Carbohydrates

Carbohydrates (CHO) are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis.

Many but not all carbohydrates have the empirical formula $C_n(H_2O)_n$, some also contain nitrogen, phosphorus or sulfur.

They are also called saccharides or sugar due to the sweet taste of the simplest member of the family.

Biomedical importance:

1. Chief source of energy (glucose) and for storage of energy (starch and glycogen).
2. Constituents of compound lipids (glycolipids) and conjugated proteins (glycoproteins).
3. Certain CHO derivatives are used as drugs such as Cardiac glycosides (digoxin) and antibiotics.
4. Their degradation products are utilized for the synthesis of other substances such as fatty acids, cholesterol, amino acids, etc.
5. Ribose is an important component of coenzymes such as ATP, NAD and as the backbone of RNA while deoxyribose is part of DNA.
6. Saccharides and their derivatives play a role in immune system, fertilization and blood clotting.
7. Deficiency of certain enzymes in CHO metabolism lead to diseases such as galactocaemia and lactose intolerance. While derangement in glucose metabolism leads to Diabetes Mellitus.

Classification:

CHO are divided into 4 major groups:

1. Monosaccharide: also called simple sugar. They can't be hydrolyzed into simpler form. They can be subdivided further :

    A. Depending upon the no. of carbon atoms they possess into triose, pentose, hexose etc.

    B. Depending upon the site of carbonyl group, whether terminal (aldehyde, aldose) or non-terminal (ketone, ketose).

2. Disaccharides: sugars that yield 2 molecules of same or different monosaccharides on hydrolysis .
3. Oligosaccharides: which yields 3-10 molecules of monosaccharides on hydrolysis.

4. Polysaccharides: yield more than 10 molecules of monosaccharides on hydrolysis . They can be subdivided further :

A. Homopolysaccharide: polymer of the same monosaccharide units, ex. : starch , glycogen .

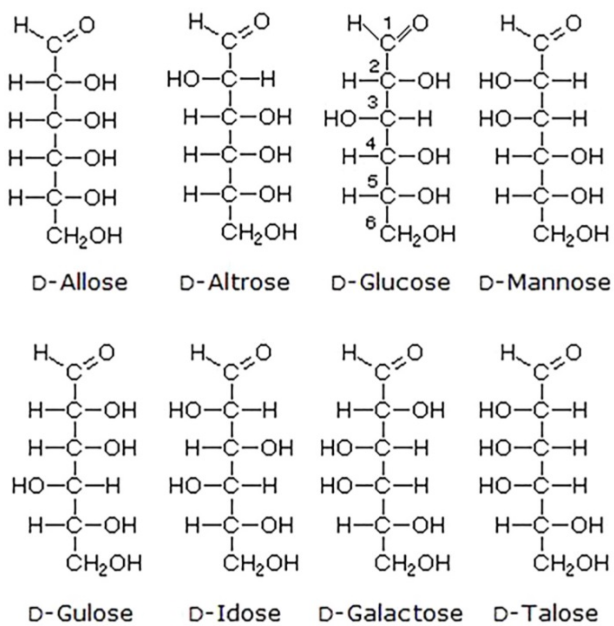
B. Heteropolysaccharide: polymer of the different monosaccharide units or their derivatives, ex.: mucopolysaccharide.

1. Monosaccharides:

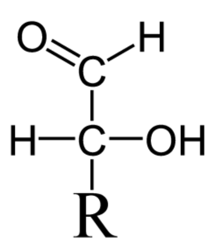
They are the simplest CHO that can't be hydrolyzed to simpler one

The structure of monosaccharides:

sugars show various forms of isomerism (compounds that are identical in composition (same chemical formula) but differ in spatial configuration). Example : Glucose, Fructose , Mannose and Galactose have the same chemical formula ($C_6H_{12}O_6$).

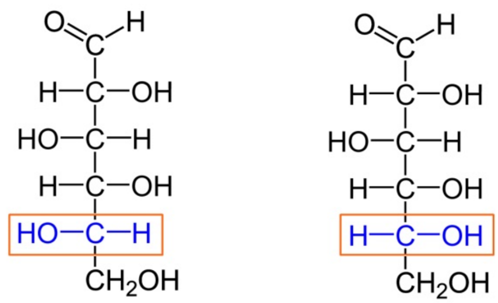


<u>Asymmetric carbon</u>: a carbon atom to which 4 different atoms or groups of atoms are attached.



Types of Isomerism:

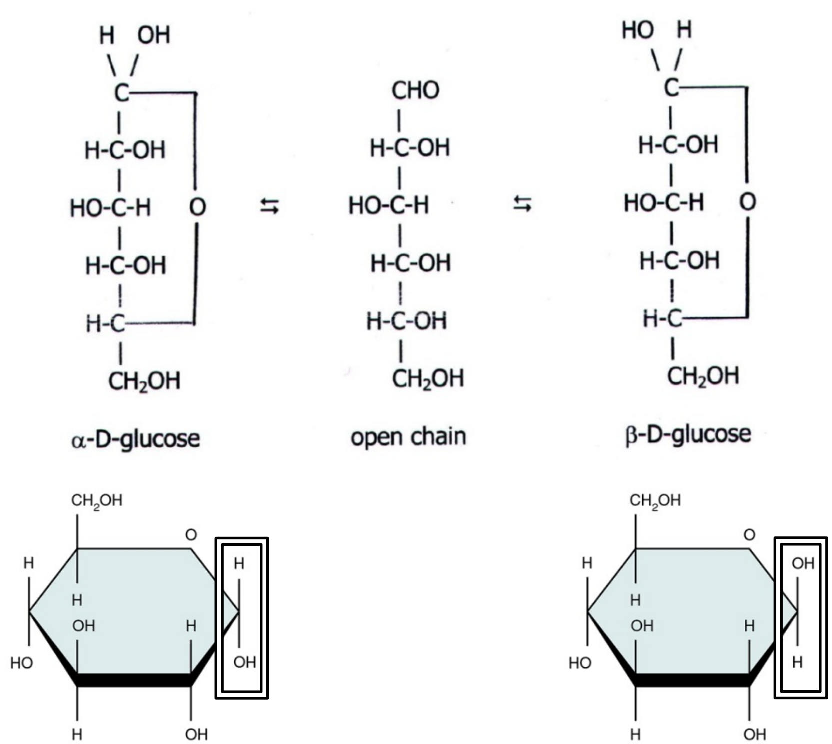
1. D and L isomerism: the orientation of H and OH groups around the carbon atom adjacent to the terminal primary alcohol carbon determine the series, ex: C_5 in glucose.
When -OH group on this carbon atom is on the right ⟶ **D- isomer**
When -OH group on this carbon atom is on the left ⟶ **L- isomer**



L- Glucose   D- Glucose

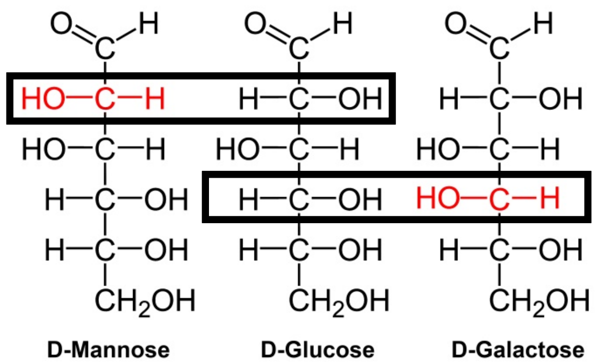
* The vast majority of sugars in human are D- sugars.

2. Alpha (α) and Beta (β) anomers: most monosaccharides exist in cyclic form as they contain 2 functional groups (carbonyl and hydroxyl groups). Ex: in case of glucose, the carbonyl group at C1 reacts with the hydroxyl group in C_5 to give six-member ring, and 2 different forms of glucose are formed:
Alpha (α) : (α-D-glucose) when the –OH group extends to the right (i.e. below the ring).
Beta (β) : **(β -D-glucose)** when the –OH group extends to the left (i.e. above the ring).

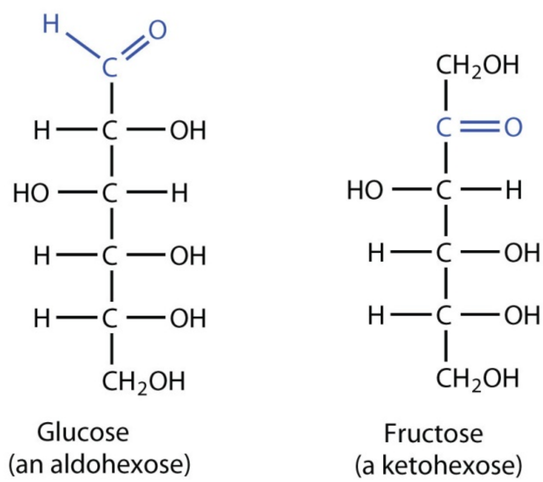


3. Epimers: are 2 monosaccharides that differ in the configuration of –H and –OH around only one specific carbon atom (with the exception of the carbonyl carbon).

Glucose and Mannose are epimers at C_2.
Glucose and Galactose are epimers at C_4.



4. Aldose and Ketose: Fructose and Glucose have the same molecular formula, but they differ in the site of the carbonyl group.
In glucose, the carbonyl group is at C_1 so it is an Aldose.
In Fructose, the carbonyl group is at C_2 so it is an Ketose.



Reactions of Carbohydrates:

1. Molisch's test: is a sensitive test for the presence of CHO.
2. Benedict's test: it is used to detect reducing sugars (whether mono or disaccharide).
3. Barfoed's test: it is used to distinguish between reducing monosaccharide from reducing disaccharide.
4. Bial's test: it is used to distinguish between pentoses and hexoses.
5. Seliwanoff's test: it is used to distinguish between aldoses and ketoses.
6. Iodine test: it is used to detect polysaccharides (starch).

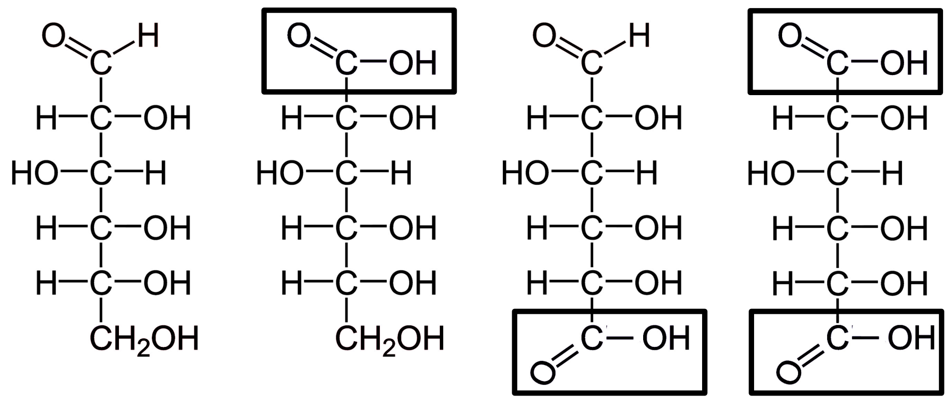
Reactions of Monosaccharides:

1. Oxidation reactions:

a. The carbonyl group of an aldose is oxidized to carboxylic acid by mild oxidizing agent to form **aldonic acid,** ex: gluconic acid.

b. Oxidation of the primary alcohol yields **uronic acid**, ex: Glucuronic acid, galacturonic acid.

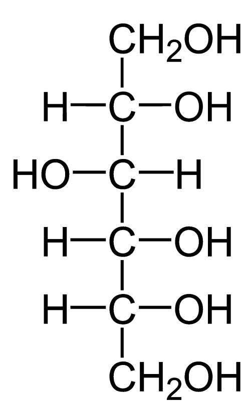
c. Oxidation of both carbonyl group and primary alcohol in aldoses yields **aldaric acid**.



D-Glucose Gluconic acid Glucuronic acid Glutaric acid

2. Reduction reaction: aldoses and ketoses can be reduced to form **Alditols (sugar alcohol)**.

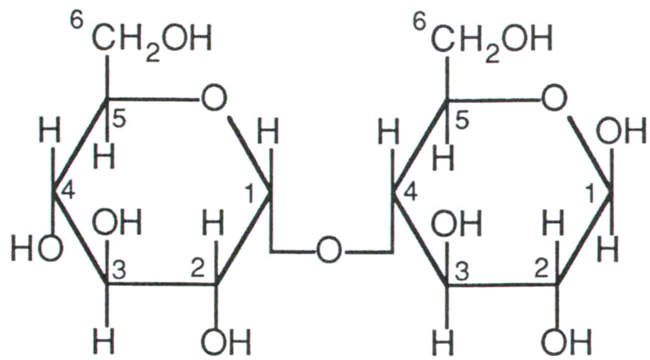
Biomedical importance: Several of them are used as sugarless sweetening agents such as Sorbitol (glucitol) and Mannitol. They are also important components of lipid. Sorbitol is also used as laxative while mannitol is used to reduce acutely raised intracranial pressure e.g., after head trauma. It is also used to treat patients with oliguric renal failure.



3. Glycosides formation: result from the condensation between the hydroxyl group of anomeric carbon atom of a monosaccharide and another compound (which may or may not be a monosaccharide).

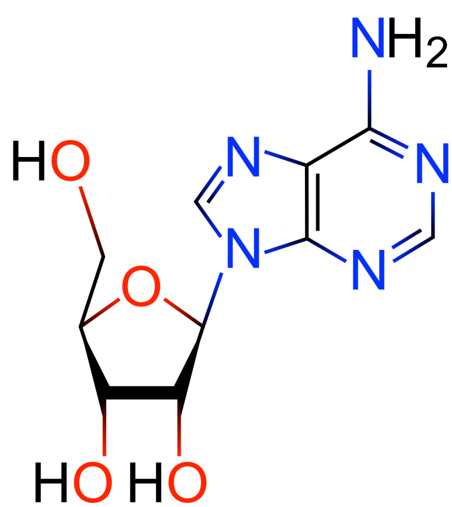
Types of glycosidic bonds:

a. **O-glycosidic bond:** results from the reaction between the hydroxyl group of anomeric carbon atom of a monosaccharide with an alcohol in presence of acid.



Maltose

b. **N- glycosidic bond:** results from the reaction between the hydroxyl group of anomeric carbon atom of a monosaccharide with an amide group, ex: adenosine (which is made from adenine and D-ribose).



Adenosine

Pentoses

Sugar	Biochemical importance
D- Ribose	structural component of nucleic acids and co-enzymes including ATP and NAD
D-Ribulose	Intermediate in the Pentose Phosphate Pathway
D-Arabinose	Constituent of Glycoproteins

Hexoses

Sugar	Biochemical importance
D- Glucose	The main metabolic fuel of the tissues. It is excreted in urine in poorly controlled diabetes mellitus.
D-Fructose	It is metabolized to glucose. Fructose intolerance leads to fructose accumulation and hypoglycemia.
D-Galactose	It is metabolized to glucose. Synthesized in mammary glands for synthesis of lactose in milk.

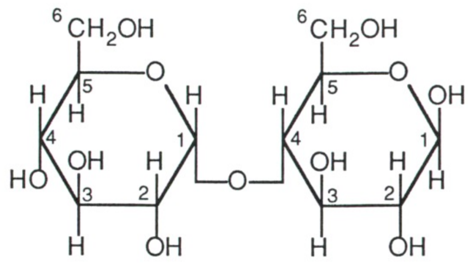
2. Disaccharides:

Disaccharide is made up of two molecules of monosaccharides that are the same or different and joined by glycosidic bond. The general molecular formula is $C_{12}H_{22}O_{11}$

The most important disaccharides of biological importance are **Maltose**, **Lactose** and **Sucrose**.

Maltose:

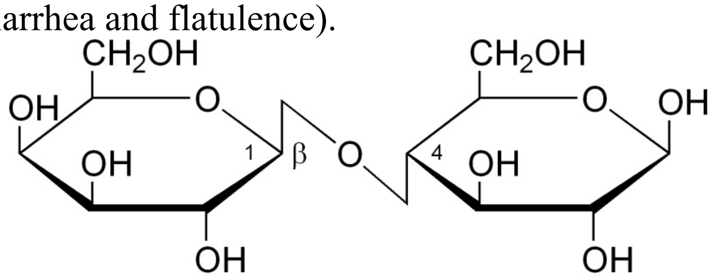
1. Consists of 2 molecules of Glucose linked by α(1→4) glycosidic bond.
2. It is an intermediate in hydrolysis of starch by acid or enzyme (amylase).
3. It is a reducing sugar, so it gives +ve result with Benedict's reagent.



Maltose

Lactose:

1. It is made up of one molecule of β-D-Galactose and one molecule of either α or β D-Glucose linked by β(1→4) glycosidic bond.
2. It is 'milk sugar'.
3. It is a reducing sugar, so it gives +ve result with Benedict's reagent.
4. Lack of lactase (the enzyme which is responsible for its hydrolysis) leads to lactose intolerance (causing diarrhea and flatulence).



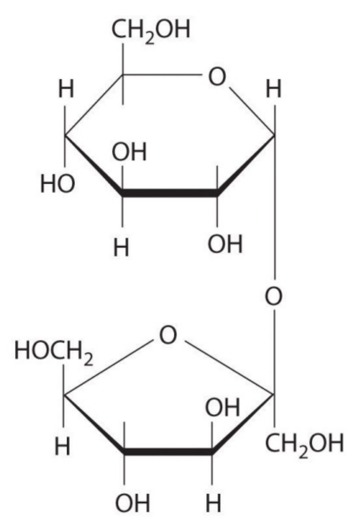
Sucrose:

1. It is made up of one molecule of α-D-Glucose and one molecule of β-D-Fructose linked by (α1→ β2) glycosidic bond.

2. It is called "table" sugar or "cane sugar". It is synthesized by plant and not by animals.

3. It is a non-reducing sugar, so it gives -ve result with Benedict's reagent.

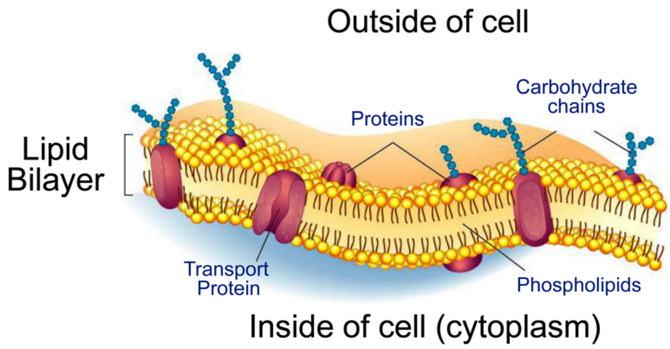
4. It is used as food preservative because at high concentration, it produces high osmotic pressure inhibiting the growth of microorganisms.



Sucrose

3. Oligosaccharides:

Oligosaccharide molecule consists of 3-10 molecules of monosaccharides. Oligosaccharides are attached covalently to the outer surface of the proteins of cell membrane forming (glycoproteins) which act as receptors. Moreover, many antibodies and coagulation factors contain oligosaccharide units.



Blood groups

Blood group antigens: Specific oligosaccharides bound to proteins (glycoproteins) and lipids (glycolipids) on membrane surfaces of RBC (Red Blood Cells) and most other cells in human body.

H-antigen

- The H antigen is found on virtually all RBCs.
- It is the building block for the production of the antigens within the ABO blood group.
- It consists of the following:

  Glucose – Galactose – N-acetylglucosamine – Galactose – Fucose.

A-antigen

- It consists of the following:

  Glucose – Galactose – N-acetylglucosamine – Galactose – Fucose

  |

  N-acetylgalactosamine

B-antigen

- It consists of the following:

  Glucose – Galactose – N-acetylglucosamine – Galactose – Fucose

  |

  Galactose

4. Polysaccharides:

They more complex substances. They yield more than 10 molecules of monosaccharides on hydrolysis . They can be subdivided further:

A. Homopolysaccharide: polymer of the same monosaccharide units, ex.: starch, glycogen, cellulose and chitin.

B. Heteropolysaccharide: polymer of the different monosaccharide units or their derivatives, ex.: Hyaluronic acid, Chondroitin and Heparin.

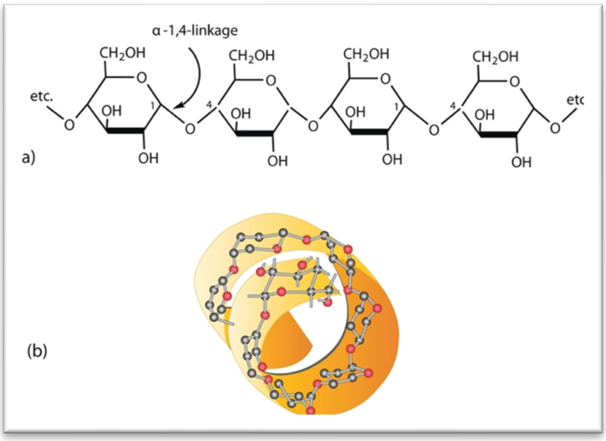
1. Starch:

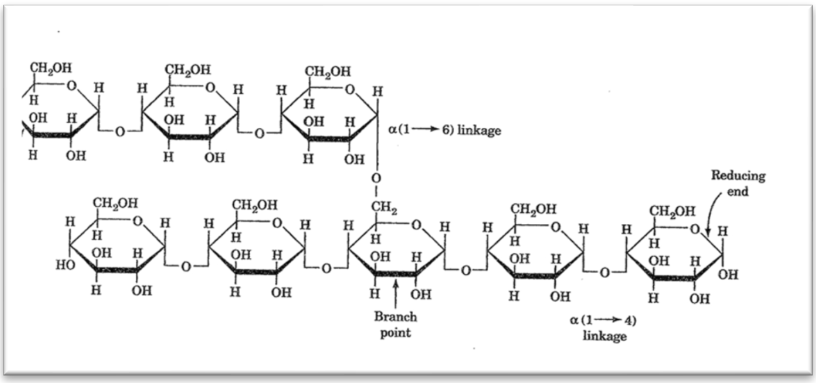
a. It is a polymer of α-D-glucose.
b. It is the most important dietary carbohydrate in cereals, potatoes and other vegetables.
c. It consists of two types of glucose polymers:

1. **Amylose** (20%), which has a non-branched structure made up entirely of α-D- Glucose joint by α(1→4) glycosidic linkage, so it is a head-to-tail polymer of up to 4000 glucose units.

2. **Amylopectin** (80%), which is highly branched chains composed of α-D-Glucose united by α(1→4) linkages while the linkages at branch points are α(1→6) linkages. The branching occurs at one in every 20-25 glucose molecules in the chain.

So starch is a heterogeneous homopolysaccharide.





Amylose **Amylopectin and Glycogen**

2. Glycogen:

a. It is the storage polysaccharide in animals and is sometimes called animal starch.
b. Like amylopectin, it is highly branched chains composed of α-D-Glucose joined by α(1→4) linkages while the linkages at branch points are α(1→6) linkages.
c. It differs from amylopectin that it has more but shorter branches. The branching occur every 12-18 glucose molecules in the chain.

d. During meals, the excess of glucose is stored in the body (liver and muscles) in form of glycogen. Between meals and during fasting, the glycogen is hydrolyzed to glucose to provide the body with its need of glucose.

3. Inulin:

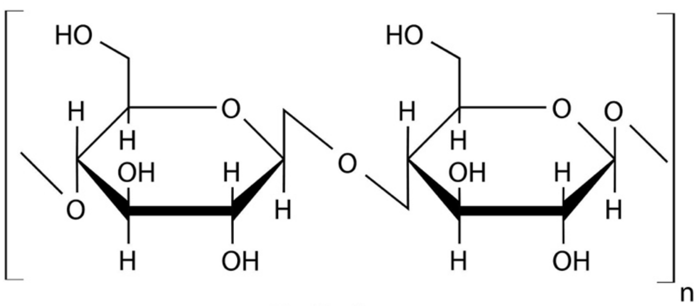
It is a homopolysaccharide of D-fructose. It has no dietary importance in human. It has low molecular weight and readily soluble in water. It is used to determine the Glomerular Filtration Rate (GFR).

4. Cellulose:

a. It is a structural polysaccharide. It is the main constituent of cell wall of plants.

b. It is an unbranched homopolysaccharide of β-D-Glucose joined by β (1→4) linkages to form long, straight chains. They are strengthened by crosslinking hydrogen bonds forming long chains of parallel cellulose molecules called Fibrils.

c. It has no dietary importance in human because human gut does not release the enzyme responsible for hydrolysis of β (1→4) linkages so he can't digest cellulose.



Cellulose

5. Mucopolysaccharide (Glycosaminoglycan):

a. They are usually composed of **amino sugar** and **uronic acid** units.

b. They may be attached to a protein molecule to form a **proteoglycan.**

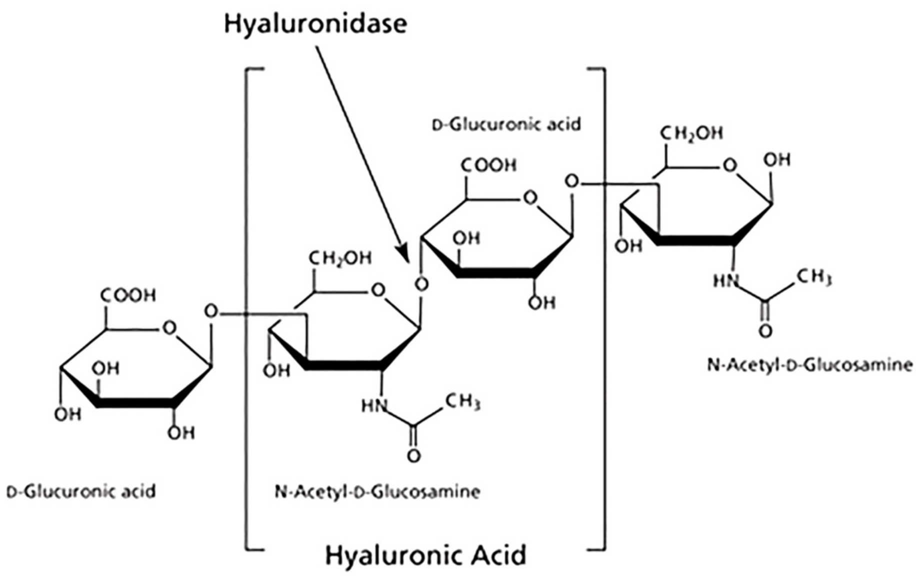
1. Hyaluronic acid:

a. A non-sulfated mucopolysaccharide.

b. It is present in bacteria and animals' tissues, including synovial fluid, the vitreous body of the eye, cartilage, and loose connective tissues.

c. It consists of an unbranched chain of repeating disaccharide units containing D-glucuronic acid and N-acetyl D-glucosamine joined by β(1→3) linkages. Each disaccharide unit is attached to the next unit by β(1→4) linkages.

d. Hyaluronidase, catalyzes the hydrolysis of β(1→4) linkages of hyaluronic acid and so decreasing its viscosity. This enzyme is present in testicular secretion, dissolving the substance surrounding the ova so facilitate the penetration of ova. It is also secreted by some pathogenic bacteria facilitating their diffusion into the tissues.

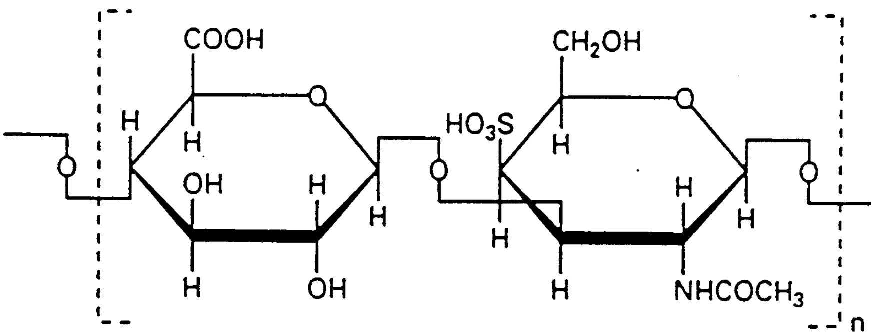


2. Chondroitin:

a. A non-sulfated mucopolysaccharide.

b. It consists of an unbranched chain of repeating disaccharide units containing D- glucuronic acid and N-acetyl D-galactosamine joined by β(1→3) linkages. Each disaccharide unit is attached to the next unit by β(1→4) linkages.

c. The sulfuric acid derivatives (chondroitin 4-sulphate and chondroitin 6-sulphate) are the major components of cell wall, cartilage, bones, cornea and connective tissues. **Why Hyaluronidase catalyzes the hydrolysis of chondroitin?**



3. Heparin:

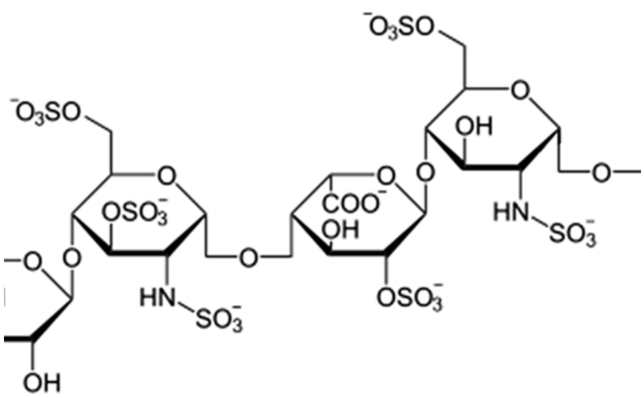
a. A highly-sulfated mucopolysaccharide.

b. It is produced by the liver.

c. It is a polymer of repeated units of L-iduronic acid and N-sulfated D-glucosamine.

d. It inhibits the formation of thrombin from prothrombin so it is widely used as injectable anticoagulant in test tubes and renal dialysis.

e. It increases the activity of lipoprotein lipase.



4. Heparan sulfate:

This molecule is present on many **cell surfaces** as a proteoglycan and is extracellular. It differs from heparin in that it contains fewer N-sulfates than heparin, and, unlike heparin, its predominant uronic acid is Glucuronic acid.

Glycoproteins and Proteoglycans:

Proteoglycans:

a. They are proteins that contain covalently linked glycosaminoglycans. The proteins are called **"core proteins"**.

b. The unbranched carbohydrate chains may form up to 95% of its weight.

c. **Functions:**

1. are found in **every tissue** of the body, mainly in the Extra Cellular Matrix (ECM) where they are bound to collagen and elastin.

2. They are negatively charged so they bind cations such as Na^+ and K^+ and thus attract water to ECM.

Glycoproteins:

a. They are proteins to which oligosaccharides are attached to. The oligosaccharides are usually branched.

b. They contain more proteins than carbohydrates.

c. **Functions:**

1. Structural molecules such as collagen.

2. Act as receptors on cell membrane for binding hormones and in cell recognition.

3. Act as transport molecule such as Transferrin, ceruloplasmin.

4. Immunoglobulins are glycoproteins.

5. Act as hormones such as Thyroid stimulating hormone (TSH) and hCG.

6. Some have a role in blood clotting such as Fibrinogen.