FUNDAMENTALS OF BIOCHEMISTRY

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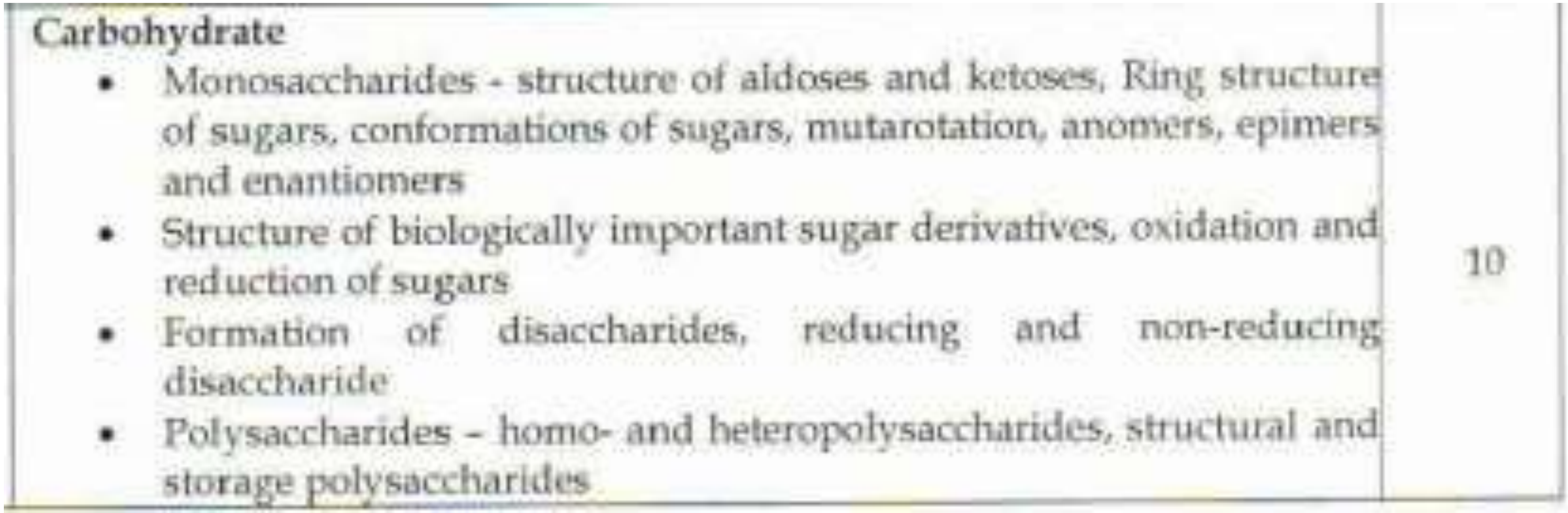
Carbohydrates

Concept Covered



Carbohydrate • Monosaccharides - structure of aldoses and ketoses, Ring structure of sugars, conformations of sugars, mutarotation, anomers, epimers and enantiomers • Structure of biologically important sugar derivatives, oxidation and reduction of sugars • Formation of disaccharides, reducing and non-reducing disaccharide • Polysaccharides - homo- and heteropolysaccharides, structural and storage polysaccharides	10

Monosaccharides

- **Carbohydrates** are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis.
- carbohydrates have the empirical formula $(\mathrm{CH2O})n$; some also contain nitrogen,
- phosphorus, or sulfur.
- There are three major size classes of carbohydrates: monosaccharides, oligosaccharides, and polysaccharides
- **Monosaccharides**, or simple sugars, consist of a single polyhydroxy aldehyde or ketone unit with two or more hydroxyl groups
- Glucose and fructose have five hydroxyl groups.
- Many of the carbon atoms to which hydroxyl groups are attached are chiral centers, which give rise to the many sugar stereoisomers found in nature
- Monosaccharides are colorless, crystalline solids that are freely soluble in

Monosaccharides

- The backbones of common monosaccharides are unbranched carbon chains in which all the carbon atoms are linked by single bonds.
- one of the carbon atoms is double-bonded to an oxygen atom to form a carbonyl group; each of the other carbon atoms has a hydroxyl group.
- If the carbonyl group is an aldehyde the monosaccharide is an **aldose**;
- if the carbonyl group is a ketone group the monosaccharide is a **ketose**.
- The simplest monosaccharides are the two three-carbon trioses: glyceraldehyde, an aldotriose, and dihydroxyacetone, a Ketotriose
- Monosaccharides with four, five, six, and seven carbon atoms in their backbones are called, respectively, tetroses, pentoses, hexoses, and heptoses. There are aldoses and ketoses of each of these chain lengths: aldotetroses and ketotetroses, aldopentoses and ketopentoses, and so on.
- Example: aldohexose D-glucose and the ketohexose D- fructose

Enantiomers

- All the monosaccharides except dihydroxyacetone contain one or more asymmetric (chiral) carbon atoms and thus occur in optically active isomeric forms
- In general, a molecule with *n* chiral centers can have 2^n stereoisomers.
- Enantiomers or optical isomers are chiral molecules which are non-superimposable mirror images of each other.
- Enantiomers have identical chemical and physical properties and are indistinguishable from each other except for the direction of rotation of the plane of polarized light.
- One enantiomer in solution rotates the plane of polarized light to the right, whereas the other rotates it to the left.
- A chiral molecule that rotates light to the right is known as 'dextrorotatory,' and its chemical name is preceded by the plus sign, e.g., (+)-lactic acid.
- Its enantiomer, which rotates the plane of polarized light to the left, is described as 'levorotatory' and the minus sign is used, e.g., (−)-lactic acid.
- This property is known as optical isomerism.

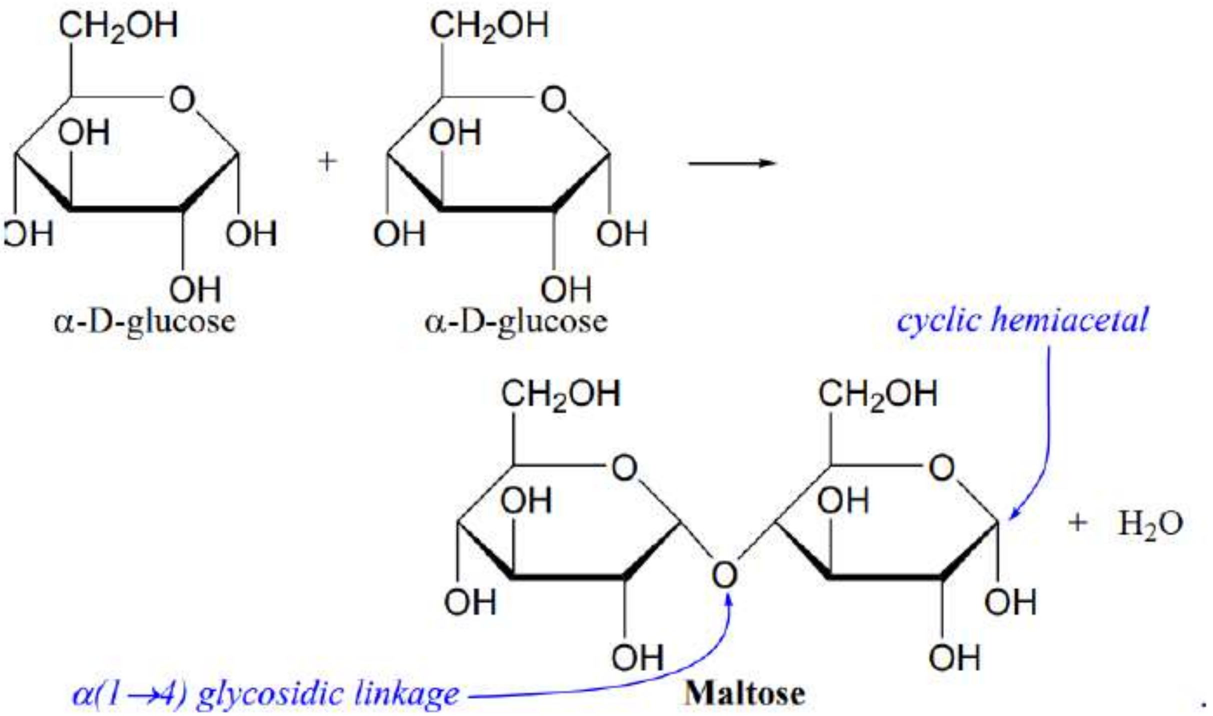
Substances Jaap van Brakel, in Philosophy of Chemistry, 2012

Diastereoisomers

- Diastereoisomers are those stereoisomers that have different configurations at one or more (but not all) stereoisomers without being mirror-images of each other.
- Anomers and epimers are both diastereomers, but an epimer is a stereoisomer that differs in configuration at any single stereogenic center, while an anomer is actually an epimer that differs in configuration at the acetal/hemiacetal carbon

Disaccharides

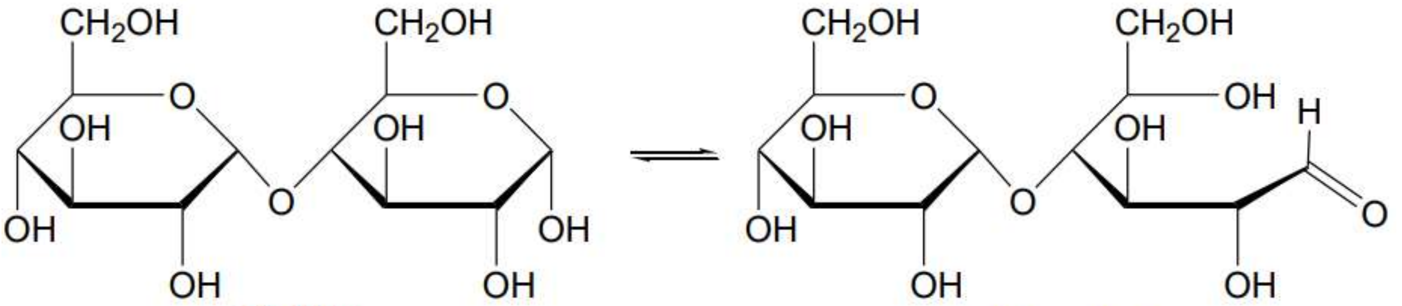
- Two monosaccharides can be linked together through a glycosidic linkage to form a **disaccharide**.



Disaccharides

- Disaccharides that contain hemiacetal groups are reducing sugars.

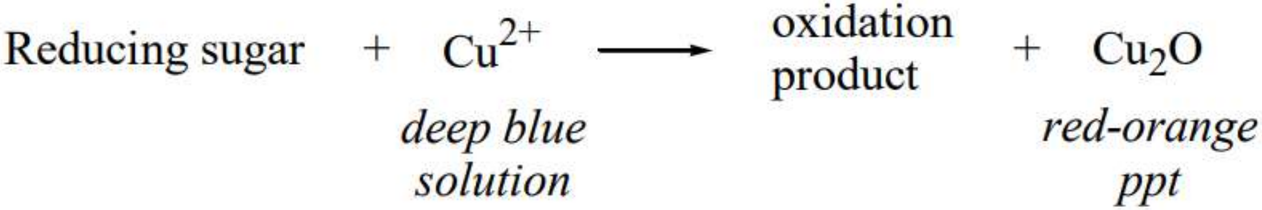
$$\text{maltose} + H_2O \xrightarrow{H^+} \text{D-glucose} + \text{D-glucose}$$



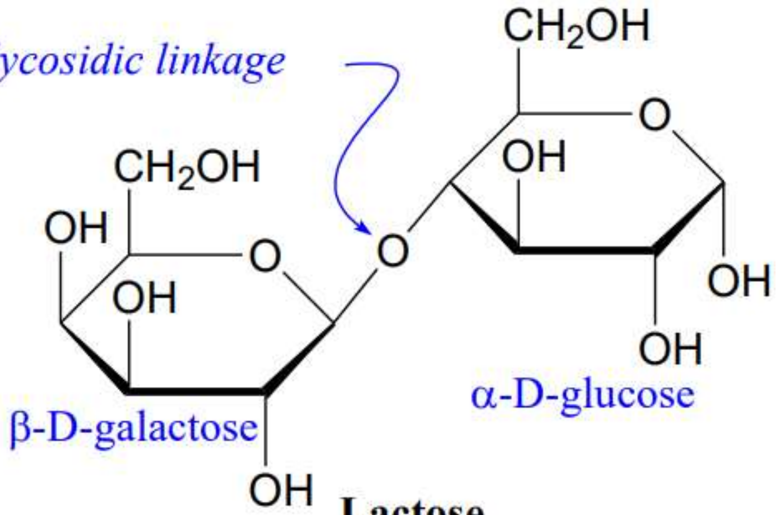
Maltose

reacts with Benedict's reagent

- Aldehydes and ketones that have an OH group on the carbon next to the carbonyl group react with a basic solution of Cu^{2+} (**Benedict's reagent**) to form a red-orange precipitate of copper(I) oxide (Cu_2O).
- Sugars that undergo this reaction are called **reducing sugars**. (All of the monosaccharides are reducing sugars.)



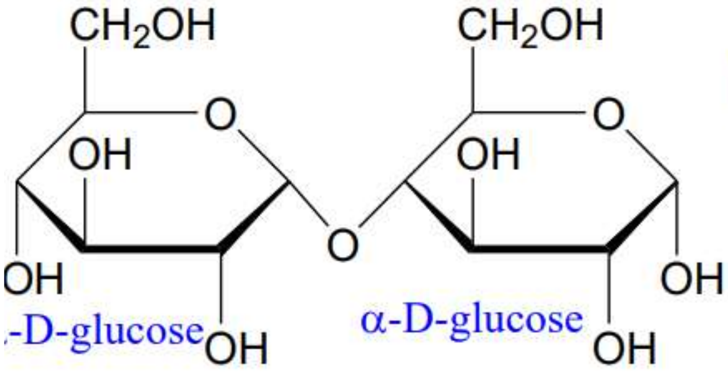
$$\text{Reducing sugar} + \underset{\textit{deep blue solution}}{Cu^{2+}} \longrightarrow \text{oxidation product} + \underset{\textit{red-orange ppt}}{Cu_2O}$$



β(1→4) glycosidic linkage

Lactose

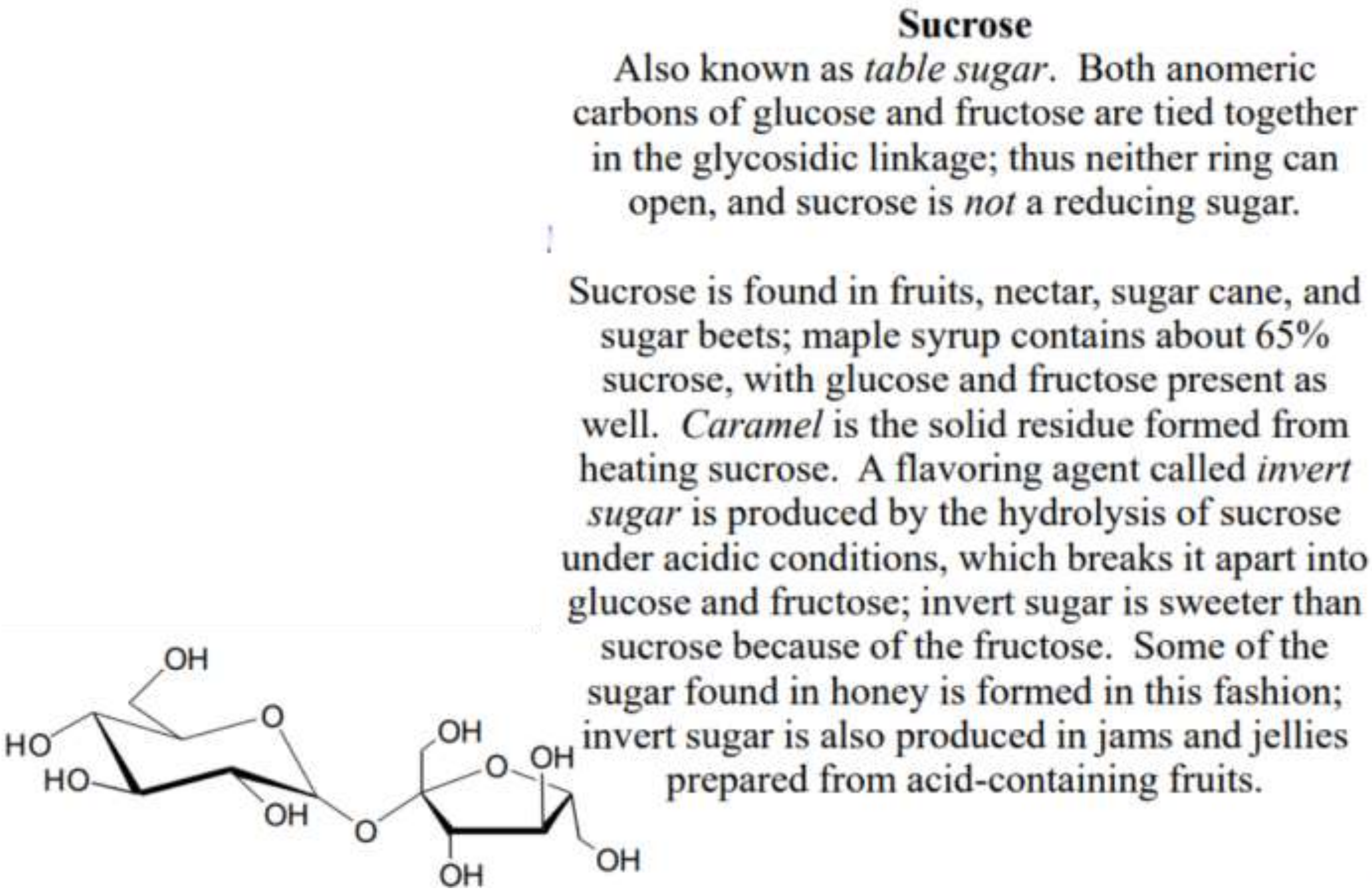
Also known as *milk sugar*. Lactose constitutes 5% of cow's milk and 7% of human milk. It is digested by the enzyme *lactase*. Pure lactose is found in whey, the watery byproduct of cheese production.



Maltose

Also known as *malt sugar*. It is produced in germinating grain (such as barley) as starch is broken down during malting, and is formed during the hydrolysis of starch to glucose during digestion.

Sucrose



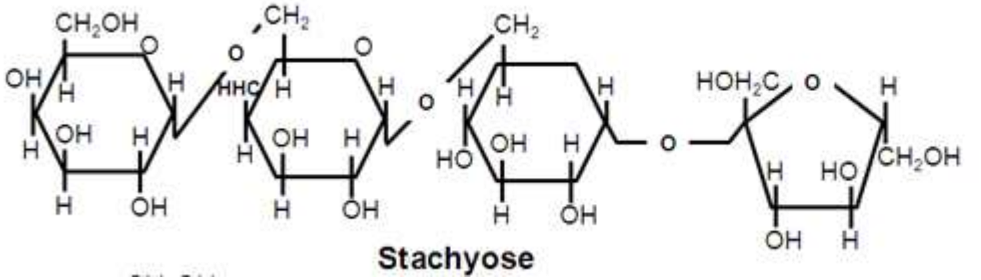
Sucrose

Also known as *table sugar*. Both anomeric carbons of glucose and fructose are tied together in the glycosidic linkage; thus neither ring can open, and sucrose is *not* a reducing sugar.

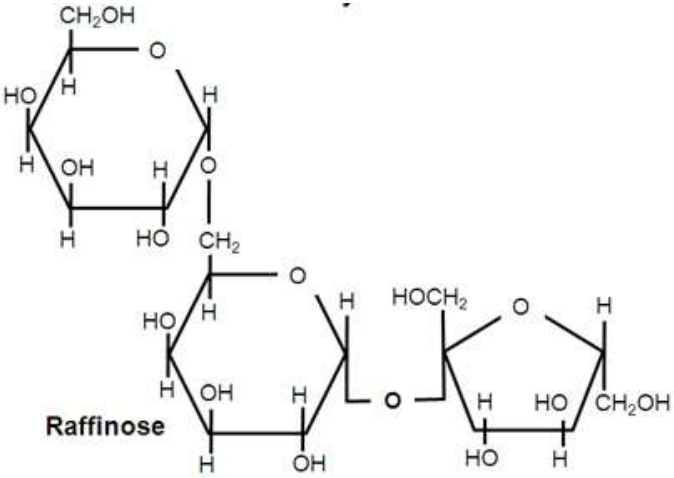
Sucrose is found in fruits, nectar, sugar cane, and sugar beets; maple syrup contains about 65% sucrose, with glucose and fructose present as well. *Caramel* is the solid residue formed from heating sucrose. A flavoring agent called *invert sugar* is produced by the hydrolysis of sucrose under acidic conditions, which breaks it apart into glucose and fructose; invert sugar is sweeter than sucrose because of the fructose. Some of the sugar found in honey is formed in this fashion; invert sugar is also produced in jams and jellies prepared from acid-containing fruits.

Oligoaccharides

- Carbohydrates having more than two or up to ten monosaccharide units are termed as oligosaccharides. Raffinose and stachyose are two major examples of oligosaccharides which consist of repetitive chains of fructose, galactose and glucose.



Stachyose



Raffinose

- Raffinose is a trisaccharide widely found in legumes and vegetables like beans, peas, soy, cabbage, brussels sprouts, and broccoli.

- Here, galactose is bonded to sucrose via a α(1 --> 6) glycosidic linkage.

- Humans are unable to digest such saccharides Thus undigested saccharides are thus fermented by colonic bacteria resulting into flatulence formation.

Polysaccharides

- Polysaccharides are polymeric carbohydrate structures, formed of repeating units (either mono- or di-saccharides) joined together by glycosidic bonds.
- Polysaccharides have a general formula of $C_x(H_2O)_y$ where x is usually a large number between 200 and 2500.
- These structures are often linear, but may contain various degrees of branching.
- They may be amorphous or even insoluble in water.
- Based on the monosccharide units, polysaccharides are broadly put into two categories
- **Homopolysaccharides :** If the polysaccharides consists of only one type of monosaccharide units, these are called homopolysaccharides.Common example of homopolysaccharide is starch which comprises of only D - glucose units.
- **Heteropolysaccharides :** When more than one type of monosaccharides are present in a polysaccharide, they are called heteropolysaccharides e.g. pectin (polymer of galactouranic acid and its methylated ester).

Storage polysaccharides

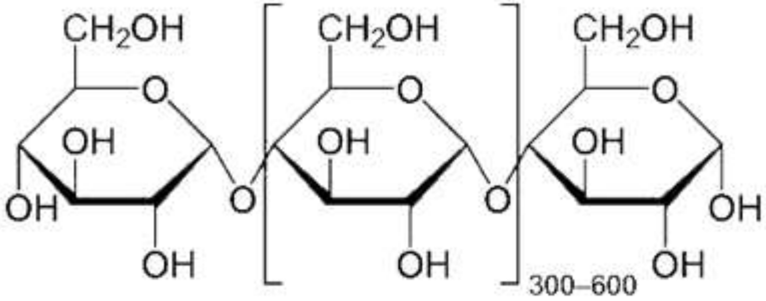
- **Starch :**

  Starch constitutes the most predominant storage polysaccharide in nature and is a characteristic storage sugar of all plant cells.

  This is abundant in tubers, like potatoes and corn seeds.

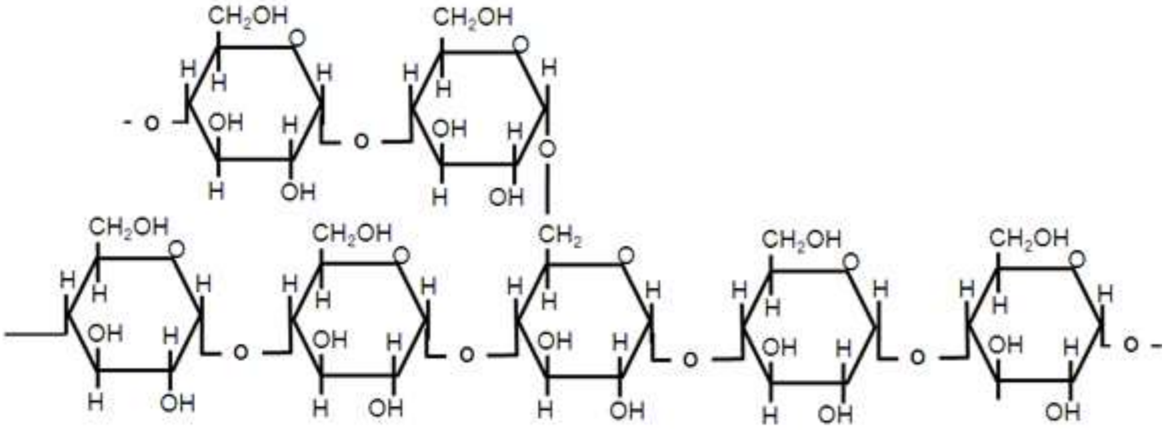
  Starch is a polymer of glucose and contains two types of glucose polymers namely

- **Amylose :** Amylose consists of linear, unbranched chains of several hundred D-glucose residues. The glucose residues are linked by a α(1 --> 4) glycosidic bond between their C1 and C4 carbon atoms. Molecular weight of such chains may extend upto 50000.



Starch

- **Amylopectin :** Amylopectin differs from amylose in being highly branched. The total number of glucose residues in a molecule of amylopectin may run into several thousands. Branching takes place with α(1 --> 6) bonds occurring every 24 to 30 glucose units.

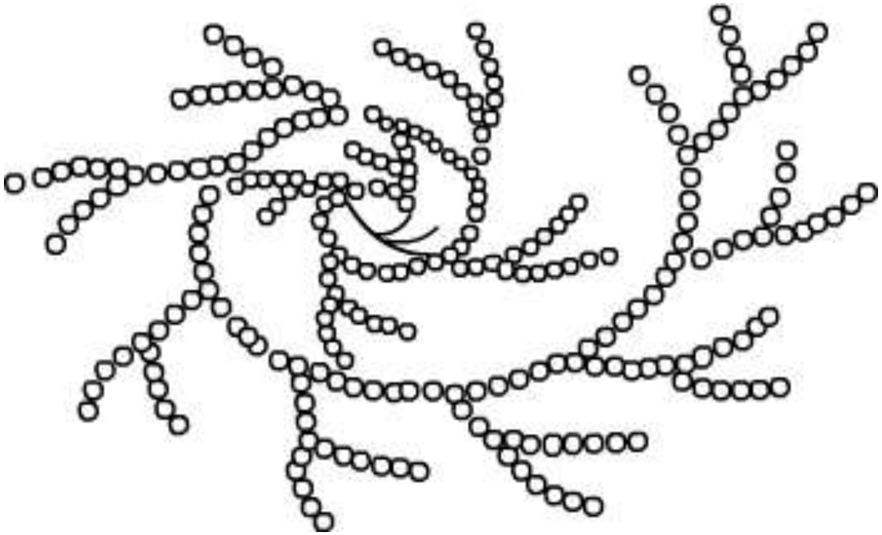


Hydrolysed starch

- **Dextrins** are mixtures of polymers of D-glucose units linked by α(1 --> 4) or α(1 --> 6) glycosidic bonds. These are low in molecular weight. When produced by heat, these are termed as pyrodextrins.
- Partial hydrolysis of starch results in a less sweet or almost flavourless **Maltodextrin**. These are easily digestable and hence act as a source of readily available energy. These can be easily derived from any starch.
- **Syrups**, such as corn syrup made are made from hydrolysis of corn starch. **Corn syrup solids**, are mildly sweet semi - crystalline or powdery amorphous products. The latter are not readily digested but partially fermented by intestinal bacteria.
- **High Fructose Corn Syrup(HFCS)** is another derivative of corn syrup which is as sweet as sugar and is often used in soft drinks.
- When starch is modified by any mechanical or chemical treatments, the resulting product is **Modified starch**.
- **Hydrogenated glucose syrup(HGS)** is produced by hydrolyzing starch, followed by its hydrogenation. The resulting syrup is used to produce sugar alcohols as well as hydrogenated oligo- and polysaccharides.
- **Polydextrose** (poly-D-glucose) is a highly-branched and synthetic polymer. It is known to possess many types of glycosidic linkages which are generated upon heating dextrose.

Glycogen

- Glycogen is the main storage polysaccharide in animal cells, a counterpart of starch in plant cells.
- Glycogen, is also a branched polysaccharide of D glucose monomer units bonded via α(1 --> 4) glycosidic linkage. The α(1 --> 6) branches in glycogen are shorter and more frequent and extensive than those in amylopectin. The overall structure is more compact here.



Glycogen

The glucose chains are organized globularly originating from a pair of molecules of glycogenin, a protein with a molecular weight of 38,000 at the core of the structure.

- Glycogen is easily converted back to glucose to provide energy.

- Both glycogen and starch are hydrolysed in the digestive tract by α - amylases present in the saliva and pancreatic juice which are secreted into the digestive tract.

- α - amylases hydrolyse the α(1 --> 4) glycosidic linkage of the outer branches of glycogen and amylopectin resulting in D-glucose, maltose and a resistant core named as "limit dextrin".

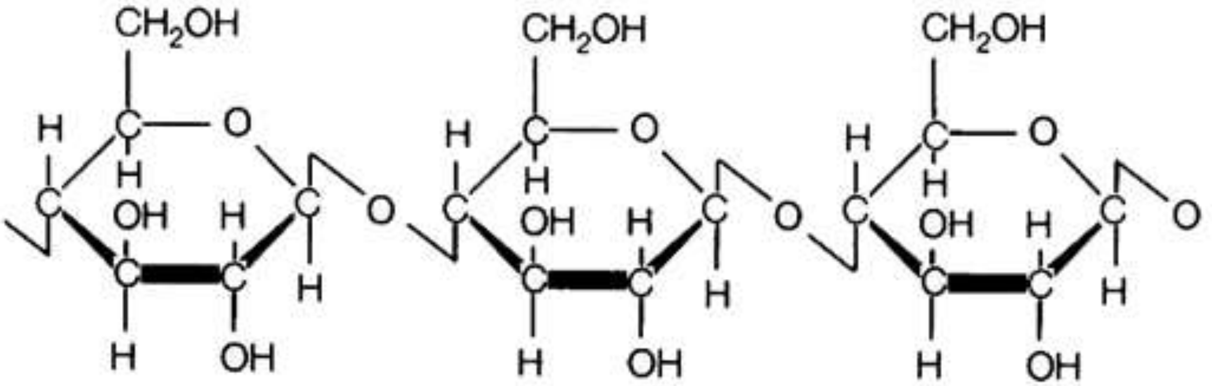
- α - amylases cannot further hydrolyse limit dextrins because of their inability to cleave α(1 --> 6) linkages. This, however, is achieved by a "debranching" enzyme, α(1 --> 6) glucosidase acting on the branch linkages.

- Together α - amylase and α(1 --> 6) glucosidase completely degrade glycogen and starch (amylopectin).

- β - amylase hydrolyses alternate α(1 --> 4) glycosidic linkages yielding mostly maltose with very little glucose.

Cellulose

- Cellulose is the major structural polysaccharide, predominant in the cell wall of the plants. Cellulose is found in cell walls of stalks, stems, trunks, woody portions of plant tissues.
- Like starch, cellulose also comprises of glucose as monomer units which are linked by β(1 --> 4) glycosidic bonds in a linear fashion. The absence of side chains allows cellulose molecules to lie close together and form a rigid structures.



- The basic structural difference between cellulose and starch or glycogen is that in cellulose, the glucose monomer units are linked by β(1 --> 4) glycosidic linkage while in amylose, amylopectin or glycogen the glycosidic linkages are α(1 --> 4).

Cellulose

Structural Polysaccharides

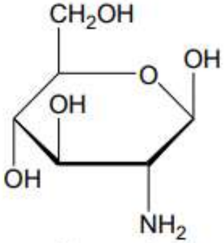
- On account of this structural difference, the main chains in glycogen or starch assume a coiled and helical conformation leading to formation of dense granules. The main chains of cellulose, on the other hand take up an extended conformation and allow lateral aggregation to form insoluble fibrils.
- Cellulose are hydrolyzed to its constituent glucose units by microorganisms that inhabit the digestive tract of termites and ruminants. The intestinal tract of termites harbors Triconympha, a parasitic microorganism, that secretes enzyme cellulase which is a cellulose hydrolysing enzyme.
- Cellulose is mostly unavailable as food for vertebrates since they cannot be digested/hydrolysed by any enzyme in them(except cattle and ruminant animals). The digestive system of cattle and ruminant animals like sheep, goats, camels etc is thus abundant with microorganisms that secrete cellulase to degrade cellulose to glucose units.

Functions

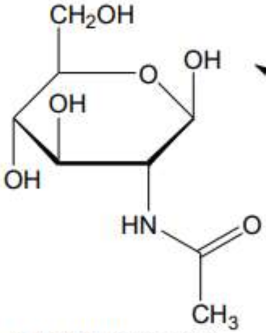
- Carbohydrates are the source of energy (~4 Kcal/g) in most diets.
- Cellulose is the major constituent of cell wall. Wood, cotton and paper are forms of cellulose.
- Carbohydrate also forms the part of some glycoproteins.
- **Hemicellulose**
- The polysaccharide components of plant cell walls other than cellulose are termed "hemicellulose" , which is extractable by dilute alkaline solutions.
- Hemicelluloses comprise almost one-third of the carbohydrates in woody plant tissue.
- The chemical structure of hemicelluloses consist of long chains of a variety of pentoses, hexoses, and their corresponding uronic acids
- Xylan is major example of a pentosan consisting of D-xylose units with β(1 --> 4) linkages

Structural Polysaccharides

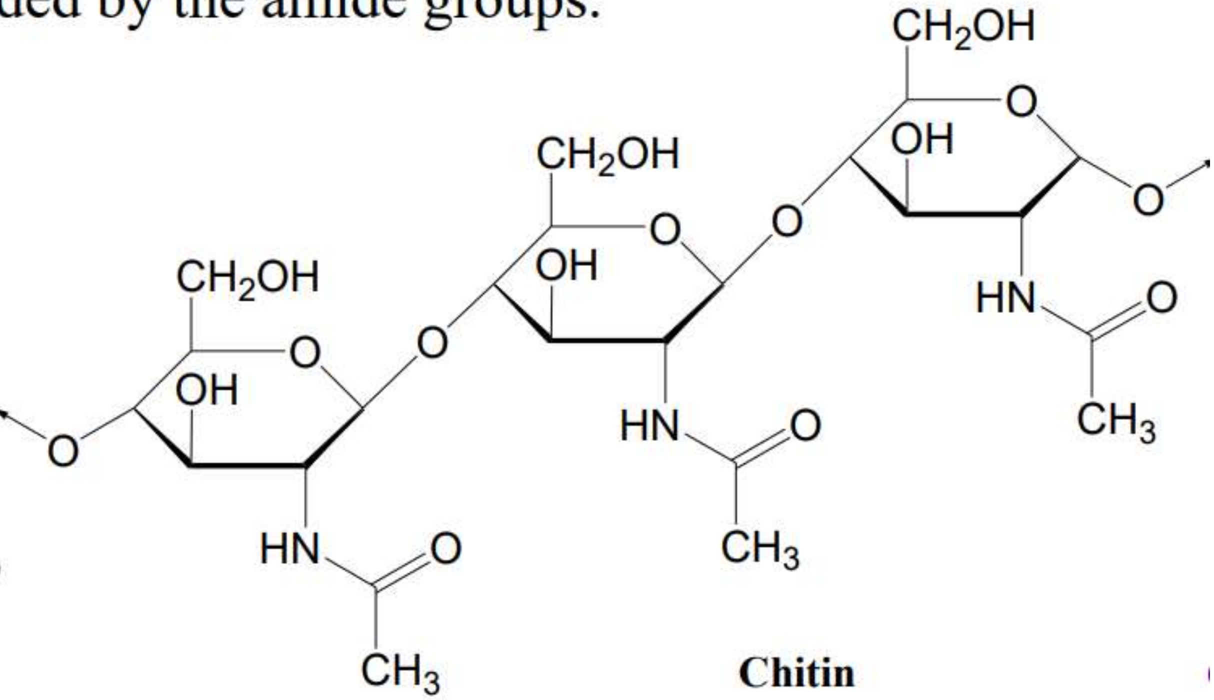
- **Chitin** is a polymer of N-acetylglucosamine, an amide derivative of the *amino sugar* glucosamine, in which one of the OH groups is converted to an amine (NH_2) group. The polymer is extremely strong because of the increased hydrogen bonding provided by the amide groups.



Glucosamine



N-Acetylglucosamine

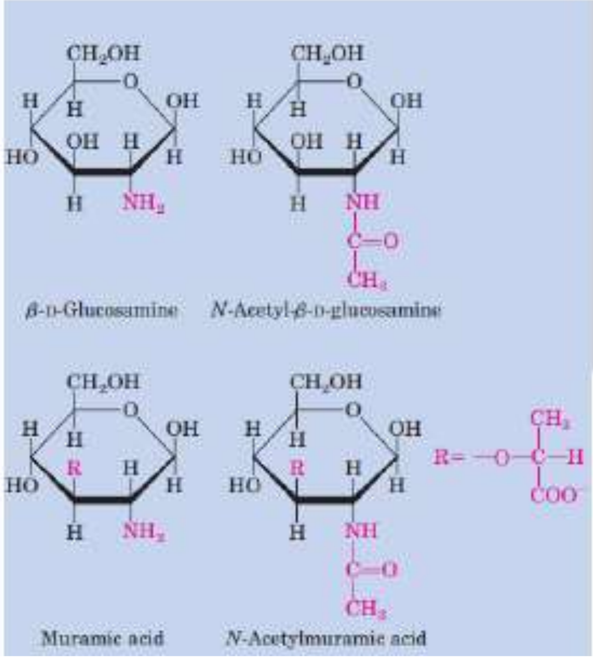


Chitin

Heteropolysaccharides

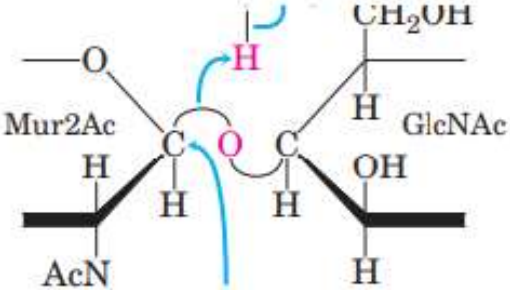
Heteropolysaccharides

The rigid component of bacterial cell walls is a heteropolymer of alternating $(\beta 1 \rightarrow 4)$-linked N-acetylglucosamine and N-acetylmuramic acid residues

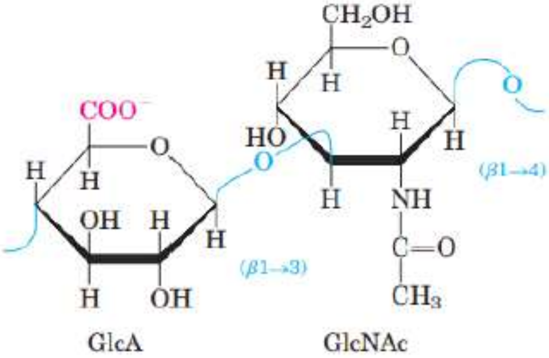
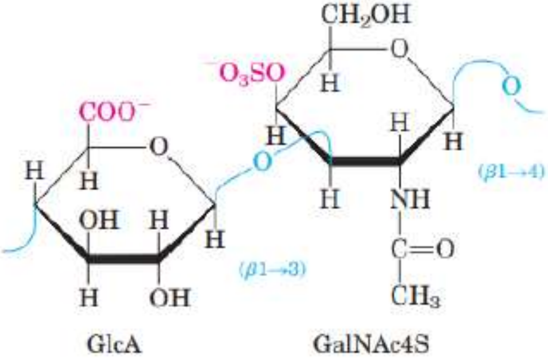
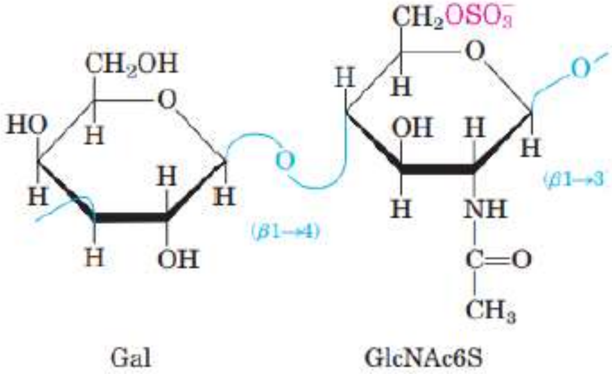
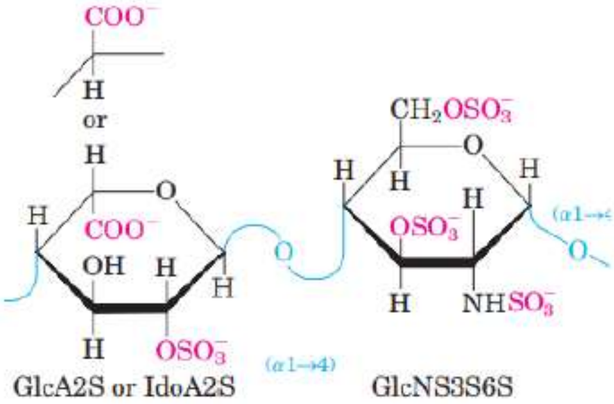


β-D-Glucosamine N-Acetyl-β-D-glucosamine

Muramic acid N-Acetylmuramic acid



Heteropolysaccharides

Glycosaminoglycan Number of disaccharides per chain	Repeating disaccharide
Hyaluronate ~50,000	
Chondroitin 4-sulfate 20–60	
Keratan sulfate ~25	
Heparin 15–90	

Heteropolysaccharides

The **glycosaminoglycan hyaluronic acid** (hyaluronnate at physiological pH) contains alternating residues of D-glucuronic acid and N-acetylglucosamine With up to 50,000 repeats of the basic disaccharide unit, hyaluronates have molecular weights greater than 1 million; they form clear, highly viscous solutions that serve as lubricants in the synovial fluid of joints and give the vitreous humor of the vertebrate eye its jelly-like consistency (the Greek hyalos means “glass”; hyaluronates can have a glassy or translucent appearance).

Hyaluronate is also an essential component of the extracellular matrix of cartilage and tendons, to which it contributes tensile strength and elasticity as a result of its strong interactions with other components of the matrix. Hyaluronidase, an enzyme secreted by some pathogenic bacteria, can hydrolyze the glycosidic linkages of hyaluronate, rendering tissues more susceptible to bacterial invasion. In many organisms, a similar enzyme in sperm hydrolyzes an outer glycosaminoglycan coat around the ovum, allowing sperm penetration. Chondroitin sulfate (Greek) contributes to the tensile strength of cartilage, tendons, ligaments, and the walls of the aorta.

Heteropolysaccharides

Dermatan sulfate (Greek) contributes to the pliability of skin and is also present in blood vessels and heart valves. In this polymer, many of the glucuronate (GlcA) residues present in chondroitin sulfate are replaced by their epimer, iduronate (IdoA).

Keratan sulfates (Greek) have no uronic acid and their sulfate content is variable. They are present in cornea, cartilage, bone, and a variety of horny structures formed of dead cells: horn, hair, hoofs, nails, and claws. Heparin is a natural anticoagulant made in mast cells (a type of leukocyte) and released into the blood, where it inhibits blood coagulation by binding to the protein antithrombin. Heparin binding causes antithrombin to bind to and inhibit thrombin, a protease essential to blood clotting. The interaction is strongly electrostatic; heparin has the highest negative charge density of any known biological macromolecule

Heteropolysaccharides

Specific carbohydratecontaining molecules act in cell-cell adhesion, cell migration during development, blood clotting, the immune response, and wound healing, to name but a few of their many roles. In most of these cases, the informational carbohydrate is covalently joined to a protein or a lipid to form a glycoconjugate, which is the biologically active molecule. Proteoglycans are macromolecules of the cell surface or extracellular matrix in which one or more glycosaminoglycan chains are joined covalently to a membrane protein or a secreted protein. The glycosaminoglycan moiety commonly forms the greater fraction (by mass) of the proteoglycan molecule, dominates the structure, and is often the main site of biological activity. In many cases the biological activity is the provision of multiple binding sites, rich in opportunities for hydrogen bonding and electrostatic interactions with other proteins of the cell surface or the extracellular matrix. Proteoglycans are major components of connective tissue such as cartilage, in which their many noncovalent interactions with other proteoglycans, proteins, and glycosaminoglycans provide strength and resilience.

Heteropolysaccharides

Glycoproteins have one or several oligosaccharides of varying complexity joined covalently to a protein. They are found on the outer face of the plasma membrane, in the extracellular matrix, and in the blood. Inside cells they are found in specific organelles such as Golgi complexes, secretory granules, and lysosomes. The oligosaccharide portions of glycoproteins are less monotonous than the glycosaminoglycan chains of proteoglycans; they are rich in information, forming highly specific sites for recognition and high-affinity binding by other proteins.

Glycolipids are membrane lipids in which the hydrophilic head groups are oligosaccharides, which, as in glycoproteins, act as specific sites for recognition by carbohydrate-binding proteins. Glycolipids are membrane lipids in which the hydrophilic head groups are oligosaccharides, which, as in glycoproteins, act as specific sites for recognition by carbohydrate-binding proteins.