Chapter 7

Carbohydrates

Sugar in the gourd and honey in the horn,
I never was so happy since the hour I was born.

Turkey in the Straw, stanza 6 (classic American folk tune)

"The Discovery of Honey"—Piero di Cosimo (1462). *(Courtesy of the Worcester Art Museum)*

OUTLINE

Carbohydrates are the single most abundant class of organic molecules found in nature. The name *carbohydrate* arises from the basic molecular formula $(CH_2O)_n$, which can be rewritten $(C \cdot H_2O)_n$ to show that these substances are hydrates of carbon, where $n = 3$ or more. Carbohydrates constitute a versatile class of molecules. Energy from the sun captured by green plants, algae, and some bacteria during photosynthesis (see Chapter 22) is stored in the form of carbohydrates. In turn, carbohydrates are the metabolic precursors of virtually all other biomolecules. Breakdown of carbohydrates provides the energy that sustains animal life. In addition, carbohydrates are covalently linked with a variety of other molecules. Carbohydrates linked to lipid molecules, or **glycolipids,** are common components of biological membranes. Proteins that have covalently linked carbohydrates are called **glycoproteins.** These two classes of biomolecules, together called **glycoconjugates,** are important components of cell walls and extracellular structures in plants, animals, and bacteria. In addition to the structural roles such molecules play, they also serve in a variety of

processes involving *recognition* between cell types or recognition of cellular structures by other molecules. Recognition events are important in normal cell growth, fertilization, transformation of cells, and other processes.

All of these functions are made possible by the characteristic chemical features of carbohydrates: (1) the existence of at least one and often two or more asymmetric centers, (2) the ability to exist either in linear or ring structures, (3) the capacity to form polymeric structures via *glycosidic* bonds, and (4) the potential to form multiple hydrogen bonds with water or other molecules in their environment.

7.1 • Carbohydrate Nomenclature

Carbohydrates are generally classified into three groups: **monosaccharides** (and their derivatives), **oligosaccharides,** and **polysaccharides.** The monosaccharides are also called **simple sugars** and have the formula $(CH_2O)_n$. Monosaccharides cannot be broken down into smaller sugars under mild conditions. Oligosaccharides derive their name from the Greek word *oligo,* meaning "few," and consist of from two to ten simple sugar molecules. Disaccharides are common in nature, and trisaccharides also occur frequently. Four- to six-sugar-unit oligosaccharides are usually bound covalently to other molecules, including glycoproteins. As their name suggests, polysaccharides are polymers of the simple sugars and their derivatives. They may be either linear or branched polymers and may contain hundreds or even thousands of monosaccharide units. Their molecular weights range up to 1 million or more.

7.2 • Monosaccharides

Classification

Monosaccharides consist typically of three to seven carbon atoms and are described either as **aldoses** or **ketoses,** depending on whether the molecule contains an aldehyde function or a ketone group. The simplest aldose is glyceraldehyde, and the simplest ketose is dihydroxyacetone (Figure 7.1). These two simple sugars are termed **trioses** because they each contain three carbon atoms. The structures and names of a family of aldoses and ketoses with three, four, five, and six carbons are shown in Figure 7.2 and 7.3. *Hexoses* are the most abundant sugars in nature. Nevertheless, sugars from all these classes are important in metabolism.

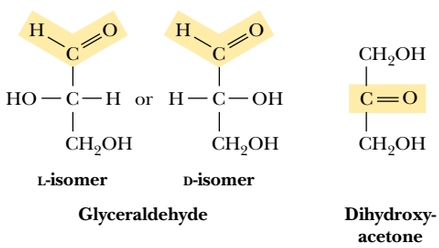


FIGURE 7.1 • Structure of a simple aldose (glyceraldehyde) and a simple ketose (dihydroxyacetone).

Monosaccharides, either aldoses or ketoses, are often given more detailed generic names to describe both the important functional groups and the total number of carbon atoms. Thus, one can refer to *aldotetroses* and *ketotetroses, aldopentoses* and *ketopentoses, aldohexoses* and *ketohexoses,* and so on. Sometimes the ketone-containing monosaccharides are named simply by inserting the letters -ul- into the simple generic terms, such as *tetruloses, pentuloses, hexuloses, heptuloses,* and so on. The simplest monosaccharides are water-soluble, and most taste sweet.

Stereochemistry

Aldoses with at least three carbons and ketoses with at least four carbons contain **chiral centers** (Chapter 4). The nomenclature for such molecules must specify the **configuration** about each asymmetric center, and drawings of these molecules must be based on a system that clearly specifies these configurations.

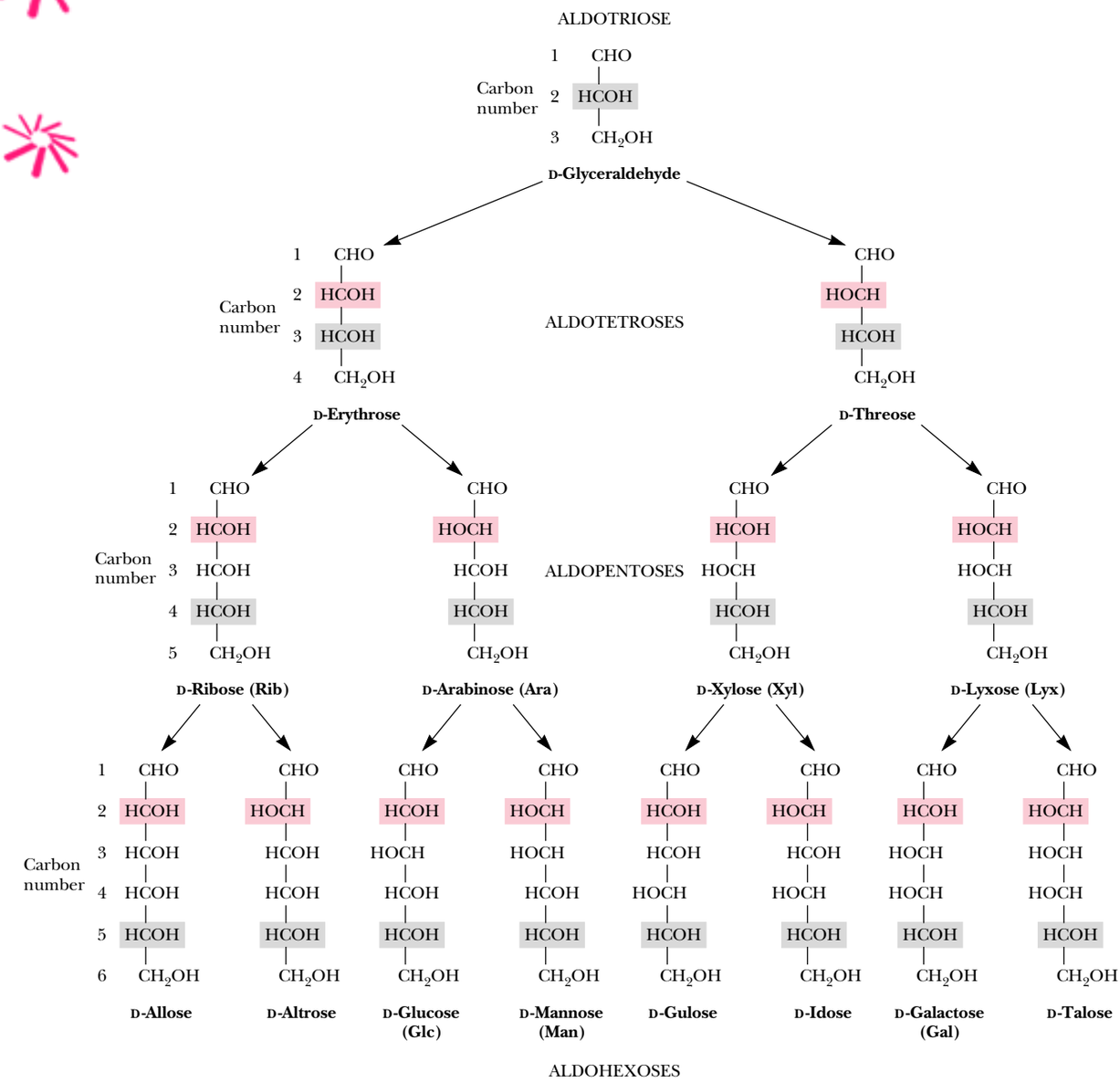


FIGURE 7.2 • The structure and stereochemical relationships of D-aldoses having three to six carbons. The configuration in each case is determined by the highest numbered asymmetric carbon (shown in gray). In each row, the "new" asymmetric carbon is shown in red.

As noted in Chapter 4, the **Fischer projection** system is used almost universally for this purpose today. The structures shown in Figures 7.2 and 7.3 are Fischer projections. For monosaccharides with two or more asymmetric carbons, the prefix D or L refers to the configuration of the highest numbered asymmetric carbon (the asymmetric carbon farthest from the carbonyl carbon). A monosaccharide is designated D if the hydroxyl group on the highest numbered asymmetric carbon is drawn to the right in a Fischer projection, as in D-glyceraldehyde (Figure 7.1). Note that the designation D or L merely relates the

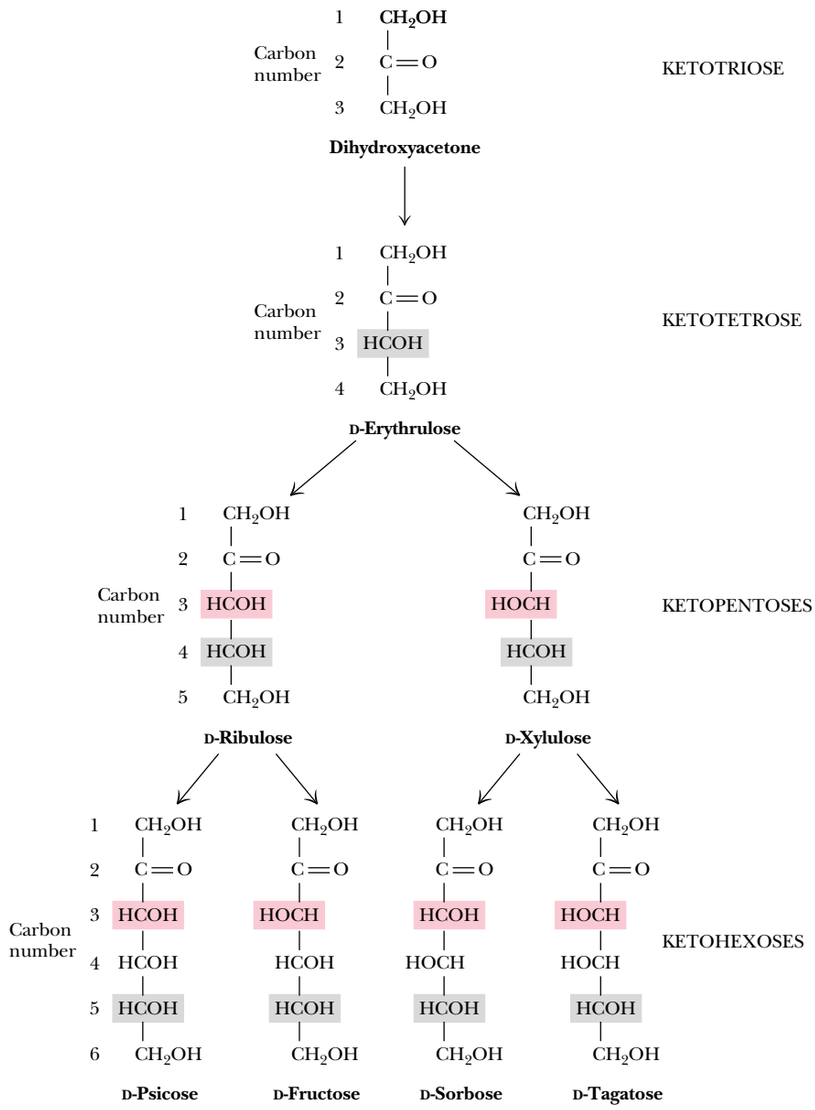


FIGURE 7.3 • The structure and stereochemical relationships of D-ketoses having three to six carbons. The configuration in each case is determined by the highest numbered asymmetric carbon (shown in gray). In each row, the "new" asymmetric carbon is shown in red.

configuration of a given molecule to that of glyceraldehyde and does *not* specify the sign of rotation of plane-polarized light. If the sign of optical rotation is to be specified in the name, the Fischer convention of D or L designations may be used along with a + (plus) or − (minus) sign. Thus, D-glucose (Figure 7.2) may also be called D(+)-glucose because it is dextrorotatory, whereas D-fructose (Figure 7.3), which is levorotatory, can also be named D(−)-fructose.

All of the structures shown in Figures 7.2 and 7.3 are D-configurations, and the D-forms of monosaccharides predominate in nature, just as L-amino acids do. These preferences, established in apparently random choices early in evolution, persist uniformly in nature because of the stereospecificity of the enzymes that synthesize and metabolize these small molecules.

L-Monosaccharides do exist in nature, serving a few relatively specialized roles. L-Galactose is a constituent of certain polysaccharides, and L-arabinose is a constituent of bacterial cell walls.

According to convention, the D- and L-forms of a monosaccharide are *mirror images* of each other, as shown in Figure 7.4 for fructose. Stereoisomers that are mirror images of each other are called **enantiomers,** or sometimes *enantiomeric pairs*. For molecules that possess two or more chiral centers, more than two stereoisomers can exist. Pairs of isomers that have opposite configurations at one or more of the chiral centers but that are not mirror images of each other are called **diastereomers** or *diastereomeric pairs*. Any two structures in a given row in Figures 7.2 and 7.3 are diastereomeric pairs. Two sugars that differ in configuration at *only one* chiral center are described as **epimers.** For example, D-mannose and D-talose are epimers and D-glucose and D-mannose are epimers, whereas D-glucose and D-talose are *not* epimers but merely diastereomers.

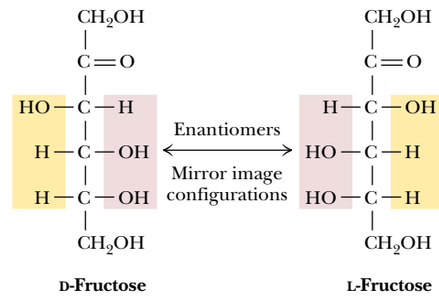
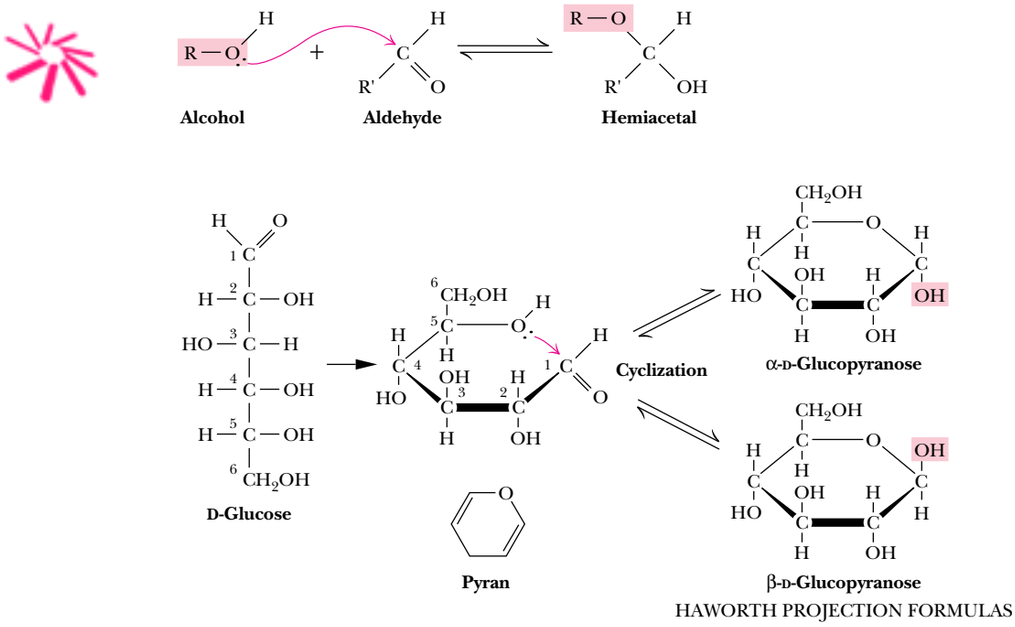


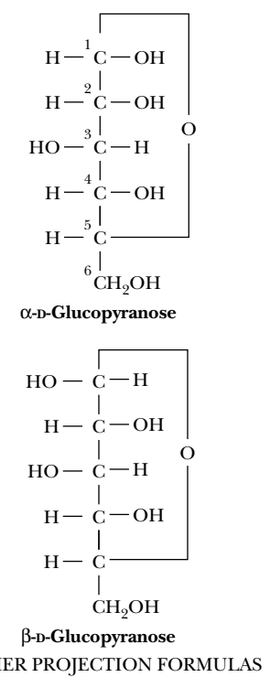
FIGURE 7.4 • D-Fructose and L-fructose, an enantiomeric pair. Note that changing the configuration only at C_5 would change D-fructose to L-sorbose.

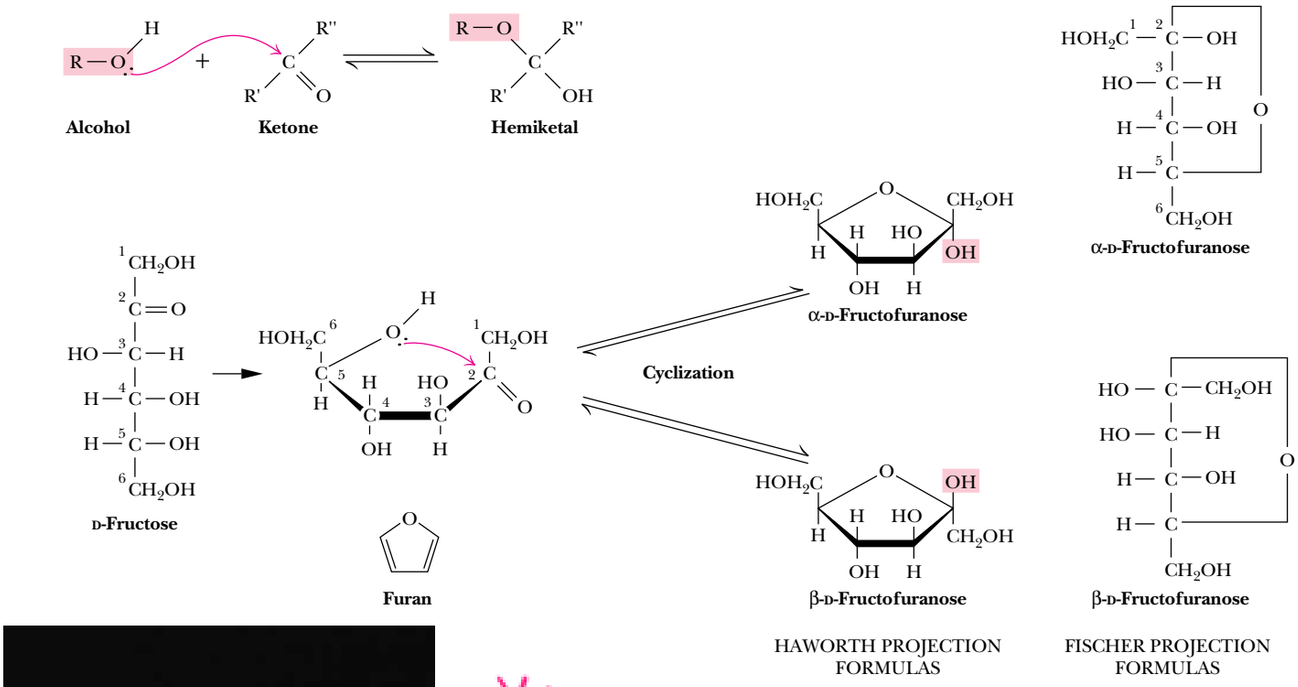
Cyclic Structures and Anomeric Forms

Although Fischer projections are useful for presenting the structures of particular monosaccharides and their stereoisomers, they ignore one of the most interesting facets of sugar structure—*the ability to form cyclic structures with formation of an additional asymmetric center.* Alcohols react readily with aldehydes to form **hemiacetals** (Figure 7.5). The British carbohydrate chemist Sir Norman Haworth showed that the linear form of glucose (and other aldohexoses) could undergo a similar *intramolecular* reaction to form a *cyclic hemiacetal.* The resulting six-membered, oxygen-containing ring is similar to *pyran* and is designated a **pyranose.** The reaction is catalyzed by acid (H^+) or base (OH^-) and is readily reversible.

FIGURE 7.5







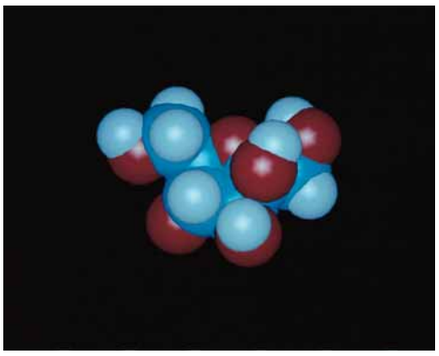


FIGURE 7.6

In a similar manner, ketones can react with alcohols to form **hemiketals.** The analogous intramolecular reaction of a ketose sugar such as fructose yields a *cyclic hemiketal* (Figure 7.6). The five-membered ring thus formed is reminiscent of *furan* and is referred to as a **furanose.** The cyclic pyranose and furanose forms are the preferred structures for monosaccharides in aqueous solution. At equilibrium, the linear aldehyde or ketone structure is only a minor component of the mixture (generally much less than 1%).

When hemiacetals and hemiketals are formed, the carbon atom that carried the carbonyl function becomes an asymmetric carbon atom. Isomers of monosaccharides that differ only in their configuration about that carbon atom are called **anomers,** designated as α or β, as shown in Figure 7.5, and the carbonyl carbon is thus called the **anomeric carbon.** When the hydroxyl group at the anomeric carbon is on the *same side* of a Fischer projection as the oxygen atom at the highest numbered asymmetric carbon, the configuration at the anomeric carbon is α, as in α-D-glucose. When the anomeric hydroxyl is on the *opposite side* of the Fischer projection, the configuration is β, as in β-D-glucopyranose (Figure 7.5).

The addition of this asymmetric center upon hemiacetal and hemiketal formation alters the optical rotation properties of monosaccharides, and the original assignment of the α and β notations arose from studies of these properties. Early carbohydrate chemists frequently observed that the optical rotation of glucose (and other sugar) solutions could change with time, a process called **mutarotation.** This indicated that a structural change was occurring. It was eventually found that α-D-glucose has a specific optical rotation, $[\alpha]_D^{20}$, of 112.2°, and that β-D-glucose has a specific optical rotation of 18.7°. Mutarotation involves interconversion of α and β forms of the monosaccharide with intermediate formation of the linear aldehyde or ketone, as shown in Figures 7.5 and 7.6.

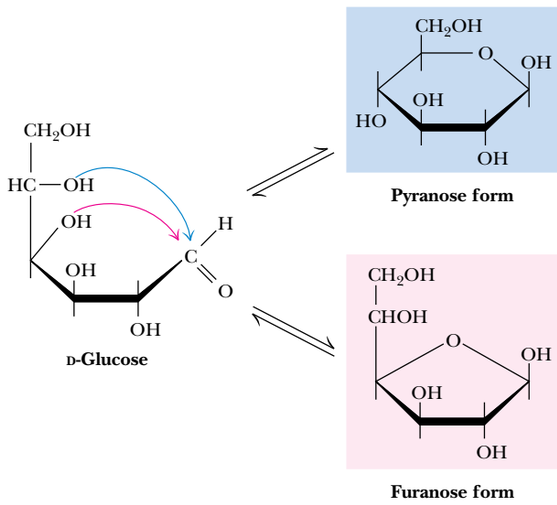


FIGURE 7.7 • D-Glucose can cyclize in two ways, forming either furanose or pyranose structures.

Haworth Projections

Another of Haworth's lasting contributions to the field of carbohydrate chemistry was his proposal to represent pyranose and furanose structures as hexagonal and pentagonal rings lying perpendicular to the plane of the paper, with thickened lines indicating the side of the ring closest to the reader. Such **Haworth projections,** which are now widely used to represent saccharide structures (Figures 7.5 and 7.6), show substituent groups extending either above or below the ring. Substituents drawn to the left in a Fischer projection are drawn above the ring in the corresponding Haworth projection. Substituents drawn to the right in a Fischer projection are below the ring in a Haworth projection. Exceptions to these rules occur in the formation of furanose forms of pentoses and the formation of furanose or pyranose forms of hexoses. In these cases, the structure must be redrawn with a rotation about the carbon whose hydroxyl group is involved in the formation of the cyclic form (Figures 7.7 and 7.8) in order to orient the appropriate hydroxyl group for ring formation. This is

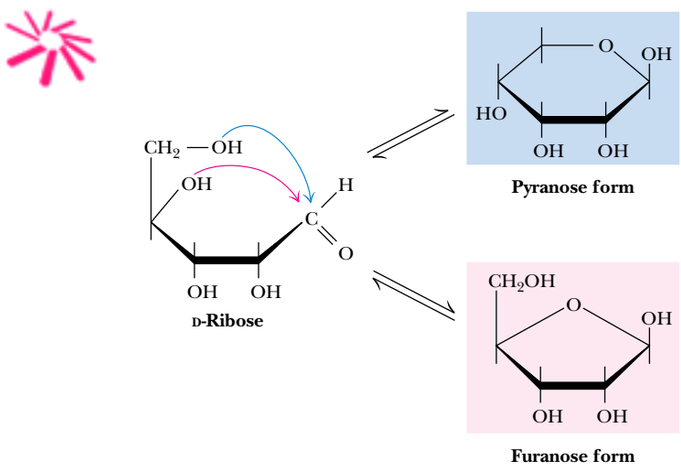


FIGURE 7.8 • D-Ribose and other five-carbon saccharides can form either furanose or pyranose structures.

merely for illustrative purposes and involves no change in configuration of the saccharide molecule.

The rules previously mentioned for assignment of α- and β-configurations can be readily applied to Haworth projection formulas. For the D-sugars, the anomeric hydroxyl group is below the ring in the α-anomer and above the ring in the β-anomer. For L-sugars, the opposite relationship holds.

As Figures 7.7 and 7.8 imply, in most monosaccharides there are two or more hydroxyl groups which can react with an aldehyde or ketone at the other end of the molecule to form a hemiacetal or hemiketal. Consider the possibilities for glucose, as shown in Figure 7.7. If the C-4 hydroxyl group reacts with the aldehyde of glucose, a five-membered ring is formed, whereas if the C-5 hydroxyl reacts, a six-membered ring is formed. The C-6 hydroxyl does not react effectively because a seven-membered ring is too strained to form a stable hemiacetal. The same is true for the C-2 and C-3 hydroxyls, and thus five- and six-membered rings are by far the most likely to be formed from six-membered monosaccharides. D-Ribose, with five carbons, readily forms either five-membered rings (α- or β-D-ribofuranose) or six-membered rings (α- or β-D-ribopyranose) (Figure 7.8). In general, aldoses and ketoses with five or more carbons can form *either* furanose or pyranose rings, and the more stable form depends on structural factors. The nature of the substituent groups on the carbonyl and hydroxyl groups and the configuration about the asymmetric carbon will determine whether a given monosaccharide prefers the pyranose or furanose structure. In general, the pyranose form is favored over the furanose ring for aldohexose sugars, although, as we shall see, furanose structures are more stable for ketohexoses.

Although Haworth projections are convenient for display of monosaccharide structures, they do not accurately portray the conformations of pyranose and furanose rings. Given C—C—C tetrahedral bond angles of 109° and C—O—C angles of 111°, neither pyranose nor furanose rings can adopt true planar structures. Instead, they take on puckered conformations, and in the case of pyranose rings, the two favored structures are the **chair conformation** and the **boat conformation,** shown in Figure 7.9. Note that the ring substituents

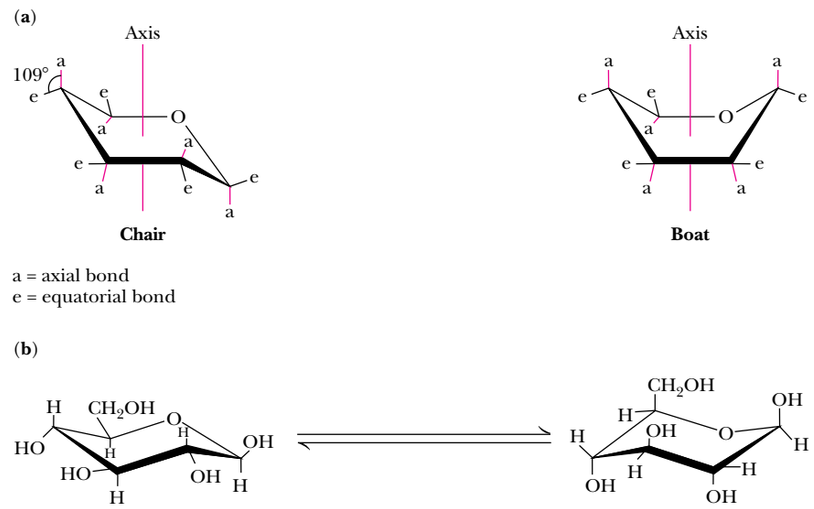


FIGURE 7.9 • (a) Chair and boat conformations of a pyranose sugar. (b) Two possible chair conformations of β-D-glucose.

in these structures can be **equatorial,** which means approximately coplanar with the ring, or **axial,** that is, parallel to an axis drawn through the ring as shown. Two general rules dictate the conformation to be adopted by a given saccharide unit. First, bulky substituent groups on such rings are more stable when they occupy equatorial positions rather than axial positions, and second, chair conformations are slightly more stable than boat conformations. For a typical pyranose, such as β-D-glucose, there are two possible chair conformations (Figure 7.9). Of all the D-aldohexoses, β-D-glucose is the only one that can adopt a conformation with all its bulky groups in an equatorial position. With this advantage of stability, it may come as no surprise that β-D-glucose is the most widely occurring organic group in nature and the central hexose in carbohydrate metabolism.

Derivatives of Monosaccharides

A variety of chemical and enzymatic reactions produce **derivatives** of the simple sugars. These modifications produce a diverse array of saccharide derivatives. Some of the most common derivations are discussed here.

Sugar Acids

Sugars with free anomeric carbon atoms are reasonably good reducing agents and will reduce hydrogen peroxide, ferricyanide, certain metals (Cu^{2+} and Ag^{+}), and other oxidizing agents. Such reactions convert the sugar to a **sugar acid.** For example, addition of alkaline $CuSO_4$ (called *Fehling's solution*) to an aldose sugar produces a red cuprous oxide (Cu_2O) precipitate:

$$\underset{\textbf{Aldehyde}}{\overset{\displaystyle O}{\overset{\|}{R}C{-}H}} + 2\,Cu^{2+} + 5\,OH^{-} \longrightarrow \underset{\textbf{Carboxylate}}{\overset{\displaystyle O}{\overset{\|}{R}C{-}O^{-}}} + Cu_2O\downarrow + 3\,H_2O$$

and converts the aldose to an **aldonic acid,** such as **gluconic acid** (Figure 7.10). Formation of a precipitate of red Cu_2O constitutes a positive test for an aldehyde. Carbohydrates that can reduce oxidizing agents in this way are referred to as **reducing sugars.** By quantifying the amount of oxidizing agent reduced by a sugar solution, one can accurately determine the concentration of the sugar. *Diabetes mellitus* is a condition that causes high levels of glucose in urine and blood, and frequent analysis of reducing sugars in diabetic patients is an important part of the diagnosis and treatment of this disease. Over-the-counter kits for the easy and rapid determination of reducing sugars have made this procedure a simple one for diabetics.

Monosaccharides can be oxidized enzymatically at C-6, yielding **uronic acids,** such as **D-glucuronic** and **L-iduronic** acids (Figure 7.10). L-Iduronic acid is similar to D-glucuronic acid, except for having an opposite configuration at C-5. Oxidation at both C-1 and C-6 produces **aldaric acids,** such as **D-glucaric acid.**

Sugar Alcohols

Sugar alcohols, another class of sugar derivative, can be prepared by the mild reduction (with $NaBH_4$ or similar agents) of the carbonyl groups of aldoses and ketoses. Sugar alcohols, or **alditols,** are designated by the addition of *-itol* to the name of the parent sugar (Figure 7.11). The alditols are linear molecules that cannot cyclize in the manner of aldoses. Nonetheless, alditols are characteristically sweet tasting, and **sorbitol, mannitol,** and **xylitol** are widely used to sweeten sugarless gum and mints. Sorbitol buildup in the eyes of dia-

FIGURE 7.10

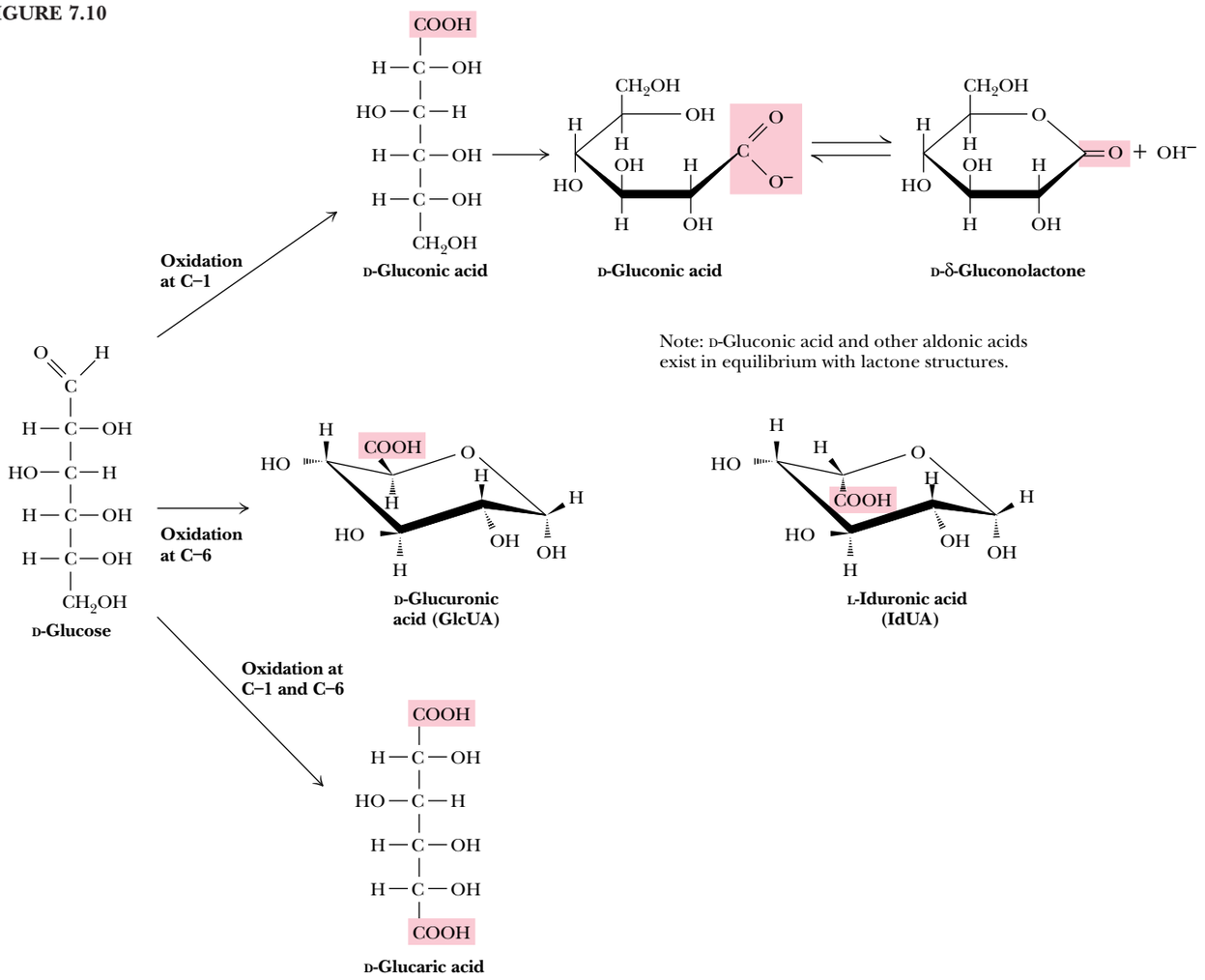
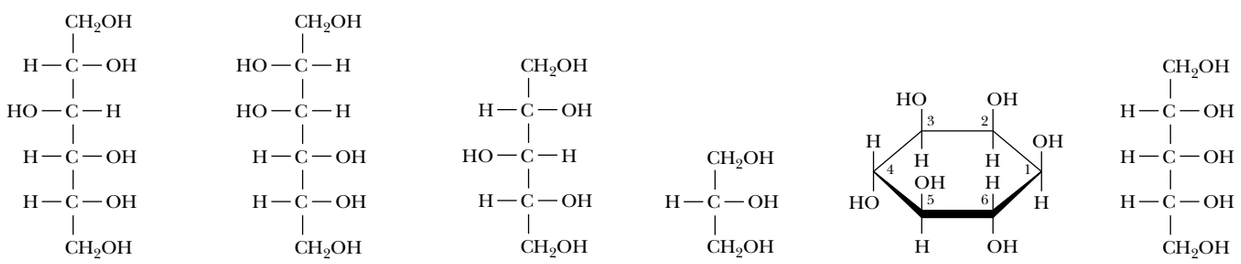


FIGURE 7.11 • Structures of some sugar alcohols.



betics is implicated in cataract formation. **Glycerol** and ***myo*-inositol,** a cyclic alcohol, are components of lipids (see Chapter 8). There are nine different stereoisomers of inositol; the one shown in Figure 7.11 was first isolated from heart muscle and thus has the prefix *myo-* for muscle. **Ribitol** is a constituent of flavin coenzymes (see Chapter 20).

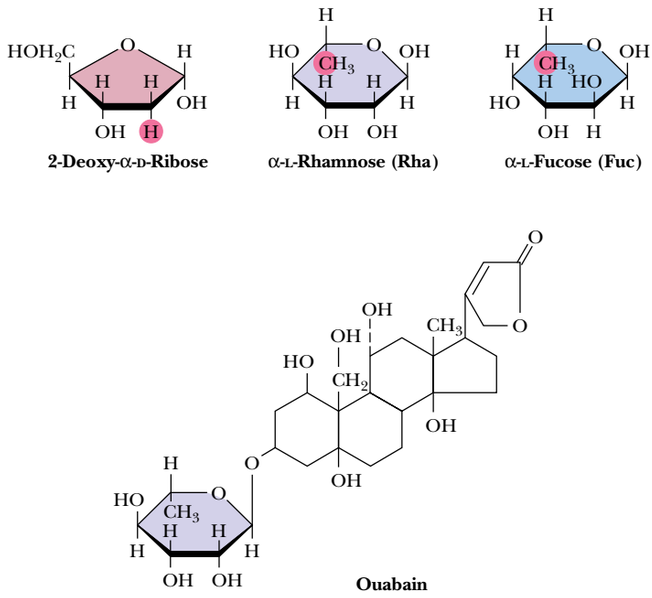


FIGURE 7.12 • Several deoxy sugars and ouabain, which contains α-L-rhamnose (Rha). Hydrogen atoms highlighted in red are "deoxy" positions.

Deoxy Sugars

The **deoxy sugars** are monosaccharides with one or more hydroxyl groups replaced by hydrogens. 2-Deoxy-D-ribose (Figure 7.12), whose systematic name is 2-deoxy-D-erythropentose, is a constituent of DNA in all living things (see Chapter 11). Deoxy sugars also occur frequently in glycoproteins and polysaccharides. L-Fucose and L-rhamnose, both 6-deoxy sugars, are components of some cell walls, and rhamnose is a component of **ouabain,** a highly toxic *cardiac glycoside* found in the bark and root of the ouabaio tree. Ouabain is used by the East African Somalis as an arrow poison. The sugar moiety is not the toxic part of the molecule (see Chapter 10).

Sugar Esters

Phosphate esters of glucose, fructose, and other monosaccharides are important metabolic intermediates, and the ribose moiety of nucleotides such as ATP and GTP is phosphorylated at the 5′-position (Figure 7.13).

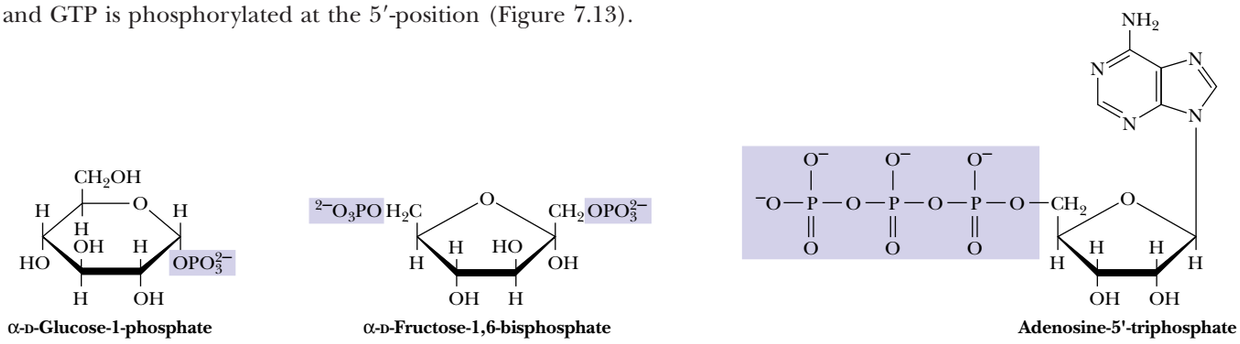


FIGURE 7.13 • Several sugar esters important in metabolism.

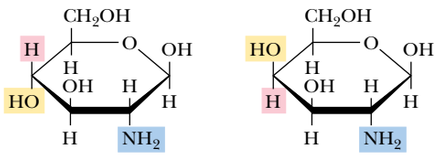


FIGURE 7.14 • Structures of D-glucosamine and D-galactosamine.

Amino Sugars

Amino sugars, including **D-glucosamine** and **D-galactosamine** (Figure 7.14), contain an amino group (instead of a hydroxyl group) at the C-2 position. They are found in many oligo- and polysaccharides, including *chitin,* a polysaccharide in the exoskeletons of crustaceans and insects.

Muramic acid and **neuraminic acid,** which are components of the polysaccharides of cell membranes of higher organisms and also bacterial cell walls, are glucosamines linked to three-carbon acids at the C-1 or C-3 positions. In muramic acid (thus named as an *ami*ne isolated from bacterial cell wall polysaccharides; *murus* is Latin for "wall"), the hydroxyl group of a lactic acid moiety makes an ether linkage to the C-3 of glucosamine. Neuraminic acid (an *ami*ne isolated from *neur*al tissue) forms a C—C bond between the C-1 of *N*-acetylmannosamine and the C-3 of pyruvic acid (Figure 7.15). The *N*-acetyl and *N*-glycolyl derivatives of neuraminic acid are collectively known as **sialic acids** and are distributed widely in bacteria and animal systems.

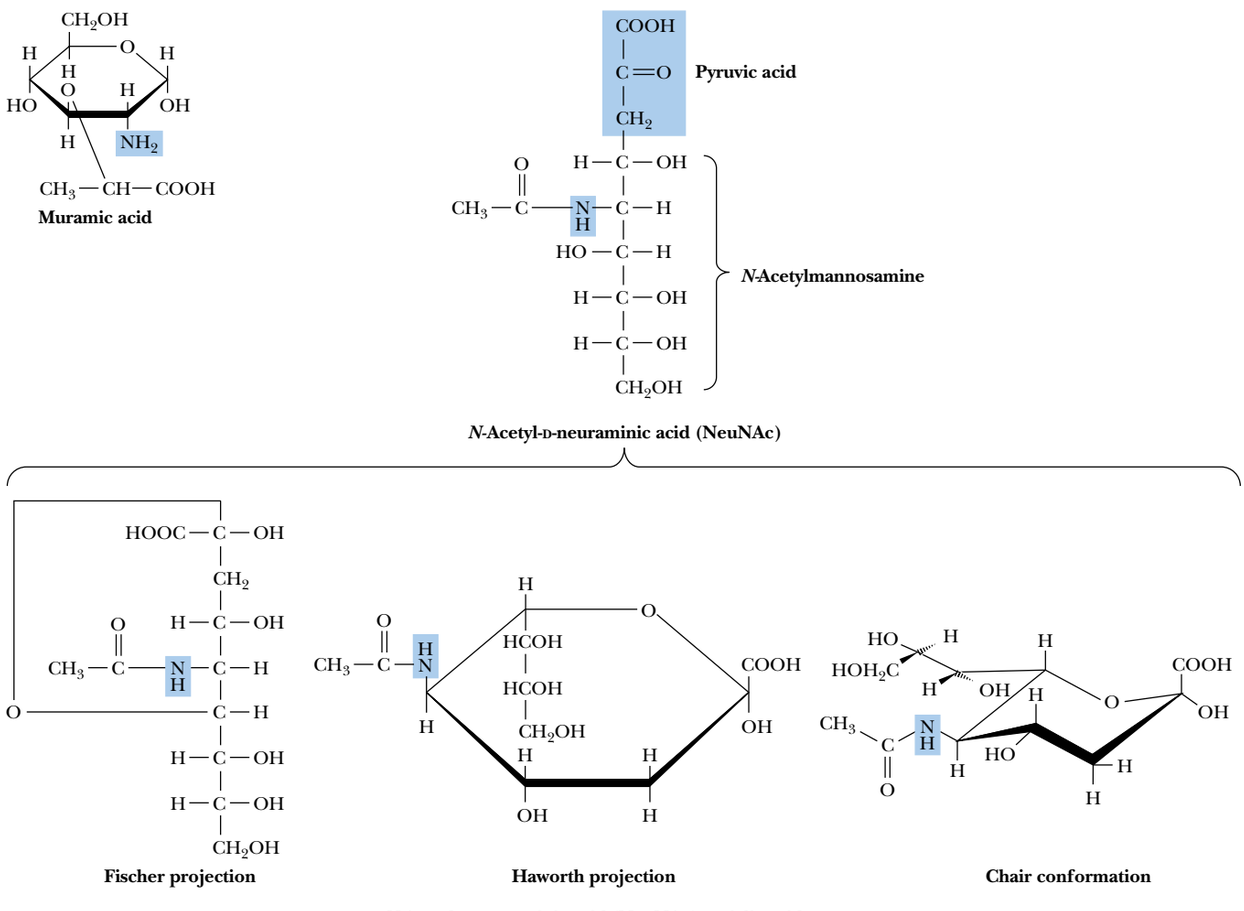


FIGURE 7.15 • Structures of muramic acid and neuraminic acid and several depictions of sialic acid.

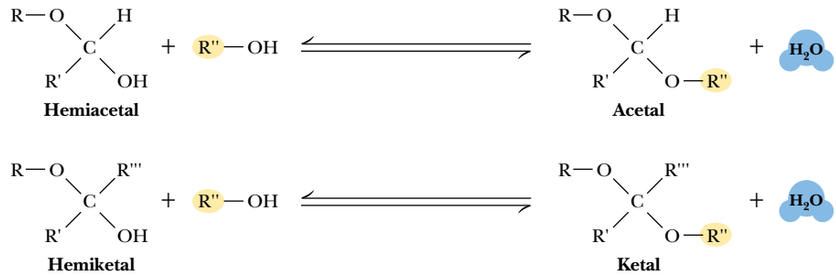


FIGURE 7.16 • Acetals and ketals can be formed from hemiacetals and hemiketals, respectively.

Acetals, Ketals, and Glycosides

Hemiacetals and hemiketals can react with alcohols in the presence of acid to form **acetals** and **ketals,** as shown in Figure 7.16. This reaction is another example of a *dehydration synthesis* and is similar in this respect to the reactions undergone by amino acids to form peptides and nucleotides to form nucleic acids. The pyranose and furanose forms of monosaccharides react with alcohols in this way to form **glycosides** with retention of the α- or β-configuration at the C-1 carbon. The new bond between the anomeric carbon atom and the oxygen atom of the alcohol is called a **glycosidic bond.** Glycosides are named according to the parent monosaccharide. For example, *methyl-β-D-glucoside* (Figure 7.17) can be considered a derivative of β-D-glucose.

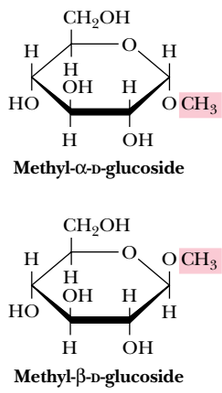


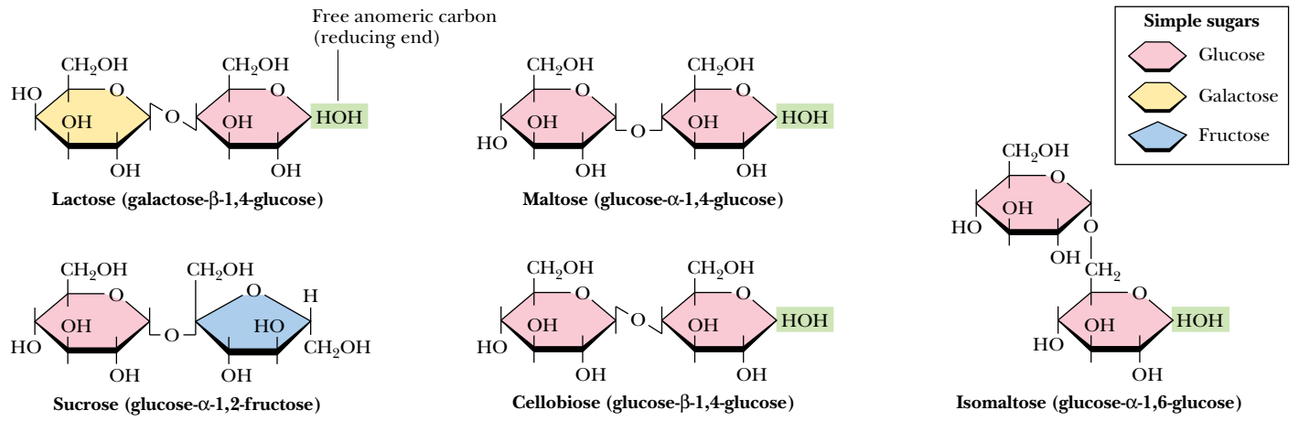
FIGURE 7.17 • The anomeric forms of methyl-D-glucoside.

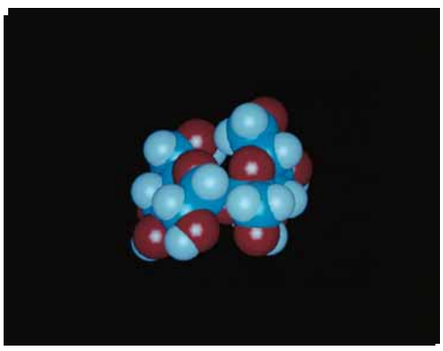
7.3 • Oligosaccharides

Given the relative complexity of oligosaccharides and polysaccharides in higher organisms, it is perhaps surprising that these molecules are formed from relatively few different monosaccharide units. (In this respect, the oligo- and polysaccharides are similar to proteins; both form complicated structures based on a small number of different building blocks.) Monosaccharide units include the hexoses glucose, fructose, mannose, and galactose and the pentoses ribose and xylose.

Disaccharides

The simplest oligosaccharides are the **disaccharides,** which consist of two monosaccharide units linked by a glycosidic bond. As in proteins and nucleic acids, each individual unit in an oligosaccharide is termed a *residue.* The disaccharides shown in Figure 7.18 are all commonly found in nature, with sucrose, maltose, and lactose being the most common. Each is a mixed acetal, with one hydroxyl group provided intramolecularly and one hydroxyl from the other monosaccharide. Except for sucrose, each of these structures possesses one free unsubstituted anomeric carbon atom, and thus each of these disaccharides is a reducing sugar. The end of the molecule containing the free anomeric carbon is called the **reducing end,** and the other end is called the **nonreducing end.** In the case of sucrose, both of the anomeric carbon atoms are substituted, that is, neither has a free —OH group. The substituted anomeric carbons cannot be converted to the aldehyde configuration and thus cannot participate in





Sucrose

FIGURE 7.18 • The structures of several important disaccharides. Note that the notation —HOH means that the configuration can be either α or β. If the —OH group is above the ring, the configuration is termed β. The configuration is α if the —OH group is below the ring as shown. Also note that sucrose has no free anomeric carbon atoms.

the oxidation–reduction reactions characteristic of reducing sugars. Thus, sucrose is *not* a reducing sugar.

Maltose, isomaltose, and cellobiose are all **homodisaccharides** because they each contain only one kind of monosaccharide, namely, glucose. **Maltose** is produced from starch (a polymer of α-D-glucose produced by plants) by the action of amylase enzymes and is a component of malt, a substance obtained by allowing grain (particularly barley) to soften in water and germinate. The enzyme **diastase,** produced during the germination process, catalyzes the hydrolysis of starch to maltose. Maltose is used in beverages (malted milk, for example), and because it is fermented readily by yeast, it is important in the brewing of beer. In both maltose and cellobiose, the glucose units are **1→4 linked,** meaning that the C-1 of one glucose is linked by a glycosidic bond to the C-4 oxygen of the other glucose. The only difference between them is in the configuration at the glycosidic bond. Maltose exists in the α-configuration, whereas cellobiose is β. **Isomaltose** is obtained in the hydrolysis of some polysaccharides (such as dextran), and **cellobiose** is obtained from the acid hydrolysis of cellulose. Isomaltose also consists of two glucose units in a glycosidic bond, but in this case, C-1 of one glucose is linked to C-6 of the other, and the configuration is α.

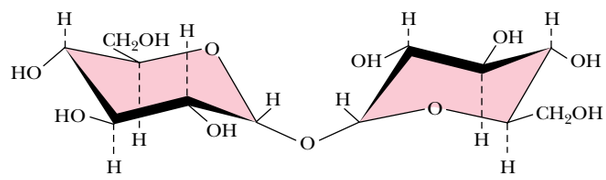
The complete structures of these disaccharides can be specified in shorthand notation by using abbreviations for each monosaccharide, α or β, to denote configuration, and appropriate numbers to indicate the nature of the linkage. Thus, cellobiose is Glcβ1–4Glc, whereas isomaltose is Glcα1–6Glc. Often the glycosidic linkage is written with an arrow so that cellobiose and isomaltose would be Glcβ1→4Glc and Glcα1→6Glc, respectively. Because the linkage carbon on the first sugar is always C-1, a newer trend is to drop the 1- or

A DEEPER LOOK

Trehalose—A Natural Protectant for Bugs

Insects use an open circulatory system to circulate **hemolymph** (insect blood). The "blood sugar" is not glucose but rather **trehalose,** an unusual, nonreducing disaccharide (see Figure). Trehalose is found typically in organisms that are naturally subject to temperature variations and other environmental stresses—bacterial spores, fungi, yeast, and many insects. (Interestingly, honeybees do not have trehalose in their hemolymph, perhaps because they practice a colonial, rather than solitary, lifestyle. Bee colonies maintain a rather constant temperature of 18°C, protecting the residents from large temperature changes.)

What might explain this correlation between trehalose utilization and environmentally stressful lifestyles? Konrad Bloch* suggests that trehalose may act as a natural cryoprotectant. Freezing and thawing of biological tissues frequently causes irreversible structural changes, destroying biological activity. High concentrations of polyhydroxy compounds, such as sucrose and glycerol, can protect biological materials from such damage. Trehalose is particularly well-suited for this purpose and has been shown to be superior to other polyhydroxy compounds, especially at low concentrations. Support for this novel idea comes from studies by P. A. Attfield,† which show that trehalose levels in the yeast *Saccharomyces cerevisiae* increase significantly during exposure to high salt and high growth temperatures—the same conditions that elicit the production of heat-shock proteins!



*Bloch, K., 1994. *Blondes in Venetian Paintings, the Nine-Banded Armadillo, and Other Essays in Biochemistry.* New Haven: Yale University Press.
†Attfield, P. A., 1987. Trehalose accumulates in *Saccharomyces cerevisiae* during exposure to agents that induce heat shock responses. *FEBS Letters* **225:**259.

1→ and describe these simply as Glcβ4Glc and Glcα6Glc, respectively. More complete names can also be used, however, so that maltose would be O-α-D-glucopyranosyl-(1→4)-D-glucopyranose. Cellobiose, because of its β-glycosidic linkage, is formally O-β-D-glucopyranosyl-(1→4)-D-glucopyranose.

β-D-lactose (O-β-D-Galactopyranosyl-(1→4)-D-glucopyranose) (Figure 7.18) is the principal carbohydrate in milk and is of critical nutritional importance to mammals in the early stages of their lives. It is formed from D-galactose and D-glucose via a β(1→4) link, and because it has a free anomeric carbon, it is capable of mutarotation and is a reducing sugar. It is an interesting quirk of nature that lactose cannot be absorbed directly into the bloodstream. It must first be broken down into galactose and glucose by **lactase,** an intestinal enzyme that exists in young, nursing mammals but is not produced in significant quantities in the mature mammal. Most humans, with the exception of certain groups in Africa and northern Europe, produce only low levels of lactase. For most individuals, this is not a problem, but some cannot tolerate lactose and experience intestinal pain and diarrhea upon consumption of milk.

Sucrose, in contrast, is a disaccharide of almost universal appeal and tolerance. Produced by many higher plants and commonly known as *table sugar,* it is one of the products of photosynthesis and is composed of fructose and glucose. Sucrose has a specific optical rotation, $[\alpha]_D^{20}$, of +66.5°, but an equimolar mixture of its component monosaccharides has a net negative rotation ($[\alpha]_D^{20}$ of glucose is +52.5° and of fructose is −92°). Sucrose is hydrolyzed by the enzyme **invertase,** so named for the inversion of optical rotation accompanying this reaction. Sucrose is also easily hydrolyzed by dilute acid, apparently because the fructose in sucrose is in the relatively unstable furanose form. Although sucrose and maltose are important to the human diet, they are not taken up directly in the body. In a manner similar to lactose, they are first hydrolyzed by **sucrase** and **maltase,** respectively, in the human intestine.

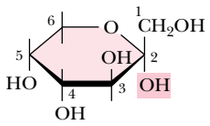
A DEEPER LOOK

Honey—An Ancestral Carbohydrate Treat

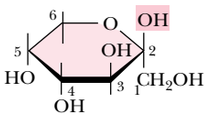
Honey, the first sweet known to humankind, is the only sweetening agent that can be stored and used exactly as produced in nature. Bees process the nectar of flowers so that their final product is able to survive long-term storage at ambient temperature. Used as a ceremonial material and medicinal agent in earliest times, honey was not regarded as a food until the Greeks and Romans. Only in modern times have cane and beet sugar surpassed honey as the most frequently used sweetener. What is the chemical nature of this magical, viscous substance?

The bees' processing of honey consists of (1) reducing the water content of the nectar (30 to 60%) to the self-preserving range of 15 to 19%, (2) hydrolyzing the significant amount of sucrose in nectar to glucose and fructose by the action of the enzyme invertase, and (3) producing small amounts of gluconic acid from glucose by the action of the enzyme **glucose oxidase.** Most of the sugar in the final product is glucose and fructose, and the final product is supersaturated with respect to these monosaccharides. Honey actually consists of an emulsion of microscopic glucose hydrate and fructose hydrate crystals in a thick syrup. Sucrose accounts for only about 1% of the sugar in the final product, with fructose at about 38% and glucose at 31% by weight.

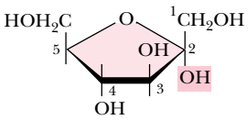
The figure shows a ^{13}C nuclear magnetic resonance spectrum of honey from a mixture of wildflowers in southeastern Pennsylvania. Interestingly, five major hexose species contribute to this spectrum. Although most textbooks show fructose exclusively in its furanose form, the predominant form of fructose (67% of total fructose) is β-D-fructopyranose, with the β- and α-fructofuranose forms accounting for 27% and 6% of the fructose, respectively. In polysaccharides, fructose invariably prefers the furanose form, but free fructose (and crystalline fructose) is predominantly β-fructopyranose.



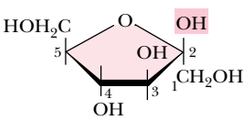
α-D-Fructopyranose



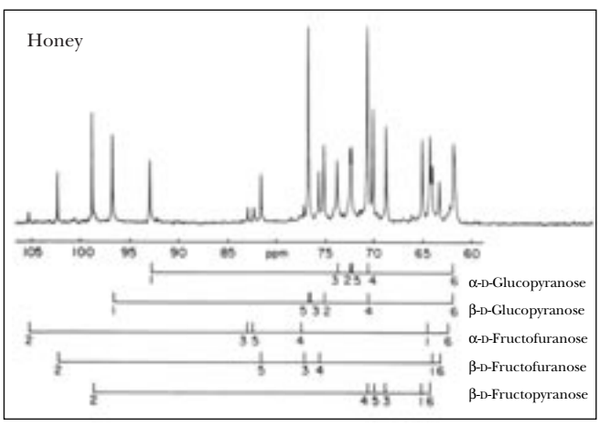
β-D-Fructopyranose



α-D-Fructofuranose

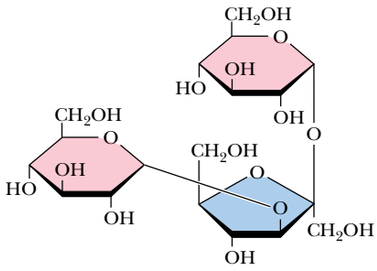


β-D-Fructofuranose

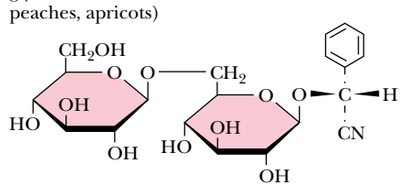


White, J. W., 1978. Honey. *Advances in Food Research* **24:**287–374.
Prince, R. C., Gunson, D. E., Leigh, J. S., and McDonald, G. G., 1982. The predominant form of fructose is a pyranose, not a furanose ring. *Trends in Biochemical Sciences* **7**:239–240.

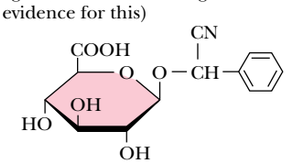
Melezitose (a constituent of honey)



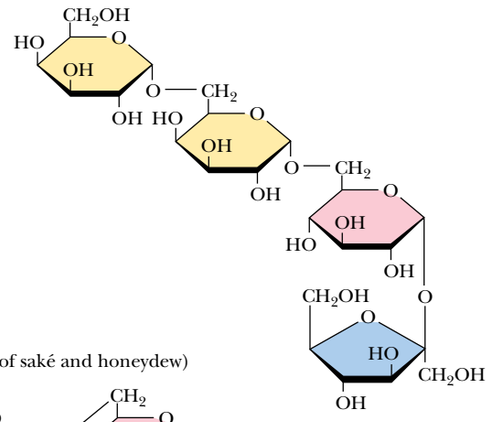
Amygdalin (occurs in seeds of *Rosaceae*; glycoside of bitter almonds, in kernels of cherries, peaches, apricots)



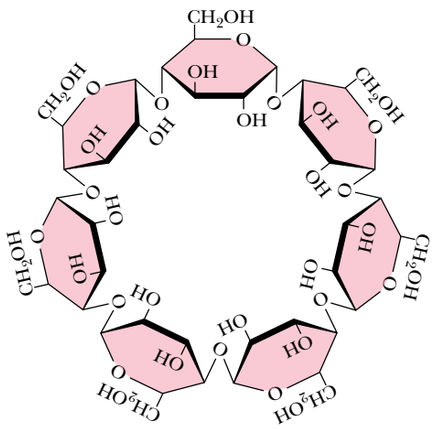
Laetrile (claimed to be an anticancer agent, but there is no rigorous scientific evidence for this)



Stachyose (a constituent of many plants: white jasmine, yellow lupine, soybeans, lentils, etc.; causes flatulence since humans cannot digest it)



Cycloheptaamylose (a breakdown product of starch; useful in chromatographic separations)



Dextrantriose (a constituent of saké and honeydew)

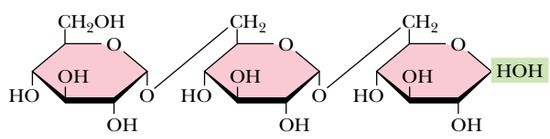
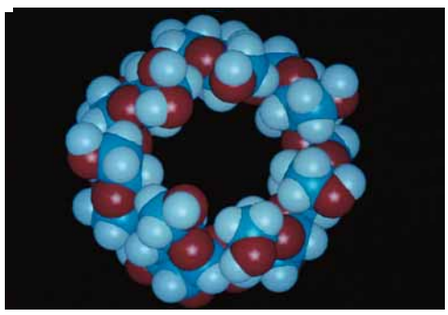


FIGURE 7.19 • The structures of some interesting oligosaccharides.

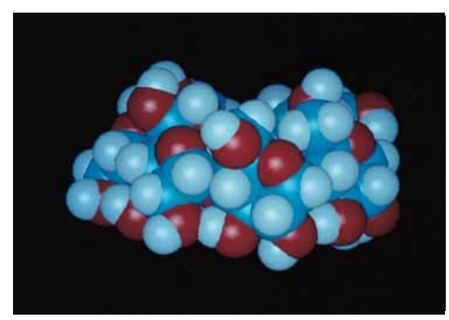


Cycloheptaamylose

Higher Oligosaccharides

In addition to the simple disaccharides, many other oligosaccharides are found in both prokaryotic and eukaryotic organisms, either as naturally occurring substances or as hydrolysis products of natural materials. Figure 7.19 lists a number of simple oligosaccharides, along with descriptions of their origins and interesting features. Several are constituents of the sweet nectars or saps exuded or extracted from plants and trees. One particularly interesting and useful group of oligosaccharides is the **cycloamyloses.** These oligosaccharides are cyclic structures, and in solution they form molecular "pockets" of various diameters. These pockets are surrounded by the chiral carbons of the saccharides themselves and are able to form stereospecific inclusion complexes with chiral molecules that can fit into the pockets. Thus, mixtures of stereoisomers of small organic molecules can be separated into pure isomers on columns of **cycloheptaamylose,** for example.

Stachyose is typical of the oligosaccharide components found in substantial quantities in beans, peas, bran, and whole grains. These oligosaccharides are not digested by stomach enzymes, but *are* metabolized readily by bacteria in the intestines. This is the source of the flatulence that often accompanies the consumption of such foods. Commercial products are now available that assist in the digestion of the gas-producing components of these foods. These products contain an enzyme that hydrolyzes the culprit oligosaccharides in the stomach before they become available to intestinal microorganisms.

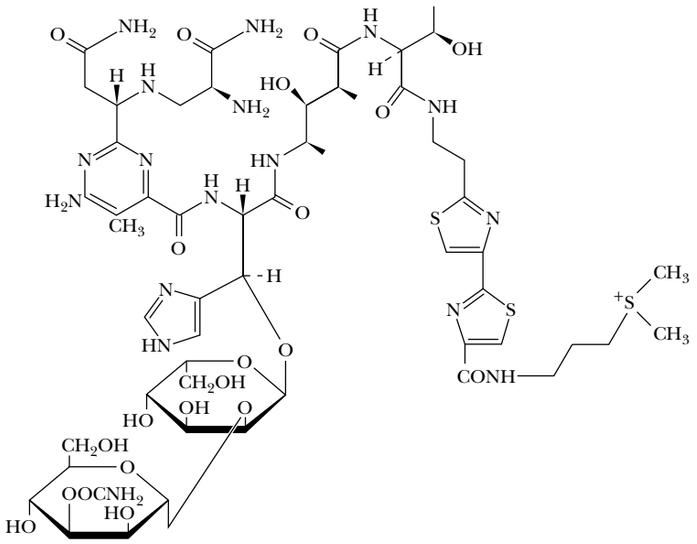


Cycloheptaamylose (side view)

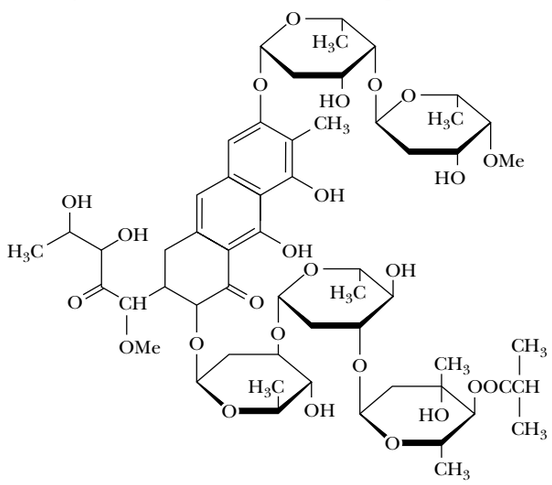
Another notable glycoside is **amygdalin,** which occurs in bitter almonds and in the kernels or pits of cherries, peaches, and apricots. Hydrolysis of this substance and subsequent oxidation yields **laetrile,** which has been claimed by some to have anticancer properties. There is no scientific evidence for these claims, and the U.S. Food and Drug Administration has never approved laetrile for use in the United States.

Oligosaccharides also occur widely as components (via glycosidic bonds) of *antibiotics* derived from various sources. Figure 7.20 shows the structures of a few representative carbohydrate-containing antibiotics. Some of these antibiotics also show antitumor activity. One of the most important of this type is **bleomycin A_2,** which is used clinically against certain tumors.

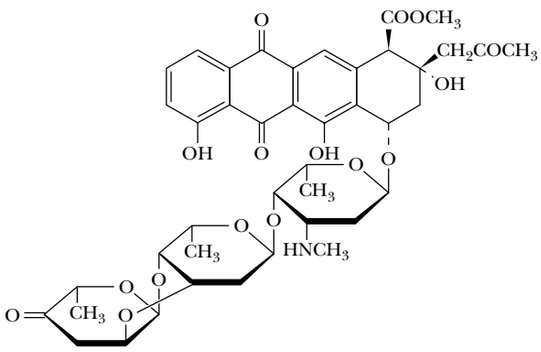
Bleomycin A_2 (an antitumor agent used clinically against specific tumors)



Aburamycin C (an antibiotic and antitumor agent)



Sulfurmycin B (active against Gram-positive bacteria, mycobacteria, and tumors)



Streptomycin (a broad spectrum antibiotic)

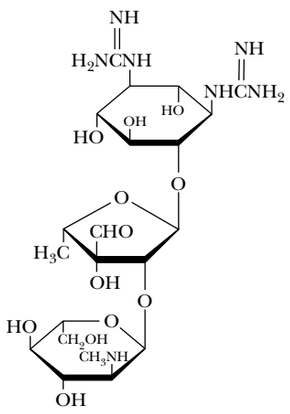


FIGURE 7.20 • Some antibiotics are oligosaccharides or contain oligosaccharide groups.

7.4 • Polysaccharides

Structure and Nomenclature

By far the majority of carbohydrate material in nature occurs in the form of polysaccharides. By our definition, polysaccharides include not only those substances composed only of glycosidically linked sugar residues but also molecules that contain polymeric saccharide structures linked via covalent bonds to amino acids, peptides, proteins, lipids, and other structures.

Polysaccharides, also called **glycans,** consist of monosaccharides and their derivatives. If a polysaccharide contains only one kind of monosaccharide molecule, it is a **homopolysaccharide,** or **homoglycan,** whereas those containing more than one kind of monosaccharide are **heteropolysaccharides.** The most common constituent of polysaccharides is D-glucose, but D-fructose, D-galactose, L-galactose, D-mannose, L-arabinose, and D-xylose are also common. Common monosaccharide derivatives in polysaccharides include the amino sugars (D-glucosamine and D-galactosamine), their derivatives (*N*-acetylneuraminic acid and *N*-acetylmuramic acid), and simple sugar acids (glucuronic and iduronic acids). Homopolysaccharides are often named for the sugar unit they contain, so that glucose homopolysaccharides are called **glucans,** while mannose homopolysaccharides are **mannans.** Other homopolysaccharide names are just as obvious: *galacturonans, arabinans,* and so on. Homopolysaccharides of uniform linkage type are often named by including notation to denote ring size and linkage type. Thus, cellulose is a *(1→4)-β-D-glucopyranan.* Polysaccharides differ not only in the nature of their component monosaccharides but also in the length of their chains and in the amount of chain branching that occurs. Although a given sugar residue has only one anomeric carbon and thus can form only one glycosidic linkage with hydroxyl groups on other molecules, each sugar residue carries several hydroxyls, one or more of which may be an acceptor of glycosyl substituents (Figure 7.21). This ability to form branched structures distinguishes polysaccharides from proteins and nucleic acids, which occur only as linear polymers.

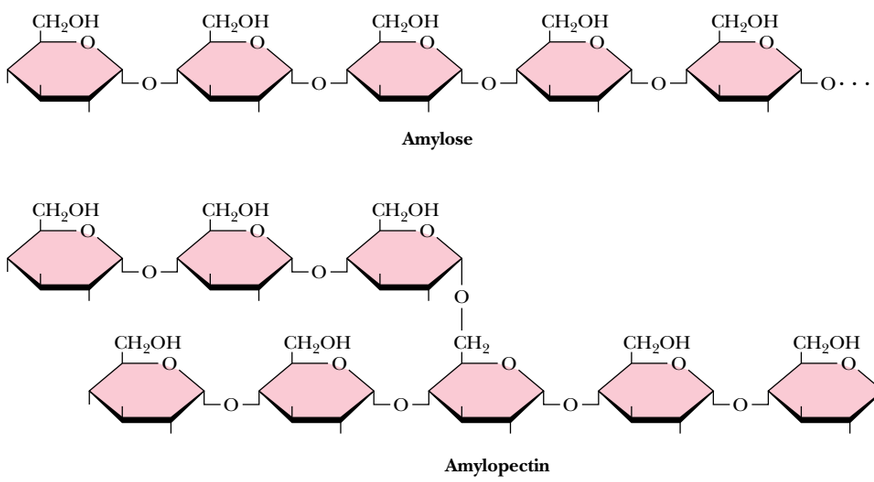


FIGURE 7.21 • Amylose and amylopectin are the two forms of starch. Note that the linear linkages are α(1→4), but the branches in amylopectin are α(1→6). Branches in polysaccharides can involve any of the hydroxyl groups on the monosaccharide components. Amylopectin is a highly branched structure, with branches occurring every 12 to 30 residues.

Polysaccharide Functions

The functions of many individual polysaccharides cannot be assigned uniquely, and some of their functions may not yet be appreciated. Traditionally, biochemistry textbooks have listed the functions of polysaccharides as storage materials, structural components, or protective substances. Thus, *starch, glycogen,* and other storage polysaccharides, as readily metabolizable food, provide energy reserves for cells. *Chitin* and *cellulose* provide strong support for the skeletons of arthropods and green plants, respectively. Mucopolysaccharides, such as the *hyaluronic acids,* form protective coats on animal cells. In each of these cases, the relevant polysaccharide is either a homopolymer or a polymer of small repeating units. Recent research indicates, however, that oligosaccharides and polysaccharides with varied structures may also be involved in much more sophisticated tasks in cells, including a variety of cellular recognition and intercellular communication events, as discussed later.

Storage Polysaccharides

Storage polysaccharides are an important carbohydrate form in plants and animals. It seems likely that organisms store carbohydrates in the form of polysaccharides rather than as monosaccharides to lower the osmotic pressure of the sugar reserves. Because osmotic pressures depend only on *numbers of molecules,* the osmotic pressure is greatly reduced by formation of a few polysaccharide molecules out of thousands (or even millions) of monosaccharide units.

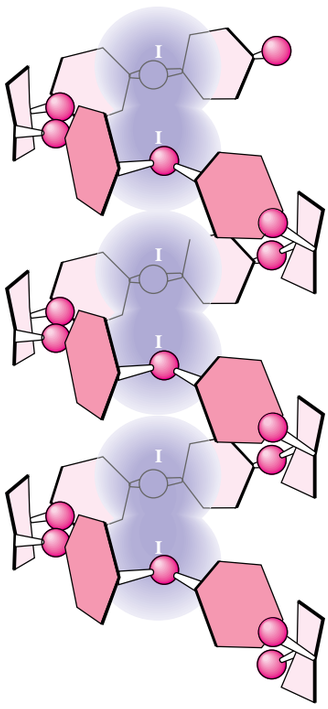


FIGURE 7.22 • Suspensions of amylose in water adopt a helical conformation. Iodine (I_2) can insert into the middle of the amylose helix to give a blue color that is characteristic and diagnostic for starch.

Starch

By far the most common storage polysaccharide in plants is **starch,** which exists in two forms: ***α*-amylose** and **amylopectin,** the structures of which are shown in Figure 7.21. Most forms of starch in nature are 10 to 30% α-amylose and 70 to 90% amylopectin. Typical cornstarch produced in the United States is about 25% α-amylose and 75% amylopectin. α-Amylose is composed of linear chains of D-glucose in $\alpha(1\rightarrow4)$ linkages. The chains are of varying length, having molecular weights from several thousand to half a million. As can be seen from the structure in Figure 7.21, the chain has a reducing end and a nonreducing end. Although poorly soluble in water, α-amylose forms micelles in which the polysaccharide chain adopts a helical conformation (Figure 7.22). Iodine reacts with α-amylose to give a characteristic blue color, which arises from the insertion of iodine into the middle of the hydrophobic amylose helix.

In contrast to α-amylose, amylopectin, the other component of typical starches, is a highly branched chain of glucose units (Figure 7.21). Branches occur in these chains every 12 to 30 residues. The average branch length is between 24 and 30 residues, and molecular weights of amylopectin molecules can range up to 100 million. The linear linkages in amylopectin are $\alpha(1\rightarrow4)$, whereas the branch linkages are $\alpha(1\rightarrow6)$. As is the case for α-amylose, amylopectin forms micellar suspensions in water; iodine reacts with such suspensions to produce a red-violet color.

Starch is stored in plant cells in the form of granules in the stroma of plastids (plant cell organelles) of two types: **chloroplasts,** in which photosynthesis takes place, and **amyloplasts,** plastids that are specialized starch accumulation bodies. When starch is to be mobilized and used by the plant that stored it, it must be broken down into its component monosaccharides. Starch is split into its monosaccharide elements by stepwise phosphorolytic cleavage of glucose units, a reaction catalyzed by **starch phosphorylase** (Figure 7.23). This is formally an $\alpha(1\rightarrow4)$-glucan phosphorylase reaction, and at each step, the prod-

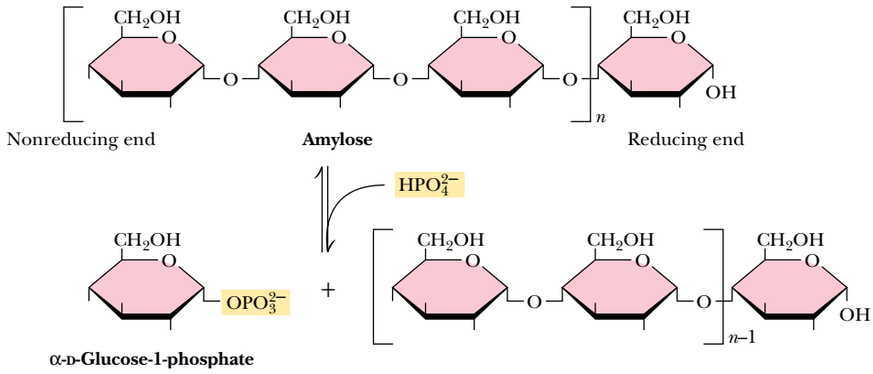


FIGURE 7.23 • The starch phosphorylase reaction cleaves glucose residues from amylose, producing α-D-glucose-1-phosphate.

ucts are one molecule of glucose-1-phosphate and a starch molecule with one less glucose unit. In α-amylose, this process continues all along the chain until the end is reached. However, the α(1→6) branch points of amylopectin are not susceptible to cleavage by phosphorylase, and thorough digestion of amylopectin by phosphorylase leaves a *limit dextrin,* which must be attacked by an α(1→6)-glucosidase to cleave the 1→6 branch points and allow complete hydrolysis of the remaining 1→4 linkages. Glucose-1-phosphate units are thus delivered to the plant cell, suitable for further processing in glycolytic pathways (see Chapter 19).

In animals, digestion and use of plant starches begins in the mouth with **salivary α-amylase** (α(1→4)-glucan 4-glucanohydrolase), the major enzyme secreted by the salivary glands. Although the capability of making and secreting salivary α-amylases is widespread in the animal world, some animals (such as cats, dogs, birds, and horses) do not secrete them. Salivary α-amylase is an **endoamylase** that splits α(1→4) glycosidic linkages only within the chain. Raw starch is not very susceptible to salivary endoamylase. However, when suspensions of starch granules are heated, the granules swell, taking up water and causing the polymers to become more accessible to enzymes. Thus, cooked starch is more digestible. In the stomach, salivary α-amylase is inactivated by the lower pH, but pancreatic secretions also contain α-amylase. **β-Amylase,** an enzyme absent in animals but prevalent in plants and microorganisms, cleaves disaccharide (maltose) units from the termini of starch chains and is an **exoamylase.** Neither α-amylase nor β-amylase, however, can cleave the α(1→6) branch points of amylopectin, and once again, α(1→6)-glucosidase is required to cleave at the branch points and allow complete hydrolysis of starch amylopectin.

Glycogen

The major form of storage polysaccharide in animals is **glycogen.** Glycogen is found mainly in the liver (where it may amount to as much as 10% of liver mass) and skeletal muscle (where it accounts for 1 to 2% of muscle mass). Liver glycogen consists of granules containing highly branched molecules, with α(1→6) branches occurring every 8 to 12 glucose units. Like amylopectin, glycogen yields a red-violet color with iodine. Glycogen can be hydrolyzed by both α- and β-amylases, yielding glucose and maltose, respectively, as products and can also be hydrolyzed by **glycogen phosphorylase,** an enzyme present in liver and muscle tissue, to release glucose-1-phosphate.

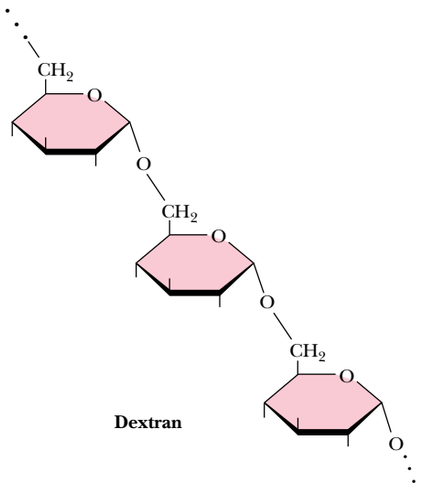


FIGURE 7.24 • Dextran is a branched polymer of D-glucose units. The main chain linkage is $\alpha(1\rightarrow6)$, but $1\rightarrow2$, $1\rightarrow3$, or $1\rightarrow4$ branches can occur.

Dextran

Another important family of storage polysaccharides are the **dextrans,** which are $\alpha(1\rightarrow6)$-linked polysaccharides of D-glucose with branched chains found in yeast and bacteria (Figure 7.24). Because the main polymer chain is $\alpha(1\rightarrow6)$ linked, the repeating unit is *isomaltose,* Glc$\alpha(1\rightarrow6)$-Glc. The branch points may be $1\rightarrow2$, $1\rightarrow3$, or $1\rightarrow4$ in various species. The degree of branching and the average chain length between branches depend on the species and strain of the organism. Bacteria growing on the surfaces of teeth produce extracellular accumulations of dextrans, an important component of *dental plaque.* Bacterial dextrans are frequently used in research laboratories as the support medium for column chromatography of macromolecules. Dextran chains cross-linked with epichlorohydrin yield the structure shown in Figure 7.25. These preparations (known by various trade names such as Sephadex and Bio-gel) are extremely hydrophilic and swell to form highly hydrated gels in water. Depending on the degree of cross-linking and the size of the gel particle, these materials form gels containing from 50 to 98% water. Dextran can also be cross-linked with other agents, forming gels with slightly different properties.

Structural Polysaccharides

Cellulose

The **structural polysaccharides** have properties that are dramatically different from those of the storage polysaccharides, even though the compositions of these two classes are similar. The structural polysaccharide **cellulose** is the most

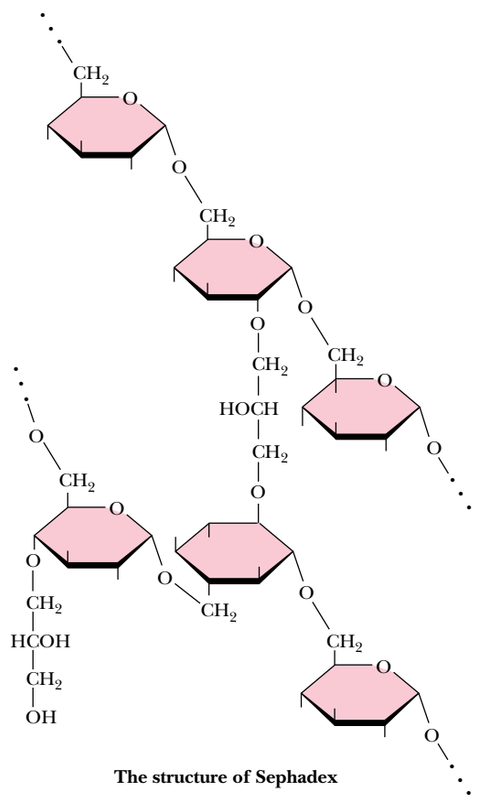


FIGURE 7.25 • Sephadex gels are formed from dextran chains cross-linked with epichlorohydrin. The degree of cross-linking determines the chromatographic properties of Sephadex gels. Sephacryl gels are formed by cross-linking of dextran polymers with *N,N′*-methylene bisacrylamide.

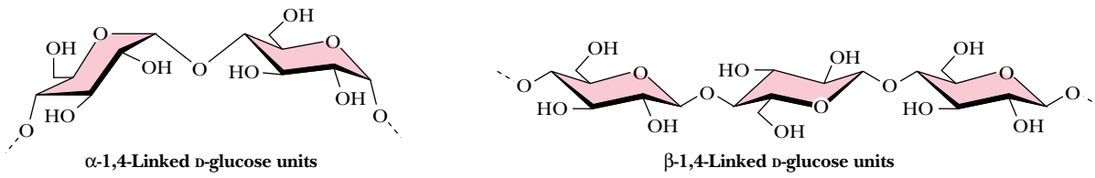


FIGURE 7.26 • (a) Amylose, composed exclusively of the relatively bent $\alpha(1\rightarrow4)$ linkages, prefers to adopt a helical conformation, whereas (b) cellulose, with $\beta(1\rightarrow4)$-glycosidic linkages, can adopt a fully extended conformation with alternating 180° flips of the glucose units. The hydrogen bonding inherent in such extended structures is responsible for the great strength of tree trunks and other cellulose-based materials.

abundant natural polymer found in the world. Found in the cell walls of nearly all plants, cellulose is one of the principal components providing physical structure and strength. The wood and bark of trees are insoluble, highly organized structures formed from cellulose and also from *lignin* (see Figure 27.35). It is awe-inspiring to look at a large tree and realize the amount of weight supported by polymeric structures derived from sugars and organic alcohols. Cellulose also has its delicate side, however. *Cotton,* whose woven fibers make some of our most comfortable clothing fabrics, is almost pure cellulose. Derivatives of cellulose have found wide use in our society. **Cellulose acetates** are produced by the action of acetic anhydride on cellulose in the presence of sulfuric acid and can be spun into a variety of fabrics with particular properties. Referred to simply as *acetates,* they have a silky appearance, a luxuriously soft feel, and a deep luster and are used in dresses, lingerie, linings, and blouses.

Cellulose is a linear homopolymer of D-glucose units, just as in α-amylose. The structural difference, which completely alters the properties of the polymer, is that in cellulose the glucose units are linked by $\beta(1\rightarrow4)$-glycosidic bonds, whereas in α-amylose the linkage is $\alpha(1\rightarrow4)$. The conformational difference between these two structures is shown in Figure 7.26. The $\alpha(1\rightarrow4)$-linkage sites of amylose are naturally bent, conferring a gradual turn to the polymer chain, which results in the helical conformation already described (see Figure 7.22). The most stable conformation about the $\beta(1\rightarrow4)$ linkage involves alternating 180° flips of the glucose units along the chain so that the chain adopts a fully extended conformation, referred to as an **extended ribbon.** Juxtaposition of several such chains permits efficient interchain hydrogen bonding, the basis of much of the strength of cellulose.

The structure of one form of cellulose, determined by X-ray and electron diffraction data, is shown in Figure 7.27. The flattened sheets of the chains lie side by side and are joined by hydrogen bonds. These sheets are laid on top of one another in a way that staggers the chains, just as bricks are staggered to give strength and stability to a wall. Cellulose is extremely resistant to hydrolysis, whether by acid or by the digestive tract amylases described earlier. As a result, most animals (including humans) cannot digest cellulose to any significant degree. Ruminant animals, such as cattle, deer, giraffes, and camels, are an exception because bacteria that live in the rumen (Figure 7.28) secrete the enzyme **cellulase,** a β-glucosidase effective in the hydrolysis of cellulose. The resulting glucose is then metabolized in a fermentation process to the benefit of the host animal. Termites and shipworms (*Teredo navalis*) similarly digest cellulose because their digestive tracts also contain bacteria that secrete cellulase.

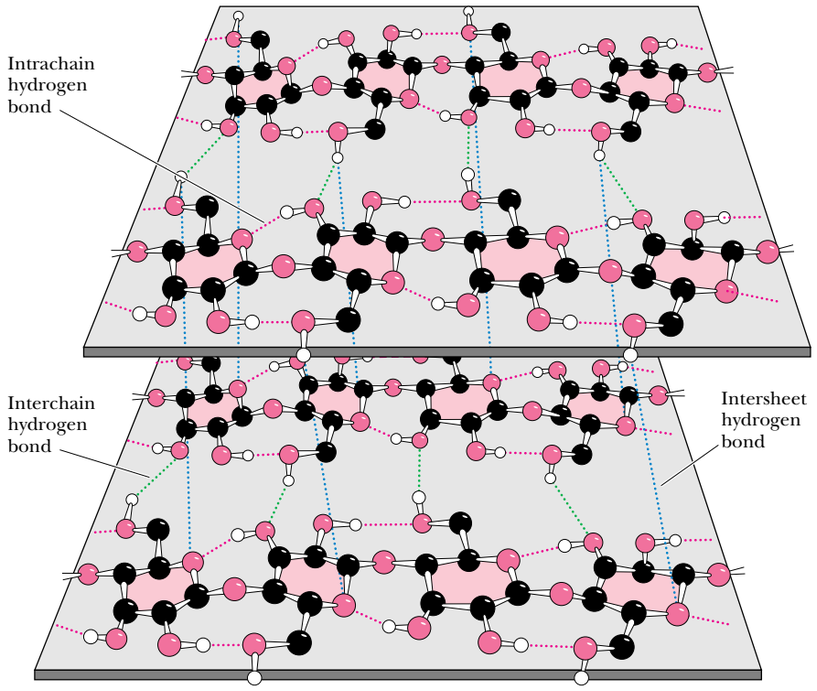


FIGURE 7.27 • The structure of cellulose, showing the hydrogen bonds (blue) between the sheets, which strengthen the structure. Intrachain hydrogen bonds are in red and interchain hydrogen bonds are in green.

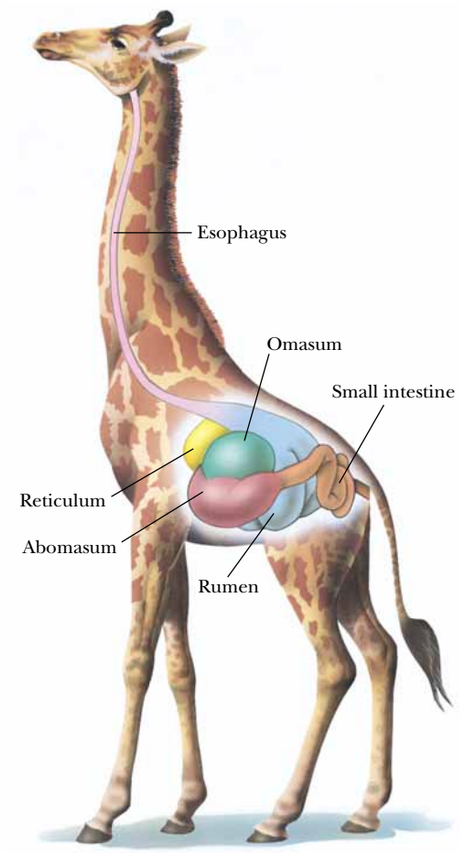


FIGURE 7.28 • Giraffes, cattle, deer, and camels are ruminant animals that are able to metabolize cellulose, thanks to bacterial cellulase in the rumen, a large first compartment in the stomach of a ruminant.

Chitin

A polysaccharide that is similar to cellulose, both in its biological function and its primary, secondary, and tertiary structure, is **chitin.** Chitin is present in the cell walls of fungi and is the fundamental material in the exoskeletons of crustaceans, insects, and spiders. The structure of chitin, an extended ribbon, is identical to cellulose, except that the —OH group on each C-2 is replaced by $—NHCOCH_3$, so that the repeating units are *N-acetyl-D-glucosamines* in $\beta(1\rightarrow4)$ linkage. Like cellulose (Figure 7.27), the chains of chitin form extended ribbons (Figure 7.29) and pack side by side in a crystalline, strongly hydrogen-bonded form. One significant difference between cellulose and chitin is whether the chains are arranged in **parallel** (all the reducing ends together at one end of a packed bundle and all the nonreducing ends together at the other end) or **antiparallel** (each sheet of chains having the chains arranged oppositely from the sheets above and below). Natural cellulose seems to occur only in parallel arrangements. Chitin, however, can occur in three forms, sometimes all in the same organism. α-*Chitin* is an all-parallel arrangement of the chains, whereas β-*chitin* is an antiparallel arrangement. In δ-*chitin,* the structure is thought to involve pairs of parallel sheets separated by single antiparallel sheets.

Chitin is the earth's second most abundant carbohydrate polymer (after cellulose), and its ready availability and abundance offer opportunities for industrial and commercial applications. Chitin-based coatings can extend the shelf life of fruits, and a chitin derivative that binds to iron atoms in meat has been found to slow the reactions that cause rancidity and flavor loss. Without such a coating, the iron in meats activates oxygen from the air, forming reactive free radicals that attack and oxidize polyunsaturated lipids, causing most of the flavor loss associated with rancidity. Chitin-based coatings coordinate the iron atoms, preventing their interaction with oxygen.

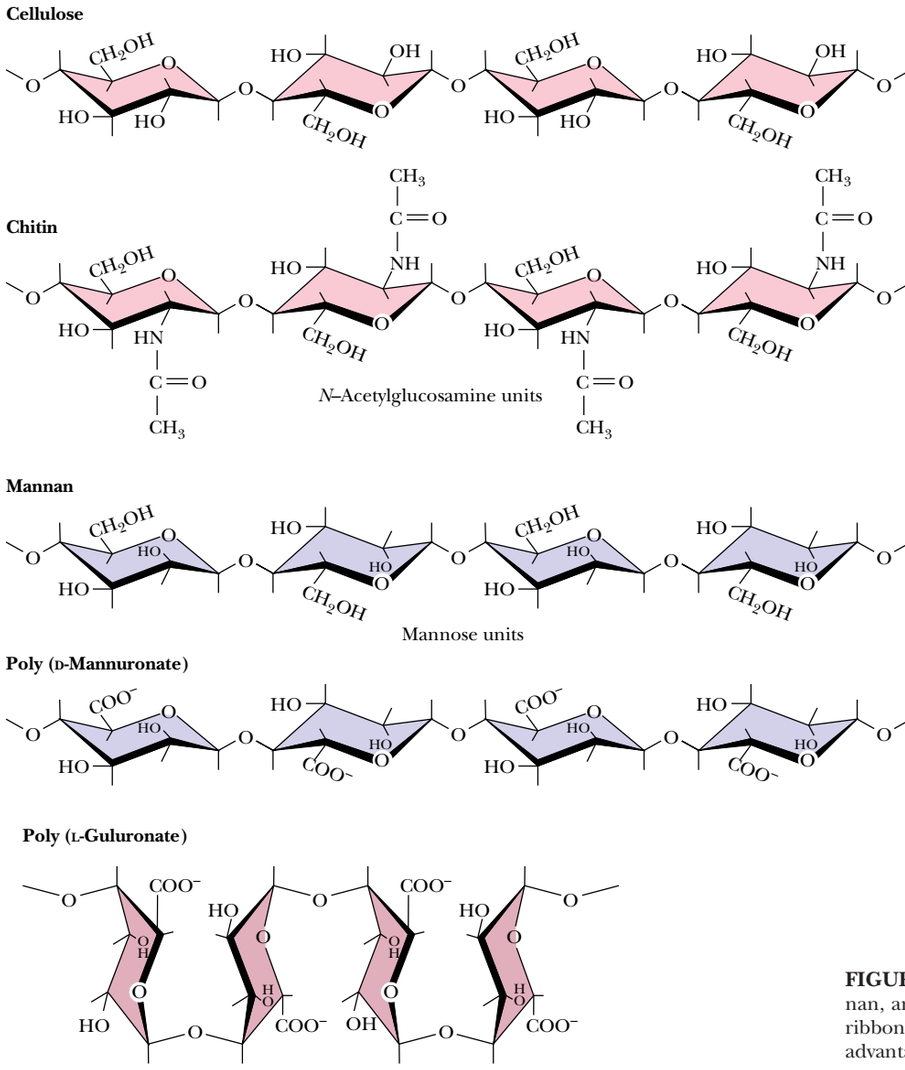


FIGURE 7.29 • Like cellulose, chitin, mannan, and poly(D-mannuronate) form extended ribbons and pack together efficiently, taking advantage of multiple hydrogen bonds.

Alginates

A family of novel extended ribbon structures that bind metal ions, particularly calcium, in their structure are the **alginate** polysaccharides of marine brown algae *(Phaeophyceae)*. These include **poly(*β*-D-mannuronate)** and **poly(*α*-L-guluronate),** which are (1→4) linked chains formed from *β-mannuronic acid* and α-*L-guluronic acid,* respectively. Both of these homopolymers are found together in most marine alginates, although to widely differing extents, and mixed chains containing both monomer units are also found. As shown in Figure 7.29, the conformation of poly(*β*-D-mannuronate) is similar to that of cellulose. In the solid state, the free form of the polymer exists in cellulose-like form. However, complexes of the polymer with cations (such as lithium, sodium, potassium, and calcium) adopt a threefold helix structure, presumably to accommodate the bound cations. For poly(*α*-L-guluronate) (Figure 7.29), the axial–axial configuration of the glycosidic linkage leads to a distinctly buckled ribbon with limited flexibility. Cooperative interactions between such buckled ribbons can only

A DEEPER LOOK

Billiard Balls, Exploding Teeth, and Dynamite—The Colorful History of Cellulose

Although humans cannot digest it and most people's acquaintance with cellulose is limited to comfortable cotton clothing, cellulose has enjoyed a colorful and varied history of utilization. In 1838, Théophile Pelouze in France found that paper or cotton could be made explosive if dipped in concentrated nitric acid. Christian Schönbein, a professor of chemistry at the University of Basel, prepared "nitrocotton" in 1845 by dipping cotton in a mixture of nitric and sulfuric acids and then washing the material to remove excess acid. In 1860, Major E. Schultze of the Prussian army used the same material, now called **guncotton,** as a propellant replacement for gunpowder, and its preparation in brass cartridges soon made it popular for this purpose. The only problem was that it was too explosive and could detonate unpredictably in factories where it was produced. The entire town of Faversham, England, was destroyed in such an accident. In 1868, Alfred Nobel mixed guncotton with ether and alcohol, thus preparing **nitrocellulose,** and in turn mixed this with nitroglycerine and sawdust to produce **dynamite.** Nobel's income from dynamite and also from his profitable development of the Russian oil fields in Baku eventually formed the endowment for the Nobel Prizes.

In 1869, concerned over the precipitous decline (from hunting) of the elephant population in Africa, the billiard ball manufacturers Phelan and Collander offered a prize of $10,000 for production of a substitute for ivory. Brothers Isaiah and John Hyatt in Albany, New York, produced a substitute for ivory by mixing guncotton with camphor, then heating and squeezing it to produce **celluloid.** This product found immediate uses well beyond billiard balls. It was easy to shape, strong, and resilient, and it exhibited a high tensile strength. Celluloid was used eventually to make dolls, combs, musical instruments, fountain pens, piano keys, and a variety of other products. The Hyatt brothers eventually formed the Albany Dental Company to make false teeth from celluloid. Because camphor was used in their production, the company advertised that their teeth smelled "clean," but, as reported in the *New York Times* in 1875, the teeth also occasionally exploded!

Portions adapted from Burke, J., 1996. *The Pinball Effect: How Renaissance Water Gardens Made the Carburetor Possible and Other Journeys Through Knowledge.* New York: Little, Brown, & Company.

be strong if the interstices are filled effectively with water molecules or metal ions. Figure 7.30 shows a molecular model of a Ca^{2+}-induced dimer of poly(α-L-guluronate).

Agarose

An important polysaccharide mixture isolated from marine red algae (*Rhodophyceae*) is **agar,** which consists of two components, **agarose** and **agaropectin.** Agarose (Figure 7.31) is a chain of alternating D-galactose and 3,6-anhydro-L-galactose, with side chains of 6-methyl-D-galactose. Agaropectin is similar, but contains in addition sulfate ester side chains and D-glucuronic acid. The three-dimensional structure of agarose is a double helix with a threefold screw axis, as shown in Figure 7.31. The central cavity is large enough to accommodate water molecules. Agarose and agaropectin readily form gels containing large amounts (up to 99.5%) of water. Agarose can be processed to remove most of the charged groups, yielding a material (trade name Sepharose) useful for purification of macromolecules in gel exclusion chromatography. Pairs of chains form double helices that subsequently aggregate in bundles to form a stable gel, as shown in Figure 7.32.

Glycosaminoglycans

A class of polysaccharides known as **glycosaminoglycans** is involved in a variety of extracellular (and sometimes intracellular) functions. Glycosaminoglycans consist of linear chains of repeating disaccharides in which one of the monosaccharide units is an amino sugar and one (or both) of the monosaccharide units contains at least one negatively charged sulfate or carboxylate group. The repeating disaccharide structures found commonly in glycosaminoglycans are

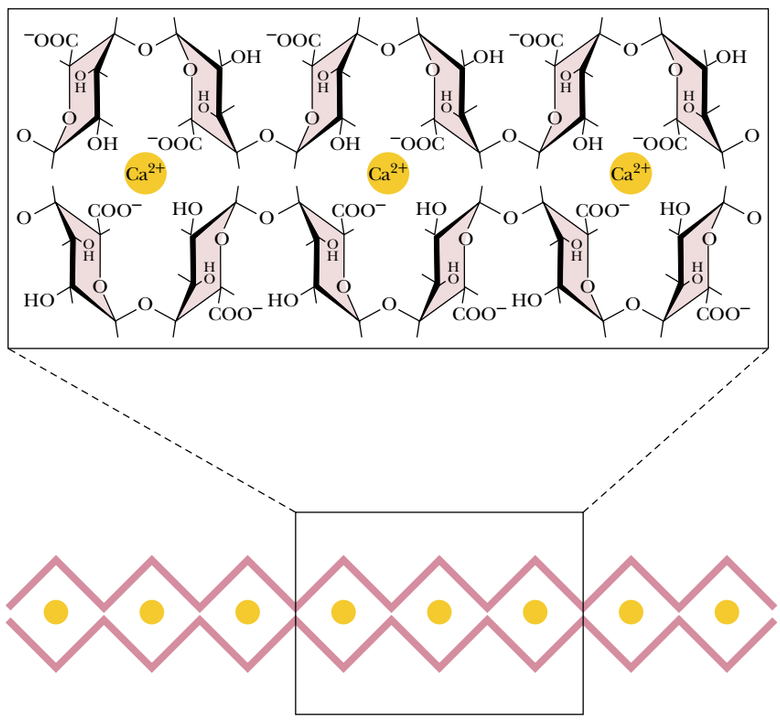


FIGURE 7.30 • Poly(α-L-guluronate) strands dimerize in the presence of Ca^{2+}, forming a structure known as an "egg carton."

shown in Figure 7.33. **Heparin,** with the highest net negative charge of the disaccharides shown, is a natural anticoagulant substance. It binds strongly to *antithrombin III* (a protein involved in terminating the clotting process) and inhibits blood clotting. **Hyaluronate** molecules may consist of as many as 25,000 disaccharide units, with molecular weights of up to 10^7. Hyaluronates are impor-

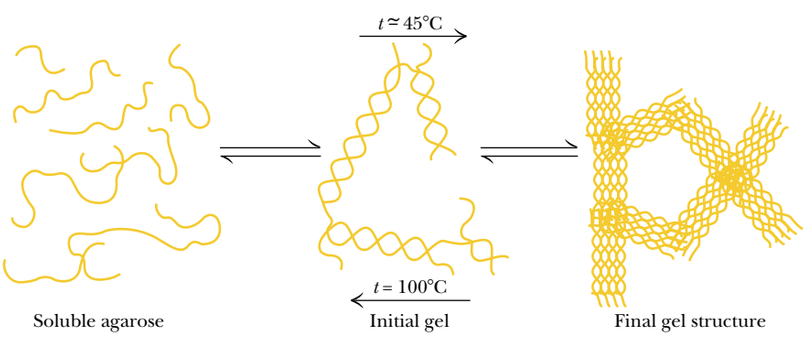


FIGURE 7.32 • The ability of agarose to assemble in complex bundles to form gels in aqueous solution makes it useful in numerous chromatographic procedures, including gel exclusion chromatography and electrophoresis. Cells grown in culture can be embedded in stable agarose gel "threads" so that their metabolic and physiological properties can be studied.

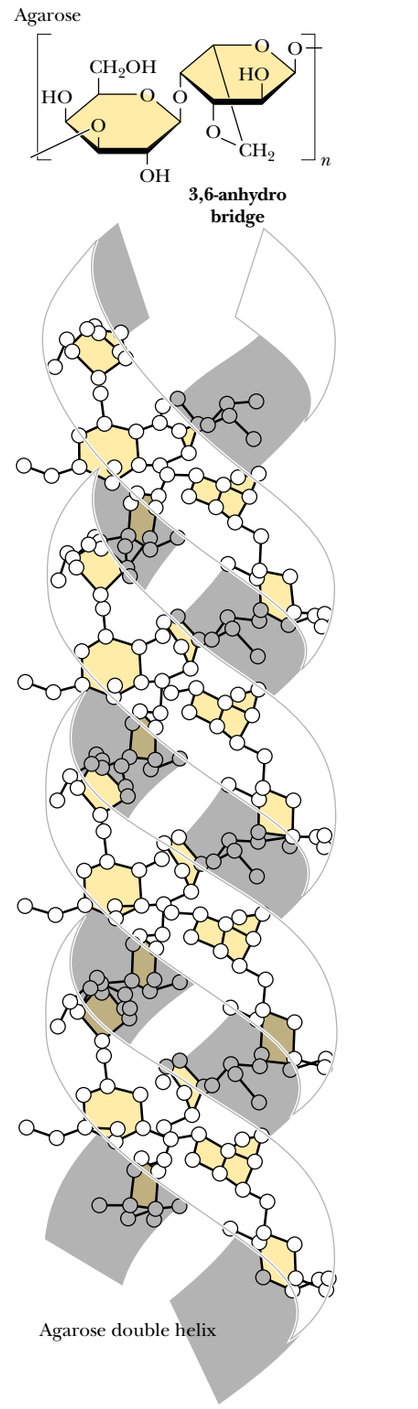


FIGURE 7.31 • The favored conformation of agarose in water is a double helix with a threefold screw axis.

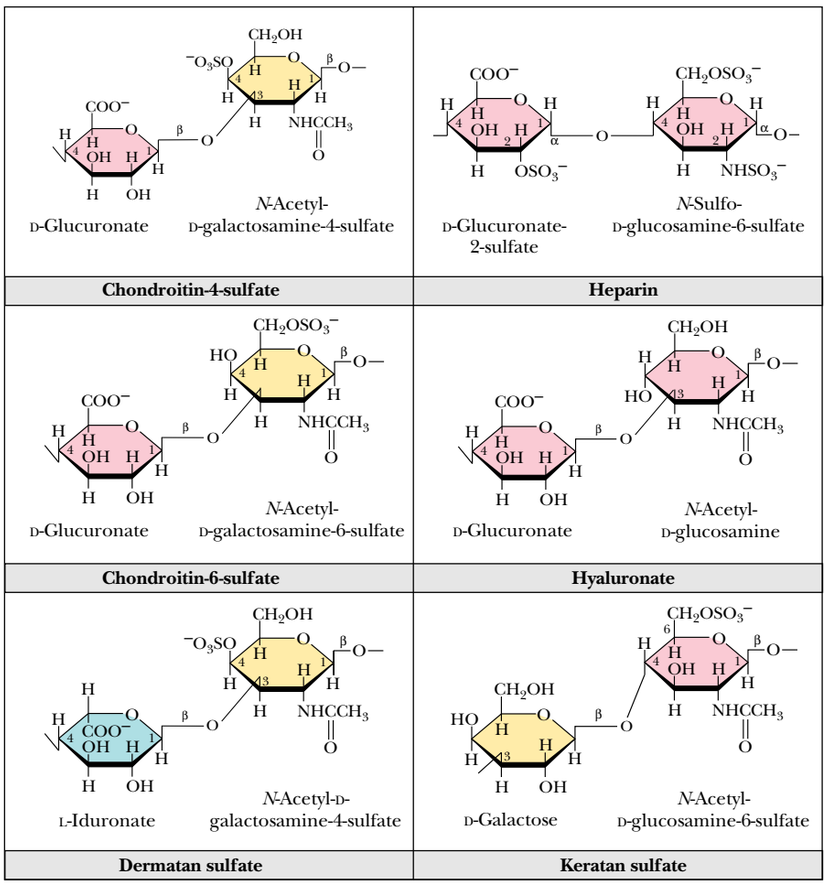


FIGURE 7.33 • Glycosaminoglycans are formed from repeating disaccharide arrays. Glycosaminoglycans are components of the proteoglycans.

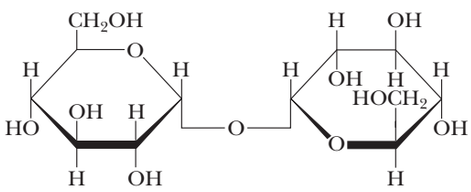
tant components of the vitreous humor in the eye and of *synovial fluid,* the lubricant fluid of joints in the body. The **chondroitins** and **keratan sulfate** are found in tendons, cartilage, and other connective tissue, whereas **dermatan sulfate,** as its name implies, is a component of the extracellular matrix of skin. Glycosaminoglycans are fundamental constituents of *proteoglycans* (discussed later).

Problems

1. Draw Haworth structures for the two possible isomers of D-altrose (Figure 7.2) and D-psicose (Figure 7.3).

2. Give the systematic name for stachyose (Figure 7.19).

3. Trehalose, a disaccharide produced in fungi, has the following structure:



a. What is the systematic name for this disaccharide?
b. Is trehalose a reducing sugar? Explain.

4. Draw a Fischer projection structure for L-sorbose (D-sorbose is shown in Figure 7.3).

5. α-D-Glucose has a specific rotation, $[\alpha]_D^{20}$, of +112.2°, whereas β-D-glucose has a specific rotation of +18.7°. What is the composition of a mixture of α-D- and β-D-glucose, which has a specific rotation of 83.0°?

6. A 0.2-g sample of amylopectin was analyzed to determine the fraction of the total glucose residues that are branch points in the structure. The sample was exhaustively methylated and then digested, yielding 50 μmol of 2,3-dimethylglucose and 0.4 μmol of 1, 2, 3, 6-tetramethylglucose.

a. What fraction of the total residues are branch points?
b. How many reducing ends does this amylopectin have?

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