Lipids

Overweight and excessive fatness is one of the fundamental problems of contemporary society, affecting not only people, but increasingly also domesticated animals. In the nineteenth century James Herriot in the cult book series "All Creatures Great and Small" memorably fought Pekingese obesity, and today the view of obese cats or horses is not uncommon.

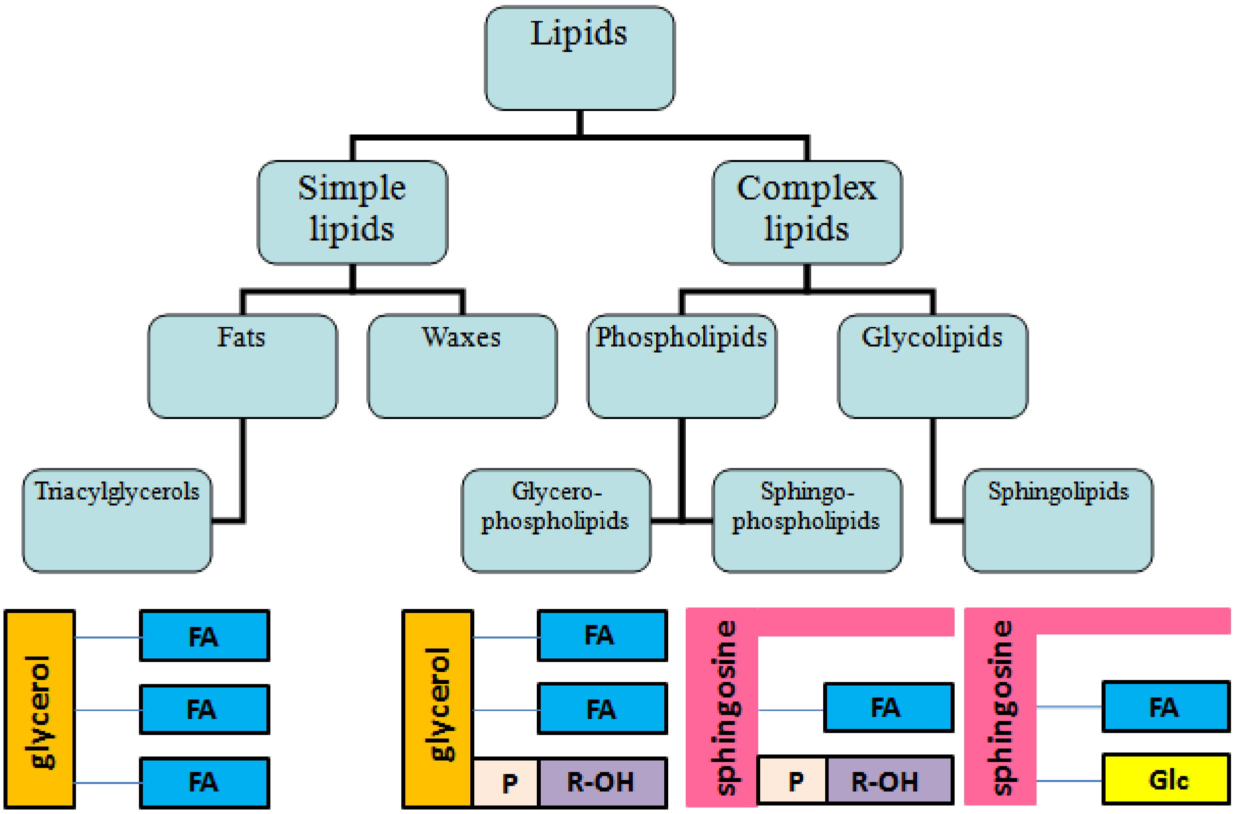
Excessively accumulating fat reserves unnecessarily burden the skeletal system and cardiovascular system. In addition, harmful substances known as xenobiotics accumulate in the fat stored in adipose tissue. Xenobiotics are sparingly soluble in water and over the years they are accumulated in the body, being a potential detrimental factors that damage the liver or cause cancer. Cholesterol deposits accumulating in blood vessels impair blood flow and, after separation from the vessels, they wander with the blood and only the incident determines in which organ they block capillaries. Caused by them blockage in the heart or brain poses an immediate threat to life. Moreover, alterations in lipid metabolism are the cause of hyperlipidemia in horses, and fat mobilisation syndrome or ketosis in cattle. These diseases are difficult to treat, and if not treated, lead to death.

However, lipids are not just a source of problems. They are valuable source of energy - oxidation of 1 gram of accumulated fat delivers two times more energy than oxidation of 1 gram of sugar. Furthermore, lipid compounds co-create cell membranes, sheath surrounding nerve fibers, act as hormones and also they are involved in digestion, processes of vision, in the regulation of the inflammatory processes, intracellular signal transduction and many others.

It results directly from the specific structure of this group of compounds, and hence, their physicochemical properties. Thus, the classification, the structure and the properties of lipids should be investigated. Generally, lipids are substances of biological origin, insoluble or sparingly soluble in water, well soluble in organic solvents such as methanol, acetone, chloroform or benzene.

Thus defined lipids are very heterogenous compounds, such as: vegetable and animal fats, phospholipids of cell membranes, waxes, steroids, fatty acids, carotenoids, even hydrocarbons. So, let's take a biochemical point of view and recognize as valid the following definition: **lipids are compounds which are hydrolyzed to fatty acids and alcohol. Mainly they are the esters of fatty acids and alcohol.** Lipid fraction obtained from biological material contains also an admixture of other insoluble

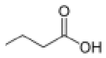
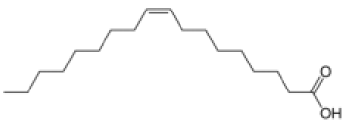
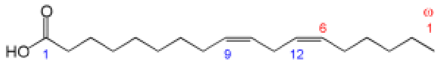
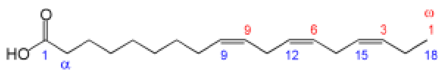
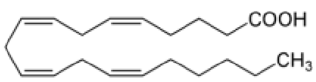
substances, such as cholesterol and other steroids (estrogens, progesterone, testosterone, cortisol, bile acids), free fatty acids, pro vitamins and vitamins (fat-soluble). These substances are defined as lipid derivatives, because they derive from lipid metabolism and can be useful to create the fat molecule. It is often said that steroids (cholesterol and its derivatives), carotenoids and fat-soluble vitamins are derivatives of isoprene, because they derive from the common component, isoprene (2-methyl-1,3-butadiene).
Let's leave them for now and focus on lipids which hydrolyze. Lipids are divided according to the following scheme:



In the diagram above, the distribution of lipids is given as schematic structure of individual types of lipids. As shown, the lipids may be esters of fatty acids (FAs) and glycerol or some other alcohol - sphingosine. Simple lipids (triacylglycerols) consists only of glycerol and fatty acids. Complex lipids beside an alcohol (glycerol or sphingosine) and FAs have other compounds. Phospholipids have phosphate residue (P) and aminoalcohol residue (R-OH), against glycolipids have sugar residue (Glc). In contrast, there are no lipids, which include both P and Glc residues.

CHEMICAL STRUCTURE

Fatty acids. Lipids found in plant and animal tissues have in their composition organic acids having a relatively simple structure with many common features, therefore it is used the general concept: fatty acids. Fatty acids are simple monocarboxylic acids with unbranched chains, which consists of even number of carbon (from 4 to 24 atoms of C), because all of them are synthesized from two-carbon fragments. Fatty acids found in lipids of higher plants and animals typically have 16 or 18 carbon atoms, 20-carbon acids are less common. For example, milk is made of butyric acid with 4 carbon atoms. Fatty acids may differ from each other (apart from the chain length) in respect of the degree of saturation of individual bonds. They may be saturated or unsaturated compounds, and in the case of unsaturated acids it is very important to know: the number of double bonds, their position in the chain and the type of isomerism (cis, trans). The most important fatty acids include:

	butyric acid
	palmitic acid
	stearic acid
	oleic acid
	linoleic acid (exogenous)
	linolenic acid (exogenous)
 	arachidonic acid (exogenous)

To memorize the structure of individual fatty acids, the use of special nomenclature abbreviations consisting of several digits, eg. 4:0 (for butyric acid) and 20:4;5,8,11,14 (for arachidonic acid) may be helpful. First number reflects the number of C atoms in the molecule, number after the colon = the number of double bonds, and number after semicolon = the position of unsaturated bonds in the chain, more precisely – it mean the number of carbon atom, where there is double bond counting from the carboxyl group. In turn, specialists involved in dietetics and nutrition calculate the position of the double bond starting from the terminal carbon atom (CH_3).
The first carbon atom is defined as α, while ω (omega) is used to indicate the "last" carbon atom in the fatty acid chain. Hence we have ω-3 fatty acids (eg. linolenic acid) - with a double bond (C=C) at the third carbon atom from the end of the carbon chain, ω-6 acids (linoleic and arachidonic) or ω-9 (oleic acid). Naturally occurring fatty acids almost always have a cis geometry. These polyunsaturated fatty acids ω-3 and ω-6, as well as vitamins, must be present in the diet of animals and humans because they are not produced in their bodies. Therefore, they are called **"essential fatty acids" (EFAs)**.

Physicochemical properties of fatty acids depend on the chain length and the number of unsaturated bonds. The longer is the chain, the higher is the melting point, and the more pronounced is hydrophobic nature (more difficult solubility in water). So-called "higher fatty acids" having 12 or more carbon atoms are practically insoluble in water. In turn, the presence of double bonds decreases the melting point. Properties of individual fatty acids affect the properties of the lipid, which is formed by them. Therefore animal fats mainly consisting of palmitic and stearic acids, have a solid consistency at room temperature, in turn oils containing ω-3 and ω-6 fatty acids are liquid under these conditions.

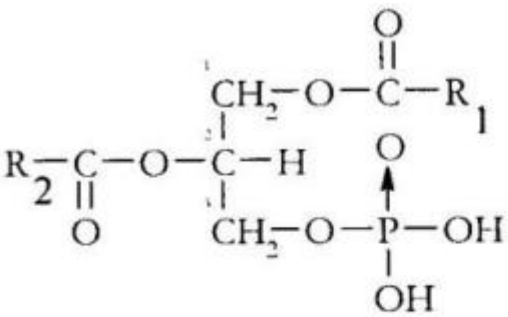
Fats are the esters of glycerol and fatty acids. Primarily they are the reserve material. Furthermore, their deposits are a heat shield (eg. in the subcutaneous tissue of animals who live in arctic conditions) and mechanical protection (sheath kidney fat). Animal fats are usually solid (except the oil from fish liver) differently from vegetable fats that are liquids in room temperature. This difference is due to the content of unsaturated fatty acids in plant oils. Although the lipids are insoluble in water, they may be transported by the blood, but only in combination with proteins, so-called apoproteins. Depending on the ratio of fat to protein, there are chylomicrons and lipoproteins: lipoproteins of very low density (VLDL), lipoproteins of low density (LDL) and lipoproteins of high density (HDL). Aforementioned lipid fractions differ not only in chemical composition but also in their functions. For example, chylomicrons transport triacylglycerols from the gastrointestinal tract into the liver, VLDL - transport triacylglycerols from the liver to peripheral tissues and HDL (containing relatively the highest proportion of protein to lipids) are responsible for transporting the lipids from peripheral tissues to the liver.

You should know the following issues:

- concepts and formulas of α- and β-monoacylglycerol, diacylglycerol, triacylglycerol
- the theory and reactions of hardening fats
- hydrolysis, including saponification of fats - reactions
- rancidity (acid, aldehyde, ketone, hydroxy-acid)
- the values characteristic for lipids (saponification, acid and iodine values)
- glycerol – structure, chemical properties

Phospholipids are divided into two groups depending on the alcohol present in their structure: <u>phosphoglycerides (glycerophospholipids)</u> and <u>sphingophospholipids</u>. Their common feature is the presence of a phosphate residue linked by ester linkage to an alcohol. Phospholipids are the main components of biological membranes. Presence of a phosphate residue makes, that in the neutral environment phospholipids are endowed with a negative charge.

Phosphoglyceride. If one fatty acid residue will be replaced by a phosphate residue in the triacylglycerol molecule, we will obtain phosphatidic acid – which is generated in the body, during the synthesis of both triglycerides and phospholipids. Usually, in the α position there is an saturated fatty acid residue, and in the β position – unsaturated fatty acid residue.
The molecule of phosphatidic acid is presented below:



phosphatidic acid

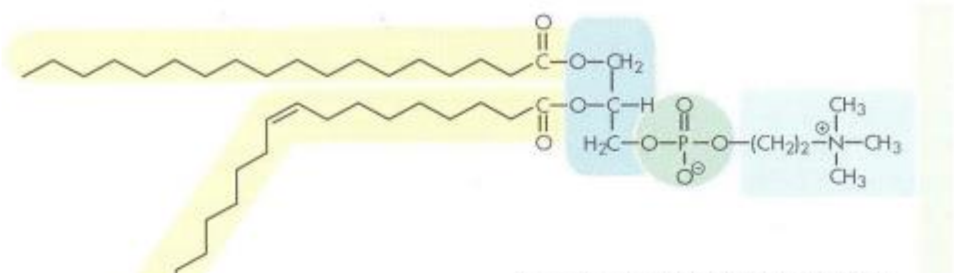
Phosphatidic acid mostly acts as a parent substance in the process of lipid biosynthesis. Primarily there are phosphoglycerides in the cell membranes. The phosphate group of phosphatidic acid is esterified by amino alcohol (choline, ethanolamine or serine) or cyclical alcohol (myoinositol) in their structure.

$HO\text{-}CH_2\text{-}NH_2$	$HO\text{-}CH_2\text{-}N^+(CH_3)_3$	$HO\text{-}CH_2\text{-}CH(\text{-}NH_2)\text{-}COOH$
ethanolamine	choline	serine

Therefore, there are 4 ester bonds in phosphoglycerides, which are located between following residues:

- glycerol and saturated fatty acid
- glycerol and unsaturated fatty acid
- glycerol and phosphoric acid
- phosphoric acid and amino alcohol or inositol.

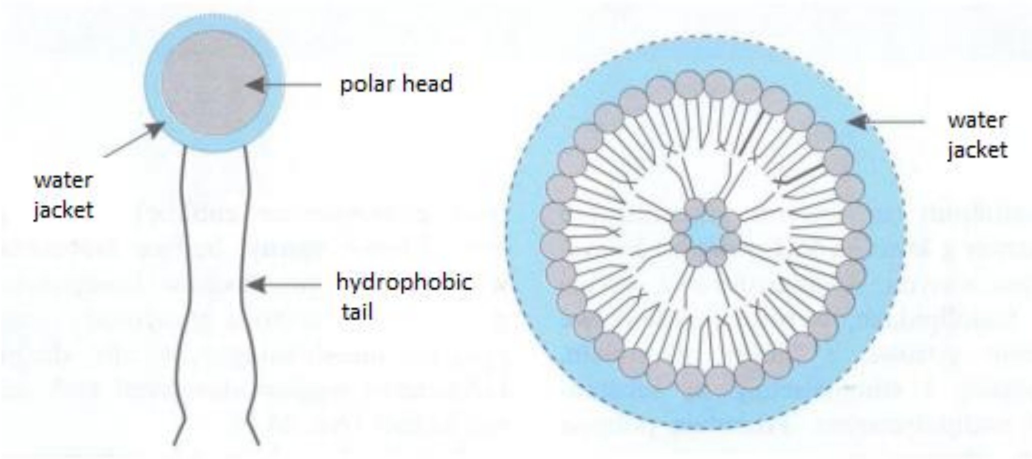
If the phosphoglyceride includes amino alcohol - ethanolamine (colamine), it is commonly called: cephalin, otherwise if there is choline in the place of ethanolamine, then it is called: lecithin.



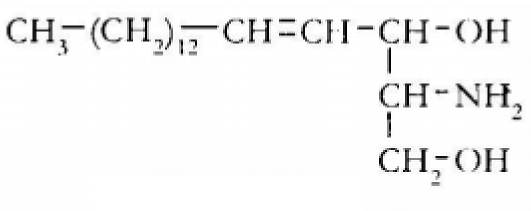
phosphatidylcholine (lecithin)

(ryc, Koolman: Biochemia, PZWL)

Besides the negative charge at the phosphate group, lecithins and cephalins also have a positive charge on the nitrogen of the amino alcohol. Consequently, these two phosphatides show no accident of electric charge - they are electrically neutral, but also highly polar in this part of their molecule. Phosphoric acid residues in combination with amino alcohols forms the polar head and the fatty acid residues - a non-polar tail. These features are the basis of lecithin and cephalin. These phosphoglycerides participate in the formation of cell membranes. The content of unsaturated bonds in the fatty acid residues and the spatial structure associated with the cis / trans isomerism affect the degree of plasticity cellular membranes and resistance to mechanical stress.

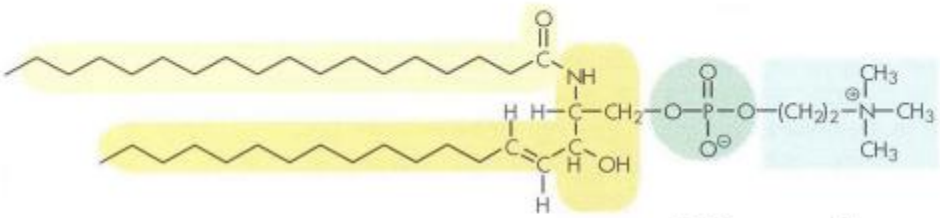


Sphingophospholipids appear in abundance in the membranes of nerve cells in the brain and nervous tissue. They differ from glycerophospholipids mainly kind of alcohol contained in their molecules. Instead of glycerol, they contain unsaturated long-chain amino alcohol (sphingosine).



sphingosine

Sphingosine is combined with the fatty acid residue by an amide bond via its amino group. This compound is a **ceramide,** which is a precursor of sphingolipids. If phosphate residue and choline are attached to ceramide, then the most important representative of sphingophospholipids: **sphingomyelin** is formed.



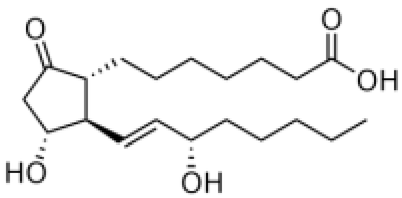
Sphingomyelin

Glycolipids consist of a ceramide and sugar residues linked by a glycosidic bond, therefore they do not have ester bonds. Cerebrosides contain a glucose (glucosylceramide) or galactose (galactosylceramide). Glycolipids, in which a sugar is esterified with sulfuric acid are the **sulfatides.** In the glycolipid molecule it is also possible the presence of polysaccharide consisting of monosaccharides and their derivatives, including N-acetylneuraminic acid, which is a typical component of gangliosides. Glycolipids present on the outside of cell membranes where they serve, among others, a signal function.

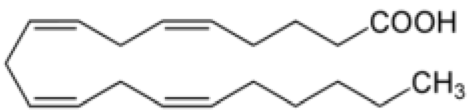
Lipid derivatives

Lipid derivatives are divided into:
- free (non-esterified) fatty acids,
- steroids,
- higher alcohols and other polar organic compounds

Within this group of compounds, fatty acids constituting the lipid components were described above. However, apart from the basic role - the component of lipids, some fatty acids are used for the synthesis of biologically important derivatives - eicosanoids. The most important representative of this group of compounds are prostaglandins. They are formed by a series of oxidation and reduction reactions of arachidonic acid, and in respect of chemical structure they are still 20-carbon acids, have only one double bond between carbons C13 and C14, and the newly formed bond between C8 and C12 make them cyclic compounds.



prostaglandin E1

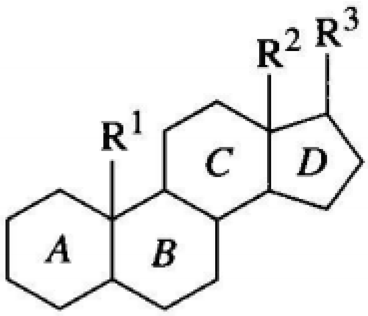


arachidonic acid

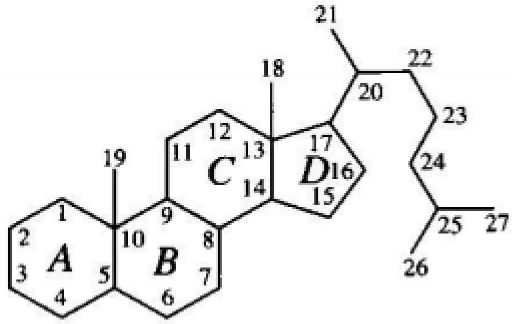
Prostaglandins are created from arachidonic acid released from the cell membrane phospholipids. They are the tissue hormones, which mean they are produced by cells of different tissues, act locally to neighboring cells causing there changes characteristic for inflammation: swelling as a result of Na^+ and water retention and increase blood flow, which results in increased temperature and tissue congestion. Commonly used acetylsalicylic acid (aspirin) acts anti-inflammatory just by inhibiting the production of prostaglandins. In addition, prostaglandins inhibit gastric acid secretion. Other groups of eicosanoids are: **leukotrienes**, which are involved in the regulation of inflammatory and allergic processes, and **thromboxanes** involved in blood clotting.

Now, let's discuss another group of lipid derivatives:

steroids. In general, this group means all compounds built on the tetracyclic carbon skeleton - cyclopentane perhydro phenanthrene.



perhydro-1,2-cyclopentano- phenanthrene



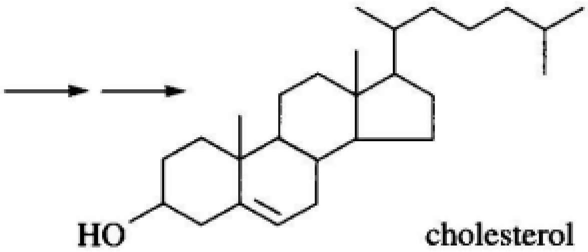
skeletal structure of cholesterol

Derivatives of this compound differ from each other the degree of unsaturation and length of the side chains R1 R2 R3. Discussing the construction of these derivatives we use the "numbering" of the rings: A, B, C and D and the numbering of carbons in the molecule, as shown in the attached drawings. Among steroids there are an important group called sterols, which have the OH group in position 3. In all steroids discussed below in place of R2 is methyl group, and in place of R1 there is almost always a methyl group (only estrogens have in place of R1 hydrogen).

The most important representative of the steroids is cholesterol.

There are characteristics of the cholesterol structure:

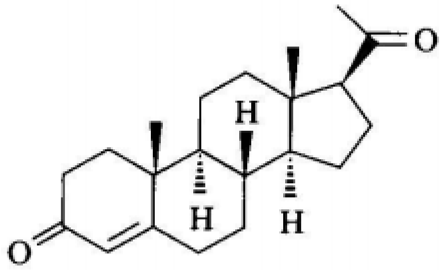
- it consists of 27 carbon atoms,
- it has a hydroxyl group in position 3
- there is one double bond between carbons C5 and C6 in the ring B.



cholesterol

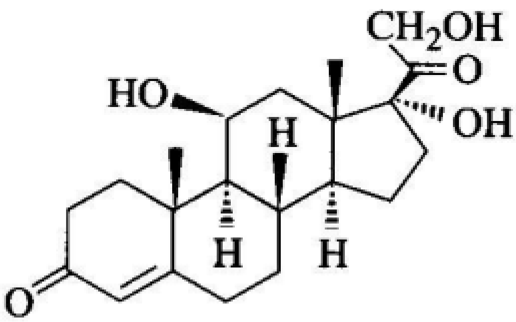
Cholesterol is present in the membranes of all mammal cells. In the nerve tissue it is a part of myelin sheath and accounts for 10-15% of dry brain mass. It is the precursor of: sex and adrenal cortex hormones, vitamin D and bile acids. Disorders of cholesterol metabolism lead to the accumulation of deposits in vessels and to the formation of gallstones. Therefore, in humans it is important to control blood cholesterol in different lipoprotein fractions. It is understood that more dangerous is high value of the concentration of cholesterol in LDL than in HDL. A high value of HDL-cholesterol (so-called "good cholesterol") provides an efficient mechanism for the removal of cholesterol from the peripheral tissues. As mentioned above, cholesterol is a precursor of the important hormones. Shortening the chain R3 gives progesterone, a compound which contains:

- 21 carbon atoms,
- double bond in chain A, between carbons C4 and C5,
- 2 ketone groups:
  - at C3 (therefore it is a steroid, not a sterol)
  - in chain R3, which means at C20.



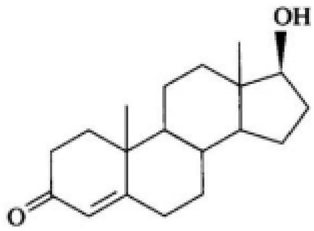
progesterone

Progesterone is a pregnancy hormone. It is a direct precursor of other sex hormones and corticosteroids. A typical hormone of adrenal cortex is cortisol. Cortisol differs from progesterone only by the appearance of the three -OH groups in the carbons C11, C17 and C21.



cortisol
(hydrocortisone)

Removal of the R3 chain and the oxidation of carbon C17 in progesterone gives testosterone.

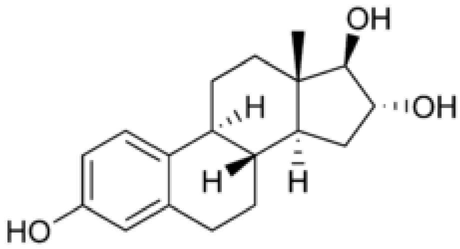


testosterone

Bigger changes are needed to converse testosterone into estrogen. In fact, estrogens differ from testosterone by three features:

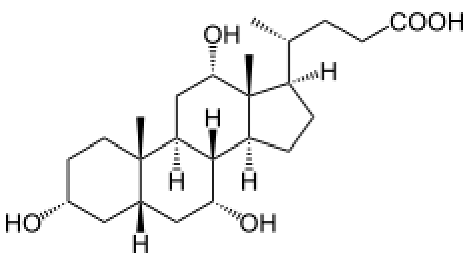
- ring A is aromatic (it has 3 double bonds),
- the lack of carbon C19 (R1)
- at C3 is -OH group.

A typical example of the estrogen is estradiol:



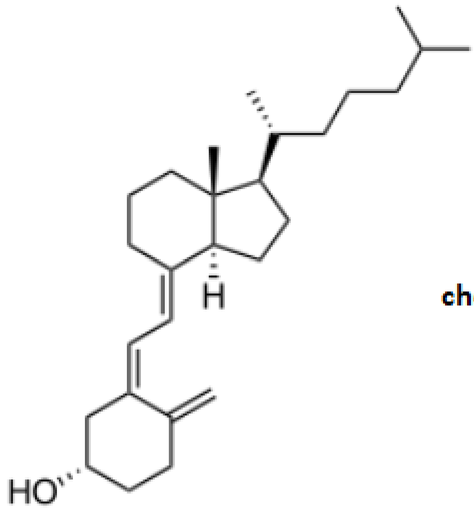
estriol

Other derivatives of cholesterol are bile acids, which main function is support the process of fat digestion by its emulsification and dissolution excreted via the bile cholesterol. As the name suggests, these compounds contain a carboxyl group, and also hydroxyl groups. However, they do not have double bonds. A typical representative of this group is cholic acid:



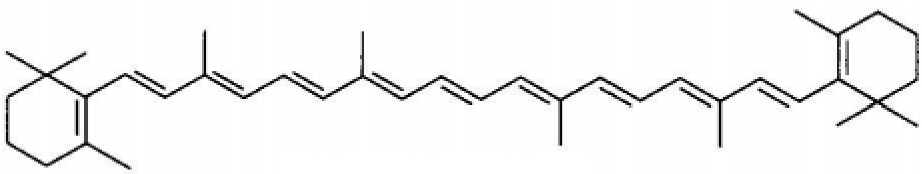
cholic acid

Vitamin D will be discussed as the last derivative of cholesterol. The name could be misleading, because this compound can be produced in the mammal's organisms, and its active form - **cholecalciferol** – acts as hormone – regulating the absorption of calcium in the gastrointestinal tract. It differs from other steroids mainly by the opening of ring B and the occurrence in its place three conjugated unsaturated bonds.

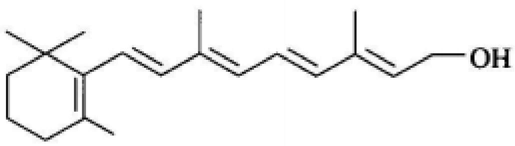


cholecalciferol

Other fat-soluble vitamins are classified as derivatives of isoprene. These compounds are apolar organic substances different than sterols and alcohols. Only vitamin A will be described here. Vitamin A is essential for the proper growth and functioning of epithelia and co-creates the retinal pigment responsible for the processes of vision. In the animal organisms it is obtained from the plant dye - β-carotene (a provitamin for vitamin A):



β-carotene



vitamin A (retinol)

If you learn given formulas, you will celebrate after test.