LIPIDS

❖ Lipids are a class of biological molecules defined by low solubility in water and high solubility in nonpolar solvents.

❖ Energy storage

❖ Key components of membranes

❖ Signal molecules in biological systems

❖ Lipids as Cofactors, and Pigments

Fatty Acids

Fatty Acids Are Hydrocarbon Derivatives

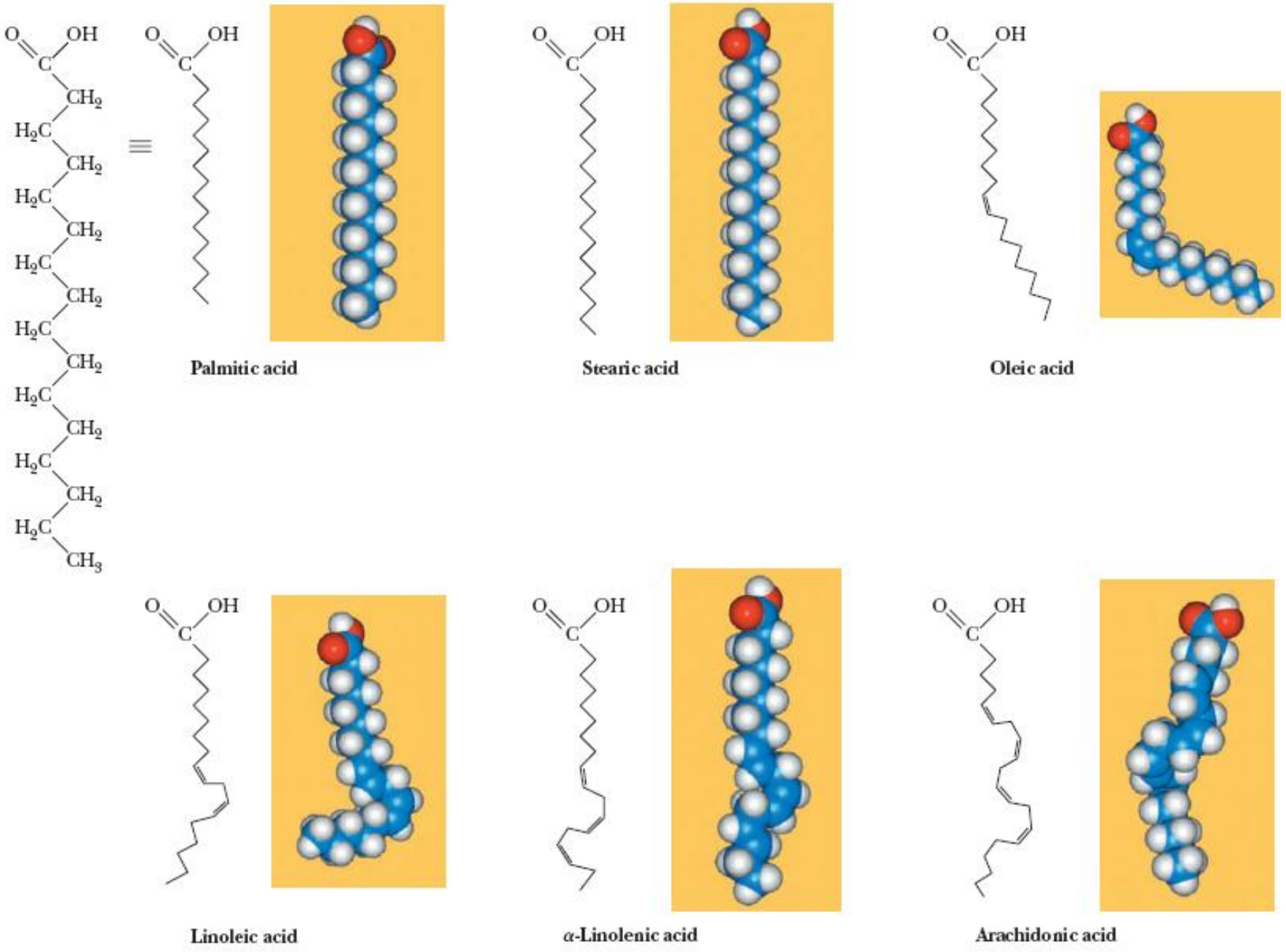
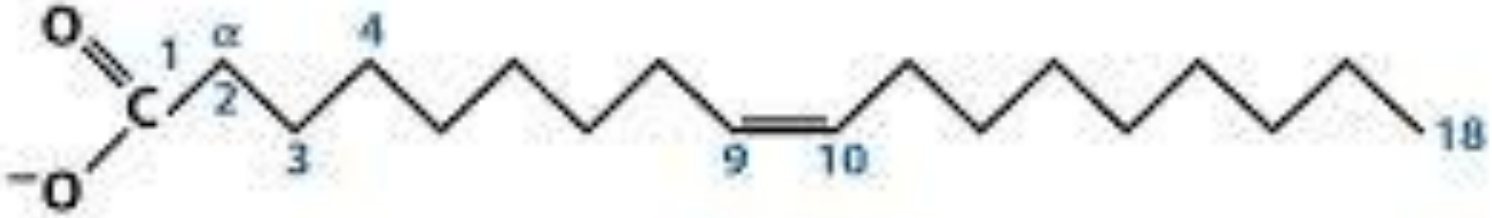


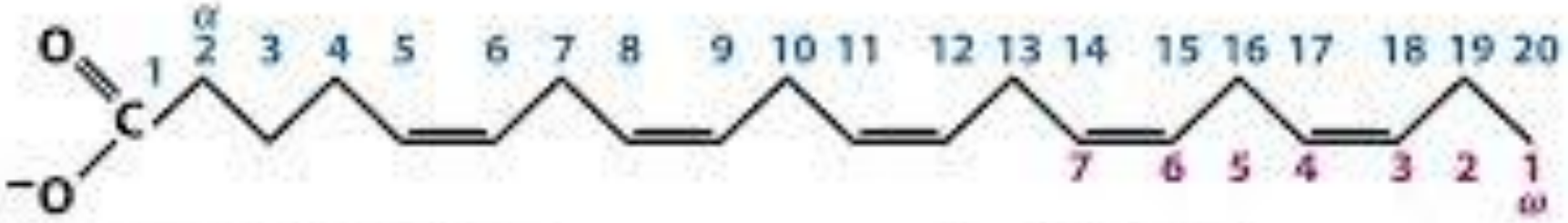
FIGURE 8.1 The structures of some typical fatty acids. Note that most natural fatty acids contain an even number of carbon atoms and that the double bonds are nearly always *cis* and rarely conjugated.

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

Carbon skeleton	*Structure**	*Systematic name†*	*Common name (derivation)*	*Melting point (°C)*
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6
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	1–0.5
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

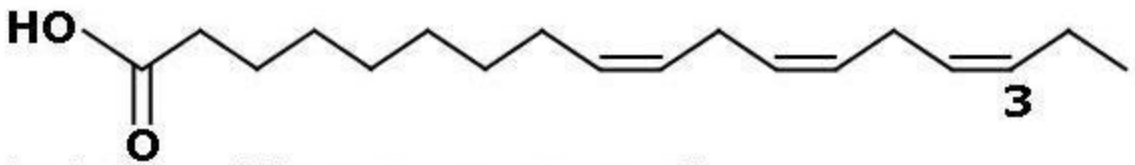


(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid

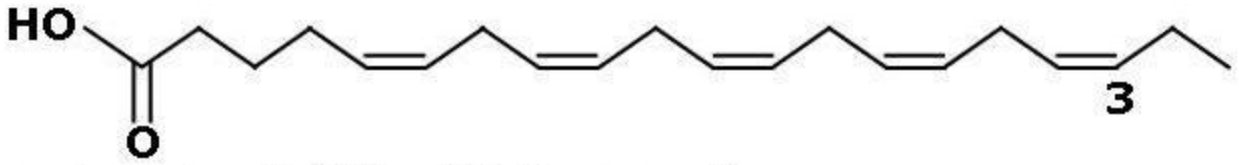


(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), an omega-3 fatty acid

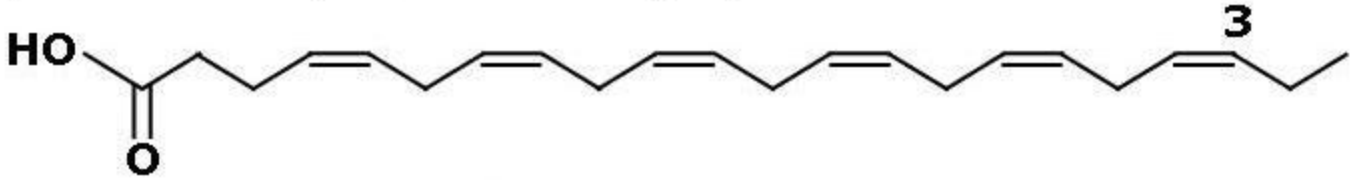
FIG. 1 OMEGA-3 AND OMEGA-6 FATTY ACIDS



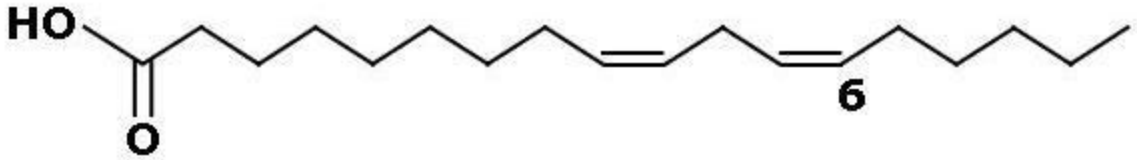
Alpha-linolenic acid (ALA, C18:3, omega-3)



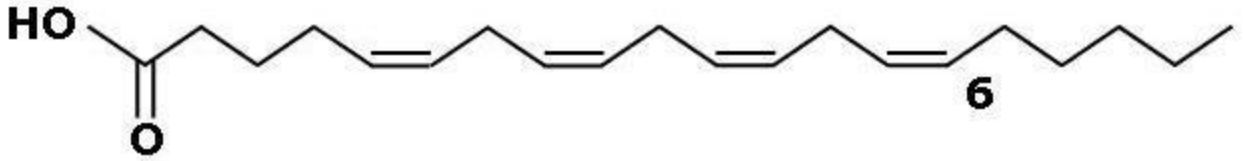
Eicosapentaenoic acid (EPA, C20:5, omega-3)



Docosahexaenoic acid (DHA, C22:6, omega-3)



Linoleic acid (LA, C18:2, omega-6)



Arachidonic acid (AA, C20:4, omega-6)

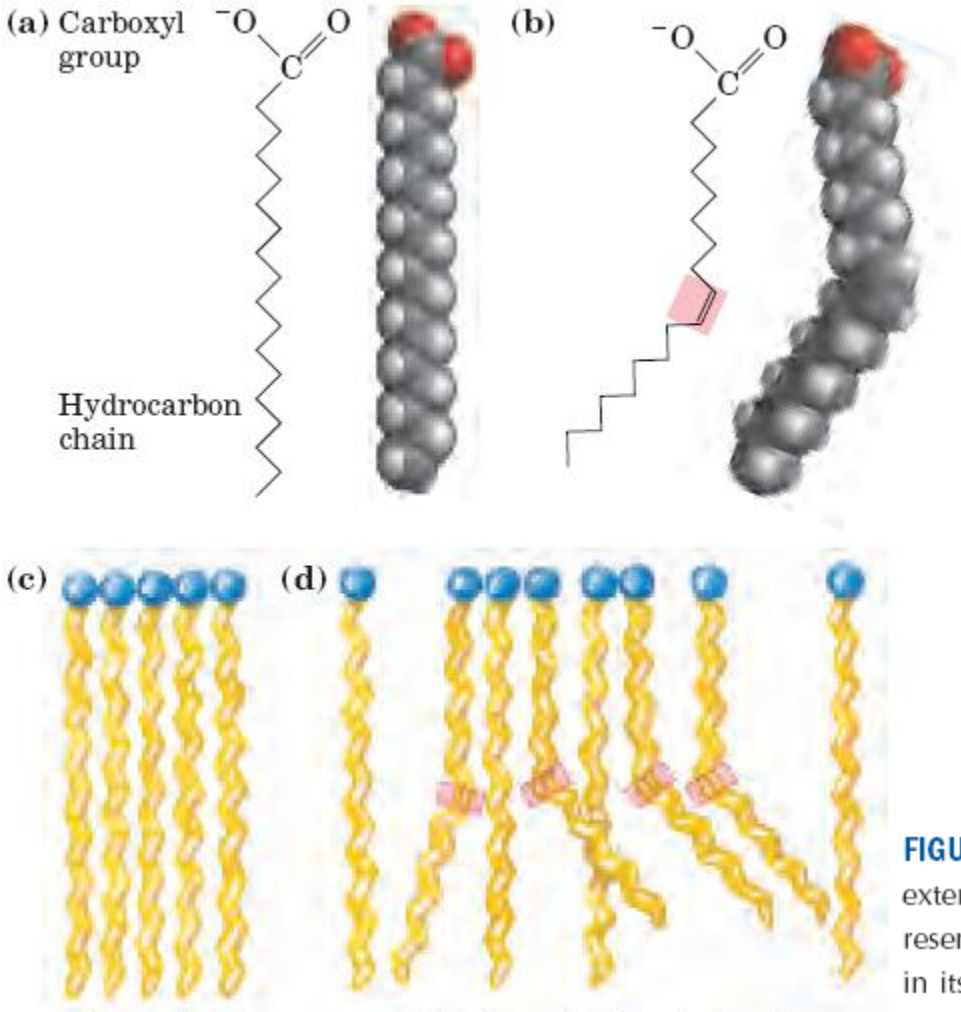


FIGURE 10–1 The packing of fatty acids into stable aggregates. The extent of packing depends on the degree of saturation. **(a)** Two representations of the fully saturated acid stearic acid (stearate at pH 7) in its usual extended conformation. Each line segment of the zigzag represents a single bond between adjacent carbons. **(b)** The cis double bond (shaded) in oleic acid (oleate) does not permit rotation and introduces a rigid bend in the hydrocarbon tail. All other bonds in the chain are free to rotate. **(c)** Fully saturated fatty acids in the extended form pack into nearly crystalline arrays, stabilized by many hydrophobic interactions. **(d)** The presence of one or more cis double bonds interferes with this tight packing and results in less stable aggregates.

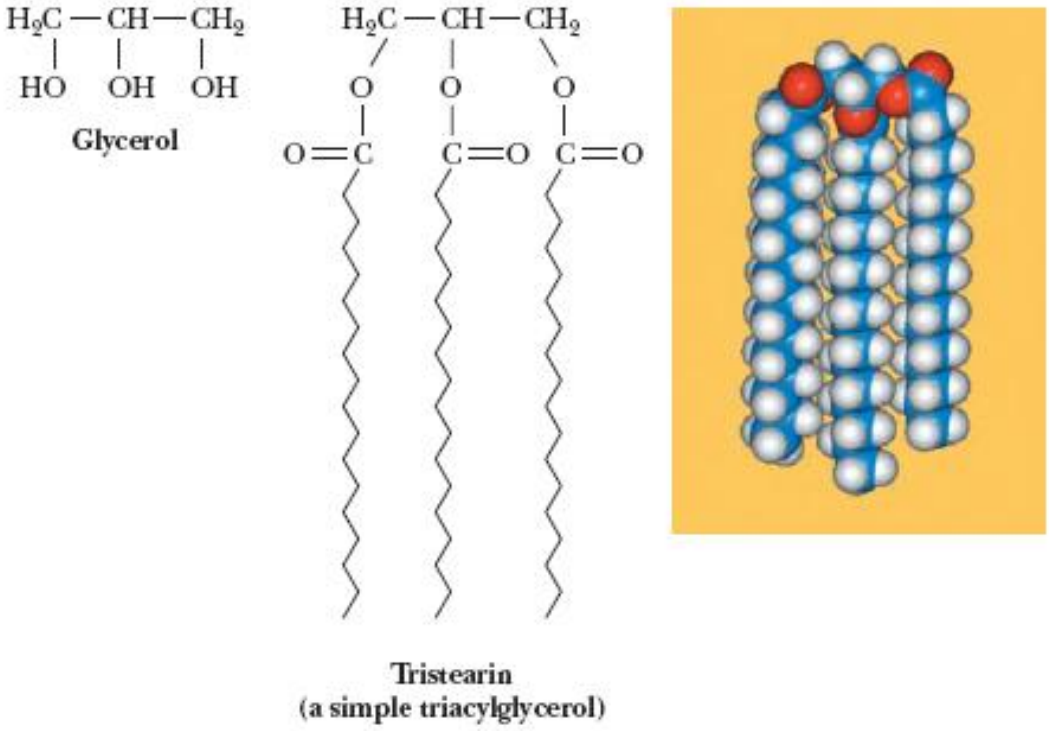
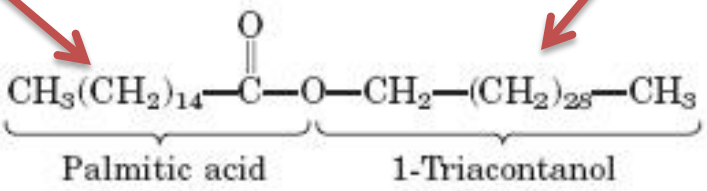


FIGURE 8.3 Triacylglycerols are formed from glycerol and fatty acids.

Fatty acids: C14 – C36

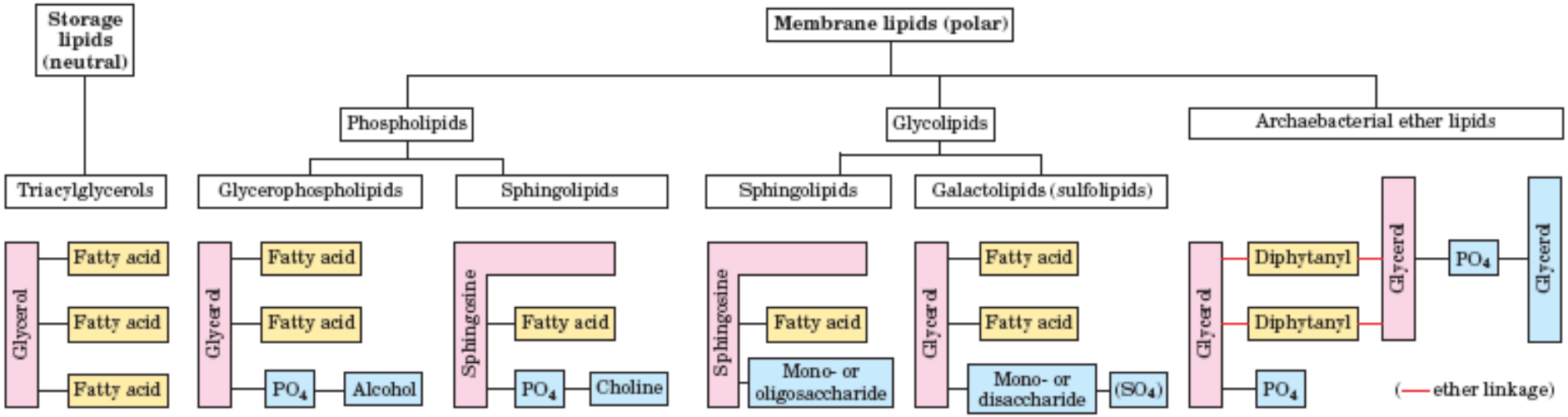
Alcohol: C16 – C30

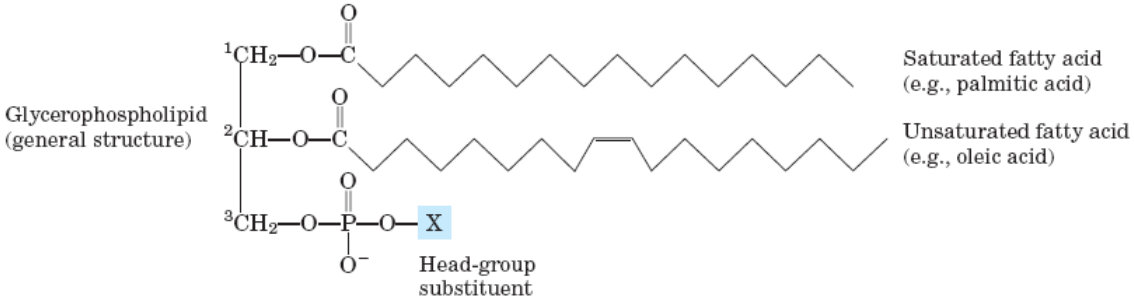


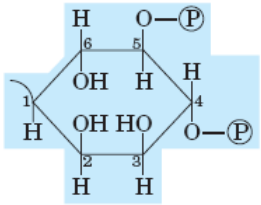
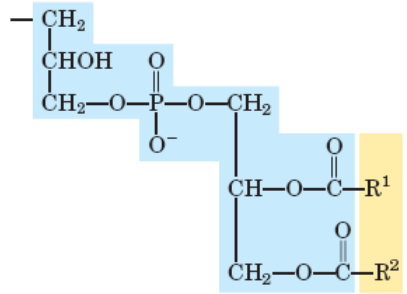
(a)

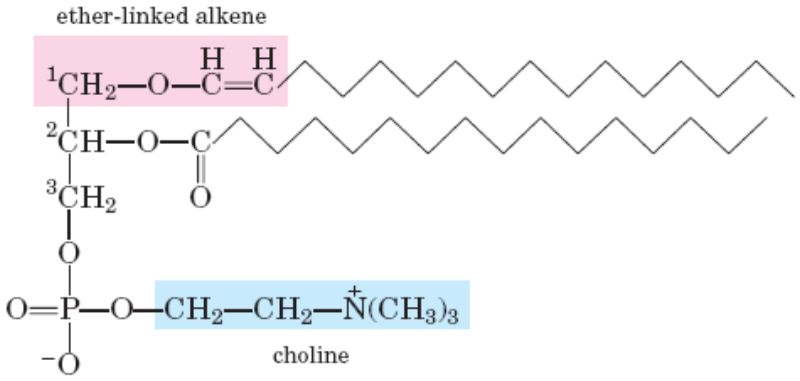
(b)

FIGURE 10–5 **Biological wax.** (a) Triacontanoylpalmitate, the major component of beeswax, is an ester of palmitic acid with the alcohol triacontanol. (b) A honeycomb, constructed of beeswax, is firm at 25 °C and completely impervious to water. The term "wax" originates in the Old English *weax*, meaning "the material of the honeycomb."

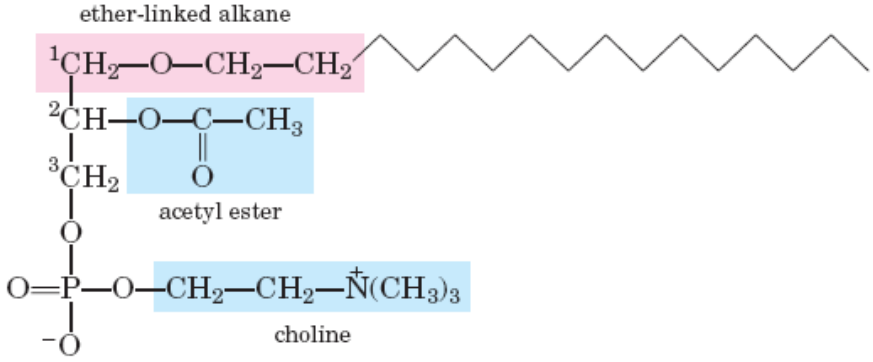

Storage lipids (neutral)
Membrane lipids (polar)
Phospholipids
Glycolipids
Archaebacterial ether lipids
Triacylglycerols
Glycerophospholipids
Sphingolipids
Sphingolipids
Galactolipids (sulfolipids)
Glycerol
Fatty acid
Fatty acid
Fatty acid
Glycerol
Fatty acid
Fatty acid
PO4
Alcohol
Sphingosine
Fatty acid
PO4
Choline
Sphingosine
Fatty acid
Mono- or oligosaccharide
Glycerol
Fatty acid
Fatty acid
Mono- or disaccharide
(SO4)
Glycerol
Diphytanyl
Diphytanyl
PO4
Glycerol
PO4
Glycerol
(— ether linkage)



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	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{OH}{CH}-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

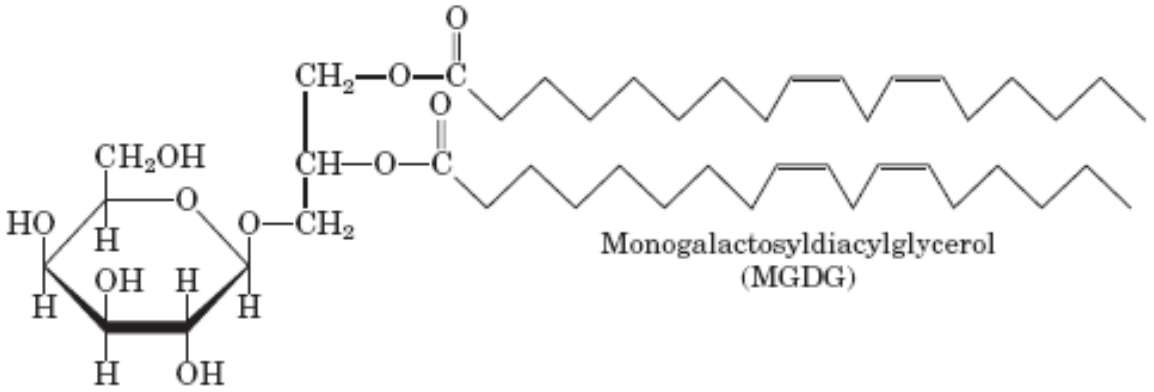


Plasmalogen

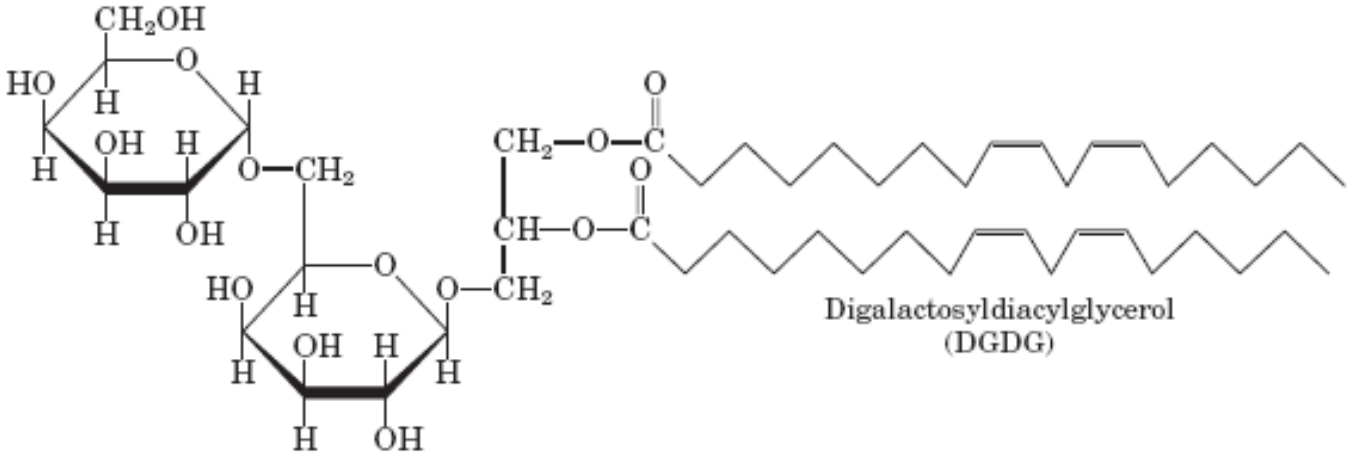


Platelet-activating factor

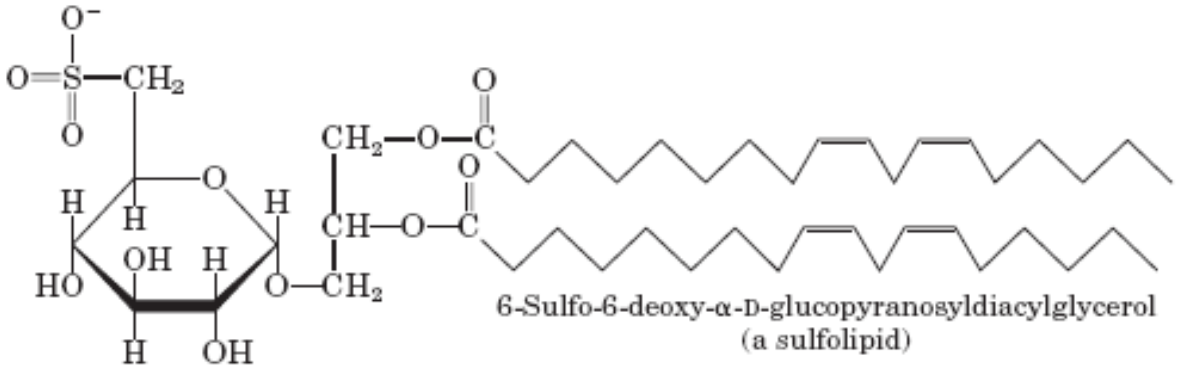
FIGURE 10–9 **Ether lipids.** Plasmalogens have an ether-linked alkenyl chain where most glycerophospholipids have an ester-linked fatty acid (compare Fig. 10–8). Platelet-activating factor has a long ether-linked alkyl chain at C-1 of glycerol, but C-2 is ester-linked to acetic acid, which makes the compound much more water-soluble than most glycerophospholipids and plasmalogens. The head-group alcohol is choline in plasmalogens and in platelet-activating factor.



Monogalactosyldiacylglycerol
(MGDG)



Digalactosyldiacylglycerol
(DGDG)



6-Sulfo-6-deoxy-α-D-glucopyranosyldiacylglycerol
(a sulfolipid)

FIGURE 10–10 Three glycolipids of chloroplast membranes. In monogalactosyldiacylglycerols (MGDGs) and digalactosyldiacylglycerols (DGDGs), almost all the acyl groups are derived from linoleic acid (18:2($\Delta^{9,12}$)) and the head groups are uncharged. In the sulfolipid 6-sulfo-6-deoxy-α-D-glucopyranosyldiacylglycerol, the sulfonate carries a fixed negative charge.

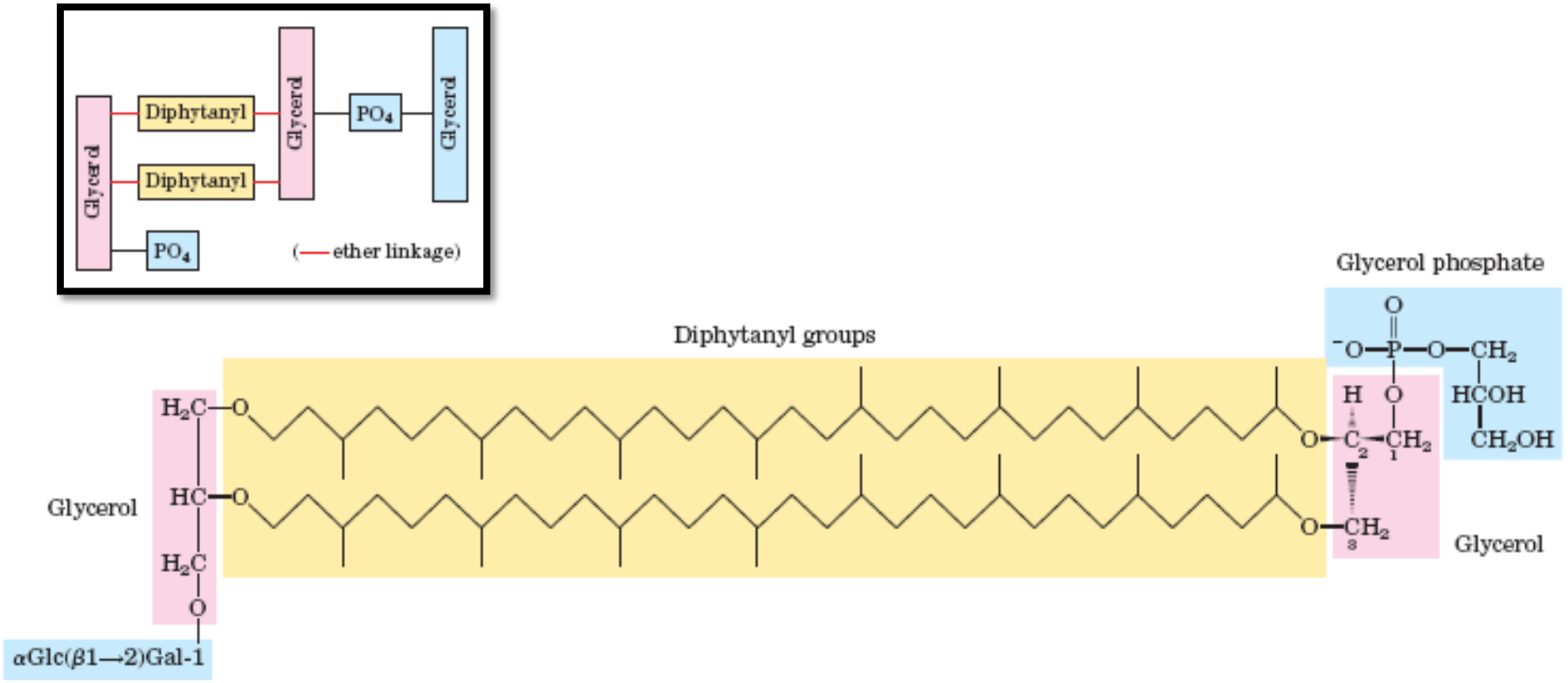
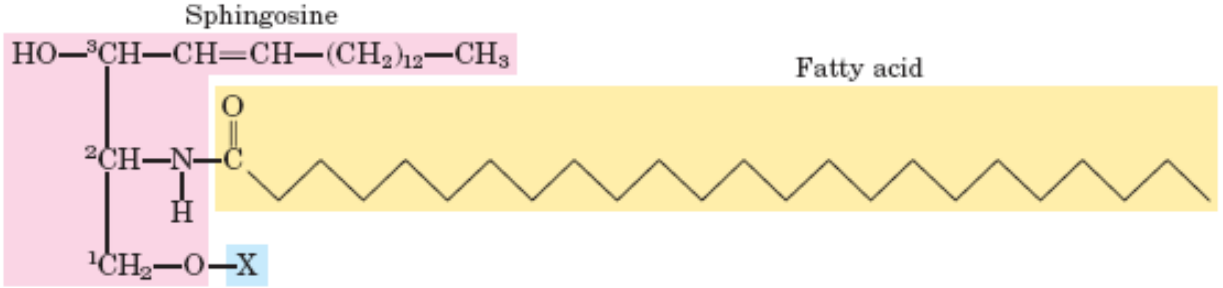
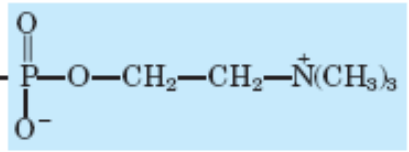
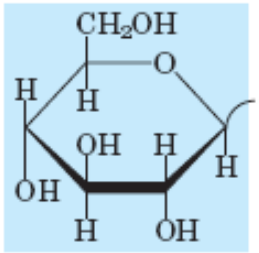
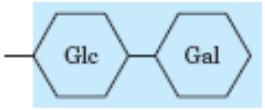
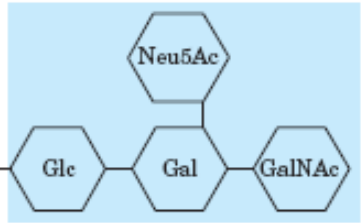
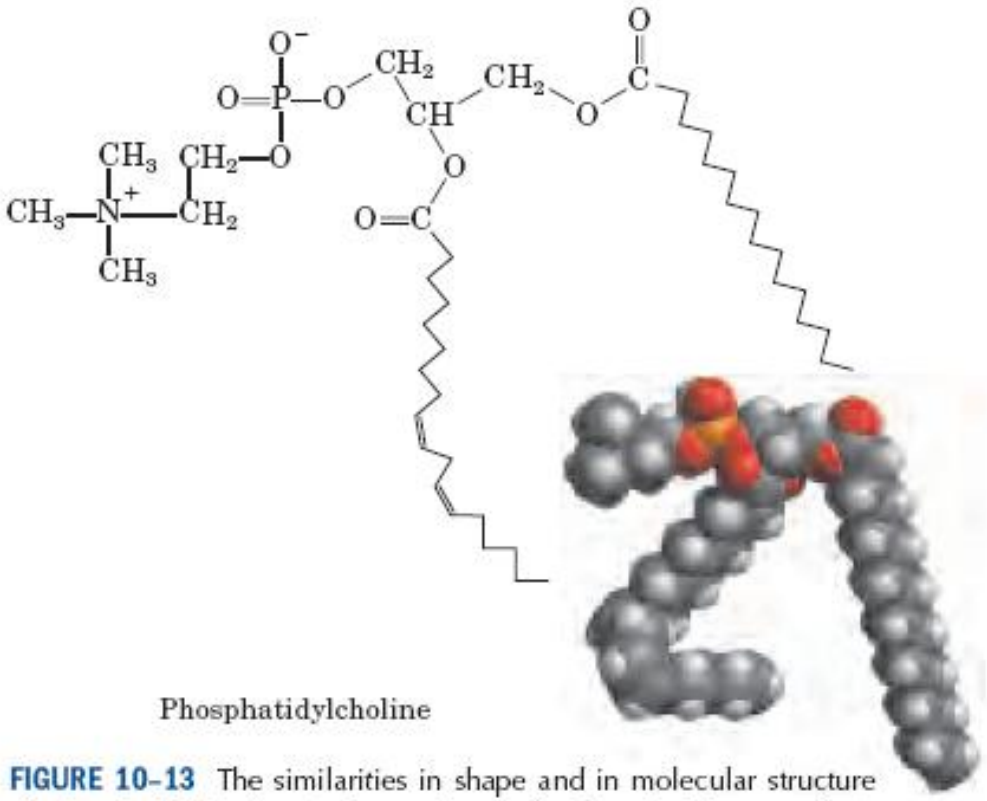


FIGURE 10–11 A typical membrane lipid of archaebacteria. In this diphytanyl tetraether lipid, the diphytanyl moieties (yellow) are long hydrocarbons composed of eight five-carbon isoprene groups condensed end-to-end (on the condensation of isoprene units, see Fig. 21–36; also, compare the diphytanyl groups with the 20-carbon phytol side chain of chlorophylls in Fig. 19–40a). In this extended form, the diphytanyl groups are about twice the length of a 16-carbon fatty acid typically found in the membrane lipids of eubacteria and eukaryotes. The glycerol moieties in the archaebacterial lipids are in the R configuration, in contrast to those of eubacteria and eukaryotes, which have the S configuration. Archaebacterial lipids differ in the substituents on the glycerols. In the molecule shown here, one glycerol is linked to the disaccharide α-glucopyranosyl-(1→2)-β-galactofuranose; the other glycerol is linked to a glycerol phosphate head group.

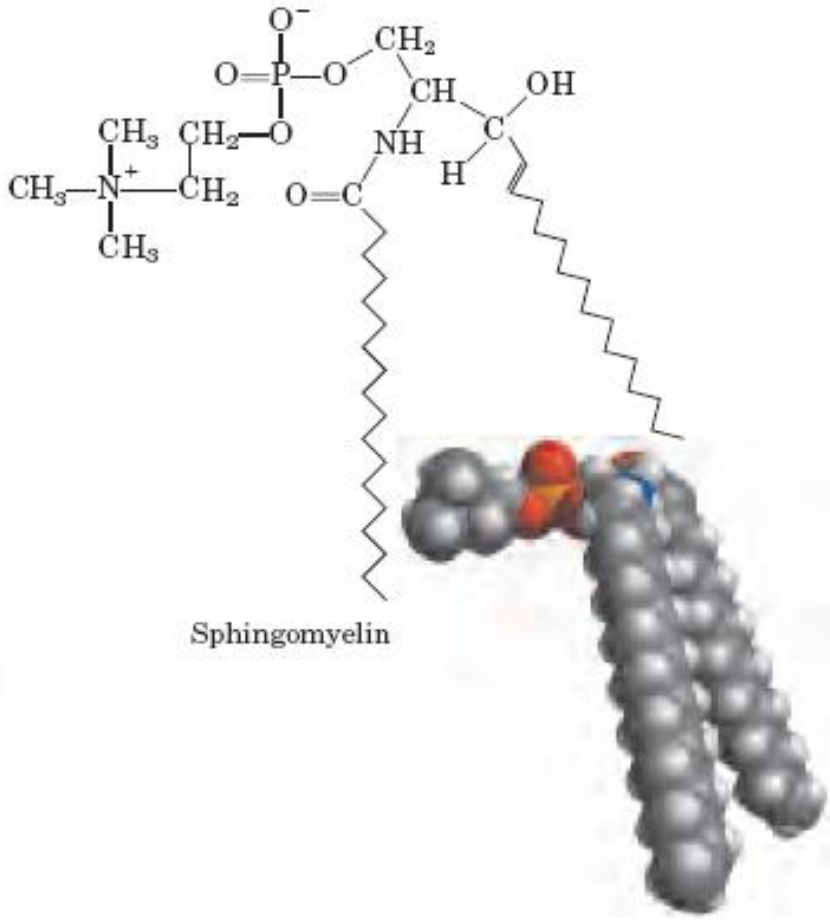
Sphingolipid (general structure)



Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	



Phosphatidylcholine



Sphingomyelin

FIGURE 10–13 The similarities in shape and in molecular structure of phosphatidylcholine (a glycerophospholipid) and sphingomyelin (a sphingolipid) are clear when their space-filling and structural formulas are drawn as here.

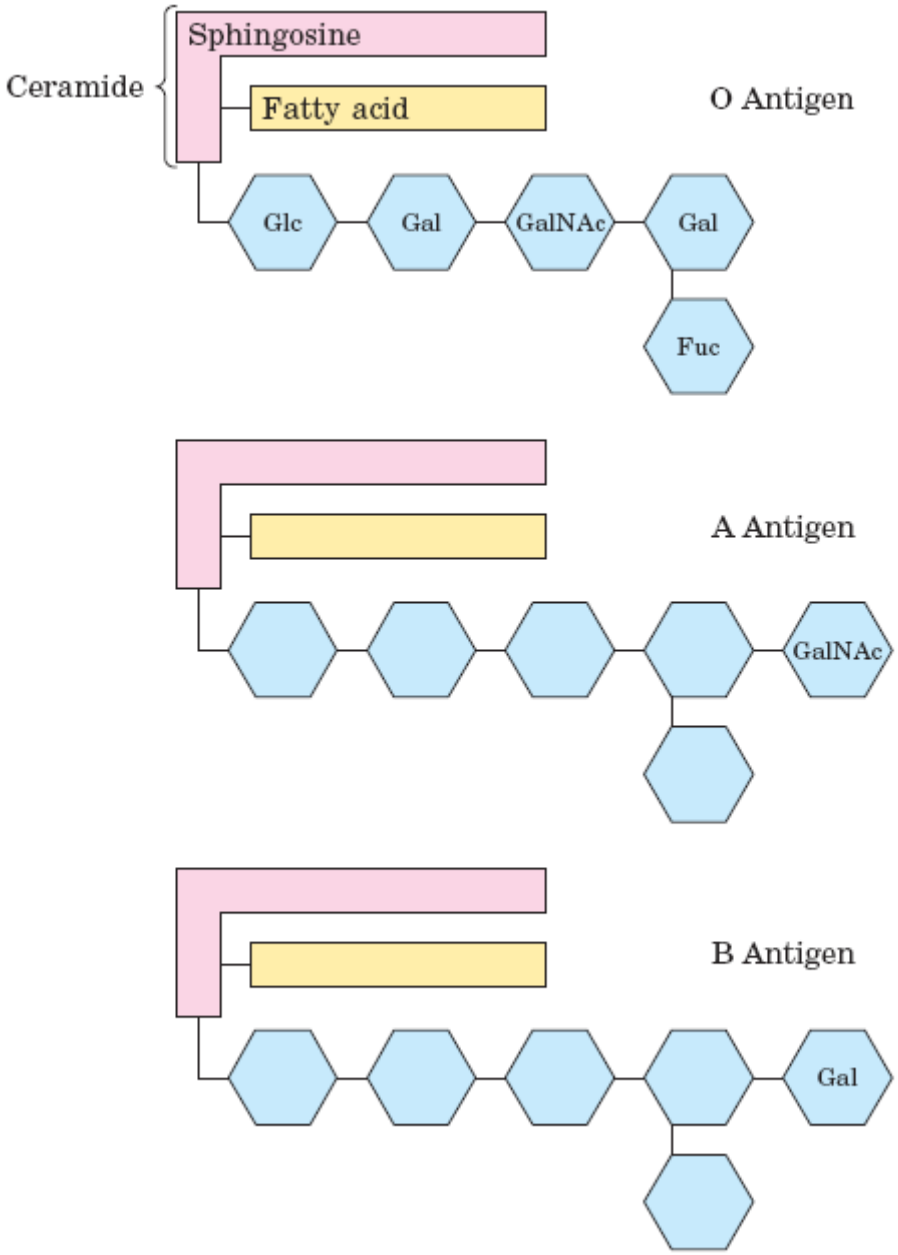


FIGURE 10–14 Glycosphingolipids as determinants of blood groups. The human blood groups (O, A, B) are determined in part by the oligosaccharide head groups (blue) of these glycosphingolipids. The same three oligosaccharides are also found attached to certain blood proteins of individuals of blood types O, A, and B, respectively. (Fuc represents the sugar fucose.)

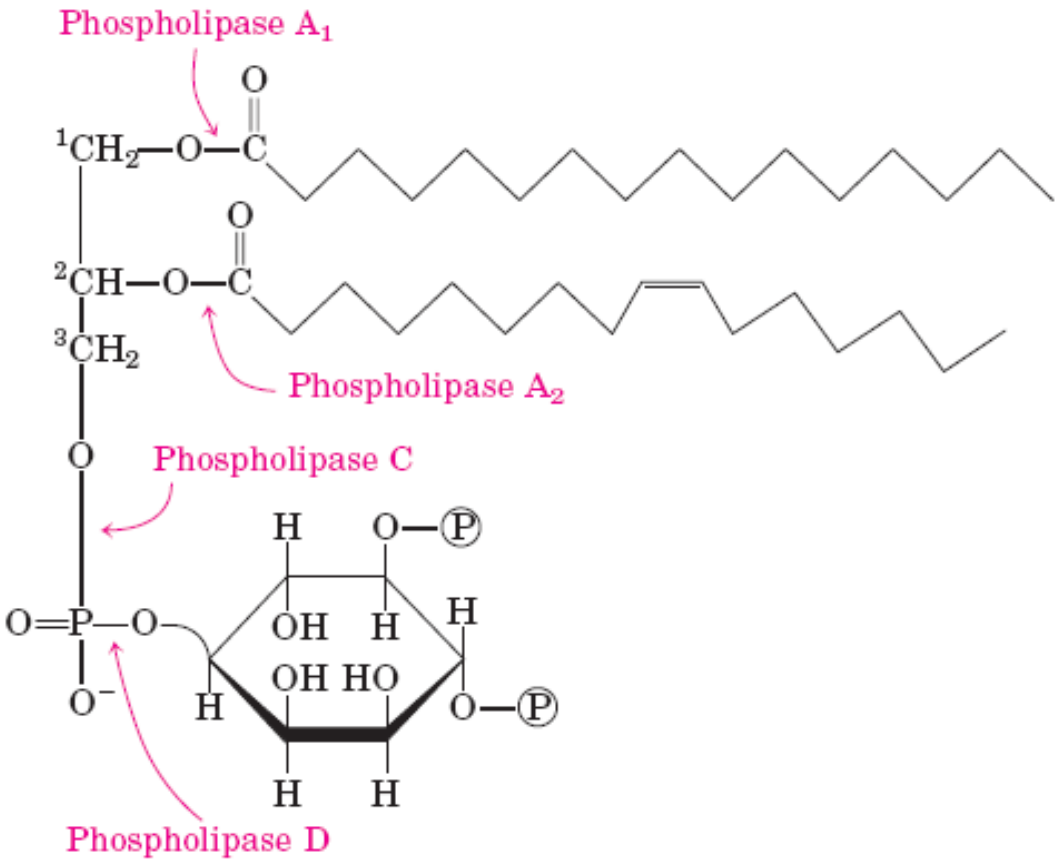


FIGURE 10–15 The specificities of phospholipases. Phospholipases A_1 and A_2 hydrolyze the ester bonds of intact glycerophospholipids at C-1 and C-2 of glycerol, respectively. Phospholipases C and D each split one of the phosphodiester bonds in the head group. Some phospholipases act on only one type of glycerophospholipid, such as phosphatidylinositol 4,5-bisphosphate (shown here) or phosphatidylcholine; others are less specific. When one of the fatty acids has been removed by a type A phospholipase, the second fatty acid is cleaved from the molecule by a lysophospholipase (not shown).

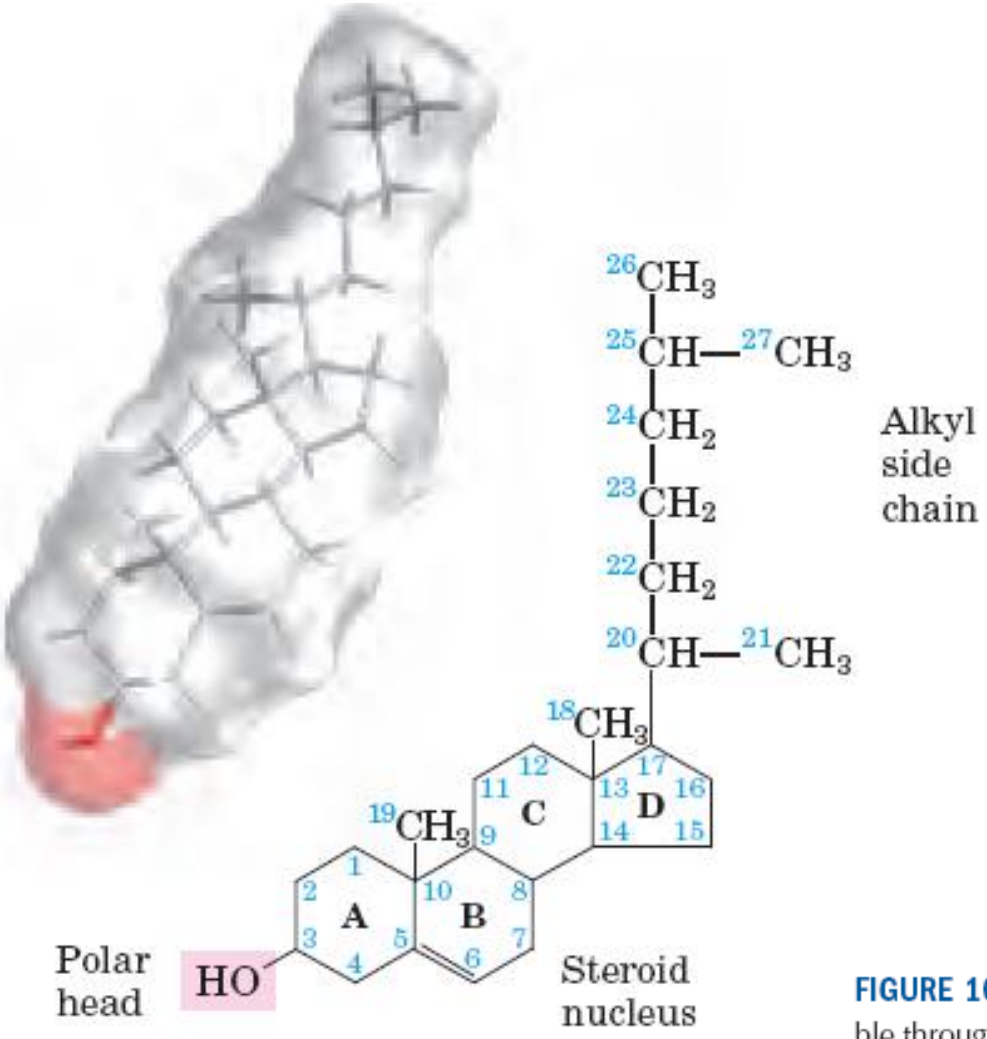
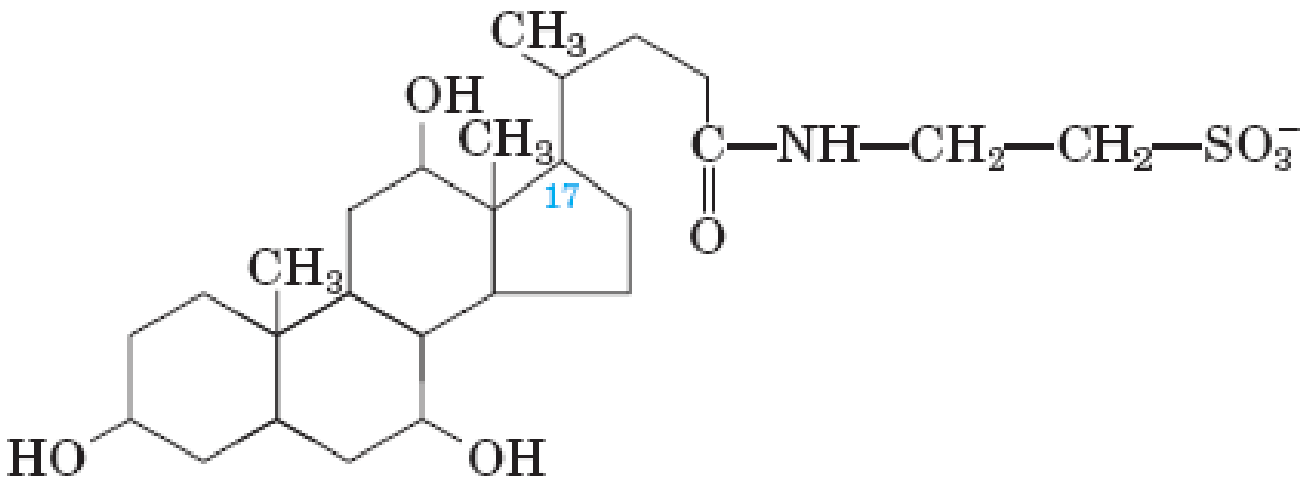
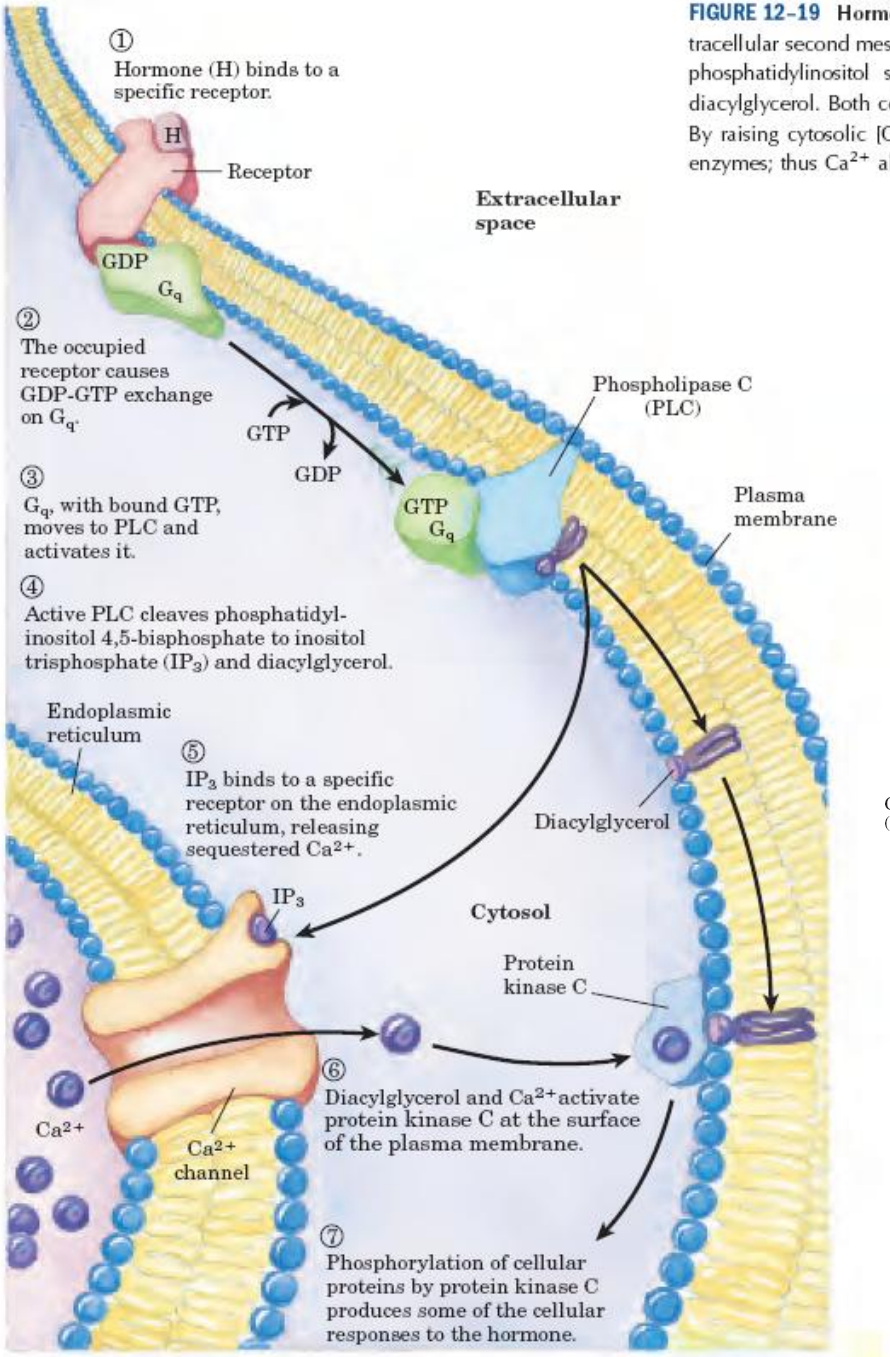


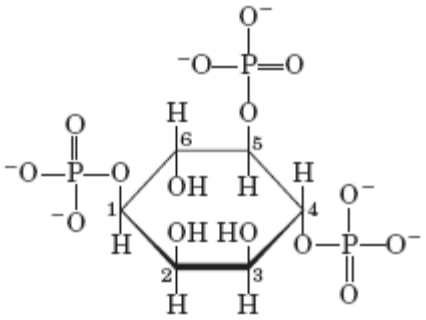
FIGURE 10–16 Cholesterol. The stick structure of cholesterol is visible through a transparent surface contour model of the molecule (from coordinates supplied by Dave Woodcock). In the chemical structure, the rings are labeled A through D to simplify reference to derivatives of the steroid nucleus, and the carbon atoms are numbered in blue. The C-3 hydroxyl group (pink in both representations) is the polar head group. For storage and transport of the sterol, this hydroxyl group condenses with a fatty acid to form a sterol ester.

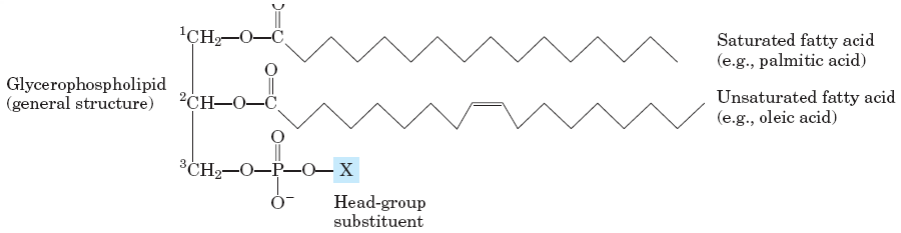


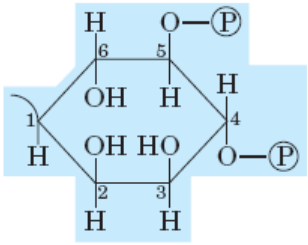
Taurocholic acid
(a bile acid)

FIGURE 12–19 Hormone-activated phospholipase C and IP_3. Two intracellular second messengers are produced in the hormone-sensitive phosphatidylinositol system: inositol 1,4,5-trisphosphate (IP_3) and diacylglycerol. Both contribute to the activation of protein kinase C. By raising cytosolic [Ca^{2+}], IP_3 also activates other Ca^{2+}-dependent enzymes; thus Ca^{2+} also acts as a second messenger.









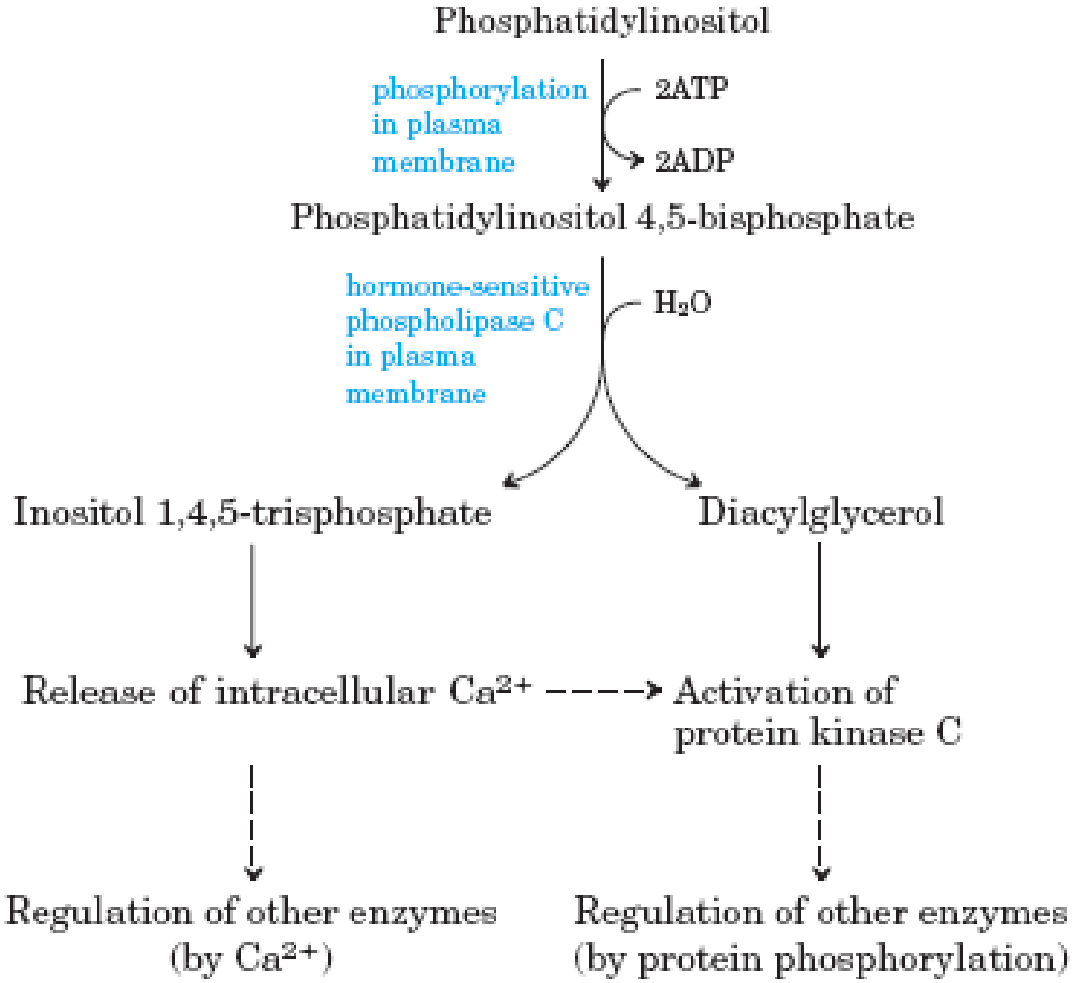
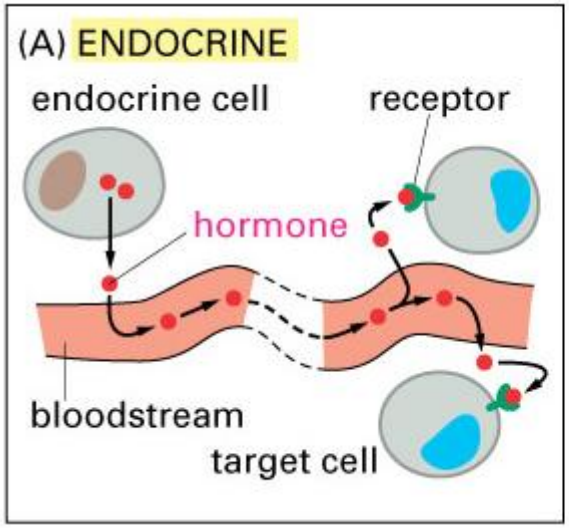
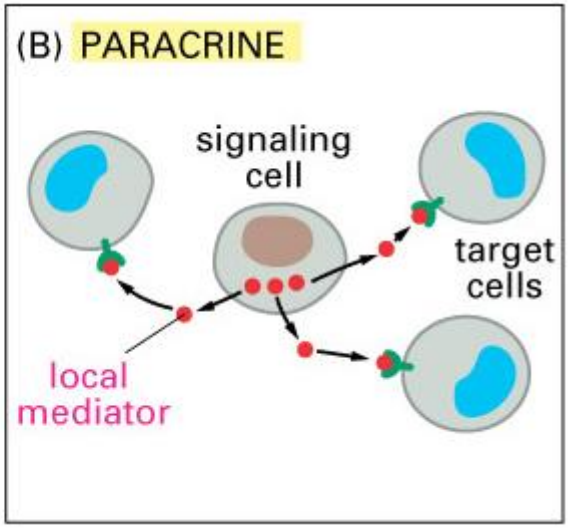
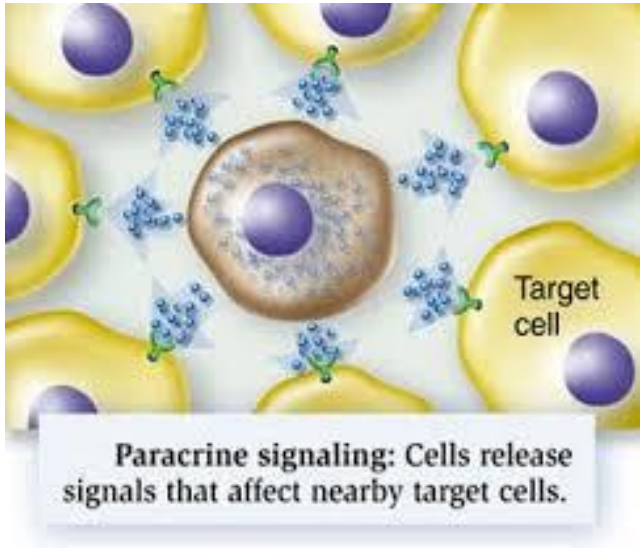


FIGURE 10–17 Phosphatidylinositols in cellular regulation. Phosphatidylinositol 4,5-bisphosphate in the plasma membrane is hydrolyzed by a specific phospholipase C in response to hormonal signals. Both products of hydrolysis act as intracellular messengers.

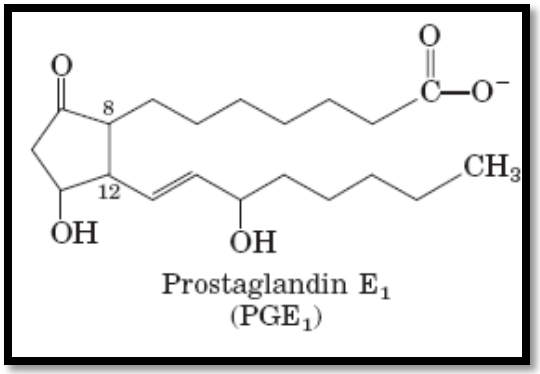
Eicosanoids

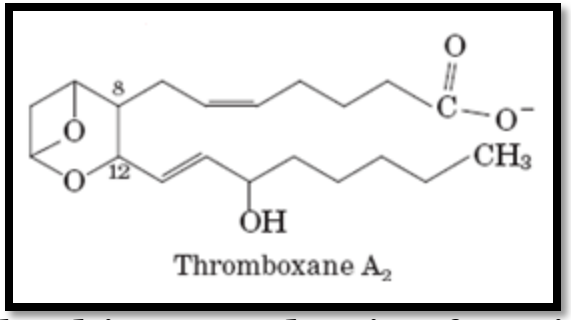


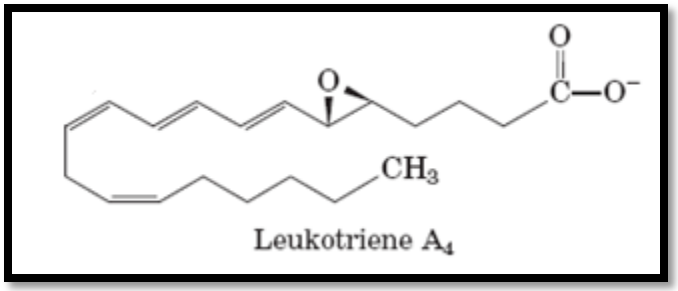




Eicosanoids Carry Messages to Nearby Cells







They are known to be involved in reproductive function; in the inflammation, fever, and pain associated with injury or disease; in the formation of blood clots and the regulation of blood pressure; in gastric acid secretion; and in a variety of other processes important in human health or disease.

All eicosanoids are derived from arachidonic acid (20:4(Δ5,8,11,14))

Greek *eikosi, "twenty*

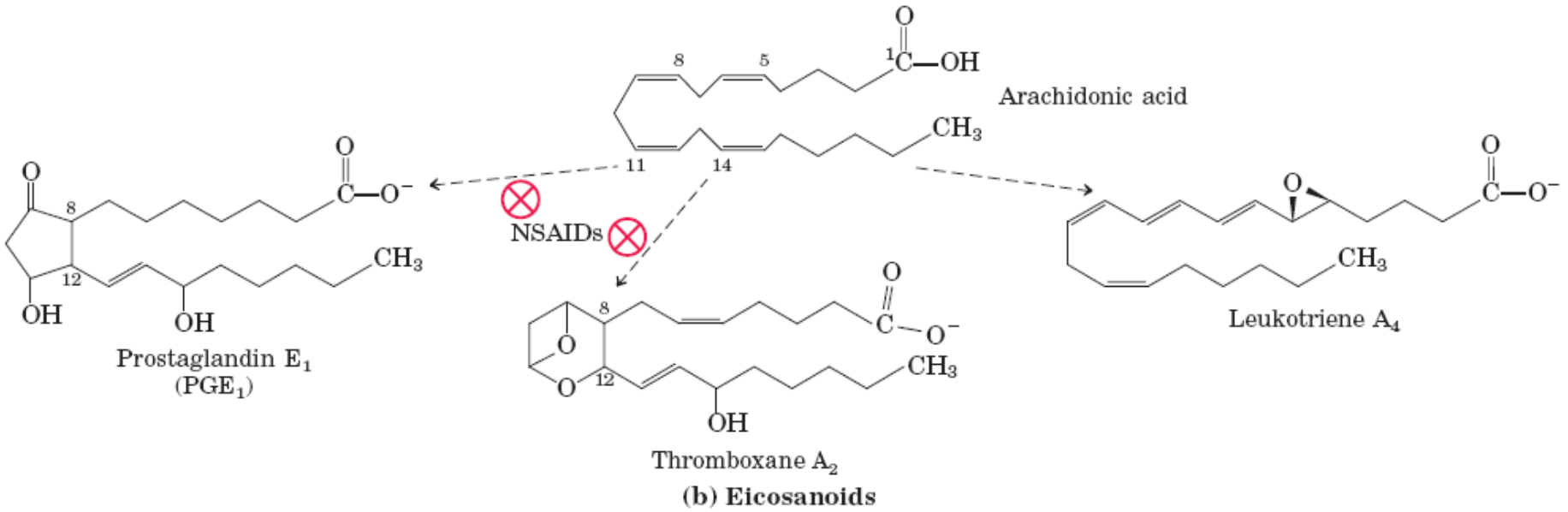
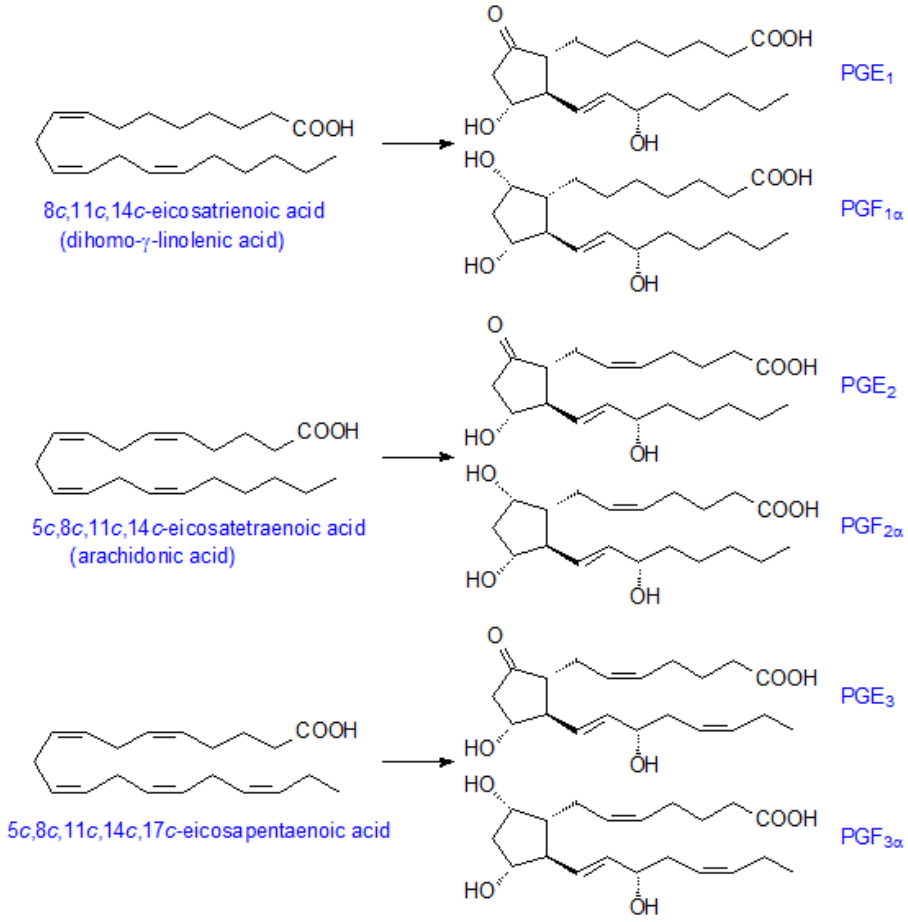


FIGURE 10–18 Arachidonic acid and some eicosanoid derivatives. **(a)** In response to hormonal signals, phospholipase A_2 cleaves arachidonic acid–containing membrane phospholipids to release arachidonic acid (arachidonate at pH 7), the precursor to various eicosanoids. **(b)** These compounds include prostaglandins such as PGE_1, in which C-8 and C-12 of arachidonate are joined to form the characteristic five-membered ring. In thromboxane A_2, the C-8 and C-12 are joined and an oxygen atom is added to form the six-membered ring. Leukotriene A_4 has a series of three conjugated double bonds. Nonsteroidal antiinflammatory drugs (NSAIDs) such as aspirin and ibuprofen block the formation of prostaglandins and thromboxanes from arachidonate by inhibiting the enzyme cyclooxygenase (prostaglandin H_2 synthase).

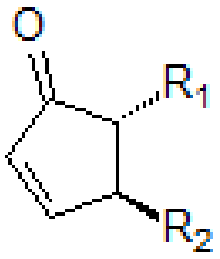
Prostaglandins (PG)



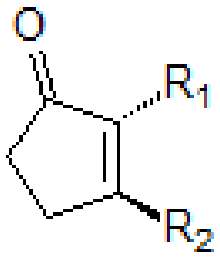
➢**Prostaglandins (PG)** contain a five-carbon ring originating from the chain of arachidonic acid.

➢Their name derives from the prostate gland, the tissue from which they were first isolated.

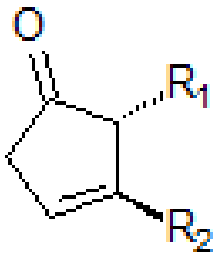
➢Two groups of prostaglandins were originally defined: **PGE**, for *ether-soluble, and **PGF,** for phosphate* (*fosfat in Swedish) buffer–soluble. Each group contains* numerous subtypes, named PGE1, PGE2, and so forth.



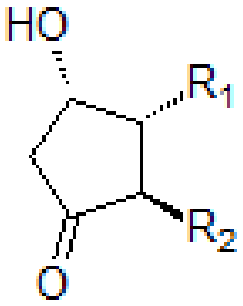
PGA



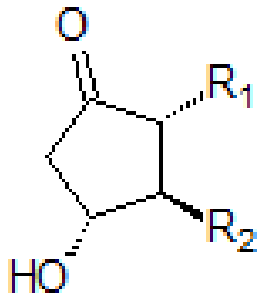
PGB



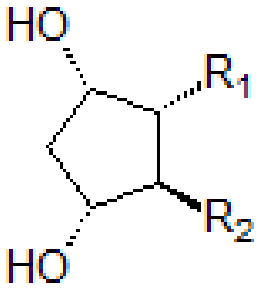
PGC



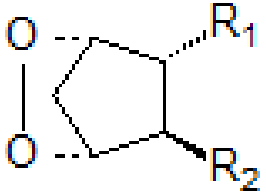
PGD



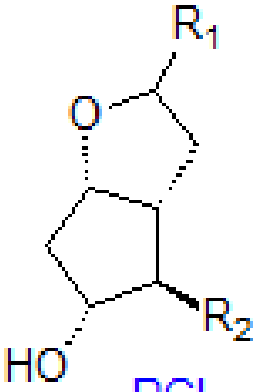
PGE



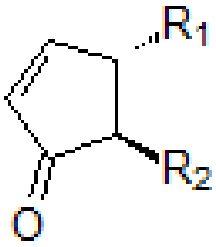
PGFα



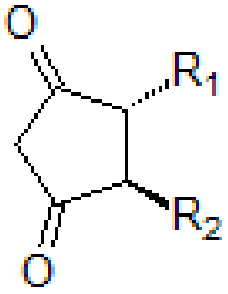
PGG
PGH



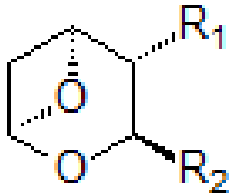
PGI



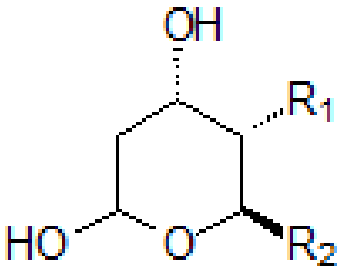
PGJ



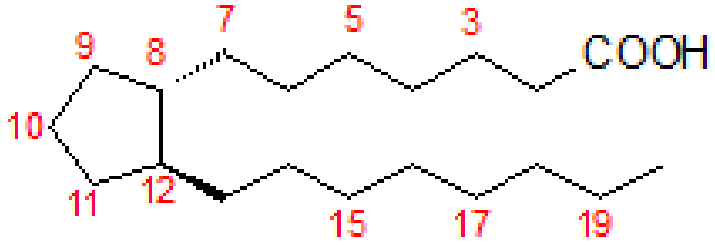
PGK



TXA



TXB

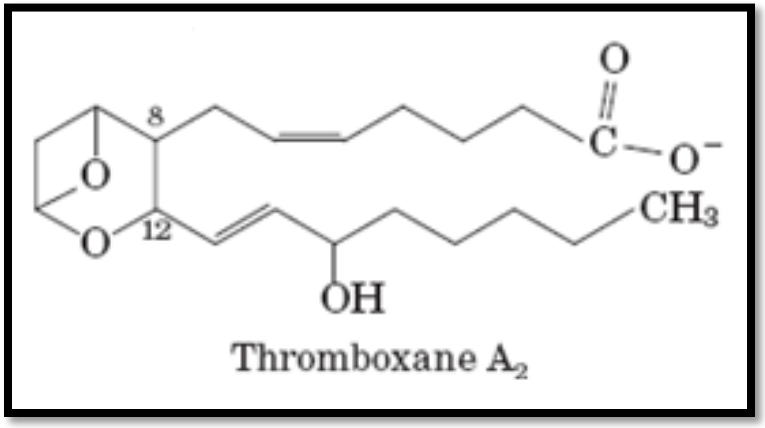


prostanoic acid

Prostaglandins (PG)

- Prostaglandins act in many tissues by regulating the synthesis of the intracellular messenger 3,5-cyclic AMP (cAMP). Because cAMP mediates the action of diverse hormones, the prostaglandins affect a wide range of cellular and tissue functions.
- Some prostaglandins stimulate contraction of the smooth muscle of the uterus during menstruation.
- Others affect blood flow to specific organs, the wake-sleep cycle, and the responsiveness of certain tissues to hormones such as epinephrine and glucagon.
- Prostaglandins in a third group elevate body temperature (producing fever) and cause inflammation and pain.

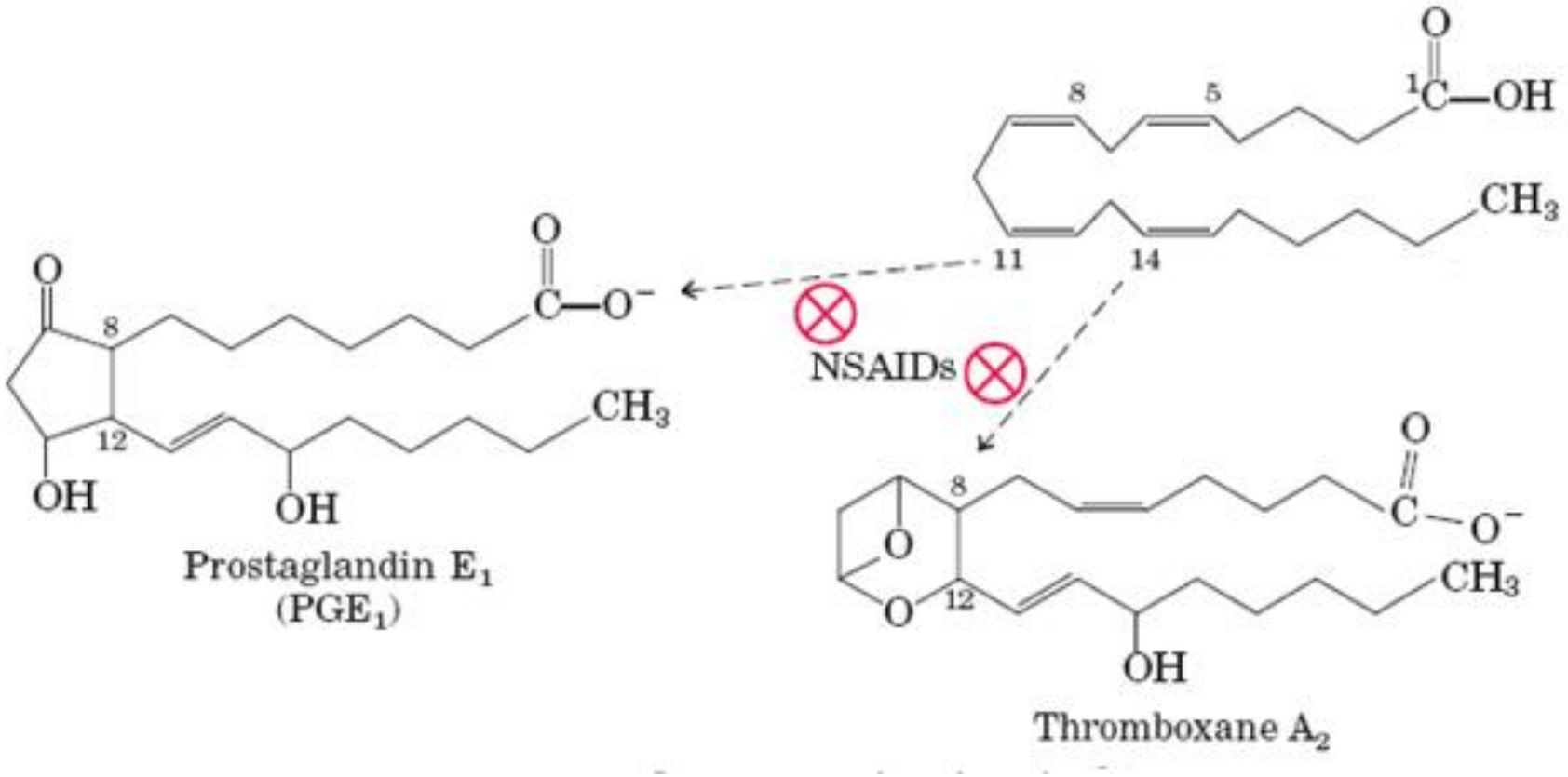
Thromboxanes



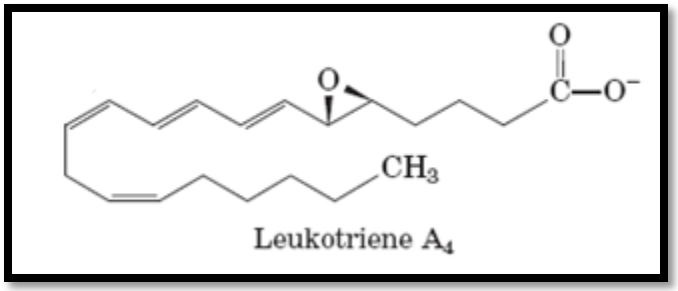
Thromboxane A_2

- The 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.

➢The nonsteroidal anti-inflammatory drugs (**NSAIDs**)— **aspirin**, **ibuprofen**, and **meclofenamate**, inhibit the enzyme prostaglandin H2 synthase (also called cyclooxygenase or COX), which catalyzes an early step in the pathway from arachidonate to prostaglandins and thromboxanes

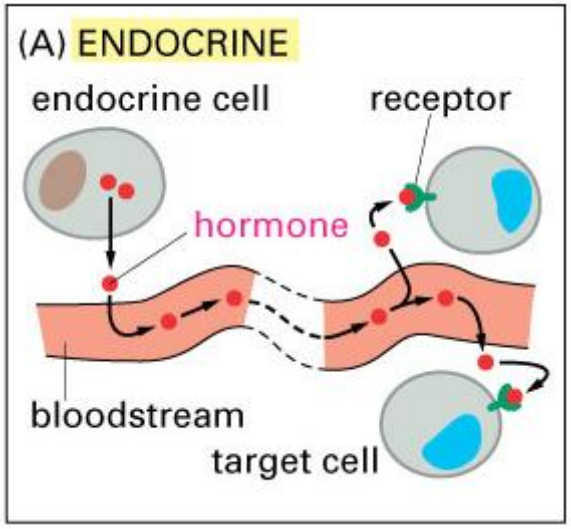


Leukotrienes

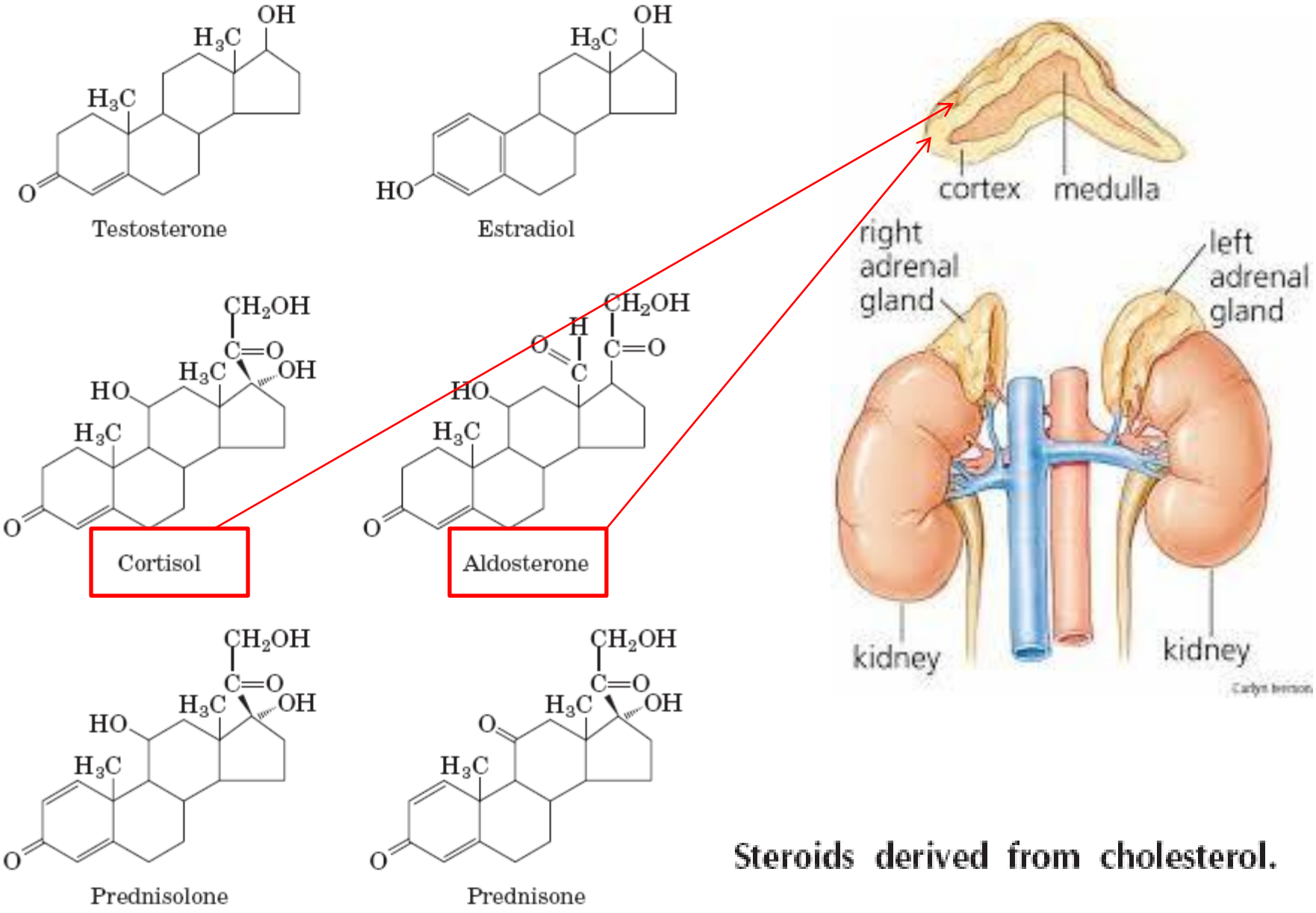


Leukotriene A_4

- Contain **three** conjugated double bonds.
- They are powerful biological signals. For example, leukotriene D4, derived from leukotriene A4, induces contraction of the muscle lining the airways to the lung. Overproduction of leukotrienes causes asthmatic attacks.
- Leukotriene synthesis is one target of **antiasthmatic** drugs such as prednisone.
- The strong contraction of the smooth muscles of the lung that occurs during anaphylactic shock is part of the potentially fatal allergic reaction in individuals hypersensitive to bee stings, penicillin, or other agents

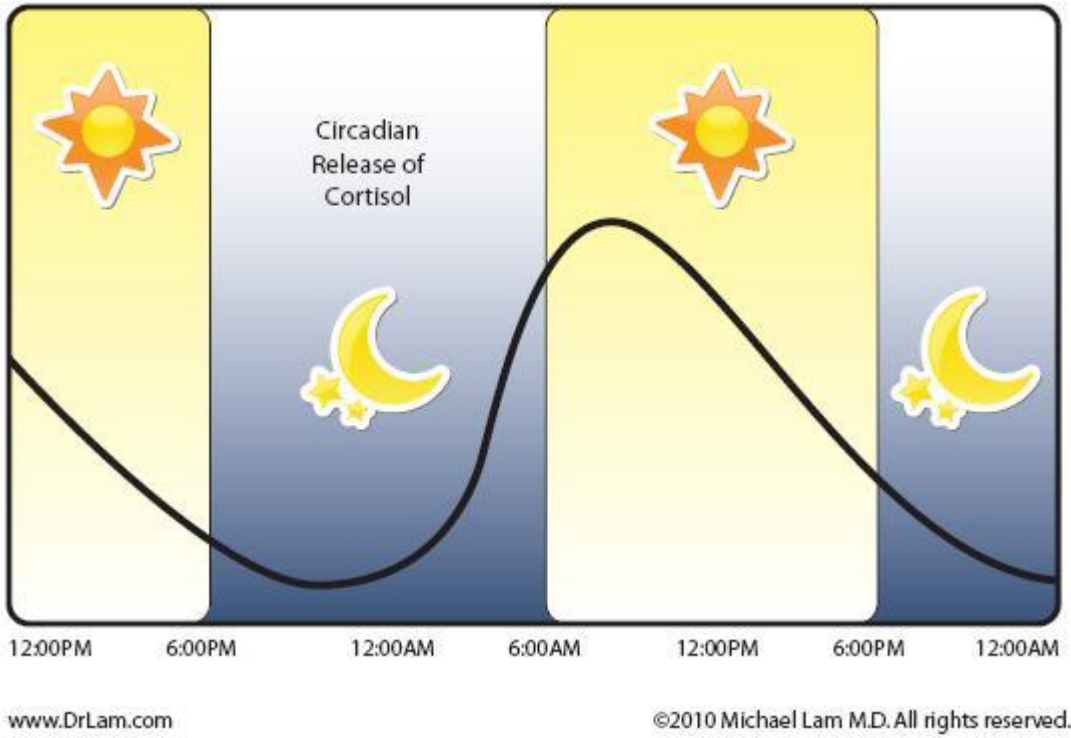


Steroid Hormones Carry Messages between Tissues



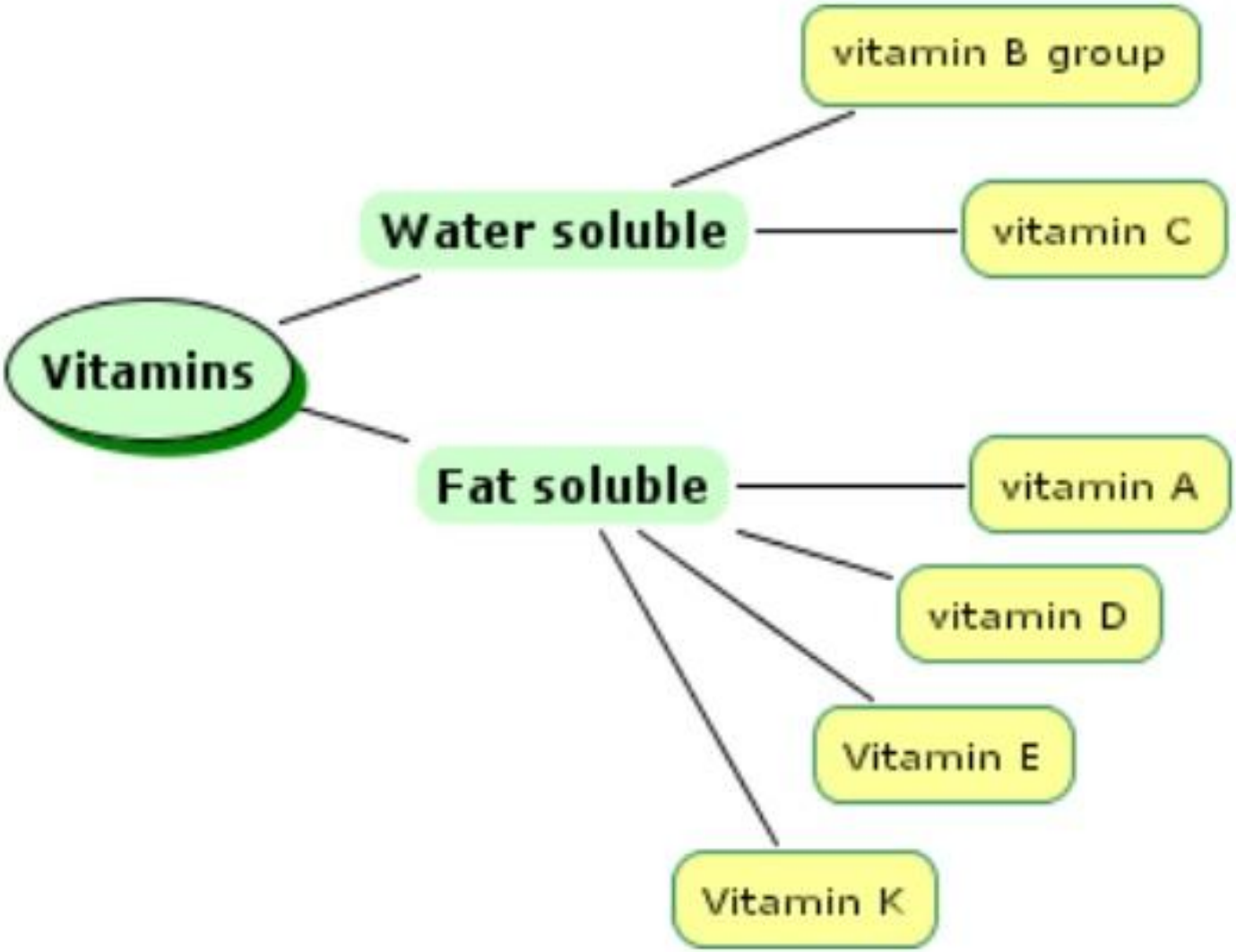
Steroids derived from cholesterol.

Steroids are oxidized derivatives of sterols; they have the sterol nucleus but lack the alkyl chain attached to ring D of cholesterol, and they are more polar than cholesterol.



Cortisol is a steroid hormone that is produced by the adrenal glands in a response to stress.

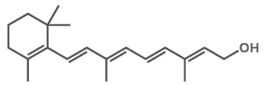
CLASSIFICATION OF VITAMINS



THE CHEMICAL STRUCTURES OF VITAMINS

Vitamins are the essential nutrients that our body needs in small amounts. More specifically, an organic compound is defined as a vitamin when it is required by an organism, but not synthesised by that organism in the required amounts (or at all). There are thirteen recognised vitamins.

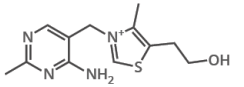
VITAMIN A



RETINOL
active form in mammalian tissues

Important for eyesight. Also strengthens immune system and keeps skin and linings of parts of the body healthy.

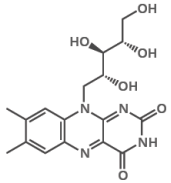
VITAMIN B1



THIAMIN
can also occur in pyrophosphate ester form

Used to keep nerves & muscle tissue healthy. Also important for processing of carbohydrates and some proteins.

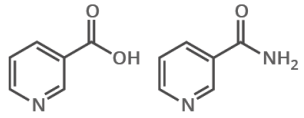
VITAMIN B2



RIBOFLAVIN
excess turns urine bright yellow

Important for body growth, red blood cell production, and keeping the eyes healthy. Also helps processing of carbohydrates.

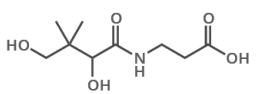
VITAMIN B3



NICOTINIC ACID **NICOTINEAMIDE**
niacin is collective name for these compounds

Helps with digestion and digestive system health. Also helps with the processing of carbohydrates.

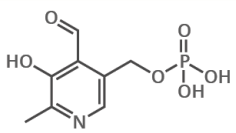
VITAMIN B5



PANTOTHENIC ACID
can also occur in pyrophosphate ester

Important for manufacturing red blood cells and maintaining a healthy digestive system. Also helps process carbohydrates.

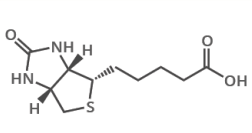
VITAMIN B6



PYRIDOXAL PHOSPHATE
active form in mammalian tissues

Helps make some brain chemicals; needed for normal brain function. Also helps make red blood cells and immune system cells.

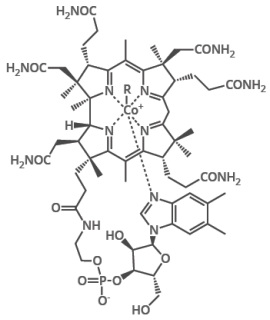
VITAMIN B7



BIOTIN
produced by intestinal bacteria

Needed for metabolism of various compounds. Often recommended for strengthening hair, but evidence is variable.

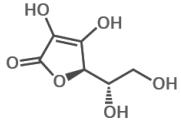
VITAMIN B12



COBALAMIN
usually contains CN as the R group

Important for the nervous system, for making red blood cells, and helps in the production of DNA and RNA.

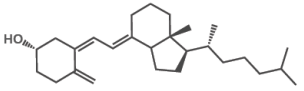
VITAMIN C



ASCORBIC ACID
deficiency can cause scurvy

Important for a healthy immune system; helps produce collagen, used to make skin and other tissues. Also helps wound healing.

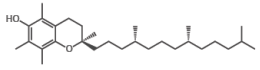
VITAMIN D



CHOLECALCIFEROL
natural form; different form used in supplements

Important for bone health and maintaining the immune system function. May also have a preventative role in cancers.

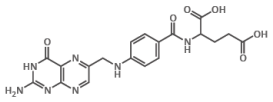
VITAMIN E



ALPHA-TOCOPHEROL
group includes tocopherols & tocotrienols

An antioxidant that helps prevent damage to cells and may have a preventative role in cancer. Also helps make red blood cells.

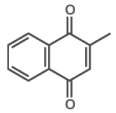
VITAMIN B9



FOLIC ACID
found as tetrahydrofolate in food

Important for brain function & mental health. Aids production of DNA & RNA. Important when tissues are growing quickly.

VITAMIN K



MENADIONE
all K vitamins are menadione or derivatives

Helps blood clot properly, & plays a key role in bone health. Newborns recieve vitamin K injections to prevent bleeding.

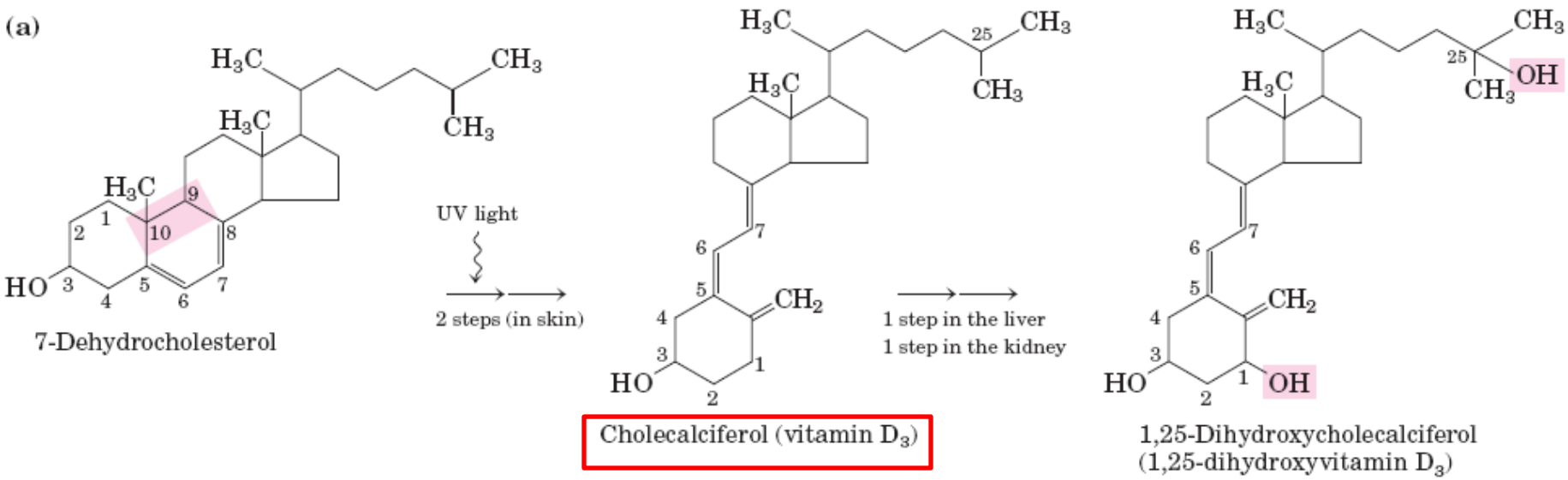
Key

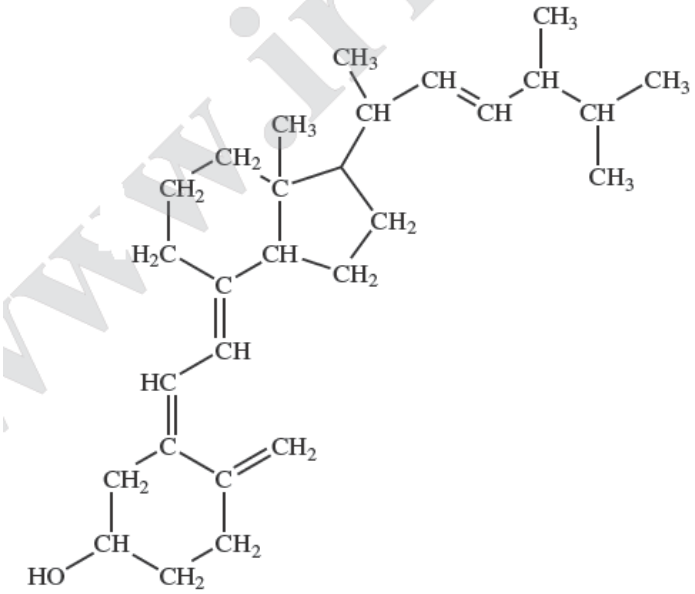
Vitamins can be divided broadly into two classes.

WATER SOLUBLE VITAMINS
These vitamins are not stored in the body. As such, generally, they are required more frequently than the fat soluble vitamins.

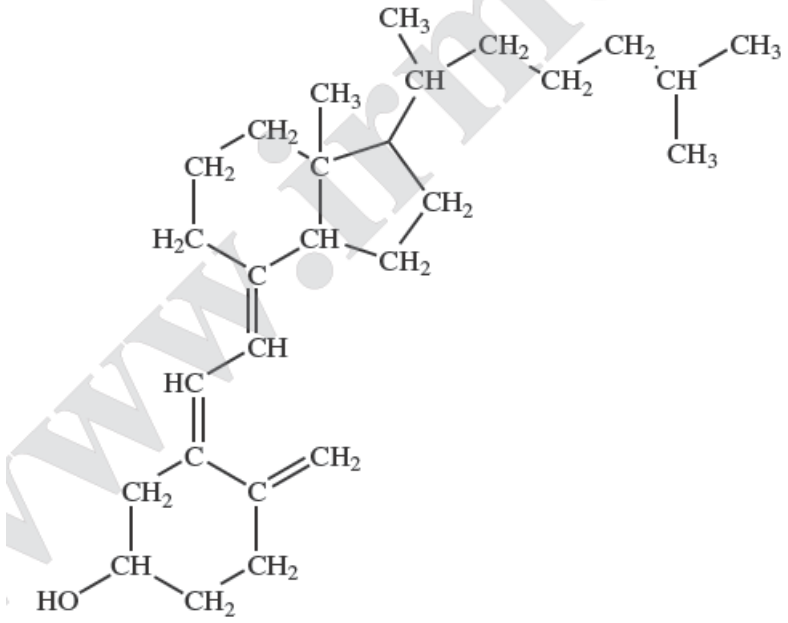
FAT SOLUBLE VITAMINS
These vitamins are stored in the liver and fatty tissues until required. As such, they can be harmful if too much is taken in.

Vitamin D is Hormone Precursor





Vitamin D_2



Vitamin D_3

➢**Vitamin D3** (cholecalciferol): is not itself biologically active, but it is converted by enzymes in the liver and kidney to 1,25-dihydroxycholecalciferol, a hormone that regulates calcium uptake in the intestine and calcium levels in kidney and bone.

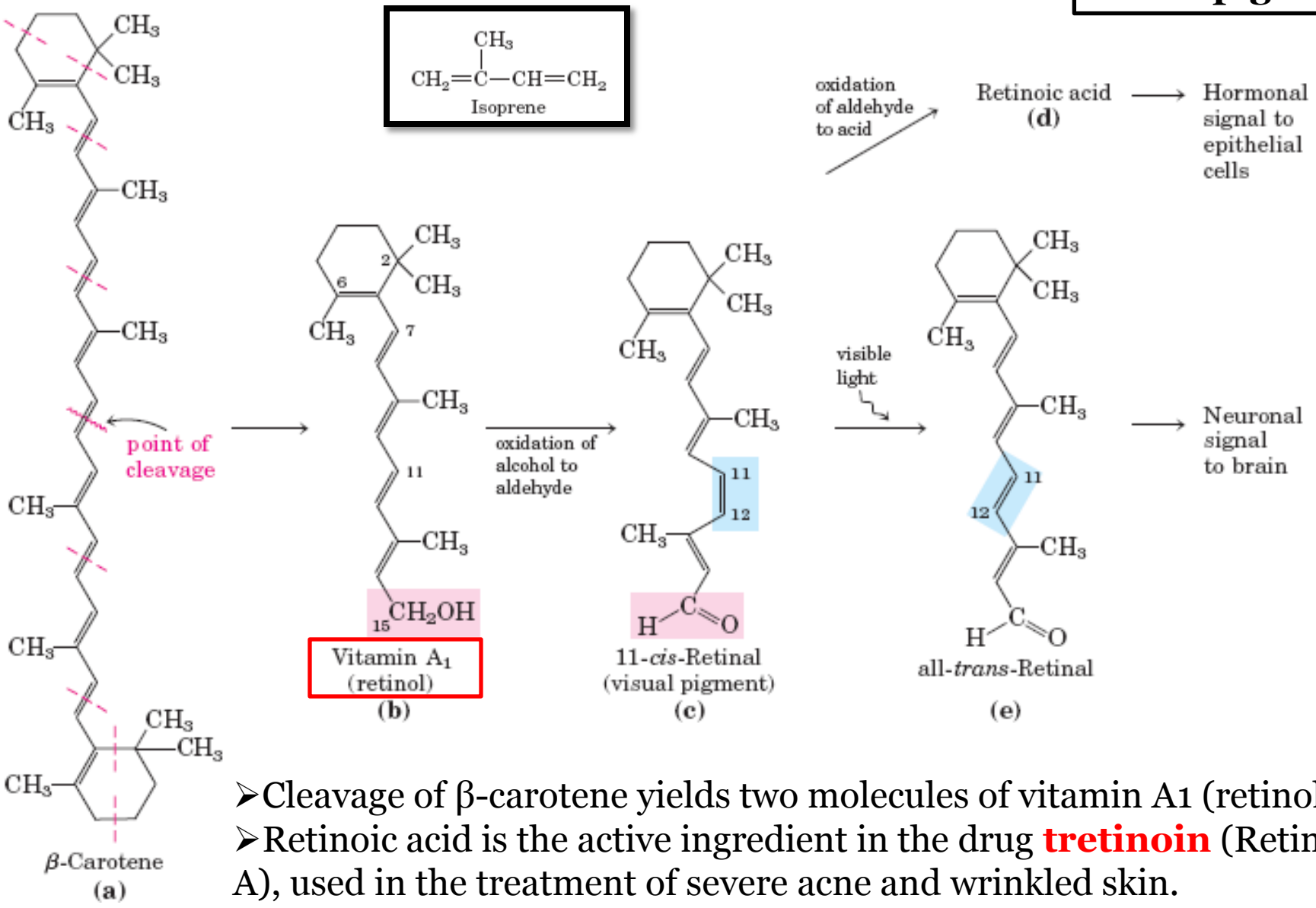
➢**Vitamin D2** (ergocalciferol) is a commercial product formed by UV irradiation of the ergosterol of yeast.

➢Vitamin D2 is structurally similar to D3, with slight modification to the side chain attached to the sterol D ring. Both have the same biological effects, and D2 is commonly added to **milk** and **butter** as a dietary supplement.

Vitamin A is Hormone Precursor

hormone

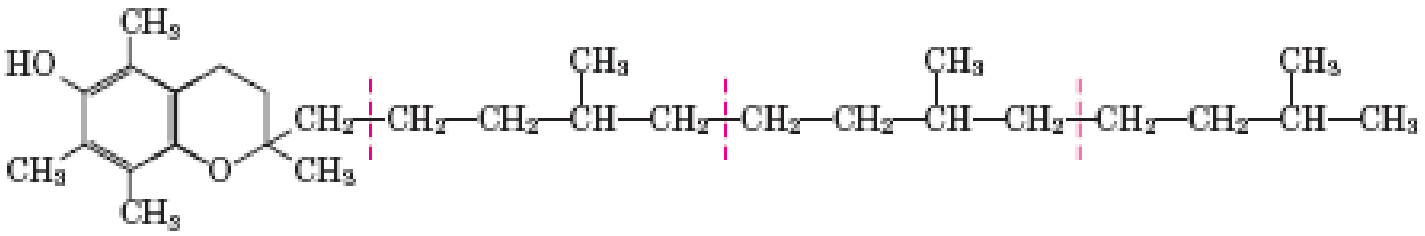
visual pigment



- Cleavage of β-carotene yields two molecules of vitamin A1 (retinol).
- Retinoic acid is the active ingredient in the drug **tretinoin** (Retin-A), used in the treatment of severe acne and wrinkled skin.

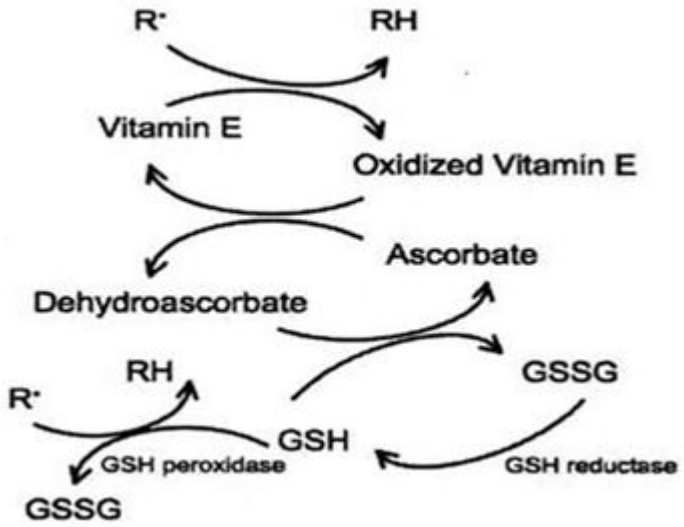
Vitamins E and K Are Oxidation-Reduction Cofactors

(a)
Vitamin E: an antioxidant



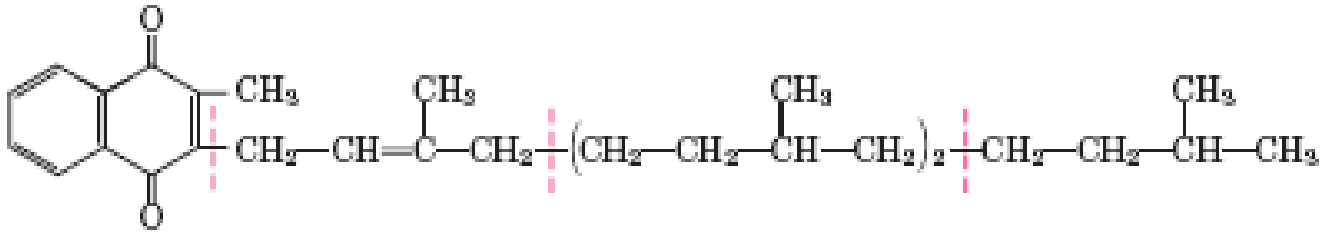
contain a substituted aromatic ring and a long isoprenoid side chain

biological antioxidants (The aromatic ring reacts with and destroys the most reactive forms of oxygen radicals and other free radicals, protecting unsaturated fatty acids from oxidation and preventing oxidative damage to membrane lipids, which can cause cell fragility)

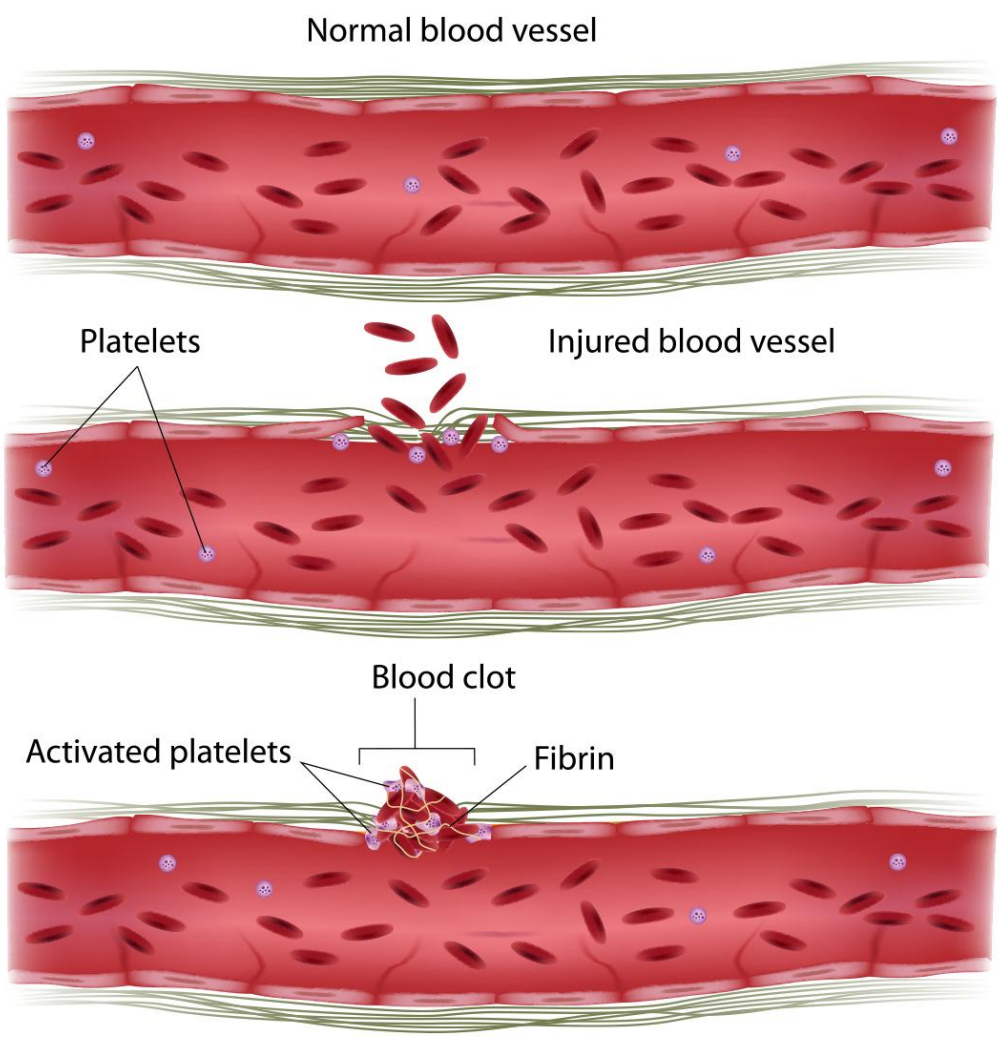


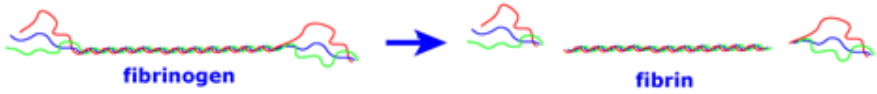
Vitamins E and K Are Oxidation-Reduction Cofactors

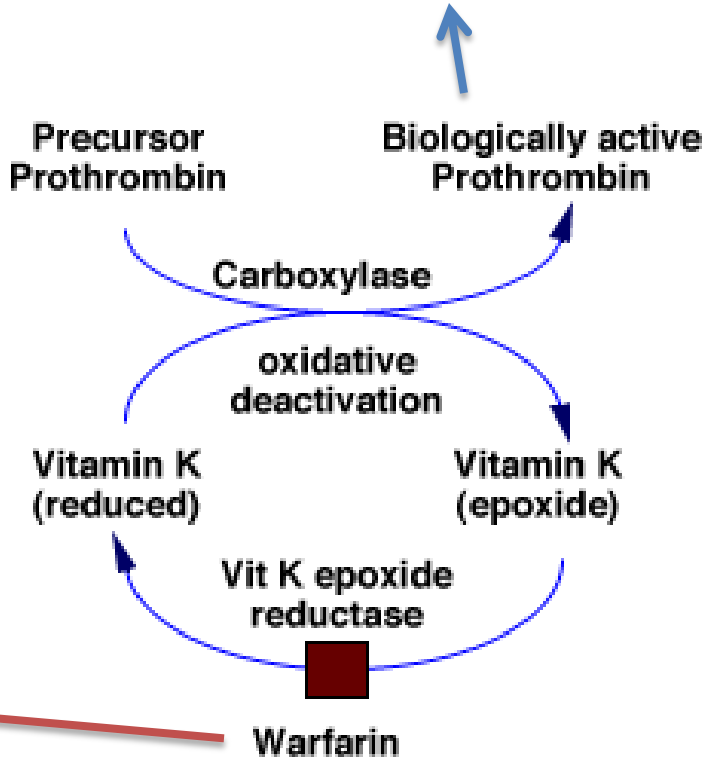
(b)
Vitamin K_1: a blood-clotting cofactor (phylloquinone)



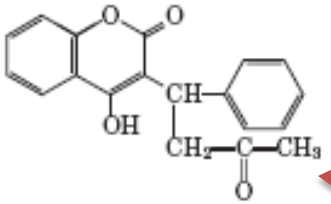
- Vitamin K1 (phylloquinone) is found in green plant leaves
- Vitamin K2 (menaquinone), is formed by bacteria residing in the vertebrate intestine



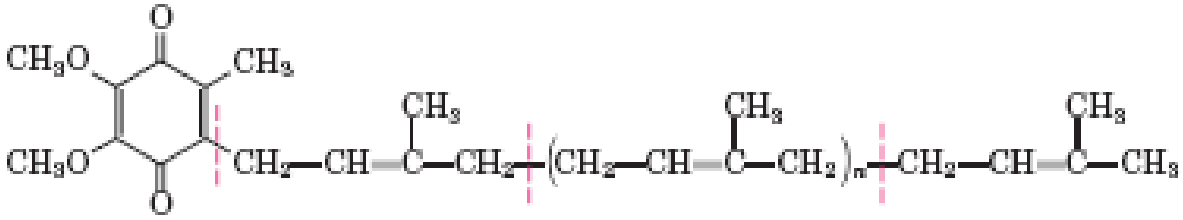




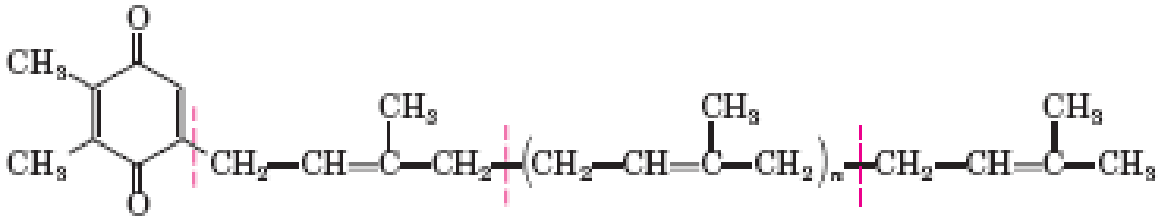
(c)
Warfarin: a blood anticoagulant



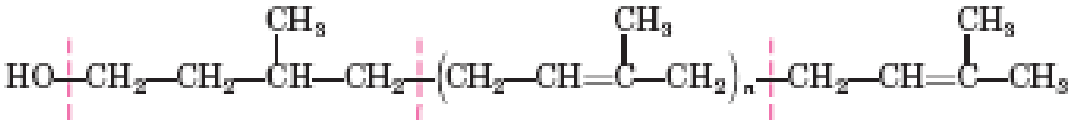
(d)
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) (n = 4 to 8)

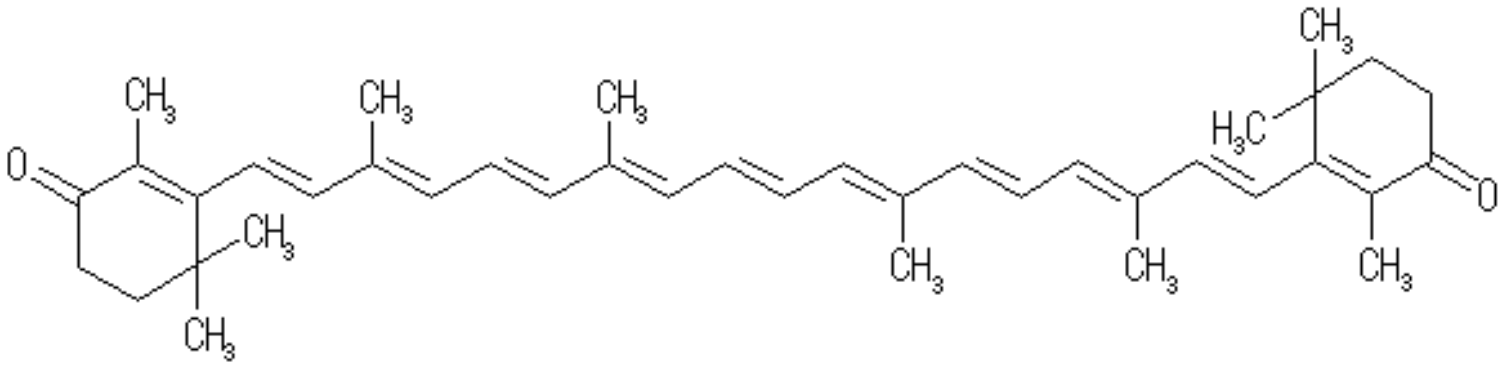


(e)
Plastoquinone: a chloroplast electron carrier (n = 4 to 8)

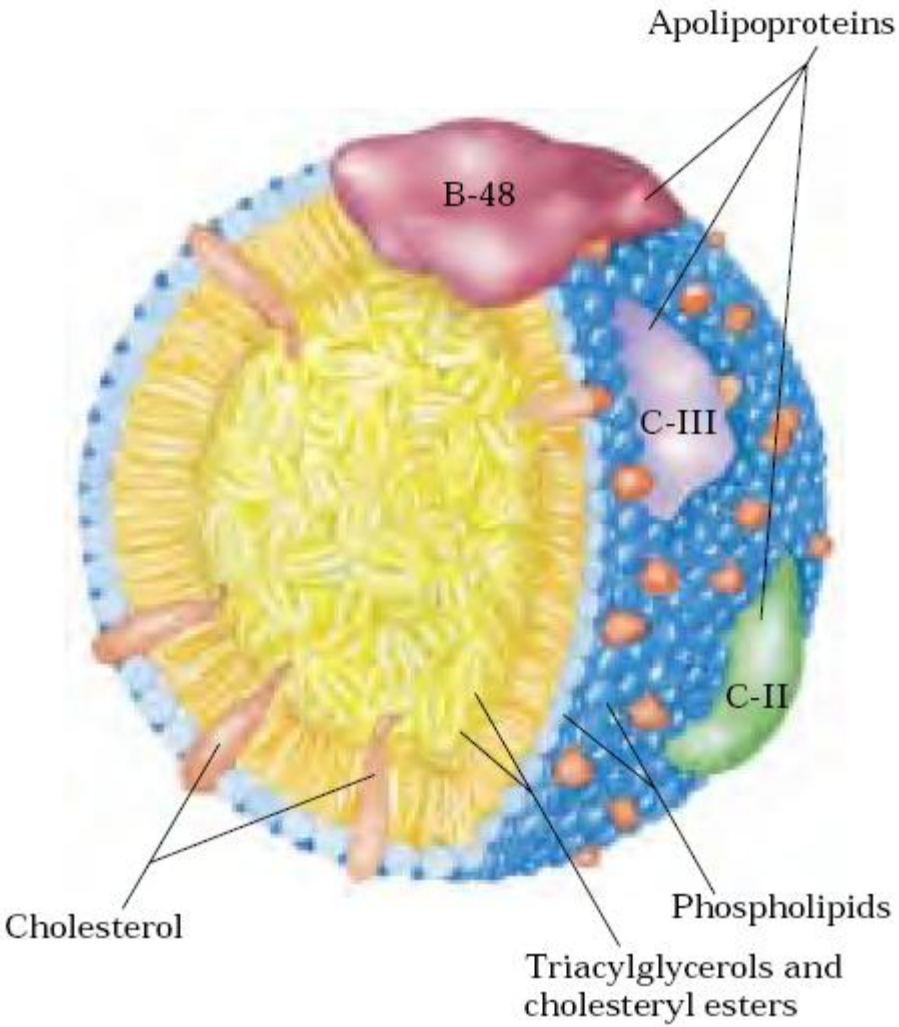


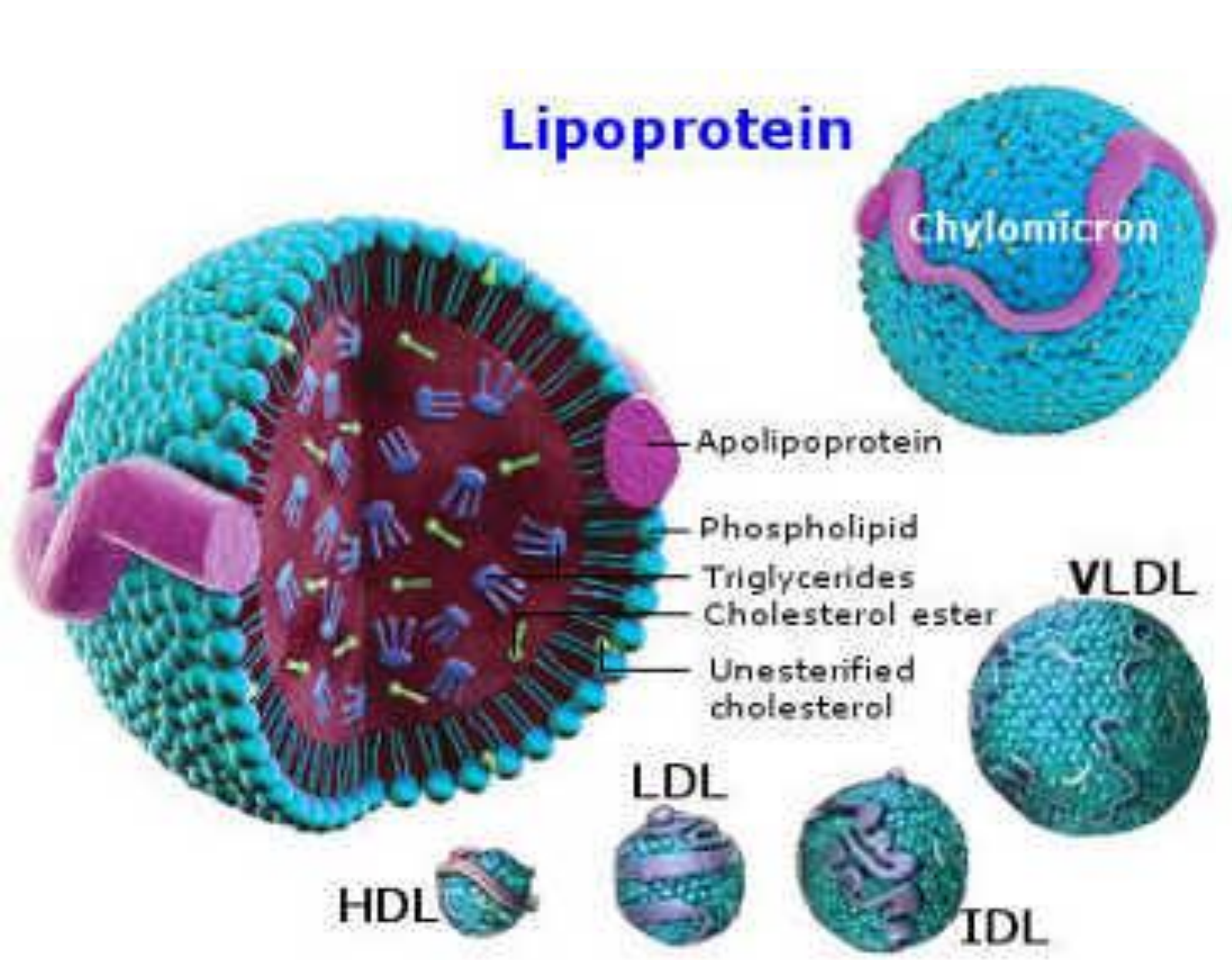
(f)
Dolichol: a sugar carrier (n = 9 to 22)

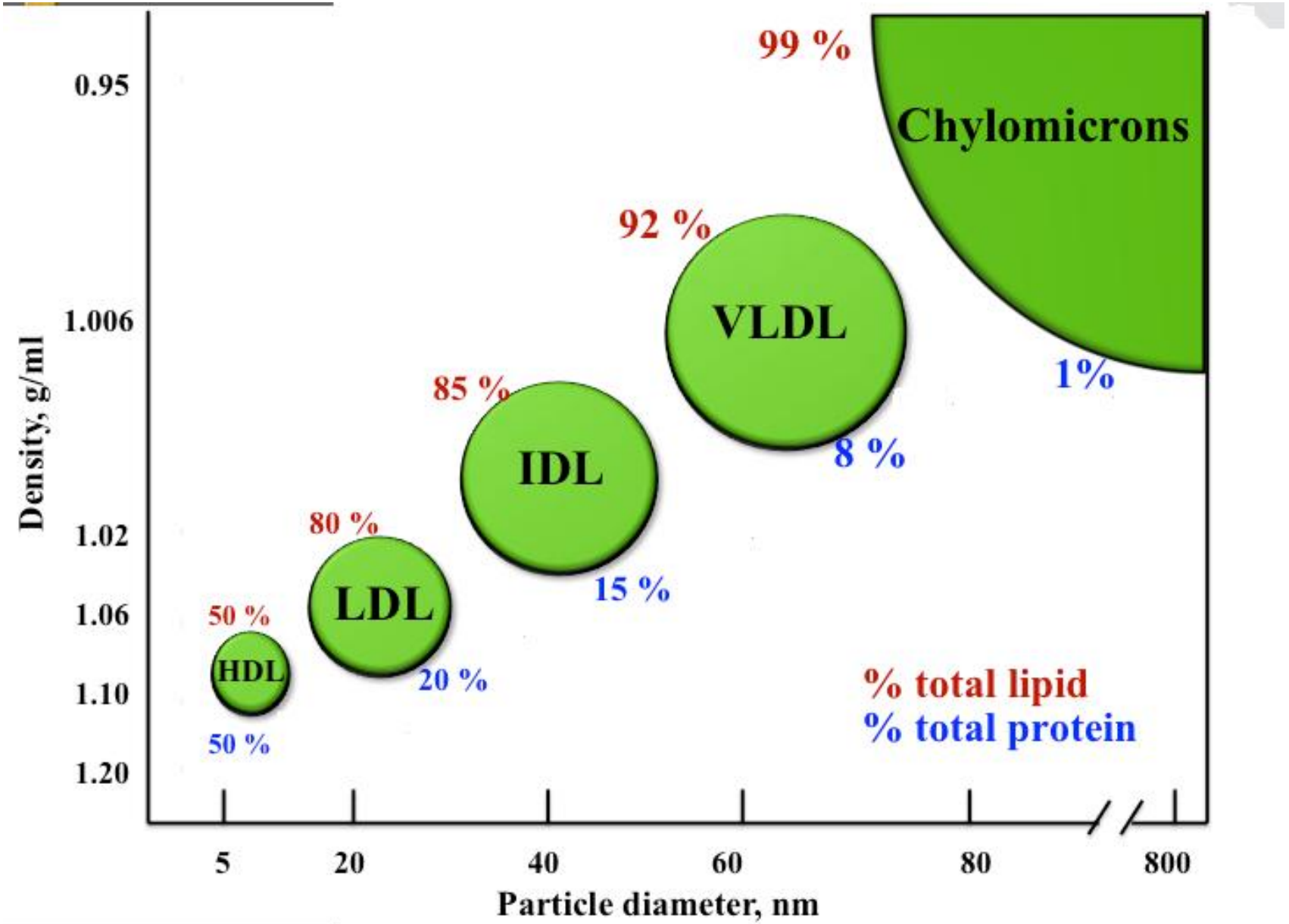




Canthaxanthin


Apolipoproteins
B-48
C-III
C-II
Cholesterol
Triacylglycerols and
cholesteryl esters
Phospholipids


Lipoprotein
Chylomicron
Apolipoprotein
Phospholipid
Triglycerides
Cholesterol ester
Unesterified cholesterol
VLDL
LDL
HDL
IDL


99 %
Chylomicrons
1%
92 %
VLDL
8 %
85 %
IDL
15 %
80 %
LDL
20 %
50 %
HDL
50 %
% total lipid
% total protein
Density, g/ml
0.95
1.006
1.02
1.06
1.10
1.20
5
20
40
60
80
800
Particle diameter, nm