

Carbohydrates

- Of the macromolecules that we will cover in this class, those involving carbohydrates are the most abundant in nature.
- Via photosynthesis, over 100 billion metric tons of CO₂ and H₂O are converted into cellulose and other plant products.
- The term carbohydrate is a generic one that refers primarily to carbon-containing compounds that contain hydroxyl, keto, or aldehydic functionalities.
Carbohydrates can range in sizes, from simple monosaccharides (sugars) to oligosaccharides,

Carbohydrates constitute more than 1/2 of organic molecules

Main role of carbo in nature

- Storage of energy - ATP/NADH/FADH/NADPH/RNA/DNA
- Structural support
- Lipid and protein modification:
 - membranes asymmetry, recognition by IgG/fertilization/virus recognition/cell cell communication

Definition: Carbohydrates, Sugars and Saccharides- are all polyhydroxy

(at least 2 OH) $C_n(H_2O)_n$ = hydrate of carbon

- Notice that there are two distinct types of monosaccharides, ketoses and aldoses. A ketose has a ketone functionality associated with it, while an aldose has an aldehyde functionality associated with it. The number of carbons is important in general nomenclature (triose = 3, pentose = 5, hexose =6,
- Notice also that when a carbon is missing a hydroxyl group, it's a big thing. It determines to a certain extent, the nomenclature associated with the compound. In one case, a carbon is a 2-deoxy sugar.

Types of Carbohydrates

Monosaccharides - Simple sugars

Single polyhydroxyl

- aldehyde - aldose
- ketone - ketose

Can't be hydrolyzed to simpler form

Disaccharide - two sugars linked together. Can be the same molecule or two different sugars. Attached together via a glycosidic linkage

Oligosaccharide - 2 to 6 monosaccharides

Polysaccharides - straight or branched long chain monosaccharides. Bonded together by glycosidic linkages

Chirality in Monosaccharides

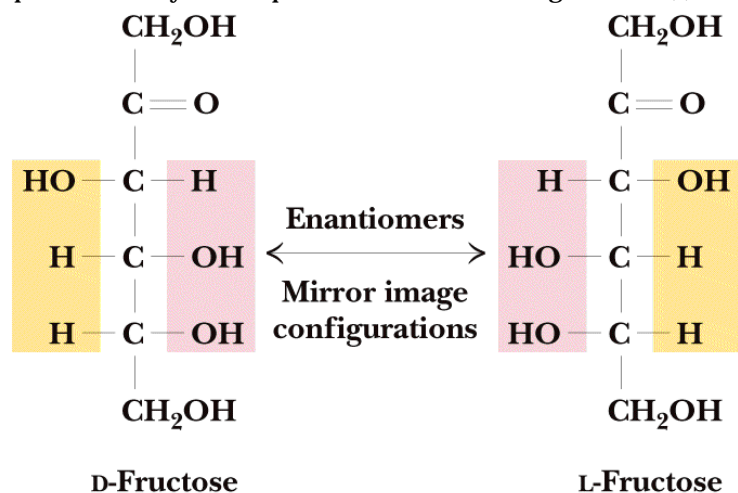
- Most simple monosaccharides have at least one chiral center. As in the case of amino acids, sugars are given D or L designations based on their similarity with D or L glyceraldehyde (shown on left).
- Since some sugars contain many chiral centers, it is necessary to designate one chiral center that will act as the reference. This chiral center is designated as the one that is

- most distant from the carbon that bears the carbonyl functionality.
- Sugars are frequently written as Fischer projections. Remember that atoms that lie on horizontal bonds are projecting towards you, while those on vertical bonds are projecting away from you.
- Compare the top and bottom structures for glyceraldehyde.
- The numbering of carbons in sugars begins at the end of the chain that is closer to the carbonyl functionality.

Stereochemistry - optically active molecules

D or L as designated by furthest asymmetric carbon from ketone or aldehyde

optical activity is independent of D or L designation D(-) fructose



Increase in number of carbons increase possible stereoisomers: Van't Hoff's Rule: A compound with n asymmetric C atoms has a maximum of 2^n possible stereoisomers

Enantiomers: Stereoisomers that are non superimposable mirror images

ex. L and D forms of sugars D-glyceraldehyde and L-glyceraldehyde

Diastereomers: Stereoisomers that are not enantiomers (mirror images)

ex. D-ribose and D-arabinose - isomers but not mirror images

Epimers: Diastereomers that differ in the configuration at a single asymmetric carbon atom (except the reference carbon)

ex. D-glucose and D-galactose are epimers because of C4. D-mannose and D-galactose are not epimers because the difference is at more than one carbon

- Epimers are two sugars that differ only in the configuration around one carbon atom of their structures.
- D-Mannose differs from D-glucose only in its configuration around carbon 2.
- D-Galactose differs from D-glucose only in its configuration around carbon 4.
- D-Galactose and D-Mannose are not epimers.

Conformational Structures

Emil Fisher - Nobel Prize 1891 Organic chemist who found the structure of D glucose

Fisher projections - place most oxidized carbon on top

Haworth Structures: carbons counted from anomeric C to clockwise from the oxygen in the ring (pyranose) or the #2 C for furanose

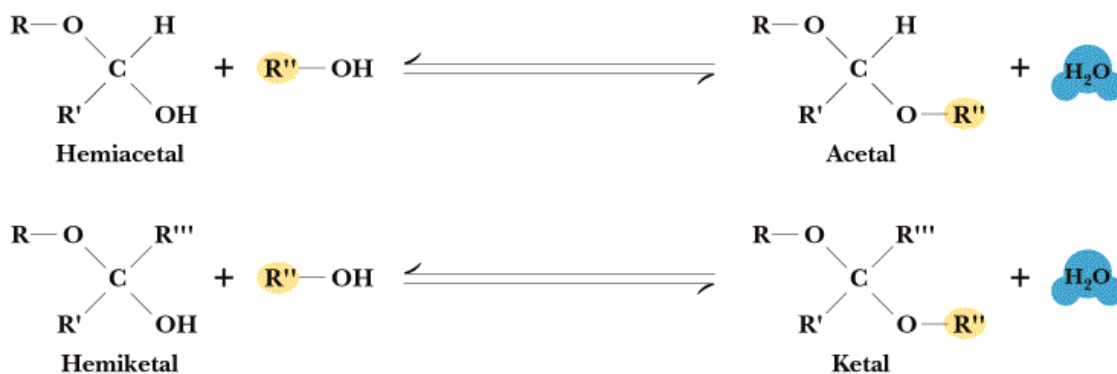
OH in down position - α form

OH in up position - β form

Cyclization of Monosaccharides:

- Carbohydrase of four carbons and up are found in cyclic forms.
- Aldehydes and ketones react reversibly with -OH on sugars
 - 5 or 6 carbon rings most stable
 - 4 carbon membered ring furan - ribose
 - 5 carbon membered ring pyran - glucose

- straight chains form hemiacetals and hemi ketals



ex of aldehyde + alcohol - hemiacetal (same for ketones)

C=O at reference carbon is reduced to OH

Formation of ring structure leads to an additional chiral carbon (anomeric carbon) This is the number one carbon in the pyranose structures, #2 for the furanoses

- In hexoses, an attack of the hydroxyl group at C-5 onto the aldehyde functionality generates a cyclic structure containing six substituents.
- One of the substituents is an oxygen, which acted as the nucleophile in the reaction.
- Notice that two different stereochemical outcomes are possible, at the new chiral center that is generated (the hemiacetal). The hydroxyl group can be on the same side (cis) of the ring as the CH₂OH moiety (beta configuration), or it can be on the opposite side (trans) of the ring as the CH₂OH moiety (alpha configuration).
- Notice the formal names for each of the two possible configurations.

D sugar ring structures form and reform so there is an intra-conversion between the α and β form. This is called mutarotation. Mutarotation occurs spontaneously or with the help of an enzyme (generally called a mutase)

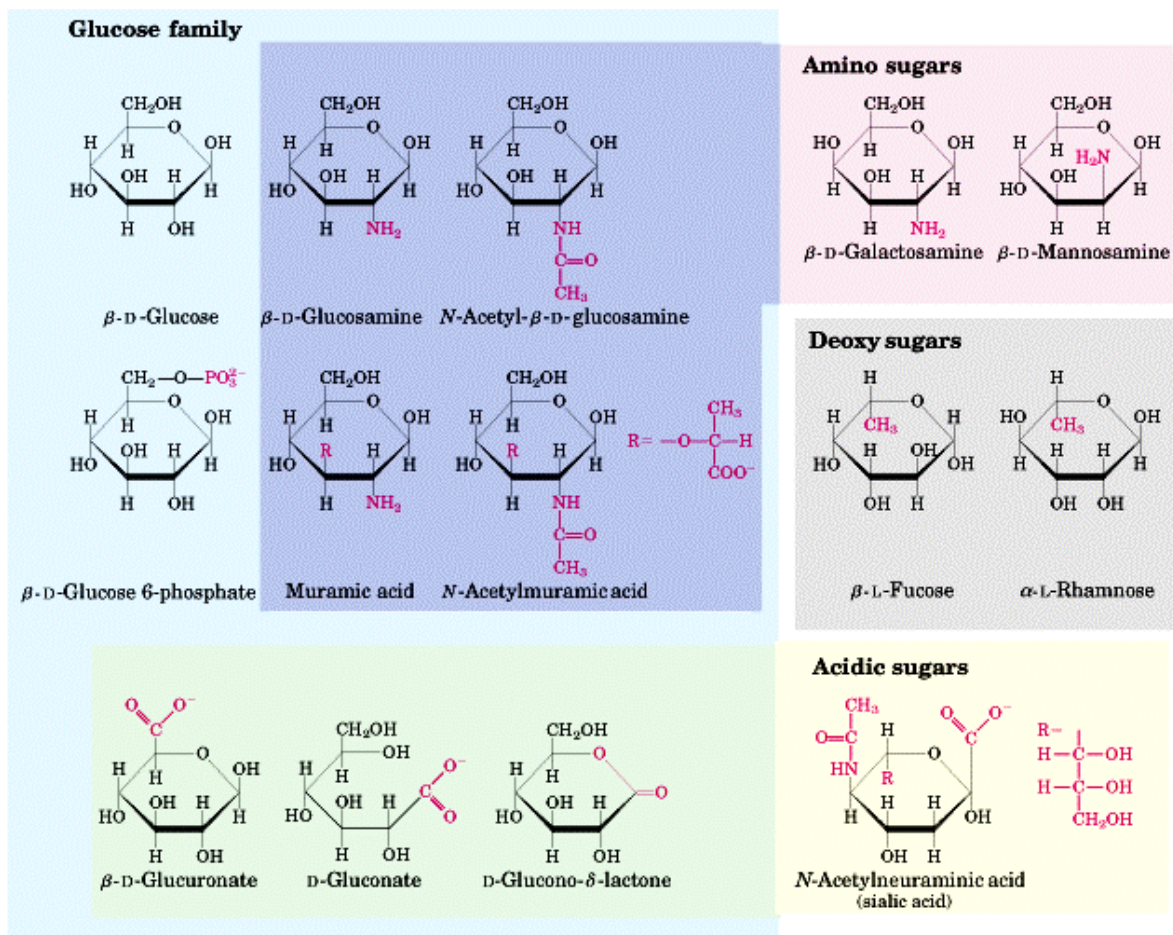
The hemi groups are ordinarily unstable and revert back to the straight chain form

In solution: D-glucose (0.02%) α -D Glucopyranoside (37%) and β -D glucopyranoside (64%) less than 1% of the furans

- pyranose and furanose are the basis for nomenclature; glucose refers to the mixtures of the different forms.

Beta and Alpha forms -

Reactions of Monosaccharides



Reducing sugars - a reduction reaction at the aldehyde or ketone groups of the sugar molecules. As sugar is being oxidized, something else is being reduced:

- Only those anomeric carbons that can mutarotate are available for reduction. ie. disaccharides only contain 1 reducing sugar
- Formation of a carboxylic acid from an aldehyde is a 2-electron oxidation.
- Notice that the sugar acts as the reductant of copper. Copper is reduced from the +2 state to the +1 state; however, the sugar is oxidized by 2 electrons.

- In the presence of Benedict's reagent (sodium citrate, sodium carbonate, and copper sulfate, reducing sugars will produce a brick-red precipitate of cuprous oxide.
- There are enzymatic methods that can be used to quantify reducing sugars such as glucose, which forms the basis of blood sugar detection by diabetics.

Phosphorylation - can form anhydride phosphoester bond.

phosphorylation alters ionic character. Locks molecule in cell.

Nucleotides are phosphorylated (ATP, GTP ...)

Deoxy sugars - without oxygen common case - ribose RNA vs. DNA

Amino sugars - Sugars with OH replaced by and NH₂. Amination usually occurs at C2 and often is acylated

Glycosaminoglycans both amino and sulfated sugars.

Heparin inhibits action of thrombin in blood clotting

-protein with sugar residues

- sugar has added C chains (acetylated), sulfur groups (sulfanated) and aminated

Important monosaccharides

Glucose - preferred source of energy for brain cells and cells without mitochondria

Fructose - ketose, 2x as sweet as sucrose. Sperm use this as major sugar/energy source for motility

Galactose - important for lactose and glycolipid production

galactosemia - genetic disorder in galactose metabolism leads to accumulation of galactose-1-phosphate in liver results in liver damage. Another version of the disease results due to lack of galactose metabolism. Galactose concentration builds up in blood leading to cataracts.

- Can result in severe mental retardation. Identification and galactose free diet helps

Disaccharide Nomenclature:

- When named, structures are considered to have their reducing ends on the right. Locate the reducing ends of the structures on the left if appropriate.
- The configuration of the anomeric carbon joining the first monosaccharide unit to the second is given (reading left to right).
- The non-reducing residue is named, and five- and six-membered ring structures are distinguished by using "furano" or "pyrano" prefixes.
- The two carbons joined by the glycosidic bond are indicated in parentheses, with an arrow connecting the two numbers.
- The second residue is then named.
- If there are subsequent residues, the subsequent glycosidic bonds are described by the same conventions.
- Non-reducing disaccharides are named as glycosides rather than glycoses. Note that a double-headed arrow is used to denote sugars that are joined by their anomeric carbons, AND, it is necessary to specify the stereochemistry at both anomeric carbons.

Important disaccharides:

sucrose = table sugar - glucose and fructose (alpha linkage)

lactose = milk sugar - galactose and glucose (beta linkage)

Lactose intolerance: lack of enzyme to break the β glycosidic linkage - leads to bloating cramps and diarrhea

Maltose - malt sugar, from breakdown of starch - 2 glucoses

Cellobiose - breakdown of cellulose 2 β (1 \rightarrow 4) glucose β linkages serve as structural sugars, α linkages serve as storage sugars

Important polysaccharides

Starch - energy reservoir in plants - made of two polysaccharides

Amylose - long unbranched glucose α (1,4) with open reducing end large tight *helical* forms. Test by iodination.

Amylopectin - polymer of α (1,4) and α (1,6) branches. Not helical.

Glycogen - storage of carbohydrates in vertebrates greatest conc. in muscles and liver.

Similar to amylopectin with more branch points - takes up less space

Cellulose - β (1,4) glucose most common structural polysaccharide in plants long non branched chains strengthened by H bonds

Chitin -

- Chitin is a linear homopolysaccharide composed of N-acetylglucosamine residues in linkages.
- Chitin differs chemically from cellulose only in the acetylated amino substituent at carbon 2.
- It forms extended fibers that are similar to those of cellulose, and is found principally in hard exoskeletons of arthropods.
- One of the major structural differences between chitin and cellulose, is that naturally occurring cellulose is composed of strands that pack against each other in parallel (non-reducing ends are together at one end), whereas chitin occurs naturally in both parallel and antiparallel stacking arrangements.

Glycoproteins - many proteins contain covalently bound carbohydrates. Many of these proteins are found associated with the cell membrane. Many more are secreted.

- Sugars are attached to the protein by either N-glycosidic or β -glycosidic bonds
- In N-linkages the amide group of an asparagine in the sequence Asn - X -Ser/Thr is linked to N-acetylglucosamine.
- In β -linked sugars, the oligosaccharide chains are covalently bonded to Ser or Thr OH group.
- Sugar addition is initiated in the endoplasmic reticulum and further modified in the golgi. The final protein is then shipped by membrane fusion to the cell membrane. Usually the outer membrane.

Proteoglycans - a class of molecules containing both carbohydrates and protein, but are mostly carbohydrates.

-Properties are more carbo than protein.

- Usually contain a main core of a protein and chains of glycosaminoglycans many cases are sulfonated and acylated often found in eye fluids, connective tissues - high viscosity and high elasticity