

# Lipids

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Lipids, widely distributed in animals and plants, comprise a heterogeneous group of substances which share the common characteristic of having little or no solubility in water, but good solubility in nonpolar substances (a substance is soluble in solvents of similar nature; polar substances dissolve in polar solvents, nonpolar substances in nonpolar solvents). Different from polypeptides or polysaccharides, lipids do not form macromolecular polymers and do not have high molecular mass.

The study of lipids is important because (1) lipids are essential components of living beings, constituting a fundamental part of cell membranes; (2) they are the main energy reserve (neutral fats) in animals; (3) they are of essential nutritional value because lipids have a high-caloric content, they transport fat-soluble vitamins, and supply indispensable compounds [essential fatty acids (FAs)] that humans cannot synthesize; and (4) they comprise a number of substances of critical physiological activity, including hormones, certain vitamins, and bile acids.

## CLASSIFICATION

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According to the complexity of the molecule, lipids can be classified into two different types: *simple* and *complex*. In addition, there are other substances associated with lipids that share

their solubility properties. Simple lipids include acylglycerols and waxes, while complex lipids include phospholipids, glycolipids, and lipoproteins. Among the compounds associated with lipids are sterols, terpenes, and vitamins that are soluble in organic solvents.

Lipid molecules contain monocarboxylic organic acids, normally referred to as FAs. Due to their biological relevance, they will be discussed first.

## FATTY ACIDS

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The FAs isolated from animal lipids are monocarboxylic and have a linear chain. Only very few of them are free; the vast majority form part of simple or complex lipids. FAs with a cyclic structure are only found in lipids from some microorganisms and seeds. FAs with branched chains are present in waxes. Animal lipids have, in general, an even number of carbon atoms (between 4 and 26 carbon atoms) and only very few FAs with an uneven number of carbon atoms have been isolated. The number of carbon atoms in a FA chain depends on the manner in which they are synthesized or degraded in animals, which is achieved through addition or subtraction of two carbon atoms at a time. FAs can be saturated, with the general chemical formula  $\text{CH}_3-(\text{CH}_2)_n-\text{COOH}$ , or unsaturated, with

double bonds in the hydrocarbon chain. The unsaturated FAs can have one or multiple double bonds. When FAs have more than one double bond, generally they are not conjugated:  $\text{—CH=CH—CH=CH—}$ , but instead

separated by a methylene group ( $\text{—CH}_2\text{—}$ ):  $\text{—CH=CH—CH}_2\text{—CH=CH—}$ . In animals, the most common FAs have 16–18 carbon atoms. FAs with even carbon number linear chain are listed in [Table 5.1](#).

**TABLE 5.1** Fatty Acids (FAs) Common in Nature

Trivial name	No. of C	Systematic name	Fusion temp. (°C)	Formula
<b>SATURATED FATS</b>				
Butyric	4	Butanoic	−7.9	$\text{CH}_3\text{—(CH}_2\text{)}_2\text{—COOH}$
Caproic	6	Hexanoic	−3.4	$\text{CH}_3\text{—(CH}_2\text{)}_4\text{—COOH}$
Caprylic	8	Octanoic	16.3	$\text{CH}_3\text{—(CH}_2\text{)}_6\text{—COOH}$
Capric	10	Decanoic	31.2	$\text{CH}_3\text{—(CH}_2\text{)}_8\text{—COOH}$
Lauric	12	Dodecanoic	43.9	$\text{CH}_3\text{—(CH}_2\text{)}_{10}\text{—COOH}$
Myristic	14	Tetradecanoic	54.1	$\text{CH}_3\text{—(CH}_2\text{)}_{12}\text{—COOH}$
Palmitic	16	Hexadecanoic	62.7	$\text{CH}_3\text{—(CH}_2\text{)}_{14}\text{—COOH}$
Stearic	18	Octadecanoic	69.9	$\text{CH}_3\text{—(CH}_2\text{)}_{16}\text{—COOH}$
Arachidic	20	Eicosanoic	75.4	$\text{CH}_3\text{—(CH}_2\text{)}_{18}\text{—COOH}$
Behenic	22	Docosanoic	80.0	$\text{CH}_3\text{—(CH}_2\text{)}_{20}\text{—COOH}$
Lignoceric	24	Tetracosanoic	84.2	$\text{CH}_3\text{—(CH}_2\text{)}_{22}\text{—COOH}$
<b>SATURATED HYDROXY ACID</b>				
Cerebronic	24	2-Hydroxytetracosanoic	−100.0	$\text{CH}_3\text{—(CH}_2\text{)}_{21}\text{—CHOH—COOH}$
<b>UNSATURATED FATS</b>				
<b>MONOETHYLENIC</b>				
Palmitoleic	16	<i>cis</i> Δ9 Hexadecenoic ω7	0.5	$\text{CH}_3\text{(CH}_2\text{)}_5\text{CH=CH(CH}_2\text{)}_7\text{COOH}$
Oleic	18	<i>cis</i> Δ9 Octadecenoic ω9	13.4	$\text{CH}_3\text{(CH}_2\text{)}_7\text{CH=CH(CH}_2\text{)}_7\text{COOH}$
Erucic	22	<i>cis</i> Δ13 Docosenoic ω9		$\text{CH}_3\text{(CH}_2\text{)}_7\text{CH=CH(CH}_2\text{)}_{11}\text{COOH}$
Nervonic	24	<i>cis</i> Δ15 Tetracosenoic ω9		$\text{CH}_3\text{(CH}_2\text{)}_7\text{CH=CH(CH}_2\text{)}_{13}\text{COOH}$
<b>DIETHYLENIC</b>				
Linoleic	18	<i>cis</i> Δ9,12 Octadecadienoic ω6	−5.0	$\text{CH}_3\text{(CH}_2\text{)}_4\text{CH=CH—CH}_2\text{—CH=CH(CH}_2\text{)}_7\text{COOH}$
<b>POLYETHYLENIC</b>				
Linolenic	18	<i>cis</i> Δ9,12,15 Octadecatrienoic ω3	−10.0	
Arachidonic	20	<i>cis</i> Δ5,8,11,14 Eicosatetraenoic ω6	−49.5	
Timnodonic	20	<i>cis</i> Δ5,8,11,14,17 Eicosapentaenoic ω3		
Clupanodonic	22	<i>cis</i> Δ7,10,13,16,19 Docosapentaenoic ω3		
Cervonic	22	<i>cis</i> Δ4,7,10,13,16,19 Docosaheptaenoic ω3		

The systematic name for the FAs results from adding the suffix “-oic” to the name of the hydrocarbon from which they derive, but commonly a trivial name is used (Table 5.1). FA carbons are numbered from the carbon that has the carboxyl group, which is considered C1. Greek letters are also used,  $\alpha$  (or C2) is the carbon adjacent to the carboxyl, and carbons  $\beta$ ,  $\gamma$ , etc. are the ones that follow. Carbon  $\omega$  (omega) is always considered the last carbon, whatever be the number of carbons in the chain. To represent each FA, a simplified notation is used, which indicates the number of carbons and number of double bonds in the chain, separated by a colon. This notation allows for the differentiation between FAs that have the same number of carbon atoms, but different numbers of carbon double bonds. For example, the notation for stearic acid is 18:0, while the notation for linolenic acid is 18:3. For unsaturated FAs, the positions of the double bonds are indicated in parentheses, with the number of the carbon where the double bond begins. For example, oleic acid is 18:1(9) and arachidonic acid is 20:4(5,8,11,14), which indicates that the double bond is located between C9 and C10 in oleic acid and between C5–C6, C8–C9, C11–C12, and C14–C15 in arachidonic acid. The symbol  $\Delta$  (delta) followed by the carbon number where the double bond begins is also used. For example, linolenic acid is 18:3 $\Delta$ 9,12,15.

Another notation is used which indicates the position of double bonds from the  $\omega$ C. For example, oleic acid is represented as 18:1 $\omega$ 9 (or n9); linoleic, 18:2 $\omega$ 6 (or n6); linolenic, 18:3 $\omega$ 3 (or n3); arachidonic, 20:4 $\omega$ 6 (or n6). Since the double bonds are separated by methylene bridges ( $-\text{CH}_2-$ ), knowing their number and position from the  $\omega$ C, the location of the other double bonds can be deduced. The  $\omega$  notation is useful when considering polyethylene acid biosynthesis.

## Fatty Acids Properties

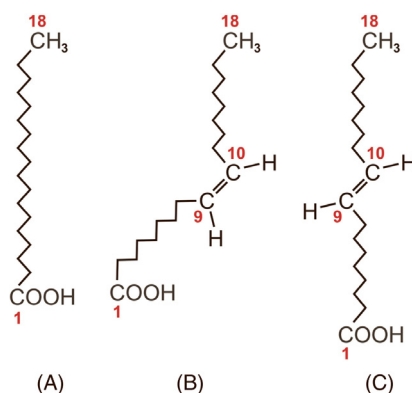
### Physical Properties

**Solubility.** FAs possess a polar group (hydrophilic) represented by the carboxyl group and a

nonpolar (hydrophobic) portion that includes the carbon chain. The water solubility of FAs decreases as the length of the carbon chain increases. FAs with more than six carbons are practically insoluble in water and soluble in organic solvents because the long hydrophobic chain prevails over the hydrophilic carboxyl group.

**Melting and boiling temperatures.** The melting temperature of FAs increases with the chain length (Table 5.1). Saturated FAs from two to eight carbons are in liquid state at 20°C, while those of longer chains are solid. The presence of double bonds decreases the melting temperature of FAs. Thus, stearic acid melts at 69.9°C and is solid at 20°C. If a double bond between C9 and C10 is inserted into stearic acid, it becomes oleic acid and the melting temperature is reduced to 13.4°C; unlike stearic acid, oleic acid is liquid at 20°C. Adding a second double bond to oleic acid, between C12 and C13 generates linoleic acid, which melts at 5°C. The boiling temperature of FAs increases with the chain length.

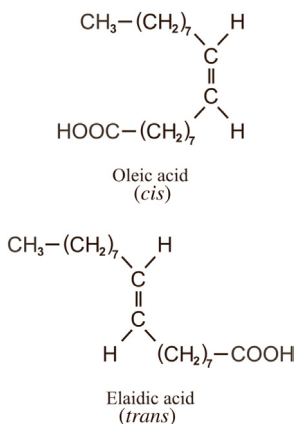
**Geometrical isomerism.** Saturated FAs adopt different spatial arrangements because the single bonds between the carbon atoms allow their free rotation. However, the extended conformation, forming a zigzag with angles of 109° between two successive links (Fig. 5.1), is more



**FIGURE 5.1** Arrangement of fatty acid (FA) carbon chains. (A) Saturated FA (stearic); (B) monoethylenic FA, *cis* configuration (oleic acid); and (C) monoethylenic FA, *trans* configuration (elaidic acid).

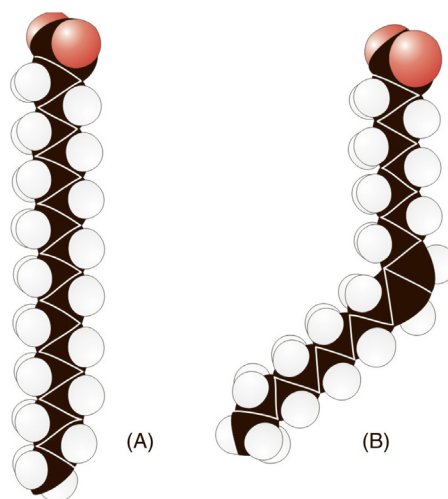
stable (with lower free energy) due to the hydrogen atoms linked to the carbon atoms of the chain.

The ethylenic or unsaturated FAs have a more rigid structure because the carbons joined by the double bond cannot rotate freely. The existence of a double bond creates the possibility of geometrical isomerism. According to the position of the substituents with respect to the plane of the double bond, *cis*–*trans* isomers can be formed:

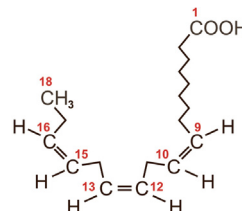


Almost all natural unsaturated FAs are *cis* isomers. The *cis* configuration produces a kink in the chain at each ethylenic bond, which causes the chain to adopt different layouts (Figs. 5.1 and 5.2), commonly exhibiting a U-shaped configuration (Fig. 5.3). In contrast, the *trans* isomers have an extended structure, similar to that of saturated chains (Fig. 5.1C). The *cis* form is less stable than the *trans* form and may be converted to the *trans* configuration by action of various agents, including heat. With an increase in temperature, oleic acid (18:1Δ9 *cis*) becomes elaidic acid (18:1Δ9 *trans*), which shows different properties.

Although natural products have great predominance of *cis* FAs, there are always a small proportion of *trans* isomers. For example, milk fat contains 4–8% of FAs in *trans* configuration. In contrast, fats subjected to hydrogenation, as



**FIGURE 5.2** Compact molecular models. (A) Saturated FA and (B) monoethylenic FA (oleic). Carbon, Black; oxygen, red; hydrogen, white.



**FIGURE 5.3** Arrangement of the carbon chain of a *cis* triethylenic FA (linolenic).

margarines, have significantly higher proportions of these isomers.

### Chemical Properties

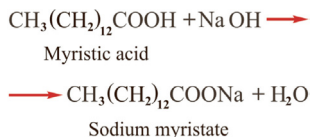
#### PROPERTIES THAT DEPEND ON THE CARBOXYL GROUP

**Acidic character.** The acidic property of a FA depends on the carboxyl group. In water soluble molecules like acetic acid, ionization occurs as follows:



Increasing the number of carbons in the lipid chain reduces its water solubility and acidic character.

*Formation of salts (soaps).* When a FA reacts with a base, a salt is formed:



Salts are designated by the name of the metal followed by the FA name with the suffix “-ate” (e.g., potassium stearate). These FA salts are called *soaps*. Soaps generated from alkaline metals (Na, K, etc.) are water soluble and act as emulsifiers or detergents. Salts formed with elements in Group II of the Periodic Table (Ca, Mg, Ba), or with any other heavy metal, are insoluble in water and organic solvents. Soaps containing calcium or magnesium precipitate and do not form foam.

*Emulsifying action of soluble soaps.* An *emulsion* is a heterogeneous mixture of two insoluble liquids causing one to disperse in small droplets within the other. A common example of emulsion is seen when mixing oil and water. Both liquids spontaneously separate, with the less dense oil forming a layer on top of the water. If the mixture is intensely shaken, the oil splits into small droplets, forming an emulsion. However, once the mixture is left unstirred, the oil droplets come together and reconstitute the initial oil top layer. If a soluble soap (sodium palmitate) is added before stirring the mixture, a stable emulsion is obtained and the oil will remain dispersed in fine droplets within the water. Soap molecules have a nonpolar carbon chain ( $\text{CH}_3-(\text{CH}_2)_{14}-$ ) that is hydrophobic (soluble in oil and insoluble in water) and a  $-\text{COONa}$  group, which ionizes ( $-\text{COO}^- + \text{Na}^+$ ) and is polar and hydrophilic (soluble in water and insoluble in oil). At the interface between oil droplets and water, soap ions are arranged with the alkyl group oriented toward the oil and the carboxylate ions positioned toward the water (Fig. 5.4). The surface of the droplets covered by the  $-\text{COO}^-$  groups is

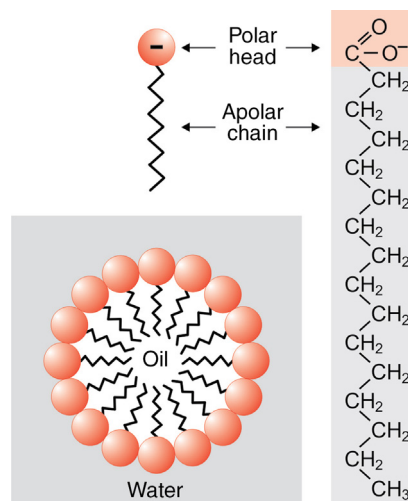
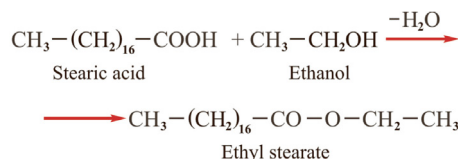


FIGURE 5.4 Emulsifying action of soluble soaps.

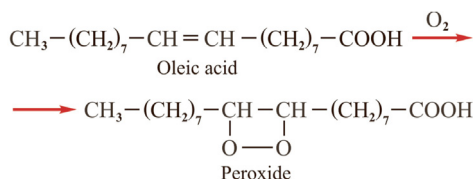
negatively charged, maintaining the droplets repelled from each other, which helps to stabilize the emulsion.

*Ester formation.* FAs form esters by reacting with alcohols:

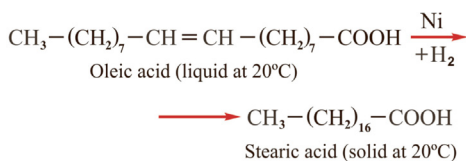


## PROPERTIES DEPENDENT ON THE CARBON CHAIN

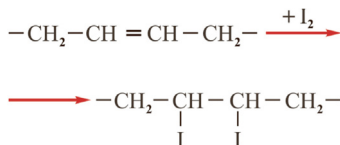
*Oxidation.* Unsaturated FAs are easily oxidized. Atmospheric oxygen oxidizes oleic acid at the level of the double bond to form peroxides. This peroxide is susceptible to further oxidation, which produces the rupture of the double bond, breaking the carbon chain into different compounds (such as short-chain monocarboxylic and dicarboxylic acids and aldehydes), which are responsible for the odor and taste, typical of rancid fats.



**Hydrogenation.** Unsaturated FAs are more abundant in nature than saturated FAs and their use in industry is important. Saturated FAs are obtained from unsaturated FAs by hydrogenation in the presence of a catalyst (Pt, Ni, or Pd). The hydrogen atoms bind to the carbon atoms that contain double bonds, transforming these into single bonds.



**Halogenation.** The double bonds of FAs can easily incorporate halogens (F, Cl, Br, and I).



This property is used to determine the degree of unsaturation of FAs in a biological sample. Most commonly iodine is used for halogenation. Under controlled conditions, the quantity of iodine consumed by a certain amount of lipid is proportional to the number of double bonds within the FAs present in the sample. *Iodine number* is defined as the amount of iodine in grams required to halogenate 100 g of lipid material.

## ESSENTIAL FATTY ACIDS

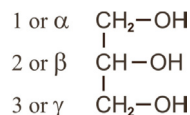
As it will be discussed in Chapter 15, animals produce FAs from the addition of two carbon atoms at a time. However, there are some FAs,

which cannot be synthesized by the body and must be supplied with the diet. These are called essential or indispensable FAs. Essential FAs include the polyethylenic or polyunsaturated *linoleic*, *linolenic*, and *arachidonic* FAs.

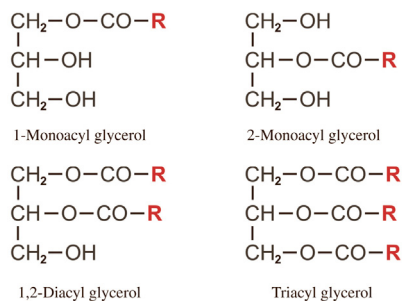
## SIMPLE LIPIDS

### Acylglycerols

Most of the FAs of the body form esters with different alcohols, preferably glycerol, generating *acylglycerols* or *acylglycerides*. Glycerol has three alcohol groups bound to each of its carbons. Glycerol carbons are designated by Arabic numerals or Greek letters. The primary carbons C1 and C3 are also named  $\alpha$  and  $\gamma$ , while C2 is named  $\beta$ .



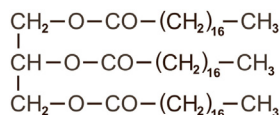
Depending on the number of alcohol groups esterified by FAs, acylglycerols are designated monoacylglycerols, diacylglycerols, or triacylglycerols. The names mono-, di-, and triglycerides, widely used, are not correct and should be abandoned. Triacylglycerols are commonly called *neutral fats*.



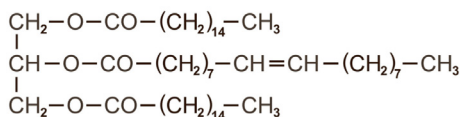
R: FA carbon chain



If the FAs are all the same, the di- and triacylglycerols are called homoacylglycerols; if they are different, the acylglycerols are named heteroacylglycerols. The more recommended designation for each acylglycerol includes the FA with the suffix “-oil” and a number that describes the position of the FA within the molecule. For example,



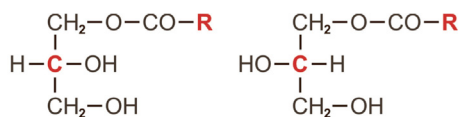
Tristearoylglycerol or tristearin  
(homotriacylglycerol)



1,3-Dipalmitoyl-2-oleyl-glycerol  
(heterotriacylglycerol)

Trivial names for homotriacylglycerols, such as tripalmitin, tristearin, or triolein, are also commonly used.

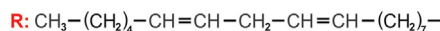
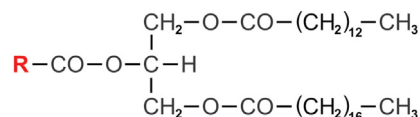
In 1-monoacylglycerol, the C2 of glycerol is asymmetric or chiral, producing two stereoisomers: D and L. According to the convention adopted for glyceraldehyde (see p. 23), the D-form is represented with the hydroxyl in C2 to the right and the L-form, with the hydroxyl to the left.



D-Monoacylglycerol      L-Monoacylglycerol  
(The asymmetric C is shown in red)

In 1,2-diacylglycerols and in di- and triacylglycerols, C2 is asymmetric when the C1 and C3 are esterified by different acyl residues. All natural compounds of this type belong to the L series.

To avoid confusions that may be created with the numbering of carbons (the primary carbons of glycerol are called either C1 or C3), the *stereospecific numbering (sn)* notation has been proposed. Glycerol is represented with the C2 hydroxyl to the left, the upper carbon is C1.



Systematic name:  
1-Myristoyl-2-linoleyl-3-stearoyl-*sn*-glycerol  
or 1-myristoyl-2-linoleyl 1-3-stearoyl-L-glycerol

## Acylglycerols Properties

### PHYSICAL PROPERTIES

**Solubility.** Acylglycerols are less dense than water and are water insoluble. In contrast, mono- and diacylglycerols are polar molecules due to their free hydroxyl groups; they have emulsifying power. Triacylglycerols are soluble in chloroform, ether, and hot alcohol. These are all solvents that are used to extract these triacylglycerols from tissues.

**Melting temperature.** The melting temperature of an acylglyceride depends on the FAs that compose them. Those containing FAs with long saturated chains melt at higher temperature, while those with FAs that are unsaturated or have short saturated chains melt at lower temperature. For example, tristearin melts at 71°C, while triolein at −17°C.

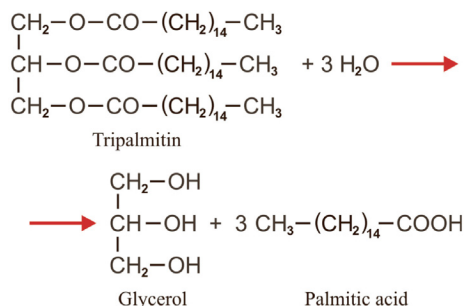
Heteroacylglycerols with unsaturated FAs are either liquid at room temperature or solids with a low melting temperature, depending on the amount of ethylenic FAs present in the molecule. Vegetable oils are rich in triacylglycerols containing long-chain unsaturated FAs.

**Isomerism.** Heteroacylglycerols exhibit structural and also optical isomerism.

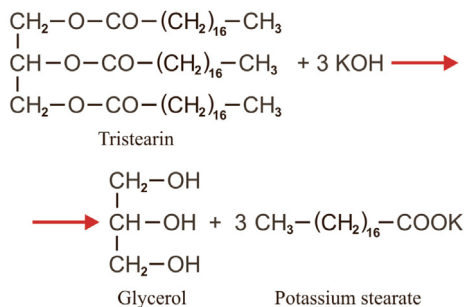
## CHEMICAL PROPERTIES

The chemical properties of acylglycerides depend mainly on their ester functions and the FA chains that constitute them.

**Hydrolysis.** Acylglycerols are hydrolyzed when heated in an aqueous acidic medium. This reaction releases FAs and glycerol.



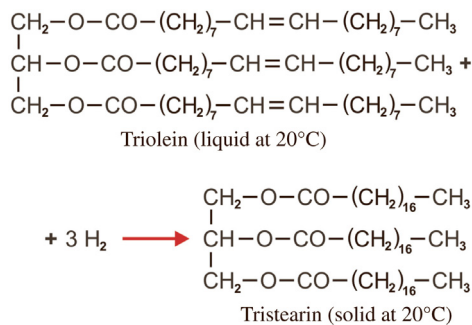
Acylglycerides are also readily cleaved when heated in the presence of a strong base (KOH or NaOH), leading to the release of glycerol and the corresponding FA salts (soaps). This process is called *saponification*.



Usually, in addition to triacylglycerols, non-ester substances exist in fats. These form the unsaponifiable fraction of fats and include hydrocarbons, free sterols, and pigments. After saponification, compounds with ester functions (acylglycerols) are converted into glycerol and soap, both of which are, unlike the original fat,

soluble in water and insoluble in ether. The unsaponifiable fraction of fat remains soluble in ether and insoluble in water, a characteristic that allows for the separation of the two groups of substances.

**Hydrogenation.** Solid fats are obtained by hydrogenation of oils in the presence of nickel as catalyst. This process is used to produce margarine. The hydrogenation of unsaturated FA from the acylglycerols in oils is only partial, which gives these fats a consistency similar to that of butter. If the hydrogenation were complete, the fats obtained would be hard. The consistency of butter is due to short-chain FAs, such as butyric and caproic. Margarine has acylglycerols with partially hydrogenated, long-chain FAs and lacks the vitamins that are present in butter.



The hydrogenation process also produces isomerization of *cis* unsaturated chains, with part of the acylglycerides becoming *trans* isomers.

**Oxidation.** Acylglycerols can undergo oxidation on their ethylenic FAs, producing compounds that are responsible for the odor and flavor that stale (rancid) fats have.

## Nutritional Importance of Fats

Lipids have a much higher caloric value than other components of a diet. One gram of fat provides 9.3 kcal (38.9 kJ), while the same amount of carbohydrates only offers 4.1 kcal (17.2 kJ). All



animals store neutral fats as energy reserve. This reserve is more important than that of carbohydrates that are rapidly depleted during fasting. Triacylglycerols are efficient molecules for the storage of energy. Nearly all of the carbon atoms in triacylglycerols are relatively less oxidized than in carbohydrates; their complete oxidation to  $\text{CO}_2$  and  $\text{H}_2\text{O}$  yields higher amounts of energy. Moreover, due to their hydrophobicity, fats practically do not retain water, unlike other reserve material, such as glycogen. This gives fat the possibility to store more energy relative to its weight.

The chemical composition of fat varies according to the site or organ where it is located within an animal. In general, fats that function as mechanical support predominantly have saturated long-chain FAs and are semisolid (perirenal fat). Fat reserves that are used as energy source are almost liquid at body temperature. The composition of reserve fat is influenced, in part, by the composition of dietary fat.

The predominant FA in animal fat reserve is oleic acid. Oleic acid is also the most abundant FA in plants; however, vegetable oils contain a high percentage of polyethylenic FAs. For example, corn oil is made up of 41.8% linoleic acid. Grape, sunflower, and peanut oils are also rich in polyunsaturated FAs. Olive oil is relatively low in these essential FAs. Fats from several species of fish contain polyunsaturated  $\omega 3$  FAs of 20–22 carbon atoms in length.

It has been observed that the consumption of diets rich in polyethylenic *cis* FAs contributes to the reduction of cholesterol concentration in people with elevated blood cholesterol. This is a valuable preventive factor for atherosclerosis. In contrast, animal fats with a higher proportion of saturated FAs or foods with *trans* unsaturated FAs favor high levels of cholesterol.

Numerous studies have shown that linoleic acid (LA, 18:2 $\Delta$ 9,12),  $\omega 3$  (or  $n 3$ ), linolenic (LNA, 18:3 $\Delta$ 9,12,15), eicosapentaenoic acid (EPA, 20:5 $\Delta$ 5,8,11,14,17), and docosahexaenoic acid (DHA, 22:6 $\Delta$ 4,7,10,13,16,19) exert a protective action against coronary heart disease. These

acids, mainly LA, have a regulatory effect on the metabolism of plasma lipoproteins (see p. 348), diminishing the production of LDL and promoting its removal. Essential FAs tend to reduce hyperlipemic effects of other diet components, such as saturated FAs, *trans* unsaturated FAs, and cholesterol. EPA and DHA help to maintain normal vascular endothelium, blood pressure, levels of plasma triacylglycerides, and prevent platelet aggregation. An adequate diet should contain a FA ratio of  $\omega 6/\omega 3$  ( $n 6:n 3$ ) of 6/1. However, the most important factor is the total amount of essential FAs. It is recommended that essential FAs provide between 1% and 2% of the total calories needed by an individual.

**Conjugated linoleic acids.** These comprise dienolic FA isomers and stereoisomers of linoleic or octadecadienoic acid (18:2 $\Delta$ 9 *cis*, 12 *cis*). They are found in foods (meat, milk, and milk products) from bovine and ovine origin. The most abundant isomer in these foods is the 9 *cis*, 11 *trans* (also called rumenic acid), the 7 *trans*, 9 *cis*, and the 11 *cis*, 13 *trans* (Fig. 5.5).

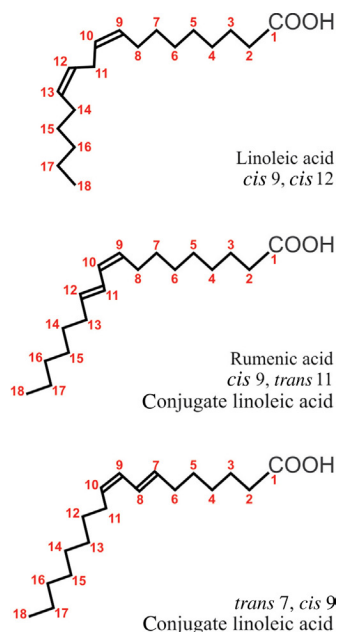


FIGURE 5.5 *trans* 7, *cis* 9 conjugated linoleic acid.

The inclusion of these acids in the diet of laboratory animals (rats and mice) showed beneficial effects, reducing body fat and weight and decreasing the incidence of malignant tumors, atherosclerosis, and diabetes. While some studies have reported similar effects in humans, there are others which present conflicting results. Until more convincing experimental evidence is obtained, ingestion of conjugated linoleic acids in amounts greater than 0.5% of the total dietary FA is not justified.

## Waxes

These types of lipids are esters of long-chain monohydric alcohols and higher FAs. For example, one of the most important components in beeswax is the ester of a 30-carbon alcohol ( $C_{30}H_{61}OH$ ) and palmitic acid. Waxes are solid at room temperature and insoluble in water. Usually they play lubricative and protective roles. For example, waxes help to lubricate the skin and provide waterproof protection to hair and feathers; bees use them to build the honeycombs. In vegetables, waxes form a protection coat over leaves and fruits. Plankton organisms are rich in waxes, and marine animals from cold regions consume them and accumulate waxes that they can store as energy reserve.

## COMPLEX LIPIDS

Complex lipids have other components in addition to the alcohols and FAs present in simple lipids. Depending on these additional components, they are divided into *phospholipids* and *glycolipids*, which contain phosphoric acid and carbohydrates, respectively. Lipoproteins are also considered complex lipids.

## Phospholipids

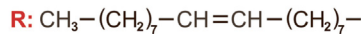
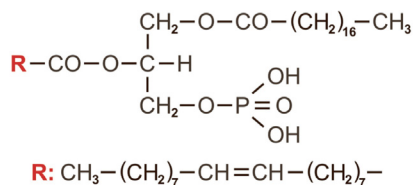
Phospholipids are complex lipids that have phosphoric acid linked by an ester bond. Some

tissues are very rich in phospholipids. They represent up to 30% of brain dry weight, while they only comprise approximately 2% of muscle dry weight. Phospholipids are constituted by an alcohol, FAs, and phosphoric acid. They are subdivided into glycerophospholipids (when the alcohol is glycerol) and sphingophospholipids (when the alcohol is sphingosine).

### Glycerophospholipids

Glycerophospholipids are the most abundant phospholipids. They are found in highest amounts in the membranes of all cells and are present in very small quantities in fat stores. In addition, glycerophospholipids are a source of physiologically active compounds. They commonly have arachidonate (at position C2), a FA that is released for the synthesis of eicosanoids (p. 349). Glycerophospholipids also participate in cell signaling systems and as an anchor for proteins in cell membranes.

Glycerophospholipids derive from *phosphatidic acids*, compounds formed by a molecule of glycerol with two of its hydroxyl groups esterified by FAs, and the third hydroxyl esterified by phosphoric acid. C2 of the glycerol moiety is asymmetric, producing stereoisomers. Natural glycerophospholipids have the L configuration. The numbering of the carbon atoms follows the rules of stereospecific numbering (*sn*). The carbon whose OH is esterified with phosphate is termed C3.

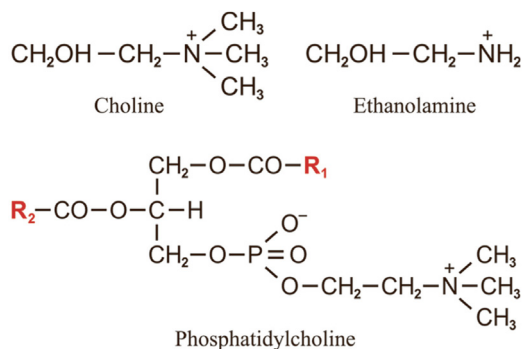


Phosphatidic acid

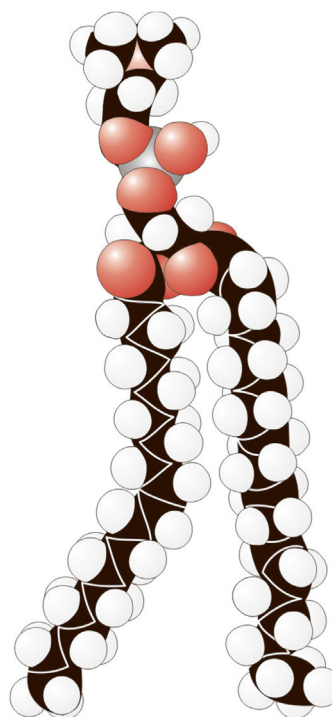
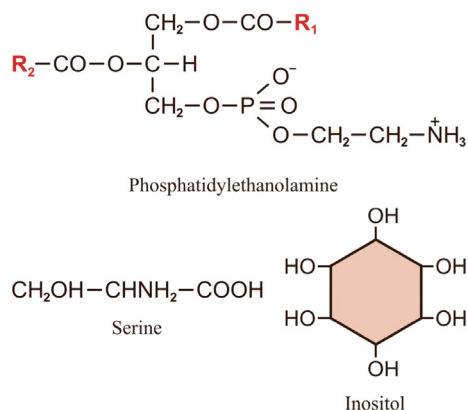
Systematic name: 1-stearoyl-2-oleyl-*sn*-glycerol-3-phosphate

Phosphatidic acids are produced in the body as intermediates in the synthesis of triacylglycerols and glycerophospholipids; however, because

they are not stored in tissues, they exist in small amounts. Generally one of the free OH groups on the phosphate moiety is esterified with another component, generating different glycerophospholipids. When the added component is the amino alcohol *choline*, the phospholipid is *phosphatidylcholine*, also known as *lecithin* (Fig. 5.6). If the amino alcohol is ethanolamine, the resulting phospholipid is *phosphatidylethanolamine* or *cephalin*.



Addition of the amino acid serine to phosphatidic acid produces *phosphatidylserine*, while addition of the cyclic polyol inositol gives *phosphatidylinositol*. Inositol is a cyclic hexalcohol; the most abundant isomer in nature is *meso*-inositol. When the six hydroxyls are esterified by phosphate, hexakisphosphate inositol or phytic acid is obtained.

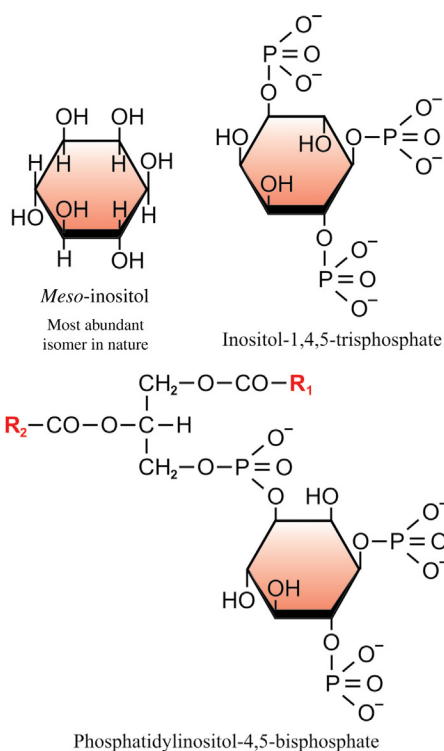


**FIGURE 5.6** Phosphatidylcholine, space filling model. C, Black; H, white; O, red; P, gray; N, pink.

At physiological pH, phosphatidylcholine and phosphatidylethanolamine are neutral molecules that behave as dipolar ions or zwitterions. Phosphatidylserine and phosphatidylinositol have a net negative charge and behave as acids.

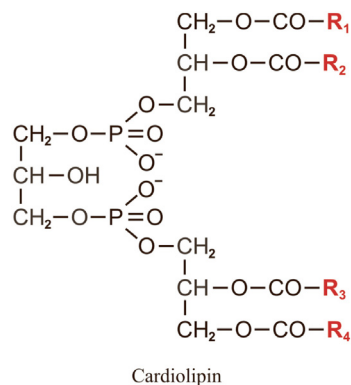
*Phosphatidylinositol bisphosphate*, unlike the phospholipids mentioned earlier, has three phosphate groups instead of one. Both of the additional phosphate groups are attached to the —OHs of the C4 and C5 of inositol. *Phosphatidylinositol bisphosphate* is found in cell membranes. In response to extracellular signals (hormones and chemical intermediates) *phosphatidylinositol bisphosphate* is hydrolyzed to diacylglycerol and inositol trisphosphate (1,4,5-trisphosphateinositol), both are products that function

as “second messengers” in signal transduction systems (p. 560).

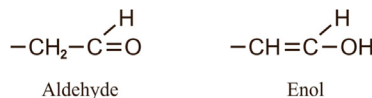


Inositol derivatives with a high proportion of phosphate groups participate in regulation of various biological processes, such as gene expression, hormone signal transduction, and metabolism among others.

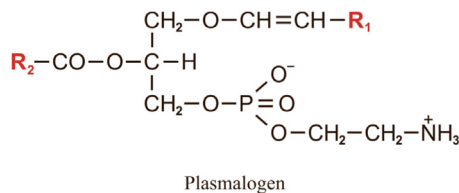
*Phosphatidylglycerol*, an acidic compound with a net negative electric charge, is usually found in the inner membrane of mitochondria and in the fluid covering the pulmonary alveolar epithelium. Another component of inner mitochondrial membranes and bacterial membranes is *cardiolipin*, formed by two phosphatidic acid molecules joined to one molecule of glycerol by phosphodiester bonds. Cardiolipin is acidic and has two negative electrical charges.



*Plasmalogens*. These compounds are glycerophospholipids that have glycerol, phosphoric acid, a nitrogenous base (choline or ethanolamine), and a FA. The difference with other phospholipids that these compounds have is, a long-chain *fatty aldehyde* linked by an ether bond to the C1 of glycerol. The fatty aldehyde easily acquires the enol form by transposition of a hydrogen and double bond change.



The enol form binds to the primary alcohol of glycerol with water loss. The fatty aldehyde can be palmital with 16 carbons, or any other aldehyde derived from FAs. Plasmalogens are found in cell membranes, especially in muscle and nerve cells.



*Properties of glycerophospholipids*. Glycerophospholipids show great diversity in the

composition of their FAs. Most glycerophospholipids have a saturated FA at *sn*-1 and another unsaturated FA at C2; however, others have two saturated or two unsaturated FAs. Phosphatidylcholine often contains palmitoyl (16:0) or stearoyl (18:0) at *sn*-1 and unsaturated residues oleyl (18:1), linoleyl (18:2), or linolenoyl (18:3) at C2. Phosphatidylethanolamine has the same saturated FAs in *sn*-1, but frequently the unsaturated acid at *sn*-2 has a longer carbon chain (20–22C). Phosphatidylinositol presents almost exclusively stearic acid (18:0) at *sn*-1 and arachidonic acid (20:4) at *sn*-2.

The glycerophospholipid molecule is amphipathic or amphiphilic, with a polar head and a nonpolar tail. The polar head comprises the free —OH groups of the phosphoryl acid moiety and the basic nitrogen of the amino alcohol, while the nonpolar region comprises the tails or carbon chains of the FAs (Fig. 5.7).

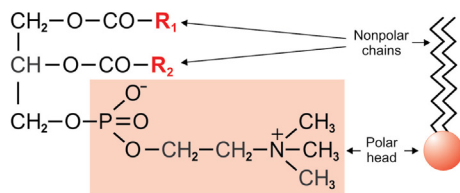
The marked polarity of glycerophospholipids is an important property of these molecules and plays an essential role in the formation of cell membranes. These molecules arrange in a double layer, with their polar heads facing the aqueous medium (either the cytosol or the external medium bathing the cell) and the nonpolar acyl chains oriented toward the membrane interior.

The venom of some snakes contains enzymes (phospholipases) that catalyze the hydrolysis of phosphoglycerides. One of these, phospholipase A<sub>2</sub>, hydrolyzes the ester function of glycerophospholipids located at position two, resulting in a structural change of the membrane and lysis

of the cell. The glycerophospholipids that result from the release of the FA at *sn*-2 by phospholipase A<sub>2</sub> are called lysoderivatives. The action of phospholipase A<sub>2</sub> on phosphatidylcholine produces a free FA and *lysophosphatidylcholine*.

Glycerophospholipids are detergents and, as such, they reduce water surface tension and stabilize the dispersion of hydrophobic compounds (cholesterol and neutral fats) in aqueous solutions. The capacity of phospholipids to function as detergents is important in bile, where they favor the solubility of cholesterol. In the lung, phospholipids prevent the collapse of the alveoli by decreasing surface tension. Type II pneumocytes of the lung secrete a substance called *surfactant* into the alveolar lumen. This is a lipoprotein complex, 80%–90% of which is composed of lipids and 10% is made by up of an 18–26 kDa proteins. Half of the surfactant lipids correspond to dipalmitoylphosphatidylcholine, an unusual compound that contains the same saturated acid, palmitic acid (16:0), in the *sn*-1 and *sn*-2 positions. Surfactant also contains phosphatidylglycerol. The ability to synthesize and excrete surfactant develops during fetal life and reaches its normal level around the 8th month of gestation. Children that are born prematurely and are deficient in surfactant suffer severe respiratory disorders (respiratory distress syndrome) due to reduced gas exchange in the alveoli. A method previously used to estimate the degree of fetal lung maturity in potential premature infants is the determination of the amount of dipalmitoylphosphatidylcholine in amniotic fluid. The lethicin to sphingomyelin ratio is now more often used for this purpose. In the newborn, the determination of these lipids can be made in the gastric content because the fetus swallows amniotic fluid during its development in uterus.

Phosphatidylinositol and other phosphoglycerides, in addition to their role as structural components of cell membranes, function as a reservoir of arachidonic acid, which will be used for the future synthesis of prostaglandins, leukotrienes,



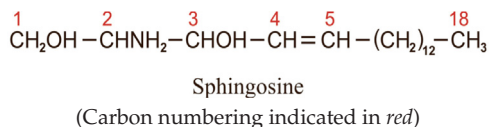
**FIGURE 5.7** Schematic representation of a glycerophospholipid.

and thromboxanes. Phosphatidylinositol also serves as an anchor for proteins, fixing them to the outer surface of the plasma membrane.

A special glycerophospholipid is the *platelet activating factor* (PAF), or 1-O-alkyl-2-acetyl-glyceryl-phosphoryl-choline. This lipid differs from phosphatidylcholine in a 16 carbon alkyl radical at *sn*-1 (linked via an ether instead of an ester bond) and an acetate moiety at *sn*-2. PAF exhibits several important actions, among which is its capacity to increase platelet aggregation, reduce blood pressure, and activate inflammatory processes.

### Sphingophospholipids

The most abundant sphingolipid is *sphingomyelin*, which is composed of: (1) an alcohol called sphingosine, (2) a FA, (3) phosphoric acid, and (4) choline. Sphingosine has 18 carbon atoms, an alcohol functional group at C1, an amine at C2, a secondary alcohol at C3, and a double bond between C4 and C5. The rest of the molecule is a saturated hydrocarbon chain.



FAs bind to sphingosine C2 amine via an amide function. This basic structure is called *ceramide* (Fig. 5.8).

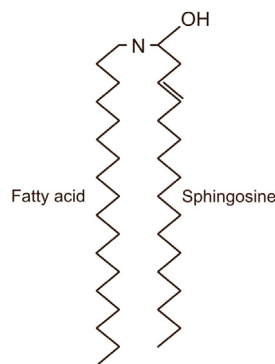
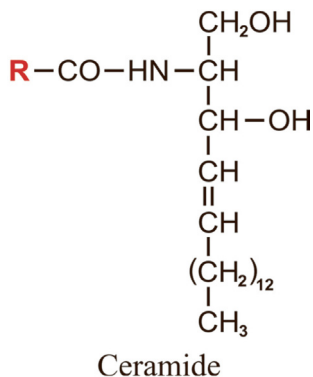
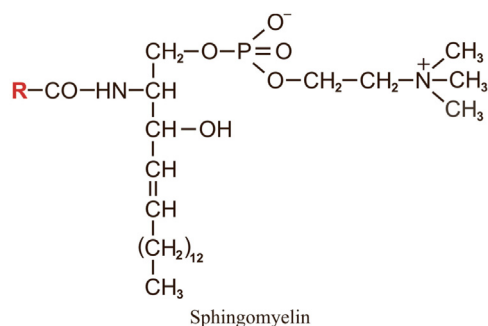


FIGURE 5.8 Schematic representation of ceramide.

The phosphoric acid esterifies the —OH at C1 of sphingosine and choline binds to the phosphate, just as it does in phosphatidylcholine.



Sphingomyelin is an important component of cell membranes; it forms the myelin sheaths of nervous tissue. Similar to other glycerophosphatides, sphingomyelin has a polar head (choline phosphate) and two nonpolar tails, represented by the hydrocarbon chains of sphingosine and the FA (Figs. 5.9 and 5.10).

### Glycolipids

These lipids have carbohydrates instead of phosphates in their molecule. The most abundant in higher animals are glycosphingolipids, mainly *cerebrosides* and *gangliosides*. They are amphipathic compounds and are found in cell membranes.



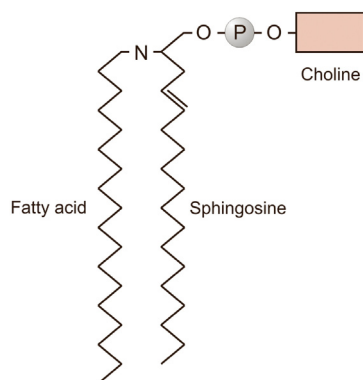


FIGURE 5.9 Schematic representation of sphingomyelin.

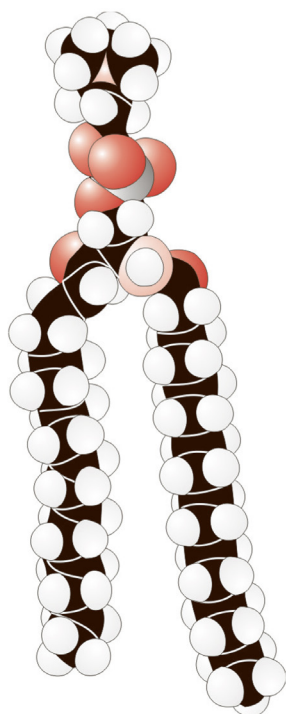


FIGURE 5.10 Space filling molecular model of sphingomyelin. C, Black; H, white; O, red; P, gray; N, pink.

### Cerebrosides

Cerebrosides are neutral compounds that consist of ceramide (sphingosine and FA) and a monosaccharide bound by a  $\beta$ -glycosidic bond to the C1 of sphingosine. Often the carbohydrate is

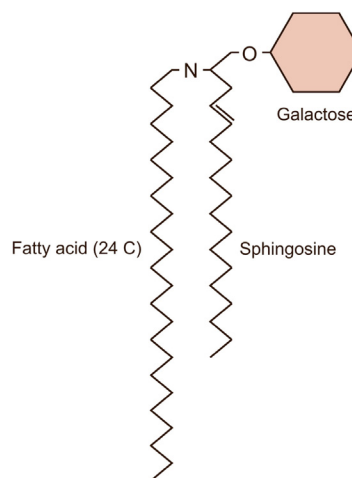


FIGURE 5.11 Schematic representation of a cerebroside.

galactose (galactocerebroside) (Fig. 5.11). The most common FAs are lignoceric and hydroxylignoceric or cerebronic acid, both of which have 24 carbons. The cerebroside containing lignoceric acid is called *kerasin*, while those having cerebronic acid are known as *phrenosin*.

Glucocerebrosides (glucose bound to ceramide) are found in very small proportions in the body, along with galactocerebrosides. Cerebrosides are abundant in brain white matter and nerve myelin sheaths and they are present in small quantity within the cell membranes of other tissues.

Brain white matter and, to a lesser extent, other tissues, also have lipids that contain sulfur. These compounds, formerly called sulfatides, are galactocerebrosides in which the monosaccharide is esterified with sulfate.

Glycosphingolipids with a more complex carbohydrate portion (di, tri, and tetrasaccharides instead of a monosaccharide) have been identified. Compounds of this type containing *N*-acetyl-galactosamine are called *globosides*.

### Gangliosides

This is another important group of glycosphingolipids, whose basic structure is similar

to that of cerebrosides, but the carbohydrate portion is of greater complexity. Linked to the ceramide, they contain an oligosaccharide composed of several hexoses and one to three acetylneuraminic acid (sialic acid) residues.

Many types of gangliosides have been recognized that differ in the number of hexoses and sialic acid residues and in the relative position of these residues. In virtually all gangliosides, the first hexose residue of the oligosaccharide attached to the ceramide is glucose, then galactose, *N*-acetyl-galactosamine, and another glucose or galactose, are subsequently attached by  $\beta$ -glycosidic bonds. Sialic acid is bound to one of the monosaccharides in the chain. According to the most commonly used notation, gangliosides are designated with the letter G followed by a subscript indicating the number of sialic acid residues existing in the molecule ( $G_M$ : mono-,  $G_D$ : di-, and  $G_T$ : trisialoganglioside). Another subscript indicates the order of migration of the compound in chromatography. The compound shown schematically in Fig. 5.12 corresponds to monosialoganglioside  $G_{M2}$ .

Gangliosides are not only a structural component of cell membranes. They also play a role as cell markers. For example, bacterial toxins, such as those of cholera, tetanus, botulism, and

diphtheria selectively bind to specific cell surface gangliosides. If the toxin is first incubated with the specific ganglioside and then placed in contact with the cell, the binding site of the toxin is blocked and it cannot bind to the cell, becoming harmless. Surface gangliosides also serve as specific binding sites for other molecules, including interferons, which are potent antiviral agents.

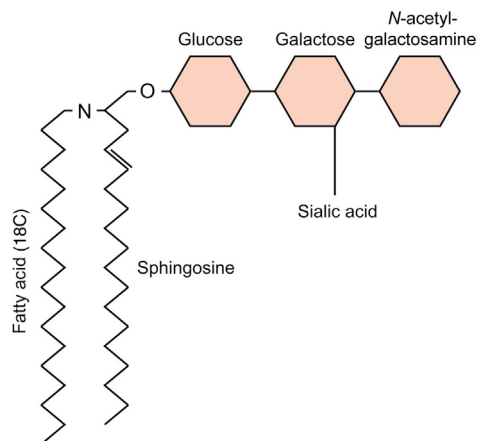
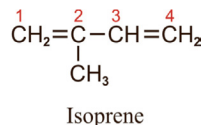
## Lipoproteins

Lipids are carried through the blood circulation in association with proteins, which allows them to be dispersed in the aqueous plasma medium. There are different types of plasma lipoproteins, which vary depending on the amount and composition of lipids that they have (pp. 62). In the lipoprotein complex, the hydrophobic lipids (triacylglycerol and cholesterol esters) are located in the interior of the molecule and the polar components (proteins, complex lipids, and free cholesterol) are arranged on the surface. Lipoproteins are also among the compounds that make up mitochondria, microsomes, and myelin membranes.

## SUBSTANCES ASSOCIATED WITH LIPIDS

### Terpenes

*Polyisoprene* or *terpenes* are hydrocarbon compounds derived from isoprene or 2-methyl-1,3-butadiene.

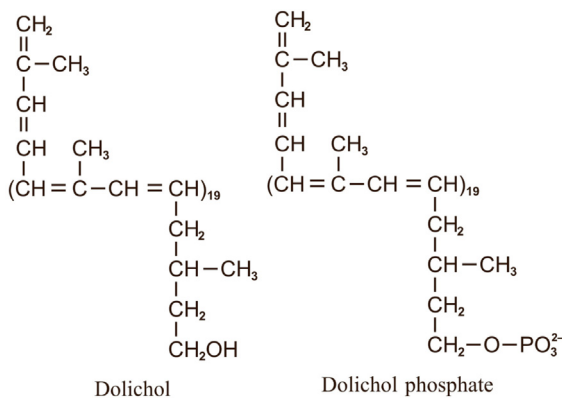


**FIGURE 5.12** Schematic representation of a ganglioside.

*Terpenes* are formed by two or more isoprene units. The binding generally takes place between C4 of one isoprene and C1 of another.

Polyisoprenes can exhibit linear structure, such as *geraniol* (composed of two isoprene units), *farnesol* (containing three isoprene units), or *squalene* (with six isoprenes). They may also form cyclic structures in vitamin A, carotenes, lanosterol, and ubiquinone.

The polyprenols belong to the terpene group of compounds; among them are *dolichol*, which has a chain of 17–21 isoprene units (85–105 carbons). Some of the double bonds of dolichol are in the *trans* configuration; the initial isoprenyl moiety, with an alcohol functional group, is saturated. When esterified with phosphate (dolichol phosphate) dolichol participates in the biosynthesis of glycoproteins (p. 317).



## Sterols

*Sterols* are cyclopentanoperhydrophenanthrene derivatives formed by perhydrophenanthrene, a saturated phenanthrene derivative (Fig. 5.13), condensed with a cyclopentane ring. Cyclopentanoperhydrophenanthrene's rings are designated by letters and the carbons are numbered as shown in Fig. 5.13. All substances that have this chemical ring structure are called *steroids*.

Many biologically important compounds are derived from cyclopentanoperhydrophenanthrene, including sexual and adrenocortical hormones, bile acids, vitamin D, and sterols (Fig. 5.14).

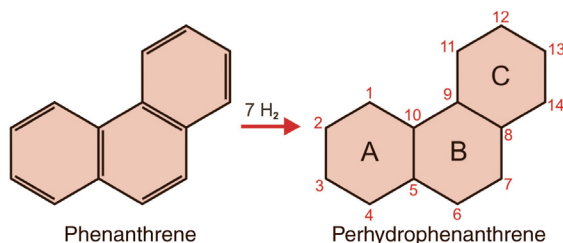


FIGURE 5.13 Carbon numbering in cyclopentanoperhydrophenanthrene.

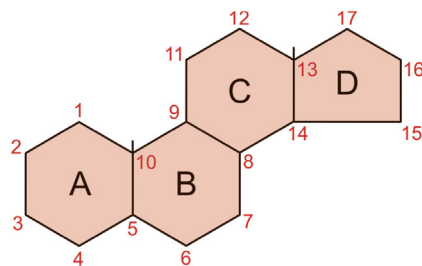
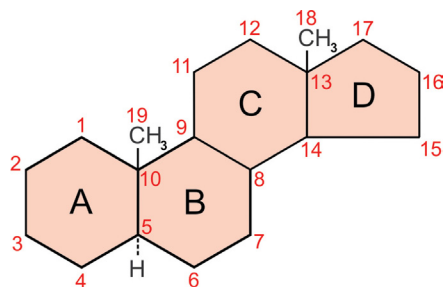


FIGURE 5.14 Cyclopentanoperhydrophenanthrene.

All cyclopentanoperhydrophenanthrene carbons are located in a plane and the substituents attached to the carbons may be located on either side of the plane creating geometric (*cis-trans*) isomerism. There are six asymmetric centers in the cyclopentanoperhydrophenanthrene ring (carbons 5, 8, 9, 10, 13, and 14), which opens the possibility for the existence of many isomers of this compound. However, in nature only isomers in C5 occur, while substituents at the remaining asymmetric carbons have the same relative position in all compounds of biological interest.

In a flat cyclopentanoperhydrophenanthrene molecule, the hydrogen or side groups can be placed above or below the plane where the carbon atoms are located. Those placed above are called  $\beta$  and the bond to the carbon is represented by a solid line; those located below are designated  $\alpha$  and a dashed line is drawn to represent the bond (Fig. 5.15).

In the majority of naturally occurring steroids, methyl groups are linked to C10 and C13 (the carbons of those methyl groups are numbered



**FIGURE 5.15** Cyclopentanoperhydrophenanthrene with methyl molecules at C10 and C13. Additional carbons numbered 18 and 19 are located above the molecular plane (indicated by a solid line). C5 hydrogen is below the molecular plane (shown by a dashed line).

19 and 18, respectively). The steroids of interest in human biochemistry have both C18 and C19 above the plane ( $\beta$ ). Methyl C10 (C19) serves as a reference; the hydrogen of C5 or any other substituent is considered  $\beta$  (*cis*) when it is on the same side of the plane as C10, or  $\alpha$  (*trans*) if it is on the opposite side.

In fact, the A, B, and C hexagonal rings of cyclopentanoperhydrophenanthrene do not lie in a plane; they adopt a more stable chair configuration. Fig. 5.16 shows the steroid conformation of the AB ring in the *trans* position.

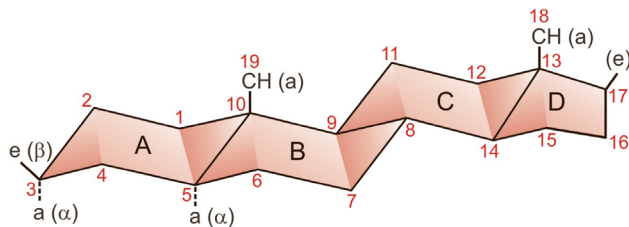
If a branched hydrocarbon chain of eight carbons is inserted on C17 and a ( $\text{—OH}$ ) hydroxyl group on C3 of cyclopentanoperhydrophenanthrene, the basic structure of a *sterol* is obtained. In these compounds, the addition of the hydroxyl group to C3 creates new *cis-trans*

isomers according to its position with respect to the methyl on C10. Sterols exist as free sterols or as esters of the C3  $\text{—OH}$  with long-chain FAs. The most abundant sterol in animal tissues is cholesterol; it exists both free and esterified. The  $\text{—OH}$  on C3 of cholesterol is in the *cis* position ( $\beta$ ) and there is a double bond between carbons five and six (Fig. 5.17). Cholesterol is insoluble in water, but easily soluble in organic solvents, such as chloroform and benzene. Increased cholesterol in blood plasma and deposition of this substance in vascular walls is commonly observed in atherosclerosis.

The spatial conformation adopted by cholesterol is shown in Fig. 5.18. The presence of the double bond between carbons five and six modifies the B ring arrangement. As there is no hydrogen at C5, there are no A/B (*cis-trans*) isomers.

Cholesterol is the raw material from which some tissues synthesize a series of compounds of high biological activity, including adrenocortical hormones, sex hormones, and bile acids. Cholesterol is present in animal fat. In plasma it is found free and esterified. It is particularly abundant in bile, where it may precipitate and form stones in the gallbladder or bile ducts (gallstones).

Another sterol present in animal organisms is 7-dehydrocholesterol (Fig. 5.19). The chemical formula of this compound is similar to that of cholesterol, except that it has an additional double bond between C7 and C8. The 7-dehydrocholesterol is a provitamin, which is converted into vitamin  $\text{D}_3$  by ultraviolet light.



**FIGURE 5.16** Spatial conformation of cyclopentanoperhydrophenanthrene. Hexagonal cycles adopt the chair configuration. This corresponds to the A/B *trans* isomer. The direction of the links is indicated by *a*, axial; *e*, equatorial.

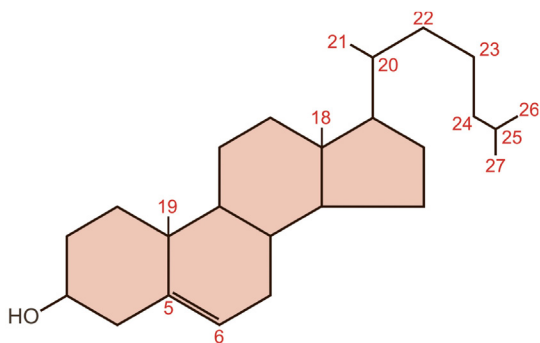


FIGURE 5.17 Cholesterol.

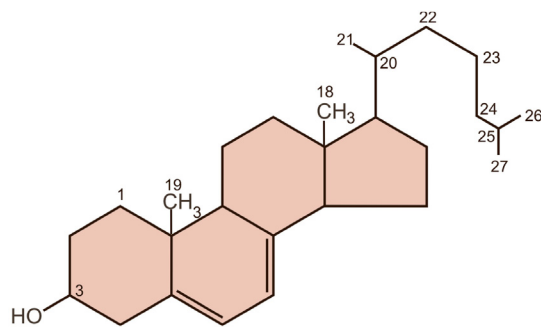


FIGURE 5.19 7-Dehydrocholesterol.

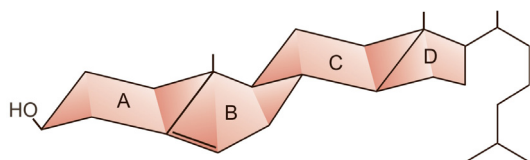


FIGURE 5.18 Spatial conformation of cholesterol. The double bond between C5 and C6 deforms the B ring.

Ergosterol is the most important plant sterol (Fig. 5.20). Its chemical structure is similar to that of 7-dehydrocholesterol, with an additional double bond between C22 and C23 and a methyl group at C24. This compound is also converted into vitamin D with exposure to sunlight.

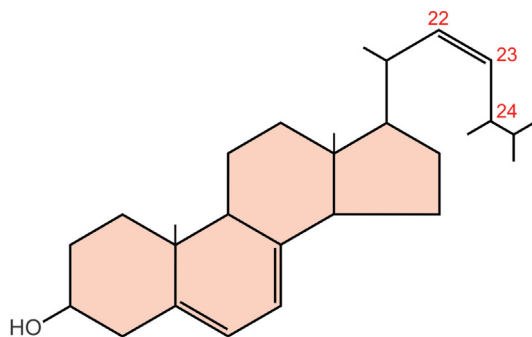


FIGURE 5.20 Ergosterol.

linoleic (18C) (18:2 $\Delta$ 9,12),  
linolenic (18:3 $\Delta$ 9,12,15), and  
arachidonic (20:4 $\Delta$ 5,8,11,14) acids.

Another notation used for unsaturated FAs is based on the position of the double bond in relation to the carbon distal to the —COOH function ( $\omega$ C). For example, oleic acid is 18:1 $\omega$ 9; linoleic, 18:2 $\omega$ 6; linolenic, 18:3 $\omega$ 3; arachidonic, 20:4 $\omega$ 6.

FA properties include the following:

1. Poor water solubility, which decreases as the carbon chain increases in length, due to the greater influence of the hydrophobic portion of the molecule over the polar —COOH group. FAs with more than six C are practically insoluble in water.
2. Melting and boiling temperatures are variable and increase with the FA carbon chain length. FAs with 1–8C are liquid at 20°C. Those with a higher number of C are solid. The presence of ethylenic bonds in FA decreases their melting temperature.
3. Geometrical isomerism, which is given by the rigidity of the ethylenic double bond of FAs. Almost all natural unsaturated FAs have a *cis* configuration. Double bonds produce angulation of the carbon chain.

## SUMMARY

*Lipids* are a heterogeneous group of substances that share the property of being poorly soluble in water but soluble in organic solvents.

*Fatty acids* (FA) are monocarboxylic organic acids and essential components of lipids. Animal lipids contain FA composed of a linear carbon chain that has an even number of carbon atoms (4–26); the most common ones have 16–18C. FA can be *saturated* or *unsaturated* and mono- and polyethylenic.

The most common saturated FAs include: butyric (4C); caproic (6C); caprylic (8C); capric (10C); lauric (12C); myristic (14C); palmitic (16C); stearic (18C); arachidic (20C); and lignoceric (24C) acids. Unsaturated FA comprise: palmitoleic (16C) (double bond between C9 and C10, indicated by the notation 16:1 $\Delta$ 9); oleic (18C) (18:1 $\Delta$ 9),

4. Acidic character, which decreases as the number of C in the chain increases.
5. Capacity to form soaps when the  $\text{—COOH}$  group reacts with a base. Soaps derived from FA and alkaline metals (Na and K) are very soluble and act as emulsifiers or detergents.
6. FAs reactivity with alcohols allows them to form esters.
7. FAs can become oxidized and unsaturated ones are more readily oxidized, forming peroxides.
8. FA can be hydrogenated in the presence of a catalyst, with the ethylene FA becoming saturated.
9. Unsaturated FA easily incorporates halogens; the amount of halogen consumed by a certain amount of acylglycerol reflects the number of double bonds in their molecule (*iodine number*).

*Lipids are classified as simple lipids*, which include acylglycerols and waxes; and *complex lipids*, which comprise phospholipids, glycolipids, and lipoproteins.

*Acylglycerols* are esters of glycerol and FA. Depending on the number of esterified alcoholic functions, acylglycerols can be monoacylglycerols, diacylglycerols, or triacylglycerols. *Triacylglycerols* are also called *triacylglycerides* or neutral fats. If FAs in the triacylglycerides are all the same, they are called *homoacylglycerols*; if they are different, *heteroacylglycerols*. Many acylglycerols exhibit optical isomerism; the common ones found in nature belong to the L series. Neutral fats are the most abundant lipids in living beings; they represent energy reserve material. The animal adipose tissue also functions as mechanical protection and thermal insulation.

*Properties of acylglycerols* include a lack of solubility in water and a melting temperature that depends on the type of FA they contain. Those having long-chain saturated FAs show higher melting temperature. The presence of unsaturated or saturated short-chain FA allows natural fats to stay in liquid state at room temperature (oils).

*Saponification* is a process that results from heating a neutral fat in the presence of a strong base (KOH and NaOH). This generates free glycerol and soaps.

*Hydrogenation* of oils leads to the formation of a solid fat (margarine). Oxidation of unsaturated FAs results first in the formation of peroxides and second it causes a break in the FA chain, which generates compounds with the taste and odor of rancid fat.

*Fats are important in nutrition*. Their caloric value (38.9 kJ/g or 9.3 kcal/g) is much higher than that of other components of the diet. *Essential FAs* are linoleic, linolenic, and arachidonic acids (polyunsaturated); humans do not synthesize them, they must be provided with food.

*Waxes* are esters of long-chain monohydric alcohols and a FA.

*Complex lipids* include:

*Phospholipids*, which are composed by an alcohol, a FA, and phosphoric acid. Depending on the type of alcohol, they are divided into *glycerophospholipids* and *sphingophospholipids*.

*Glycerophospholipids* are main components of cell membranes; they are derivatives of *phosphatidic acid*, which is composed of glycerol esterified by FAs in C1 and C2 and phosphoric acid in C3. Generally, one of the  $\text{—OH}$  groups in the phosphate of phosphatidic acid is esterified by an amino alcohol. Depending on the amino alcohol, the glycerophospholipid could be *phosphatidylcholine*, *phosphatidylethanolamine*, *phosphatidylserine*, or *phosphatidylinositol*. Phosphatidylinositol-4,5-bisphosphate participates on cell signal transduction systems. Hydrolysis of the ester linking the FA to C2 produces a *lysoderivative*.

*Plasmalogens* are similar to glycerophospholipids, but they contain a fatty aldehyde instead of a FA.

*Glycerophospholipids* are *amphipathic*, with a polar head (which includes a  $\text{—OH}$  group of phosphate, the basic N of amino alcohols, and the  $\text{—OH}$  groups of serine and inositol) and a nonpolar chain (constituted by the FA carbon chains).

*Sphingophospholipids*. The most abundant is *sphingomyelin*, which is formed by:

1. A 18C alcohol (sphingosine).
2. FA (The FA does not form an ester, but an amide bond with the sphingosine  $\text{—NH}_2$  group of C2).
3. Phosphoric acid.
4. Choline.
5. FA and sphingosine form *ceramide*, which is the basic structure of various sphingolipids.

*Glycolipids* have no phosphate. They include cerebroside, gangliosides, and sulfolipids.

*Cerebrosides* are formed by ceramide and a monosaccharide joined by  $\beta$ -glycosidic bond to the C1 of sphingosine. The monosaccharide of cerebroside is commonly galactose and the FA usually is 24C long (lignoceric in *keratin* and cerebronic in *phrenosin*). Cerebrosides are abundant in brain white matter and myelin sheaths.

*Gangliosides* are formed by ceramide, an oligosaccharide composed of several hexoses and 1–3 N-acetylneuraminic acid residues. Gangliosides function as marker molecules on the surface of membranes, which can be readily recognized by other molecules (toxins and interferon).

*Sulfolipids* or *sulfatides* are galactocerebrosides that contain sulfur.



*Lipoproteins* are complexes containing a hydrophobic lipid core (triacylglycerol and esterified cholesterol) and a polar surface, formed by proteins, complex lipids, and free cholesterol.

*Substances associated to lipids* refer to the following:

*Terpenes*, which are isoprene derivatives. Some have a linear molecule (geraniol, farnesol, squalene, and polyprenols), others present cyclic structures (vitamin A, carotenes, lanosterol, ubiquinone). A polyprenol of interest is *dolichol*, which has 17–21 isoprene units.

*Sterols* are derivatives of *cyclopentanoperhydrophenanthrene*. All carbons in this structure are in one plane, which allows the presence of geometric isomerism. When a chemical group on one of the C is on the same side of the plane as the methyl on C10, it is considered *cis* or  $\beta$ -isomer. In contrast, if the group is placed on the other side, the isomer is *trans* or  $\alpha$ .

All substances in this group (sterols, sexual and adrenocortical hormones, bile acids, and vitamin D) are generically called *steroids*.

*Cholesterol* is a sterol with a branched chain of eight carbons bound to C17, a hydroxyl group on C3, and a double bond between C5 and C6. It is only found in animal tissues. Steroidal hormones and bile acids are

synthesized from cholesterol. *7-Dehydrocholesterol* is a provitamin that can be activated by UV into vitamin D. In plants, the major sterol is *ergosterol*.

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