

Chapter 9

Carbohydrates: Sugars, Saccharides, Glycans

長庚大學生物化學科
吳嘉霖 老師
分機：5159

Carbohydrates have numerous functions in biochemistry:

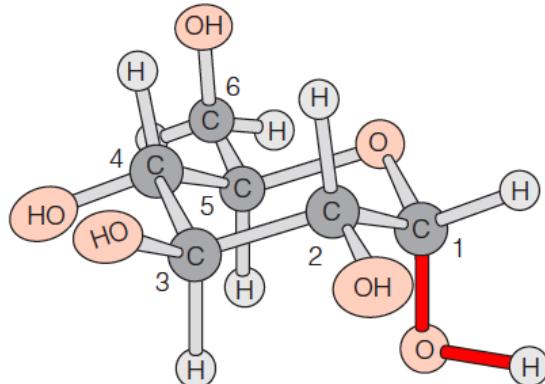
- generating and storing biological energy
- molecular recognition (as in the immune system)
- cellular protection (as in bacterial and plant cell walls)
- cell signaling
- cell adhesion
- biological lubricants
- controlling protein trafficking
- maintaining biological structure (e.g., cellulose).

Representative carbohydrates:

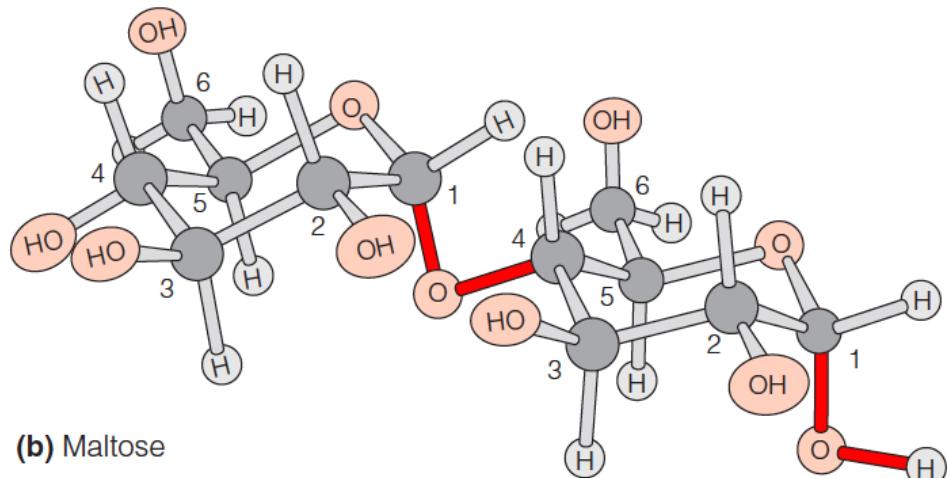
- The three compounds shown here are composed entirely of C, H, and O, with glucose forming the monomer for the oligomer and the polymer.

a) Glucose, a monosaccharide.

b) Maltose(麥芽糖), a disaccharide containing two glucose units.



(a) Glucose



(b) Maltose

Representative carbohydrates:

c) A portion of a molecule of amylose(直鏈澱粉), a glucose polymer found in starch.

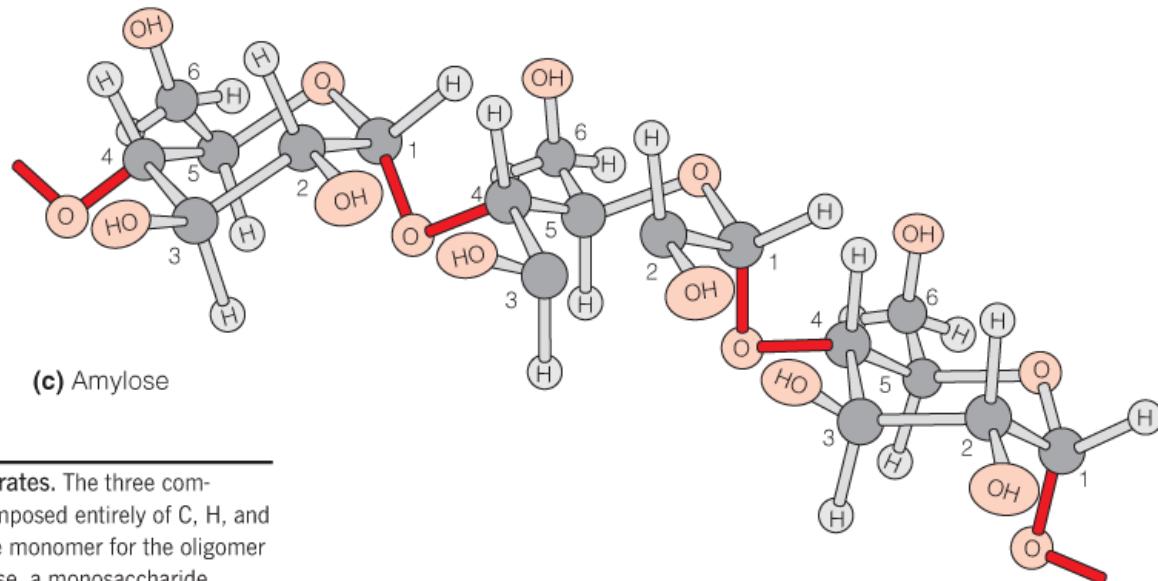


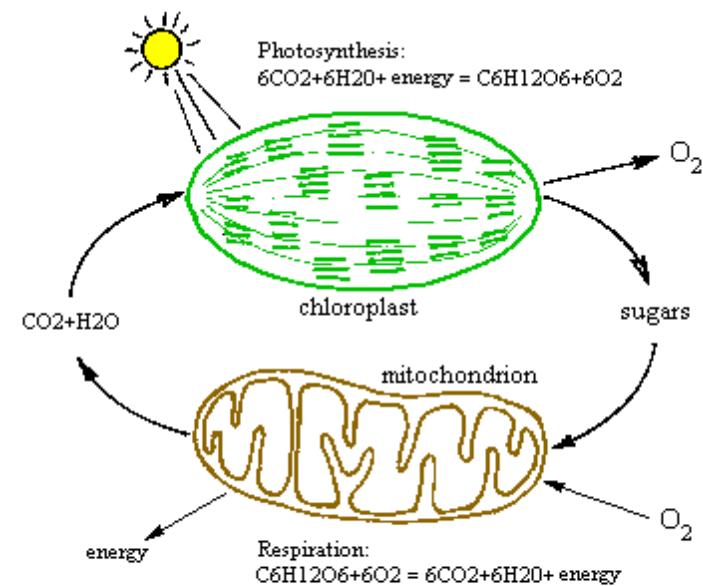
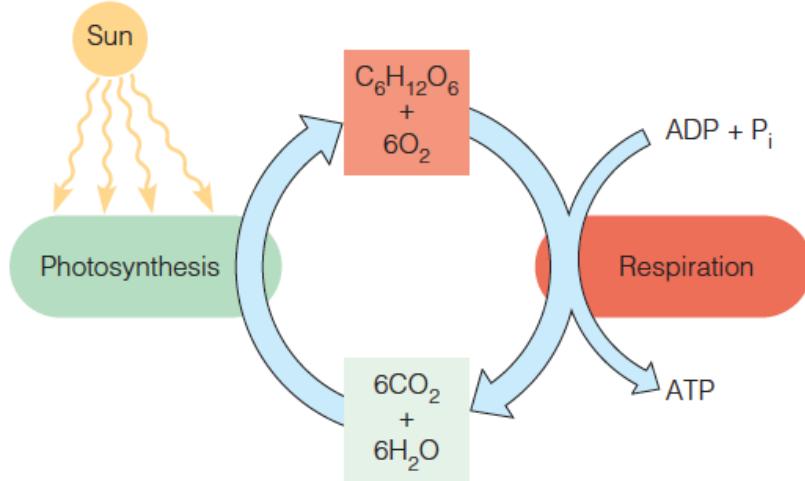
FIGURE 9.1

Representative carbohydrates. The three compounds shown here are composed entirely of C, H, and O, with glucose forming the monomer for the oligomer and the polymer. (a) Glucose, a monosaccharide. (b) Maltose, a disaccharide containing two glucose units. (c) A portion of a molecule of amylose, a glucose polymer found in starch.

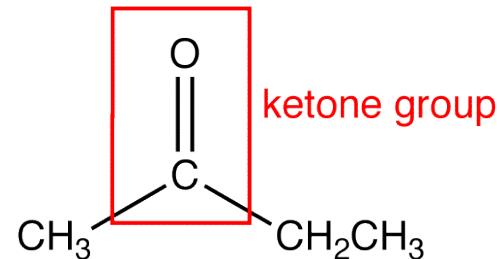
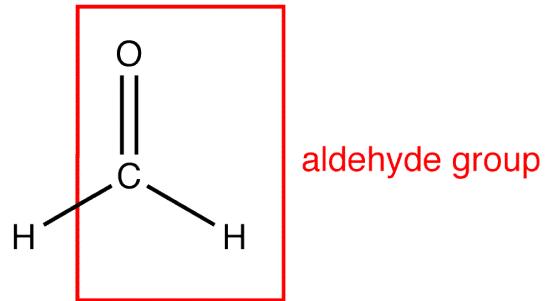
The Basic Processes of Photosynthesis

The carbon cycle in nature:

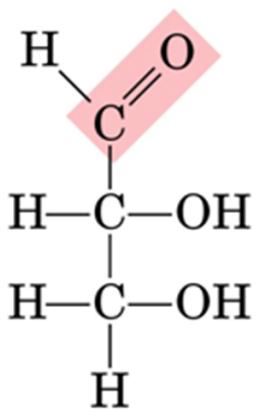
- **Carbon dioxide** and **water** are combined through photosynthesis to form carbohydrates.
- In both photosynthetic and nonphotosynthetic organisms these carbohydrates can be reoxidized to regenerate CO₂ and H₂O.
- Part of the energy obtained from both photosynthesis and fuel oxidation is captured in ATP.



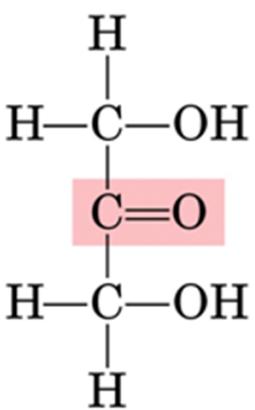
- **Carbohydrate:** a polyhydroxyaldehyde or polyhydroxyketone, or a substance that gives these compounds on hydrolysis
- **Monosaccharide:** a carbohydrate that cannot be hydrolyzed to a simpler carbohydrate
- Building blocks of all carbohydrates
 - They have the general formula $C_nH_{2n}O_n$, where n varies from 3 to 8
 - **Aldose**(醛糖): a monosaccharide containing an **aldehyde group**
 - **Ketose**(酮糖): a monosaccharide containing a **ketone group**



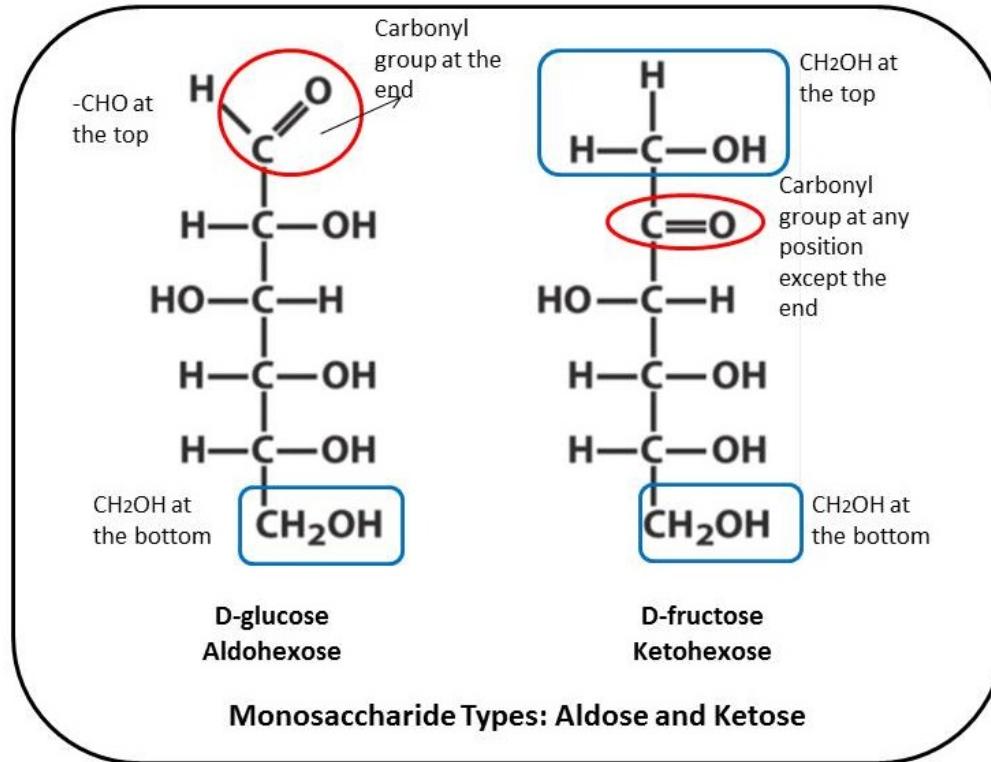
Monosaccharides



Aldose

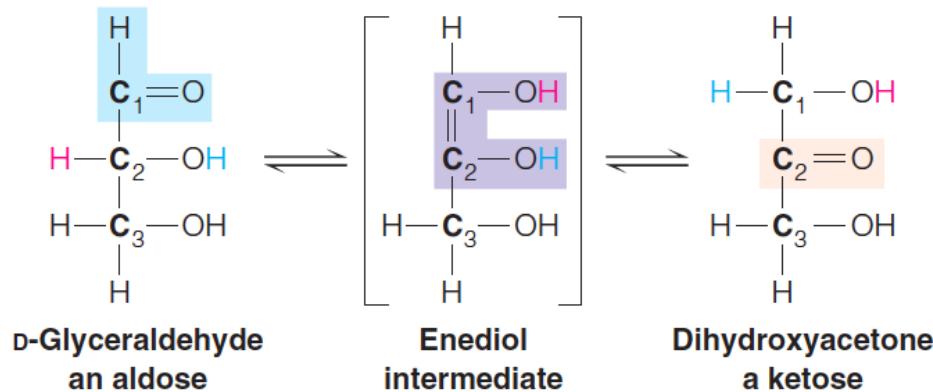


Ketose



Namrata Heda

Monosaccharides



Trioses are the simplest monosaccharides (含三個碳).

- The two triose tautomers illustrate the difference between aldose(醛糖) and ketose(酮糖) monosaccharides, also called more descriptively aldotriose and ketotriose, respectively.
- D-Glycerolaldehyde and Dihydroxylaseacetone are **tautomers** (structure isomers differing in location of hydrogen atoms and double bond).
- The enediol intermediate through which they are interconverted is unstable and cannot be isolated.

The Nobel Prize in Chemistry 1902

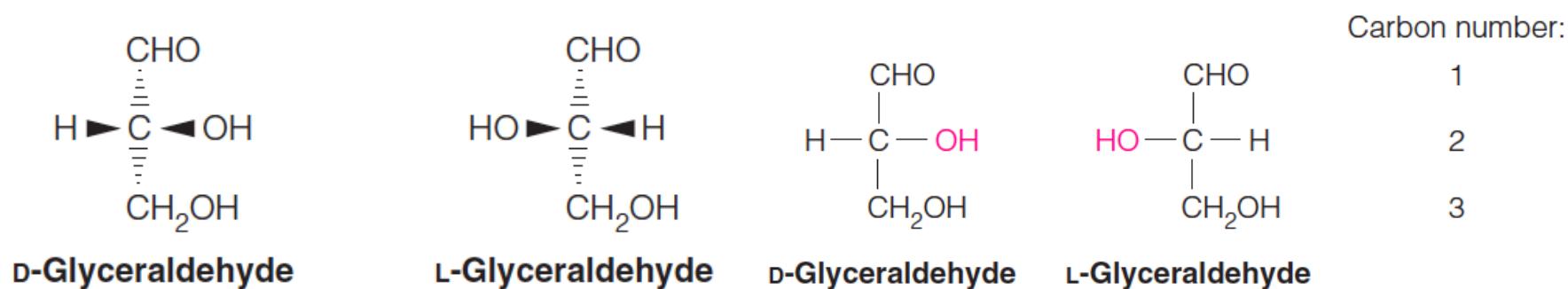


Hermann Emil Fischer

in recognition of the extraordinary services he has rendered by his work on sugar and purine syntheses".

Monosaccharides

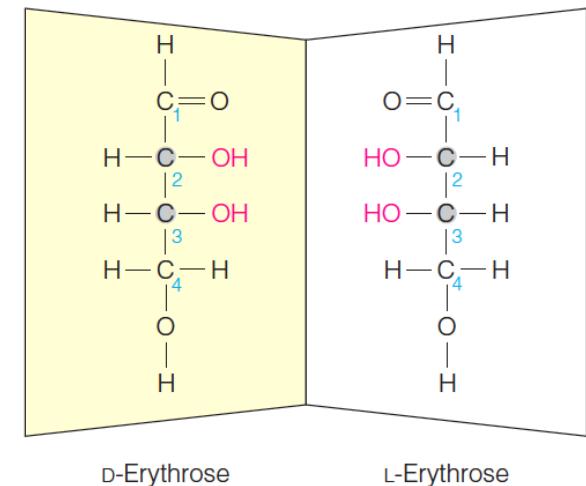
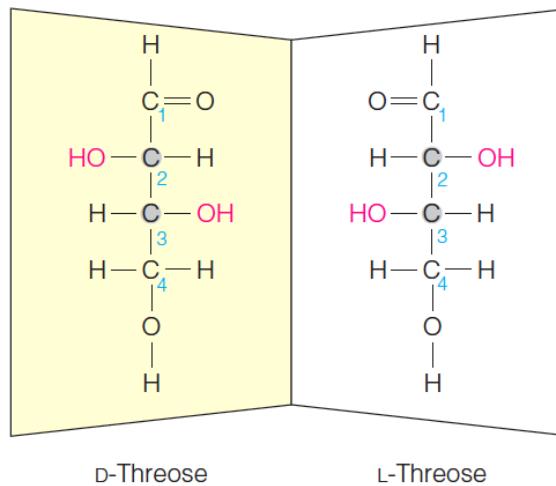
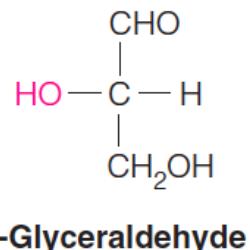
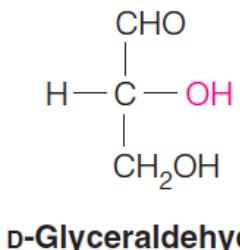
- The most compact way to represent enantiomers is to use a **Fischer projection**.
- In a Fischer projection the bonds that are drawn horizontally are imagined as coming toward you; those drawn vertically are receding.



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 chiral carbon on the right
- L-monosaccharide:** a monosaccharide that, when written as a Fischer projection, has the -OH on its penultimate chiral carbon on the left



Stereoisomers of carbohydrate and amino acid

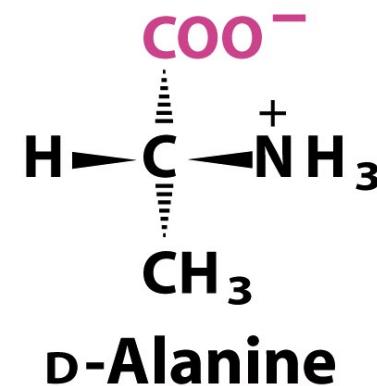
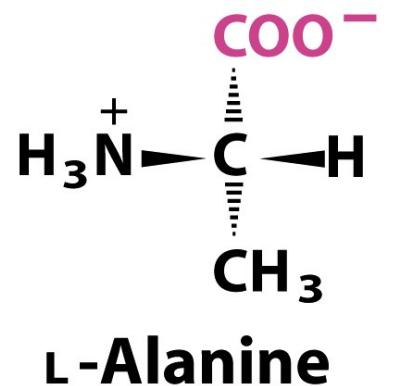
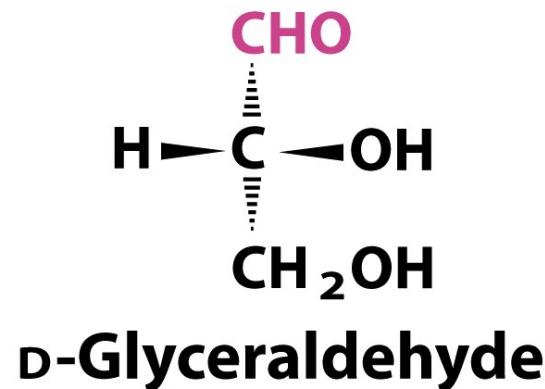
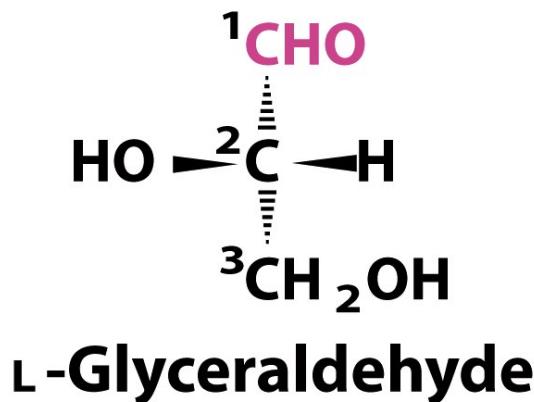
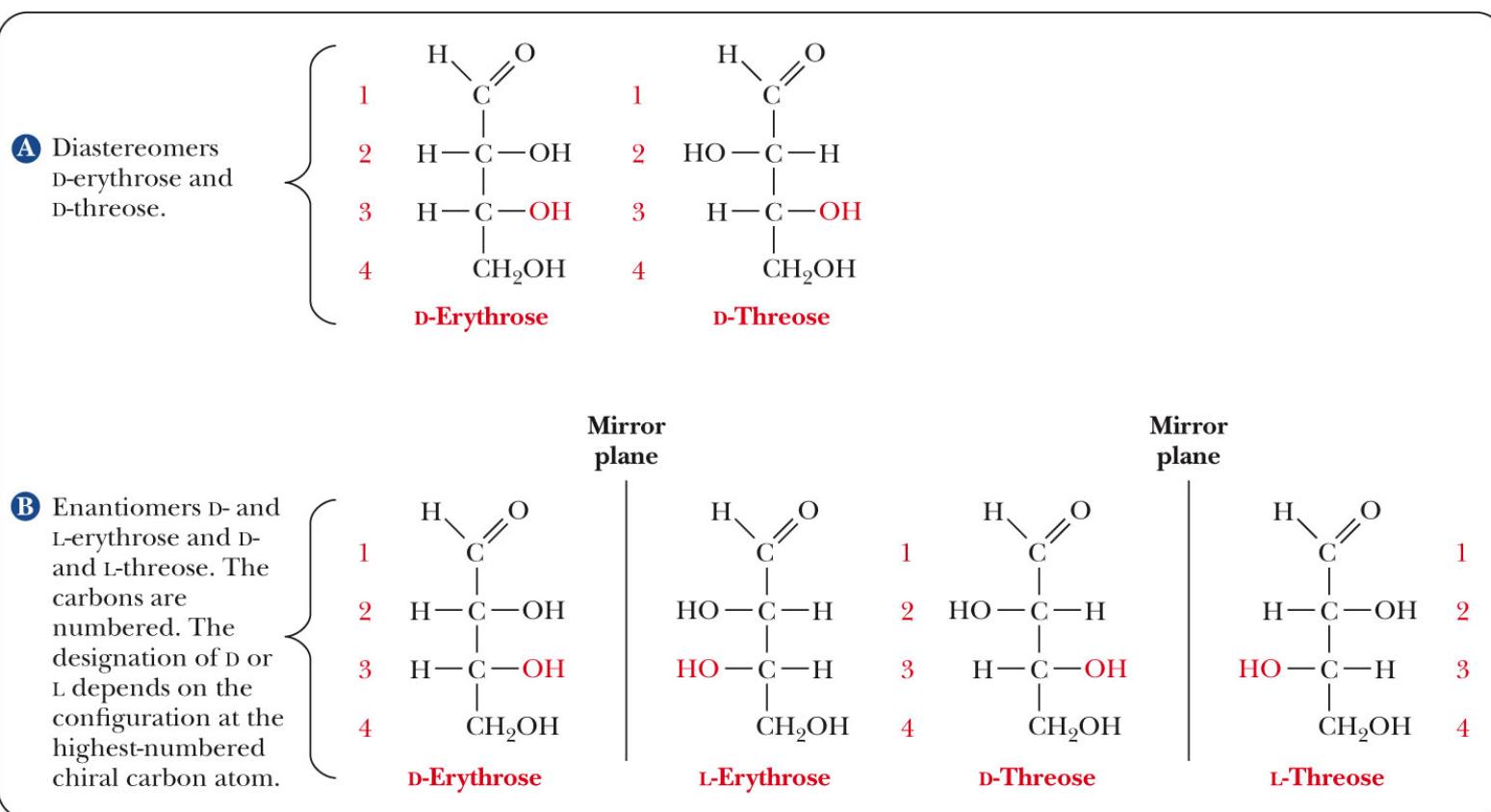


Figure 3-4
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W.H. Freeman and Company

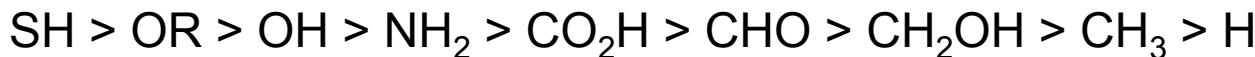
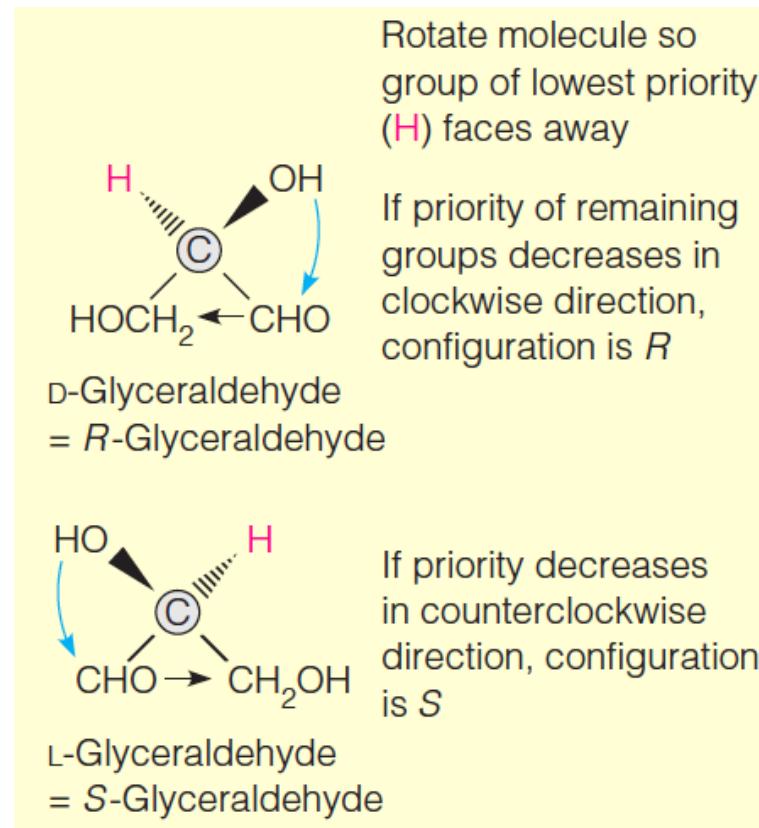
- **Diastereomers:** stereoisomers that are not mirror images
 - example: D-erythrose and D-threose are diastereomers
- **Enantiomers:** stereoisomers that are **mirror images**
 - example: D-erythrose and L-erythrose are enantiomers



Monosaccharides

R–S nomenclature:

In this notation, D-glyceraldehyde is *R-glyceraldehyde*, and L-glyceraldehyde is *S-glyceraldehyde*.



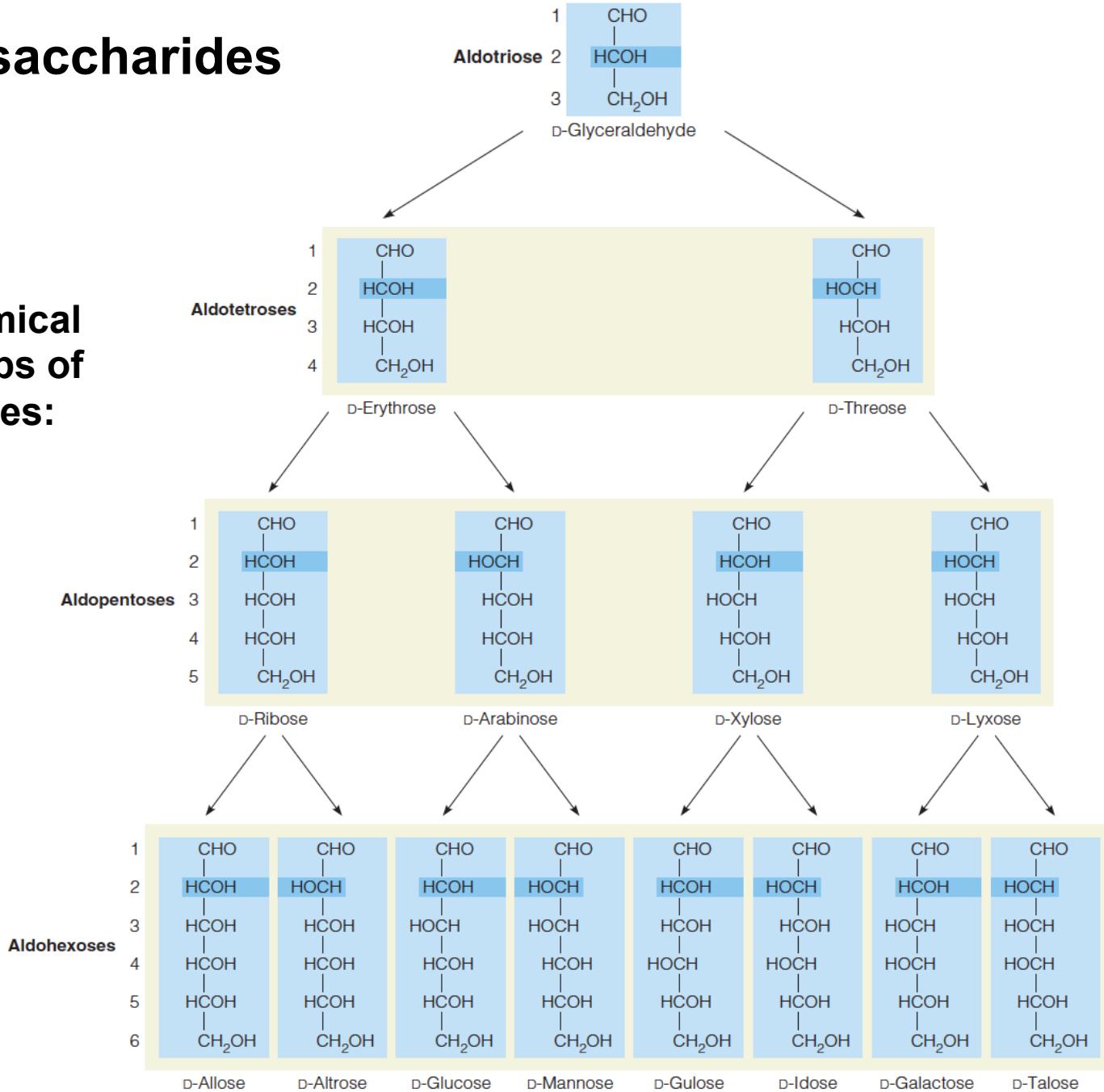
Monosaccharides

TABLE 9.1 Examples of occurrence and biochemical roles of monosaccharides

| Monosaccharides | Natural Occurrence | Physiological Role ^a |
|------------------|--|--|
| Trioses | | |
| Glyceraldehyde | Widespread (as phosphate) | The 3-phosphate is an intermediate in glycolysis |
| Dihydroxyacetone | Widespread (as phosphate) | The 1-phosphate is an intermediate in glycolysis |
| Tetroses | | |
| D-Erythrose | Widespread | The 4-phosphate is an intermediate in carbohydrate metabolism |
| Pentoses | | |
| D-Arabinose | Some plants, tuberculosis bacilli | Plant glycosides, cell walls |
| L-Arabinose | Widely distributed in plants, bacterial cell walls | Constituent of cell walls, plant glycoproteins |
| D-Ribose | Widespread, in all organisms | Constituent of RNA and ribonucleotides |
| D-Xylose | Woody materials | Constituent of plant polysaccharides |
| Hexoses | | |
| D-Galactose | Widespread | Milk (as part of lactose); structural polysaccharides |
| L-Galactose | Agar, other polysaccharides; component of lactose | Polysaccharide structures |
| D-Glucose | Widespread | Major energy source for animal metabolism; structural role in cellulose |
| D-Mannose | Plant polysaccharides, animal glycoproteins | Polysaccharide structures |
| D-Fructose | A major plant sugar; part of sucrose | Intermediate in glycolysis (phosphate esters) |
| Heptoses | | |
| D-Sedoheptulose | Many plants | Intermediate in Calvin cycle in photosynthesis and pentose phosphate pathway |

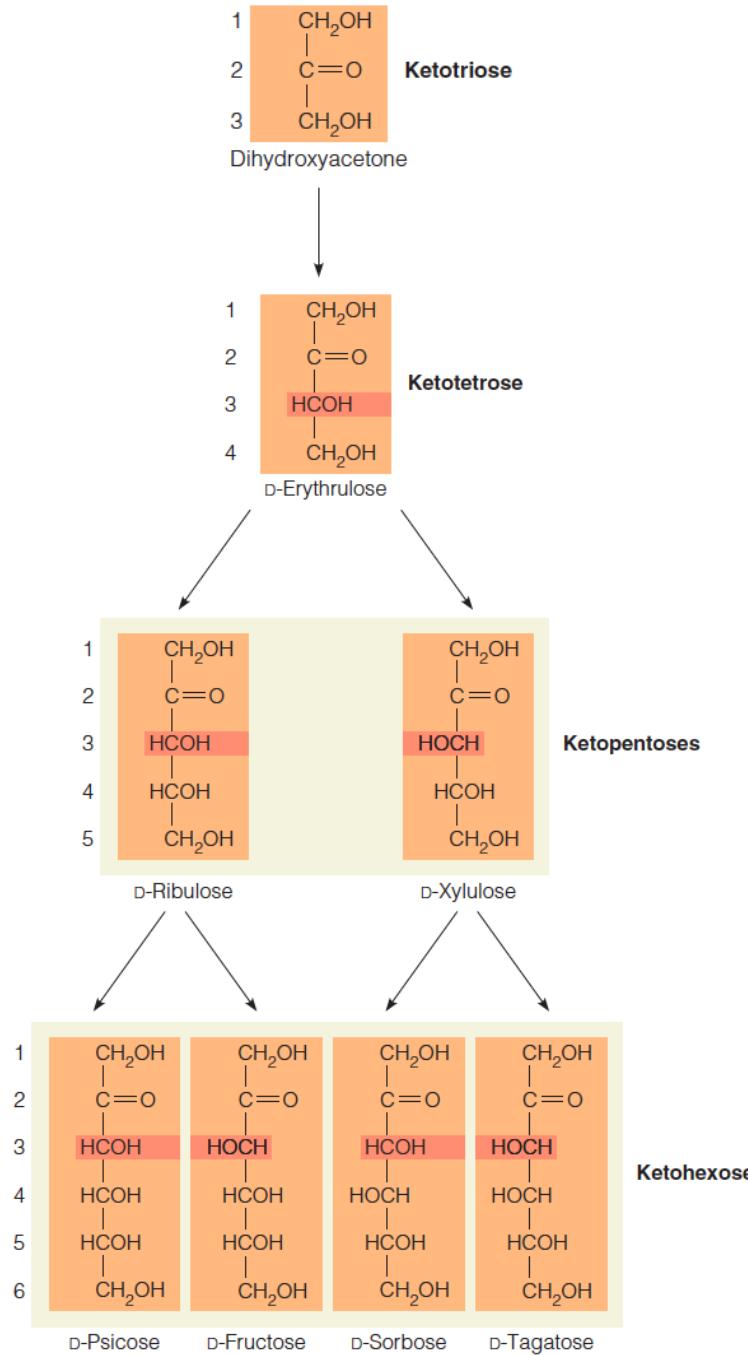
Monosaccharides

Stereochemical relationships of the D-aldoses:



Monosaccharides

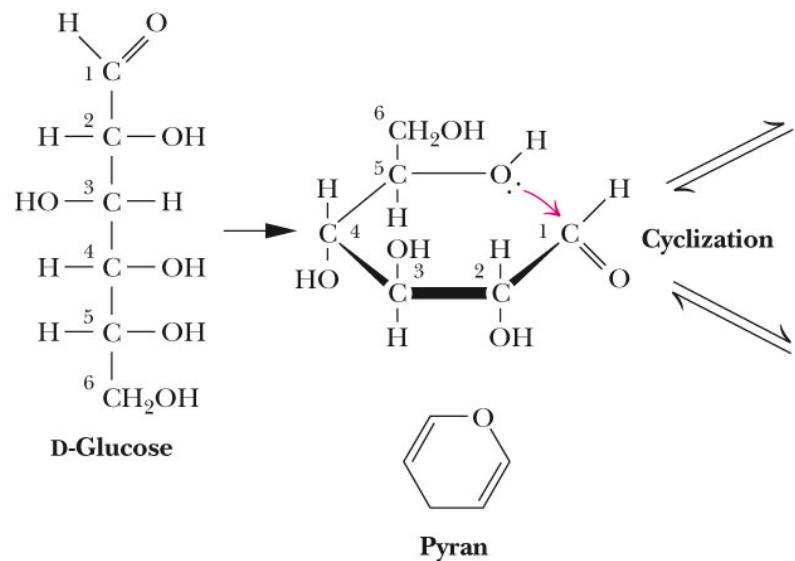
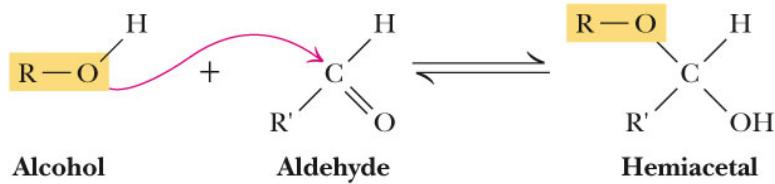
Stereochemical relationships of the D-ketoses:



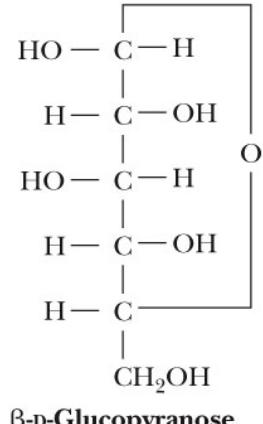
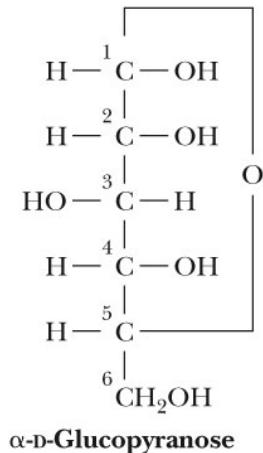
What Happens if a Sugar Forms a Cyclic Molecule?

- 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**

Formation of a Cyclic Hemiacetal



HAWORTH PROJECTION FORMULAS



FISCHER PROJECTION FORMULAS

Cyclic Structure

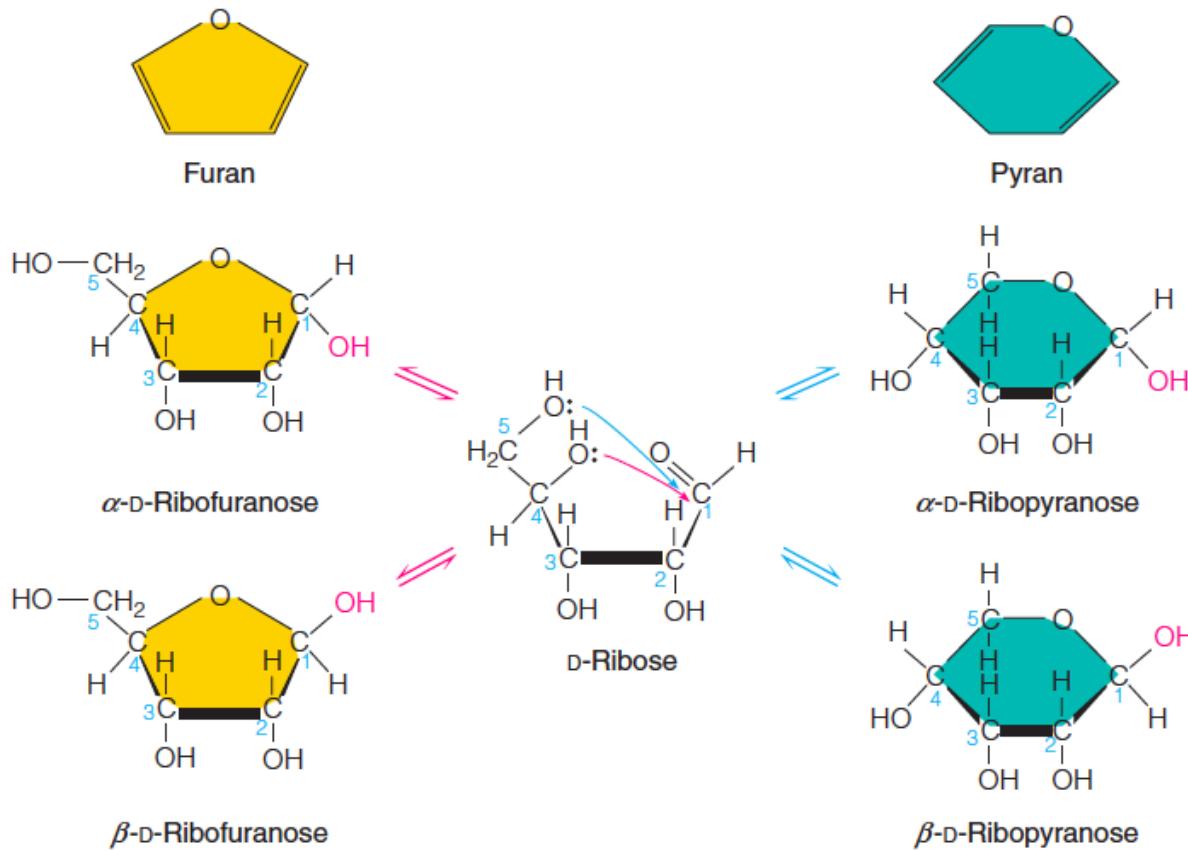
- Monosaccharides have -OH and C=O groups in the same molecule and exist almost entirely as five- and six-membered cyclic hemiacetals
 - **anomeric carbon:** the new stereocenter resulting from cyclic hemiacetal formation
 - **anomers:** carbohydrates that differ in configuration only at their anomeric carbons

Haworth Projections

- A **six-membered** hemiacetal ring is shown by the infix - **pyran-** (pyranose)
- A **five-membered** hemiacetal ring is shown by the infix - **furan-** (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

Monosaccharides

- Monosaccharides with five or more carbons exist preferentially in five- or six-membered ring structures (*Haworth projections*), resulting from internal hemiacetal formation.
- Two anomeric forms, and are possible, α and β .



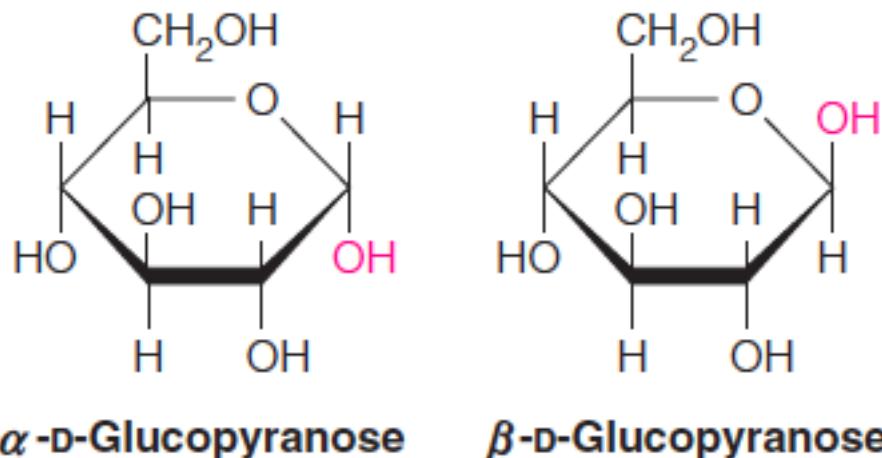
Monosaccharides

TABLE 9.2 Relative amounts of tautomeric forms for some monosaccharide sugars at equilibrium in water at 40°C

| Monosaccharide | Relative Amount (%) | | | | Total Furanose |
|----------------|---------------------|-------------------|--------------------|-------------------|----------------|
| | α -Pyranose | β -Pyranose | α -Furanose | β -Furanose | |
| Ribose | 20 | 56 | 6 | 18 | 24 |
| Lyxose | 71 | 29 | — ^a | — ^a | <1 |
| Altrose | 27 | 40 | 20 | 13 | 33 |
| Glucose | 36 | 64 | — ^a | — ^a | <1 |
| Mannose | 67 | 33 | — ^a | — ^a | <1 |
| Fructose | 3 | 57 | 9 | 31 | 40 |

Monosaccharides

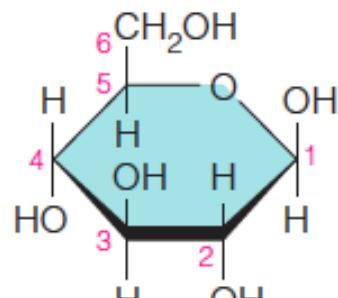
- The hexoses also exist primarily in ring forms under physiological conditions.
- As with the aldopentoses, two kinds of rings are found: five-membered furanoses and six-membered pyranoses.
- In each case, α and β anomers are possible.
- An example, illustrated by *Haworth projections*, follows:



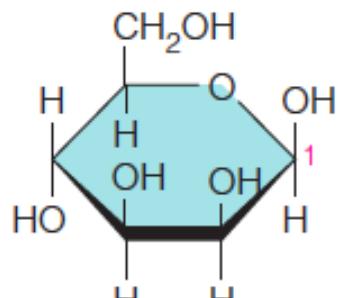
Monosaccharides

The four most common hexoses:

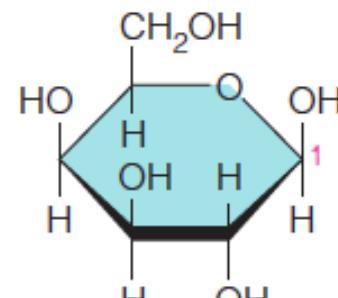
- These Haworth projections represent the D enantiomers.
- Only the β anomers are shown.



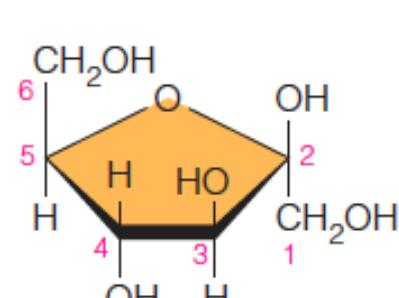
β -D-Glucopyranose



β -D-Mannopyranose



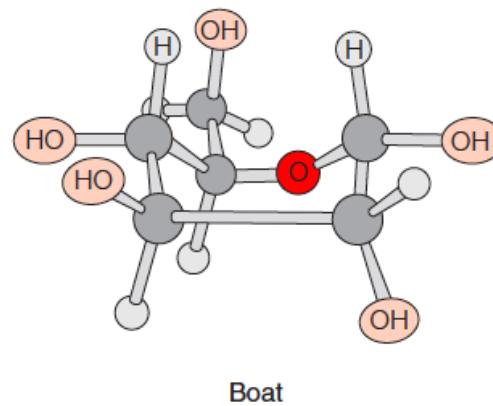
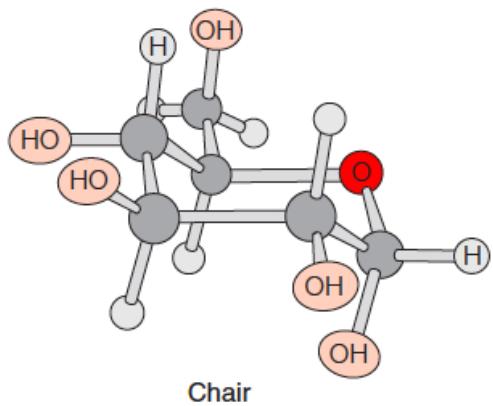
β -D-Galactopyranose



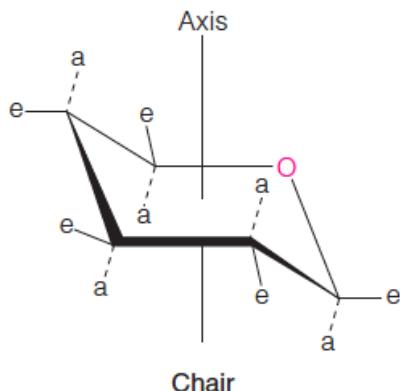
β -D-Fructofuranose

Monosaccharides

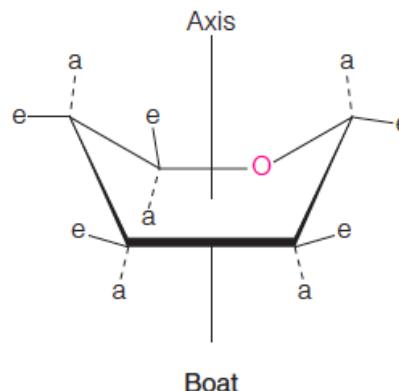
- Hexoses can exist in boat and chair conformations.
- Usually the chair is more stable.



(a)



Chair

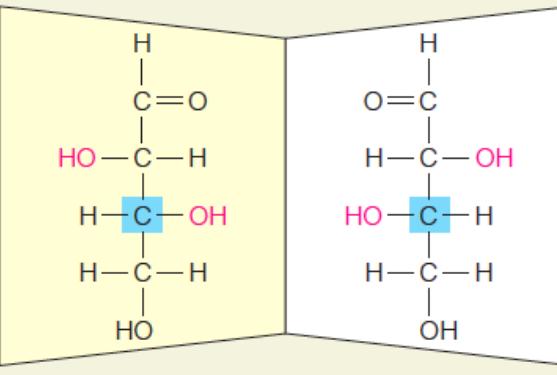
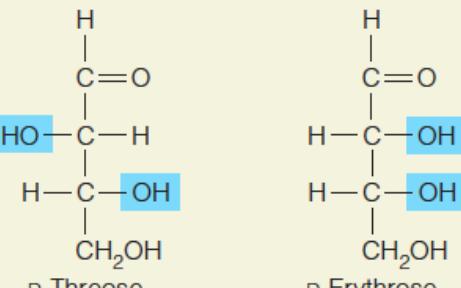
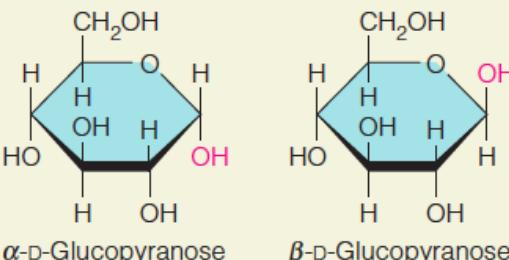


Boat

(b)

Monosaccharides

A summary of terminology describing the structure of sugar molecules:

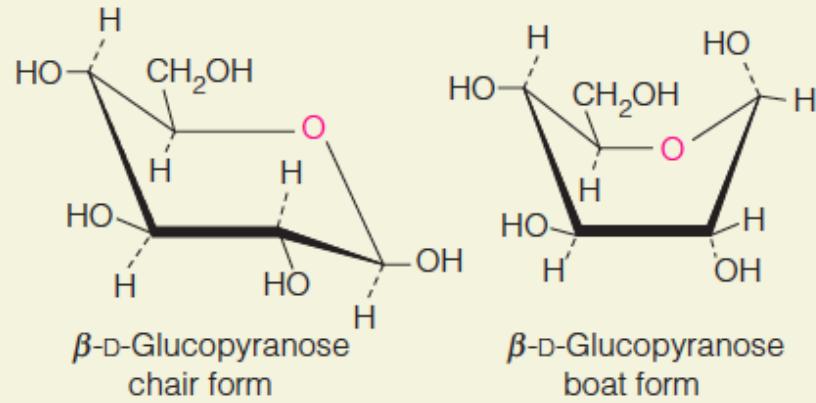
| Configurational isomers | |
|---|---|
| Enantiomers Stereoisomers that are mirror images of one another |  <p>D-Threose L-Threose</p> |
| Diastereomers Stereoisomers that are not mirror images of one another |  <p>D-Threose D-Erythrose</p> |
| Anomers | |
| Anomers Stereoisomers that differ in configuration at the anomeric carbon |  <p>α-D-Glucopyranose β-D-Glucopyranose</p> |

Monosaccharides

The different ring conformations produced by slightly different bond angles are called **conformational isomers**

Conformational isomers

Molecules with the same stereochemical configuration, but differing in three-dimensional conformation



Chair form is more stable

Derivatives of the Monosaccharides

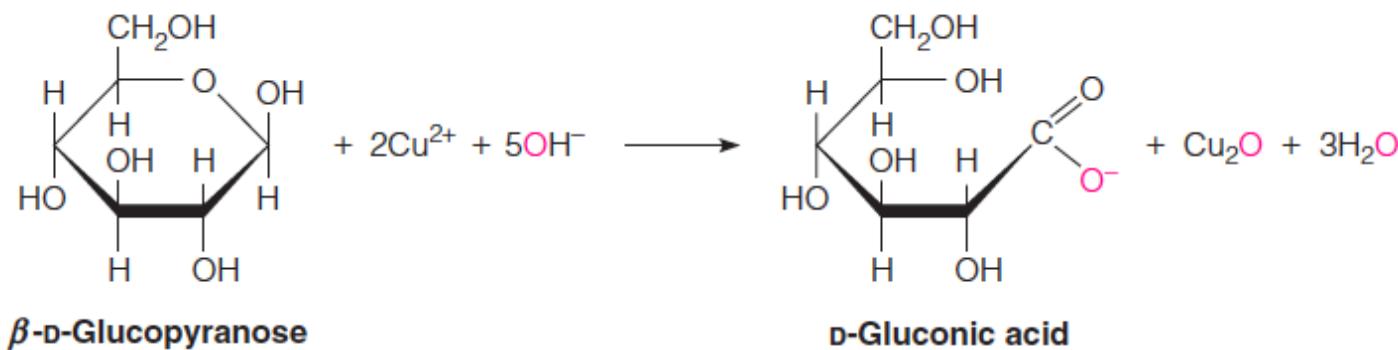
- Sugar phosphates** are important intermediates in metabolism, functioning as activated compounds in syntheses.

TABLE 9.3 Some biochemically important phosphate esters of monosaccharides

| Name | Structure | $\Delta G^\circ{}^a$ (kJ/mol) | pK_{a1} | pK_{a2} |
|----------------------------------|-----------|----------------------------------|-----------|-----------|
| D-Glyceraldehyde-3-phosphate | | ~ -12 | 2.10 | 6.75 |
| β -D-Glucose-1-phosphate | | -20.9 | 1.10 | 6.13 |
| β -D-Glucose-6-phosphate | | -13.8 | 0.94 | 6.11 |
| α -D-Fructose-6-phosphate | | -13.8 | 0.97 | 6.11 |

Reaction of Monosaccharides

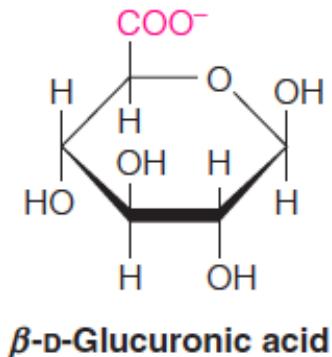
- Oxidation of monosaccharides can proceed in several ways, depending upon the oxidizing agent used.
- For example, mild oxidation of an aldose with alkaline Cu(II) (**Fehling's solution**) produces the **aldonic acids**, as in the following example:



Red precipitate of Cu_2O is a classic sugar test for diabetes (to test excess sugar in urine)

Derivatives of the Monosaccharides

- Enzyme-catalyzed oxidation of monosaccharides gives other products, including **uronic acids** such as **glucuronic acid** (葡萄糖醛酸), in which oxidation has occurred at carbon 6.
- Uronic acids are, important constituents of certain natural polysaccharides.

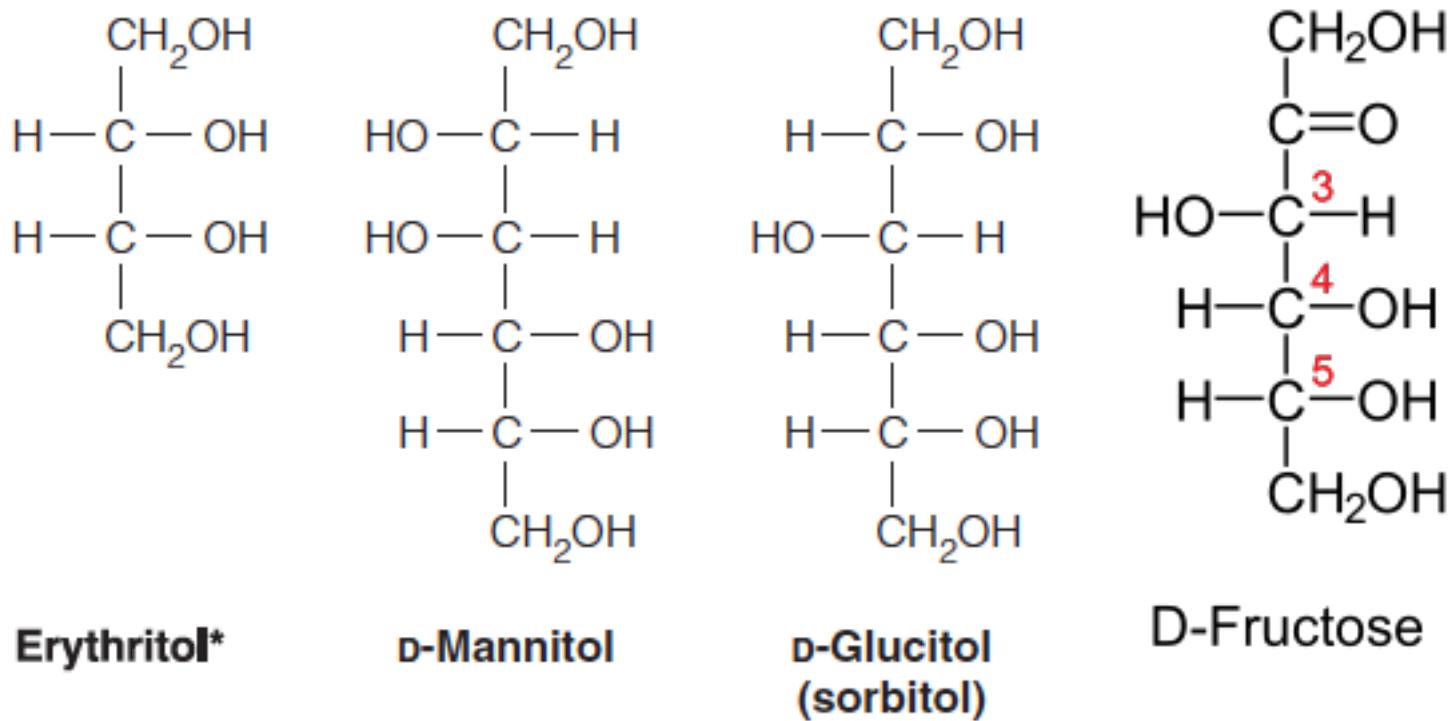


Many wastes in the human body are excreted in the urine as their glucuronate salts.

L-iduronic acid, is the major uronic acid component of the glycosaminoglycans (GAGs) dermatan sulfate, and heparin, is a component of some structural complexes such as **proteoglycans**.

Derivatives of the Monosaccharides (alditols)

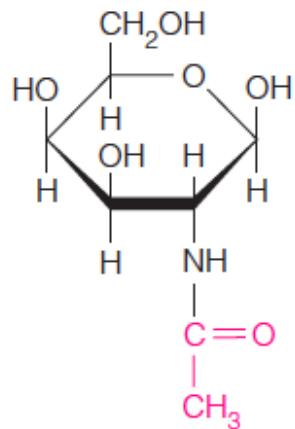
- Reduction of the carbonyl group on a sugar gives rise to the class of **polyhydroxy compounds** called **alditols**(糖醇). Important naturally occurring ones are *erythritol*, *D-mannitol*, and *D-glucitol*, often called *sorbitol*.



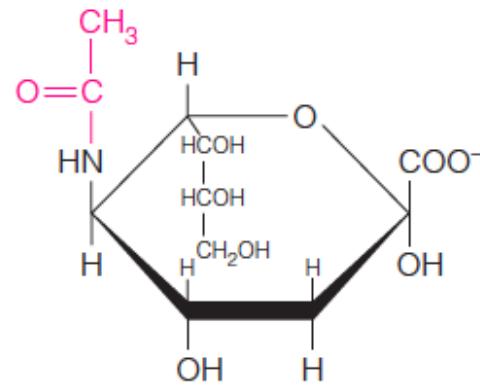
糖尿病患 Sorbitol 堆積在眼球造成白內障(cataracts)

Derivatives of the Monosaccharides (amino sugar)

Two amino derivatives of simple sugars are widely distributed in natural polysaccharides:



β -D-N-Acetylgalactosamine

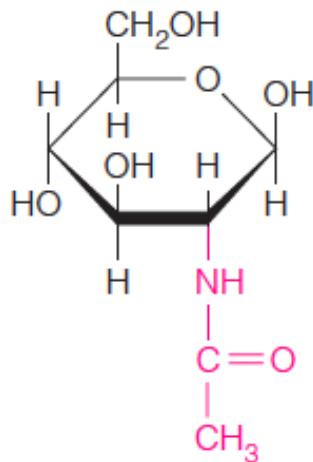


N-Acetylneuraminic acid
(sialic acid)

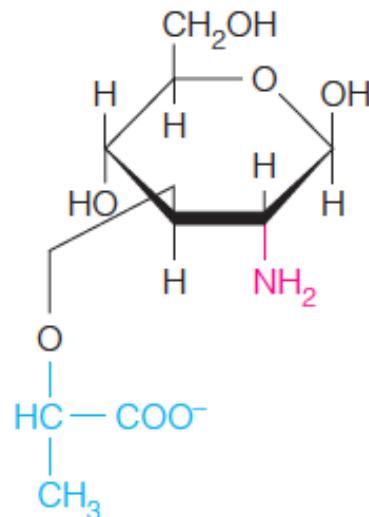
glucosamine and galactosamine, derived from glucose and galactose, respectively.

Derivatives of the Monosaccharides (amino sugar)

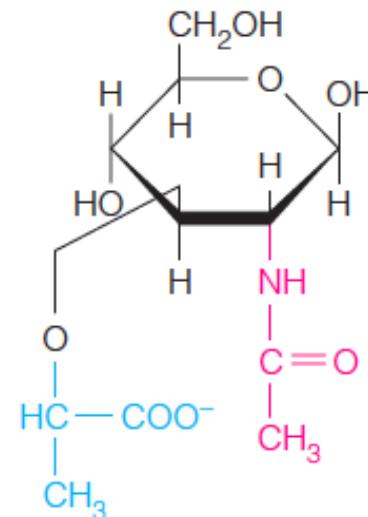
- Amino sugars are found in many polysaccharides.



β -D-N-Acetylglucosamine



Muramic acid



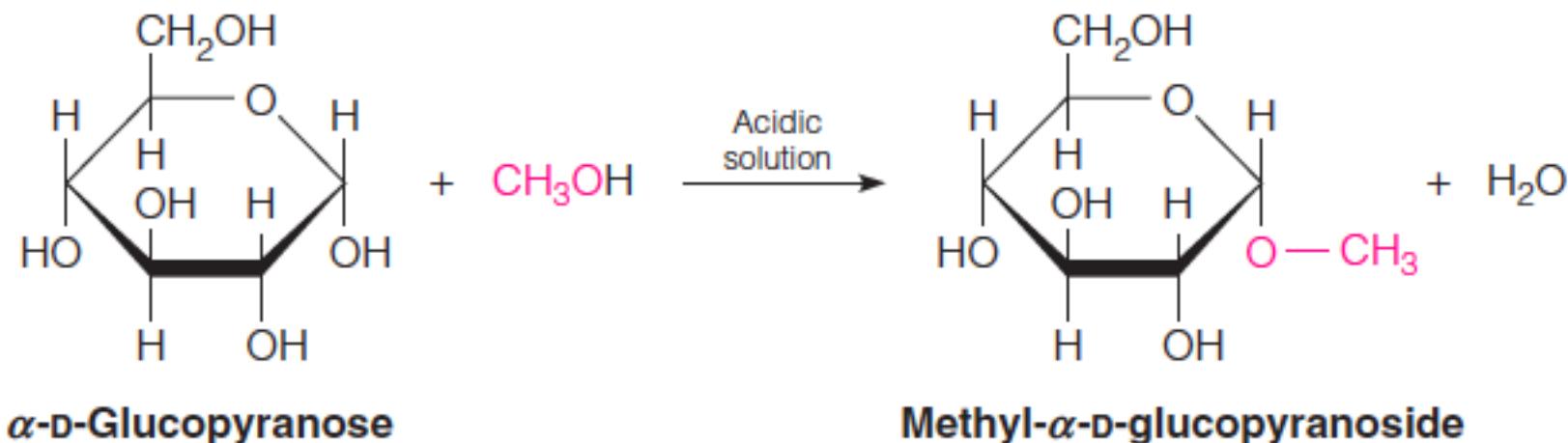
N-Acetylmuramic acid

Abbreviations for some common monosaccharide residues

| Monosaccharides | |
|--|--------------------|
| Arabinose | Ara |
| Fructose | Fru |
| Fucose | Fuc |
| Galactose | Gal |
| Glucose | Glc |
| Lyxose | Lyx |
| Mannose | Man |
| Ribose | Rib |
| Xylose | Xyl |
| Monosaccharide Derivatives | |
| Gluconic acid | GlcA |
| Glucuronic acid | GlcUA |
| Galactosamine | GalN |
| Glucosamine | GlcN |
| <i>N</i> -Acetylgalactosamine | GalNAc |
| <i>N</i> -Acetylglucosamine | GlcNAc (or NAG) |
| Muramic acid | Mur |
| <i>N</i> -Acetylmuramic acid | MurNAc (or NAM) |
| <i>N</i> -Acetylneuraminic acid (or sialic acid) | NeuNAc (or Sia) |

Glycosides

- A sugar is bound to another functional group via a **glycosidic bond**
- Elimination of water between the anomeric hydroxyl of a cyclic monosaccharide and the hydroxyl group of another compound yields an **O-glycoside**.
- The acetal bond formed is referred to as a glycosidic bond.
- A simple example is the formation of methyl- α -D-glucopyranoside:

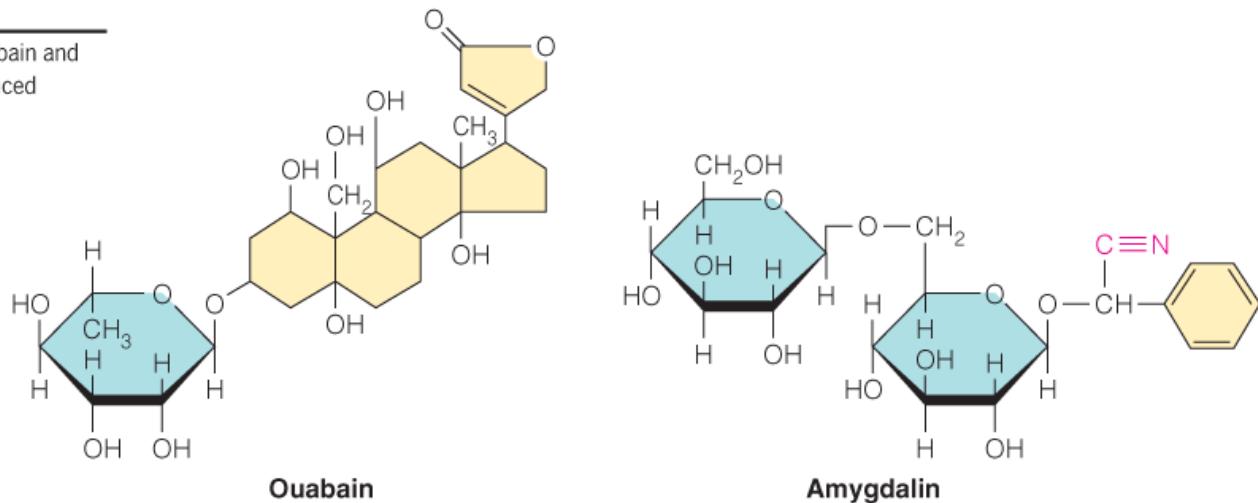


Two naturally occurring glycosides

Ouabain and **amygdalin** are highly toxic glycosides produced by plants.

FIGURE 9.14

Two naturally occurring glycosides. Ouabain and amygdalin are highly toxic glycosides produced by plants.



Ouabain inhibits the action of enzymes that pump Na^+ & K^+ ions across cell membranes to maintain necessary electrolyte balance

Amygdalin, found in seeds of bitter almonds, this glycoside yields **hydrogen cyanide (HCN)** upon hydrolysis.

氫化氫(HCN)，又稱氫氰酸。標準狀態下為氣體，劇毒且致命，無色而苦，並有杏仁氣味

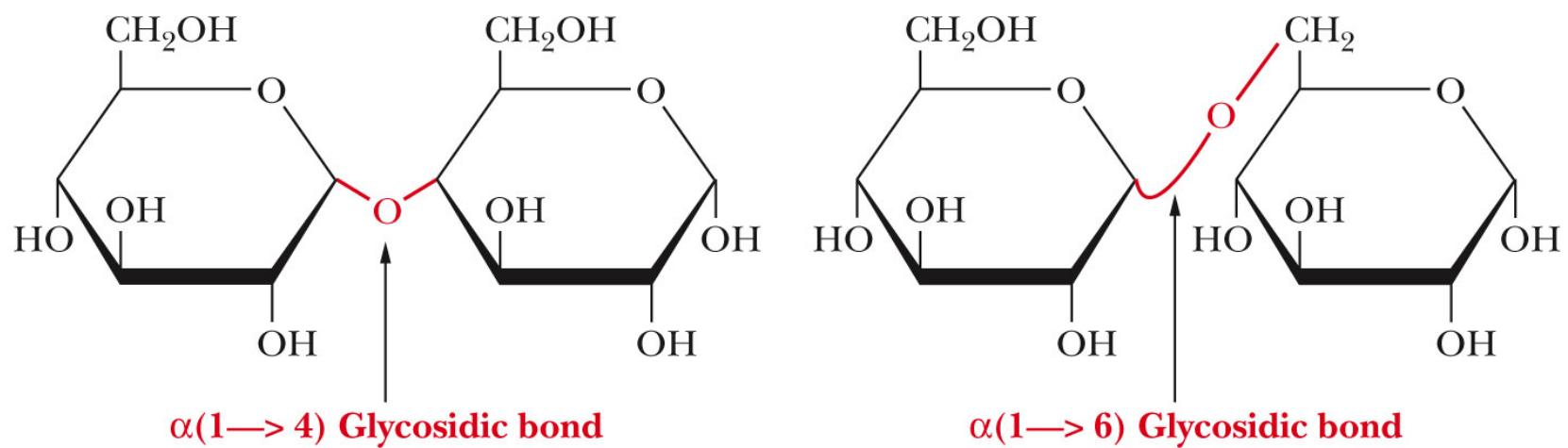
Oligosaccharides

The simplest and biologically most important oligosaccharides are the disaccharides, made up of **two residues**

TABLE 9.5 Occurrence and biochemical roles of some representative disaccharides

| Disaccharide | Structure | Natural Occurrence | Physiological Role |
|-----------------------------|---|--|--|
| Sucrose | $\text{Glc}\alpha(1 \rightarrow 2)\text{Fru}\beta$ | Many fruits, seeds, roots, honey | A final product of photosynthesis, used as primary energy source in many organisms |
| Lactose | $\text{Gal}\beta(1 \rightarrow 4)\text{Glc}$ | Milk, some plant sources | A major animal energy source |
| α, α -Trehalose | $\text{Glc}\alpha(1 \rightarrow 1)\text{Glc}\alpha$ | Yeast, other fungi, insect blood | A major circulatory sugar in insects; used for energy |
| Maltose | $\text{Glc}\alpha(1 \rightarrow 4)\text{Glc}$ | Plants (starch) and animals (glycogen) | The dimer derived from the starch and glycogen polymers |
| Cellobiose polymer | $\text{Glc}\beta(1 \rightarrow 4)\text{Glc}$ | Plants (cellulose) | The dimer of the cellulose |
| Gentiobiose | $\text{Glc}\beta(1 \rightarrow 6)\text{Glc}$ | Some plants (e.g., gentians) | Constituent of plant glycosides and some polysaccharides |

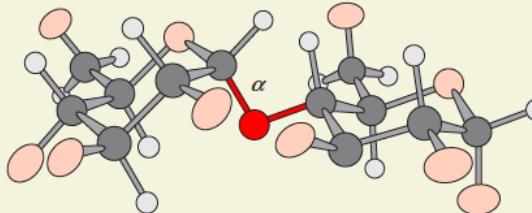
- **Glycosidic linkages** can take various forms; the anomeric carbon of one sugar to any of the -OH groups of another sugar to form an α - or β -glycosidic linkage



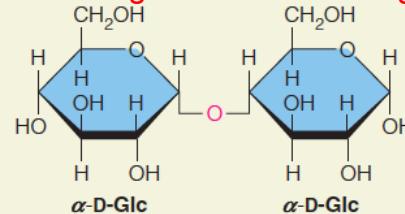
Oligosaccharides

(a) Disaccharides with α -connections

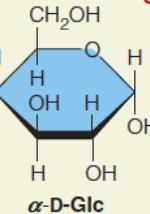
Maltose:
 α -D-glucopyranosyl
(1 \rightarrow 4) α -D-glucopyranose



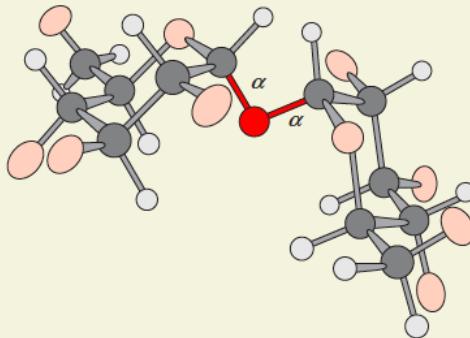
Nonreducing end



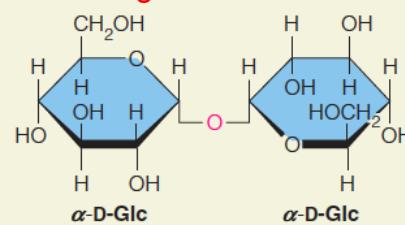
Reducing end



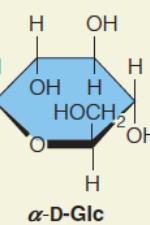
α,α -Trehalose:
 α -D-glucopyranosyl
(1 \rightarrow 1) α -D-glucopyranose



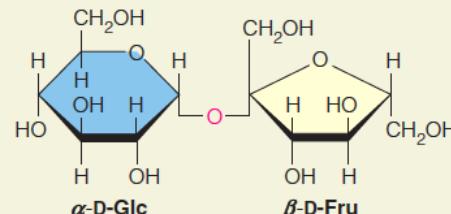
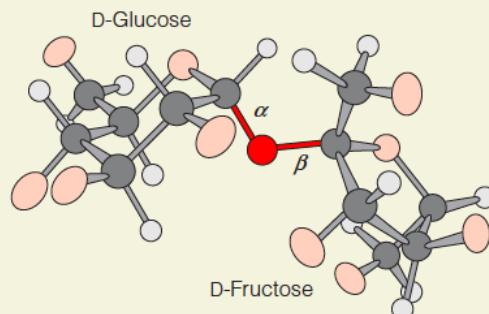
Nonreducing end



Nonreducing end

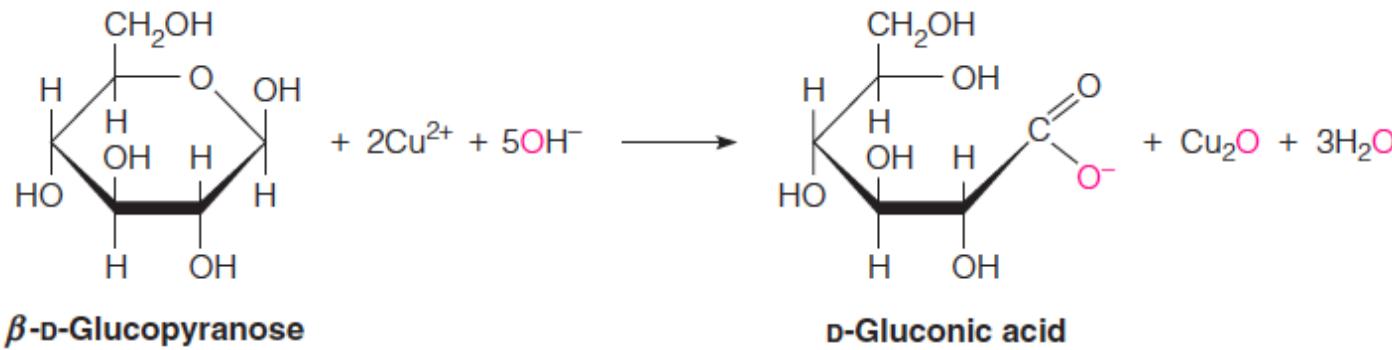


Sucrose:
 α -D-glucopyranosyl
(1 \rightarrow 2) β -D-fructofuranoside



Reducing sugar: Contains a **free anomeric carbon** and thus a potential free aldehyde group could be oxidized by Fehling's solution.

- Oxidation of monosaccharides can proceed in several ways, depending upon the oxidizing agent used.
- For example, mild oxidation of an aldose with alkaline Cu(II) (*Fehling's solution*) produces the **aldonic acids**, as in the following example:

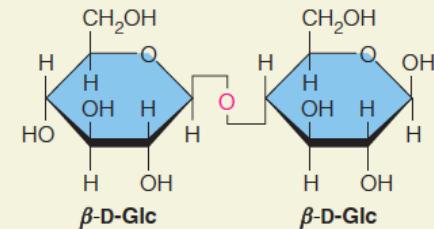
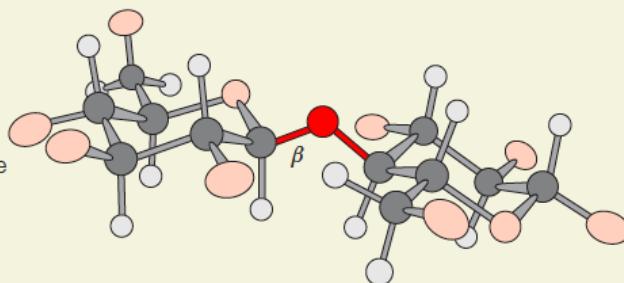


Red precipitate of Cu₂O is a classic sugar test for diabetes (to test excess sugar in urine)

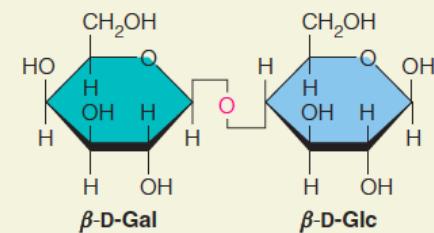
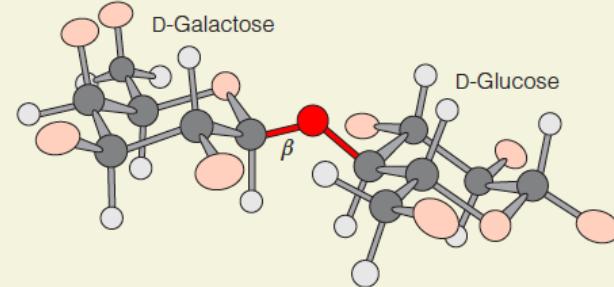
Oligosaccharides

(b) Disaccharides with β connections

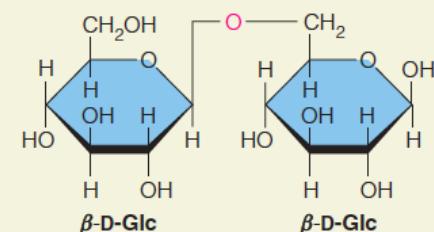
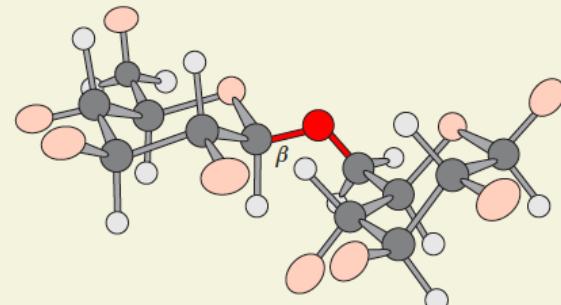
Cellobiose:
 β -D-glucopyranosyl
(1 \rightarrow 4) β -D-glucopyranose



Lactose:
 β -D-galactopyranosyl
(1 \rightarrow 4) β -D-glucopyranose



Gentiobiose:
 β -D-glucopyranosyl
(1 \rightarrow 6) β -D-glucopyranose



Oligosaccharides

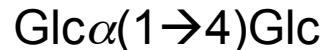
Writing the Structure of Disaccharides:

- For example, we can write the structure of sucrose as:



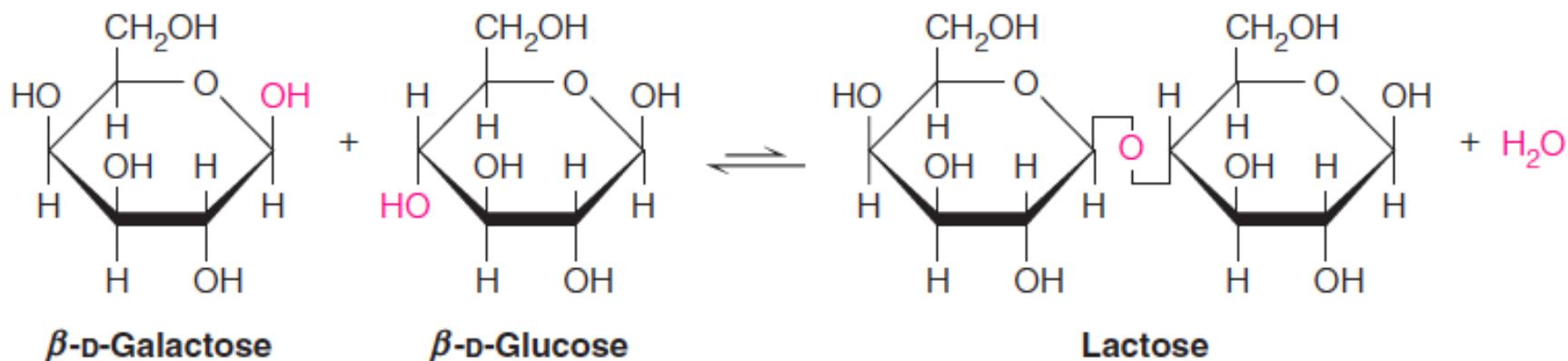
- Often, the D- and p or f are omitted under normal circumstances.

- For example, the structure of maltose can be written as:



Oligosaccharides

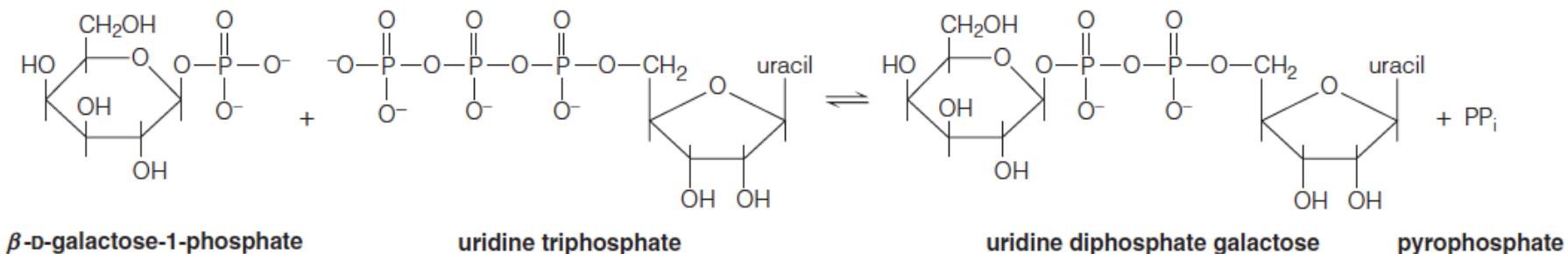
- Formation of the glycosidic bond between two monomers in an oligosaccharide is a **condensation reaction**, involving the **elimination of a molecule of water**.
- Thus, we might expect the synthesis of lactose to proceed as follows:



- Like the phosphodiester bond in nucleic acid and amide bond in proteins, the glycosidic bond is metastable.
- Enzymes control its hydrolysis.

Oligosaccharides

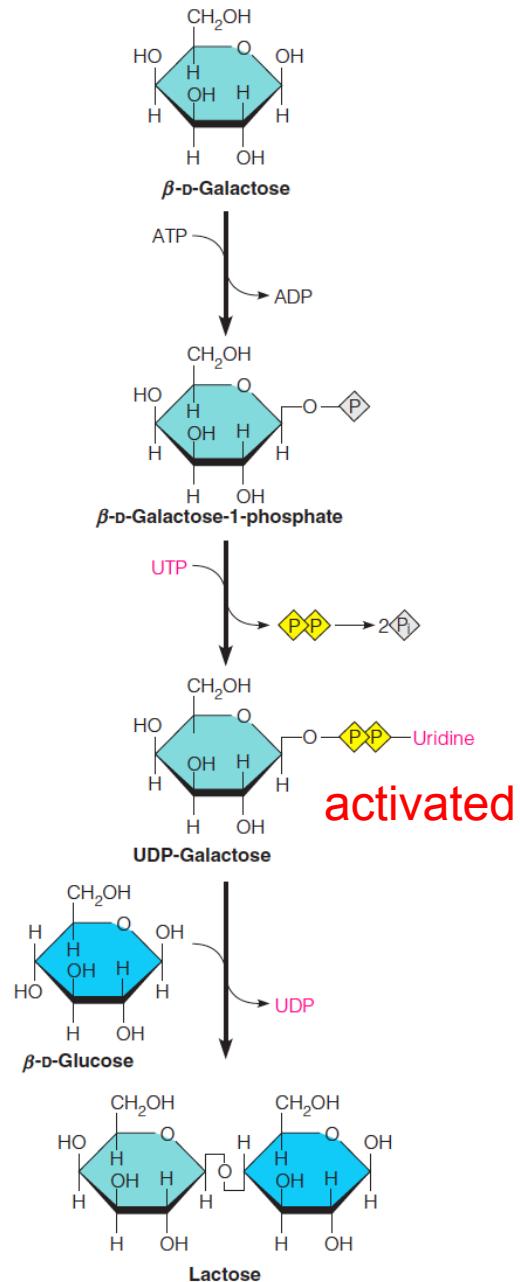
- For **glycan** (多聚醣) biosynthesis those activated monomers are usually *nucleotide-linked sugars*.
- Phosphoric esters are particularly important in the metabolism of sugars to provide energy
- The activated sugar molecule in lactose biosynthesis is **uridine diphosphate galactose (UDP-galactose or UDPGal)**, a nucleotide-linked sugar formed by reaction of uridine triphosphate with galactose-1-phosphate.



Oligosaccharides

Enzymatic formation of lactose:

- The reaction shown occurs in the formation of milk in mammary tissue.
- Galactose is phosphorylated by ATP, then transferred to uridine diphosphate (UDP).
- UDP-galactose transfers galactose to glucose, with the accompanying cleavage of a phosphate bond.
- The reaction is catalyzed by the enzyme **lactose synthase**.



Some bacteria carry out the synthesis of **dextran** (聚葡萄糖), an $\alpha(1 \rightarrow 6)$ -linked polymer of glucose with $\alpha(1 \rightarrow 2)$, $\alpha(1 \rightarrow 3)$, or $\alpha(1 \rightarrow 4)$ branch points.

Several bacteria growing in the human oral cavity synthesize large quantities of dextran, which contributes toward formation of dental plaque (牙菌斑).

These excessive sucrose consume may cause obesity.

Polysaccharides (Amylose, amylopectin, glycogen)

- The principal storage polysaccharides are **amylose** and **amylopectin**, which together constitute starch in plants, and **glycogen**, which is stored in animal and microbial cells.
- **Amylose**, a linear polymer involving exclusively $\alpha(1 \rightarrow 4)$ links between adjacent glucose residues.
- **Amylopectin** and **glycogen** are both branched polymers contain $\alpha(1 \rightarrow 4)$ and $\alpha(1 \rightarrow 6)$ links
- The branches in glycogen are somewhat more frequent and shorter than those in amylopectin, and glycogen usually has higher molecular weight.
- They are homopolysaccharides of the class called **glucans**, the polymer of glucose.

Polysaccharides (Amylose, amylopectin, glycogen)

- Both starch and glycogen are stored in granules within cells
- Glycogen is deposited in the liver, which acts as a central energy storage organ in many animals.
- Glycogen is also abundant in muscle tissue, where it is more immediately available for energy release.
- Glycogen and the components of starch—amylose and amylopectin—are storage polysaccharides.

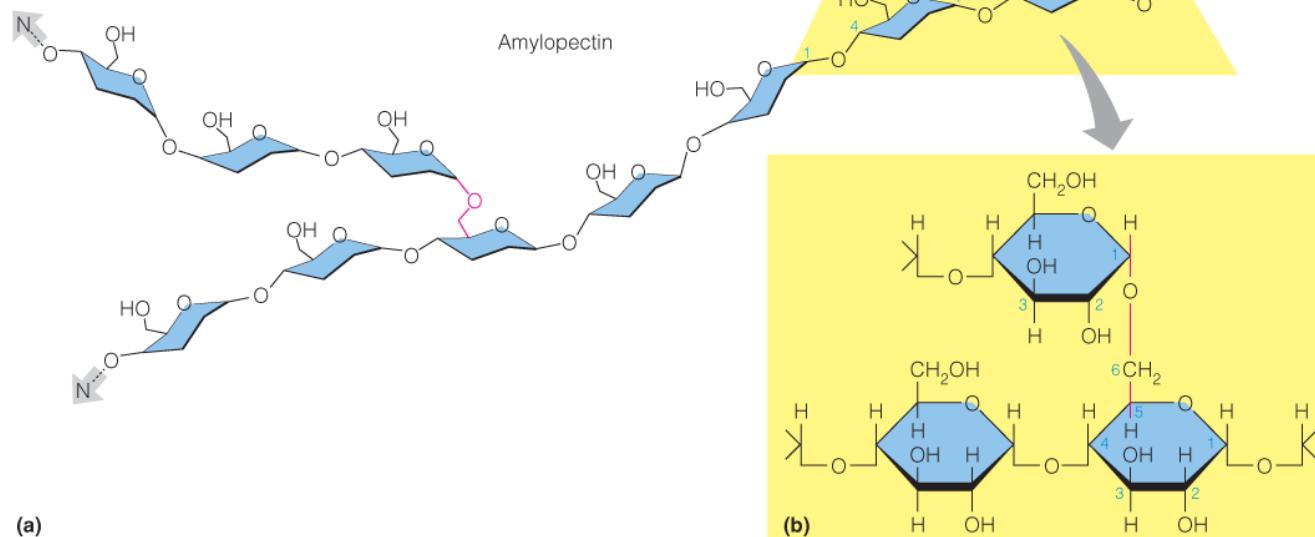
Polysaccharides (Amylose, amylopectin, glycogen)

Amylopectin, a branched glucan:

The branches in glycogen are somewhat more frequent and shorter than those in amylopectin, and glycogen is usually of higher molecular weight, but in most respects the structures of these two polysaccharides are very similar.

FIGURE 9.18

Amylopectin, a branched glucan. (a) The primary structure of amylopectin. Nonreducing ends (N) and reducing ends (R) are indicated. (b) Detailed structure of a branch point. To simplify the figure some ring hydroxyls are not shown.

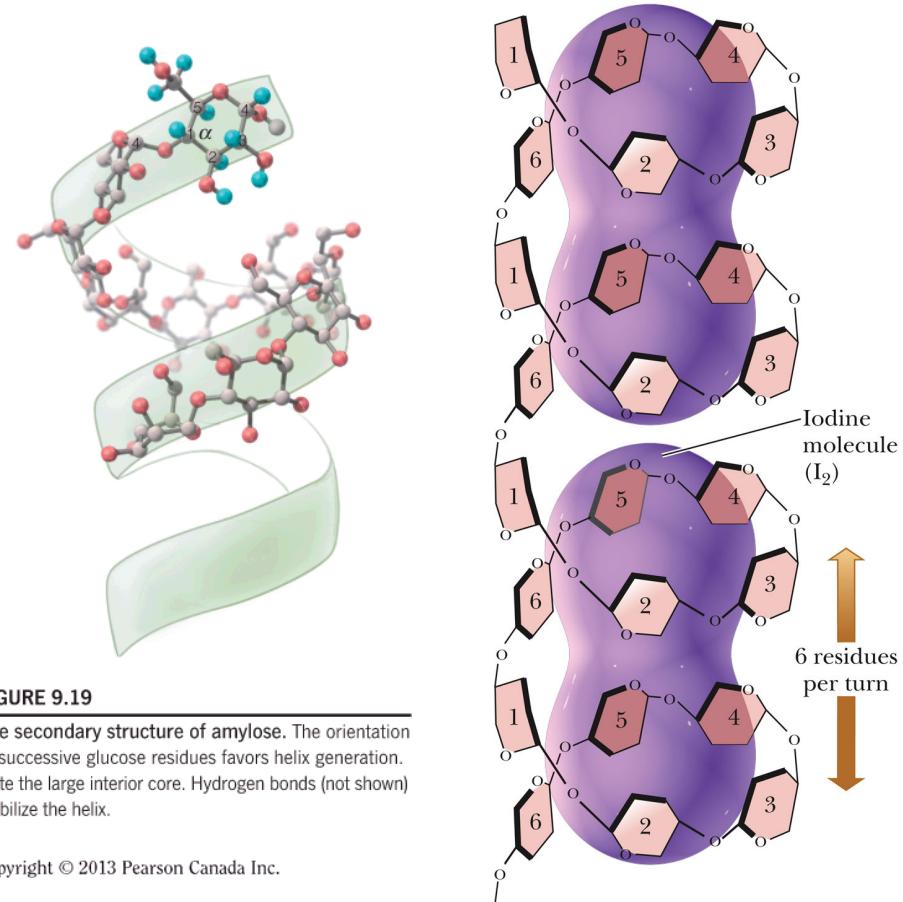


Polysaccharides (Amylose, amylopectin, glycogen)

The secondary structure of amylose:

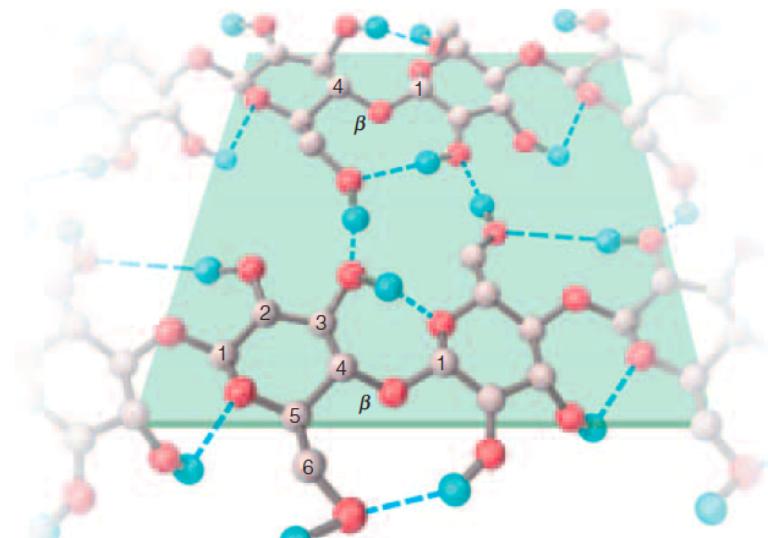
- The orientation of successive glucose residues favors helix generation.
- Note the large interior core.
- Hydrogen bonds (not shown) stabilize the helix.

The branch structure of amylopectin and glycogen inhibits the formation of helices



Polysaccharides (Cellulose)

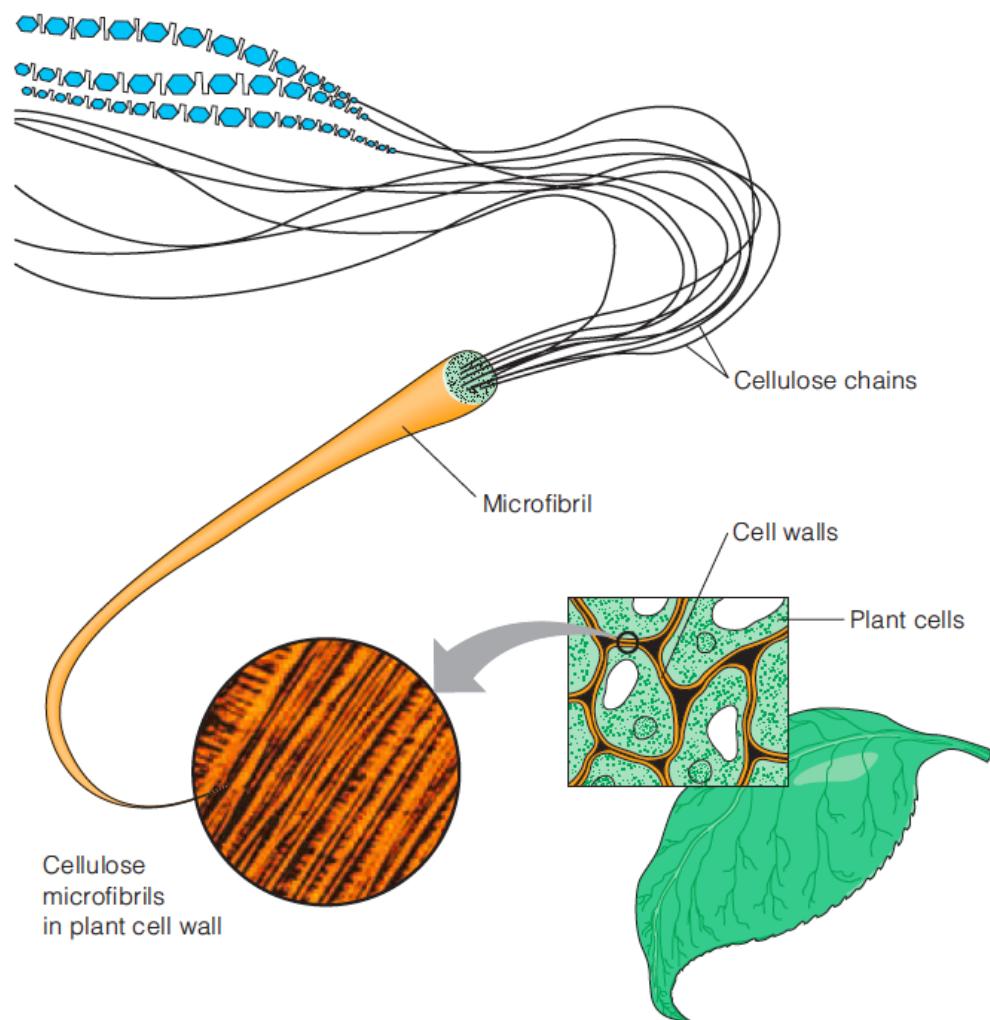
- **Cellulose:** the major structural component of plants, especially wood and plant fibers
- Like amylose, cellulose a linear polymer of D-glucose, but the sugar residues are connected by $\beta(1 \rightarrow 4)$ linkages.
- The $\beta(1 \rightarrow 4)$ linkages of cellulose generate a planar structure.
- The parallel cellulose chains are linked together by a network of hydrogen bonds.



Polysaccharides (Cellulose)

Organization of plant cell walls:

- Microfibrils of cellulose are embedded in a matrix of hemicellulose.
- Note that the fibers are laid down in a crosshatched pattern to give strength in all directions.



The marine invertebrate called *tunicate*, such as the sea squirt (海鞘), contain considerable quantities of cellulose in their hard outer mantle



Polysaccharides (Cellulose)

Ruminant such as cows can digest cellulose only because their digestive tracts contain symbiotic bacteria that produce the necessary **cellulases**.

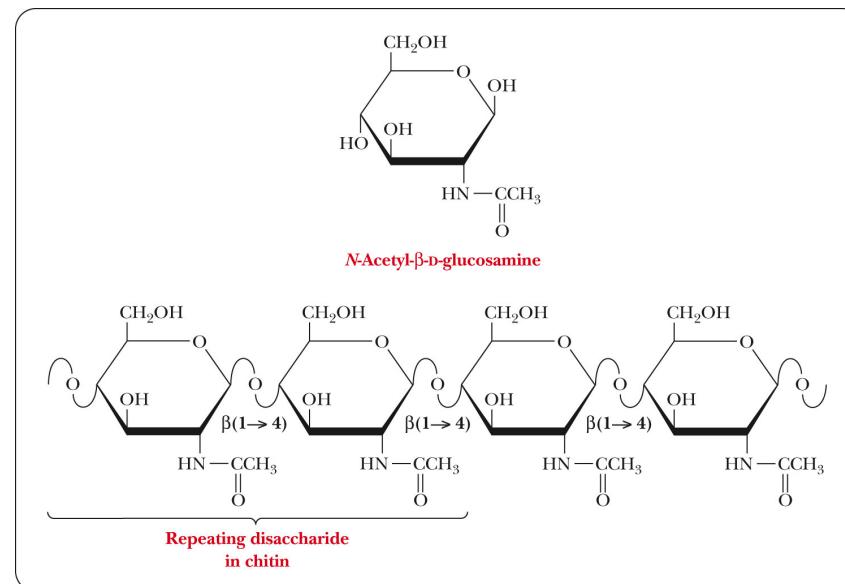
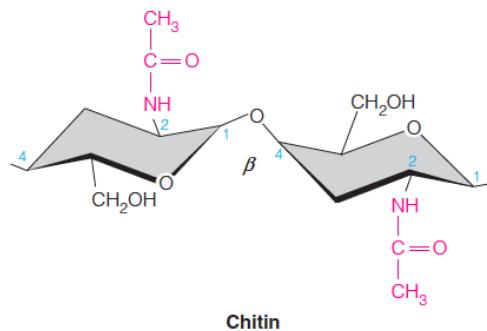
Termites manage to eat woody substances because their guts harbor protozoas capable of cellulose digestion and their salivary glands also produce a cellulase.

Many fungi also produce such enzymes, which is why some mushrooms can live in wood as carbon source.



Polysaccharides (Chitin)

- **Chitin:** the major structural component of the exoskeletons of invertebrates, such as insects and crustaceans; 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

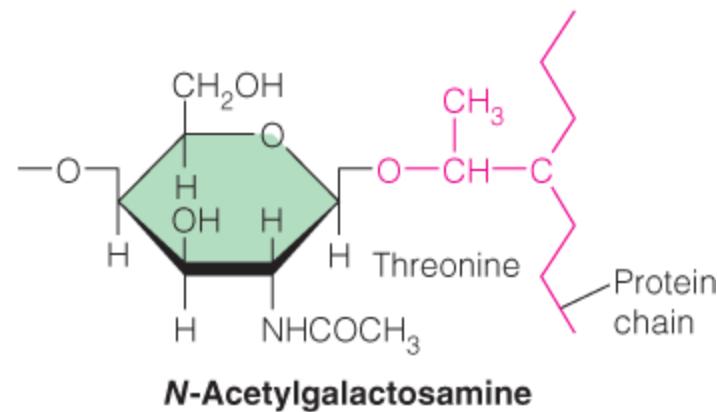
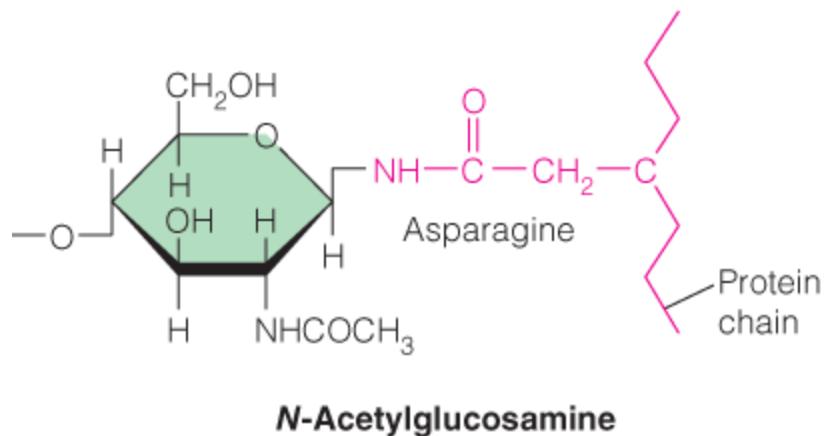


Polysaccharides (Glycosaminoglycans)

- The major structural polysaccharides in vertebrate animals are the ***glycosaminoglycans***, formerly called ***mucopolysaccharides***.
- **Chondroitin sulfate and keratan sulfate:** components of connective tissue
- **Hyaluronic acid(玻尿酸):** a component of the vitreous humor of the eye and the lubricating fluid of joints
- **Heparin:** natural anticoagulant
- **Dermatan sulfates** found mostly in skin, but also in blood vessels.

Polysaccharides (Glycosaminoglycans)

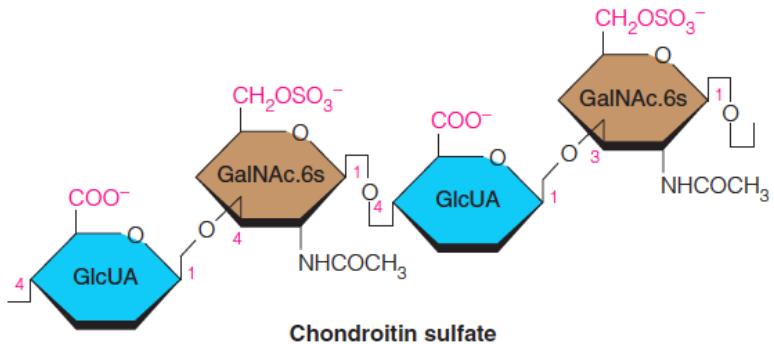
- All are polymers of repeating disaccharide units, in which one of the sugars is either *N*-acetylgalactosamine or *N*-acetylglicosamine or one of their derivatives.
- All are acidic (anionic), through the presence of either sulfate or carboxylate groups.



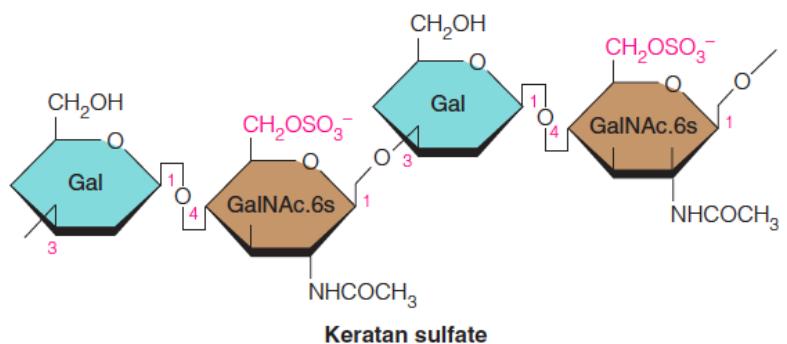
Polysaccharides (Glycosaminoglycans)

Repeating structures of some glycosaminoglycans:

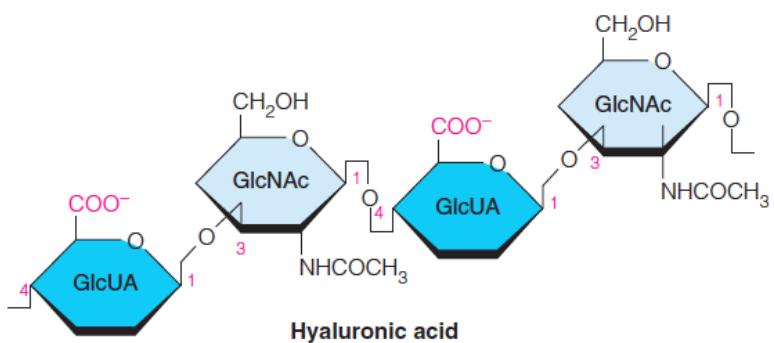
- In each case, the repeating unit is a disaccharide, of which two are shown for each structure.



Chondroitin sulfate



Keratan sulfate



Hyaluronic acid

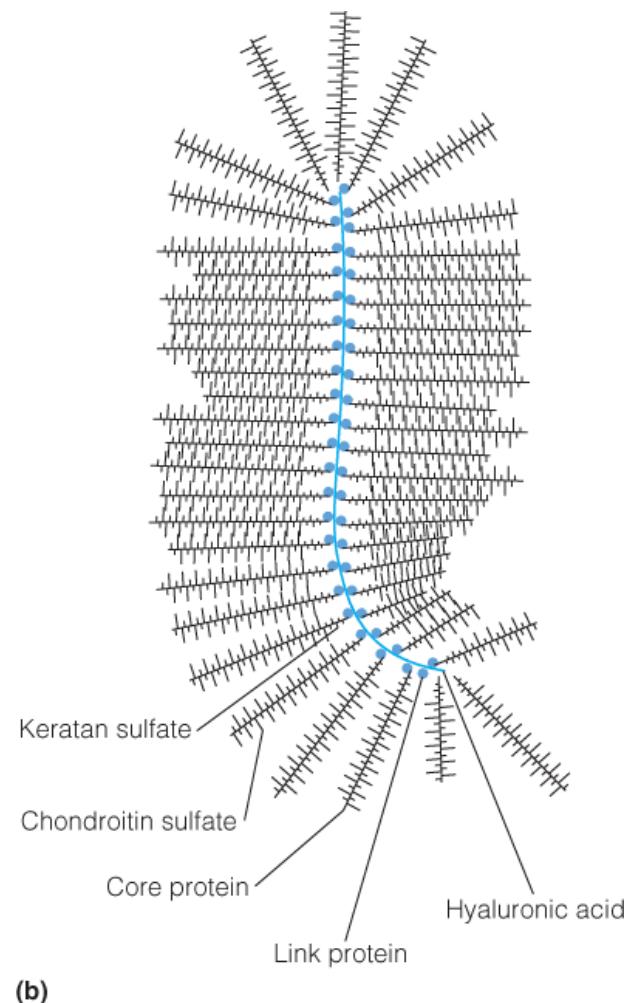
FIGURE 9.23

Proteoglycan structure in bovine cartilage. **(a)** An electron micrograph of a proteoglycan aggregate. **(b)** A schematic drawing of the same structure. Keratan sulfate and chondroitin sulfate are covalently linked to extended core protein molecules. The core proteins are noncovalently attached to a long hyaluronic acid molecule with the aid of a link protein.

(a) Reprinted from *Collagen and Related Research* 3:489–504, J. A. Buckwalter and L. Rosenberg. © 1983, with permission from Elsevier.



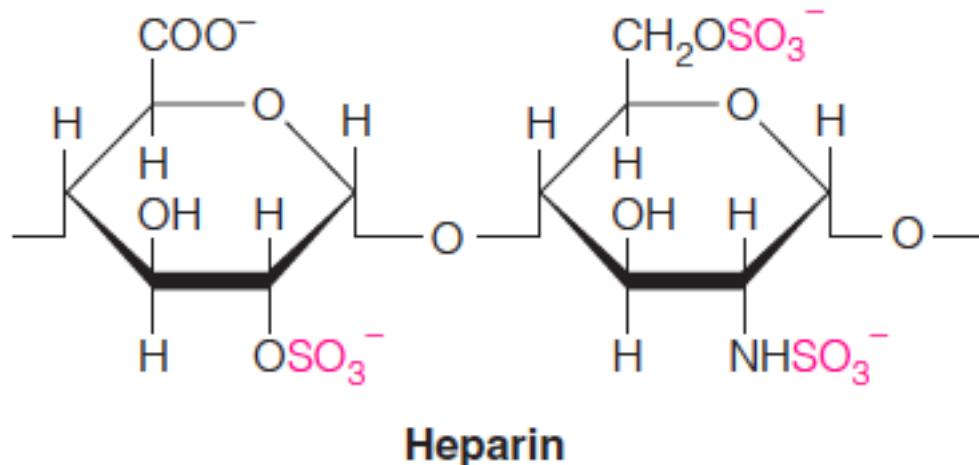
(a)



(b)

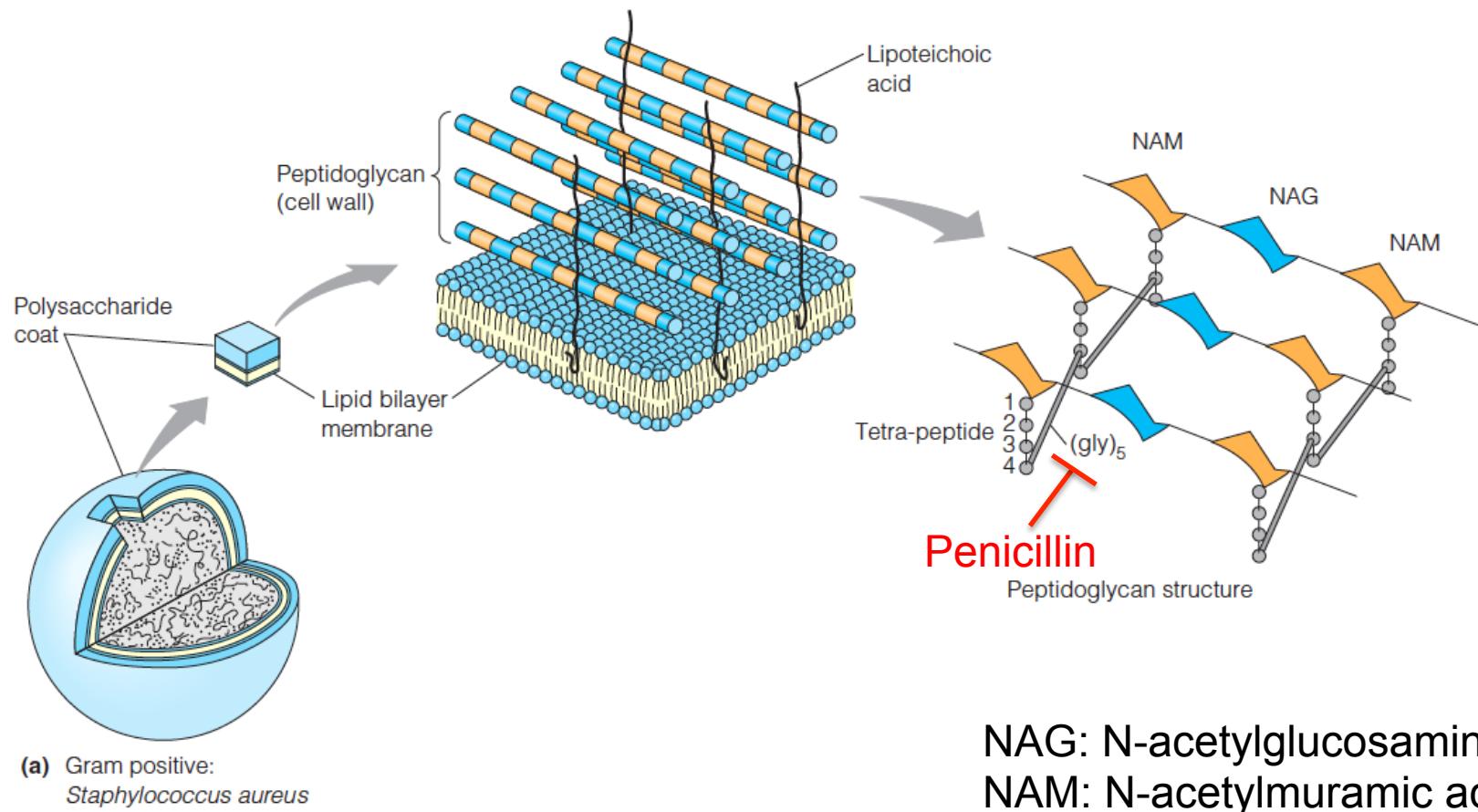
Polysaccharides (Glycosaminoglycans)

- A highly sulfated glycosaminoglycan is **heparin**.
- Heparin appears to be a **natural anticoagulant** and is found in many body tissues.
- It binds strongly to a blood protein, antiprothrombin III, and the complex inhibits enzymes of the blood clotting process.
- Therefore, heparin is used medicinally to inhibit clotting in blood vessels.



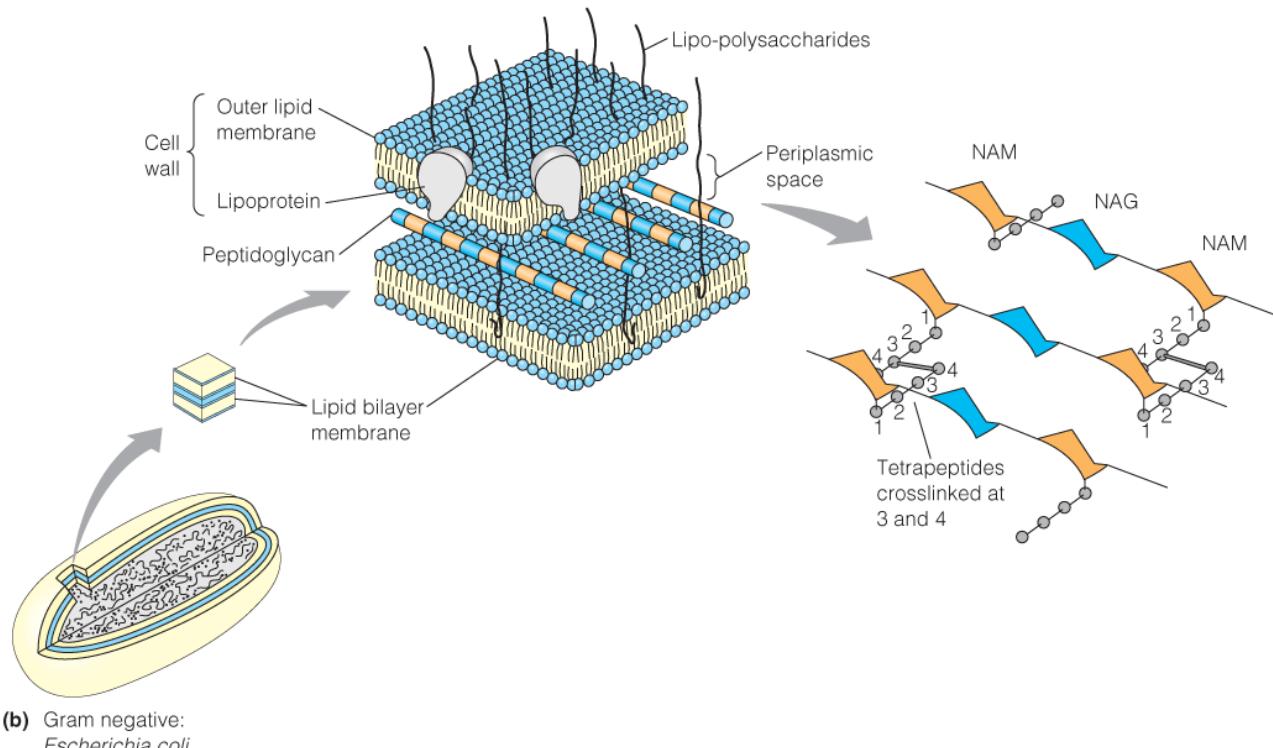
Polysaccharides (Bacterial cell wall)

- The cell wall of a **Gram-positive** bacterium, *S. aureus*, consists of a ***thick peptidoglycan layer*** made up of polysaccharide chains and short peptides.
- The peptides are cross-linked by **glycine pentapeptides**.



Polysaccharides (Bacterial cell wall)

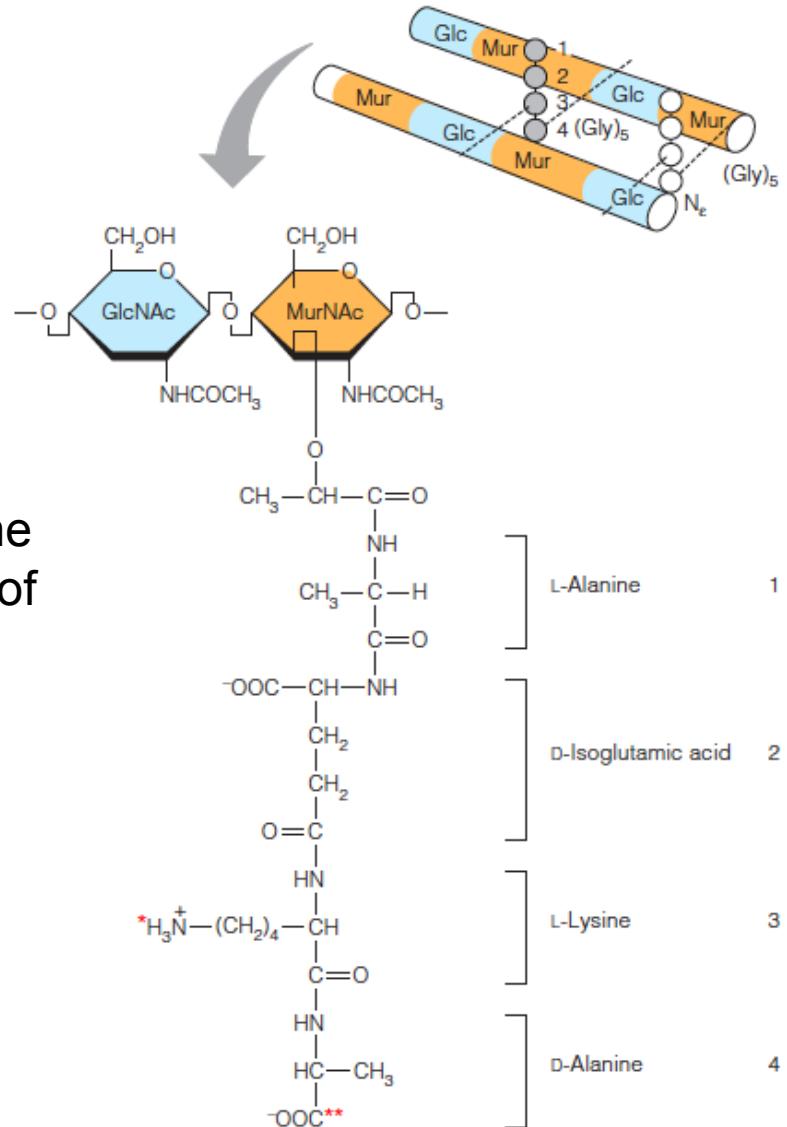
- The cell wall of a **Gram-negative** bacterium, *E. coli*, has a **thin peptidoglycan layer** and an **outer lipid membrane**.
- The cross-links here are between tetrapeptides attached to the **N-acetylmuramic acid (NAM)** residues in adjacent chains



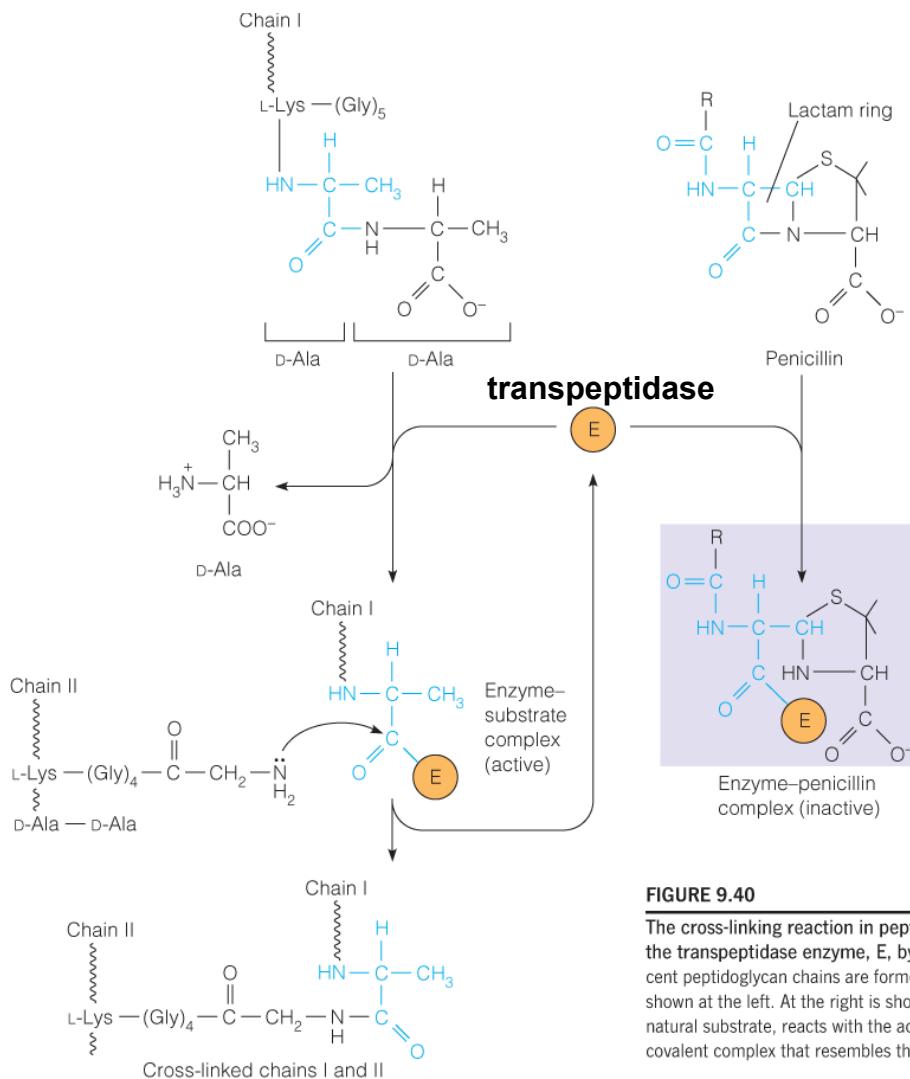
Polysaccharides (Bacterial cell wall)

The peptidoglycan layer of Gram-positive bacteria:

- Cross-links between the peptides are formed by pentaglycine chains between the α -amino group of the **lysine** (*) on one chain and the C-terminal carboxyl group of the **alanine** (**) on an adjacent chain.



Cross-linking reaction in peptidoglycan synthesis



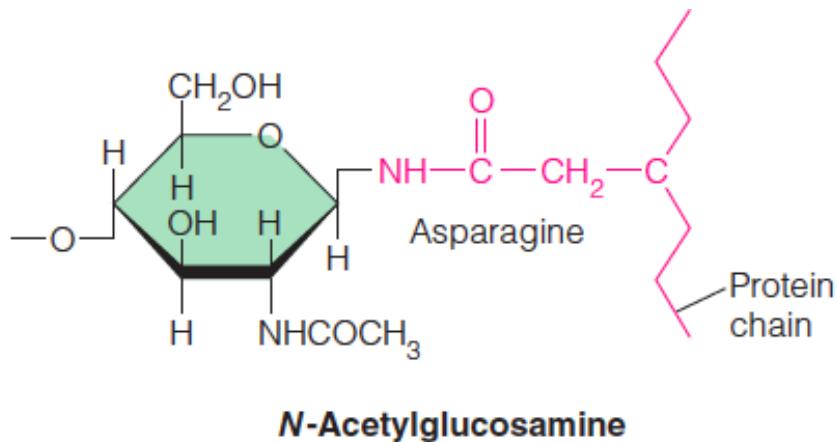
- Cross-links between adjacent peptidoglycan chains are formed by the action of a **transpeptidase enzyme**, as shown at the left.
- At the right is shown how **penicillin**, a structural **analog of the natural substrate**, reacts with the active form of the enzyme to form an inactive covalent complex that resembles the enzyme–substrate complex.

FIGURE 9.40

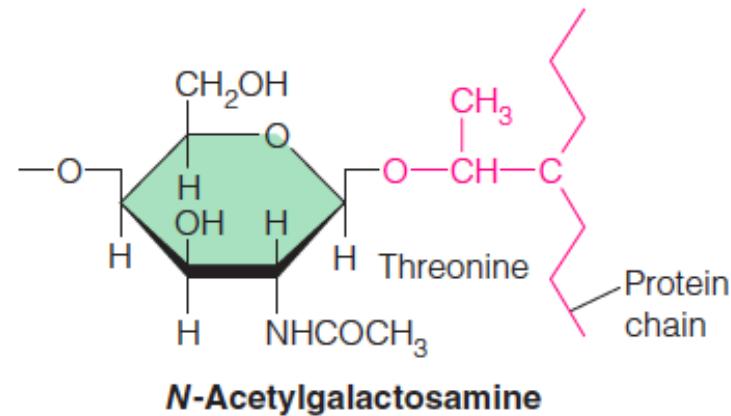
The cross-linking reaction in peptidoglycan synthesis (left) and inhibition of the transpeptidase enzyme, E, by penicillin (right). Cross-links between adjacent peptidoglycan chains are formed by the action of a transpeptidase enzyme, as shown at the left. At the right is shown how penicillin, a structural analog of the natural substrate, reacts with the active form of the enzyme to form an inactive covalent complex that resembles the enzyme–substrate complex.

Glycoproteins

- Oligosaccharides and proteins can be linked to form glycoproteins in two ways:
 - **O-linked** glycans are attached *via threonine* or *serine* hydroxyls.
 - **N-linked** glycans *via asparagine* amino groups.



***N*-linked**

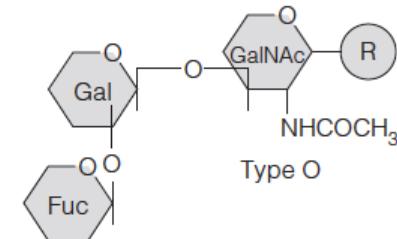


***O*-linked**

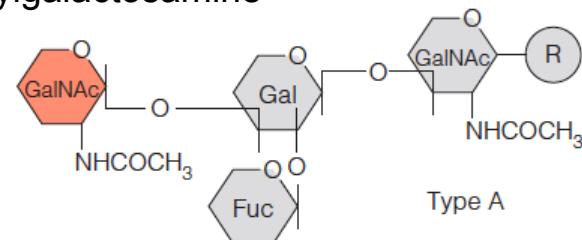
Glycoproteins

The ABO blood group antigens:

- The O oligosaccharide does not elicit antibodies in most humans.
- The A and B antigens are formed by addition of GalNAc or Gal, respectively, to the O oligosaccharide.
- Each of the A and B antigens can elicit a specific antibody.
- R can represent either a protein molecule or a lipid molecule.

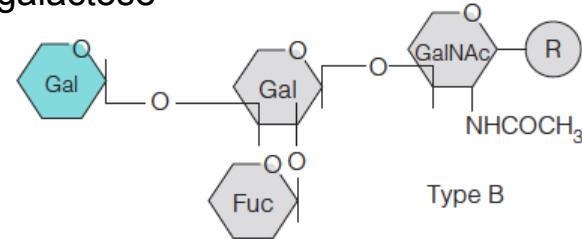


N-acetylgalactosamine



Type A

galactose



Type B

Glycoproteins

TABLE 9.6 Transfusion relationships among ABO blood types

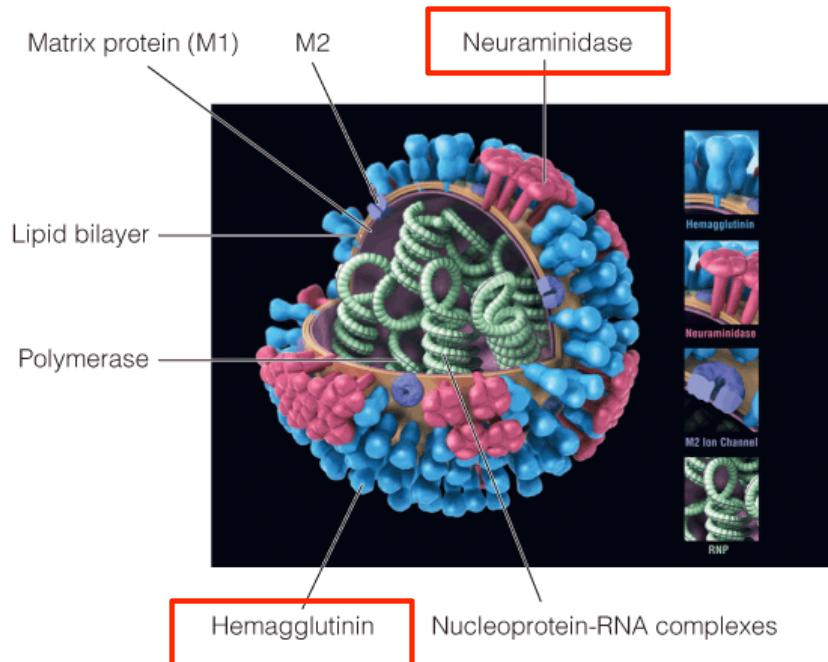
| Person Has Blood Type: | Makes Antibodies Against: | Can Safely Receive Blood from: | Can Safely Donate Blood to: |
|------------------------|---------------------------|--------------------------------|-----------------------------|
| O | A, B | O | O, A, B, AB |
| A | B | O, A | A, AB |
| B | A | O, B | B, AB |
| AB | None | O, A, B, AB ^a | AB |

The blood group substances are a set of antigenic oligosaccharides attached to the surfaces of red cells.

Glycoproteins

The structure of the influenza virus:

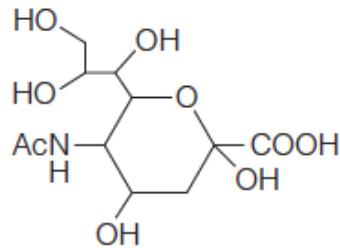
- The 13,600-nucleotide RNA genome is packaged within the sphere, about 120 nm in diameter.
- The spikes on the virion exterior include the **hemagglutinin** molecule and a spike that terminates in four **neuraminidase** molecules.
- **Hemagglutinin** can bind to host cell's **sialic acid** in cell surface glycoproteins or glycolipid.
- Release of virus from infected cells required cleavage of the sialic acid from the rest of each oligosaccharide chain, and this carried out by viral **neuraminidase**.



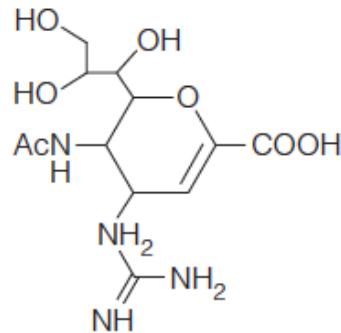
Glycoproteins

Rational design of neuraminidase inhibitors:

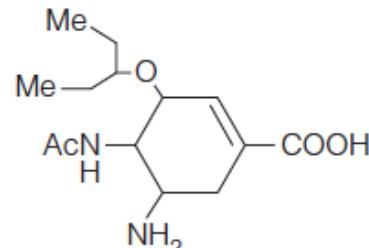
- Sialic acid analogs inhibit the neuraminidase and block the release of viral particles from infected cell.
- Structures of sialic acid, zanamivir, and oseltamivir.



Sialic acid



Zanamivir



Oseltamivir

Oligosaccharides as Cell Markers

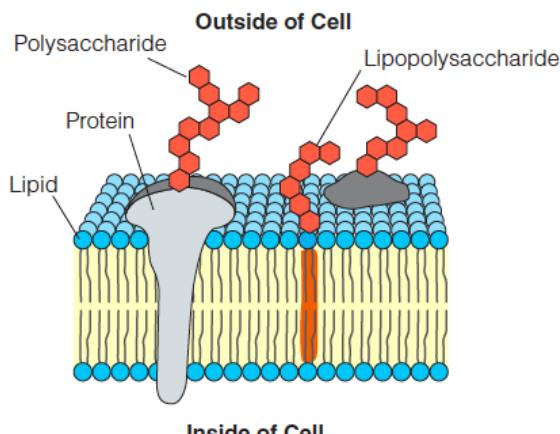
- Some animal cells have an extremely thick coating of polysaccharides called a ***glycocalyx*** (literally “sugar coat”).
- Glycocalyx oligosaccharides interact with other substances:
 - With bacteria in the intestine.
 - With collagen of the intercellular matrix in some other tissues.

Oligosaccharides as Cell Markers

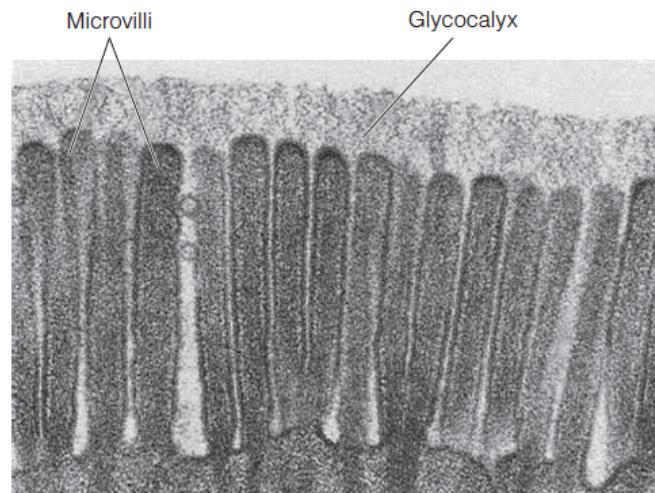
Cell surface recognition factors:

a) Schematic view of a lipid membrane.

b) Electron micrograph of the surface of an intestinal epithelial cell. The cellular projections, called *microvilli*, are covered on their outer surface by a layer of branched polysaccharide chains attached to proteins in the cell membrane. This carbohydrate layer, called the **glycocalyx**, is **found on many animal cell surfaces**.



(a) Cell surface oligosaccharides

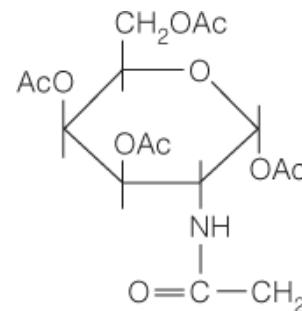


(b) Polysaccharide glycocalyx

Oligosaccharides as Cell Markers

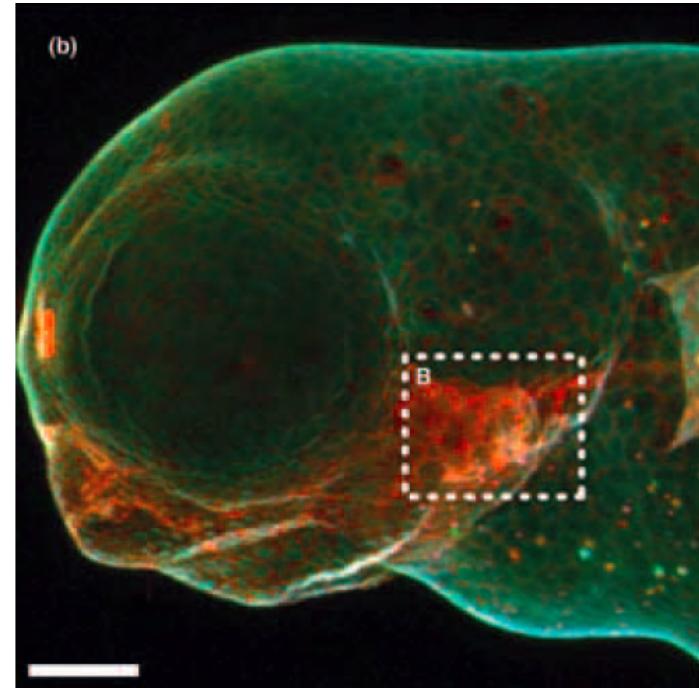
Imaging cell surface glycoproteins in living cells:

- Zebrafish embryos were allowed to incorporate an azido derivative of GalNAc.
- At fixed intervals the embryos were treated with a fluorescent reagent that couples to the azido group in the incorporated analog.



Fluorescent
reagent reaction

Peracetyl *N*-azidoacetylgalactosamine



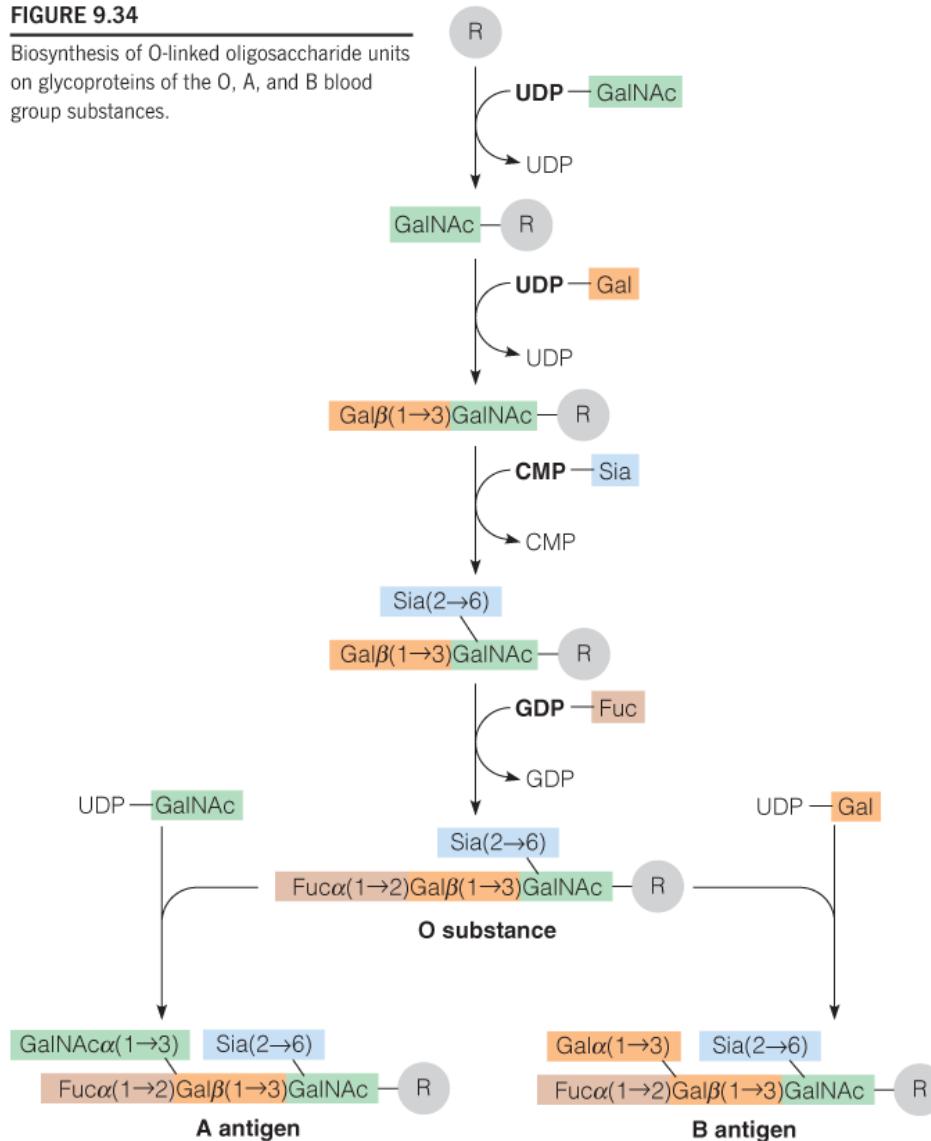
Copyright © 2013 Pearson Canada Inc.

Ac₄GalNAz: incorporated into mucin-type O-linked glycoprotein

O-linked oligosaccharides: Blood group antigen

FIGURE 9.34

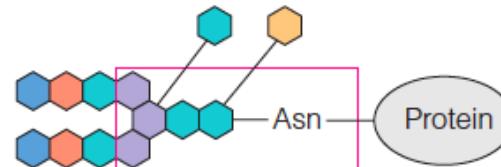
Biosynthesis of O-linked oligosaccharide units on glycoproteins of the O, A, and B blood group substances.



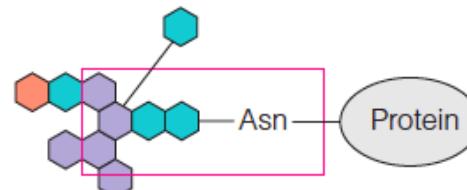
N-linked oligosaccharide: Glycoproteins

Structures of the major types of asparagine-linked (*N*-linked) oligosaccharides:

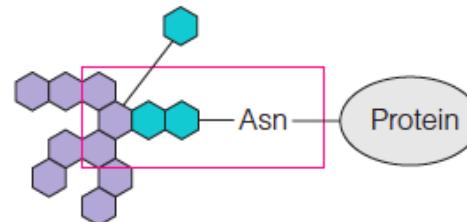
- The red boxes contain the pentasaccharide core common to all known *N*-linked structures.



Complex



Hybrid



High-mannose

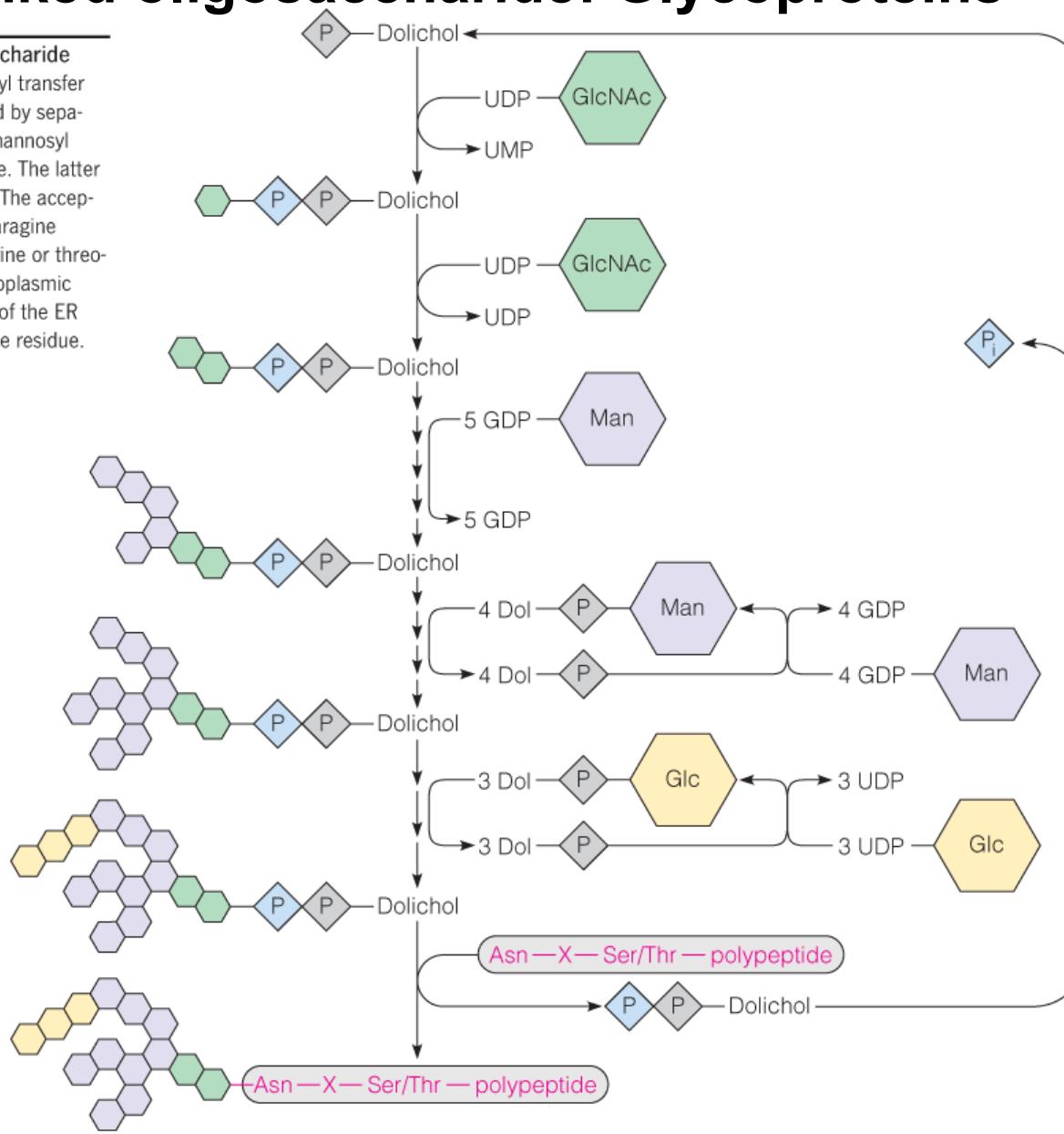
Key:

| | | |
|--------|-----|-----|
| GlcNAc | Man | Gal |
| Sia | Fuc | |

N-linked oligosaccharide: Glycoproteins

FIGURE 9.36

Biosynthesis of the lipid-linked oligosaccharide intermediate. The five sequential mannosyl transfer reactions from GDP-mannose are catalyzed by separate glycosyltransferases, as are the four mannosyl transfers from dolichol phosphate mannose. The latter is synthesized in turn from GDP-mannose. The acceptor site on the polypeptide chain is an asparagine residue two positions to the N side of a serine or threonine. The whole process occurs in the endoplasmic reticulum, with translocation to the lumen of the ER occurring after transfer of the fifth mannose residue.



Dolichol phosphate, a lipid carrier contains 18-20 C₅ isoprenoid compound.

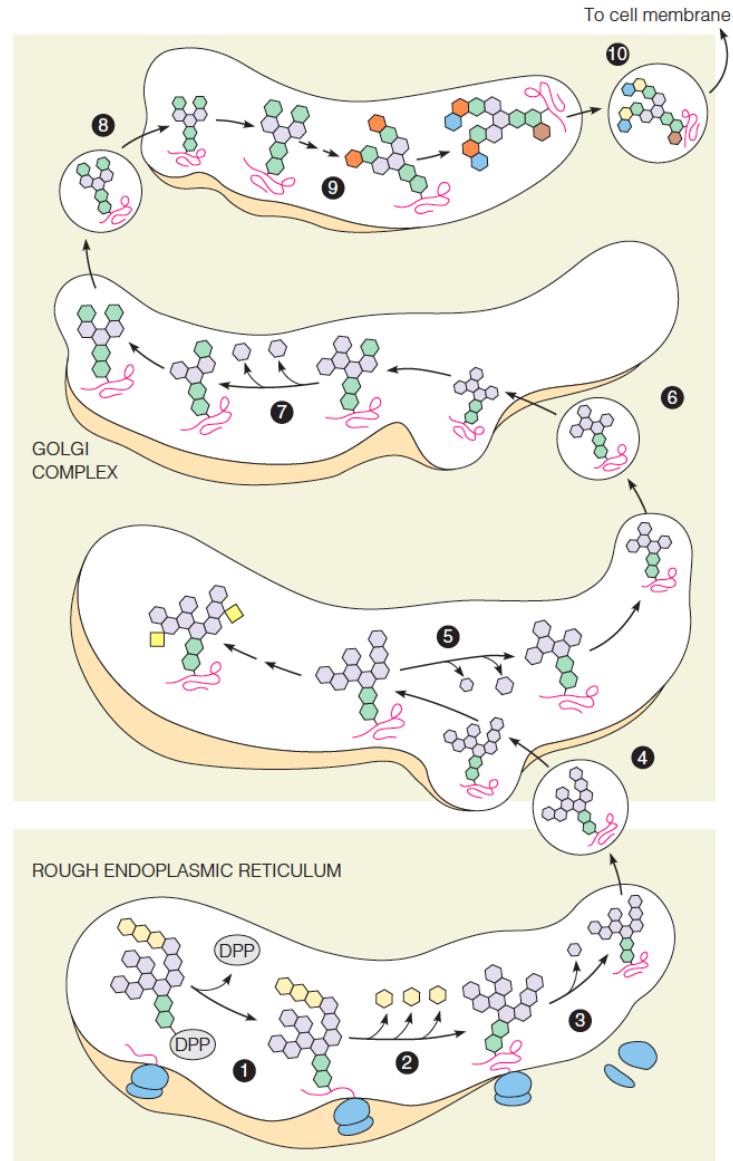
Glycoconjugates of Interest

Schematic pathway of oligosaccharide processing on newly synthesized glycoproteins:

I-cell disease: lysosomes contain very low acid hydrolase

Key:

- Yellow hexagon: Glucose
- Purple hexagon: Mannose
- Green hexagon: N-Acetylglucosamine
- Brown hexagon: Fucose
- Orange hexagon: Galactose
- Blue hexagon: Sialic acid
- DPP: Dolichol pyrophosphate
- Yellow diamond: Phosphate
- Ribosome with growing peptide chain: Blue oval with pink tail



I-cell (Inclusion-cell) disease

I-cell disease is an autosomal recessive disorder caused by a deficiency of glycosyltransferase, which phosphorylates **mannose** residues to **mannose-6-phosphate** on N-linked glycoproteins in the Golgi apparatus within the cell.

Without mannose-6-phosphate to target them to the lysosomes, the enzymes (acid hydrolase) are transported from the Golgi to the extracellular space, resulting in large intracellular inclusions of molecules requiring lysosomal degradation in patients with the disease

I-cell disease : Mucolipidosis II (黏脂症第二型)

- mental retardation
- developmental delay
- high forehead
- puffy eyelids
- flat nasal bridge
- macroglossia (large tongue)
- coarsening of facial features

通常會在10歲前因肺炎或充血性心臟衰竭死亡

