CHAPTER 10 LIPIDS

p.343

Classification of Lipids

- **Based on the structure and function**
  - **Lipids that do not contain fatty acids: cholesterol, terpenes, …**
  - **Lipids that contain fatty acids (complex lipids)**
    - **Storage lipids and membrane lipids**

10.1 Storage Lipids

- The fats and oils used almost universally as stored forms of energy in living organisms are derivatives of fatty acids.

Fatty Acids Are Hydrocarbon Derivatives

- Fatty acids are carboxylic acids with hydrocarbon chains ranging from 4 to 36 carbons long (C_4 to C_{36}).
- A simplified nomenclature for unbranched fatty acids specifies the chain length and number of double bonds, separated by a colon (Fig. 10–1a).

p.343

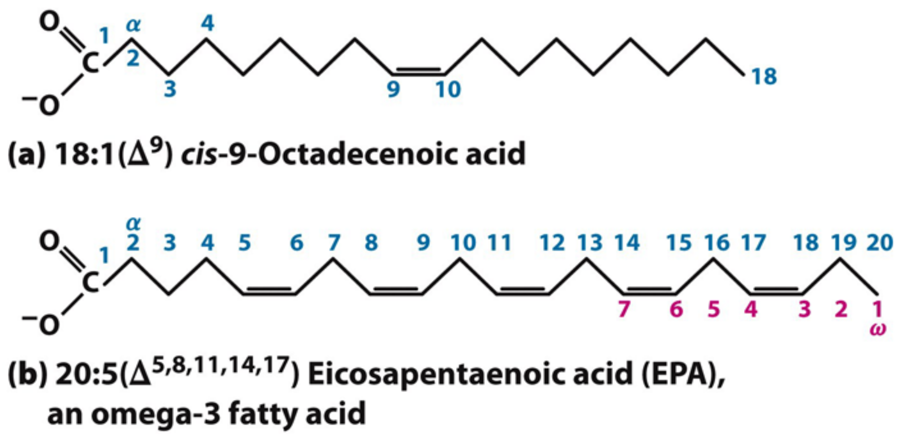


FIGURE 10–1 Two conventions for naming fatty acids.

p.343

TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1 to –0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	1–5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	−11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	−49.5		

p.344

- **The most commonly occurring fatty acids have even numbers of carbon atoms in an unbranched chain of 12 to 24 carbons.**
- **The family of polyunsaturated fatty acids (PUFAs) with a double bond between the third and fourth carbon from the methyl end of the chain are of special importance in human nutrition.**
- **PUFAs with a double bond between C-3 and C-4 are called omega-3 (ω-3) fatty acids, and those with a double bond between C-6 and C-7 are omega-6 (ω-6) fatty acids.**

p.344

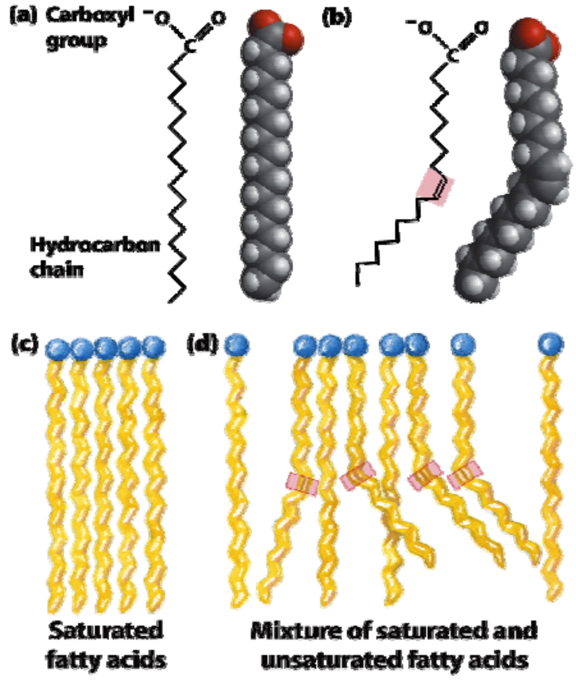


FIGURE 10–2 The packing of fatty acids into stable aggregates.

p.345

Triacylglycerols Are Fatty Acid Esters of Glycerol

- The simplest lipids constructed from fatty acids are the triacylglycerols, also referred to as triglycerides, fats, or neutral fats. Triacylglycerols are composed of three fatty acids each in ester linkage with a single glycerol (Fig. 10–3).

p.346

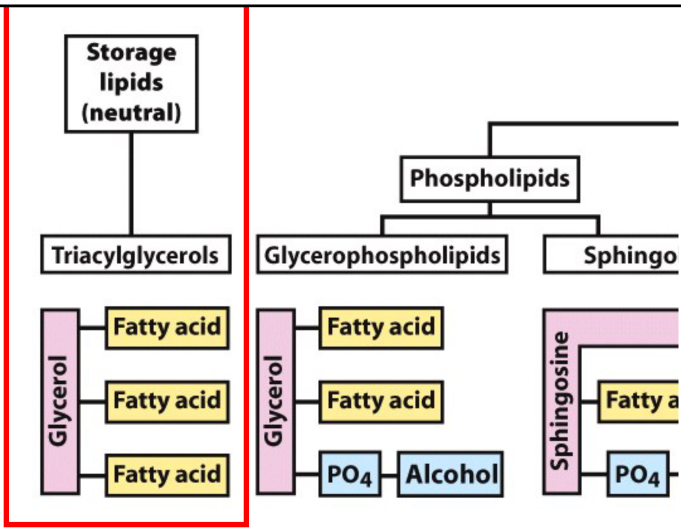


FIGURE 10–7 Some common types of storage and membrane lipids.

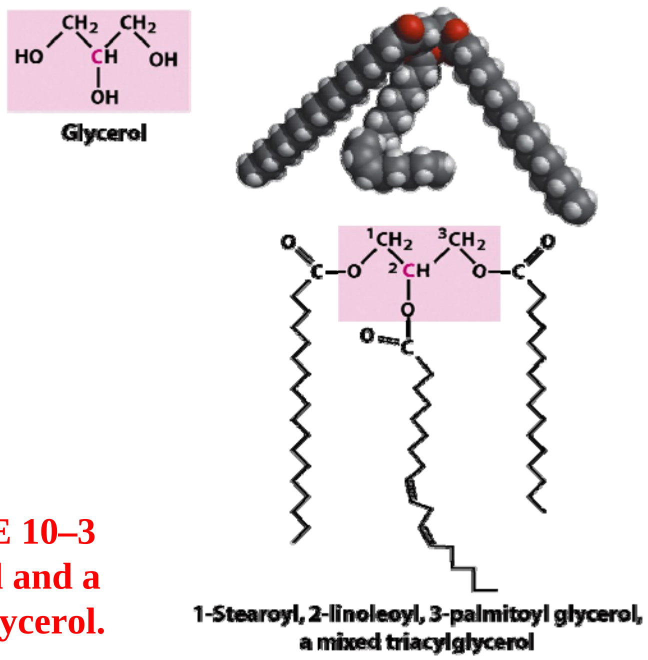


FIGURE 10–3 Glycerol and a triacylglycerol.

p.346

Triacylglycerols Provide Stored Energy and Insulation

- In vertebrates, specialized cells called adipocytes, or fat cells, store large amounts of triacylglycerols as fat droplets that nearly fill the cell (Fig. 10–4a).
- Triacylglycerols are also stored as oils in the seeds of many types of plants, providing energy and biosynthetic precursors during seed germination (Fig. 10–4b). Adipocytes and germinating seeds contain lipases, enzymes that catalyze the hydrolysis of stored triacylglycerols, releasing fatty acids for export to sites where they are required as fuel.

p.346

Fat stores in cells

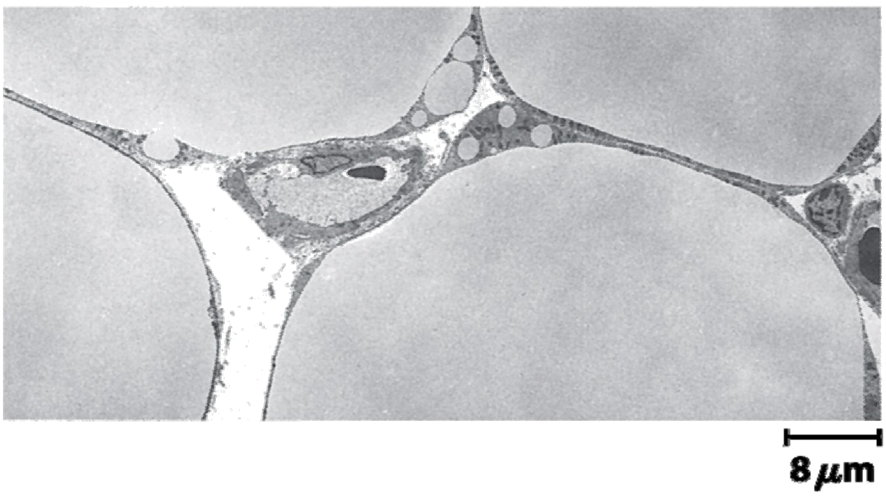


FIGURE 10-4(a) 4 guinea pig adipocytes

p.346

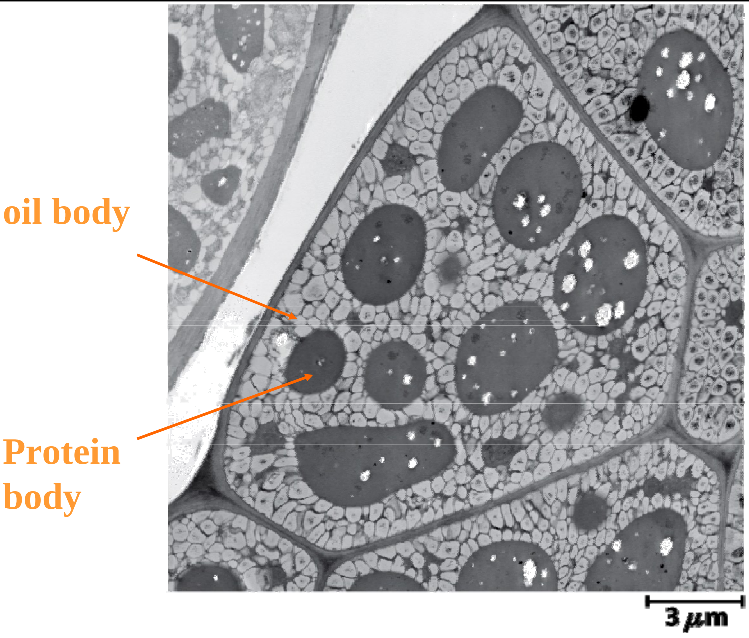


Figure 10–4(b) Cotyledon cell from a seed of *Arabidopsis*

p.346

- **Two significant advantages to using triacylglycerols as stored fuels:**

(1) the carbon atoms of fatty acids are more reduced than those of sugars, and oxidation of triacylglycerols yields more than twice as much energy.

(2) Triacylglycerols are hydrophobic and therefore unhydrated, the organism that carries fat as fuel does not have to carry the extra weight of water of hydration.

p.347

Partial Hydrogenation of Cooking Oils Produces Trans Fatty Acids

- Most natural fats, such as those in vegetable oils, dairy products, and animal fat, are complex mixtures of simple and mixed triacylglycerols. These contain a variety of fatty acids differing in chain length and degree of saturation (Fig. 10–5).
- Many fast foods are deep-fried in partially hydrogenated vegetable oils and therefore contain high levels of trans fatty acids (Table 10–2).

p.347

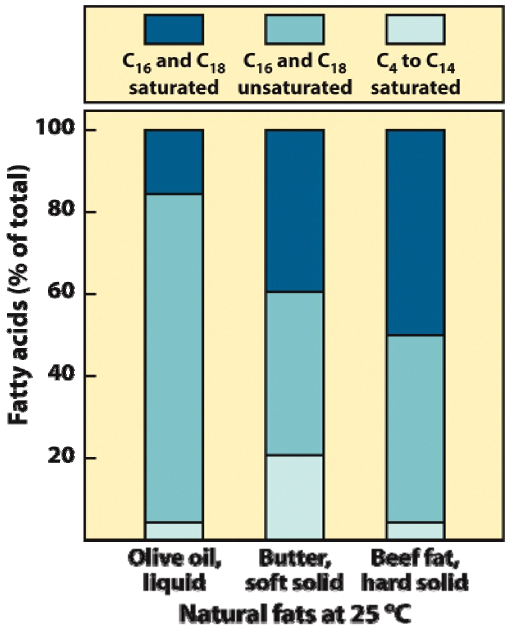


FIGURE 10–5 Fatty acid composition of three food fats.

p.348

Trans Fatty Acids in Foods

- partial dehydrogenation of unsaturated fatty acids
- A trans double bond allows a given fatty acid to adopt an extended conformation.
- Trans fatty acids can pack more regularly, and show higher melting points than cis forms.
- Consuming trans fats increases risk of cardiovascular disease
  - Avoid deep-frying partially hydrogenated vegetable oils
  - Current trend: reduce trans fats in foods (Wendy's, KFC)

TABLE 10–2 Trans Fatty Acids in Some Typical Fast Foods and Snacks

	Trans fatty acid content: In a typical serving (g)	Trans fatty acid content: As % of total fatty acids
French fries	4.7–6.1	28–36
Breaded fish burger	5.6	28
Breaded chicken nuggets	5.0	25
Pizza	1.1	9
Corn tortilla chips	1.6	22
Doughnut	2.7	25
Muffin	0.7	14
Chocolate bar	0.2	2

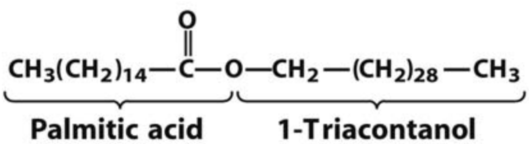
p.348

Waxes

- Waxes are esters of long-chain saturated and unsaturated fatty acids with long-chain alcohols
- Insoluble and have high melting points
- Variety of functions:
  - Storage of metabolic fuel in plankton (浮游生物)
  - Protection and pliability for hair and skin in vertebrates
  - Waterproofing of feathers in birds
  - Protection from evaporation in tropical plants and ivy
  - Used by people in lotions, ointments, and polishes

Wax: the material of the honeycomb

- Beeswax is a mixture of a large number of lipids, including esters of triacontanol, and a long-chain palmitic acid.



10.2 Structural Lipids in Membranes

- In glycerophospholipids and some sphingolipids, a polar head group is joined to the hydrophobic moiety by a phosphodiester linkage; these are the **phospholipids**.
- Other sphingolipids lack phosphate but have a simple sugar or complex oligosaccharide at their polar ends; these are the **glycolipids** (Fig. 10–7).

p.349

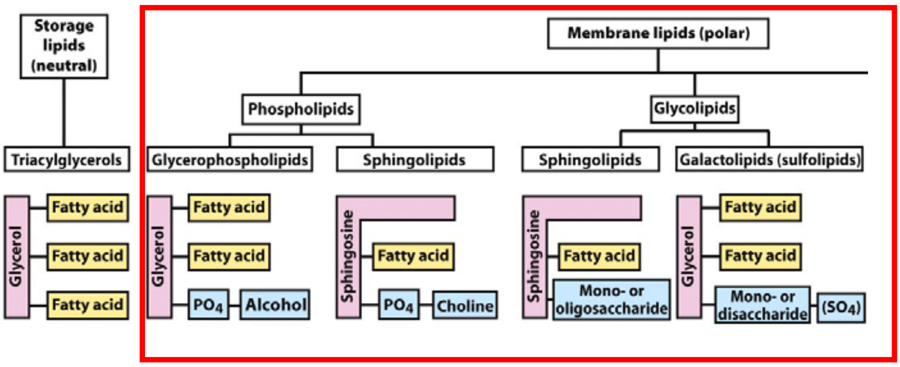


FIGURE 10–7 Some common types of storage and membrane lipids.

p.350

Glycerophospholipids Are Derivatives of Phosphatidic Acid

- Glycerophospholipids, also called phosphoglycerides, are membrane lipids in which two fatty acids are attached in ester linkage to the first and second carbons of glycerol.

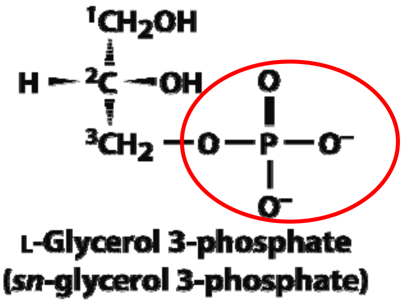
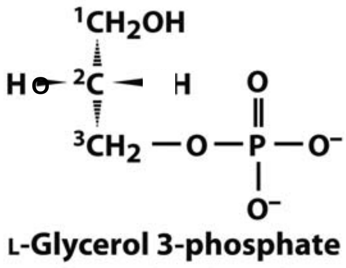


FIGURE 10–8 the backbone of phospholipids. p.350



backbone of phospholipids

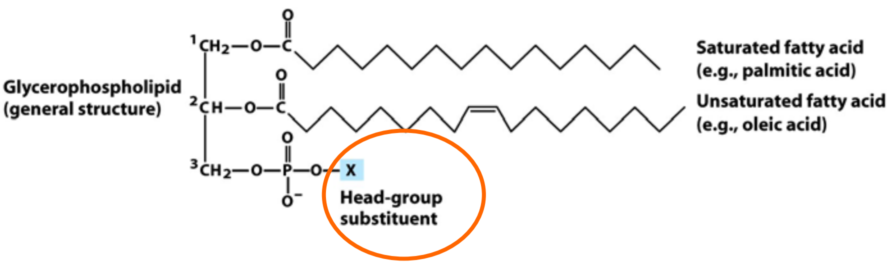
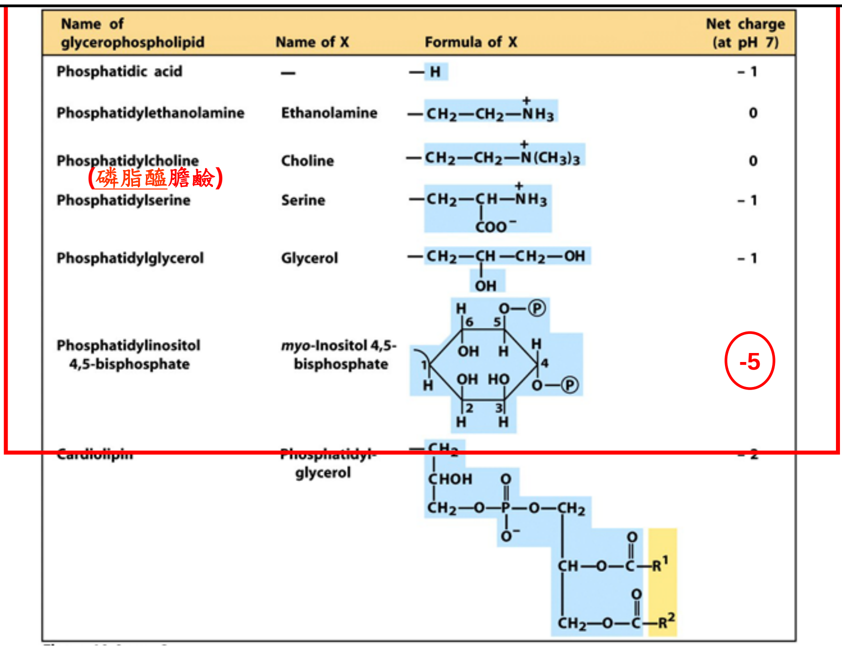


FIGURE 10–9 Glycerophospholipids.

p.351



Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	$-H$	-1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine (磷脂醯膽鹼)	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-CH(COO^-)-\overset{+}{N}H_3$	-1
Phosphatidylglycerol	Glycerol	$-CH_2-CH(OH)-CH_2-OH$	-1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		-5
Cardiolipin	Phosphatidyl-glycerol	$-CH_2-CHOH-CH_2-O-P(O)(O^-)-O-CH_2-CH(O-C(O)-R^1)-CH_2-O-C(O)-R^2$	-2

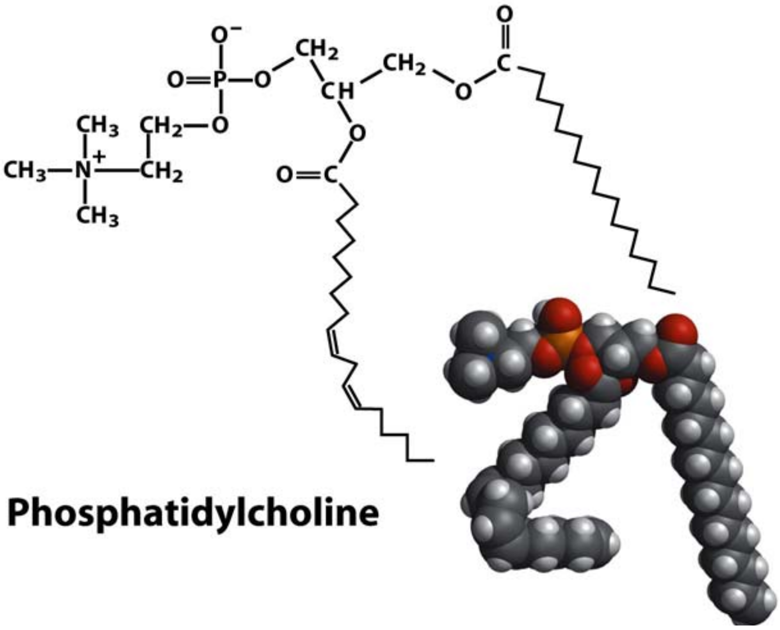
FIGURE 10-9 Part 2

p.351

- The properties of head groups determine the surface properties of membranes
- Different organisms have different membrane lipid head group compositions
- Different tissues have different membrane lipid head group compositions

Examples of Glycerophospholipids:
Phosphatidylcholine (磷脂醯膽鹼,卵磷脂)

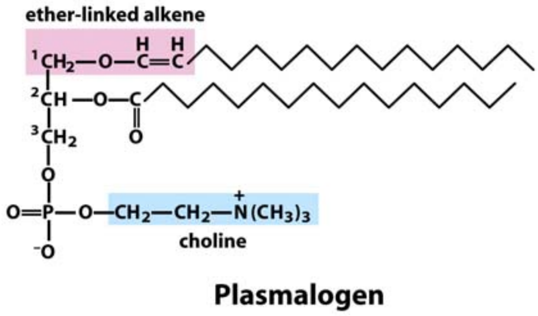
- Phosphatidylcholine is the major component of most eukaryotic cell membranes
- Many prokaryotes, including *E. coli* cannot synthesize this lipid; their membranes do not contain phosphatidylcholine



Some Glycerophospholipids Have Ether-Linked Fatty Acids

- Some animal tissues and some unicellular organisms are rich in ether lipids, in which one of the two acyl chains is attached to glycerol in ether, rather than ester, linkage.

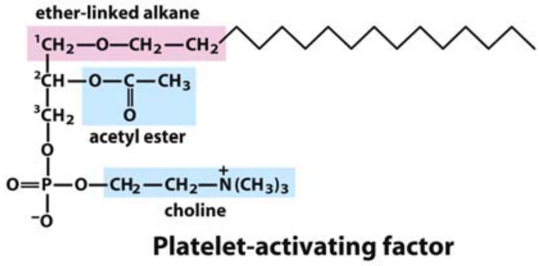
Ether lipids: Plasmalogen



- Vinyl ether analog of phosphatidylethanolamine
- Common in vertebrate heart tissue
- Also found in some protozoa and anaerobic bacteria
- Function is not well understood
  - Resistant to cleavage by common lipases but cleaved by few specific lipases
  - Increase membrane rigidity?
  - Sources of signaling lipids?
  - May be antioxidants?

p.351

Ether lipids: Platelet-activating factor



- Aliphatic ether analog of phosphatidylcholine
- Acetic acid has esterified position C2
- <u>First signaling lipid to be identified</u>
- Stimulates aggregation of blood platelets
- Plays role in mediation of inflammation

p.351

Chloroplasts Contain Galactolipids and Sulfolipids

- **The second group of membrane lipids are those that predominate in plant cells: the galactolipids, in which one or two galactose residues are connected by a glycosidic linkage to C-3 of a 1,2-diacylglycerol.**

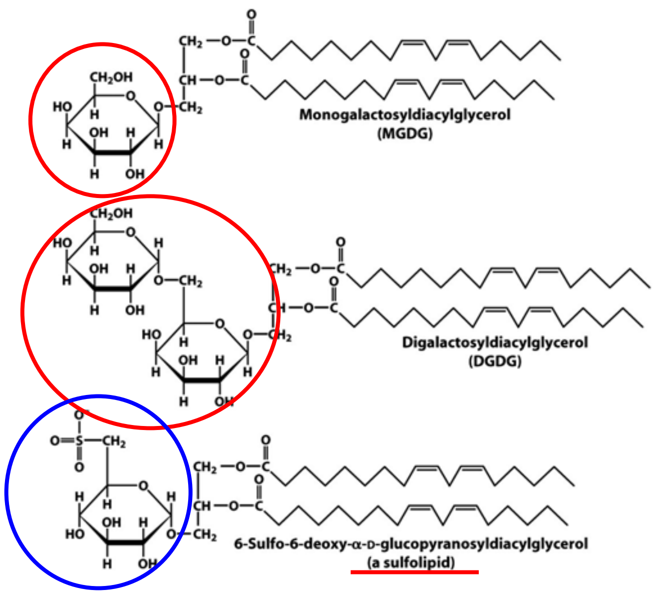
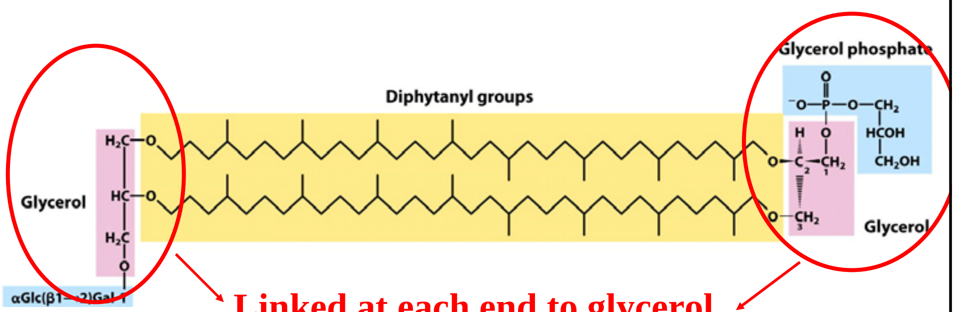


Fig. 10–11 Three glycolipids of chloroplast thylakoid membranes

p.352

Archaea contain unique membrane lipids

- Most of the archaea live in ecological extreme conditions (e.g. high temperatures, low pH, high ionic strength).
- The have membrane lipids containing long-chain branched hydrocarbons linked at each end to glycerol through **ether bonds**.
- Ether bonds are more stable to hydrolysis at low pH and high temperatures.
- These archaea lipids are twice the length of phospholipids and sphingolipids, and can span the full width of the surface membrane.



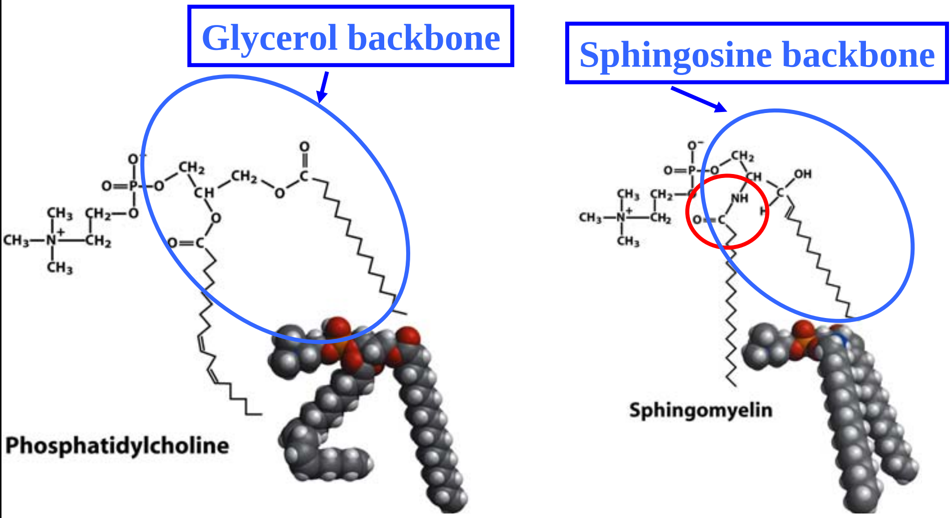
Linked at each end to glycerol through ether bonds
General name:
glycerol dialkyl glycerol tetraethers

FIGURE 10–12 A typical membrane lipid of archaea.

p.353

Sphingolipids Are Derivatives of Sphingosine

- Sphingolipids (神經鞘脂質), the fourth large class of membrane lipids, also have a polar head group and two nonpolar tails
- The backbone of sphingolipids is NOT glycerol. The backbone of sphingolipids is a long-chain amino alcohol, sphingosine
- A fatty acid is joined to sphingosine via an amide linkage rather than an ester linkage as usually seen in lipids
- A polar head group is connected to sphingosine by a glycosidic or phosphodiester linkage
- The sugar-containing glycosphingolipids are found largely in the outer face of plasma membranes



Sphingolipids

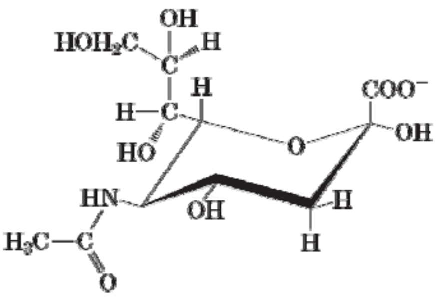
- There are three subclasses of sphingolipids.

(1) Sphingomyelins (神經鞘磷脂質) contain phosphocholine or phosphoethanolamine as their polar head group and are therefore classified along with glycerophospholipids as phospholipids (Fig. 10–7). Sphingomyelin is abundant in myelin sheath(髓鞘)that surrounds some nerve cells in animals

(2) Glycosphingolipids, which occur largely in the outer face of plasma membranes, have head groups with one or more sugars connected directly to the —OH at C-1 of the ceramide moiety

p.354

(3) Gangliosides, the most complex sphingolipids, have oligosaccharides as their polar head groups and one or more residues of *N*-acetylneuraminic acid (Neu5Ac), a sialic acid, at the termini.



N-Acetylneuraminic acid (a sialic acid)
(Neu5Ac)

p.354

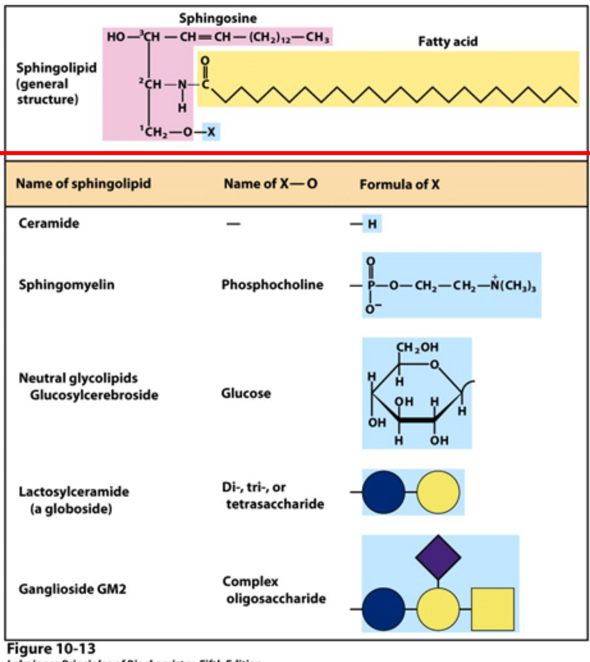


Figure 10-13
Lehninger Principles of Biochemistry, Fifth Edition

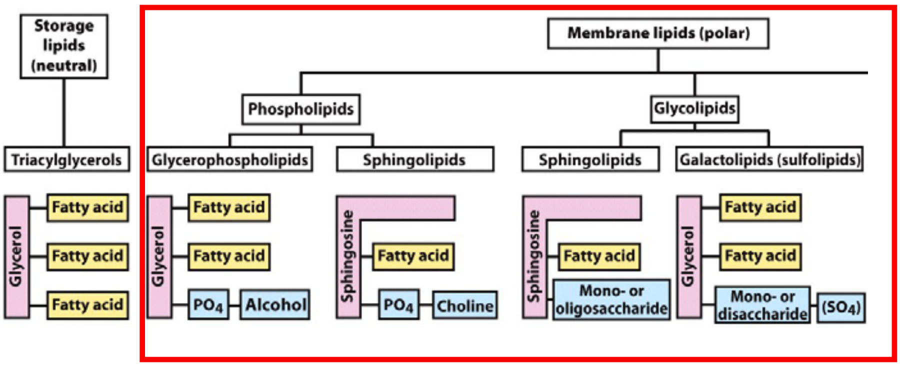


FIGURE 10–7 Some common types of storage and membrane lipids.

Glycosphingolipids and Blood Groups

- The blood groups are determined in part by the type of sugars located on the head groups in glycosphingolipids.
- The structure of sugar is determined by a expression of specific glycosyltransferases
  - Individuals with no active glycosyltransferase will have the O antigen
  - Individuals with a glycosyltransferase that transfers an N-acetylgalactosamine group have A blood group
  - Individuals with a glycosyltransferase that transfers a galactose group to phosphate will have B blood group

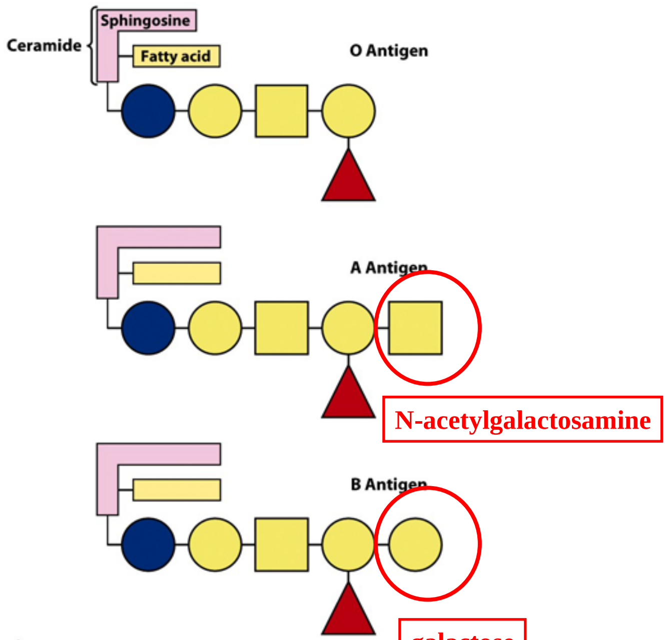


Figure 10-15
Lehninger Principles of Biochemistry, Fifth Edition

Phospholipids and sphingolipids are degraded in lysosome

- For each hydrolyzable bond in glycerophospholipids, there is a specific hydrolytic enzyme in lysosome.
- Phospholipases of the A type remove one of the two fatty acids (These esterases do not attach the ether bond of plasmalogens), producing a lysophospholipid. Lysophospholipases remove the remaining fatty acid.
- Gangliosides are degraded by a set of lysosomal enzymes the remove sugar units. A genetic defect leads to accumulation of gangliosides in the cell with severe medical consequences. (see box 10-2)

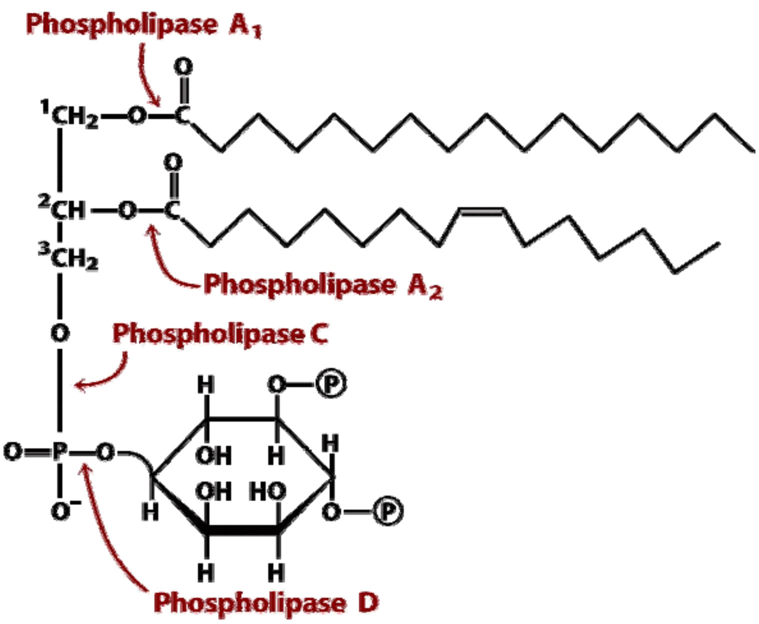
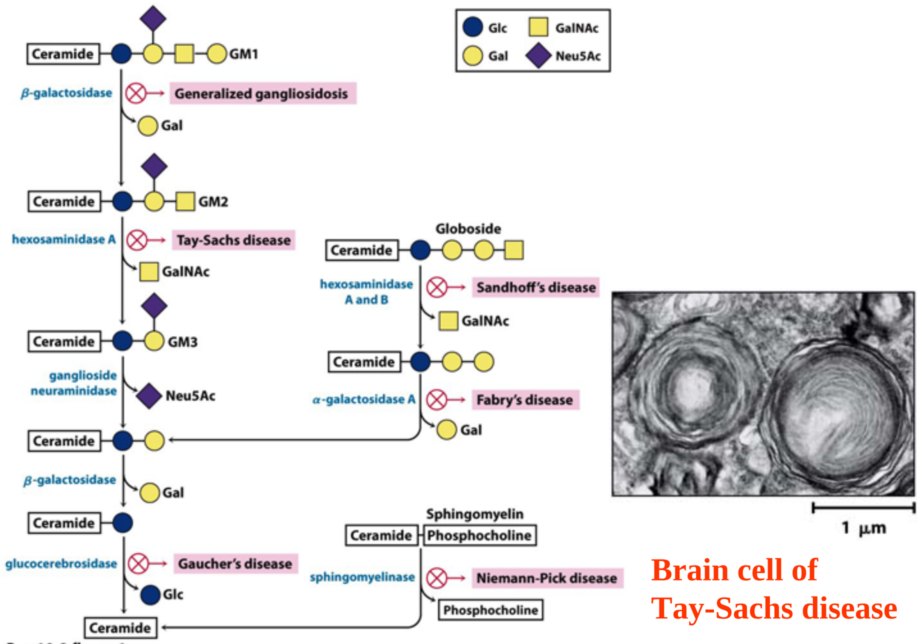


FIGURE 10–16 The specificities of phospholipases.

p.355



Brain cell of Tay-Sachs disease

Box 10-2 figure 1
Lehninger Principles of Biochemistry, Fifth Edition

Sterols(固醇) Have Four Fused Carbon Rings

- **Sterols are structural lipids present in the membranes of most eukaryotic cells. The characteristic structure of this fifth group of membrane lipids is the steroid (類固醇) nucleus, consisting of four fused rings, three with six carbons and one with five (Fig. 10–17).**
- **Cholesterol (膽固醇), the major sterol in animal tissues, is amphipathic, with a polar head group (the hydroxyl group at C-3) and a nonpolar hydrocarbon body, about as long as a 16-carbon fatty acid in its extended form.**

p.355

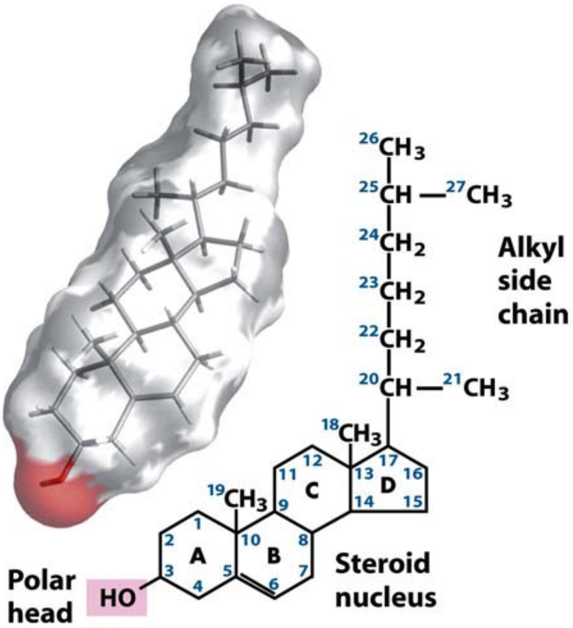
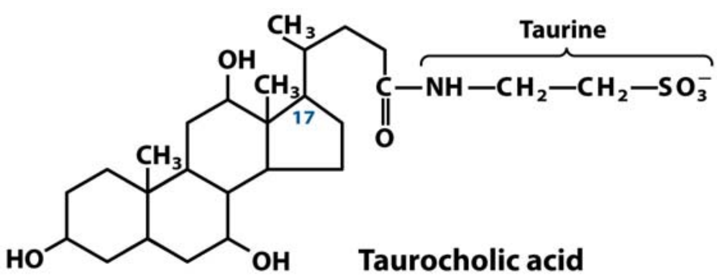


FIGURE 10–17 Cholesterol.

p.355

- **Bile acids (膽酸)** are polar derivatives of cholesterol that act as detergents in the intestine, emulsifying dietary fats to make them more readily accessible to digestive lipases.



Taurocholic acid
(a bile acid)

p.357

Physiological Role of Sterols

- Cholesterol and related sterols are present in the membranes of most eukaryotic cells.
  - Modulate fluidity and permeability
  - Thicken the plasma membrane
  - Most bacteria lack sterols
- Mammals obtain cholesterol from food and synthesize it *de novo* in the liver
- Cholesterol, bound to proteins, is transported to tissues via blood vessels
  - Cholesterol in low-density lipoproteins tends to deposit and clog arteries
- Many hormones are derivatives of sterols

Steroid Hormones

- Steroids are oxidized derivatives of sterols
- Steroids have the sterol nucleus, but lack the alkyl chain found in cholesterol. This makes them more polar than cholesterol.
- Steroid hormones are synthesized in gonads and adrenal glands from cholesterol
- They are carried through the body in the blood stream, usually attached to carrier proteins
- Many of the steroid hormones are male and female sex hormones

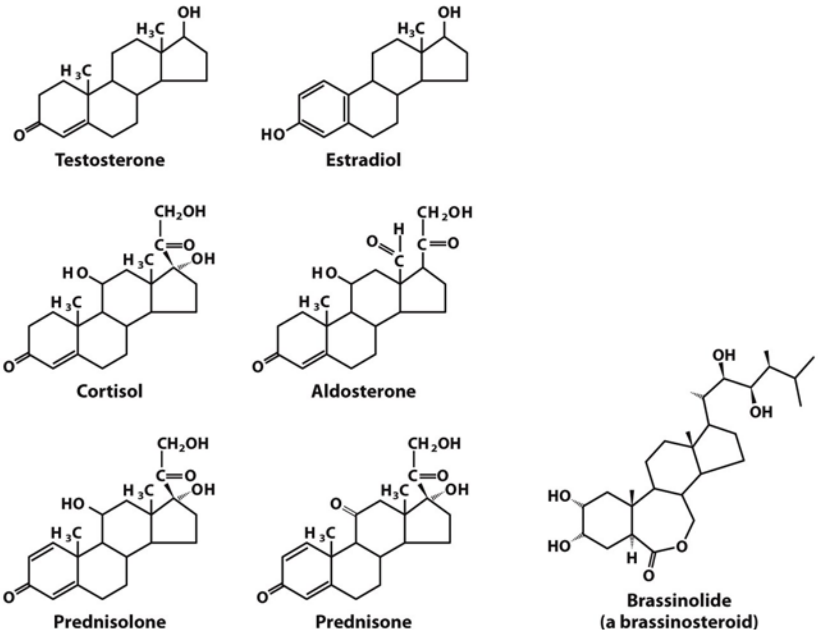


FIGURE 10–19 Steroids derived from cholesterol.

p.359

10.3 Lipids as Signals, Cofactors, and Pigments

Eicosanoids Carry Messages to Nearby Cells

Ecosanoids are paracrine hormones, are are present in small amounts but play vital roles as signaling molecules between nearby cells

- **All eicosanoids are derived from arachidonic acid (花生酸) (20:4($\Delta^{5,8,11,14}$)) (Fig. 10–18), the 20-carbon polyunsaturated fatty acid from which they take their general name. There are three classes of eicosanoids:**

  (1) Prostaglandins (PG) contain a five-carbon ring originating from the chain of arachidonic acid.

p.357

(2) **Thromboxanes** have a six-membered ring containing an ether. They are produced by platelets (also called thrombocytes) and act in the formation of blood clots and the reduction of blood flow to the site of a clot.

(3) **Leukotrienes** contain three conjugated double bonds.

Functions:

- **Inflammation and fever (prostaglandins)**
- **Formation of blood clots (thromboxanes)**
- **Smooth muscle contraction in lungs (leukotrienes)**
- **Smooth muscle contraction in uterus (prostaglandins)**

p.358

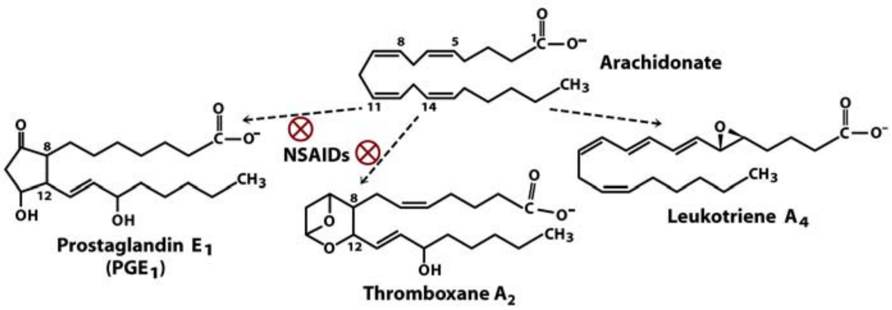


Figure 10-18
Lehninger Principles of Biochemistry, Fifth Edition

Vitamins A and D Are Hormone Precursors

- **Vitamin D_3**, also called **cholecalciferol**, is normally formed in the skin from 7-dehydrocholesterol in a photochemical reaction driven by the UV component of sunlight (Fig. 10–20a).
- **Vitamin A (retinol)**, in its various forms, functions as a hormone and as the visual pigment of the vertebrate eye (Fig. 10–21).

p.360

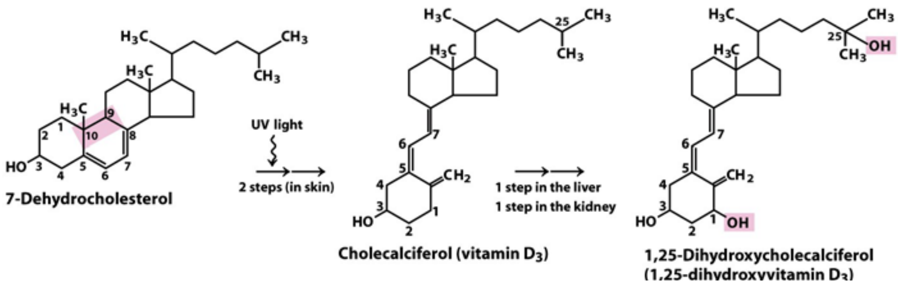


FIGURE 10–20 Vitamin D_3 production and metabolism.

p.360

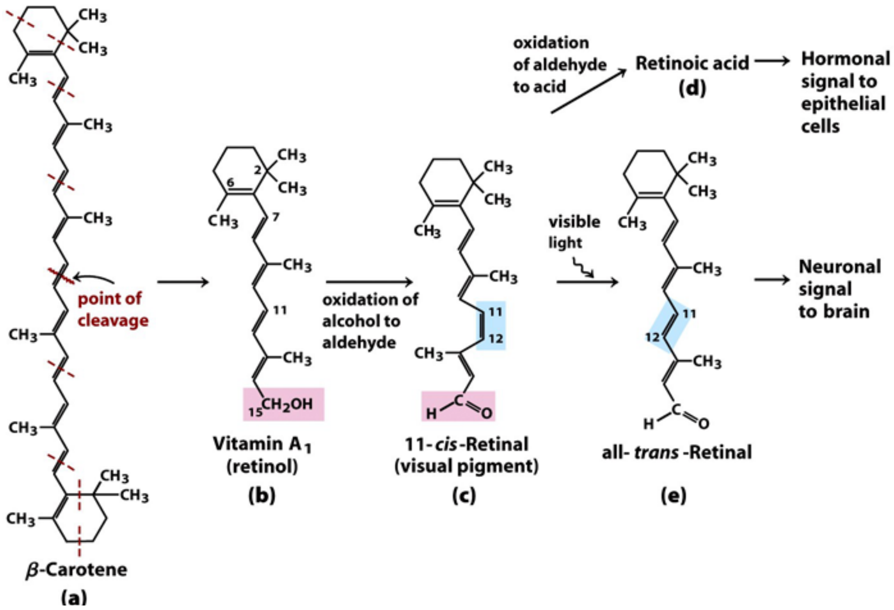


FIGURE 10–21 Vitamin A_1 and its precursor and derivatives.

Vitamins E and K and the Lipid Quinones Are Oxidation-Reduction Cofactors

- **Vitamin E** is the collective name for a group of closely related lipids called **tocopherols**, all of which contain a substituted aromatic ring and a long isoprenoid side chain (Fig. 10–22a).
- The aromatic ring of **vitamin K** (Fig. 10–22b) undergoes a cycle of oxidation and reduction during the formation of active prothrombin, a blood plasma protein essential in blood clotting.

FIGURE 10-22(a-c)

(a)
Vitamin E: an antioxidant

(b)
Vitamin K$_1$: a blood-clotting cofactor (phylloquinone)

(c)
Warfarin: a blood anticoagulant

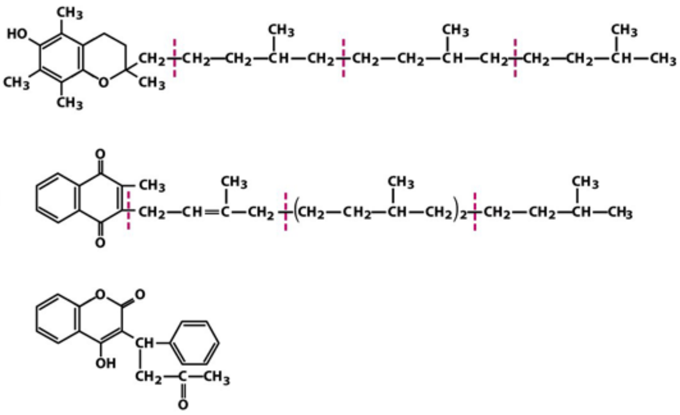


Figure 10-22a-c
Lehninger Principles of Biochemistry, Fifth Edition

p.362

FIGURE 10-22(d-f)

(d)
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) (*n* = 4 to 8)

(e)
Plastoquinone: a chloroplast electron carrier (*n* = 4 to 8)

(f)
Dolichol: a sugar carrier (*n* = 9 to 22)

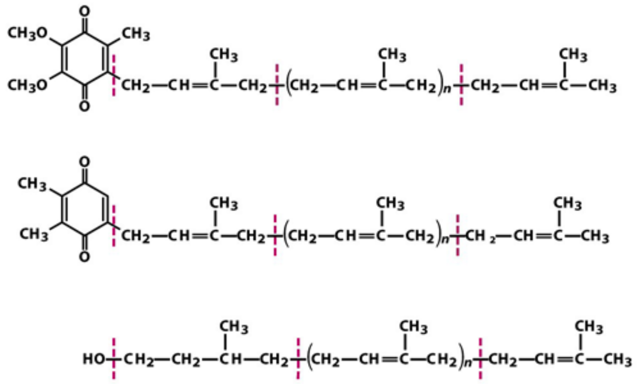


Figure 10-22d-f
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FIGURE 10–22 Some other biologically active isoprenoid compounds or derivatives.

p.362

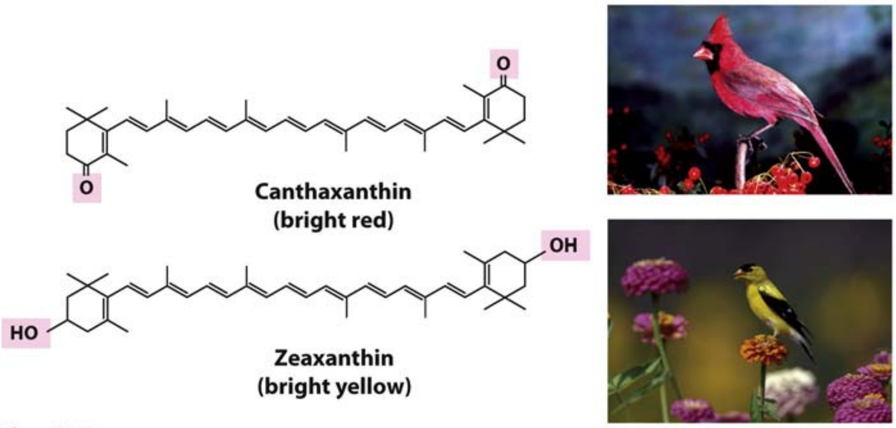

Figure 10-23
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FIGURE 10–23 Lipids as pigments in plants and bird feathers.

p.363

10.4 Working with Lipids

- Some methods commonly used in lipid analysis are shown in Figure 10–24.

  (1) Lipid Extraction Requires Organic Solvents

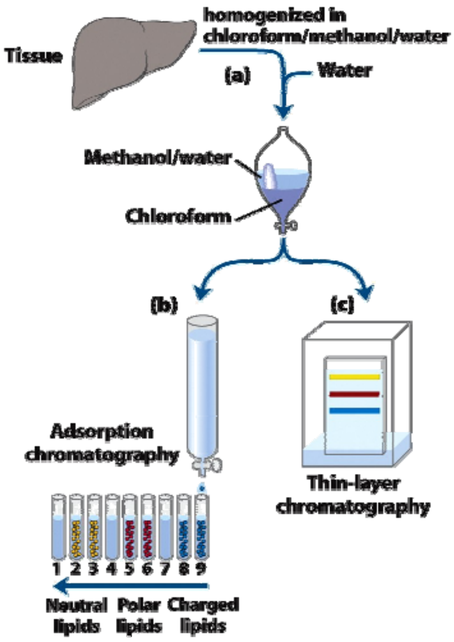
  (2) Adsorption Chromatography Separates Lipids of Different Polarity

  (3) Gas-Liquid Chromatography Resolves Mixtures of Volatile Lipid Derivatives

  (4) Specific Hydrolysis Aids in Determination of Lipid Structure

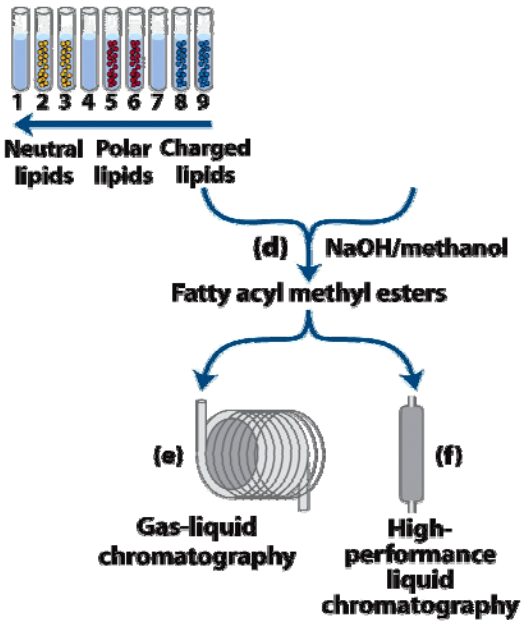
p.363

FIGURE 10–24 Part 1



p.364

FIGURE 10–24 Part 2



p.364

FIGURE 10–24 Part 3

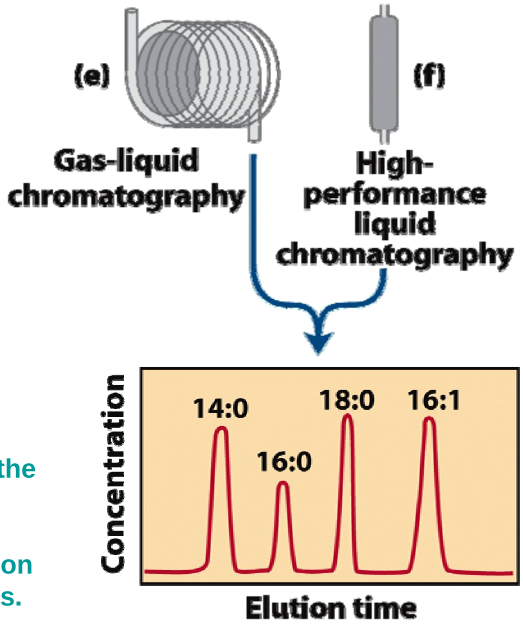


FIGURE 10–24 Common procedures in the extraction, separation, and identification of cellular lipids.

p.364

(5) Mass Spectrometry Reveals Complete Lipid Structure

(6) Lipidomics Seeks to Catalog All Lipids and Their Functions

- The structural lipids of membranes include both glycerophospholipids and sphingolipids, separate categories in Table 10–3. Each method of categorization has its advantages.

p.365

TABLE 10–3 Eight Major Categories of Biological Lipids

Category	Category code	Examples
Fatty acids	FA	Oleate, stearoyl-CoA, palmitoylcarnitine
Glycerolipids	GL	Di- and triacylglycerols
Glycerophospholipids	GP	Phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine
Sphingolipids	SP	Sphingomyelin, ganglioside GM2
Sterol lipids	ST	Cholesterol, progesterone, bile acids
Prenol lipids	PR	Farnesol, geraniol, retinol, ubiquinone
Saccharolipids	SL	Lipopolysaccharide
Polyketides	PK	Tetracycline, aflatoxin B_1

p.366