Chapter 19: Lipids

1. Be familiar with the physical and chemical properties and biological function of each of the families of lipids.
2. Write the structures of simple examples of each of the classes of lipids. Name the common lipids.
3. Know the method of synthesizing glycerides and the reactions of glycerides: esterification, hydrolysis, saponification, and hydrogenation.
4. Understand the functions of prostaglandins in physiological processes. Know how aspirin reduces pain. Be familiar with the steroid hormones. Understand the role of the lipoproteins in triglyceride and cholesterol transport in the body.
5. Appreciate the roles of HDL, LDL, and cholesterol in heart disease.
6. Know the structure and functions of cell membranes.

Introduction

There are four major classes of bioorganic substances: carbohydrates, lipids, proteins are the four major classes of bioorganic substances. In the previous chapter 18 we considered the first of these classes, carbohydrates. We now turn our attention to the second of the bioorganic classes, the compounds we call lipids.

Lipids known as fats provide a major way of storing chemical energy and carbon atoms in the body. Fats also surround and insulate vital body organs, providing protection from mechanical shock and preventing excessive loss of heat energy. Phospholipids, glycolipids, and cholesterol (a lipid) are the basic components of cell membranes. Several cholesterol derivatives functions as chemical messengers in the body.

19.1 Structure and Classification of Lipid
Structural Characteristics

Lipids are a diverse group of biological substances made up primarily or exclusively of **nonpolar groups**. Lipids are grouped together on the basis of solubility in oganic or non polar solvents. Lipids are insoluble in water (or polar solvent). Lipids vary greatly in structure and function. Lipids are nonpolar: As the hydrocarbon component (the alkyl group) of an organic compound increases in size, the relative contribution of a polar functional group to the physical properties of the molecule decreases. Lipids have larger nonpolar alkyl groups and are insoluble or poorly soluble in water. As the size of an alkyl group increases in an organic compound, the water solubility of the compound decreases. As a result of their nonpolar character, lipids typically dissolve more readily in nonpolar solvents such as acetone, ether, chloroform, and benzene, than in water. This solubility characteristic is of extreme importance in cells because lipids tend to associate into nonpolar groups and barriers, as in the cell membranes that form boundaries between and within cells. Besides having important roles in membranes, lipids are stored and used in cells as an energy source. Other lipids form parts of cellular regulatory mechanisms. Lipids link covalently with carbohydrates to form glycolipids and with proteins to form lipoproteins.

- **hydrophobic** or water hating- water insoluble nonpolar molecule.
- **hydrophilic** or water loving- water soluble polar molecule.

They are classified on the basis of solubility not on any functional groups

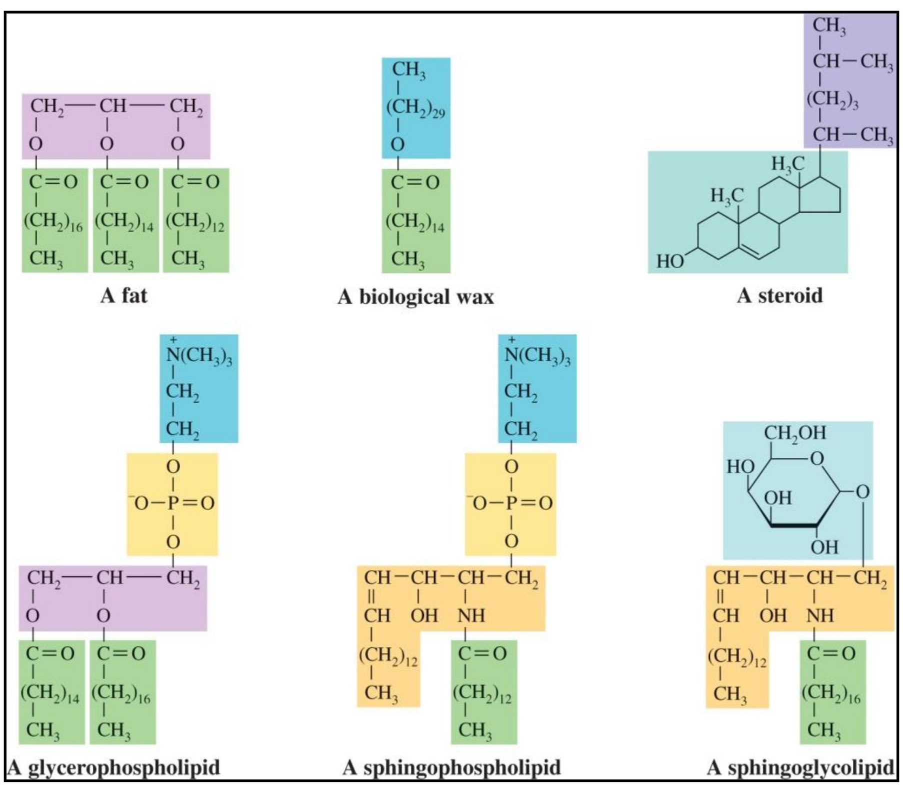
- **Insoluble** or sparingly soluble **in water**
- **Soluble in non-polar** organic **solvents**

Lipid Classification

For purposes of simplicity of study lipids are divided into five categories based on their function:

- **Energy-storage lipids** – A fat, triacylglycerols or triglycerides.
- **Membrane lipids** - phospholipids, sphingoglycolipids, and cholesterol
- **Emulsification lipids** - bile acids, soaps and detergents
- **Chemical messenger lipids** - steroid hormones, eicosanoids, and prostaglandins
- **Protective-coating lipids -** biological waxes
- **Fat-soluble vitamins-**

Lipids exhibit structural diversity and some are esters, some are amides, and some are alcohols (acyclic and cyclic) and some are polycyclic.



19.2 Fatty Acids: Lipid Building Blocks

They are long, unbranched chain carboxylic acid carboxylic acids with inear(unbranched) carbon chain - Fatty acids are naturally occuring monocarboxylic acids which nearly all have an even number of carbon atoms.

Saturated fatty acids

Even # of Carbon atoms:

Long chain fatty acids: C_{12} - C_{26}: three most abundant are palmitic acid (16:0), stearic acid (18:0)

Medium chain fatty acids: C_6 - C_{11}

Short-chain fatty acids: C_4 - C_5

Two Types: Saturated - all C-C bonds are single bonds

Most abundant saturated fatty acids

Numbering starts from the end of -COOH group

See structural notation: it indicates number of C atoms

Example - Lauric acid has 12 C atoms and no double bonds so it is (12:0).

Table 1: Saturated and Unsaturated Fatty Acid

Saturated Fatty Acids	
Caproic Acid (6)	$CH_3(CH_2)_4CO_2H$
Caprylic Acid (8)	$CH_3(CH_2)_6CO_2H$
Capric Acid (10)	$CH_3(CH_2)_8CO_2H$
Lauric Acid (12)	$CH_3(CH_2)_{10}CO_2H$
Myristic Acid (14)	$CH_3(CH_2)_{12}CO_2H$
Palmitic Acid (16)	$CH_3(CH_2)_{14}CO_2H$
Stearic Acid (18)	$CH_3(CH_2)_{16}CO_2H$
Arachidic Acid (20)	$CH_3(CH_2)_{18}CO_2H$
Lignoceric Acid (24)	$CH_3(CH_2)_{22}CO_2H$

*Occur as major fatty acids in human storage fats.

Unsaturated fatty acids

Monosunsaturated: one C=C bond. Most abundant is oleic acid (18:1)

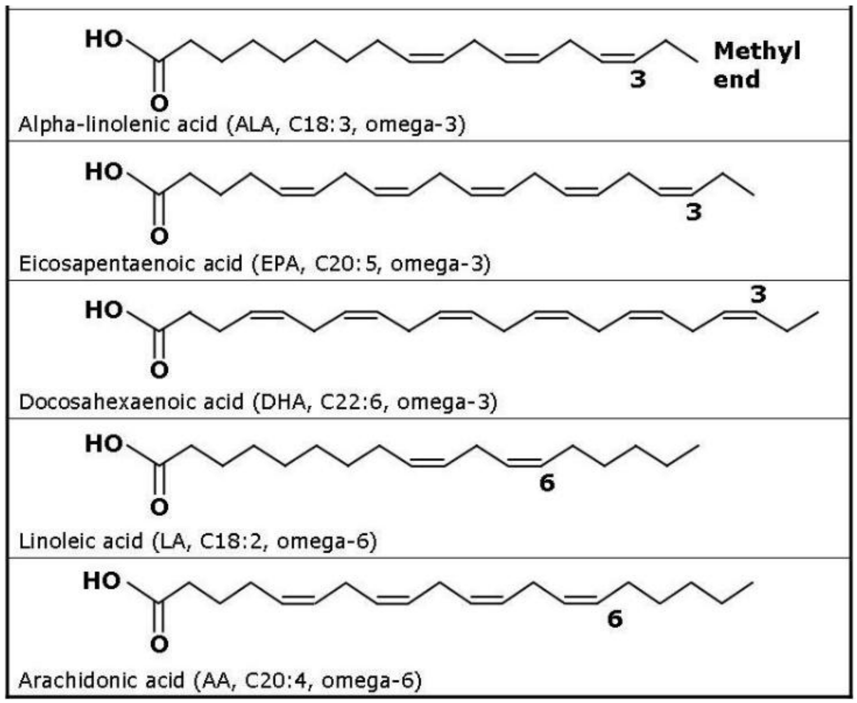
Numbering of unsaturated fatty acids starts from the other end of COOH

See structural notation: it indicates number of C atoms E.g., 18:2 – 18 carbons, 2 double bonds.

Unsaturated Fatty Acids	
Crotonic Acid (4:1)2	$CH_3CH{=}CHCO_2H$
Palmitoleic Acid (16:1)9 OMEGA 7	$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$
Oleic acid* (18:1)9 OMEGA 9	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$

Polyunsaturated fatty acids: 2 or more C=C bonds present - up to six double bonds are present in fatty acids. In most unsaturated fatty acids, the cis isomer predominates; the trans isomer is rare and cis configuration imparts lower melting points than their saturated counterparts; the greater the degree of unsaturation, the lower the melting point.

Important polyunsaturated fatty acids: omega-3 and omega-6 fatty acids



Scientists differentiate fatty acids by the characteristics of their molecules. The two principal essential fatty acids are Omega-6 (n-6) series and the Omega-3(n-3) series. The number indicates the position of the first double carbon bond when counting from a specified end of the molecule.

Omega refers to number carbon atoms in the hydrocabon chain at the terminal end of chain after the last double bond.

Essential Fatty Acids: Must be part of diet. They are fatty acids that cannot be produced by the body and are necessary for proper metabolism. The OMEGA 6 and OMEGA 3 fatty acids are referred to as Essential Fatty Acids (**EFA**).

Omega-6 Series

Linoleic Acid (LA) -- LA is the essential fatty acid from which Gamma Linolenic Acid (GLA) is derived.

Gamma linolenic Acid (GLA) -- GLA is found primarily in mother's milk and Evening Primrose seeds. Moderate but variable amounts are found in borage and blackcurrant seeds.

Dihomogamma linolenic Acid (DGLA) -- DGLA is found in mother's milk and organ meats such as spleens, kidneys and adrenals.

Arachidonic Acid (AA) -- AA is found in meats, dairy products and seafood such as shrimps and prawns.

Omega-3 Series

Alpha linolenic Acid (ALA) -- ALA is found in green, leafy vegetables and linseed (GLA) oils.

Eicosapentaenoic (EPA) -- EPA is found primarily in marine and fish oils.

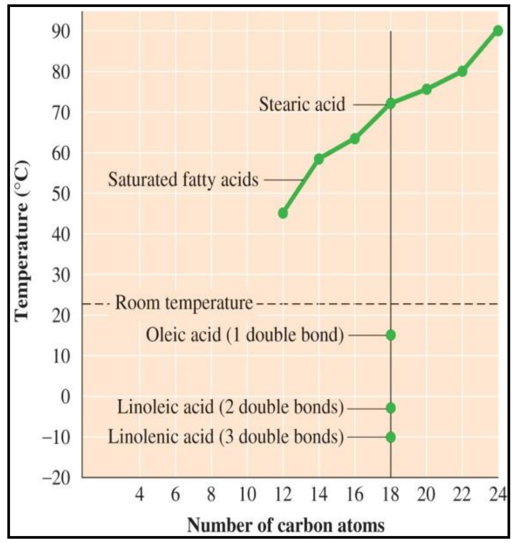
Docosahexaenoic (DHA) -- DHA found primarily in marine and fish oils.

19.3 Physical Properties of Fatty Acids

Water solubility: Short chain fatty acids have some solubility whereas long chain fatty acids are insoluble. Short chain fatty acids are sparingly soluble because of carboxylic acid polar group

Physical properties such as melting point depends on the number of C atoms and degree unsaturation.

Melting Point: Depends Upon: Length of carbon chain. Also degree of unsaturation (number of double bonds in a molecule



Physical properties of triglycerides depend on their fatty acid components Melting point of the triglycerides increases as the number of carbons in their hydrocarbon chains increases and as the number of double bonds decreases.

Triglycerides rich in unsaturated fatty acids are generally liquid at room temperature and are called oils. Triglycerides rich in saturated fatty acids are generally semisolids or solids at room temperature and are called fats.

Effect of unsaturation on physical properties

Saturated fatty acids

Hydrocarbon chains of the saturated fatty acids can lie parallel with strong London dispersion forces between their chains; they pack into well-ordered, compact crystalline forms and melt above room temperature as exemplified in animal facts.

Unsaturated fatty acids

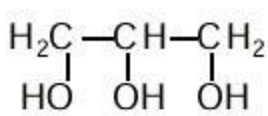
Hydrocarbon chains have a less ordered structure and dispersion forces between them are weaker in unsaturated fatty acids because of the **cis** configuration of the double bonds in unsaturated fatty acids, thei; these triglycerides have melting points below room temperature as exemplified in triglycerides found fish and polar bears.

19.4 Energy-Storage Lipids: Triacylglycerols

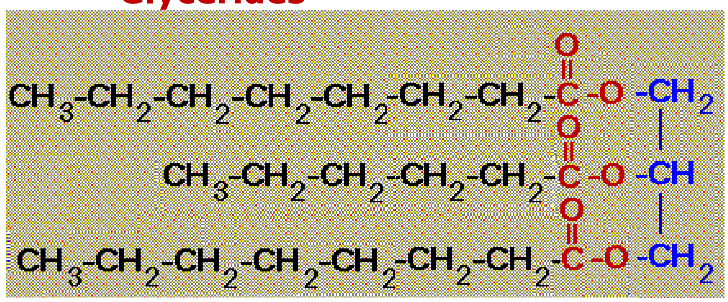
Simple Triacylglycerols: Three identical fatty acids are esterified. Naturally occurring simple triacylglycerols are rare

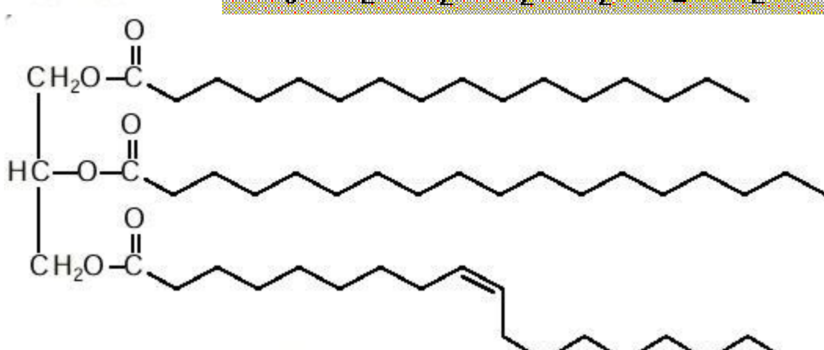
Mixed Triacylglycerols: A triester formed from the esterification of glycerol with more than one kind of fatty acid. In nature mostly mixed triacylglycerols are found and are different even from the same source depending on the feed, e.g., corn, peanut and wheat -fed cows have different triacylglycerols.

Glycerides



GLYCEROL





α-PALMITO-β-STEARO-α'-OLEIN

Triacylglycerols are concentrated primarily in special cells (adipocytes) Nearly filled with the material.

9.5 Dietary Considerations and Triacylglycerols

In the past two decades, considerable research has been carried out concerning the role dietary factors as a cause of disease (obesity, diabetes, cancer, hypertension, and atherosclerosis). Numerous studies have shown that, in general, nations whose citizens have hit dietary intakes of triacylglycerols (fats and oils) tend to have higher incidences of her disease and certain types of cancers. This is the reason for concern that the typical Americ; diet contains too much fat and the call for Americans to reduce their total dietary fat intake. According to U.S. Department of Agriculture (USDA) Food Guide or the Dietary Approaches to Stop Hypertension (DASH) Eating Plan, it is recommended for WEIGHT MANAGEMENT a daily diet should have less than 10 percent of calories from saturated fatty acids and less than 300 mg/day of cholesterol, and keep trans fatty acid consumption as low as possible.

Contrary to recommendations, however, there are several areas of the world when high dietary fat intake does not translate into high risks for cardiovascular disease, obesity, and certain types of cancers. These exceptions, which include some Mediterranean; countries and the Inuit people of Greenland, suggest that relationships between direct triglyceride intake and risk factors for disease involve more than simply the total amount of triglycerides taken in.

Effect of high Fructose Corn Syrup (HFCS) on the Obesity and LDL bad fats in the blood stream

Recent studies indicate Obesity and type 2 diabetes are occurring at epidemic rates in the United States and many parts of the world are could also come from the high fructose levels in the diets. The "obesity epidemic" appears to have emerged largely from changes in our diet to reduce dietary fats and reduced physical activity. An important but not well-appreciated dietary change has been the substantial increase in the amount of dietary fructose consumption from high intake of sucrose and high fructose corn syrup, a common sweetener used in the food industry. A high flux of fructose to the liver, the main organ capable of metabolizing this simple carbohydrate, perturbs glucose metabolism and glucose uptake pathways, and leads to a significantly enhanced rate of triglyceride (TG) in the form of HDL, driven by the high flux of glycerol and acyl portions of TG molecules from fructose breakdown. These metabolic disturbances appear to underlie the induction of insulin resistance commonly observed with high fructose feeding in both humans and animal models. The emerging evidence from recent epidemiological and biochemical studies clearly suggests that the high dietary intake of fructose has rapidly become an important causative factor in the development of the metabolic disorders leading to obesity. **There is an urgent need for increased public awareness** of the risks associated with high fructose consumption and greater efforts should be made to curb the supplementation of packaged foods with high fructose additives.

Lipoproteins

Lipoproteins are composed of a neutral core of cholesterol and triacylglycerols. These molecules are very hydrophobic and in the intestine become coated with an outer shell of apoproteins, phospholipids and nonesterified cholesterol. These other molecules become oriented such that their hydrophobic tails are facing the central core and their hydrophilic portions face the aqueous environment of the plasma. The lipids in the core are obtained from the diet (fat) or de novo synthesis. The lipoproteins leave the intestines in the form of chylomicrons. There are 4 different lipoproteins found in the blood that are clinically important. They vary in their densities, size and triglyceride/cholesterol ester ratios. Chylomicrons are the largest and least dense. In increasing order of density, the remainder are VLDL, LDL and HDL.

Four major groups of plasma lipoproteins.

a) Chylomicrons

Transports dietary triglyceride from the gut to the liver, adipose tissue and muscle. They appear in the bloodstream after a meal and transport dietary triglycerides from the gut to sites where the triglycerides are used and stored.

b) Very low-density lipoproteins (VLDL)

They transport triglycerides and cholesterol that are synthesized by the liver to similar sites for utilization or storage. Many people with high triglycerides and cholesterol make too much VLDL in the liver because of an inherited tendency. Transports mostly triglyceride, some cholesterol, from liver to the periphery. When **chylomicrons** and VLDL reach capillary beds in various tissues such as muscle or fat, an enzyme breaks down triglycerides into fatty acids and glycerol. The remaining chylomicron remnants continue to circulate until they are taken up or absorbed by the liver.

c. Low-density lipoproteins (LDL)

The VLDL remnants are converted primarily to **LDL**, which is removed from the circulation mostly by being absorbed into liver cells. For liver cell absorption of LDL to occur, the LDL must bind to the LDL receptor on the cell surface. People with **familial hypercholesterolemia** lack these receptors, and the result is they have LDL-cholesterol levels that are often two or three times normal. The LDL-cholesterol complex is small and dense compared to chylomicrons and VLDL, and when it is present in high concentrations it tends to deposit inside the blood vessel wall. This contributes to **atherosclerosis** (the build-up of fatty plaque in the arteries; "hardening of the arteries").

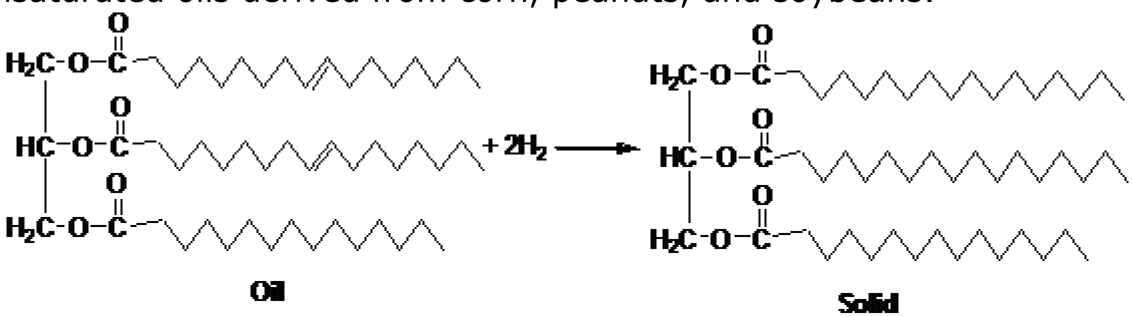
d. High-density lipoproteins (HDL)

They have a different function in the body. It removes excess cholesterol from cells and helps transport it back to the liver. High HDL levels are associated with a reduced risk of heart disease and low levels with an increased risk of early heart disease. For this reason HDL-cholesterol is known as the "good" cholesterol. However, we don't yet have any direct evidence that increasing HDL can prevent or treat heart disease. Involved in "reverse transport" of cholesterol from cells to the liver

19.6 Chemical Reactions of Triacylglycerols

The reduction of triglycerides with unsaturated fatty acids

The process of converting fats to oils is called hardening and involves c**atalytic reduction** of some or all of an oil's carbon-carbon double bonds. in practice, the process is controlled to produce a fat of a desired consistency the resulting fats are sold for cooking (Crisco, Spray, and others) margarine and other butter substitutes are produced by partial hydrogenation of polyunsaturated oils derived from corn, peanuts, and soybeans.

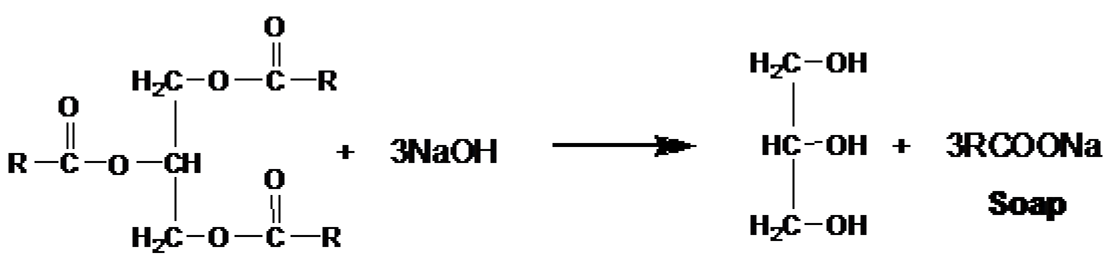


Trans fatty acids

Hardening results in the isomerization of some cis-fatty acids to trans-fatty because catalytic hydrogenation is to some degree reversible.

Hydrolysis in basic solution (Saponification): Produce salt of fatty acid and glycerol

$$RCOOR' + NaOH \rightarrow RCOONa \text{ (soap)} + R'OH$$



Oxidation of Triglycerides

Double bonds in triacylglycerols are subject to oxidation with oxygen in air (an oxidizing agent)-Leads to C=C breakage.

Remember that oxidation of alkenes may result into two short chain molecules – an aldehydes or a carboxylic acid:

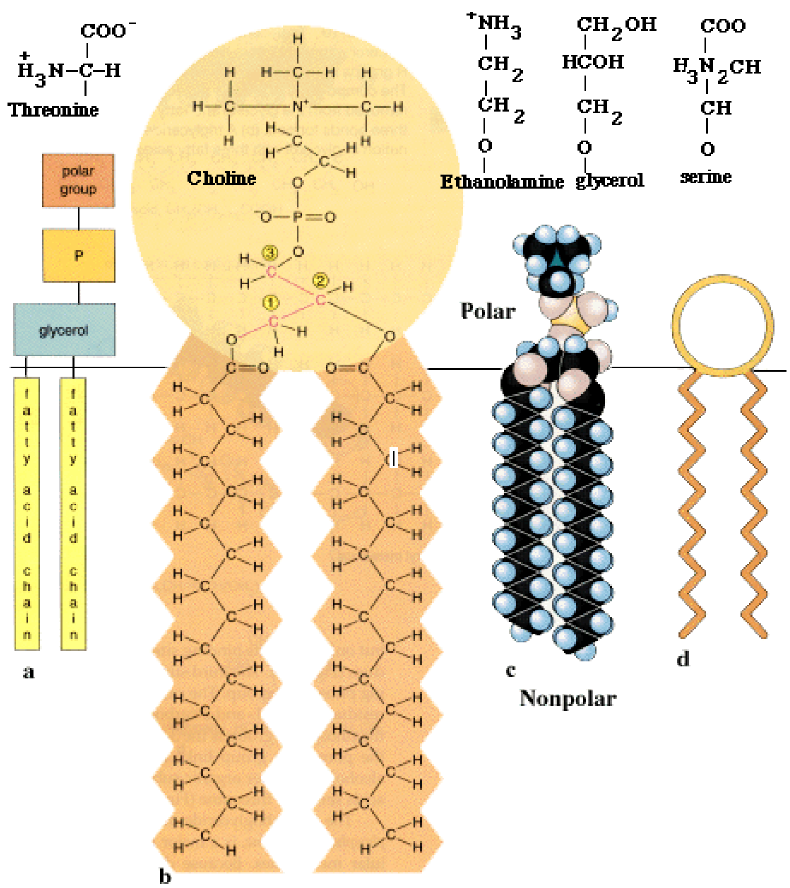
The aldehydes and/or carboxylic acids so produced often have objectionable odors - fats and oils are said to be *rancid*

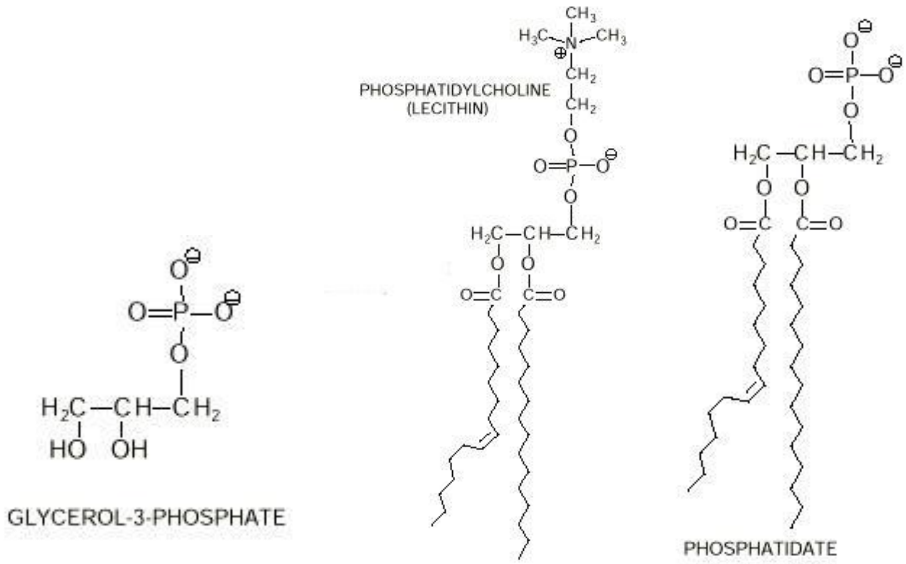
To avoid this unwanted oxidation process antioxidants are added as preservatives, e.g., Vitamin C and vitamin E are good antioxidant preservatives.

19.7 Membrane Lipids: Phospholipids

The Primary lipids of biological membranes are Phospholipids, a group of phosphate-containing molecules with structures related to the triglycerides. In most common phospholipids, called phosphoglycerides, glycerol forms the backbone of the molecule but only two of its binding sites link to fatty acid residues. The third site links instead to a bridging phosphate group. The carbon linked to the phosphate group is called the 3-carbon; the carbons attached to fatty acid residues are the 1 and 2 carbons. The other end of the phosphate bridge links to another organic subunit, most commonly a nitrogen-containing alcohol. Other organic subunits that may link at this position include the amino acids serine and threonine and a sugar, inositol.

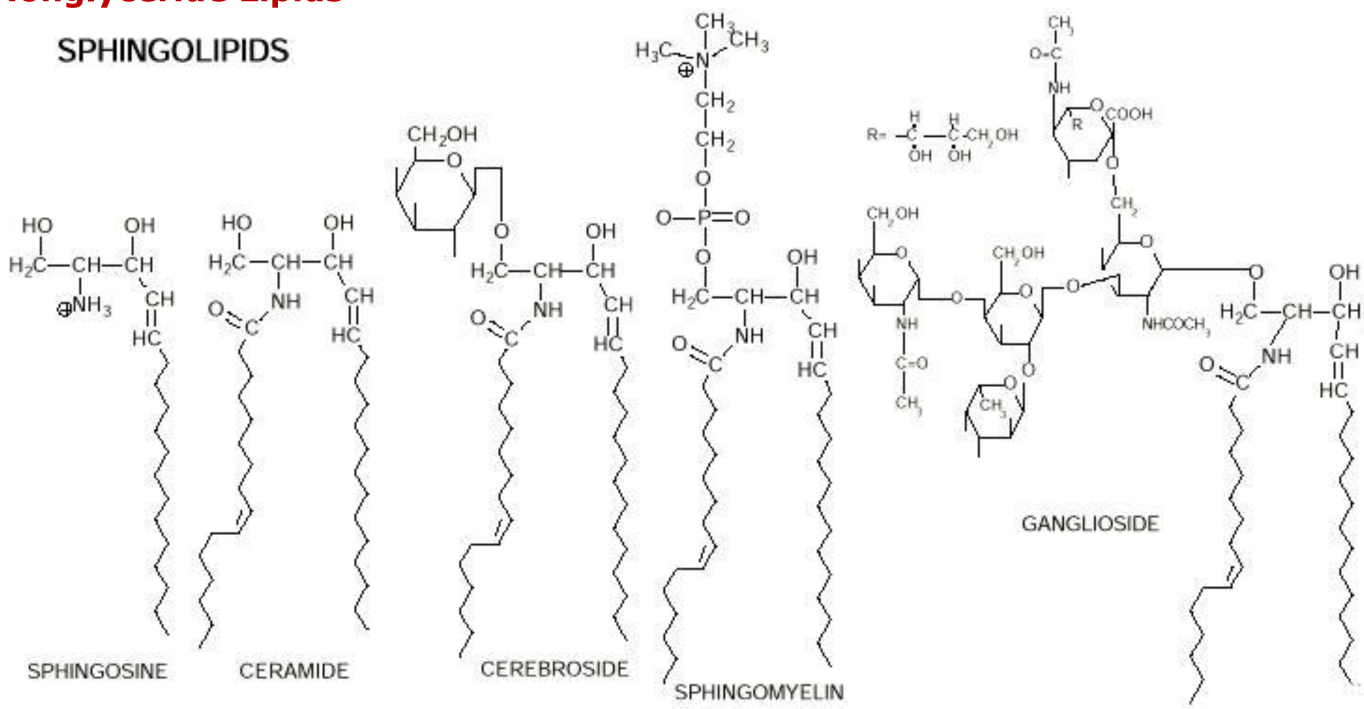
Phosphatidycholine (lecithin) is a major lipid component of cellular membranes. Because different fatty acids may bind at the 1 and 2 carbons of the glycerol residue in phosplipids of this type, phosphatidyl choline is actually a family of closely relate molecules differing in the particular fatty acids present. The colored blocks represents the arrangement of subunits in phospholipids (a). Structure (b) represents the formula for phosphatidy choline, a common membrane phospholipid. (c) is the space-filling model of phosphatidyl choline and (d) is a diagram widely used to depict a phopholipid molecule. The circle represents the polar end of the molecule and the zigzag lines the nompolar carbon chains of the fatty acid residues.





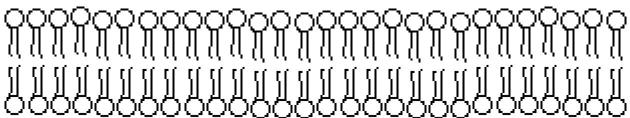
19.8 Membrane Lipids: Sphingoglycolipids

Nonglyceride Lipids



19.9 Membrane Lipids: Cholesterol
19.10 Cell Membranes
Plasma membrane
Planar lipid bilayers

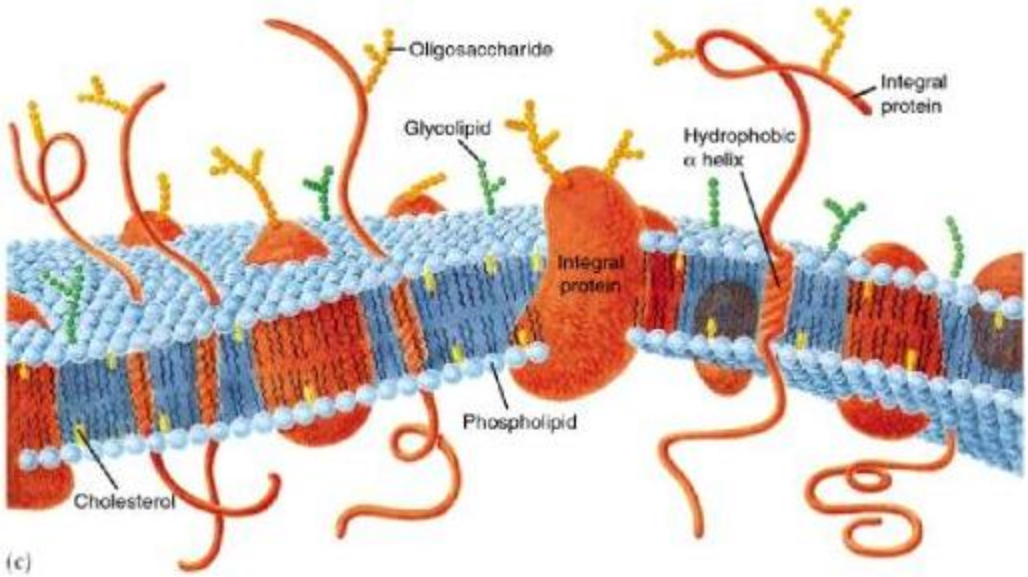
Biological membranes are bilipid layers . In a real cell the membrane phospholipids create a spherical three dimensional lipid bilayer shell around the cell. However, they are often represented two-dimensionally as:



Each  represents a phospholipid. The circle, or head, is the negatively charged phosphate group and the two tails are the two highly hydrophobic hydrocarbon chains of the phospholipid. The tails of the phospholipids orient towards each other creating a hydrophobic environment within the membrane. This leaves the charged phosphate groups facing out into the hydrophilic environment. The membrane is approximately 5 nm thick. This bilipid layer is semipermeable, meaning that some molecules are allowed to pass freely (diffuse) through the membrane. The lipid bilayer is virtually impermeable to large molecules, relatively impermeable to molecules as small as charged ions, and quite permeable to lipid soluble low molecular weight molecules. Its substantial permeability to water molecules is not well understood. Molecules that can diffuse through the membrane due so at differing rates depending upon their ability to enter the hydrophobic interior of the membrane bilayer.

The Fluid Mosaic Model

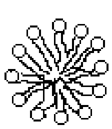
Lipid bilayers are fluid, and individual phospholipids diffuse rapidly throughout the two dimensional surface of the membrane. This is known as the fluid mosaic model of biological membranes (mosaic because it includes proteins, cholesterol, and other types of molecules besides phospholipids). The phospholipids can move to the opposite side of a bacterial cell membrane in a few minutes at room temperature. That's is a distance several thousand times the size of the phospholipid. Membrane proteins diffuse throughout the membrane in the same fashion, though at a slower pace because of their massive size (a phospholipid may be 650 d (daltons, or MW), and a medium sized protein can be 100,000 d). From time to time a given phospholipid will "flip-flop" through the membrane to the opposite side, but this is uncommon. To do so required the hydrophilic head of the phospholipid to pass fully through the highly hydrophobic interior of the membrane, and for the hydrophobic tails to be exposed to the aqueous environment.



19.11 Emulsification Lipids: Bile Acids

Emulsification, Hydrolysis and Micelle Formation

Bile salts play their first critical role in lipid assimilation by promoting emulsification. As derivatives of cholesterol, bile salts have both hydrophilic and hydrophobic domains (i.e. they are amphipathic). On exposure to a large aggregate of triglyceride, the hydrophobic portions of bile salts intercalate into the lipid, with the hydrophilic domains remaining at the surface. Such coating with bile salts aids in breakdown of large aggregates or droplets into smaller and smaller droplets. Hydrolysis of triglyceride into monoglyceride and free fatty acids is accomplished predominantly by pancreatic lipase. The activity of this enzyme is to clip the fatty acids at positions 1 and 3 of the triglyceride, leaving two free fatty acids and a 2-monoglyceride. Lipase is a water-soluble enzyme, and with a little imagination, it's easy to understand why emulsification is a necessary prelude to its efficient activity. Shortly after a meal, lipase is present within the small intestine in rather huge quantities, but can act only on the surface of triglyeride droplets. For a given volume of lipid, the smaller the droplet size, the greater the surface area, which means more lipase molecules can get to work. As monoglycerides and fatty acids are liberated through the action of lipase, they retain their association with bile salts and complex with other lipids to form structures called micelles.

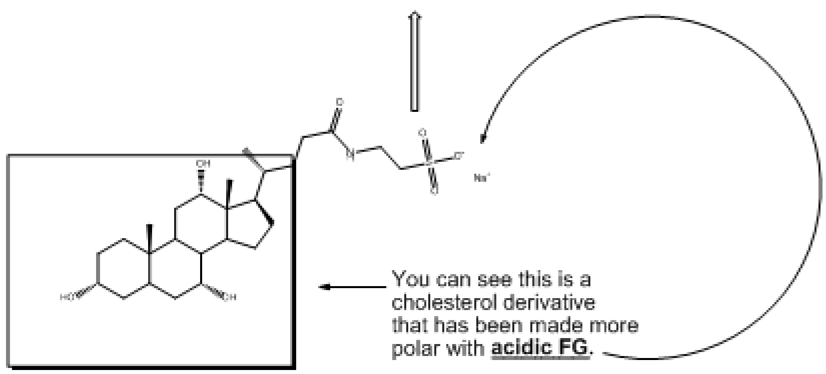


Micelles are essentially small aggregates of mixed lipids and bile salts suspended within the ingesta. As the ingesta is mixed, micelles bump into the brush border and the lipids, including monoglyceride and fatty acids, are absorbed. Lipids are absorbed by a mechanism distinctly different from what we've seen for monosaccharides and amino acids. The major products of lipid digestion - fatty acids and 2-monoglycerides - enter the enterocyte by simply diffusing across the plasma membrane. Once inside the enterocyte, fatty acids and monoglyceride are transported into the endoplasmic reticulum, where they are used to synthesize triglyeride! Beginning in the endoplasmic reticulum and continuing in the Golgi, triglyceride is packagedwith cholesterol, lipoproteins and other lipids into particles called chylomicrons.

Bile acids

Bile acids are tri- or dihydroxy cholesterol derivatives. The carbon 17 side chain of cholesterol has been oxidized to a carboxylic acid.

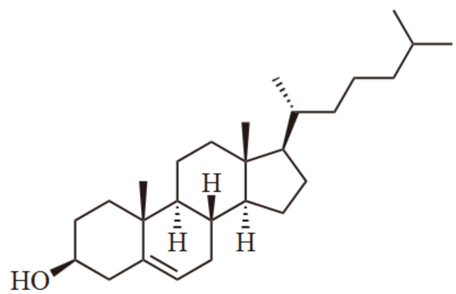
The oxidized acid side chain is bonded to an amino acid (either glycine or taurine) through an amide linkage. Bile is a fluid containing emulsifying agents (Bile acids) secreted by the liver, stored in the gallbladder, and released into the small intestine during digestion.



sodium taurocholate

Cholesterol

Cholesterol is a waxy steroid metabolite found in the cell membranes and transported in the blood plasma of all animals. It is an essential structural component of mammalian cell membranes, where it is required to establish proper membrane permeability and fluidity. In addition, cholesterol is an important component for the manufacture of bile acids, steroid hormones, and several fat-soluble vitamins. Cholesterol is the principal sterol synthesized by animals, but small quantities are synthesized in other eukaryotes, such as plants and fungi. It is almost completely absent among prokaryotes, which include bacteria.



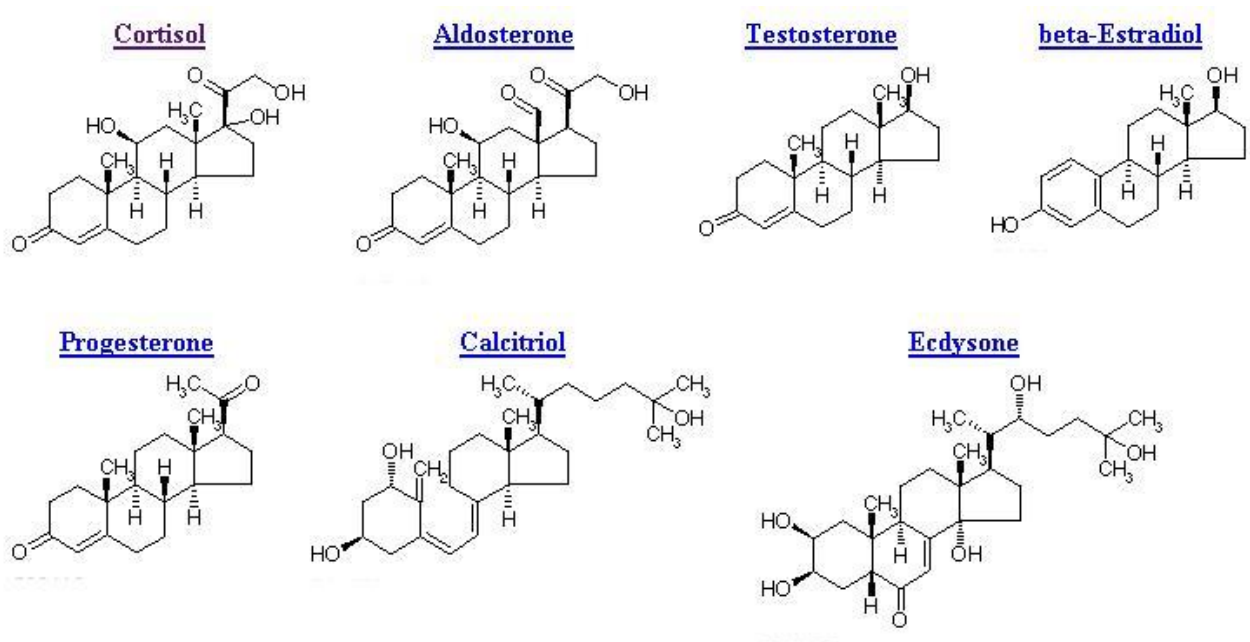
Atherosclerosis, cholesterol and low density lipoproteins (LDL)

Atherosclerosis is a condition in which patchy deposits of fatty material (atheromas or atherosclerotic plaques) develop in the walls of medium-sized and large arteries, leading to reduced or blocked blood flow. The LDL-cholesterol complex is small and dense compared to chylomicrons and VLDL, and when it is present in high concentrations it tends to deposit inside the blood vessel wall. This contributes to **atherosclerosis** (the build-up of fatty plaque in the arteries; "hardening of the arteries").

19.12 Messenger Lipids: Steroid Hormones

Fats similar to, and usually synthesized from, cholesterol. Nearly all of the classic hormones are proteins or smaller peptides; they don't get inside a cell (the membrane keeps them out); instead, they bind to, and initiate, cell changes from the outside. The exceptions are the thyroxines (from the thyroid) and the steroid hormones. They move into the cell, bind with receptors, and initiate changes in the way a cell regenerates itself or synthesizes new compounds.

Because the steroid hormones stimulate cell growth, either by changing the internal structure or increasing the rate of proliferation, they are often called anabolic steroids. Estrogen, an ovarian steroid, when secreted into the bloodstream, will be bound within a short time by internal receptors inside those cells that need estrogen for their growth; the unused portion is partially broken down, mostly in the liver, and partially stored in a less active form by adipose tissue.



Glucocorticoids

The glucocorticoids get their name from their effect of raising the level of blood sugar (glucose). One way they do this is by stimulating the liver to convert fat and protein into intermediate metabolites that are ultimately converted into glucose.

The most abundant glucocorticoid is **cortisol** (also called hydrocortisone). Cortisol and the other glucocorticoids also have a potent anti-inflammatory effect on the body. They depress the immune response, especially cell-mediated immune responses.

For this reason glucocorticoids are widely used in therapy:

- to reduce the inflammatory destruction of rheumatoid arthritis and other autoimmune diseases
- to prevent the rejection of transplanted organs
- to control asthma

Mineralocorticoids

The mineralocorticoids get their name from their effect on mineral metabolism. The most important of them is the steroid **aldosterone**. Aldosterone acts on the kidney promoting the reabsorption of salt into the blood and the maintenance of normal blood pressure. The secretion of aldosterone is stimulated by:

- angiotensin II
- ACTH (as is that of cortisol)
- a high level of potassium ions in the blood

Androgens

The adrenal cortex secretes precursors to androgens such as testosterone. In sexually-mature males, this source is so much lower than that of the testes that it is probably of little physiological significance. However, excessive production of adrenal androgens can cause premature puberty in young boys. In females, the adrenal cortex is a major source of androgens. Their hypersecretion may cause some masculinization in adult females, producing a masculine pattern of body hair and cessation of menstruation. The principal androgen (male sex hormone) is testosterone. This steroid is manufactured by the interstitial (Leydig) cells of the testes. Secretion of testosterone increases sharply at puberty and is responsible for the development of the so-called secondary sexual characteristics (e.g., beard) of men. Testosterone is also essential for the production of sperm.

Anabolic steroids

A number of synthetic androgens are used for therapeutic purposes. Unfortunately, these drugs also promote an increase in body weight and muscle strength. This has made them increasingly popular with athletes: weight lifters, cyclists, professional football players, etc. Often these athletes take doses 100 time greater than those used in standard therapy. Such illicit use carries dangers (besides being banned from an event because of a positive drug test): acne, a decrease in libido, testicle size, and sperm counts to name a few.

Estrogens

They are primarily responsible for the conversion of girls into sexually-mature women.

- development of breasts
- further development of the uterus and vagina
- broadening of the pelvis
- growth of pubic and axillary hair
- increase in adipose (fat) tissue
- participate in the monthly preparation of the body for a possible pregnancy
- participate in pregnancy if it occurs

Estrogens also have non-reproductive effects.

They antagonize the effects of the parathyroid hormone, minimizing the loss of calcium from bones and thus helping to keep bones strong.

They promote blood clotting.

Progesterone

Progesterone is also a steroid. It has many effects in the body, some having nothing to do with sex and reproduction. Here we shall focus on the role of progesterone in the menstrual cycle and pregnancy.

How estrogens and progesterone achieve their effects

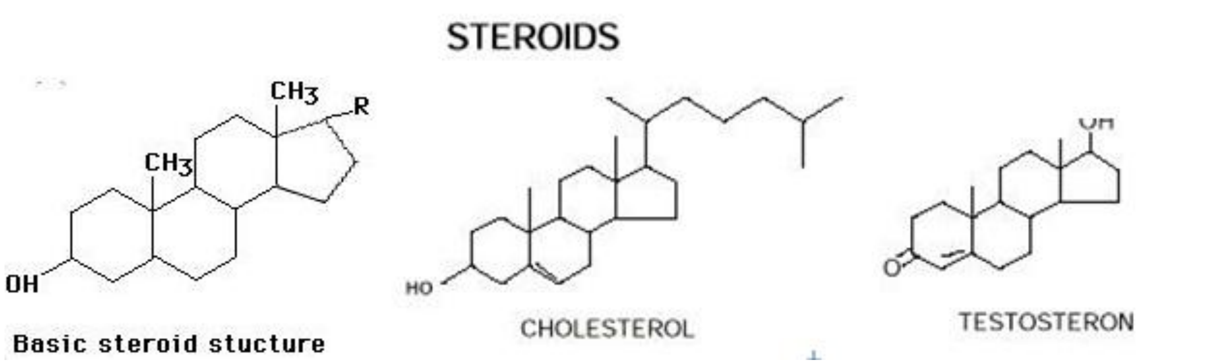
Steroids like estrogens and progesterone are small, hydrophobic molecules able to diffuse freely into cells (all cells). In "target" cells, they bind to receptor proteins located in the cytoplasm and/or nucleus. The hormone-receptor complex enters the nucleus (if it formed in the cytoplasm) and binds to specific sequences of DNA, called the estrogen (or progesterone) response elements Response elements are located in the promoters of genes. The hormone-receptor complex acts as a transcription factor (often recruiting other transcription factors to help) which turns on (sometimes off) transcription of those genes. gene expression in the cell produces the response.

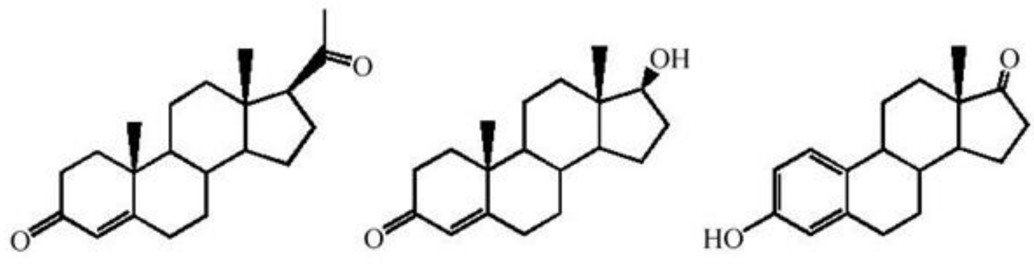
Oral contraceptives: the "pill"

The feedback inhibition of GnRH secretion by estrogens and progesterone provides the basis for the most widely-used form of contraception. Dozens of different formulations of synthetic estrogens, progestins (progesterone relatives) or both are available. Their inhibition of GnRH prevents the mid-cycle surge of LH and ovulation. Hence there is no egg to be fertilized.

Usually the preparation is taken for about three weeks and then stopped long enough for normal menstruation to occur.

The main side-effects of the pill stem from an increased tendency for blood clots to form (estrogen enhances clotting of the blood).





progesterone testosterone oestrone

19.13 Messenger Lipids: Eicosanoids

The functions of prostaglandins in physiological processes

Essential fatty acids in the cell membranes serve as stores from which prostaglandins are formed. Like essential fatty acids, prostaglandins were discovered in 1943. Prostaglandins regulate bodily functions in the heart, kidneys, liver, lungs, brain, nerves and the immune system**.** They are fatty acid metabolites (derived from arachidonic acid) formed by enzyme cyclooxygenase. They are autacoid hormones, are widely distributed in many tissues, and exert diverse biological effects, including vasodilation, smooth muscle contraction or relaxation, and regulation of renal function**.** Prostaglandins are important for the regulation of a host of bodily functions including:

- inflammation, swelling, & pain
- pressure in the eye, joints or blood vessels
- secretions from mucus membranes and their viscosity
  smooth muscle & autonomic reflexes, gastrointestinal, arterial, ear, heart
- water retention
- blood clotting ability
- allergic response
- rheumatoid arthritis
- nerve transmission
- steroid production & hormone synthesis

In human beings, there are three families of prostaglandins, each of which is derived from a different fatty acid. One prostaglandin, Prostaglandin E1, derived from Gamma linolenic Acid (GLA) and Dihomogamma linolenic Acid (DGLA), is believed to be responsible for controlling several critical functions in the body.

Do we need a dietary supplement of fatty acids to produce Prostaglandins?

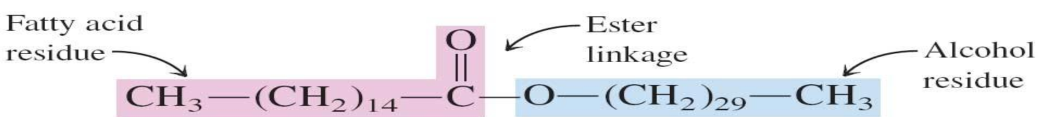
Until recently, it was thought that the normal dietary intake of vegetable oils was sufficient for most people to ensure adequate supplies of cis-LA for synthesis of Prostaglandin E1. However, it is now known that processing these oils for use in food may in some circumstances convert a substantial proportion of cis-LA into biologically inactive trans isomer. The trans form of LA is incapable of being converted into biologically active cis-GLA and cannot give rise to Prostaglandin E1. Moreover, the trans isomer competes with and inhibits the use of the remaining cis form. Efamol Pure Evening Primrose Oil (EPO) is a direct source of GLA, whereas Efamol's marine oils provide EPA and DHA.

More examoles of [Leukotriene]()

[Check this site for details of medications by their Generic names]()

19.14 Protective-Coating Lipids: Biological Waxes

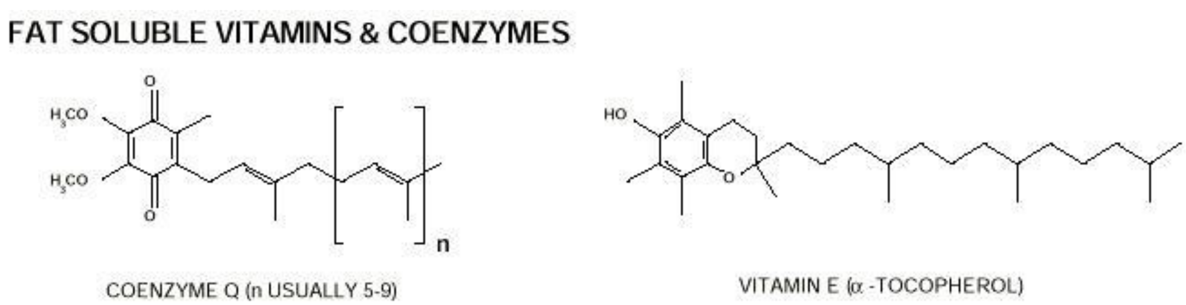
Biological waxes are complex mixtures containing high molar mass lipid esters.



A component of beeswax

Table 18.2 Some Typical Waxes

Type	Structural Formula	Source	Uses
Beeswax	$CH_3(CH_2)_{14}—\overset{O}{\overset{\|}{C}}—O—(CH_2)_{29}CH_3$	Honeycomb	Candles, shoe polish, wax paper
Carnauba wax	$CH_3(CH_2)_{24}—\overset{O}{\overset{\|}{C}}—O—(CH_2)_{29}CH_3$	Brazilian palm tree	Waxes for furniture, cars, floors, shoes
Jojoba wax	$CH_3(CH_2)_{18}—\overset{O}{\overset{\|}{C}}—O—(CH_2)_{19}CH_3$	Jojoba	Candles, soaps, cosmetics



Chemistry at a Glance: Types of Lipids and How They Function

Chemical Connections: The Fat Content of Tree Nuts and Peanuts; Artificial Fat Substitutes; The Cleansing Action of Soap; Trans Fatty Acids and Blood Cholesterol Levels; Steroid Drugs in Sports; The Mode of Action for Anti-Inflammatory Drugs