

Lipids

- **heterogeneous group of water-insoluble, oily or greasy substances**
- **Soluble in non-polar solvents** (e.g. benzene or ether), but **not with the polar solvents.**
- *lipids do not form polymers.*
- serve as **fuel molecules** highly concentrated energy stores
- signal molecules
- components of cell membranes, and carriers of fat soluble vitamins, e.g. A, D, E and K.
- A layer of subcutaneous fat acts as thermal **insulator** and acts as a **cushion**, which protects several delicate organs by absorbing mechanical shocks.
- Both lipids and lipid derivatives serve as vitamins and hormones

Fatty acids

- The building blocks of most lipids are fatty acids
- The **fatty acid** molecule consists of a long hydrocarbon chain with a polar carboxyl group at its end

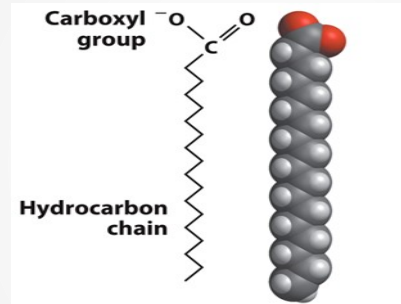


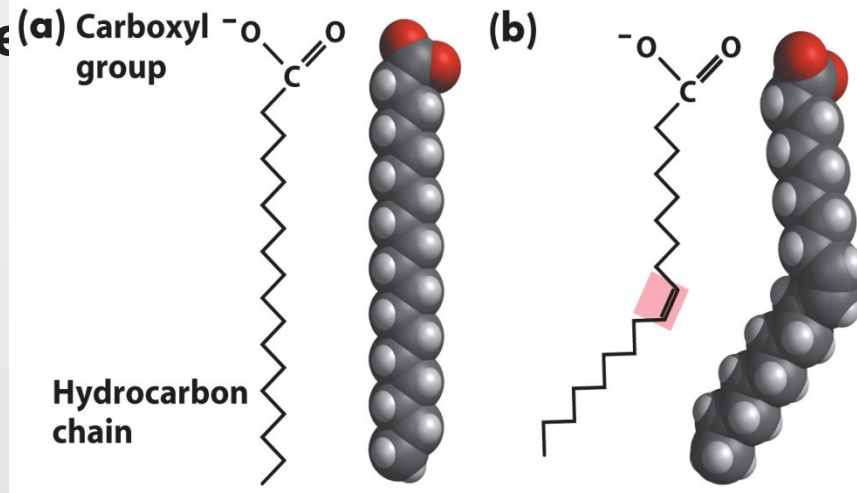
Figure 10-2a
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- fatty acid molecule contains both polar (hydrophilic) and non-polar (hydrophobic) regions; such molecules are called **amphipathic molecules**.
- the carboxylate rapidly ionizes at the physiological pH to form the carboxylate ion (COO⁻) The carboxylate ion has polar characteristics, with high affinity for water (hydrophilic).
- hydrocarbon chain accounts for predominantly non-polar

- Naturally occurring fatty acids contain even number of carbon atoms (most contain 14 to 24).
- Most abundant are the fatty acids containing 16 or 18 carbon atoms.
- There are two types of fatty acids depending on the hydrocarbon chains

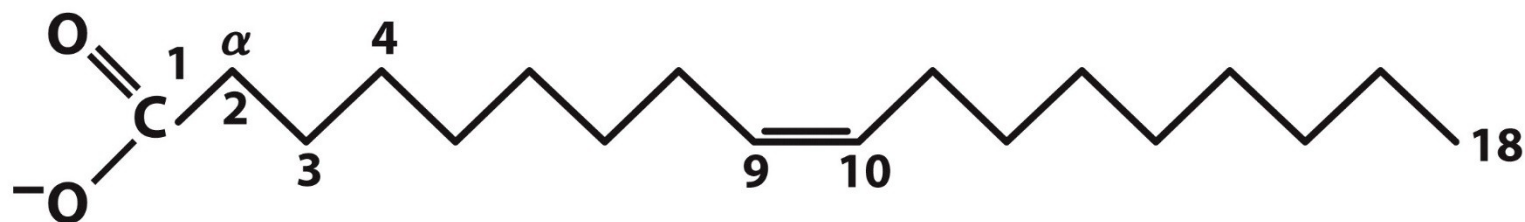
1. **Unsaturated fatty acids** - containing one or more double bonds,

2. **saturated** any double bonds

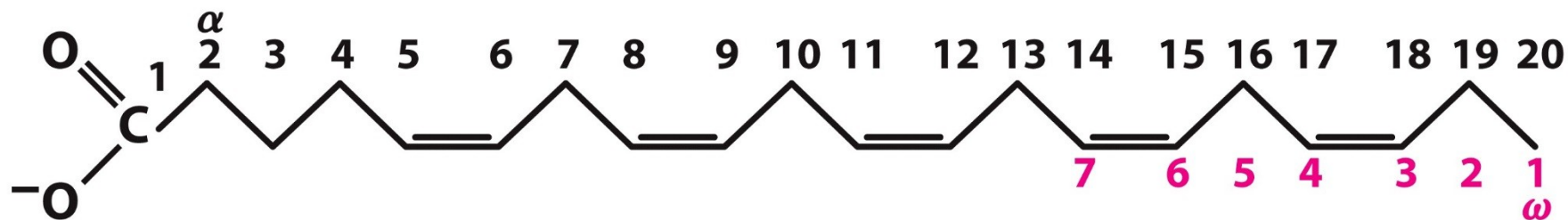


Nomenclature

- The nomenclature of fatty acids is based on the following characteristics of the hydrocarbon chain:
 1. Chain length
 2. Presence of double bonds and their positions.
- the abbreviation 18;1 indicates an 18-carbon fatty acid having a single double bond.
- Δ^h indicates position of these bonds; for example, Δ^9 indicates double bond at C-9, starting from the carboxyl end.
- An 18-C saturated fatty acid with one double bond is called octadecanoic acid: octa (8) and deca (ten) imply chain length (18 carbons). with double bonds, at C-9, and C-12, is called octadecadienoic acid and that having three double bonds, at C-9, C-12 and C-15 positions, is called octadeca-trienoic acid



(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid



**(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA),
an omega-3 fatty acid**

Figure 10-1
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Functions: Fatty acids perform following functions in the body:

- 1. Membrane lipids:** They are the components of the more complex membrane lipids.
- 2. Fuel molecules:** They are components of stored fat in the form of triacylglycerols.
- 3. Hormones:** Derivatives of fatty acids serve as hormones (such as prostaglandins) and **intracellular second messengers** (such as IP3 and DAG).
- 4.** Numerous proteins are covalently modified by fatty acids. Palmitic acid and myristic acid, for example, are directly attached to some proteins.

Properties

- **Solubility**

Fatty acids are insoluble in water and other polar solvents, and soluble in the non-polar solvents.

- **Melting Point**

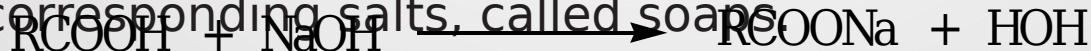
Melting point of fatty acids is dependent on two factors:

1. Level of unsaturation of hydrocarbon chain: The melting point falls as the number of double bonds increases.

- **2. Chain length** of fatty acid: Increase in chain length results in elevating the melting point. Saturated fatty acids of less than eight carbon atoms are liquid at physiological temperature, whereas those containing more than 10 are solids at this temperature

- **Soap Formation**

Fatty acids react with alkalies, such as NaOH or KOH, to produce the corresponding salts, called soaps.

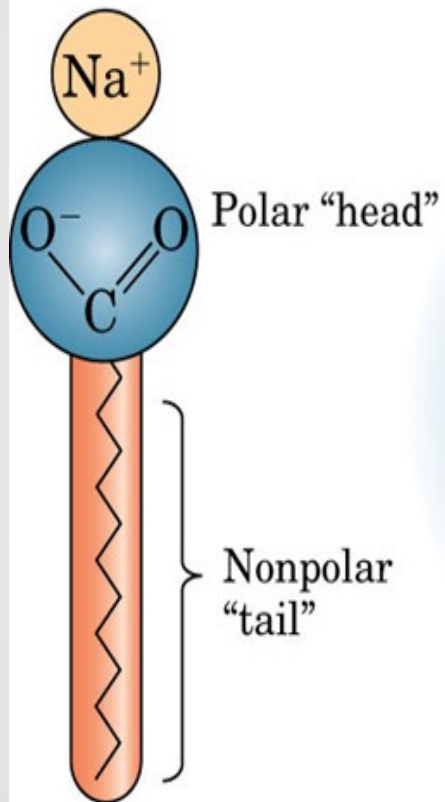


Fatty acid

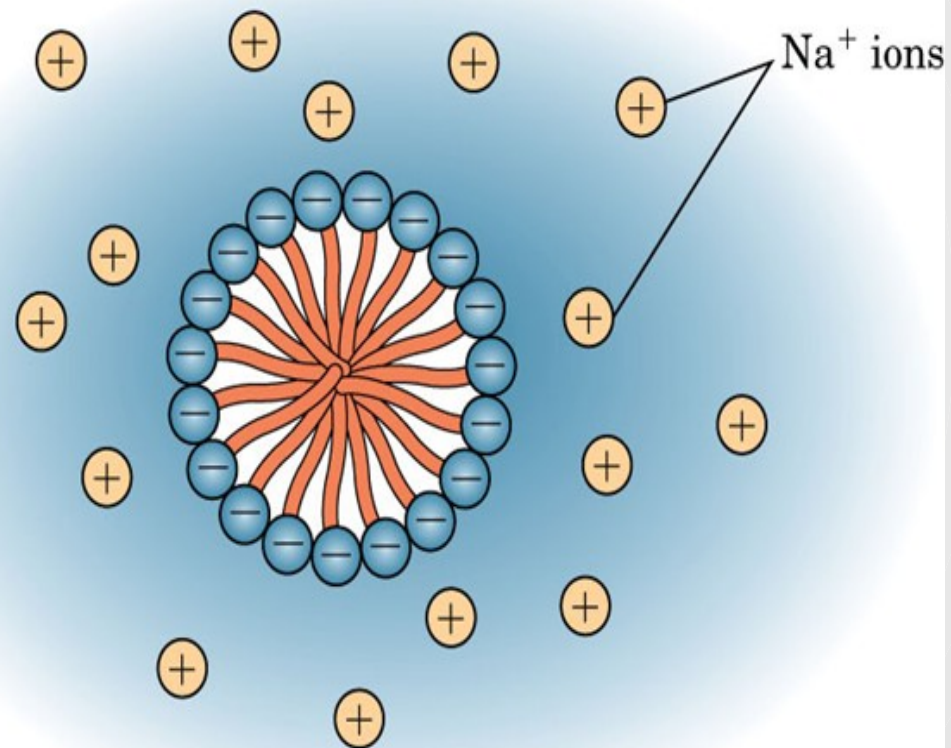
Soap

- Soaps are amphipathic molecules where the ionized carboxyl group constitutes the polar head, and the hydrocarbon tail forms the non-polar portion.
- *Because of their amphipathic nature, soaps can disperse oily or greasy substances into finer droplets; the process is called **emulsification***
- The hydrophilic polar portion of the soap molecule remains at the surface, forming a stable cover, whereas the hydrocarbon tail extends into the interior to cause the dispersion

(a) A soap



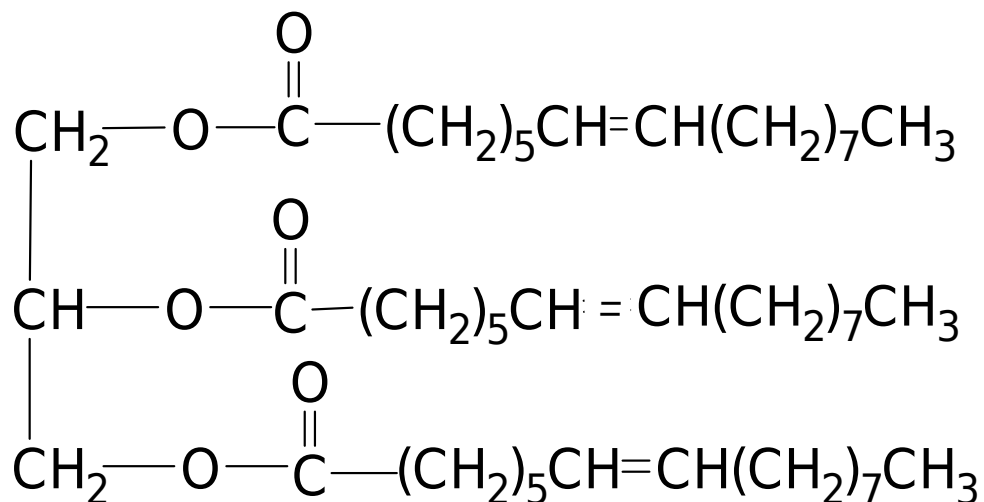
(b) Cross section of a soap micelle in water



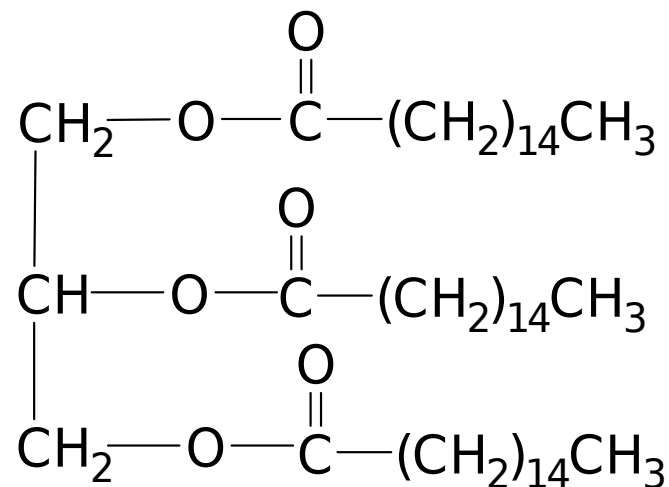
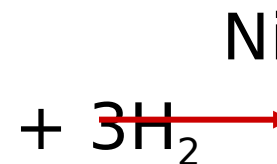
Hydrogenation

- The double bonds of unsaturated fatty acids can be hydrogenated in the presence of catalysts, e.g. nickel to yield the corresponding saturated fatty acids.

Hydrogenation



glyceryl Trioleate
(triolein)



glyceryl

Halogenation

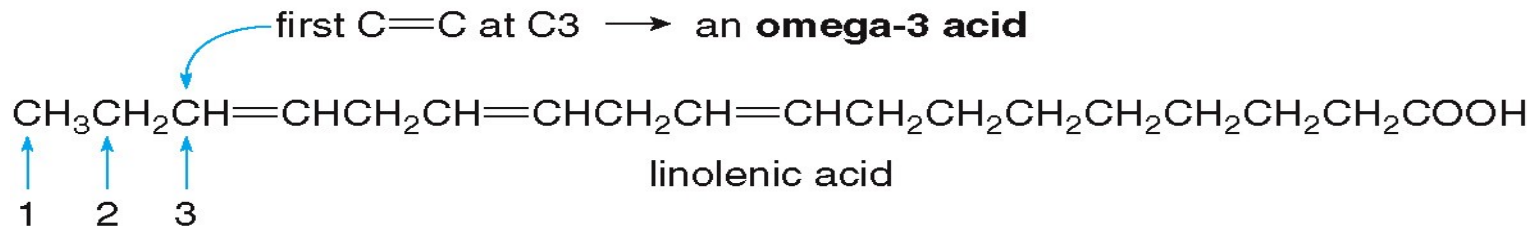
- Double bonds of unsaturated *fatty acids* are capable of adding halogens, the result of which are dihalogen fatty acids.
- This property is often used to assess the extent of unsaturation in fats and oils via reaction with iodine to obtain the so-called **iodine number** (number of gm of iodine required to saturate 100 gm of the lipid).
- The higher the iodine number, the more unsaturated the oil.

Oxidation

- Unsaturated fatty acids can spontaneously react with atmospheric oxygen to form fatty acid peroxides, fatty acids epoxides and fatty acid aldehydes.
- Fat which undergoes oxidation becomes **rancid**.
- Rancid fat is unpleasant in taste and smell and can be toxic.
- Rancidity is prevented by anti-oxidants, e.g. vitamin E.
- Degree of rancidity is measured by **acid**

Essential Fatty Acids

- fatty acids that can't be synthesized by the body and must be supplied from the diet
- e.g. **linoleic acid** and **linolenic acid**



Biomedical Importance

Essential fatty acids are important for following reasons:

1. *Membrane components*: They are components of phospholipids and form biomembranes.
2. *Structural elements*: they are present in high concentrations in the lipids associated with structural elements of tissues.

Classification of Lipids

- Lipids are classified into three groups- **simple lipids, compound lipids** and **derived lipids**
- Simple lipids are esters of fatty acids with alcohol.
- Compound lipids contain, besides fatty acids and alcohols, non-lipid polar groups like phosphate, carbohydrates, etc.
- Substances derived from the above

Simple Lipids

- The major simple lipids are the triacylglycerols and the waxes.
- They are neutral molecules they lack any polar group
- Hydrophobic and water repellent.
- They serve as major fuel reserves in the animal and the plant cells.

Triacylglycerols

- Triacylglycerols are the simplest and the most abundant lipids
- fatty acid esters of glycerol and are the major storage fats in animal cells.

Structure: A triacylglycerol molecule is an ester of three fatty acids and a trihydroxy-alcohol, called glycerol

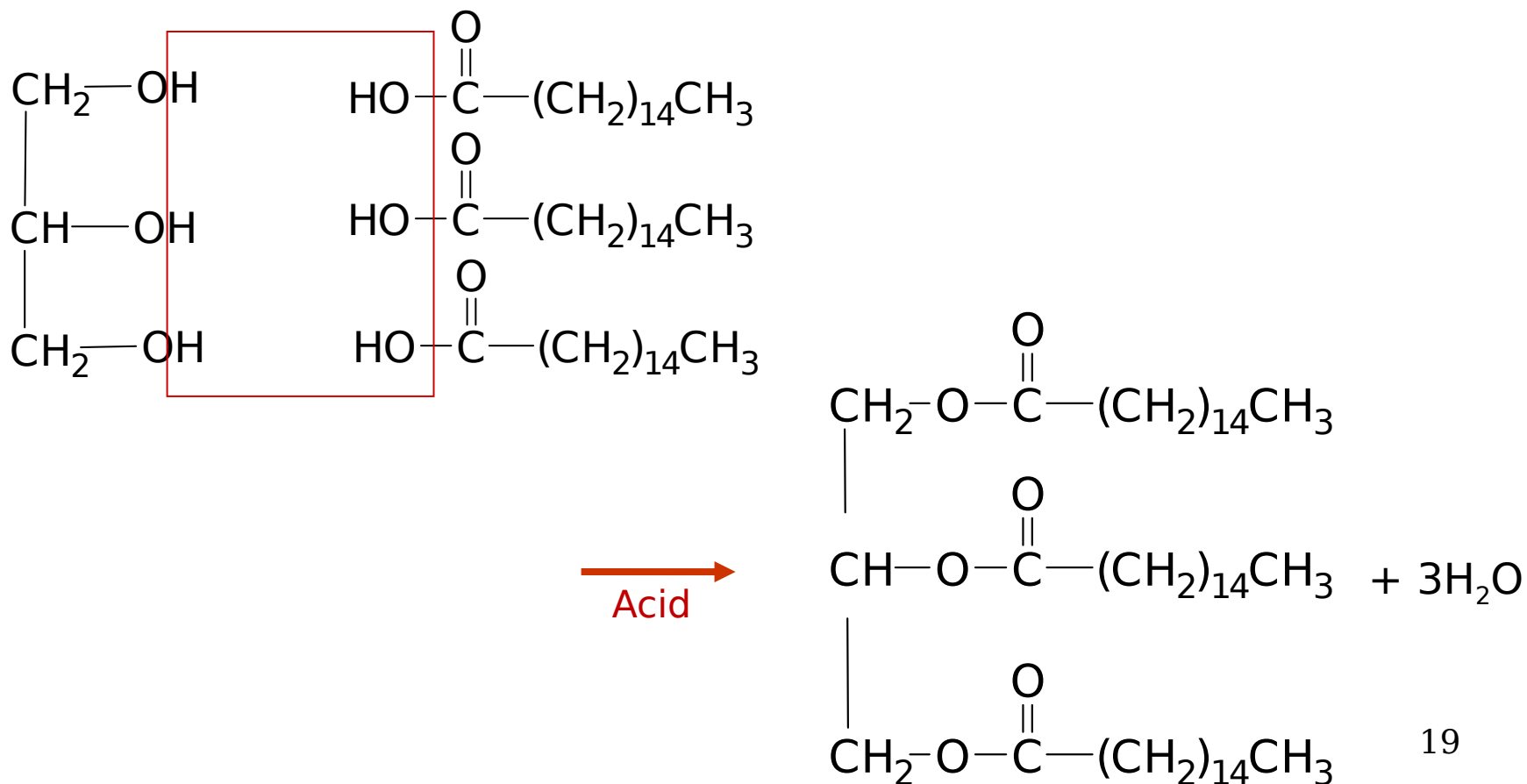
- the 2nd carbon is chiral.

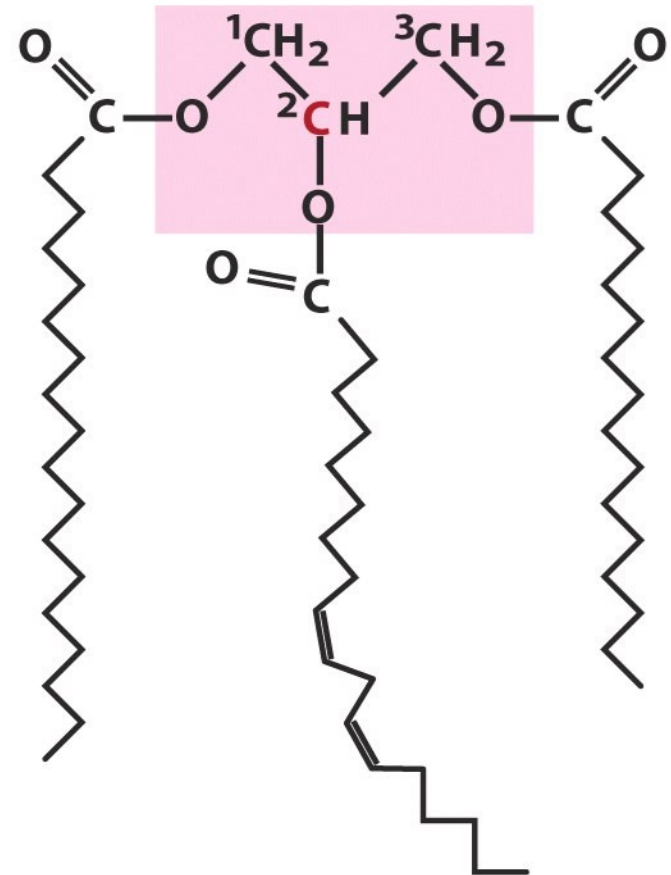
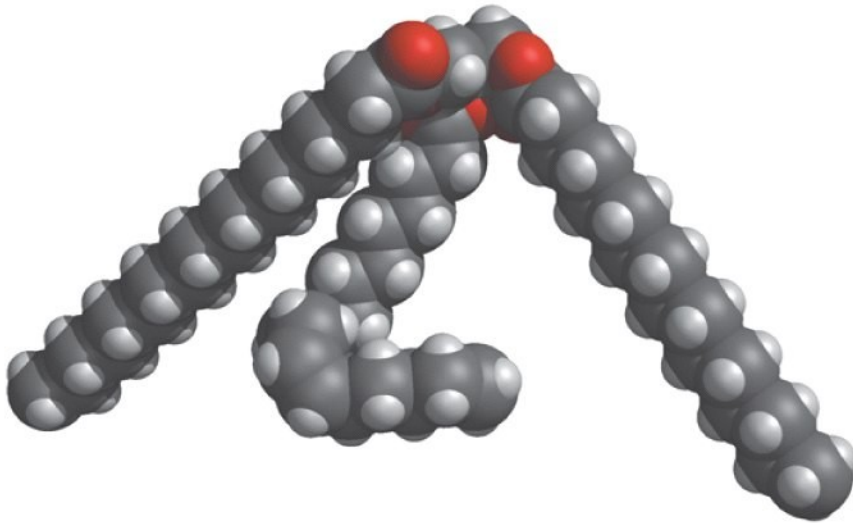
Esterification

glycerol

three fatty acids

triacylglycerol



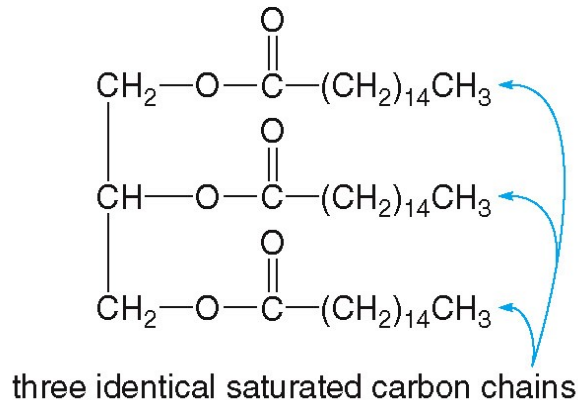


**1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol**

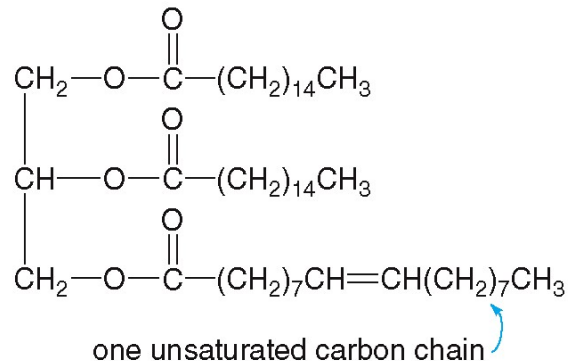
- There are two types of Triacylglycerols
 1. Simple triacylglycerols - have all three hydroxyl groups of the glycerol esterified to the same fatty acid.
 2. Mixed triacylglycerols - one of the three hydroxyls are esterified to a different fatty acid
- Oils, butter, and other food fats are complex mixtures of simple and mixed triacylglycerols containing fatty acids of varying chain lengths and

Triacylglycerols (Triglycerides)

Simple triacylglycerols have three identical fatty acid side chains.



Mixed triacylglycerols have two or three different fatty acids.



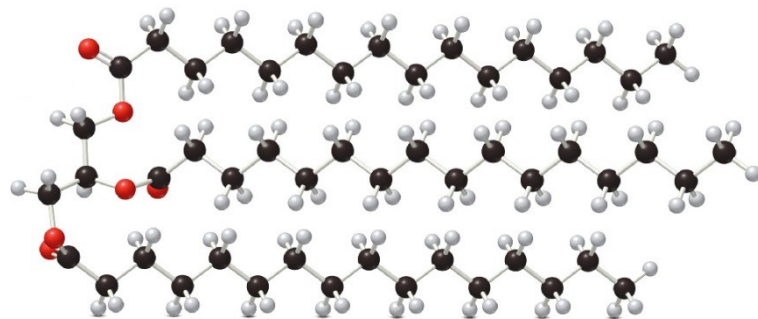
Triacylglycerols (Triglycerides)

Saturated triacylglycerols contain only saturated fatty acids.

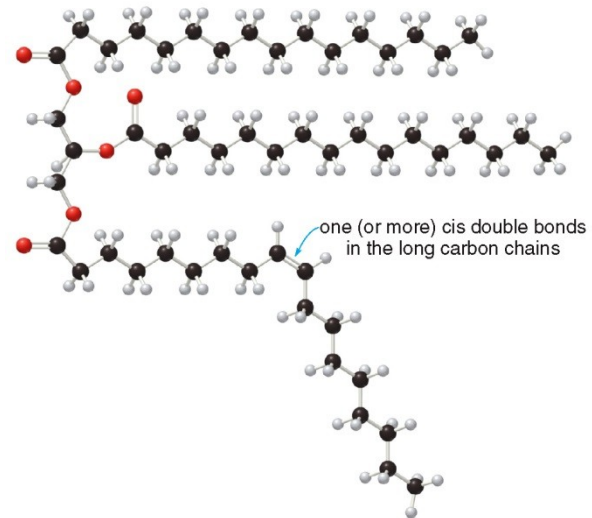
Monounsaturated triacylglycerols have 1 C=C bond.

Polyunsaturated triacylglycerols have many C=C bonds.

Increasing the number of double bonds in the fatty acid chain decreases the melting point of the triacylglycerol.



a saturated triacylglycerol



Triacylglycerols (Triglycerides)

Fat: is a triacylglycerol that is solid at room temperature.

Made by more saturated fatty acids (Saturated triacylglycerols).

Meat, milk, butter and cheese (animal sources).



Oil: is a triacylglycerol that is liquid at room temperature.

Made by more unsaturated fatty acids (Unsaturated triacylglycerol).

Corn, cotton seed, safflower and sunflower (plant sources).



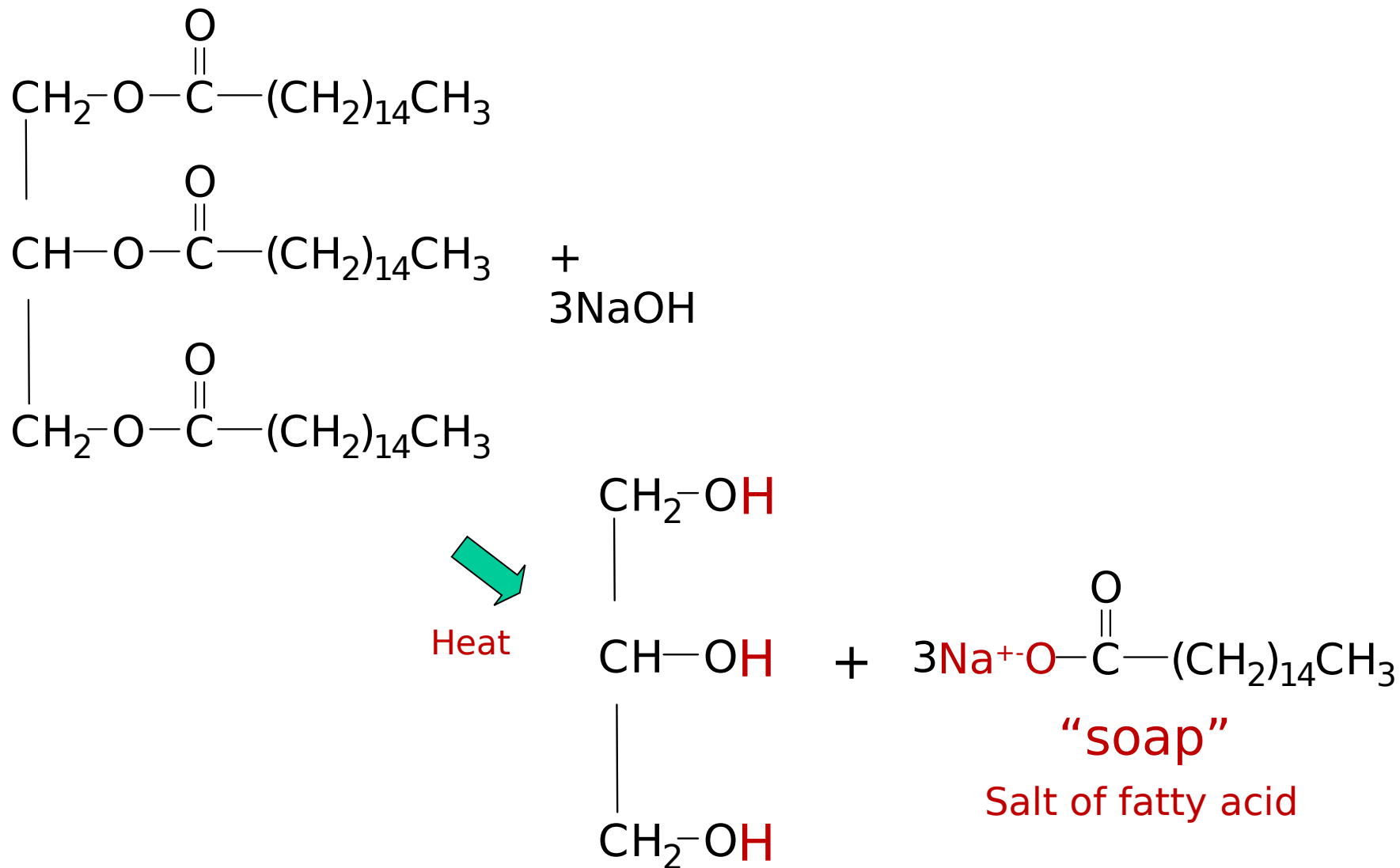
Both are colorless, odorless, and tasteless.

Properties: Properties of a triacylglycerol depend on the nature of the constituent fatty acids.

1. *Melting point:* Triacylglycerols containing only saturated fatty acids, such as tristearin and tripalmitin, are solids at physiologic temperature (37°C) since melting point of the saturated fatty acids is relatively higher. Conversely, the triacylglycerol that contain only unsaturated fatty acids, such as²⁵

- *Solubility:* triacylglycerols *insoluble in water*. However, they are *soluble in the non-polar solvents*, such as ether, benzene and chloroform.
- *Hydrolysis:* Triacylglycerols undergo hydrolysis when boiled with strong acids
- *Hydrolysis of triacylglycerols by alkalis, such as NaOH and KOH, is called **saponification*** yields a mixture of sodium or potassium salts of the fatty acids (called soaps) and glycerol
- **Saponification number:** The number of milligrams of KOH required to saponify the free and combined fatty acids in one gram of a given fat

3- Saponification

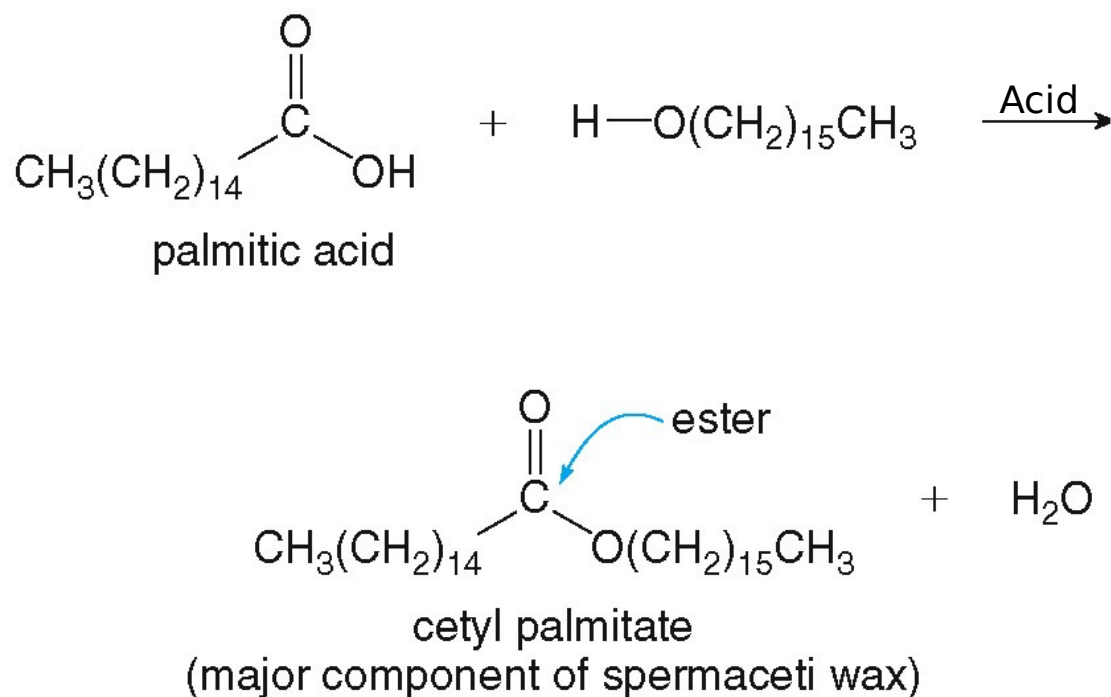


Waxes

- Waxes are esters of long chain unsaturated fatty acids, having 14–36 carbon atoms, with long chain alcohols (consisting of 16–22 carbons)

Waxes

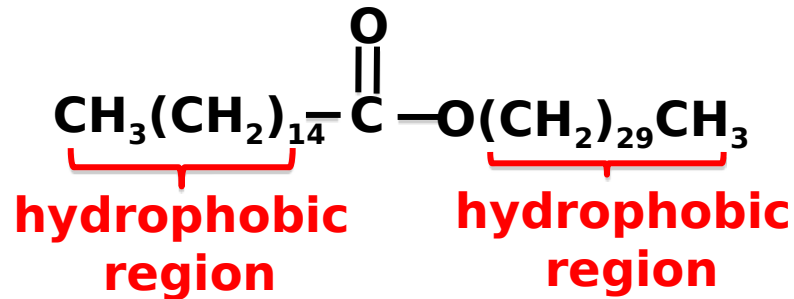
For example, shown below is the formation of **spermaceti wax**, isolated from the heads of sperm whales.



Waxes

Because of their long nonpolar C chains, waxes are very **hydrophobic**.

Beeswax
(myricyl palmitate)



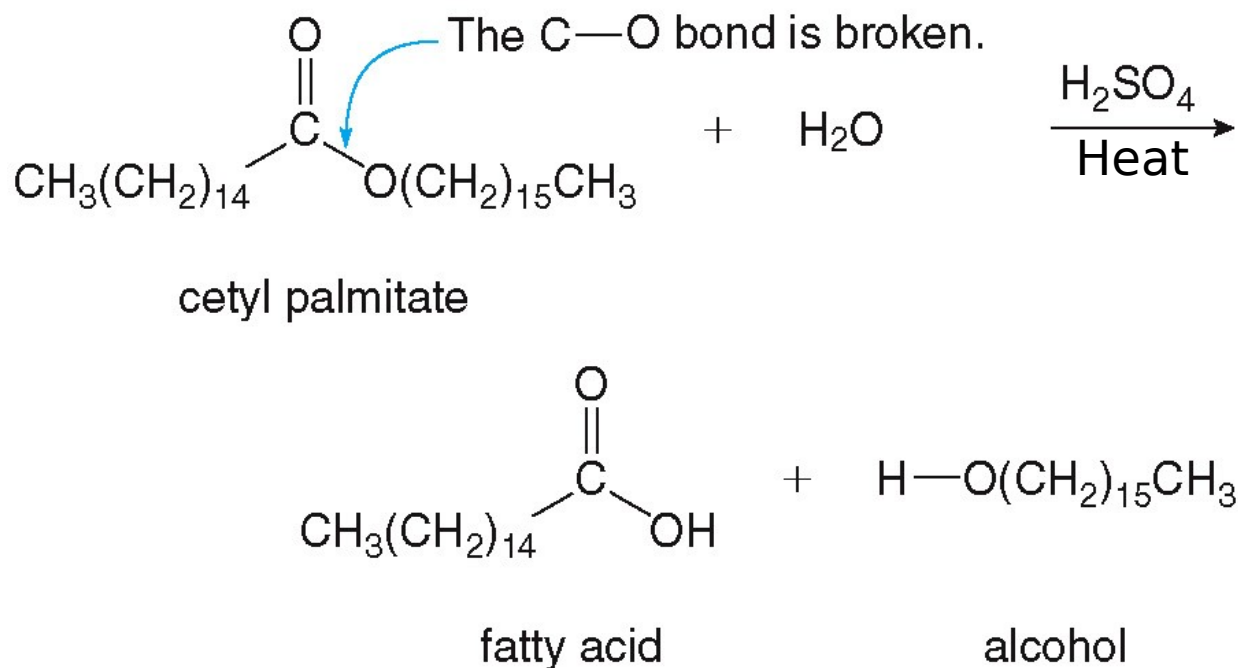
They form **protective coatings**:

- In plants, they help prevent loss of water and damage from pests.
- In humans and animals, provide waterproof coating on skin and fur.



Waxes

Hydrolysis reaction: like other esters, waxes are hydrolyzed.



Compound Lipids

- Compound lipids contain additional non-lipid portion.
- The compound lipids are amphipathic molecules.
- They can be subclassified into the following categories:
 1. **Phospholipids** which contain an additional phosphate group.
 2. **Glycolipids** which contain carbohydrate groups

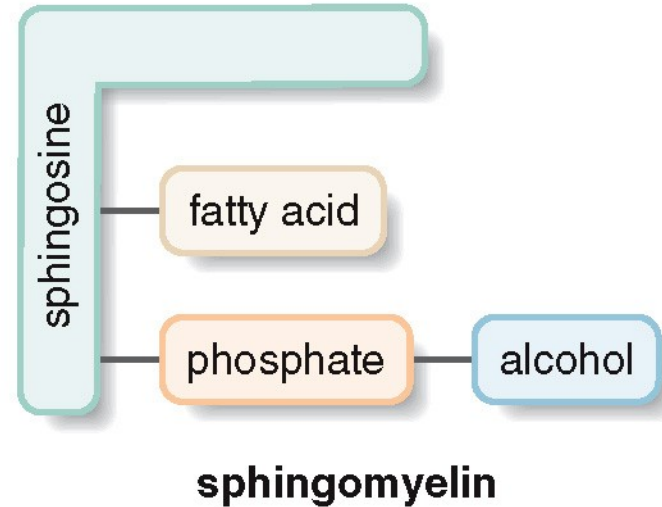
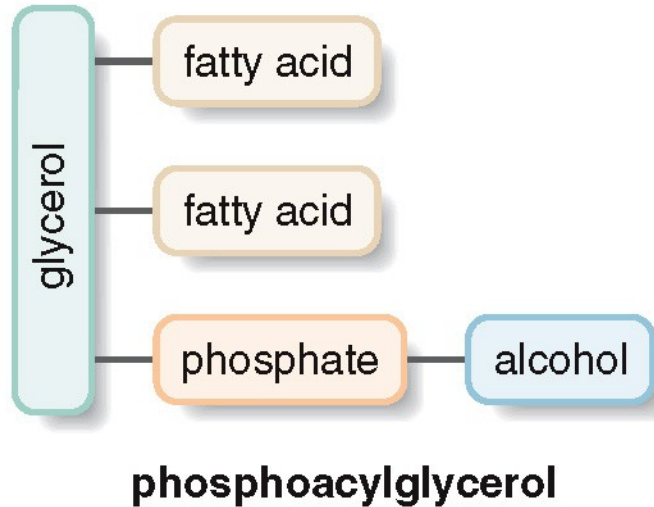
Phospholipids

- These are amphipathic molecules with non-polar aliphatic (hydrocarbon) “*tails*” and polar (phosphoryl-X) “*heads*”.
- They are major components of the biological membranes
- Phospholipids can be further subdivided into two groups: **phosphoglycerides** and **sphingomyelins** depending the type of alcohol they contain
- **Phosphoglycerides** contain **Glycerol phosphate** as an alcohol while an **amino alcohol sphingosine** is present in the

phospholipids

Phospholipids are lipids that contain a P atom.

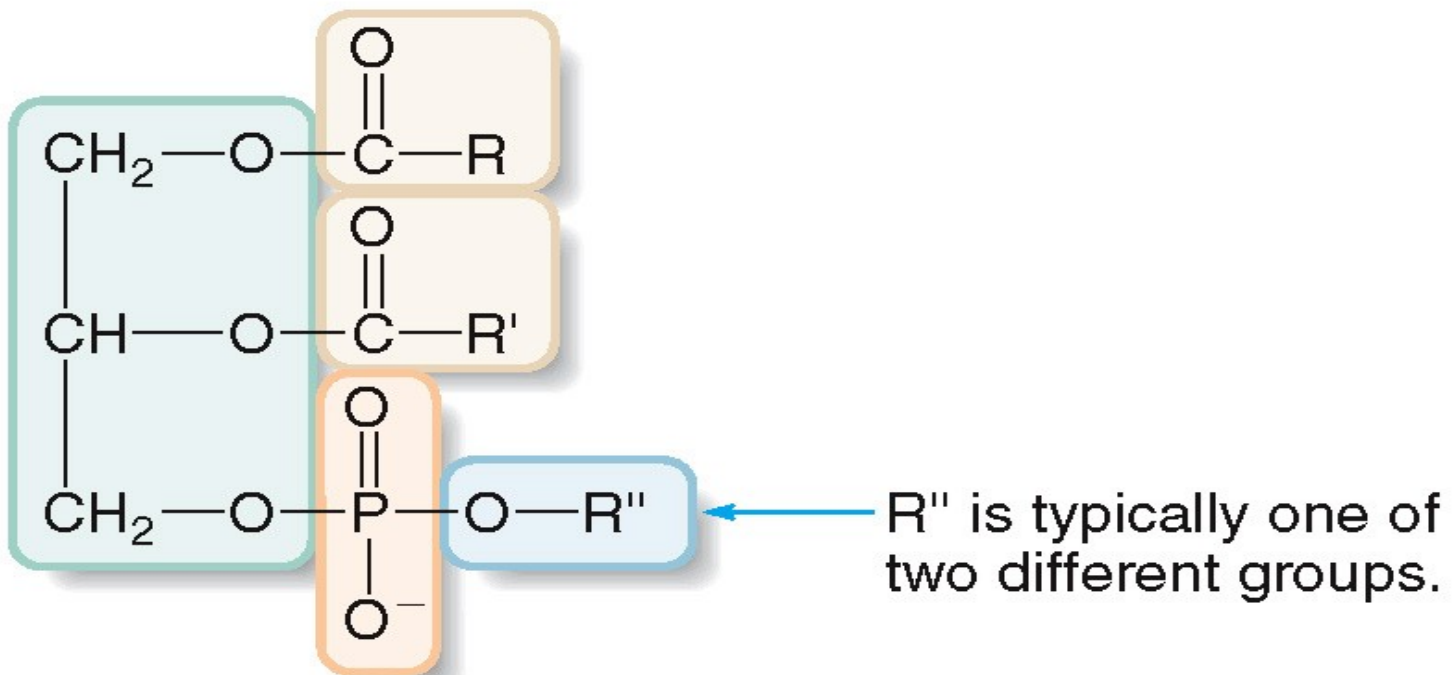
Two common types:



Phosphoglycerides

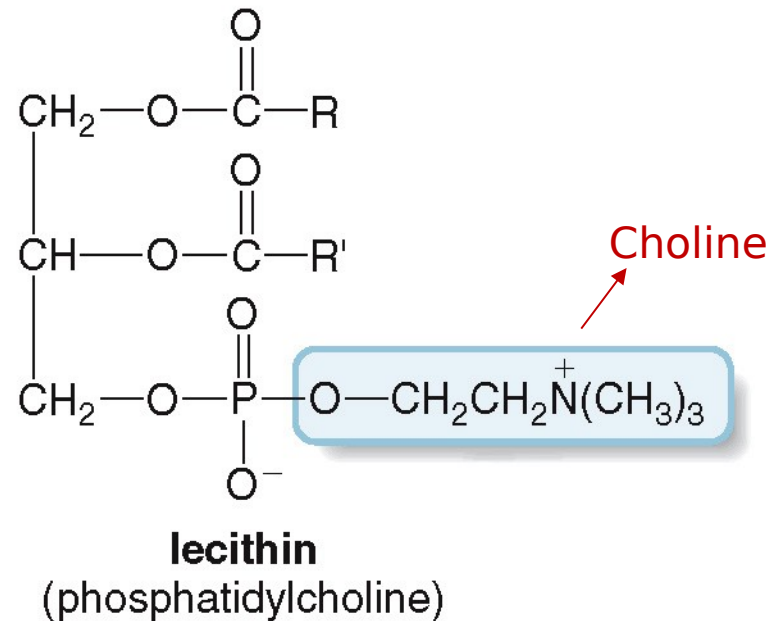
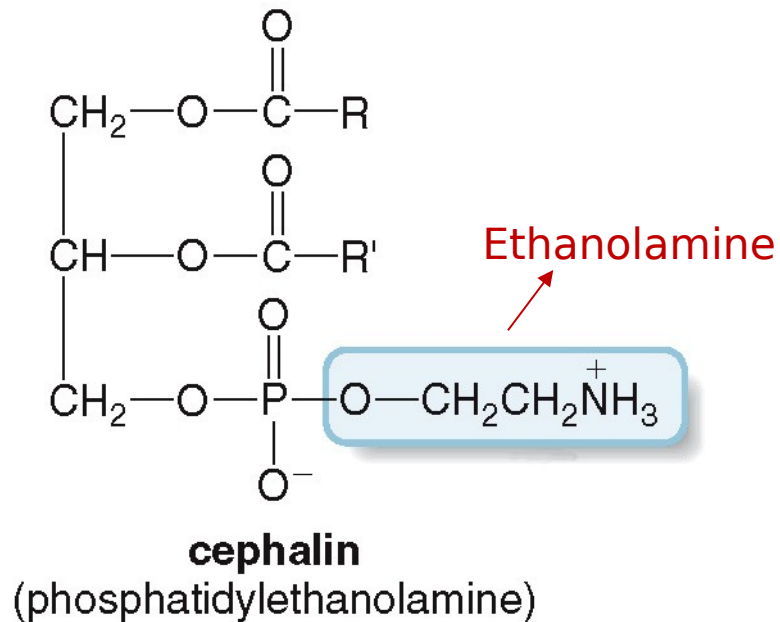
- similar to that of triacylglycerol – two fatty acids are esterified to two of the carbon atoms of glycerol except the third carbon that is esterified to phosphoric acid.
- The structure formed is **phosphatidic acid** or **phosphatide** molecule
- derived from phosphatidic acid by attachment of a polar alcohol group to the phosphate group (of phosphatidic acid) by a phosphodiester bond.
- Also known as diacylglycerol 3-phosphate

General structure



phospholipids

If the alcohol attached is ethanolamine the compound is called cephalin
Lecithin uses choline as an alcohol



Functions of phosphoglycerides

1. Membrane lipids: Phosphoglycerides are easily the most abundant membrane lipids They form *lipid bilayer structures* because of their amphipathic nature.

2. Surfactants: dipalmitoyl phosphatidylcholine (dipalmitoyl lecithin), serves a special function as the major constituent of lung surfactant.

- It is secreted by cells in the alveolar wall. It reduces surface tension by

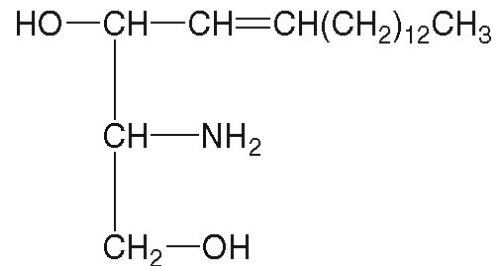
Sphingomyelins

- Contain the alcohol **sphingosine** (Greek word, “*sphingein*” means to bind tightly).
- The hydroxyl groups in sphingosine are present at carbons 1 and 3, and amino group is present at carbon 2
- A fatty acid gets attached at the amino group at C-2 to form a sphingosine derivative called **ceramide**.
- The hydroxyl groups at C-1 in ceramide carries a variable substituent (a *phosphorylbase*, e.g. phosphocholine, phosphoethanolamine). The *phosphorylbase* forms the polar head group of the³⁹ sphingomyelin.

phospholipids

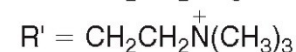
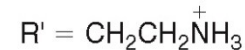
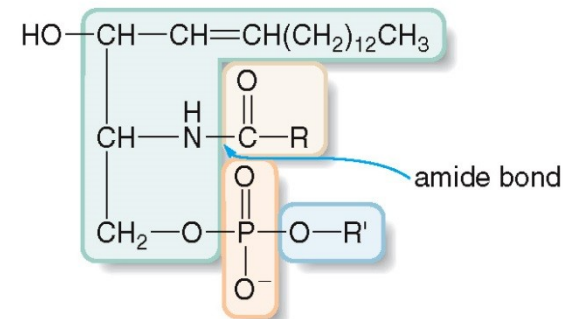
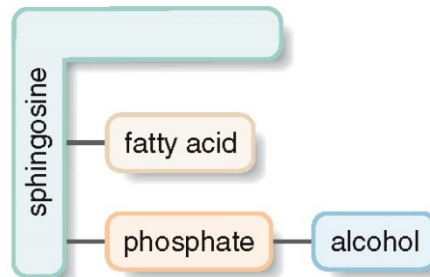
2. Sphingomyelins: They differ in two ways:

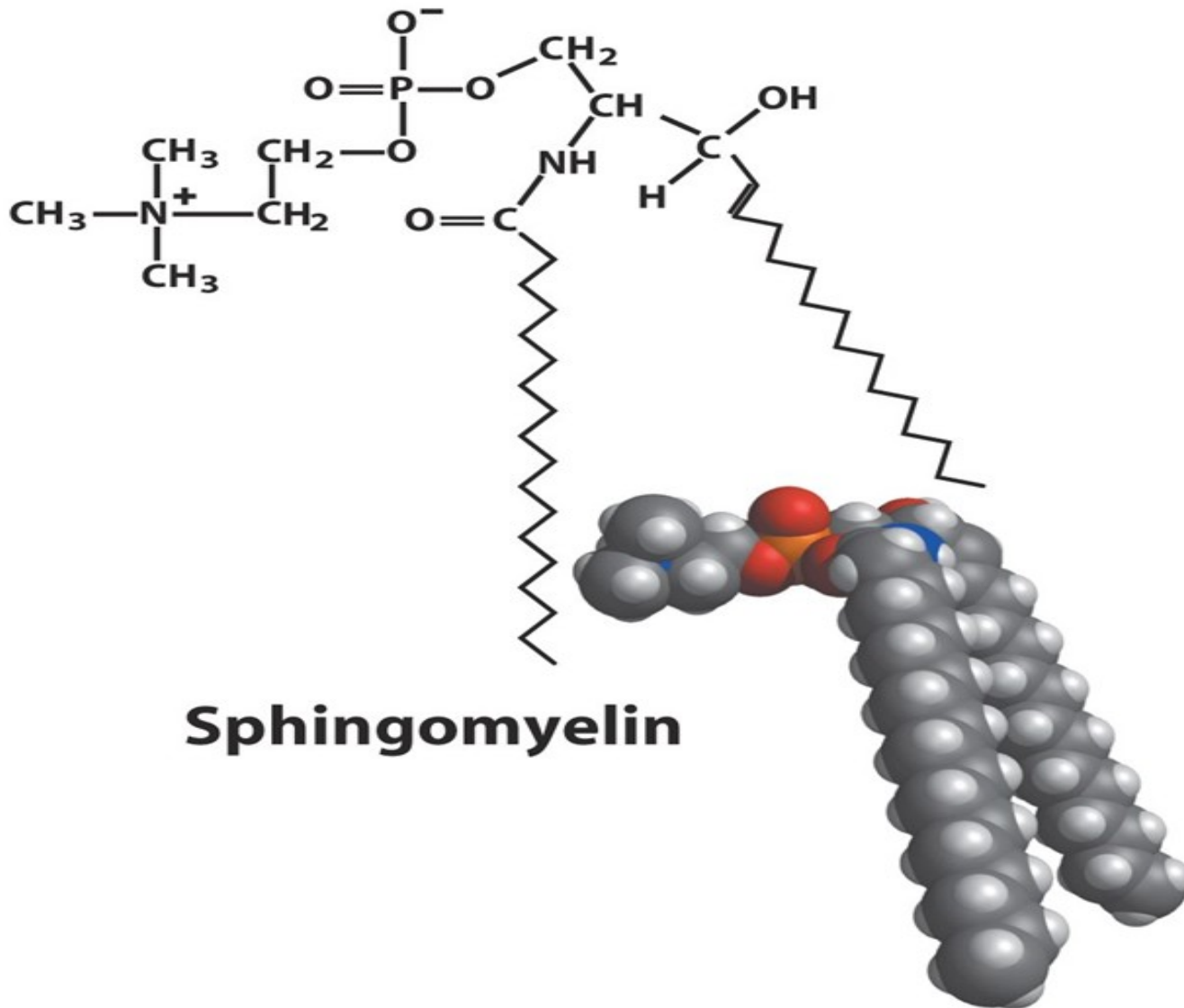
They do not contain a glycerol backbone, they have a **sphingosine backbone** instead.



sphingosine

They **do not contain an ester**; their single fatty acid is bonded to the backbone by an **amide bond**.





- sphingomyelin molecule has two hydrophobic tails. Only one of these comes from a fatty acid; the other one is the hydrocarbon tail of sphingosine itself

Glycolipids

The glycolipids are formed by attachment of a carbohydrate component (mono- or oligosaccharide) to ceramide

- commonly referred to as **glycosphingolipids** (Greek word, *glykos* means “sweet”) because of presence of sphingosine backbone.
- Depending on the nature of the carbohydrate component attached, **four types of glycolipids** are recognized: **cerebrosides, sulphatides,**

- ***Cerebrosides***: a monosaccharide is attached to ceramide.
- The monosaccharide is commonly either galactose (**galactocerebroside**) or glucose (**glucocerebroside**).
- Galactocerebroside is the most common cerebroside found in membranes.
- Glucocerebroside serves primarily as an intermediate in the synthesis and degradation of the more complex glycosphingolipids.

- ***Sulphatides:*** These are **sulphuric acid esters** of galactocerebroside, found predominantly in **nervous tissue**.
- ***Globosides:*** They contain **two or more sugars** (oligosaccharide chain) attached to ceramide.
- ***Gangliosides:*** They are similar to globosides except that they also contain **sialic acid**. They are found primarily in the ganglion cells of the central

Functions of Glycolipids

- 1.** The glycolipids are essential components of **biological membranes** (though less abundant than phosphoglycerides)
- 2.** Sphingolipids are known to play a role in **cell-cell interactions, growth, and development**. They are highly antigenic,
- 3.** The gangliosides act as **receptors**

Derived Lipids

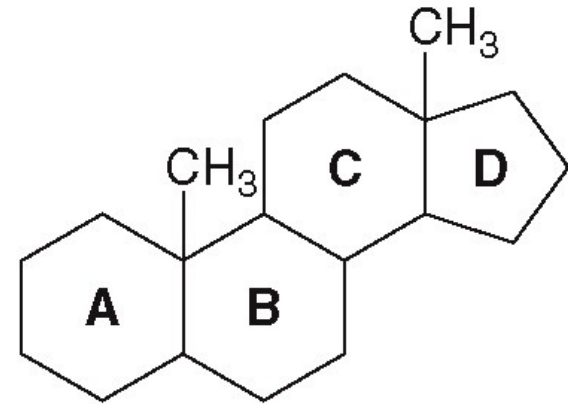
- Unsaponifiable compounds obtained by hydrolysis of simple or compound lipids
- **Steroids**
*Steroids are complex molecules consisting of **four fused carbon rings**.*
- There is a phenanthrene nucleus made of three six-membered rings (A, B and C rings) and a cyclopentane which forms D ring.
- *The alcohol derivatives of steroids, in which one or more OH groups are present in the steroid nucleus, are termed **sterols**.*
- Cholesterol, ergosterol, coprosterol and

- cholesterol is a very important molecule
being precursor for three useful compounds: the **bile acids**, the **steroid hormones**, and **vitamin D**.
- Cholesterol is an essential component of all biological membranes.
- With its ring system and a solitary

Steroids

Steroids have:

- A steroid nucleus which is 4 carbon rings.
- Attached groups that make the different types of compounds.
- No fatty acids.

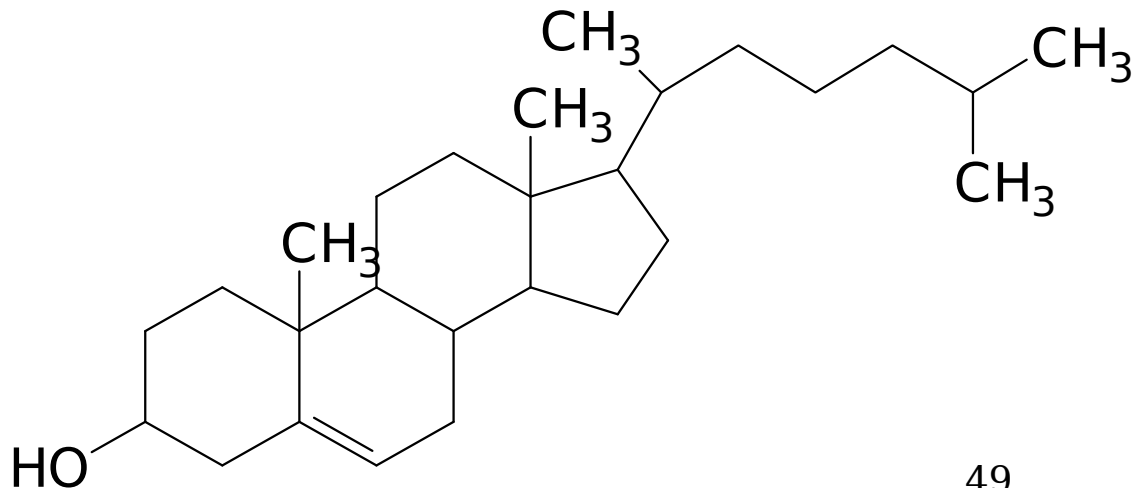


steroid skeleton
(steroid
nucleus)

Cholesterol

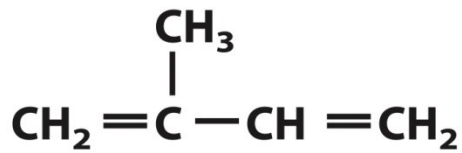
Cholesterol:

- Is the most abundant steroid in the body.
- Insoluble in water (need a water soluble carrier).
- Has methyl CH_3 - groups, alkyl chain, and -OH attached to the steroid nucleus.



Steroid Hormones

Made from Cholesterol

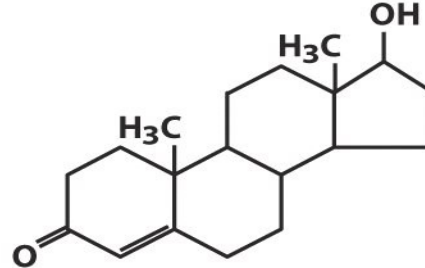


Isoprene

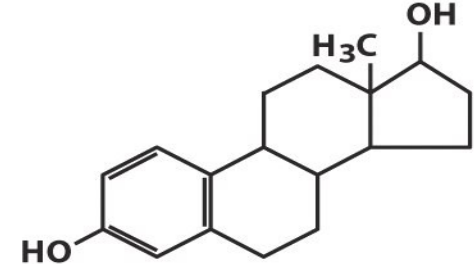
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Multistep

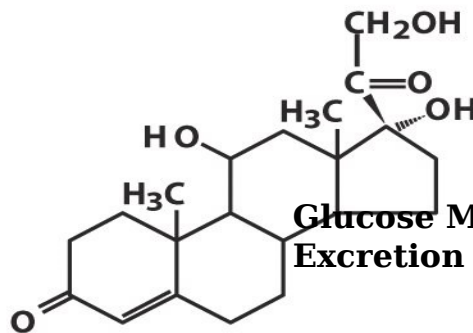
Cholesterol



Testosterone

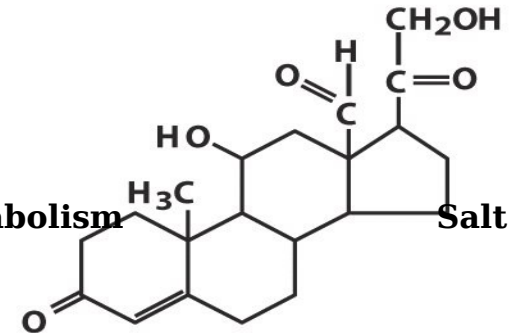


Estradiol



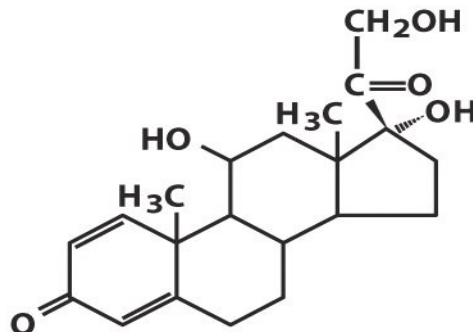
Cortisol

Glucose Metabolism
Excretion

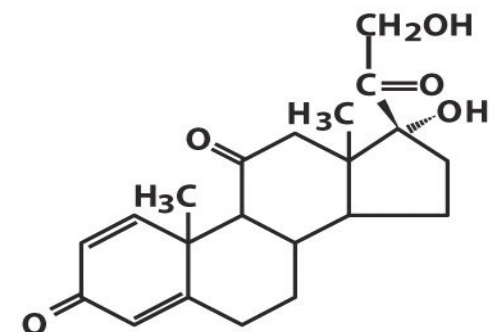


Aldosterone

Salt



Prednisolone



Prednisone

Anti-inflammatory

Lipoproteins

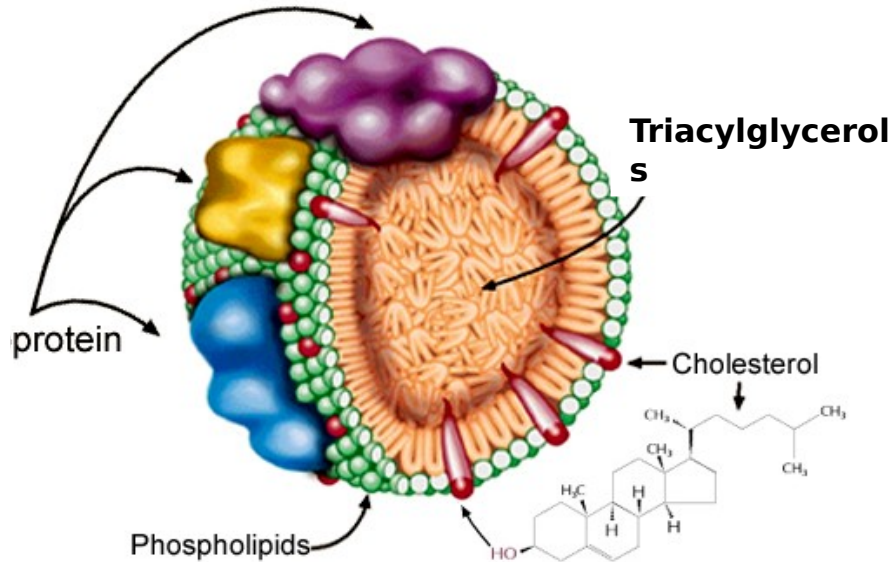
- Lipoproteins are molecular complexes consisting of lipids and proteins
- A lipoprotein particle is a spherical structure having a hydrophobic core wrapped in an amphipathic coating
- The **core** contains cholesterol esters and triacylglycerols, which, because of their non-polar nature, always avoid contact with water
- The amphipathic **coat** contains phospholipids, free cholesterol, and proteins.

- **Functions**

The lipoprotein particles have three important functions in human body.

- First, they transport the dietary fat from the intestinal mucosa, where it is absorbed, to liver by **exogenous lipid transport**
- The second role is to transfer triacylglycerols and cholesterol from liver to other tissues by **endogenous lipid transport**
- The third function is to transport cholesterol from extrahepatic tissues to the liver by **reverse cholesterol transport**

Lipoproteins



Water-soluble form of lipids
(soluble in blood)

Spherical particles

Polar surface and nonpolar inner

transporting lipids through the bloodstream to tissues where they are stored
Used for energy, or to make hormones.