BIOL 157: BIOLOGICAL CHEMISTRY

Lecture 15:

Lipids

Lecturer:

Christopher Larbie, *PhD*

Introduction

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

- As molecules that are largely hydrocarbon in nature, lipids represent highly reduced forms of carbon and, upon oxidation in metabolism, yield large amounts of energy.

- Lipids are thus the molecules of choice for metabolic energy storage.

- The lipids found in biological systems are either **hydrophobic** (containing only nonpolar groups) or **amphipathic,** which means they possess both polar and nonpolar groups. The hydrophobic nature of lipid molecules allows membranes to act as effective barriers to more polar molecules. In this lecture, we shall discuss the chemical and physical properties of the various classes of lipid molecules.

Fatty Acids

- A fatty acid is composed of a long hydrocarbon chain (“tail”) and a terminal carboxyl group (or “head”).
- The carboxyl group is normally ionized under physiological conditions.
- Fatty acids occur in large amounts in biological systems, but rarely in the free, uncomplexed state.
- They typically are esterified to glycerol or other backbone structures.
- Most of the fatty acids found in nature have an even number of carbon atoms (usually 14 to 24). Certain marine organisms, however, contain substantial amounts of fatty acids with odd numbers of carbon atoms.

- Fatty acids are either **saturated** (all carbon–carbon bonds are single bonds) or **unsaturated** (with one or more double bonds in the hydrocarbon chain).
- If a fatty acid has a single double bond, it is said to be **monounsaturated**, and if it has more than one, **polyunsaturated**.
- Fatty acids can be named or described in at least three ways. For example, a fatty acid composed of an 18-carbon chain with no double bonds can be called by its systematic name (octadecanoic acid), its common name (stearic acid), or its shorthand notation, in which the number of carbons is followed by a colon and the number of double bonds in the molecule (18:0 for stearic acid). Stearic acid (18:0) and palmitic acid (16:0) are the most common saturated fatty acids in nature.

- Unsaturated fatty acids are slightly more abundant in nature than saturated fatty acids, especially in higher plants.

- The most common unsaturated fatty acid is **oleic acid,** or 18:1(9), with the number in parentheses indicating that the double bond is between carbons 9 and 10. The number of double bonds in an unsaturated fatty acid varies typically from one to four, but, in the fatty acids found in most bacteria, this number rarely exceeds one.

- The double bonds found in fatty acids are nearly always in the *cis* configuration. This causes a bend or “kink” in the fatty acid chain. This bend has very important consequences for the structure of biological membranes.

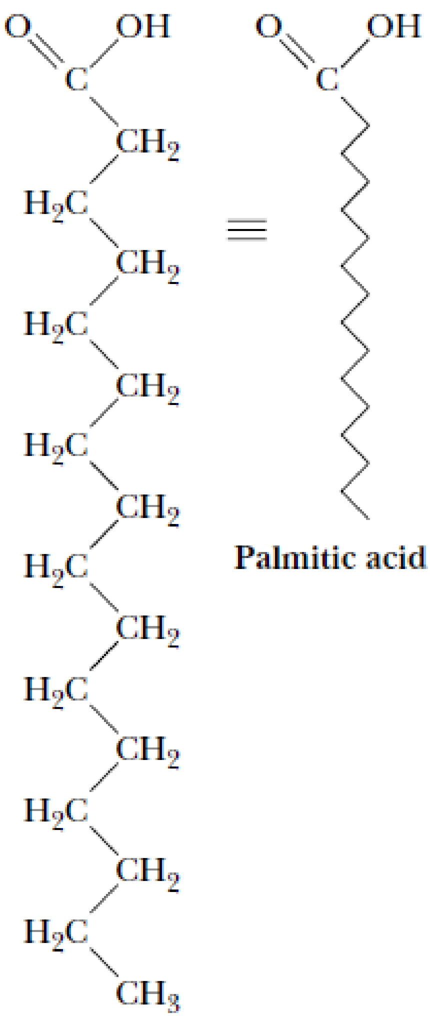
Common Biological Fatty Acids

Common Biological Fatty Acids

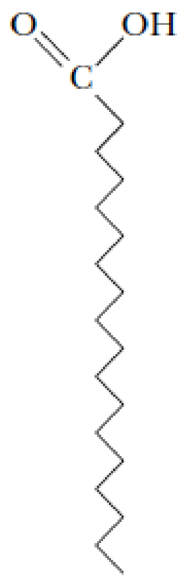
Number of Carbons	Common Name	Systematic Name	Symbol	Structure
Saturated fatty acids				
12	Lauric acid	Dodecanoic acid	12:0	$CH_3(CH_2)_{10}COOH$
14	Myristic acid	Tetradecanoic acid	14:0	$CH_3(CH_2)_{12}COOH$
16	Palmitic acid	Hexadecanoic acid	16:0	$CH_3(CH_2)_{14}COOH$
18	Stearic acid	Octadecanoic acid	18:0	$CH_3(CH_2)_{16}COOH$
20	Arachidic acid	Eicosanoic acid	20:0	$CH_3(CH_2)_{18}COOH$
22	Behenic acid	Docosanoic acid	22:0	$CH_3(CH_2)_{20}COOH$
24	Lignoceric acid	Tetracosanoic acid	24:0	$CH_3(CH_2)_{22}COOH$
Unsaturated fatty acids (all double bonds are *cis*)				
16	Palmitoleic acid	9-Hexadecenoic acid	16:1	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$
18	Oleic acid	9-Octadecenoic acid	18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
18	Linoleic acid	9,12-Octadecadienoic acid	18:2	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$
18	α-Linolenic acid	9,12,15-Octadecatrienoic acid	18:3	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$
18	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	18:3	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$
20	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	20:4	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$
24	Nervonic acid	15-Tetracosenoic acid	24:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$

Essential and Non-essential fatty acids

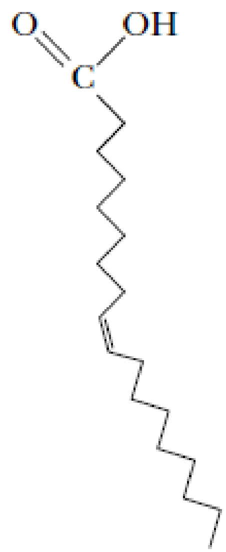
- Some fatty acids are not synthesized by mammals and yet are necessary for normal growth and life.
- These are *essential fatty acids* and include **linoleic** and **γ-linolenic acids.** These must be obtained by mammals in their diet (specifically from plant sources).
- **Arachidonic acid,** which is not found in plants, can only be synthesized by mammals from linoleic acid.
- At least one function of the essential fatty acids is to serve as a precursor for the synthesis of **eicosanoids,** such as *prostaglandins,* a class of compounds that exert hormone-like effects in many physiological processes.



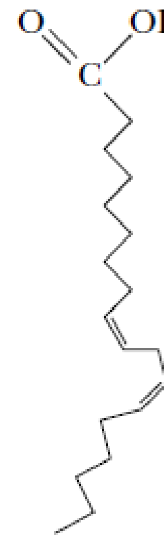
Palmitic acid

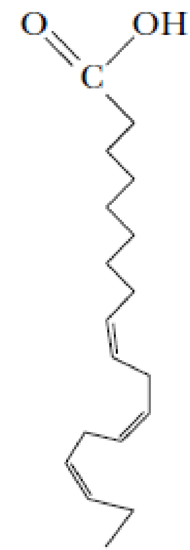


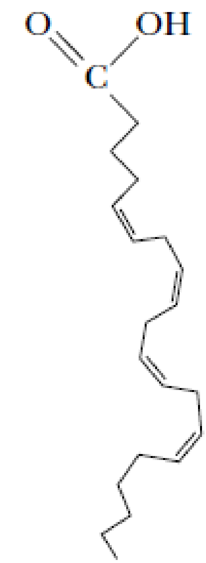
Stearic acid



Oleic acid







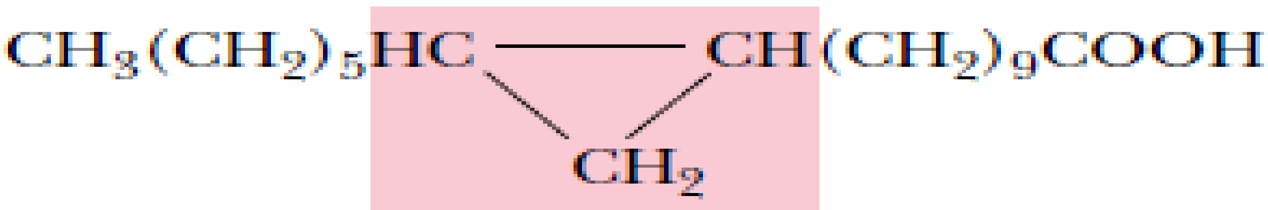
Modified Fatty Acids

- In addition to unsaturated fatty acids, several other modified fatty acids are found in nature.

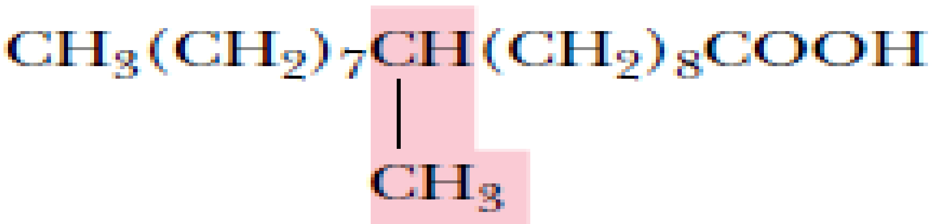
- Microorganisms, for example, often contain branched-chain fatty acids, such as **tuberculostearic acid**. When these fatty acids are incorporated in membranes, the methyl group constitutes a local structural perturbation in a manner similar to the double bonds in unsaturated fatty acids.

- Some bacteria also synthesize fatty acids containing cyclic structures such as cyclopropane, cyclopropene, and even cyclopentane rings.

Lactobacillic acid



Tuberculostearic acid



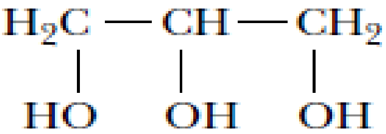
Triacylglycerols

- Triacylglycerols are a major energy reserve and the principal neutral derivatives of glycerol found in animals.

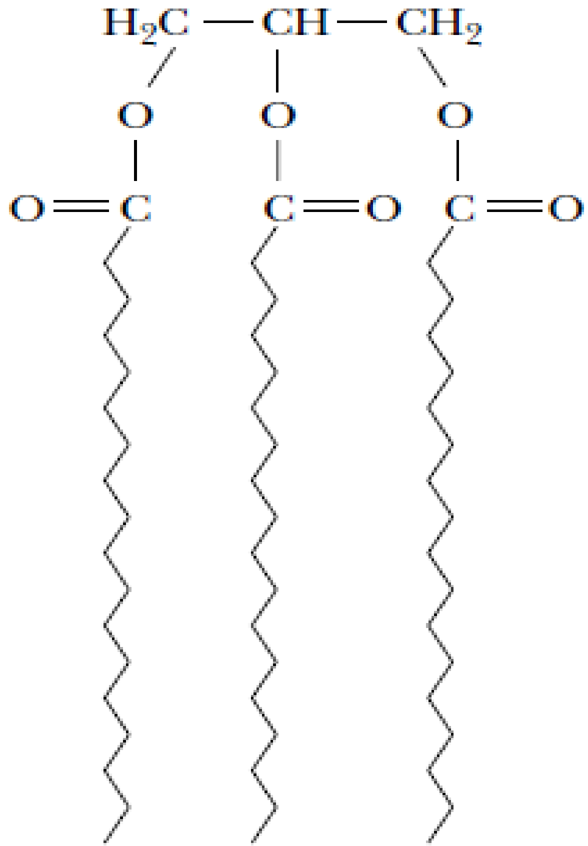
- These molecules consist of a glycerol esterified with three fatty acids.

- If all three fatty acid groups are the same, the molecule is called a **simple triacylglycerol**. Examples include tristearoylglycerol (common name *tristearin*) and trioleoylglycerol (*triolein*). **Mixed triacylglycerols** contain two or three different fatty acids.

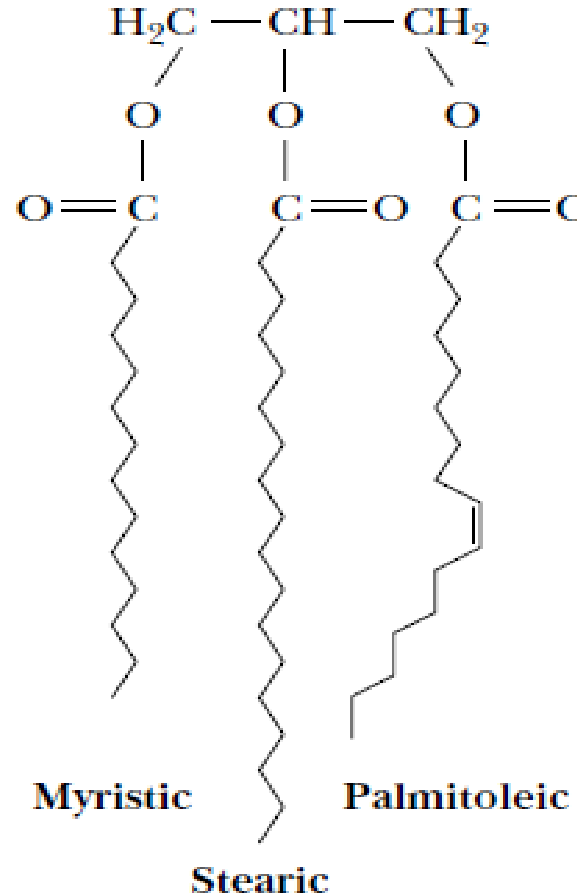
- Triacylglycerols in animals are found primarily in the adipose tissue (body fat), which serves as a depot or storage site for lipids. Monoacylglycerols and diacylglycerols also exist, but are far less common than the triacylglycerols. Most natural plant and animal fat is composed of mixtures of simple and mixed triacylglycerols.



Glycerol



Tristearin
(a simple triacylglycerol)



A mixed triacylglycerol

- Acylglycerols can be hydrolyzed by heating with acid or base or by treatment with lipases. Hydrolysis with alkali is called saponification and yields salts of free fatty acids and glycerol.

- One method used potassium hydroxide (*potash*) leached from wood ashes to hydrolyze animal fat (mostly triacylglycerols). When the fatty acids esterified at the first and third carbons of glycerol are different, the second carbon is asymmetric.

- The various acylglycerols are normally soluble in benzene, chloroform, ether, and hot ethanol. Although triacylglycerols are insoluble in water, mono- and diacylglycerols readily form organized structures in water, owing to the polarity of their free hydroxyl groups.

- Triacylglycerols are rich in highly reduced carbons and thus yield large amounts of energy in the oxidative reactions of metabolism.

- Complete oxidation of 1 g of triacylglycerols yields about 38 kJ of energy, whereas proteins and carbohydrates yield only about 17 kJ/g.

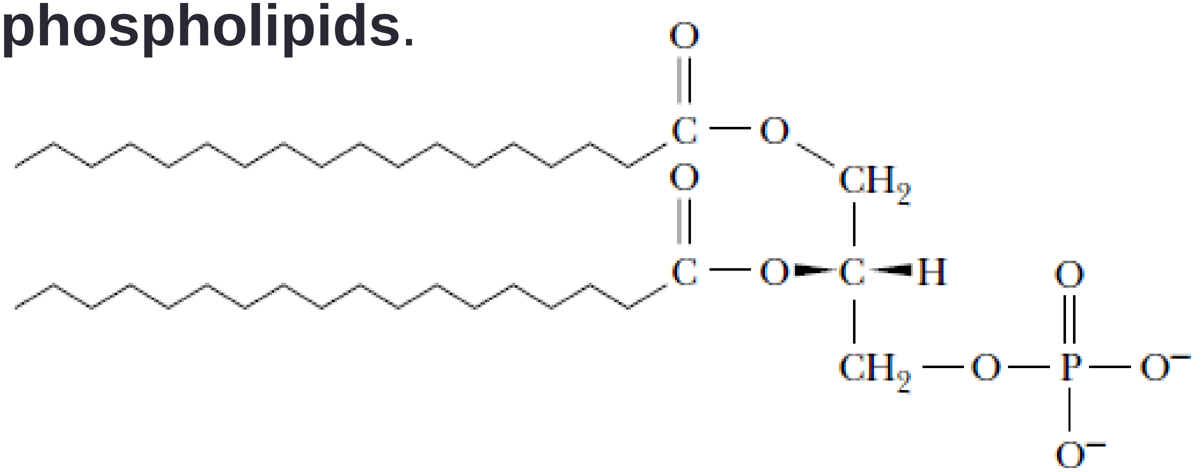
- Also, their hydrophobic nature allows them to aggregate in highly anhydrous forms, whereas polysaccharides and proteins are highly hydrated.

- For these reasons, triacylglycerols are the molecules of choice for energy storage in animals. Body fat (mainly triacylglycerols) also provides good insulation. Whales and Arctic mammals rely on body fat for both insulation and energy reserves.

Glycerophospholipids

- A 1,2-diacylglycerol that has a phosphate group esterified at carbon atom 3 of the glycerol backbone is a glycerophospholipid, also known as a *phosphoglyceride* or a *glycerol phosphatide*.

- These lipids form one of the largest classes of natural lipids and one of the most important. They are essential components of cell membranes and are found in small concentrations in other parts of the cell. It should be noted that all glycerophospholipids are members of the broader class of lipids known as **phospholipids**.



Common Phospholipids

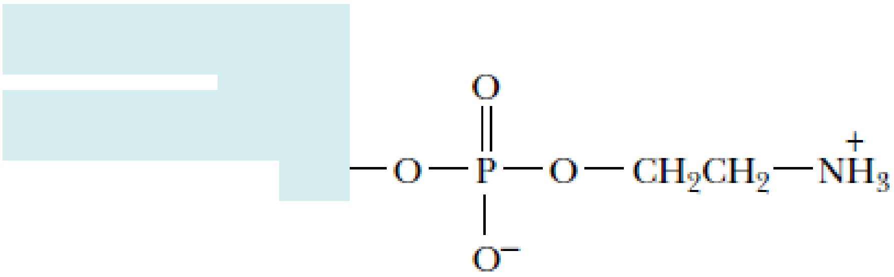
- Phosphatidic acid, the parent compound for the glycerol-based phospholipids, consists of glycerol-3-phosphate, with fatty acids esterified at the 1- and 2-positions.
- Phosphatidic acid is found in small amounts in most natural systems and is an important intermediate in the biosynthesis of the more common glycerophospholipids. In these compounds, a variety of polar groups are esterified to the phosphoric acid moiety of the molecule.
- The phosphate, together with such esterified entities, is referred to as a "head" group.

- Phosphatides with choline or ethanolamine are referred to as phosphatidylcholine (known commonly as lecithin) or phosphatidylethanolamine, respectively. These phosphatides are two of the most common constituents of biological membranes.

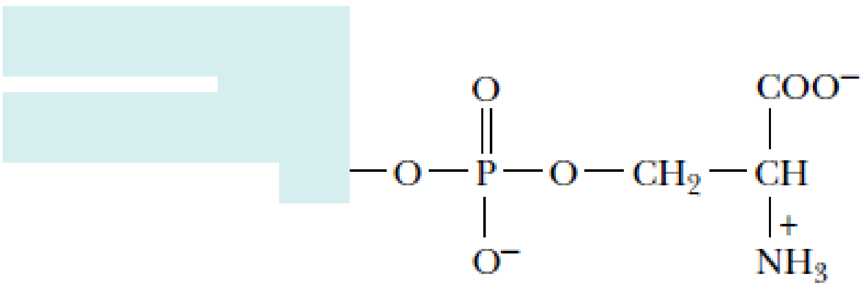
- Other common *head groups* found in phosphatides include glycerol, serine, and inositol.

- Another kind of glycerol phosphatide found in many tissues is diphosphatidylglycerol. First observed in heart tissue, it is also called cardiolipin. In cardiolipin, a phosphatidylglycerol is esterified through the C-1 hydroxyl group of the glycerol moiety of the head group to the phosphoryl group of another phosphatidic acid molecule.

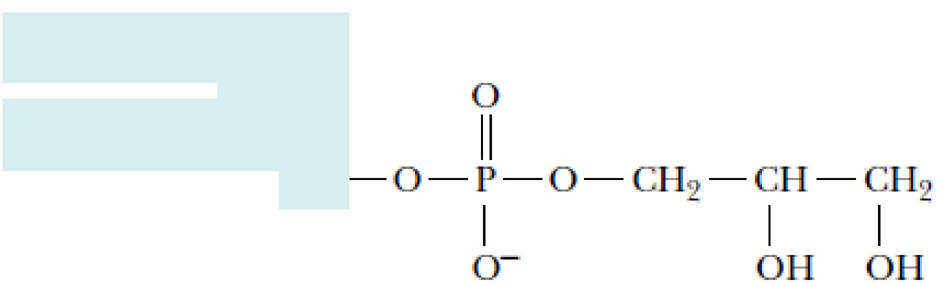
GLYCEROLIPIDS WITH OTHER HEAD GROUPS:



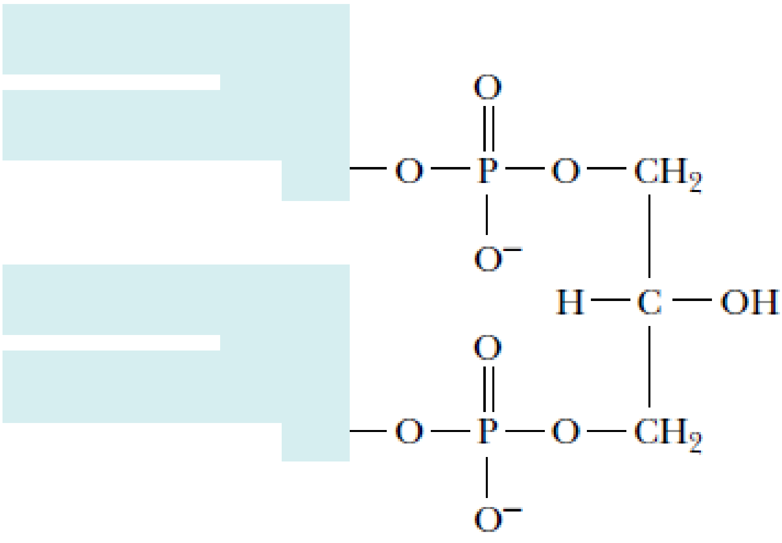
Phosphatidylethanolamine



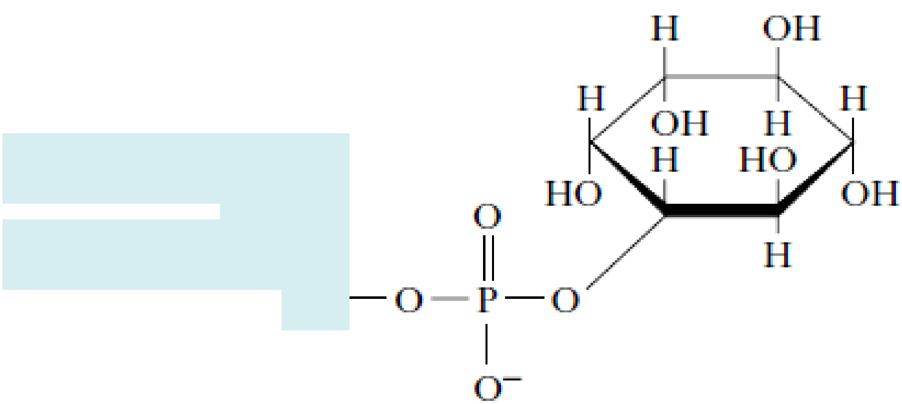
Phosphatidylserine



Phosphatidylglycerol

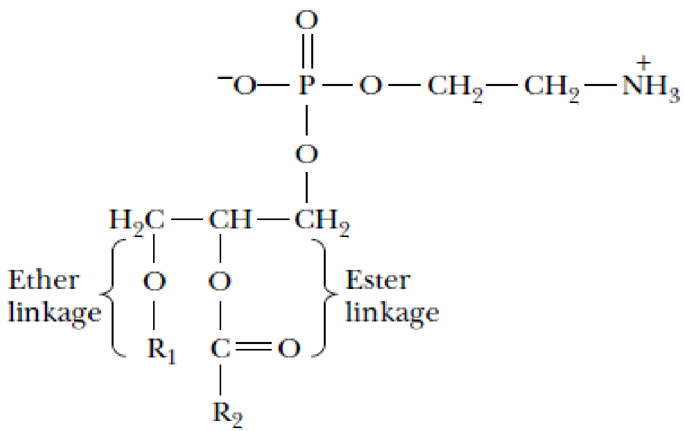


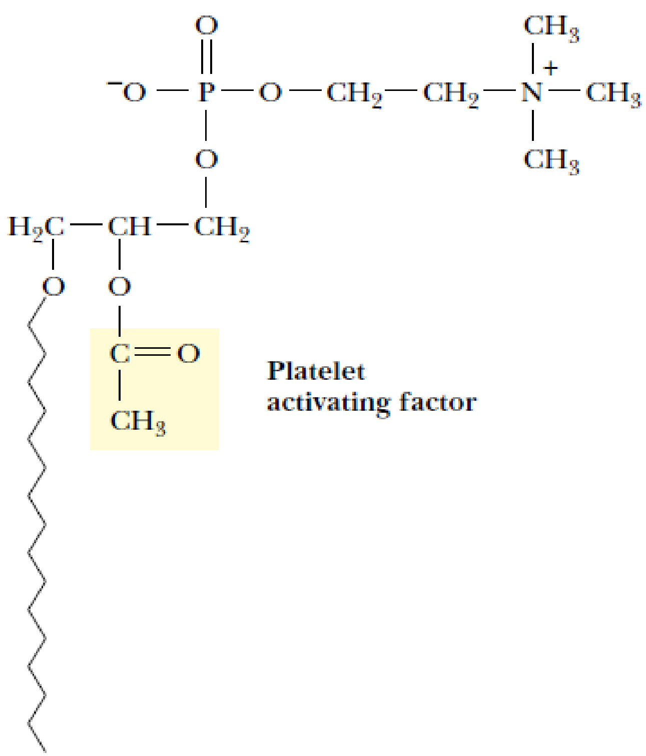
Diphosphatidylglycerol (Cardiolipin)



Phosphatidylinositol

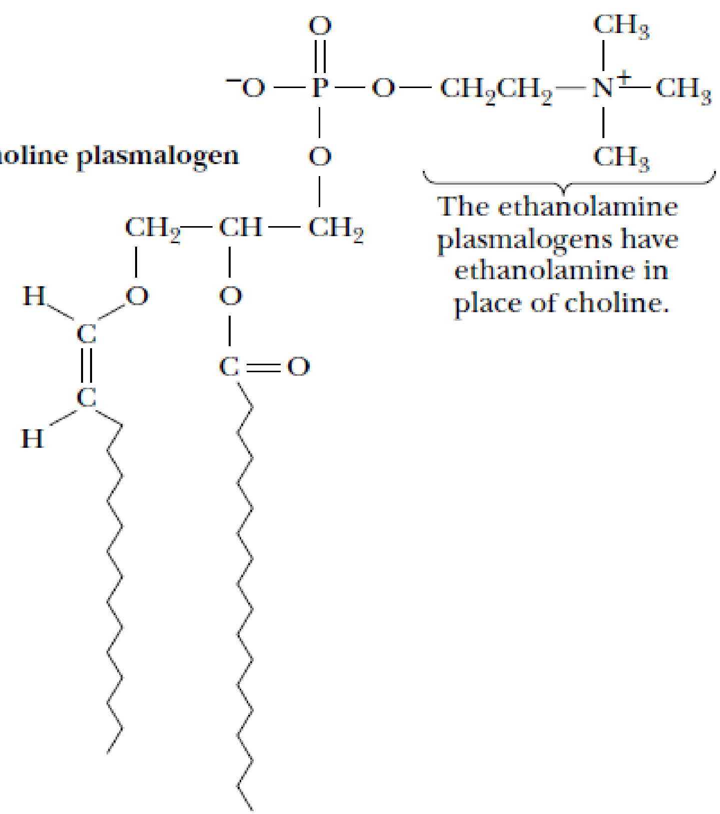
Ether Glycerophospholipids





Platelet activating factor

Choline plasmalogen



- Ether glycerophospholipids possess an ether linkage instead of an acyl group at the C-1 position of glycerol.

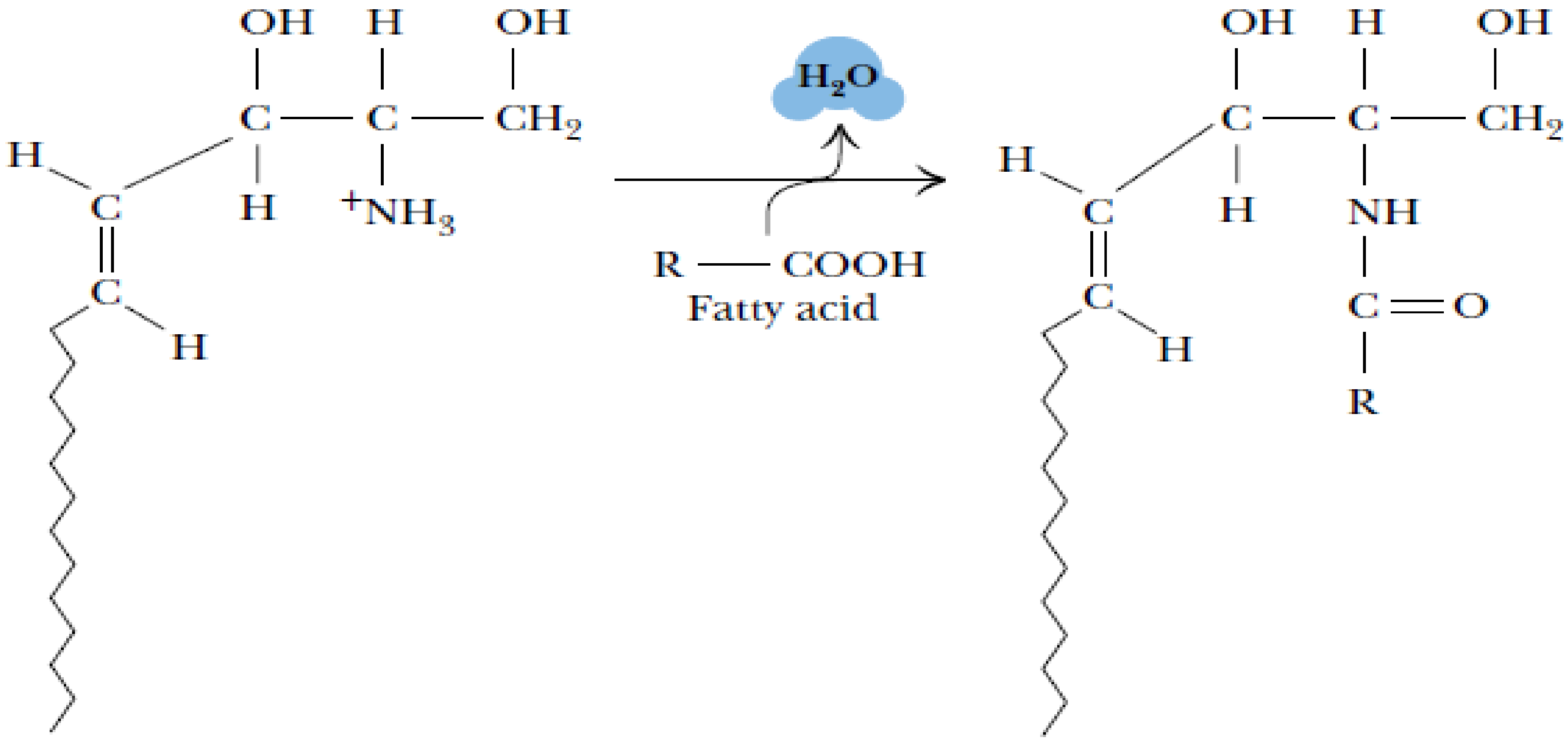
- One of the most versatile biochemical signal molecules found in mammals is **platelet activating factor**, or PAF, a unique ether glycerophospholipid.

- The alkyl group at C-1 of PAF is typically a 16-carbon chain, but the acyl group at C-2 is a 2-carbon acetate unit.

- By virtue of this acetate group, PAF is much more water-soluble than other lipids, allowing PAF to function as a soluble messenger in signal transduction.

- Plasmalogens are ether glycerophospholipids in which the alkyl moiety is *cis*-α,β-unsaturated.
- Common plasmalogen head groups include choline, ethanolamine, and serine.
- These lipids are referred to as phosphatidal choline, phosphatidal ethanolamine, and phosphatidal serine.

Sphingolipids

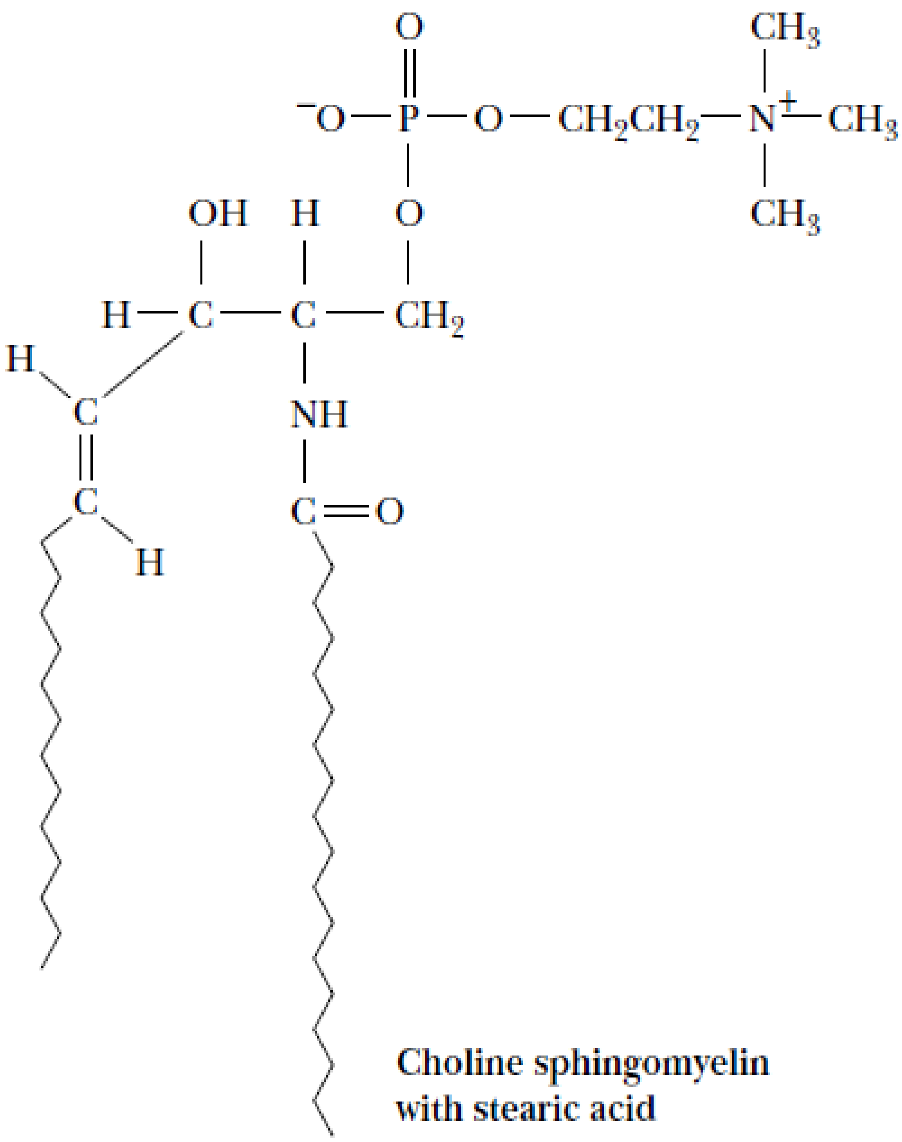


Sphingosine

Ceramide

- Sphingolipids represent another class of lipids found frequently in biological membranes. An 18-carbon amino alcohol, sphingosine, forms the backbone of these lipids rather than glycerol.

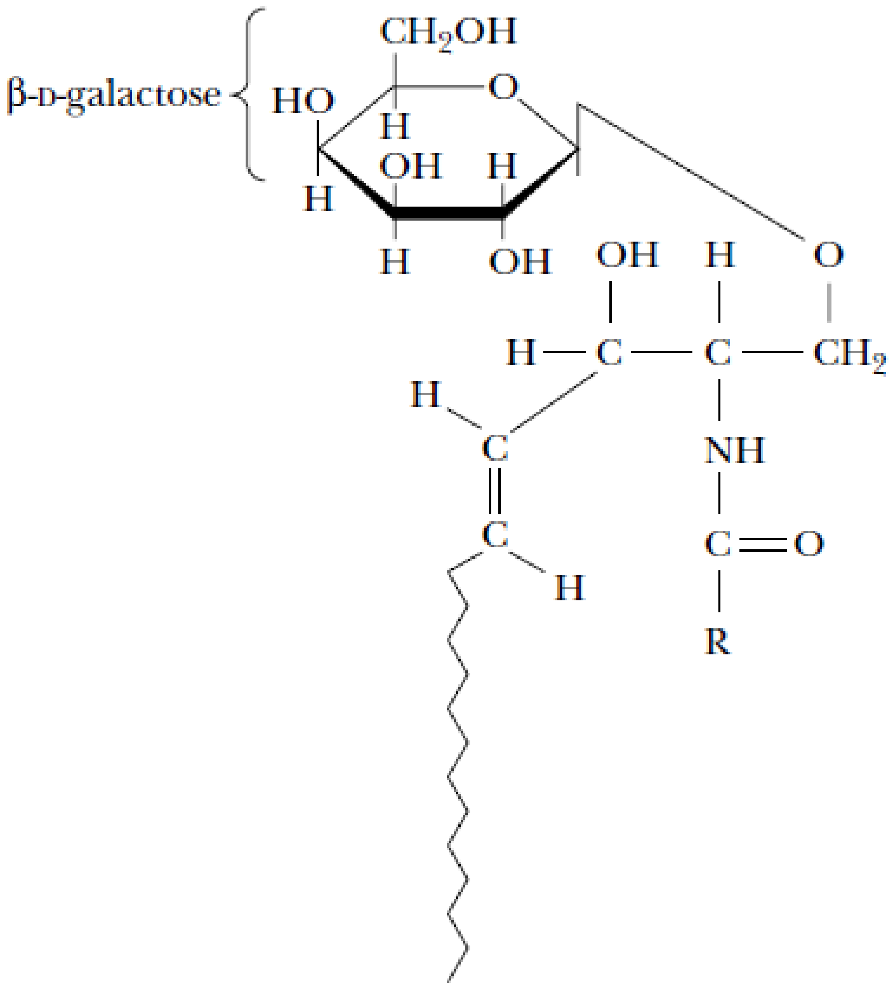
- Sphingomyelins represent a phosphorus-containing subclass of sphingolipids and are especially important in the nervous tissue of higher animals. A sphingomyelin is formed by the esterification of a phosphorylcholine or a phosphorylethanolamine to the 1-hydroxy group of a ceramide.



Choline sphingomyelin with stearic acid

- Glycosphingolipids are important components of muscle and nerve membranes in animals and they consist of a ceramide with one or more sugar residues in a β-glycosidic linkage at the 1-hydroxyl moiety.

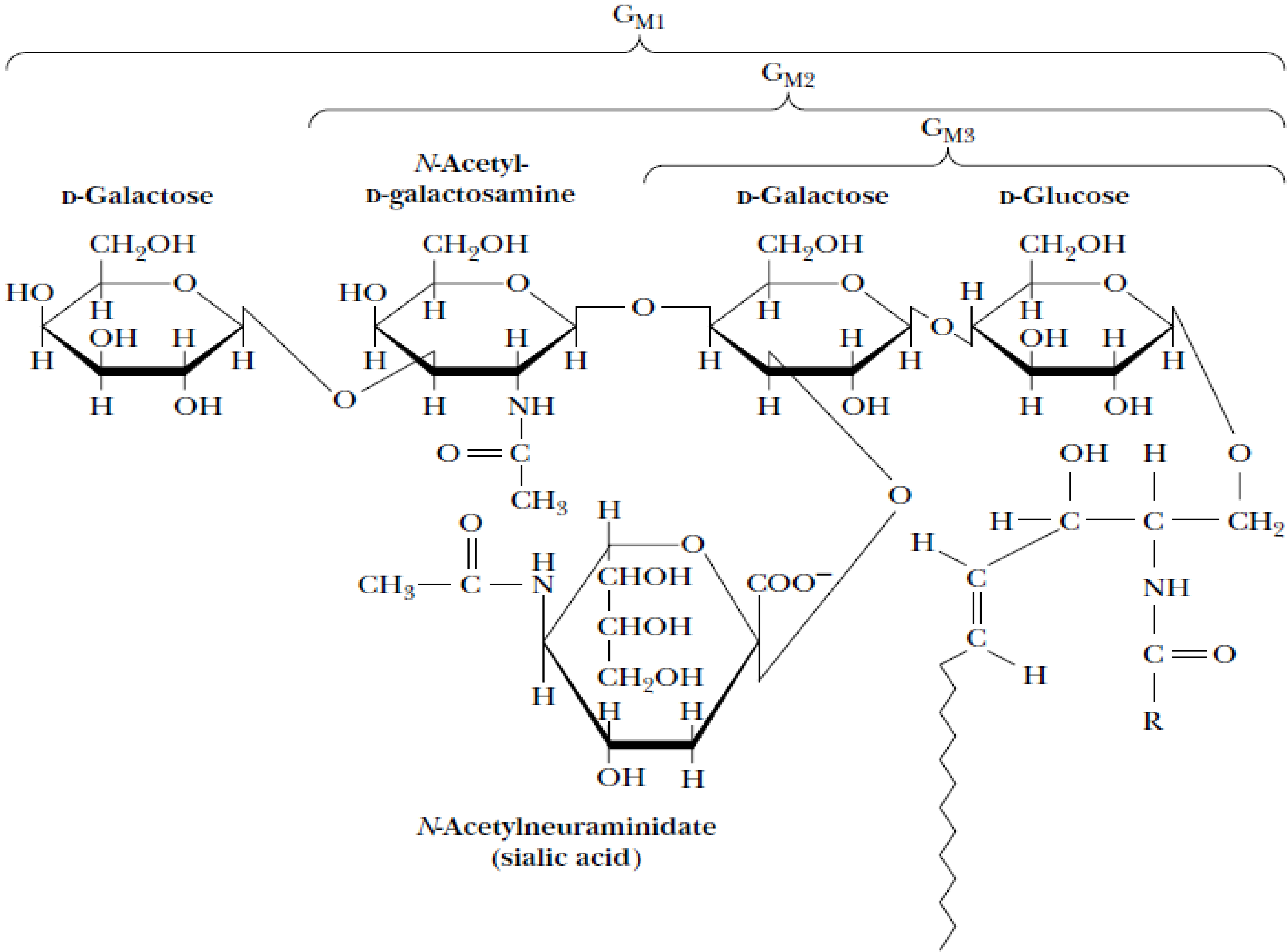
- The neutral glycosphingolipids contain only neutral (uncharged) sugar residues. When a single glucose or galactose is bound in this manner, the molecule is a cerebroside.



A cerebroside

- Gangliosides are formed when a sulphate is esterified at the 3-position of the galactose to make a sulphatide and are more complex glycosphingolipids that consist of a ceramide backbone with three or more sugars esterified, one of these being a sialic acid such as *N*-acetyl neuraminic acid.

- These latter compounds are referred to as *acidic glycosphingolipids,* and they have a net negative charge at neutral pH.



Gangliosides G_{M1}, G_{M2}, and G_{M3}

- The glycosphingolipids have a number of important cellular functions, despite the fact that they are present only in small amounts in most membranes.

- Glycosphingolipids at cell surfaces appear to determine, at least in part, certain elements of tissue and organ specificity. Cell–cell recognition and tissue immunity appear to depend upon specific glycosphingolipids.

- Gangliosides are present in nerve endings and appear to be important in nerve impulse transmission.

- A number of genetically transmitted diseases involve the accumulation of specific glycosphingolipids due to an absence of the enzymes needed for their degradation. Such is the case for ganglioside GM2 in the brains of *Tay-Sachs disease* victims, a rare but fatal disease characterized by a red spot on the retina, gradual blindness, and loss of weight, especially in infants and children.

Waxes

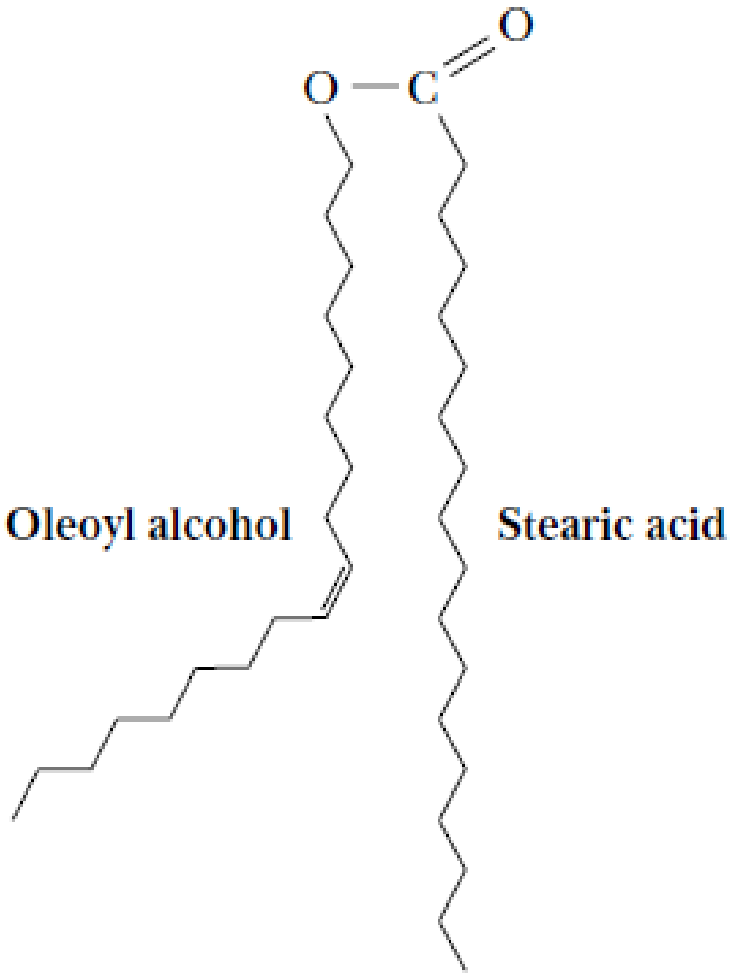
- Waxes are esters of long-chain alcohols with long-chain fatty acids. The resulting molecule can be viewed (in analogy to the glycerolipids) as having a weakly polar head group (the ester moiety itself) and a long, nonpolar tail (the hydrocarbon chains).

- Fatty acids found in waxes are usually saturated. The alcohols found in waxes may be saturated or unsaturated and may include sterols, such as cholesterol.

- Waxes are water-insoluble due to the weakly polar nature of the ester group. As a result, this class of molecules confers water-repellant character to animal skin, to the leaves of certain plants, and to bird feathers. The glossy surface of a polished apple results from a wax coating.

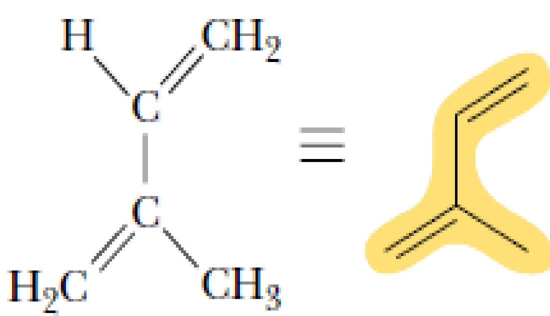
- Carnauba wax, obtained from the fronds of a species of palm tree in Brazil, is a particularly hard wax used for high gloss finishes, such as in automobile wax, boat wax, floor wax, and shoe polish.

- Lanolin, a component of wool wax, is used as a base for pharmaceutical and cosmetic products because it is rapidly assimilated by human skin.

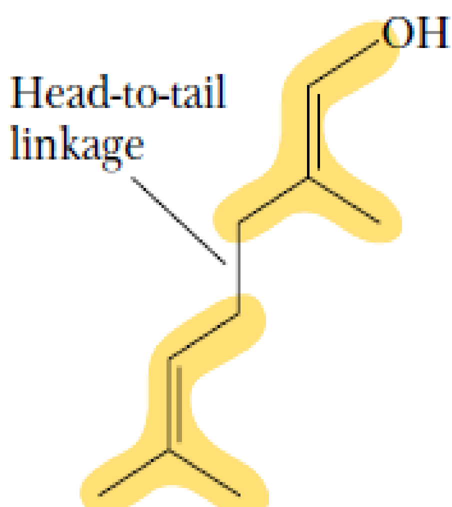


Terpenes

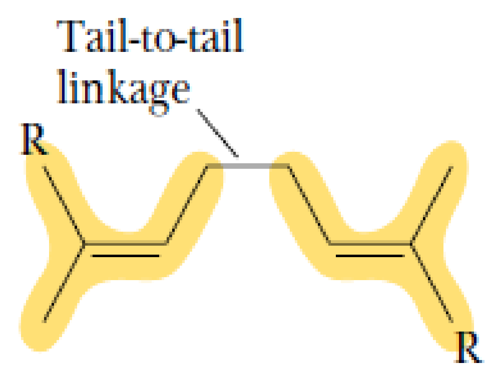
- The terpenes are a class of lipids formed from combinations of two or more molecules of 2-methyl-1,3-butadiene (isoprene; a five-carbon unit that is abbreviated C5). A monoterpene (C10) consists of two isoprene units, a sesquiterpene (C15) consists of three isoprene units, a diterpene (C20) has four isoprene units, and so on. Isoprene units can be linked in terpenes to form straight chain or cyclic molecules, and the usual method of linking isoprene units is head to tail.



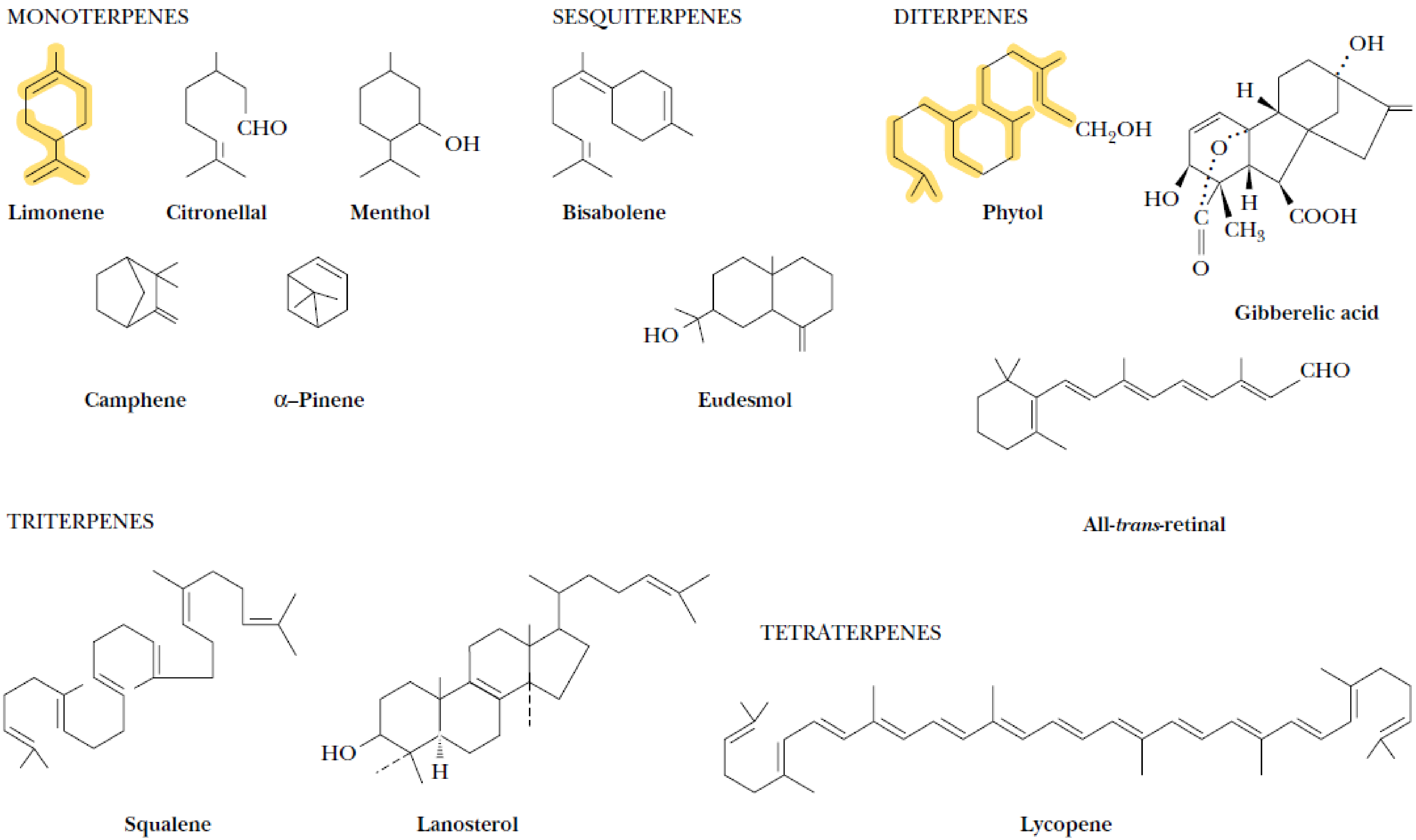
Isoprene



Geraniol



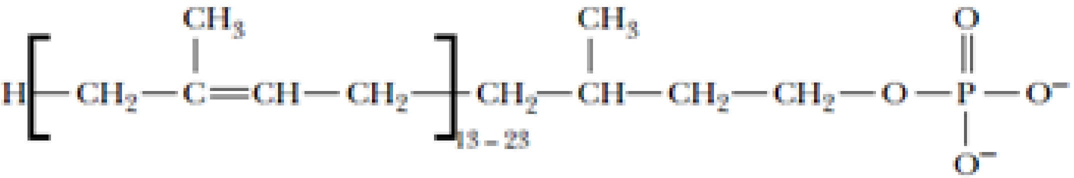
- Monoterpenes occur in all higher plants, while sesquiterpenes and diterpenes are less widely known.



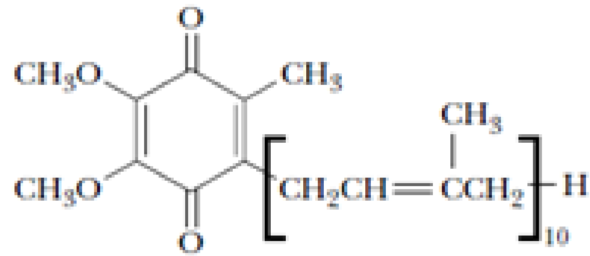
- The triterpenes are C30 terpenes and include squalene and lanosterol, two of the precursors of cholesterol and other steroids.

- Tetraterpenes (C40) are less common but include the carotenoids, a class of colourful photosynthetic pigments. β-Carotene is the precursor of vitamin A, while lycopene, similar to β-carotene but lacking the cyclopentene rings, is a pigment found in tomatoes.

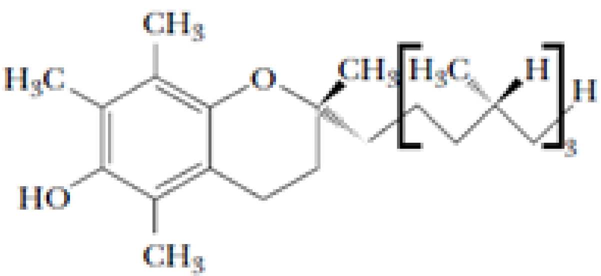
- Long-chain polyisoprenoid molecules with a terminal alcohol moiety are called polyprenols. The dolichols, one class of polyprenols, consist of 16 to 22 isoprene units and, in the form of dolichyl phosphates, function to carry carbohydrate units in the biosynthesis of glycoproteins in animals. Polyprenyl groups serve to *anchor* certain proteins to biological membranes.



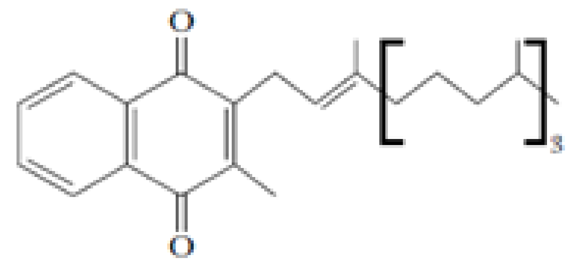
Dolichol phosphate



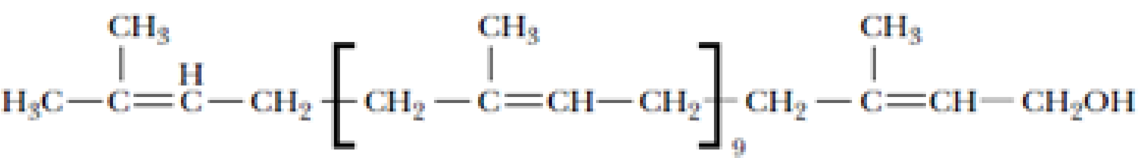
Coenzyme Q (Ubiquinone, UQ)



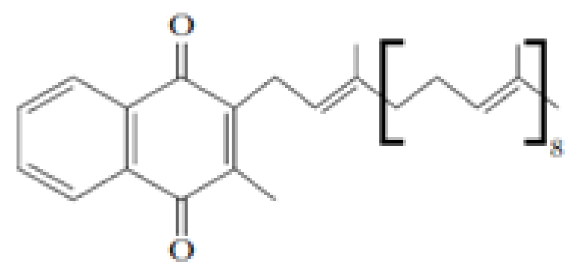
Vitamin E (α-tocopherol)



Vitamin K_1
(phylloquinone)



Undecaprenyl alcohol (bactoprenol)

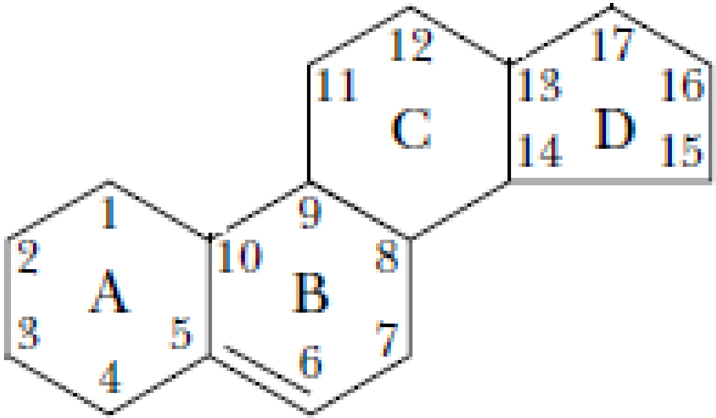


Vitamin K_2
(menaquinone)

Steroids

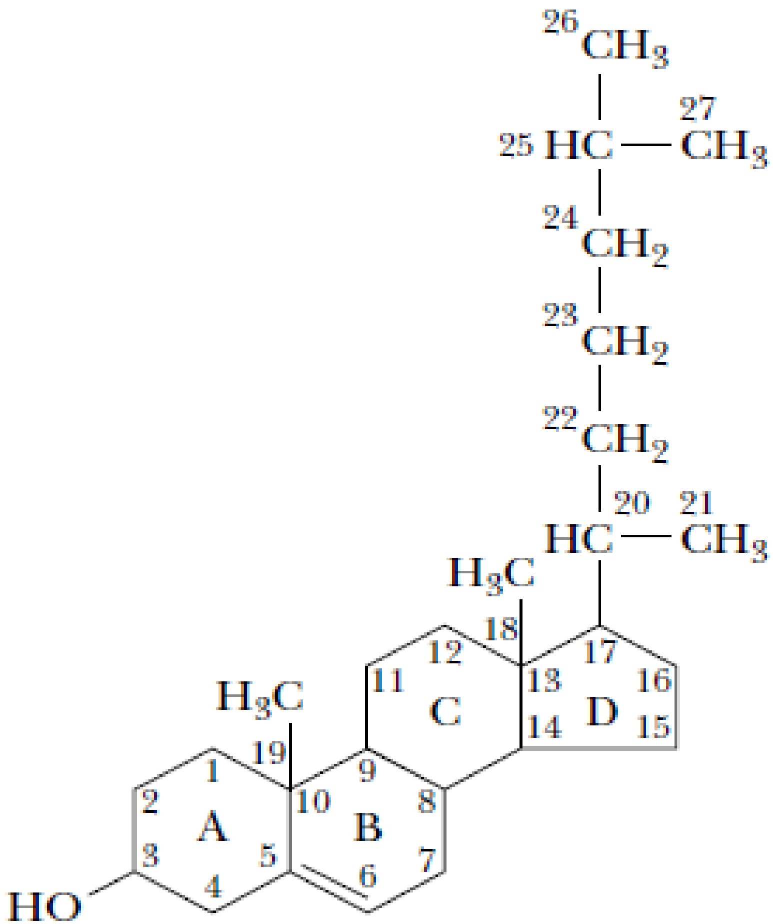
- The steroids are characterised by the fusoin of a four-ring system called the cyclopentanoperhydrophenanthrene (phenanthrene is three aromatic rings).

- The steroid nucleus has the three fused cyclohexane rings (A,B, and C) together with the cyclopentane ring (D).



Cholesterol

- A large and important class of terpene-based lipids is the steroids.
- This molecular family, whose members effect an amazing array of cellular functions, is based on a common structural motif of three six-membered rings and one five-membered ring all fused together.
- Cholesterol is the most common steroid in animals and the precursor for all other animal steroids.



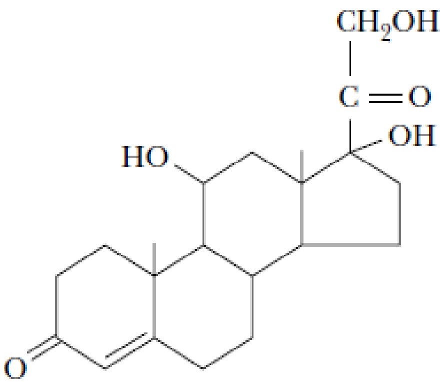
Cholesterol

- Cholesterol is a principal component of animal cell plasma membranes, and much smaller amounts of cholesterol are found in the membranes of intracellular organelles.

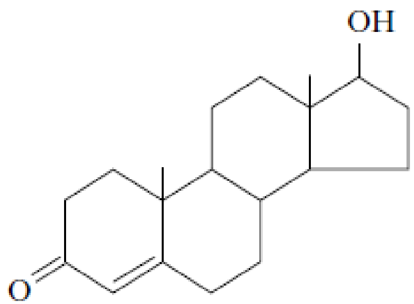
- The relatively rigid fused ring system of cholesterol and the weakly polar alcohol group at the C-3 position have important consequences for the properties of plasma membranes.

- Cholesterol is also a component of *lipoprotein complexes* in the blood, and it is one of the constituents of *plaques* that form on arterial walls in *atherosclerosis.*

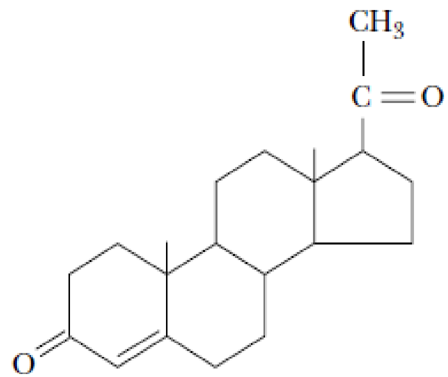
Steroid Hormones



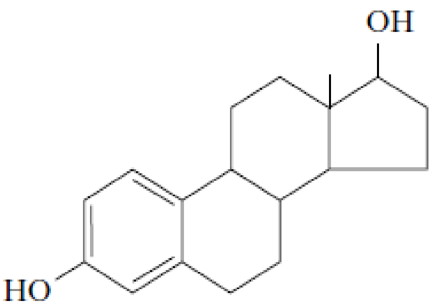
Cortisol



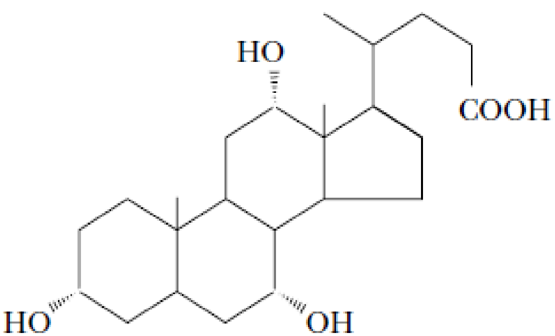
Testosterone



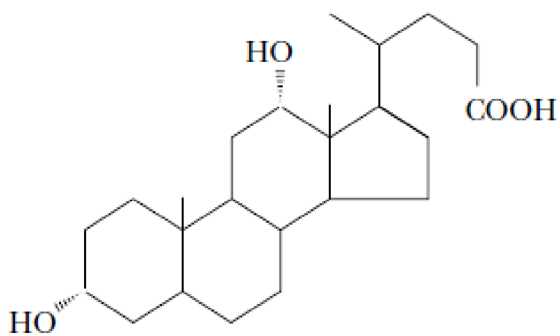
Progesterone



Estradiol



Cholic acid



Deoxycholic acid

- Steroids derived from cholesterol in animals include five families of hormones (the androgens, estrogens, progestins, glucocorticoids and mineralocorticoids) and bile acids.

- Androgens such as testosterone and estrogens such as estradiol mediate the development of sexual characteristics and sexual function in animals.

- The progestins such as progesterone participate in control of the menstrual cycle and pregnancy.

- Glucocorticoids (for example cortisol) participate in the control of carbohydrate, protein, and lipid metabolism, whereas the mineralocorticoids regulate salt (Na^+, K^+, and Cl^-) balances in tissues.

- The bile acids (including cholic and deoxycholic acid) are detergent molecules secreted in bile from the gallbladder that assist in the absorption of dietary lipids in the intestine.

Soaps

- Soaps are sodium and potassium salts of long chain fatty acids.

- They are commonly formed when acylglycerols are heated in the presence of an alkali.

- This process of alkali hydrolysis of glycerides is called saponification. Animal fat or vegetable oil is mixed with NaOH and heated for some hours.

- Sodium soaps are less soluble and less expensive that potassium soaps. Liquid soaps and shaving creams usually contain potassium soaps.

- Detergents are sodium and potassium salts of long chain alky sulphates or sulphonates. Soiudm lauryl (dodecyl) sulphate and sodium p-dodecylbenzenesulphonate are examples of detergents.

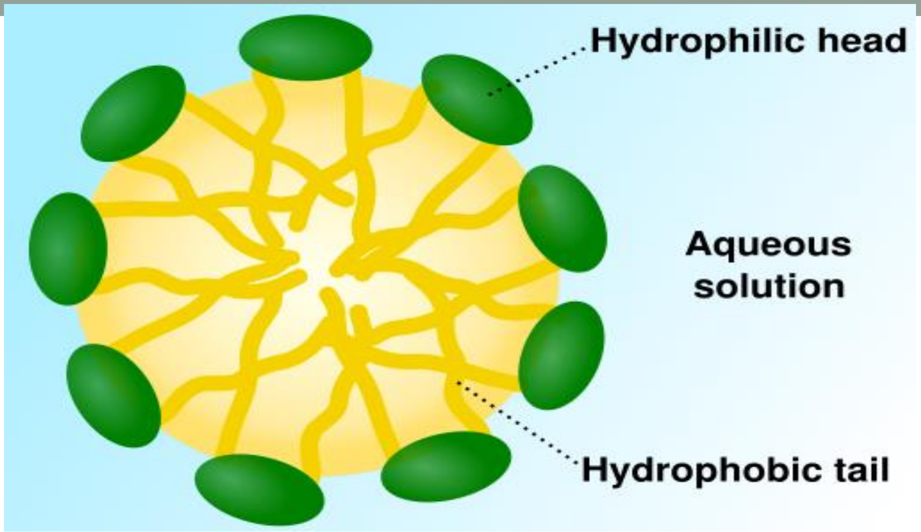
- Detergents and soaps are amphipathic molecules, composed of hydrophilic and hydrophobic parts. They are said to have polar heads and hydrophobic tails.

Cleansing action of detergents – micelle formation

- In the presence of detergent which has both polar and non-polar groups, the hydrophobic part interact with the organic dirt, while the polar part interact with the water and with agitation, the dirt is removed and broken into small droplets called micelles.

- The soap is said to have emulsified the organic dirt so that it can be rinsed away.

- In the micelle, the carboxylate head is exposed to the aqueous medium while the hydrocarbon tail extend into the greasy dirt. Due to negative charges on the head portion at the surface, repulsive forces prevent the micelles from coalescing.



- The main disadvantage of soaps is that in hard water containing Ca^{2+} and Mg^{2+} ions, the soaps are precipitated.
- Before any lather is formed, all the metallic ions have to be precipitated.
- Not only is the soap wasted, some undesirable deposits are formed on the clothing and other surfaces.

Rancidification

- **Rancidification**, the product of which can be described as **rancidity**, is the chemical decomposition of fats, oils and other lipids. When these processes occur in food, undesirable odours and flavours can result. In some cases, however, the flavours can be desirable (as in aged cheeses). In processed meats, these flavours are collectively known as warmed-over flavour. Three pathways for rancidification are recognized.
-
- ***Hydrolytic rancidity***
- Hydrolytic rancidity occurs when water splits fatty acid chains away from the glycerol backbone in triglycerides (fats). The chemical term is ester hydrolysis. Usually this hydrolysis process goes unnoticed, since most fatty acids are odourless and tasteless.

Oxidative rancidity

- Oxidative rancidity is associated with the degradation by oxygen in the air. Via a free radical process, the double bonds of an unsaturated fatty acid can undergo cleavage, releasing volatile aldehydes and ketones. This process can be suppressed by the exclusion of oxygen or by the addition of antioxidants. Oxidation primarily occurs with unsaturated fats.
-
- ***Microbial rancidity***
- Microbial rancidity refers to a process in which microorganisms, such as bacteria, use their enzymes such as lipases to break down fat. This pathway can be prevented by sterilization.

Reducing rancidification

- Antioxidants are often added to fat-containing foods to delay the onset or slow the development of rancidity due to oxidation. Natural antioxidants include polyphenols (for instance flavonoids), ascorbic acid (vitamin C) and tocopherols (vitamin E). Synthetic antioxidants include butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), TBHQ, propyl gallate and ethoxyquin.

- Rancidification can be decreased, but not completely eliminated, by storing fats and oils in a cool, dark place with little exposure to oxygen or free radicals, since heat and light accelerate the rate of reaction of fats with oxygen.

- Antimicrobial agents can also delay or prevent rancidification by inhibiting the growth of bacteria or other micro-organisms.

- Oxygen scavenging technology can be used to remove oxygen from food packaging and therefore prevent oxidative rancidification.

Parameters for characterizing lipids

Acid Number: This is the number of milligrams (mg) of KOH required to neutralize the free fatty acids present in 1 gram of fat or oil. It gives a measure of the extent of rancidity of fats.

Iodine Number: This is the number of grams of iodine absorbed by 100 grams of fat or oil. This absorbed iodine adds across the double bond present in the fat or oil. Therefore the iodine number shows the degree of unsaturation of fat or oil.

Saponification Number: This is the number of milligram of KOH required to saponify 1 gram of fat. It is determined by hydrolysis of fat in excess of standard alcoholic KOH followed by the determination of the excess alkali by titration with standard acid.

Peroxide Number: This refers to the amount in millimoles of oxygen taken per kilogram of oil. It measures the extent to which oxygen has been taken up by an oil to form peroxides. Therefore, it shows the freshness of an oil.

Thiobarbituric acid (TBA) Test: This is a measure of secondary product of lipid peroxidation, malonaldehyde. It involves the reaction of malonaldehyde with TBA to give coloured products the intensity of which gives the degree of peroxidation of fats.