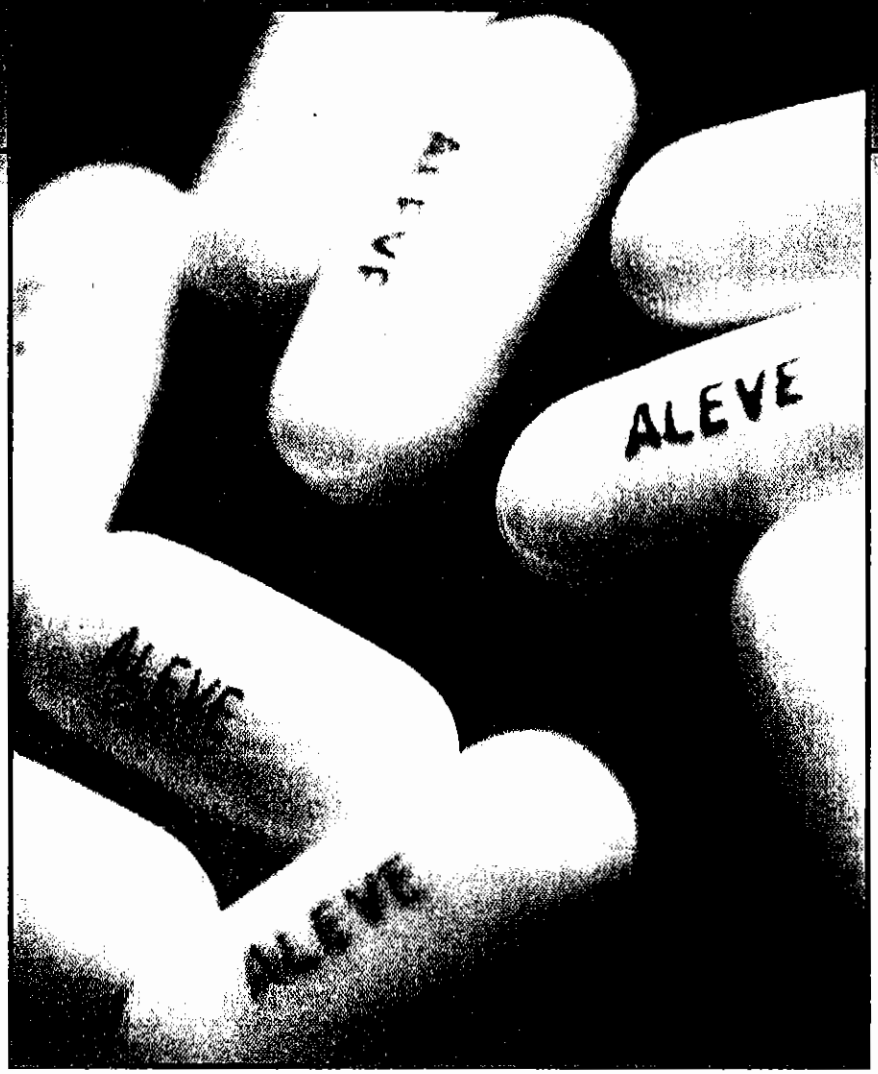
CHAPTER

8



Some drugs display versatility and serendipity in their actions. They often show therapeutic benefits against diseases for which they were not originally intended. The anti-inflammatory drugs Celebrex, naproxen (Aleve), Vioxx, and others are very effective in relieving the pain of individuals with rheumatoid arthritis, osteoarthritis, and other related diseases. Inflammatory processes are initiated by the production of a class of lipids called the prostaglandins. The anti-inflammatory drugs inhibit the synthesis of prostaglandins. Although direct, clinical evidence is not yet available, it has been suspected by medical researchers that the disintegration of brain cells in Alzheimer's disease patients is caused by a process of inflammation. Is it possible that anti-inflammatory drugs may prevent or at least lessen the symptoms of Alzheimer's disease? The National Institute of Aging in the National Institutes of Health recently conducted such a study on 2500 individuals over the age of 70 years. The trial individuals were divided into three groups to receive Celebrex or naproxen or a placebo. The goal of the study was to determine if the inflammatory drugs lowered the risk of Alzheimer's disease. After 3 years the trial was suspended because an unusually large number of individuals taking naproxen suffered a heart attack or stroke. The trial had to be stopped, but the group will continue to be monitored in the future to see if there is any decline in the development of Alzheimer's disease.
(© Mario Tama/Getty Images.)

Lipids: Structure and Biological Function

Lipids are a class of biomolecules whose distinctive characteristic is their solubility behavior. Because of their hydrophobic nature, they are more soluble in nonpolar solvents such as diethyl ether, methanol, and hexane than in water. Because they are defined by their physical *behavior* rather than their chemical *structure* (like amino acids and carbohydrates), we may expect to find a great variety of chemical structures among the lipid class of molecules. In addition to the expected elements of carbon and hydrogen, which lend nonpolar character, lipids may also contain oxygen, nitrogen, and phosphorus. The chemical functional groups most common to the lipids are carbon–carbon single and double bonds, aldehydes and ketones, carboxylate esters, phosphate esters, amines, and amides. We have discussed in earlier chapters how chemical diversity among biomolecular structure always leads to a diversity of biological function. This is true also for the **lipids**.

The lipids are probably best known for their role in energy metabolism. In most organisms, the principal molecules for long-term energy storage are the **nonpolar lipids** called **fats**. The **fatty acids**, components of the nonpolar lipids, are important energy molecules especially in the heart, brain, and adipose tissues. The **polar lipids**, some nitrogen and phosphorus containing, are important components of biological membranes. **Biological membranes**, which are composed primarily of lipids and proteins, form molecular boundaries around all cells and cell organelles. They give the cell its shape and form and protect its contents from the outside environment (see Chapter 9). The **steroid** class of lipids is represented by **cholesterol**, which is found in membranes and also serves as a precursor for many hormones. Miscellaneous lipids present in only minor quantities in the cell are involved as light-absorbing pigments (β-carotene, retinal), enzyme cofactors (vitamin K), hormones (estrogens, testosterone), signal molecules (prostaglandins), and electron carriers (ubiquinone).

In this chapter we will first introduce the structures of the various lipid families and then turn to a discussion of their biological roles. In the next chapter we focus on the chemical architecture and transport activities of biological membranes, with emphasis on the roles of lipids and proteins.

8.1 Fatty Acids

Learning Objective

Know the chemical structures and understand the biological importance of the naturally occurring fatty acids.

Fatty Acid Structure

Fatty acids are biomolecules containing a carboxyl functional group (—COOH) connected to an unbranched aliphatic chain (Figure 8.1). These structural features give them a split personality: One end is polar and sometimes ionic (the carboxyl group), whereas the opposite end (the hydrocarbon chain) has nonpolar properties. (In Section 2.2, we called such molecules **amphiphilic**.) Fatty acids are rarely found in a free form in cells and tissues but are most often bound in fats (triacylglycerols and other lipids). The number of carbon atoms in a fatty acid can range from 4 (as found in butter) to as many as 36 (found in the brain). Most fatty acids found in nature, however, contain between 12 and 24 carbon atoms, with those containing 16 and 18 carbons the most prevalent. Table 8.1 provides a list of names and structures of the most common naturally occurring fatty acids.

Several general rules are followed for the cellular construction of fatty acids (Table 8.2). Because fatty acids are synthesized by combining the C_2 units of acetic acid (CH_3COOH), almost all contain an even number of carbon atoms. The hydrocarbon chain, which is almost always unbranched, can consist of all carbon–carbon single bonds (**saturated fatty acids**) or one or more carbon–carbon double bonds (**unsaturated fatty acids**) (see Figure 8.1). For monounsaturated acids, the double bond is usually between carbons 9 and 10 (C1 is the carboxyl carbon). For diunsaturated

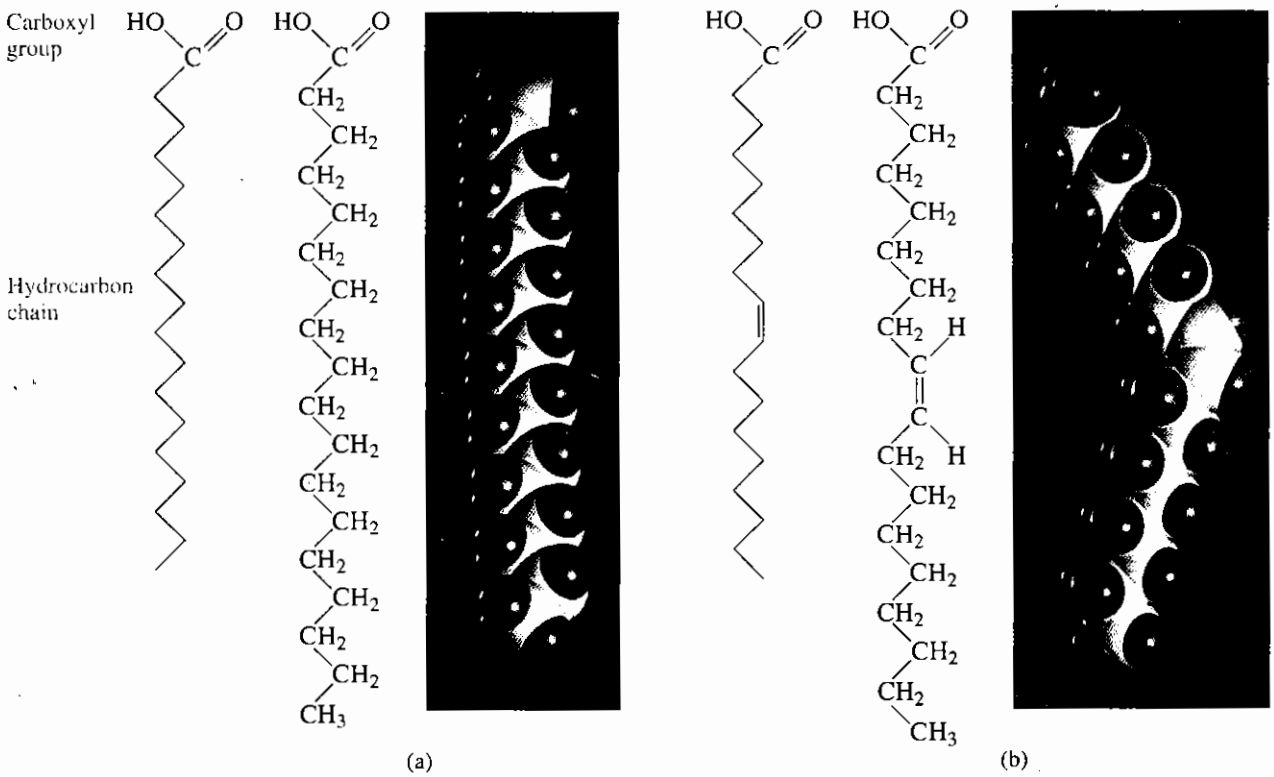


Figure 8.1 The structures of two fatty acids: (a) octadecanoic acid, a saturated acid, and (b) 9-octadecenoic acid, an unsaturated acid. The fatty acids are shown in three forms, an abbreviated structure, where a zigzag line represents the hydrocarbon chain; a structure showing all carbon and hydrogen atoms; and space-filling models showing the actual shape of each molecule. (© Tripos, Inc.)

Table 8.1
Structures and names of common, naturally occurring fatty acids

Number of Carbons[a]	Common Name	Systematic Name	Abbreviated Symbol[b]	Structure[c]
12	Lauric acid	*n*-Dodecanoic acid	12:0	$CH_3(CH_2)_{10}COOH$
14	Myristic acid	*n*-Tetradecanoic acid	14:0	$CH_3(CH_2)_{12}COOH$
16	Palmitic acid	*n*-Hexadecanoic acid	16:0	$CH_3(CH_2)_{14}COOH$
16	Palmitoleic acid	*n*-Hexadecenoic acid	$16:1^{\Delta 9}$	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$
18	Stearic acid	*n*-Octadecanoic acid	18:0	$CH_3(CH_2)_{16}COOH$
18	Oleic acid	*n*-Octadecenoic acid	$18:1^{\Delta 9}$	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
18	Linoleic acid	—	$18:2^{\Delta 9,12}$	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
18	Linolenic acid	—	$18:3^{\Delta 9,12,15}$	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$
20	Arachidonic acid	—	$20:4^{\Delta 5,8,11,14}$	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$
20	EPA	Eicosapentaenoic acid	$20:5^{\Delta 5,8,11,14,17}$	
22	DHA	Docosahexaenoic acid	$22:6^{\Delta 4,7,10,13,16,19}$	

[a] Note that all have an even number of carbons.
[b] Indicates the number of carbon atoms and the position of the carbon–carbon double bonds.
[c] All double bonds are cis.

acids, the second double bond is most often between carbons 12 and 13. Note in Table 8.2 that multiple double bonds are not conjugated (—CH=CH—CH=CH—) but are separated by one methylene group (—CH=CH—CH_2—CH=CH—). Fatty acids with two or more double bonds are called **polyunsaturated**. Double bonds in naturally occurring fatty acids are almost always of the cis configuration.

Table 8.2
General rules for the structures of naturally occurring fatty acids

1. Most fatty acids have an even number of carbon atoms.
2. The hydrocarbon chain is almost always unbranched.
3. Most carbon–carbon bonds are single; however, fatty acids may contain one, two, or more carbon–carbon double bonds.
4. Double bonds are most often cis.
5. For monounsaturated fatty acids, the double bond is usually between carbons 9 and 10.
6. If more than one carbon–carbon double bond is present they are not conjugated but are separated by a methylene unit.

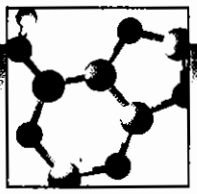
Because of the many varieties of fatty acids present in nature, a special, abbreviated nomenclature system has been developed. This system indicates the total number of carbon atoms, the number of carbon–carbon double bonds, and the position of each double bond. Fatty acids also have common names, which are more often used than their official names. **Lauric acid** (dodecanoic acid), a fatty acid with 12 carbon atoms and no carbon–carbon double bonds, is designated in the abbreviated form as 12:0. **Linoleic acid**, with 18 carbon atoms and two carbon–carbon double bonds (at C9–C10 and C12–C13), is $18{:}2^{\Delta 9,12}$. [This is read 18:2 delta (Δ) 9,12.] This nomenclature is used to define each fatty acid in Table 8.1.

Before You Go On

1. Review Figure 8.1 and Tables 8.1 and 8.2 to answer the following questions.
   a. Draw each of the fatty acids listed below in two forms as shown in Figure 8.1, namely, zig-zag form and the form showing all carbon and hydrogen atoms.
      Myristic acid
      Linoleic acid
      Arachidonic acid
   b. The systematic name for linoleic acid is 9,12-octadecadienoic acid. What is the systematic name for linolenic acid?
   c. The common name for the saturated acid with 20 carbons is arachidic acid. What is the systematic name? Write the abbreviated symbol.
   d. Draw the structure for the fatty acid EPA.
   e. Write the abbreviated symbol for the monounsaturated fatty acid with 20 carbon atoms. Where is the most likely position of the double bond for the acid found in humans?

Physical and Chemical Properties of Fatty Acids

The physical properties of fatty acids can be predicted from a knowledge of their structures. They are all soluble in organic solvents, such as alcohols, hexane, and diethyl ether. The smaller chain acids acetic (2:0), propanoic (3:0), and butanoic (4:0) are infinitely soluble in H_2O; however, solubility decreases with increasing chain length. Lauric acid (12:0) is soluble in water to the extent of 0.06 g per gram of water. Fatty acids greater than 12:0 are increasingly insoluble in water. The saturated acids with 10 or more carbons are waxy solids at room temperature. All saturated acids with fewer than 10 carbons and all unsaturated acids are oily liquids at room temperature. The double bonds put "kinks" in the hydrocarbon chains of the unsaturated fatty acids (see Figure 8.1b). These molecules cannot line up in a fully extended form

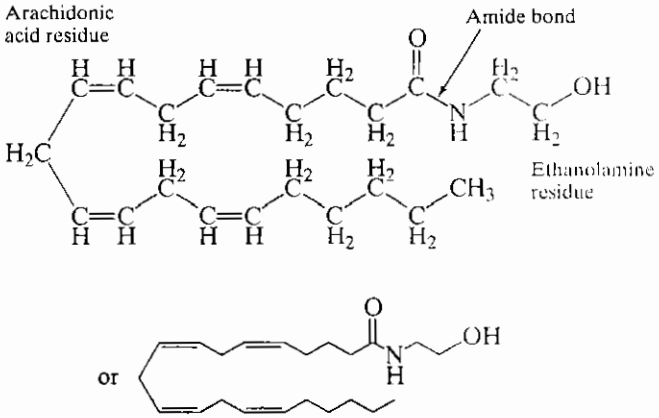


8 - 1

Window on Biochemistry

Anandamide: Pain Relief and Chocolate Cravings

Arachidonic acid ($20{:}4^{\Delta 5,8,11,14}$) has recently received attention for its involvement in brain chemistry. **Anandamide**, a product of the metabolism of arachidonic acid, has been found in the brains of humans, pigs, and other animals. It has also been isolated from cocoa and chocolate products. The name for this new molecule comes from the Sanskrit word *ananda*, which means internal bliss. Anandamide, produced by the combination of arachidonic acid with ethanolamine (see structure), is a neurotransmitter involved in the control of pain and regulation of movement. Researchers have found that stimulating nerve cells in the dorsal striatum region causes the cells to release anandamide. The newly discovered signaling molecule is the natural ligand for the cannabinoid receptor, CB-1. The CB-1 receptor is present in high concentrations in the cerebellum and basal ganglia where motor effects are mediated and in the hippocampus which controls memory, mood, cognition, coordination, sleep, and appetite. For example, when the body senses pain, anandamide is released and it binds to the CB-1 receptor sending a message to suppress pain. The CB-1 receptor is part of the G-protein receptor system involved in signal transduction (Special Topic I). When pain subsides, anandamide, which is no longer needed, is hydrolyzed to arachidonic acid and ethanolamine by an enzyme called fatty acid amide hydrolase. Chemicals that inhibit the hydrolase, and hence prolong the natural pain-relieving action of anandamide, may be potent analgesics (pain-relieving drugs). CB-1 is also the protein receptor that binds and mediates the central nervous system (CNS) effects of the cannabinoids, especially Δ^9-tetrahydrocannabinol (THC), an active ingredient in marijuana. The discovery of anandamide and similar compounds in cocoa powder may explain the craving for chocolate that many people experience. These chemicals in chocolate turn on the same receptor in the brain as marijuana. Research on the biochemistry of anandamide and its receptor may eventually lead to new and better treatments for pain relief, mood and anxiety disorders (depression, etc.), and sleep disorders. Although marijuana is used legally and illegally for treatment of some of these conditions, it has many undesirable side effects. Drugs for treatment of movement disorders such as Parkinson's disease and Tourette's syndrome may also be discovered from this research.

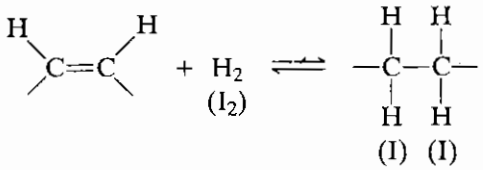


to pack together in a crystalline array as is the case for saturated fatty acids. Although larger chain fatty acids are insoluble in water, they appear to dissolve in dilute aqueous NaOH or KOH solutions. This is because an acid–base reaction takes place, forming the Na^+ or K^+ salt of the acids:

$$\underset{\text{Lauric acid}}{CH_3(CH_2)_{10}COOH} + NaOH \longrightarrow \underset{\text{Sodium laurate (a soap)}}{CH_3(CH_2)_{10}COO^-Na^+} + H_2O$$

The Na^+ or K^+ salts of fatty acids are called **soaps**. The soaps appear to dissolve in water, but they do not form true solutions. The amphiphilic molecules aggregate into molecular arrangements called **micelles** (see Section 2.2). Soaps are able to remove grease and other stains from cloth and skin by coating the oily residues with their hydrophobic tails and at the same time extending their ionic salt heads into the water. Free fatty acids under physiological conditions are present as carboxylate salts (ions) since their pK_a values are between 4 and 5. Therefore, the names of fatty acids under physiological conditions should end with *-ate*, indicating salts: laurate, myristate, oleate, and so on.

The chemical reactivity of the hydrocarbon chains of fatty acids depends on the extent of unsaturation. Saturated chains of fatty acids are relatively unreactive. Unsaturated chains display the usual reactivity of carbon–carbon double bonds. For example, hydrogen or halogen atoms may be added:



The hydrogenation process is used to produce solid fats from oils, and the iodine addition reaction has been used to measure experimentally the number of double bonds in a fatty acid sample. The double bonds of unsaturated fatty acids are attacked also by oxygen. The process, called **autooxidation**, results in complex, yellow products such as smaller, odoriferous aldehydes and acids from the degradation of the unsaturated hydrocarbon chains.

8.2 Nonpolar Lipids—Triacylglycerols

Learning Objective
Know the chemical structures and understand the biological function(s) of the nonpolar lipids, triacylglycerols.

Triacylglycerol Structure

The primary biological role of the fatty acids is to serve as metabolic fuel for cells. The acids are ingested and stored for future energy use in **triacylglycerols**. When energy is needed, the fatty acids are released in a free form by enzyme-catalyzed hydrolysis reactions, bound to serum albumin in the blood, and circulated throughout an organism. In heart and skeletal muscle, fatty acids, which have hydrocarbon structures similar to fossil fuels, are oxidized to CO_2 and H_2O with release of large amounts of energy. The stored fatty acids are especially efficient for energy production because the hydrocarbon chains are in a highly reduced state. As we shall see in Chapters 15 and 18, the complete oxidative metabolism of fatty acids produces twice as much energy per gram as for carbohydrates.

Oil from these canola plants is a rich source of polyunsaturated fatty acids. (© Carl Purcell/Photo Researcher.)

Almost all fatty acids present in nature are found as constituents of the **nonpolar lipids** called **triacylglycerols**. The basic foundation molecule of the triacylglycerols is the trihydroxyl compound **glycerol**. Each hydroxyl group can be linked to a fatty acid by esterification (Figure 8.2). The esterification process can occur in a stepwise manner to produce intermediate monoacylglycerols and diacylglycerols (either 1,2 or 1,3). Simple triacylglycerols, which are rare in nature, have three identical fatty acids, whereas the more common mixed triacylglycerols have two or three different fatty acids. The polar hydroxyl groups of glycerol and the polar (and sometimes ionic) carboxyl group of each fatty acid are tied up in neutral ester linkages, so triacylglycerols are nonpolar, hydrophobic molecules. As we can predict by inspection of the structures, triacylglycerols are insoluble in water but soluble in nonpolar solvents. [Recall that oil and vinegar salad dressings separate into two phases, a lower layer of vinegar (4% acetic acid in H_2O) and an upper layer of vegetable oil (mixtures of triacylglycerols).] Triacylglycerols are extracted from plant and animal tissue using solvent systems such as chloroform–methanol and hexane–isopropanol mixtures. Triacylglycerols isolated from animal tissues are called **fats** and are solids at room temperature because they contain predominately saturated fatty acids. Triacylglycerol mixtures from plant seeds are termed **oils** and contain mainly unsaturated acids. Table 8.3 compares the fatty acid content of several plant and animal triacylglycerol mixtures. Nutmeg oil is the source of trimyristin (contains three molecules of myristic acid, 14:0), one of the few simple triacylglycerols found in nature.

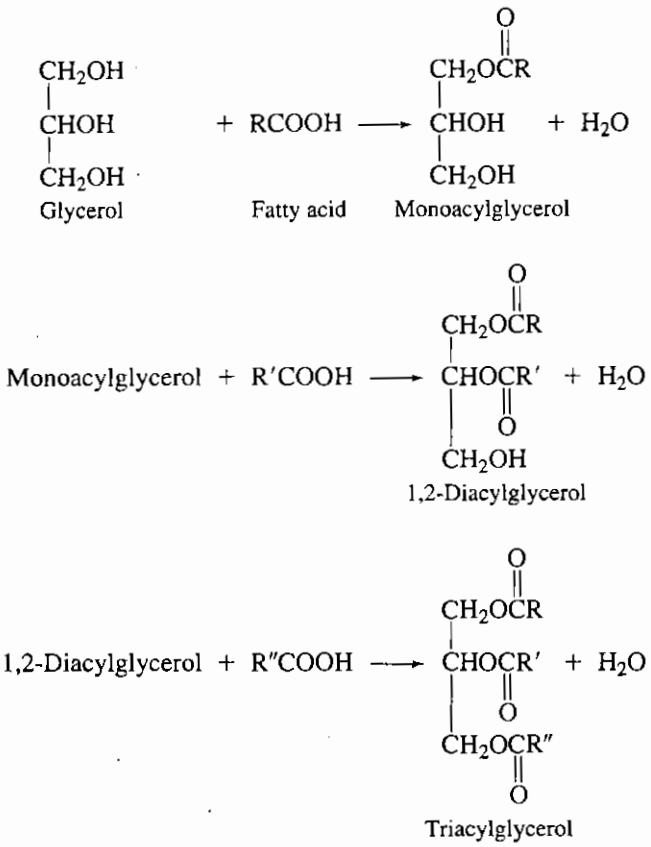


Figure 8.2 The stepwise addition of fatty acids to glycerols to the final stage of a triacylglycerol. Ester bonds hold the acyl groups to the glycerol backbone. R, R′, R″ are aliphatic saturated or unsaturated hydrocarbon chains of variable lengths.

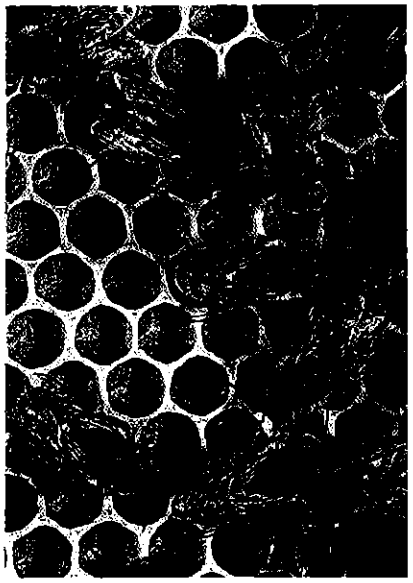
Table 8.3
Fatty acid content of common oils and fats. The fatty acids are present in triacylglycerol form. The numbers represent percentage of each fatty acid in an oil.

	Fatty Acids				
	Saturated				*Unsaturated*
Source	C_4–C_{12}	C_{14}	C_{16}	C_{18}	$C_{16} + C_{18}$
Canola oil	—	—	5	1	94
Olive oil	2	2	13	3	80
Butter	10	11	29	10	40
Beef fat	2	2	29	21	46
Coconut oil	60	18	11	2	8
Corn oil	—	2	10	3	85
Palm oil	—	2	40	6	52
Nutmeg oil	7	90	3	—	—
Peanut oil	—	5	8	3	84
Soybean oil	—	2	10	3	85
Sunflower oil	—	—	6	3	91

Before You Go On...

1. Draw the structure for a triacylglycerol containing the following fatty acids:

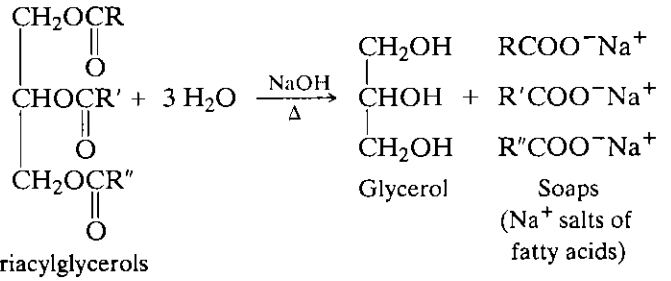
   Oleic acid at C1
   Myristic acid at C2
   Palmitic acid at C3



The primary component of beeswax is a nonpolar ester of palmitic acid. (© William J. Webber/Visuals Unlimited.)

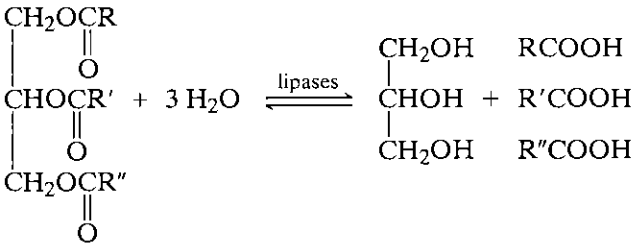
Triacylglycerol Reactivity

Ester Hydrolysis The chemical behavior of triacylglycerols depends mainly on the reactivity of the ester linkages. In an important commercial process called **saponification**, each ester is hydrolyzed in a reaction catalyzed by NaOH to produce glycerol and soaps:



In ancient times soaps were prepared by boiling animal fats with wood ash, which contains lye (NaOH). Soaps have been replaced largely by synthetic detergents, such as sodium dodecyl sulfate (SDS; see Section 3.5), which do not form precipitates or a bathtub ring in hard water the way sodium salts of fatty acids do.

Hydrolysis of triacylglycerols also occurs under physiological conditions; however, the catalysts are enzymes called **lipases**. These enzymes are present in the intestines and in fat cells (adipocytes), where they release fatty acids for energy metabolism:



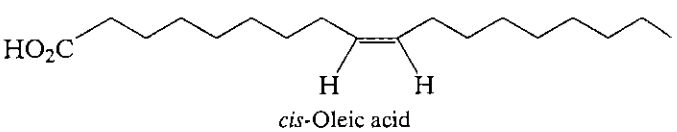
8 - 2

Window on Biochemistry

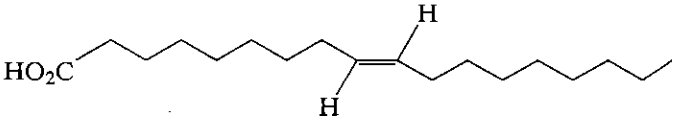
How Much Trans Fat Is in Your Food?

Food manufacturers often use the chemical process of partial hydrogenation to make vegetable oils more spreadable and to inhibit spoilage. However, hydrogenation leads to the formation of **trans fatty acids** or **trans fats** in the triacylglycerols (see Figure 8.3). An example is oleic acid, which in nature exists primarily in the cis configuration; its hydrogenation may lead to the production of *trans*-oleic acid, a trans fatty acid (see figure). When oils and fats are digested in the body, all of the fatty acids are released from the triacylglycerols including saturated, cis-unsaturated, and trans-unsaturated fatty acids. The freed fatty acids are carried in the bloodstream and distributed to cells for energy metabolism (Chapter 18).

There is now substantial medical evidence that the dietary consumption of trans fatty acids has contributed to the epidemic of coronary heart disease in the Western world, especially in the United States. In fact, epidemiological studies at Harvard University provide data showing that trans fat consumption may be a contributing factor in at least 30,000 premature coronary heart disease deaths per year. Metabolic studies reveal, specifically, that trans fats have an adverse effect on blood lipid levels. Dietary trans fats increase low density lipoprotein (LDL, "bad") cholesterol and decrease high density lipoprotein (HDL,



cis-Oleic acid



trans-Oleic acid

In Chapter 18 we discuss this important cellular reaction in detail.

Reactions of Carbon–Carbon Bonds Reactions of triacylglycerols do not involve only the ester linkages. The double bonds of unsaturated fatty acids in the triacylglycerols may be attacked by oxygen (autooxidation, see p. 236) or may react with hydrogen or halogen just as we saw with the free fatty acids (see p. 236).

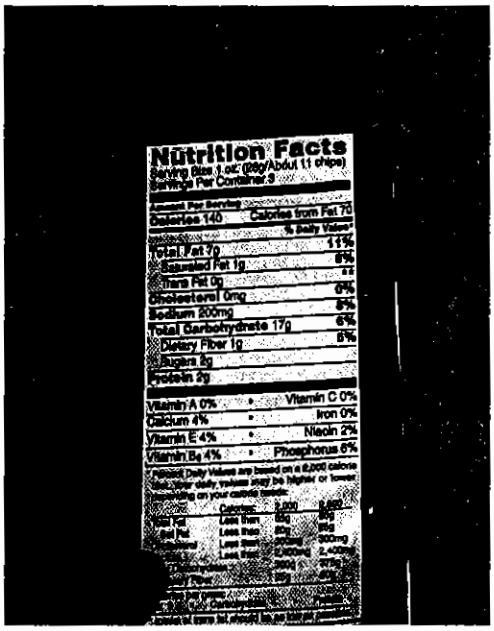
Autooxidation Highly purified vegetable oils are clear, colorless, and virtually odorless. The yellow color and strong odor of old or rancid fats and oils results from autooxidation of unsaturated fatty acid chains in the triacylglycerols. The rate of oil deterioration may be slowed by two processes: reducing the number of unsaturated fatty acids by partial hydrogenation (see later) or by adding a chemical preservative such as butylated hydroxytoluene (BHT). BHT slows oxidation by trapping radical intermediates which are produced by the destruction of carbon–carbon double bonds by oxygen.

Partial Hydrogenation The preparation of oleomargarine (a butter substitute that contains a higher content of desirable polyunsaturated fatty acids and is more spreadable than butter) involves the **partial hydrogenation** of liquid vegetable oils, usually corn oil. The commercial hydrogenation process carried out by food manufacturers consists of heating the oil in the presence of hydrogen gas and metal, usually nickel, catalysts. Partial hydrogenation is used for two primary reasons:

1. It reduces the number of double bonds in the fatty acids and raises the oil's melting point. This changes the oil into a firm, but spreadable solid like "soft" stick and tub margarine or shortening.
2. Hydrogenation decreases the number of double bonds, reduces the rate of autooxidation, and therefore inhibits rancidity. Unsaturated fatty acids like linolenic acid ($18{:}3^{\Delta 9,12,15}$) and linoleic acid ($18{:}2^{\Delta 9,12}$) are especially vulnerable to reaction with oxygen.

"good") cholesterol (see Section 18.5). The quantitative, deleterious impact of trans fats is at least twice that of the "not-so-healthy" saturated fats.

After reviewing the mounting evidence against trans fats, the U.S. Food and Drug Administration (FDA) in 1999 recommended that it was good dietary practice to avoid the consumption of trans fats. At that time, however, few food processing companies listed separately the amount of trans fat present in a product. That number is usually included as part of the "saturated fat." Foods that often contain trans fat include french fries, donuts, cookies, crackers, "soft" margarines, and processed foods that list "partially hydrogenated vegetable oil" as an ingredient. The FDA has now ruled that as of January 1, 2006, food manufacturers must list the *trans* fat content separately from the total fat (saturated and unsaturated) content on the standard Nutrition Facts label. Some companies have voluntarily started this labeling program early (see figure).



(Reprinted with permission from Chem. Eng. News
© 2003 American Chemical Society.)

The partial hydrogenation process does, however, have a major drawback as some of the original cis carbon–carbon double bonds rearrange to trans double bonds during the chemical process (Figure 8.3). New medical research shows that the products, **trans fatty acids** or **trans fats**, have a strong influence on plasma cholesterol levels and are linked to an increase of coronary heart disease (see Window on Biochemistry 8-2).

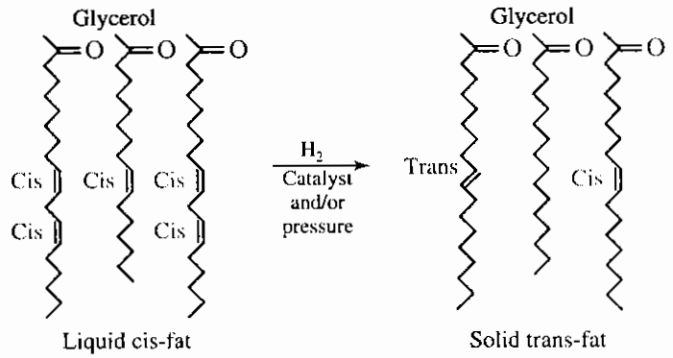


Figure 8.3 The commercial hydrogenation of vegetable oils often leads to trans fatty acids.

Biological Properties of Triacylglycerols

The triacylglycerols have two primary biological roles, energy metabolism and temperature insulation. They serve as the molecular form for storage of the important fuel molecules, fatty acids. (In comparison, the fuel molecule glucose is stored in the form of starch and glycogen in plants and animals, respectively). Triacylglycerols are present in oily droplets in the cytoplasm of plant and animal cells. **Adipocytes** are animal cells specialized for fat storage (Figure 8.4). Almost the entire volume of each cell is filled by a fat droplet. These cells serve as storage depots of metabolic fuel. Enzymes called **lipases** are present in adipocytes to catalyze the release of fatty acids. Triacylglycerols are also present below the skin layer of animals, especially those living in polar regions, to insulate against temperature extremes.

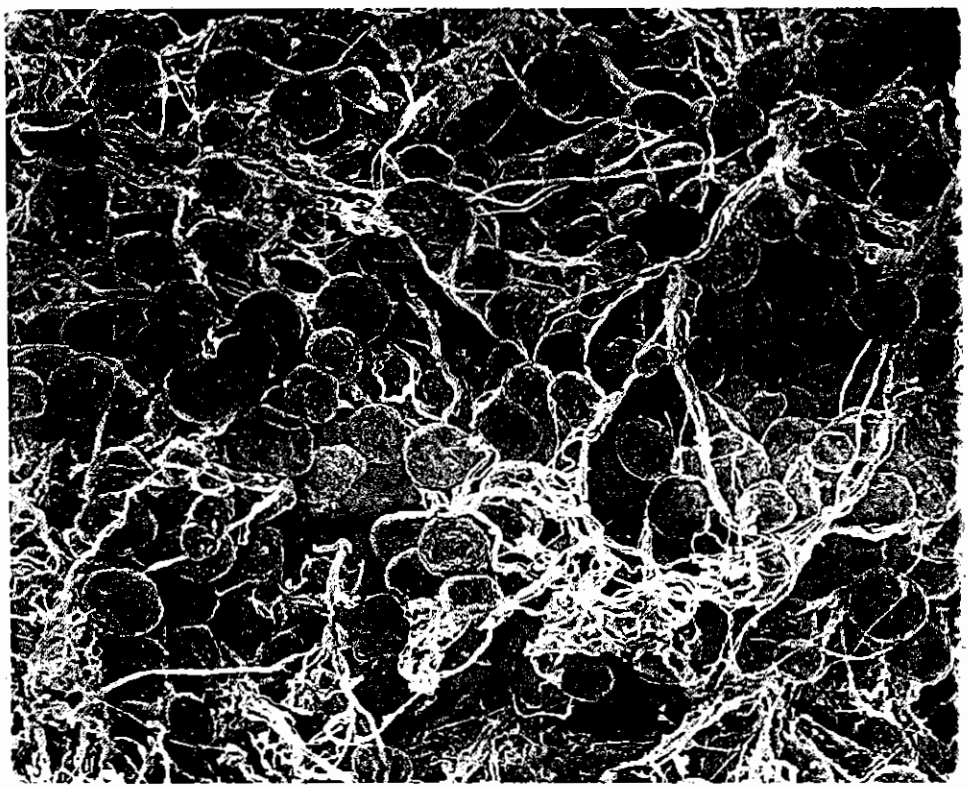


Figure 8.4 A scanning electron micrograph of adipocytes (*red*). Adipocytes are specialized fat storage cells. (© Fred E. Hossler/ Visuals Unlimited.)

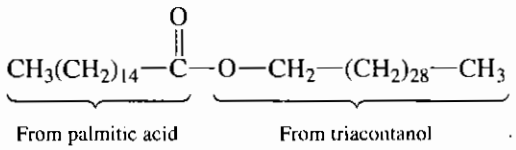


Figure 8.5 Beeswax, an important derivative of fatty acids, is a nonpolar lipid composed of palmitic acid in ester linkage to the alcohol triacontanol.

The fatty acids, in addition to being found in triacylglycerols, are also present in other derivative forms. Chemically related to the triacylglycerols are nonpolar lipids called **waxes**, which serve many biological roles such as protective coatings for plant leaves, lubrication of skin, and water repellency for the feathers of waterfowl. Representative of the waxes is beeswax, an ester composed of palmitic acid (16:0) and the alcohol triacontanol, a compound containing an unbranched saturated chain of 30 carbons (Figure 8.5).

8.3 Polar Lipids

Learning Objective

Recognize the chemical components, chemical properties, and biological function(s) of the polar lipids.

The nonpolar class of lipids, represented by the very hydrophobic triacylglycerols, serve as storage molecules for metabolic fuel. The **polar lipids** are a class of lipids that have some structural features that are similar to the nonpolar triacylglycerols; however, they also have some polar, even ionic, character that gives them quite different biological functions. The special functions of polar lipids are due to their **amphiphilic** nature: They have both nonpolar and polar structural features. The dual nature of the polar lipids allows them to combine with protein molecules for the construction of biological membranes, which provide a protective shield around cells and cellular organelles. The membrane forms a permeable barrier that selects some molecules for passage but not others. The polar lipids are found almost exclusively in membranes and are not stored in adipocytes as energy molecules like the triacylglycerols.

In this section, we discuss the chemical structures for the polar lipids and the properties that make them well suited for membrane construction. As a preview for this section, Figure 8.6 compares the structural features of nonpolar lipids (triacylglycerols) with polar lipids found in membranes. Two types of polar lipids are introduced: **glycerophospholipids** and **sphingolipids**. (The steroid cholesterol, also a lipid, is present in membranes; however, because of its very different chemical structure and additional biological properties, it is explored in a separate section.)

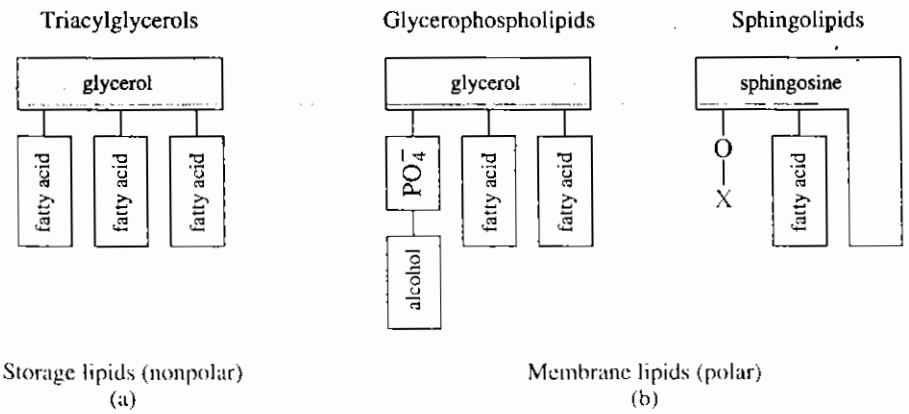


Figure 8.6 Structural features of storage and membrane lipids. (a) The storage lipids are composed of nonpolar triacylglycerols. (b) The membrane lipids are composed of the glycerophospholipids and sphingolipids, which have polar and nonpolar regions. Specific members of the polar lipid class that have various X substituents are shown in later figures.

Glycerophospholipids

The foundation molecule for the glycerophospholipids is **1,2-diacylglycerol-3-phosphate**, which has the generic name **phosphatidic acid** (Figure 8.7a). The fatty acids linked by ester bonds to the glycerol molecule are the same variety as found in triacylglycerols. Fatty acids with 16 and 18 carbons are most prevalent. Both saturated and unsaturated hydrocarbon chains are found; however, an analysis of many glycerophospholipids has uncovered a preference for saturated fatty acids at position 1 and for unsaturated fatty acids at position 2. (Note that the term "phosphatidic acid" actually refers to a group of many molecules that differ by the identity of the two fatty acids.)

The third hydroxyl group of glycerol is esterified by phosphoric acid. Because phosphoric acid is triprotic, it is able to react with up to three alcohol moieties to form mono-, di-, and triesters. In the glycerophospholipids, a second alcohol is esterified

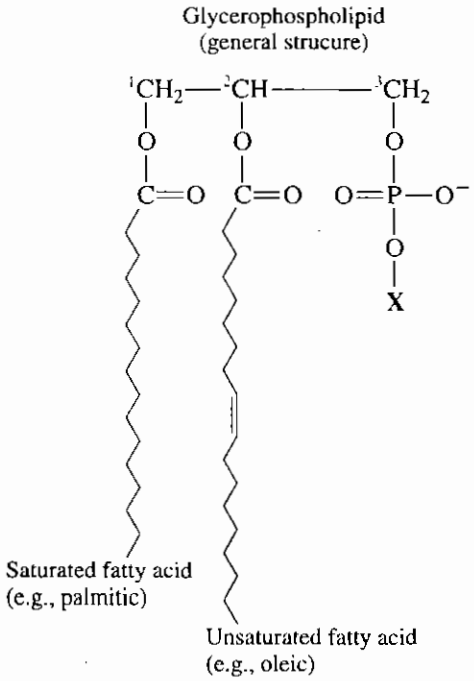
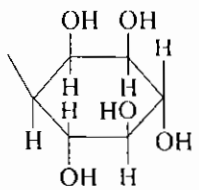


Figure 8.7 Phosphatidic acid is the foundation molecule for the glycerophospholipids. It contains two fatty acids in ester linkage to glycerol (at carbons 1 and 2) and a phosphate in ester linkage to glycerol (C3). The X moiety in (a) phosphatidic acid is H. A variety of saturated or unsaturated fatty acids may be present. The four major types of glycerophospholipids are (b) phosphatidylethanolamines, (c) phosphatidylcholines, (d) phosphatidylserines, and (e) phosphatidylinositols.

Name of X	Structure of X	Name of Glycerophospholipids
(a) Hydrogen	—H	Phosphatidic acid
(b) Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	Phosphatidylethanolamine
(c) Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	Phosphatidylcholine
(d) Serine	$-CH_2-CH(\overset{+}{N}H_3)-COO^-$	Phosphatidylserine
(e) Inositol		Phosphatidylinositol

with the phosphate group. That alcohol is usually one of the following: the amino alcohols **ethanolamine** or **choline**, the amino acid **serine**, or the polyhydroxy compound **inositol** (Figure 8.7b–e). The four resulting polar lipids are named by combining "phosphatidyl" with the alcohol name, for example, **phosphatidylethanolamine**. With the exception of inositol, all of the alcohols have an amino or other functional group that becomes ionic at physiological pH. Except for phosphatidylethanolamine and phosphatidylcholine, all of the glycerophospholipids are electrically charged at cellular pH. We should by now see a major structural difference when comparing triacylglycerols and glycerophospholipids. Triacylglycerols are nonpolar and hydrophobic. The glycerophospholipids, on the other hand, have highly polar and sometimes electrically charged regions on the molecule in addition to nonpolar regions. Therefore, we can distinguish two structural features in the glycerophospholipids: a polar head and nonpolar tails. These characteristics are essential for membrane structure.

Sphingolipids

A second group of polar lipids found in membranes are the **sphingolipids**. This major class of lipids is represented by three subclasses: **ceramides**, **sphingomyelins**, and **glycosphingolipids**. Here the foundation molecule is the 18-carbon amino alcohol **sphingosine** (Figure 8.8a), rather than the simple glycerol molecule. Sphingosine has two functional groups (amino and hydroxyl) that can be chemically modified to make a variety of sphingolipids.

The amino group at C2 of sphingosine may be linked via an amide bond with a fatty acid. The resulting molecule is called a ceramide and has a polar head (hydroxyl group on C1 of sphingosine) and two nonpolar tails (Figure 8.8b). Another class of sphingolipids uses the amino and hydroxyl groups to link additional units. The **sphingomyelins**, the only phosphorus-containing sphingolipids, contain a fatty acid on the amino group (like the ceramides) and a phosphocholine unit esterified with the hydroxyl group (see Figures 8.6b and 8.8c). This results in a molecule with a polar (in fact, ionic) head and two nonpolar tails similar to the glycerophospholipids. Although the sphingomyelins are found in plasma membranes, they are probably best known and named for their presence in the myelin sheath, where they insulate nerve axons.

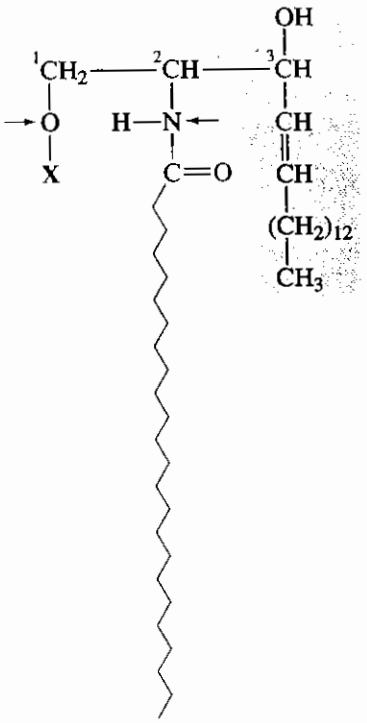
A third subclass of the sphingolipids is represented by the **glycosphingolipids**. These carbohydrate-containing lipids use the ceramides as foundation molecules. The **cerebrosides** consist of ceramide with a monosaccharide unit in glycosidic linkage at the hydroxyl group at C1 of sphingosine (Figure 8.8d). The carbohydrates commonly found are glucose, galactose, and *N*-acetylgalactosamine (see Section 7.3). Cerebrosides, as the name implies, are abundant in the membranes of the brain and nervous system. The most complex sugar-containing lipids are the **gangliosides**, which contain a polar head composed of several carbohydrate units linked by glycosidic bonds (Figure 8.8e). Like the cerebrosides, these are abundant in brain and nerve membranes. In addition to their role in biological membrane structure, the glycosphingolipids are also involved in other specialized cellular functions, including recognition events at cell surfaces (see Section 7.5 on glycoproteins), tissue specificity of cell association, and transmission of nerve impulses. These important functions explain some of the major medical and clinical consequences of improper metabolism of the glycosphingolipids. In **Tay-Sachs disease**, for example, a specific ganglioside accumulates in the brain and spleen because the enzyme that is responsible for its degradation is lacking. This genetic disease results in slow development, paralysis, blindness, and, finally, death by the age of 3 to 4 years.

Polar Lipids and Membranes

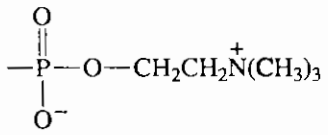
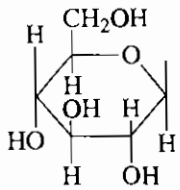
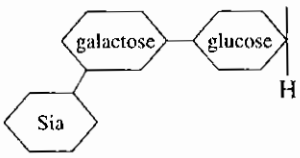
We have observed a variety of chemical structures for the polar lipids we call glycerophospholipids and sphingolipids. In spite of chemical differences, these molecules serve a similar biological role as structural units in membranes. Their similar features,

Figure 8.8 The foundation molecule for the sphingolipids is sphingosine, which is derivatized at the amino group on C2 with a fatty acid and at the hydroxyl group on C1 with an X substituent. (a) The arrows point to the amino and hydroxyl groups of sphingosine that are derivatized to make sphingolipids. The four major types of sphingolipids are (b) ceramides, (c) sphingomyelins, (d) cerebrosides, and (e) gangliosides. Sia = *N*-acetylneuraminic acid (sialic acid).

Sphingolipid
(general structure)



(a)

Name of **X**	Structure of **X**	Name of Sphingolipid
(b) Hydrogen	—H	Ceramide
(c) Phosphocholine		Sphingomyelin
(d) Glucose		Glucosylcerebroside
(e) Complex oligosaccharide		Ganglioside

a polar region and a nonpolar region, endow them with their common biological ch
acteristic. We have observed that salts of fatty acids with a polar (ionic) head an
single nonpolar tail assemble spontaneously into spherical structures called **micell**
The polar lipids represented by the glycerophospholipids and sphingolipids each h
a polar (and sometimes ionic) head and *two* hydrophobic tails. Because of the ex
space taken by the nonpolar tails, these lipids are unable to assemble into micell

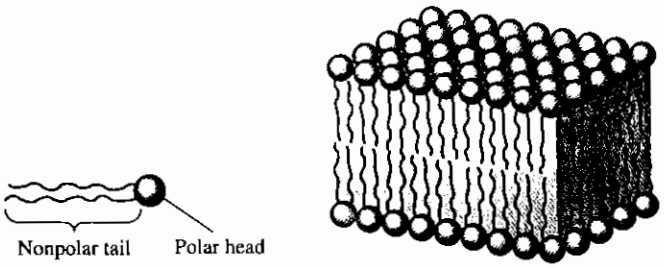


Figure 8.9 Assembly of polar lipids with ionic heads and nonpolar tails into bilayer sheets. The nonpolar tails cluster in the interior of the bilayer. Hydrophobic interactions provide stabilizing energy to hold the bilayer together.

Instead, they form **bilayers**, composed of two monolayers or sheets of polar lipids (Figure 8.9). The nonpolar side of each sheet combines by hydrophobic interactions to exclude water in the central region of the bilayer. The bilayer provides a structural framework for membrane assembly.

8.4 Steroids and Other Lipids

Learning Objective
Know the chemical structures and understand the biological properties of the steroids and other lipids.

The two large classes of lipids previously covered, the triacylglycerols and the polar lipids, perform functions in energy storage and biological membrane construction, respectively. A lipid extraction of cells and tissues contains many more lipid classes in addition to these two. In this section a potpourri of lipids and their functions are explored.

Steroids

Animal Steroids—Cholesterol One of the most well known and best studied of the lipid groups is the **steroid** class. The steroids all have the characteristic fused-ring system of three six-membered rings labeled A, B, and C and one five-membered ring called the D ring (Figure 8.10a). Ketones, alcohols, double bonds, and hydrocarbon chains decorate the ring system in various types of steroids. **Cholesterol**, the best known steroid, has a hydroxyl group on the A ring, a double bond in ring B, and hydrocarbon chains attached at several locations (Figure 8.10b). Although the chemical

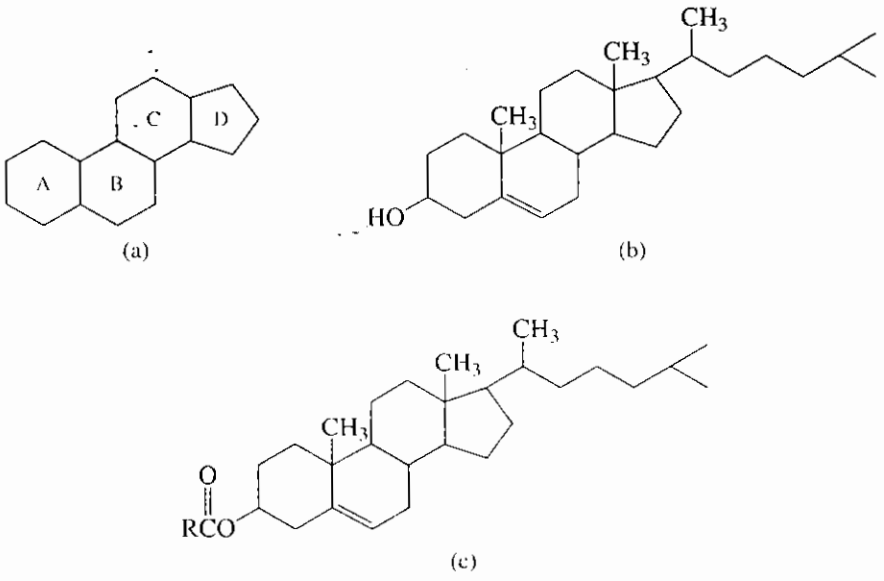


Figure 8.10 (a) The molecular structure common to all steroids showing the four fused rings, A, B, C, and D. (b) Cholesterol has a polar head (hydroxyl group) and a nonpolar tail (hydrocarbon skeleton). (c) A cholesteryl ester formed between the cholesterol hydroxyl group and a fatty acid with a long aliphatic side chain, R.

structure is quite different from lipids previously studied, the cholesterol molecule is amphiphilic with a polar head (the —OH group) and an extensive nonpolar region (the fused rings and hydrocarbon tails). Indeed, cholesterol and some of its derivatives accompany the glycerophospholipids and sphingolipids in biological membranes. The most chemically reactive portion of the cholesterol structure is the hydroxyl group. Under physiological conditions, it is common for a fatty acid to be esterified at this position (Figure 8.10c).

Cholesterol and its ester derivatives are abundant in plasma proteins called **lipoproteins** whose function is to transport the cholesterol to peripheral tissue for use in construction of membranes and as a biosynthetic precursor for steroid hormones and other biologically active products. We discuss the roles of cholesterol and lipoproteins in the development of **atherosclerosis** in Chapter 18. The cholesterol molecule, which is found almost exclusively in animal tissue, is derived from units of five carbons called **isoprene** (2-methyl-1,3-butadiene, Figure 8.11a). Multiples of these C_5 building blocks are combined to make compounds with 10, 15, and eventually 30 carbons to synthesize the characteristic fused-ring system of the steroids. Cholesterol is the starting point for biosynthesis of the steroid hormones and the bile acids. Several steroid hormones, including estradiol (female sex hormone), testosterone (male sex hormone), and cortisol (glucose metabolism regulator), are pictured in Figure 8.11b–d. Enzyme-catalyzed oxidation reactions on the cholesterol ring system lead to the bile acids (Figure 8.11e,f). Two important bile acids in humans are **cholic acid** and its glycine derivative, **glycocholic acid**. Note that these compounds have acidic functional groups with protons that dissociate at physiological pH to produce ionic structures called **bile salts**. The bile salts are stored in the gallbladder and secreted into the intestines to help solubilize, digest, and absorb dietary fats.

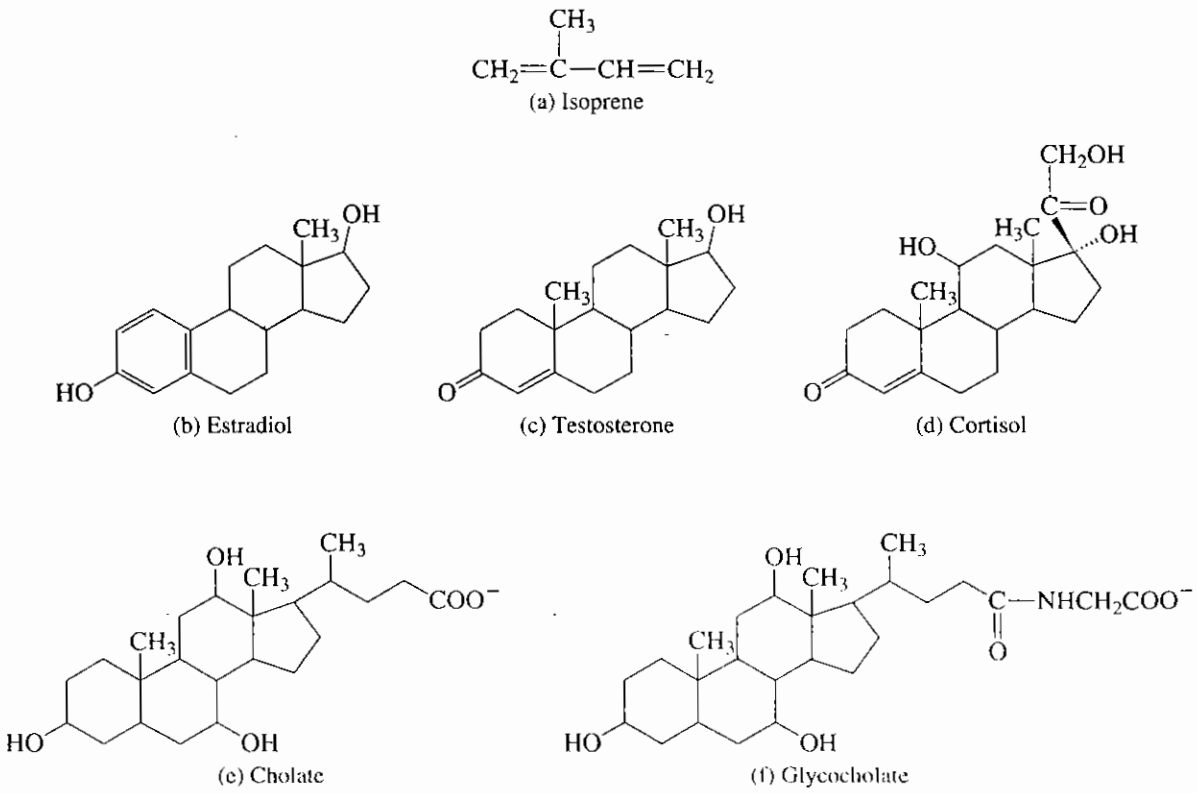


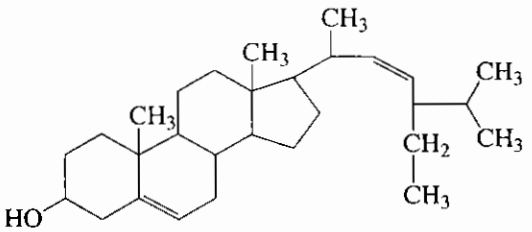
Figure 8.11 Structures of the isoprene unit and bioactive products produced from cholesterol: (a) isoprene, or 2-methyl-1,3-butadiene, a building block for the steroid ring system and for other terpenes; (b) estradiol, a female sex hormone; (c) testosterone, a male sex hormone; (d) cortisol, a regulator of glucose metabolism; (e) cholate, a bile salt derived from cholic acid; and (f) glycocholate, a bile salt derived from glycocholic acid.

Before You Go On...

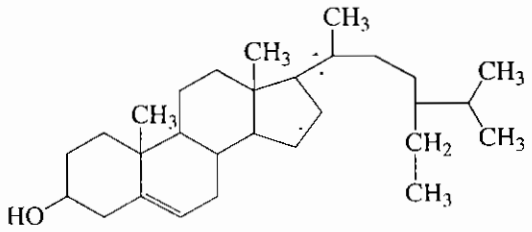
1. Under physiological conditions, the hydroxyl functional group of the cholesterol molecule is often esterified with a fatty acid. These derivatives are called cholesteryl esters. Draw the structure of the ester formed between cholesterol and palmitic acid. (***Hint:*** See Figure 8.10c.)
2. Review the structures of the bile salts cholate and glycocholate (Figure 8.11) and explain how they function to help solubilize dietary fats.

Phytosterols At one time, steroids were thought to be present only in animals; however, sterols with structures similar to cholesterol have been isolated from plants. The plant steroids are derived from isoprenes, just like cholesterol (Section 18.4), and they are essential constituents in plant membrane structure.

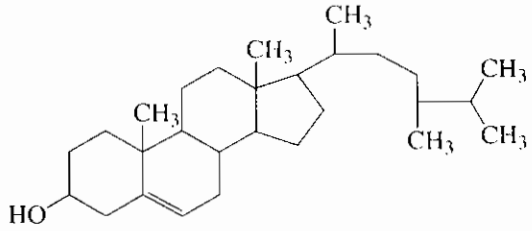
Three major **phytosterols** have been identified: **stigmasterol**, **β-sitosterol**, and **campesterol** (Figure 8.12). They differ from cholesterol in the placement of methyl and ethyl groups and in unsaturation on the side chain. The phytosterols are especially abundant in corn oil, rice bran, wheat germ, soybeans, and other vegetables. These foods are often referred to as "nutraceuticals" or "functional foods" because they contain ingredients that may provide a health benefit beyond the traditional nutrients present. For example, the phytosterols have significant health benefits and have received therapeutic use in Europe for years. Medical studies prove that the phytosterols decrease the level of LDL cholesterol in the blood. A daily serving (about 3 tablespoons; 4–5 g of phytosterol) of the specialized margarines Benecol and Take Control causes a 10–15% decrease in serum cholesterol after a few months of use.



Stigmasterol



β-Sitosterol



Campesterol

Figure 8.12 Major steroid components of plant membranes.

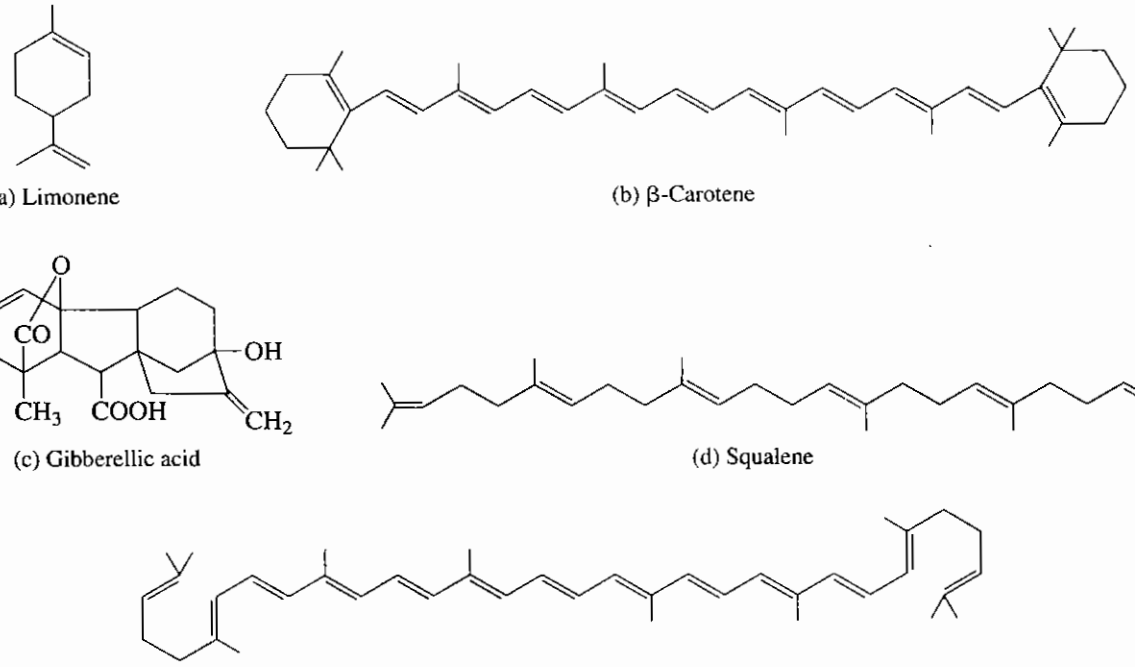


Figure 8.13 Important terpenes found in plants and animals: (a) limonene, found in citrus fruits, where it provides the distinct odor; (b) β-carotene, the source of the orange color in carrots (the precursor of vitamin A); (c) gibberellic acid, a plant growth hormone; (d) squalene, an intermediate in cholesterol synthesis; and (e) lycopene, the red pigment of tomatoes.

β-Sitosterol is also known to benefit sufferers of benign prostatic hyperplasia (BPH, enlarged prostate). Recent research has also provided evidence that β-sitosterol may inhibit the growth of human prostate cancer cells. For further information on the therapeutic use of phytosterols, see Window on Biochemistry 18-2.

Terpenes

The lipid class of **terpenes** includes all molecules biosynthesized from the isoprenes. (According to this definition, cholesterol and its derivatives are also in this class.) Important terpenes in plants and animals include **limonene**, **β-carotene**, **gibberellic acid**, **squalene**, and **lycopene** (Figure 8.13). Many of these compounds provide the colors and odors associated with plants. Squalene is an intermediate in the biosynthesis of plant and animal steroids (see Section 18.4).

Eicosanoids

The **eicosanoids** are a class of lipids characterized by their localized, short-lived hormone-like activities (they often act for only a few seconds) and very low cellular concentrations. Better known hormones, such as adrenaline and insulin, are synthesized in endocrine glands, and transported, via the blood, to target cells throughout the body, where they influence cellular metabolism by binding to protein receptors in the plasma membrane and relaying a message to the cell's interior by the process of signal transduction (Special Topic I). In contrast, the eicosanoids act in their local environment—the cells in which they are produced; however, their actions are initiated also by signal transduction like the traditional hormones. The list of biological functions and activities associated with the eicosanoids is long and diverse (Table 8.4). The initial discovery and many subsequent studies of eicosanoid action were carried out by Ulf von Euler, Sune Bergstrom, and Bengt Samuelsson, three Swedish biochemists.

Table 8.4
Biological Activities of the Eicosanoids

1. Initiate the inflammatory response, pain, and fever associated with injury (cuts, scrapes, blisters, etc.) and diseases (osteoarthritis and rheumatoid arthritis).
2. Promote the blood clotting process (platelet aggregation) and regulate blood pressure (some prostaglandins are vasodilators).
3. Control of some reproductive functions, for example, inducing labor, and a possible role in male infertility.
4. Regulate temperature and the sleep/wake cycle in animals.
5. Promote smooth muscle contraction.

There are three subclasses of eicosanoids: **prostaglandins**, **thromboxanes**, and **leukotrienes**. All three classes are derived from the 20-carbon, polyunsaturated arachidonic acid ($20{:}4^{\Delta 5,8,11,14}$), but each type has a unique chemical structure (Figure 8.14). The prostaglandins, which were first isolated from the prostate gland, contain a five-membered ring substituted with two side chains and functional groups, including a carboxylic acid, hydroxyl groups, ketones, and carbon–carbon double bonds.

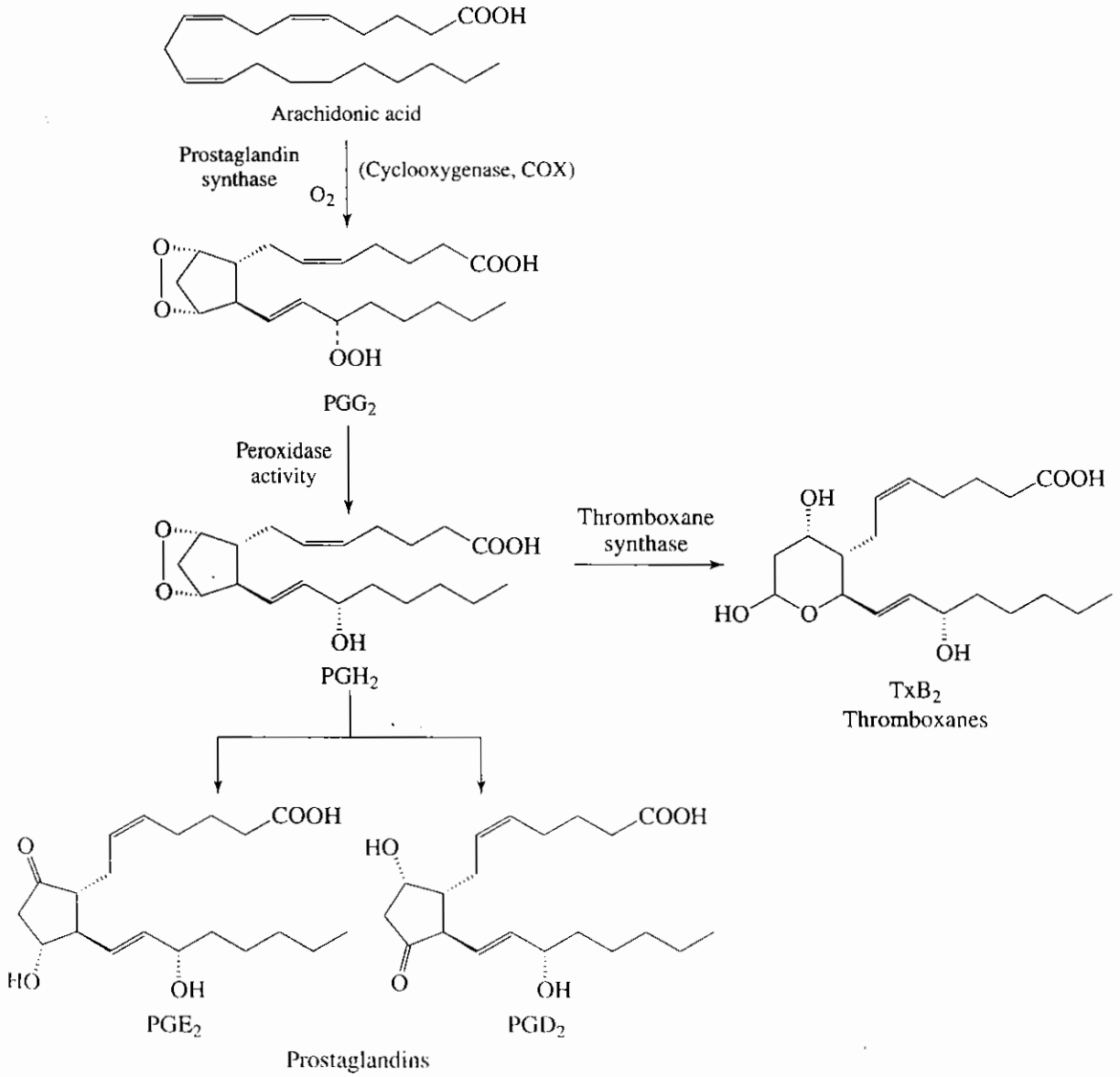


Figure 8.14 Synthesis of prostaglandins and thromboxanes from arachidonic acid via the cyclic pathway.

Eicosanoids: are paracrine hormones; substances that act only on site cells near the point of synthesis instead of being transported in the blood to act on other cells or tissues.
Eicosanoids are derived from membrane lipids and mainly from Arachodonic acid
[20:4($\Delta^{5,8,11,14}$]

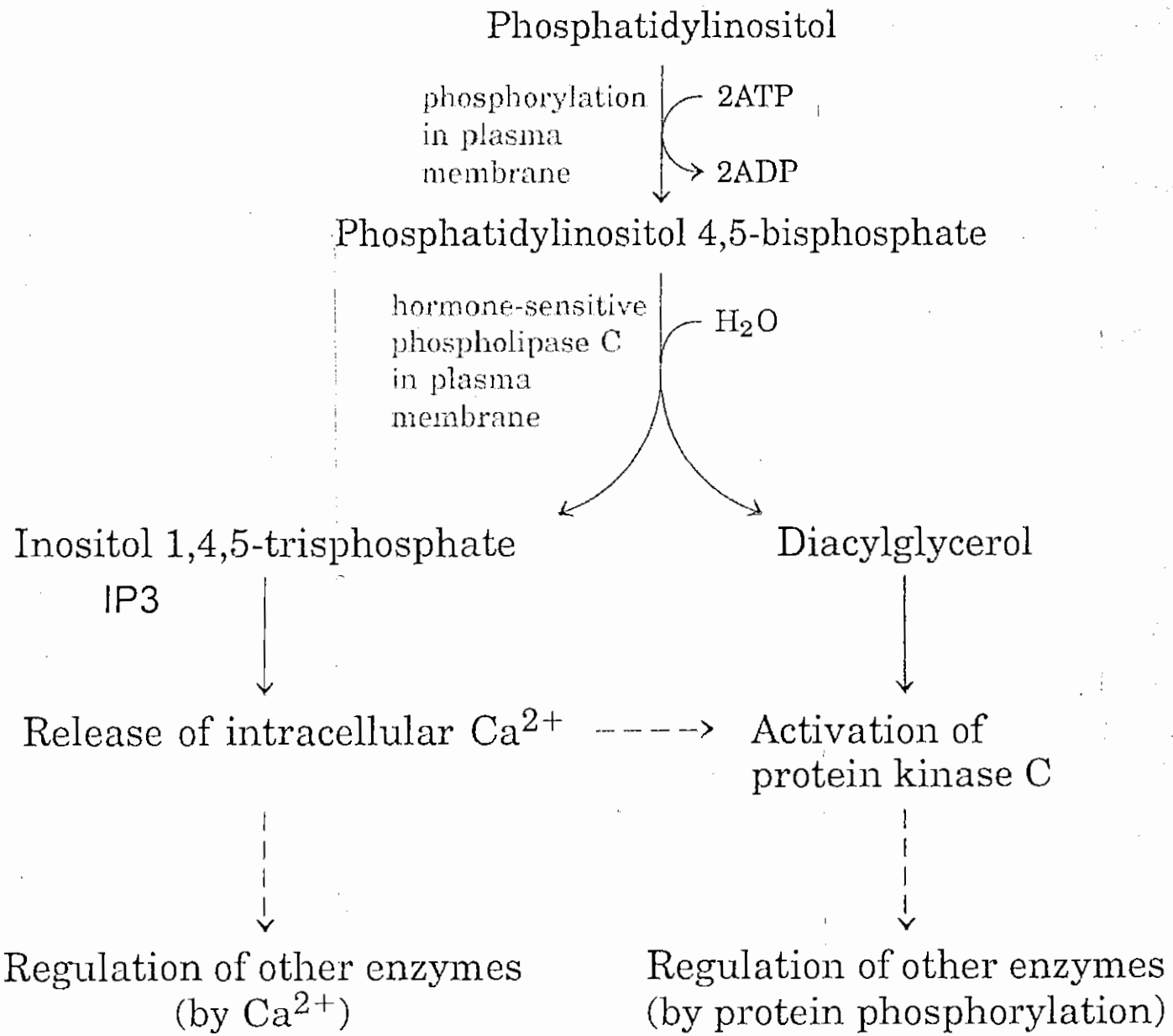
1- Prostaglandins

•C20 compounds
• Five carbon ring
• affect a wide range of cellular and tissue function
•Act at low concentration and are involved in the production of pain and fever, regulation of blood pressure, blood coagulation and reproduction
•Produced and used locally
• Regulate the synthesis of the intracellular messenger (cAMP) which mediate the action of different hormones.
-Stimulate the contraction of smooth muscle in uterus
-Affect the blood flow
-Elevate the body temperature and mediate the inflammation and pain

2- Thromboxanes:

Six-memebred ring containing an ether, produced by the platelets (thrombocytes) and play role in formation of the blood clots

3- Leukotriens: contain conjugated double bonds, found in the leukocytes, powerful biological signals, induce contraction of muscles lining the airways of the lung. Over production cause asthmatic attack


Phosphatidylinositol
phosphorylation in plasma membrane
2ATP
2ADP
Phosphatidylinositol 4,5-bisphosphate
hormone-sensitive phospholipase C in plasma membrane
H_2O
Inositol 1,4,5-trisphosphate
IP3
Diacylglycerol
Release of intracellular Ca^{2+}
Activation of protein kinase C
Regulation of other enzymes (by Ca^{2+})
Regulation of other enzymes (by protein phosphorylation)

The eicosanoids are produced in virtually all mammalian tissues and organs. Prostaglandins and thromboxanes are synthesized by the **cyclic pathway** of arachidonic acid metabolism (Figure 8.14), whereas the leukotrienes are produced by the **linear pathway** of arachidonic acid metabolism. The cyclic pathway begins with the reaction of arachidonic acid with oxygen, catalyzed by **prostaglandin synthase**, an enzyme with two catalytic activities, oxygenase and peroxidase. The enzyme is also called **cyclooxygenase (COX)** because it forms the five-membered cyclic structure. The first important intermediate, prostaglandin H_2 (PGH_2), is the precursor for other prostaglandins and for the thromboxanes. Each tissue type has its own set of eicosanoids. The compounds PGE_2 and PGD_2 (Figure 8.14) have been discovered in the brains of mammals, including humans. These two prostaglandins are especially concentrated in the preoptic area, the sleep center of the brain. Experiments in rats, monkeys, and humans show that PGD_2 promotes physiological sleep and PGE_2 induces wakefulness.

The COX Enzymes Several isoenzymatic forms of COX have been identified in humans and other animals. **COX-1**, a constitutive enzyme, is expressed in most tissues at all times. It is probably needed for cell maintenance and has general housekeeping duties, especially in the stomach and gastrointestinal (GI) tract.

COX-2 is an induced enzyme synthesized in response to inflammatory stimuli such as injury or disease. The induction of COX-2 leads to elevated levels of the prostaglandins that cause the pain and swelling associated with the inflammatory response. Some relief from the pain may be achieved by taking aspirin, which is an analgesic (painkiller), antipyretic (fever reducer), and anti-inflammatory agent. The common, over-the-counter **nonsteroidal anti-inflammatory drugs (NSAIDs)** such as aspirin, ibuprofen, naproxen, and indomethacin (Figure 8.15a) act by inhibiting both COX-1 and COX-2, thus reducing the production of prostaglandins (Figure 8.14).

However, the NSAIDs have undesirable side effects such as gastric ulceration and other problems including stomach bleeding. COX inhibitors are now better designed and more selective for COX-2. Three painkilling drugs that act by inhibiting COX-2 but not COX-1 have been approved by the FDA: Bextra, Celebrex, and Vioxx (Figure 8.15b). The COX-2 inhibitors have been prescribed to millions of patients since the mid 1990s for the treatment of rheumatoid arthritis, osteoarthritis, and acute pain without the side effects of the nonspecific NSAIDs. All three drugs are now under close scrutiny by the FDA because recent studies have shown that the drugs may increase the risk of heart attack and stroke.

Epidemiological studies on COX-1 and COX-2 inhibitors have provided surprise evidence that the drugs may prevent other diseases including some cancers and Alzheimer's disease. The induced COX-2 has been found to be overexpressed in some cancer cells compared to normal tissue. This leads to the overproduction of prostaglandins that are known to promote tumorigenesis and cell proliferation. Good, preliminary clinical results have been found in the treatment of colorectal cancer by the COX inhibitors. There is also some evidence that damage in the brains of Alzheimer's patients is due to an inflammatory process, which has encouraged the study of COX inhibitors for treatment of the disease. A clinical trial testing the prevention of Alzheimer's disease by Celebrex and naproxen (Aleve) has been suspended because of an increased incidence of heart attacks and strokes.

A third isoenzyme, **COX-3**, was reported in 2002. This enzyme seems to be the site of the inhibitory action of **acetaminophen**, the widely used analgesic and antipyretic. Acetaminophen inhibits neither COX-1 nor COX-2, so it displays no measurable anti-inflammatory action.

Thromboxanes and Leukotrienes The **thromboxanes**, also derived from the cyclic arachidonate pathway, are characterized by a six-membered ring containing oxygen (Figure 8.14). The thromboxanes were first isolated from blood platelets (thrombocytes), where they are thought to facilitate the formation of blood clots. The action

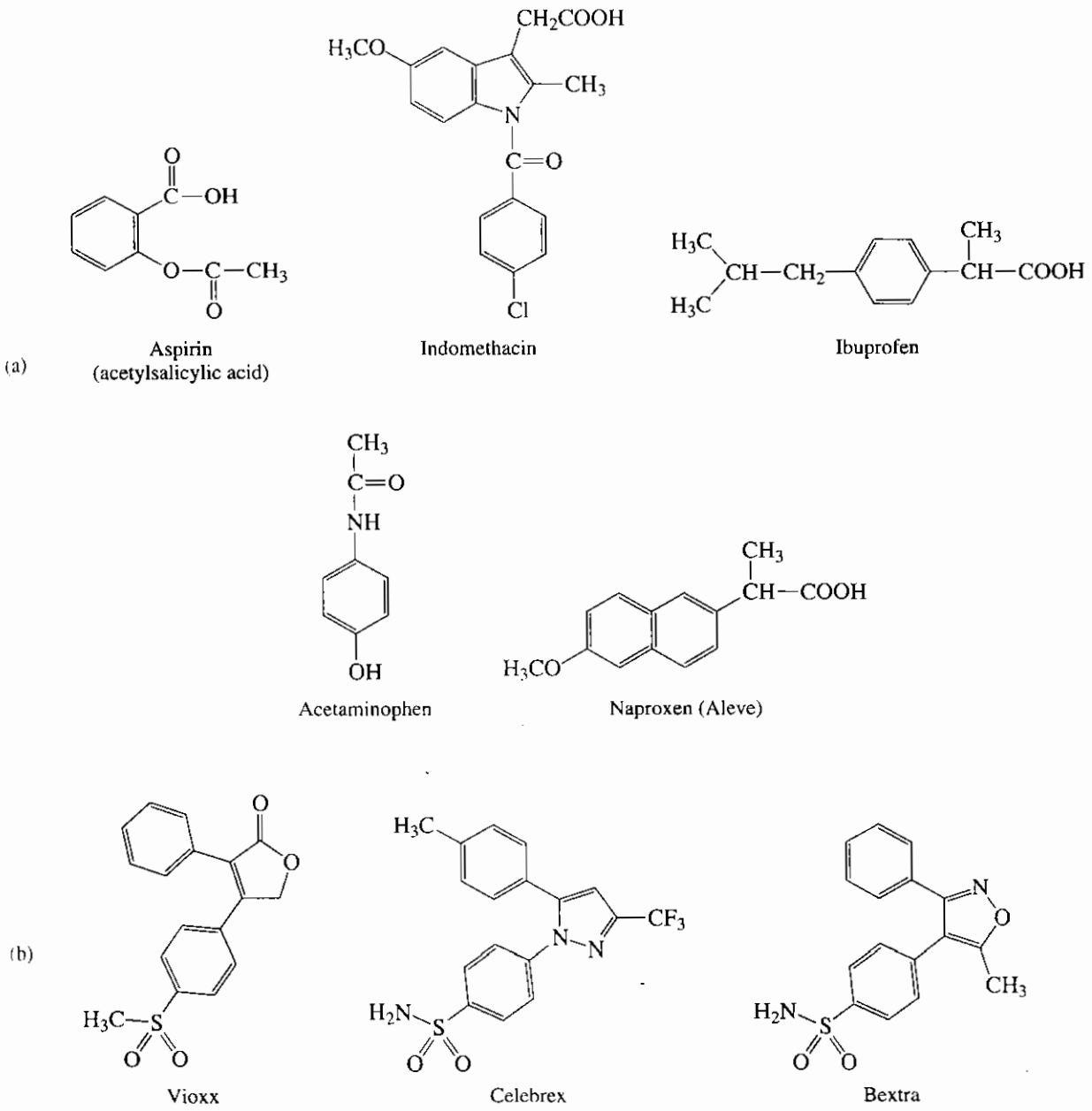


Figure 8.15 Painkilling drugs. (a) Some nonsteroidal anti-inflammatory drugs (NSAIDs). These drugs relieve pain by inhibiting COX-1 and COX-2 (except for acetaminophen, which inhibits COX-3). (b) Anti-inflammatory drugs that act as COX-2 inhibitors. (© 2004 D. Voet and J.G. Voet. Biochemistry, Third Ed.)

of aspirin in blood thinning and preventing heart attacks and strokes may be caused in part by inhibition of COX and thus lowering of the concentration of thromboxanes and prostaglandins.

The **leukotrienes** are produced by the arachidonic pathway shown in Figure 8.16. This biosynthetic route is initiated by enzymes called **lipoxygenases** which catalyze oxygenation (but not cyclization) of arachidonic acid. The leukotrienes are named after white blood cells (leukocytes), from which they were first extracted. The structural characteristics that separate leukotrienes from other eicosanoids are the linear chain (no rings) and the presence of three conjugated double bonds. The leukotrienes cause the contraction of smooth muscle, especially in the lungs. Asthmatic attacks and allergic reactions may be caused by overproduction of leukotrienes.

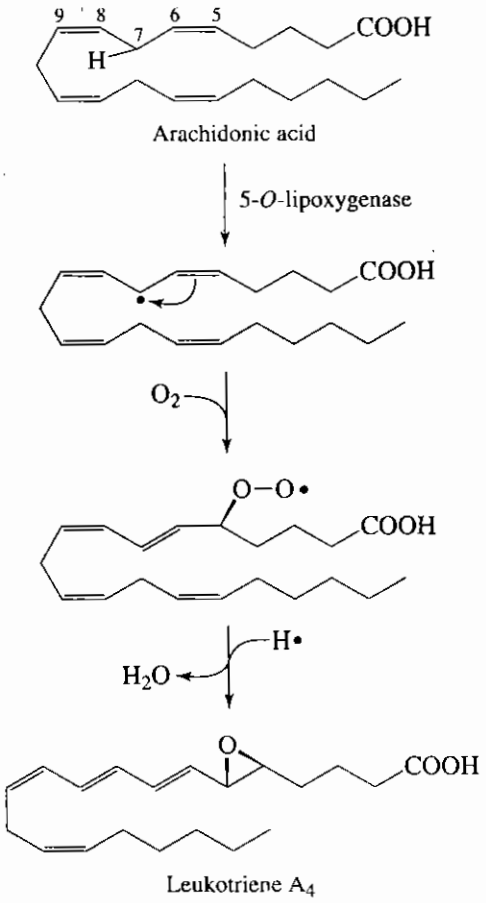


Figure 8.16 Synthesis of leukotrienes from arachidonic acid via the linear pathway. (© 2004 D. Voet and J.G. Voet. Biochemistry, Third Ed.)

Lipid-Soluble Vitamins

In Section 6.1, we identified two classes of vitamins, those that are water soluble and those that are fat soluble. Here we only briefly mention the biological properties of the fat-soluble vitamins and wait until later chapters to study their roles in nutrition and metabolism. This lipid-soluble group of vitamins can be classified as terpenes (derived from isoprenes), but because of their importance in human health they are usually considered a separate category of lipids. The most important compounds to consider here are vitamins A, D, E, and K. Table 8.5 provides the names, chemical characteristics, and the most significant biological functions for the fat-soluble vitamins.

Table 8.5
Common fat-soluble vitamins and their biological functions

Vitamin	Common Name	Chemical Characteristics	Biological Function
A	Retinol	A terpene with 20 carbons	Absorption of light in vision
D	Several forms; one is D_3 (cholecalciferol)	Formed from cholesterol by ultraviolet radiation	Regulation of calcium and phosphorus metabolism
E	α-Tocopherol	Aromatic ring with long hydrocarbon chain	Antioxidant; prevents oxidation damage to cellular membranes
K	Vitamin K	Bicyclic ring system with long hydrocarbon chain	Regulates blood clotting; bone formation

Pheromones

Some organisms release chemical signals into the environment that alter the behavior of members of the same species or of organisms they interact with. Most often the behavior is linked to sexual attraction, but it may also involve trail markings and defense alarms (natural repellants). These hormone-like signaling substances are called **pheromones**. Although all organisms, including humans, may release and respond to pheromones, the most studied are those from insects. The compound **muscalure**, which is a long-chain hydrocarbon (Figure 8.17a), is secreted by the common female housefly to attract a male partner. The sex attractant used by a honeybee queen in her nuptial flight is **9-ketodecenoic acid** (Figure 8.17b).

Plants also use chemical signal molecules to communicate with one another, with themselves, and with other species. Plant pheromones, which are usually released from leaves, flowers, and fruit, play important roles in plant development and survival. Three types of plant-to-plant communication have been identified:

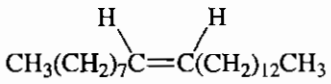
- **intraspecific**, or interactions with plants of the same species
- **interspecific**, or interactions with plants of other species
- **autosignaling**, or a plant communicating with itself

A bean plant infested with spider mites illustrates an example of such interactions. The infested plant releases volatile organic compounds (mite repellants) that cover leaves of the same plant and also spread to other bean plants in the same area.

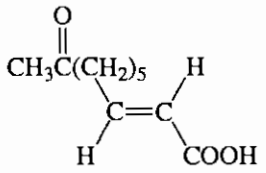
Some of the most common plant chemical signaling molecules include ethylene (Figure 8.17c), methyl salicylate (Figure 8.17d), and methyl jasmonate (Figure 8.17e). **Ethylene** acts to control the growth of tobacco plants by slowing the spread of plants that overgrow a neighboring tobacco plant. **Methyl salicylate** (the major odorous

The female gypsy moth secretes chemicals called pheromones to attract a male. (© Gary Meszaros/ Visuals Unlimited.)

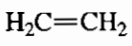
Figure 8.17 The molecular structures for insect and plant pheromones: (a) muscalure (housefly); (b) 9-keto-*trans*-2-decenoic acid (honeybees); (c) ethylene, (d) methyl salicylate; and (e) methyl jasmonate.



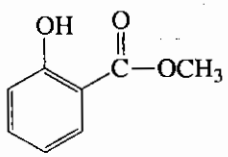
(a) Muscalure



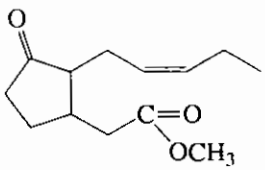
(b) 9-Keto-*trans*-2-decenoic acid



(c) Ethylene



(d) Methyl salicylate



(e) Methyl jasmonate

Electron Carriers

The final group of lipids to be considered here are those that serve as electron carriers for the oxidation–reduction reactions of energy metabolism. **Ubiquinone (coenzyme Q)**, a primary component of the mitochondrial electron transport chain in animals, is named for its ubiquitous presence in cells. **Plastoquinone**, a compound in plant chloroplasts, serves as an electron carrier for the production of adenosine triphosphate (ATP) generated by light absorption (photosynthesis). **Menaquinone** is the primary electron carrier of bacteria. All these compounds function as redox cofactors, cycling between oxidized and reduced states as they shuttle electrons from one biomolecule to another (see Chapter 18).

(Age fotostock/SUPERSTOCK.)

Because of the very positive effects of dietary fish oils, the American Heart Association now recommends that individuals without heart disease eat fish two or more times per week (provides about 1–1.5 g EPA and DHA) or take fish oil, at least 300–500 mg of EPA plus DHA in capsule form daily. It is suggested that heart patients with high levels of LDL cholesterol and triacylglycerols in the blood should take about 1 g of fish oil daily. Individuals should always consult their family physician before beginning any therapeutic treatment and be under the care of their physician during this period. Recommendations on dietary fish from the U.S. Food and Drug Administration and the American Heart Association come with at least two cautionary statements: (1) Daily intake of fish oil above 3 g may cause bleeding, and (2) some types of fish may contain high levels of mercury. Pregnant women and women who might become pregnant should avoid eating shark, swordfish, king mackerel, or other fish that may be contaminated with mercury.

Study Questions

1. Draw structures for the following fatty acids.
   a. EPA **b.** DHA
2. Part of mercury's toxic effects are due to reaction with a particular amino acid residue in proteins. Name the amino acid residue and show the reaction using Hg^{+}.
3. Would you expect to find the two fatty acids EPA and DHA in meat from pigs that have been fed a diet consisting only of corn? (***Hint:*** See Table 8.3.)

References

Dalton, L., 2004. Methylmercury toxicology probed. *Chem. Eng. News* Jan. 19:70–71.

Din, J., Newby, D., and Flapan, A., 2004. Omega 3 fatty acids and cardiovascular disease—fishing for a natural treatment. *Br. Med. J.* 328.30–35.

Kris-Etherton, P., Harris, W., and Appell, L., 2002. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 106:2747. *http://www.circulationaha.org*