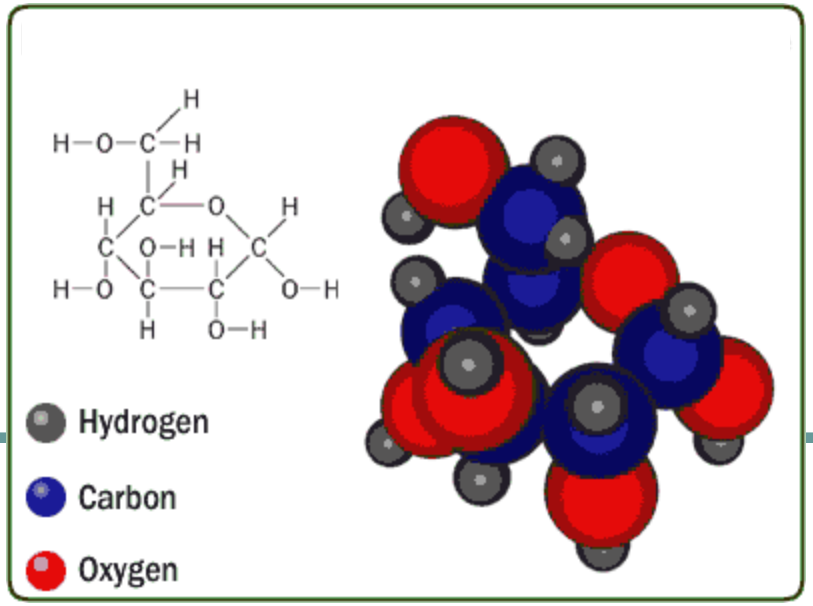
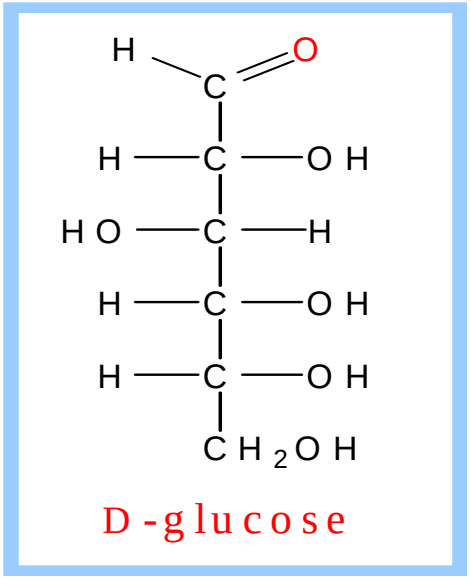
CHEMISTRY OF CARBOHYDRATES

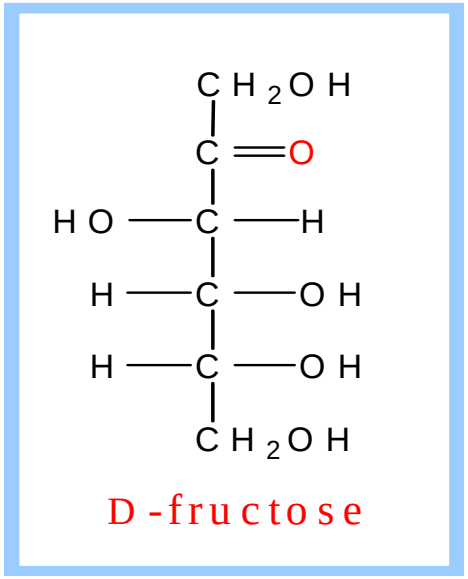


DEFINITION

- **Carbohydrates are polyhydroxy aldehydes or ketones or compounds which yield these on hydrolysis.**



D-glucose



D-fructose

BIOMEDICAL IMPORTANCE

1. Most abundant dietary source of energy.
2. Also serve as storage form of energy – Glycogen.
3. Participate in the structure of cell membrane & cellular functions (cell growth, adhesion and fertilization).
4. Mucopolysaccharides form the ground substance of mesenchymal tissues.
5. Certain carbohydrate derivatives are used as drugs, like cardiac glycosides / antibiotics.

ASSOCIATED DISORDERS

- Derangement in Glucose metabolism – Diabetes Mellitus.
- Inherited deficiency of certain enzymes in metabolic pathways of different carbohydrates cause diseases.
  - Glycogen storage disorders
  - Galactosemia
  - Hereditary fructose intolerence
  - Lactose intolerance, etc.

SOURCES

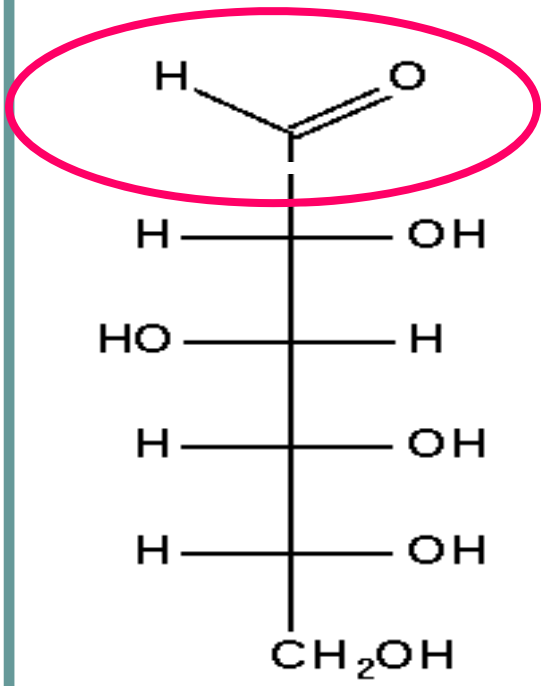
CLASSIFICATION

- Based on number of sugar units present.
  - **Monosaccharides**.
    - Cannot be hydrolyzed further into simpler forms.
  - **Disaccharides**.
    - Yield 2 molecules of same or different monosaccharide units on hydrolysis.
  - **Oligosaccharides**.
    - Yield 3-10 molecules of monosaccharide units on hydrolysis.
  - **Polysaccharides**.
    - Yield more than 10 molecules of same or different monosaccharide units on hydrolysis.
    - Homo- & Heteropolysaccharides.

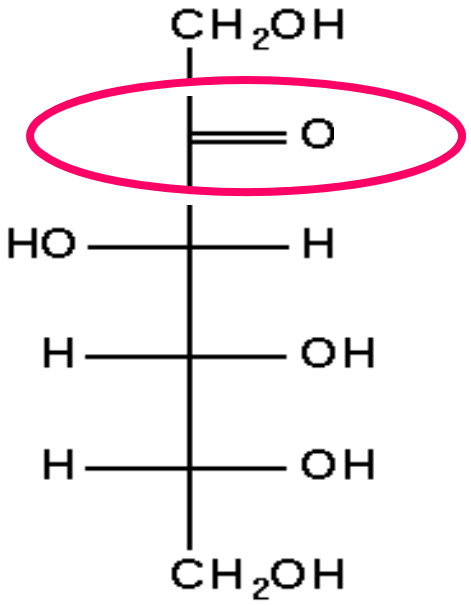
MONOSACCHARIDES

- Simplest group of carbohydrates, cannot be further hydrolysed.
- General formula : $C_n(H_2O)_n$
- Categorization of monosaccharides is based on
  - the Functional Group. (Aldehyde or keto)
  - the Number of Carbon atoms.

MONOSACCHARIDES BASED ON FUNCTIONAL GROUP



ALDOSE



KETOSE

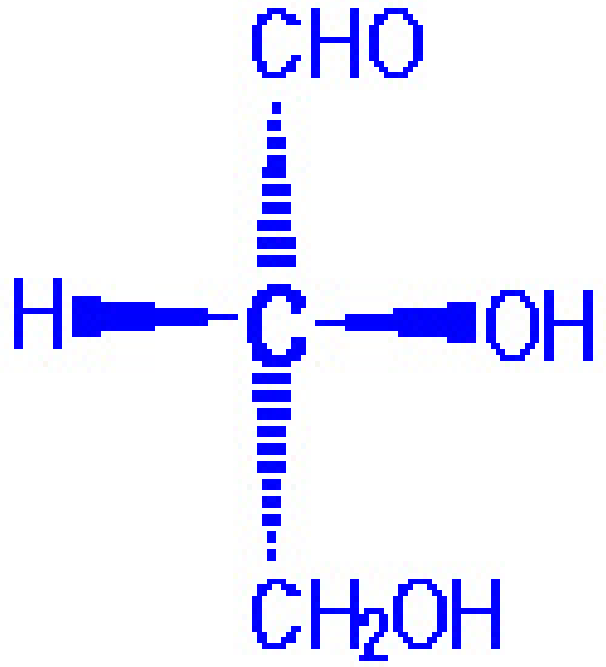
COMMON MONOSACCHARIDES

No. of C atoms	Generic name	Aldoses	Ketoses
3	Triose	Glyceraldehyde	Dihydroxy acetone
4	Tetrose	Erythrose	Erythrulose
5	Pentose	Ribose Xylose	Rilulose Xylulose
6	Hexose	Glucose Galactose	Fructose
7	Heptose	Glucoheptose	Sedoheptulose

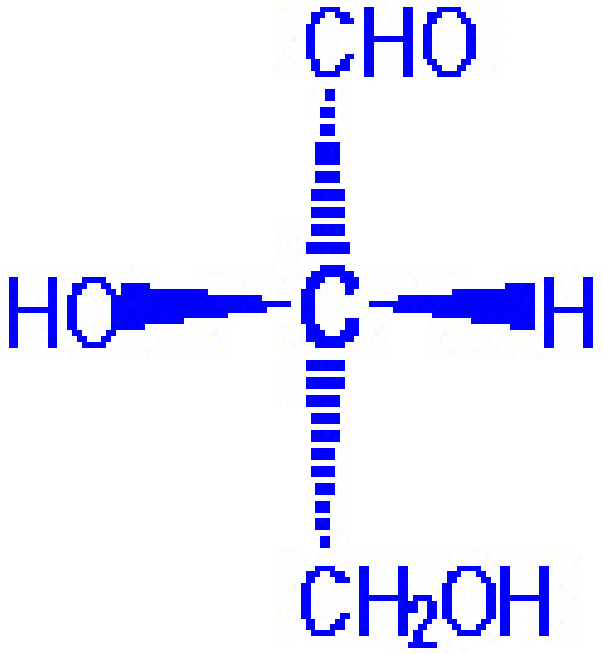
STEREOISOMERS

- Compounds having same structural formula, but differ in spatial configuration.
- Asymmetric Carbon atom: Attached to four different atoms or groups.
- Vant Hoff's rule: The possible isomers (2^n) of a given compound is determined by the number of asymmetric carbon atoms (n).
- Reference C atom: Penultimate C atom, around which mirror images are formed.

GLYCERALDEHYDE STEREOISOMERS

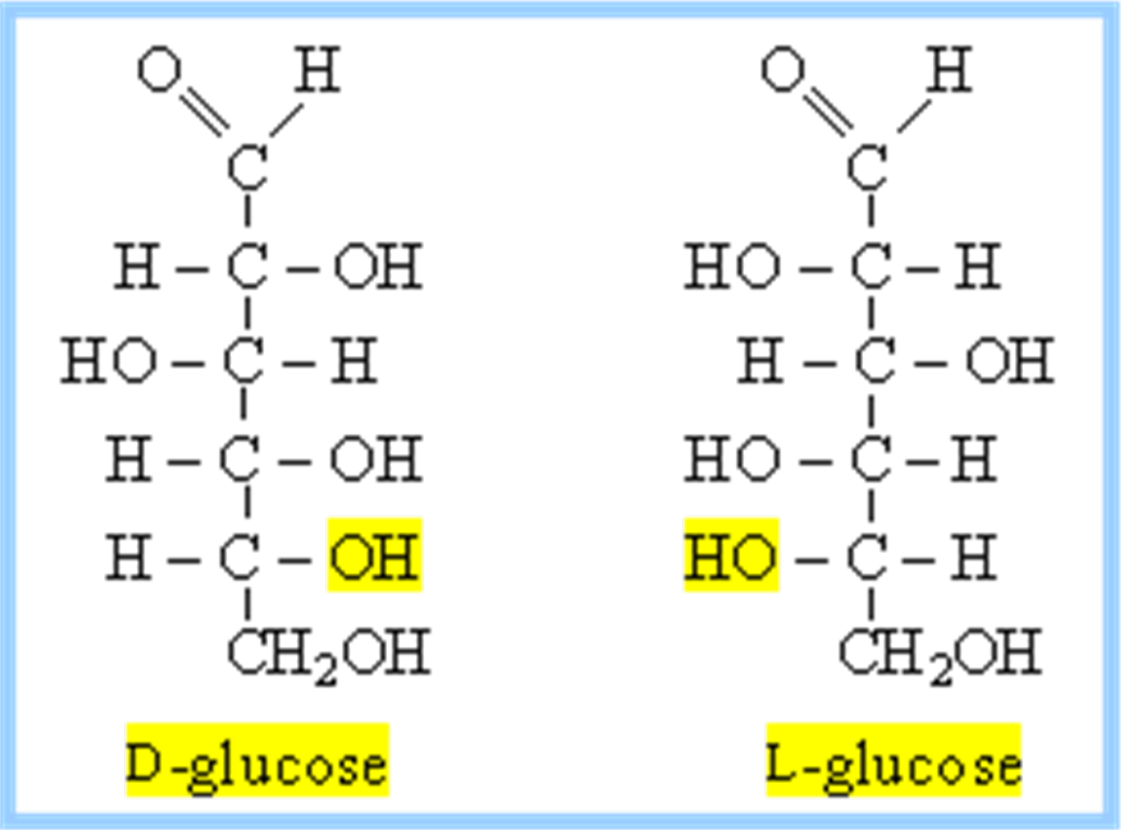


D-Glyceraldehyde



L-Glyceraldehyde

D & L ISOMERISM OF GLUCOSE

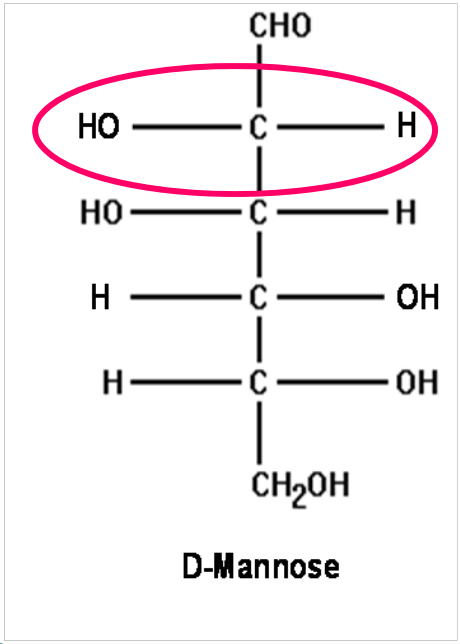


OPTICAL ACTIVITY

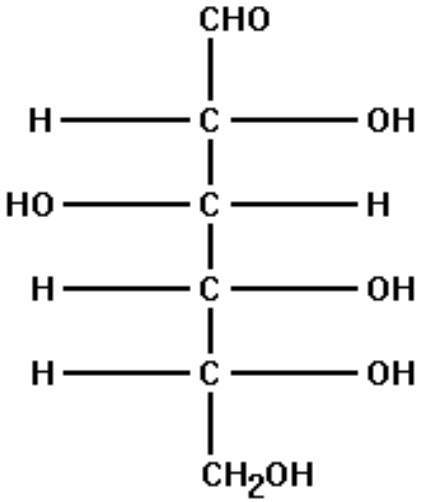
- **Dextrorotatory (+) : If the sugar solution turns the plane of polarized light to right.**
- **Levorotatory (–) : If the sugar solution turns the plane of polarized light to left.**
- **Racemic mixture: Equimolar mixture of optical isomers has no net rotation.**

EPIMERISM

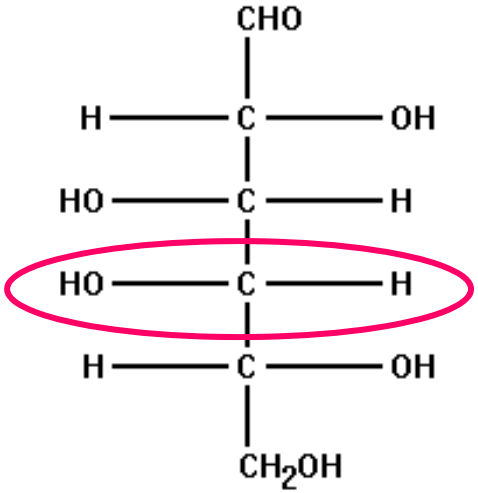
- **Sugars are different from one another, only in configuration with regard to a single C atom (other than the reference C atom).**



D-Mannose



D-Glucose



D-Galactose

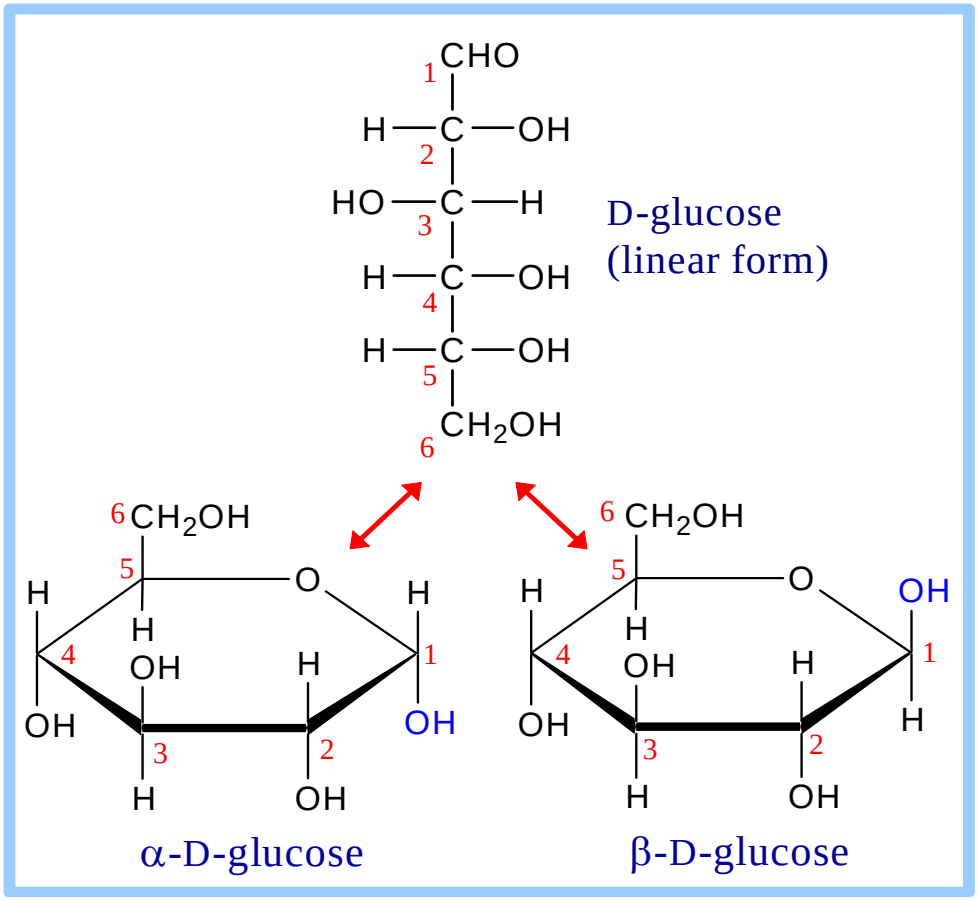
MUTAROTATION & ANOMERISM

- When D-glucose is crystallised at room temp. and a fresh solution is prepared, its specific rotation of polarised light is + 112.2^{O};but after 12-18 hrs it changes to + 52.5^{0}. If initial crystallisation takes place at 98^{0} C, initial rotation is $+19^{0}$, which also changes to 52.5^{0}.

- Anomers are produced by spatial configuration with reference to 1^{st} C atom in aldoses and 2^{nd} C atom in ketoses.

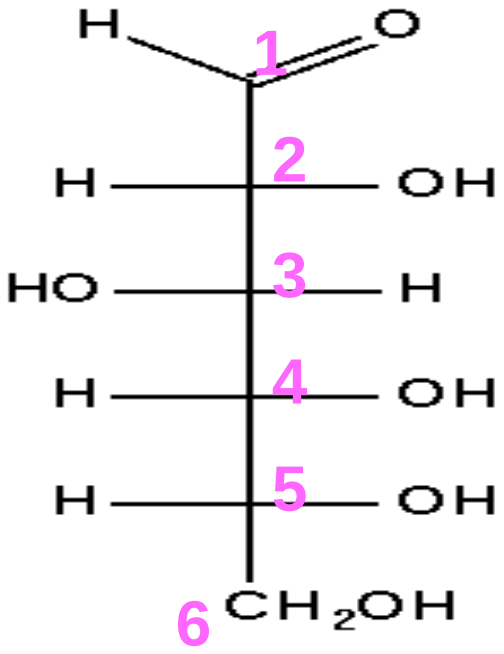
- So, total 32 isomers are there for glucose.

α AND ß ANOMERS OF D-GLUCOSE

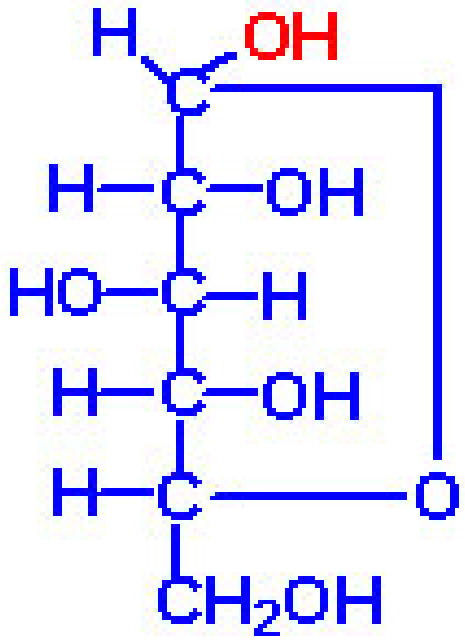


DIFFERENT REPRESENTATIONS OF GLUCOSE STRUCTURE

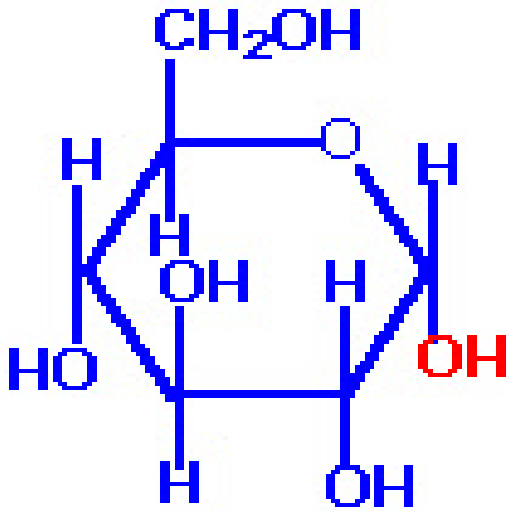
OPEN CHAIN PROJECTION



FISCHER'S FORMULA

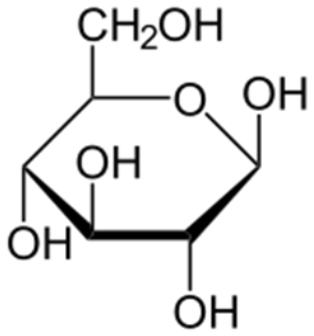


HAWORTH FORMULA

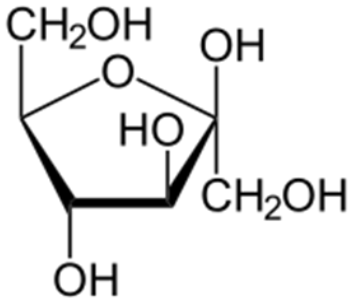


GLUCOSE VS. FRUCTOSE

- β D glucopyranose is the stable form of glucose and it exhibits the dextro rotation.
- Fructose exits as β D furanose & exhibits laevo rotation.



β D glucopyranose



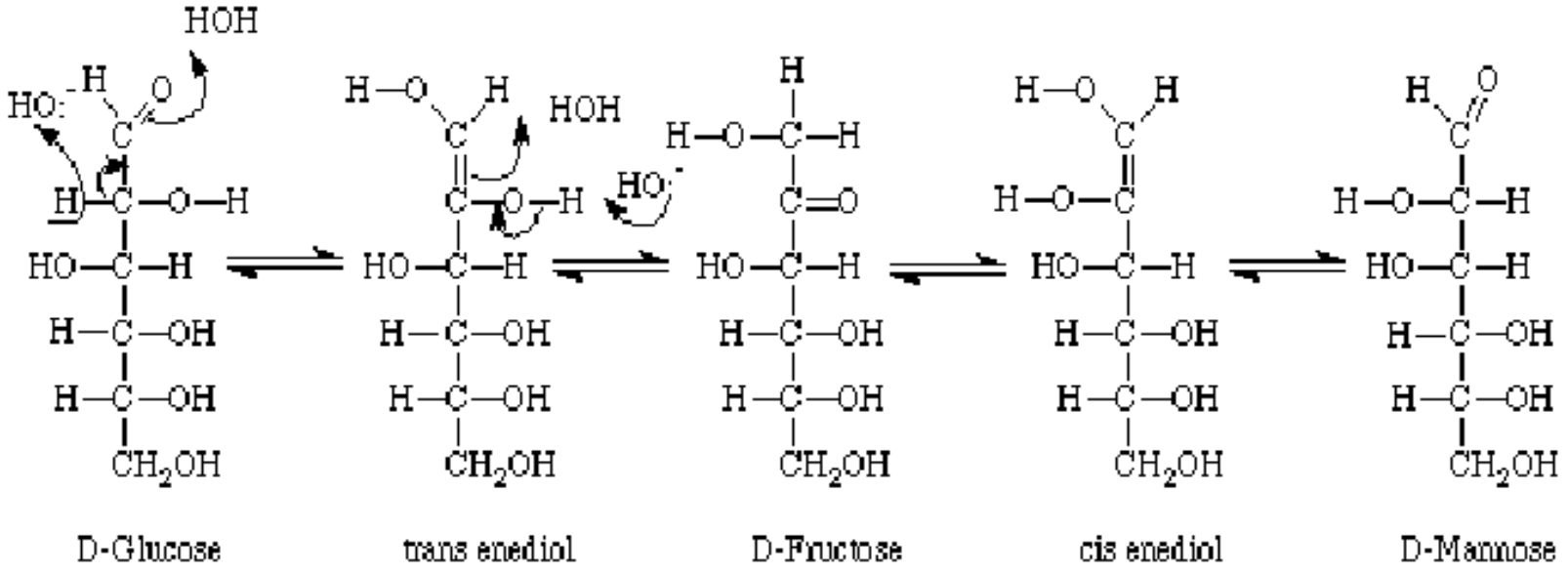
β D fructofuranose

REACTIONS OF MONOSACCHARIDES

- Tautomerization or Enolization.
- Reducing properties.
- Oxidation.
- Reduction.
- Dehydration.
- Formation of Esters
- Glycoside formation.

ENEDIOL FORMATION

- **In mild alkaline solutions, carbohydrates containing free sugar group tautomerises to form *enediols*, where 2 –OH groups are attached to double-bonded carbon.**

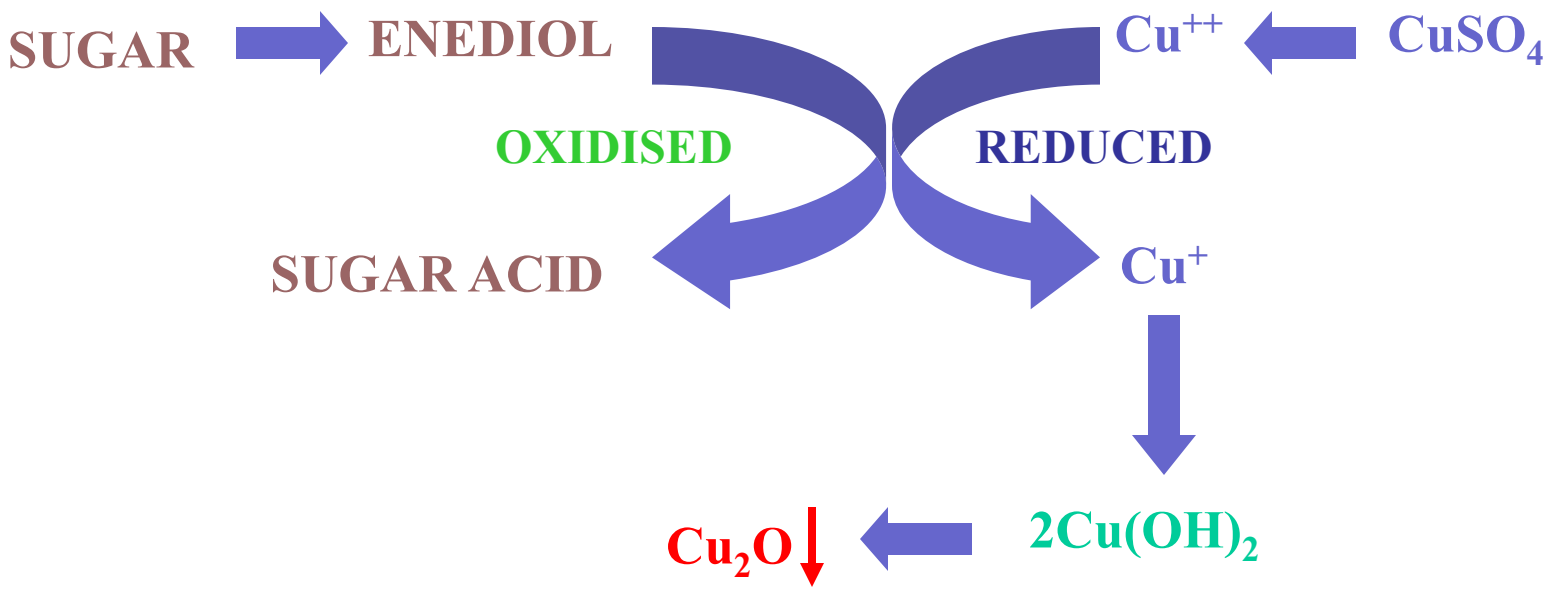


REDUCING PROPERTIES

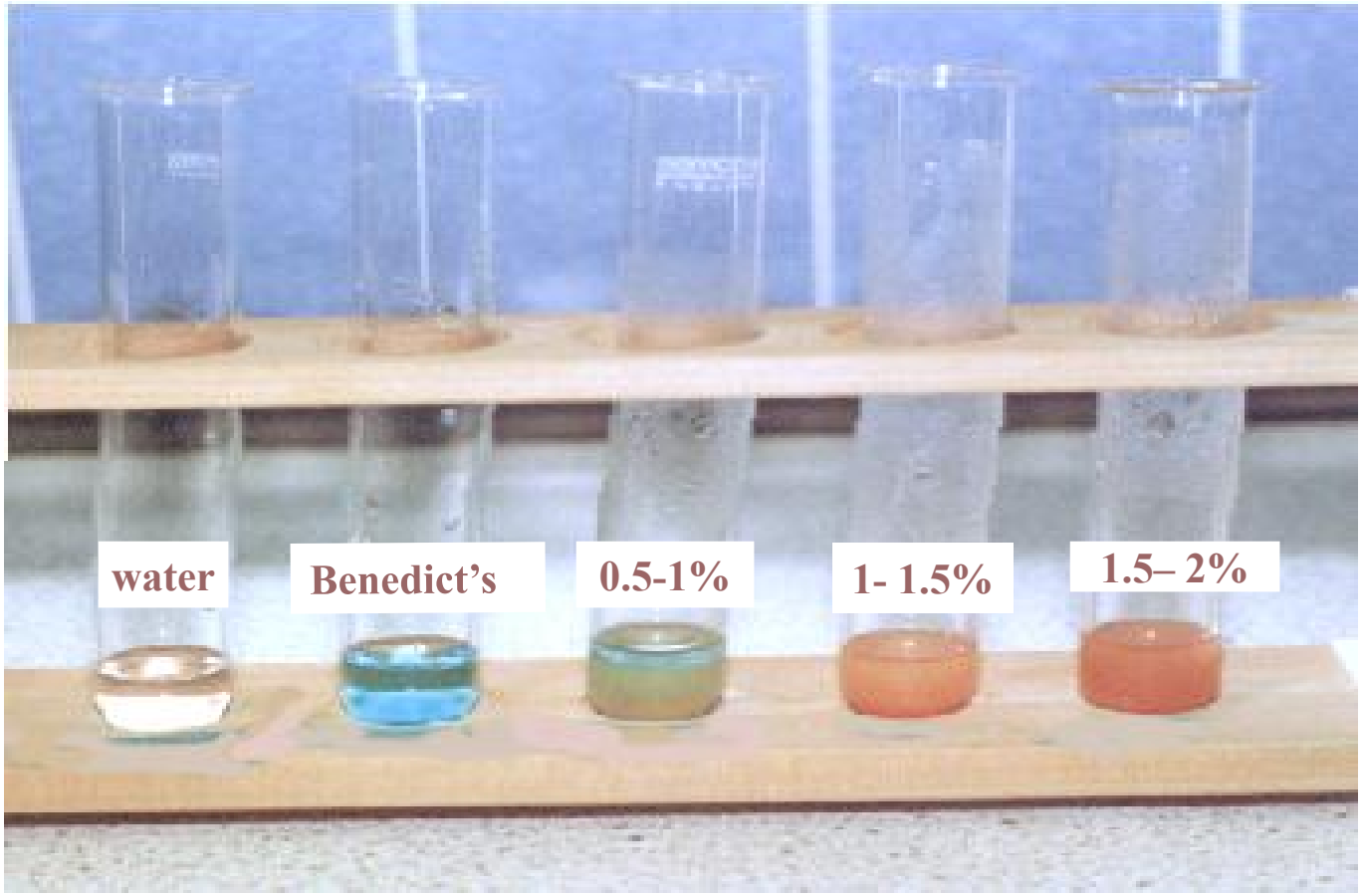
- Attributed to the free aldehyde or keto group of anomeric carbon.
- Tests done to identify the reducing action of sugars include :
  - Benedict's test.
  - Barfoed's test.
  - Fehling's test.
  - Osazone test.
- Reduction is more efficient in alkaline medium than in acidic medium.

BENEDICT'S TEST: PRINCIPLE

REAGENT: Na_2CO_3, CuSO4, Na citrate

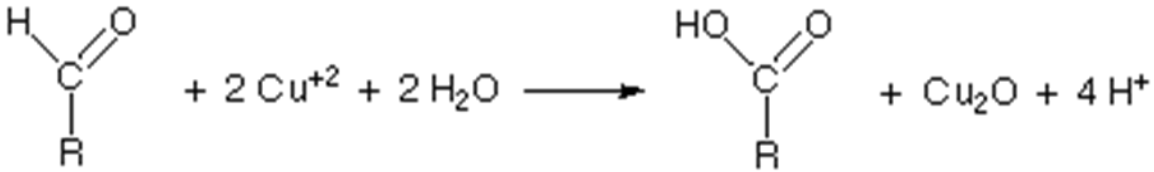


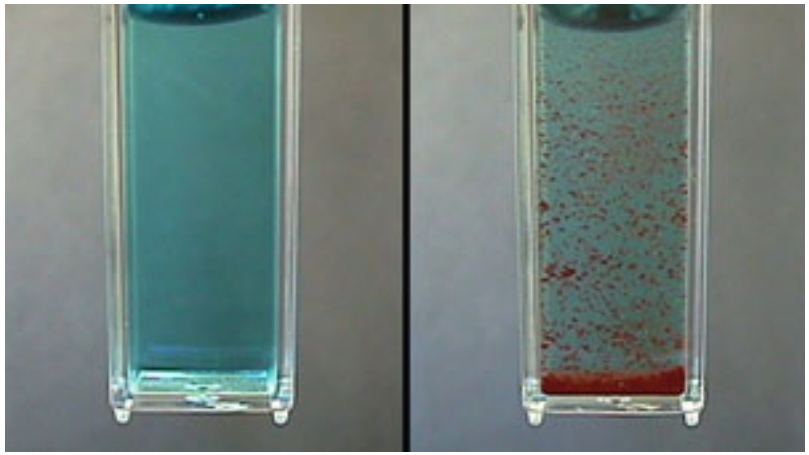
BENEDICT'S TEST



BARFOED'S TEST

- **Reducing monosaccharides are oxidized by the copper ion in solution to form a carboxylic acid and a reddish precipitate of cuprous oxide within three minutes.**

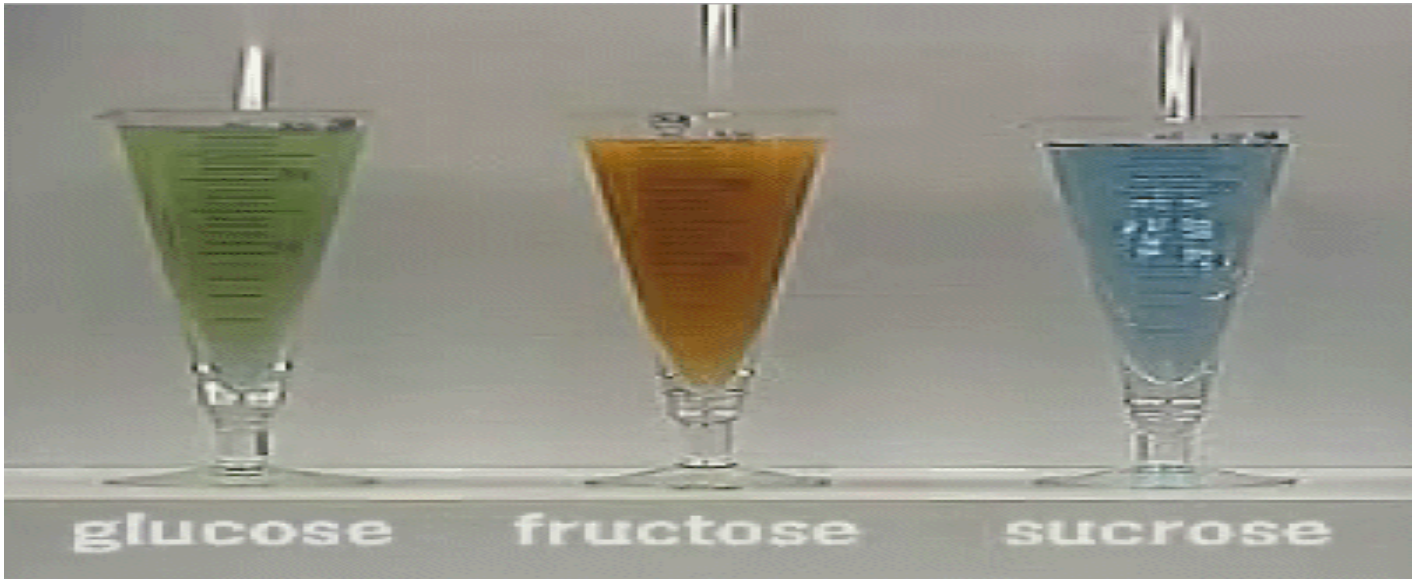




Red scum at bottom

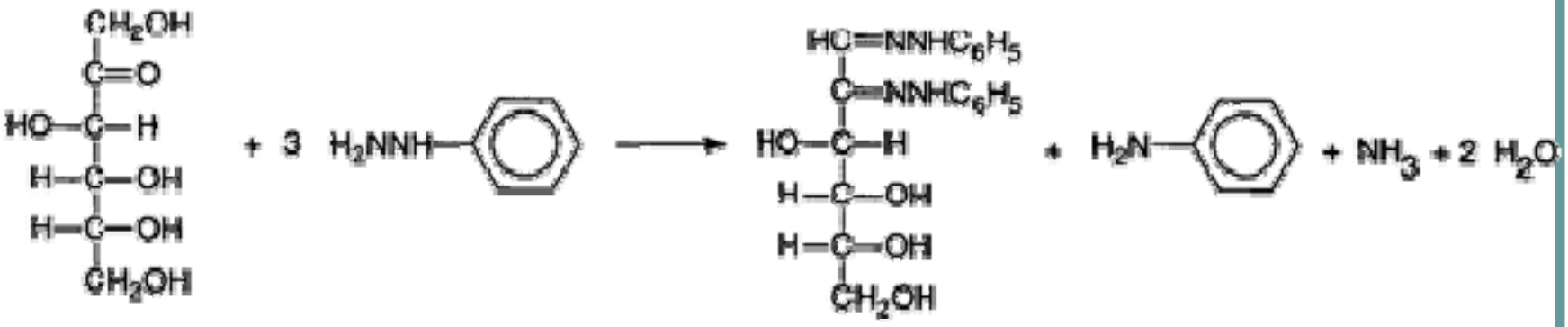
FEHLING'S TEST

- **Fehling I:$CuSO_4$**
- **Fehling II: K-Na- tartrate + NaOH**
- **Fehling's reagent: Equal volumes of Fehling I and Fehling II are mixed to form a deep blue solution.**



OSAZONE FORMATION

- Phenylhydrazine in acetic acid, when boiled with reducing sugars, forms osazones.

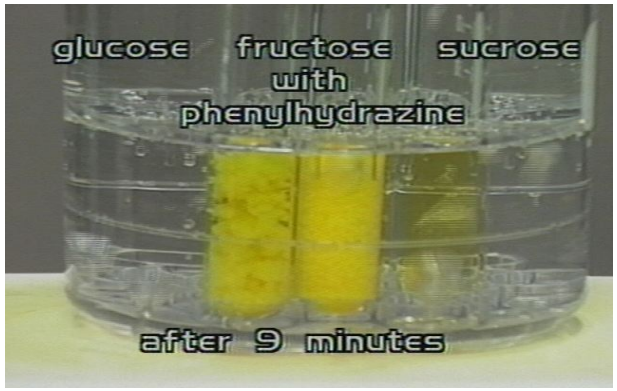


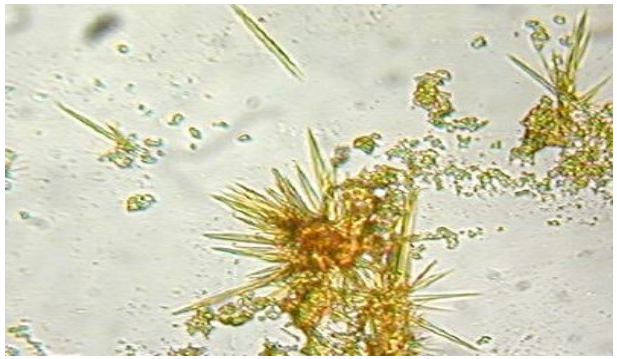
FRUCTOSE

PHENYL HYDRAZINE

FRUCTOSAZONE

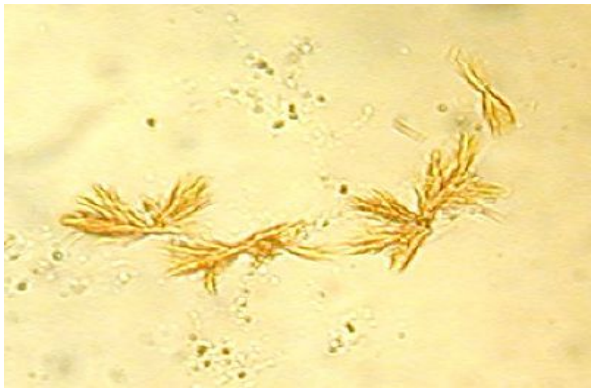
OSAZONE CRYSTALS





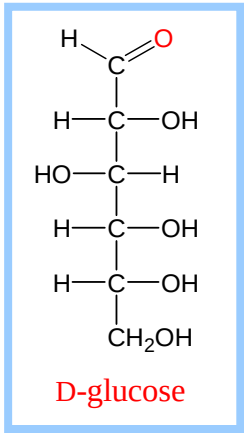
LACTOSAZONE: HEDGEHOG SHAPED

GLUCOSAZONE:NEEDLE SHAPED



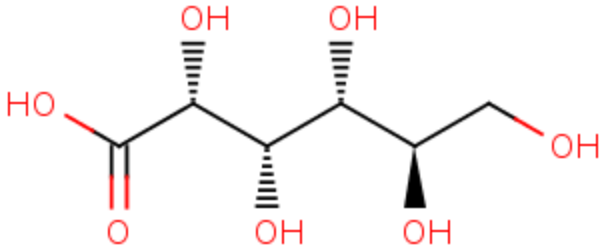
MALTOSAZONE: SUNFLOWER SHAPED

OXIDATION

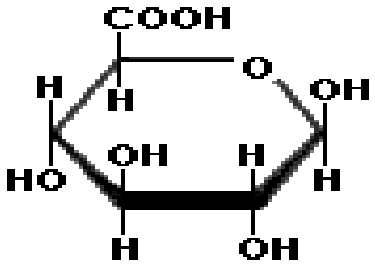


D-glucose

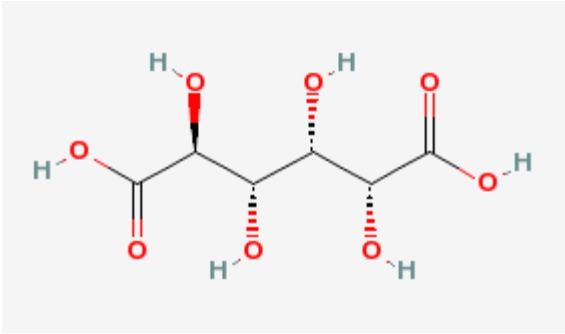
Gluconic acid



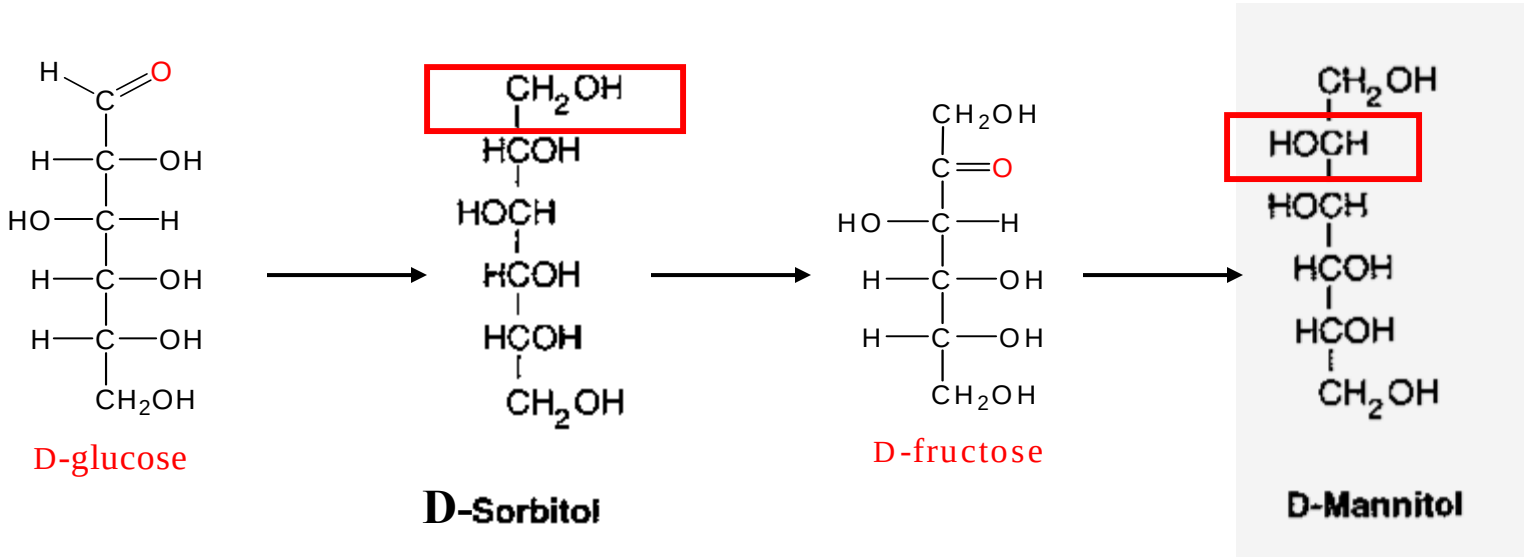
Glucuronic acid



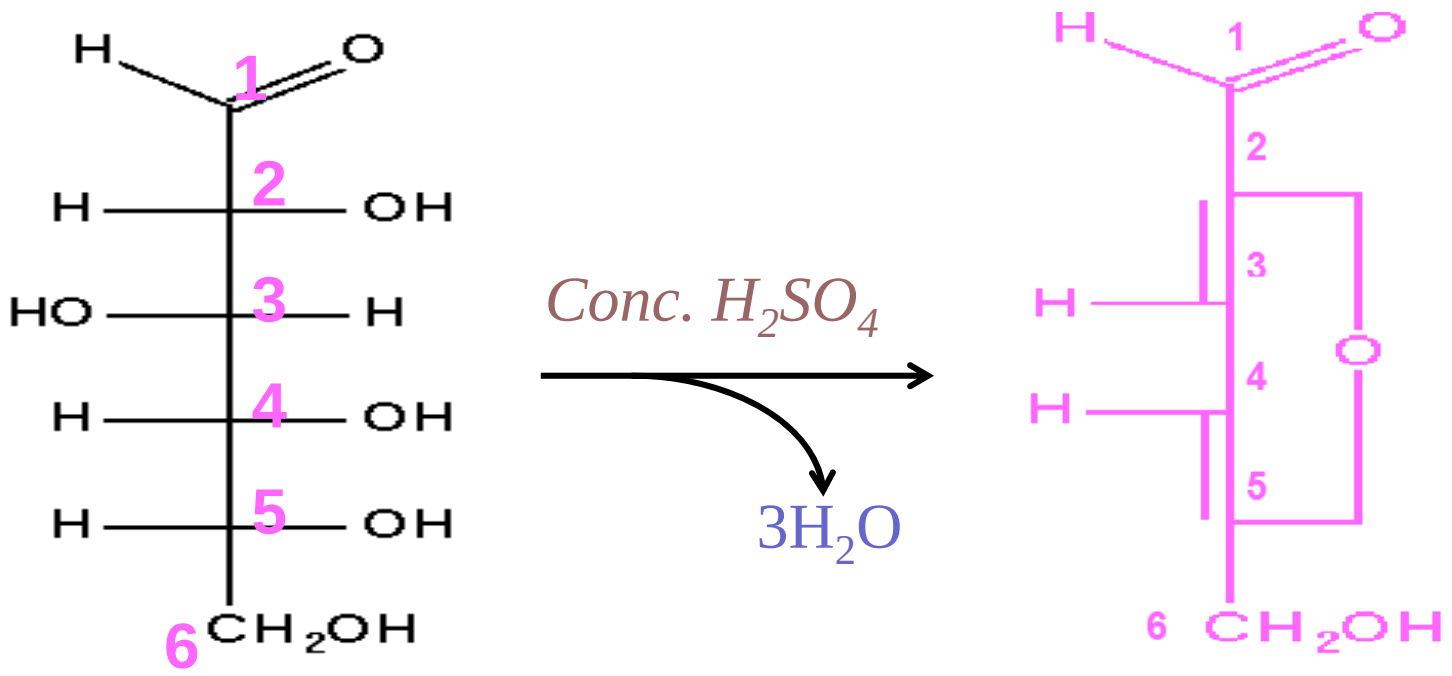
Glucosaccharic acid



REDUCTION



DEHYDRATION



- **Furfurals condense with phenolic compounds (α-naphthol) to form coloured products.**
  - **Basis of the "Molisch test".**

FORMATION OF ESTERS

- Esterification of alcoholic groups of mono-saccharides with phosphoric acid is a common reaction in metabolism.
- Examples :
  - Glucose-6-phosphate, and
  - Glucose-1-phosphate.
- ATP donates the phosphate moiety.

GLYCOSIDE FORMATION

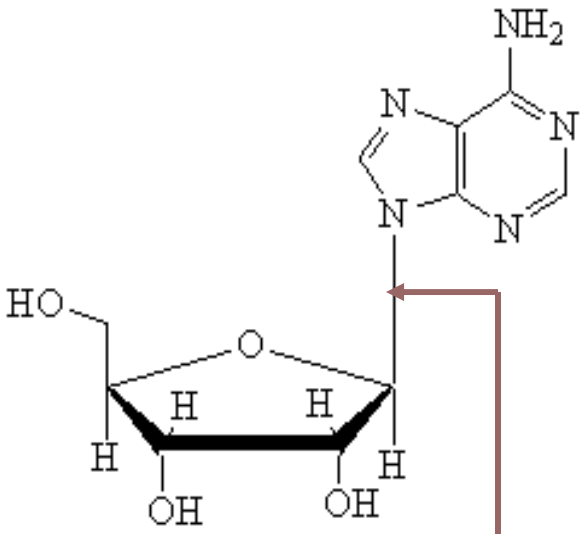
- The hydroxyl group of anomeric carbon of a carbohydrate can join with a hydroxyl group of another carbohydrate or some other compound to form a glycoside and the bond so formed is known as glycosidic bond.

  eg. R-OH + HO-R' → R-O-R' + H_2O

- The non-carbohydrate moiety is known as aglycone – phenol, sterol, bases, CH_3OH, glycerol.

- Glycosidic bond can be N-linked or, O-linked.

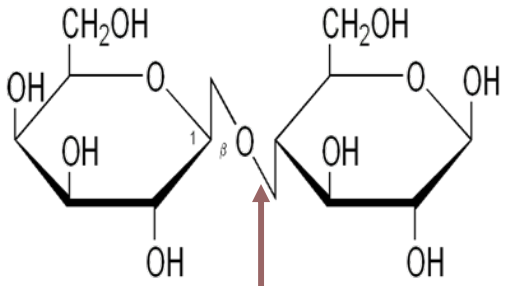
N & O GLYCOSIDIC LINKAGE



Adenosine

N-Glycosidic linkage

Lactose



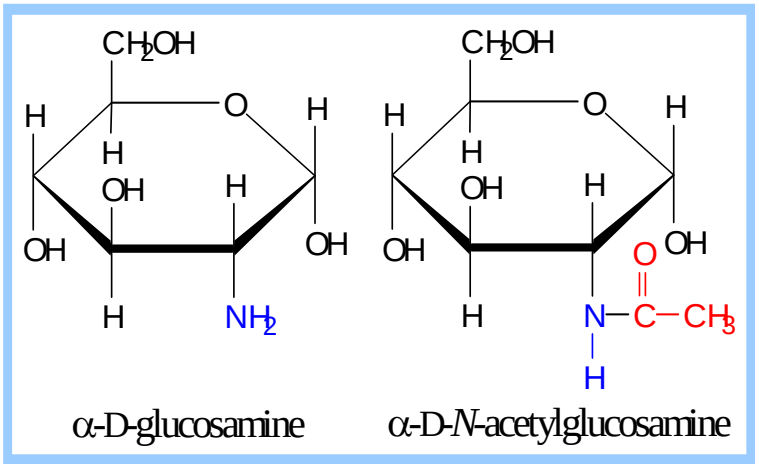
O- Glycosidic linkage

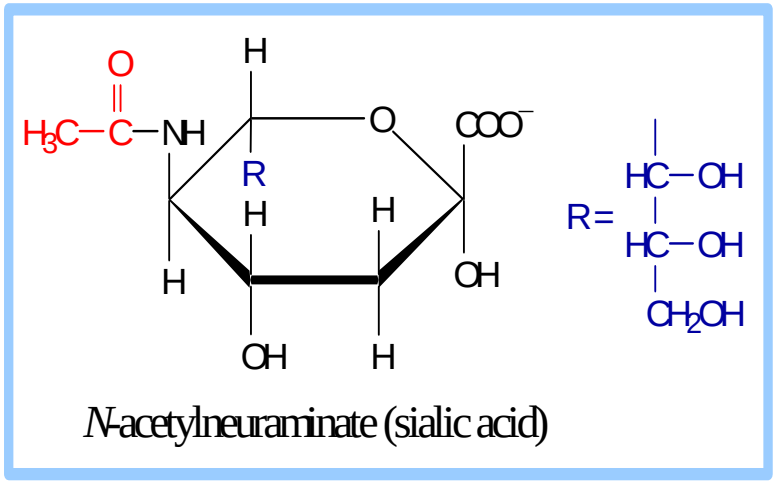
BIOMEDICAL IMPORTANCE OF GLYCOSIDES

- Cardiac Glycosides – Digoxin, Digitoxin
  - Used in cardiac insufficiency.
  - Contain steroids as aglycone component.
- Ouabain – Sodium pump inhibitor.
- Streptomycin – Antibiotic
- Phloridzin – cause renal damage, glycosuria.
  - Obtained from root & bark of apple tree.
  - Blocks the transport of sugar across the mucosal cells of small intestine & also renal tubular epithelium.

AMINO SUGARS

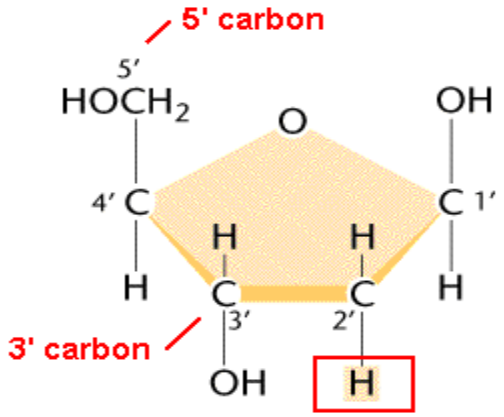
- **Amino groups are substituted for hydroxy groups of sugars.**



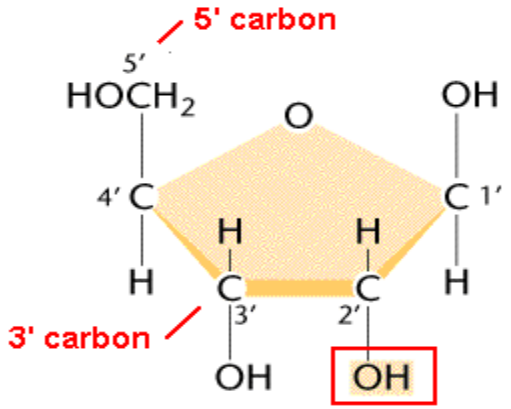


DEOXY SUGARS

- Oxygen of the hydroxyl group is removed to form deoxy sugars.
- Non reducing and non osazone forming.
- Important part of nucleic acids.



2-Deoxyribose



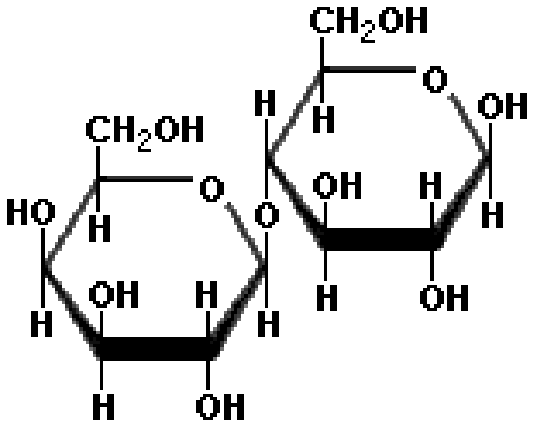
Ribose

DISACCHARIDES

- **Two monosaccharides combined together by glycosidic linkage.**
  - **Reducing : Maltose, Lactose – with free aldehyde or keto group.**
  - **Non-reducing : Sucrose, Trehalose – no free aldehyde or keto group.**

SUCROSE

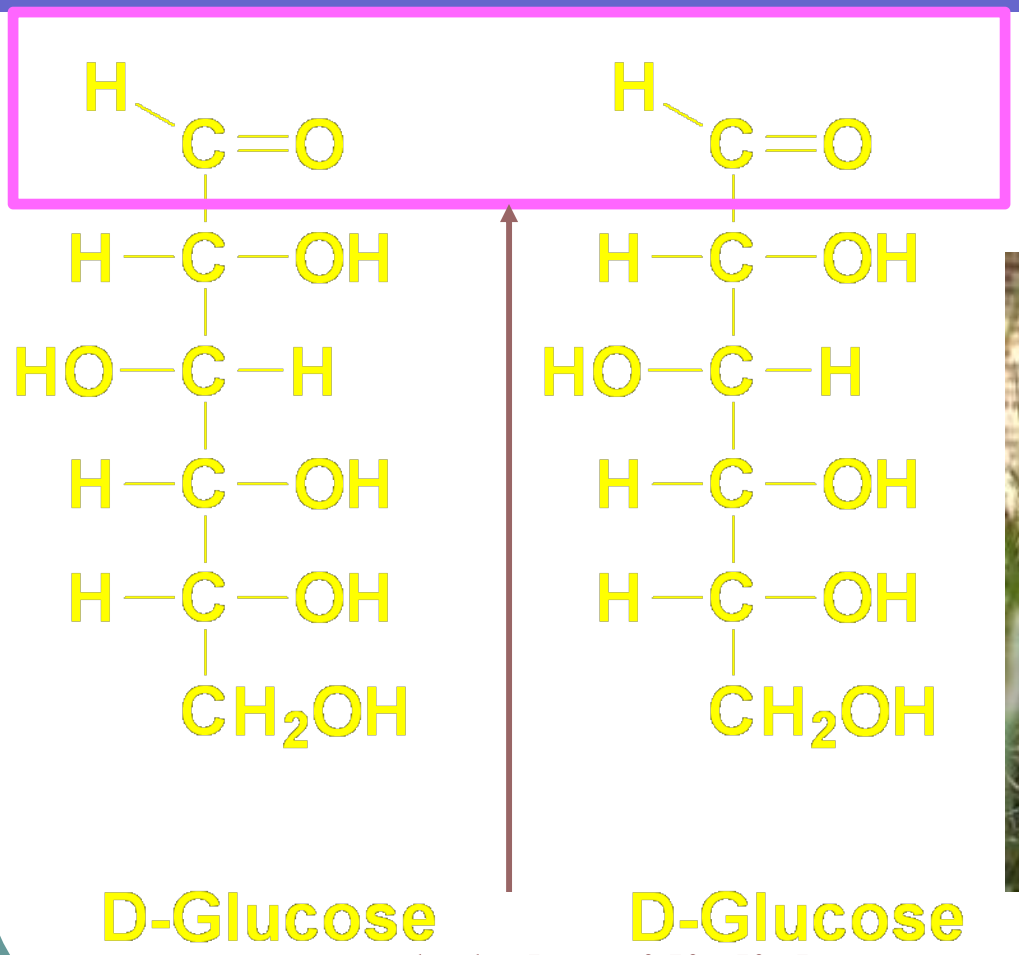
- Cane sugar.
- α-D-glucose & β-D-fructose units held together by (α1→ β2) glycosidic bond.
- Reducing groups in both are involved in bond formation, hence non reducing.



INVERT SUGAR

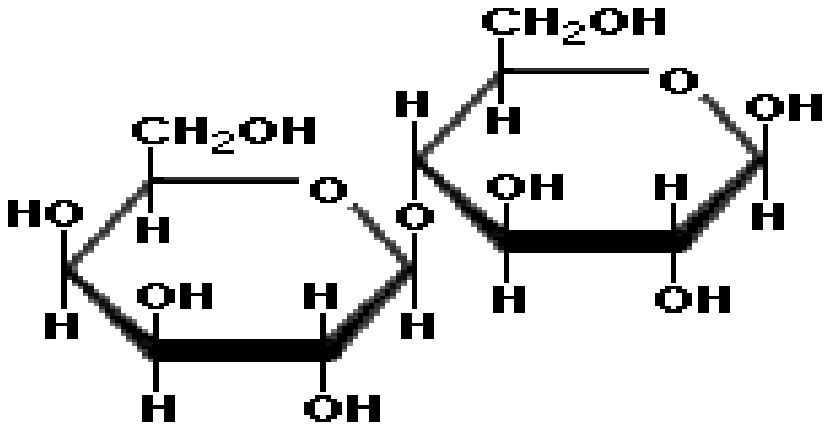
- Sucrose is dextrorotatory. ($+66.5^0$)
- During hydrolysis, sucrose is first split into α-D-glucopyranose & β-D-fructofuranose (both dextrorotatory).
- β-D-fructofuranose is less stable and immediately converted to β-D-fructopyranose (strongly levorotatory).
- Net rotation : -28.2^0.
- Sweeter than sucrose.

TREHALOSE



α 1- 1 glycosidic linkage

LACTOSE



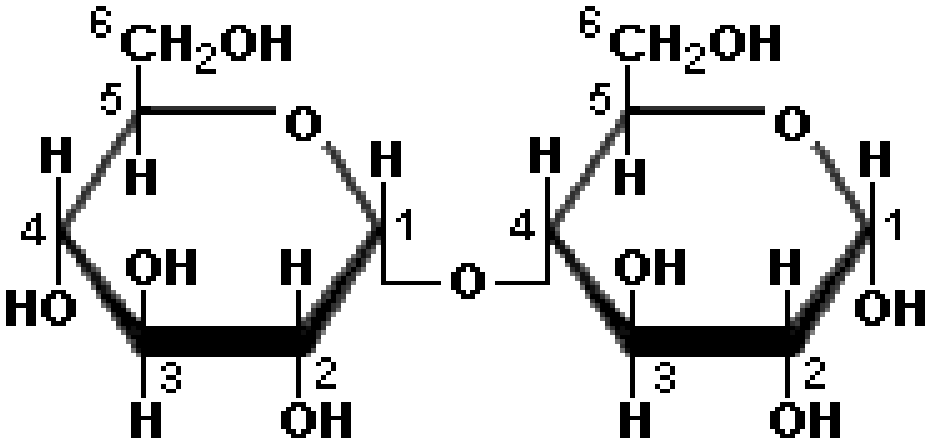
- Present in milk.
- β-D-galactose & β-D-glucose units held together by β (1→4) glycosidic bond.

MALTOSE

- Malt sugar.

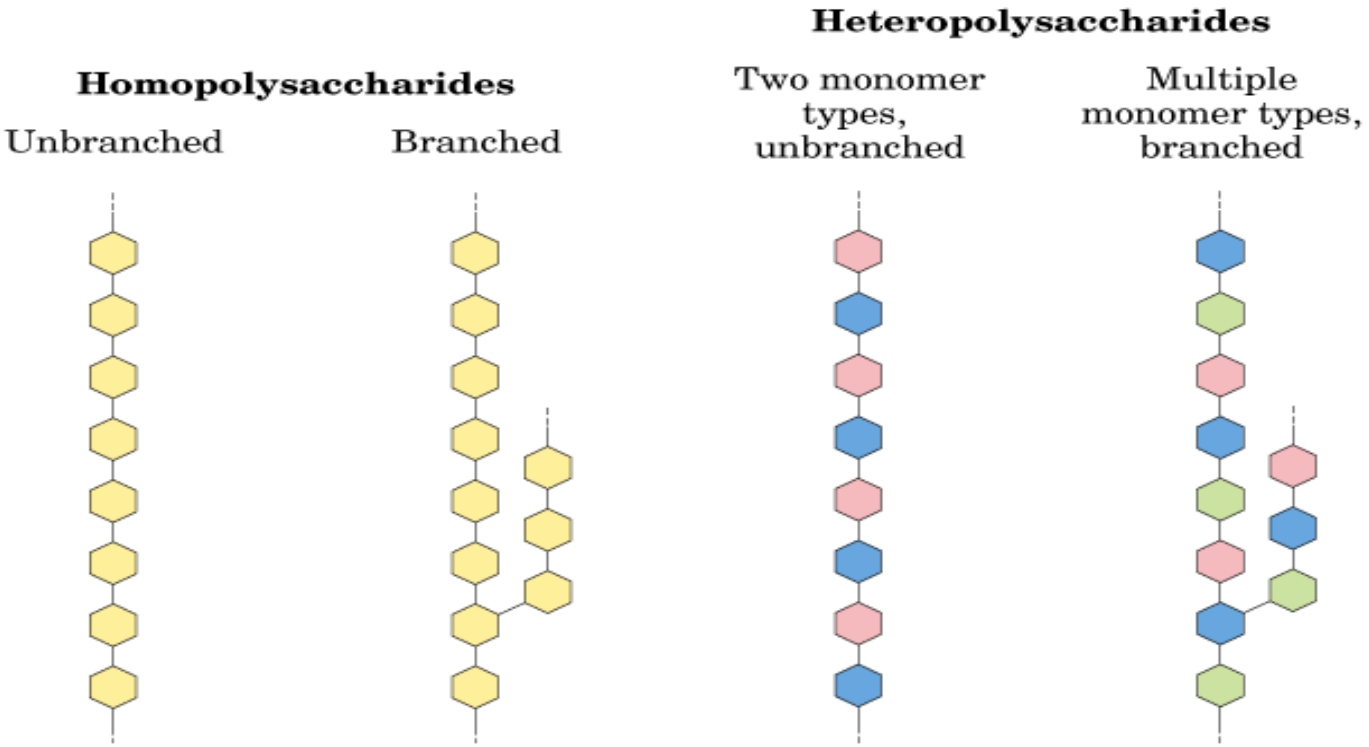
Produced during the course of digestion of starch by the enzyme amylase.

- Two α-D-glucose units held together by α (1→4) glycosidic bond.



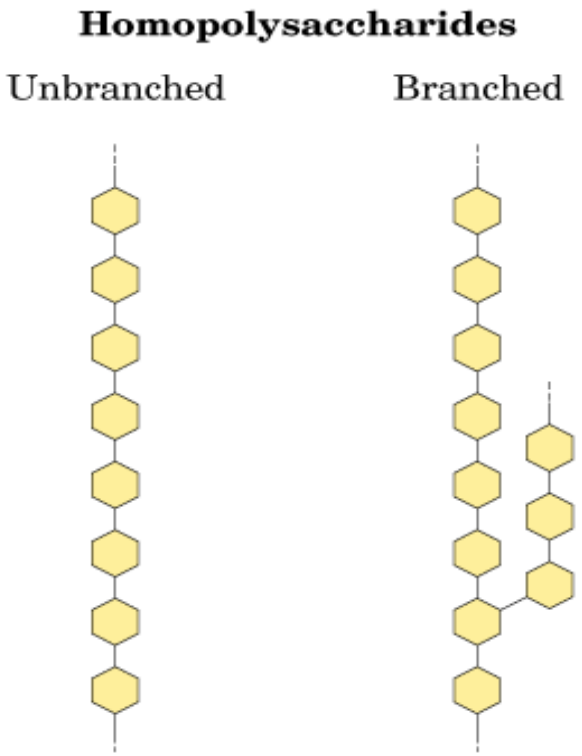
POLYSACCHARIDE

- **Repeat units of monosaccharides or their derivatives held together by glycosidic bonds.**

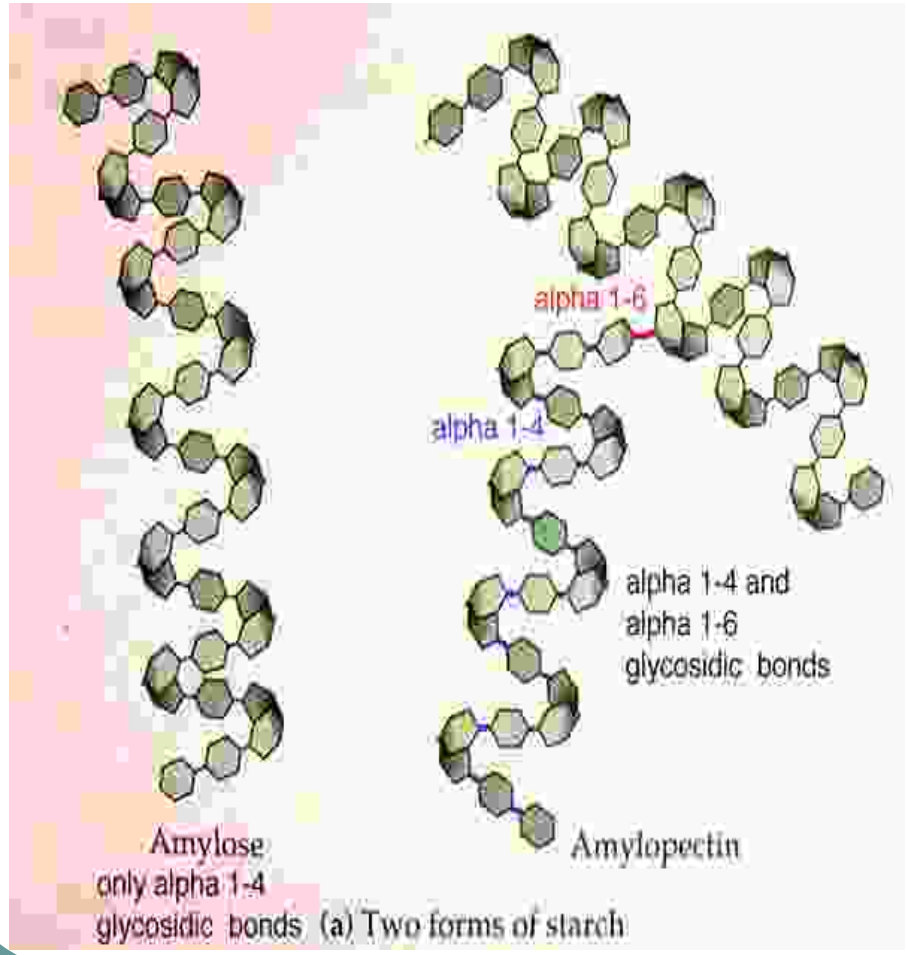


HOMOPOLYSACCHARIDES

- Starch
- Glycogen
- Cellulose
- Inulin
- Dextrans
- Chitin



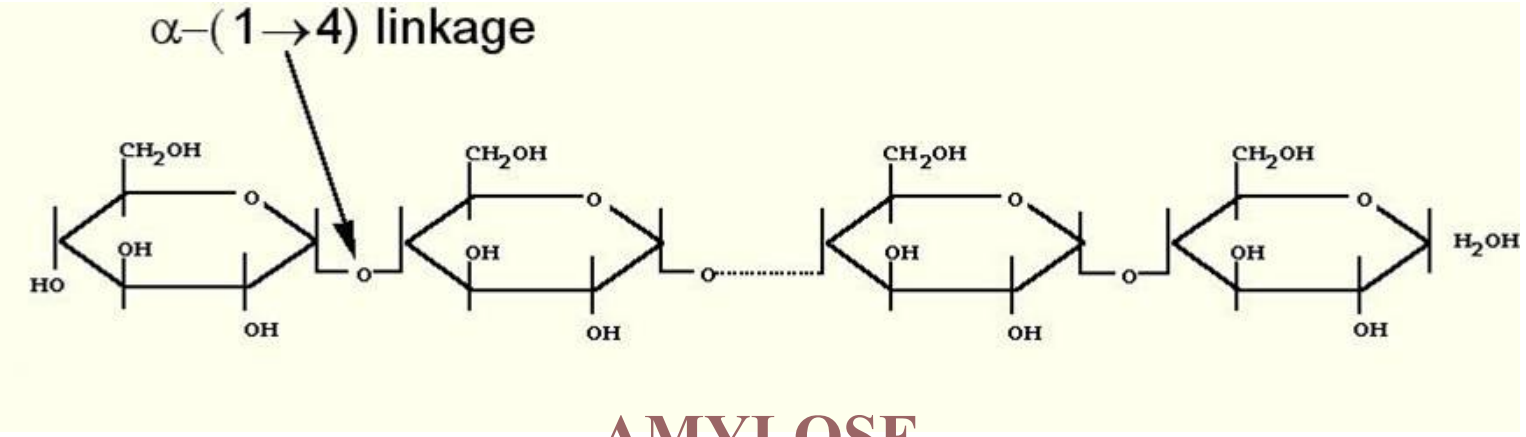
STARCH



- Carbohydrate reserve of plants. Present in Cereals, Roots, Tuber, Vegetables.
- Consists of Amylose (water soluble) & Amylopectin (water insoluble).

AMYLOSE

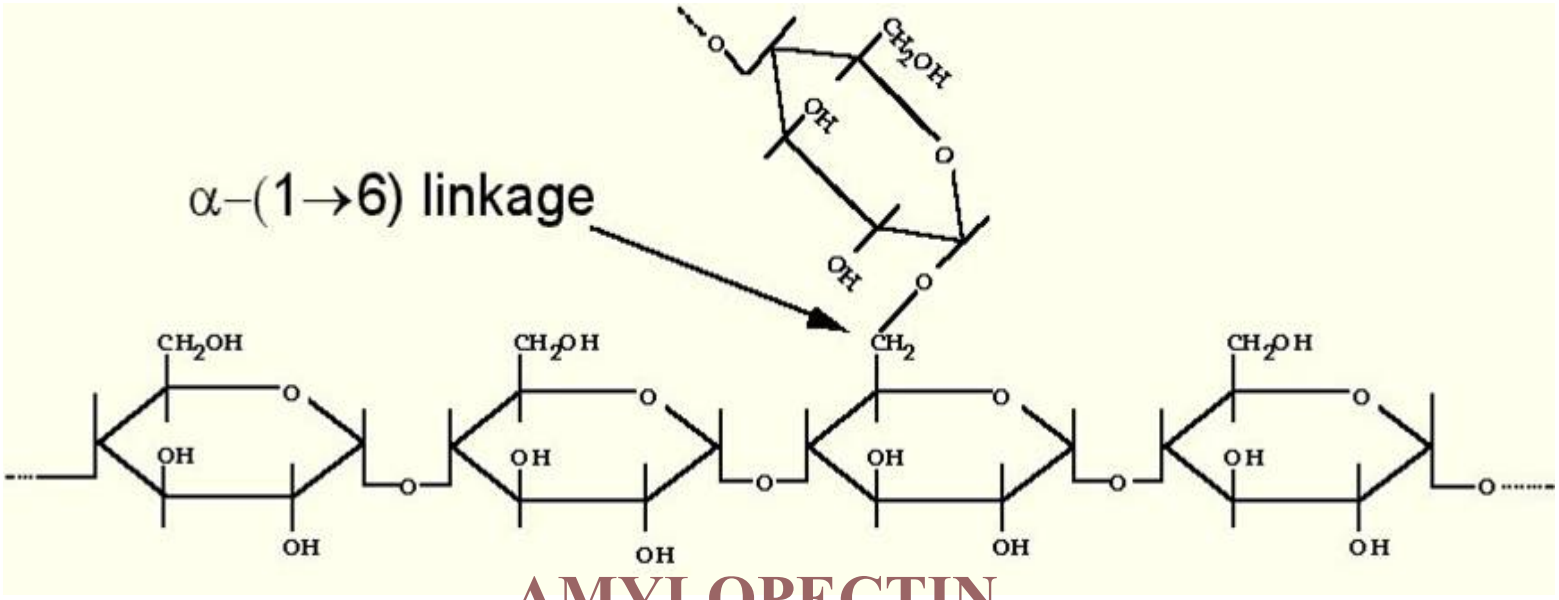
- **Long unbranched chain.**
- **200 – 20,000 D-glucose units held together by α (1→4) glycosidic linkages.**



AMYLOSE

AMYLOPECTIN

- **Branched chain. (α 1→6 glycosidic bonds at branches).**
- **20 – 30 glucose units per branch.**



AMYLOPECTIN

HYDROLYSIS OF STARCH

- Colour disappears with heating and reappears when cooled.
- Starch is non reducing.
- Hydrolysis for a short time: Violet colour due to Amylopectin (non reducing).
- Further hydrolysis: Red colour due to Erythrodextrin (reducing).
- Later Achrodextrin & Maltose (both reducing).

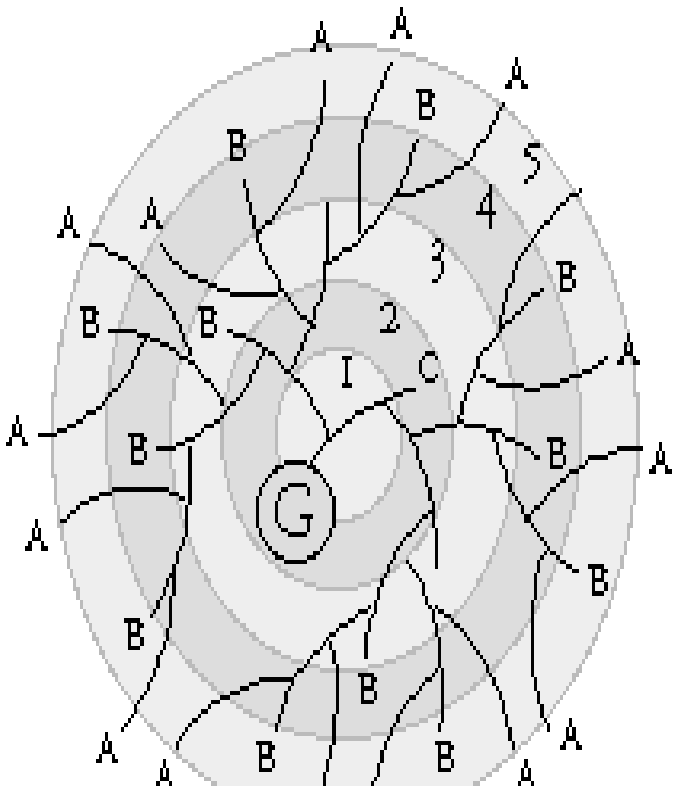
ACTION OF AMYLASE

- **Starch** —(Salivary & pancreatic α-amylase or ß-amylase)→ **Dextrins** → **α/ß-Maltose**

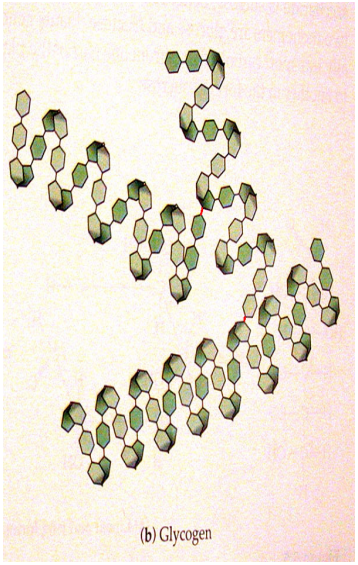
- **Amylopectin** —(ß-amylase)→ **Limit dextrin** + **Maltoses**

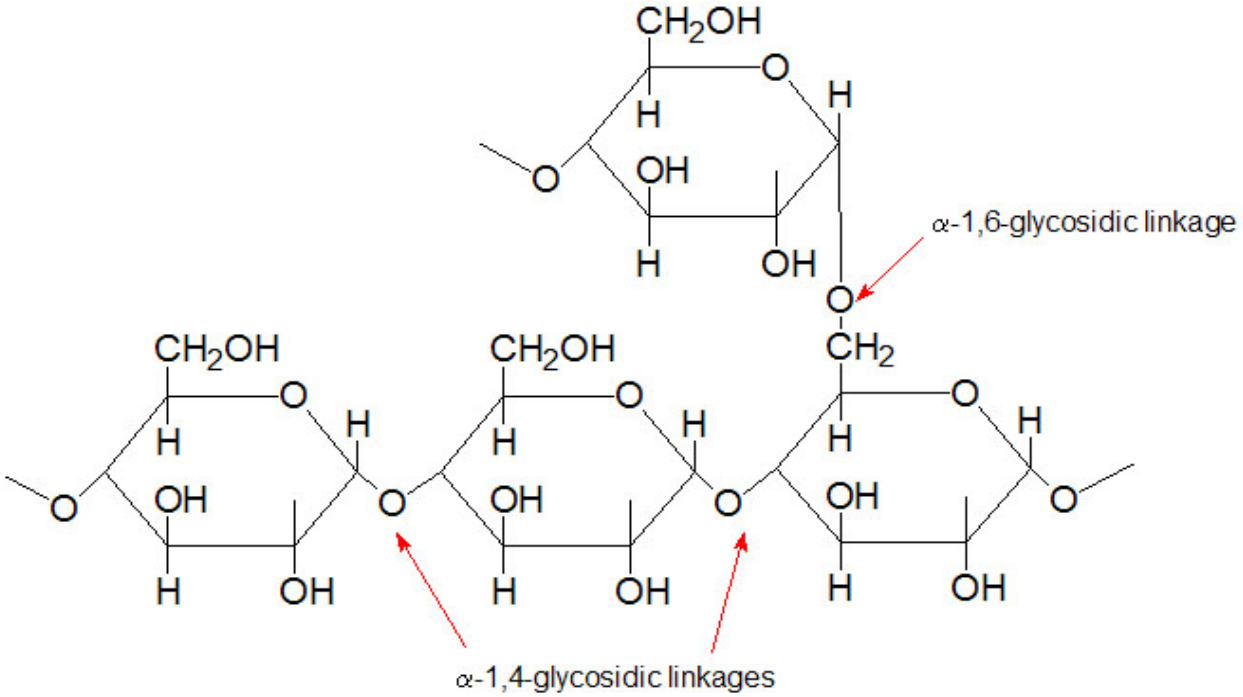
GLYCOGEN

- Reserve carbohydrate in animals. Stored in liver & muscle.
- Forms red-brown/brown-violet colour with iodine.
- Contains primer protein: Glycogenin.
- More branched and compact than amylopectin. Every 11th sugar molecule has a branch.

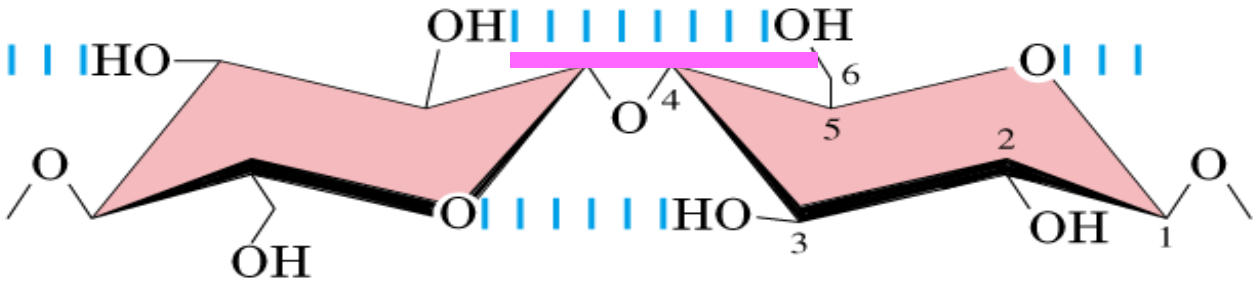


GLYCOGEN STRUCTURE





CELLULOSE

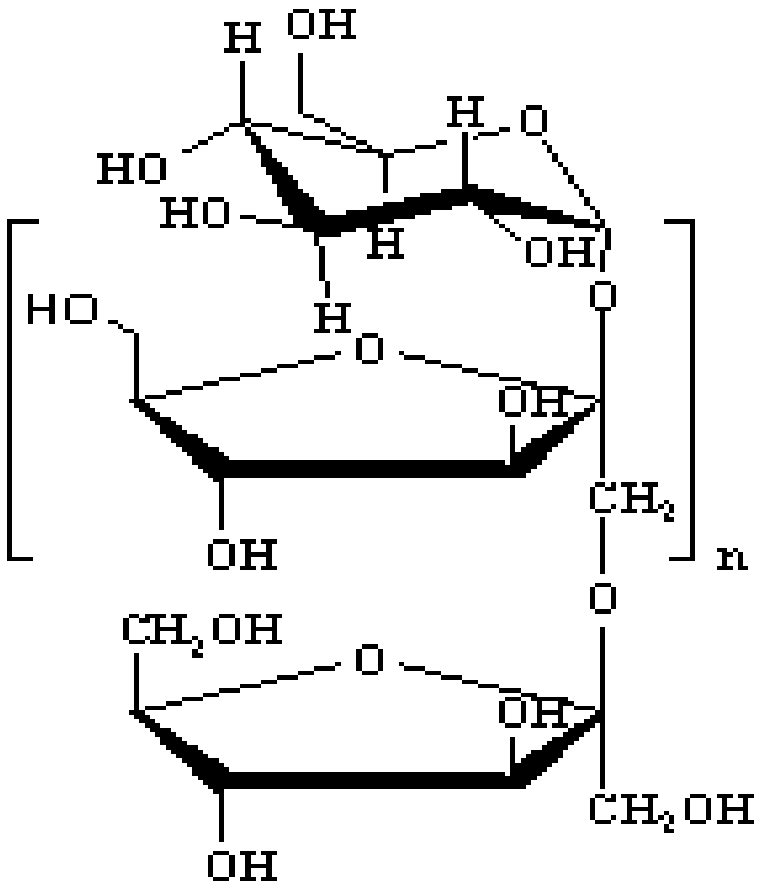


(β1→4)-linked D-glucose units

(a)

- **Chief carbohydrate in plants.**
- **Made up of glucose units combined with cellobiose bridges.**
- **No branching point.**
- **Cannot be digested by human due to absence of Cellobiase.**

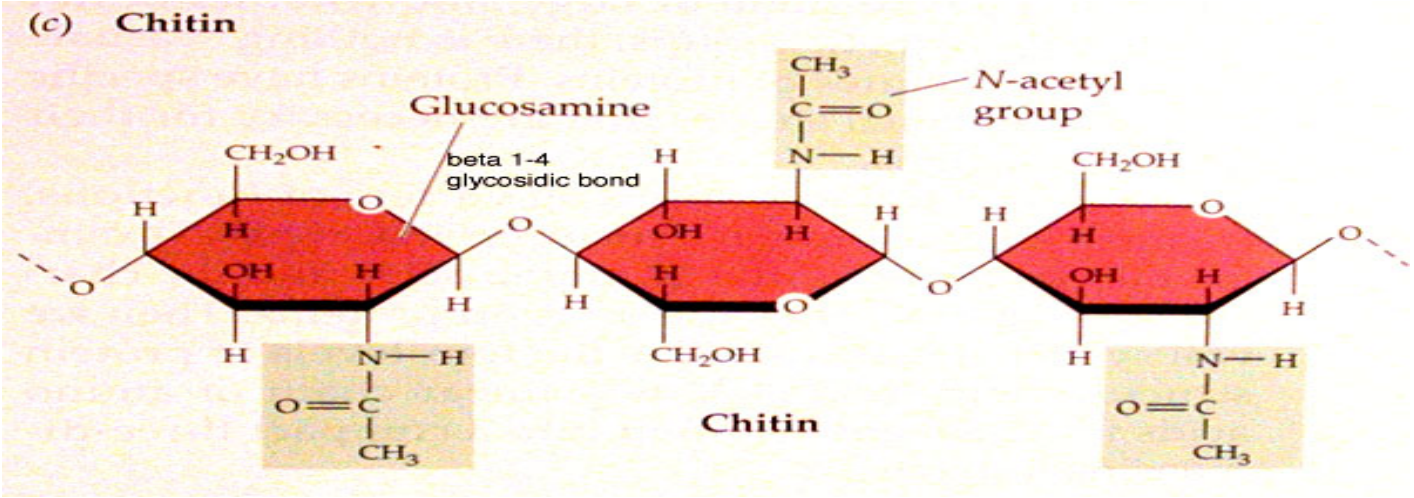
INULIN



- Inulin is made up of D-fructose units with repeating ß-1,2 linkages.
- It acts as a marker for glomerular filtration since it is not synthesized, metabolized but filtered completely by glomerulus.

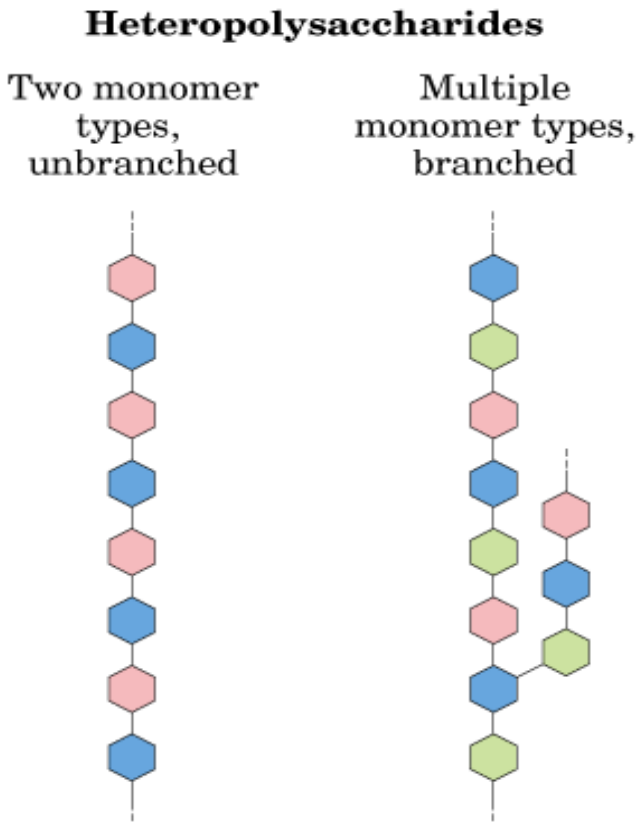
CHITIN

- Chitin is found in crustaceans eg.lobsters,crabs,shrimps,insects.
- Composed of N-acetyl glucosamine units joined by ß-1,4 glycosidic linkages.



HETEROPOLYSACCHARIDES

- **Agar**
- **Mucopolysaccharides:**
  - ✓ **Hyaluronic acid**
  - ✓ **Heparin**
  - ✓ **Chondroitin sulphate**
  - ✓ **Keratan sulphate**
  - ✓ **Dermatan sulphate**

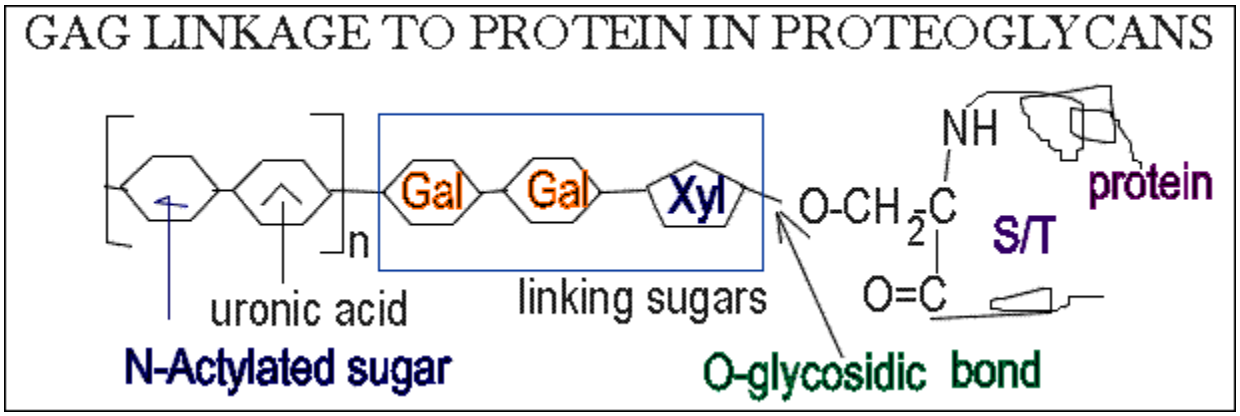


AGAR

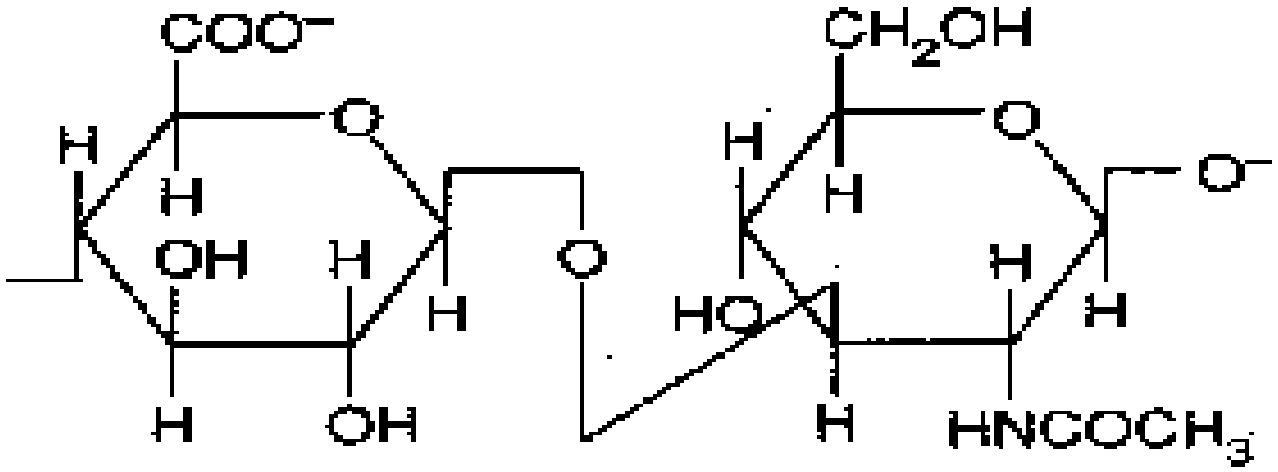
- Prepared from sea weeds.
- Contains Galactose, Glucose and other sugars.
- Used as supporting medium for immunodiffusion & immunoelectrophoresis.
- Agarose contains Galactose combined with3,6 anhydrogalactose units.
- Agarose is used as matrix for electrophoresis.

MUCOPOLYSACCHARIDES

- Also known as GAG.
- Made up of repeating units of sugar derivatives (aminosugars and uronic acids).
- Acetylated amino groups, sulfates and carboxyl groups are generally present.

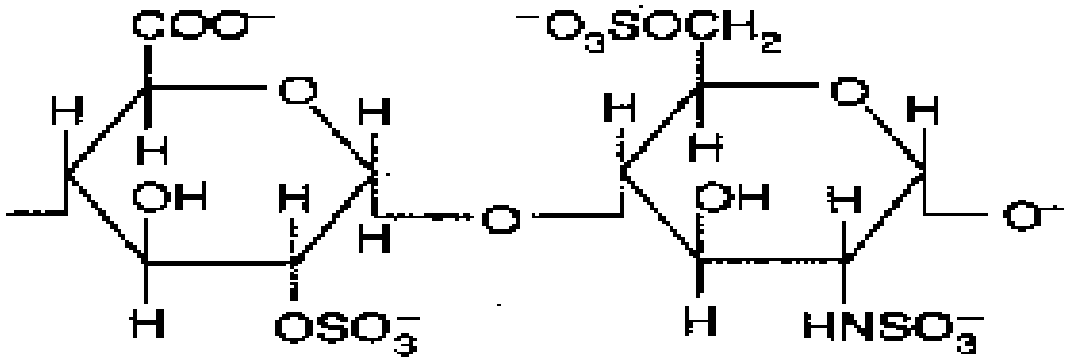


HYALURONIC ACID



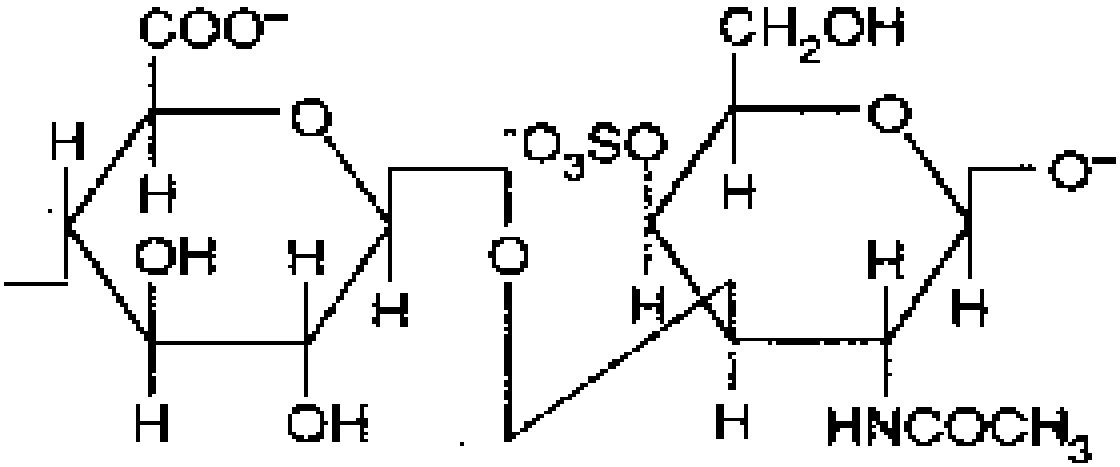
- Present in connective tissues, tendons, synovial fluid and vitreous humor.
- Composed of repeating units of N-acetyl glucosamine → ß-1,4 glucuronic acid → ß-1,3 N-acetyl glucosamine.

HEPARIN



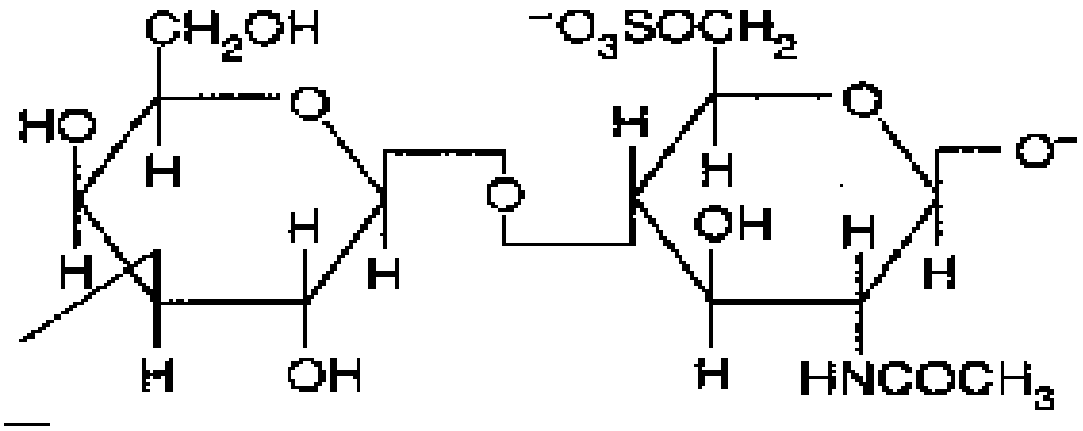
- **Anticoagulant. Bind and activate Antithrombin III, which in turn activates Thrombin, Factor X & Factor IX.**
- **Present in lung, spleen and monocytes.**
- **Contains repeating units of sulphated glucosamine → α-1,4 L-iduronic acid.**
- **Sulphated: Heparan sulphate**

CHONDROITIN SULPHATE



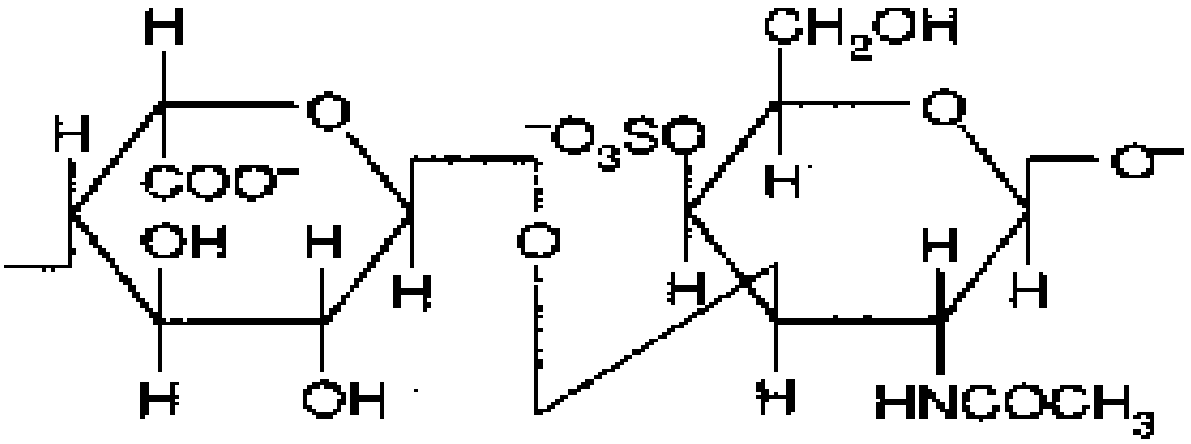
- **Present in ground substances of connective tissues of cartilages, bones & tendons.**
- **Composed of Glucuronic acid → ß-1,3 N-acetyl galactosamine sulphate → ß-1,4 and so on.**

KERATAN SULPHATE



- Only GAG not having Uronic acid.
- Found in cornea and tendons.
- Repeating units are Galactose & N-acetyl galactosamine in ß linkage.

DERMATAN SULPHATE



- Found in skin, blood vessels & heart vessels.
- Contains L-iduronic acidand N-acetyl galactosamine in ß-1,3 linkage.

MUCOPLYSACCHARIDOSIS

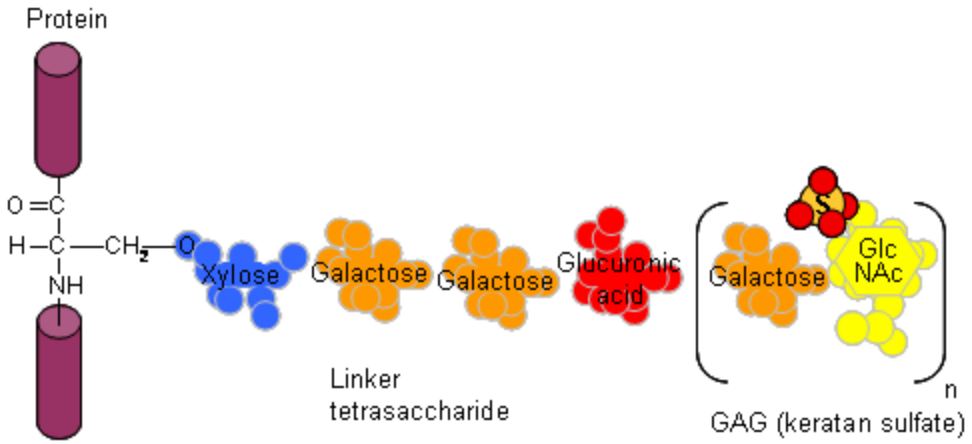
NAME	ENZYME DEFECT	URINARY METABOLITES
MPS I : Hurler's	α -L-Iduronidase	Dermatan sulfate Heparan sulfate
MPS II: Hunter's	Iduronate sulphatase	Dermatan sulfate Heparan sulphate
MPS IIIA: San Filippo A MPS IIIB: San Filippo B MPS IIIC: San Filippo C MPS IIID: San Filippo D	Sulfamidase α-N-acetyl glucosaminidase Acetyl transferase N-acetyl glucosamine 6 sulfatase	Heparan sulfate Heparan sulfate Heparan sulfate Heparan sulfate

MUCOPLYSACCHARIDOSIS

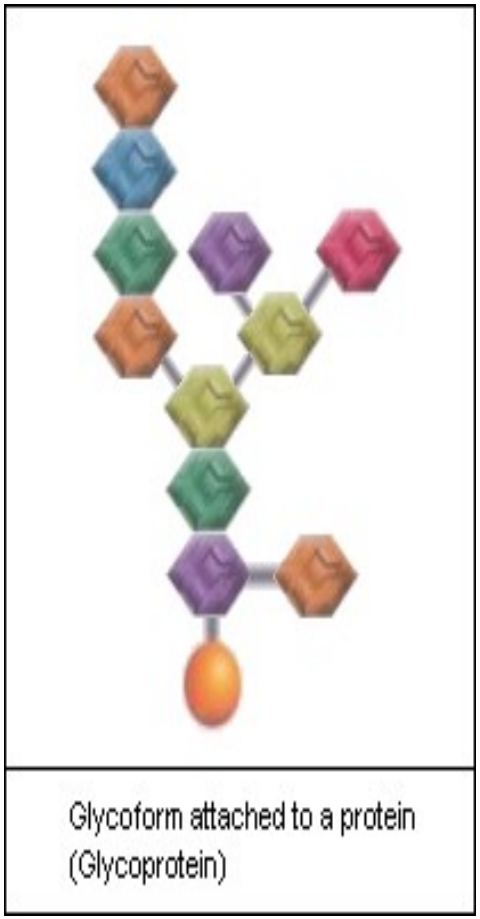
NAME	ENZYME DEFECT	URINARY METABOLITES
MPS IVA: Morquio A MPS IVB: Morquio B	Galactosamine 6 sulfatase ß-galactosidase	Keratan sulfate, Chondroitin 6-sulfate
MPS VI: Maroteaux-Lamy	Arylsulfatase B	Keratan sulfate
MPS VII: Sly	ß-glucuronidase	Dermatanan sulphate

PROTEOGLYCANS & GLYCOPROTEINS

- **Proteoglycans:** When carbohydrate chains are attached to a polypeptide chain.
- **Glycoproteins:** Carbohydrate content ≤ 10%.
- **Mucoprotein:** Carbohydrate content ≥10%



Proteoglycan



Glycoform attached to a protein (Glycoprotein)


Thank You