Would "looking-glass milk" be nutritious?

17 Carbohydrates

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Learning Goals

1. Explain the difference between complex and simple carbohydrates and know the amounts of each recommended in the daily diet.
2. Apply the systems of classifying and naming monosaccharides according to the functional group and number of carbons in the chain.
3. Determine whether a molecule has a chiral center.
4. Explain stereoisomerism.
5. Identify monosaccharides as either D- or L-.
6. Draw and name the common monosaccharides using structural formulas.
7. Given the linear structure of a monosaccharide, draw the Haworth projection of its α- and β-cyclic forms and vice versa.
8. By inspection of the structure, predict whether a sugar is a reducing or a nonreducing sugar.
9. Discuss the use of the Benedict's reagent to measure the level of glucose in urine.
10. Draw and name the common disaccharides and discuss their significance in biological systems.
11. Describe the difference between galactosemia and lactose intolerance.
12. Discuss the structural, chemical, and biochemical properties of starch, glycogen, and cellulose.

CHEMISTRY CONNECTION

Chemistry Through the Looking Glass

In his children's story *Through the Looking Glass*, Lewis Carroll's heroine Alice wonders whether "looking-glass milk" would be good to drink. As we will see in this chapter, many biological molecules, such as the sugars, exist as two stereoisomers, *enantiomers*, that are mirror images of one another. Because two mirror-image forms occur, it is rather remarkable that in our bodies, and in most of the biological world, only one of the two is found. For instance, the common sugars are members of the D-family, whereas all the common amino acids that make up our proteins are members of the L-family. It is not too surprising, then, that the enzymes in our bodies that break down the sugars and proteins we eat are *stereospecific*, that is, they recognize only one mirror-image isomer. Knowing this, we can make an educated guess that "looking-glass milk" could not be digested by our enzymes and therefore would not be a good source of food for us. It is even possible that it might be toxic to us!

Pharmaceutical chemists are becoming more and more concerned with the stereochemical purity of the drugs that we take. Consider a few examples. In 1960 the drug thalidomide was commonly prescribed in Europe as a sedative. However, during that year, hundreds of women who took thalidomide during pregnancy gave birth to babies with severe birth defects. Thalidomide, it turned out, was a mixture of two enantiomers. One is a sedative; the other is a teratogen, a chemical that causes birth defects.

One of the common side effects of taking antihistamines for colds or allergies is drowsiness. Again, this is the result of the fact that antihistamines are mixtures of enantiomers. One causes drowsiness; the other is a good decongestant.

One enantiomer of the compound carvone is associated with the smell of spearmint; the other produces the aroma of caraway seeds or dill. One mirror-image form of limonene smells like lemons; the other has the aroma of oranges.

The pain reliever ibuprofen is currently sold as a mixture of enantiomers, but one is a much more effective analgesic than the other.

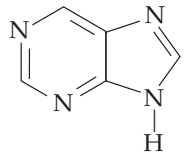
Taste, smell, and the biological effects of drugs in the body all depend on the stereochemical form of compounds and their interactions with cellular enzymes or receptors. As a result, chemists are actively working to devise methods of separating the isomers in pure form. Alternatively, methods of conducting stereospecific syntheses that produce only one stereoisomer are being sought. By preparing pure stereoisomers, the biological activity of a compound can be much more carefully controlled. This will lead to safer medications.

In this chapter we will begin our study of stereochemistry, the spatial arrangement of atoms in molecules, with the carbohydrates. Later, we will examine the stereochemistry of the amino acids that make up our proteins and consider the stereochemical specificity of the metabolic reactions that are essential to life. A more complete treatment of stereochemistry is found in Appendix D: Stereochemistry and Stereoisomers Revisited.

Introduction

Emil Fischer's father, a wealthy businessman, once said that Emil was too stupid to be a businessman and had better be a student. Lucky for the field of biochemistry, Emil did just that. Originally he wanted to study physics, but his cousin Otto Fischer convinced him to study chemistry. Beginning as an organic chemist, Fischer launched a career that eventually led to groundbreaking research in biochemistry. By following his career, we get a glimpse of the entire field.

Early on, Fischer discovered the active ingredients in coffee and tea, caffeine and theobromine. Eventually he discovered their structures and synthesized them in the laboratory. In work that he carried out between 1882 and 1906, Fischer demonstrated that adenine and guanine, along with some other compounds found in plants and animals, all belonged to one family of compounds. He called these the purines. All the purines have the same core structure and differ from one another by the functional groups attached to the ring.



Purine core structure

We will study the purines in Chapter 24 where we will learn that these are two of the essential components of the genetic molecules DNA and RNA. We will see that DNA is a double helix. Each strand of the helix is made up of a backbone of alternating sugars (ribose in RNA and deoxyribose in DNA) and phosphoryl groups. The purines are one of the two types of nitrogenous bases that we will study. They project into the helix. By reading the order of these nitrogenous bases, we can decipher the genetic code of an organism.

The structure of the purines and pyrimidines was first described in Section 16.2. It is discussed in much more detail in Sections 24.1 and 24.2.

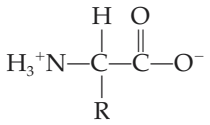
In 1884 Fischer began his monumental work on sugars. In 1890 he established the stereochemical nature of all sugars, and between 1891 and 1894 he worked out the stereochemical configuration of all the known sugars and predicted all the possible stereoisomers. Stereochemistry is the study of molecules that have two mirror-image isomers. We will find, as Fischer did, that nature has "selected" only one of the two mirror-image forms for common use in biological systems. Fischer studied virtually all the sugars, but one of his greatest successes was the synthesis of glucose, fructose, and mannose, three six-carbon sugars. We will learn much more about the structure and function of carbohydrates, as well as about stereochemistry in this chapter.

The structure of simple sugars and the function in biological systems are discussed in Sections 17.2 and 17.4. Stereochemistry is discussed in Section 17.3.

Between 1899 and 1908, Fischer turned his attention to proteins. He developed methods to separate and identify individual amino acids and discovered an entirely new class, the cyclic amino acids (those with ring structures). Fischer also worked on protein synthesis from the amino acids. He demonstrated the nature of the peptide bond and discovered how to make small peptides in the laboratory.

As we will learn in Chapter 19, amino acids are all characterized by a common core structure, having both a carboxyl group and an amino group.

We will study the amino acids and the structure of proteins in Chapter 19.



Amino acid core structure

The peptide bond that forms between amino acids is actually an amide bond between these two groups.

See also Section 16.4, A Preview of Amino Acids, Proteins, and Protein Synthesis.

While each of the amino acids has a common core, they differ from one another in the nature of a side chain, or R group. The amino acids are classified based on the properties they acquire from these R groups.

Quite late in his career, Fischer even got around to studying the fats, a heterogenous group of substances characterized by their hydrophobic nature. In Chapter 18, we will study the incredibly diverse family of fats, or lipids.

Fischer's personal life was not as happy as his professional life. His wife died after only seven years of marriage, leaving Fischer with three sons. One son died in World War I and another committed suicide at the age of twenty-five. However, his third son, Hermann Otto Laurenz Fischer, followed in his father's footsteps, becoming a professor of biochemistry at the University of California at Berkeley.

In 1902, Fischer was awarded the Nobel Prize for his work on sugar and purine synthesis. But a glance at all of his accomplishments helps us to realize that this great man, who began his career as an organic chemist, established the field of biochemistry through his extraordinary studies of the molecules of life.

17.1 Types of Carbohydrates

Learning Goal 1

We begin our study of biochemistry with the carbohydrates. Carbohydrates are produced in plants by photosynthesis (Figure 17.1). Natural carbohydrate sources such as grains and cereals, breads, sugar cane, fruits, milk, and honey are an important source of energy for animals. **Carbohydrates,** especially glucose, are the

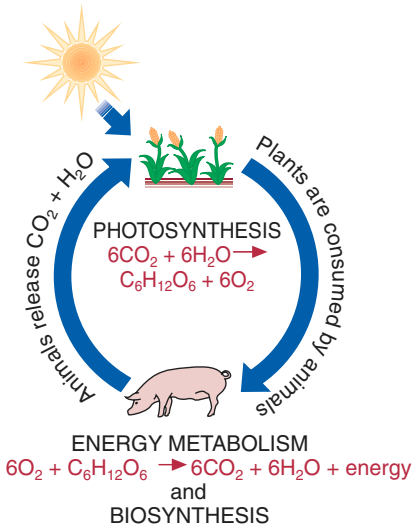


Figure 17.1
Carbohydrates are produced by the process of photosynthesis, which uses the energy of sunlight to produce hexoses from CO_2 and H_2O. The plants use these hexoses to harvest energy and produce ATP to fuel cellular function and to produce macromolecules, including starch, cellulose, fats, nucleic acids, and proteins. Animals depend on plants as a source of organic carbon. The hexoses are metabolized to generate ATP and are used as precursors for the biosynthesis of carbohydrates, fats, proteins, and nucleic acids.

A kilocalorie is the same as the calorie referred to in the "count-your-calories" books and on nutrition labels.

See A Human Perspective: Tooth Decay and Simple Sugars.

primary energy source for the brain and nervous system and can be used by many other tissues. When "burned" by cells for energy, each gram of carbohydrate releases approximately four kilocalories of energy.

A healthy diet should contain both complex carbohydrates, such as starches and cellulose, and simple sugars, such as fructose and sucrose. However, the quantity of simple sugars, especially sucrose, should be minimized because large quantities of sucrose in the diet promote obesity and tooth decay.

Complex carbohydrates are better for us than the simple sugars. Starch, found in rice, potatoes, breads, and cereals, is an excellent energy source. In addition, the complex carbohydrates, such as cellulose, provide us with an important supply of dietary fiber.

It is hard to determine exactly what percentage of the daily diet *should* consist of carbohydrates. The *actual* percentage varies widely throughout the world, from 80% in the Far East, where rice is the main component of the diet, to 40–50% in the United States. Currently, it is recommended that about 58% of the calories in the diet should come from carbohydrates and that no more than 10% of the daily caloric intake should be sucrose. The U.S. Department of Agriculture has adopted a food pyramid to show the recommended amounts of various foods in the diet (Figure 17.2). The foods at the bottom of the pyramid, grains (breads, cereals, rice, pasta), and at the next level, fruits and vegetables, should be the most abundant in our diet. These food groups are our major sources of dietary carbohydrates.

Question 17.1

What is the current recommendation for the amount of carbohydrates that should be included in the diet? Of the daily intake of carbohydrates, what percentage should be simple sugar?

Question 17.2

Distinguish between simple and complex sugars. What are some sources of complex carbohydrates?

Monosaccharides such as glucose and fructose are the simplest carbohydrates because they contain a single (*mono-*) sugar (***saccharide***) unit. **Disaccharides,** including sucrose and lactose, consist of two monosaccharide units joined through

A HUMAN PERSPECTIVE

Tooth Decay and Simple Sugars

How many times have you heard the lecture from parents or your dentist about brushing your teeth after a sugary snack? Annoying as this lecture might be, it is based on sound scientific data that demonstrate that the cause of tooth decay is plaque and acid formed by the bacterium *Streptococcus mutans* using sucrose as its substrate.

Saliva is teeming with bacteria in concentrations up to one hundred million (10^8) per milliliter of saliva! Within minutes after you brush your teeth, sticky glycoproteins in the saliva adhere to tooth surfaces. Then millions of oral bacteria immediately bind to this surface.

Although all oral bacteria adhere to the tooth surface, only *S. mutans* causes dental caries, or cavities. Why does this bacterium cause cavities when all the others do not? The answer lies in the special enzyme called *glucosyl transferase* that is found on the surface of *S. mutans* cells.

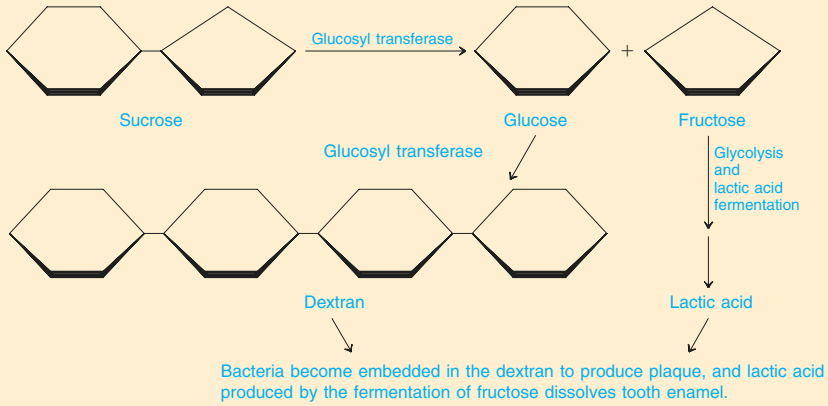
Glucosyl transferase is a very specific enzyme. It can act only on the disaccharide sucrose, which it breaks down into glucose and fructose. As the accompanying diagram shows, the enzyme then adds the glucose to a growing polysaccharide chain called *dextran,* which adheres tightly to both the tooth enamel and the bacteria. *Plaque* is made up of huge masses of bacteria, embedded in dextran, adhering to the tooth surface.

This is just the first stage of cavity formation. Note in the accompanying figure that the second sugar released by the cleavage of sucrose is fructose. The bacteria use the fructose in the energy-harvesting pathways of glycolysis and lactic acid fermentation. Production of lactic acid decreases the pH on the tooth surface and begins to dissolve calcium from the tooth enamel.

Why is the acid not washed away from the tooth surface? After all, we produce about 1 L of saliva each day, which should dilute the acid and remove it from the tooth surface. The problem is the dextran plaque; it is not permeable to saliva, and thus plaque keeps the bacteria and the lactic acid localized on the enamel.

What measures can we take to prevent tooth decay? Practice good oral hygiene: brushing after each meal and flossing regularly reduce plaque buildup. Eat a diet rich in calcium; this helps to build strong tooth enamel. Include many complex carbohydrates in the diet; these cannot be used by glucosyl transferase and will not lead to the formation of acid. Further, the complex carbohydrates from fruits and vegetables help prevent decay by mechanically removing plaque from tooth surfaces. Avoid sucrose-containing snacks between meals. Studies have shown that the consumption of a sucrose-rich dessert with a meal, followed by brushing, does not produce many cavities. However, even small amounts of sugar ingested between meals are very cariogenic.

Researchers have developed a vaccine that prevents tooth decay in rats. Such a vaccine may one day be available for humans.



Action of the glucosyl transferase of *Streptococcus mutans*, which is responsible for tooth decay.

bridging oxygen atoms. Such a bond is called a **glycosidic bond. Oligosaccharides** consist of three to ten monosaccharide units joined by glycosidic bonds. The largest and most complex carbohydrates are the **polysaccharides,** which are long, often highly branched, chains of monosaccharides. Starch, glycogen, and cellulose are all examples of polysaccharides.

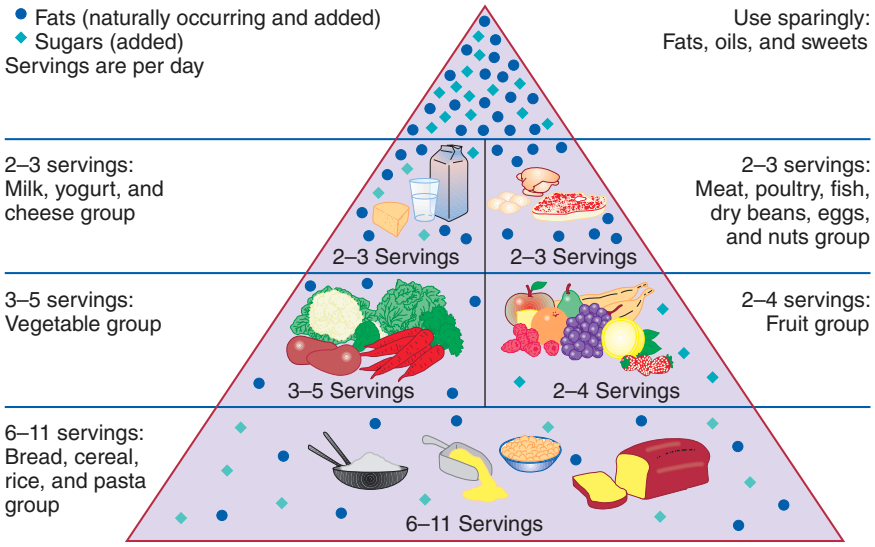


Figure 17.2
The U.S. Department of Agriculture has adopted a food pyramid to explain that carbohydrates in the form of cereals, grains, fruits, and vegetables should make up the majority of our diet. Fats and sweets should be consumed sparingly. Source: U.S. Department of Agriculture.

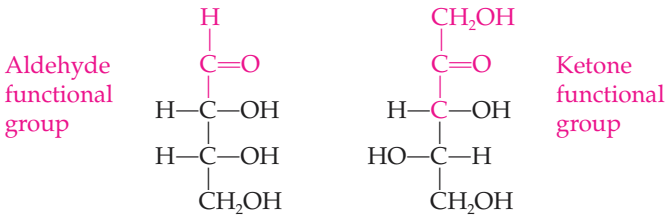
17.2 Monosaccharides

Monosaccharides are composed of carbon, hydrogen, and oxygen, and most are characterized by the general formula $(CH_2O)_n$, in which n is any integer from 3 to 7. As we will see, this general formula is an oversimplification because several biologically important monosaccharides are chemically modified. For instance, several blood group antigen and bacterial cell wall monosaccharides are substituted with amino groups. Many of the intermediates in carbohydrate metabolism carry phosphate groups. Deoxyribose, the monosaccharide found in DNA, has one fewer oxygen atom than the general formula above would predict.

The importance of phosphorylated sugars in metabolic reactions is discussed in Sections 15.4 and 21.3.

Learning Goal 2

Monosaccharides can be named on the basis of the functional groups they contain. A monosaccharide with a ketone (carbonyl) group is a **ketose.** If an aldehyde (carbonyl) group is present, it is called an **aldose.** Because monosaccharides also contain many hydroxyl groups, they are sometimes called *polyhydroxyaldehydes* or *polyhydroxyketones*.

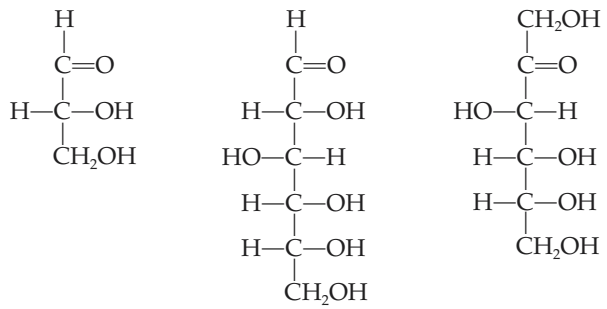


An aldose A ketose

Another system of nomenclature tells us the number of carbon atoms in the main skeleton. A three-carbon monosaccharide is a ***tri*ose,** a four-carbon sugar is a ***tet*rose,** a five-carbon sugar is a ***pen*tose,** a six-carbon sugar is a ***hex*ose,** and so on. Combining the two naming systems gives even more information about the structure and composition of a sugar. For example, an aldotetrose is a four-carbon sugar that is also an aldehyde.

In addition to these general names, each monosaccharide has a unique name. These names are shown in blue for the following structures. Because the monosaccharides can exist in several different isomeric forms, it is important to provide the complete name. Thus the complete names of the following structures are

D-glyceraldehyde, D-glucose, and D-fructose. These names tell us that the structure represents one particular sugar and also identifies the sugar as one of two possible isomeric forms (D- or L-).



Aldose	Aldose	Ketose
Triose	Hexose	Hexose
Aldotriose	Aldohexose	Ketohexose
D-Glyceraldehyde	D-Glucose	D-Fructose

Question 17.3

What is the structural difference between an aldose and a ketose?

Question 17.4

Explain the difference between:

a. A ketohexose and an aldohexose
b. A triose and a pentose

17.3 Stereoisomers and Stereochemistry

Stereoisomers

Learning Goal 3 Learning Goal 4 Learning Goal 5

The prefixes D- and L- found in the complete name of a monosaccharide are used to identify one of two possible isomeric forms called **stereoisomers.** By definition, each member of a pair of stereoisomers must have the same molecular formula and the same bonding. How then do isomers of the D-family differ from those of the L-family? D- and L-isomers differ in the spatial arrangements of atoms in the molecule.

Stereochemistry is the study of the different spatial arrangements of atoms. A general example of a pair of stereoisomers is shown in Figure 17.3. In this example the general molecule C-abcd is formed from the bonding of a central carbon to four different groups: a, b, c, and d. This results in two molecules rather than one. Each isomer is bonded together through the exact *same* bonding pattern, yet they are *not* identical. If they were identical, they would be superimposable one upon the other; *they are not*. They are therefore stereoisomers. These two stereoisomers have a mirror-image relationship that is analogous to the mirror-image relationship of the left and right hands (see Figure 17.3b).

Build models of these compounds using toothpicks and gumdrops of five different colors to prove this to yourself.

Two stereoisomers that are nonsuperimposable mirror images of one another are called a pair of **enantiomers.** Molecules that can exist in enantiomeric forms are called **chiral molecules.** The term simply means that as a result of different three-dimensional arrangements of atoms, the molecule can exist in two mirror-image forms. For any pair of nonsuperimposable mirror-image forms (enantiomers), one is always designated D- and the other L-.

For a more detailed discussion of stereochemistry, see Appendix D, Stereochemistry and Stereoisomers Revisited.

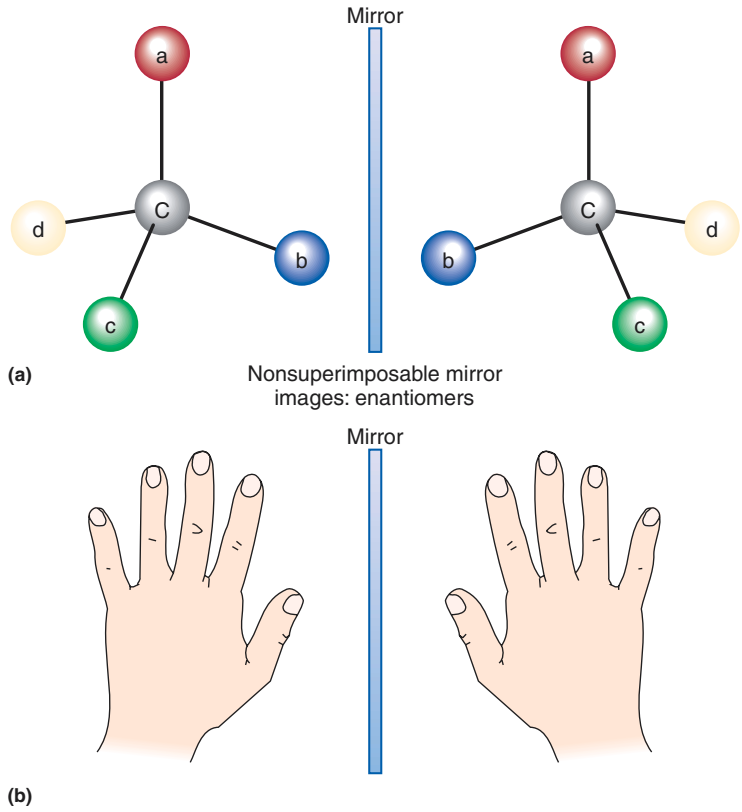


Figure 17.3
(a) A pair of enantiomers for the general molecule C-abcd. (b) Mirror-image right and left hands.

A carbon atom that has four different groups bonded to it is called an **asymmetric** (or chiral) **carbon** atom. Any molecule containing a chiral carbon can exist as a pair of enantiomers. Consider the simplest carbohydrate, **glyceraldehyde,** which is shown in Figure 17.4. Note that the second carbon is bonded to four different groups. It is therefore a chiral carbon. As a result, we can draw two enantiomers of glyceraldehyde that are nonsuperimposable mirror images of one another. Larger biological molecules typically have more than one chiral carbon.

Rotation of Plane-Polarized Light

Stereoisomers can be distinguished from one another by their different optical properties. Each member of a pair of stereoisomers will rotate plane-polarized light in different directions.

The polarimeter, measurement of the rotation of plane-polarized light, and the calculation of specific rotation are discussed in detail in Appendix D, Stereochemistry and Stereoisomers Revisited.

As we learned in Chapter 3, white light is a form of electromagnetic radiation that consists of many different wavelengths (colors) vibrating in *planes* that are all perpendicular to the direction of the light beam (Figure 17.5a). To measure optical properties of enantiomers, scientists use special light sources to produce *monochromatic light*, that is, light of a single wavelength. The monochromatic light is passed through a polarizing material, like a Polaroid lens, so that only waves in one plane can pass through. The light that emerges from the lens is *plane-polarized light* (Figure 17.5b).

Applying these principles, scientists have developed the *polarimeter* to measure the ability of a compound to change the angle of the plane of plane-polarized light (Figure 17.5c). The polarimeter allows the determination of the specific rotation of a compound, that is, the measure of its ability to rotate plane-polarized light.

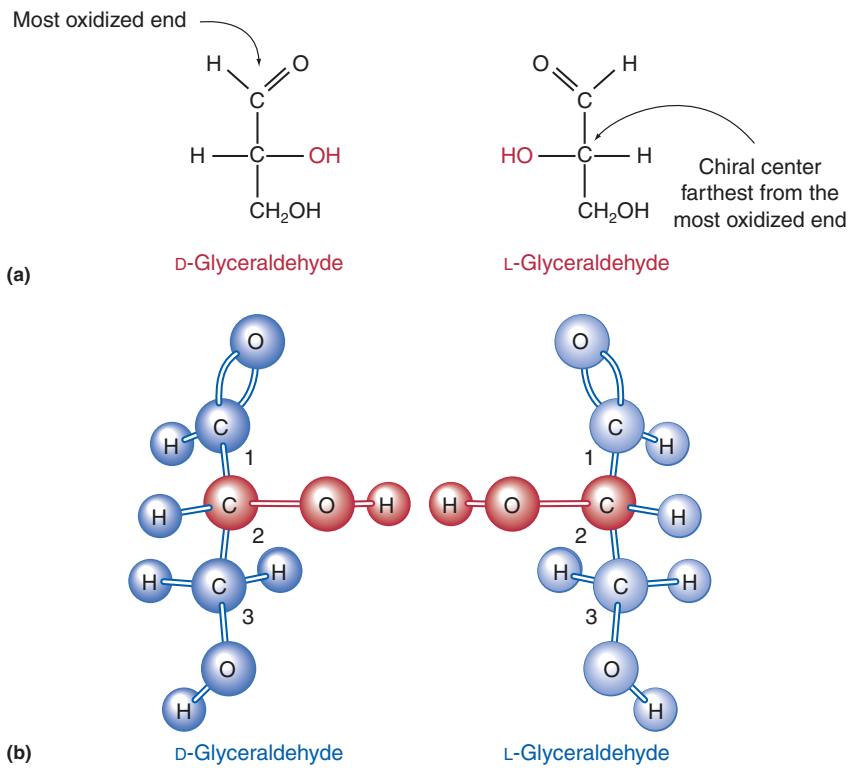


Figure 17.4
(a) Structural formulas of D- and L-glyceraldehyde. The end of the molecule with the carbonyl group is the most oxidized end. The D- or L-configuration of a monosaccharide is determined by the orientation of the functional groups attached to the chiral carbon farthest from the oxidized end. In the D-enantiomer the —OH is to the right. In the L-enantiomer, the —OH is to the left. (b) A three-dimensional representation of D- and L-glyceraldehyde.

Some compounds rotate light in a clockwise direction. These are said to be *dextrorotatory* and are designated by a plus sign (+) before the specific rotation value. Other substances rotate light in a counterclockwise direction. These are called *levorotatory* and are indicated by a minus sign (−) before the specific rotation value.

The Relationship between Molecular Structure and Optical Activity

In 1848, Louis Pasteur was the first to see a relationship between the structure of a compound and the effect of that compound on plane-polarized light. In his studies of winemaking, Pasteur noticed that salts of tartaric acid were formed as a by-product. It is a tribute to his extraordinary powers of observation that he noticed that two types of crystals were formed and that they were mirror images of one another. Using a magnifying glass and forceps, Pasteur separated the left-handed and right-handed crystals into separate piles. When he measured the optical activity of each of the mirror-image forms and of the original mixed sample, he obtained the following results:

- A solution of the original mixture of crystals was optically inactive.
- But both of the mirror-image crystals were optically active. In fact, the specific rotation produced by each was identical in magnitude but was of opposite sign.

Although Pasteur's work opened the door to understanding the relationship between structure and optical activity, it was not until 1874 that the Dutch chemist van't Hoff and the French chemist LeBel independently came up with a basis for the observed optical activity: tetrahedral carbon atoms bonded to four different atoms or groups of atoms. Thus, two enantiomers, which are identical to one another in all other chemical and physical properties, will rotate plane-polarized light to the same degree, but in opposite directions.

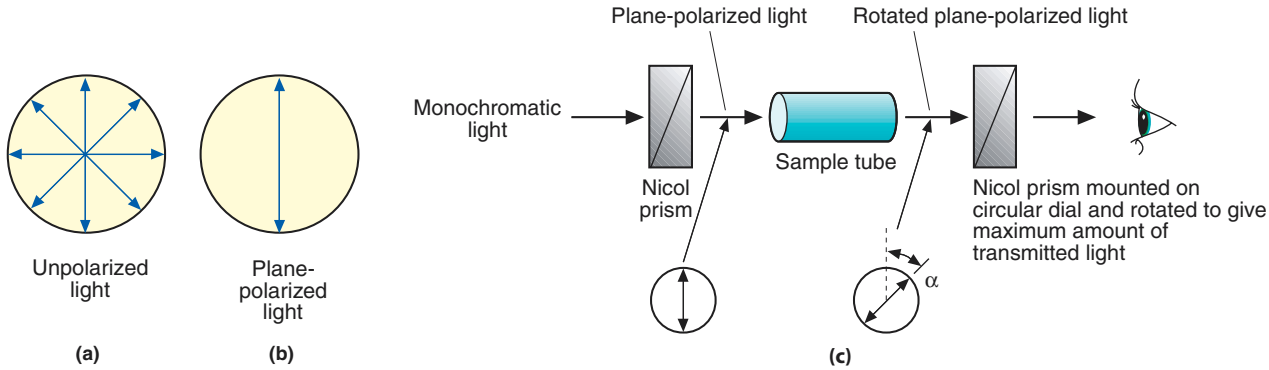
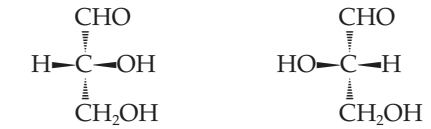


Figure 17.5
Light as wave motion. (a) Viewed from the end of the axis of propagation, light contains waves traveling in many planes. (b) Plane-polarized light contains light traveling in only one plane. (c) Schematic drawing of a polarimeter.

Fischer Projection Formulas

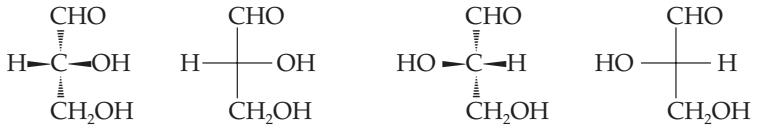
Let's take another look at the aldotriose glyceraldehyde to learn a convenient way to represent the structure of sugars that was devised by Emil Fischer. The **Fischer Projection** is a two-dimensional drawing of a molecule that shows a chiral carbon at the intersection of two lines and with horizontal lines representing bonds projecting out of the page and vertical lines representing bonds that project into the page. For sugars, the aldehyde or ketone group, the most oxidized carbon, is always represented at the "top."

Let's look again at Figure 17.4b. We can represent these ball-and-stick models with three-dimensional wedge drawings:



D-Glyceraldehyde L-Glyceraldehyde

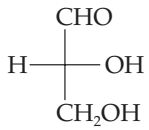
Remember that in the wedge diagram, the solid wedges represent bonds directed toward the reader. The dashed wedges represent bonds directed away from the reader and into the page. In these molecules, the center carbon in the representation is the only chiral carbon in the structure. To convert these wedge representations to a Fischer Projection, simply use a horizontal line in place of each solid wedge and use a vertical line to represent each dashed wedge. The chiral carbon is represented by the point at which the vertical and horizontal lines cross, as shown below.



D-Glyceraldehyde L-Glyceraldehyde

The D- and L- System of Nomenclature

In 1891 Emil Fischer devised a nomenclature system that would allow scientists to distinguish between enantiomers. Fischer knew that there are two enantiomers of glyceraldehyde that rotated plane-polarized light in opposite directions. He did not have the sophisticated tools needed to make an absolute connection between the structure and the direction of rotation of plane-polarized light. He simply decided that the (+) enantiomer would be the one with the hydroxyl group of the chiral carbon on the right:

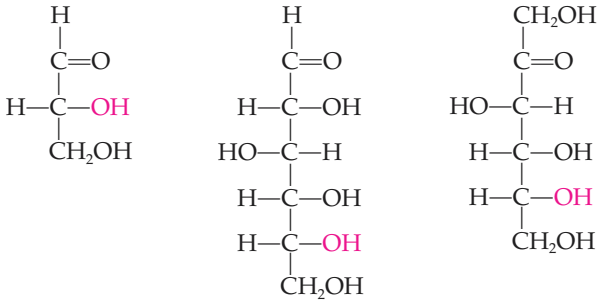


D-Glyceraldehyde

The enantiomer that rotated plane-polarized light in the (−) or levorotatory direction, he called L-glyceraldehyde (Figure 17.4).

It was not until 1952 that researchers were able to demonstrate that Fischer had guessed correctly when he proposed the structures of the (+) and (−) enantiomers of glyceraldehyde.

While specific rotation is an experimental value that must be measured, the D- and L- designations of all other monosaccharides are determined by comparison of their structures with D- and L-glyceraldehyde. Sugars with more than three carbons will have more than one chiral carbon. *By convention,* it is the position of the hydroxyl group on the chiral carbon farthest from the carbonyl group (the most oxidized end of the molecule) that determines whether a monosaccharide is in the D- or L- configuration. If the —OH group is on the right, the molecule is in the D-configuration. If the —OH group is on the left, the molecule is in the L-configuration. Almost all carbohydrates in living systems are members of the D-family.



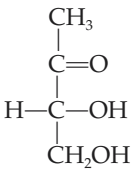
D-Glyceraldehyde D-Glucose D-Fructose

The structures and designations of D- and L-glyceraldehyde are defined by convention. In fact, the D- and L- terminology is generally applied only to carbohydrates and amino acids. For organic molecules the D- and L- convention has been replaced by a new system that provides the absolute configuration of a chiral carbon. This system, called the (R) and (S) system, is described in Appendix D, Stereochemistry and Stereoisomers Revisited.

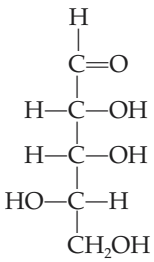
Question 17.5

Indicate whether each of the following molecules is an aldose or a ketose.

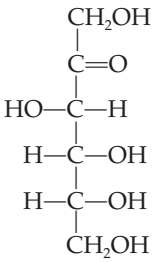
a.



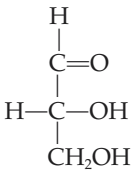
b.



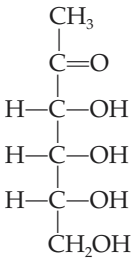
c.



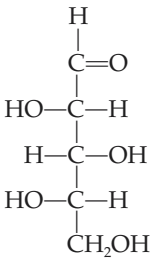
d.



e.



f.



Question 17.6

Determine the configuration (D- or L-) for each of the molecules in Question 17.5.

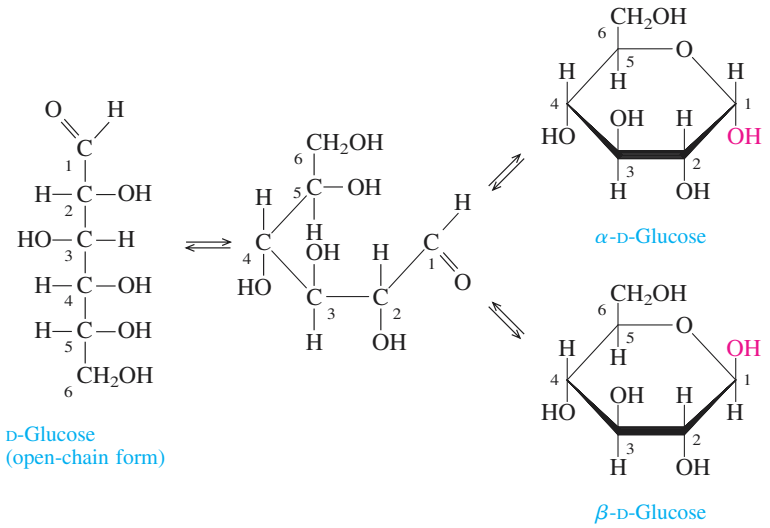


Figure 17.6
Cyclization of glucose to give α- and β-D-glucose. Note that the carbonyl carbon (C-1) becomes chiral in this process, yielding the α- and β- forms of glucose.

17.4 Biologically Important Monosaccharides

Learning Goal 6

Monosaccharides, the simplest carbohydrates, have backbones of from three to seven carbons. There are many monosaccharides, but we will focus on those that are most common in biological systems. These include the five- and six-carbon sugars: glucose, fructose, galactose, ribose, and deoxyribose.

Glucose

Glucose is the most important sugar in the human body. It is found in numerous foods and has several common names, including dextrose, grape sugar, and blood sugar. Glucose is broken down in glycolysis and other pathways to release energy for body functions.

The concentration of glucose in the blood is critical to normal body function. As a result, it is carefully controlled by the hormones insulin and glucagon. Normal blood glucose levels are 100–120 mg/100 mL, with the highest concentrations appearing after a meal. Insulin stimulates the uptake of the excess glucose by most cells of the body, and after 1–2 hr, levels return to normal. If blood glucose concentrations drop too low, the individual feels lightheaded and shaky. When this happens, glucagon stimulates the liver to release glucose into the blood, reestablishing normal levels. We will take a closer look at this delicate balancing act in Section 23.6.

The molecular formula of glucose, an aldohexose, is $C_6H_{12}O_6$. The structure of glucose is shown in Figure 17.6, and the method used to draw this structure is described in Example 17.1.

EXAMPLE 17.1 ***Drawing the Structure of a Monosaccharide***

Learning Goal 6

Draw the structure for D-glucose.

Solution

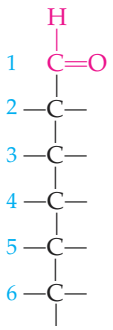
Glucose is an aldohexose.

Step 1. Draw six carbons in a straight vertical line; each carbon is separated from the ones above and below it by a bond:

Continued—

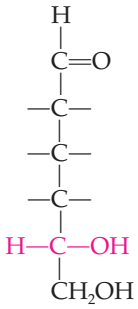
EXAMPLE 17.1 *—Continued*

Step 2. The most highly oxidized carbon is, by convention, drawn as the uppermost carbon (carbon-1). In this case, carbon-1 is an aldehyde carbon:

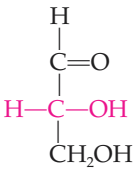


Most oxidized end of carbon chain; aldehyde

Step 3. The atoms are added to the next to the last carbon atom, at the bottom of the chain, to give either the D- or L-configuration as desired. Remember, when the —OH group is to the right, you have D-glucose. When in doubt, compare your structure to D-glyceraldehyde!



D-Isomer



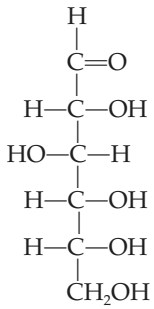
D-Glyceraldehyde

Compare chiral carbons farthest from the carbonyl group

Step 4. All the remaining atoms are then added to give the desired carbohydrate. For example, one would draw the following structure for D-glucose.

Continued—

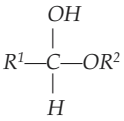
EXAMPLE 17.1 *—Continued*



D-Glucose

The positions for the hydrogen atoms and the hydroxyl groups on the remaining carbons must be learned for each sugar. For instance, the complete structures of D-fructose and D-galactose are shown later in this section.

Hemiacetal structure,



and formation are described in Section 14.4.

The term *intramolecular* tells us that the reacting carbonyl and hydroxyl groups are part of the same molecule.

In actuality the open-chain form of glucose is present in very small concentrations in cells. It exists in cyclic form under physiological conditions because the carbonyl group at C-1 of glucose reacts with the hydroxyl group at C-5 to give a six-membered ring. In the discussion of aldehydes, we noted that the reaction between an aldehyde and an alcohol yields a **hemiacetal.** When the aldehyde portion of the glucose molecule reacts with the C-5 hydroxyl group, the product is a cyclic *intramolecular hemiacetal*. For D-glucose, two isomers can be formed in this reaction (see Figure 17.6). These isomers are called α- and β-D-glucose. The two isomers formed differ from one another in the location of the —OH attached to the hemiacetal carbon, C-1. Such isomers, differing in the arrangement of bonds around the hemiacetal carbon, are called **anomers.** In the α-anomers, the C-1 (anomeric carbon) hydroxyl group is below the ring, and in the β-anomers, the C-1 hydroxyl group is above the ring. Like the stereoisomers discussed previously, the α and β forms can be distinguished from one another because they rotate plane-polarized light differently.

In Figure 17.6 a new type of structural formula, called a **Haworth projection,** is presented. Although on first inspection it appears complicated, it is quite simple to derive a Haworth projection from a structural formula, as Example 17.2 shows.

EXAMPLE 17.2 ***Drawing the Haworth Projection of a Monosaccharide from the Structural Formula***

Learning Goal 7

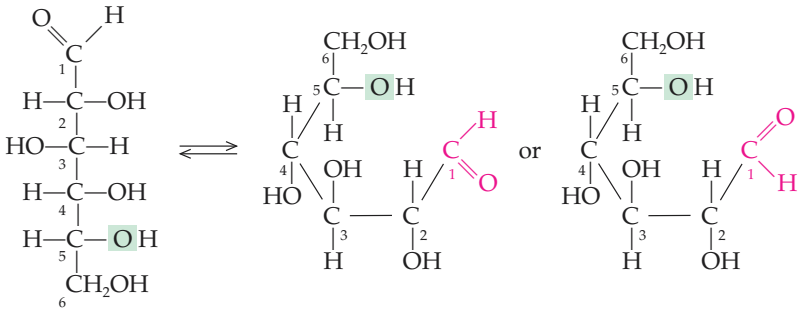
Draw the Haworth projections of α- and β-D-glucose.

Solution

1. Before attempting to draw a Haworth projection, look at the first steps of ring formation shown here:

Continued—

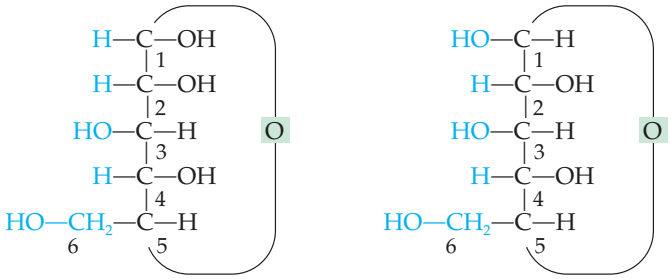
EXAMPLE 17.2 *—Continued*



Glucose (open chain) ⇌ Glucose (intermediates in ring formation)

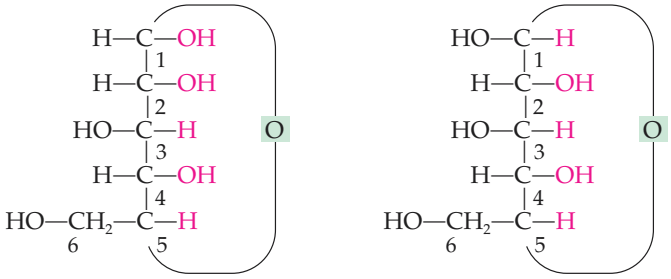
Try to imagine that you are seeing the molecules shown above in three dimensions. Some of the substituent groups on the molecule will be above the ring, and some will be beneath it. The question then becomes: How do you determine which groups to place above the ring and which to place beneath the ring?

2. Look at the two-dimensional structural formula. Note the groups (drawn in blue) to the left of the carbon chain. These are placed above the ring in the Haworth projection.



α-D-Glucose β-D-Glucose

3. Now note the groups (drawn in red) to the right of the carbon chain. These will be located beneath the carbon ring in the Haworth projection.

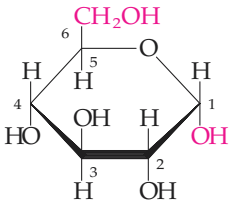


α-D-Glucose β-D-Glucose

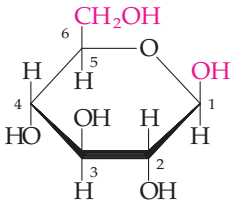
Continued—

EXAMPLE 17.2 *—Continued*

4. Thus in the Haworth projection of the cyclic form of any D-sugar the —CH_2OH group is always "up." When the —OH group at C-1 is also "up," *cis* to the —CH_2OH group, the sugar is β-D-glucose. When the —OH group at C-1 is "down," *trans* to the —CH_2OH group, the sugar is α-D-glucose.



Haworth projection
α-D-Glucose



Haworth projection
β-D-Glucose

Question 17.7

Refer to the linear structure of D-galactose. Draw the Haworth projections of α- and β-D-galactose.

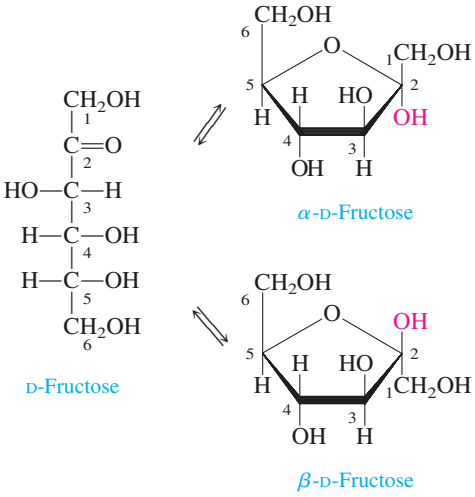
Question 17.8

Refer to the linear structure of D-ribose. Draw the Haworth projections of α- and β-D-ribose. Note that D-ribose is a pentose.

Fructose

Fructose, also called levulose and fruit sugar, is the sweetest of all sugars. It is found in large amounts in honey, corn syrup, and sweet fruits. The structure of fructose is similar to that of glucose. When there is a —CH_2OH group instead of a —CHO group at carbon-1 and a —C═O group instead of CHOH at carbon-2, the sugar is a ketose. In this case it is D-fructose.

Cyclization of fructose produces α- and β-D-fructose:

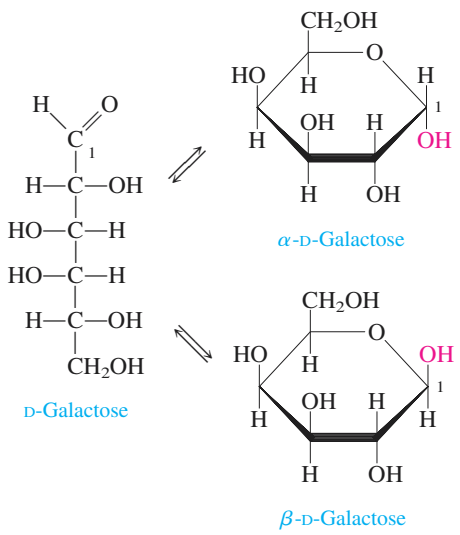


Fructose is a ketose, or ketone sugar. Recall that the reaction between an alcohol and a ketone yields a **hemiketal.** Thus the reaction between the C-2 keto group and the C-5 hydroxyl group in the fructose molecule produces an *intramolecular hemiketal.* Fructose forms a five-membered ring structure.

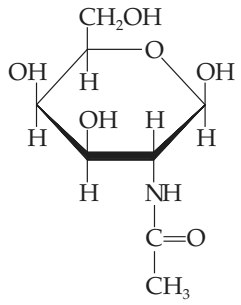
Hemiketal formation is described in Section 14.4.

Galactose

Another important hexose is **galactose.** The linear structure of D-galactose and the Haworth projections of α-D-galactose and β-D-galactose are shown here:

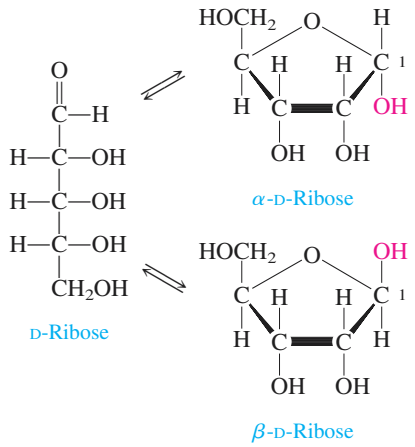


Galactose is found in biological systems as a component of the disaccharide lactose, or milk sugar. This is the principal sugar found in the milk of most mammals. β-D-Galactose and a modified form, β-D-*N*-acetylgalactosamine, are also components of the blood group antigens.

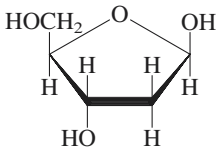


Ribose and Deoxyribose, Five-Carbon Sugars

Ribose is a component of many biologically important molecules, including RNA, and various coenzymes, a group of compounds required by many of the enzymes that carry out biochemical reactions in the body. The structure of the five-carbon sugar D-ribose is shown in its open-chain form and in the α- and β-cyclic forms.



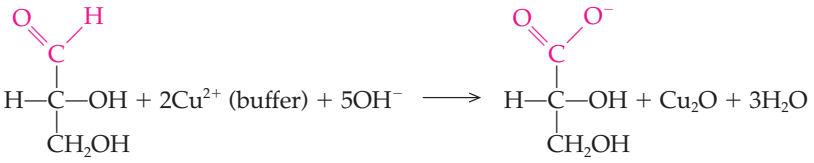
DNA, the molecule that carries the genetic information of the cell, contains 2-deoxyribose. In this molecule the —OH group at C-2 has been replaced by a hydrogen, hence the designation "2-deoxy," indicating the absence of an oxygen.



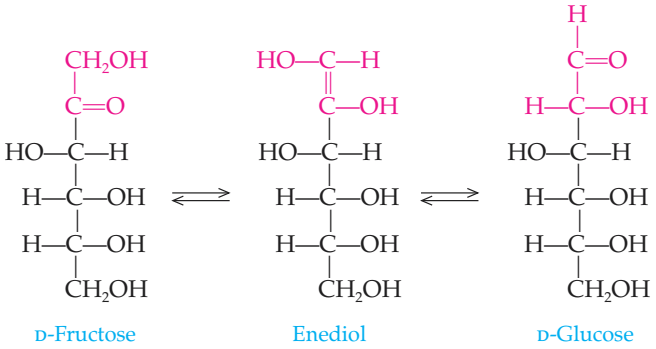
Reducing Sugars

Learning Goal 8 Learning Goal 9

The aldehyde group of aldoses is readily oxidized by the Benedict's reagent. Recall that the **Benedict's reagent** is a basic buffer solution that contains Cu^{2+} ions. The Cu^{2+} ions are reduced to Cu^{+} ions, which, in basic solution, precipitate as brick-red Cu_2O. The aldehyde group of the aldose is oxidized to a carboxylic acid, which undergoes an acid-base reaction to produce a carboxylate anion.



Although ketones generally are not easily oxidized, ketoses are an exception to that rule. Because of the —OH group on the carbon next to the carbonyl group, ketoses can be converted to aldoses, under basic conditions, via an *enediol reaction:*

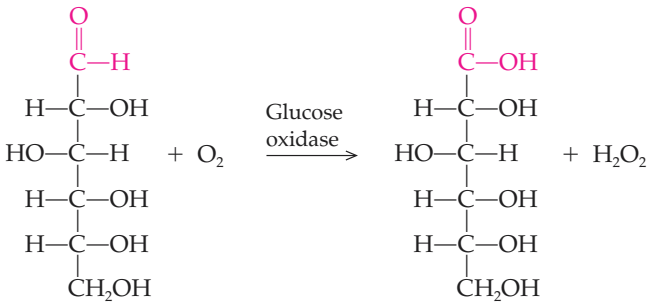


The name of the enediol reaction is derived from the structure of the intermediate through which the ketose is converted to the aldose: It has a double bond (ene), and it has two hydroxyl groups (diol). Because of this enediol reaction, ketoses are also able to react with Benedict's reagent, which is basic. Because the metal ions in the solution are reduced, the sugars are serving as reducing agents and are called **reducing sugars.** All monosaccharides and all the common disaccharides, except sucrose, are reducing sugars.

For many years the Benedict's reagent was used to test for *glucosuria*, the presence of excess glucose in the urine. Individuals suffering from *Type I insulin-dependent diabetes mellitus* do not produce the hormone insulin, which controls the uptake of glucose from the blood. When the blood glucose level rises above 160 mg/100 mL, the kidney is unable to reabsorb the excess, and glucose is found in the urine. Although the level of blood glucose could be controlled by the injection of insulin, urine glucose levels were monitored to ensure that the amount of insulin injected was correct. The Benedict's reagent was a useful tool because the amount of Cu_2O formed, and hence the degree of color change in the reaction, is directly proportional to the amount of reducing sugar in the urine. A brick-red color indicates a very high concentration of glucose in the urine. Yellow, green, and blue-green solutions indicate decreasing amounts of glucose in the urine, and a blue solution indicates an insignificant concentration.

See A Clinical Perspective: Diabetes Mellitus and Ketone Bodies in Chapter 23.

Use of Benedict's reagent to test urine glucose levels has largely been replaced by chemical tests that provide more accurate results. The most common technology is based on a test strip that is impregnated with the enzyme glucose oxidase and other agents that will cause a measurable color change. In one such kit, the compounds that result in color development include the enzyme peroxidase, a compound called orthotolidine, and a yellow dye. When a drop of blood is placed on the strip, the glucose oxidase catalyzes the conversion of glucose into gluconic acid and hydrogen peroxide.



D-Glucose D-Gluconic acid

The enzyme peroxidase catalyzes a reaction between the hydrogen peroxide and orthotolidine. This produces a blue product. The yellow dye on the test strip simply serves to "dilute" the blue end product, thereby allowing greater accuracy of the test over a wider range of glucose concentrations. The test strip remains yellow if there is no glucose in the sample. It will vary from a pale green to a dark blue, depending on the concentration of glucose in the urine sample.

Frequently, doctors recommend that diabetics monitor their *blood* glucose levels multiple times each day because this provides a more accurate indication of how well the diabetic is controlling his or her diet. Many small, inexpensive glucose meters are available that couple the oxidation of glucose by glucose oxidase with an appropriate color change system. As with the urine test, the intensity of the color change is proportional to the amount of glucose in the blood. A photometer within the device reads the color change and displays the glucose concentration. An even newer technology uses a device that detects the electrical charge

Actually, glucose oxidase can only oxidize β-D-glucose. However, in the blood there is an equilibrium mixture of the α and β anomers of glucose. Fortunately, α-D-glucose is very quickly converted to β-D-glucose.

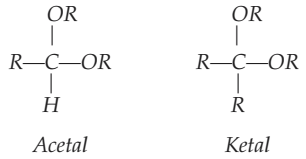
generated by the oxidation of glucose. In this case, it is the amount of electrical charge that is proportional to the glucose concentration.

17.5 Biologically Important Disaccharides

Learning Goal 10

Recall that disaccharides consist of two monosaccharides joined through an "oxygen bridge." In biological systems, monosaccharides exist in the cyclic form and, as we have seen, they are actually hemiacetals or hemiketals. Recall that when a hemiacetal reacts with an alcohol, the product is an *acetal,* and when a hemiketal reacts with an alcohol, the product is a *ketal.* In the case of disaccharides, the alcohol comes from a second monosaccharide. The acetals or ketals formed are given the general name *glycosides,* and the carbon-oxygen bonds are called *glycosidic bonds.*

Acetals and ketals are described in Section 14.4:



Glycosidic bond formation is nonspecific; that is, it can occur between a hemiacetal or hemiketal and any of the hydroxyl groups on the second monosaccharide. However, in biological systems, we commonly see only particular disaccharides, such as maltose (Figure 17.7), lactose (see Figure 17.9), or sucrose (see Figure 17.10). These specific disaccharides are produced in cells because the reactions are catalyzed by enzymes. Each enzyme catalyzes the synthesis of one specific disaccharide, ensuring that one particular pair of hydroxyl groups on the reacting monosaccharides participates in glycosidic bond formation.

Maltose

If an α-D-glucose and a second glucose are linked, as shown in Figure 17.7, the disaccharide is **maltose,** or malt sugar. This is one of the intermediates in the hydrolysis of starch. Because the C-1 hydroxyl group of α-D-glucose is attached to C-4 of another glucose molecule, the disaccharide is linked by an α (1 → 4) glycosidic bond.

Maltose is a reducing sugar. Any disaccharide that has a hemiacetal hydroxyl group (a free —OH group at C-1) is a reducing sugar. This is because the cyclic structure can open at this position to form a free aldehyde. Disaccharides that do not contain a hemiacetal group on C-1 do not react with the Benedict's reagent and are called **nonreducing sugars.**

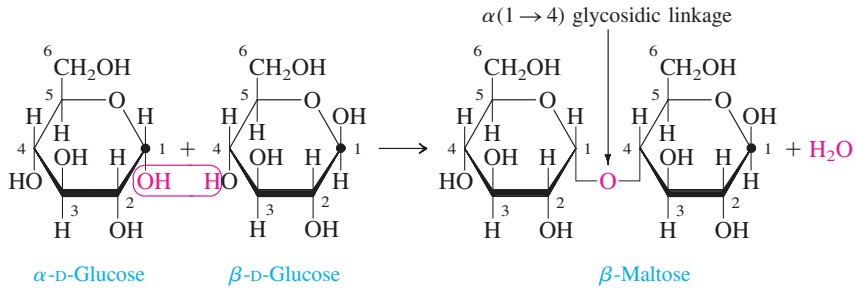


Figure 17.7
Glycosidic bond formed between the C-1 hydroxyl group of α-D-glucose and the C-4 hydroxyl group of β-D-glucose. The disaccharide is called β-maltose because the hydroxyl group at the reducing end of the disaccharide has the β-configuration.

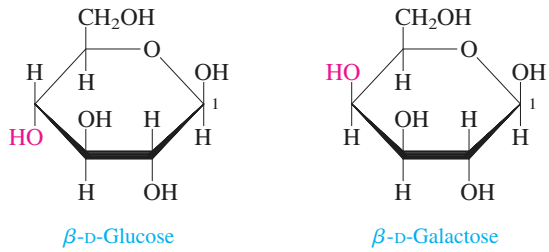


Figure 17.8
Comparison of the cyclic forms of glucose and galactose. Note that galactose is identical to glucose except in the position of the C-4 hydroxyl group.

Lactose

Learning Goal 11

Milk sugar, or **lactose,** is a disaccharide made up of one molecule of β-D-galactose and one of either α- or β-D-glucose. Galactose differs from glucose only in the configuration of the hydroxyl group at C-4 (Figure 17.8). In the cyclic form of glucose the C-4 hydroxyl group is "down," and in galactose it is "up." In lactose the C-1 hydroxyl group of β-D-galactose is bonded to the C-4 hydroxyl group of either an α- or β-D-glucose. The bond between the two monosaccharides is therefore a β(1 → 4) glycosidic bond (Figure 17.9).

Lactose is the principal sugar in the milk of most mammals. To be used by the body as an energy source, lactose must be hydrolyzed to produce glucose and galactose. Note that this is simply the reverse of the reaction shown in Figure 17.9. Glucose liberated by the hydrolysis of lactose is used directly in the energy-harvesting reactions of glycolysis. However, a series of reactions is necessary to convert galactose into a phosphorylated form of glucose that can be used in cellular metabolic reactions. In humans the genetic disease **galactosemia** is caused by the absence of one or more of the enzymes needed for this conversion. A toxic compound formed from galactose accumulates in people who suffer from galactosemia. If the condition is not treated, galactosemia leads to severe mental retardation, cataracts, and early death. However, the effects of this disease can be avoided entirely by providing galactosemic infants with a diet that does not contain galactose. Such a diet, of course, cannot contain lactose and therefore must contain no milk or milk products.

Glycolysis is discussed in Chapter 21.

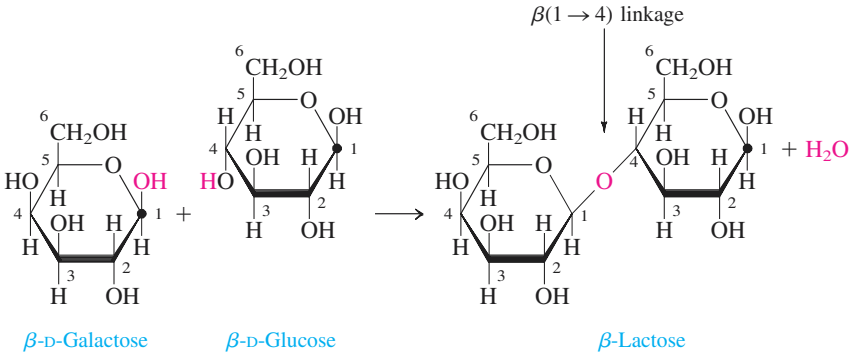


Figure 17.9
Glycosidic bond formed between the C-1 hydroxyl group of β-D-galactose and the C-4 hydroxyl group of β-D-glucose. The disaccharide is called β-lactose because the hydroxyl group at the reducing end of the disaccharide has the β-configuration.

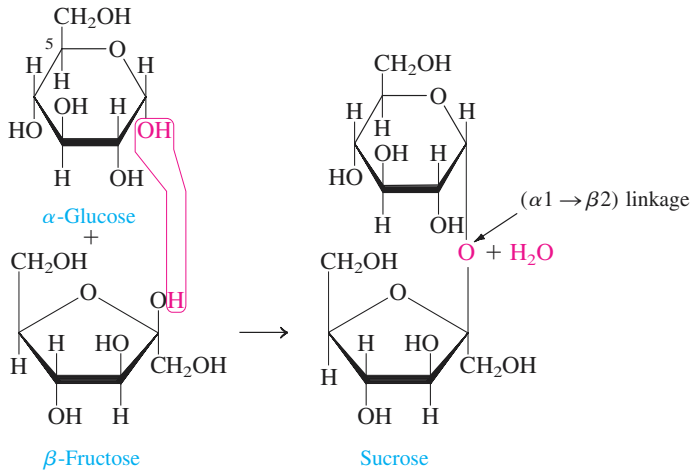


Figure 17.10
Glycosidic bond formed between the C-1 hydroxyl of α-D-glucose and the C-2 hydroxyl of β-D-fructose. This bond is called an (α1 → β2) glycosidic linkage. The disaccharide formed in this reaction is sucrose.

A HUMAN PERSPECTIVE

Blood Transfusions and the Blood Group Antigens

The first blood transfusions were tried in the seventeenth century, when physicians used animal blood to replace human blood lost by hemorrhages. Unfortunately, many people died as a result of this attempted cure, and transfusions were banned in much of Europe. Transfusions from human donors were somewhat less lethal, but violent reactions often led to the death of the recipient, and by the nineteenth century, transfusions had been abandoned as a medical failure.

In 1904, Dr. Karl Landsteiner performed a series of experiments on the blood of workers in his laboratory. His results explained the mysterious transfusion fatalities, and blood transfusions were reinstated as a lifesaving clinical tool. Landsteiner took blood samples from his coworkers. He separated the blood cells from the serum, the liquid component of the blood, and mixed these samples in test tubes. When he mixed serum from one individual with blood cells of another, Landsteiner observed that, in some instances, the serum samples caused clumping, or *agglutination,* of red blood cells (RBC). The agglutination reaction always indicated that the two bloods were incompatible and transfusion could lead to life-threatening reactions. As a result of many such experiments, Landsteiner showed that there are four human blood groups, designated A, B, AB, and O.

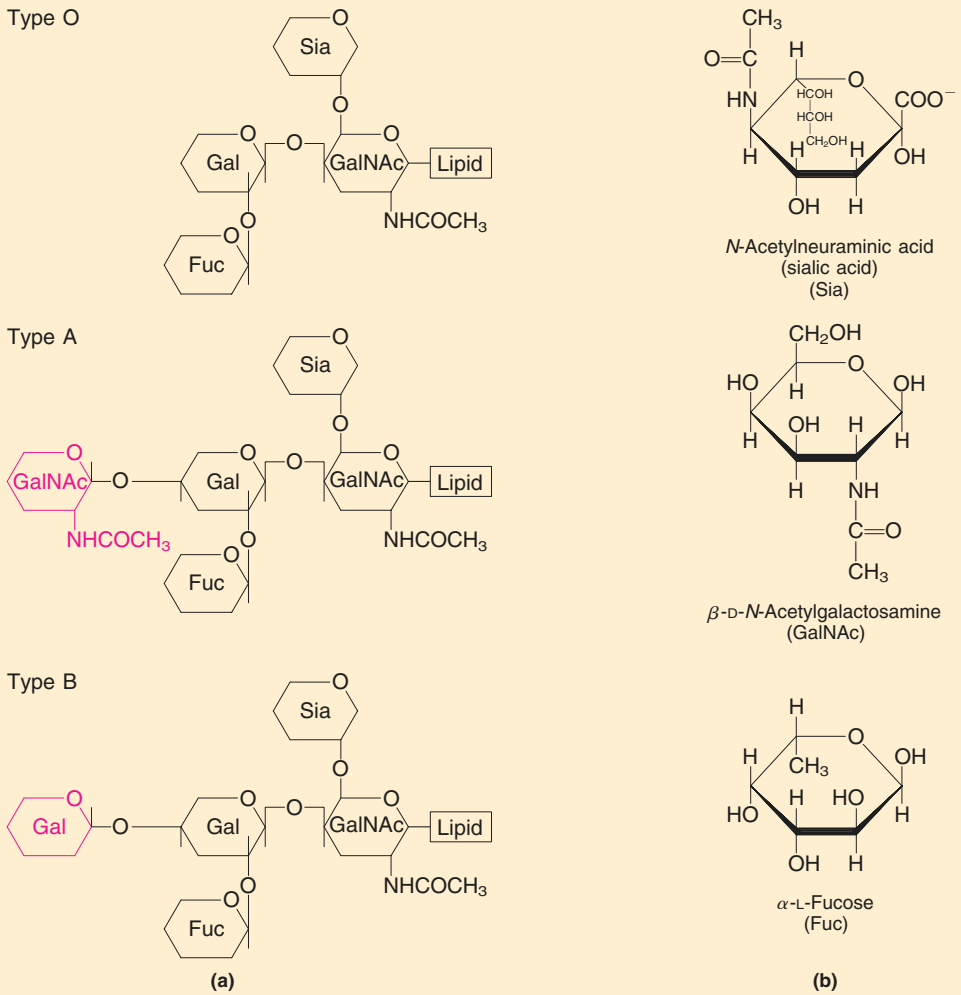
We now know that differences among blood groups reflect differences among oligosaccharides attached to the proteins and lipids of the RBC membranes. The oligosaccharides on the RBC surface have a common core, as shown in the accompanying figure, consisting of β-D-*N*-acetylgalactosamine, galactose, *N*-acetylneuraminic acid (sialic acid), and L-fucose. It is the terminal monosaccharide of this oligosaccharide that distinguishes the cells of different blood types and governs the compatibility of the blood types.

The A blood group antigen has β-D-*N*-acetylgalactosamine at its end, whereas the B blood group antigen has α-D-galactose. In type O blood, neither of these sugars is found on the cell surface; only the core oligosaccharide is present. Some of the oligosaccharides on type AB blood cells have a terminal β-D-*N*-acetylgalactosamine, whereas others have a terminal α-D-galactose.

Why does agglutination occur? The clumping reaction that occurs when incompatible bloods are mixed is an antigen-antibody reaction. Antigens are large molecules, often portions of bacteria or viruses, that stimulate the immune defenses of the body to produce protective antibodies. Antibodies bind to the foreign antigens and help to destroy them.

People with type A blood also have antibodies against type B blood (anti-B antibodies) in the blood serum. If the person with type A blood receives a transfusion of type B blood, the anti-B antibodies bind to the type B blood cells, causing clumping and destruction of those cells that can result in death. Individuals with type B blood also produce anti-A antibodies and therefore cannot receive a transfusion from a type A individual. Those with type AB blood are considered to be *universal recipients* because they have neither anti-A nor anti-B antibodies in their blood. (If they did, they would destroy their own red blood cells!) Thus in emergency situations a patient with type AB blood can receive blood from an individual of any blood type without serious transfusion reactions. Type O blood has no A or B antigens on the RBC but has both anti-A and anti-B antibodies. Because of the presence of both types of antibodies, type O individuals can receive transfusions only from a person who is also type O. On the other hand, the absence of A and B antigens on the red blood cell surface means that type O blood can be safely transfused into patients of any blood type. Hence type O individuals are *universal donors.*

Many adults, and some children, are unable to hydrolyze lactose because they do not make the enzyme *lactase.* This condition, which affects 20% of the population of the United States, is known as **lactose intolerance.** Undigested lactose remains in the intestinal tract and causes cramping and diarrhea that can eventually lead to dehydration. Some of the lactose is metabolized by intestinal bacteria that release organic acids and CO_2 gas into the intestines, causing further discomfort. Lactose intolerance is unpleasant, but its effects can be avoided by a diet that excludes milk and milk products. Alternatively, the enzyme that hydrolyzes lactose is available in tablet form. When ingested with dairy products it breaks down the lactose, preventing symptoms.



Schematic diagram of the blood group oligosaccharides. (a) Only the core oligosaccharide is found on the surface of type O red blood cells. On type A red blood cells, β-D-*N*-acetylgalactosamine is linked to the galactose (Gal) of the core oligosaccharide. On type B red blood cells, a galactose molecule is found attached to the galactose of the core oligosaccharide. (b) The structures of some of the unusual monosaccharides found in the blood group oligosaccharides.

Sucrose

Sucrose is also called table sugar, cane sugar, or beet sugar. Sucrose is an important carbohydrate in plants. It is water soluble and can easily be transported through the circulatory system of the plant. It cannot be synthesized by animals. High concentrations of sucrose produce a high osmotic pressure, which inhibits the growth of microorganisms, so it is used as a preservative. Of course, it is also widely used as a sweetener. In fact, it is estimated that the average American consumes 100–125 pounds of sucrose each year. It has been suggested that sucrose in the diet is undesirable because it represents a source of empty calories; that is, it contains no vitamins or minerals. However, the only negative association that has been

scientifically verified is the link between sucrose in the diet and dental caries, or cavities (see A Human Perspective: Tooth Decay and Simple Sugars on p. 493).

Sucrose is a disaccharide of α-D-glucose joined to β-D-fructose (Figure 17.10). The glycosidic linkage between α-D-glucose and β-D-fructose is quite different from those that we have examined for lactose and maltose. This bond involves the anomeric carbons of *both* sugars! This bond is called an (α1 → β2) glycosidic linkage, since it involves the C-1 anomeric carbon of glucose and the C-2 anomeric carbon of fructose (noted in red in Figure 17.10). Because the (α1 → β2) glycosidic bond joins both anomeric carbons, there is no hemiacetal group. As a result, sucrose will not react with Benedict's reagent and is not a reducing sugar.

17.6 Polysaccharides

Starch

Learning Goal 12

A polymer (Section 12.5) is a large molecule made up of many small units, the monomers, held together by chemical bonds.

Most carbohydrates that are found in nature are large polymers of glucose. Thus a polysaccharide is a large molecule composed of many monosaccharide units (the monomers) joined in one or more chains.

As seen in Figure 17.1, plants have the ability to use the energy of sunlight to produce monosaccharides, principally glucose, from CO_2 and H_2O. Although sucrose is the major transport form of sugar in the plant, starch (a polysaccharide) is the principal storage form in most plants. These plants store glucose in starch granules. Nearly all plant cells contain some starch granules, but in some seeds, such as corn, as much as 80% of the cell's dry weight is starch.

Starch is a heterogeneous material composed of the glucose polymers **amylose** and **amylopectin.** Amylose, which accounts for about 80% of the starch of a plant cell, is a linear polymer of α-D-glucose molecules connected by glycosidic bonds between C-1 of one glucose molecule and C-4 of a second glucose. Thus the glucose units in amylose are joined by α(1 → 4) glycosidic bonds. A single chain can contain up to four thousand glucose units. Amylose coils up into a helix that repeats every six glucose units. The structure of amylose is shown in Figure 17.11.

Enzymes are proteins that serve as biological catalysts. They speed up biochemical reactions so that life processes can function. These enzymes are called α(1 → 4) glycosidases because they cleave α(1 → 4) glycosidic bonds.

Amylose is degraded by two types of enzymes. They are produced in the pancreas, from which they are secreted into the small intestine, and the salivary glands, from which they are secreted into the saliva. α-*Amylase* cleaves the glycosidic bonds of amylose chains at random along the chain, producing shorter polysaccharide chains. The enzyme β-*amylase* sequentially cleaves the disaccharide maltose from the reducing end of the amylose chain. The maltose is hydrolyzed into glucose by the enzyme *maltase.* The glucose is quickly absorbed by intestinal cells and used by the cells of the body as a source of energy.

Amylopectin is a highly branched amylose in which the branches are attached to the C-6 hydroxyl groups by α(1 → 6) glycosidic bonds (Figure 17.12). The main chains consist of α(1 → 4) glycosidic bonds. Each branch contains 20–25 glucose units, and there are so many branches that the main chain can scarcely be distinguished.

Glycogen

Glycogen is the major glucose storage molecule in animals. The structure of glycogen is similar to that of amylopectin. The "main chain" is linked by α(1 → 4) glycosidic bonds, and it has numerous α(1 → 6) glycosidic bonds, which provide many branch points along the chain. Glycogen differs from amylopectin only by having more and shorter branches. Otherwise, the two molecules are virtually identical. The structure of glycogen is shown in Figure 17.12.

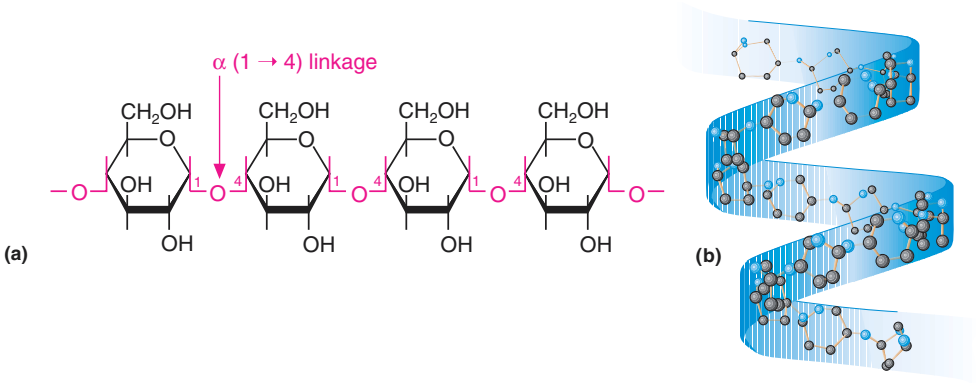


Figure 17.11
Structure of amylose. (a) A linear chain of α-D-glucose joined in α(1 → 4) glycosidic linkage makes up the primary structure of amylose. (b) Owing to hydrogen bonding, the amylose chain forms a left-handed helix that contains six glucose units per turn.

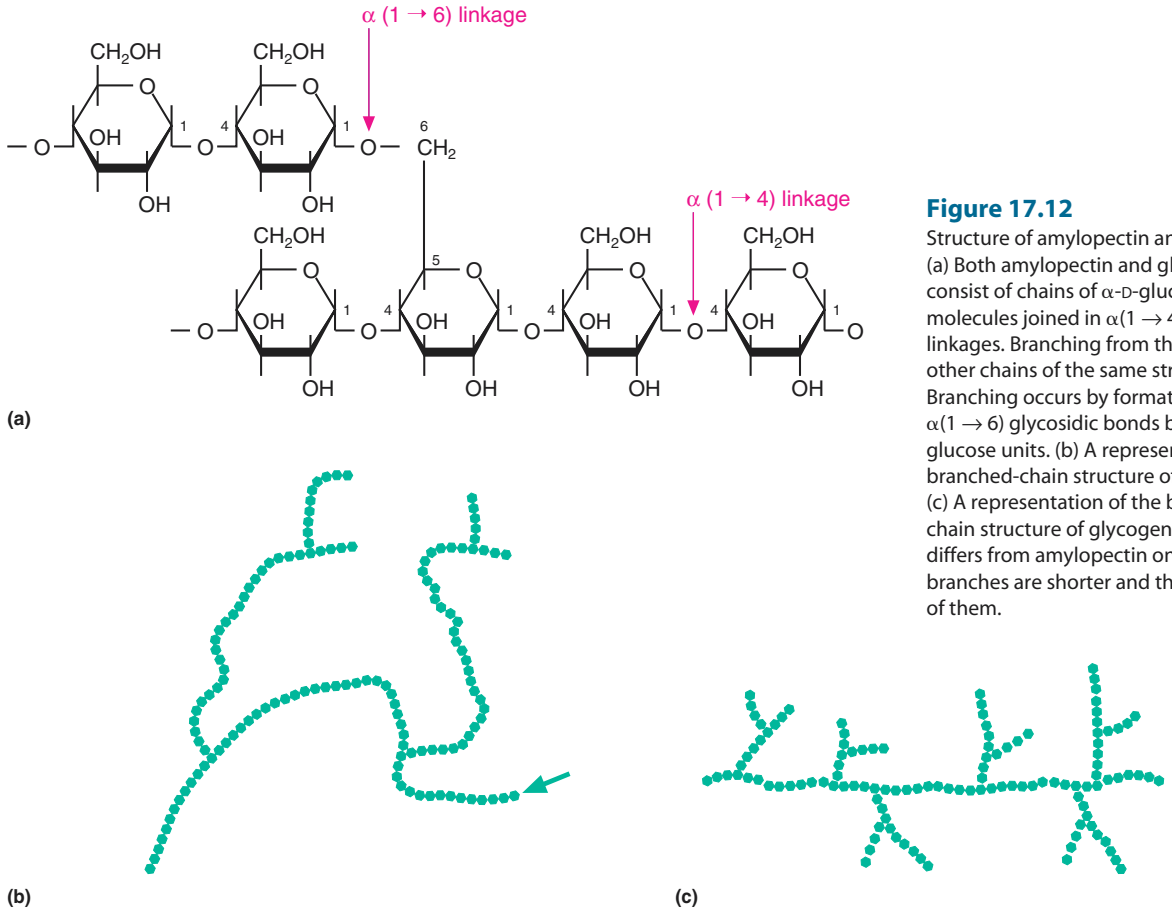


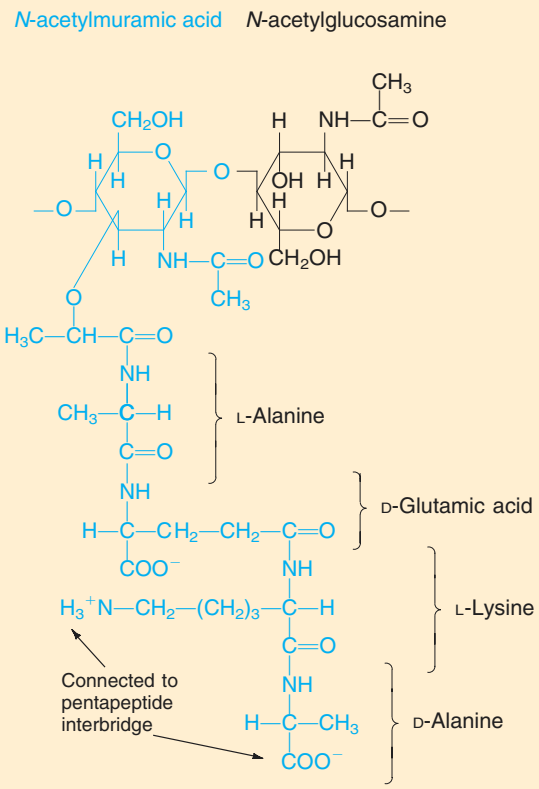
Figure 17.12
Structure of amylopectin and glycogen. (a) Both amylopectin and glycogen consist of chains of α-D-glucose molecules joined in α(1 → 4) glycosidic linkages. Branching from these chains are other chains of the same structure. Branching occurs by formation of α(1 → 6) glycosidic bonds between glucose units. (b) A representation of the branched-chain structure of amylopectin. (c) A representation of the branched-chain structure of glycogen. Glycogen differs from amylopectin only in that the branches are shorter and there are more of them.

A CLINICAL PERSPECTIVE

The Bacterial Cell Wall

The major component of bacterial cell walls is a complex polysaccharide known as a *peptidoglycan*. The name tells us that this structure consists of sugar molecules (-glycan) and peptides (peptido-; short polymers of amino acids).

As the accompanying structure shows, the carbohydrate portion of the peptidoglycan is a polymer of alternating units of two modified glucose molecules called *N-acetylglucosamine* and *N-acetylmuramic acid*. These two unusual monosaccharides

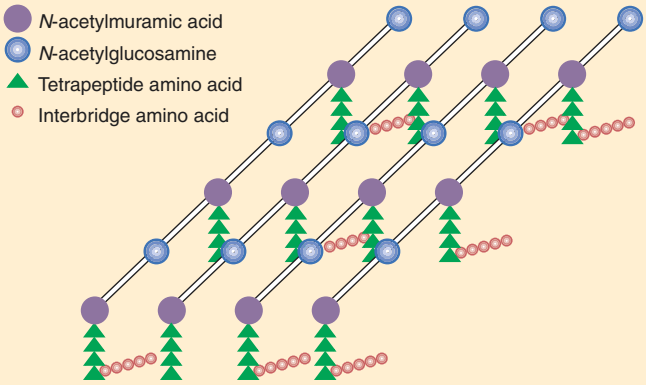


Structures of *N*-acetylglucosamine and *N*-acetylmuramic acid in β(1 → 4) glycosidic linkage. Note the tetrapeptide bridge linked to the *N*-acetylmuramic acid.

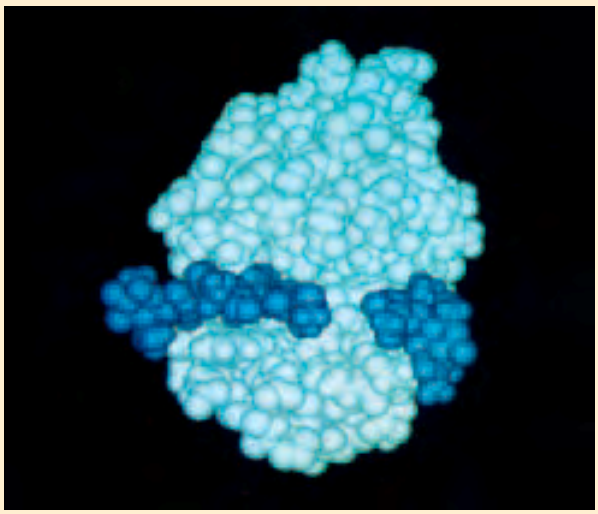
Glycogen is stored in the liver and skeletal muscle. Glycogen synthesis and degradation in the liver are carefully regulated. As we will see in Section 21.7, these two processes are intimately involved in keeping blood glucose levels constant.

Cellulose

The most abundant polysaccharide, indeed the most abundant organic molecule in the world, is **cellulose,** a polymer of β-D-glucose units linked by β(1 → 4) glycosidic bonds (Figure 17.13). A molecule of cellulose typically contains about 3000 glucose



The three-dimensional structure of one layer of peptidoglycan.



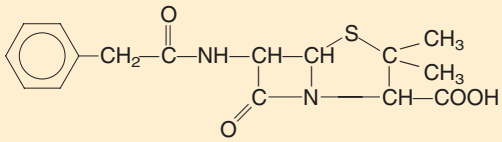
Conformation of lysozyme bound to its substrate. The enzyme binds with a six-sugar portion of the bacterial cell wall and cleaves it. The substrate fits into a deep crevice on the surface of the enzyme.

are joined by a β(1 → 4) glycosidic bond. In addition, each *N*-acetylmuramic acid is bonded to a tetrapeptide, a chain of four amino acids.

The structural strength of the cell wall is a result of pentapeptide cross-bridges that link the repeat units to one another (see the figure at the left). Millions of such cross-linkages produce an enormous peptidoglycan molecule, dozens of layers thick, around the bacterium. This thick wall is very rigid. It allows the bacterium to maintain its shape and protects it from bursting if the salt concentration of the environment is too low (hypotonic conditions).

Our bodies are constantly being assaulted by a variety of bacteria, and as you might expect, we have evolved protective mechanisms to minimize the damage. For instance, the enzyme *lysozyme*, found in tears and saliva, catalyzes the hydrolysis of the β(1 → 4) glycosidic bonds of peptidoglycan. As the accompanying figure shows, the enzyme has a deep groove on the surface (the active site) that a six-sugar unit of the cell wall can slip into like a bank card into the slot of an automatic teller machine. Lysozyme then catalyzes bond breakage and destroys the cell wall of the bacterium.

The penicillins are antibiotics that interfere with bacterial cell wall synthesis. The human body has no structures similar to the bacterial cell wall, so treatment with penicillins selectively destroys the bacteria, causing no harm to the patient. In practice, however, it must always be remembered that some individuals may develop an allergy to penicillins.



Penicillin G

The penicillins inhibit the enzyme that catalyzes the formation of the cross-linkage between the tetrapeptides. The antibiotic binds irreversibly to the active site of that enzyme so that it cannot bind to the tetrapeptide tail. Thus no cross-linkage can be made. Without the rigid, highly cross-linked peptidoglycan, the bacterial cells rupture and die.

units, but the largest known cellulose, produced by the alga *Valonia*, contains 26,000 glucose molecules.

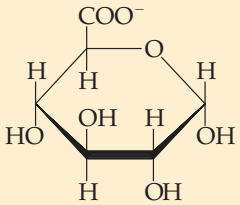
Cellulose is a structural component of the plant cell wall. The unbranched structure of the cellulose polymer and the β(1 → 4) glycosidic linkages allow cellulose molecules to form long, straight chains of parallel cellulose molecules called *fibrils*. These fibrils are quite rigid and are held together tightly by hydrogen bonds; thus it is not surprising that cellulose is a cell wall structural element.

In contrast to glycogen, amylose, and amylopectin, cellulose *cannot* be digested by humans. The reason is that we cannot synthesize the enzyme *cellulase*, which can

A MEDICAL PERSPECTIVE

Monosaccharide Derivatives and Heteropolysaccharides of Medical Interest

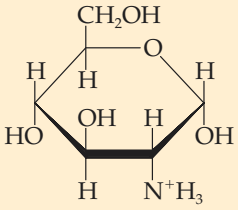
Many of the carbohydrates with important functions in the human body are either derivatives of simple monosaccharides or are complex polymers of monosaccharide derivatives. One type of monosaccharide derivatives, the uronates, is formed when the terminal—CH_2OH group of a monosaccharide is oxidized to a carboxylate group. α-D-Glucuronate is a uronate of glucose:



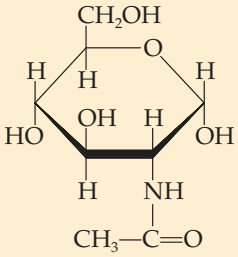
α-D-Glucuronate

In liver cells, α-D-glucuronate is bonded to hydrophobic molecules, such as steroids, to increase their solubility in water. When bonded to the modified sugar, steroids are more readily removed from the body.

Amino sugars are a second important group of monosaccharide derivatives. In amino sugars one of the hydroxyl groups (usually on carbon-2) is replaced by an amino group. Often these are found in complex oligosaccharides that are attached to cellular proteins and lipids. The most common amino sugars, D-glucosamine and D-galactosamine, are often found in the *N*-acetyl form. *N*-acetylglucosamine (see A Clinical Perspective: The Bacterial Cell Wall on pp. 514–515) is a component of bacterial cell walls and *N*-acetylgalactosamine is a component of the A, B, O blood group antigens (see preceding, A Human Perspective: Blood Transfusions and the Blood Group Antigens).

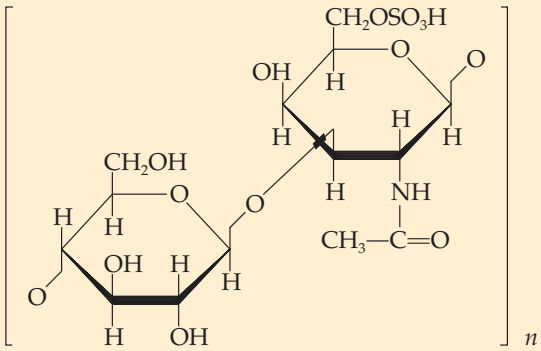


α-D-Glucosamine



α-D-*N*-Acetylglucosamine

Heteropolysaccharides are long-chain polymers that contain more than one type of monosaccharide, many of which are amino sugars. As a result, they are often referred to as *glycosaminoglycans*, which include chondroitin sulfate, hyaluronic acid, and heparin. Hyaluronic acid is abundant in the fluid of joints and in the vitreous humor of the eye. Chondroitin sulfate is an important component of cartilage; and heparin has anticoagulant function. The structures of the repeat units of these polymers are shown below.



Repeat unit of chondroitin sulfate

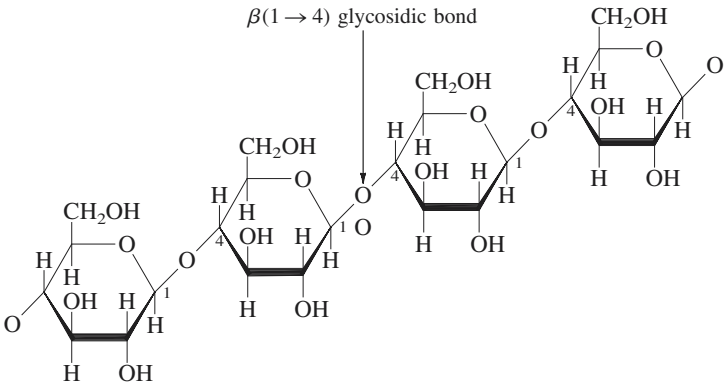
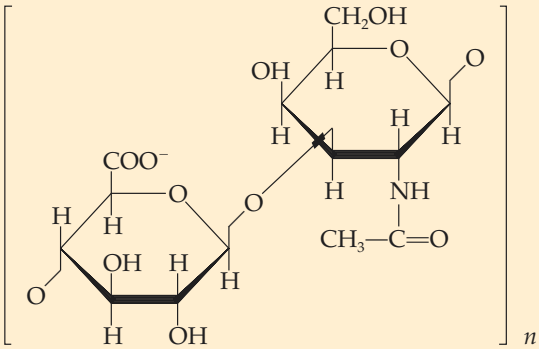
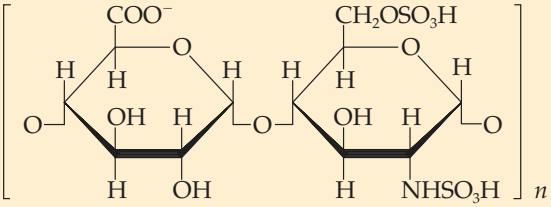


Figure 17.13
The structure of cellulose.



Repeat unit of hyaluronic acid



Repeat unit of heparin

Two of these molecules have been studied as potential treatments for osteoarthritis, a painful, degenerative disease of the joints. The amino sugar D-glucosamine is thought to stimulate the production of collagen. Collagen is one of the main components of articular cartilage, which is the shock-absorbing cushion within the joints. With aging, some of the D-glucosamine is lost, leading to a reduced cartilage layer and to the onset and progression of arthritis. It has been suggested that ingestion of D-glucosamine can actually "jump-start" production of cartilage and help repair eroded cartilage in arthritic joints.

It has also been suggested that chondroitin sulfate can protect existing cartilage from premature breakdown. It absorbs large amounts of water, which is thought to facilitate diffusion of nutrients into the cartilage, providing precursors for the synthesis of new cartilage. The increased fluid also acts as a shock absorber.

Studies continue on the effect that D-glucosamine and chondroitin sulfate have on degenerative joint disease. To date the studies are inconclusive because a large placebo effect is observed with sufferers of osteoarthritis. Many people in the control groups of these studies also experience relief of symptoms when they receive treatment with a placebo, such as a sugar pill.

Capsules containing D-glucosamine and chondroitin sulfate are available over the counter, and many sufferers of osteoarthritis prefer to take this nutritional supplement as an alternative to any nonsteroidal anti-inflammatory drugs (NSAID), such as ibuprofen. Although NSAID can reduce inflammation and pain, long-term use of NSAID can result in stomach ulcers, damage to auditory nerves, and kidney damage.

hydrolyze the β(1 → 4) glycosidic linkages of the cellulose polymer. Indeed, only a few animals, such as termites, cows, and goats, are able to digest cellulose. These animals have, within their digestive tracts, microorganisms that produce the enzyme cellulase. The sugars released by this microbial digestion can then be absorbed and used by these animals. In humans, cellulose from fruits and vegetables serves as fiber in the diet.

What chemical reactions are catalyzed by α-amylase and β-amylase? **Question 17.9**

What is the function of cellulose in the human diet? How does this relate to the structure of cellulose? **Question 17.10**

Summary

17.1 Types of Carbohydrates

Carbohydrates are found in a wide variety of naturally occurring substances and serve as principal energy sources for the body. Dietary carbohydrates include complex carbohydrates, such as starch in potatoes, and simple carbohydrates, such as sucrose.

Carbohydrates are classified as *monosaccharides* (one sugar unit), *disaccharides* (two sugar units), *oligosaccharides* (three to ten sugar units), or *polysaccharides* (many sugar units).

17.2 Monosaccharides

Monosaccharides that have an aldehyde as their most oxidized functional group are *aldoses*, and those having a ketone group as their most oxidized functional group are *ketoses*. They may be classified as *trioses*, *tetroses*, *pentoses*, and so forth, depending on the number of carbon atoms in the carbohydrate.

17.3 Stereoisomers and Stereochemistry

Stereoisomers of monosaccharides exist because of the presence of *chiral* carbon atoms. They are classified as D- or L- depending on the arrangement of the atoms on the chiral carbon farthest from the aldehyde or ketone group. If the —OH on this carbon is to the right, the stereoisomer is of the D-family. If the —OH group is to the left, the stereoisomer is of the L-family.

Each member of a pair of stereoisomers will rotate plane-polarized light in different directions. A polarimeter is used to measure the direction of rotation of plane-polarized light. Compounds that rotate light in a clockwise direction are termed dextrorotatory and are designated by a plus sign (+). Compounds that rotate light in a counterclockwise direction are called levorotatory and are indicated by a minus sign (−).

The *Fischer Projection* is a two-dimensional drawing of a molecule that shows a chiral carbon at the intersection of two lines. Horizontal lines represent bonds projecting out of the page and vertical lines represent bonds that project into the page. The most oxidized carbon is always represented at the "top" of the structure.

17.4 Biologically Important Monosaccharides

Important monosaccharides include *glyceraldehyde*, *glucose*, *fructose*, and *ribose*. Monosaccharides containing five or six carbon atoms can exist as five-membered or six-membered rings. Formation of a ring produces a new chiral carbon at the original carbonyl carbon, which is designated either α or β depending on the orientation of the groups. The cyclization of an aldose produces an intramolecular *hemiacetal*, and the cyclization of a ketose yields an intramolecular *hemiketal*.

Reducing sugars are oxidized by the *Benedict's reagent*. All monosaccharides and all common disaccharides, except sucrose, are reducing sugars. At one time Benedict's reagent was used to determine the concentration of glucose in urine.

17.5 Biologically Important Disaccharides

Important disaccharides include *lactose* and *sucrose*. Lactose is a disaccharide of β-D-galactose bonded β(1 → 4) with D-glucose. In *galactosemia*, defective metabolism of galactose leads to accumulation of a toxic by-product. The ill effects of galactosemia are avoided by exclusion of milk and milk products from the diet of affected infants. Sucrose is a dimer composed of α-D-glucose bonded (α1 → β2) with β-D-fructose.

17.6 Polysaccharides

Starch, the storage polysaccharide of plant cells, is composed of approximately 80% amylose and 20% amylopectin. *Amylose* is a polymer of α-D-glucose units bonded α(1 → 4). Amylose forms a helix. Amylopectin has many branches. Its main chain consists of α-D-glucose units bonded α(1 → 4). The branches are connected by α(1 → 6) glycosidic bonds.

Glycogen, the major storage polysaccharide of animal cells, resembles amylopectin, but it has more, shorter branches. The liver reserve of glycogen is used to regulate blood glucose levels.

Cellulose is a major structural molecule of plants. It is a β(1 → 4) polymer of D-glucose that can contain thousands of glucose monomers. Cellulose cannot be digested by animals because they do not produce an enzyme capable of cleaving the β(1 → 4) glycosidic linkage.

Key Terms

aldose (17.2)
amylopectin (17.6)
amylose (17.6)
anomer (17.4)
asymmetric carbon (17.3)
Benedict's reagent (17.4)
carbohydrate (17.1)
cellulose (17.6)
chiral molecule (17.3)
disaccharide (17.1)
enantiomers (17.3)
Fischer Projection (17.3)
fructose (17.4)
galactose (17.4)
galactosemia (17.5)
glucose (17.4)
glyceraldehyde (17.3)
glycogen (17.6)
glycosidic bond (17.1)
Haworth projection (17.4)
hemiacetal (17.4)
hemiketal (17.4)
hexose (17.2)
ketose (17.2)
lactose (17.5)
lactose intolerance (17.5)
maltose (17.5)
monosaccharide (17.1)
nonreducing sugar (17.5)
oligosaccharide (17.1)

pentose (17.2)
polysaccharide (17.1)
reducing sugar (17.4)
ribose (17.4)
saccharide (17.1)
stereochemistry (17.3)
stereoisomers (17.3)
sucrose (17.5)
tetrose (17.2)
triose (17.2)

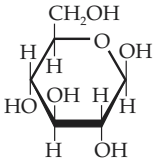
Questions and Problems

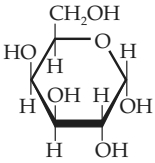
Types of Carbohydrates

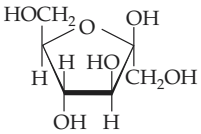
17.11 What is the difference between a monosaccharide and a disaccharide?
17.12 What is a polysaccharide?
17.13 Read the labels on some of the foods in your kitchen, and see how many products you can find that list one or more carbohydrates among the ingredients in the package. Make a list of these compounds, and attempt to classify them according to parent structure (e.g., monosaccharides, disaccharides, polysaccharides).
17.14 Some disaccharides are often referred to by their common names. What are the chemical names of (a) milk sugar, (b) beet sugar, and (c) cane sugar?
17.15 How many kilocalories of energy are released when 1 g of carbohydrate is "burned" or oxidized?
17.16 List some natural sources of carbohydrates.
17.17 Draw and provide the names of an aldohexose and a ketohexose.
17.18 Draw and provide the name of an aldotriose.

Monosaccharides

17.19 Identify each of the following sugars. Label each as either a hemiacetal or a hemiketal:

a.


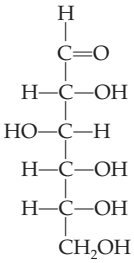
c.


b.


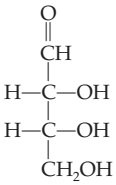
17.20 Draw the open-chain form of the sugars in Problem 17.19.
17.21 Draw all of the different possible aldotrioses of molecular formula $C_3H_6O_3$.
17.22 Draw all of the different possible aldotetroses of molecular formula $C_4H_8O_4$.

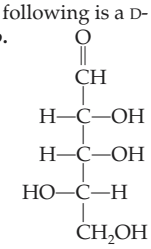
Stereoisomers and Stereochemistry

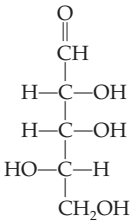
17.23 Is there any difference between dextrose and D-glucose?
17.24 The structure of D-glucose is shown. Draw its mirror image.

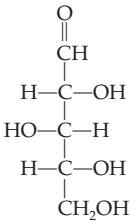


17.25 How are D- and L-glyceraldehyde related?
17.26 Determine whether each of the following is a D- or L-sugar:

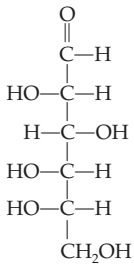
a.


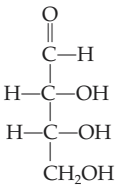
b.


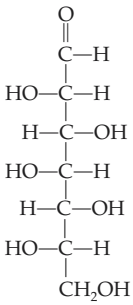
c.


d.


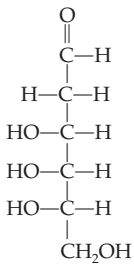
17.27 Define the term *stereoisomer.*
17.28 Define the term *enantiomer.*
17.29 Define the term *chiral carbon.*
17.30 Draw an example of a molecule with one or more chiral carbons. Note the carbon or carbons that are chiral with asterisks (*).
17.31 Explain how a polarimeter works.
17.32 What is plane-polarized light?
17.33 Draw a Fischer Projection formula for each of the following compounds. Indicate each of the chiral carbons with asterisks (*).

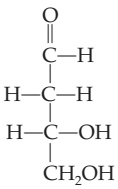
a.


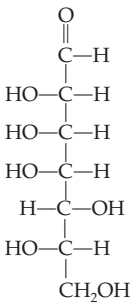
b.


c.


17.34 Draw a Fischer Projection formula for each of the following compounds. Indicate each of the chiral carbons with asterisks (*).

a.


b.


c.


Biologically Important Monosaccharides

17.35 Why does cyclization of D-glucose give two isomers, α- and β-D-glucose?
17.36 Draw the structure of the open chain form of D-fructose, and show how it cyclizes to form α- and β-D-fructose.

17.37 Which of the following would give a positive Benedict's Test?
a. Sucrose **c.** β-Maltose
b. Glycogen **d.** α-Lactose

17.38 Why was the Benedict's reagent useful for determining the amount of glucose in the urine?

17.39 Describe what is meant by a pair of enantiomers. Draw an example of a pair of enantiomers.

17.40 What is a chiral carbon atom?

17.41 When discussing sugars, what do we mean by an intramolecular hemiacetal?

17.42 When discussing sugars, what do we mean by an intramolecular hemiketal?

Biologically Important Disaccharides

17.43 Maltose is a disaccharide isolated from amylose that consists of two glucose units linked α(1 → 4). Draw the structure of this molecule.

17.44 Sucrose is a disaccharide formed by linking α-D-glucose and β-D-fructose by an (α1 → β2) bond. Draw the structure of this disaccharide.

17.45 What is the major biological source of lactose?

17.46 What metabolic defect causes galactosemia?

17.47 What simple treatment prevents most of the ill effects of galactosemia?

17.48 What are the major physiological effects of galactosemia?

17.49 What is lactose intolerance?

17.50 What is the difference between lactose intolerance and galactosemia?

Polysaccharides

17.51 What is the difference between the structure of cellulose and the structure of amylose?

17.52 How does the structure of amylose differ from that of amylopectin and glycogen?

17.53 What is the major physiological purpose of glycogen?

17.54 Where in the body do you find glycogen stored?

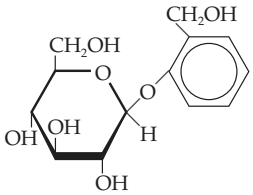
17.55 Where are α-amylase and β-amylase produced?

17.56 Where do α-amylase and β-amylase carry out their enzymatic functions?

Critical Thinking Problems

1. The six-member glucose ring structure is not a flat ring. Like cyclohexane, it can exist in the chair conformation. Build models of the chair conformation of α- and β-D-glucose. Draw each of these structures. Which would you predict to be the more stable isomer? Explain your reasoning.

2. The following is the structure of salicin, a bitter-tasting compound found in the bark of willow trees:



Salicin

The aromatic ring portion of this structure is quite insoluble in water. How would forming a glycosidic bond between the aromatic ring and β-D-glucose alter the solubility? Explain your answer.

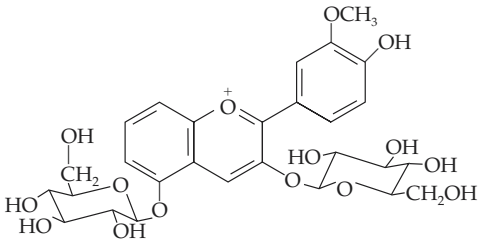
3. Ancient peoples used salicin to reduce fevers. Write an equation for the acid-catalyzed hydrolysis of the O-glycosidic bond of salicin. Compare the aromatic product with the structure of acetylsalicylic acid (aspirin). Use this information to develop a hypothesis explaining why ancient peoples used salicin to reduce fevers.

4. Chitin is a modified cellulose in which the C-2 hydroxyl group of each glucose is replaced by

This nitrogen-containing polysaccharide makes up the shells of lobsters, crabs, and the exoskeletons of insects. Draw a portion of a chitin polymer consisting of four monomers.

5. Pectins are polysaccharides obtained from fruits and berries and used to thicken jellies and jams. Pectins are α(1 → 4) linked D-galacturonic acid. D-Galacturonic acid is D-galactose in which the C-6 hydroxyl group has been oxidized to a carboxyl group. Draw a portion of a pectin polymer consisting of four monomers.

6. Peonin is a red pigment found in the petals of peony flowers. Consider the structure of peonin:



Why do you think peonin is bonded to two hexoses? What monosaccharide(s) would be produced by acid-catalyzed hydrolysis of peonin?