CBCS 3rd Semester
Core Course VII
Paper: Fundamentals of Biochemistry

Unit 1: Carbohydrates

Structure and Biological importance: Monosaccharides, Disaccharides, Polysaccharides and Glycoconjugates

By-
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Definition

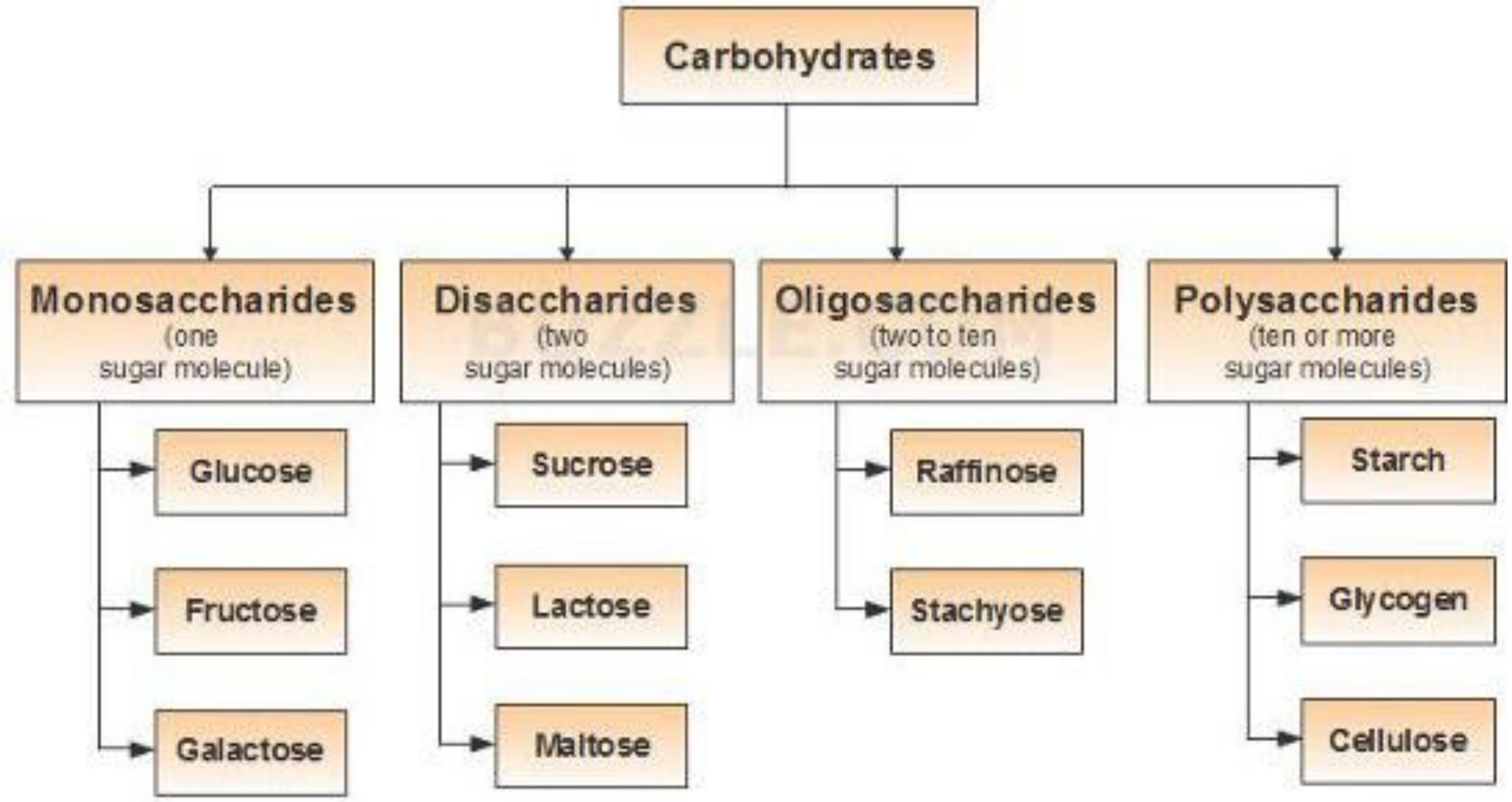
- The carbohydrates are a group of naturally occurring carbonyl compounds (aldehydes or ketones) that also contain several hydroxyl groups.
- It may also include their derivatives which produce such compounds on hydrolysis.
- They are the most abundant organic molecules in nature and also referred to as “saccharides”.
- The carbohydrates which are soluble in water and sweet in taste are called as “sugars”.

Structure of Carbohydrates

- Carbohydrates consist of carbon, hydrogen, and oxygen. The general empirical structure for carbohydrates is $(CH_2O)_n$.
  They are organic compounds organized in the form of aldehydes or ketones with multiple hydroxyl groups coming off the carbon chain.
- The building blocks of all carbohydrates are simple sugars called monosaccharides.
  A monosaccharide can be a polyhydroxy aldehyde (aldose) or a polyhydroxy ketone (ketose)

- The carbohydrates can be structurally represented in any of the three forms:
- 1. Open chain structure.
  2. Hemi-acetal structure.
  3. Haworth structure.
- Open chain structure – It is the long straight-chain form of carbohydrates.
- Hemi-acetal structure – Here the 1st carbon of the glucose condenses
  with the -OH group of the 5th carbon to form a ring structure.
- Haworth structure – It is the presence of the pyranose ring structure

Classification of Carbohydrates



Monosaccharides

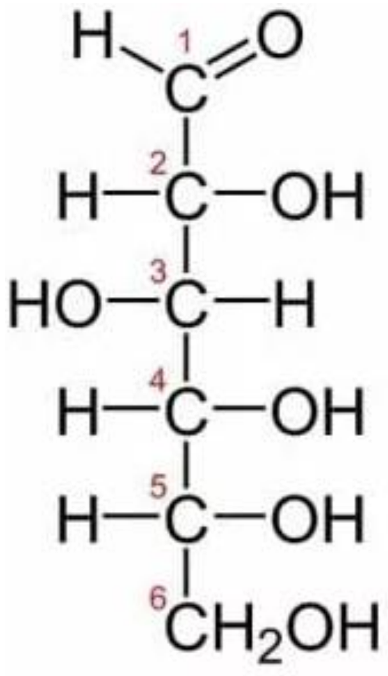
- The simple carbohydrates include single sugars (monosaccharides) and polymers, oligosaccharides, and polysaccharides.

- Simplest group of carbohydrates and often called simple sugars
since they cannot be further hydrolyzed.

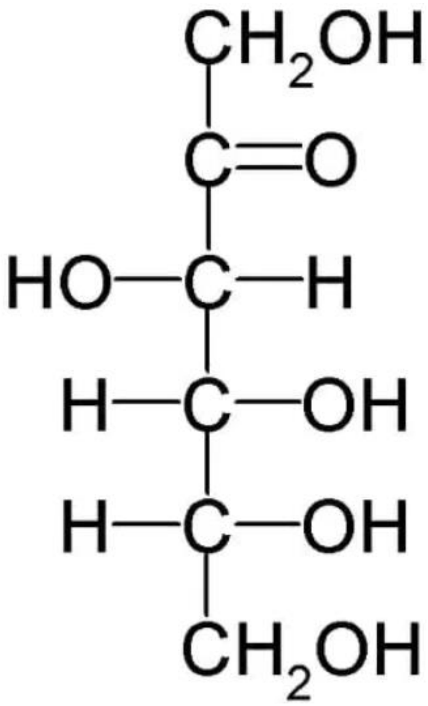
- Colorless, crystalline solid which are soluble in water and insoluble in a non-polar solvent.
- These are compound which possesses a free aldehyde or ketone group.
- The general formula is $C_n(H_2O)n$or $C_nH_{2n}O_n$.
- They are classified according to the number of carbon atoms they contain and also on the basis of the functional group present.
- The monosaccharides thus with 3,4,5,6,7… carbons are called trioses, tetroses, pentoses, hexoses, heptoses, etc., and also as aldoses or ketoses depending upon whether they contain aldehyde or ketone group.
- Examples: Glucose, Fructose, Erythrulose, Ribulose.

Chemical Structure of some monosaccharides

Glucose



Fructose



Properties of Monosaccharides

- Most monosaccharides have a sweet taste (fructose is sweetest; 73% sweeter than sucrose).
  They are solids at room temperature.

- They are extremely soluble in water: – Despite their high molecular weights, the presence of large numbers of OH groups make the monosaccharides much more water-soluble than most molecules of similar MW.

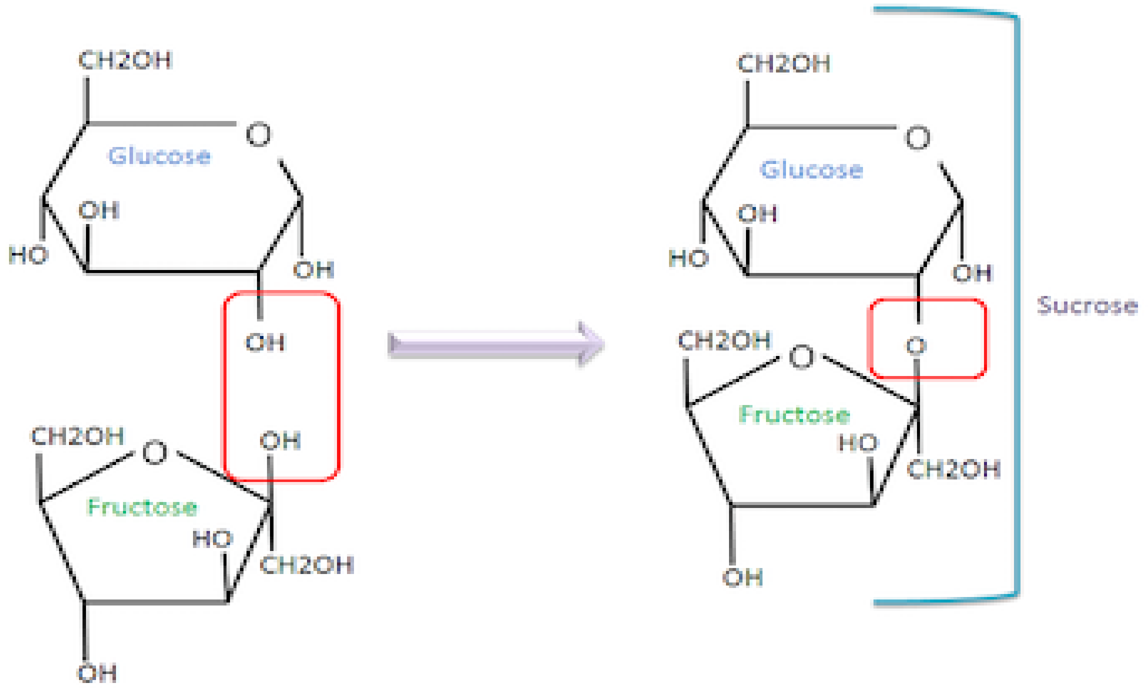
- Glucose can dissolve in minute amounts of water to make a syrup (1 g / 1 ml H_2O).

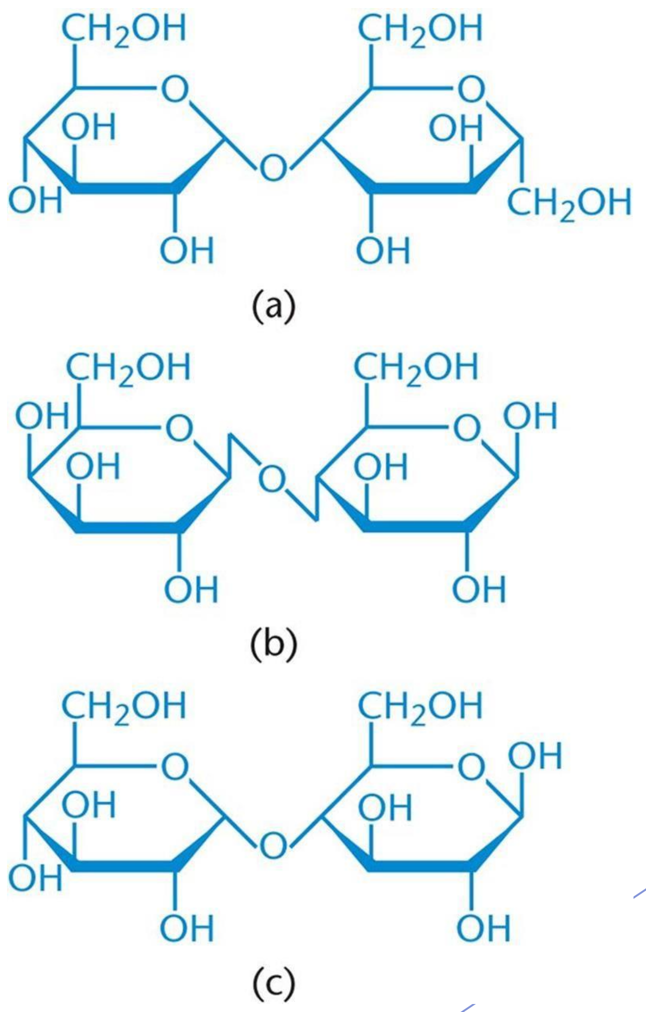
Disaccharides

- Two monosaccharides connected by a glycosidic bond.
- Disaccharide, also called double sugar, any substance that is composed of two molecules of simple sugars (monosaccharides) linked to each other.
- Disaccharides are crystalline water-soluble compounds. The monosaccharides within them are linked by a glycosidic bond (or glycosidic linkage), the position of which may be designated α- or β- or a combination of the two (α-,β-).
- Glycosidic bonds are cleaved by enzymes known as glycosidases. The three major disaccharides are sucrose, lactose, and maltose.

- Sucrose, which is formed following photosynthesis in green plants, consists of one molecule of glucose and one of fructose bonded via an α-,β-linkage. Lactose (milk sugar), found in the milk of all mammals, consists of glucaose and galactose connected by a β-linkage.
- Maltose, a product of the breakdown of starches during digestion, consists of two molecules of glucose connected via an α-linkage. Another important disaccharide, trehalose, which is found in single-celled organisms and in many insects, also consists of two molecules of glucose and an α-linkage, but the linkage is distinct from the one found in maltose.

Structure of disaccharides





Significance of disaccharides

- More specifically, a disaccharide results when two monosaccharides are joined in a chemical process called **dehydration synthesis**, which causes two monosaccharides to combine, losing a water molecule in the process. This process is also known as a **condensation reaction.** Here we see an example of the formation of the disaccharide sucrose, formed from the combination of the monosaccharides fructose and glucose.

Oligosaccharides

- Oligosaccharides are compound sugars that yield 2 to 10 molecules of the same or different monosaccharides on hydrolysis.

- The monosaccharide units are joined by glycosidic linkage.

- Based on the number of monosaccharide units, it is further classified as disaccharide, trisaccharide, tetrasaccharide etc.

- s Oligosaccharides yielding 2 molecules of monosaccharides on hydrolysis is known as a disaccharide, and the ones yielding 3 or 4

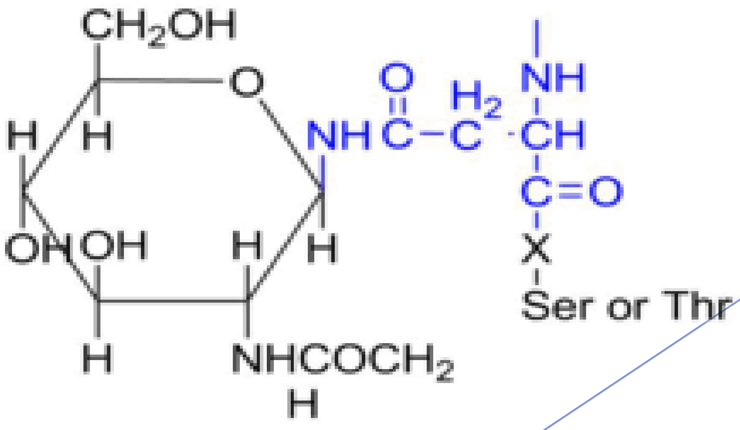
Structure of oligosaccharide

- They are normally present as glycans: oligosaccharide chains linked to lipids or to compatible amino acid side chains in proteins, by N- or O-glycosidic bonds. N-Linked oligosaccharides are always pentasaccharides attached to asparagine via a beta linkage to the amine nitrogen of the side chain.
- Alternately, O-linked oligosaccharides are generally attached to threonine or serine on the alcohol group of the side chain. Not all natural oligosaccharides occur as components of glycoproteins or glycolipids. Some, such as the raffinose series, occur as storage or transport carbohydrates in plants. Others, such as maltodextrins or cellodextrins, result from the microbial breakdown of larger polysaccharides such as starch or cellulose.

N-linked Oligosaccharides

- N-Linked glycosylation involves oligosaccharide attachment to asparagine via a beta linkage to the amine nitrogen of the side chain. The process of N-linked glycosylation occurs cotranslationally, or concurrently while the proteins is being translated. Since it is added cotranslationally, it is believed that N-linked glycosylation helps determine the folding of polypeptides due to the hydrophilic nature of sugars. All N-linked oligosaccharides are pentasaccharides: five monosaccharides long.

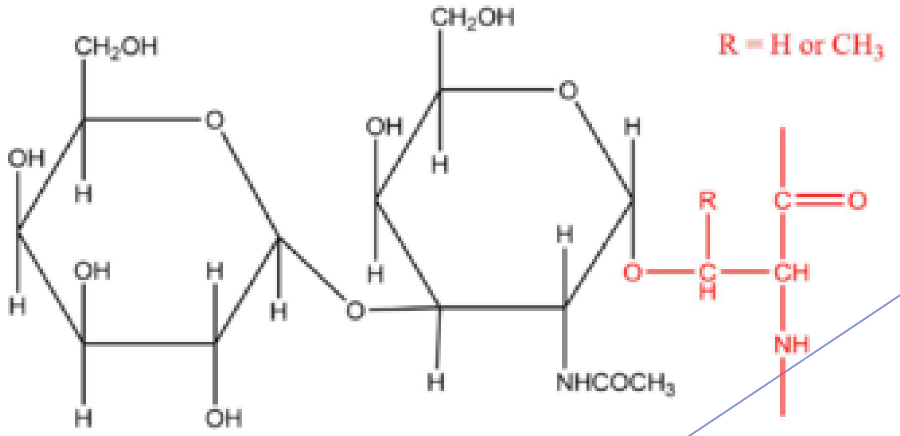
An example of an *N*-linked oligosaccharide, shown here with GlcNAc. X is any amino acid except proline.



O-Linked oligosaccharides

- Oligosaccharides that participate in O-linked glycosylation are attached to threonine or serine on the hydroxyl group of the side chain. O-linked glycosylation occurs in the Golgi apparatus, where monosaccharide units are added to a complete polypeptide chain. Cell surface proteins and extracellular proteins are O-glycosylated. Glycosylation sites in O-linked oligosaccharides are determined by the secondary and tertiary structures of the polypeptide, which dictate where glycosyltransferases will add sugars.

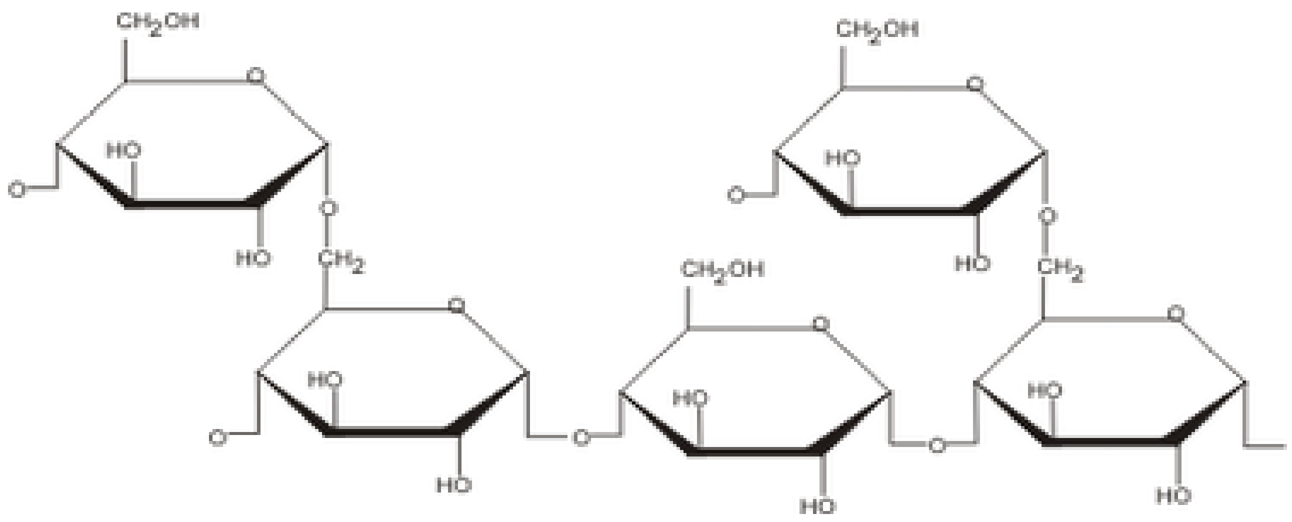
example of an O-linked oligosaccharide with β-Galactosyl-(1n3)-α-N-acetylgalactosaminyl-Ser/Thr.



Polysaccharides

- They are also called as “glycans”.
- Polysaccharides contain more than 10 monosaccharide units and can be hundreds of sugar units in length.
- They yield more than 10 molecules of monosaccharides on hydrolysis.
- Polysaccharides differ from each other in the identity of their recurring monosaccharide units, in the length of their chains, in the types of bond linking units and in the degree of branching.
- They are primarily concerned with two important functions ie. Structural functions and the storage of energy.

Structure of polysaccharides



The two types of glycosidic bonds (alpha-1,4 and alpha-1,6) in glycogen are shown.

Function of polysaccharide

- Polysaccharides have several roles.
- Polysaccharides such as starch, glycogen, and dextrans are all stored in the liver and muscles to be converted to energy for later use.
- Amylose and Amylopectin are polysaccharides of starch.
- Amylose has a linear chain structure made up of hundreds of glucose molecules that is linked by a alpha 1,4 glycosidic linkage. Due to the nature of these alpha 1,4 bonds, the macromolecule often assumes a bent shape. The starch molecules form a hollow helix that is suitable for easy energy access and storage. This gives starch a less fibrous quality and a more granule-like shape which is better suited for storage. Unlike the linear structure of Amylose, the Amylopectin starches are branched containing an alpha 1,6 glycosidic linkage about every 30 glucose units. Like amylose it is a homopolymer composed of many glucose units

- Glycogen is found in animals, and it is branched like amylopectin. It is formed by mostly alpha 1,4 glycosidic linkages but branching occurs more frequently than in amylopectin as alpha 1,6 glycosidic linkages occur about every ten units. Other polysaccharides have structural functions. For example, cellulose is a major component in the structure of plants. Cellulose is made of repeating beta 1,4-glycosidic bonds. These beta 1,4-glycosidic bonds, unlike the alpha 1,4 glycosidic bonds, force celullose to form long and sturdy straight chains that can interact with one another through hydrogen bonds to form fibers

Functions of carbohydrates

- Carbohydrates are widely distributed molecules in plant and animal tissues. In plants and arthropods, carbohydrates from the skeletal structures, they also serve as food reserves in plants and animals. They are important energy source required for various metabolic activities, the energy is derived by oxidation.

- Living organisms use carbohydrates as accessible energy to fuel cellular reactions. They are the most abundant dietary source of energy (4kcal/gram) for all living beings.
- Carbohydrates along with being the chief energy source, in many animals, are instant sources of energy. Glucose is broken down by glycolysis/ Kreb's cycle to yield ATP.
- Serve as energy stores, fuels, and metabolic intermediates. It is stored as glycogen in animals and starch in plants.

- Stored carbohydrates act as an energy source instead of proteins.

- They form structural and protective components, like in the cell wall of plants and microorganisms. Structural elements in the cell walls of bacteria (peptidoglycan or murein), plants (cellulose) and animals (chitin).

- Carbohydrates are intermediates in the biosynthesis of fats and proteins.

- Carbohydrates aid in the regulation of nerve tissue and is the energy source for the brain.
- Carbohydrates get associated with lipids and proteins to form surface antigens, receptor molecules, vitamins, and antibiotics.
- Formation of the structural framework of RNA and DNA (ribonucleic acid and deoxyribonucleic acid).
- They are linked to many proteins and lipids. Such linked carbohydrates are important in cell-cell communication and in interactions between cells and other elements in the cellular environment.
- In animals, they are an important constituent of connective tissues.
- Carbohydrates that are rich in fiber content help to prevent constipation.
- Also, they help in the modulation of the immune system.

- They re-further classified depending on the type of molecules produced as a result of hydrolysis.
- They may be homopolysaccharidese, containing monosaccharides of the same type or heteropolysaccharides i.e., monosaccharides of different types.
- Examples of Homopolysaccharides are starch, glycogen,
cellulose, pectin.
- Heteropolysaccharides are Hyaluronic acid, Chondroitin monosaccharides are known as trisaccharides and tetrasaccharides respectively and so on.

- The general formula of disaccharides is $C_n(H_2O)_{n-1}$ and that of trisaccharides is $C_n(H_2O)_{n-2}$ and so on.
- Examples: Disaccharides include sucrose, lactose, maltose,etc.
- Trisaccharides are Raffinose, Rabinose.

Properties of Carbohydrates

Physical & Chemical Properties

Physical Properties of Carbohydrates

- **Stereoisomerism** – Compound shaving the same structural formula but they differ in spatial configuration. Example: Glucose has two isomers with respect to the penultimate carbon atom. They are D-glucose and L-glucose.

- **Optical Activity** – It is the rotation of plane-polarized light forming (+) glucose and (-) glucose.

- **Diastereo isomers** – It the configurational changes with regard to C_2, C_3, or C_4 in glucose. Example: Mannose, galactose.

- **Annomerism** – It is the spatial configuration with respect to the first carbon atom in aldoses and second carbon atom in ketoses.

Chemical Properties of Carbohydrates

- **Osazone formation**: Osazone are carbohydrate derivatives when sugars are reacted with an excess of phenylhydrazine. eg. Glucosazone
- **Benedict's test:** Reducing sugars when heated in the presence of an alkali gets converted to powerful reducing species known as enediols. When Benedict's reagent solution and reducing sugars are heated together, the solution changes its color to orange-red/ brick red.
- **Oxidation:** Monosaccharides are reducing sugars if their carbonyl groups oxidize to give carboxylic acids. In Benedict's test, D-glucose is oxidized to D-gluconic acid thus, glucose is considered a reducing sugar.
- **Reduction to alcohols:** The C=O groups in open-chain forms of carbohydrates can be reduced to alcohols by sodium borohydride, $NaBH_4$, or catalytic hydrogenation (H_2, Ni, EtOH/H_2O). The products are known as "alditols".

Glycosylated Biomolecules

- In biology, glycosylation is the process by which a carbohydrate is covalently attached to an organic molecule, creating structures such as glycoproteins and glycolipids.
- Glycoproteins have distinct Oligosaccharide structures which have significant effects on many of their properties, affecting critical functions such as antigenicity, solubility, and resistance to proteases. Glycoproteins are relevant as cell-surface receptors, cell-adhesion molecules, immunoglobulins, and tumor antigens.

Gycolipids

- Glycolipids are important for cell recognition, and are important for modulating the function of membrane proteins that act as receptors.
- Glycolipids are lipid molecules bound to oligosaccharides, generally present in the lipid bilayer.
- Additionally, they can serve as receptors for cellular recognition and cell signaling.
- The head of the oligosaccharide serves as a binding partner in receptor activity.
- The binding mechanisms of receptors to the oligosaccharides depends on the composition of the oligosaccharides that are exposed or presented above the surface of the membrane.
- There is great diversity in the binding mechanisms of glycolipids, which is what makes them such an important target for pathogens as a site for interaction and entrance. For example, the chaperone activity of glycolipids has been studied for its relevance to HIV infection.

Glycoconjugates

- Glycoconjugates is the general classification for carbohydrates covalently linked with other chemical species such as proteins, peptides, lipids and saccharides. Glycoconjugates are formed in processes termed glycosylation.

- Glycoconjugates are very important compounds in biology and consist of many different categories such as glycoproteins, glycopeptides, peptidoglycans, glycolipids, glycosides and lipopolysaccharides. They are involved in cell–cell interactions, including cell–cell recognition; in cell–matrix interactions; in detoxification processes.

- Generally the carbohydrate part(s) play an integral role in the function of a glycoconjugate; prominent examples of this are NCAM and blood proteins where fine details in the carbohydrate structure determine cell binding or not or lifetime in circulation.
- Although the important molecular species DNA, RNA, ATP, cAMP, cGMP, NADH, NADPH, and coenzyme A all contain a carbohydrate part, generally they are not considered as glycoconjugates.

- Glycocojugates is covalent linking of carbohydrates antigens to protein scaffolds with goal of achieving a long term immunological response in body. Immunization with glycoconjugates successfully induced long term immune memory against carbohydrates antigens. Glycoconjugate vaccines was introduced since the 1990s have yielded effective results against influenza and meningococcus.

Functions of Glycoconjugates

- Glycoconjugates are molecules of carbohydrate bonded to other compounds, such as protein and lipid. Forms of these molecules serve various functions in connective tissue, including cell-to-cell communication and cross-linkages between proteins.
- The presence of glycoconjugates in connective tissue is also critical for maintaining fluid content of the tissue, because of the highly negative charge of some of these molecules that serves to bind water.
- The ability of connective tissue to retain water is diminished with aging as the content of glycoconjugates, particularly proteoglycan aggregates of the extracellular matrix, significantly decreases.
- In addition, there is an increase in glycoconjugate degradation and decrease in synthesis that further contribute to decreased fluid content and connective tissue degeneration.

Modulation of Enzymes

- Glycoconjugates (glycolipids and glycoproteins) are posttranslational modifications of lipids and proteins, respectively, mediated by specific enzymes, the so-called glycosyltransferases. The improper operation of these enzymes leads to aberrant glycosylation patterns, one of the most significant marks of several pathologies such as cancer, congenital disorders, and autoimmune diseases.
- Glycomimetics able to interact and interfere with the activity of these enzymes have been developed as therapeutics to be applied in the treatment of these pathologies. Representative examples of drugs marketed or under clinical studies will be highlighted in the succeeding text.

THANK YOU