Bio-organic chemistry

Lecture #12

Saponifiable and unsaponifiable lipids. Their classification. Features of the structure of neutral lipids (fats, oils), their structure and chemical properties.

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Lipids are family of substances that are soluble in nonpolar solvents but insoluble in water. So, lipids are defined in terms of a property and not in terms of their structure. Lipids can be isolated from every cells by extraction.

Lipids major roles in human biochemistry are:

1. They store energy within fat cells

Energy is stored in the form of glycogen for quick energy when we need it. However, the burning of fats gives more than twice as much energy as the burning of the equal weight of carbohydrates.

2. They are parts of membranes that separate compartments from each other.

Most body constituents, for example carbohydrates and proteins are soluble in water. For membranes that separate compartments containing aqueous solutions the body needs insoluble compounds. Lipids provide these membranes.

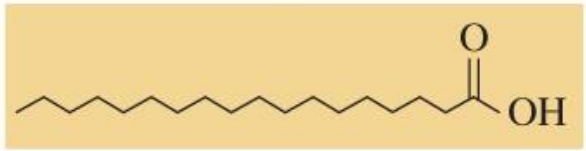
3. They serve as chemical messengers. Primary messengers such as steroid hormones, deliver signals from one part of the body to another part. Secondary messengers, such as prostaglandins and thromboxanes, mediate the hormonal response.

Lipids are

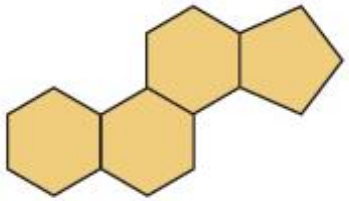
- biomolecules that contain fatty acids or a steroid nucleus
- soluble in organic solvents, but not in water
- named for the Greek word *lipos*, which means “fat”
- extracted from cells using nonpolar organic solvents
- natural components of cell membranes, fat-soluble vitamins, and steroid hormones.

There are 2 types of lipids;

those that contain the structural component of a fatty acid; and



those that contain the structural component of a four-member steroid molecule.

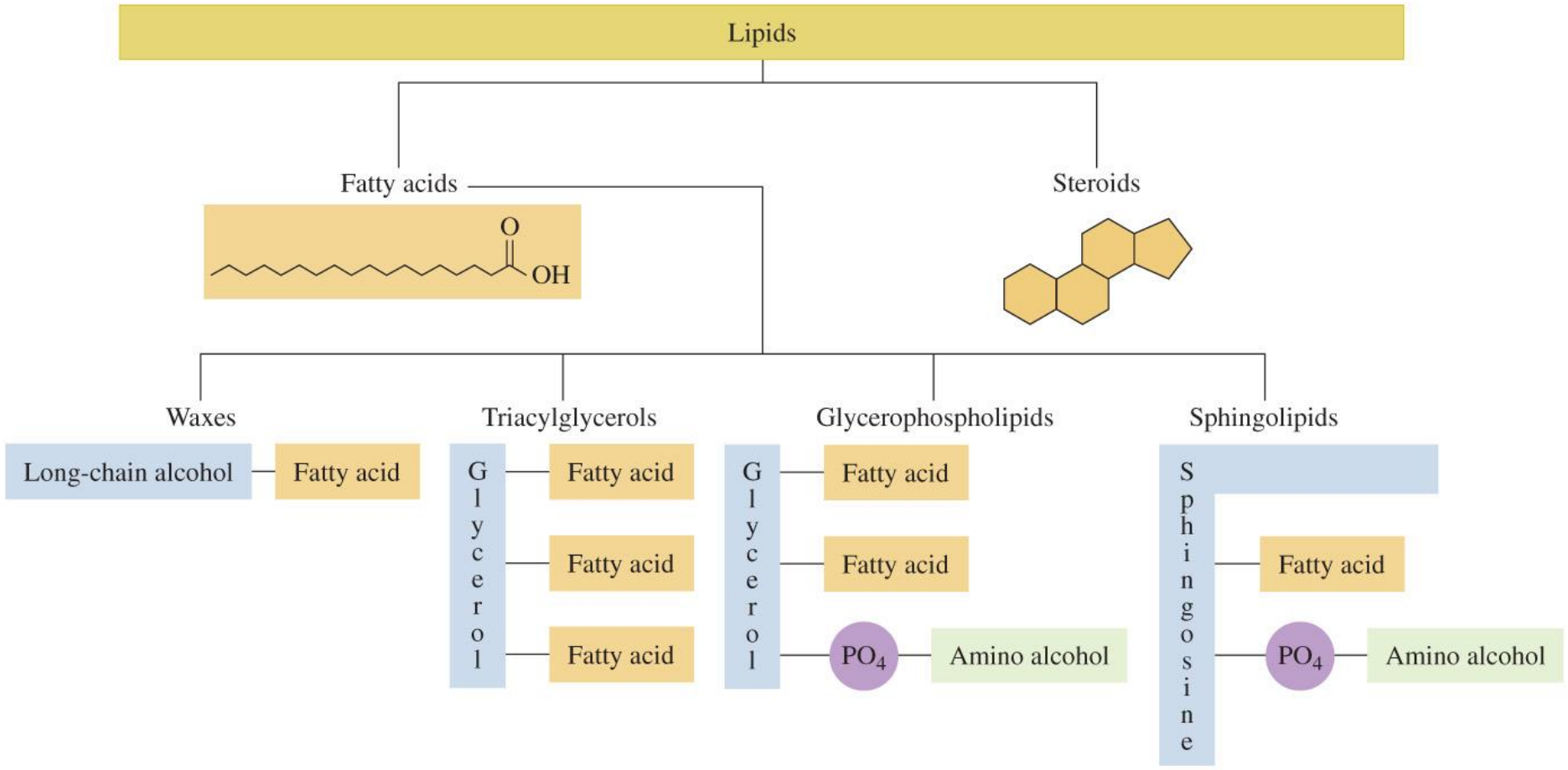


The lipids that contain fatty acids are

- waxes,
- fats and oils (triacylglycerols),
- glycerophospholipids, and
- prostaglandins.

The types of lipids that do not contain fatty acid chains are steroids.

Types of Fatty Acid Lipids

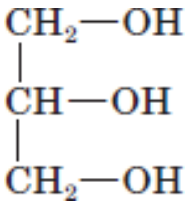


Hydrolyzable lipids

Simple lipids

Triglycerides are triesters of **glycerol and long-chain carboxylic acids** called **fatty acids.**

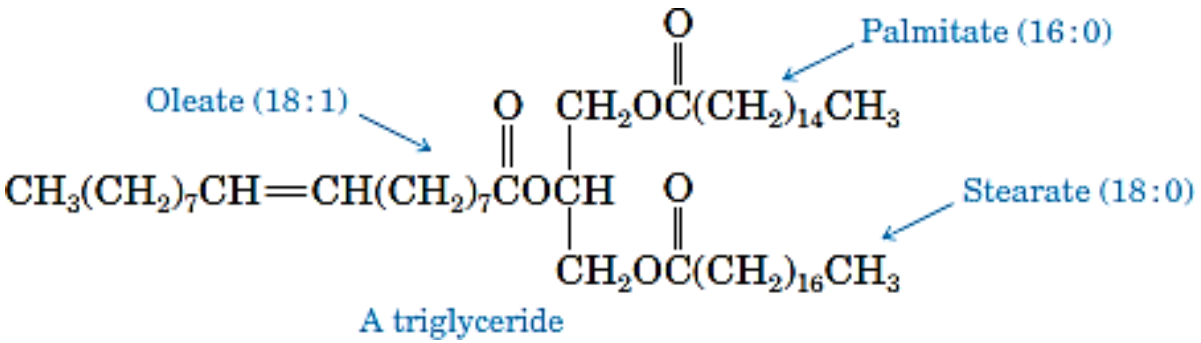
Animal fats and plant oils are triglycerides.



Glycerol

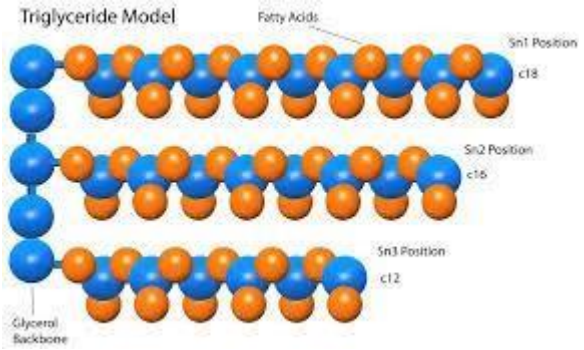
In triglycerides all hydroxy groups of glycerol are **esterified**.

Although some of the molecules contain three identical fatty acids, in most cases two
or three different acids are present. For example,



A triglyceride

The hydrophobic character of triglycerides is caused by the long hydrocarbon chains. This makes the triglycerides insoluble in water.



Animal fats are solids at room temperature, and **those from plants and fish are usually liquids.** Liquid fats are often called **oils**.

Solid animal fats contain saturated fatty acids, whereas vegetable oils contain high amounts of unsaturated fatty acids.

In human fats unsaturated fatty acids predominate. Their ratio with saturated fatty acids is approx. 3:2.

In natural triglycerides the 2nd position of glycerol usually is occupied by unsaturated fatty acid.

Average percentage of fatty acids of some common fats and oils

	Saturated fatty acids			Unsaturated fatty acids			
	Myristic (C14)	Palmitic (C16)	Stearic (C18)	Oleic (C18)	Linoleic* (C18)	Linolenic* (C18)	Other
Animal fats							
Beef tallow	6.3	**27.4**	14.1	49.6	2.5	-	0.1
Butter	11	**29**	9.2	26.7	3.6	-	17.9
Lard	1.3	28.3	11.9	**47.5**	6.0	-	5.0
Vegetable oils							
Linseed	-	6.3	2.5	19.0	24.1	**47.4**	0.7
Olive	-	6.9	2.3	**84.4**	4.6	-	1.8
Soybean	0,1	9.8	2.4	28.9	**52.3**	3.6	2.7
Sunflower	-	6.1	2.6	**25.1**	**66.2**	-	-

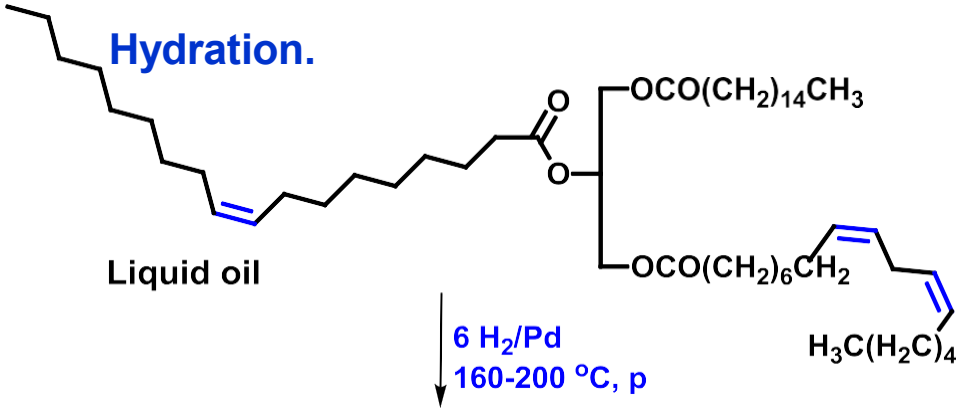
*Linoleic and linolenic acids are essential (they must be consumed as part of the diet).

Chemical properties of fats

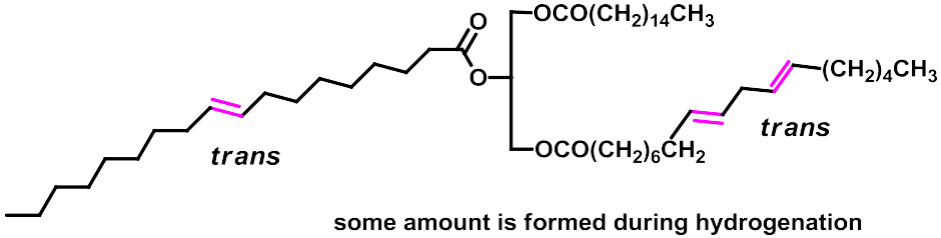
Hydrolysis (saponification) was discussed at ester properties.

Addition reactions. Unsaturated residues of fatty acids undergo addition reactions with halogens, ammonia, water and other.

Hydration.



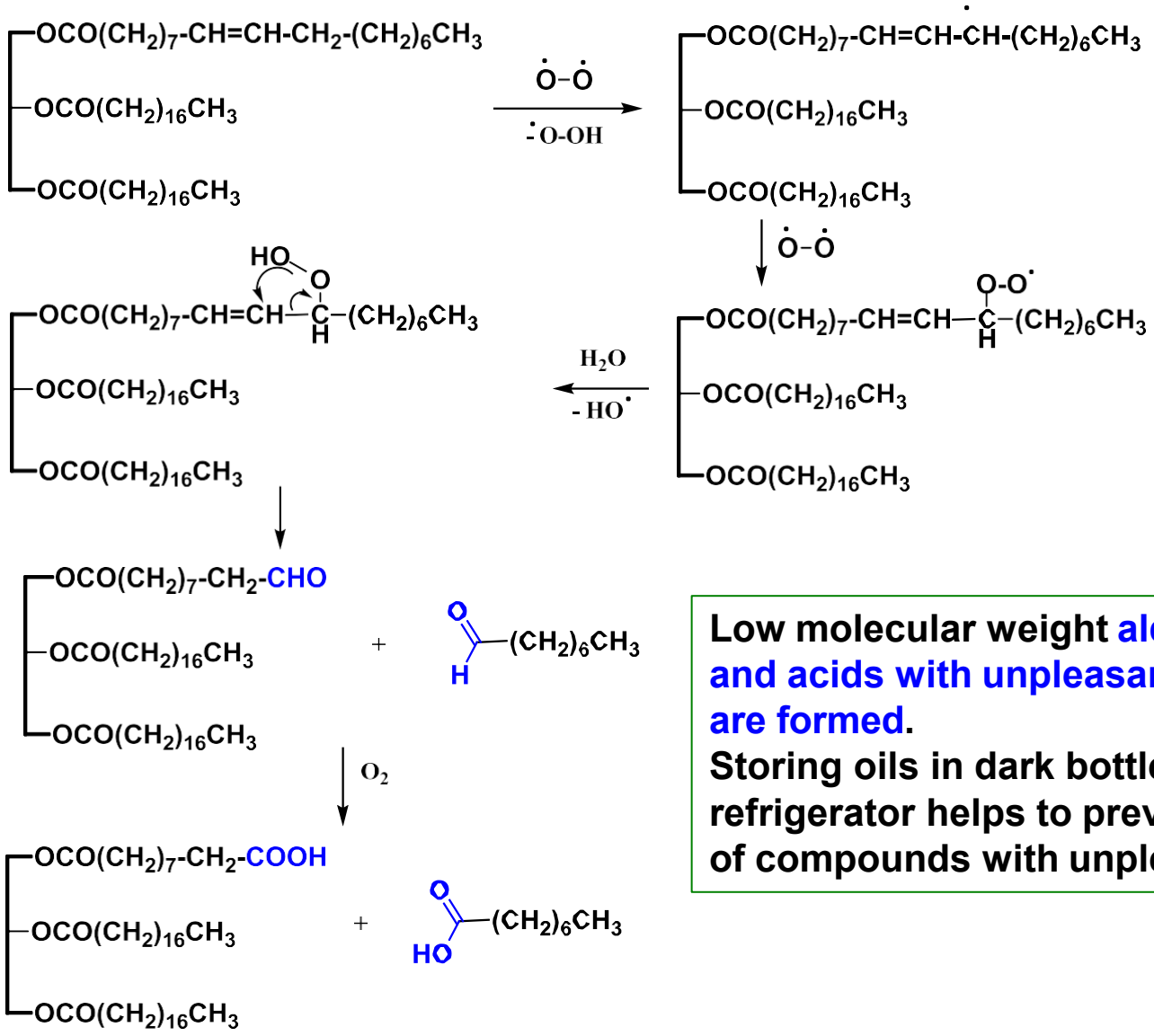
The reaction is used for the production of solid fats from liquid ones.



some amount is formed during hydrogenation

Margarine is also made by partial hydrogenation of vegetable oils. Because less hydrogen is used margarine contains more unsaturation than fully hydrogenated fats. **The hydrogenation process is the source of trans fatty acids.** For example, margarine contains ~ 35% *cis*-acids and 12% *trans*- acids. For comparison, butter contains > 50% *cis*-acids and 3-4% *trans*-acids. **Triglycerides containing *trans*-acids increase level of low density lipoproteins (bad cholesterol) in blood (negative effect).**

Autooxidation

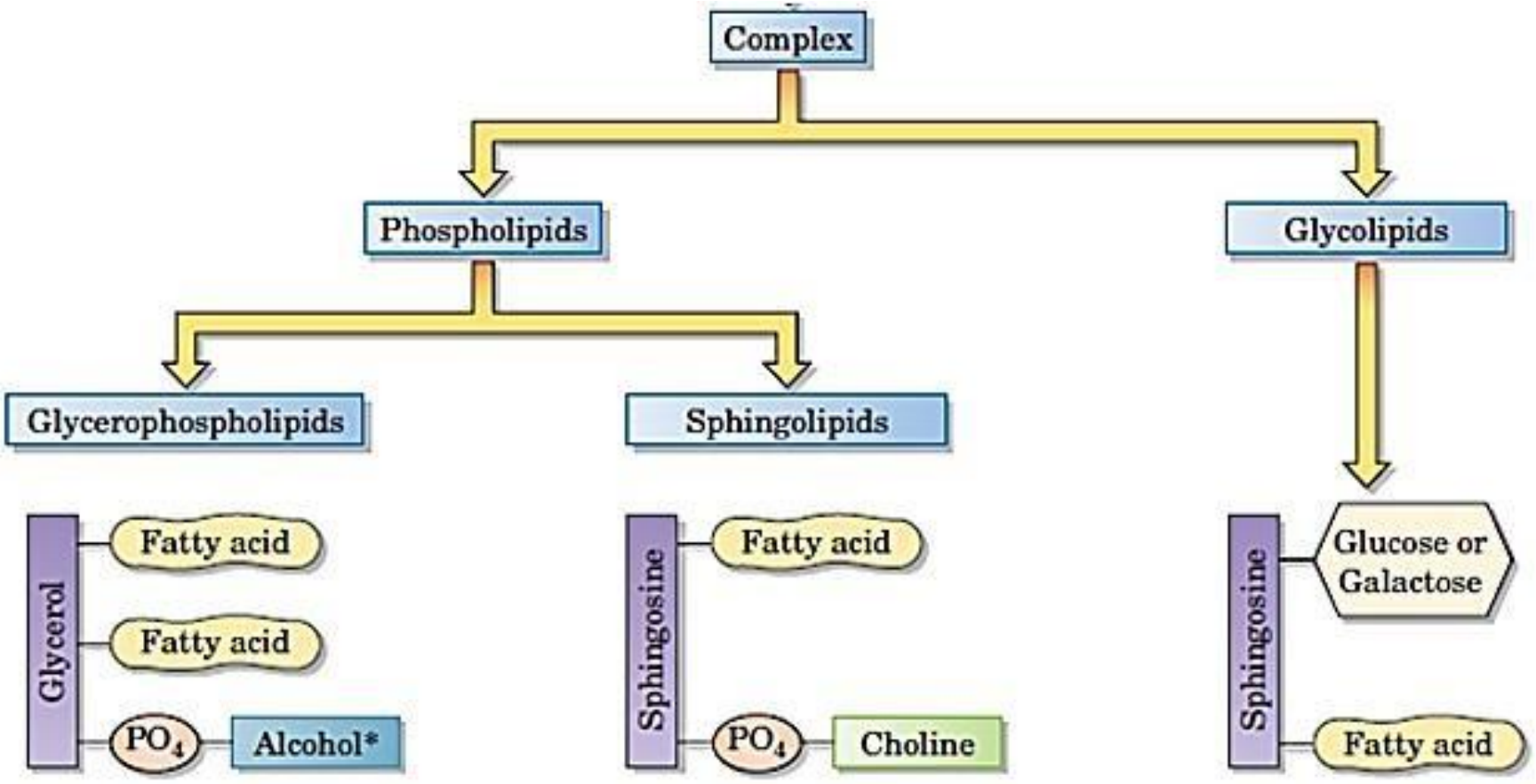


Low molecular weight aldehydes, ketones, and acids with unpleasant tastes and odors are formed.
Storing oils in dark bottles and in refrigerator helps to prevent the formation of compounds with unpleasant tastes.

Hydrolyzable lipids

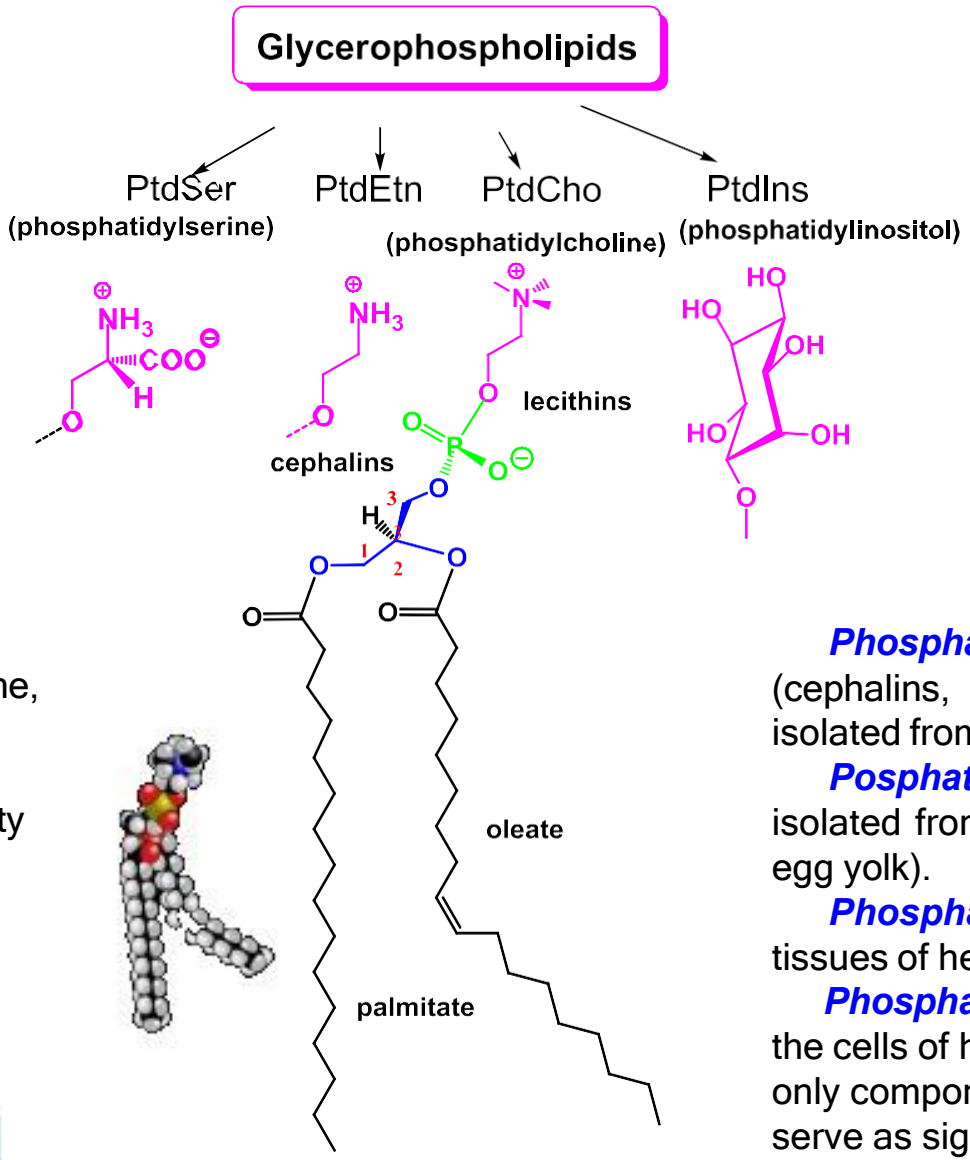
Complex lipids

Complex lipids constitute the main components of membranes.



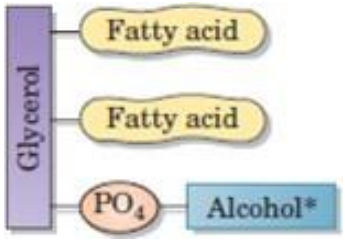
Phospholipids

Glycerophospholipids are membrane components throughout the body. The alcohol is glycerol. Glycerophospholipid structure includes both polar and nonpolar parts within one molecule.



At the 1st C – saturated fatty acid;
At the 2nd C – unsaturated fatty acid
At the 3rd C – phosphate residue.

Polar part – phosphate group and ionized amino group of serine, aminoethanol or choline.
Nonpolar part – fatty acid residues



Phosphatidylethanolamines (cephalins, greek *kephale - head)* isolated from brain tissues.

Posphatidylcholines (lecithins) isolated from egg yolk (greek *lekithos* – egg yolk).

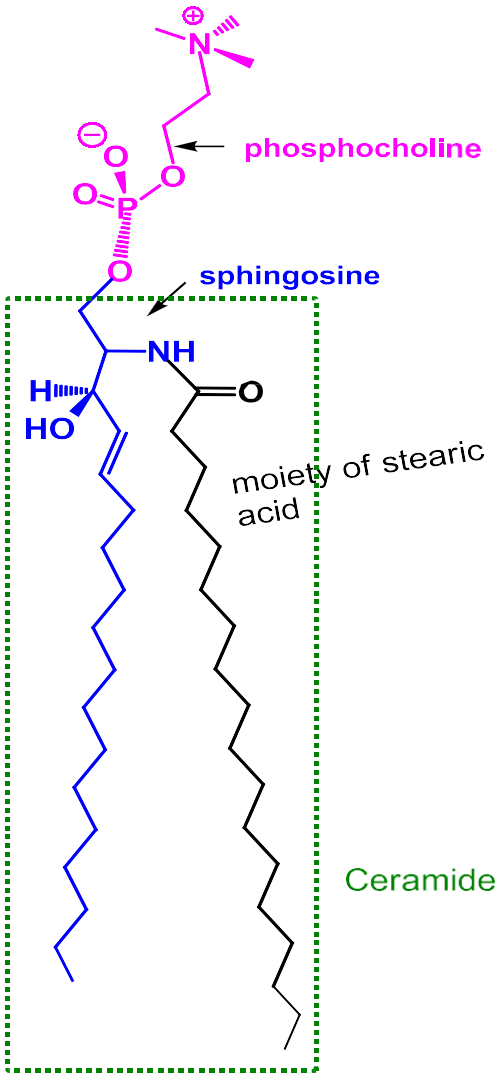
Phosphatidylserines isolated from tissues of heart, brain and liver.

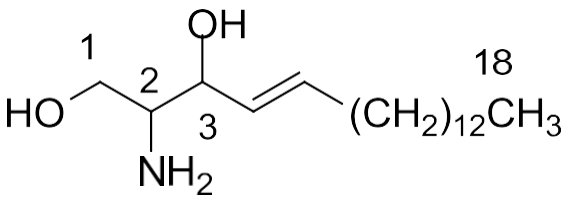
Phosphatidylinosotols isolated from the cells of heart and liver. They are not only components of membranes but serve as signaling molecules, as well.

Phospholipids

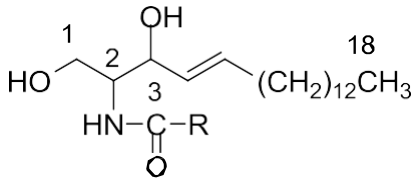
Sphingolipids

Sphingomyelin

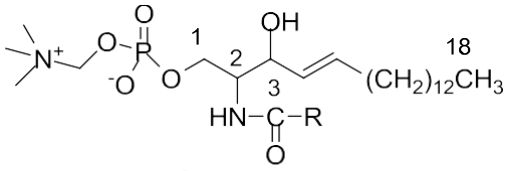




Sphingosine

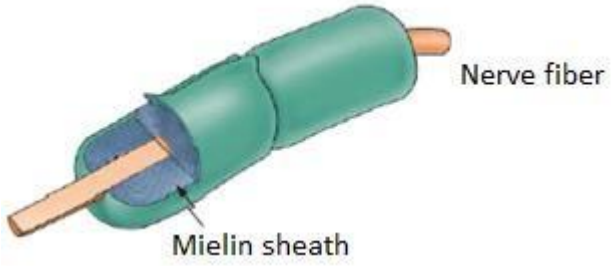


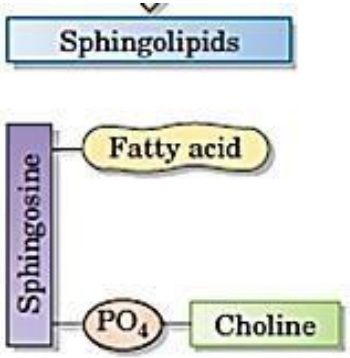
Ceramide



Sphingomyelin

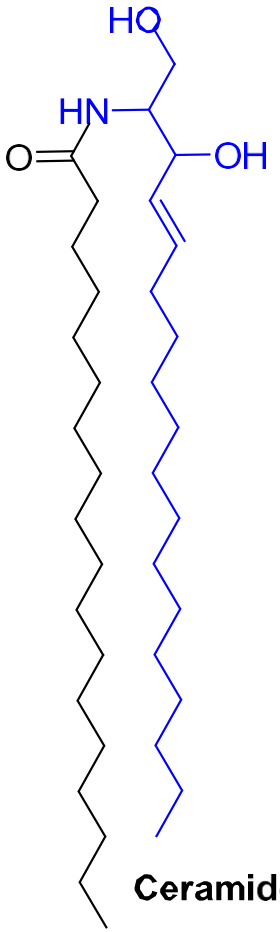
Sphingomyelins are the main components of coating of nerve axons, called the myelin sheath, which provides insulation and allows conduction of electrical signals. The myelin sheath consists of 70% lipids and 30% proteins in the lipid bilayer structure.





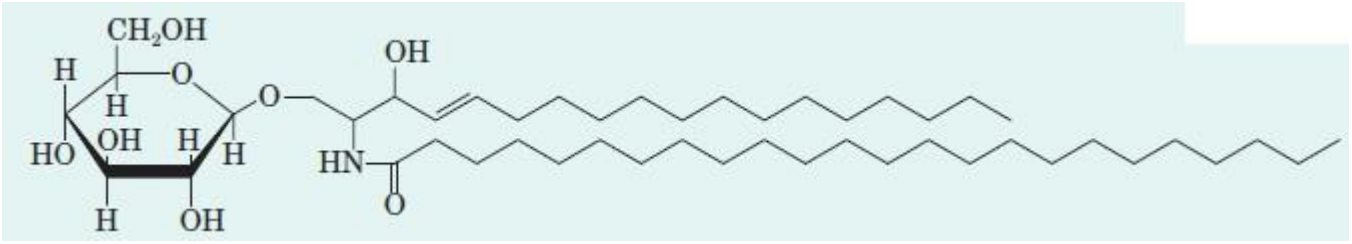
Glycolipids

Glycolipids are complex lipids that contain carbohydrates and ceramides. One group– cerebrosides, consists of ceramide mono- or oligosacharides. Other groups, such as gangliosides, contain a more complex carbohydrate structure.

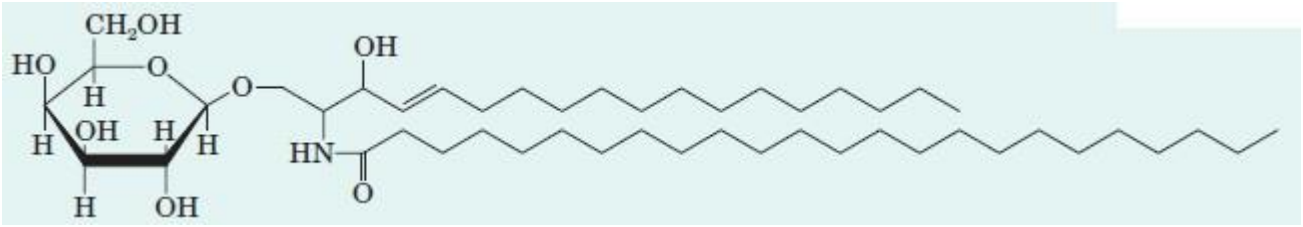


Ceramide

Glucocerebroside



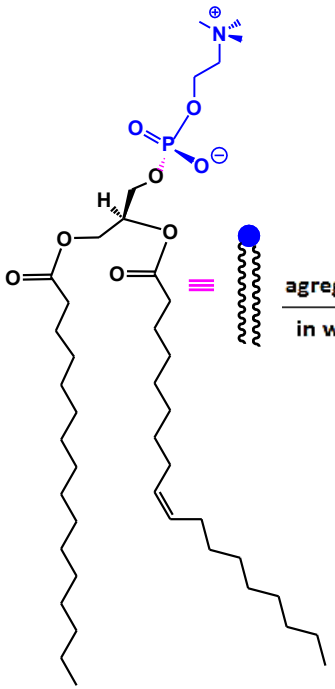
Galactocerebroside

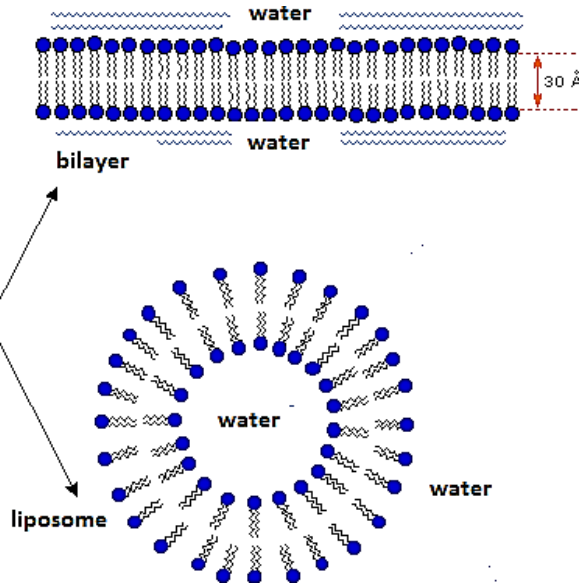


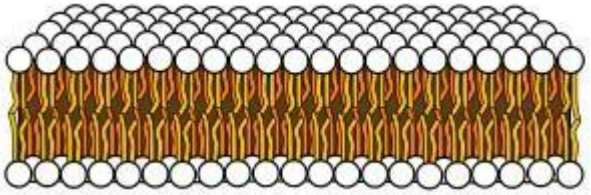
In cerebrosides, the fatty acid of the ceramide part may contain either C18 or C24 chains. Glucose or galactose are connected with ceramide by β-glycosidic bond.

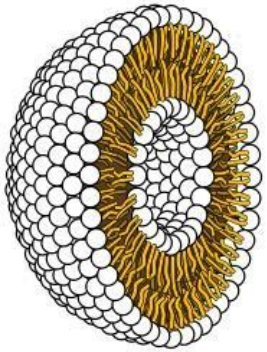
Cerebrosides occur primarily in the brain (7% of the brain dry weight).

Phosphatidylcholine



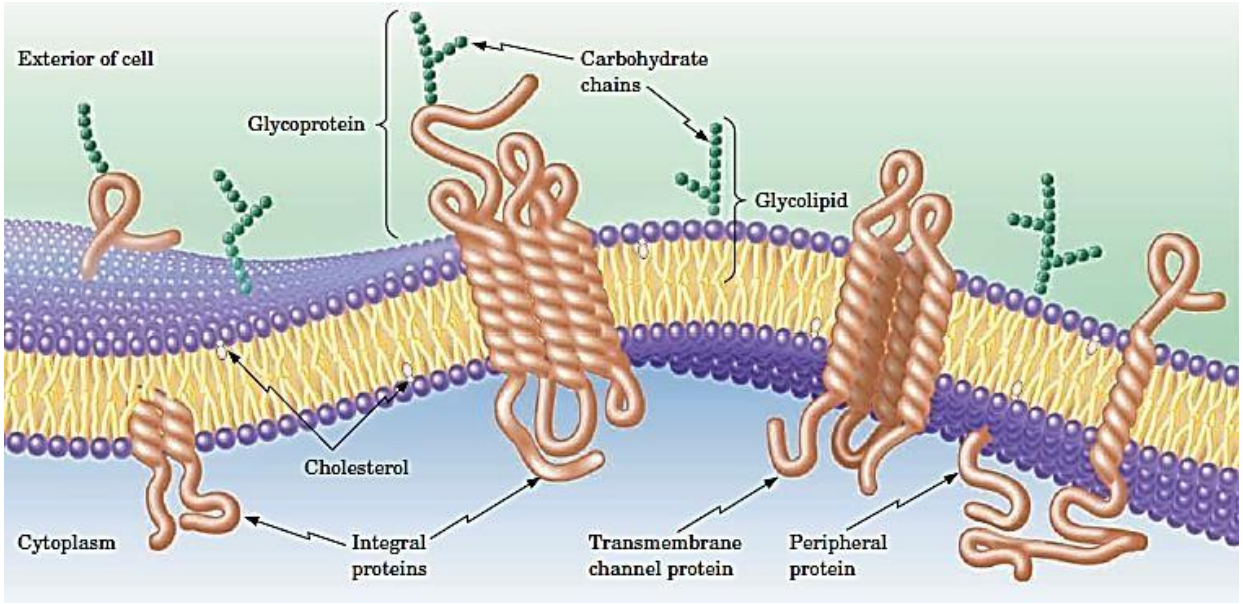






Liposome

The fluid mosaic model of membrane. Proteins are embedded in the lipid matrix



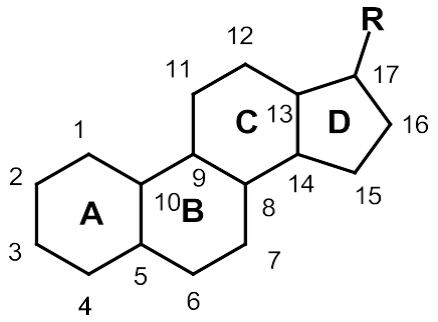
Non-hydrolyzable lipids

Steroids

Steroids are **non-hydrolyzable lipids**. Steroids are compounds containing four fused carbocyclic rings. Steroids are completely different in structure from the discussed lipids. They are normally not esters, although some of them are. Steroids are closely related in structure but are highly diverse in function.

This group of lipids involves:

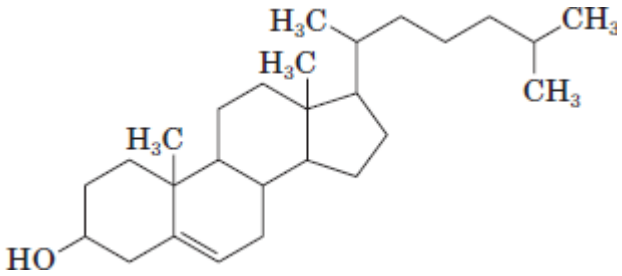
- **Cholesterol**
- **Sex and adrenocorticoid hormones**
- **Bile acids**
- **Vitamins D**



Cholesterol

Cholesterol is the most abundant steroid in human body (200-300 g in adult) and the most important.

Cholesterol

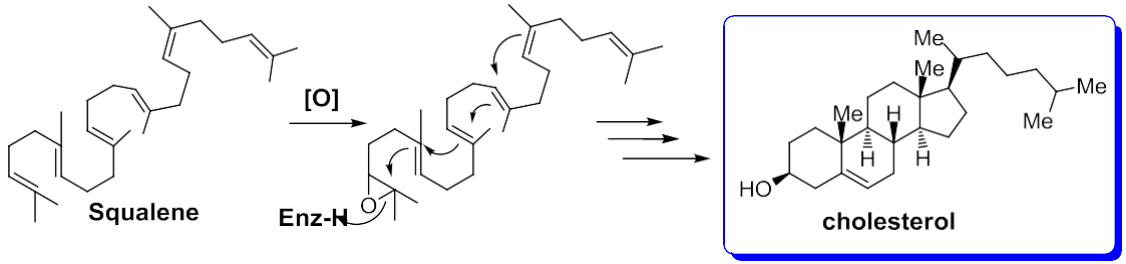


Cholesterol functions:

- **A membrane component in all animal cells**
- **Initial compound for the biosynthesis of such bioactive substances as sex and adrenocorticoid hormones and bile acids**

A human gallstone is almost pure cholesterol (∅ 5 mm)

Cholesterol is synthesized in a human liver from terpene - squalene.

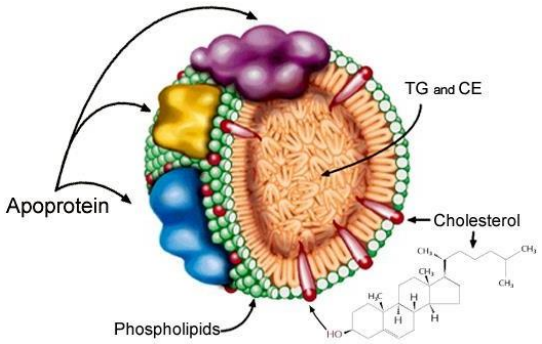


Cholesterol in the body is in a dynamic state. It constantly circulates in the blood. Cholesterol and esters of cholesterol, being hydrophobic, need a water-soluble carrier to circulate in the aqueous medium of blood.

Carriers of cholesterol are lipoproteins (Spherically shaped clusters containing both protein and lipid molecules). Most lipoproteins contain a core of hydrophobic lipid molecules surrounded by a shell of hydrophilic protein and phospholipid molecules.

There are four kinds of lipoproteins

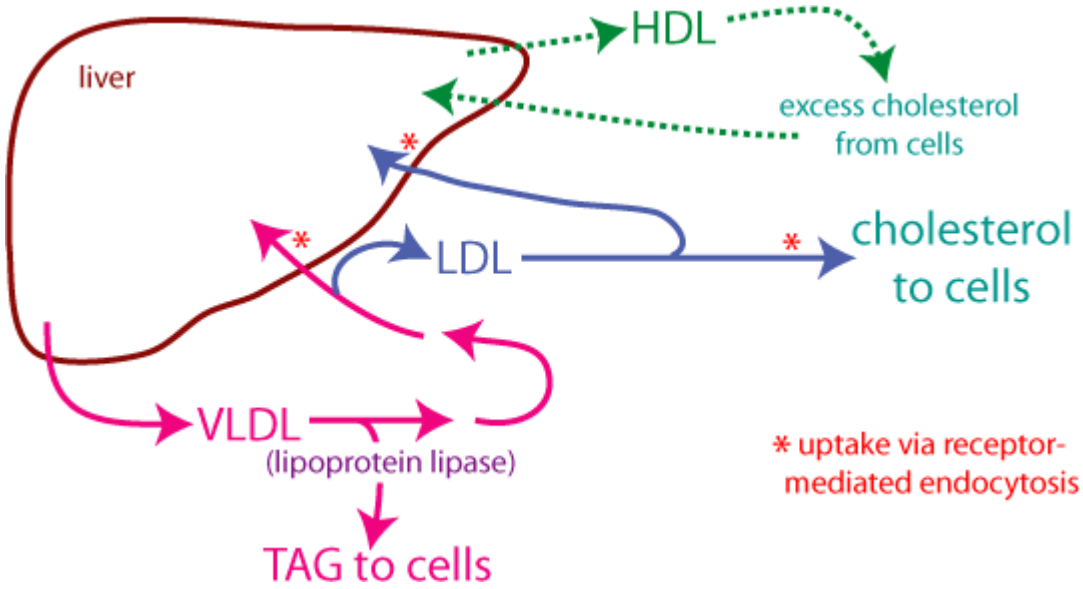
- **High density lipoprotein (HDL)** ('good cholesterol'). It consists of 33% protein and 30% cholesterol.
- **Low density lipoproteins (LDL)** ('bad cholesterol'). Constitution of LDL approx. 25% protein and 50% cholesterol.
- **Very low density lipoprotein (VLDL).** Mostly carries triglycerides synthesized by the liver.
- **Chylomicrons,** which carry dietary lipids synthesized in the intestines.



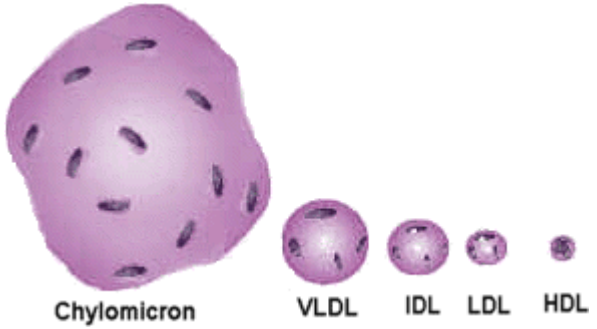
Schematic view of lipoprotein

The LDL carries cholesterol to the cells. In the cells enzyme break down lipoprotein and liberate free cholesterol. In this manner, the cell can use cholesterol as a component of membrane. This is the normal fate of LDL and the normal course of cholesterol transport. If the cell contains enough cholesterol, LDL does not enter the cell and cholesterol accumulates in the blood. **This accumulation can happen even with low intake of dietary cholesterol.** So, both genetics and diet play a role in determining cholesterol levels in the blood.

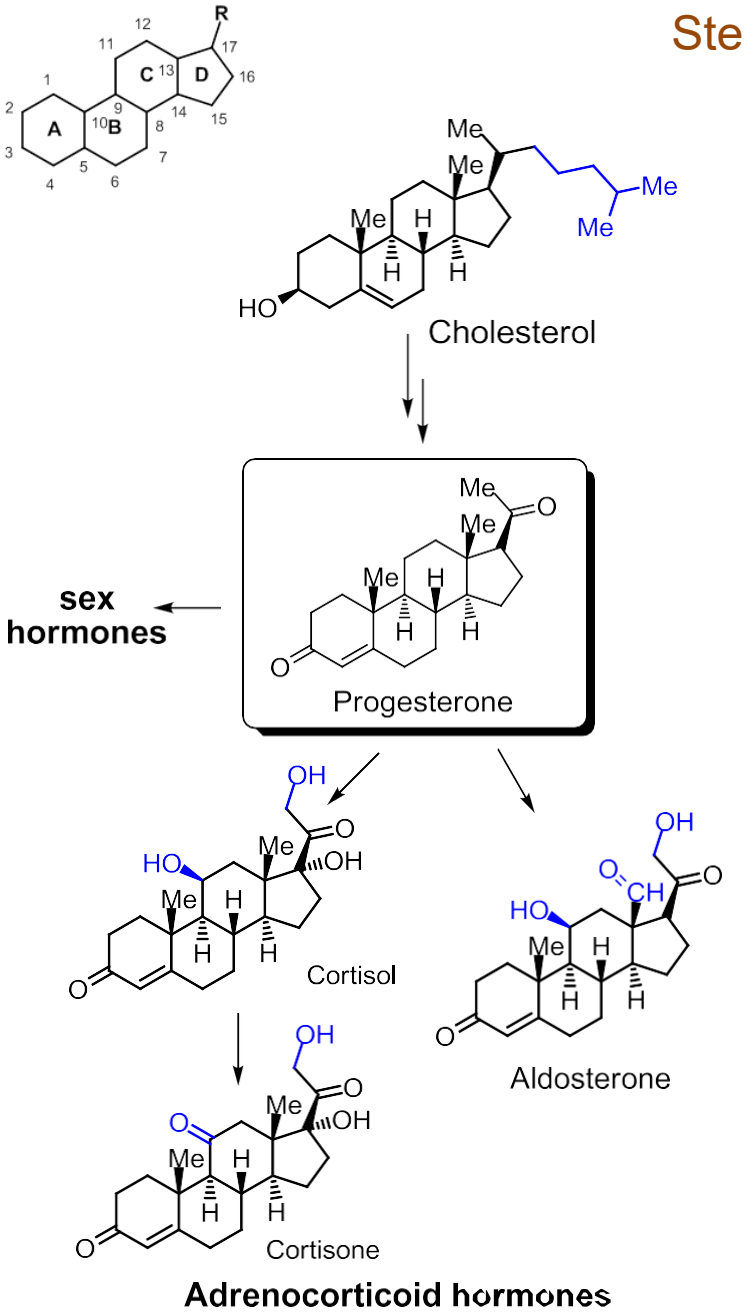
HDL transports cholesterol from peripheral tissues to the liver for the synthesis of bile acids and steroid hormones. It is desirable to have high level of HDL in the blood because it removes cholesterol from bloodstream.



Relative Sizes of Lipoproteins



Steroid hormones



Cholesterol is a starting material for the synthesis of steroid hormones. In this process, cholesterol is oxidized and the side chain at D ring is shortened to two C atoms. The 3-HO group is oxidized to ketone group to give **progesterone**. Progesterone serves as starting compound for both sex hormones and adrenocorticoid hormones.

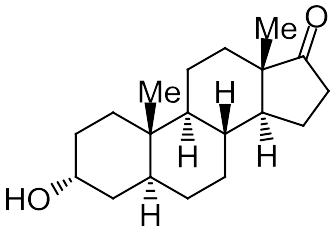
Adrenocorticoid hormones are products of the adrenal glands. They are classified into two groups according to function: **Mineralocorticoids** regulate the concentration of ions (mainly Na^+ and K^+) and **glucocorticoids** that control carbohydrate metabolism. ***Aldosterone*** is one of the most important mineralocorticoids. Increased secretion of aldosterone enhances the reabsorption of Na^+ and Cl^- ions in the kidney and increases the loss of K^+.

The function of ***Cortisol*** is to increase the glucose and glycogen concentration in the body. Fatty acids and amino acids from body proteins are transported to the liver, which under the influence of cortisol produces glucose and glycogen from these sources.

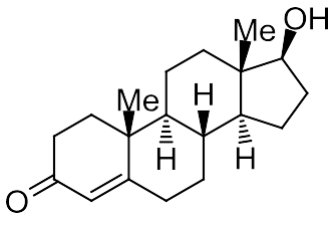
Cortisol and cortisone possess anti-inflammatory effects. They or similar synthetic derivatives (e.g. prednisone) are used to treat such diseases as rheumatoid arthritis, and bronchial asthma.

Sex hormones

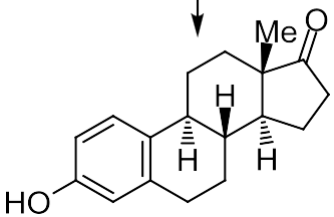
They are classified into **1) male sex hormones (androgens); 2) female sex hormones (estrogens); 3) pregnancy hormones (progestins)**. Some of them are synthesized in genital glands, some - in adrenal cortex.



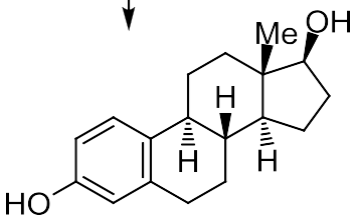
Androsterone



Testosterone

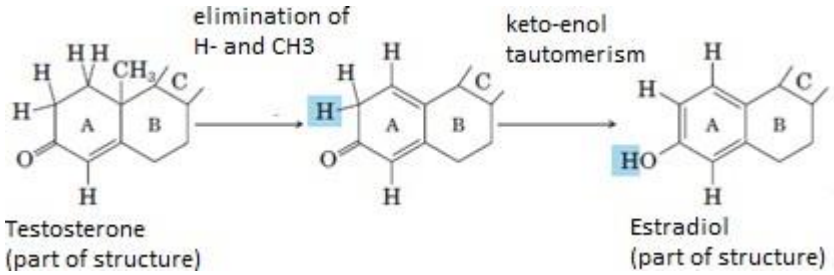


Estrone



Estradiol

Estradiol is synthesized from testosterone



Testosterone is secreted primarily in the testicles of males and the ovaries of females, although small amounts are also secreted by the adrenal glands.

In men, testosterone plays a key role in the development of male reproductive tissues such as the testis and prostate as well as promoting secondary sexual characteristics such as increased muscle, bone mass, and the growth of body hair. In addition, testosterone is essential for health and well-being as well as the prevention of osteoporosis.

Estradiol *in vivo* is interconvertible with estrone; estradiol to estrone conversion being favored. Estradiol has not only a critical impact on reproductive and sexual functioning, but also affects other organs, including the bones. Estradiol is also present in males, being produced as an active metabolic product of testosterone. The serum levels of estradiol in males (14 - 55 pg/mL) are roughly comparable to those of postmenopausal women (< 35 pg/mL).

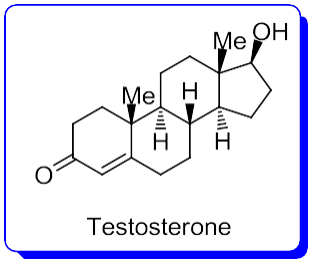
Anabolic steroids

Testosterone as male hormone is responsible for the buildup of muscles in men. For this reason many athletes have taken this drug in an effort to increase their muscular development.

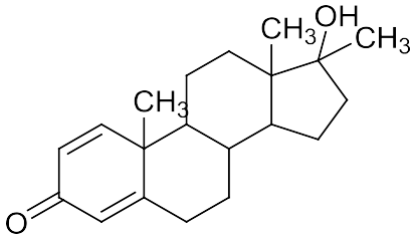
However, testosterone has two disadvantages:

1. Besides the effect on muscles it affects secondary sexual characteristics and can result in undesired side effects.
2. It is not very effective when taken orally and must be injected to achieve the best result.

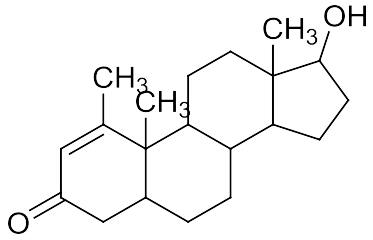
For this reason, a large number of synthetic anabolic steroids have been developed. For example:



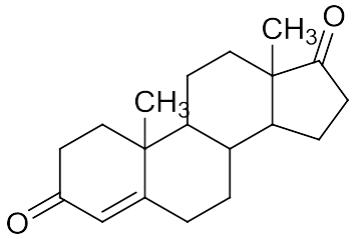
Testosterone



Methandienone



Methenolone



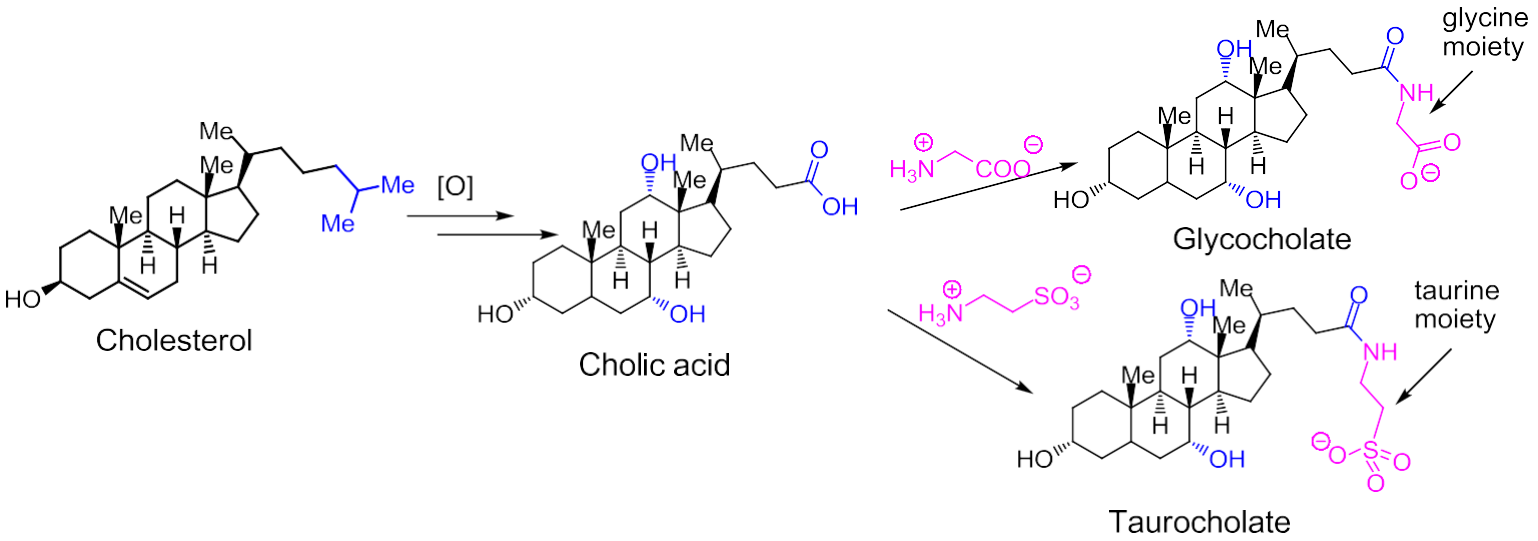
4-Androstene-3,17-dione
(prohormone)

Some women athletes use anabolic steroids, as well. Because their bodies produce only small amount of testosterone, women have much more to gain from anabolic steroids than men.

Another way to increase concentration is to use prohormones, which the body converts to testosterone. An example of prohormone is 4-androstenedione.

Bile acids

Bile acids are oxidation products of cholesterol. First the cholesterol is oxidized to the trihydroxy derivative, and the aliphatic chain is oxidized to the carboxylic acid. The latter, in turn, forms an amide bond with an amino acid, either glycine or taurine.



Bile salts are very good detergents. One end of the molecule is strongly hydrophylic because of the negative charge. Hydroxy groups are also directed to one side of the molecule. The rest of the molecule is largely hydrophobic. Thus, bile salts can disperse dietary lipids in the small intestine into the emulsions and thus, facilitate digestion. The dispersion of dietary lipids by bile salts is similar to the action of soap on dirt.

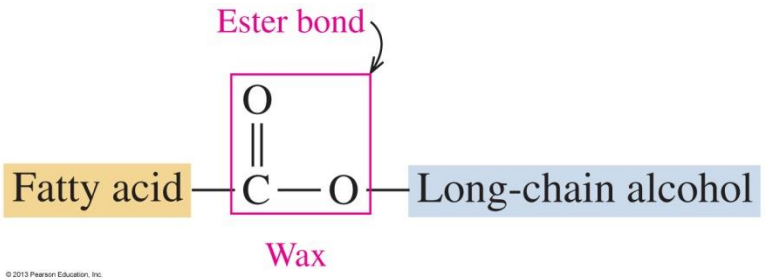
Because bile salts are eliminated in the feces, they remove excess cholesterol in two ways: (1) they are themselves breakdown products of cholesterol (cholesterol is eliminated via bile salts); (2) they solubilize deposited cholesterol in the form of bile-salts-cholesterol particles.

Waxes

Waxes are

esters of saturated fatty acids and long-chain alcohols each containing 14 to 30 carbon atoms.

coatings that prevent loss of water from leaves of plants.



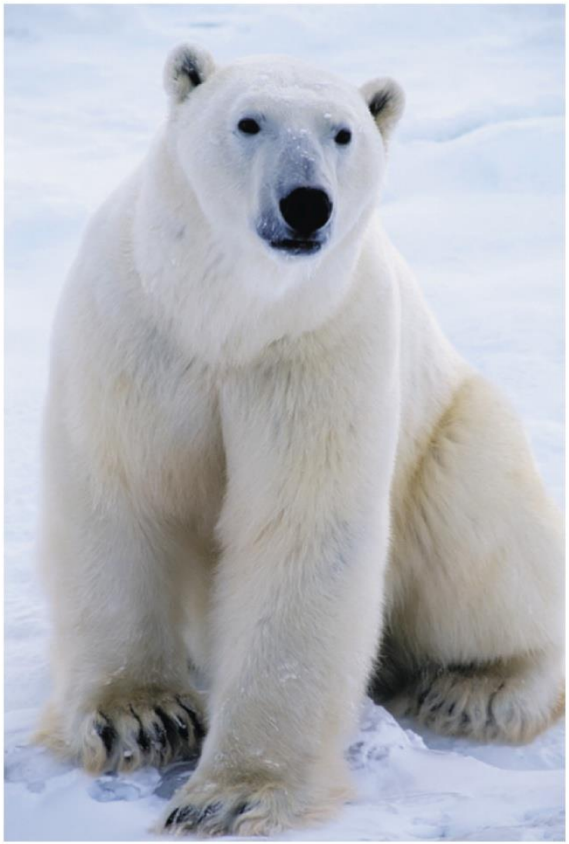
Typical Waxes

TABLE 17.2 Some Typical Waxes

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

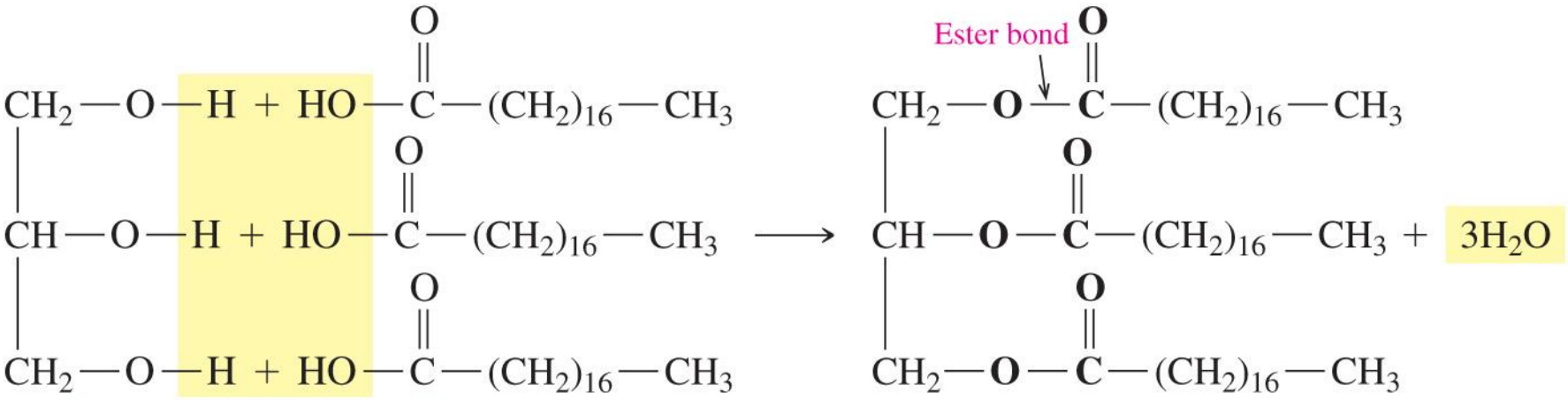
Fats and Oils: Triacylglycerols

Fats and oils are
also called **triacylglycerols**.
triesters of glycerol.
produced by esterification.
formed when the hydroxyl groups of glycerol
react with the carboxyl groups of fatty acids.
a major form of energy storage for animals.



Triacylglycerols

In a **triacylglycerol**, glycerol forms ester bonds with three fatty acids.



Base Hydrolysis (Saponification)

In **base hydrolysis (saponification)**,
a triacylglycerol reacts with heat and a strong base.
a triacylglycerol splits into glycerol and the salts of fatty acids (soap).
a solid soap that can be molded into a desired shape is produced when NaOH is used.
a softer, liquid soap is produced when KOH is used.
polyunsaturated oils produce softer soaps.