LIPIDS

Classification, functions and structure

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Lipids are non-polar (hydrophobic) compounds, insoluble in water, but soluble in organic solvents.

Lipids have a very heterogeneous chemical structure and play very different functions.
LIPID FUNCTIONS

The biological functions of the lipids are very diverse:

- **Fats and oils** - are the principal stored forms of energy in many organisms,

- **Phospholipids and sterols** - make up about half the mass of biological membranes.

- **Steroid hormones** - sex hormones, glucocorticoides and mineralocorticoides

- **Liposoluble vitamins** - vitamins A, D, E and K

**Energy storage**
- Fats stored in adipose tissue.

**Cell membrane structure**
- Creates a barrier for the cell.
- Controls flow of materials.

**Hormones and Vitamins**
- Hormones - communication between cells.
- Vitamins - assist in the regulation of biological processes.
Lipids are classified into 2 general groups:

I. Non-hydrolysable (non-saponifiable) lipids:

- Derived lipids:
  - Fatty acids
  - Fatty alcohols
  - Fatty aldehydes
  - Hydrocarbons

- Terpenes: fat soluble Vitamin A, E and K
  (made up of repeating isoprene units).

- Sterols and steroids:
  - Cholesterol
  - Vitamin D
  - Androgens and estrogens (Sex hormones)
  - Adrenal corticosteroids
  - Bile acids
II. Hydrolysable (saponifiable) lipids

• Simple Lipids – consist from only two components:
  a) Triglycerides (neutral fats and oils – storage lipids): Esters of three molecules of fatty acids plus one molecule of glycerol;

b) Waxes: Composed of esters of fatty acids with alcohol other than glycerol;
• **Complex Lipids** *(membrane lipids)*—consist from more than two components

a) **Phospholipids:**
   - **glycerophospholipids** - composed of glycerol, fatty acids, and phosphoric acid bound to a nitrogenous base.
   - **sphingophospholipids (sphingomyelins):** containing sphingosine, fatty acids, phosphoric acid, choline, and no glycerol;

b) **Glycolipids (Sphingoglycolipids):**
   - **Cerebrosides:** contains sphingosine, fatty acid and galactose (or glucose).
   - **Gangliosides:** contains sphingosine, fatty acid and an oligosaccharide
   - **Sulpholipids:**
     Sulphur-containing glycolipids.
The principal classes of storage and membrane lipids

- **Storage lipids (neutral)**
  - Triacylglycerols

- **Membrane lipids (polar)**
  - Phospholipids
    - Glycerophospholipids
    - Sphingolipids
  - Glycolipids
    - Sphingolipids

- **Glycerol**
  - Fatty acid
  - Fatty acid
  - Fatty acid

- **Glycerol**
  - Fatty acid
  - Fatty acid
  - PO₄
  - Alcohol

- **Sphingosine**
  - Fatty acid
  - PO₄
  - Choline

- **Sphingosine**
  - Fatty acid
  - Mono- or oligosaccharide
Fatty acids

Fatty acids are present in all organisms as components of storage and membrane lipids.

The naturally occurring fatty acids are carboxylic acids with unbranched hydrocarbon chains of 12–24 carbon atoms. Most naturally occurring fatty acids have an even number of carbon atoms.

\[
\text{CH}_3(\text{CH}_2)_n\text{COOH}
\]

Some fatty acids contain one or more double bonds, and are therefore “unsaturated.” Double bonds in fatty acids usually have the cis configuration.
1. **Saturated fatty acids:** general formula \( \text{C}_n\text{H}_{2n+1}\text{COOH} \); have no double bonds in the chain.

- \( \text{C}_{11}\text{H}_{23}\text{COOH} \) (\( \text{CH}_3-(\text{CH}_2)_{10}-\text{COOH} \)) - lauric acid \( (\text{C}_{12}) \)
- \( \text{C}_{13}\text{H}_{27}\text{COOH} \) (\( \text{CH}_3-(\text{CH}_2)_{12}-\text{COOH} \)) - myristic acid \( (\text{C}_{14}) \)
- \( \text{C}_{15}\text{H}_{31}\text{COOH} \) (\( \text{CH}_3-(\text{CH}_2)_{14}-\text{COOH} \)) - palmitic acid \( (\text{C}_{16}) \)
- \( \text{C}_{17}\text{H}_{35}\text{COOH} \) (\( \text{CH}_3-(\text{CH}_2)_{16}-\text{COOH} \)) - stearic acid \( (\text{C}_{18}) \)

The conformation of carbon chain is a zigzag. For example-

Palmitic acid:
2. The unsaturated acids with one double bond (monounsaturated acids) - \( \text{C}_n\text{H}_{2n-1}\text{-COOH} \):

**palmitoleic acid** \( \text{C}_{16}:\Delta^9 \)

\[
\text{C}_{15}\text{H}_{29}\text{COOH} \quad \text{CH}_3-(\text{CH}_2)_5-\text{CH}=\text{CH}-(\text{CH}_2)_7-\text{COOH}
\]

**oleic acid** \( \text{C}_{18}:\Delta^9 \)

\[
\text{C}_{17}\text{H}_{33}\text{COOH} \quad \text{CH}_3-(\text{CH}_2)_7-\text{CH}=\text{CH}-(\text{CH}_2)_7-\text{COOH}
\]
3. The unsaturated acid with two double bounds – $\text{C}_n\text{H}_{2n-3}\text{-COOH}$:

**linoleic acid** $\text{C}_{18}:\Delta^{9,12}$ $\text{C}_{17}\text{H}_{31}\text{COOH}$

$\text{CH}_3-(\text{CH}_2)_4\text{-CH=CH-CH}_2\text{-CH=CH-(CH}_2)_7\text{-COOH}$

4. The unsaturated acids with three double bounds – $\text{C}_n\text{H}_{2n-5}\text{-COOH}$:

**linolenic acid** $\text{C}_{18}:\Delta^{9,12,15}$ $\text{C}_{17}\text{H}_{29}\text{COOH}$

$\text{CH}_3\text{-CH}_2\text{CH=CH-CH}_2\text{-CH=CH-CH}_2\text{-CH=CH-(CH}_2)_7\text{-COOH}$
5. The unsaturated acids with four double bounds

\[ C_nH_{2n-7}-COOH: \]

**arachidonic acid**  
\[ C_{20}\Delta^{5,8,11,14} \]  
\[ C_{19}H_{31}COOH \]

All polyunsaturated fatty acids: *arachidonic, linoleic* and *linolenic acid* are essential fatty acids - they are not produced in human organism and have to be supplied in the diet. They are indispensable components of nutrition.
Animal fats and vegetable oils are the most widely occurring lipids. Although they look different – animal fats such as butter and lard (fat) are solids, and vegetable oils are liquids – their structures are closely related. Chemically, fats and oil are triacylglycerols (also called triglycerides), esters of glycerol with three long-chain carboxylic acids.

Triglycerides are completely unpolar, hydrophobic compounds, called neutral lipids.
Triacylglycerols Are Fatty Acid Esters of Glycerol
The chemical properties of triglyceride

1. One of the most important properties of triacylglycerols is their chemical hydrolysis in the both acid and basic medium. For example:

\[
\begin{align*}
\text{CH}_2\text{OH} & + \text{C}_{17}\text{H}_{33}\text{COOH} \\
\text{CH}_2\text{OH} & + \text{C}_{15}\text{H}_{31}\text{COOH} \\
\text{CH}_2\text{OH} & + \text{C}_{17}\text{H}_{35}\text{COOH} \\
\text{NaOH} & \\
\text{H}_2\text{O(OH)} & \\
\end{align*}
\]

\text{Palmitooleooleostearin} \\
\text{Glycerol}

- oleic acid
- palmitic acid
- stearic acid
- sodium oleate
- sodium palmitate
- sodium stearate
2. The second major reaction is the reaction of hydrogenation of fats, which are used in the conversion of liquid oils into solid fat:
- are common constituents of cellular membranes. They are composed of glycerol, fatty acids and phosphoric acid bound to a polar head group – an alcohol (X):
Glycerophospholipids Are Derivatives of Phosphatidic Acid

Glycerol + 2 fatty acids + phosphoric acid = phosphatidic acid or phosphatidate:

\[
\begin{align*}
\text{Glycerol} & \quad \text{H}_2\text{C} & \quad \text{O} & \quad \text{C} & \quad \text{R}_2 \\
\text{R}_1 & \quad \text{O} & \quad \text{C} & \quad \text{O} & \quad \text{CH} \\
& \quad \text{H}_2\text{C} & \quad \text{O} & \quad \text{P} & \quad \text{O}^- \\
\end{align*}
\]

phosphatidate

In phosphatidic acid the hydroxyls at C1 & C2 of glycerol are esterified to fatty acids and the C3 hydroxyl is esterified to Pi.

Pi is in turn esterified to OH of a polar head group (X):

serine, choline, ethanolamine or inositol.
HO-CH₂CH₂NH₃⁺   \hspace{1cm} \text{Ethanolamine}

HO-CH₂CH₂N(CH₃)₃⁺ \hspace{1cm} \text{Choline}

HO-CH₂CH-\text{NH}_2\text{COO}⁻ \hspace{1cm} \text{Serine}

\{ \hspace{1cm} \text{Aminoalcohols}

\hspace{1cm} \text{Hydroxyynamiino acid}

\text{Inositol} \hspace{1cm} \text{Cyclic polyalcohol}
Glycerophospholipids are named for their polar head groups:

<table>
<thead>
<tr>
<th>Glycerophospholipid</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphatidylcholine</td>
<td><img src="" alt="Phosphatidylcholine" /></td>
</tr>
<tr>
<td>Phosphatidylethanolamine</td>
<td><img src="" alt="Phosphatidylethanolamine" /></td>
</tr>
<tr>
<td>Phosphatidylserine</td>
<td><img src="" alt="Phosphatidylserine" /></td>
</tr>
<tr>
<td>Phosphatidylinositol</td>
<td><img src="" alt="Phosphatidylinositol" /></td>
</tr>
</tbody>
</table>
Each glycerophospholipid includes:

- a **polar** region: $P_i$, and the polar head group ($X$)
- **non-polar** hydrocarbon tails of fatty acids ($R_1, R_2$).
Glycerophospholipids are amphipathic - they have **hydrophilic** (polar) and **hydrophobic** (nonpolar) portions located at separate parts of each molecule. As a result, the lipid components are arranged in a continuous **bimolecular bilayer**. The polar portions of the constituent molecules lie in the two bilayer faces, while the nonpolar portions constitute the interior of the bilayer.
The lipidic bilayer forms the cell membranes:
- Sphingophospholipids (sphingomyelins) and glycolipids - are the second large class of membrane lipids, also have a polar head and two nonpolar tails, but unlike glycerophospholipids they contain no glycerol.

All sphingolipids contain one molecule of the long-chain unsaturated amino alcohol sphingosine.
In all sphingolipids sphingosine is bound by an amide bond to a fatty acid and forms a **ceramide**:

\[
\text{CH}_3(\text{CH}_2)_{12}\text{CH}=\text{CH}−\text{CH}−\text{OH} \quad \text{Ceramide} \\
\text{CH}−\text{NH}−\text{CO}−\text{R} \quad \text{CH}_2−\text{OH}
\]
Sphingophospholipids (Sphingomyelins) contain phosphocholine or phosphoethanolamine as their polar head group, and are therefore classified as phospholipids.

Sphingomyelins are present in plasma membranes of animal cells; the myelin sheath which surrounds and insulates the axons of myelinated neurons is a good source of sphingomyelins, and gives them their name.
Glycolipids (sphingoglycolipids) occur largely in the outer surface of the plasma membrane.

- **Cerebrosides** have a single sugar (glucose or galactose) linked to ceramide:

![Chemical structure of Galactocerebroside]
Gangliosides, the most complex sphingolipids, contain a ceramide and an oligosaccharide fragment. Gangliosides make up about 6% of the membrane lipids in the gray matter of the human brain and play an important role in molecular recognition.

Glycosphingolipids are the determinants of blood types
Steroids are the organic compounds containing the steroid nucleus – a tetracyclic system, consisting of three cyclohexane rings (A, B, C) and a cyclopentane ring (D), called steran (or by systematic nomenclature - ciclopentanperhidrofenantren). We refer to steroids cholesterol, steroid hormones, bile acids, vitamin D.
The most important steroid is **Cholesterol**

It is a vital constituent of cell membranes and the precursor of steroid hormones and bile salts, yet its deposition in arteries has been associated with heart disease.
In animal tissues, especially in the liver, adrenals and plasma lipids cholesterol is esterified by a variety of fatty acids and most frequently by essential fatty acids, thus forming *cholesterol esters*:
STEROID HORMONS

There are four groups of steroid hormones: gestagens - progesterone (corpus luteum hormone), corticosteroids (adrenal cortex hormones), androgens (male sex hormones), estrogens (female sex hormones).

At the basis of the chemical structure of the gestagens and corticosteroids, is a saturated hydrocarbon - pregnane (10,13-dimethyl-17-ethylsteran) – with 21 carbon atoms.

Pregnane is the parent of progesterone and several adrenocortical hormones.

Progesterone is a steroid hormone secreted by the corpus luteum of the ovary, or by placenta. He has the ability to transform the endometrium, favoring implantation of the fertilized egg in the uterine mucosa during pregnancy.
Corticosteroids (adrenal cortex hormones) regulates the carbohydrate metabolism (glucocorticoids) and hydro-saline metabolism (mineralocorticoids).

The most important representative of glucocorticoids is cortisol (11β-,17α-, 21-trihydroxy-pregnen-4-dione-3,20). It acts as an antagonist of insulin, increasing blood glucose, activating the gluconeogenesis in the liver (the synthesis of glucose).

The most important mineralocorticoid is aldosterone, produced in the zona glomerulosa of the adrenal cortex. It works especially at the level of distal and collectors tubules of the nephron, stimulating the reabsorption of sodium and water and excretion of potassium, resulting in increased blood volume and blood pressure.
At the basis of the chemical structure of the androgens is the hydrocarbon **androstan** (10,13-dimethyl-steran) – with 19 carbon atoms. The main male sex hormones are **androsterone** and **testosterone**.

Androgens stimulate the development and functions of male genital glands and the development of male secondary sexual signs. They are synthesized in the testes, adrenal, and in very small quantities in ovary.
Estrogens (feminine sex hormones)

At the basis of the chemical structure of the estrogens is the hydrocarbon estrane – with 18 carbon atoms. The most important estrogen hormones are estrone and estradiol. In estrogens the A ring is aromatic.

Estrogens are produced in the female sexual glands, but also in small quantities in the adrenal gland and testicles. Estrogens stimulate the development and female genital glands, development of female secondary sexual signs, and together with gestagens regulate ovulation, fertilization, pregnancy.
At the basis of the chemical structure of bile acids is the hydrocarbon \textit{cholan} with 24 \textbf{carbon atoms}, which is oxidised to \textit{5β-cholanic acid}. Bile acids are obtained by its hydroxylation in positions 3, 7 and 12.

In the human body bile acids are synthesized from cholesterol. Bile acids contribute to the emulsification of food fats, activate the enzyme lipase, which catalyzes the hydrolysis of fats. Human bile contains several bile acids including \textit{cholic acid} and its amides with glycine (\textit{glycocholic acid}) or taurine (\textit{taurocholic acid}).
VITAMIN D –

- Refers to a group of fat-soluble vitamins responsible for increasing intestinal absorption of calcium, iron, magnesium, phosphate and zinc. Vitamin D has a significant role in calcium homeostasis and metabolism. Insufficiency of vitamin D leads to rickets in children.

- In humans, the most important compounds are vitamin D₃ (also known as cholecalciferol) and vitamin D₂ (ergocalciferol). The major natural source of the vitamin is the synthesis of vitamin D (specifically cholecalciferol) in the skin dependent on sun exposure (specifically UVB radiation). Cholecalciferol and ergocalciferol can be ingested from the diet.
Sinteza vitaminei $D_3$ (colecalciferolului):

Formation of vitamin $D_2$ (ergocalciferol)
Vitamin D from the diet or dermal synthesis from sunlight is biologically inactive; activation requires enzymatic conversion (hydroxylation) in the liver and kidney. In the liver, cholecalciferol (vitamin D₃) is converted to calcidiol, which is also known as 25-hydroxycholecalciferol (25(OH)D₃). Part of the calcidiol is converted by the kidneys to calcitriol (1,25-dihydroxycholecalciferol), the biologically active form of vitamin D.

Calcitriol acts as a hormone, regulating the intestinal absorption of calcium and concentration of calcium and phosphate in the bloodstream, promoting the healthy growth and remodeling of bone. Calcitriol also affects neuromuscular and immune function.

As vitamin D is synthesized in adequate amounts by most mammals exposed to sunlight, it is not strictly a vitamin, and may be considered a hormone.
Terpenes, known as the isoprenoids, is a group of structurally heterogeneous chemical compounds, which are widespread in nature. Their structure is based on the structure of the isoprene:

![Isoprene structure]

Terpene fragments can be found in the composition of fat-soluble vitamins: A, E, K.
Carotenoids

- is a group of terpenes, widespread in plants as vegetal pigments (in carrot, tomato, maize, etc.). Their molecules contain a large number of conjugated double bonds and, therefore, they are colored substances. For natural carotenoids trans configuration of double bonds is characteristic. For example, β-carotene:
In the body the molecule of \(\beta\)-carotene under the action of the enzyme \textit{carotinase}, splits into two molecules of \textit{vitamin A}, which is further oxidized to trans-retinal:

\[
\text{Retinol (vitamin A)} \quad \text{Retinal}
\]

In the retina under the action of the enzyme \textit{trans-retinal isomerase} the trans-retinal turns into cis-retinal, and then binds to a protein \textit{opsin} forming a photosensitive pigment \textit{rhodopsin}, which participates in the visual process. Vitamin A is contained in fish oil, egg yolk, etc. The insufficiency of vitamin A in the body disturbs the normal growth, the mechanism of vision, and decreases body's resistance to infections.
Vitamin E (α-tocopherol)

- is a hydroquinone derivative with isoprene fragments. It is found naturally in vegetable oils. Vitamin E in the human body plays an important role, functioning as an antioxidant. Its main biological function is to enhance fertility.
Vitamin K
- represents a derivative of 1,4-naphthoquinone with the isoprene chains. Possesses an antihemoragic action and is necessary to ensure a normal blood clotting. In medicine is used its synthetic analogue – vicasol.

![Chemical structures of Vitamin K2 and Vicasol]