Carbohydrates

Dr. Diala Abu-Hassan, DDS, PhD

Dr.abuhassand@gmail.com

All images were taken from Campbell textbook except where noted

What Are Carbohydrates?

Carbohydrates are members of a large class of naturally occurring polyhydroxy ketones and aldehydes

Aldose A monosaccharide that contains an aldehyde carbonyl group.

Ketose A monosaccharide that contains a ketone carbonyl group

Have many hydroxyl groups on adjacent carbons together with either an aldehyde or ketone group

Roles of Carbohydrates

Major energy sources

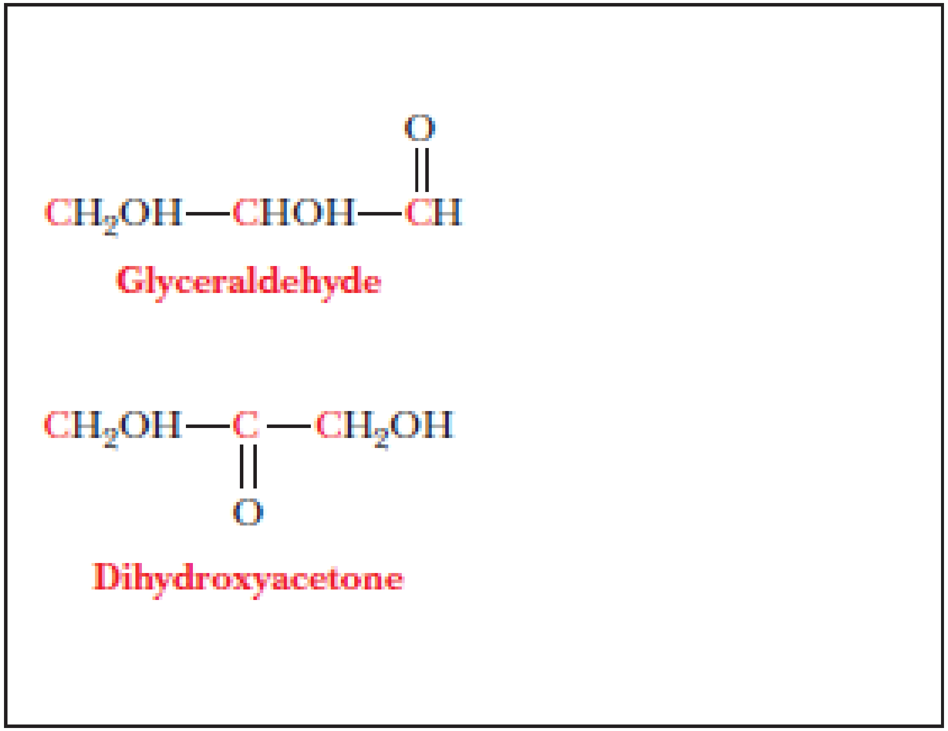
Oligosaccharides play a key role in **cell–cell interactions** and **immune recognition.**

Polysaccharides are essential **structural components** of several classes of organisms such as cellulose (a major component of grass and trees)

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)

Classification-Aldoses and ketoses



$CH_2OH—CHOH—\overset{\overset{O}{\|}}{C}H$

Glyceraldehyde

$CH_2OH—\underset{\underset{O}{\|}}{C}—CH_2OH$

Dihydroxyacetone

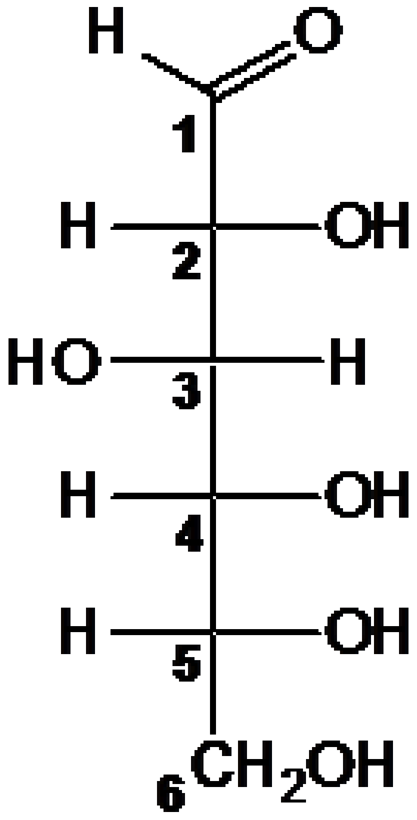
1 A comparison of glyceraldehyde (an aldotriose) and dihydroxyacetone (a ketotriose).

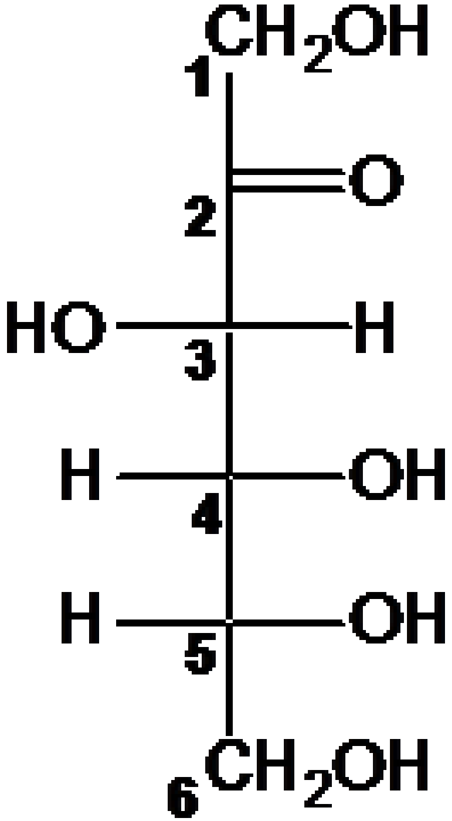
Nomenclature: aldo- or keto- + latin number + ose

Most common sugars are aldoses rather than ketoses

Classification

- By the number of carbon atoms they contain
  - Triose
  - Tetrose
  - Pentose
  - Hexose
  - Heptose
  - …

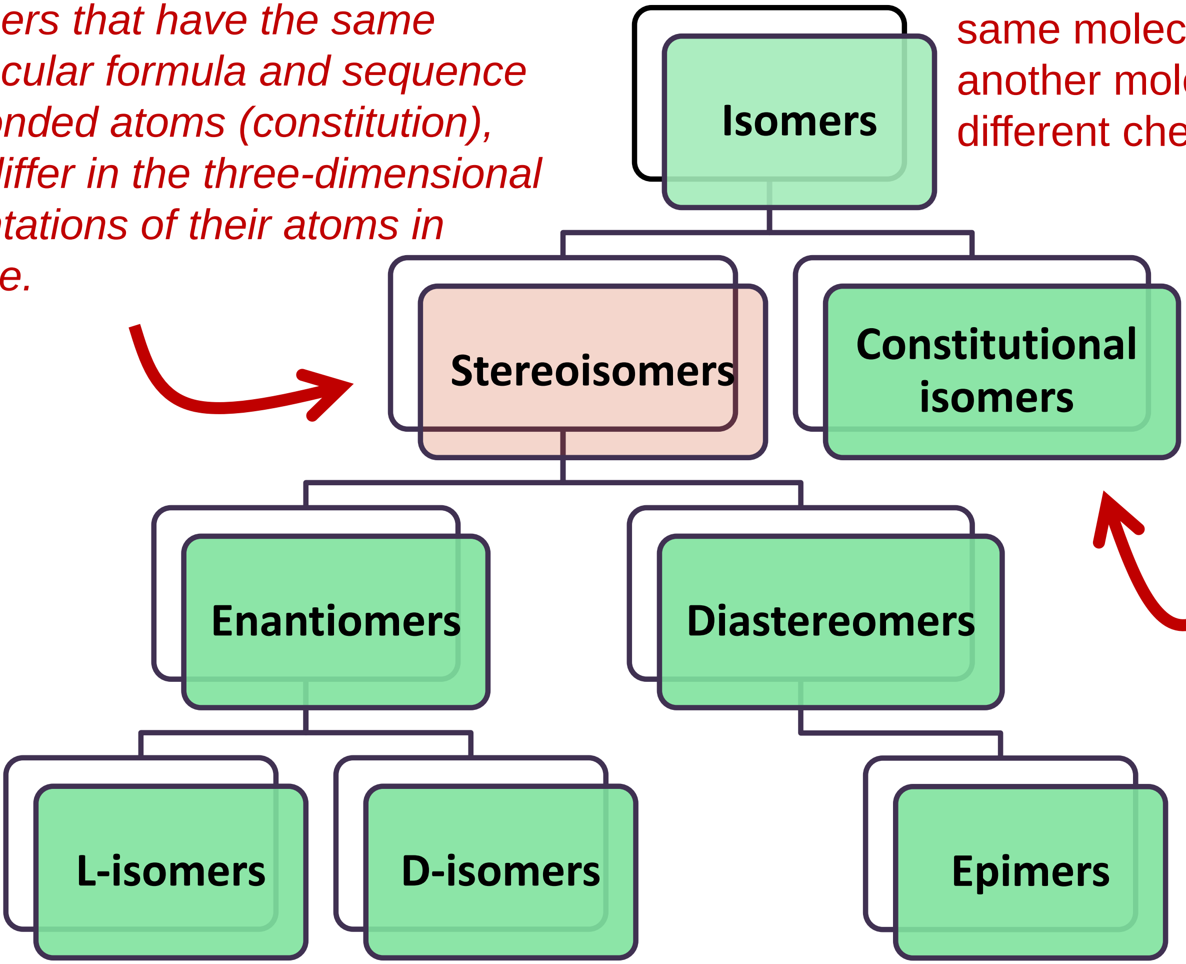




Isomerism

An *isomer* is a molecule with the same molecular formula as another molecule, but with a different chemical structure.

Isomers that have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space.



Isomers

Stereoisomers

Constitutional isomers

Enantiomers

Diastereomers

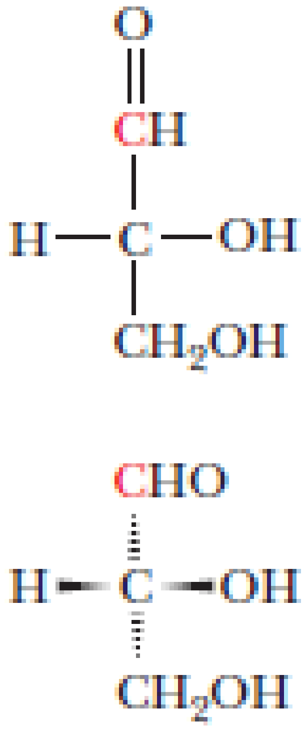
L-isomers

D-isomers

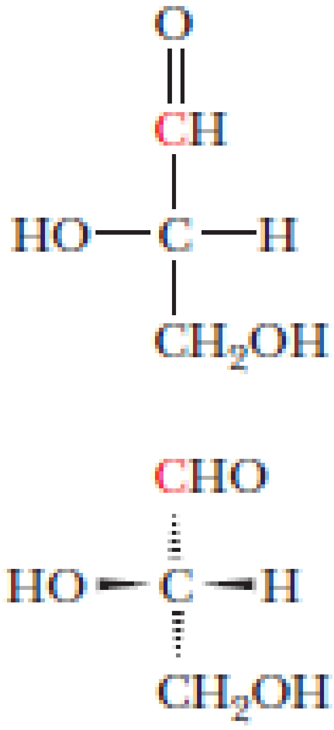
Epimers

Molecules with the same molecular formula, but have different bonding patterns and atomic organization.

Optical isomers (stereoisomers)



D-Glyceraldehyde



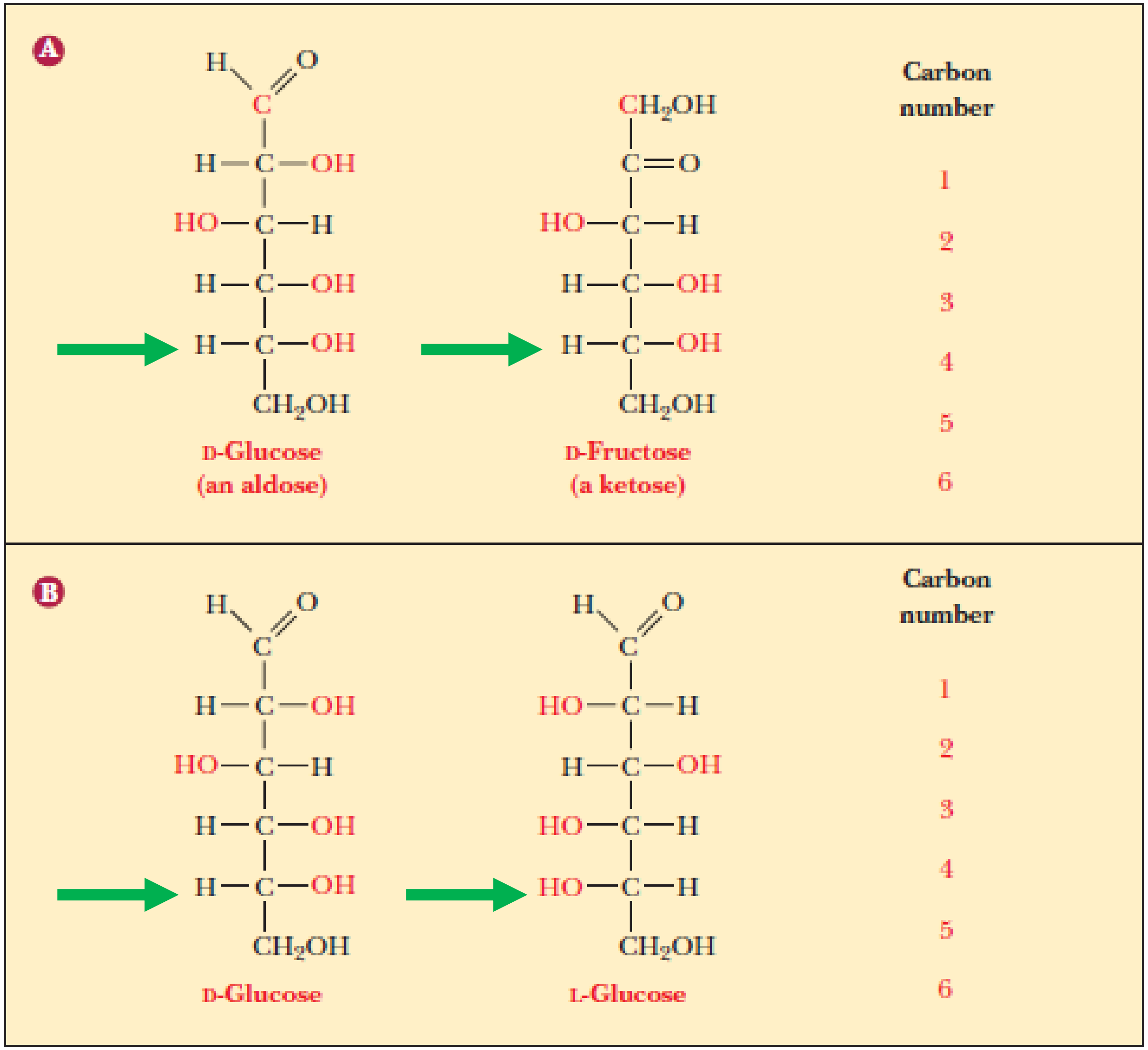
L-Glyceraldehyde

Enantiomers

More Cs, more stereoisomers

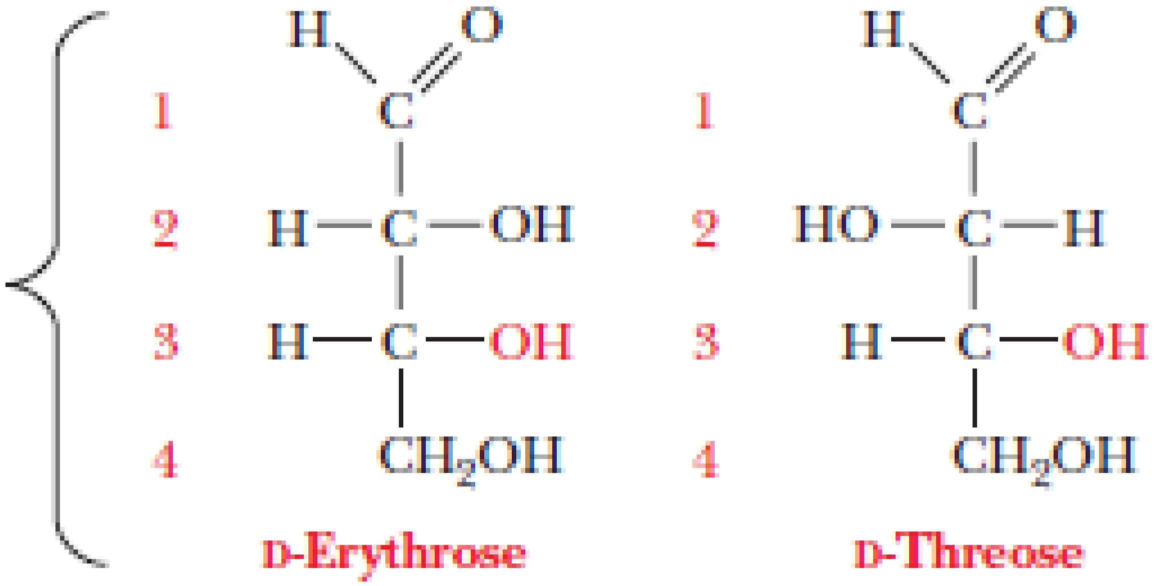
D sugars, rather than L sugars, predominate in nature

How to determine chiral carbons?



Stereoisomers of an aldotetrose

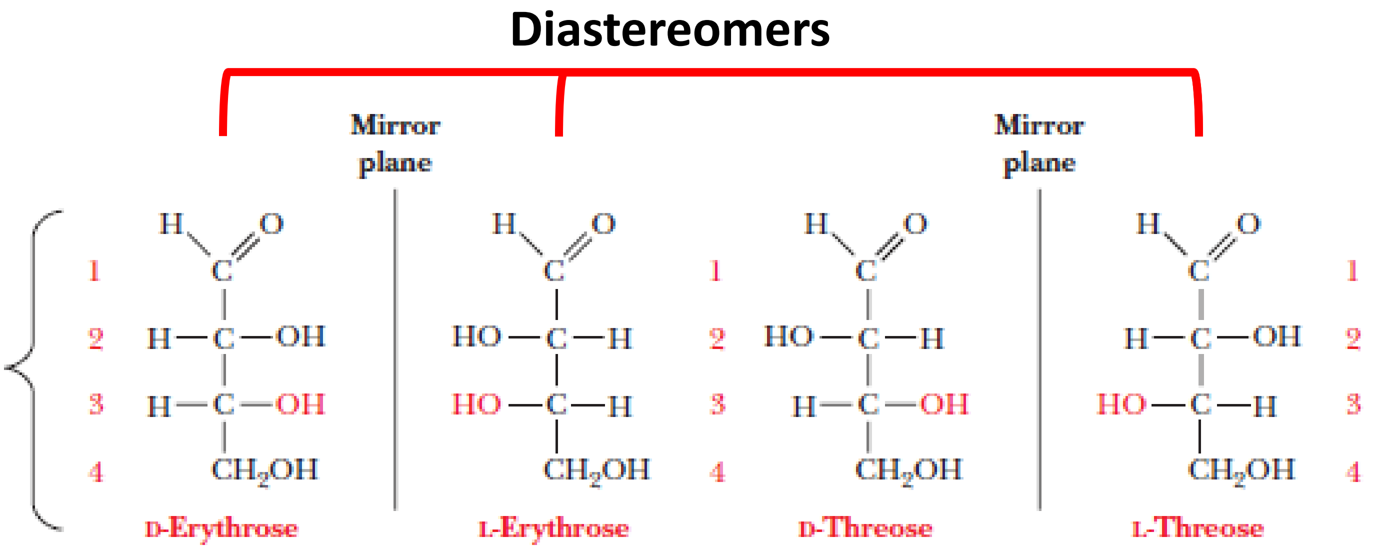
Number of stereoisomers=2^n, n is the number of chiral carbons



A Diastereomers D-erythrose and D-threose.

Stereoisomers of an aldotetrose

Diastereomers: non-superimposable, non-mirror image stereoisomers

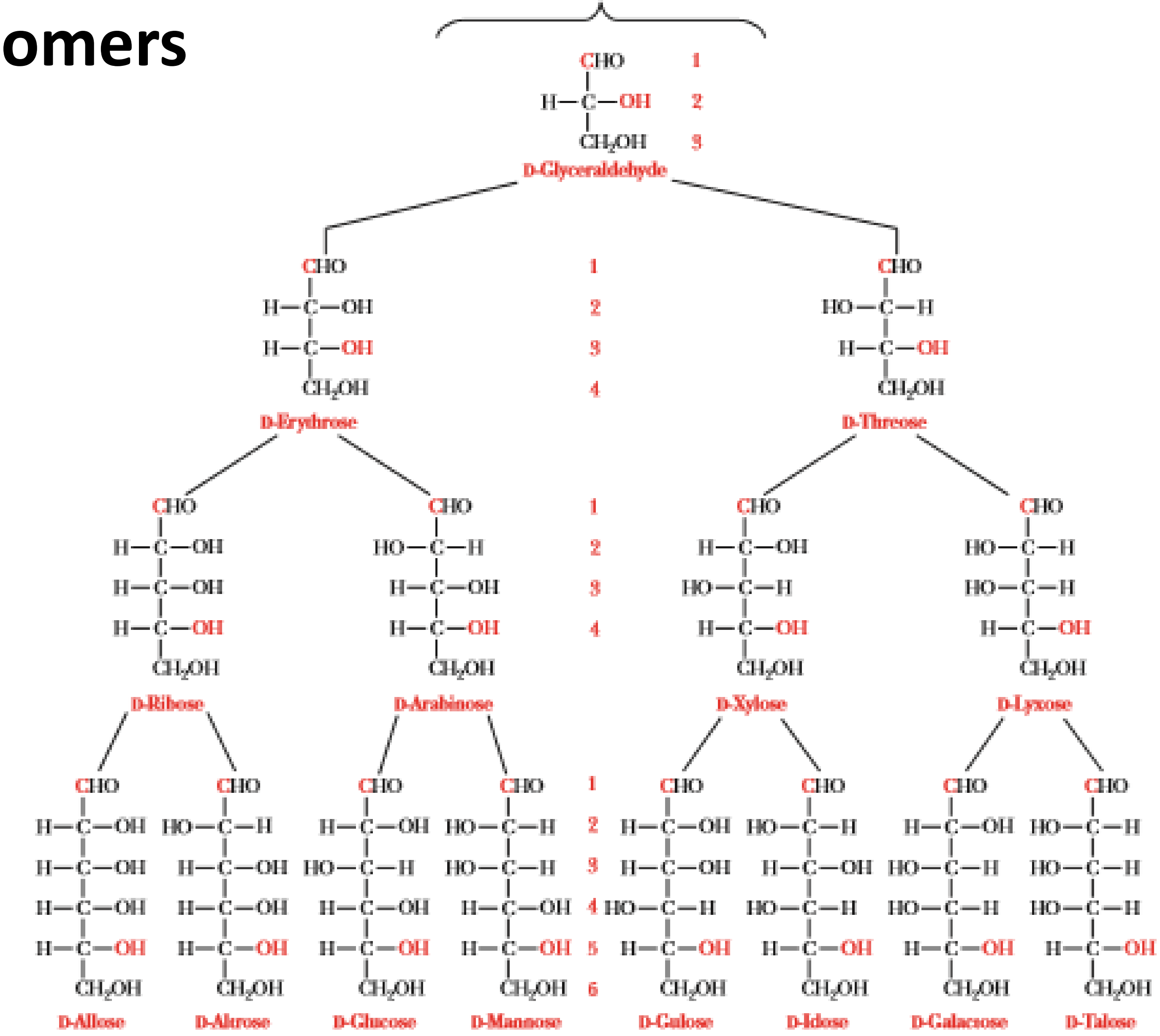


B Enantiomers D- and L-erythrose and D- and L-threose. The carbons are numbered. The designation of D or L depends on the configuration at the highest-numbered chiral carbon atom.

FIGURE 16.3 Stereoisomers of an aldotetrose.

Epimers are diastereomers that differ in the configuration at only **ONE** chiral carbon D-erythrose and D-threose are epimers.

Stereoisomers



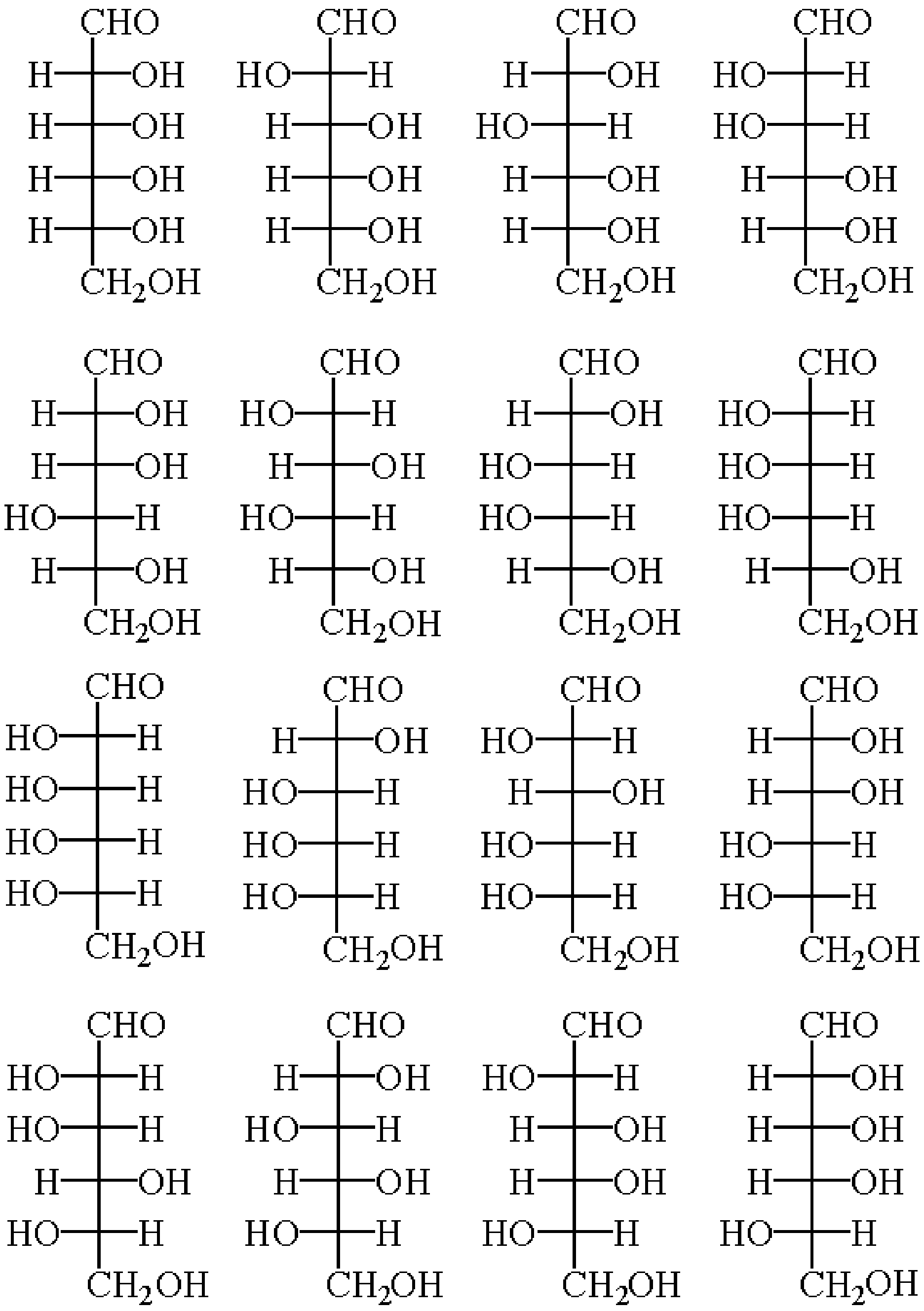
Ⓐ Aldoses containing from three to six carbon atoms, with the numbering of the carbon atom shown. Note that the figure shows only half the possible isomers. For each isomer shown, there is an enantiomer that is not shown, the L series.

Isomers of glucose

2^n (n is the number of chiral carbons in a sugar molecule)

Search for:

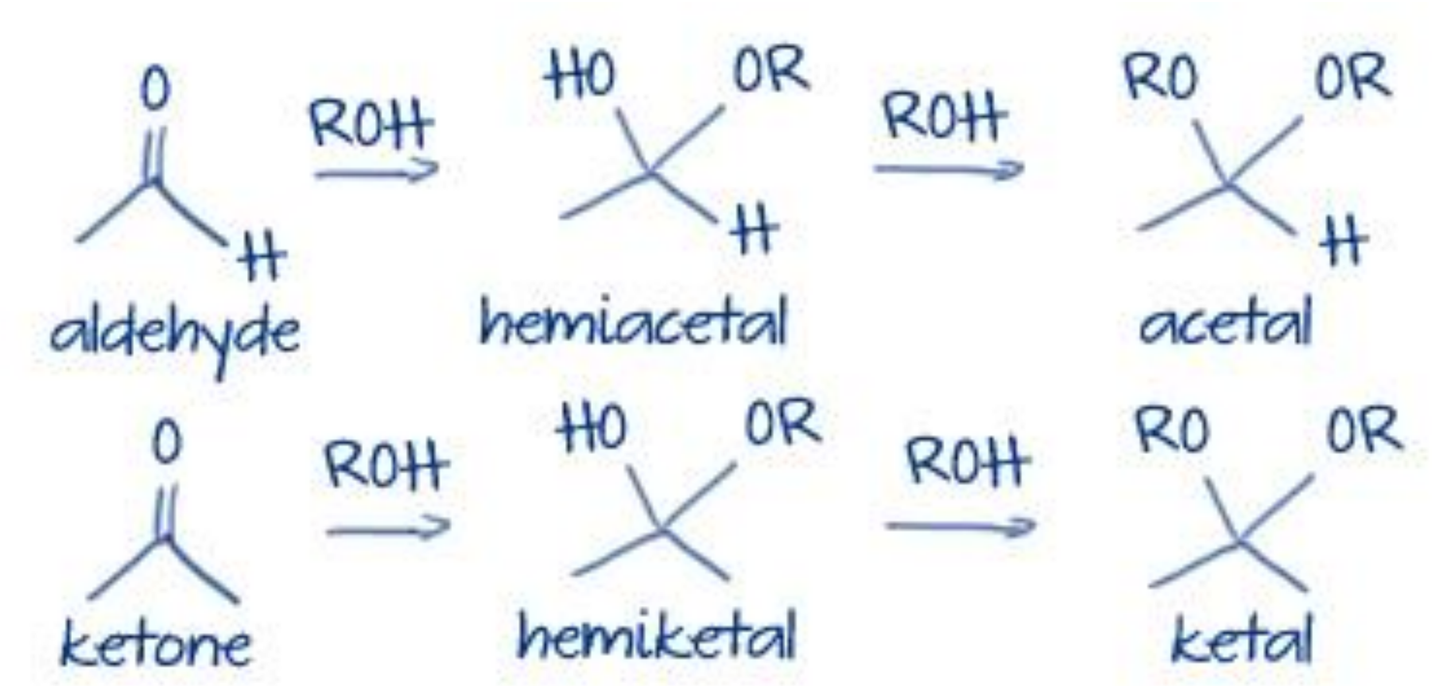
- Glucose,
- Galactose
- Mannose



16 Aldohexoses

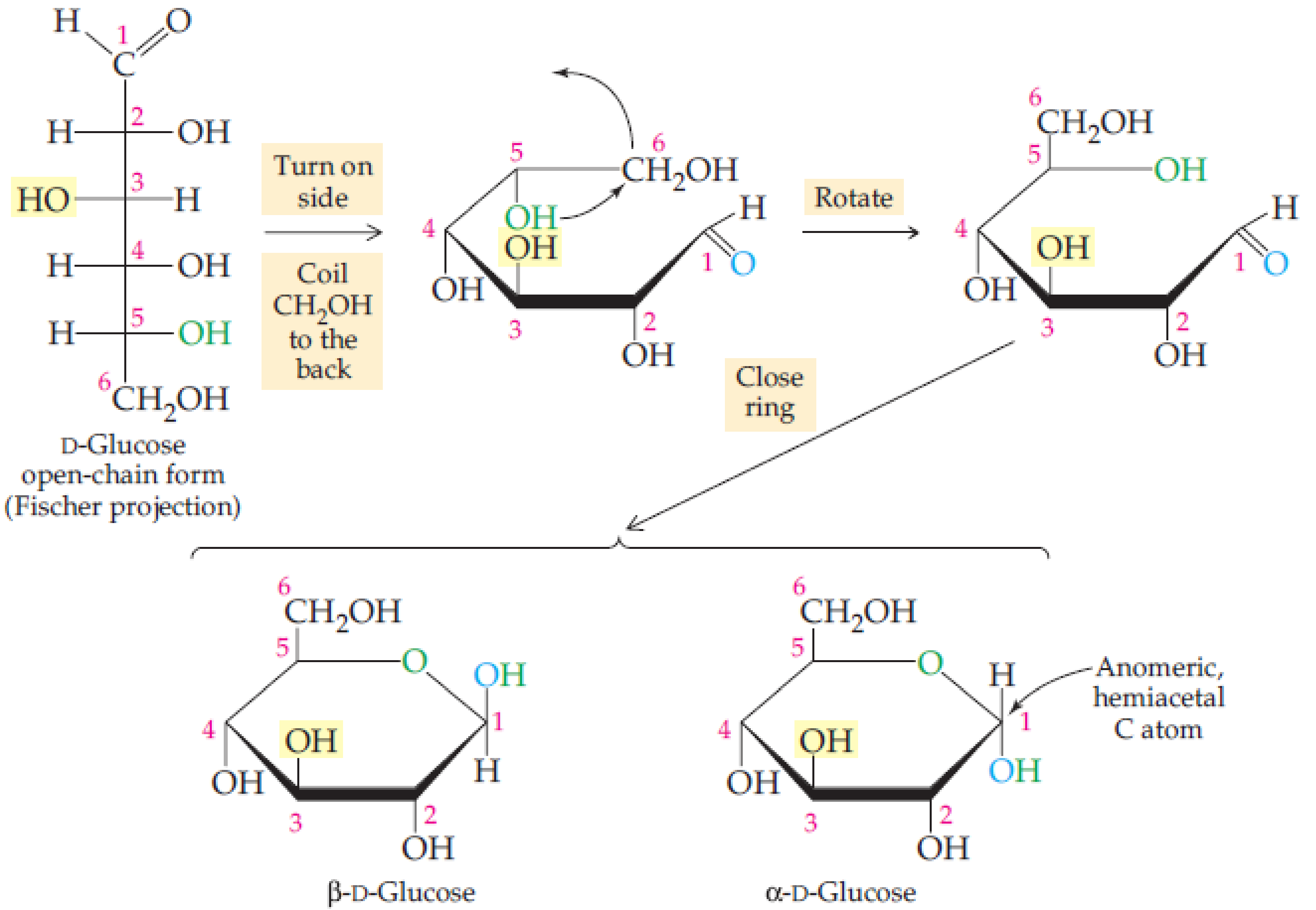
Acetal/ketal vs. hemiacetal/hemiketal

Hemiacetal and hemiketal: ether and alcohol on same carbon
Acetal and ketal: two ethers on same carbon

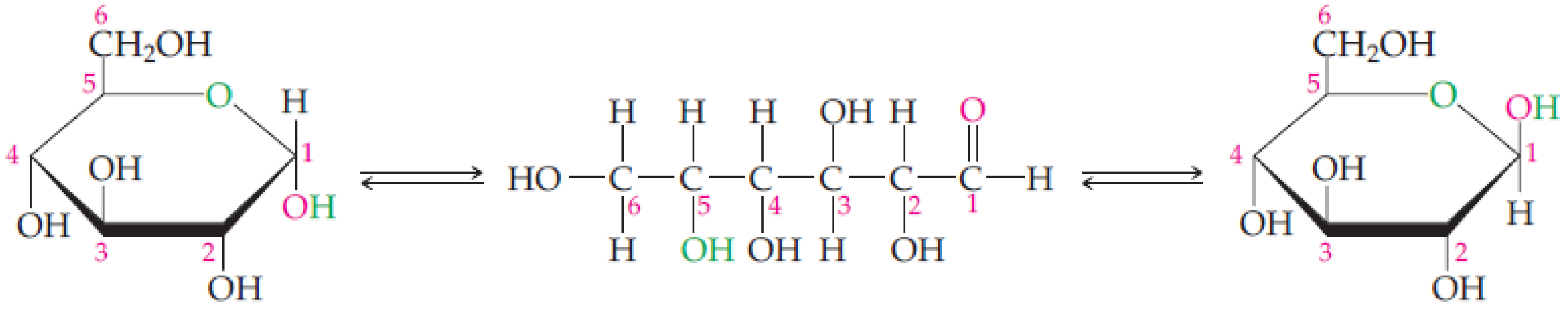


What is the difference between hemiacetal and hemiketal and the difference between acetal and ketal?

Structure of Glucose



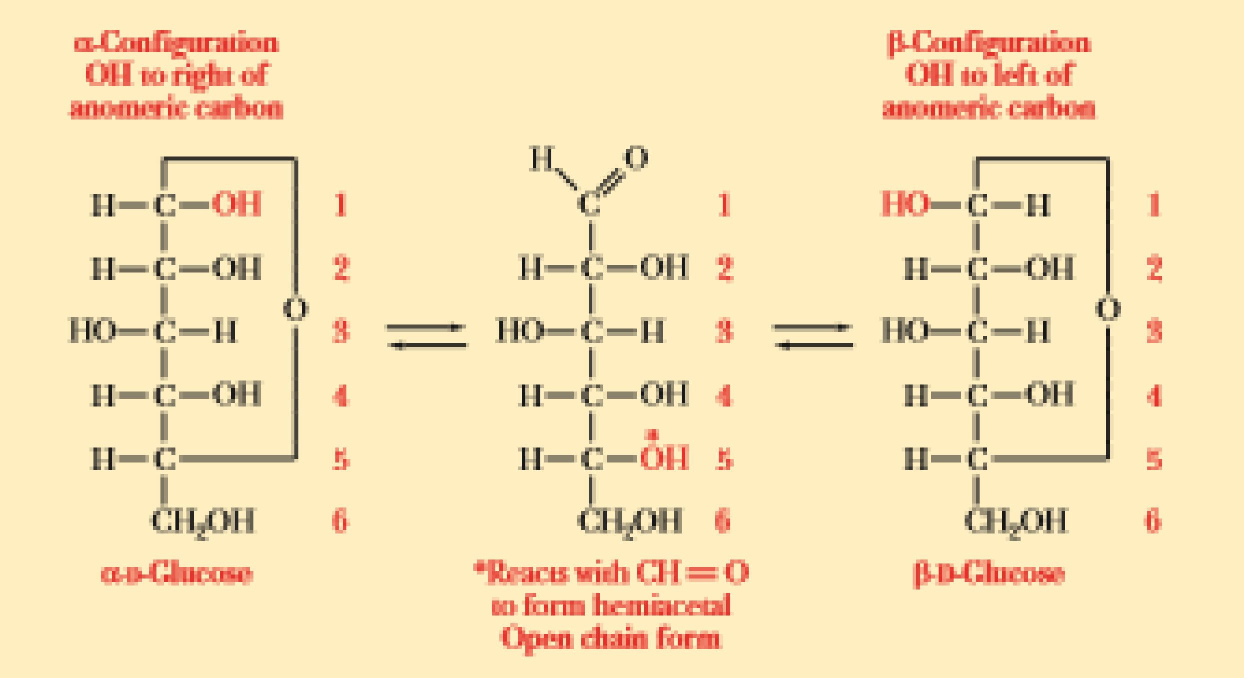
Structure of Glucose



α-D-Glucose ⇌ Open-chain D-Glucose ⇌ β-D-Glucose

(36%) (0.02%) (64%)

Glucose anomers-alpha and beta

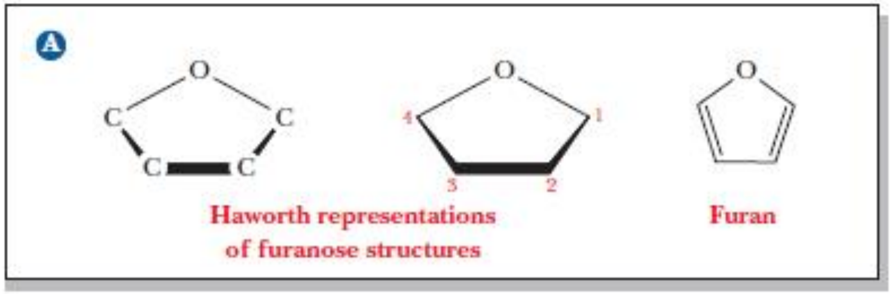


Fischer projection formulas of three forms of glucose

In some molecules, any anomer can be used

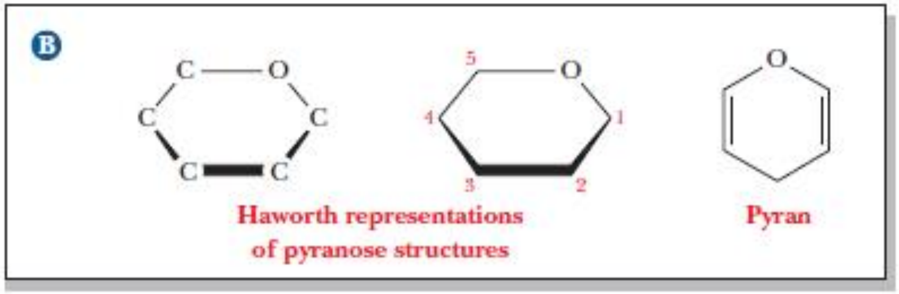
In other sugars, only one anomer is used, e.g. only β-D-ribose and β-D-deoxyribose are found in RNA and DNA, respectively.

Structural representation of sugars



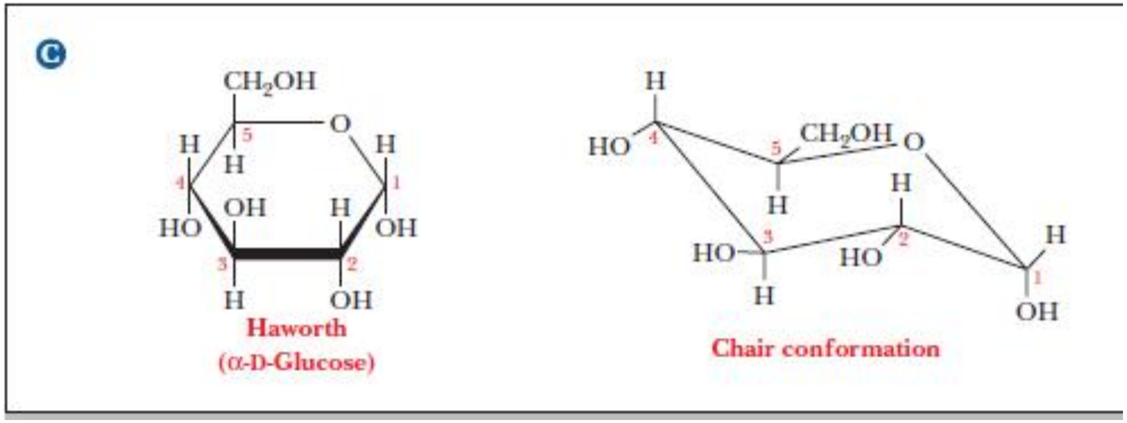
Haworth representations of furanose structures

Furan



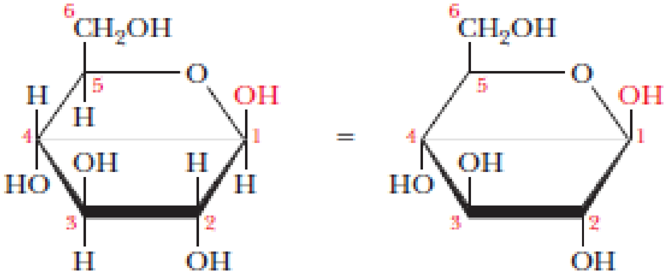
Haworth representations of pyranose structures

Pyran

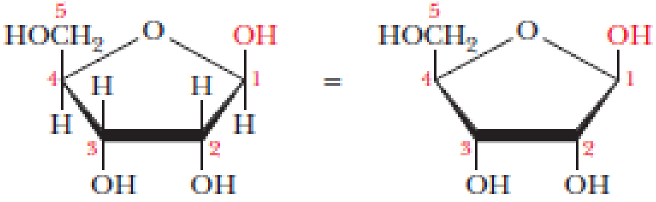


Haworth (α-D-Glucose)

Chair conformation



β-D-Glucose (β-D-Glucopyranose)



β-D-Ribose (β-D-Ribofuranose)

Carbohydrates

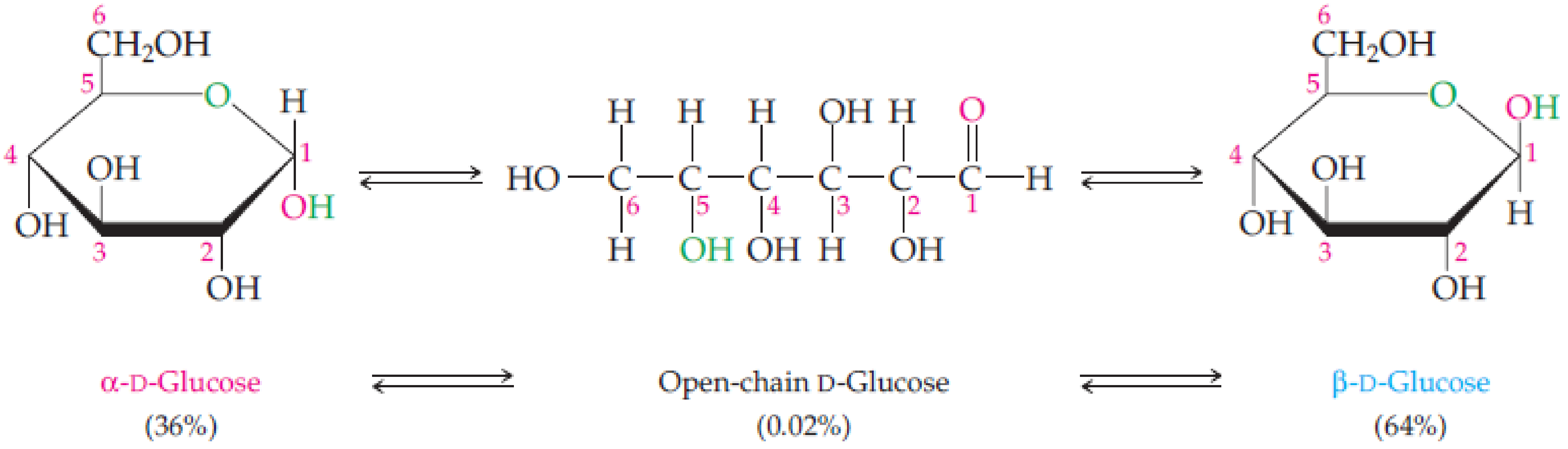
- **Mono- (one), Oligo- (a few) and (many) Polysaccharides**

- **Monosaccharides (simple sugar)** a carbohydrate with three to seven carbon atoms. General formula $C_n(H_2O)_n$.

- A monosaccharide can be a polyhydroxy aldehyde **(aldose)** or a polyhydroxy ketone **(ketose)**

Glucose

- The most important simple carbohydrate in human metabolism.
- It is the final product of carbohydrate digestion and provides acetyl groups for entry into the citric acid cycle as acetyl-SCoA

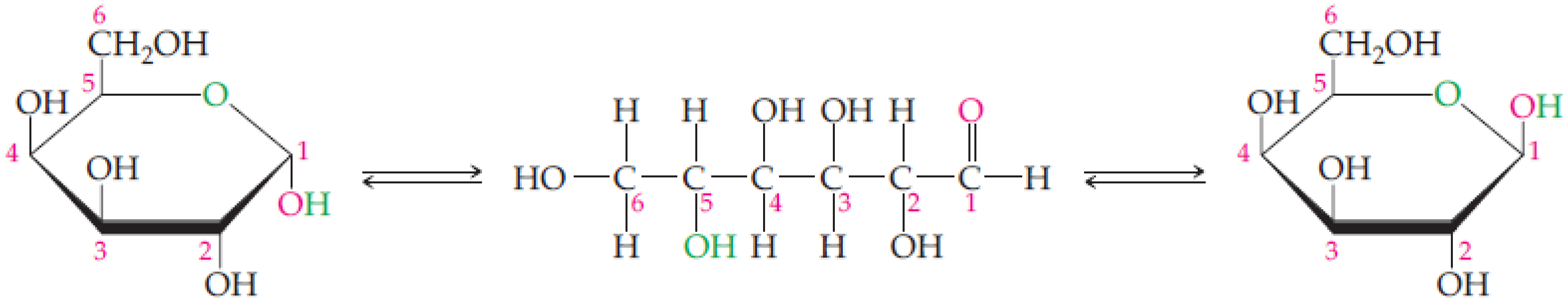


Galactose

- Plant gums and pectins
- A component of the disaccharide lactose (milk sugar)
- Is produced from lactose during digestion.
- Is converted to glucose to provide energy
- Is synthesized from glucose to produce lactose for milk and compounds needed in brain tissue.

Jam with galactose in the pectin that stiffens it

Galactose



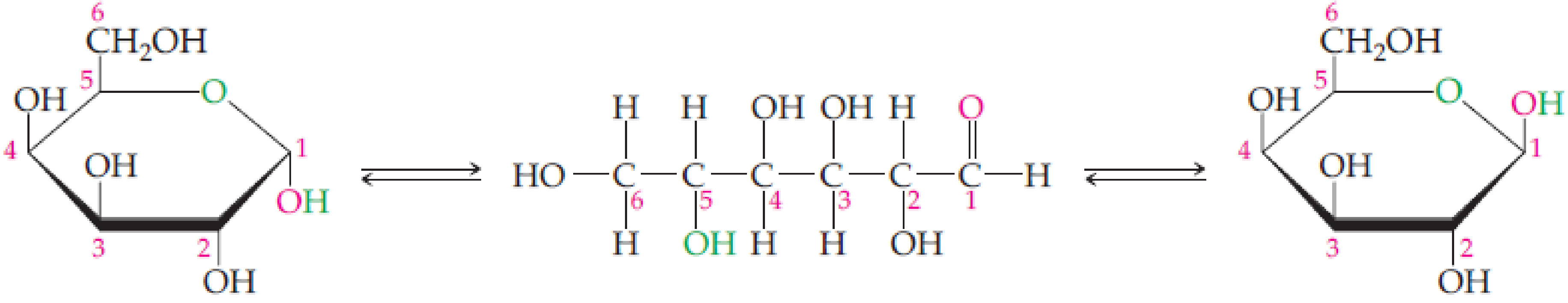
α-D-Galactose Open-chain galactose β-D-Galactose

An aldohexose

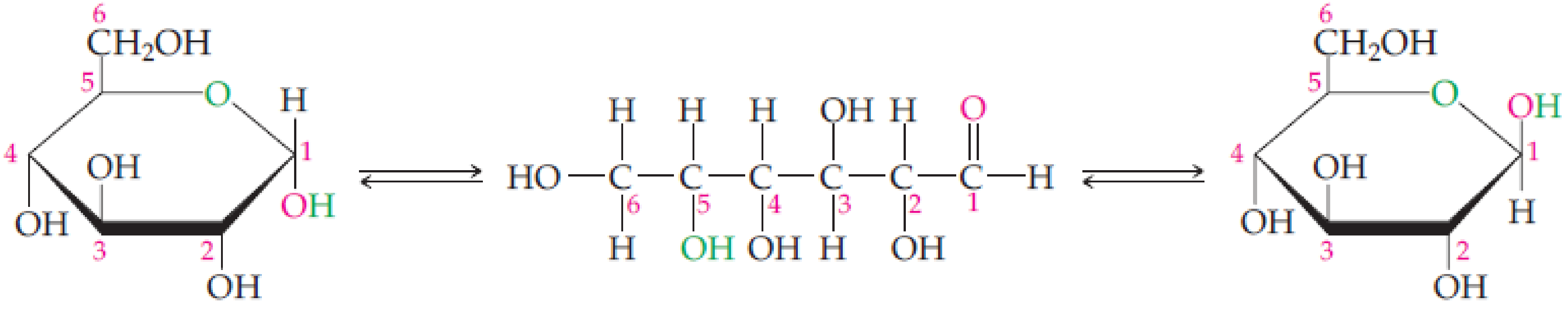
It differs from glucose only in the orientation of the OH group at C4.

Galactose vs Glucose

Galactose



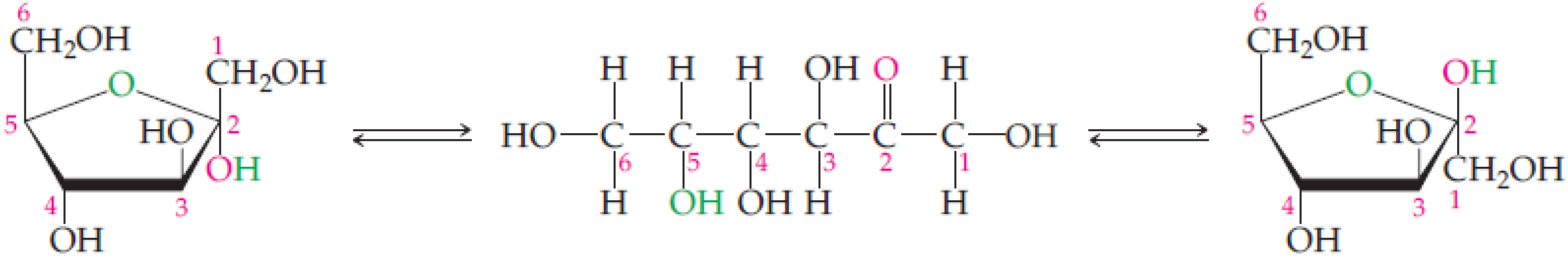
Glucose



Fructose

- D-Fructose, often called levulose or fruit sugar
- honey and many fruits.
- one of the two monosaccharides combined in the disaccharide sucrose.
- Fructose is produced commercially in large quantities by hydrolysis of cornstarch to make high fructose corn syrup (HFCS).

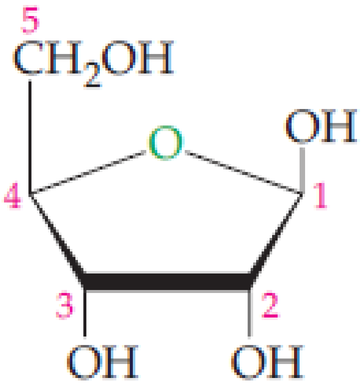
Fructose



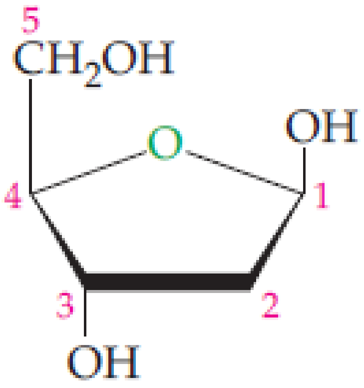
α-D-Fructose Open-chain D-Fructose β-D-Fructose

- Like glucose and galactose, fructose is a 6-carbon sugar.
- A ketohexose
- It forms a five-membered rings in solution

Ribose and 2-Deoxyribose



β-D-Ribose



β-D-2-Deoxyribose

- Both are 5-carbon aldehyde sugars.
- Important as parts of larger biomolecules, such as coenzyme A , ATP, cyclic AMP and in oxidizing and reducing agent coenzymes.
- 2-deoxyribose differs from ribose by the absence of one oxygen atom, that in the OH group at C2.
- Both exist as mixtures of open-chain and cyclic hemiacetal forms.

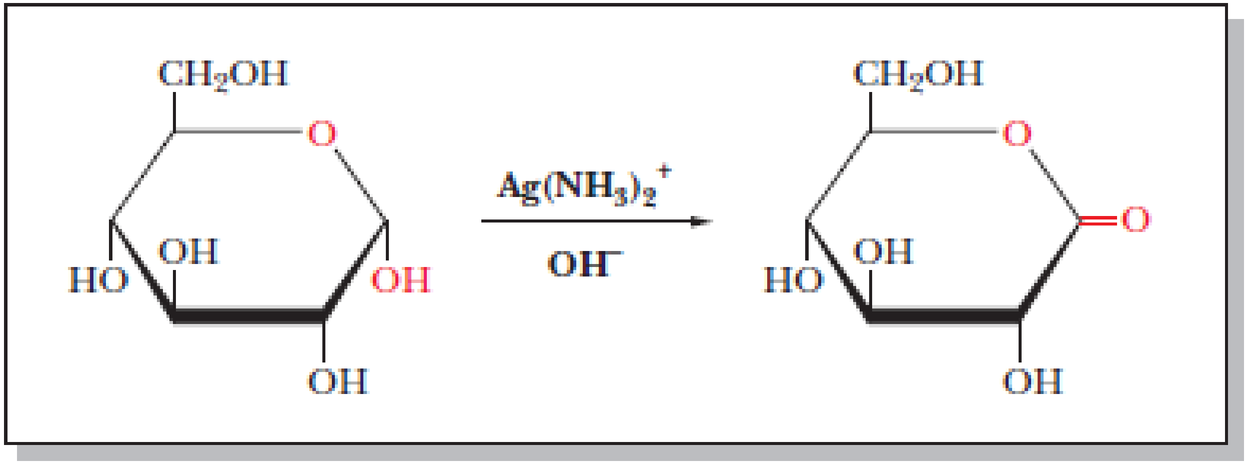
Reactions of Monosaccharides

Oxidation-Reduction Reactions

Oxidation

Aldehyde → Carboxylic acid
Cyclic aldose → Lactone
Ketose → Aldose

Oxidation of a sugar to a lactone



- Carbohydrates that react with oxidizing agents are classified as **reducing sugars (they reduce the oxidizing agent).**

- **Glucose** can be detected **specifically** by the enzyme **glucose oxidase.**

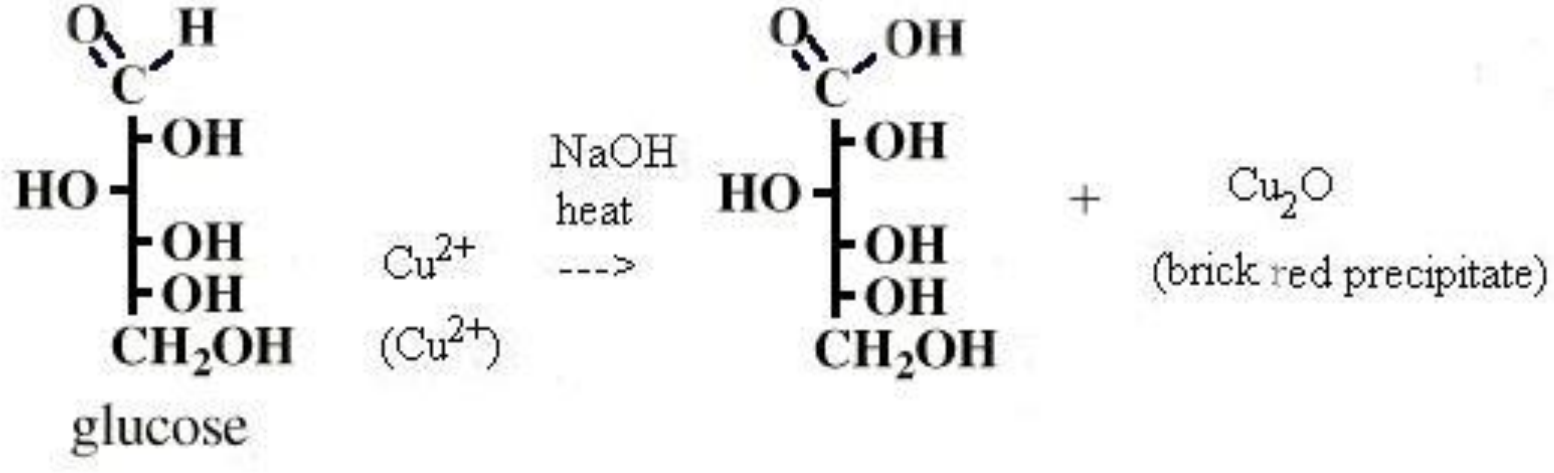
© Thomson Learning/Charles D. Winters

■ FIGURE 16.10 **A silver mirror produced by an aldehyde.** After the addition of Tollens reagent to an aldehyde, a silver mirror has been deposited in the inside of this flask.

Biochemical application on sugar oxidation

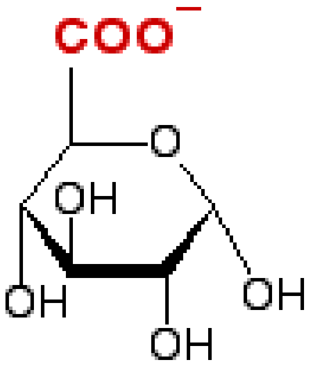
- Vitamin C (ascorbic acid) is an unsaturated lactone.
- Air oxidation of ascorbic acid, followed by hydrolysis of the ester bond, leads to loss of activity as a vitamin.
- A lack of fresh food can cause vitamin C deficiencies, which, in turn, can lead to scurvy

Benedict’s test

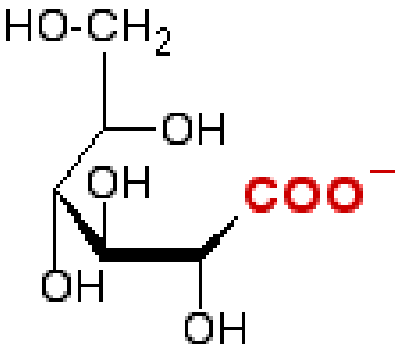


Sugar acids (oxidation)

- Where is it oxidized? What does it form?



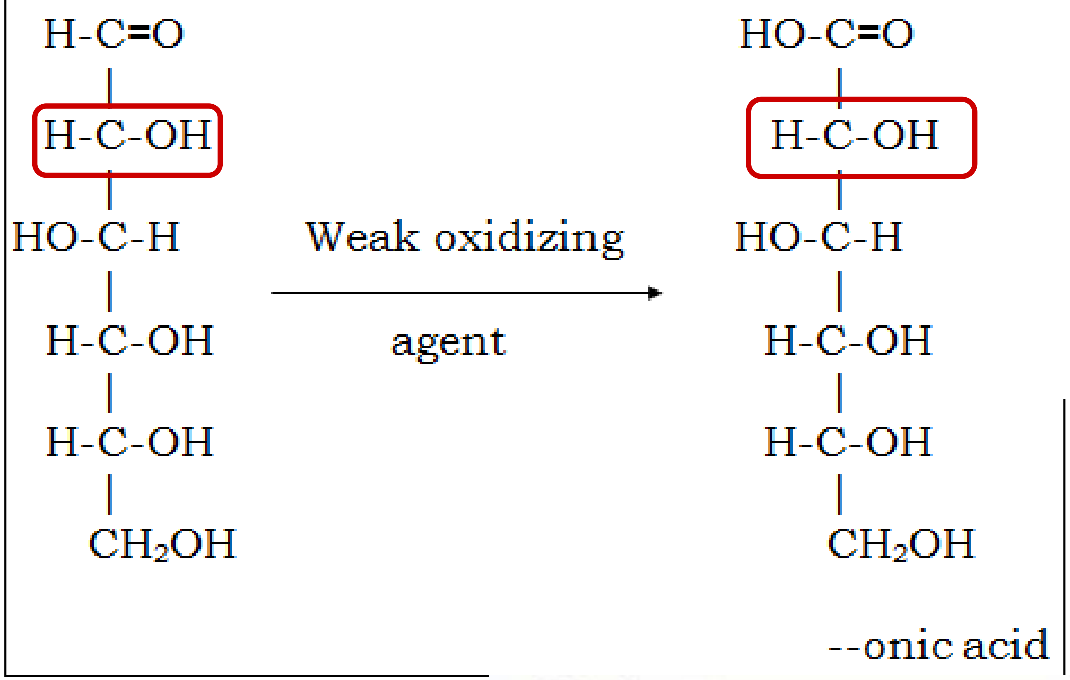
α-D-glucuronate
(D-glucuronic acid, **GlcUA**)
from **oxidation of glucose C6 OH**

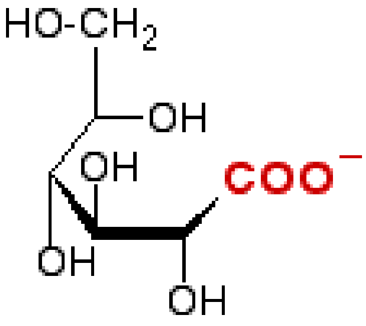


D-gluconate
(D-gluconic acid, **GlcA**)
from **oxidation of glucose C1 aldehyde)**

Example 1

a. Weak oxidizing agent

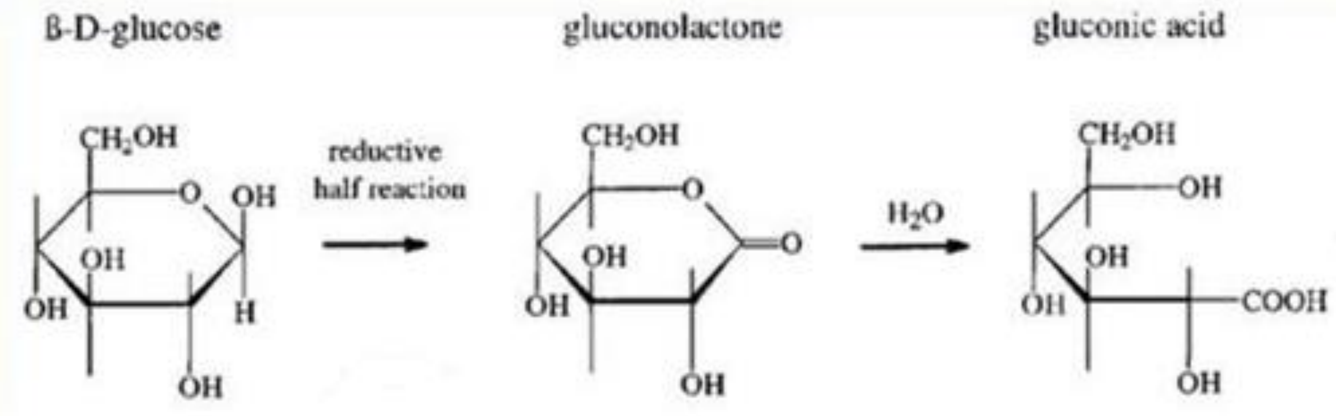




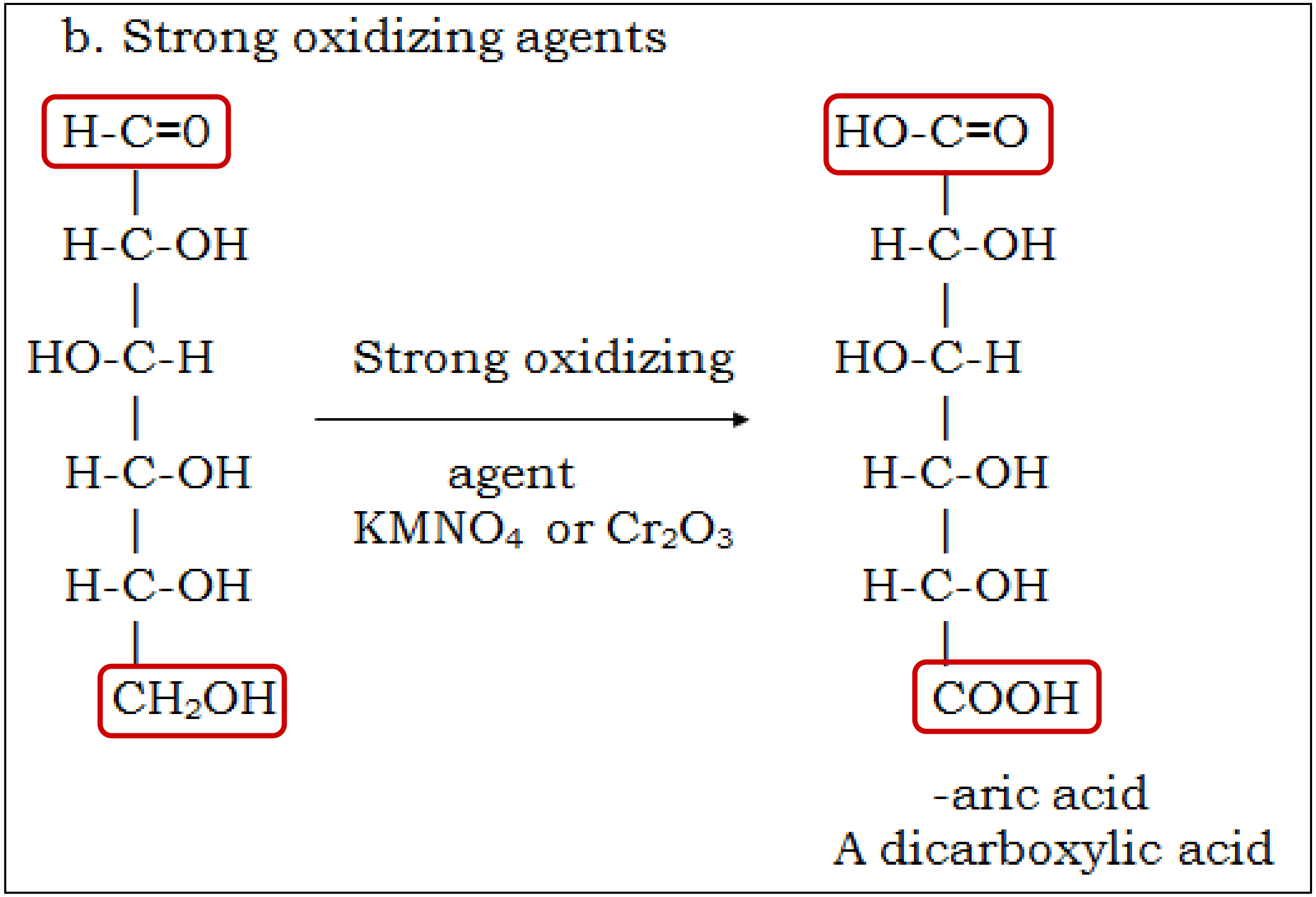
D-gluconate

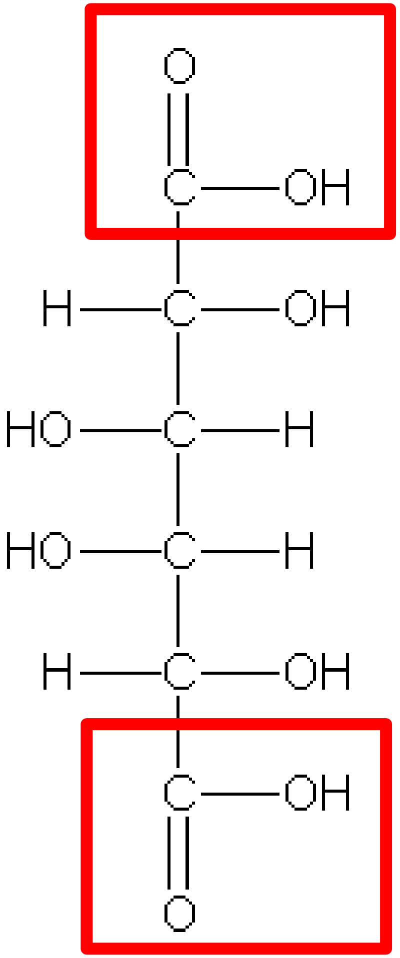
(D-gluconic acid, **GlcA**)

from **oxidation of glucose C1 aldehyde)**



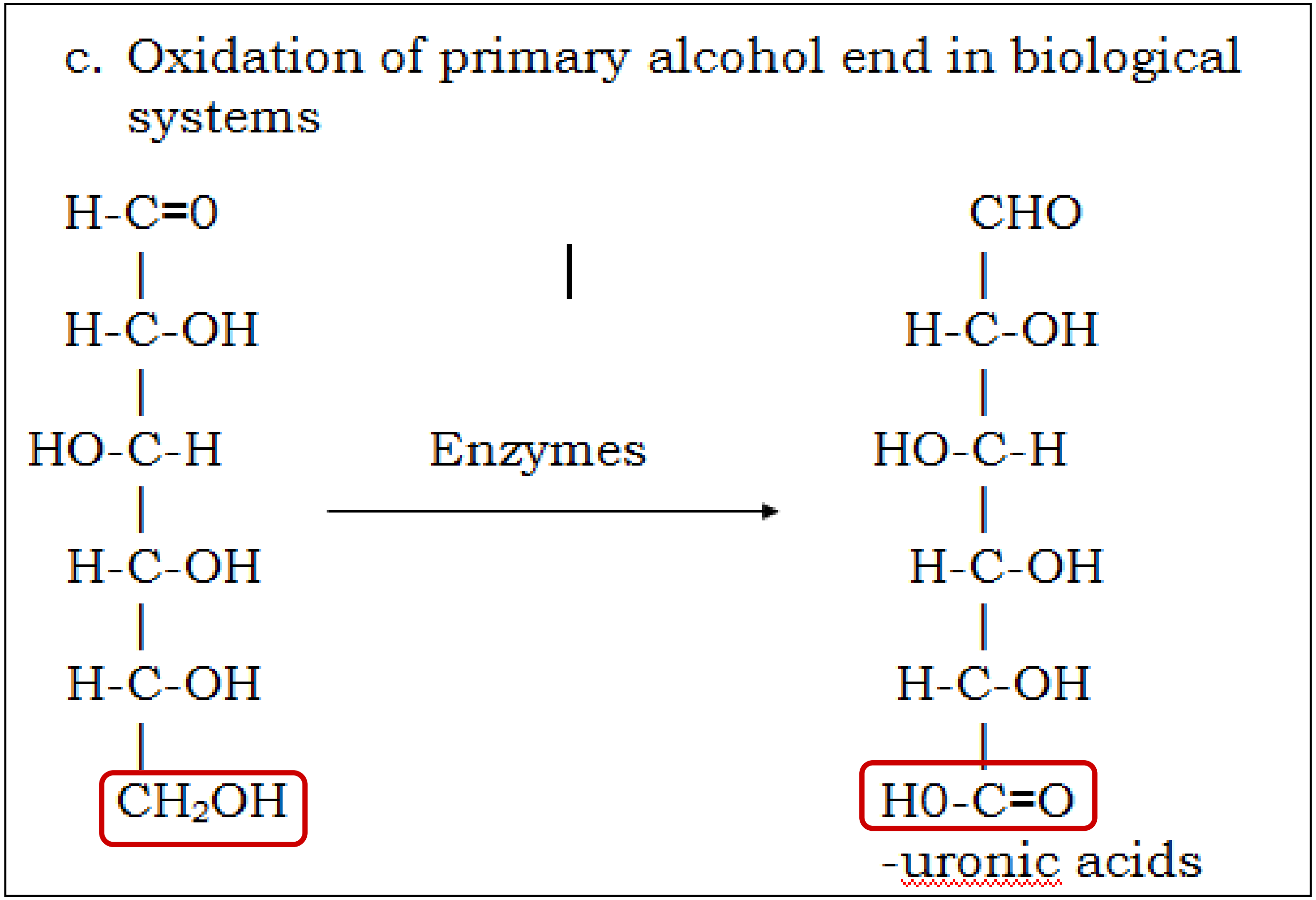
Example 2



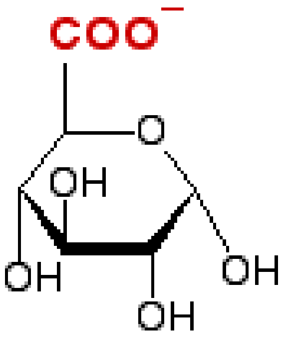


galactaric acid

Example 3



c. Oxidation of primary alcohol end in biological systems



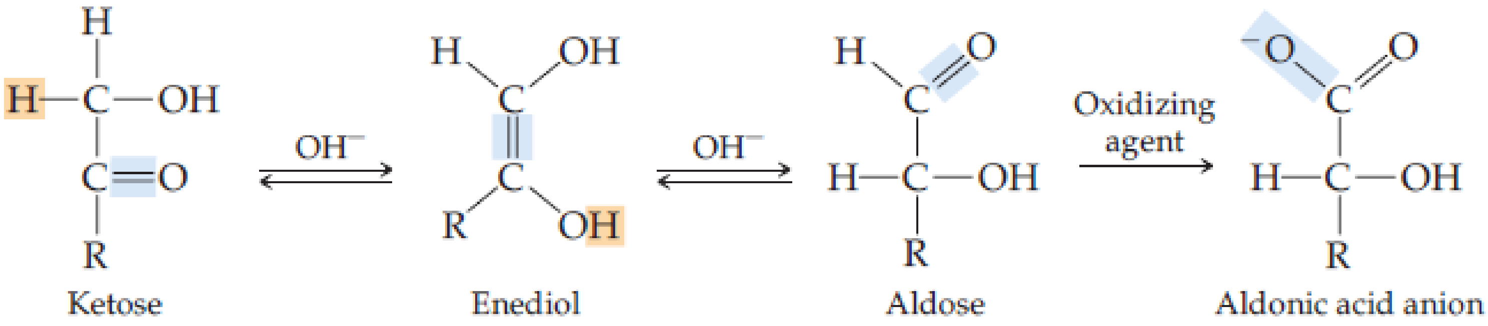
α-D-glucuronate

(D-glucuronic acid, **GlcUA**)

from **oxidation of glucose C6 OH**

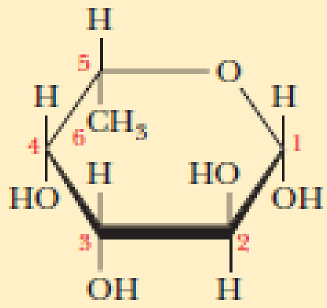
Ketoses can become aldoses

- In basic solution, ketoses are also reducing sugars.
- Rearrangement.

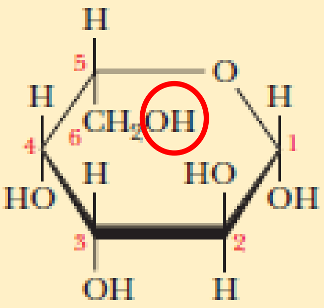


Reduced sugars (deoxy sugars)

L-fucose (L-6-deoxygalactose) is found in the carbohydrate portions of some glycoproteins including the ABO blood-group antigens.

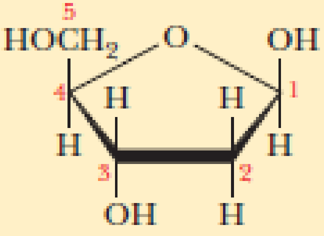


β-L-Fucose
(6-Deoxy-β-L-galactose)

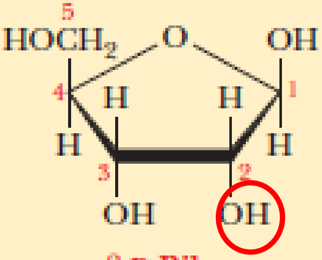


β-L-Galactose

D-2-deoxyribose is found in DNA

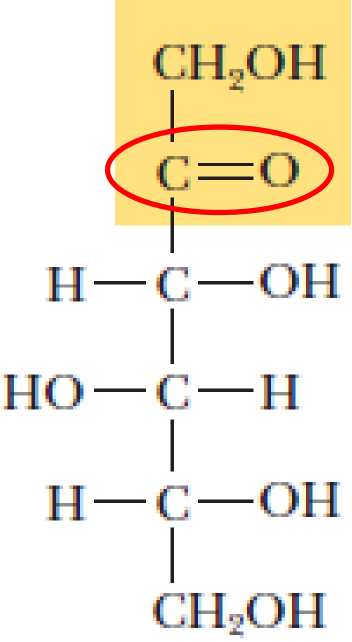


β-D-Deoxyribose
(2-Deoxy-β-D-ribose)

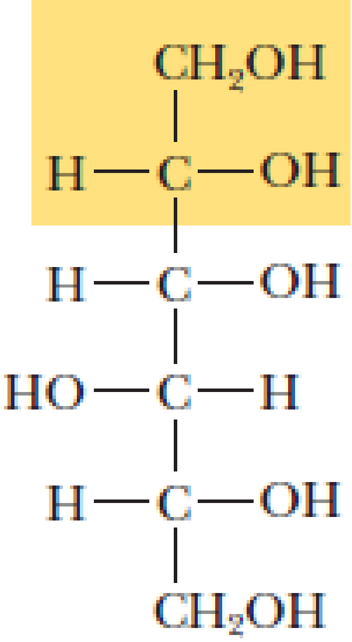


β-D-Ribose

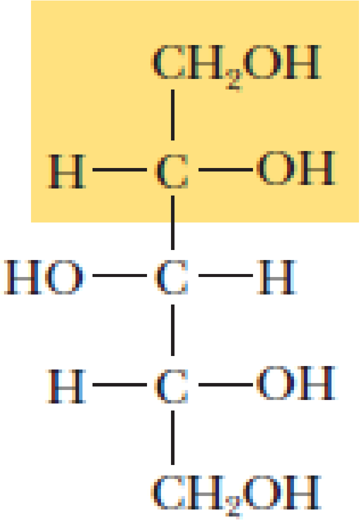
Reduced sugars (polyhydroxy alcohols or alditols)



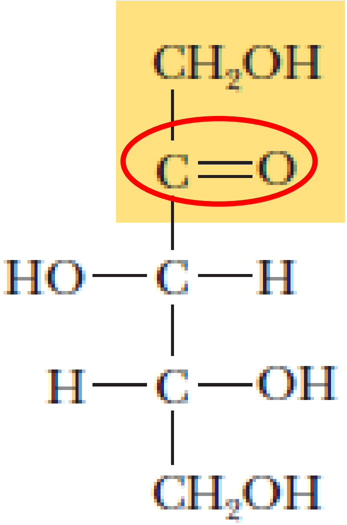
D-Sorbose



D-Sorbitol



D-Xylitol

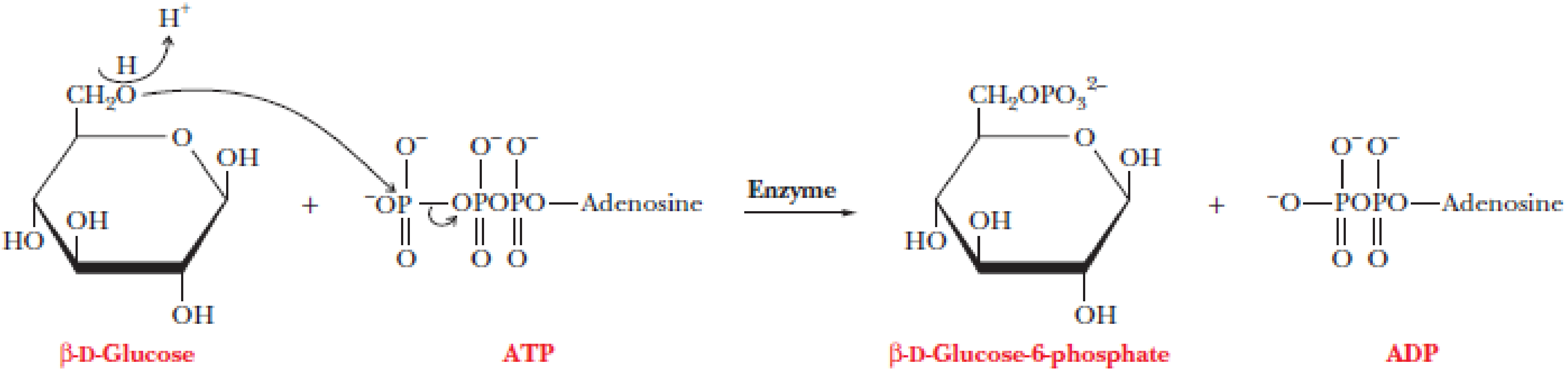


D-Xylulose

Sorbitol and xylitol are used commercially as sweeteners in sugarless chewing gum and candy.

Reactions of Monosaccharides

Esterification of sugars

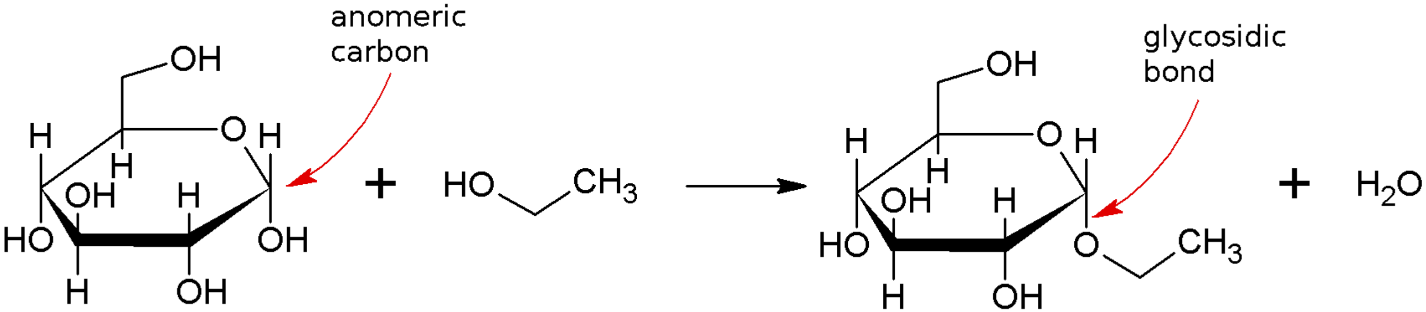


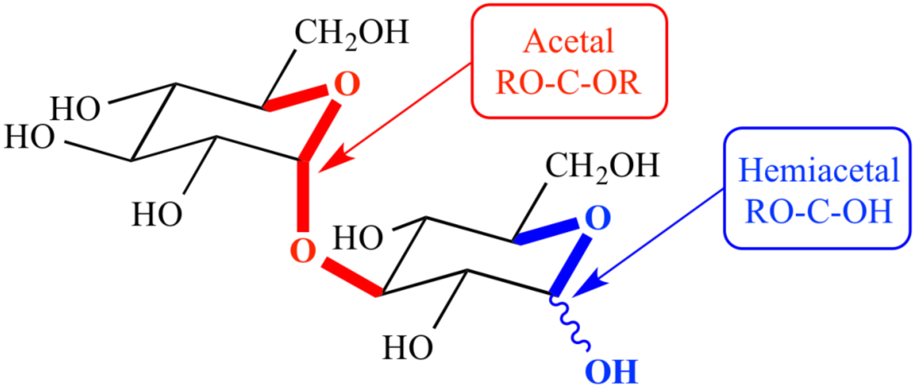
Phosphate esters formation (phosphorylated sugars)

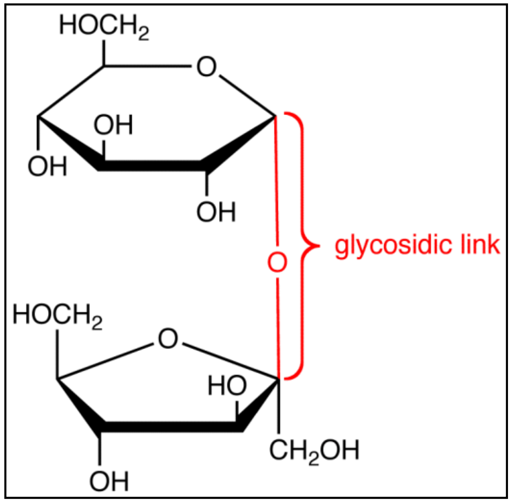
Important for the metabolism of sugars

O-Glycosides

- What is the reacting functional group? Where does it react? What are the end products? Where are they used?

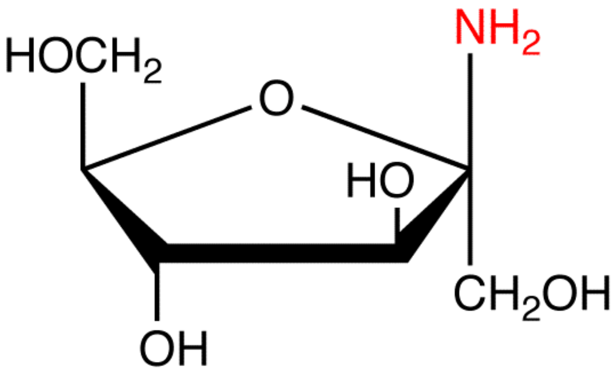




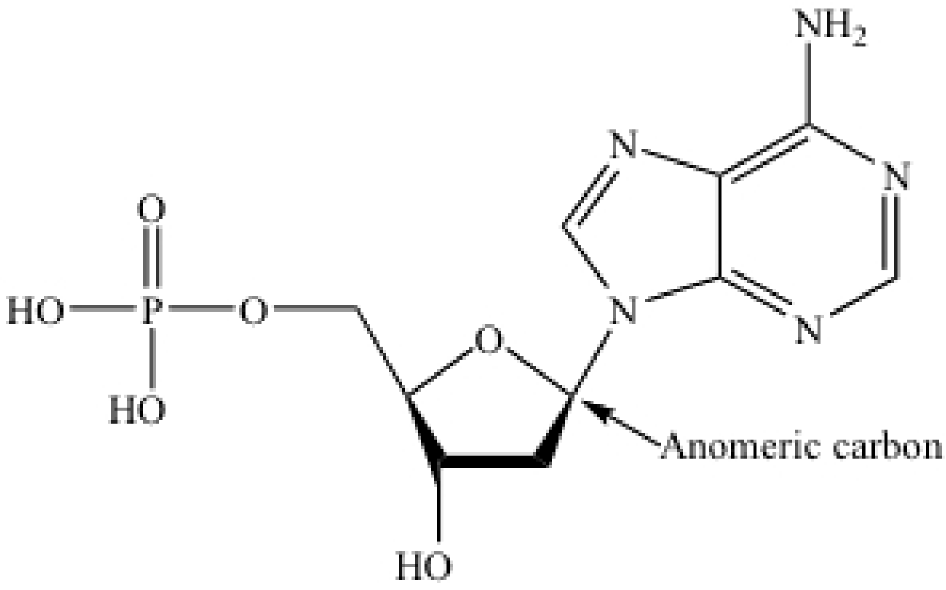


N-glycosides

- What is the reacting functional group? Where does it react? What are the end products? Where are they used?
- Examples: nucleotides (DNA and RNA)

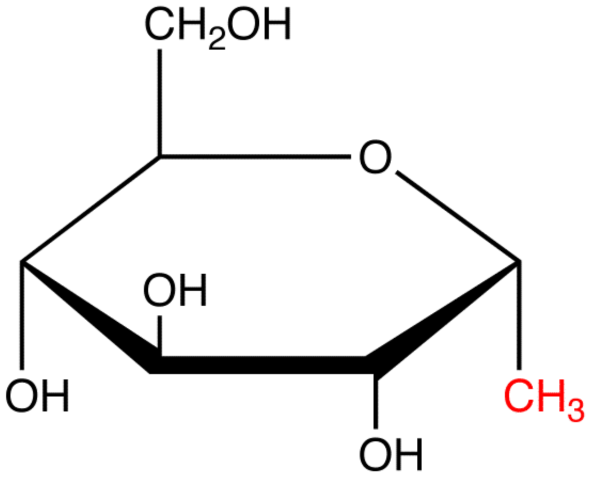


N-glycoside

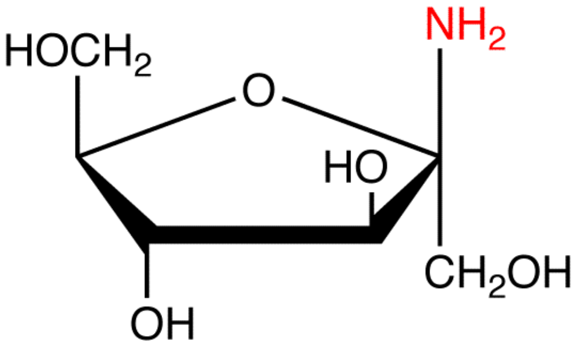


Note

- Glycosides derived from furanoses are called **furanosides**, and those derived from pyranoses are called **pyranosides,** regardless if they are N- or O-linkded.



C-glycoside

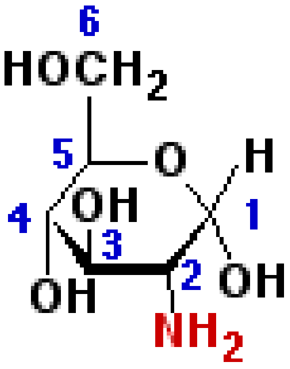


N-glycoside

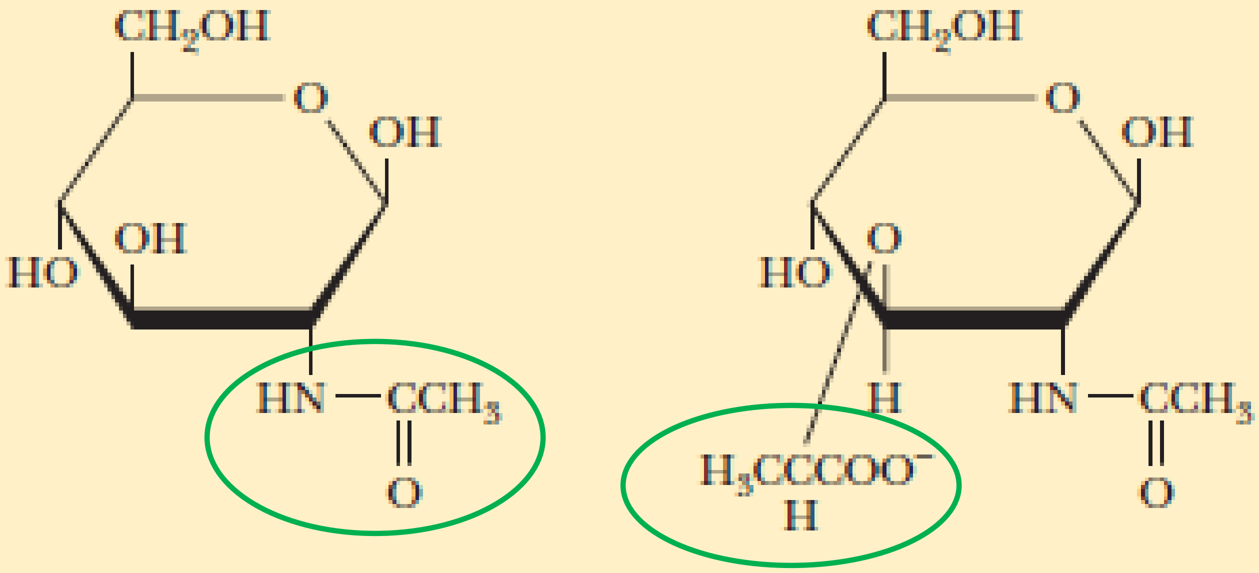
Sugar derivatives

Amino sugars

An amino group (—NH2) or one of its derivatives is substituted for the hydroxyl group of the parent sugar.



α-D-2-glucosamine
(GlcN)



N-Acetyl-β-D-glucosamine

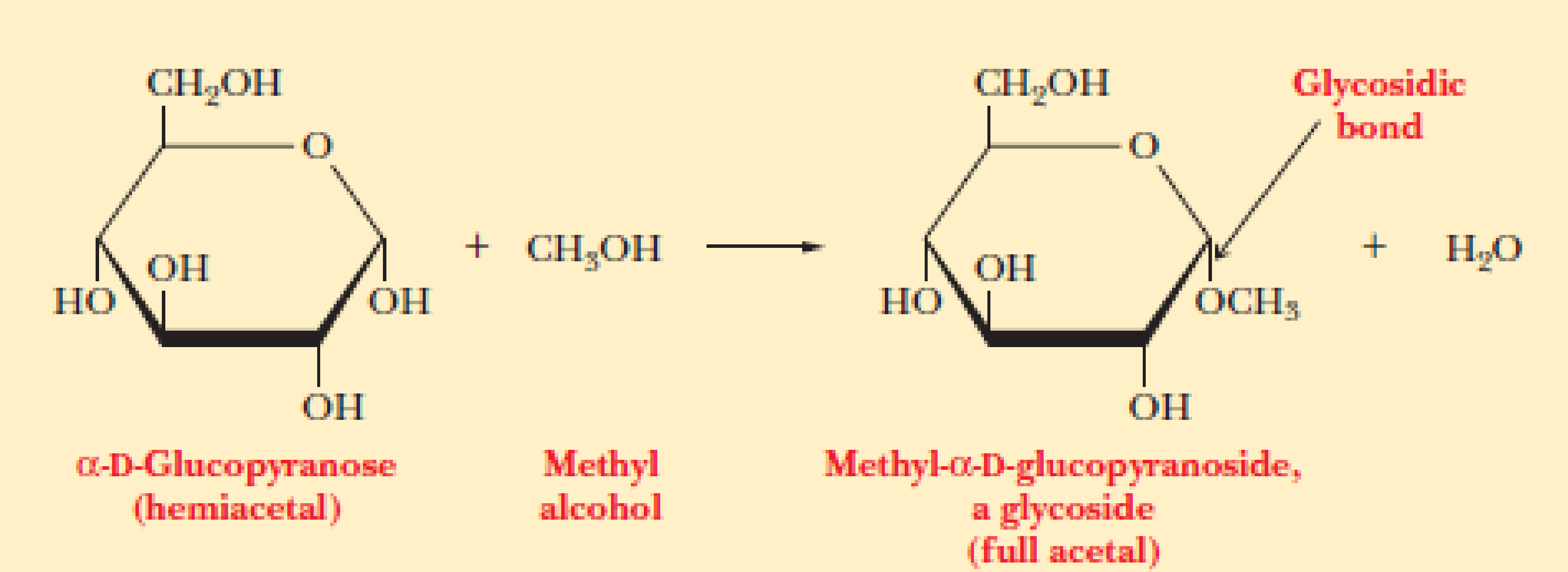
N-Acetylmuramic acid

Components of bacterial cell walls

Reactions of Monosaccharides

Reaction with Alcohols: Glycoside Formation

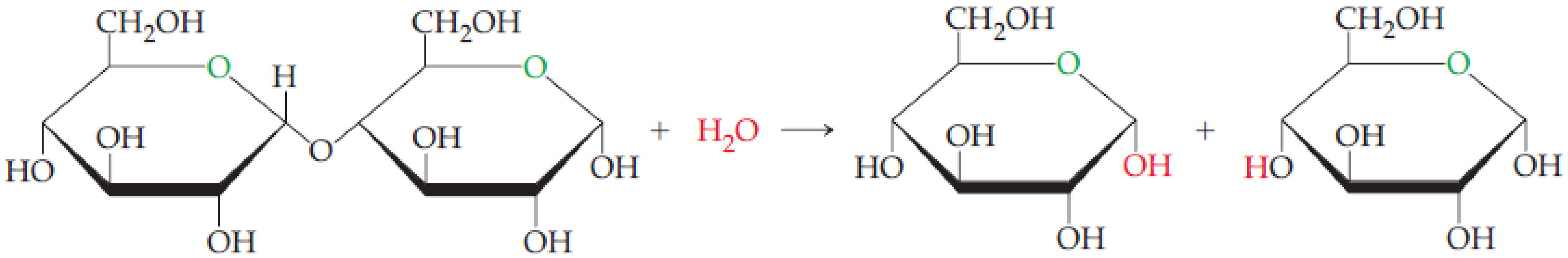
Hemiacetals react with alcohols with the loss of water to yield acetals



- Monosaccharides are cyclic hemiacetals that react with alcohols to form acetals (**glycosides).**
- O-glycosides not N-glycosides
- **Furanosides are** glycosides derived from furanoses**,** and **pyranosides are** glycosides derived from pyranoses**.**

Hydrolysis of a disaccharide

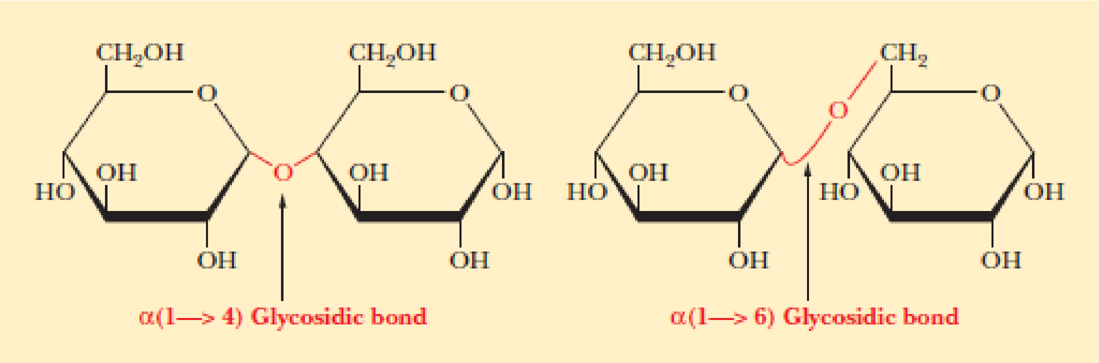
- Hydrolysis reaction takes place during digestion of all carbohydrates.



Reactions of Monosaccharides

Glycosidic bond between monosaccharides

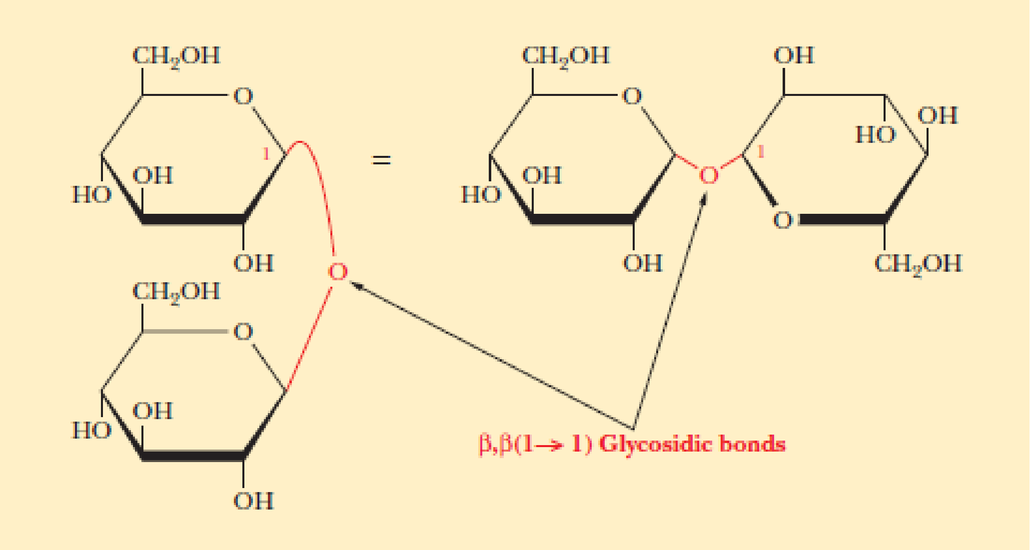
2 glucose molecules



Chemical natures of oligo-and polysaccharides depend on:

Monosaccharides linked together

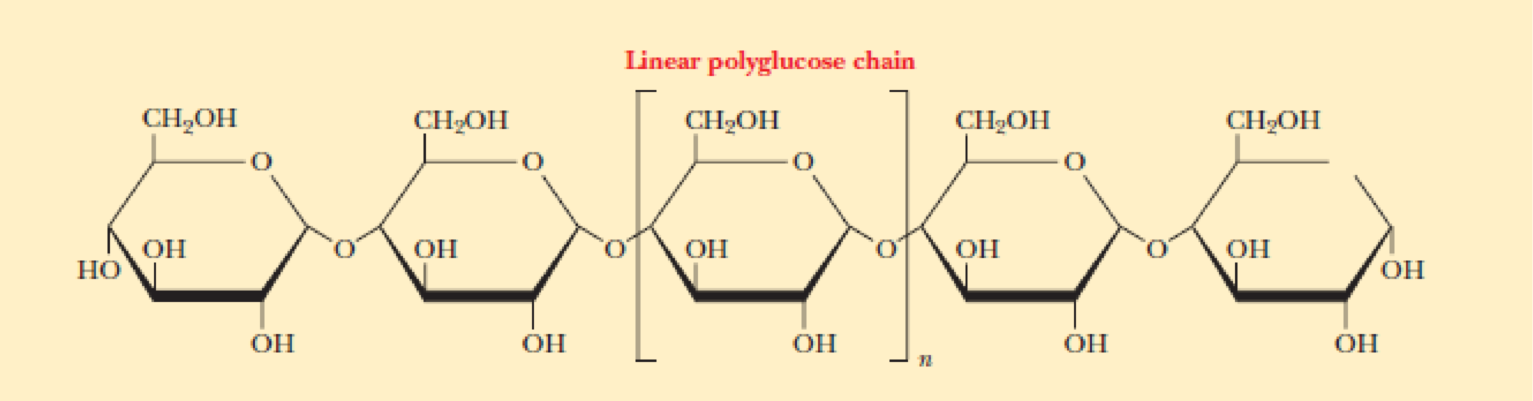
The type of glycosidic bond formed (anomer type and carbons linked)



Linear and branched-chain polymers of α-D-glucose

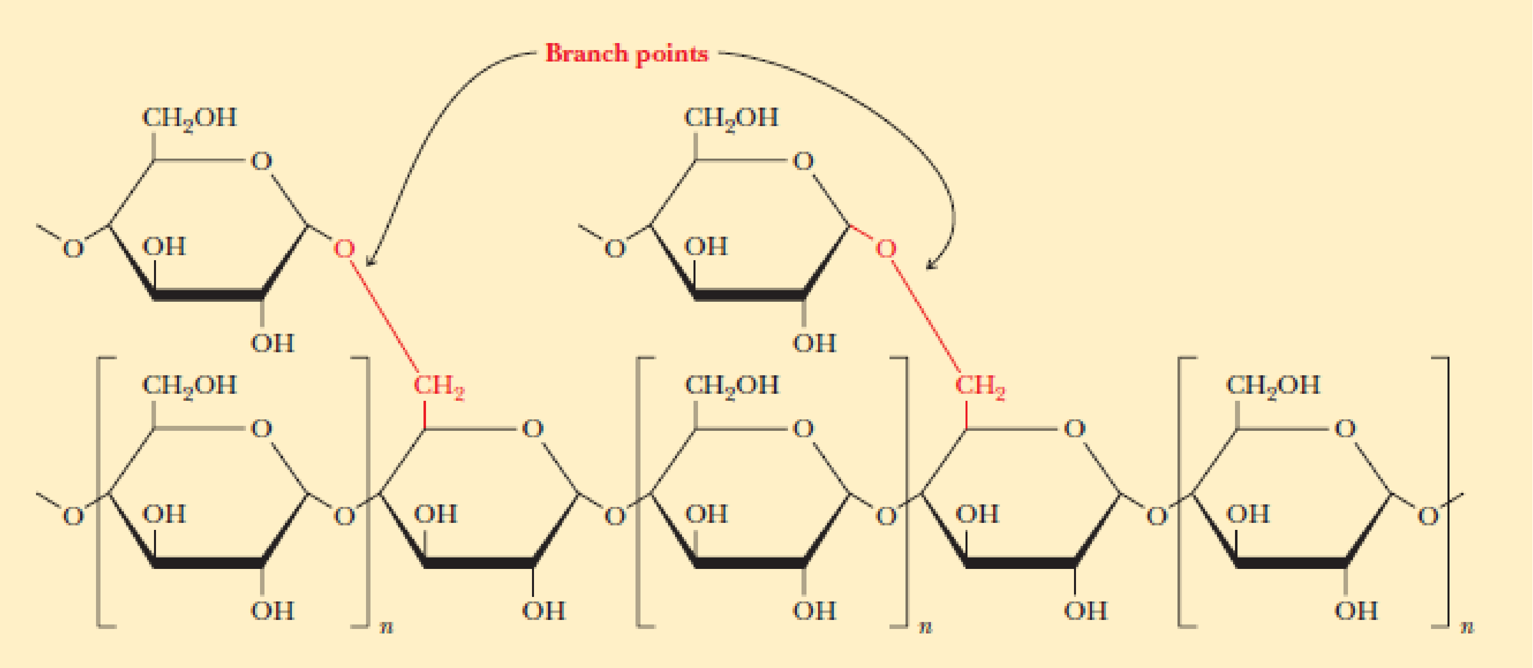
A

The linear polyglucose chain occurs in amylose. All glycosidic bonds are α(1→4).

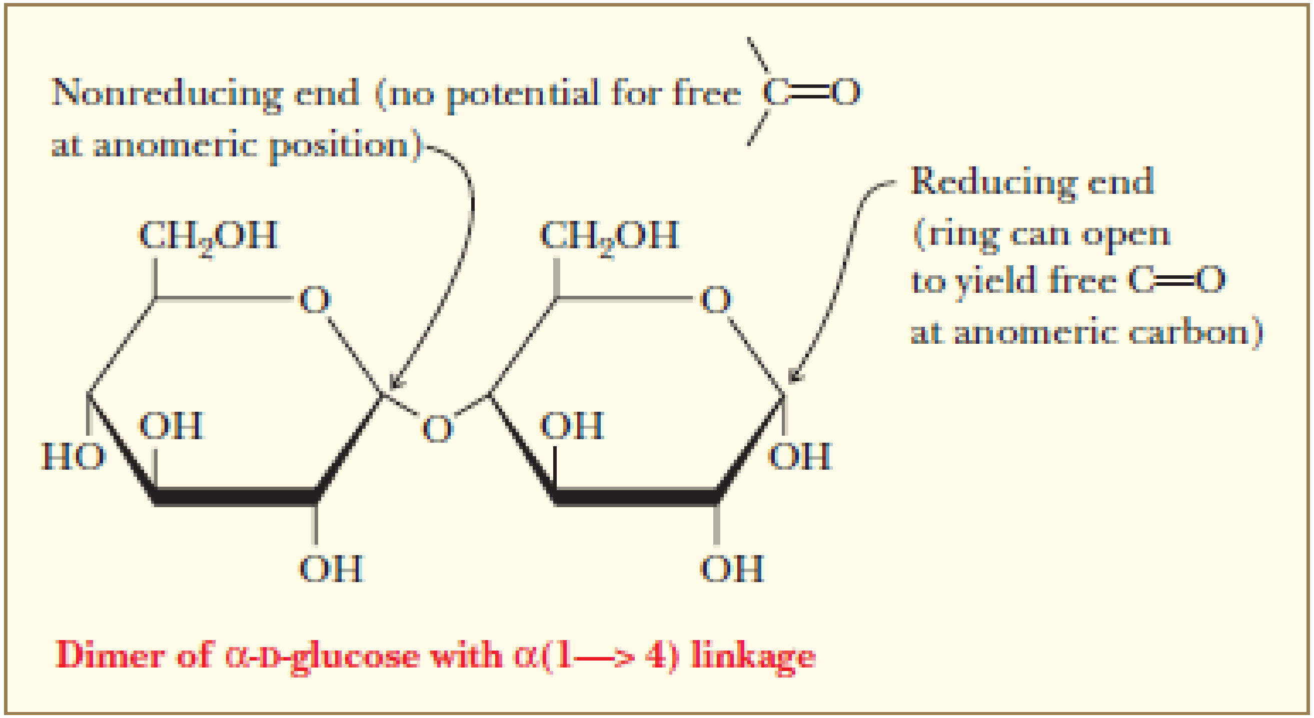


B

The branched-chain polymer occurs in amylopectin and glycogen. Branched-polyglucose-chain glycosidic bonds are α(1→6) at branched points, but all glycosidic bonds along the chain are α(1→4).



Polysaccharides and reducing sugars



Nonreducing end (no potential for free C=O at anomeric position)

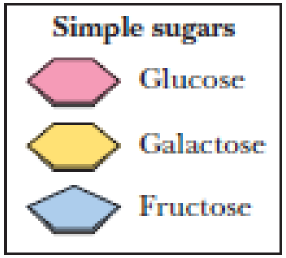
Reducing end (ring can open to yield free C=O at anomeric carbon)

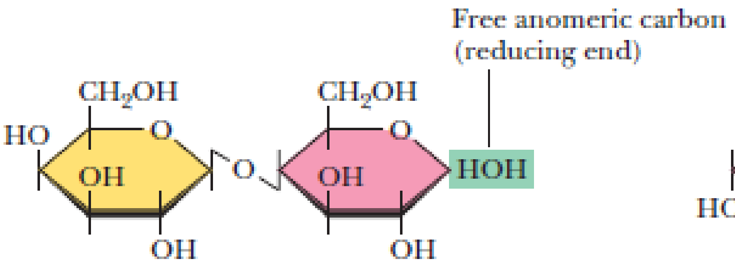
Dimer of α-D-glucose with α(1—> 4) linkage

FIGURE 16.17 **Reducing sugars.** A disaccharide with a free hemiacetal end is a reducing sugar because of the presence of a free anomeric aldehyde carbonyl or potential aldehyde group.

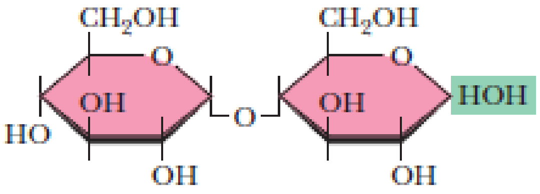
Oligosaccharides

Disaccharides are Oligosaccharides

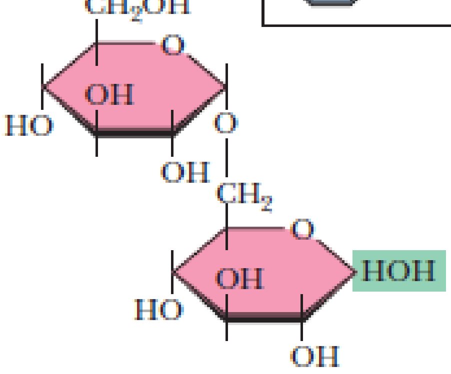


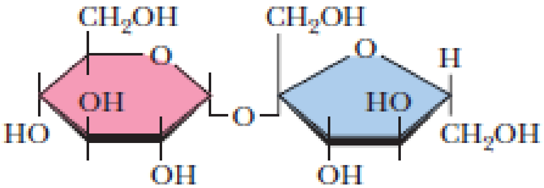


Lactose (galactose-β-1,4-glucose)

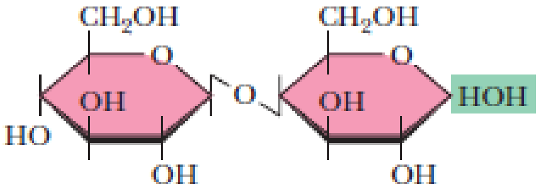


Maltose (glucose-α-1,4-glucose)





Sucrose (glucose-α-1,2-fructose)



Cellobiose (glucose-β-1,4-glucose)

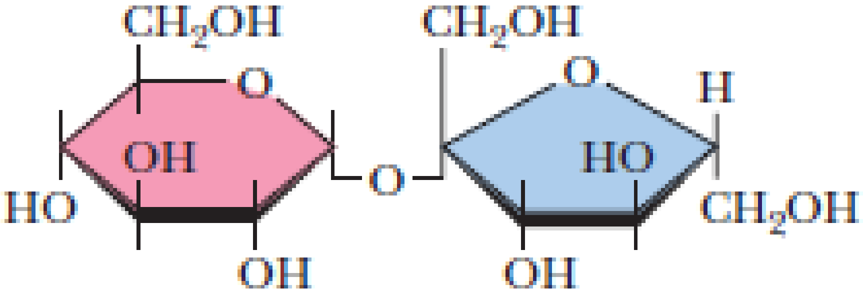
Isomaltose (glucose-α-1,6-glucose)

Distinctions of disaccharides

- The 2 specific sugar monomers involved and their stereoconfigurations (D- or L-)
- The carbons involved in the linkage (C-1, C-2, C-4, or C-6)
- The order of the two monomer units, if different (example: galactose followed by glucose)
- The anomeric configuration of the OH group on carbon 1 of each residue (α or β)

Sucrose

- **Common table sugar, cane sugar, beet sugar**
- Hydrolysis of sucrose yields one molecule of D-glucose and one molecule of D-fructose.
- The 50:50 mixture of glucose and fructose (invert sugar) is sweeter than sucrose and is used as a food additive.



Sucrose (glucose-α-1,2-fructose)

- No hemiacetal group because a 1,2 link joins both anomeric carbon atoms.
- Sucrose is not reducing because it does not have a hemiacetal group
- Sucrose is the only common disaccharide that is not a reducing sugar.

Biochemical Application: Synthetic sugars and sweetness

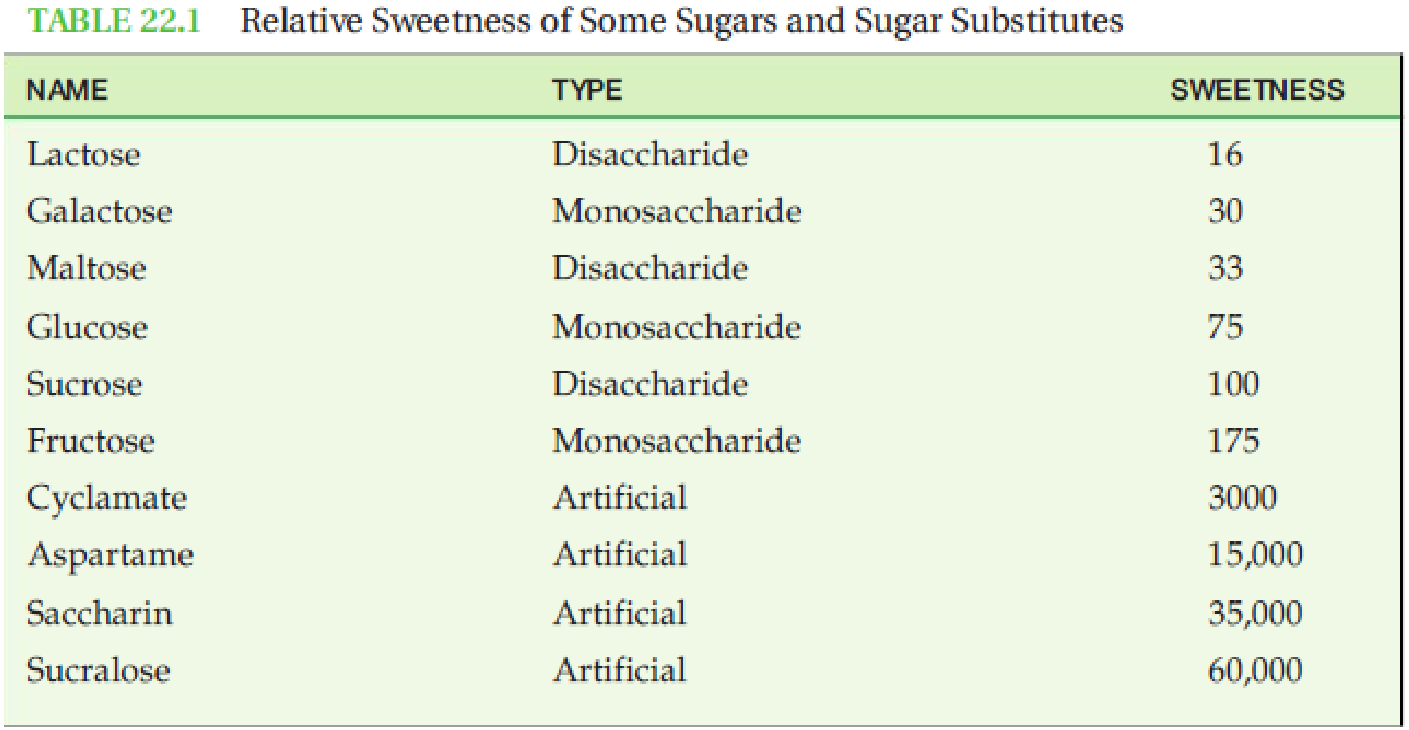
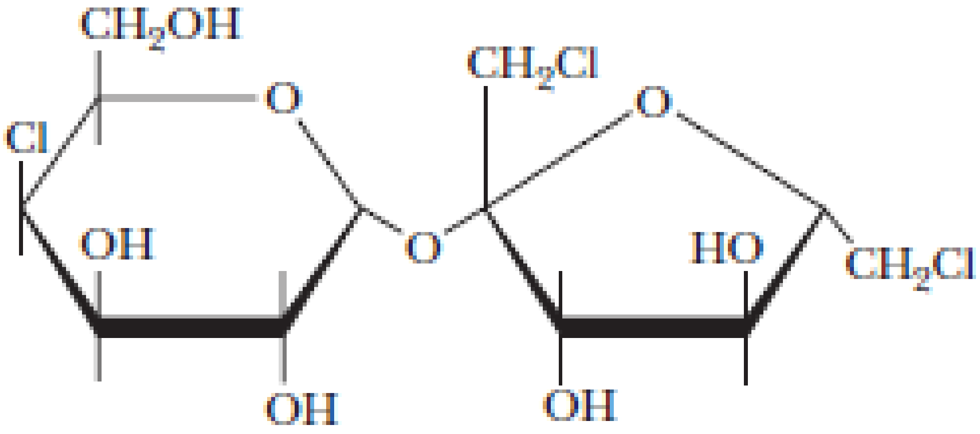


TABLE 22.1 Relative Sweetness of Some Sugars and Sugar Substitutes

NAME	TYPE	SWEETNESS
Lactose	Disaccharide	16
Galactose	Monosaccharide	30
Maltose	Disaccharide	33
Glucose	Monosaccharide	75
Sucrose	Disaccharide	100
Fructose	Monosaccharide	175
Cyclamate	Artificial	3000
Aspartame	Artificial	15,000
Saccharin	Artificial	35,000
Sucralose	Artificial	60,000

Biochemical application: Sucralose

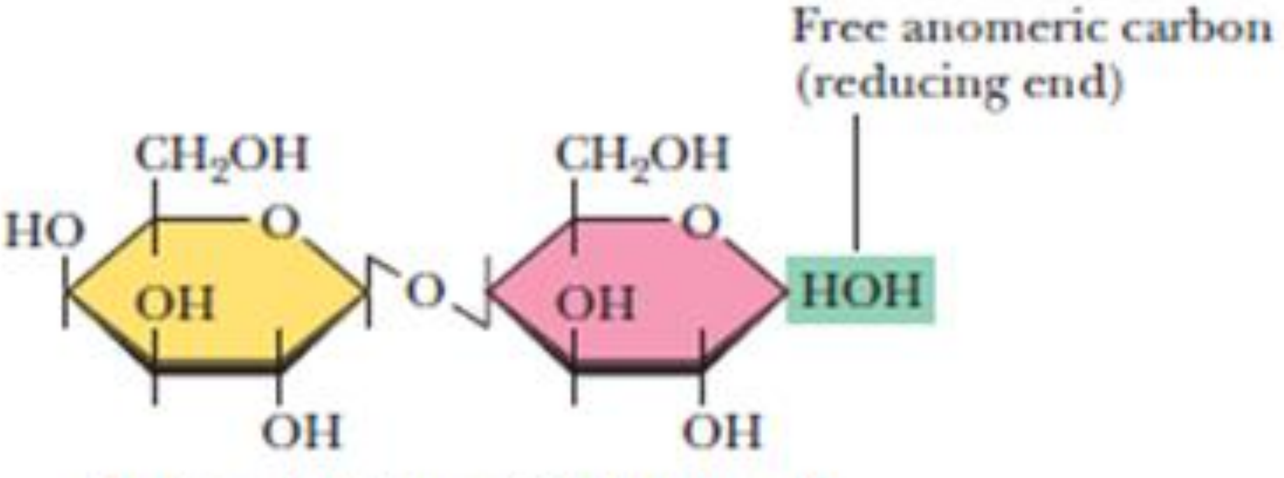


Sucralose

FIGURE 16.20 **The structure of sucralose.** Note that sucralose (marketed under the trade name Splenda) differs from sucrose in the substitution of chlorine for three hydroxyls.

Lactose (milk sugar)

- Human milk is about 7% lactose.
- A disaccharide of β-D-galactose and either α or β-D-glucose.
- The two monosaccharides are connected by a β-1,4 link.
- A reducing sugar because the glucose ring (on the right) is a hemiacetal at C1.



Lactose (galactose-β-1,4-glucose)

Clinical hint-Lactose intolerance

© Thomson Learning/ Charles D. Winters

■ **Dairy substitutes for the lactose intolerant.** These products help those with lactose intolerance meet their calcium needs.

- Is prevalent in adults in all populations.
- Due to lactase enzyme deficiency.
- Because lactose remains in the intestines rather than being absorbed, it raises the osmolarity, which draws in excess water.
- Intestinal bacteria ferment lactose to produce lactate, carbon dioxide, hydrogen gas, and methane resulting in bloating, cramps, and diarrhea.
- Lactose free food, the use of commercial enzyme preparations and Lactaid, milk that has been treated with lactase to reduce its lactose content

Clinical application

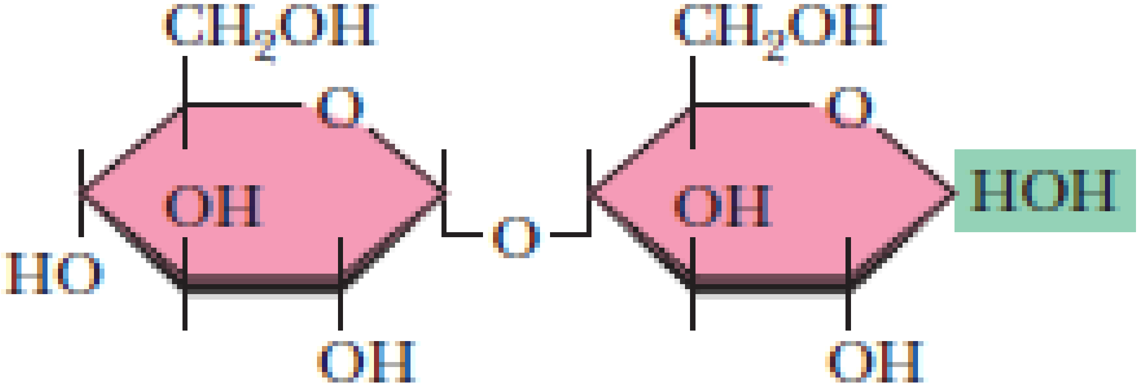
- Galactosemia: Missing a galactose-metabolizing enzyme can result in galactosemia where nonmetabolized galactose accumulates within cells and is converted to the hydroxy sugar galactitol, which cannot escape cells. Water is drawn into cells and the swelling causes cell damage, particularly in the brain, resulting in severe and irreversible retardation. It also causes cataract.

Maltose (Malt sugar)

- Present in fermenting grains
- Can be prepared by enzyme-catalyzed degradation of starch.
- Used in prepared foods as a sweetener.
- Produced during starch digestion by α-amylase in the small intestine
- Hydrolyzed to glucose by maltase.

Maltose

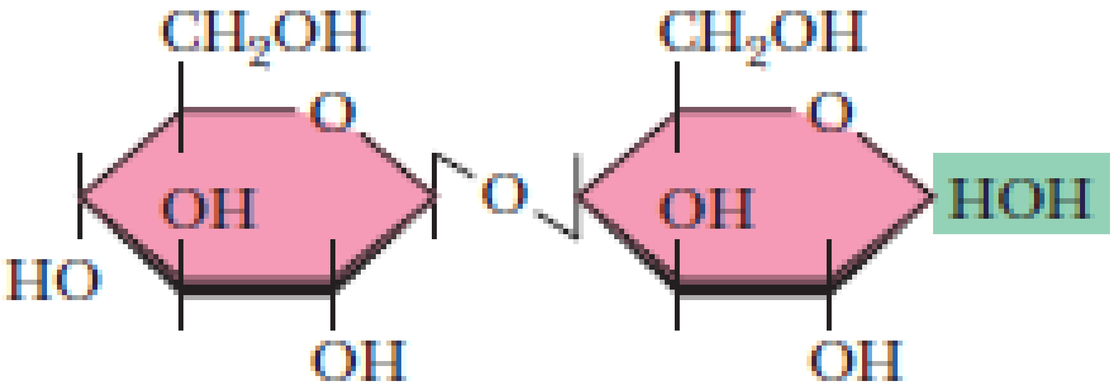
- Two -D-glucose molecules are joined in maltose by an **α-1,4 link**
- It is both an acetal (at C1 in the left-side glucose) and a hemiacetal (at C1 in the right-side glucose).
- The hemiacetal group on the right can react with an oxidizing agent, thus maltose can be a reducing sugar.



Maltose (glucose-α-1,4-glucose)

Cellobiose

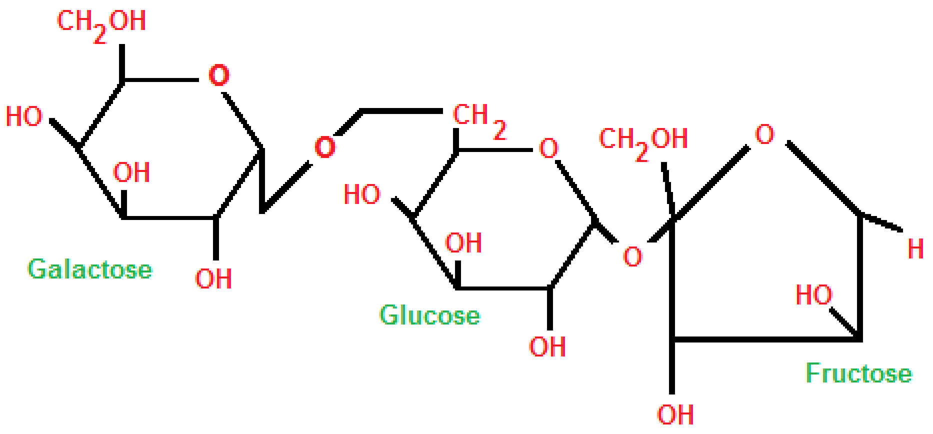
- A disaccharide that is obtained from the hydrolysis of cellulose
- Two -D-glucose molecules are joined by a **<u>β-1,4 link</u>**
- It is both an acetal (at C1 in the left-side glucose) and a hemiacetal (at C1 in the right-side glucose).
- The hemiacetal group on the right can react with an oxidizing agent, thus maltose can be a reducing sugar.



Cellobiose (glucose-β-1,4-glucose)

Oligosaccharides: Raffinose

- What are oligosaccharide?
- Example: raffinose
- It is found in Found in beans and vegetables like cabbage, brussel, sprouts, broccoli, asparagus.



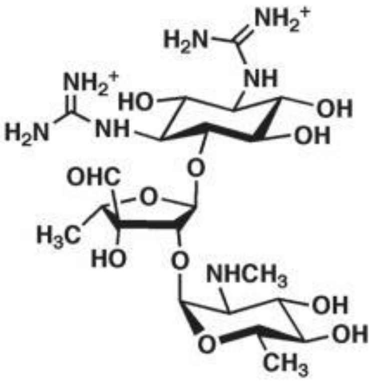
Humans lack the alpha-galactosidase enzyme that is needed to break down raffinose, but intestinal bacteria can ferment it into hydrogen, methane, and other gases.

Homework

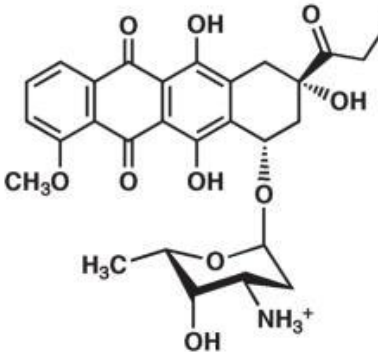
1. Recognize the monosaccharides that make up raffinose.
2. What is the monosaccharide that is attached to *what* disaccharide?

Oligosaccharides as drugs

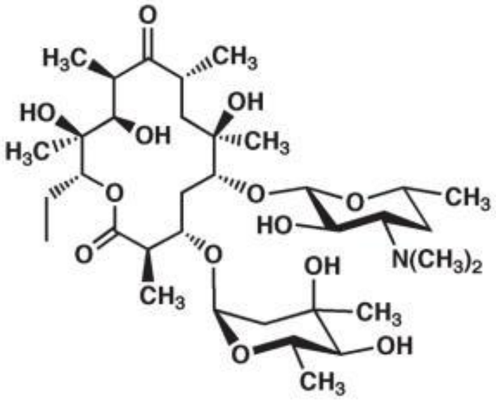
- Streptomycin and erythromycin (antibiotics)
- Doxorubicin (cancer chemotherapy)
- Digoxin (cardiovascular disease)



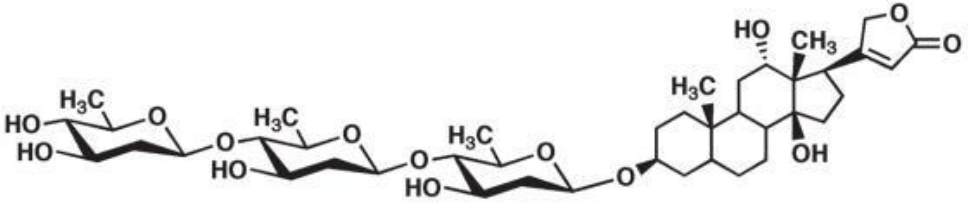
Streptomycin



Doxorubicin



Erythromycin A

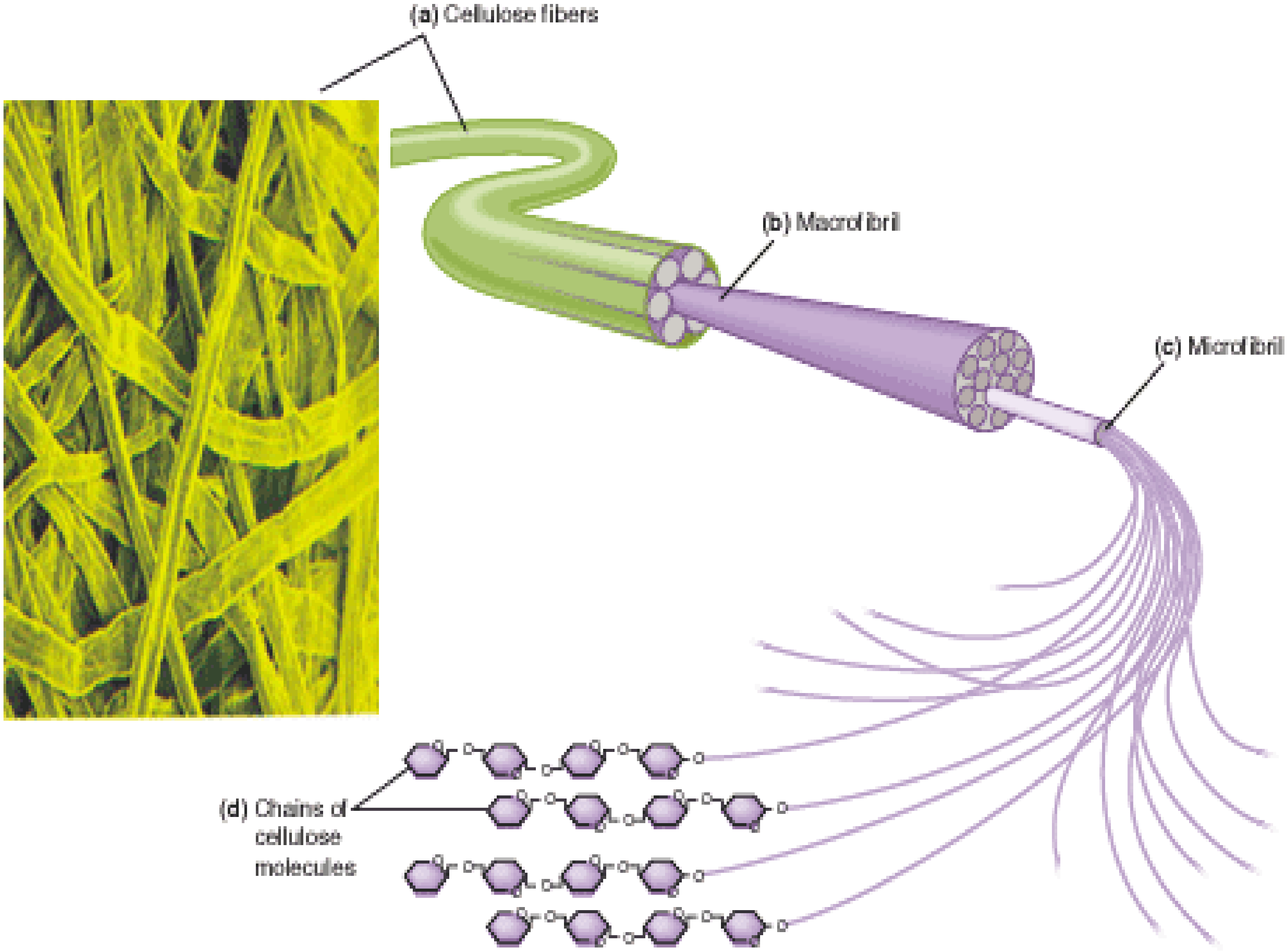


Digoxin

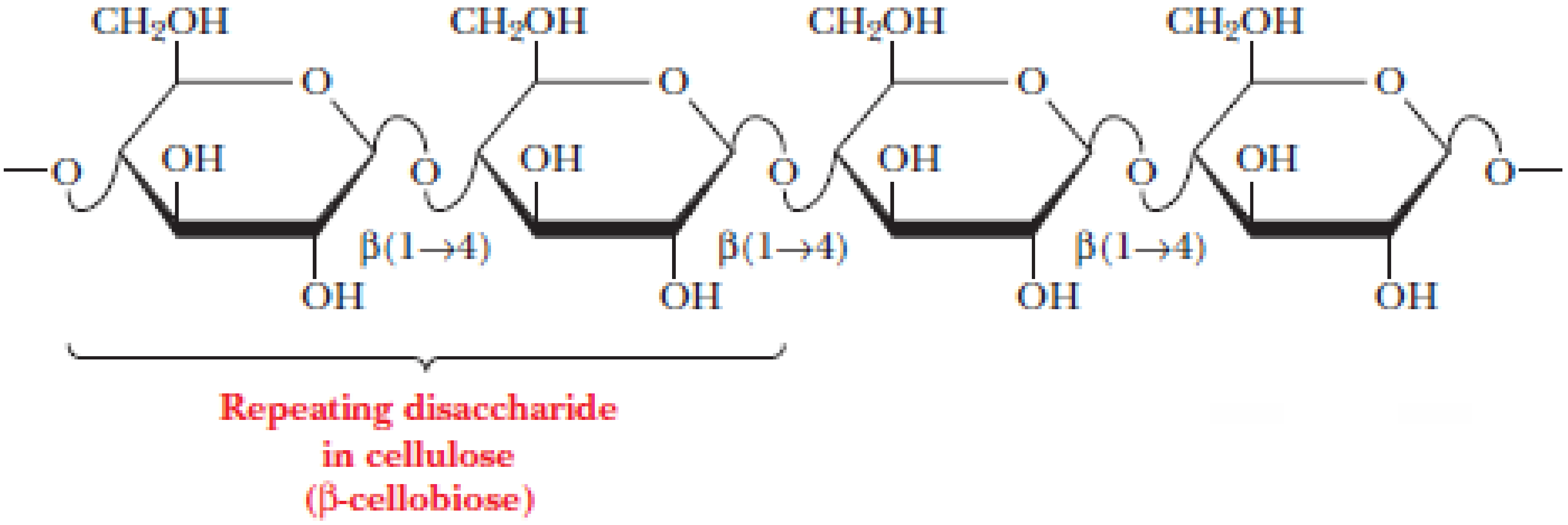
Polysaccharides

- Homopolysaccharide: a polymer that consists of only one type of monosaccharide
- Heteropolysaccharide a polymer that consists of more than one type of monosaccharide
- Glucose is the most common monomer

Cellulose

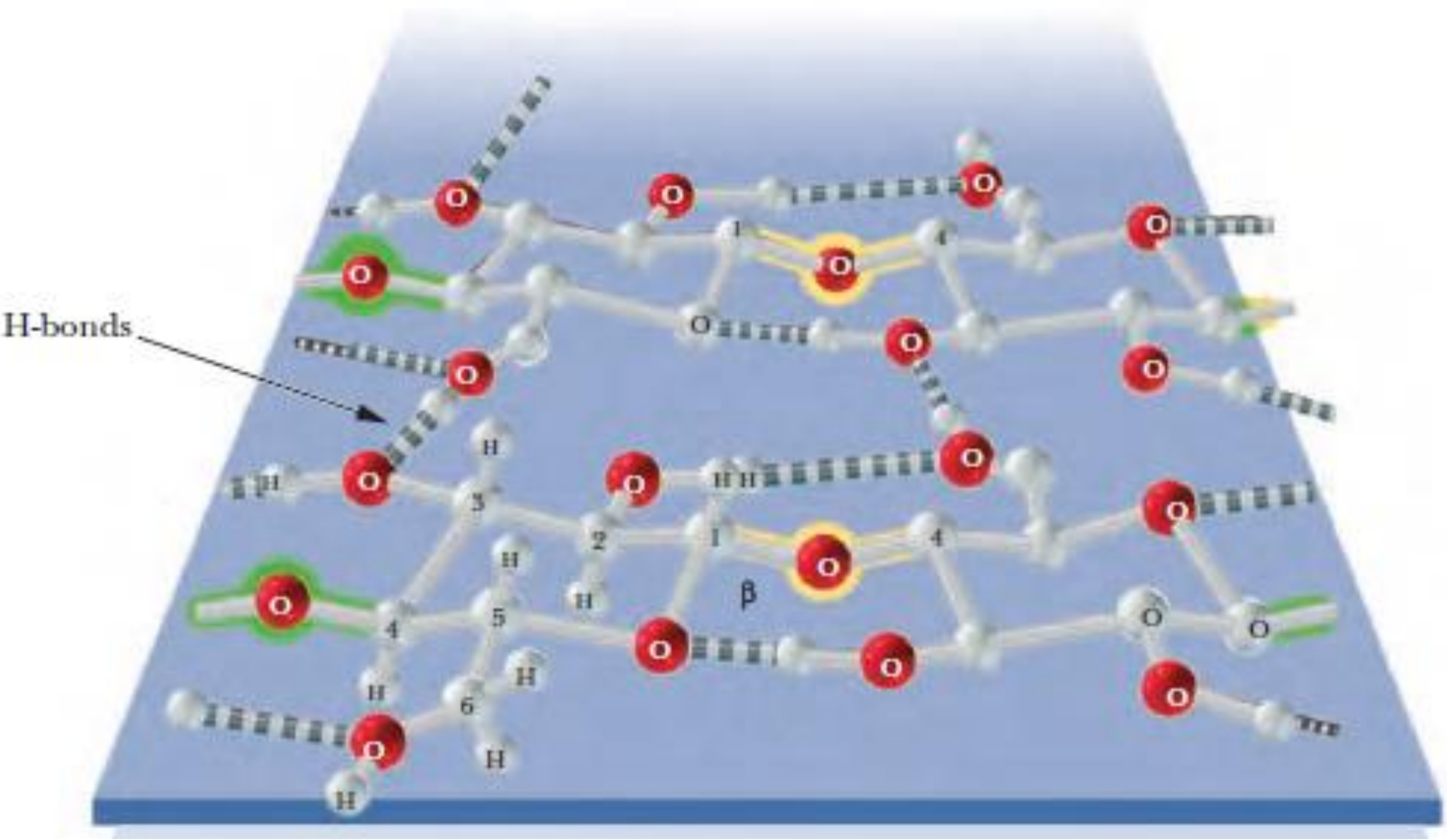

(a) Cellulose fibers
(b) Macrofibril
(c) Microfibril
(d) Chains of cellulose molecules

Cellulose



- Animals lack cellulases enzymes that hydrolyze cellulose to glucose.
- Cellulases are found in the bacteria that inhabit the digestive tracts of insects and grazing animals, such as cattle and horses.

H-bonds in cellulose



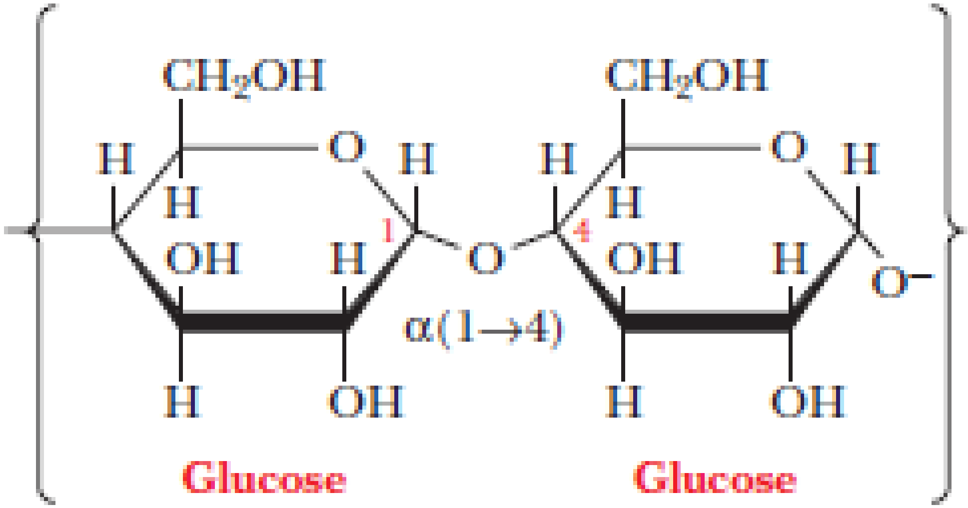
Application: Fibers and health

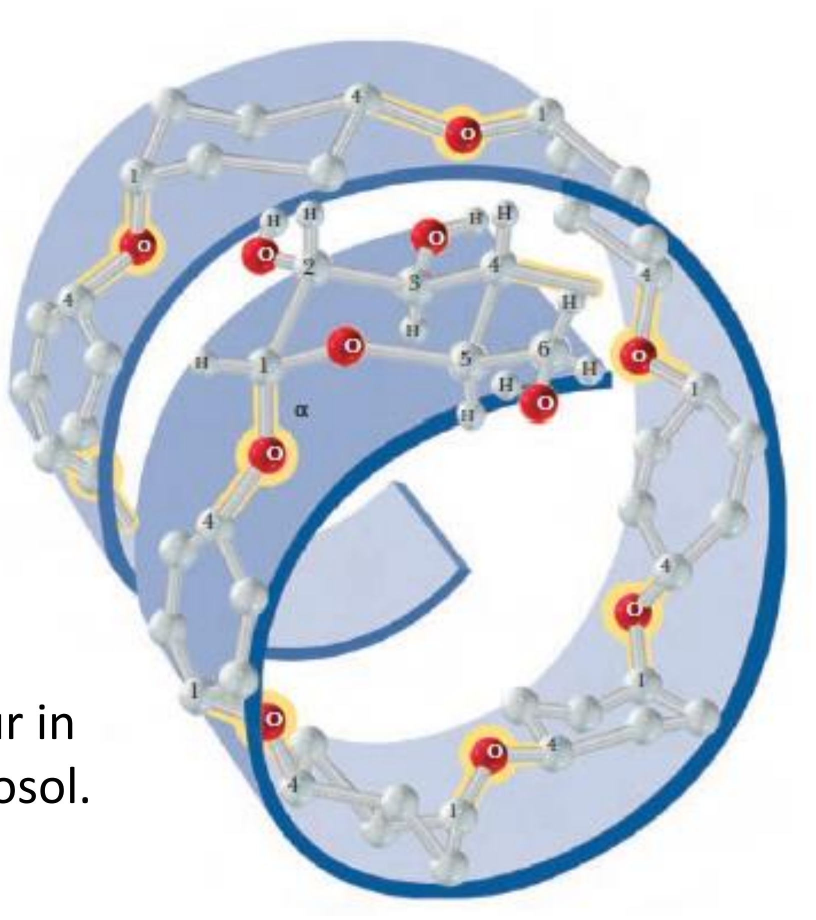
- Stimulate peristaltic action


© Foodcollection.com/Alamy

- Bind to toxic substances in foods they get exported from the body, thus preventing them from damaging the lower intestine or being reabsorbed there
- Bind carcinogens, thus prevent cancer
- Bind cholesterol resulting in less amount in the blood
- Fewer calories

Starch

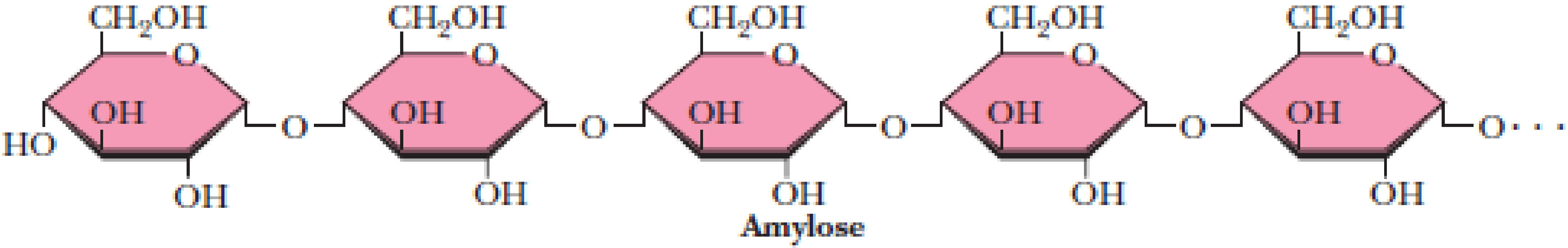




Starches are polymers of α-D-glucose that occur in plant cells, usually as starch granules in the cytosol.

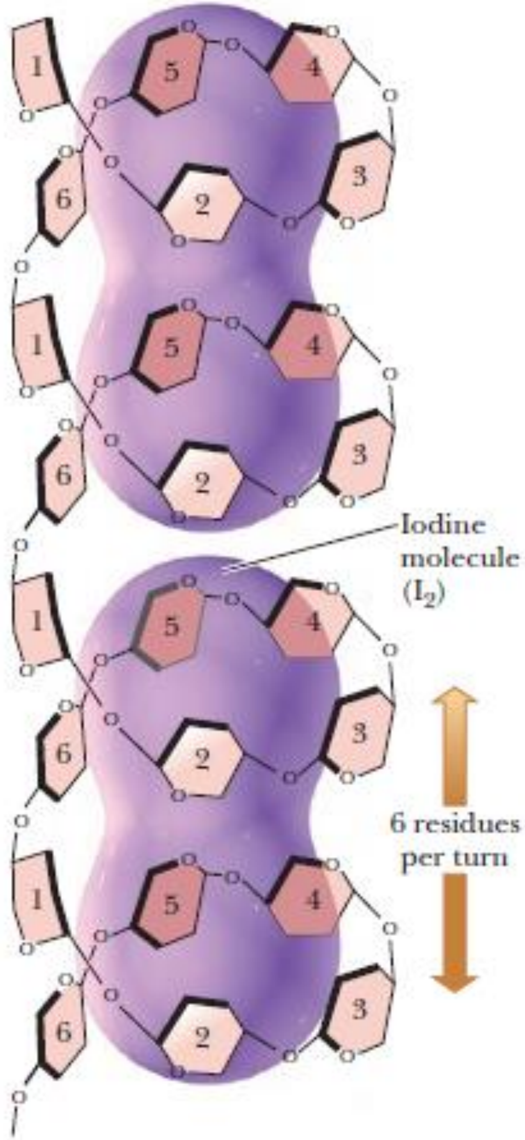
Types of starches

Amylose



α (1-4)

Types of starches



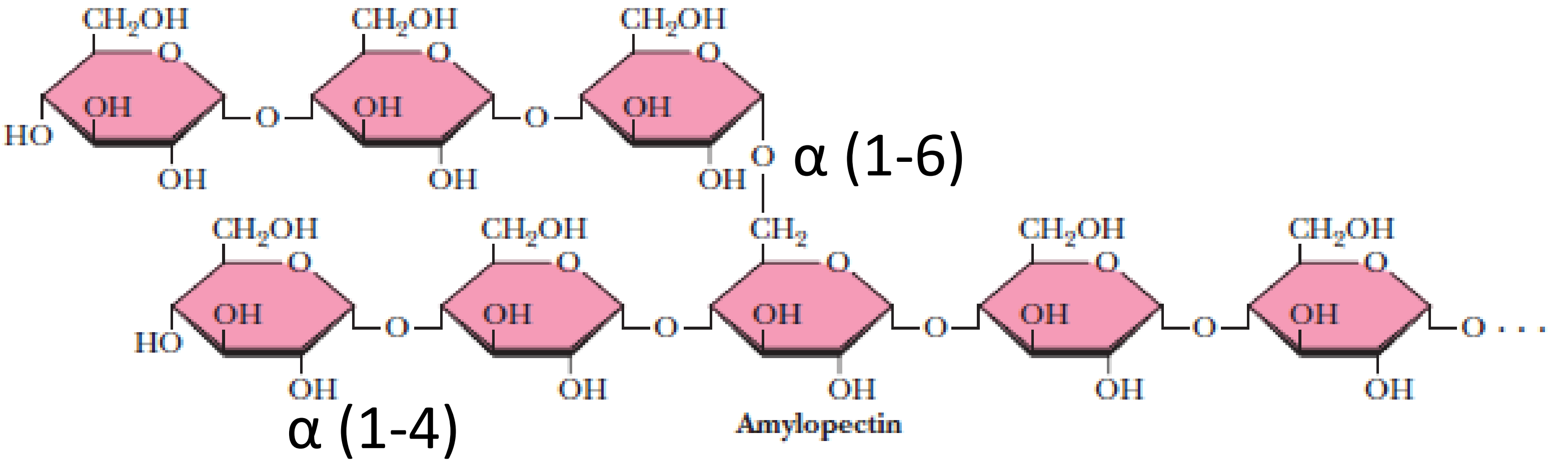
Amylose forms a helix with six residues per turn.

Iodine molecules can fit inside the helix to form a starch–iodine complex (dark-blue color)

Types of starches

Amylopectin

No known preferred conformation for amylopectin
Branch points occur about every 25 residues



Amylopectin and glycogen react with iodine to produce a red-brown product, not blue.

Amylases

- Starches are storage molecules
- Both plants and animals contain enzymes that hydrolyze starches (α- and β-amylase)
- Both enzymes attach α(1-4) linkages

α- amylase	**β-amylase**
Endoglycosidase	Exoglycosidase
Acts on glycosidic linkages along the chain	Acts on the nonreducing end of the polymer
Produces glucose and maltose	Produces maltose (glucose dimer)

Amylase action on amylose and amylopectin

- Amylose can be completely degraded to glucose and maltose by the two amylases
- Amylopectin is not completely degraded by the two amylases because the branching linkages are not attacked.
- Debranching enzymes degrade the α(1-6) linkages

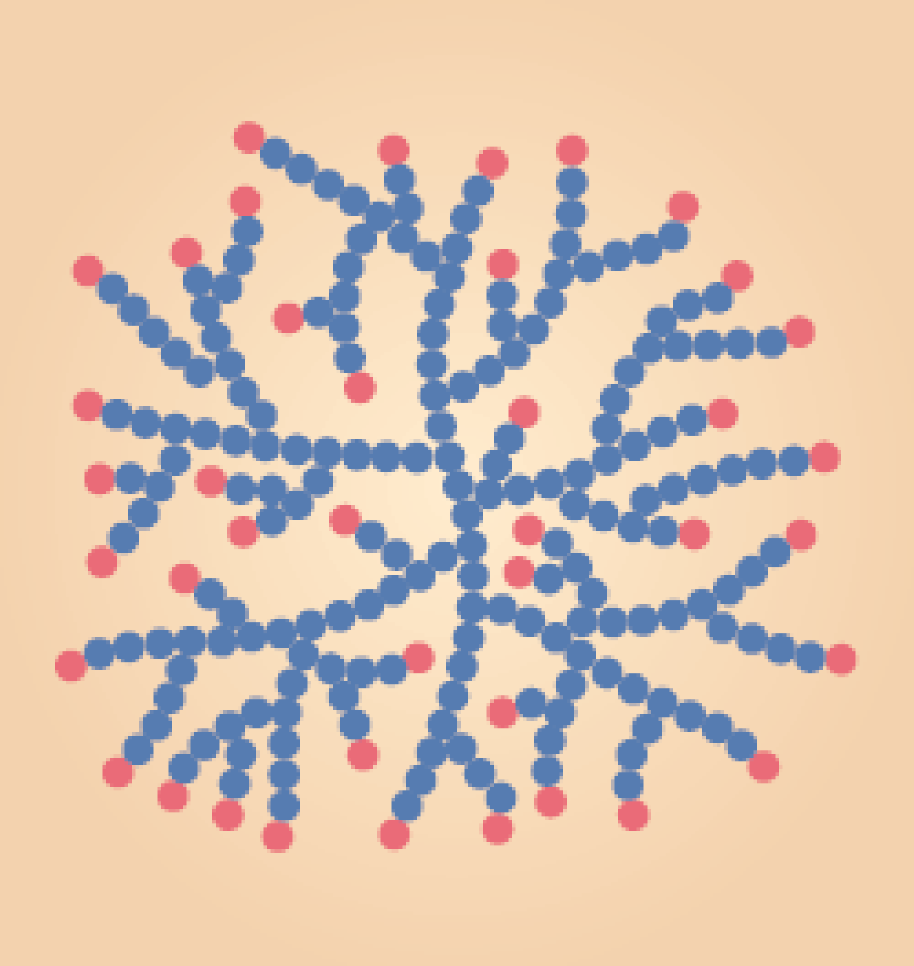
Glycogen

- glycogen is more highly branched than starch

- Branch points occur about every 10 residues in glycogen

- α (1-4) linkage in main chain
- α (1-6) linkage at branches

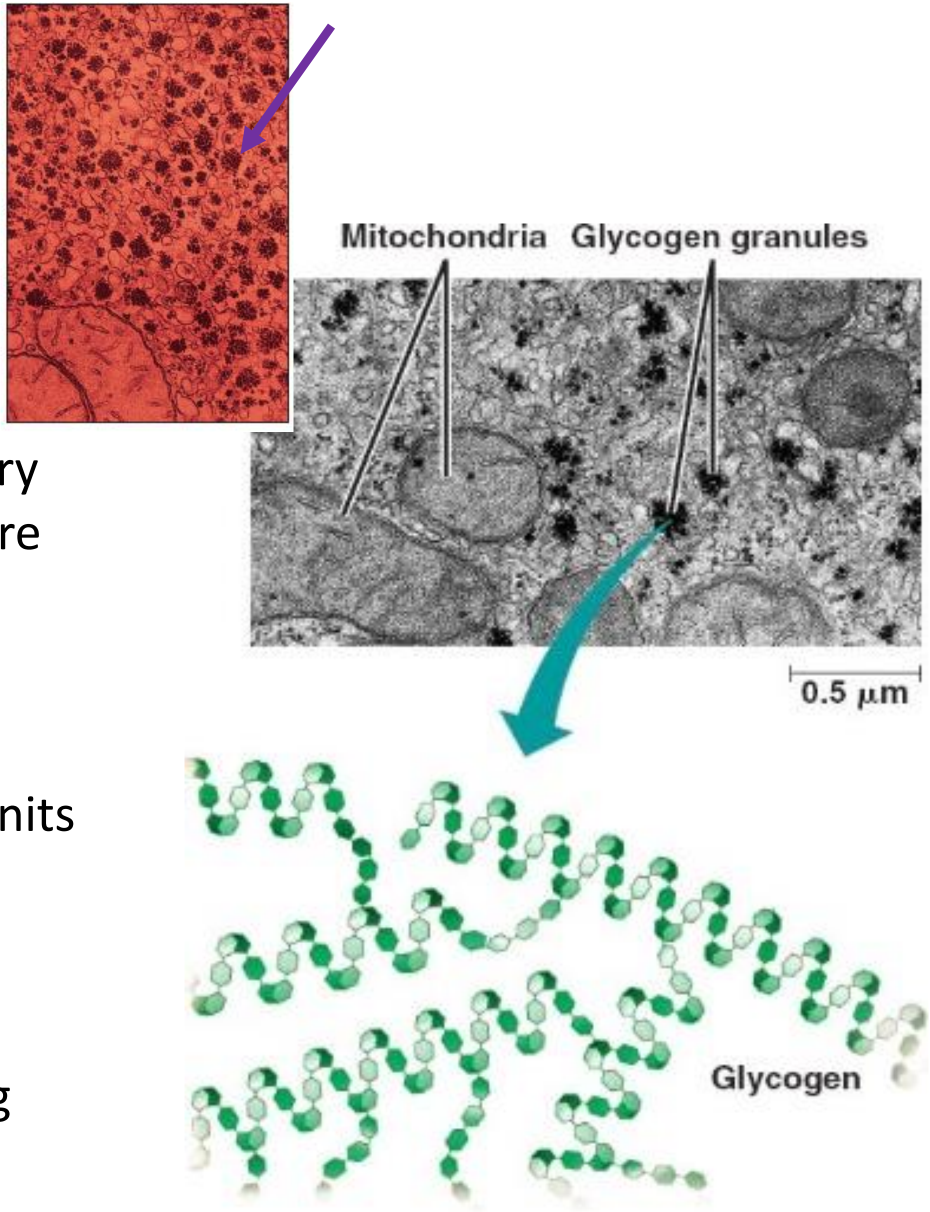
- The average chain length is 13 glucose residues
- 12 layers of branching



Glycogen

Glycogen

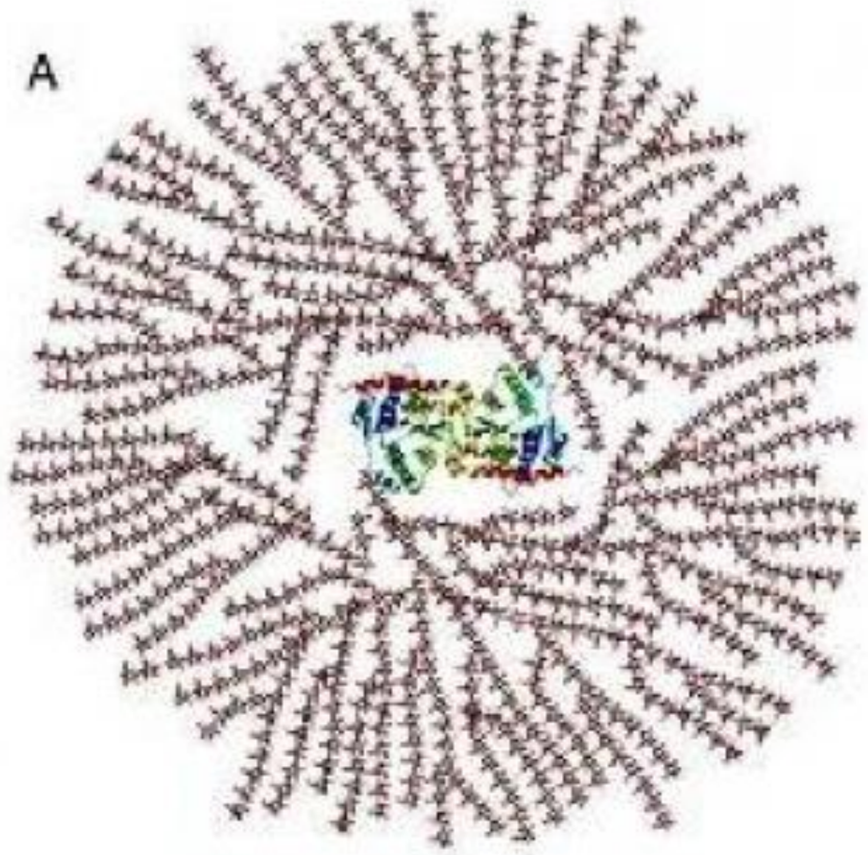
- Glycogen is found in granules in animal cells particularly in well-fed liver and muscle cells
- Some athletes (long-distance runners) try to build up their glycogen reserves before a race by eating large amounts of carbohydrates.
- Degradative enzymes remove glucose units from glycogen when energy is needed
- Glycogen phosphorylase cleaves one glucose at a time from the non-reducing end of a branch to produce glucose-1-phosphate



bio1151.nicerweb.com

Glycogen

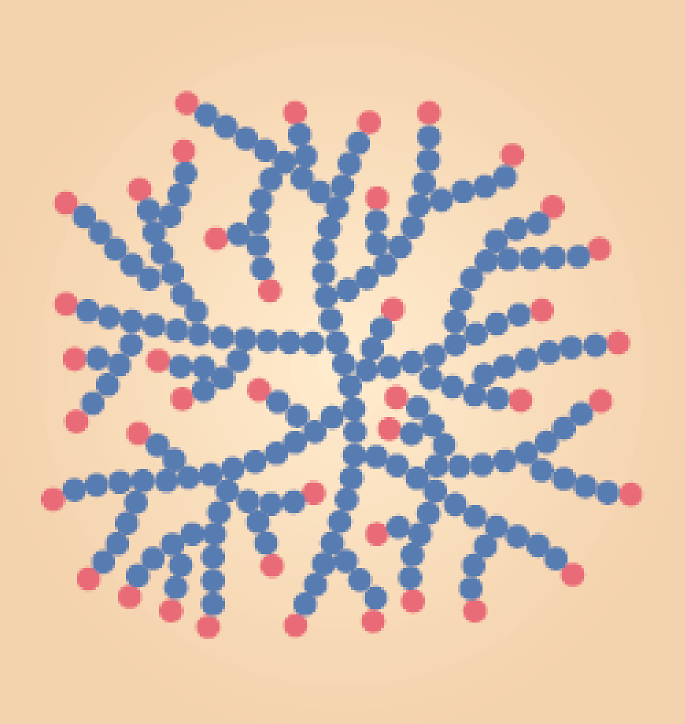
- Debranching enzymes complete the breakdown of glycogen.
- The number of branch points is important because:
- 1. A more branched polysaccharide is more water soluble and does not crystallize.
- 2. Easy access to glucose residues: when energy is needed quickly, the glycogen phosphorylase has more potential targets if there are more branches, allowing a quicker mobilization of glucose.



www.diapedia.org

Amylopectin versus glycogen

Amylopectin

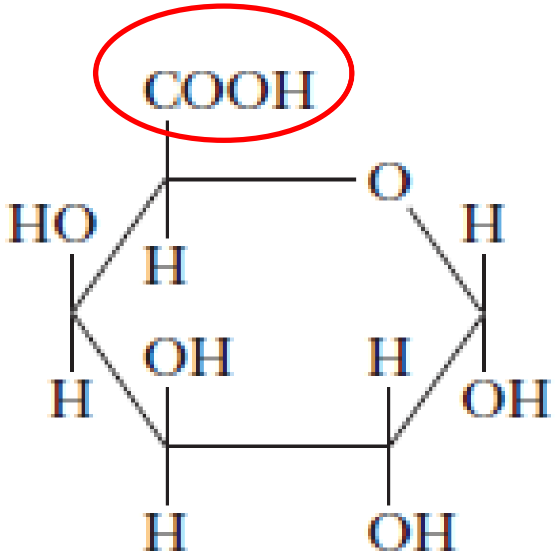


Glycogen

- Branching is more in glycogen: Branch points occur about every 10 residues in glycogen and about every 25 residues in amylopectin.
- Source

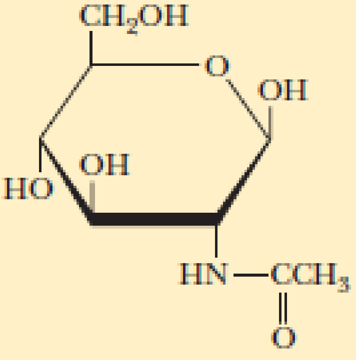
Pectin

- A polysaccharide of plant cell wall
- A polymer made up mostly of D-galacturonic acid
- D-galacturonic acid is a galactose derivative
- A gelling agent in yogurt, fruit preserves, jams, and jellies.

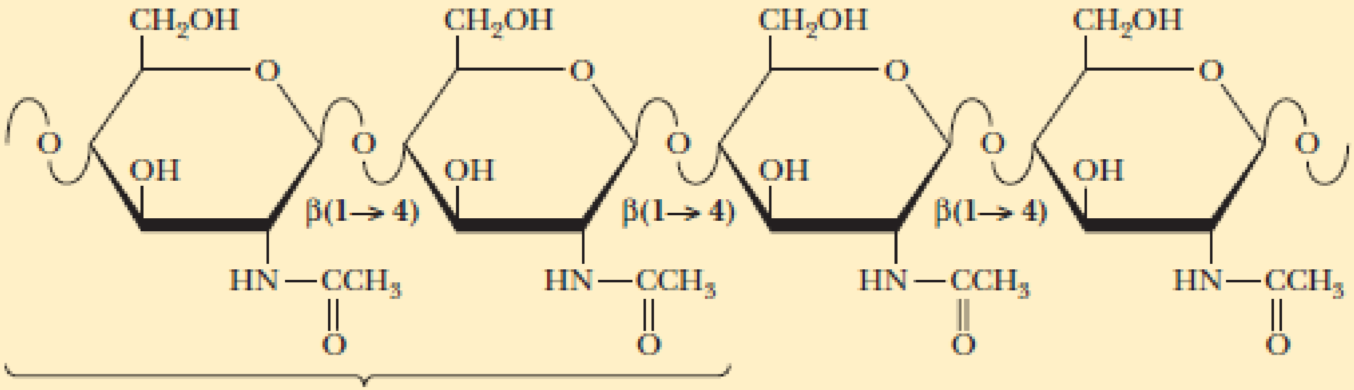


D-Galacturonic acid

Chitin



N-Acetyl-β-D-glucosamine



Repeating disaccharide in chitin

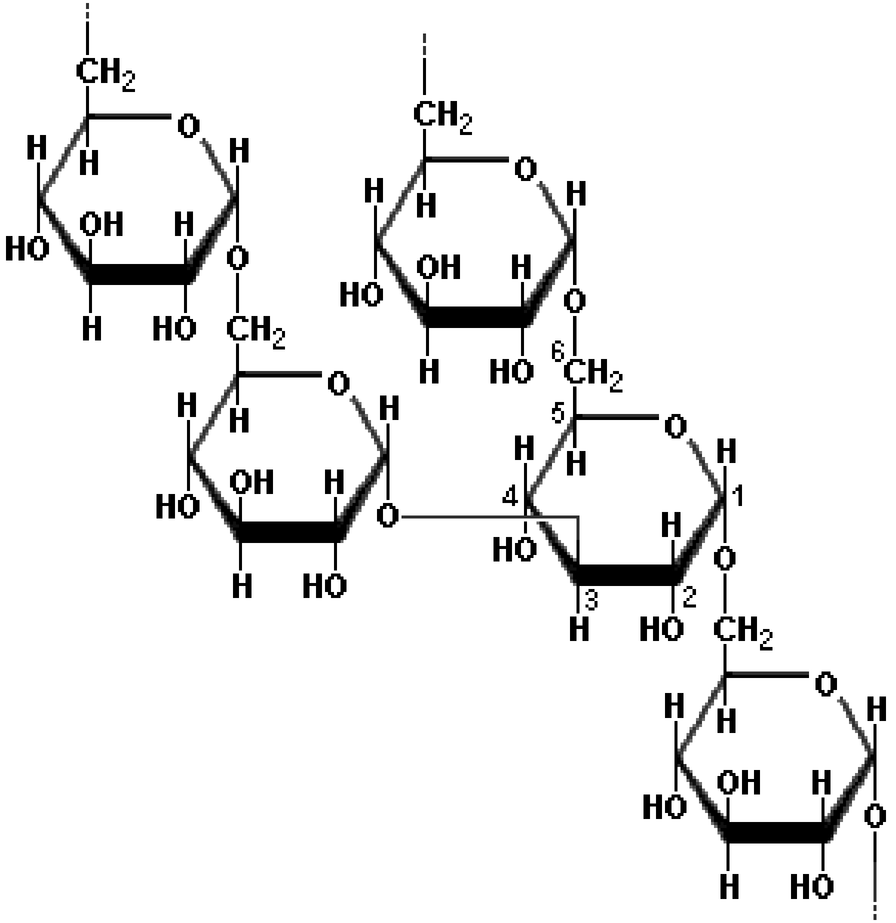
Has a structural role

Mechanical strength because of H-bonds between strands.

A major structural component of the exoskeletons of invertebrates such as insects and crustaceans (a group that includes lobsters and shrimp), and the cell walls of algae, fungi, and yeasts.

Dextran

- A storage polysaccharide
- Yeast and bacteria
- α-(1-6)-D-glucose with branched chains
- Branches: 1-2, 1-3, or 1-4



Are polysaccharides reducing?

- A sample that contains only a few molecules of a large polysaccharide, each molecule with a single reducing end, might well produce a negative test because there are not enough reducing ends to detect.

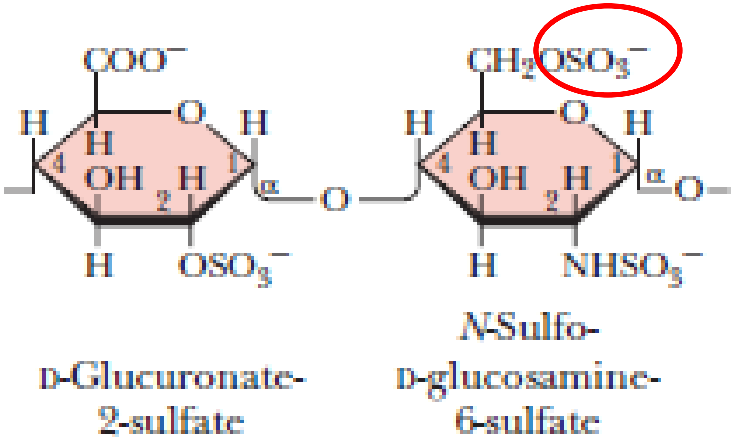
Glycoseaminoglycans (GAGs)

Polysaccharides that have a repeating disaccharide

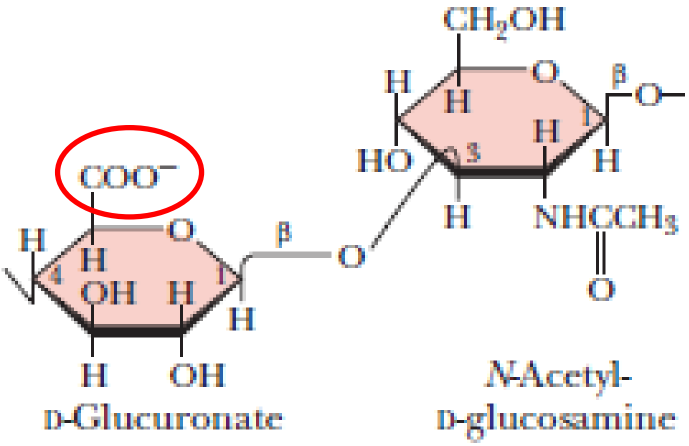
One of the sugars is an amino sugar

At least one of the sugars has a negative charge due to the presence of a sulfate group or a carboxyl group

GAGs are linked to proteins to form proteoglycans



Heparin



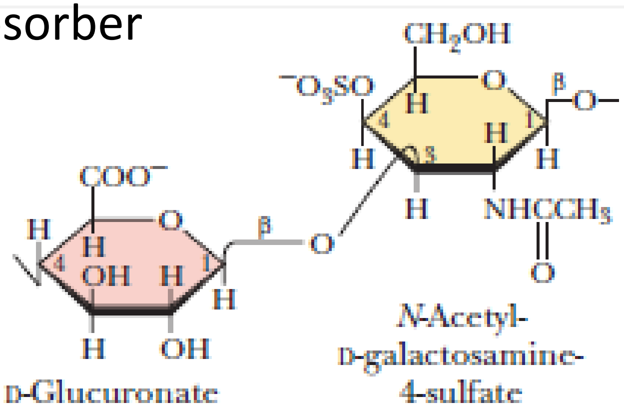
Hyaluronate

Heparin is a natural anticoagulant

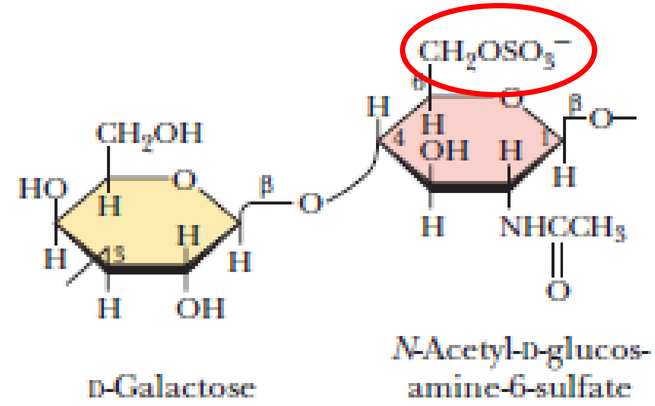
Hyaluronic acid is a component of the vitreous humor of the eye and of the lubricating fluid of joints

Glycoseaminoglycans (GAGs)

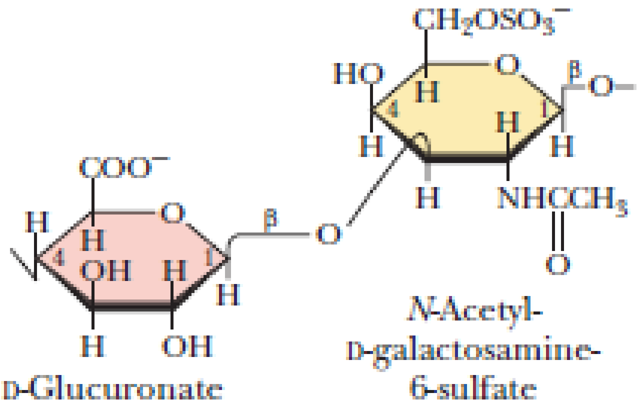
GAGs are highly polar and attract water, thus act as a lubricant or as a shock absorber



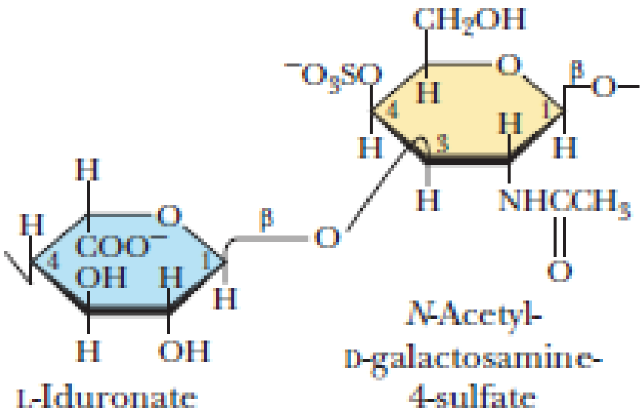
Chondroitin-4-sulfate



Keratan sulfate



Chondroitin-6-sulfate



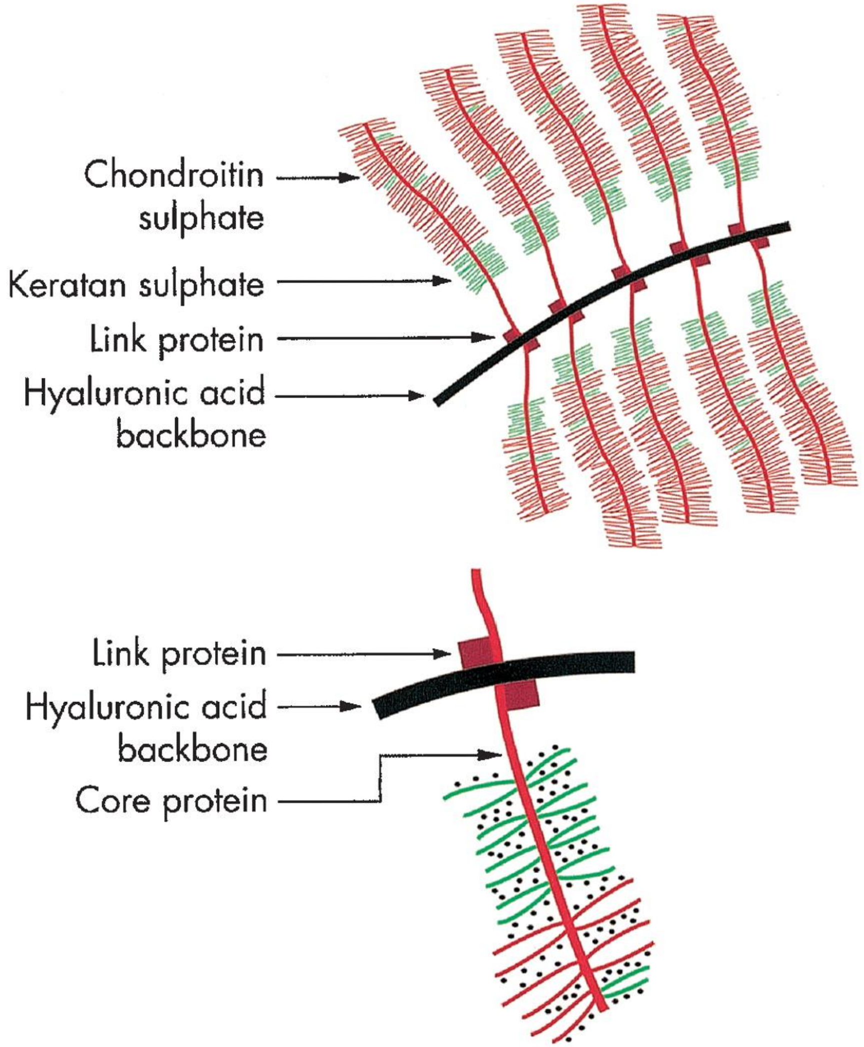
Dermatan sulfate

Localization and function of GAG

GAG	Localization	Comments
Hyaluronate	synovial fluid, **vitreous humor, ECM of loose connective tissue**	**the lubricant fluid , shock absorbing** As many as 25,000 disaccharide units
Chondroitin sulfate	**cartilage**, bone, heart valves	**most abundant GAG**
Heparan sulfate	basement membranes, components of cell surfaces	contains higher acetylated glucosamine than heparin
Heparin	component of intracellular granules of mast cells lining the arteries of the lungs, liver and skin	**A natural anticoagulant**
Dermatan sulfate	skin, blood vessels, heart valves	
Keratan sulfate	cornea, bone, cartilage aggregated with chondroitin sulfates	Only one not having uronic acid

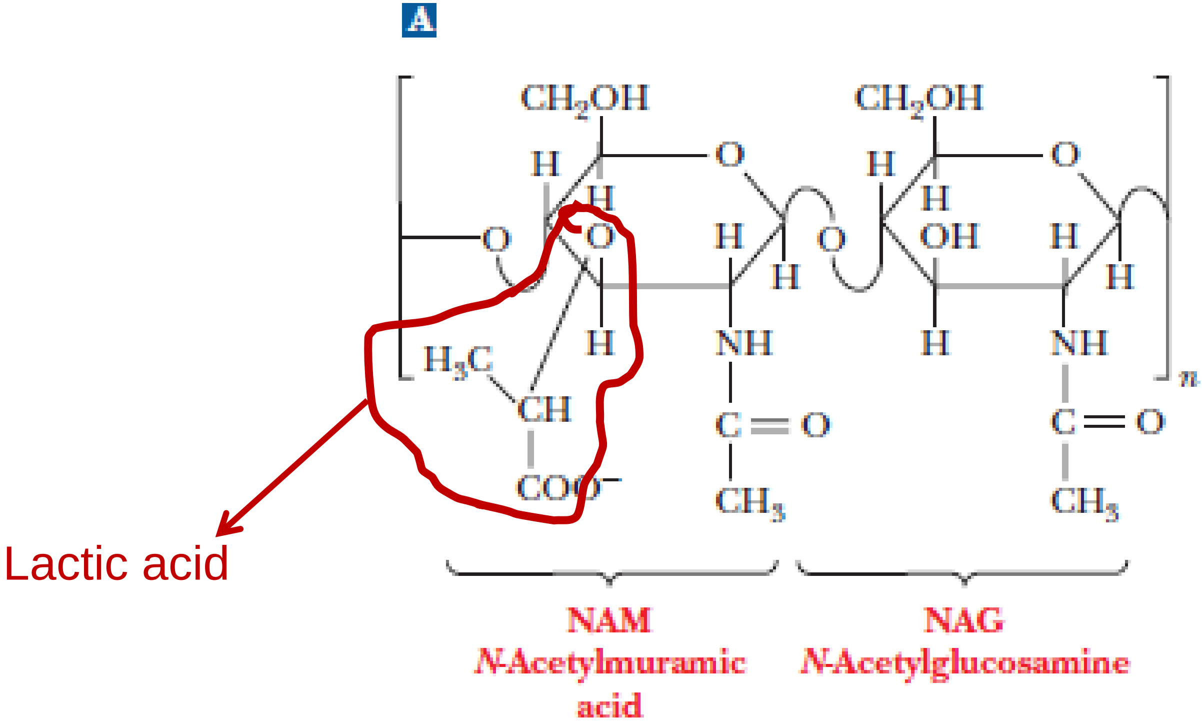
Proteoglycans

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



Polysaccharides in bacterial cell wall

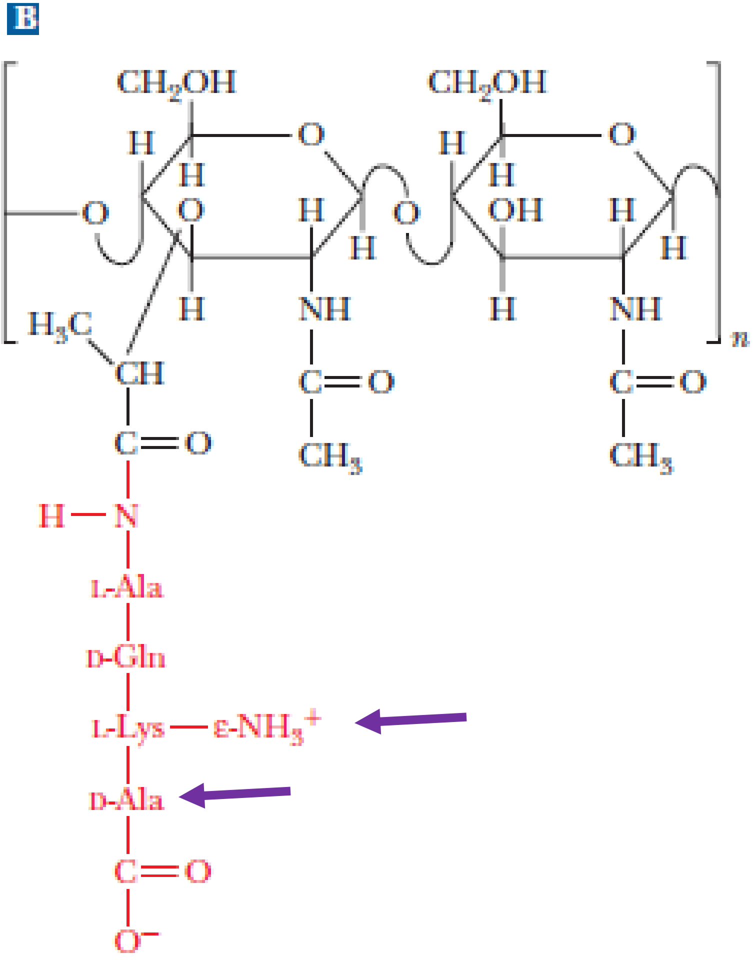
- Heteropolysaccharides are major components of bacterial cell walls

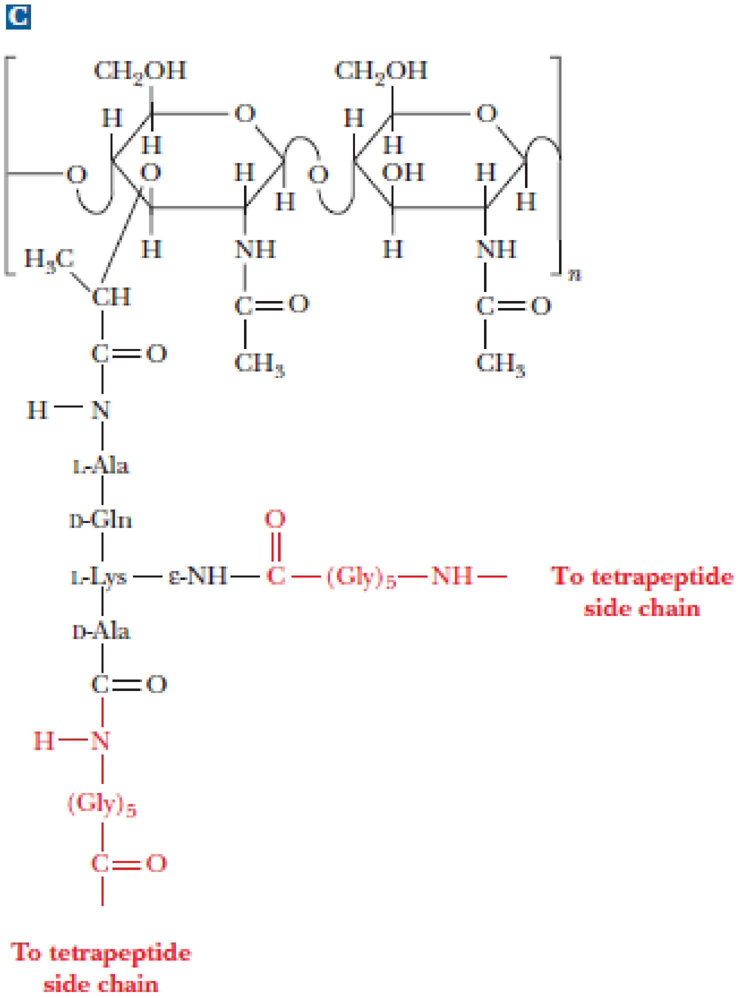


- *N*-Acetylmuramic acid is found only in prokaryotic cell walls; it does not occur in eukaryotic cell walls.

Polysaccharides in bacterial cell wall

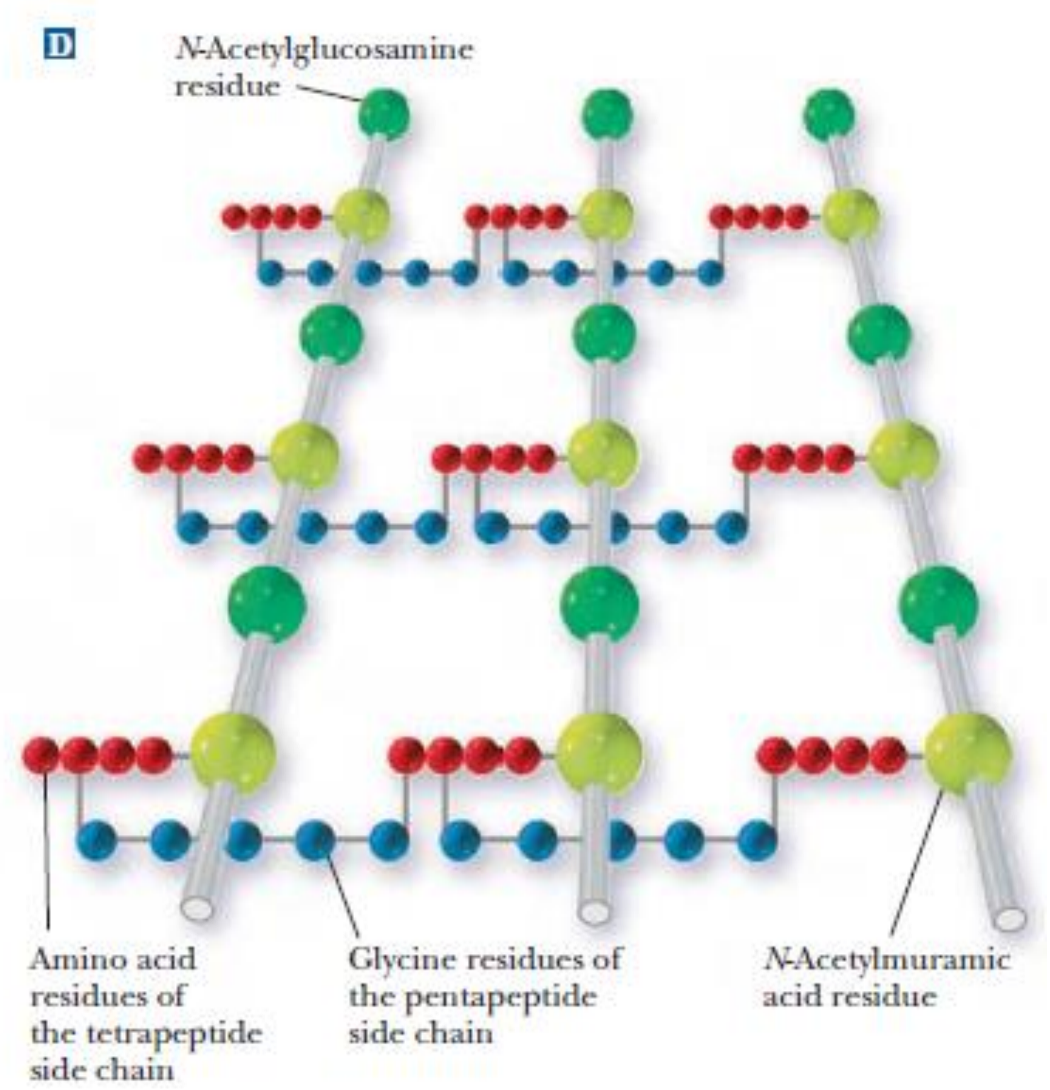
- Polysaccharides are cross-linked by peptides.





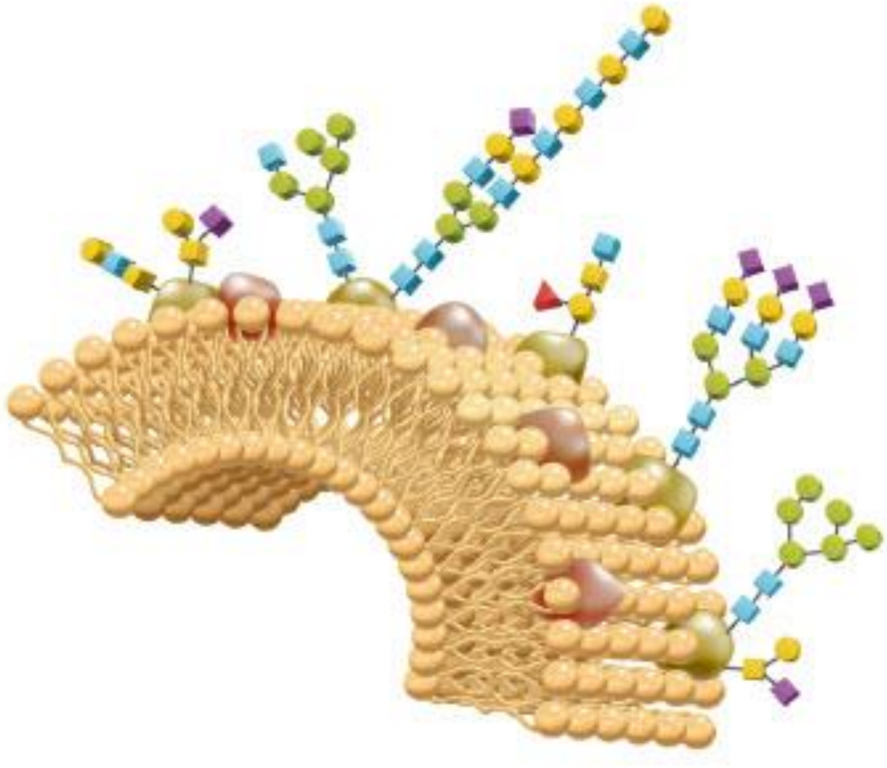
Polysaccharides in bacterial cell wall

Peptidoglycan is the material that results from the crosslinking of polysaccharides by peptides



Glycoproteins

- Glycoproteins contain carbohydrate residues attached to the polypeptide chain
- Example: antibodies.



chromblog.thermoscientific.com

Glycoproteins

- The carbohydrates of glycoproteins are linked to the protein component through either *O*-glycosidic or *N*-glycosidic bonds
  - The *N*-glycosidic linkage is through the amide group of asparagine (Asn, N)
  - The *O*-glycosidic linkage is to the hydroxyl of serine (Ser, S), threonine (Thr, T) or hydroxylysine (hLys)

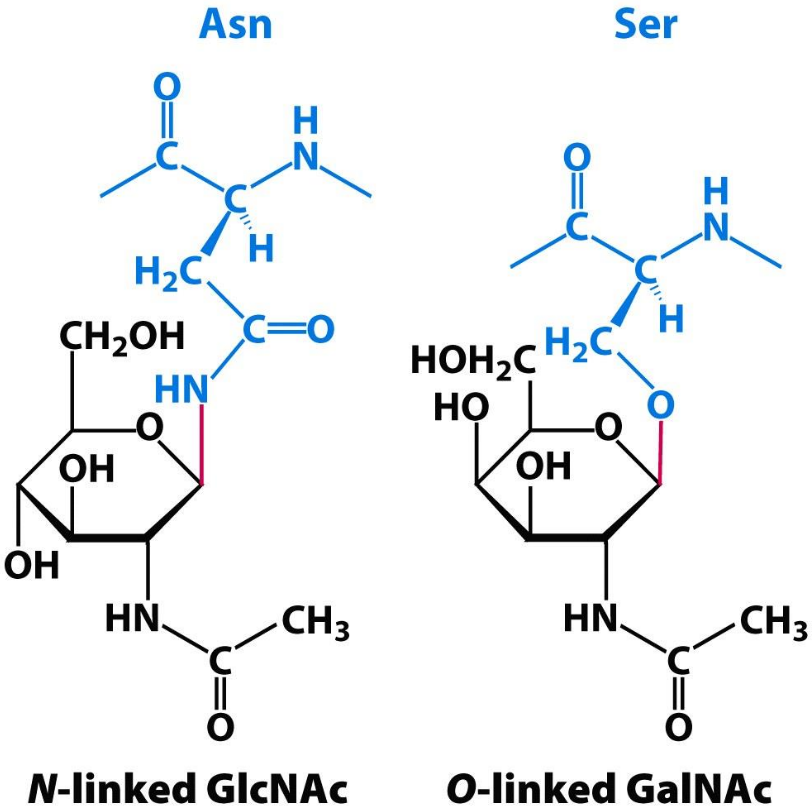


Figure 11.15
Biochemistry, Seventh Edition
© 2012 W. H. Freeman and Company

chromblog.thermoscientific.com

Significance of protein-linked sugars

- Soluble proteins as well as membrane proteins
- Purpose:
  - Protein folding
  - Protein targeting
  - prolonging protein half-life
  - Cell-cell communication
  - Signaling

Carbohydrates as **antigenic determinants-ABO blood groups**

- Carbohydrates act as **antigenic determinants,** the portions of an antigenic molecule that antibodies recognize and bind.

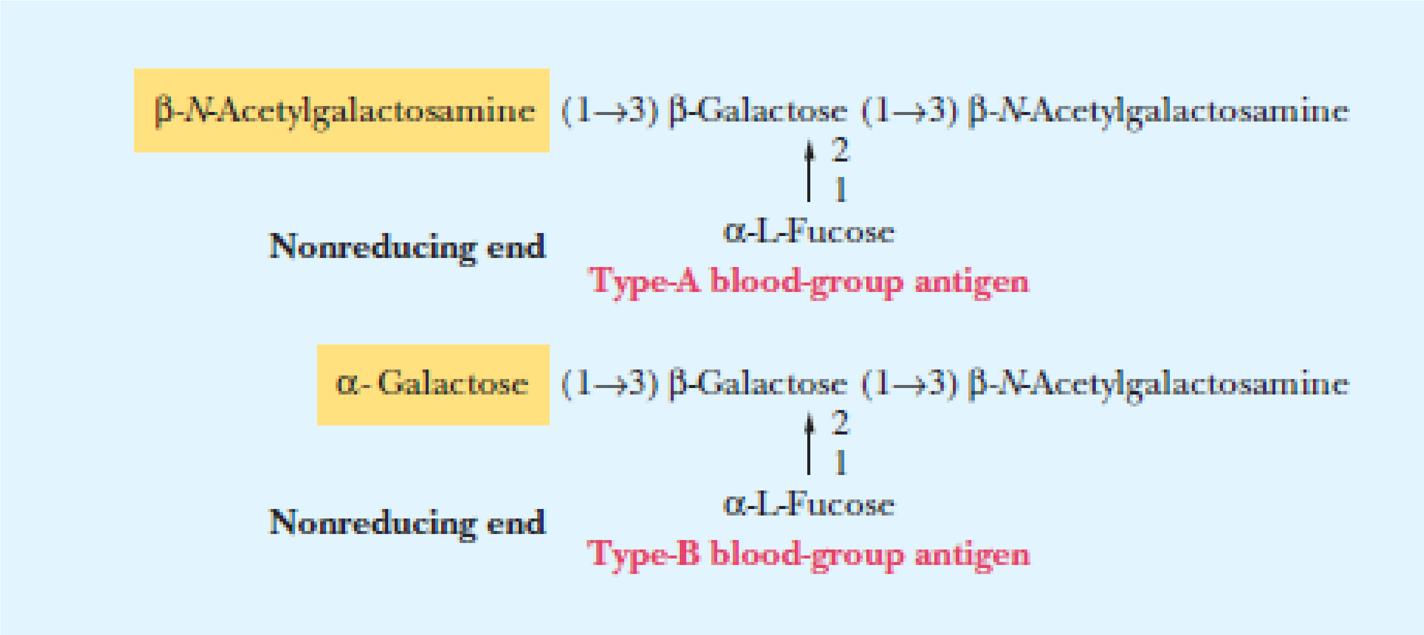
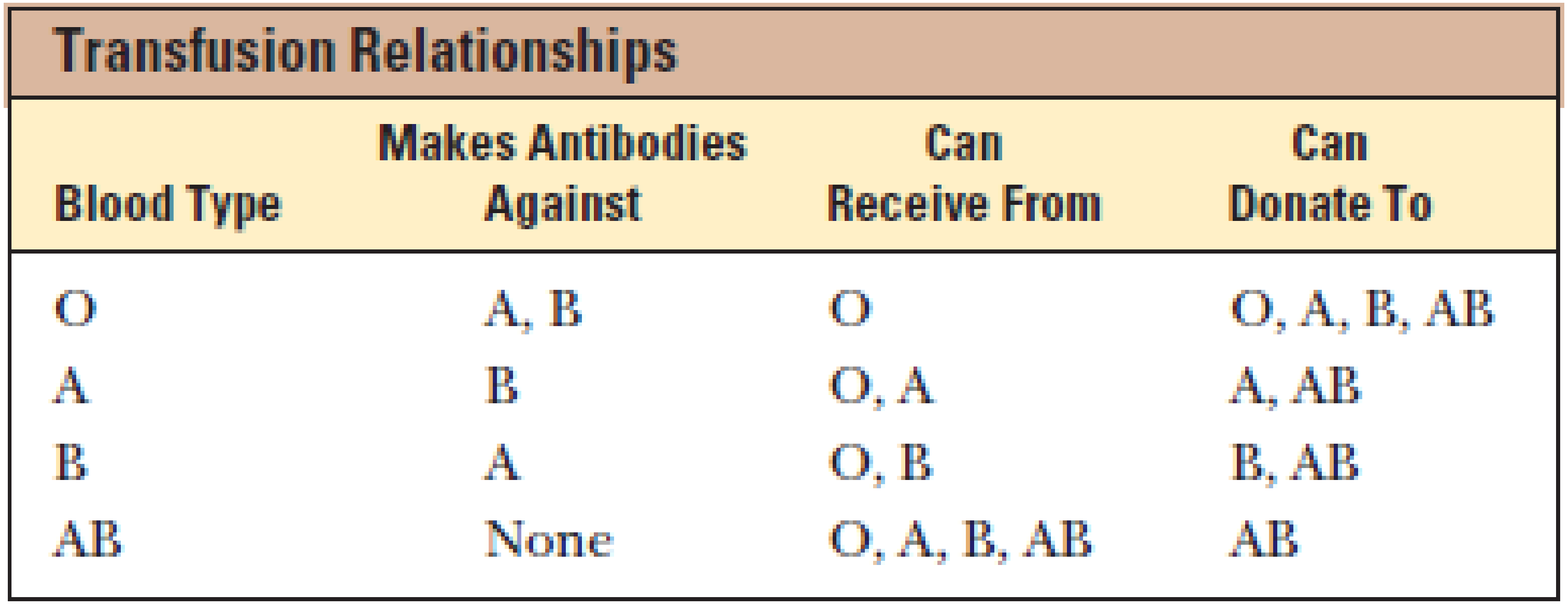


FIGURE 16.30 **The structures of the blood-group antigenic determinants.**

chromblog.thermoscientific.com

Glycoprotein and blood transfusion

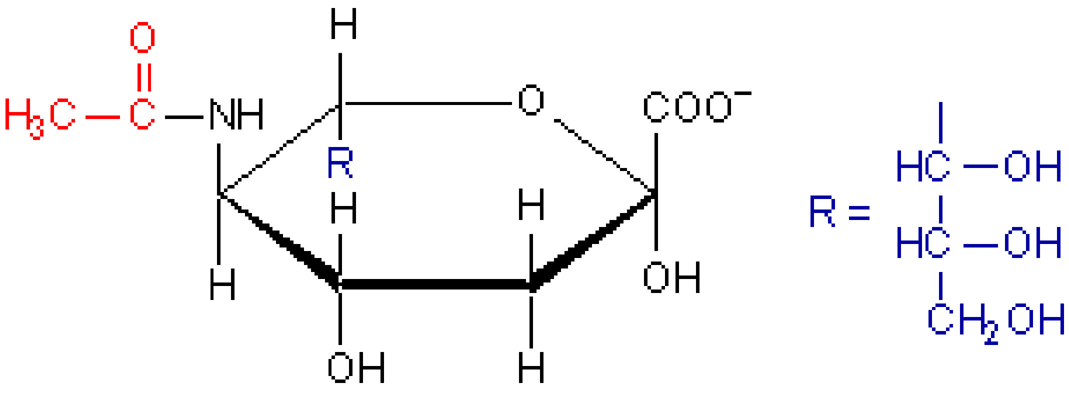


Transfusion Relationships

Blood Type	Makes Antibodies Against	Can Receive From	Can Donate 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	AB

Sialic acid

- *N*-acetylneuraminate
- Precursor: the amino sugar, neuraminic acid
- Location: a terminal residue of oligosaccharide chains of glycoproteins and glycolipids.



N-acetylneuraminate (sialic acid)

Low carbohydrate diet

Thomson Learning/Charles D. Winters

- More carbohydrates, more insulin, more fat synthesis and storage and inhibition of fat burning