

Topic goals

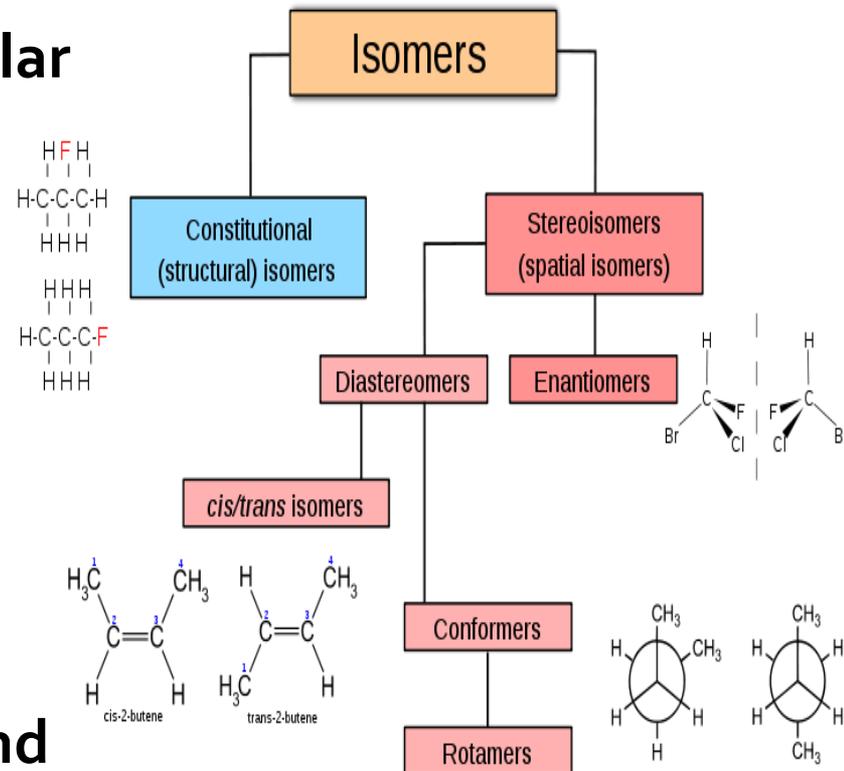
- Two major goals:
 - 1. Monosaccharides: to recognize their structure, properties, & their stereochemistry
 - 2. The nature of di-, oligo-, & polysaccharides

LECTURES OUTLINE

- 1. Monosaccharide structures
 - ✓ Aldoses and ketoses
 - ✓ Optical isomers
 - Fischer projections
 - Enantiomers, Diastereomers, & Epimers
 - ✓ Cyclic structures
 - Hemiacetals and hemiketals
 - Anomers & Haworth projections
 - Furanoses and pyranoses
- 2. Monosaccharide reactions
 - ✓ Oxidation-reductions, Esterification, glycosides, & Sugar derivatives
- 3. Oligosaccharides
 - ✓ Sucrose & Lactose
- 4. Polysaccharides
 - ✓ Cellulose & starch (Forms of starch: Amylose & Amylopectin)
 - ✓ Glycogen
 - ✓ Chitin
 - ✓ Cell walls
 - ✓ Glycosaminoglycans
- 5. Glycoproteins

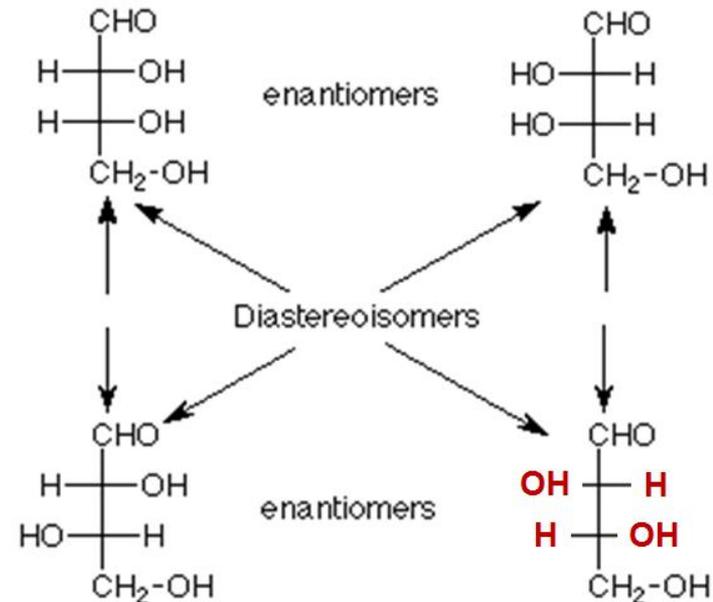
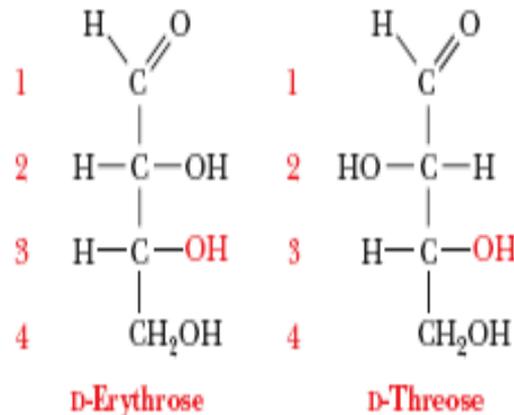
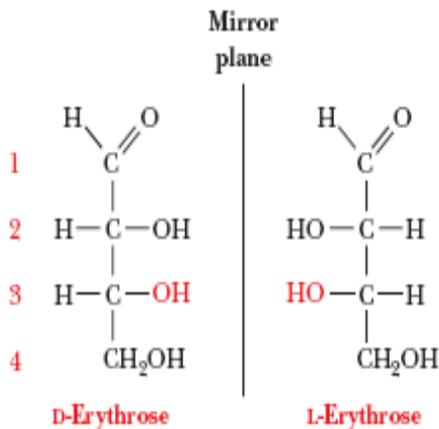
Isomers

- Greek: isos = "equal", méros = "part"
- Compounds with the same molecular formula but different structural formulas
- Isomers do not necessarily share similar properties, unless they also have the same functional groups
- There are two main forms of isomerism: structural isomerism and stereoisomerism (spatial isomerism)



Isomers

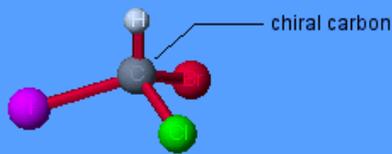
- 1. Structural (constitutional) isomers: the atoms and functional groups are joined together in different ways (2° vs. 3° alcohol)
- 2. Stereoisomers: the bond structure is the same, but the geometrical positioning of atoms and functional groups in space differs
 - ✓ Enantiomers: non-superimposable mirror-images
 - ✓ Diastereomers: NOT mirror-images



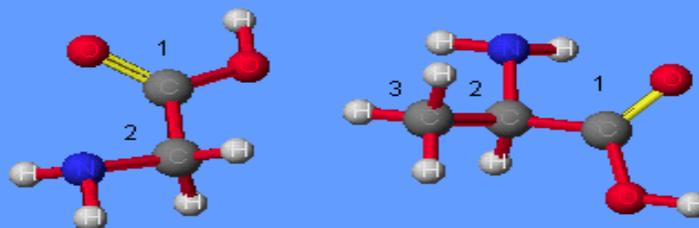
Chirality

- A chiral carbon is one that has four different "groups" attached to it
- In stereoisomers, a chiral carbon is called a stereocenter
- Achiral means NOT chiral
- The possible number of stereoisomers that we can have is 2^n (where n is the number of chiral carbons)

Chiral Carbons



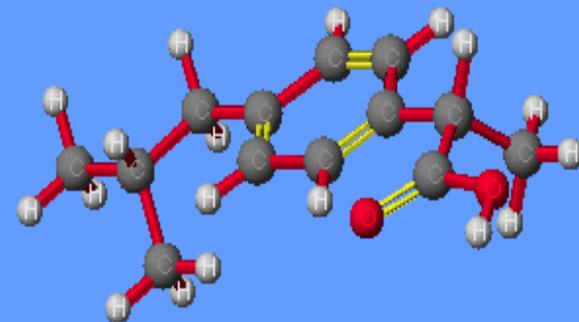
Which carbons are chiral?



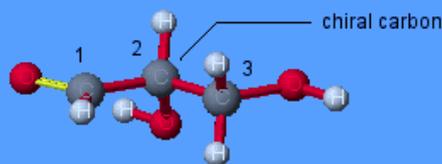
Glycine

Alanine

(s)-Ibuprofen
or Advil



Bromochloriodomethane

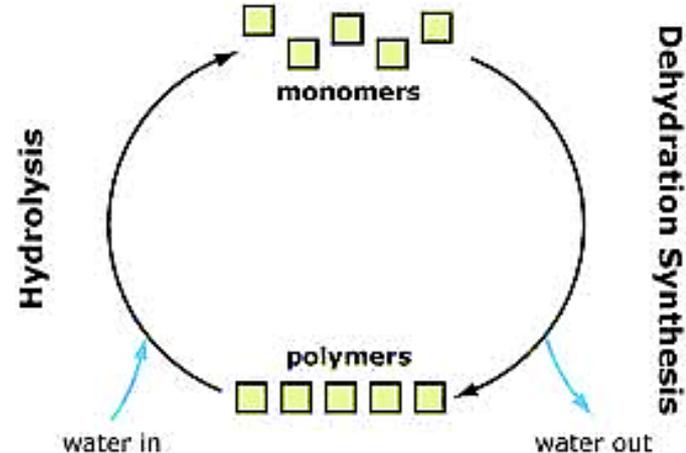


Glyceraldehyde

Ketose sugar

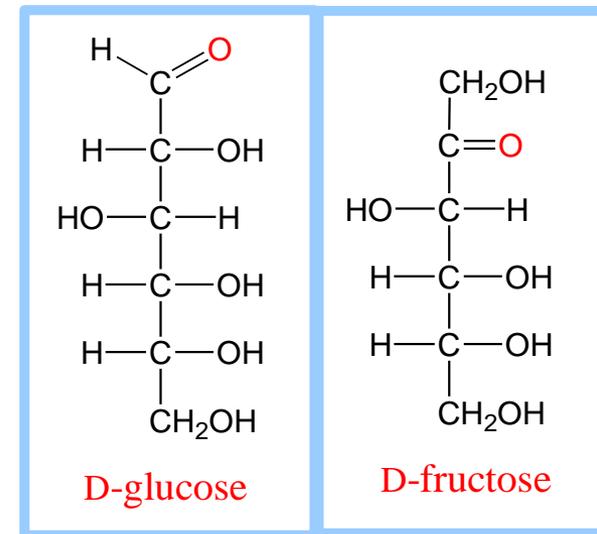
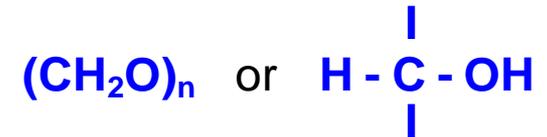
Biomacromolecules

- **Subunits:** the small building blocks (precursors) used to make macromolecules
- **Macromolecules:** large molecules made of subunits
 - ✓ Carbohydrates (monosaccharides)
 - ✓ Proteins (amino acids)
 - ✓ Nucleic acids (nucleotides)
 - ✓ Lipids (fatty acids)
- Except for lipids, these macromolecules are also considered polymers
- **Relationship (monomers and polymers)**
- **How water is removed?**
 - ✓ 1: "H" & "OH"
 - ✓ 2: 2 "H" & "O"



Carbohydrates "Saccharides"

- Carbohydrates: glycans that have the following basic formula (n varies from 3-8)
- Monosaccharide: a carbohydrate that cannot be hydrolyzed to a simpler carbohydrate
- It is a polyhydroxy (aldehyde) or (ketone), or a substance that gives these compounds on hydrolysis
- Building blocks of all carbohydrates
- Aldose: a monosaccharide containing an aldehyde group (glyceraldehyde is the simplest)
- Ketose: a monosaccharide containing a ketone group (dihydroxyacetone is the simplest)



Carbohydrates - Functions

- **1. Major energy source**
- **2. Intermediates in the biosynthesis of other basic biochemical entities (fats and proteins)**
- **3. Associated with other entities (vitamins & antibiotics)**
- **4. On cells surfaces: cell–cell interactions & immune recognition, activation of growth factors**
- **5. Structural tissues: polysaccharides (cellulose & bacterial cell walls)**

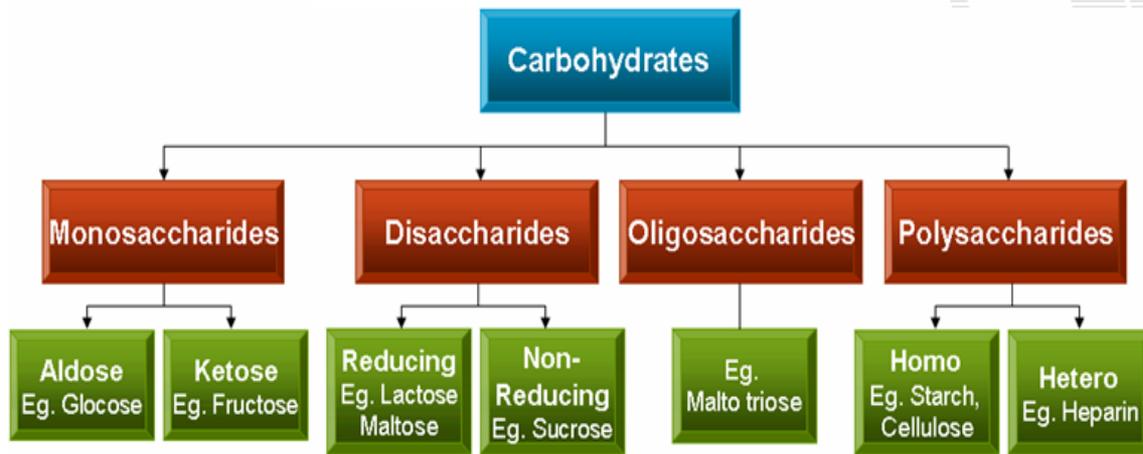
Carbohydrates - Forms

- **Monosaccharides** – carbohydrates that cannot be hydrolyzed to simpler carbohydrates (glucose or fructose)
- **Disaccharides** – carbohydrates that can be hydrolyzed into two monosaccharide units (sucrose → glucose & fructose)
- **Oligosaccharides** – carbohydrates that can be hydrolyzed into a few monosaccharide units (fructo-oligosaccharides (FOS), found in many vegetables)
- **Polysaccharides** – carbohydrates that are polymeric sugars (starch or cellulose)

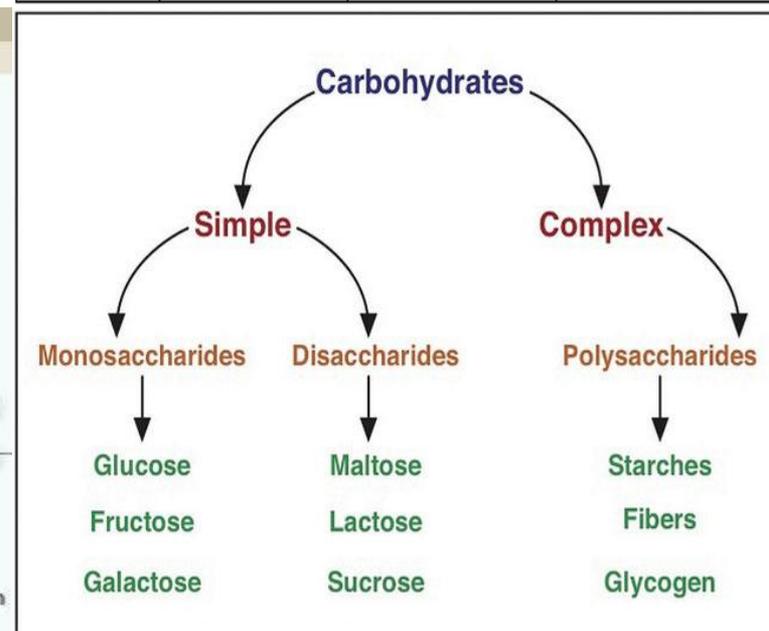
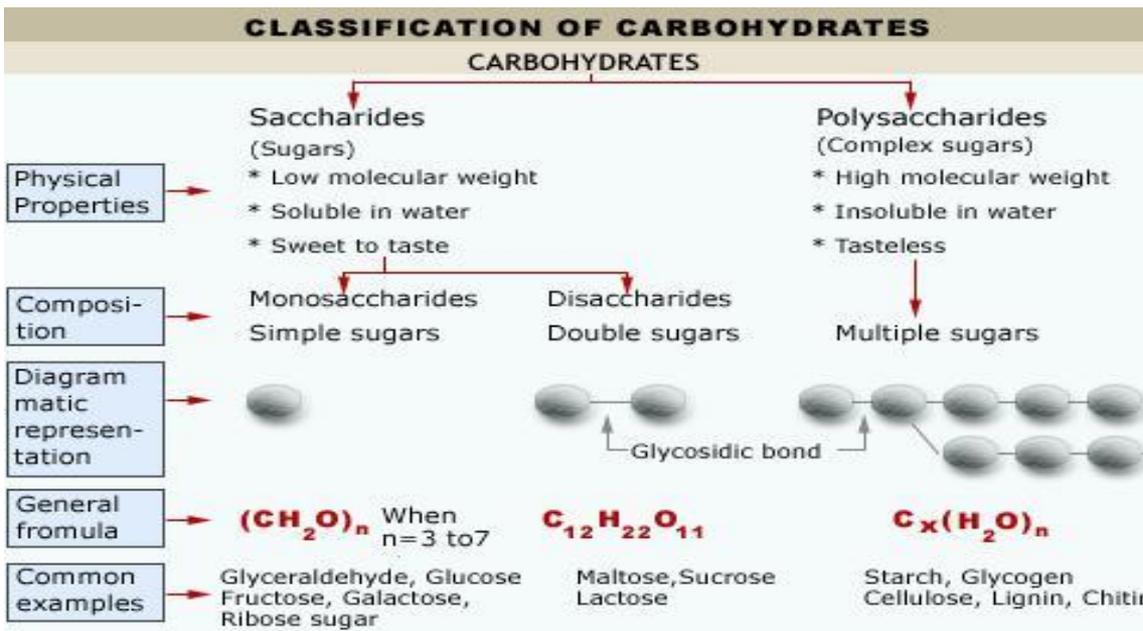
Carbohydrates – natural forms

- Most carbohydrates are found naturally in bound form rather than as simple sugars
 - ✓ Polysaccharides (starch, cellulose, inulin, gums)
 - ✓ Glycoproteins and proteoglycans (hormones, blood group substances, antibodies)
 - ✓ Glycolipids (cerebrosides, gangliosides)
 - ✓ Glycosides
 - ✓ Mucopolysaccharides (hyaluronic acid)
 - ✓ Nucleic acids (DNA, RNA)

Carbohydrates - Classification

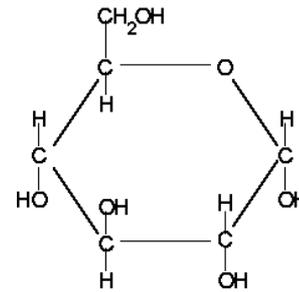


Carbon Atoms	General terms	Aldehydes	Ketones
3	Triose	Aldotriose	Keto triose
4	Tetrose	Aldotetrose	Ketotetrose
5	Pentose	Aldopentose	Ketopentose
6	Hexose	Aldohexose	Ketohexose
7	Heptose	Aldoheptose	Ketoheptose

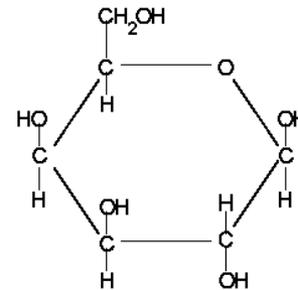


Common Monosaccharides

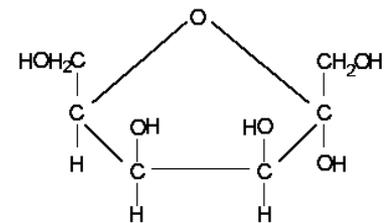
- Glucose, fructose, galactose, mannose: All are 6 carbon hexoses: 6 Cs, 12 Hs, 6 Os
- Arrangement of groups & atoms differs which accounts for varying sweetness
- Glucose:
 - ✓ Mild sweet flavor
 - ✓ Known as blood sugar
 - ✓ Essential energy source
 - ✓ Found in every disaccharide and polysaccharide
- Fructose:
 - ✓ Sweetest sugar, found in fruits and honey
 - ✓ Added to soft drinks, cereals, deserts
- Galactose:
 - ✓ Hardly tastes sweet & rarely found naturally as a single sugar



Glucose



Galactose

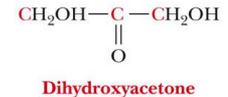
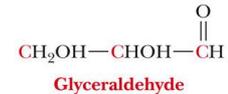


Fructose

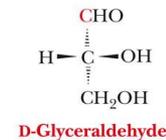
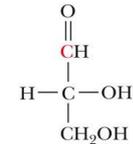
Monosaccharides

- Monosaccharides are classified by their number of carbon atoms
- Trioses are simplest carbohydrate monosaccharides
- Glyceraldehyde contains a stereocenter and exists as a pair of enantiomers
- Mirror-images stereoisomers are called enantiomers

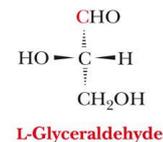
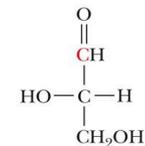
1 A comparison of glyceraldehyde (an aldotriose) and dihydroxyacetone (a ketotriose).



2 The structure of D-glyceraldehyde and a space-filling model of D-glyceraldehyde.

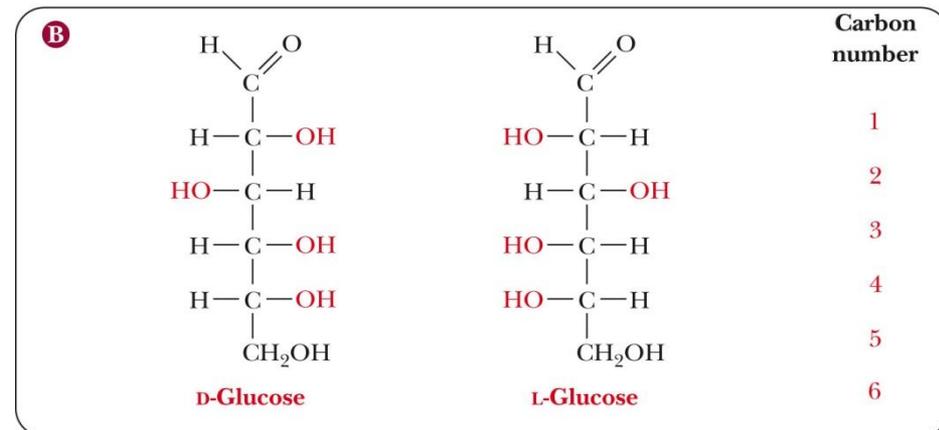
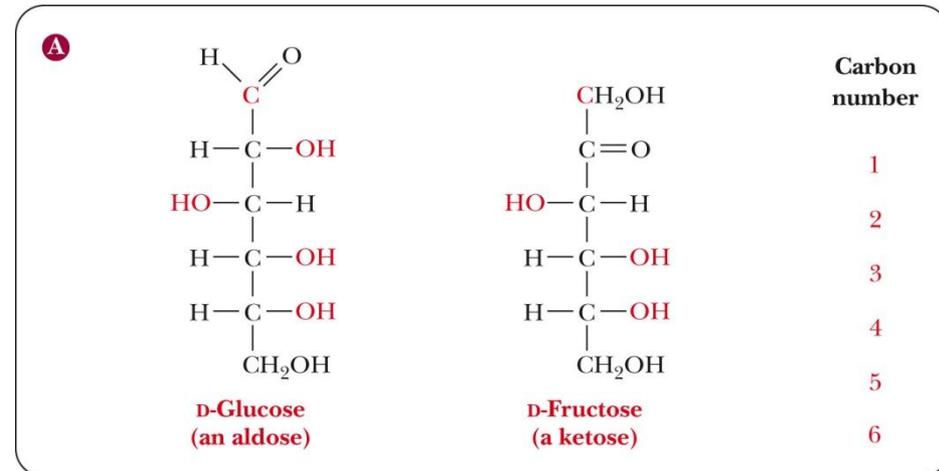


3 The structure of L-glyceraldehyde and a space-filling model of L-glyceraldehyde.



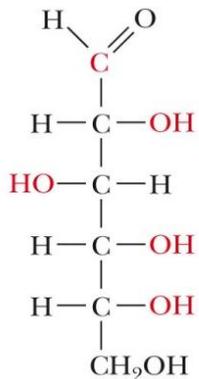
The two dimensional representation Fischer Projections

- Fischer projection: bonds are written in a two dimensional representation showing the configuration of tetrahedral stereocenters
- Horizontal lines represent bonds projecting forward
- Vertical lines represent bonds projecting to the rear

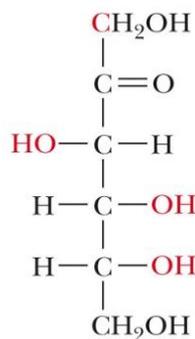


D,L Monosaccharides

- According to the conventions proposed by Fischer
 - ✓ **D-monosaccharide:** a monosaccharide that, when written as a Fischer projection, has the -OH on its penultimate carbon on the right
 - ✓ **L-monosaccharide:** a monosaccharide that, when written as a Fischer projection, has the -OH on its penultimate carbon on the left



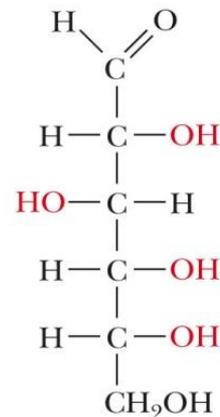
D-Glucose
(an aldose)



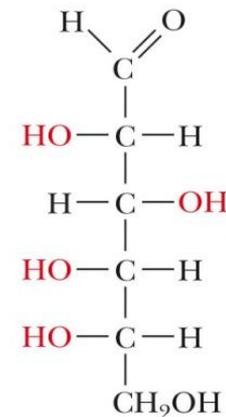
D-Fructose
(a ketose)

Carbon
number

1
2
3
4
5
6



D-Glucose



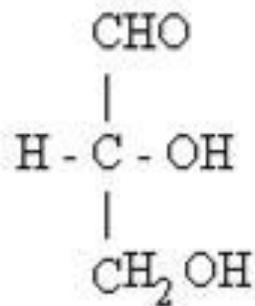
L-Glucose

Carbon
number

1
2
3
4
5
6

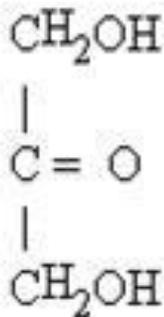
Trioses

- The simplest aldose & ketose
- Three carbon units
- D & L isomers in both sugars



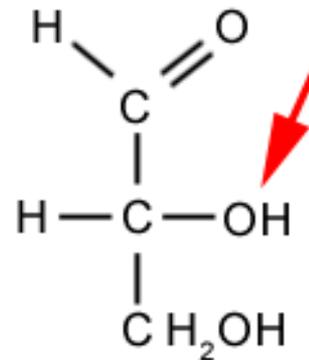
Glyceraldehyde

(An aldotriose of sugar)

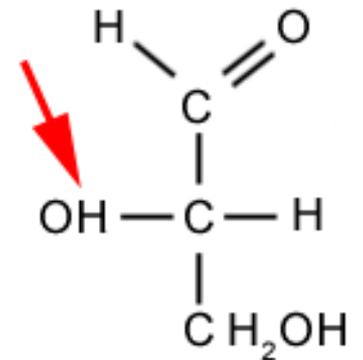


Dihydroxyacetone

(A ketotriose sugar)



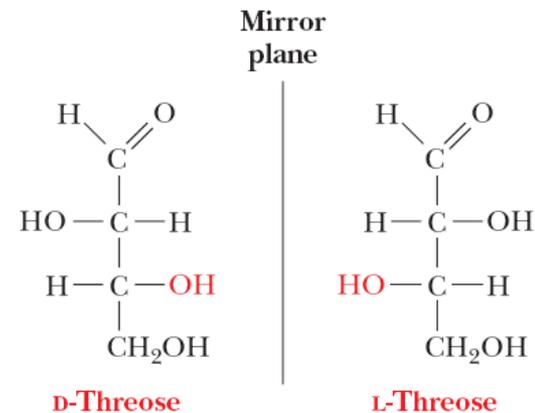
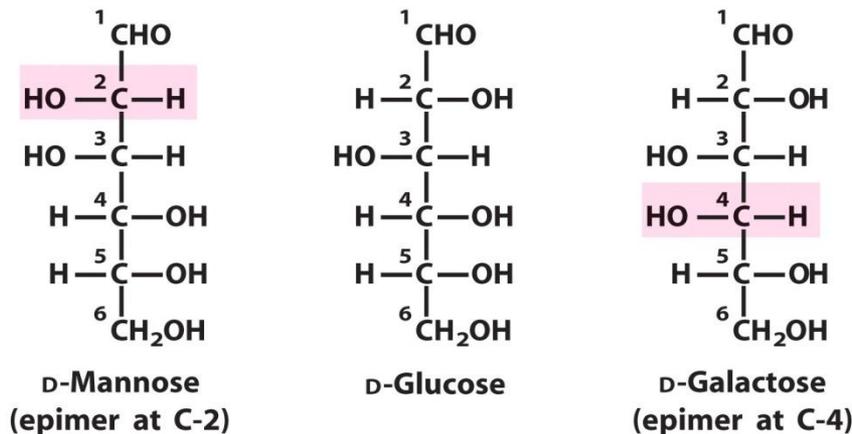
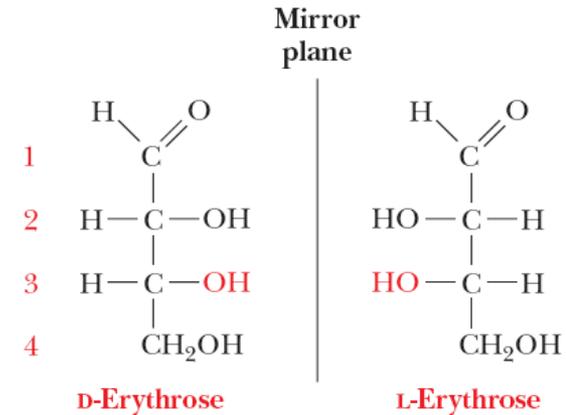
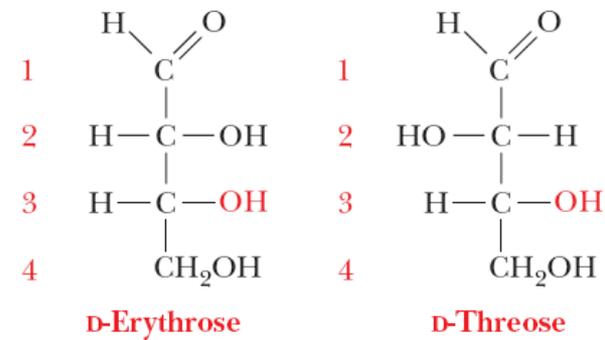
D-Glyceraldehyde



L-Glyceraldehyde

Aldotetroses

- Enantiomers: stereoisomers that are mirror images
 - example: D-erythrose and L-erythrose
- Diastereomers: stereoisomers that are not mirror images
 - example: D-erythrose and D-threose
- Epimers – stereoisomers that differ only in configuration about one chiral center

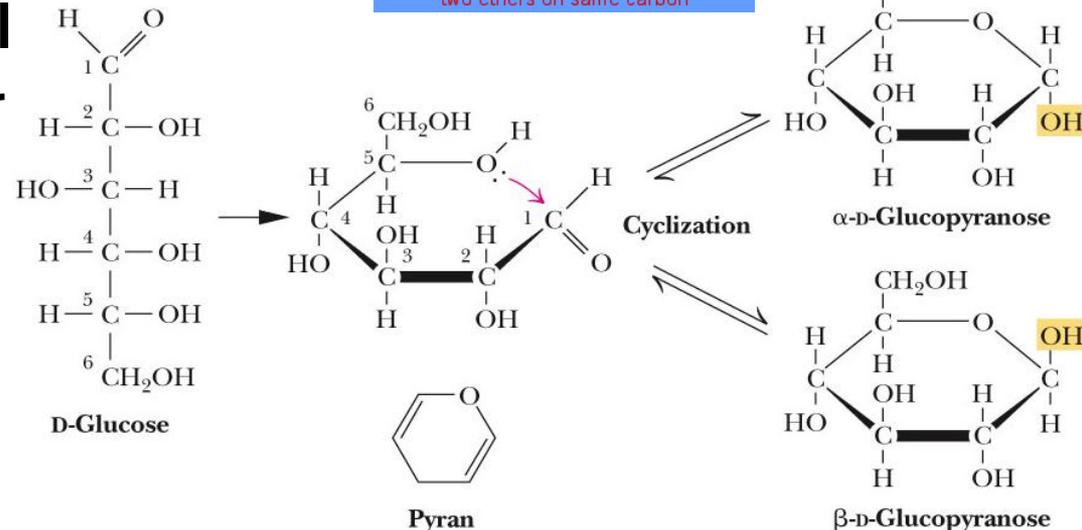
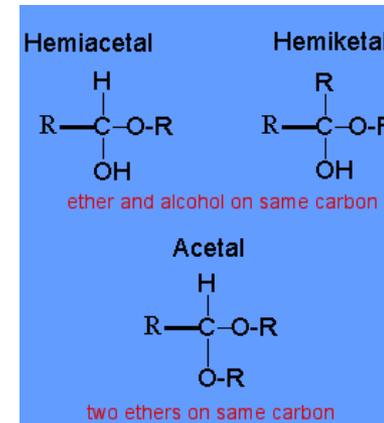
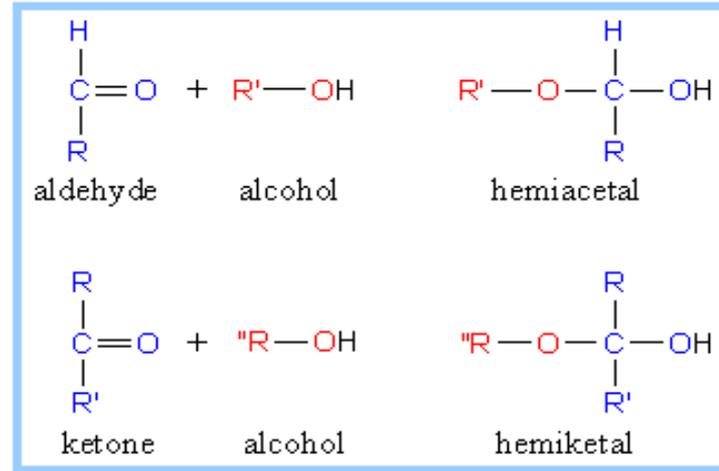


Pentoses & Hexoses

- Aldopentoses have three chiral carbons, & there are 2^3 possible stereoisomers
- Aldohehexoses have four chiral carbons and 2^4 stereoisomers
- Some stereoisomers are much more common in nature
- D sugars, rather than L sugars, predominate in nature (For example, in living organisms, only D-ribose & D-deoxyribose are found in RNA and DNA, respectively)
- Most of the sugars we encounter in nature, especially in foods, contain either five or six carbon atoms

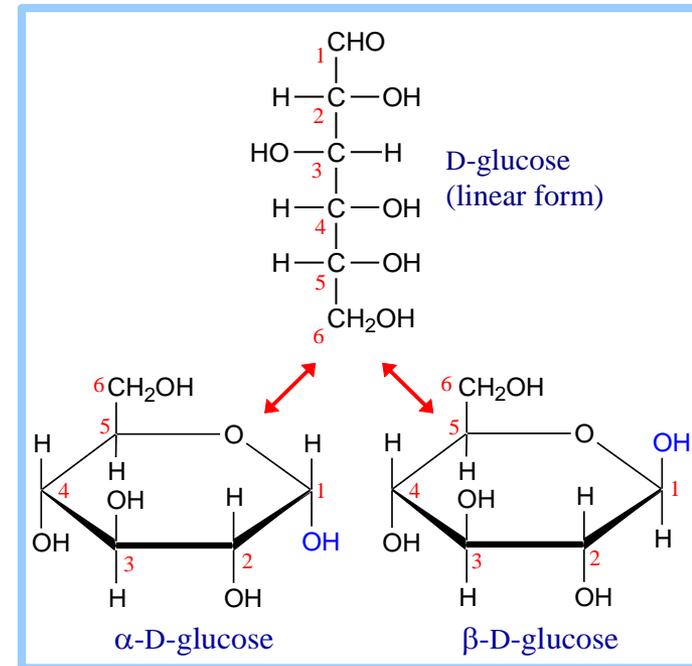
Cyclization of sugars

- Cyclization of sugars takes place due to interaction between functional groups on distant carbons, C₁ to C₅, to make a cyclic hemiacetal
- Cyclization using C₂ to C₅ results in hemiketal formation
- In both cases, the carbonyl carbon is new chiral center and becomes an anomeric carbon
- Anomers: differ only at their anomeric carbon, either α or β

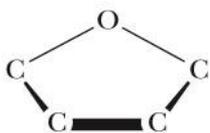


Haworth Projections

- Haworth projections
 - ✓ Five- & six-membered hemiacetals are represented as planar pentagons or hexagons
 - ✓ Most commonly written with the anomeric carbon on right & hemiacetal oxygen to the back right
 - ✓ The designation β - means that anomeric carbon -OH is cis to the terminal -CH₂OH; α - means that it is trans



A

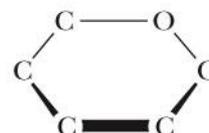


Haworth representations
of furanose structures

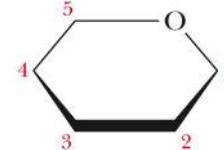


Furan

B



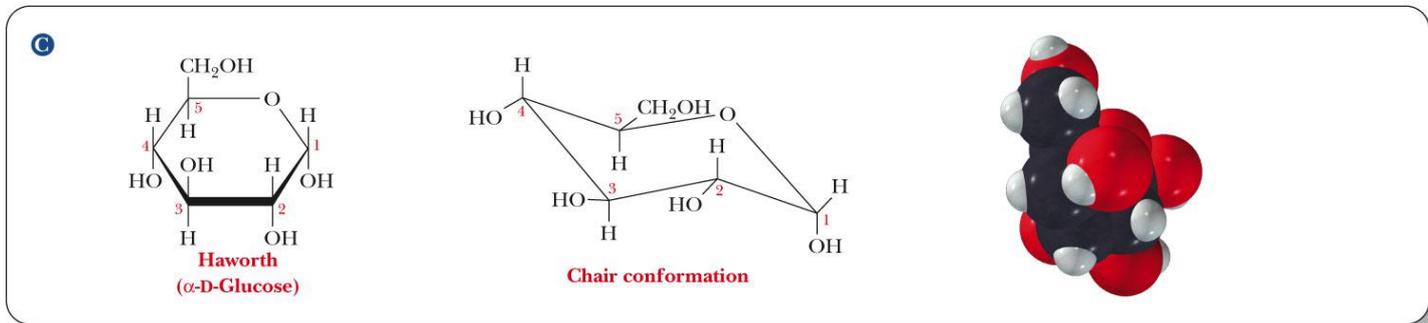
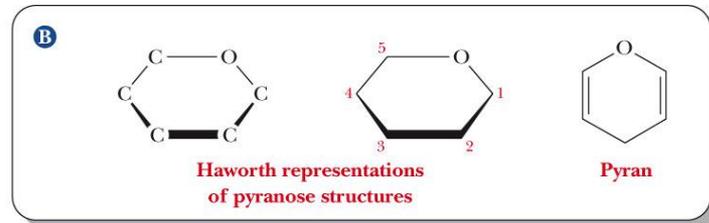
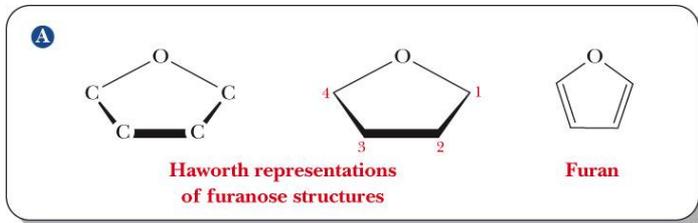
Haworth representations
of pyranose structures



Pyran

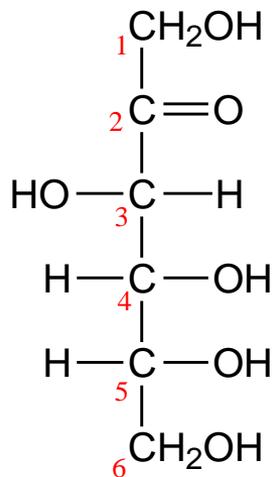
Haworth Projections (Cont'd)

- ✓ A six-membered hemiacetal ring is called pyranose
- ✓ A five-membered hemiacetal ring is called furanose
- ✓ Five-membered rings are so close to being planar that Haworth projections are adequate to represent furanoses
- ✓ For pyranoses, the six-membered ring is more accurately represented as a strain-free chair conformation

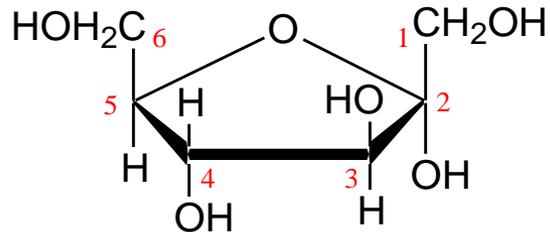


Haworth Projections (Cont'd)

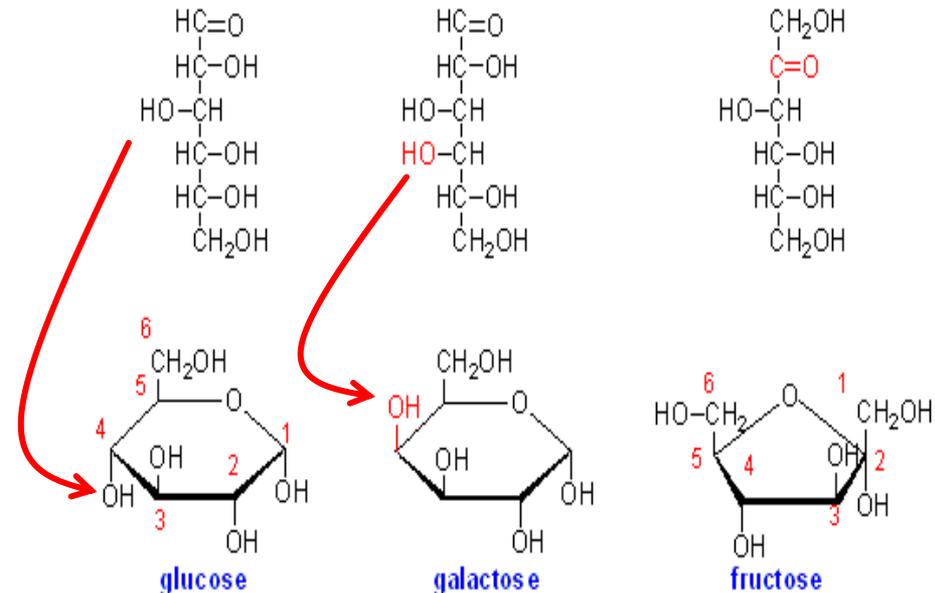
- Fructose forms either
 - a 6-member pyranose ring, by reaction of the C2 keto group with the OH on C6, or
 - a 5-member furanose ring, by reaction of the C2 keto group with the OH on C5



D-fructose (linear)



α -D-fructofuranose



glucose

galactose

fructose

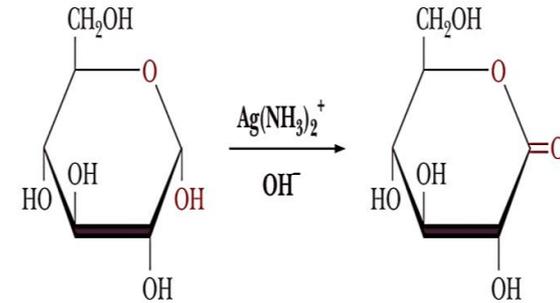
Modified Sugars

Reaction of Monosaccharides

Reducing Sugars - Oxidation

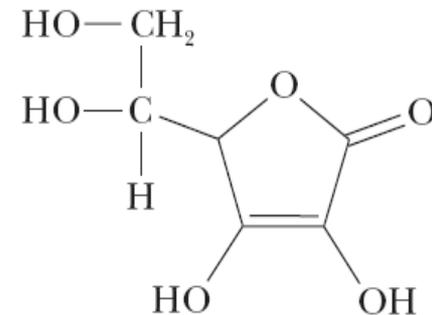
- Oxidation-reduction reactions: energy metabolism vs. photosynthesis

- Reducing sugar (oxidation process): one that reduces an oxidizing agent



- Oxidation of a cyclic hemiacetal form gives a lactone

- Reducing vs. non-reducing sugars (all monosaccharides, aldoses & ketoses). Also, most disaccharides (sucrose?)

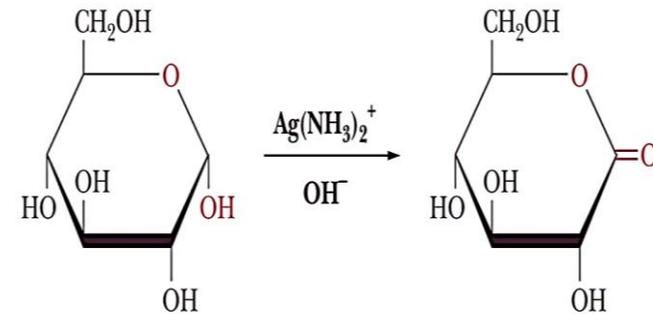


Ascorbic acid
(Vitamin C)

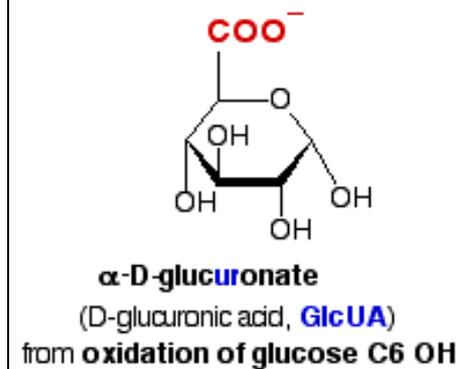
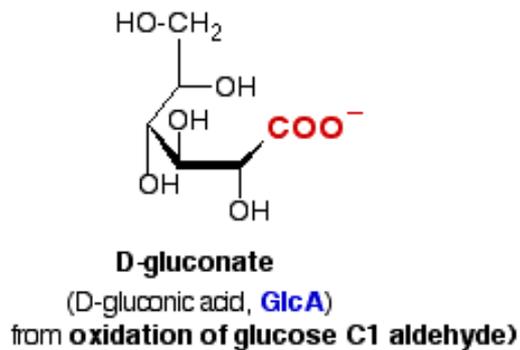
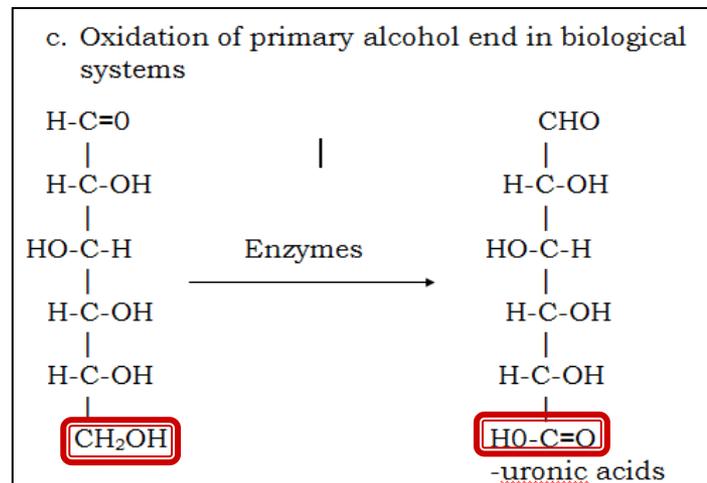
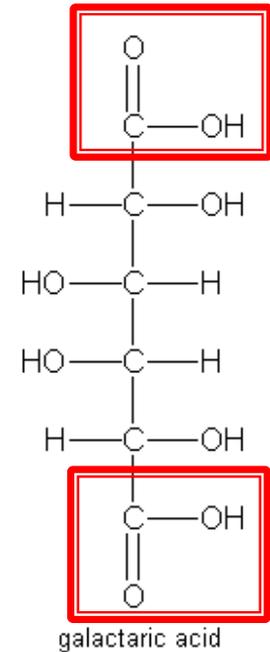
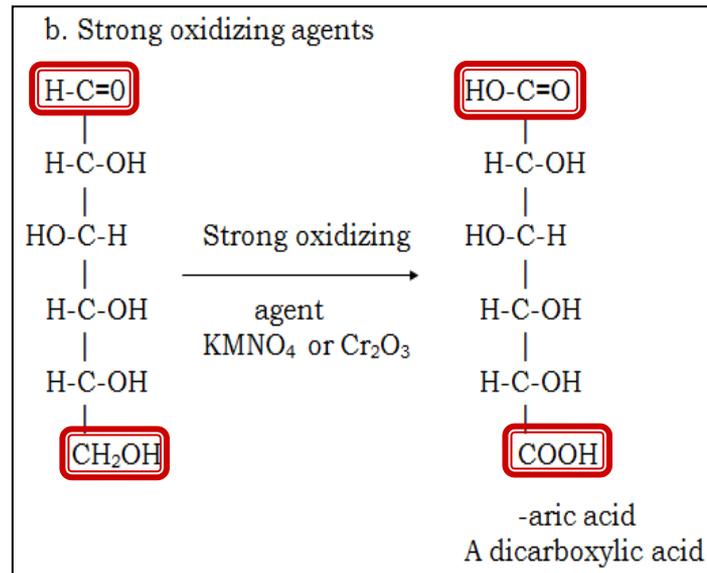
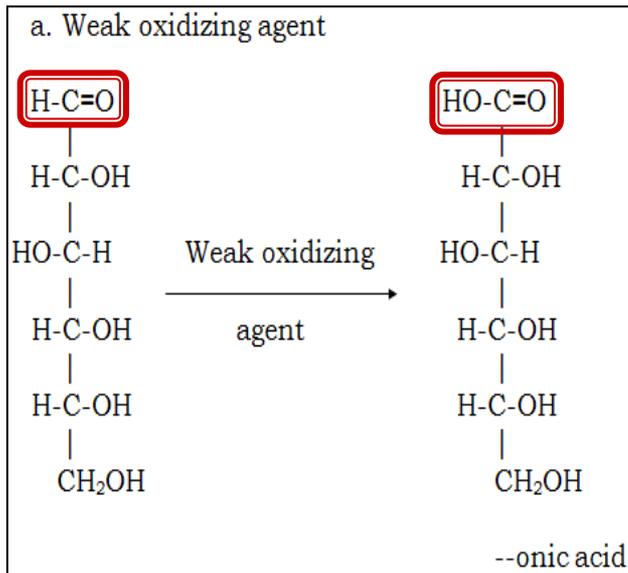
- Oxidation of ketoses to carboxylic acids does not occur

Tests for reducing sugars

- Tollens solution (oxidizing agent); silver ammonia complex ion, $\text{Ag}(\text{NH}_3)_2^+$:
 - ✓ Silver precipitates as a silver mirror
 - ✓ If anomeric carbons are involved in glycosidic linkage, there will be a negative Tollens reagent test
 - ✓ If another anomeric carbon is not bonded and is free, there will be a positive Tollens reagent test
- Specific for glucose: detection of glucose, but not other reducing sugars, is based on the use of the enzyme glucose oxidase



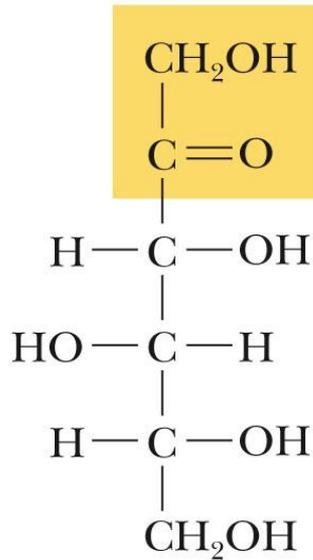
Reaction of Monosaccharides Oxidation



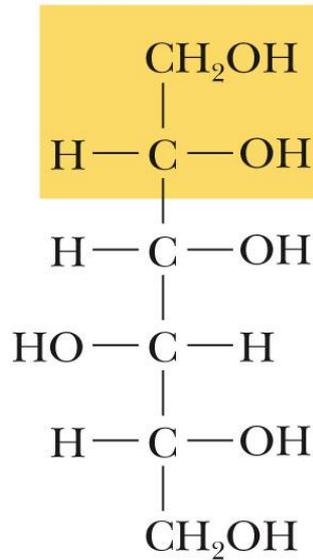
Reaction of Monosaccharides

Reduction

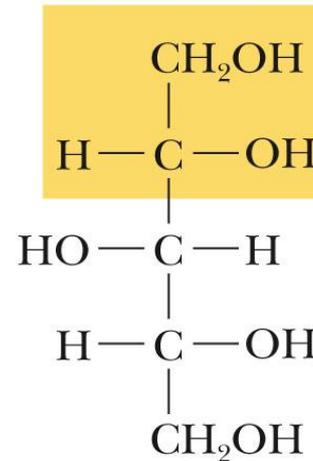
- 1. Reduction of the carbonyl group to a hydroxyl group by a variety of reducing agents (eg. NaBH_4)
 - The product is a polyhydroxy compound called an alditol
 - Xylitol & sorbitol: derivatives of xylulose & sorbose, have commercial importance (sweeteners in sugarless chewing gum & candy)



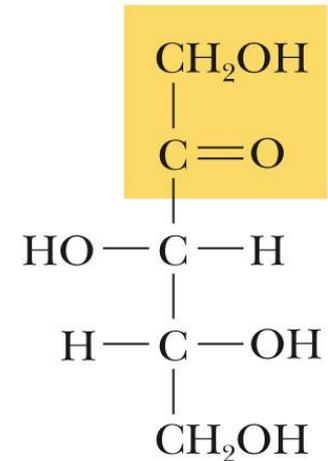
D-Sorbose



D-Sorbitol



D-Xylitol

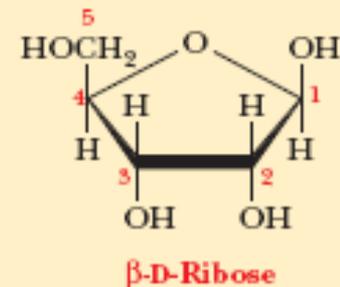
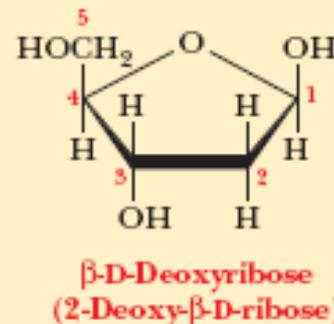
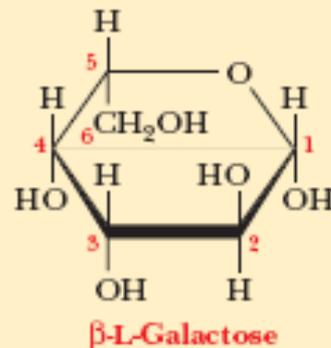
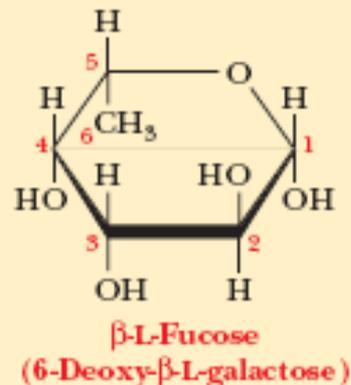


D-Xylulose

Reaction of Monosaccharides

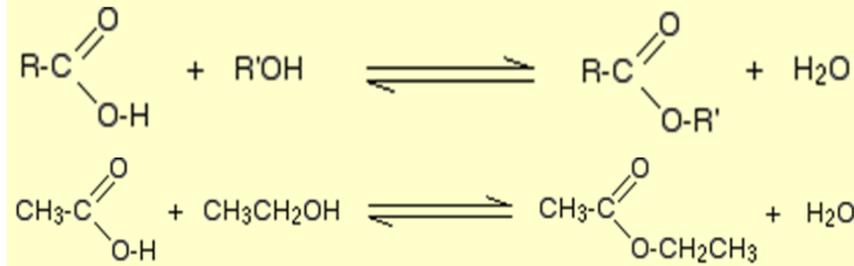
Reduction

- 2. Deoxy sugars, a hydrogen atom is substituted for one of the hydroxyl groups of the sugar
 - L-fucose (L-6-deoxygalactose): some glycoproteins including the ABO blood-group antigens
 - D-2-deoxyribose: in DNA

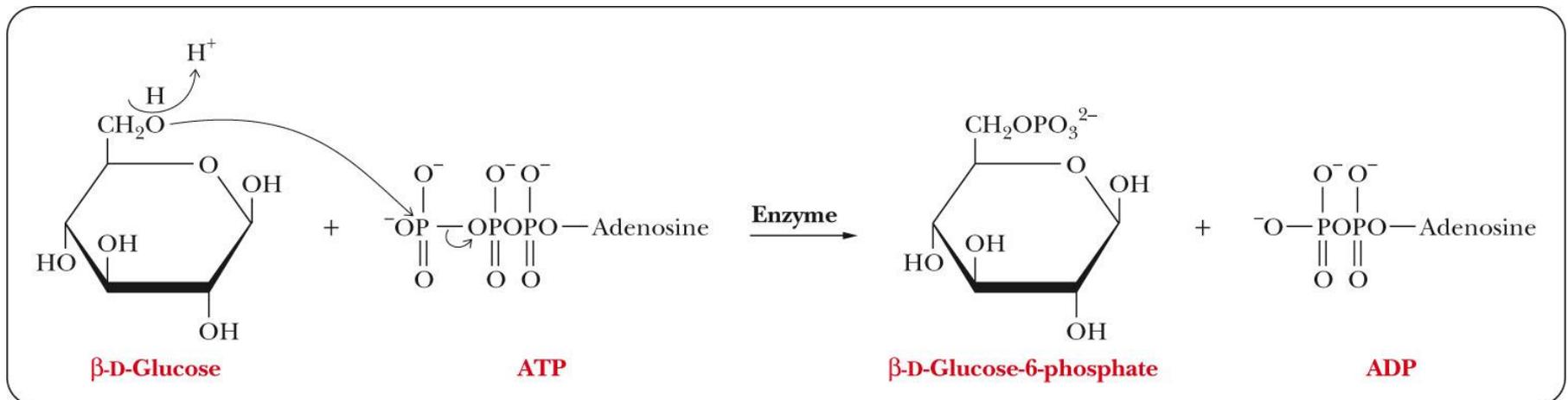


Esterification

Phosphoric Esters



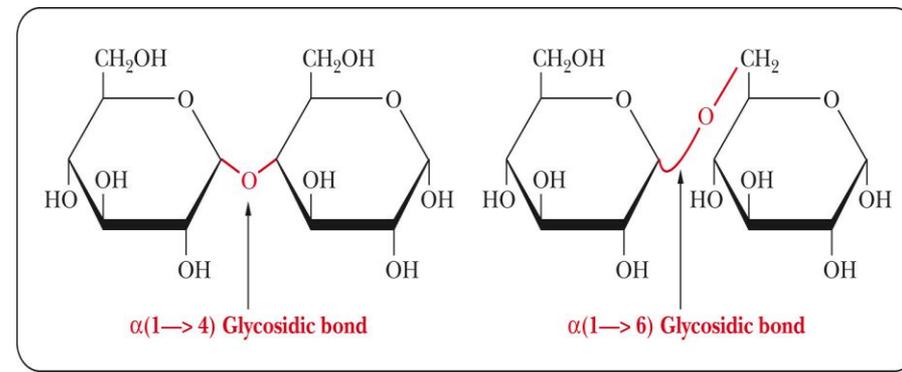
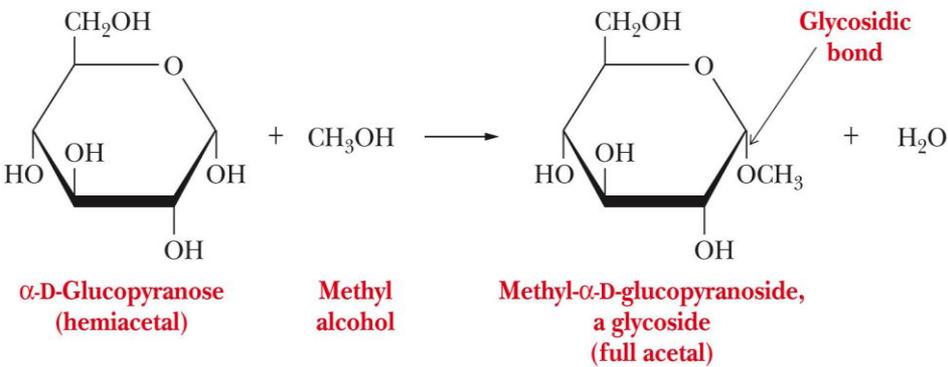
- Hydroxyl groups behave exactly like alcohols; they can react with acids and derivatives of acids to form esters
- The phosphate esters are particularly important because they are the usual intermediates in the breakdown of carbohydrates to provide energy
- Frequently formed by transfer of a phosphate group from ATP (adenosine triphosphate) to give the phosphorylated sugar & ADP (adenosine diphosphate)



Glycosidic Bond Formation

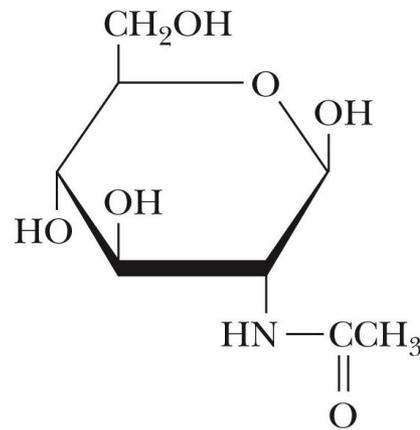
formation of full acetal

- **Glycoside:** the -OH of the anomeric carbon is replaced by -OR
 - ✓ Those derived from furanoses are furanosides; those derived from pyranoses are pyranosides
 - ✓ **Glycosidic bond:** bond from the anomeric carbon to the -OR group
 - ✓ This type of reaction involves the anomeric carbon of the sugar in its cyclic form
 - ✓ This is the basis for the formation of (di/oligo/poly)saccharides. Nature of them depends on types & linkages (Two Different Disaccharides of α -D-Glucose)

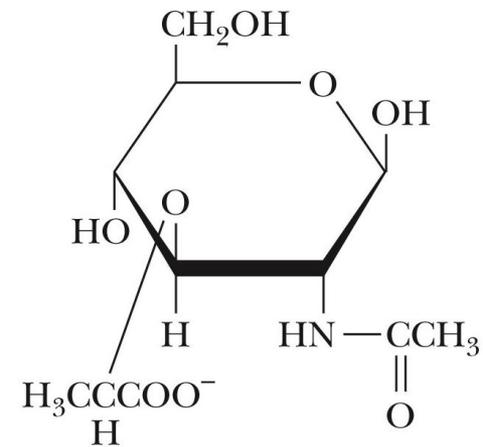


Glycosidic Bond Formation

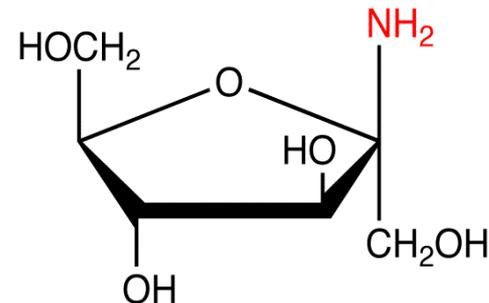
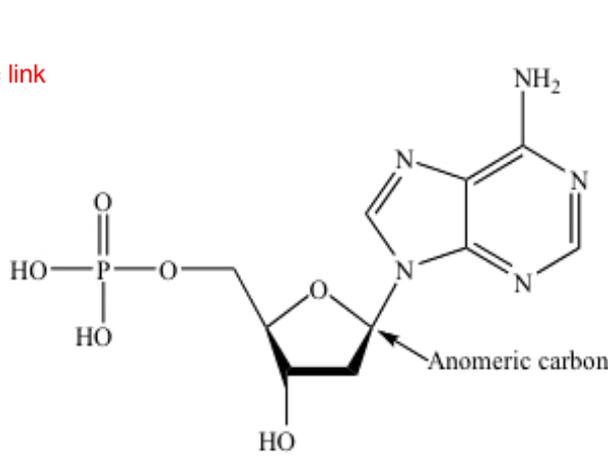
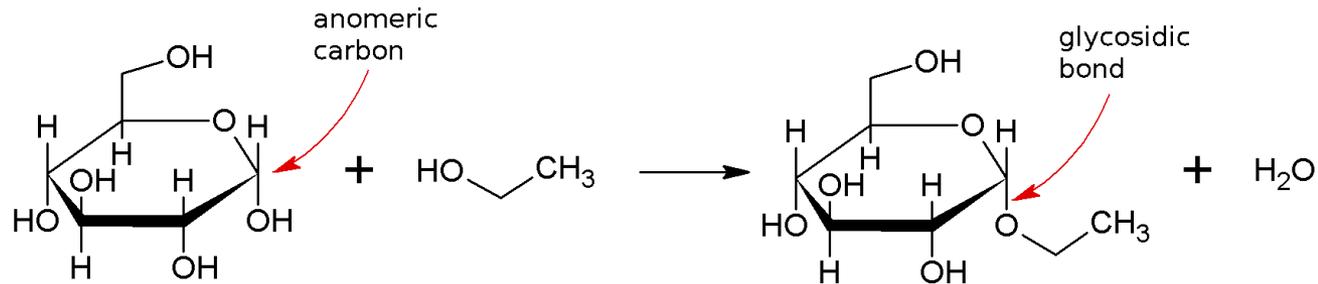
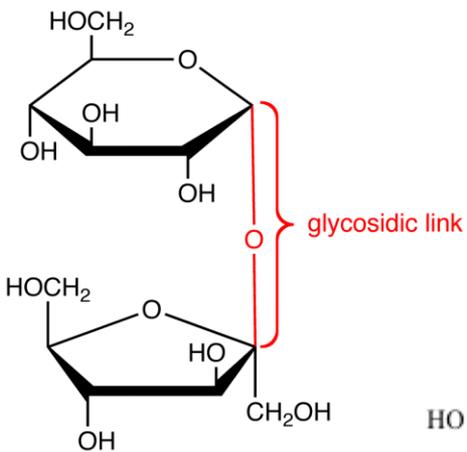
- Glycosides can be linked by:
- O- (an O-glycoside)
- N- (a glycosylamine)
- S- (a thioglycoside)
- C- (a C-glycoside)



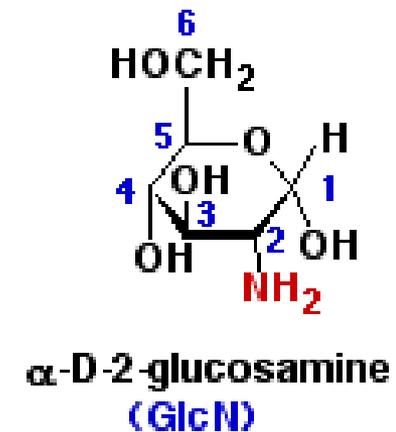
N-Acetyl- β -D-glucosamine



N-Acetylmuramic acid



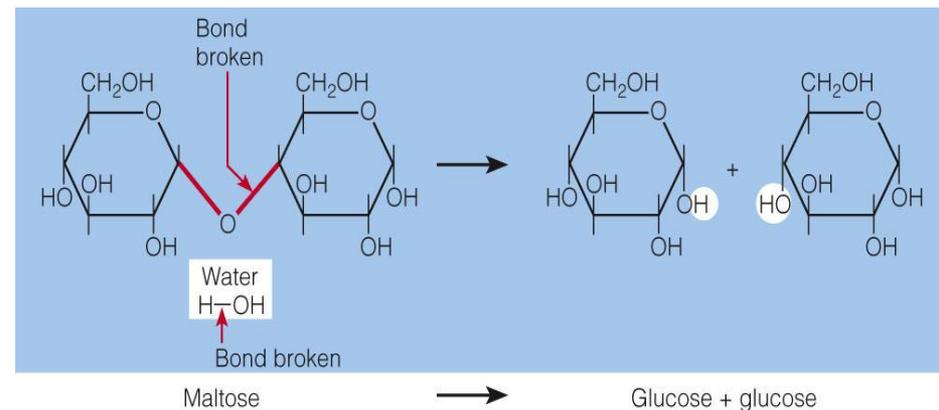
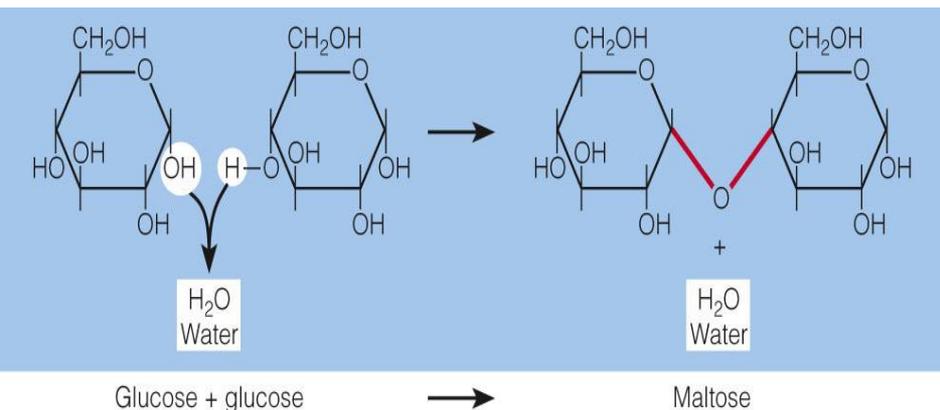
N-glycoside



α -D-2-glucosamine (GlcN)

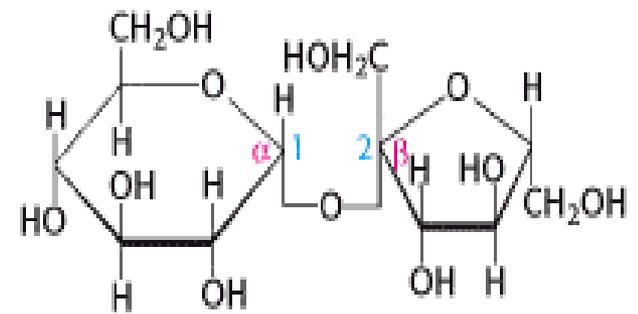
Disaccharides

- Pairs of monosaccharides, one of which is always glucose
- Condensation reactions link monosaccharides together
- Hydrolysis reactions split them & commonly occurs during digestion
- Maltose is produced during the germination of seeds and fermentation
- Sucrose is refined from sugarcane, tastes sweet, and is readily available
- Lactose is found in milk and milk products

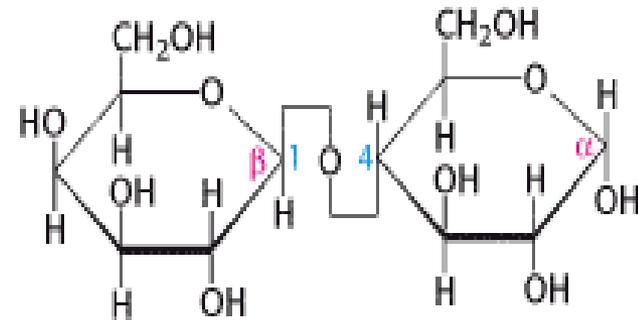


Disaccharides

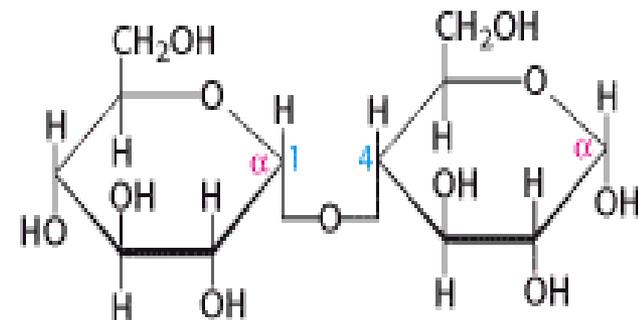
- Naming (common vs. systematic)
- Reducing vs. non-reducing
- Sucrose
 - ✓ Table sugar: D-glucose & D-fructose (α -1,2-glycosidic bond)
- Lactose
 - ✓ D-galactose & D-glucose (β -1,4-glycosidic bond). Galactose is a C-4 epimer of glucose
- Maltose
 - ✓ Two units of D-glucose (α -1,4-glycosidic bond)
 - ✓ Formed from the hydrolysis of starch



Sucrose
(α -D-Glucopyranosyl-(1 \rightarrow 2)- β -D-fructofuranose)



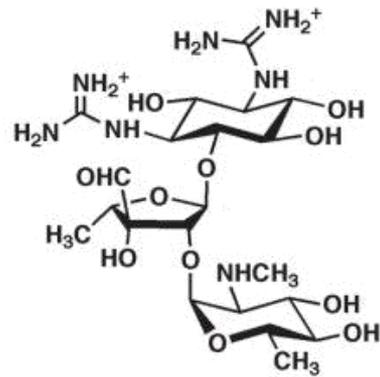
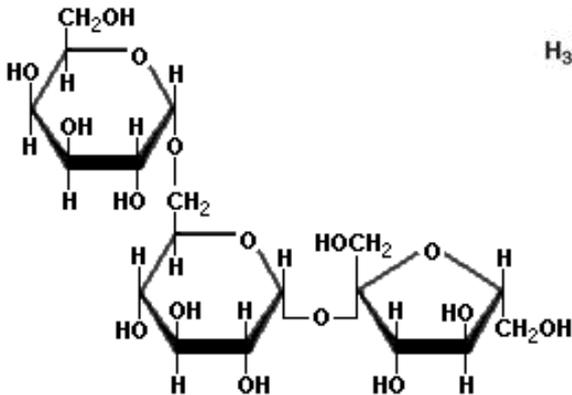
Lactose
(β -D-Galactopyranosyl-(1 \rightarrow 4)- α -D-glucopyranose)



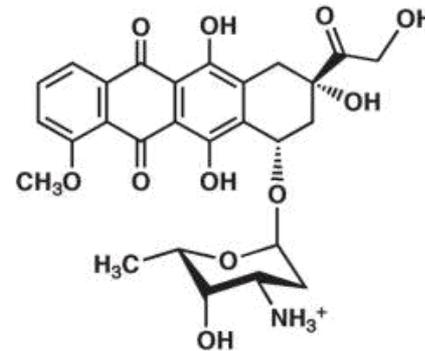
Maltose
(α -D-Glucopyranosyl-(1 \rightarrow 4)- α -D-glucopyranose)

Oligosaccharides

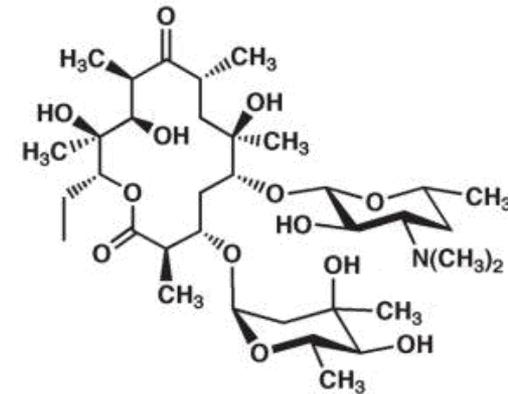
- Raffinose; found in peas and beans
- Composed of galactose, fructose, and glucose



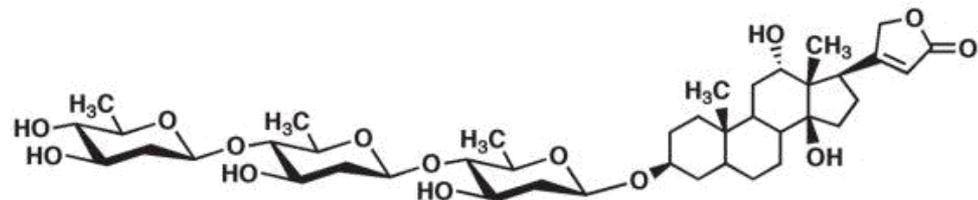
Streptomycin



Doxorubicin



Erythromycin A



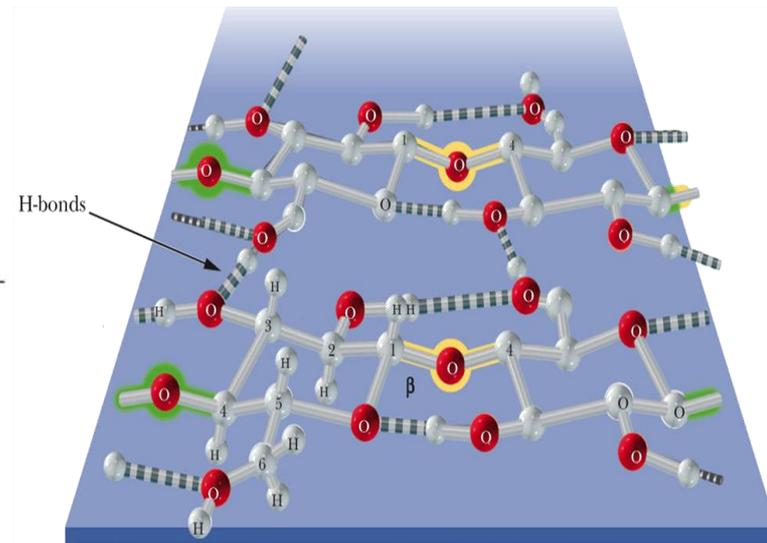
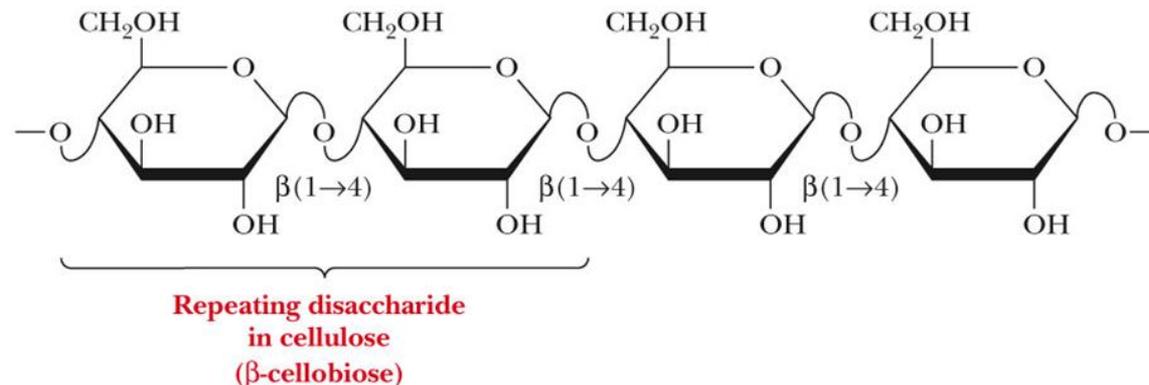
Digoxin

Structures and Function of Polysaccharides

- Polysaccharides:
 - ✓ Homopolysaccharide
 - ✓ Heteropolysaccharide
- Glucose is the most common monomer
- Mostly homo, however, if hetero, it will be two monosaccharides in a repeating sequence
- Complete characterization of a polysaccharide: monomers, sequence & type of glycosidic linkage
- Cellulose & chitin: β -glycosidic linkages, and both are structural materials
- Starch and glycogen: α -glycosidic linkages, and they serve as carbohydrate storage polymers in plants and animals, respectively

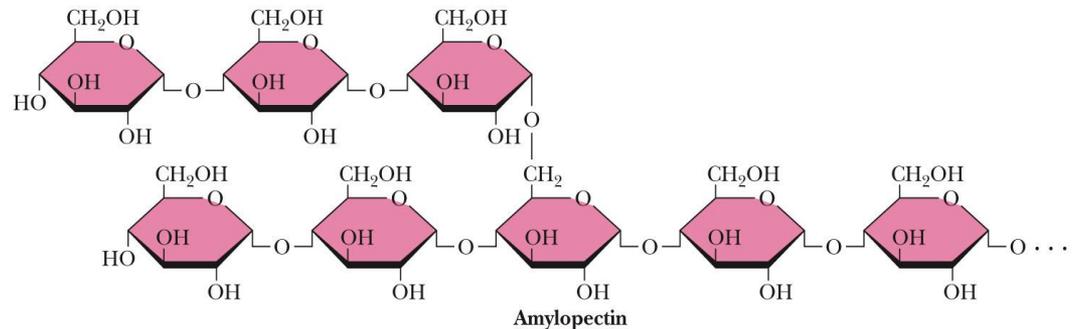
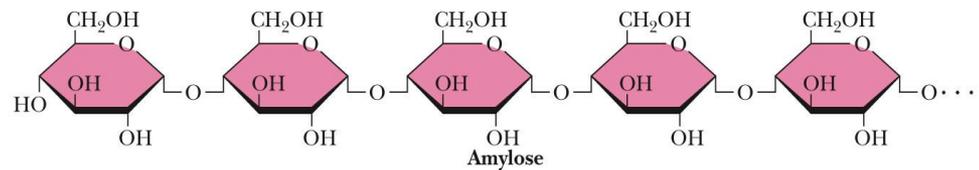
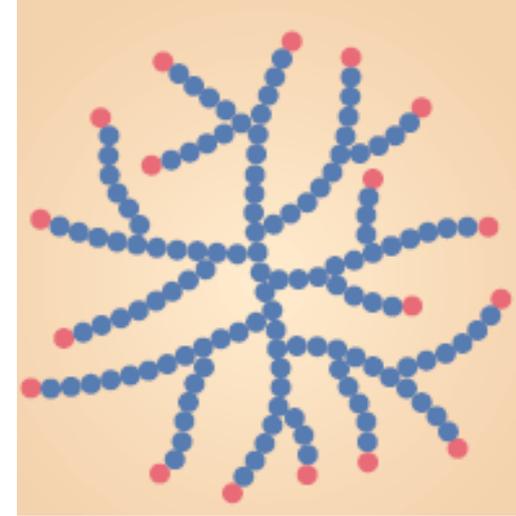
Cellulose

- The major structural component of plants, especially wood and plant fibers
- A linear polymer of approximately 2800 D-glucose units per molecule joined by β -1,4-glycosidic bonds
- Extensive intra- and intermolecular hydrogen bonding between chains
- Cellulases, animals?



Starch

- Energy storage in plants
- A polymers of α -D-glucose units
- A mylose: continuous, unbranched chains of up to 4000 α -D-glucose units joined by α -1,4-glycosidic bonds
- Amylopectin: a highly branched polymer consisting of 24-30 units of D-glucose joined by α -1,4-glycosidic bonds and branches created by α -1,6-glycosidic bonds

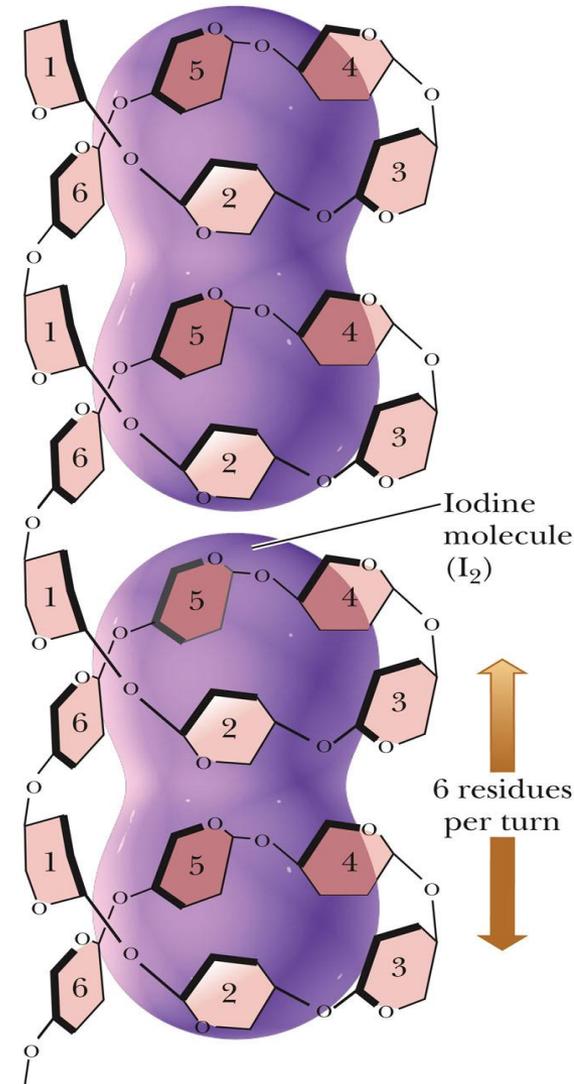


Starch

- Amylases catalyze hydrolysis of α -1,4-glycosidic bonds
- β -amylase is an exoglycosidase and cleaves from the non-reducing end of the polymer
- α -amylase is an endoglycosidase and hydrolyzes glycosidic linkages anywhere along the chain to produce glucose and maltose
- Can amylose & amylopectin be completely degraded to glucose and maltose by the two amylases?
- Debranching enzymes catalyze the hydrolysis of α -1,6-glycosidic bonds

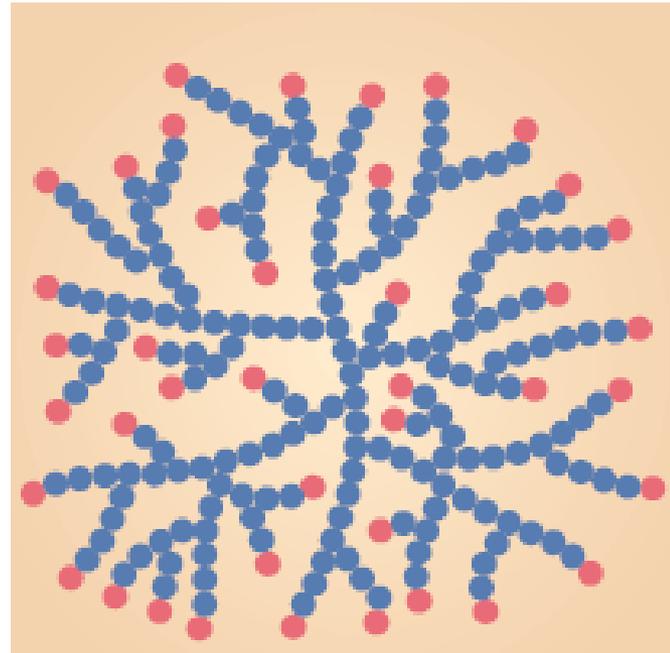
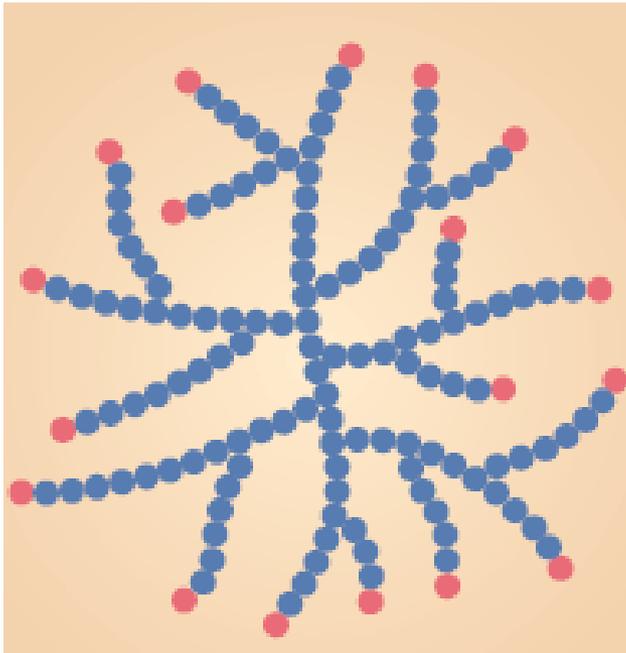
Iodine can Fit Inside Amylose to Form Starch-Iodine Complex

- Amylose occurs as a helix with six residues per turn
- Iodine molecules can fit parallel to the long axis of the helix
- Six turns of the helix, containing 36 glycosyl residues, are required to produce the characteristic blue color of the complex



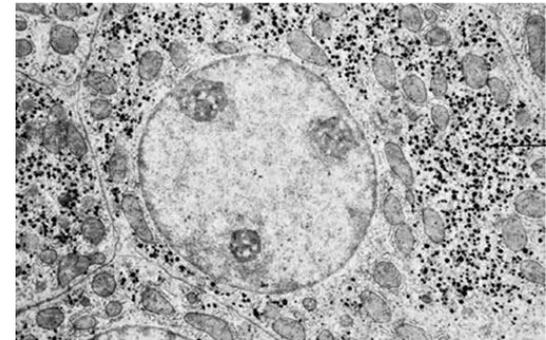
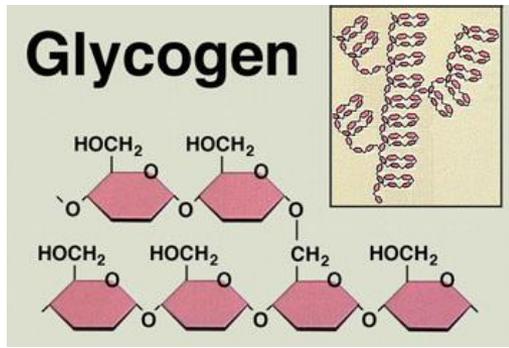
Glycogen

- A branched-chain polymer of α -D-glucose (amylopectin)
- Consists of a chain of $\alpha(1 \rightarrow 4)$ linkages with $\alpha(1 \rightarrow 6)$ linkages
- Glycogen is more highly branched (≈ 10 residues)
- The average chain length is 13 glucose residues
- At the heart of every glycogen molecule is a protein called Glycogenin



Glycogen

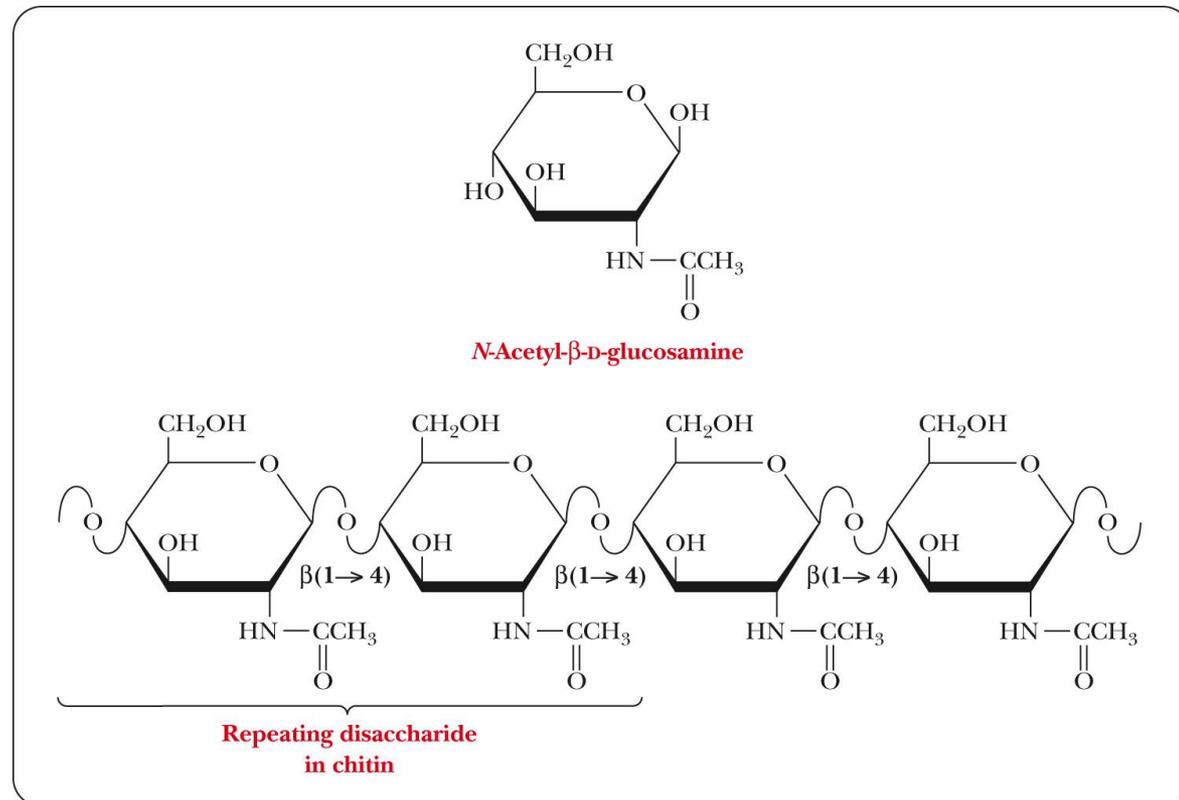
- Found in animal cells in granules (similar to the starch)
- Granules: liver and muscle cells, but hardly in other cell types
- Various degradative enzymes:
 - ✓ Glycogen phosphorylase: cleaves one glucose at a time from the nonreducing end of a branch to produce glucose-1-P
 - ✓ Debranching enzymes
- Is the number of branch points significant?
 - ✓ The higher, the higher the water solubility (plant vs. animals)
 - ✓ The higher, the higher potential targets for enzymes (plant vs. animals)



Chitin

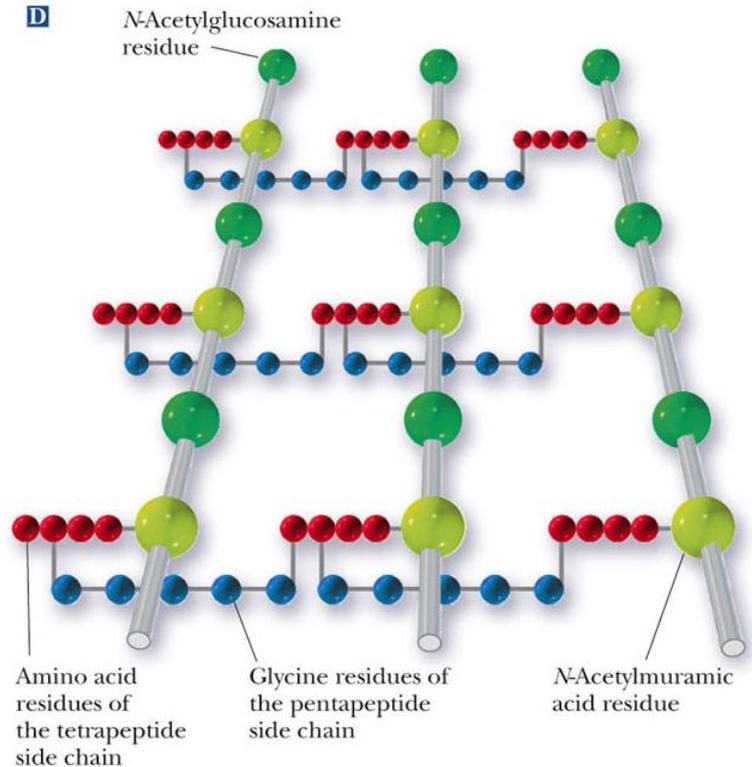
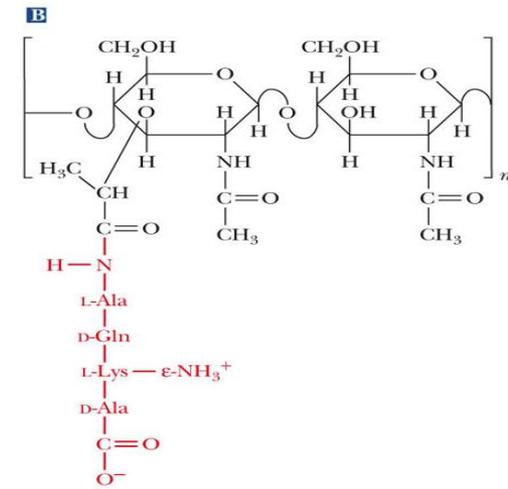
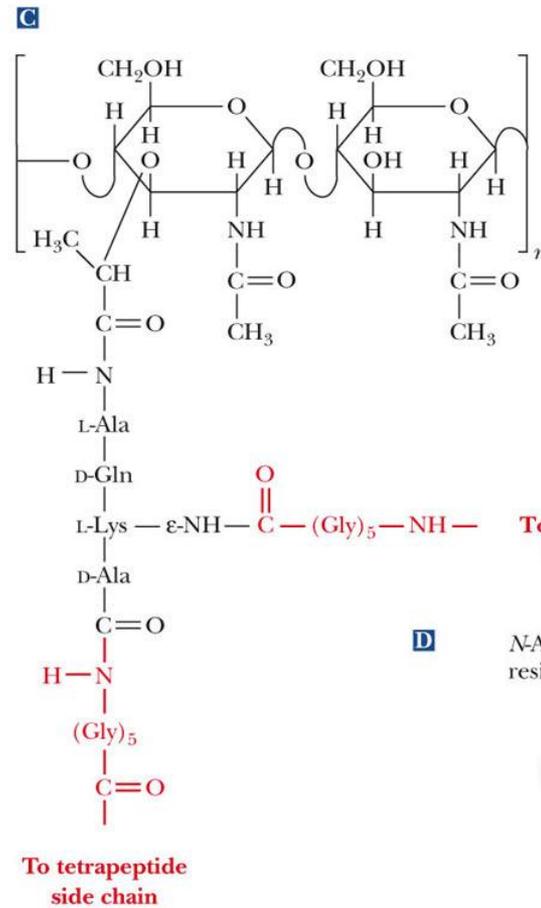
- The major structural component of the exoskeletons of invertebrates, such as insects; also occurs in cell walls of algae, fungi, and yeasts

- Composed of units of N-acetyl- β -D-glucosamine joined by β -1,4-glycosidic bonds



Bacterial cell walls

- Prokaryotic cell walls are constructed on the framework of the repeating unit NAM-NAG joined by β -1,4-glycosidic bonds



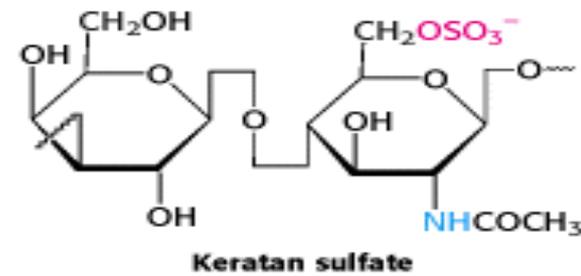
To tetrapeptide side chain

To tetrapeptide side chain

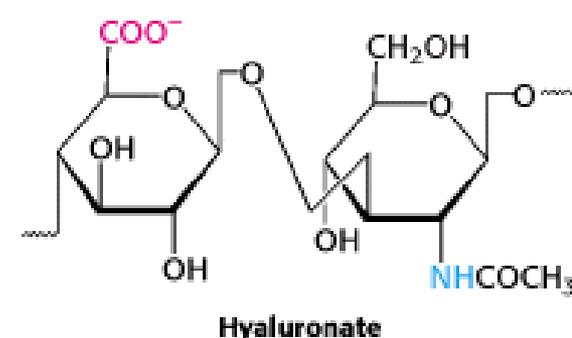
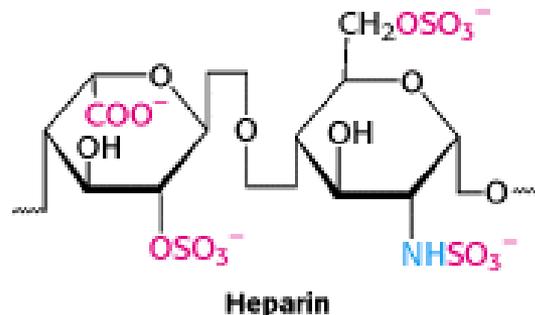
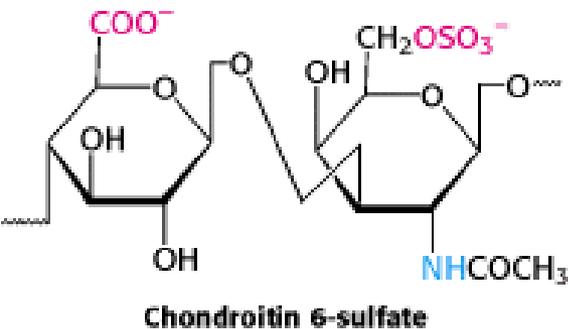
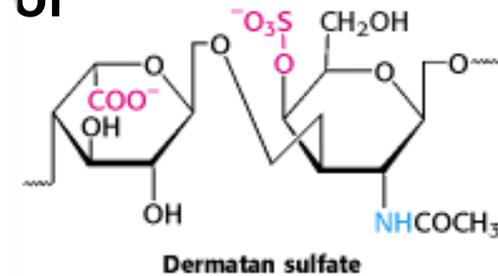
NAM
N-Acetylmuramic acid

NAG
N-Acetylglucosamine

Glycosaminoglycans



- Polysaccharides based on a repeating disaccharide where one of the monomers is an amino sugar and the other has a negative charge due to a sulfate or carboxylate group
 - ✓ Heparin: natural anticoagulant
 - ✓ Hyaluronic acid: a component of the vitreous humor of the eye and the lubricating fluid of joints
 - ✓ Chondroitin sulfate and keratan sulfate: components of connective tissue



Localization and function of GAG

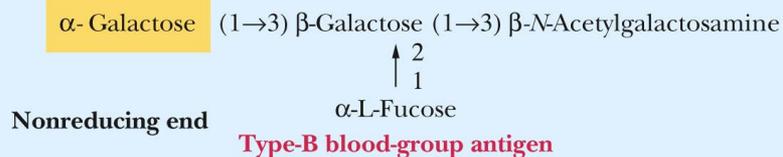
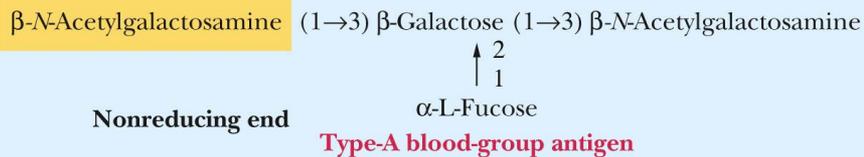
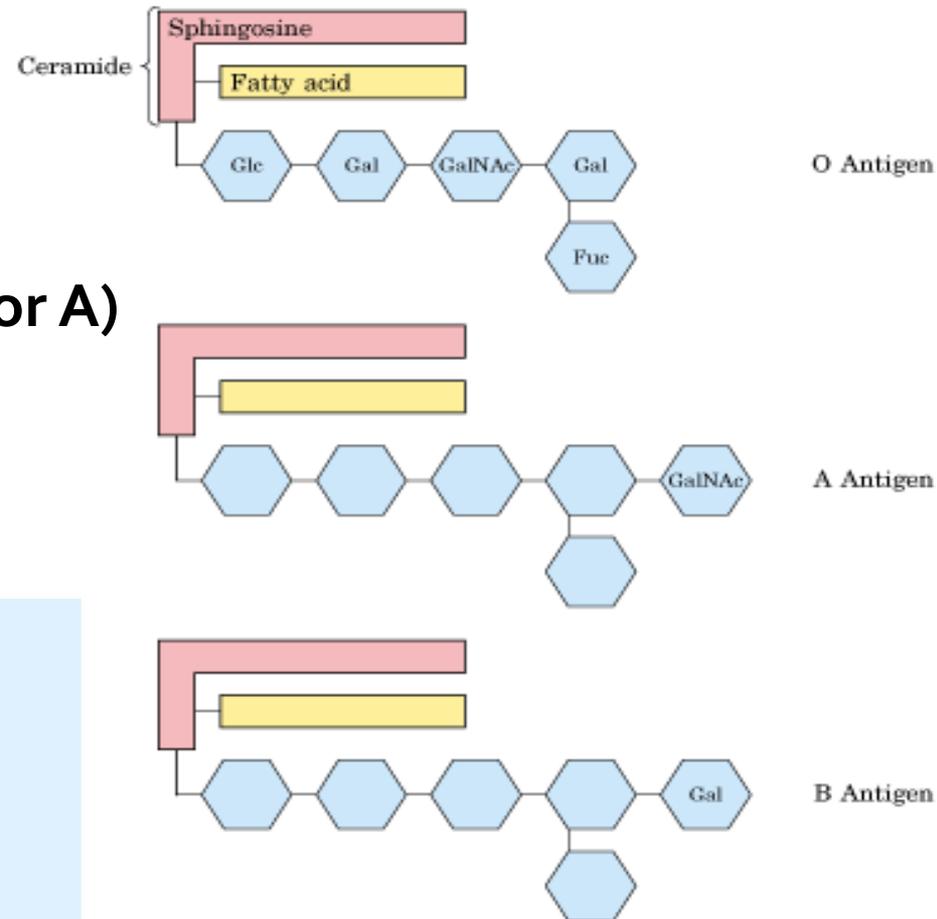
GAG	Localization	Comments
Hyaluronate	<i>synovial fluid, vitreous humor, ECM of loose connective tissue</i>	<i>the lubricant fluid , shock absorbing</i> As many as 25,000 disaccharide units
Chondroitin sulfate	<i>cartilage, bone, heart valves</i>	<i>most abundant GAG</i>
Heparan sulfate	<i>basement membranes, components of cell surfaces</i>	contains higher acetylated glucosamine than heparin
Heparin	component of <i>intracellular granules of mast cells</i> lining the arteries of the lungs, liver and skin	<i>A natural anticoagulant</i>
Dermatan sulfate	<i>skin, blood vessels, heart valves</i>	
Keratan sulfate	<i>cornea, bone, cartilage aggregated with chondroitin sulfates</i>	

Glycoproteins

- **Contain carbohydrate units covalently bonded to a polypeptide chain**
- ✓ **antibodies are glycoproteins**
- ✓ **Oligosaccharide portion of glycoproteins act as antigenic determinants**
- ✓ **Among the first antigenic determinants discovered were the blood group substances**
- ✓ **In the ABO system, individuals are classified according to four blood types: A, B, AB, and O**
- ✓ **At the cellular level, the biochemical basis for this classification is a group of relatively small membrane-bound carbohydrates**

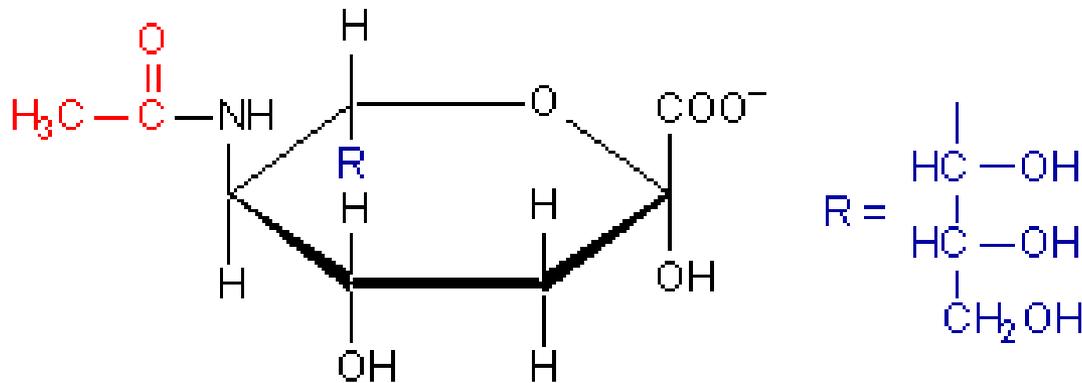
Structures of Blood-Group Antigenic Determinants

- Three different structures:
 - ✓ A, B, and O
- The difference:
 - ✓ N-acetylgalactosamine (for A)
 - ✓ Galactose (for B)
 - ✓ None (for O)



Sialic acid

- *N*-acetylneuraminate, (*N*-acetylneuraminic acid, also called sialic acid) is derived from the amino sugar, neuraminic acid and is often found as a terminal residue of oligosaccharide chains of glycoproteins giving glycoproteins negative charge



N-acetylneuraminate (sialic acid)

Proteoglycans

- Lubricants
- Structural components in connective tissue
- Mediate adhesion of cells to the extracellular matrix
- Bind factors that stimulate cell proliferation

