH 2OH
5
O
4
1
OH
HO
2
3
OH
O
6
CH 2OH
5
O
4
OH
1
2
3
OH
OH
α -orientation
α -Maltose


α -1,4-glycosidic linkage
6
CH 2OH
5
O
4
1
OH
HO
2
3
OH
O
6
CH 2OH
5
O
OH
4
OH
1
2
3
OH
β-orientation
β-Maltose


1–4
glycosidic
linkage
CH2OH
O
H
H
1
HO
OH
H
H
OH
O
4
CH2OH
O
H
H
OH
H
OH
H
OH

Maltose

❖ Isomaltose is similar to maltose but the linkage is α-1,6-glucosidic. It is **one of the hydrolysis products of starch and glycogen by amylase.**



Polysaccharides

- **Polysaccharides are carbohydrates of high molecular weight. They are widely distributed in nature. Upon hydrolysis by acid or specific enzyme, monosaccharides or its derivatives are produced.**

- **Polysaccharides are classified chemically & functionally as follows:**
- **1- Homogeneous polysaccharides:** These are polysaccharides which **give single type of sugar on hydrolysis** as D-glucose units or D-fructose units.
- **2-Heterogeneous polysaccharides:** These are polysaccharides which **give on hydrolysis different type of sugars associated with other substances.** **e.g.** D-Glucosamine, D-glucuronic acid, N-acetyl neuraminic acid. etc.

Different homopolysaccharides of biological importance:

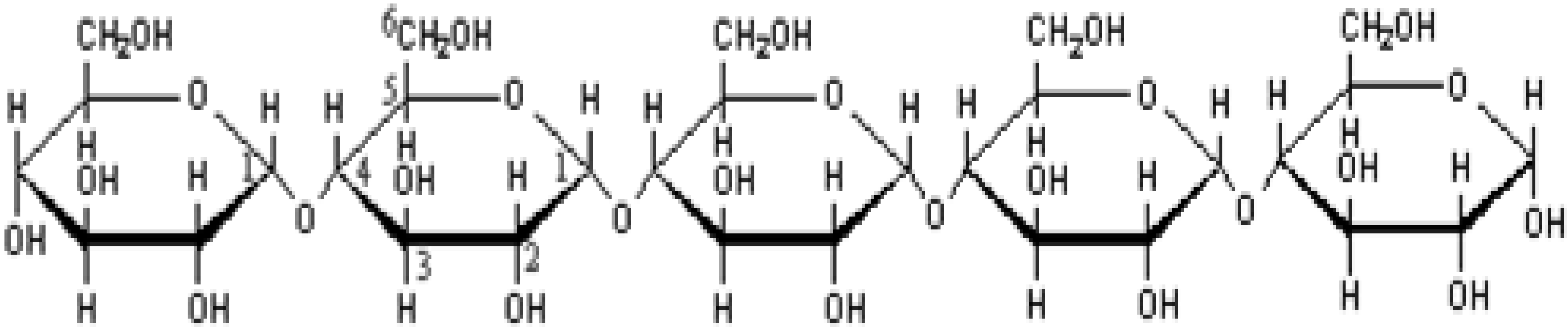
- **1- Starch:**

- It is the storage form of carbohydrates in plants (never present in animals).

- On hydrolysis, it gives only glucose and so it is called **glucosans**.

- It consists of two types of molecules, **amylose** and **amylopectin**

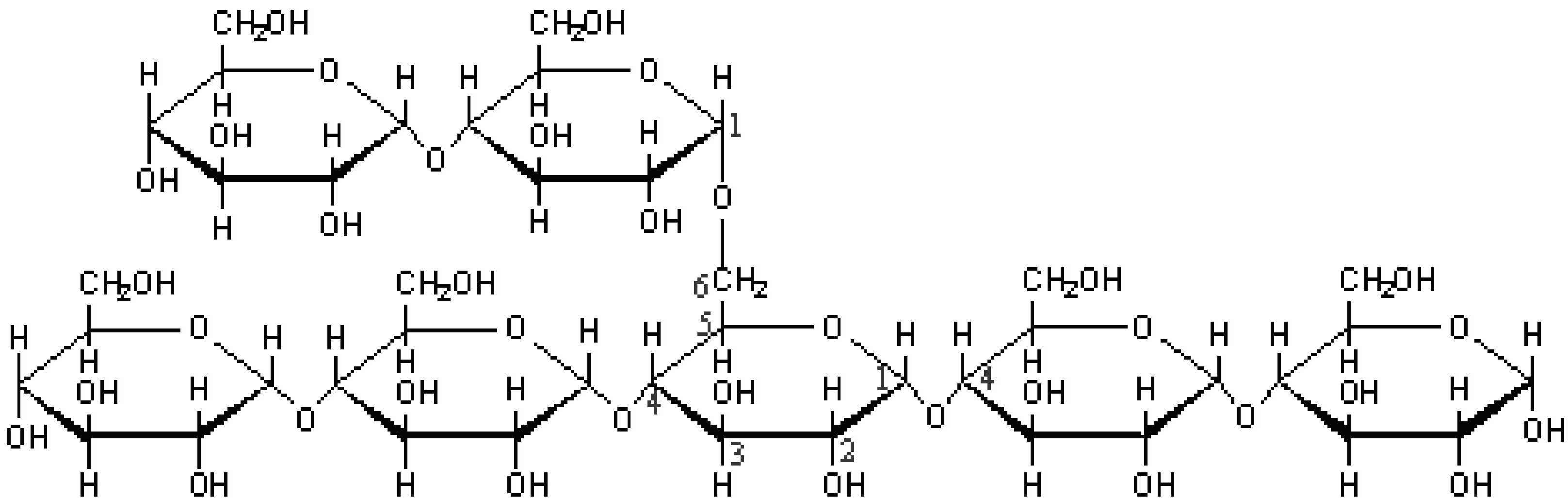
Structure of amylose:



Long, non-branched chain of **α glucose units** linked together by α-1,4 glucosidic bond.

Forms 15-20% of the starch granules.

Structure of amylopectin



Branched chain of α glucose units linked together by α-1,4 glucosidic bond while at the branching point, it forms α- 1, 6 glucosidic bond

Forms 80-85% of the starch granules.

- **Hydrolysis of starch occurs either by:**
  - Dilute mineral acids and called acid hydrolysis which results in <u>complete hydrolysis</u> to α glucose units .
  - Enzymes as **<u>α-amylase</u>** (salivary & pancreatic) which results in <u>partial hydrolysis</u> producing smaller molecules called dextrins and maltose.

Salivary amylase → **Incomplete digestion of starch (Dextrin mainly)**

Pancreatic amylase → **Complete digestion (Maltose)**

- The products of starch hydrolysis occur according to the following sequence:
- **Starch → Amylodextrin (the earliest dextrin produced) → Erythrodextrin → Achrodextrin → Isomaltose → Maltose → Glucose.**

- **(N.B.***)*: The difference between maltose and isomaltose in the bond position as it is α-1, 4 in maltose but α-1, 6 in isomaltose (i.e. at the point of branching of starch).

- It is to be noted that hydrolysis of starch by boiling with dilute acids ends in the formation of glucose.

2- Glycogen (animal starch):

- It is the reserve carbohydrate of animals, and hence the name **animal starch.**
- It is similar in its structure to amylopectin
- It is **highly branched** formed of **α** 1, 4 link and 1, 6 at the site of branching.
- Each branch is made of **12-14 glucose units**.

  (It has shorter and more numerous chains)
- **It is stored in liver &muscle.**

Functions of glycogen :

- Liver glycogen maintains normal blood glucose concentration especially during the early stage of fasting (between meals). After 12 -18 hours fasting, liver glycogen is depleted.
- Muscle glycogen acts as a source of energy within the muscle itself especially during muscle contraction.

3- Cellulose:

- It is **unbranched** polysaccharides, it is long straight chains of **β - glucose units** linked together by **β 1,4glucosidic bond.**
- It is the main structural molecules in cell walls of plants. Cotton is almost pure cellulose.
- Many mammals including humans cannot digest cellulose of diet because of the **absence of digestive enzyme that attacks β-linkage.**

(β 1,4 linkages are not hydrolized by **α amylase**)

- The presence of cellulose in diet is important because it increases the bulk of stool.
- This stimulate intestinal peristalses & prevent constipation (<u>laxative</u>).
- Cellulose is a constituent of dietary fibers. These fibers help in <u>decreasing absorption of toxic compounds and reduce the incidence of cancer colon.</u>
- Cellulose can be utilized & serve as a source of energy in herbivores because their gut contains bacterial enzyme that can attack β-linkage.

Heteropolysaccharides

- They are polysaccharides formed of more than one type of simple sugar units.
- They include the "**glycosaminoglycans**", formerly called the mucopolysaccharides **and** the **oligosaccharide chains of the glycoproteins**

Glycosaminoglycans (GAGs)

- They are unbranched, long chain (usually > 50 sugar units) heteropolysaccharides composed of a **repeating disaccharide unit**, usually made up of an amino sugar and a uronic acid.

amino sugar	**uronic acid**

- **The amino group** of the amino sugar (D-glucosamine or D- galactosamine) **is usually acetylated or sulfated, eliminating its positive charge and giving it a negative charge.**

- The amino sugar may also be sulfated on C-4 or C-6, giving it extra negative charges.

- The uronic acid (D-glucuronic acid or L-iduronic acid) may be sulfated.

- **Only in one GAG, <u>the keratan sulfate</u>, there is no uronic acid but there is galactose instead.**

❖ *L-iduronic acid: the 5 epimer of D-glucuronic acid*

- **Six classes of GAGs are present in our body, namely:**

a. Hyaluronic acid
b. Chondroitin sulfate
c. Dermatan sulfate
d. Keratan sulfate
e. Heparin
f. Heparan sulfate

a. **Hyaluronic acid:**

- It is formed of repeating units of **N-acetyl glucosamine & β-glucuronic acid.**
- It is present in cartilage, connective tissue, synovial fluid, vitreous humor of the eye, embryonic tissue & in the zona pellucida around the ovum.
- **The only GAG that does not contain sulfate.**

- **Function of hyaluronic acid:**

-It is present in synovial fluid. So, it acts as a lubricant &facilitates the joint movement.

-It makes cartilage compressible.

-It makes extracellular matrix loose because of **its ability to attract water**.

-It permits cell migration during wound repair.

-It permits cell migration during morphogenesis, i.e. differentiation of cells in the form of organs & tissues in the early embryo.

- **(N.B.**)

-It facilitates cell migration. It is produced in increased amounts by tumor cells. This facilitates migration of these cells through the extracellular matrix & spread of the tumor

-**Hyaluronidase** enzyme secreted by certain bacteria causes destruction of this cement substance , helps spread of infection **so it is called spreading factor**

-Also this enzyme is present in acrosomal cap of sperms, invades the tissues of the ova causing destruction of hyaluronic acid &helps its fertilization by the sperms.

b. Chondroitin sulfate:

- The repeating disaccharide unit is **N- acetyl galactosamine sulfate & glucuronic acid.**
- It is found in cartilage, bone, cornea & other connective tissues.
- The most abundant of the GAG.
- The high content of chondroitin sulfate in cartilage contributes to its compressibility and **its amount in cartilage diminishes with age** which may be related to the development of **osteoarthritis**.

C.Dermatan sulfate:

It is the major GAG in **arterial smooth muscles** and may play a role in the development of **atherosclerosis**. It is also present in skin , heart valves, cornea & sclera.

D.Keratan sulfate:

It does not contain any uronic acid.(D-galactose + N-acetyl-D-glucosamine-6-sulfate)

There are two types of keratan sulfate:

keratan sulfate I: found in cornea (to make it transparent)

keratan sulfate II: found in cartilage and increases in cartilage with age.

E. Heparin:

- It is formed of sulfated glucosamine & sulfated glucuronic acid or sulfated L-iduronic acid (**little GlcUA residues and many IdUA residues**).
- It differs from other GAGs in that it is mostly found in cells (granules of mast cells and basophils) rather than in connective tissue matrix.
- Its concentration in blood is very low.

- It is anticoagulant by **activation of antithrombin III** (***Antithrombin*** *(AT) is a small protein molecule that inactivates several enzymes of the coagulation system.*) which **inactivates thrombin** (*serine protease that converts soluble fibrinogen into insoluble strands of fibrin*), **and** also because of binding and inactivating factors IX & XI.

- It releases lipoprotein lipase *"attached to the luminal surface of endothelial cells in capillaries "* & activates it. lipoprotein lipase digests plasma lipids leading to clearing of plasma, so heparin & lipoprotein lipase are called **clearing factors.**

F. Heparan sulfate:

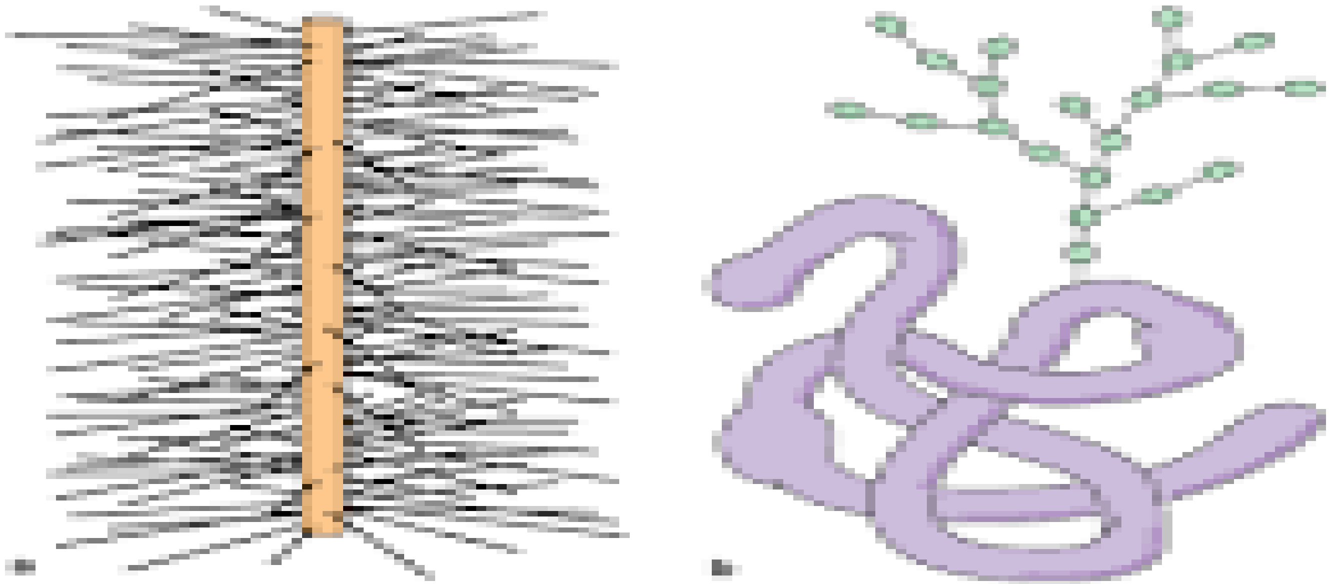
- It differs from heparin in the amount of uronic acid and the sulphate attached to glucosamine. (i.e. **it contains more glucuronic acid but less sulphated glucosamine**).

- It is present in the form of a **proteoglycan** on the surface of many cells with the core protein forming an integral protein of the plasma membrane of the cells. **It is probably related to cell-cell interaction as well as attachment of the cell to the surrounding medium.**

- In vascular endothelium heparan sulfate binds the enzyme lipoprotein lipase on the outer surface of the cell membrane facing the blood.

- **Some tumor cells have less heparan sulfate on their surface, which may explain the lack of adhesiveness of these cells to the surrounding medium and their ability to metastasize**

Proteoglycans and glycoproteins



With the exception of hyaluronic acid , all GAGs contain a sulfate and are covalently linked to a core protein , forming a proteoglycan monomer. The protein forms only about 5%of the molecule.
A glycoprotein is a conjugated protein containing one or more oligosaccharide chains, lacking a serial repeat units covalently attached to its polypeptide chain.