Biochemistry 1

Lipids

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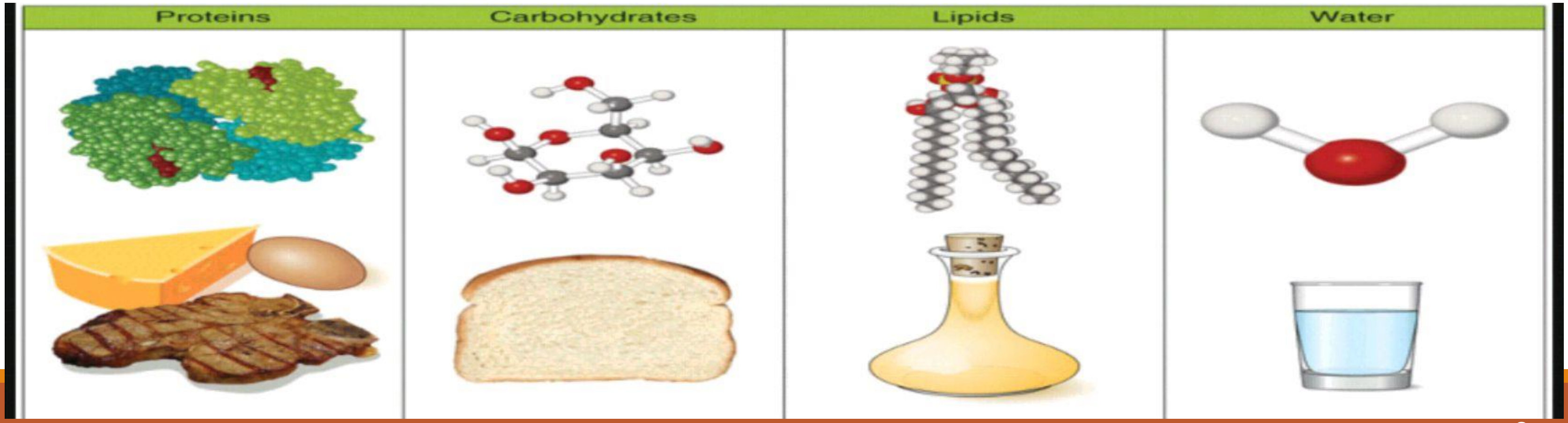
Biomedical Importance

The lipids are a heterogeneous group of compounds, including fats, oils, steroids, waxes, and related compounds, which are related more by their physical than by their chemical properties. They have the common property of being:

(1) Relatively insoluble in water.

(2) Soluble in nonpolar solvents such as ether and chloroform.



Biomedical Importance

They are important dietary constituents not only because of their high energy value but also because of the fat-soluble vitamins and the essential fatty acids contained in the fat of natural foods. Fat is stored in adipose tissue, where it also serves as a thermal insulator in the subcutaneous tissues and around certain organs. Nonpolar lipids act as electrical insulators, allowing rapid propagation of depolarization waves along myelinated nerves. Combinations of lipid and protein (lipoproteins) are important cellular constituents, occurring both in the cell membrane and in the mitochondria, and serving also as the means of transporting lipids in the blood. Knowledge of lipid biochemistry is necessary in understanding many important biomedical areas, eg, obesity, diabetes mellitus, atherosclerosis, and the role of various polyunsaturated fatty acids in nutrition and health.

LIPIDS ARE CLASSIFIED AS SIMPLE OR COMPLEX

1. Simple lipids: Esters of fatty acids with various alcohols.

a. Fats: Esters of fatty acids with glycerol. Oils are fats in the liquid state.

b. Waxes: Esters of fatty acids with higher molecular weight monohydric alcohols.

2. Complex lipids: Esters of fatty acids containing groups in addition to an alcohol and a fatty acid.

a. Phospholipids: Lipids containing, in addition to fatty acids and an alcohol, a phosphoric acid residue. They frequently have nitrogen containing bases and other substituents, eg, in glycerophospholipids the alcohol is glycerol and in sphingophospholipids the alcohol is sphingosine.

b. Glycolipids (glycosphingolipids): Lipids containing a fatty acid, sphingosine, and carbohydrate.

c. Other complex lipids: Lipids such as sulfolipids and aminolipids. Lipoproteins may also be placed in this category.

3. Precursor and derived lipids: These include fatty acids, glycerol, steroids, other alcohols, fatty aldehydes, and ketone bodies, hydrocarbons, lipid-soluble vitamins, and hormones. Because they are uncharged, acylglycerols (glycerides), cholesterol, and cholesteryl esters are termed neutral lipids.

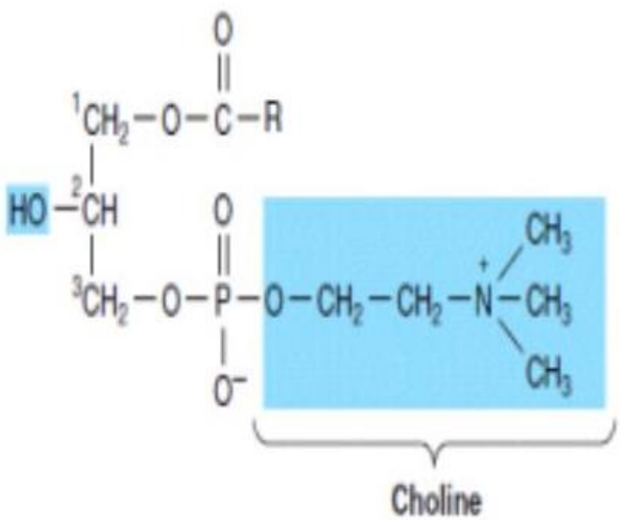
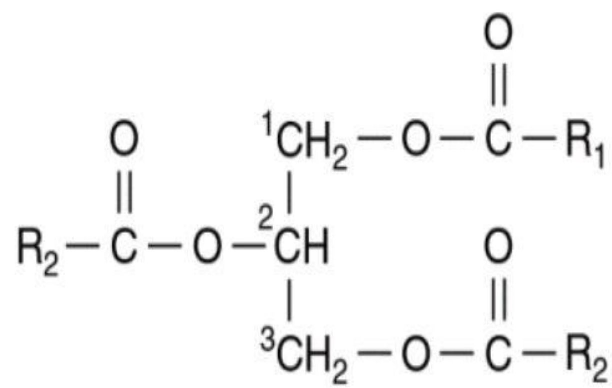


Figure 14-9. Lysophosphatidylcholine (lysolecithin).



4–6. Triacylglycerol.

Fatty Acids

Systematic nomenclature names the fatty acid after the hydrocarbon with the same number and arrangement of carbon atoms, with –oic being substituted for the final –e. Thus, saturated acids end in -anoic, eg, octanoic acid, and unsaturated acids with double bonds end in -enoic, eg, octadecenoic acid (oleic acid). Carbon atoms are numbered from the carboxyl carbon (carbon No. 1). The carbon atoms adjacent to the carboxyl carbon (Nos. 2, 3, and 4) are also known as the α, β, and γ carbons, respectively, and the terminal methyl carbon is known as the ω or n-carbon. Various conventions use Δfor indicating the number and position of the double bonds; eg, Δ9 indicates a double bond between carbons 9 and 10 of the fatty acid; ω9 indicates a double bond on the ninth carbon counting from the ω- carbon. In animals, additional double bonds are introduced only between the existing double bond (eg, ω9, ω6, or ω3) and the carboxyl carbon, leading to three series of fatty acids known as the ω9, ω6, and ω3 families, respectively.

18:1;9 *or* Δ^9 18:1

$$\overset{18}{C}H_3(CH_2)_7\overset{10}{C}H=\overset{9}{C}H(CH_2)_7\overset{1}{C}OOH$$

or

ω9,C18:1 *or* n–9, 18:1

$$\underset{n}{\overset{\omega}{CH_3}}\underset{17}{\overset{2}{CH_2}}\overset{3}{CH_2}\overset{4}{CH_2}\overset{5}{CH_2}\overset{6}{CH_2}\overset{7}{CH_2}\overset{8}{CH_2}\underset{10}{\overset{9}{CH}}=\underset{9}{\overset{10}{CH}}(CH_2)_7\underset{1}{\overset{18}{C}}OOH$$

Figure 14–1. Oleic acid. n – 9 (n minus 9) is equivalent to ω9.

Fatty acids may be further subdivided as follows:

(1) Monounsaturated (monoethenoid, monoenoic) acids, containing one double bond.

(2) Polyunsaturated (polyethenoid, polyenoic) acids, containing two or more double bonds.

(3) Eicosanoids: These compounds, derived from eicosa- (20-carbon) polyenoic fatty acids, comprise the prostanoids, leukotrienes (LTs), and lipoxins (LXs).

Prostanoids include prostaglandins (PGs), prostacyclins (PGIs), and thromboxanes (TXs)., acting as local hormones; they have important physiologic and pharmacologic activities. They are synthesized in vivo by cyclization of the center of the carbon chain of 20-carbon (eicosanoic) polyunsaturated fatty acids (eg, arachidonic acid) to form a cyclopentane ring. A related series of compounds, the thromboxanes,have the cyclopentane ring interrupted with an oxygen atom (oxane ring). Three different eicosanoic fatty acids give rise to three groups of eicosanoids characterized by the number of double bonds in the side chains, eg, PG1, PG2, PG3. Different substituent groups attached to the rings give rise to series of prostaglandins and thromboxanes, labeled A, B, etc—eg, the "E" type of prostaglandin (as in PGE2) has a keto group in position 9, whereas the "F" type has a hydroxyl group in this position. The leukotrienesand lipoxinsare a third group of eicosanoid derivatives formed via the lipoxygenase pathway, respectively. Leukotrienes cause broncho-constriction as well as being potent proinflammatory agents and play a part in asthma.

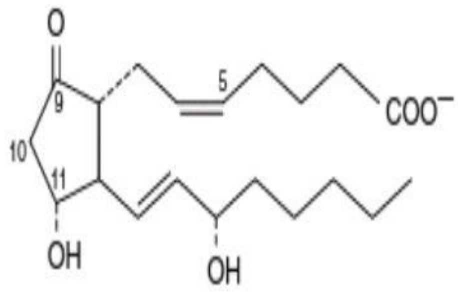


Figure 14–2. Prostaglandin E_2 (PGE_2).

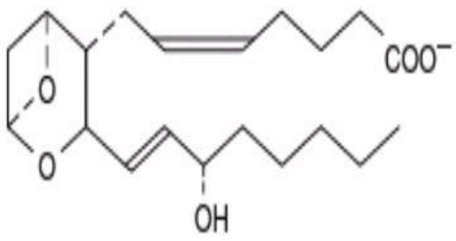


Figure 14–3. Thromboxane A_2 (TXA_2).

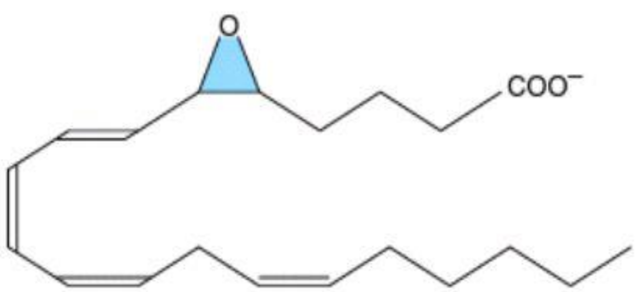


Figure 14–4. Leukotriene A_4 (LTA_4).

Most Naturally Occurring Unsaturated Fatty Acids Have cis Double Bonds

The carbon chains of saturated fatty acids form a zigzag pattern when extended, as at low temperatures. At higher temperatures, some bonds rotate, causing chain shortening, which explains why biomembranes become thinner with increases in temperature. A type of geometric isomerism occurs in unsaturated fatty acids, depending on the orientation of atoms or groups around the axes of double bonds, which do not allow rotation. If the acyl chains are on the same side of the bond, it is cis-, as in oleic acid; if on opposite sides, it is trans-, as in elaidic acid, the trans isomer of oleic acid.

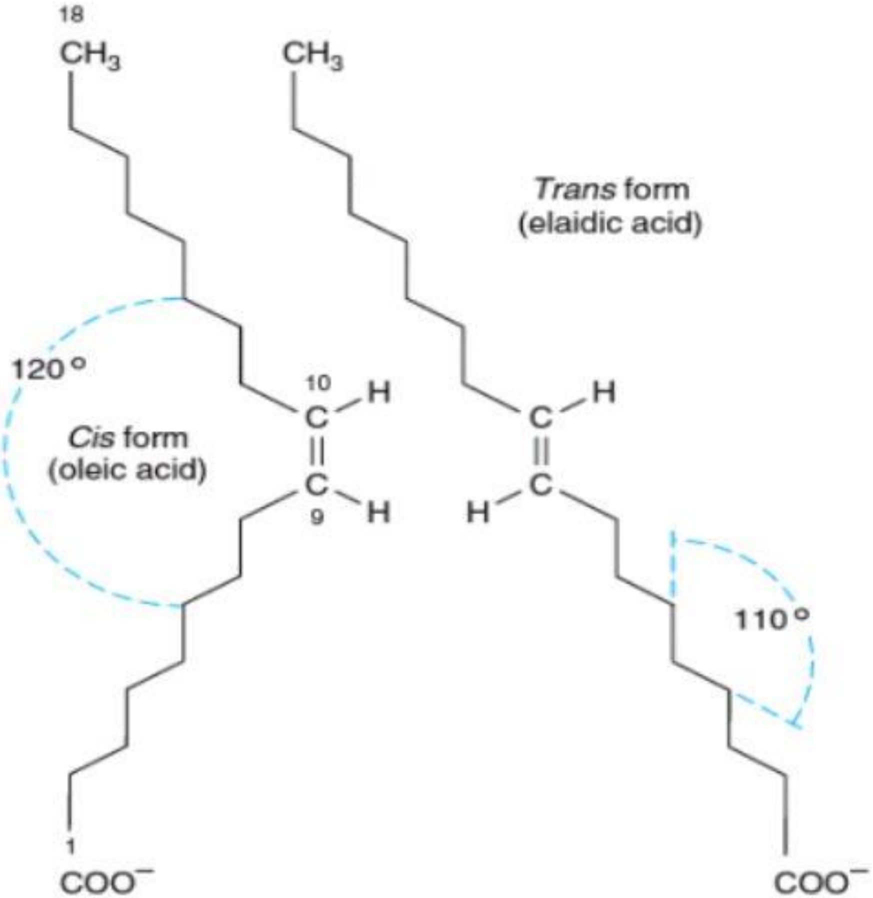


Figure 14–5. Geometric isomerism of Δ^9, 18:1 fatty acids (oleic and elaidic acids).

Table 14–2. Unsaturated fatty acids of physiologic and nutritional significance.

Number of C Atoms and Number and Position of Double Bonds	Family	Common Name	Systematic Name	Occurrence
Monoenoic acids (one double bond)				
16:1;9	ω7	Palmitoleic	*cis*-9-Hexadecenoic	In nearly all fats.
18:1;9	ω9	Oleic	*cis*-9-Octadecenoic	Possibly the most common fatty acid in natural fats.
18:1;9	ω9	Elaidic	*trans*-9-Octadecenoic	Hydrogenated and ruminant fats.
Dienoic acids (two double bonds)				
18:2;9,12	ω6	Linoleic	all-*cis*-9,12-Octadecadienoic	Corn, peanut, cottonseed, soybean, and many plant oils.
Trienoic acids (three double bonds)				
18:3;6,9,12	ω6	γ-Linolenic	all-*cis*-6,9,12-Octadecatrienoic	Some plants, eg, oil of evening primrose, borage oil; minor fatty acid in animals.
18:3;9,12,15	ω3	α-Linolenic	all-*cis*-9,12,15-Octadecatrienoic	Frequently found with linoleic acid but particularly in linseed oil.
Tetraenoic acids (four double bonds)				
20:4;5,8,11,14	ω6	Arachidonic	all-*cis*-5,8,11,14-Eicosatetraenoic	Found in animal fats and in peanut oil; important component of phospholipids in animals.
Pentaenoic acids (five double bonds)				
20:5;5,8,11,14,17	ω3	Timnodonic	all-*cis*-5,8,11,14,17-Eicosapentaenoic	Important component of fish oils, eg, cod liver, mackerel, menhaden, salmon oils.
Hexaenoic acids (six double bonds)				
22:6;4,7,10,13,16,19	ω3	Cervonic	all-*cis*-4,7,10,13,16,19-Docosahexaenoic	Fish oils, phospholipids in brain.

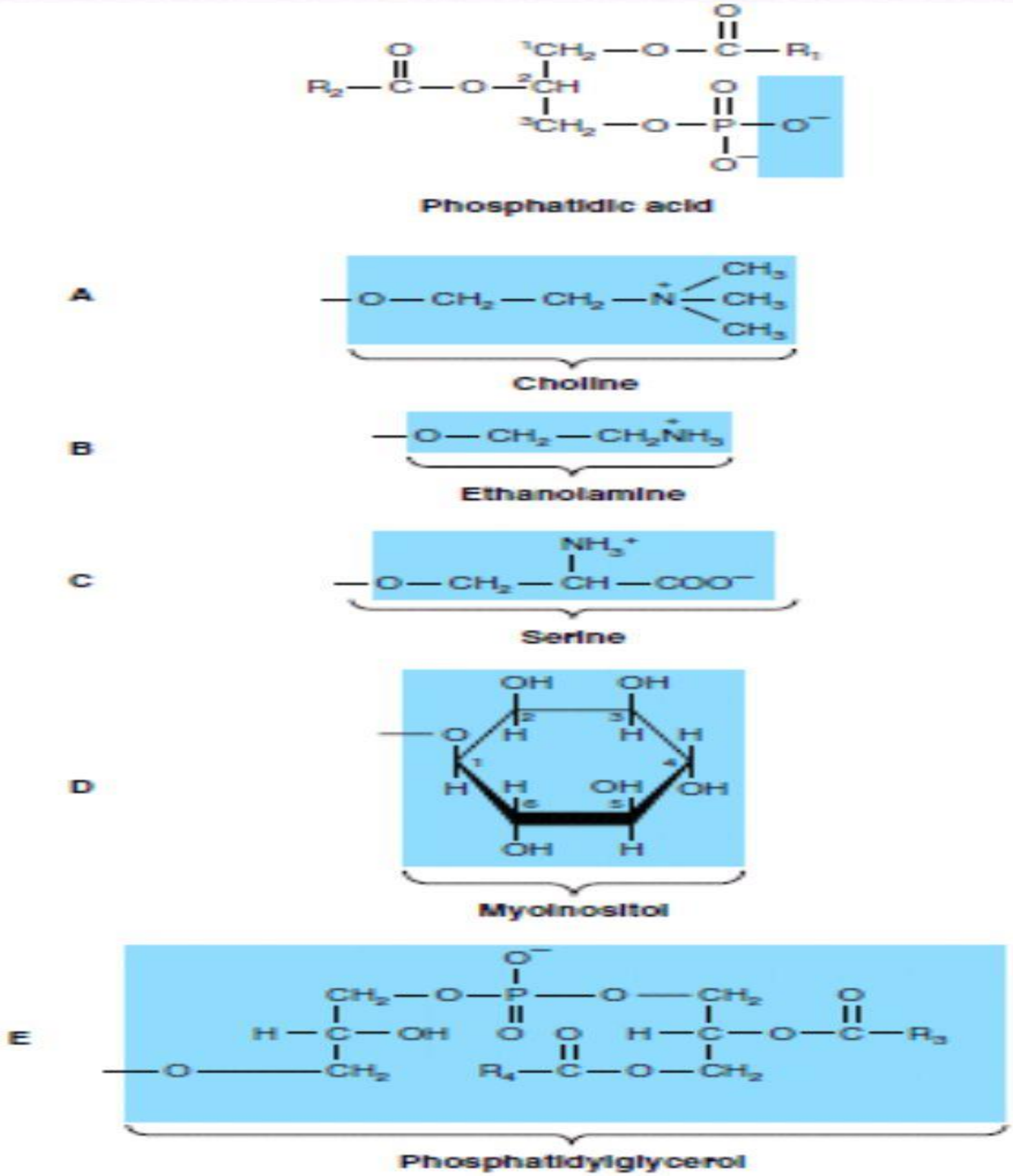


Figure 14–8. Phosphatidic acid and its derivatives. The O^- shown shaded in phosphatidic acid is substituted by the substituents shown to form in **(A)** 3-phosphatidylcholine, **(B)** 3-phosphatidylethanolamine, **(C)** 3-phosphatidylserine, **(D)** 3-phosphatidylinositol, and **(E)** cardiolipin (diphosphatidylglycerol).

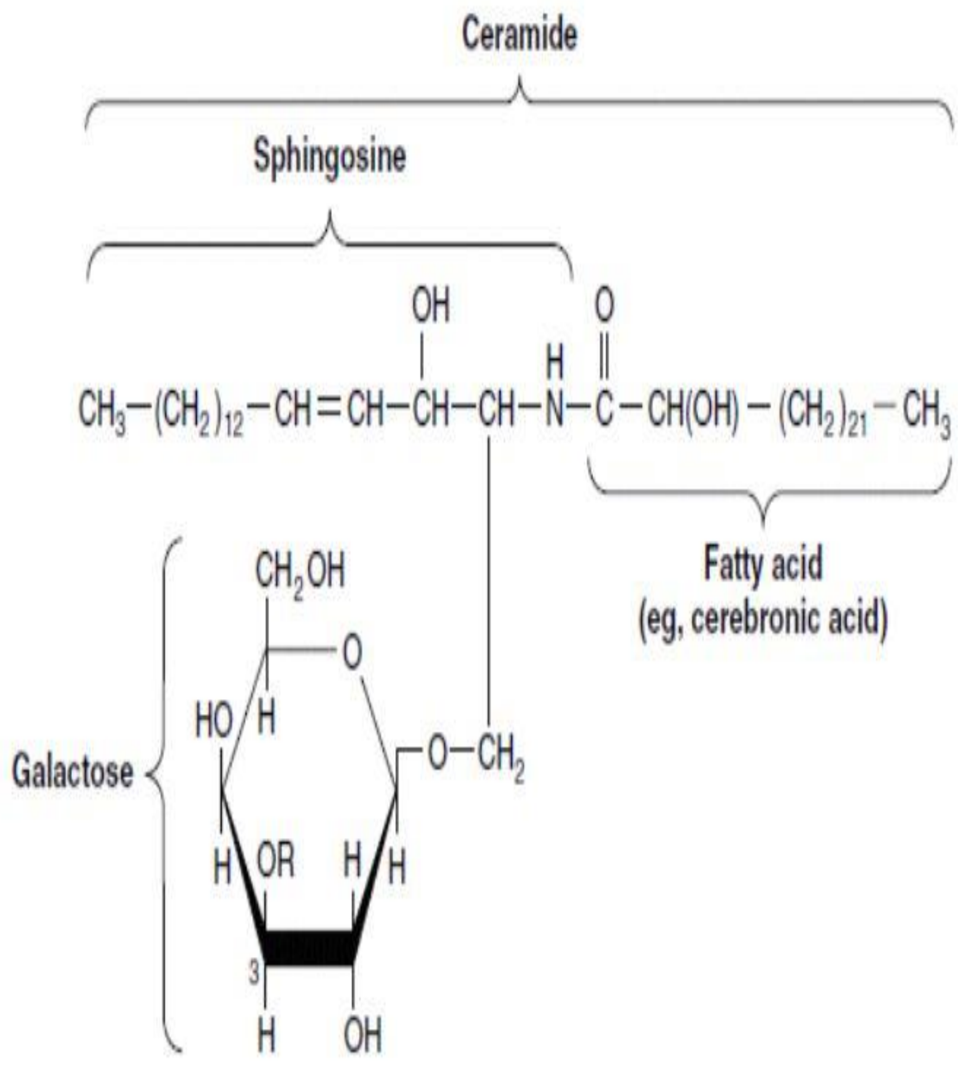


Figure 14–12. Structure of galactosylceramide (galactocerebroside, R = H), and sulfogalactosylceramide (a sulfatide, $R = SO_4^{2-}$).

Steroids

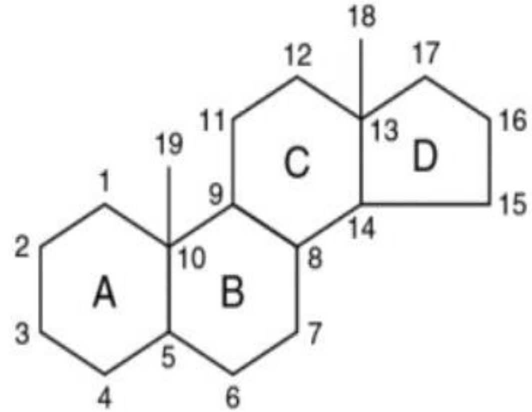


Figure 14–14. The steroid nucleus.

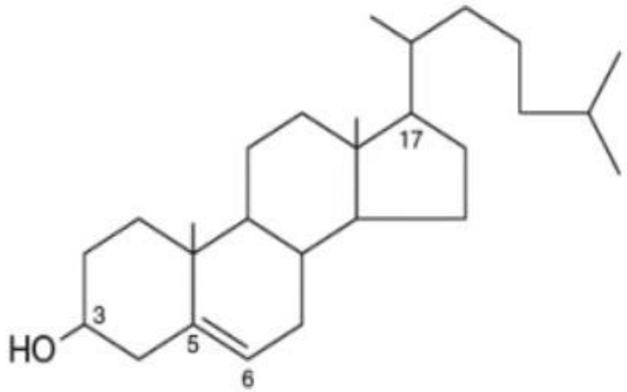


Figure 14–17. Cholesterol, 3-hydroxy-5,6-cholestene.

Ergosterol Is a Precursor of Vitamin D, Ergosterol occurs in plants and yeast and is important as a precursor of vitamin D (Figure 14–18). When irradiated with ultraviolet light, it acquires antirachitic properties consequent to the opening of ring B.

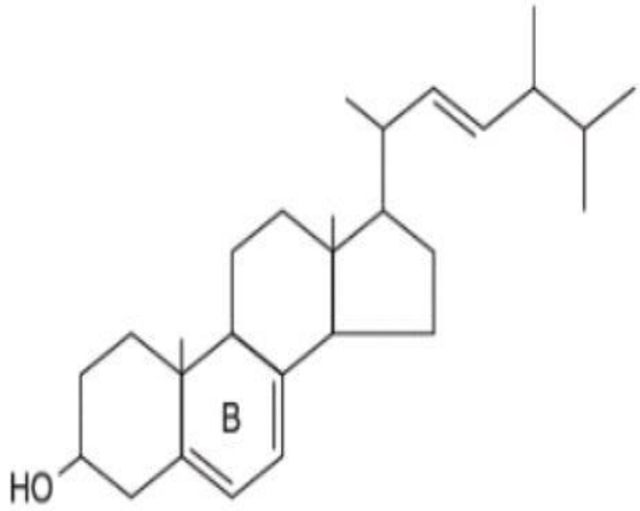


Figure 14–18. Ergosterol.

AMPHIPATHIC LIPIDS SELF-ORIENT AT OIL:WATER INTERFACES

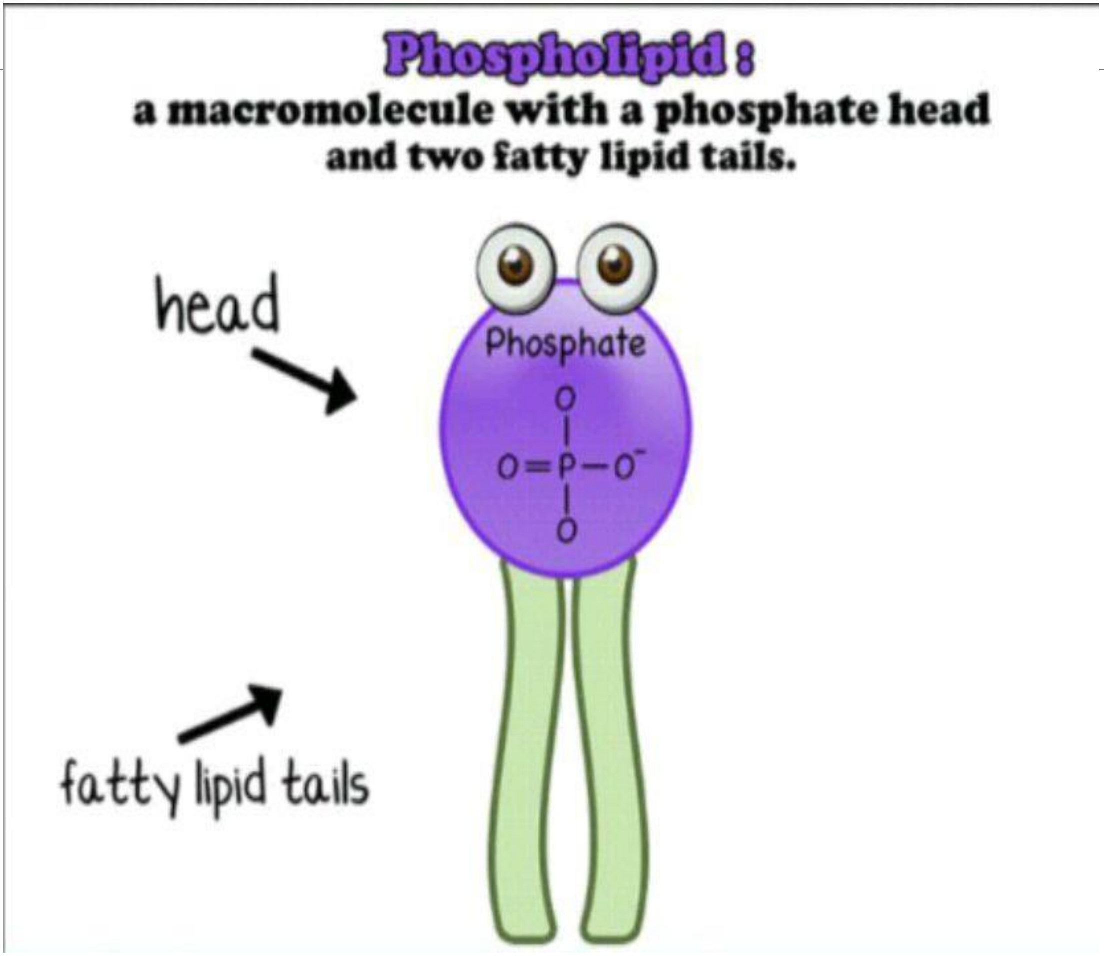
They Form Membranes, Micelles, Liposomes, & Emulsions.

Lipids are insoluble in water since they contain a predominance of nonpolar (hydrocarbon) groups.

Fatty acids, phospholipids, sphingolipids, bile salts, and, to a lesser extent, cholesterol contain polar groups.

Therefore, part of the molecule is hydrophobic,or water-insoluble; and part is hydrophilic,or water-soluble.

They become oriented at oil:water interfaces with the polar group in the water phase and the nonpolar group in the oil phase. A bilayer of such amphipathic lipids has been regarded as a basic structure in biologic membranes.


Phospholipid :
a macromolecule with a phosphate head
and two fatty lipid tails.
head
Phosphate
fatty lipid tails

When a critical concentration of these lipids is present in an aqueous medium, they form micelles.

Aggregations of bile salts into micelles and liposomes and the formation of mixed micelles with the products of fat digestion are important in facilitating absorption of lipids from the intestine.

They consist of spheres of lipid bilayers that enclose part of the aqueous medium. They are of potential clinical use—particularly when combined with tissuespecific antibodies—as carriers of drugs in the circulation, targeted to specific organs, eg, in cancer therapy.

In addition, they are being used for gene transfer into vascular cells and as carriers for topical and transdermal delivery of drugs and cosmetics.

Emulsions are much larger particles, formed usually by nonpolar lipids in an aqueous medium. These are stabilized by emulsifying agents such as amphipathic lipids (eg, lecithin), which form a surface layer separating the main bulk of the nonpolar material from the aqueous phase (Figure 14–22).

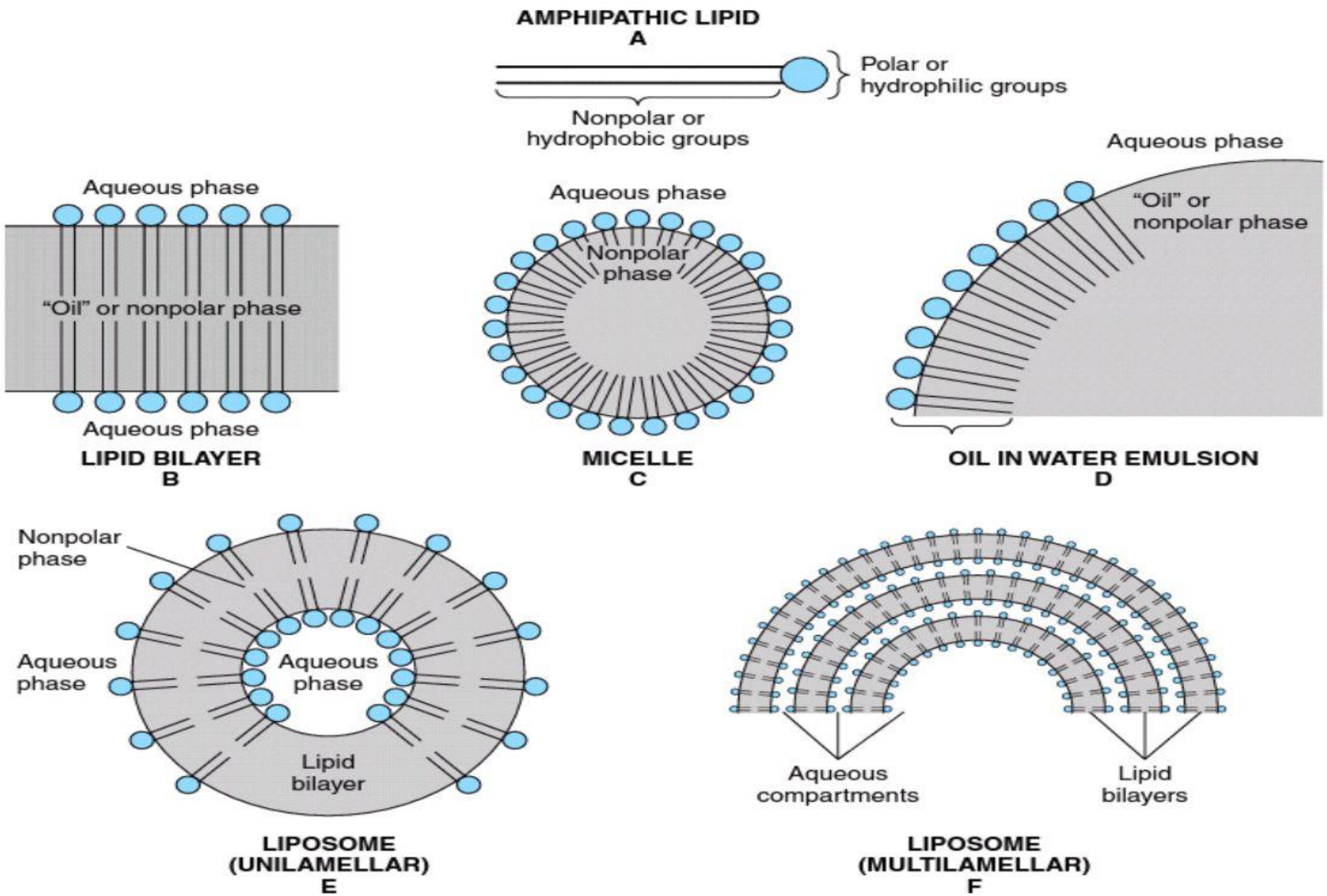
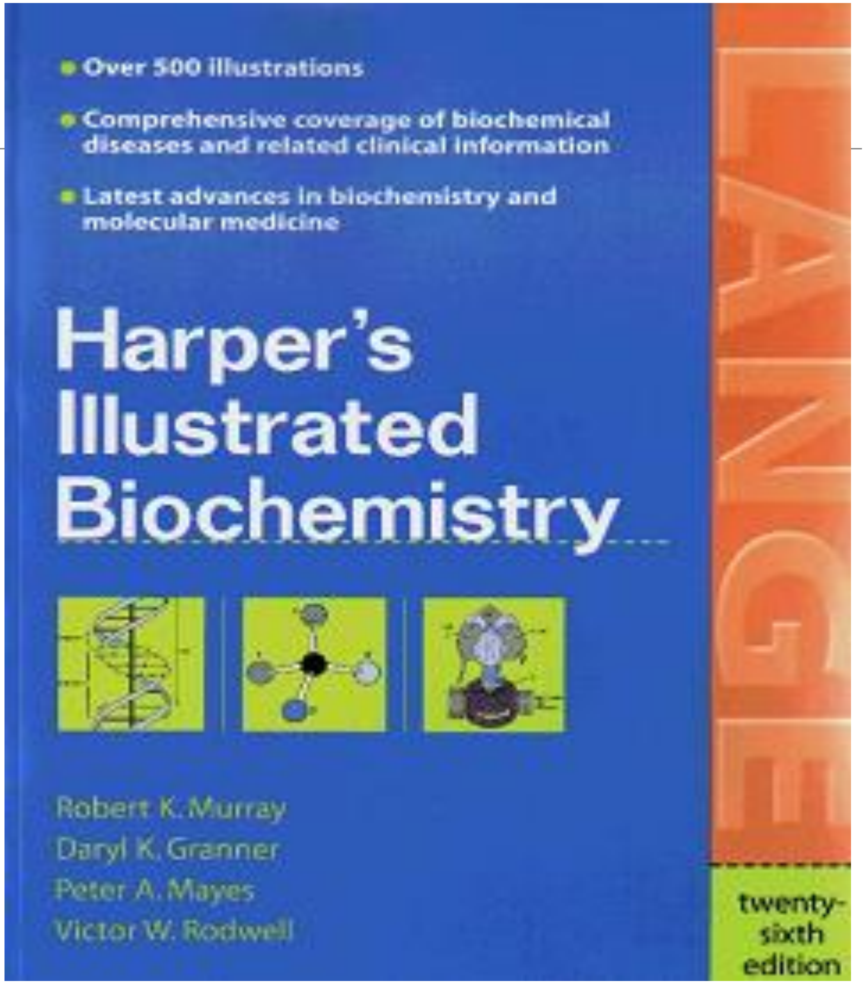


Figure 14–22. Formation of lipid membranes, micelles, emulsions, and liposomes from amphipathic lipids, eg, phospholipids.

Reference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