

III- LIPIDS OF BIOLOGICAL IMPORTANCE

ILOs:

By the end of the course, students should be able to:

- 1. Define and identify the major classes of lipids in the human body and in our diet.*
- 2. Classify the fatty acids and recognize their general structure and importance in the body.*
- 3. List the types and functions of eicosanoids.*
- 4. Define simple lipids and classify them into two main subgroups.*
- 5. Recognize the components and properties of triacylglycerol.*
- 6. Illustrate the basic structure of the different classes of conjugated lipids and recognize their importance.*
- 7. Identify the types and function of sterols.*
- 8. Identify the types of steroid hormones.*
- 9. Recognize carotenoids and their functions.*

CONTENTS:

- I. Definition, importance and classification of lipids*
- II. Fatty Acids:*
 - Nomenclature, classifications and examples
 - Physical and chemical properties of fatty acids
- III. Eicosanoids*
 - Properties, classification and functions of eicosanoids
- IV. Simple Lipids:*
 - Classification and properties of neutral fats and waxes
- V. Compound Lipids:*
 - Types and importance of phospholipids
 - Types and importance of glycolipids
- VI. Derived Lipids*
 - Classification and importance of steroids (sterols, bile acids and steroid hormones)
 - Types and importance of carotenoids

LIPIDS OF BIOLOGICAL IMPORTANCE

Definition:

Lipids are organic compounds, which have the following common properties:

- 1- They are esters of fatty acids or substances associated with them in nature.
- 2- Most of them are insoluble in water but soluble in fat solvents (nonpolar solvents) e.g. benzene, chloroform, acetone and ether.

Biomedical Importance:

Lipids are important dietary constituents because of

- Their high energy value (9 kcal /gm).
- The fat-soluble vitamins and the essential fatty acids contained in the fat of natural foods.
- Lipids are found primarily in three compartments in the body: plasma, adipose tissue and biological membranes.

Classification:

Lipids are classified into three main groups:

I. Simple lipids: Esters of **fatty acids with various alcohols** which have two subtypes.

a. Neutral fats: Esters of three fatty acids with glycerol.

b. Waxes: Esters of **fatty acids** with **higher** molecular weight **monohydric alcohols**.

II. Compound lipids: In addition to esters of fatty acids with alcohol, they contain other groups. They include:

a. Phospholipids: Lipids containing **phosphate** in addition to fatty acids and alcohol.

b. Glycolipids (glycosphingolipids): containing a fatty acid, sphingosine, and **carbohydrate**.

III. Derived lipids: They are produced by hydrolysis of the first two groups or they are present in association with them in nature.

Fatty Acids

Fatty acids occur mainly as esters in natural fats and oils, but also occur in the unesterified form as free fatty acids in the plasma. Fatty acids that occur in natural fats are usually monocarboxylic acids containing an even number of carbon atoms. The chain may be saturated (containing no double bonds) or unsaturated (containing one or more double bonds).

Nomenclature

Carbon atoms are numbered from the carboxyl carbon (carbon No. 1). The carbon atoms adjacent to the carboxyl carbon are numbered as 2, 3...etc and are also known as α , β ...etc, carbons respectively.

The terminal methyl group is known as the ω carbon which is used to indicate the site of a double bond. For example: $\omega 9$ indicates a double bond on the ninth carbon counting from the terminal methyl group.

Examples:



The position of the double bonds is also shown by the Greek letter Δ (delta) e.g. Δ^9 indicates a double bond between carbons 9 and 10 as in palmitoleic acid (counted from the terminal carboxylic group).

A- Classification of Fatty acids According to The Presence of Double Bonds:

I- Saturated Fatty Acids (SFA):

They contain no double bonds and further classified according to the length of the chain into: **short chain** (from C_2 to C_6), **medium chain** (from C_8 to C_{10}), **long chain** (from C_{12} to C_{22}) and **very long chain** ($\geq C_{24}$). All have the following general formula:

$\text{CH}_3\text{-}(\text{CH}_2)_n\text{-} \text{COOH}$ ($n = \text{Total number of carbons} - 2$), for example:

Chain length	Name	C_{No}	Chemical formula
Short	- Acetic acid	C_2	$\text{CH}_3\text{-COOH}$
	- Butyric acid	C_4	$\text{CH}_3\text{-(CH}_2)_2\text{-COOH}$
	- <i>Caproic acid</i>	C_6	$\text{CH}_3\text{-(CH}_2)_4\text{-COOH}$
Medium	- Capric acid	C_{10}	$\text{CH}_3\text{-(CH}_2)_8\text{-COOH}$
Long	- Palmitic acid	C_{16}	$\text{CH}_3\text{-(CH}_2)_{14}\text{-COOH}$
	- Stearic acid	C_{18}	$\text{CH}_3\text{-(CH}_2)_{16}\text{-COOH}$
	- <i>Arachidic acid</i>	C_{20}	$\text{CH}_3\text{-(CH}_2)_{18}\text{-COOH}$
Very long	- Lignoceric acid	C_{24}	$\text{CH}_3\text{-(CH}_2)_{22}\text{-COOH}$

The most important saturated fatty acids include:

- Palmitic and stearic acids which are widely distributed in animal fats.
- Palmitic acid is the commonest fatty acid in human tissues.

Sources:

Examples of foods containing a high proportion of saturated fat include animal fat products such as cream, cheese, butter, other whole milk dairy products and fatty meats. Certain vegetable products have high saturated fat content, such as coconut oil and palm oil.

Biomedical importance

Increased intake of saturated fatty acids may lead to increase in plasma cholesterol levels and incidence of coronary heart disease.

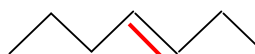
II- Unsaturated Fatty Acids (USFA):

They contain one or more double bonds. Most of the double bonds present in USFA are of the cis type and they are liquid at room temperature. USFA containing trans-double bonds are solid at room temperature.

In case of polyunsaturated fatty acids (PUFA), each two double bonds are separated by a methylene group (CH₂) as follows: **-CH=CH-CH₂-CH=CH-CH₂-**



Cis double bond of PUFA



Trans double bond

A- Trans Fatty acids:

Trans fatty acids are formed mainly during the hydrogenation of liquid vegetable oils (during the manufacture of margarine).

Sources:

Very small amounts of trans-unsaturated fatty acids are found in butter but the main source in the human diet is from **partially hydrogenated vegetable oils (eg, margarine)**. They are present in many commercial baked foods as cakes and cookies, frozen pizza and most fried foods.

Biomedical importance:

Trans fatty acids compete with essential fatty acids and may exacerbate essential **fatty acid deficiency**. Moreover, they are structurally similar to saturated fatty acids and have comparable effects in the promotion of **hypercholesterolemia** and **atherosclerosis**.

B- Cis Fatty acids:

They are classified according to the number of double bonds in their chains into two main groups:

1- Monoenoic acids: contain one double bond.

2- Polyenoic acids: they have more than one double bond in their structure, termed polyunsaturated fatty acids (PUFA). They include two important families which are $\omega 3$ & $\omega 6$ PUFA. **The most important examples of unsaturated fatty acids include:**

1-Monoenoic acids	$\text{CH}_3 (\text{CH}_2)_n \text{CH}=\text{CH} (\text{CH}_2)_x \text{COOH}$
- Palmitoleic acid ($\omega 7,16:1$)	$\text{CH}_3 (\text{CH}_2)_5 \text{CH}=\text{CH} (\text{CH}_2)_7 \text{COOH}$
- Oleic acid ($\omega 9,18:1$)	$\text{CH}_3 (\text{CH}_2)_7 \text{CH}=\text{CH} (\text{CH}_2)_7 \text{COOH}$
- Nervonic acid ($\omega 9,24:1$)	$\text{CH}_3 (\text{CH}_2)_7 \text{CH}=\text{CH} (\text{CH}_2)_{13} \text{COOH}$

2-Polyenoic acids	
A- ω3 PUFA:	$\text{CH}_3.\text{CH}_2.(\text{CH}=\text{CH}.\text{CH}_2)_x.(\text{CH}_2)_y.\text{COOH}$
- α-Linolenic acid (ω3,18:3)	$\text{CH}_3.\text{CH}_2.(\text{CH}=\text{CH}.\text{CH}_2)_3.(\text{CH}_2)_6.\text{COOH}$
- Timnodonic acid (ω3,20:5)	$\text{CH}_3.\text{CH}_2.(\text{CH}=\text{CH}.\text{CH}_2)_5.(\text{CH}_2)_2.\text{COOH}$
B- ω6 PUFA:	$\text{CH}_3.(\text{CH}_2)_n.(\text{CH}=\text{CH}.\text{CH}_2)_x.(\text{CH}_2)_y.\text{COOH}$
- Linoleic acid (ω6, 18:2)	$\text{CH}_3.(\text{CH}_2)_4.(\text{CH}=\text{CH}.\text{CH}_2)_2.(\text{CH}_2)_6.\text{COOH}$
- Arachidonic acid (ω6, 20:4)	$\text{CH}_3.(\text{CH}_2)_4.(\text{CH}=\text{CH}.\text{CH}_2)_4.(\text{CH}_2)_2.\text{COOH}$

Importance of PUFA

- 1- They are important for synthesis of **phospholipids**.
- 2- Formation of **eicosanoids** such as prostaglandins, prostacyclins, thromboxanes, leukotrienes and lipoxins.

Comparison between different types of unsaturated fatty acids:

	Monoenoic acids	Polyenoic acids	
		ω6PUFAs	ω3 PUFAs
Sources	are present in all animal and vegetable oils. Olive oil is a particular rich source.	are present in nuts, olives, various oils as sunflower, cottonseed and corn oil.	are present in plant oils as flaxseed and canola and in fish oil.
		Linoleic acid (18:2) is the precursor of ω6 family	α-Linolenic acid (18:3) is the precursor of ω3 family
Biomedical importance	Intake has beneficial health effects as: -Decreased plasma cholesterol	Intake of ω6 PUFAs may lead to: -decreased plasma cholesterol	Intake of ω3 PUFAs may reduce the incidence of cardiovascular disease as they: -lower the blood pressure, -lower plasma triacylglycerol levels -decrease the tendency to thrombosis

B- Nutritional Classification of Fatty Acids:

a)- Essential Fatty Acids: They are not synthesized in our body, so it is essential to take them in diet. They include α linolenic and linoleic acids.

Arachidonic acid is synthesized in our bodies from linoleic but in its absence, arachidonic acid might be considered as an essential fatty acid.

Deficiency of essential fatty acids produces: Dermatitis in infants, fatty liver, growth retardation as well as defective sperms, brain and retina.

b)- Non Essential Fatty Acids: They include all other fatty acids because they are formed in our body in good amounts mainly from carbohydrates. It is not essential to take them in diet.

Physical Properties of Fatty Acids

1. Solubility in water:

- Fatty acids containing up to six carbons are completely soluble in water.
- Longer chain fatty acids are insoluble in water but soluble in fat solvents.

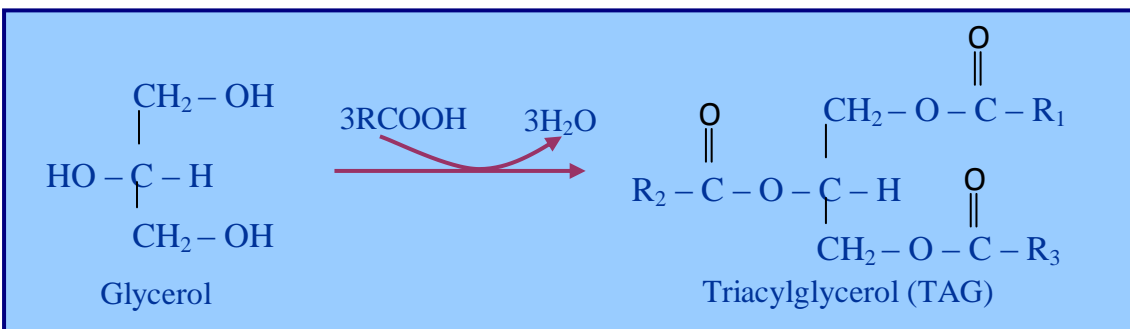
2. Physical state at room temperature:

- The lower members of saturated fatty acids are liquid at room temperature and volatile.
- They have irritant odor and bad taste.
- Those higher than ten carbons are solids.
- Unsaturated long chain fatty acids are liquids due to the presence of cis double bonds.

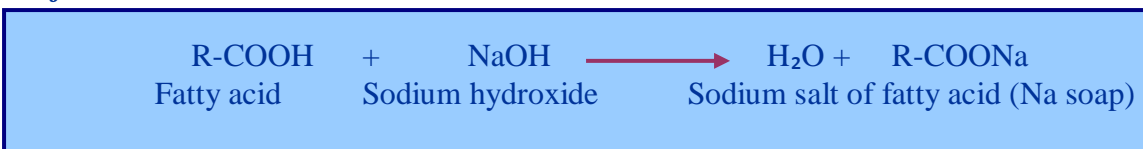
Chemical Reactions of Fatty Acids

I- Reactions due to carboxylic group:

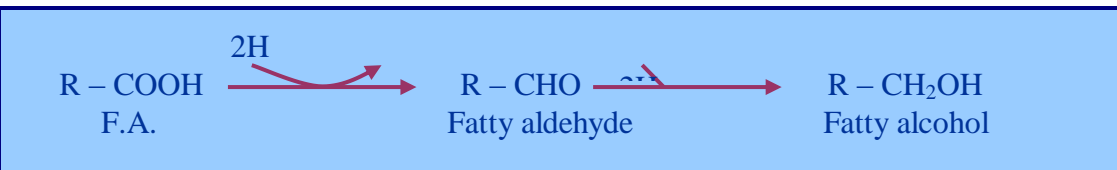
1. Ester formation:



2. Salt formation:

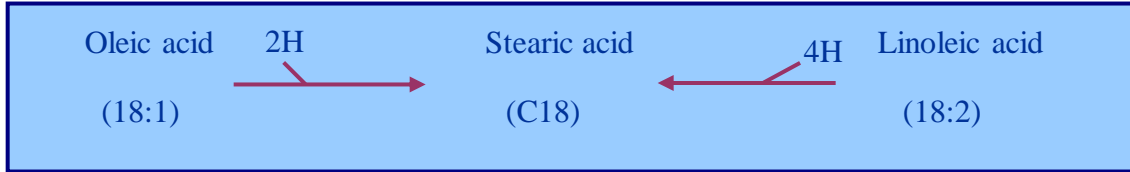


3- Reduction:

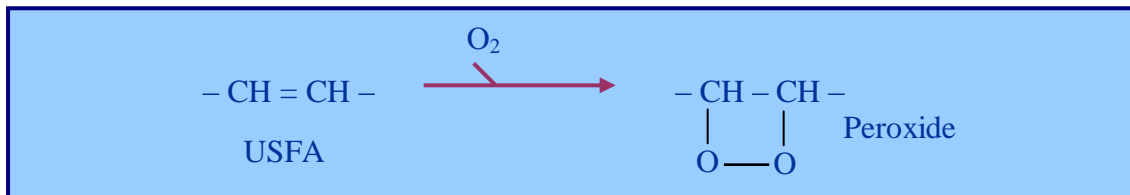


II- Reactions due to presence of double bonds (USFA) :

1- Addition of hydrogen: Each double bond reacts with two hydrogen atoms to give the corresponding saturated fatty acid as follows:



2- Addition of oxygen: The presence of double bond makes fatty acids sensitive to oxidation. Double bonds react with oxygen to form the corresponding peroxides as follows:



Peroxide has a bad taste. Further oxidation produces splitting of the fatty acid chain and results in formation of lower chain aldehydes and acids. Therefore, oxidation of USFA by hydrogen peroxide produces destruction of lipoproteins of plasma and cell membranes (lipid peroxidation).

Eicosanoids

They are characterized by the following common properties:

- 1) They are synthesized from PUFA with 20 carbon atoms mainly arachidonic acid.
- 2) They have 20 carbon atoms.
- 3) They are produced by most mammalian tissues.
- 4) They have physiological and pharmacological actions.
- 5) They are hormone- like molecules. They are autocrine and paracrine regulators.
- 6) The subscript number in an eicosanoid name indicates the number of double bonds in the molecule e.g. PGE₁, PGE₂ and PGE₃ contain one, two and three double bonds respectively.

Classification:

They are classified into 2 main groups:

A- Cyclic compounds (prostanoids):

- 1- Prostaglandins (PG)
- 2- Prostacyclins (PGI)
- 3- Thromboxanes (TX)

B- Acyclic compounds:

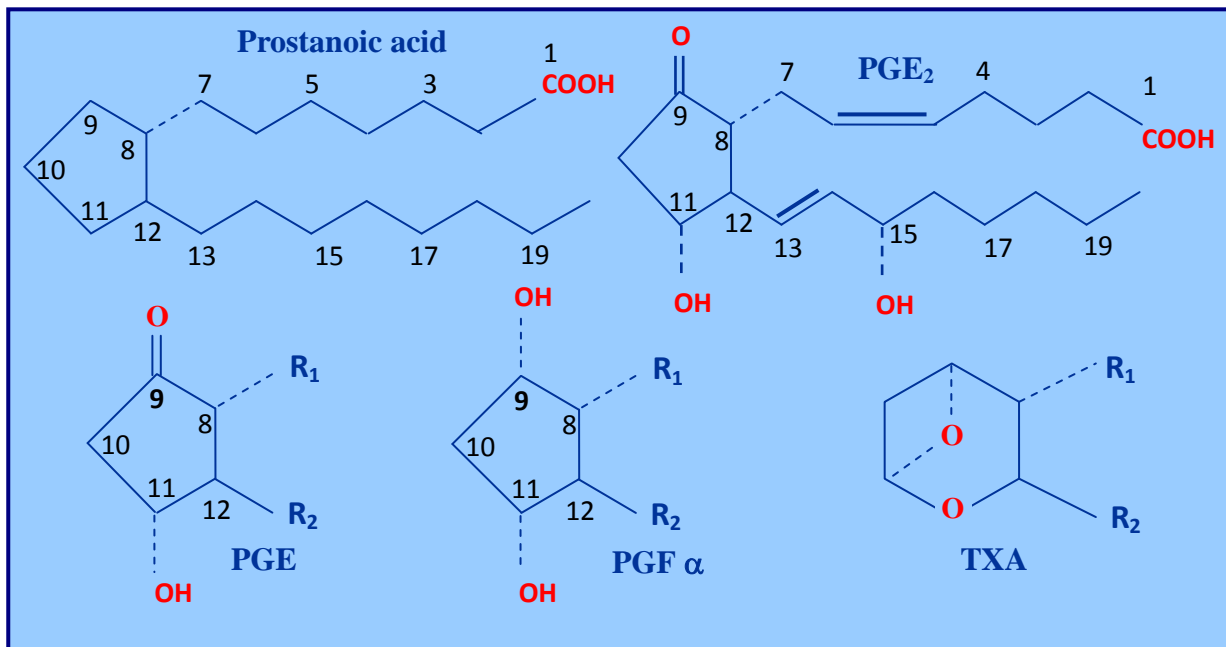
- 1- Leukotrienes (LT)
- 2- Lipoxins (LX)

1. Prostaglandins:

- They are derivatives of the C₂₀ hypothetical compound termed prostanoic acid.
 - They were first discovered in the secretion of prostatic gland hence, the name prostaglandins. However, **they are discovered in most human tissues both in males and females.**
 - All prostaglandins have a cyclopentane ring in the middle of the molecule (from C₈-C₁₂).
 - **There are many types of prostaglandins e.g.: PGA, PGB, PGE, PGF, PGG & PGH.**
- In human tissues the most important members are:**

1-PGE: They are ether soluble and contain a ketone group at C₉.

2-PGF: They are soluble in phosphate buffer and contain a hydroxyl group at C₉.

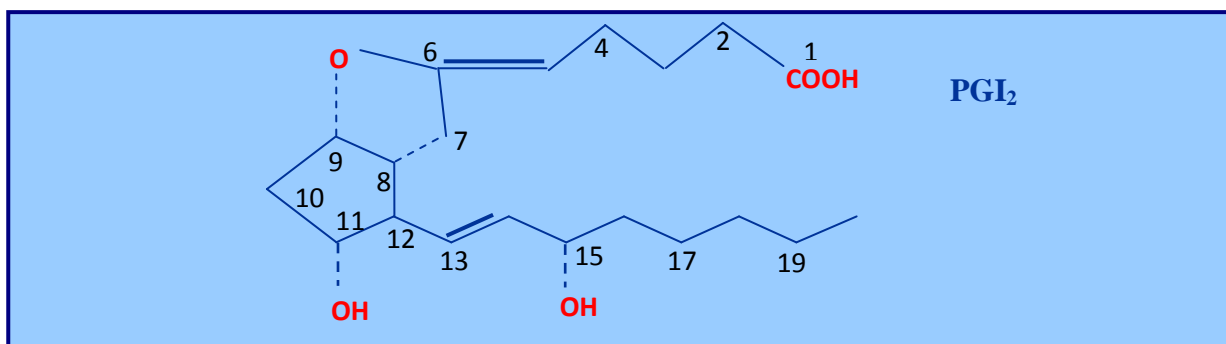


2. Thromboxanes (TX):

They are characterized by the presence of an oxane ring (containing 2 oxygen atoms) e.g. TXA₂. They are formed by platelets.

3. Prostacyclins (PGI):

They contain an additional ring in their structure.

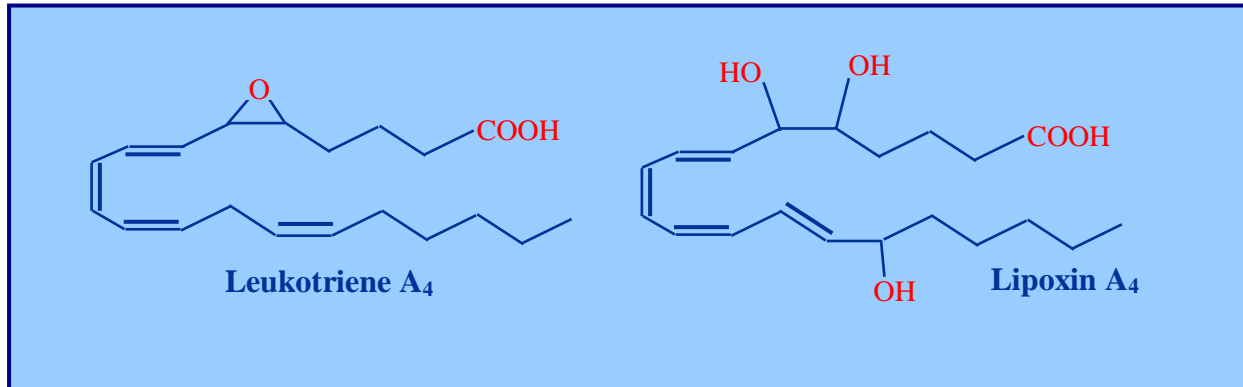


4. Leukotrienes (LT):

They are acyclic compounds and characterized by presence of three conjugated double bonds. They are secreted from leukocytes, platelets and mast cells.

5. Lipoxins (LX):

They are also acyclic compounds containing four conjugated double bonds but they contain more oxygen than LT. They are secreted from arterial walls.

**Importance and Functions of Eicosanoids (see lipid metabolism)****I- Simple Lipids**

They are esters of fatty acids with alcohols. According to the types of alcohols, there are two main sub-groups:

- 1. Neutral fats or triacylglycerol (TAG):** They are esters of three fatty acids with glycerol.
- 2. Waxes:** They are esters of one fatty acid with long chain monohydroxyalcohol higher than glycerol.

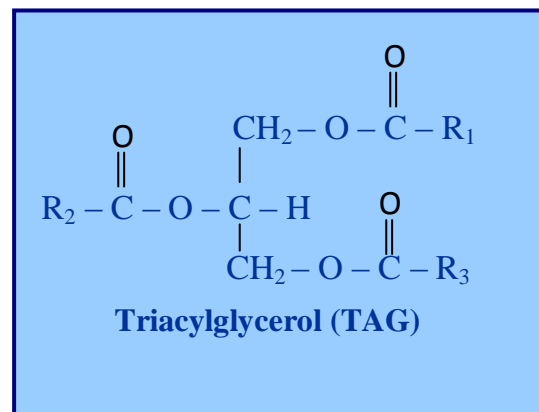
Examples of waxes:

- True wax (bee's wax): It is ester of palmitic acid (C16) with mericyl alcohol (C30).
- Cholesteryl esters.
- Vitamin A (retinol) esters.
- Vitamin D (calciferol) esters.

Triacylglycerol (Triglyceride):

They contain glycerol alcohol, which is colorless, odorless and has a sweet taste. It is liquid and soluble in water.

The fatty acids present in TAG are usually of different types (mixed TAG).



Neutral fats are classified into two sub-groups:

a) Oils: They are liquid at room temperature due to their high content of USFA.

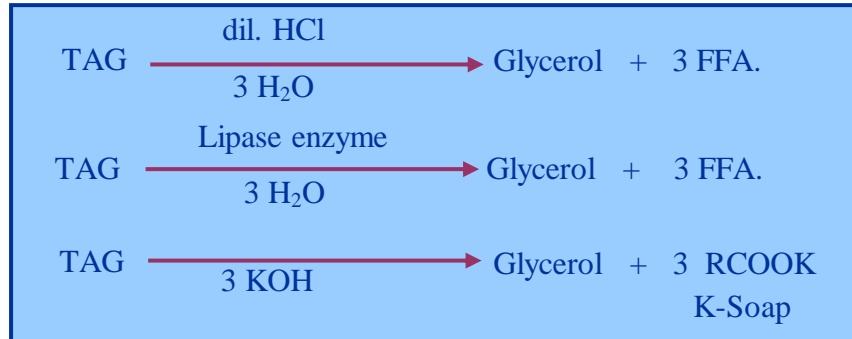
b) Solid fats: They are solid at room temperature due to their high content of long chains SFA.

Physical Properties of Neutral Fats:

- Pure, freshly prepared TAGs are colorless, odorless and tasteless. The yellow color of fats and oils is due to the presence of certain pigments e.g. carotenoids.
- They are insoluble in water but soluble in fat solvents.

Chemical Properties of Neutral Fats:**A- Addition of hydrogen (reduction or hardening):**

It is the addition of hydrogen through the double bonds to convert USFA into SFA. So the liquid oils will be converted into solid fats or margarine and hence the name (hardening).

B- Hydrolysis of TAG:**1. Acid hydrolysis:****2. Enzymatic hydrolysis:****3. Alkaline hydrolysis (saponification):****Rancidity:**

It is the development of bad odor and taste (bad flavor) of fats and oils.

Rancidity is due to exposure of fats or oils to high temperature, oxygen, moisture or humidity, light and metals (act as catalysts).

Types of Rancidity:**a) Hydrolytic rancidity:**

It is due to the hydrolysis of TAG by lipase enzyme (which is also present in bacteria) especially in presence of high temperature and moisture. Lipase causes release of short chain fatty acids which are volatile and have bad odor.

b) Oxidative rancidity:

Oils which are rich in USFA are more liable to develop this type of rancidity. Oxidation of USFA produces peroxides, lower chain fatty acids, fatty aldehydes and ketones. They have bad odor and bitter taste.

Protection against rancidity:

Addition of antioxidants e.g. vitamin E, phenols and quinones help to protect the USFA against oxidation and decrease the rate of development of rancidity.

II- Compound Lipids

They contain fatty acids, alcohols and other groups. According to the type of the attached group they are classified into:

- 1- **Phospholipids:** Containing phosphate radicals.
- 2- **Glycolipids:** Containing carbohydrate radicals.

1- Phospholipids

They are classified according to the alcohol present into two main sub-groups:

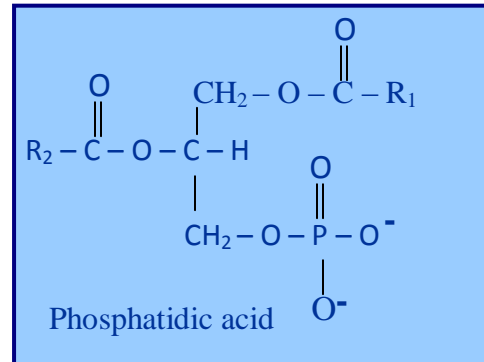
- A- **Glycerophospholipids:** Containing glycerol.
- B- **Sphingomyelin:** Containing sphingosine (sphingol).

A- Glycerophospholipids(Glycerophosphatides):

They are phospholipids containing glycerol. They include phosphatidic acid and its derivatives as follows:

1. Phosphatidic acid (Diacylglycerolphosphate):

On hydrolysis: It gives one glycerol, one saturated fatty acid (usually at position 1), one unsaturated fatty acid (usually at position 2), and phosphoric acid.



2. Lecithin (Phosphatidylcholine):

It is formed of phosphatidic acid and choline. It is usually present in the cell membranes especially in the liver, lung and brain. It is also present in blood plasma.

3. Cephalin (Phosphatidylethanolamine):

It is formed of phosphatidic acid and ethanolamine. It is present in the cell membranes and blood plasma.

4. Phosphatidylserine:

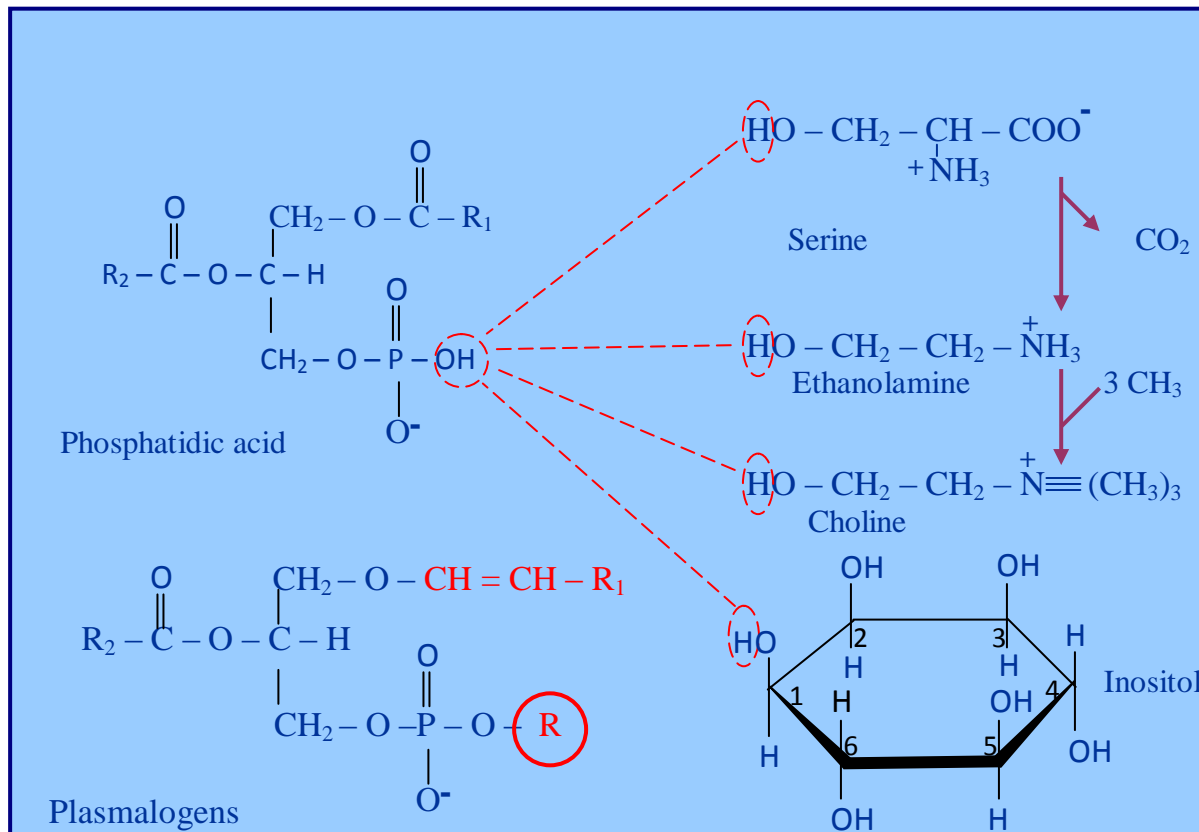
It is formed of phosphatidic acid and serine amino acid. It is present in cell membranes.

5. Phosphatidylinositol (Lipositol):

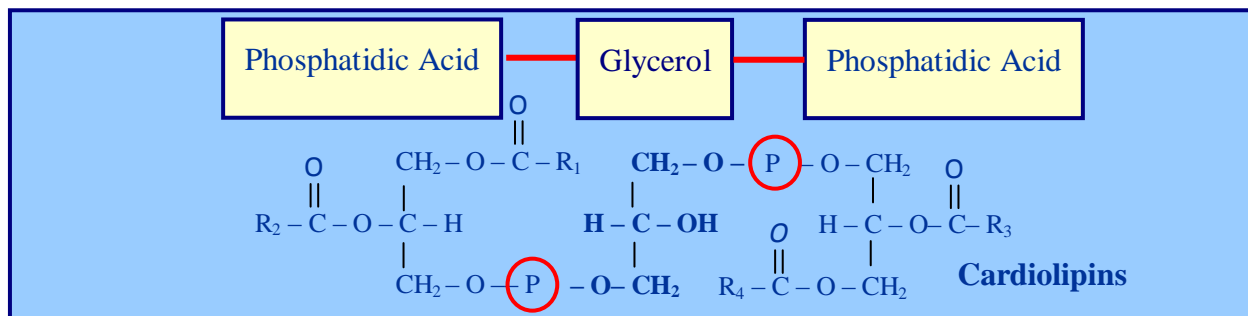
It is formed of phosphatidic acid and inositol. It is present in cell membranes. Phosphatidylinositol 4,5-bisphosphate (PIP₂) acts as secondary messenger in the process of intracellular signal transduction (explained later on).

6. Phosphatidylglycerol:

It is formed of phosphatidic acid and glycerol.



7- Cardiolipins (Diphosphatidylglycerol): They are formed of two molecules of phosphatidic acid connected by a molecule of glycerol. So, they contain 4 FAs, 3 glycerol and 2 phosphates. They form an important component of inner mitochondrial membrane.



8- Plasmalogens:

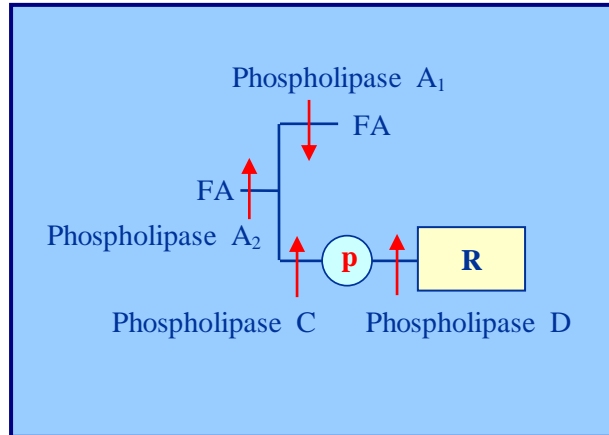
Plasmalogens are a type of **ether phospholipid** characterized by the presence of an enol form of fatty alcohol in ether linkage at the position-1, a fatty acid at the position-2 and an R group at the position-3. The R-group is in the form of **ethanolamine or choline**. Plasmalogens are found in numerous human tissues e.g. nervous and cardiovascular system. Reduced levels of brain tissue plasmalogens have been associated with **Alzheimer Disease**.

Hydrolysis of glycerophospholipids

-They are hydrolyzed by a group of enzymes termed phospholipases (PLA₁, PLA₂, PLC and PLD).

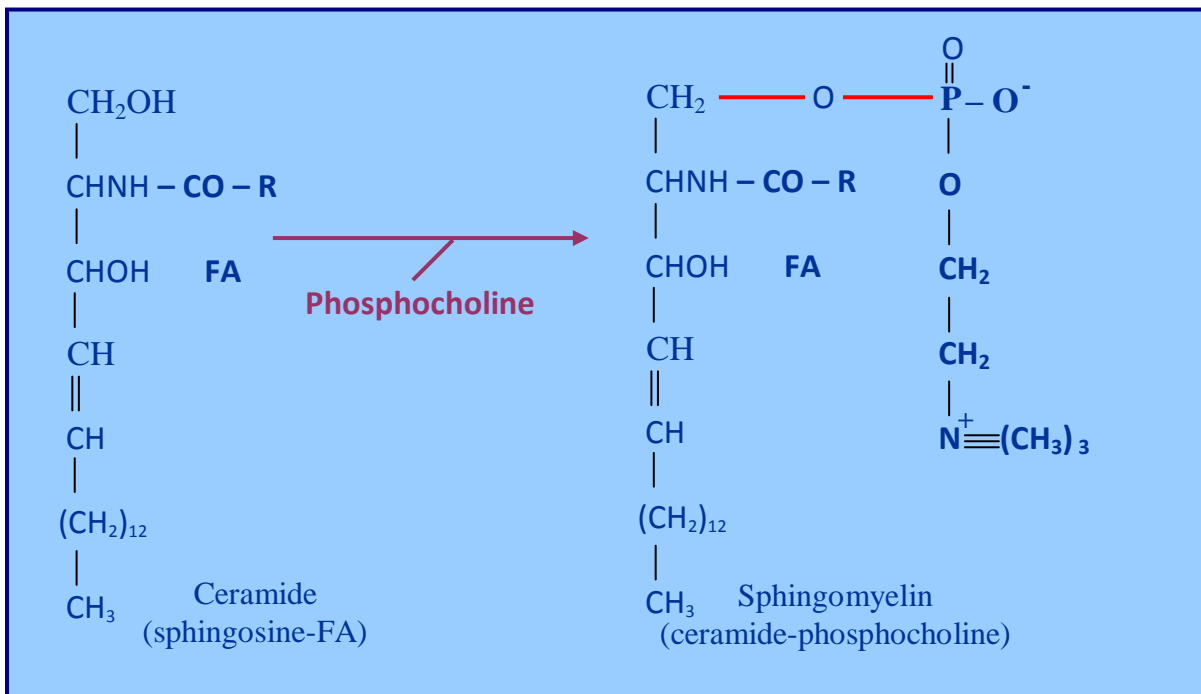
-Phospholipase D is not present in humans, but present only in plants. **Snake venom toxins** contain lecithinase enzyme with PLA₂ activity, when injected into blood, it converts phospholipids present in cell membranes of RBCs into lysophospholipids.

Therefore, snake venom toxins produce hemolysis of RBCs, which causes death if not treated by antitoxins.



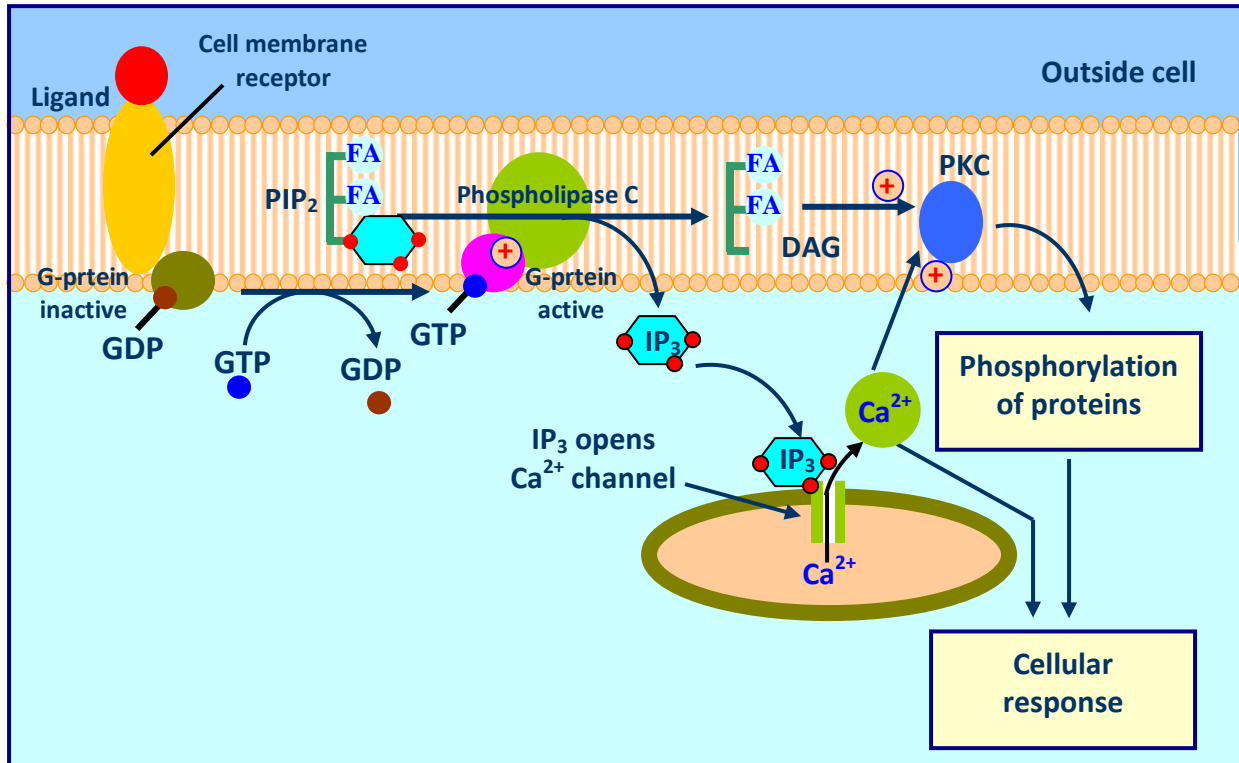
B- Sphingomyelin:

This type is present in cell membranes specially of the lungs and brain mainly in the myelin sheath. It contains **sphingosine** (sphingol) which is an 18 carbon amino alcohol. **Fatty acids** are linked to sphingosine by an amide bond to form ceramide, which is connected to **phosphocholine** to form sphingomyelin.



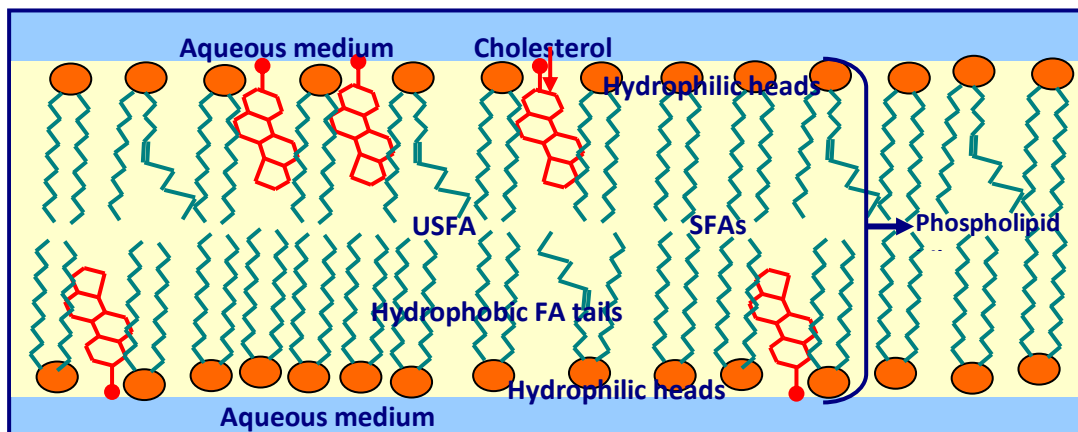
Importance and Functions of Phospholipids:

- 1) Phospholipids are **amphipathic molecules** that contain non-polar groups of fatty acid side chains and polar groups of glycerol, phosphate, serine, ethanolamine, choline and inositol. They form micelles in water.
- 2) They are good **emulsifying factors**, important for digestion and absorption of dietary fats.
- 3) They are good **hydrotropic substances**; they prevent deposition of cholesterol as cholesterol stones (biliary calculi).
- 4) They are important constituents of **plasma lipoproteins**.
- 5) They provide arachidonic acid for synthesis of **eicosanoids**.
- 6) They are essential for blood clotting, as they provide the **platelet activating factor (PAF)**, which is a **plasmalogen** that contains choline, palmityl alcohol at position 1 and acetic acid at position 2.
- 7) **Lung surfactant** is formed mainly of dipalmitoyl-lecithin, the lack of which is responsible for respiratory distress syndrome in premature infants.
 - Lecithin/Sphingomyelin ratio (**L/S ratio**) is a marker of fetal lung maturity. The pulmonary secretions from the fetal lungs into amniotic fluid maintains the level of lecithin and sphingomyelin equally until 32-33 weeks gestation, afterward the lecithin concentration begins to increase significantly while sphingomyelin remains nearly the same.
 - L/S ratio of 2 or more indicates fetal lung maturity and L/S ratio of less than 1.5 is associated with a high risk of infant respiratory distress syndrome.
 - If preterm delivery is necessary and L/S ratio is low the mother may need to receive steroids to increase the fetus surfactant production in the lungs.
- 8) **Intracellular signal transduction:** Receptor interaction with specific ligand (molecule) at cell membrane produces activation of **G-proteins** that produce activation of phospholipase C. **Phospholipase C** converts phosphatidylinositol 4,5-bisphosphate (**PIP₂**) into inositol-trisphosphate (**IP₃**) and diacylglycerol (**DAG**). **IP₃** and **DAG** act as second messengers. **IP₃** increases **release of intracellular Ca²⁺** from intracellular storage sites. **DAG and Ca²⁺** are capable of **activating protein kinase C (PKC)** which produces phosphorylation of certain proteins. The phosphorylated proteins are responsible for producing the specific cellular response. **Many chemical transmitters** (e.g. acetylcholine, histamine and serotonin), **hormones** (e.g. vasopressin and α -1 receptors for epinephrine and norepinephrine) and **growth factors** act through activation of phospholipase C.



- 9) They are important constituents of lipid bilayer in **cell membranes**: membrane lipids are **amphipathic**; having both hydrophilic region and a hydrophobic region. Because of their structure, when phospholipids are added to water, they form **phospholipid bilayer**, so that the phosphate and other polar groups form heads and make contact with water (outer layer) and the hydrophobic hydrocarbon tails are restricted to water-free areas (inner layer).

Increased unsaturated fatty acids (**USFA**) content (at C2 of phospholipids) will increase membrane fluidity because, the **kinks** of the *cis*-double bonds prevent the packing of phospholipids closely together, keeping them away from each other, and allow greater mobility. Straight hydrocarbon tails of saturated fatty acids interact strongly with each other decreasing membrane fluidity.



2- Glycolipids

They are formed of ceramide (sphingosine alcohol and fatty acid) and a carbohydrate radical. They include the following types:

A- Cerebrosides:

They contain either galactose (galactocerebrosides) or glucose (glucocerebrosides). They are widely distributed in brain tissues and brain centers. All are characterized by the presence of 24 carbon fatty acids e.g. cerebronic acid (α -hydroxylignoceric acid), nervonic acid or lignoceric acid.

B- Sulpholipids (Sulphatides):

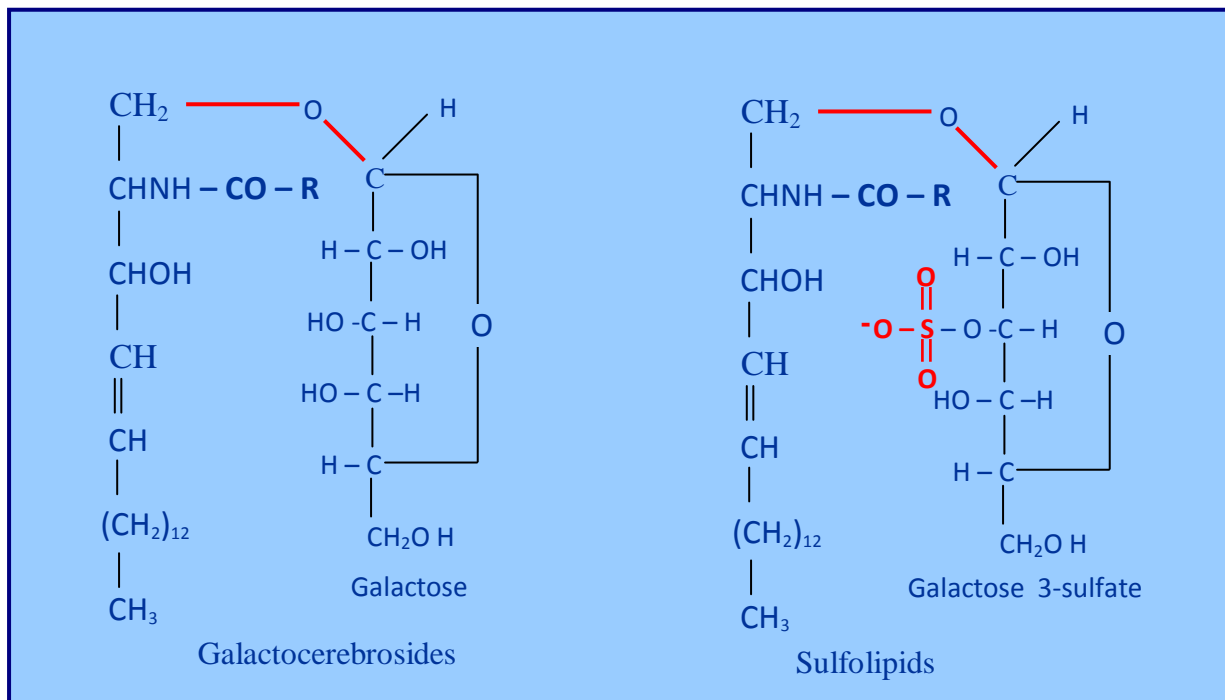
They are present in the liver, muscles and testis. They have the same structure as cerebrosides **but there is a sulphate group** attached to the hydroxyl group of C3 of galactose.

C- Gangliosides:

They are formed of ceramide connected to a complex carbohydrate radical containing mixture of glucose, galactose, amino sugars and NANA. The fatty acid usually contains 18 carbon atoms e.g. oleic acid or stearic acid.

Importance of glycolipids:

They are found mainly in brain tissues, myelin sheath and cell membrane of RBCs. They are components of cell membrane receptors for hormones and external stimuli, also they provide recognition properties.



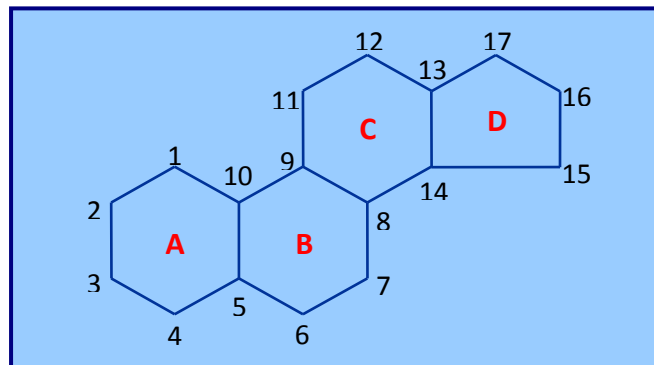
III- Derived Lipids

They are produced by hydrolysis of either simple or conjugated lipids or they are associated with lipids in nature. They include the following:

1. Fatty acids.
2. Alcohols.
3. Steroids.
4. Carotenoids.
5. Fat soluble vitamins: vitamins A, D, E & K.

STEROIDS

They are compounds containing steroid nucleus. This nucleus is composed of four fused rings with 17 carbon atoms. It is named as cyclo-pentano-perhydro-phenanthrene ring (CPPP).



Classification of steroids

They include the following groups:

- 1- Sterols.
- 2- Bile acids.
- 3- Steroid hormones.

Sterols

Sterols mean solid alcohols. They include the following groups:

- 1- Zoo sterols:** They are present in animals and humans e.g. cholesterol.
- 2- Phytosterols:** They are present in higher plants e.g. sitosterols. They have no physiologic importance.
- 3- Mycosterols:** They are present in lower plants (yeast and fungi) e.g. ergosterol.

Cholesterol

Sources: Exogenous (Dietary): The richest sources are egg yolk, red meat, liver, kidney, butter and brain. It is the most important animal sterol.

Endogenous: Every cell can synthesize its own cholesterol (from acetyl Co A). Plasma cholesterol is synthesized by the liver and intestine.

Forms: It is present either free (nonesterified) or esterified with fatty acid to form cholesteryl-ester. Free cholesterol contains 27 carbon atoms.

Distribution of cholesterol: It is widely distributed in all tissues but higher concentrations are present in the nervous tissue, liver, adrenals, gonads, skin and adipose tissue.

Plasma level of cholesterol: Normally it ranges from **120 to 200 mg/dL** (30% as free cholesterol and 70% as cholesteryl-esters).

Importance and derivatives of cholesterol:

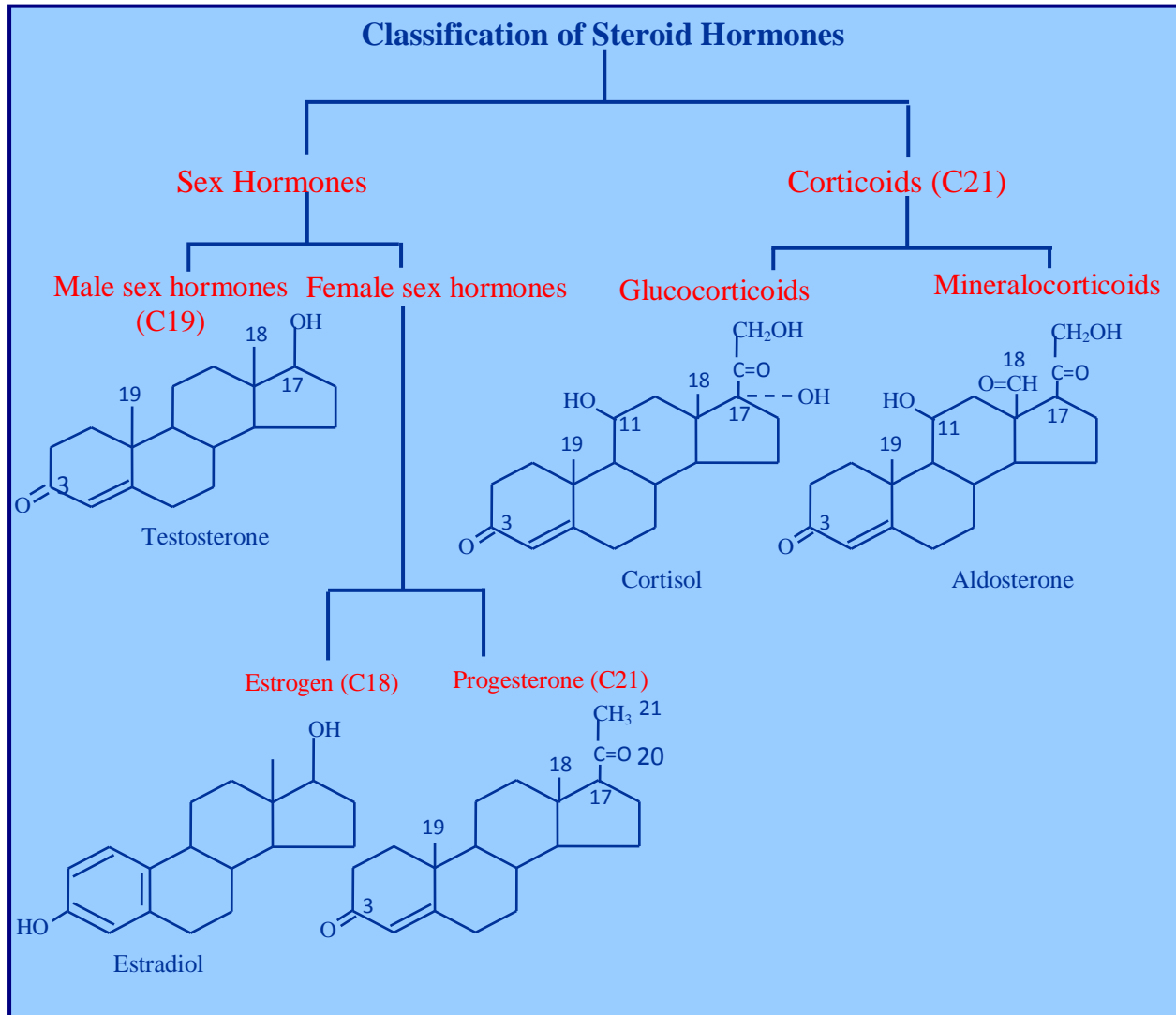
- 1- It is converted into bile acids and bile salts in the liver.
- 2- It is the precursor of all steroid hormones.
- 3- It can be oxidized in the liver into 7-dehydrocholesterol which can be converted into vitamin D₃ under the skin by ultraviolet rays.
- 4- It is an important constituent of cell membranes. Cholesterol moderates **fluidity** of cell membranes:
 - **At warm temperatures**, cholesterol makes the membrane less fluid by limiting the movement of the fatty acid tails of phospholipids (it cannot move to the same extent as FA).
 - **At low temperature** cholesterol decreases the close packing of phospholipids, increasing fluidity and decreasing gel formation.

Excretion of cholesterol:

- It is mainly excreted from the body in bile in the form of bile salts.
- *Less amounts are excreted as cholesterol, cholesteryl-esters and dihydrocholesterol.*
- *In the large intestine cholesterol is reduced by intestinal bacteria to give coprostanol which is excreted mainly in stool.*

Hazards of hypercholesterolemia: Increased plasma level of cholesterol predisposes to atherosclerosis and coronary heart diseases. The recommended level is **< 200 mg/dL** to decrease the risk of atherosclerosis and coronary heart disease.

Steroid Hormones



Carotenoids

- They are fat soluble pigments yellow to red in color.
- They are widely distributed in plants and responsible for many colors of fruits and vegetables e.g. orange, apricot, apple, tomato and carrots. They are also found in human and animal fats, milk, butter and egg yolk.
- They are precursors of vitamin A that have an important role in vision and normal development.
- They are powerful antioxidants that can help in the prevention of certain human diseases, such as atherosclerosis or cancer.
- They enhance immune response against infections.

FORMATIVE ASSESSMENT

- 1- Which one of the following statements concerning choline is true?
- It is an essential nutrient
 - It is a constituent of cardiolipin
 - It is a constituent of ceramide
 - It is a constituent of lung surfactant
- 2- The activation of phospholipase C associated with a cell membrane initiates a chemical signal most directly involving
- Arachidonic acid
 - cAMP
 - Inositol triphosphate
 - Prostaglandins

Key Answers

1	2
d	c

- **On biochemical basis explain:**

- Snake venoms cause hemolysis of RBCs? (key words: lecithinase enzyme with PLA_2 activity, lysophospholipid)
- Phospholipids are important for intracellular signal transduction? (key words: G-proteins, phospholipase C, PIP_2 , IP_3 and DAG act as second messengers, intracellular Ca^{2+} , PKC, phosphorylation of certain proteins)

- **Mention:**

- An $\omega 6$ non-essential PUFA. (Arachidonic acid)

REFERENCES

- ❖ Harper's Illustrated Biochemistry
- ❖ Lippincott's Illustrated Reviews: Biochemistry