# LIPIDS

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- A category of organic compounds that are insoluble in water and have a greasy feel
- lipids are a chemically diverse group of compounds, the common and defining feature of which is their insolubility in water due to lack of a polar group.
- diverse functions.

- **are non-polar** (hydrophobic) organic compounds, insoluble in water, soluble in organic solvents (ether, acetone, carbontetrachloride).
- They contain carbon, hydrogen, and oxygen; sometimes nitrogen and phosphorus.
- In most cases they yield fatty acids on hydrolysis.

- Lipids can be defined as “a group of naturally occurring substances, consisting of higher fatty acids, their naturally occurring compounds and substances found naturally in chemical association with them”.
- Biological molecules that are insoluble in aqueous solutions and soluble in organic solvents are classified as lipids. Only similarity in these compounds is that they yield fatty acids after hydrolysis.

# FUNCTIONS OF LIPIDS

- Storage form of energy
- Structural component of cell membrane.
- Precursor of many steroid hormones, vitamin D
- Act as thermal insulator
- Protection of internal organs

# FUNCTIONS OF LIPIDS

- Helps in absorption of fat soluble vitamins
- Lipoproteins transporting lipids
- Fats serve as surfactants by reducing surface tension.
- Improve taste and palatability.
- Acts as electric insulators in neurons.

# CLASSIFICATION OF LIPIDS

Simple lipid

Complex lipid

Derived lipids

# SIMPLE LIPIDS

**They are esters of FA with various alcohols**

**D/U the type of alcohols these are subclassified as**

| Neutral fats or oils | Waxes |
| --- | --- |
| Alcohol is GLYCEROL | Alcohol is other than glycerol |

# COMPLEX/ COMPOUND LIPIDS

These are esters of FA with alcohol containing additional[prosthetic] groups.

Subclassified according to the type of prosthetic group

- Phospholipids
- Glycolipids
- Lipoproteins

# DERIVED LIPIDS

**These are the derivatives obtained on the hydrolysis of group 1 and group 2 lipids which possess the characteristics of lipids.**

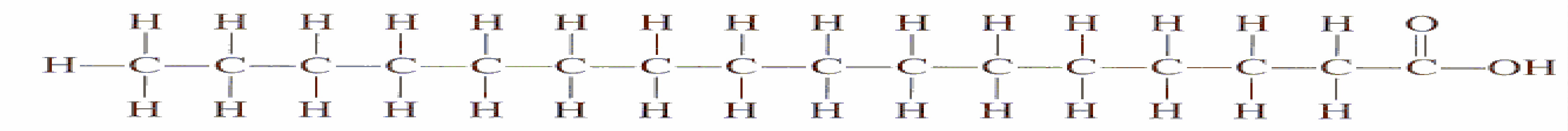
| Example | | | |
|---|---|---|---|
| Fatty acids | Steroids | Cholesterol | Vitamin A and D |

# FATTY ACIDS

- **Fatty acids** are naturally occurring carboxylic acids with an unbranched hydro-carbon chain and an even number of carbon atoms.
- The pathway by which fatty acids are biosynthesized they almost always contain an even number of carbon atoms.
- Long-chain fatty acids (12 to 26 carbon atoms) are found in meats and fish
- medium-chain fatty acids (6 to 10 carbon atoms) and short-chain fatty acids (fewer than 6 carbon atoms) occur primarily in dairy products.

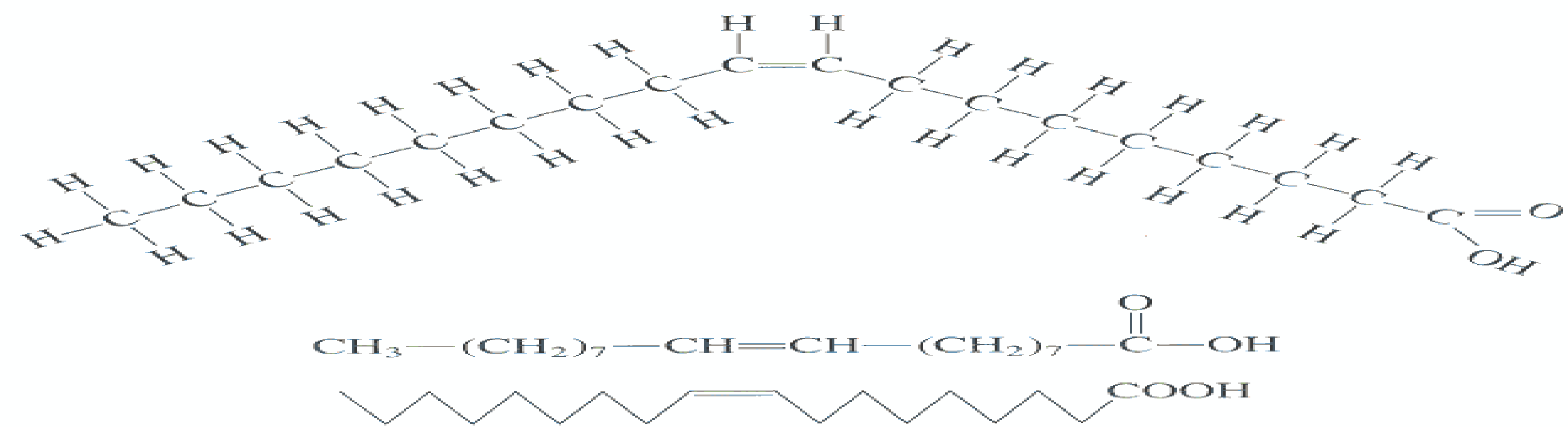
There are saturated and  unsaturated Fatty acids.

- ***Saturated fatty acid*** : Fatty acid chains that contain only carbon-carbon single bonds are referred to as **saturated (**Palmitic acid)



Hexadecanoic acid (palmitic acid)

- ***Unsaturated fatty acid*** : **Those molecules that contain one or more double bonds are said to be unsaturated. There are mono- and polyunsaturated fatty acids (Oleic acid)**



# Naming a Fatty Acid

- suffix '**oic acid**' to the name of the parent hydrocarbon.
- total number of carbon atoms + the number and position of double bonds
- Are ionized at physiological pH, so usually written as '**ate**' rather than 'oic acid'.
- A C18 saturated fatty acid would be called **octadecanoate/ octadecanoic acid [ octadeca + ane + oic acid]**
- A C18 monounsaturated fatty acid **octadecenoate/ octadecenoic acid [octadeca + ene + oic acid]**
- A C18 fatty acid with two double bonds **octadecadienoate/ octadecadienoic acid [ octadeca + di + ene + oic acid]**

- In nonsystematic shorthand notation, we show the number of carbon atoms and the number of any double bonds in the structure.
- A fatty acid with 18 carbons and no double bonds is designated 18:0,
- while one with 18 carbons and two double bonds is 18:2.
- The **carbon atoms in fatty acids are numbered from the carboxylic acid residue**,
- The position of double bonds is described using the number of the first carbon involved in the bond (e.g. Δ9 shows a double bond between carbons 9 and 10 of the fatty acid chain).
- The configuration of the double bonds in most unsaturated fatty acids is ***cis***; so called because the two hydrogens on the carbon atoms either side of the double bond are on the same side of the molecule (Latin, *cis* meaning on this side of).

# Omega-3 fatty acids

- also called **ω-3 fatty acids** or ***n*-3 fatty acids** are polyunsaturated fatty acids (PUFAs) with a double bond (C=C) at the third carbon atom from the end of the carbon chain.
- The fatty acids have two ends, the carboxylic acid (-COOH) end, which is considered the beginning of the chain, thus "alpha", and the methyl ($CH_3$) end, which is considered the "tail" of the chain, thus "omega." The way in which a fatty acid is named is determined by the location of the first double bond, counted from the methyl end, that is, the omega (ω-) or the n- end.

# Saturated Fatty Acids

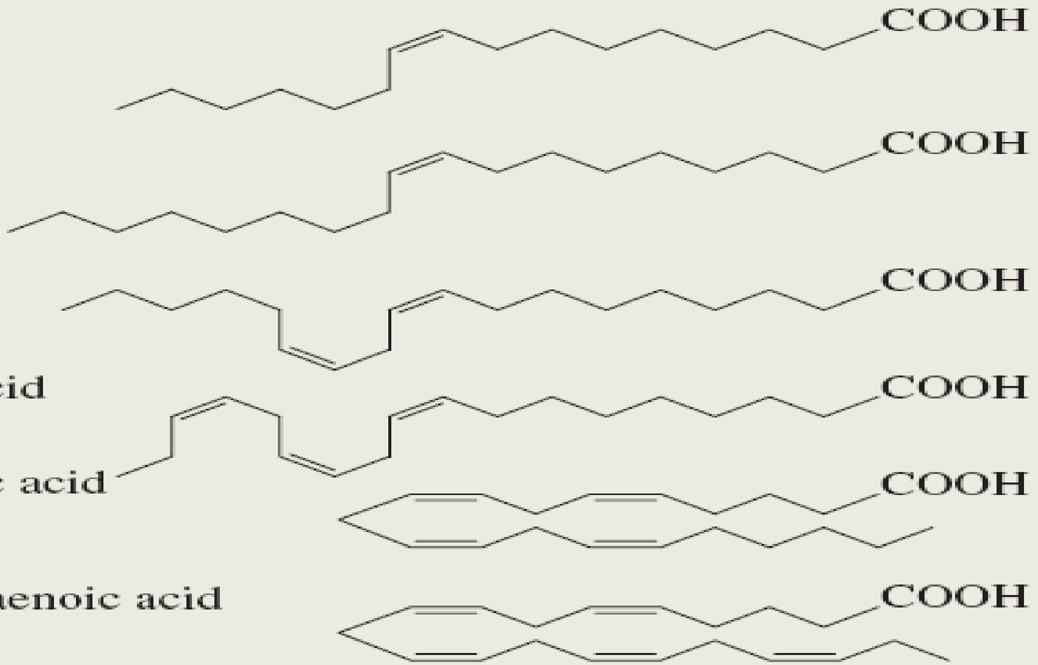
| SN | Saturated Fatty Acid | No. of Carbons | Name | Formula |
|---|---|---|---|---|
| 1 | Acetic Acid | 2 | n-Ethanoic acid | $CH_3COOH$ |
| 2 | Propionic Acid | 3 | n-Propanoic acid | $CH_3CH_2COOH$ |
| 3 | Butyric Acid | 4 | n- Butanoic acid | $C_3H_7COOH$ |
| 4 | Caproic Acid | 6 | n- Hexanoic acid | $C_5H_{11}COOH$ |
| 5 | Caprylic Acid | 8 | n-Octanoic acid | $C_7H_{15}COOH$ |
| 6 | Capric Acid | 10 | n- Decanoic acid | $C_9H_{19}COOH$ |
| 7 | Lauric Acid | 12 | n-Dodecanoic acid | $C_{11}H_{23}COOH$ |
| 8 | Myristic Acid | 14 | n-Tetradecanoic acid | $C_{13}H_{27}COOH$ |
| 9 | Palmitic acid | 16 | n-Hexadecanoic acid | $C_{15}H_{31}COOH$ |
| 10 | Stearic Acid | 18 | n- Octadecanoic acid | $C_{17}H_{35}COOH$ |
| 11 | Arachidic Acid | 20 | n-Eicosanoic acid | $C_{19}H_{39}COOH$ |
| 12 | Behemic Acid | 22 | n-Docosanoic acid | $C_{21}H_{43}COOH$ |
| 13 | Lignoceric Acid | 24 | n-Tetracosanoic acid | $C_{23}H_{47}COOH$ |
| 14 | Cerotic Acid | 26 | n-Hexacosanoic acid | $C_{25}H_{51}COOH$ |
| 15 | Montanic Acid | 28 | n-Octacosanoic acid | $C_{27}H_{55}COOH$ |

# Unsaturated Fatty Acids

| SN | Unsaturated Fatty Acid | No. of Carbons | Name | Formula |
|---|---|---|---|---|
| 1 | Palmitoleic Acid | 16:1 (Δ9) | 9-Hexadecenoic acid | $C_{15}H_{29}COOH$ |
| 2 | Oleic Acid | 18:1 (Δ9) | 9-Octadecenoic acid | $C_{17}H_{33}COOH$ |
| 3 | Linoleic Acid | 18:2 (Δ9,12) | 9,12-Octadecadienoic acid | $C_{17}H_{31}COOH$ |
| 4 | Linolenic Acid | 18:3 (Δ9,12,15) | 9,12,15 Octadecatrienoic acid | $C_{17}H_{29}COOH$ |
| 5 | Arachidonic Acid | 20:4 (Δ5,8,11,14) | 5,8,11,14 Icosatetraenoic acid | $C_{19}H_{31}COOH$ |

| Number of carbons | Common name | Systematic name | Structure | Melting point °C |
|---|---|---|---|---|
| **Saturated** | | | | |
| 12 | lauric acid | dodecanoic acid |  COOH | 44 |
| 14 | myristic acid | tetradecanoic acid |  COOH | 58 |
| 16 | palmitic acid | hexadecanoic acid |  COOH | 63 |
| 18 | stearic acid | octadecanoic acid |  COOH | 69 |
| 20 | arachidic acid | eicosanoic acid |  COOH | 77 |

| | | | |
|---|---|---|---|
| 16 | palmitoleic acid | (9Z)-hexadecenoic acid | 0 |
| 18 | oleic acid | (9Z)-octadecenoic acid | 13 |
| 18 | linoleic acid | (9Z,12Z)-octadecadienoic acid | −5 |
| 18 | linolenic acid | (9Z,12Z,15Z)-octadecatrienoic acid | −11 |
| 20 | arachidonic acid | (5Z,8Z,11Z,14Z)-eicosatetraenoic acid | −50 |
| 20 | EPA | (5Z,8Z,11Z,14Z,17Z)-eicosapentaenoic acid | −50 |



# FUNCTIONS OF FATTY ACIDS

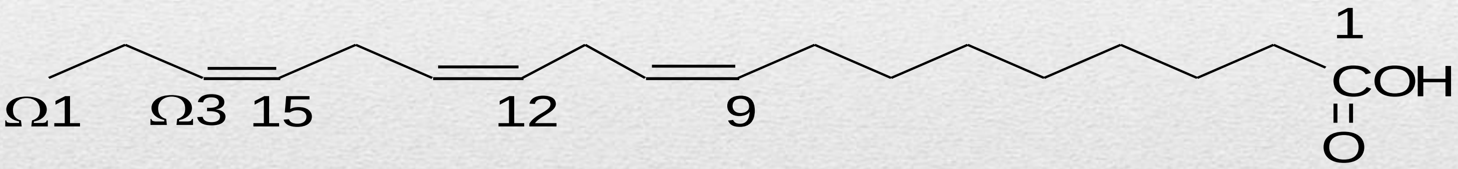
- make **glycerophospholipids** and **sphingolipids** that are essential components of biological membranes.
- Numerous proteins are **covalently modified** by fatty acids. Myristate (C14:0) and palmitate (C16:0) are directly attached to some proteins, while phosphatidylinositol is covalently linked to the C terminus of other proteins via a complex glycosylated structure.
- act as **fuel molecules**, being stored as **triacylglycerols**, and broken down to generate energy.
- Derivatives of fatty acids serve as **hormones** (such as the prostaglandins) and **intracellular second messengers** (such as DAG and IP3).

# Essential Fatty Acids (EFA)

There are TWO essential fatty acids.

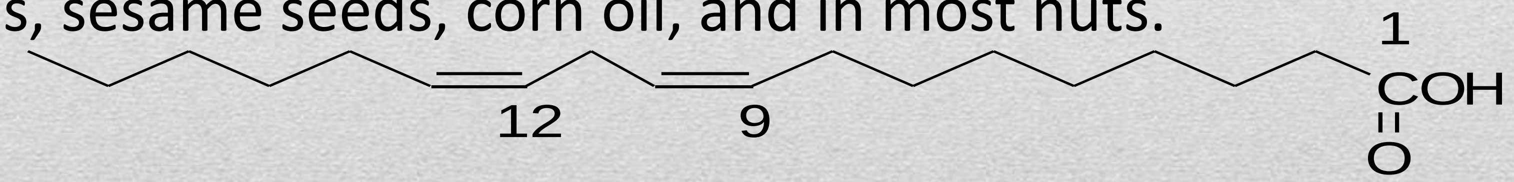
Essential means you NEED to get them from the diet because the body cannot manufacture them.

- α-linolenic acid (LNA or ALA): an omega-3 fatty acid




ALA
α-Linolenic acid

- Linoleic acid (LA): an omega-6 fatty acid found abundantly in soy oil, sunflower seeds, pumpkin seeds, sesame seeds, corn oil, and in most nuts.




Linoleic acid

cis-9,12-Octadecadienoic aicd, 18:2($\Delta^{9,12}$)

# Functions of EFA

- Essential fatty acids are required for the membrane structure and function.
- Transport of cholesterol.
- Formation of lipoproteins.
- Prevention of fatty liver etc.
- They are also needed for the synthesis of another important group of compounds, namely eicosanoids.

# PROPERTIES OF FATTY ACIDS

- depend on their **chain length** and the **number of double bonds**.
- Shorter chain length of FA; lower melting temperatures.
- Unsaturated fatty acids have lower melting temperatures than saturated fatty acids of the same chain length, whilst the corresponding polyunsaturated fatty acids have even lower melting temperatures.

# Saturated FA

- Fatty acids up to C10 (capric acid) are liquid at ordinary temperature; whereas the higher members are solid.
- Melting point increases with chain length.
- Acetic and Butyric acid mix in water in all proportions and the solubility of the higher acids decreases with chain length.
- Above C10 the acids are essentially insoluble in water.
- The liquid fatty acids from C2 to C10 are volatile with steam, the volatility decreases as the carbon chain increases.

# Unsaturated FA

- All naturally occurring unsaturated fatty acids are liquid at room temperature.
- Generally insoluble in water.
- All fatty acids whether saturated or unsaturated are soluble in organic solvents.
- With exception of Acetic acid, fatty acids are lighter than water; that is their specific gravity is less than water.

# SIMPLE LIPIDS

**They are esters of FA with various alcohols**

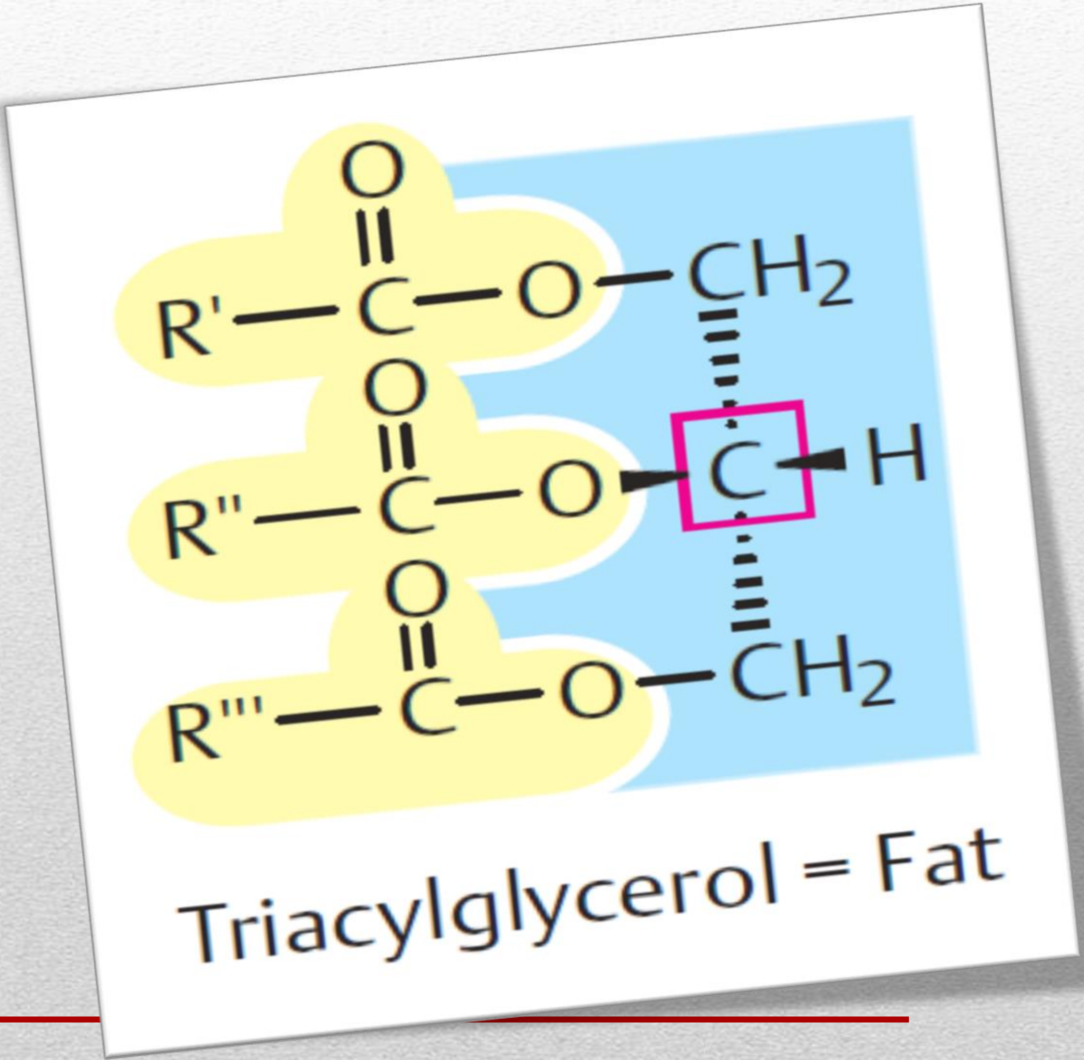
**D/U the type of alcohols these are subclassified as**

| Neutral fats or oils | Waxes |
| --- | --- |
| Alcohol is GLYCEROL | Alcohol is other than glycerol |

# NEUTRAL FATS OR OILS

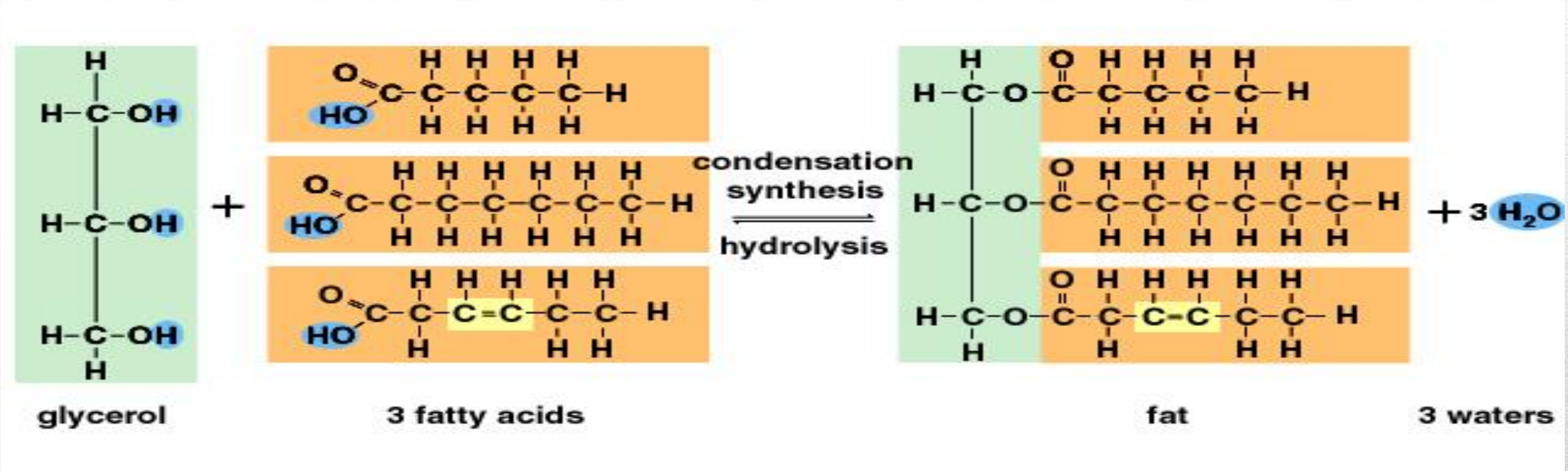
Esters of FA with alcohol GLYCEROL

Uncharged



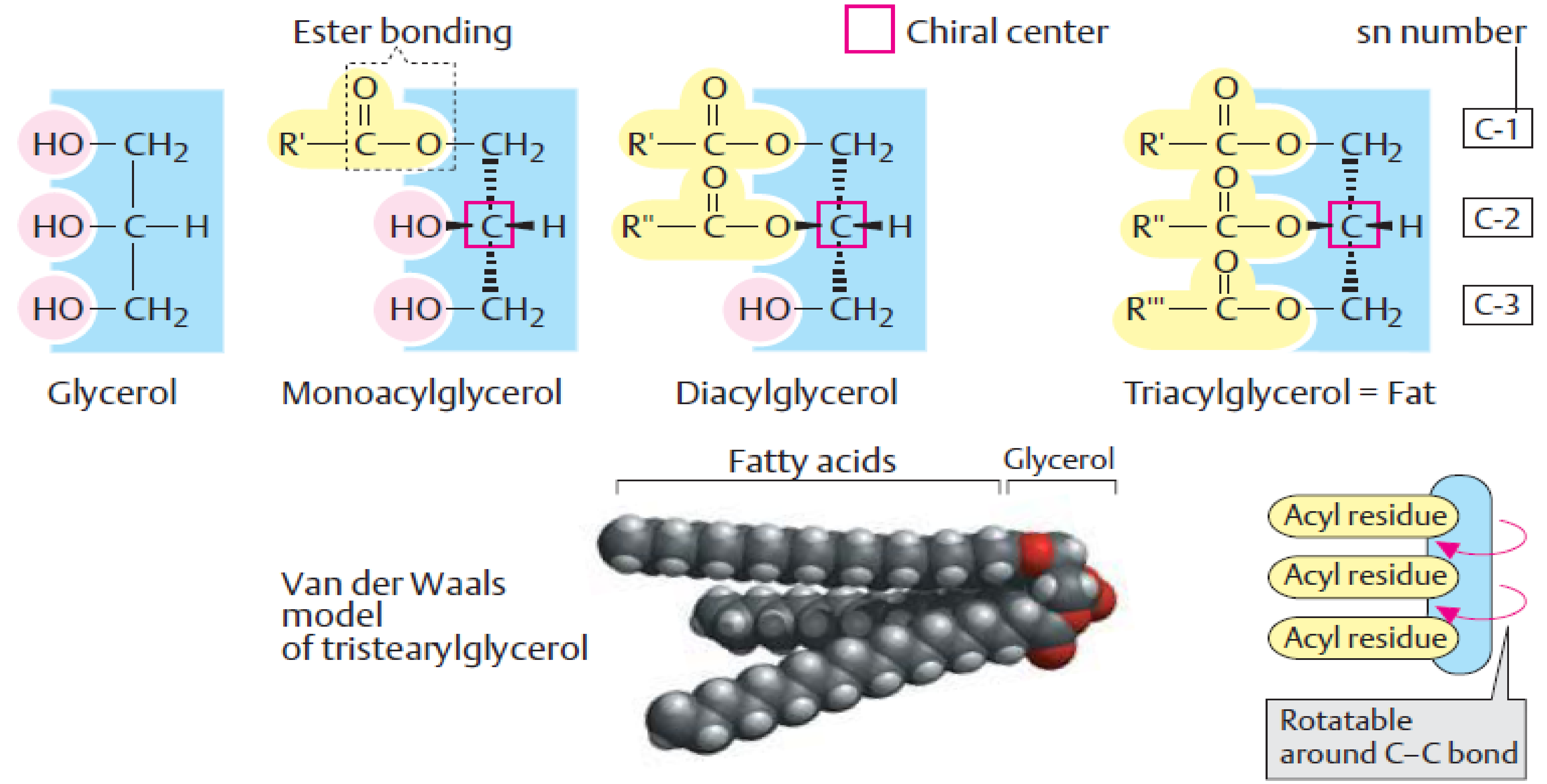
# Fats and Oils

- **=3 fatty acids + Glycerol**
  - A **fatty acid** is a long hydrocarbon chain with a carboxyl (acid) group at one end. (-COOH)
    - Because the carboxyl group is a polar group, fatty acids can be slightly soluble in water.
    - Most fatty acids in cells contain 16 to 18 carbon atoms per molecule. The longer the chain the less water soluble it is.
  - **Glycerol** is a water-soluble compound with three hydroxyl groups.


condensation
synthesis
hydrolysis
glycerol
3 fatty acids
fat
3 waters

- **Triglycerides** are glycerol joined to three fatty acids by condensation synthesis.
  - **Fats** are triglycerides containing saturated fatty acids (e.g., butter is solid at room temperature).  Generally from animals
  - **Oils** are triglycerides with unsaturated fatty acids (e.g., corn oil is liquid at room temperature).  Generally from plants
  - **Animals use fat rather than glycogen for long-term energy storage; fat stores more energy.(9cal/g)

## B. Structure of fats



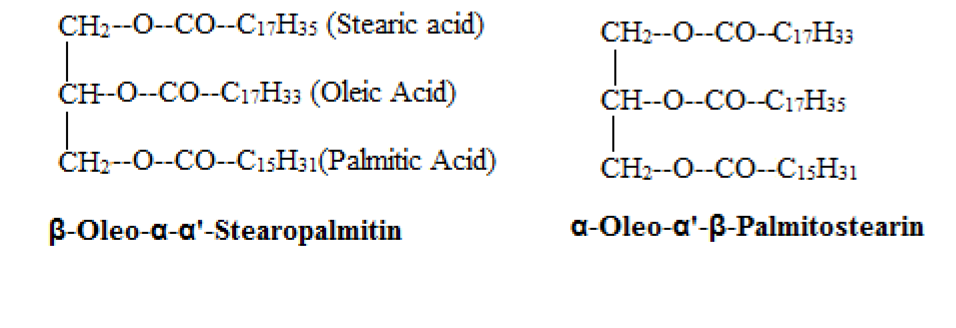
# Types of TG

- **Simple Triglycerides:**

Those triglycerides having the same kind of fatty acids in all three positions are called **Simple Triglycerides** and are named after the fatty acids they contain like Tributyrin, Tristearin & Triolein etc.

- **Mixed:**

Most naturally occurring triglycerides are **mixed**, they contain two or more fatty acids. To name the mixed TGs, the name & position of each fatty acid must be specified.



# Physical Properties of Fat/ Oils

- Insoluble in water, but readily soluble in organic solvents like alcohol, ether, chloroform etc.
- Greasy in touch and leave an oily impression on paper.
- Pure TGs are tasteless, odourless, colourless and neutral in reaction.
- After exposure to air for sometimes, they become acidic & develop yellow colour due to partial hydrolysis & oxidation of unsaturated fatty acids present in it.
- Fats used in food have specific flavour & colour. The flavour is attributed to the presence of certain foreign substances absorbed by the fat either from its natural environment or acquired during the processing of fats.
- The colour of butter, human fats & egg yolk is due to the presence of carotene and xanthophyll contained in them.

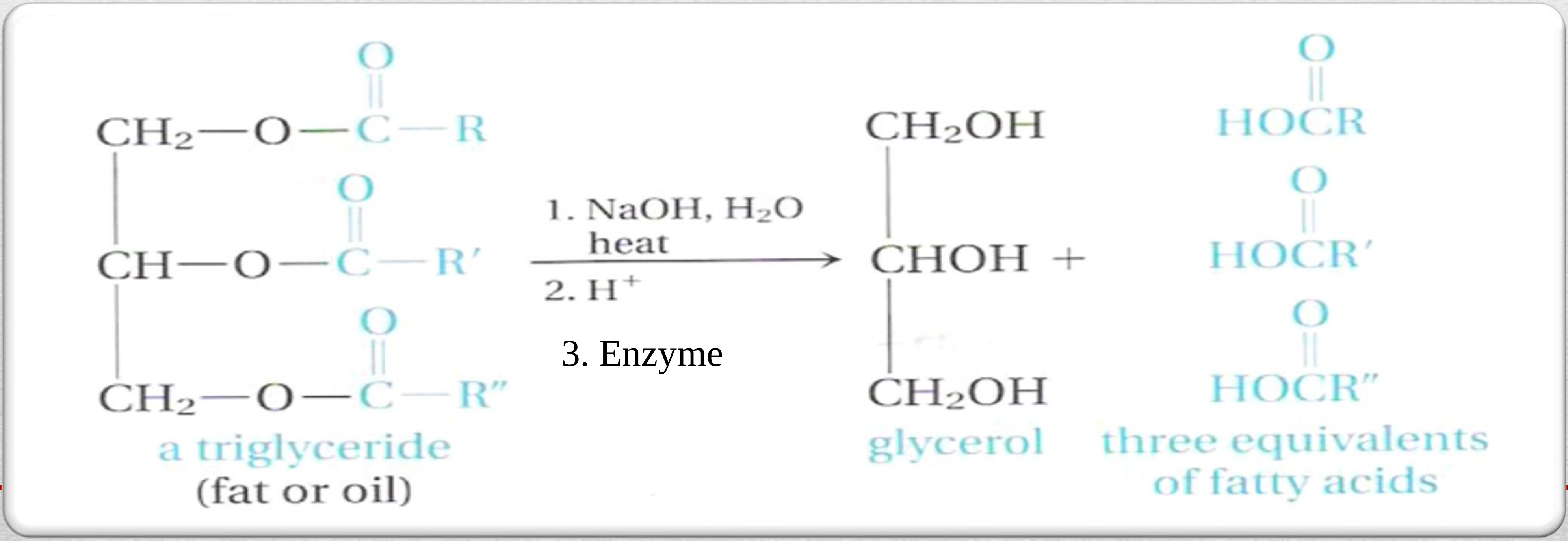
# Physical Properties of Fat/ Oils

- Hardness of fats depends upon the relative amount of saturated & unsaturated fatty acids present in them. Fats containing saturated fatty acids are solid at room temperature; whereas fats having unsaturated fatty acids are liquid.
- Fats have lesser specific gravity than water, and therefore float in water.
- **Emulsification:** Though fats are insoluble in water, they can be broken down into minute droplets and dispersed in water. This is emulsion. A satisfactory emulsion is one which is stable and which contains very minute fat droplets with diameter less than 0.5 microns. Emulsification greatly increases the surface area of the fats, and this is an essential requisite for digestion of fats in the intestines.

# CHEMICAL PROPERTIES OF FATS/ OILS

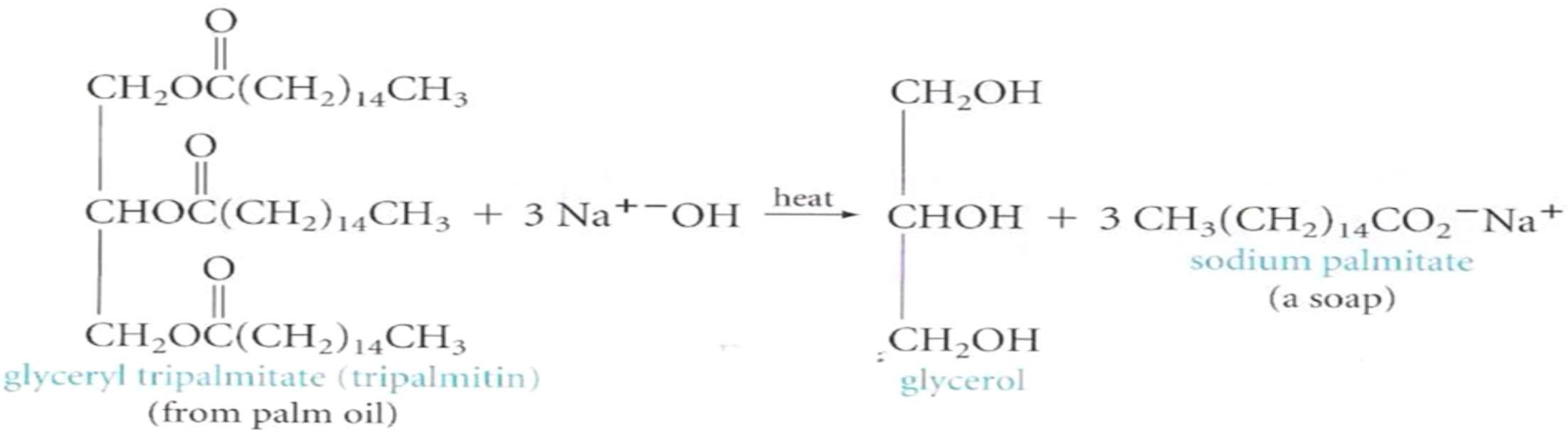
# HYDROLYSIS

- Glycerides are readily hydrolyzed in to their component that is fatty acids and glycerol. Hydrolysis can be accompanied by heating with water at high temperature & pressure preferably with addition of catalysts such as acids. On ordinary pressure, reaction is very slow.



# Saponification

When a fat or oil is heated with alkali, the ester is converted to glycerol and the salts of fatty acids. The reaction is illustrated here with the saponification of glyceryl tripalmitate.



# Soaps

- are sodium or potassium salt of fatty acids.
- Potassium soaps are soft and soluble in water; but sodium soaps are hard and less soluble in water.
- The soaps are good cleaning agents because they are effective emulsifying agents. Dirt is held to the surface by greasy substances.
- Soaps being good emulsifying agent lower the surface tension also. The greasy materials are emulsified by the soaps and dirt is carried away with them in washing.

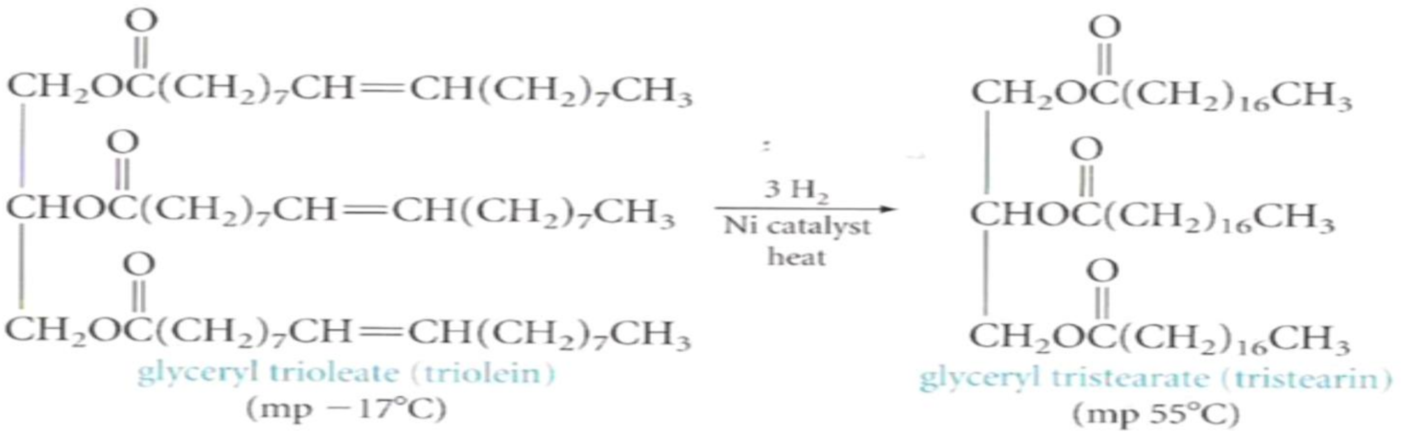
- **Saponification number** is defined as the "milligrams of KOH required to saponify one gram of fat".
- The saponification number provides information about the average molecular size of fatty acids present in triglycerides.

# Hydrogenation

- Unsaturated glycerides of fats may be hydrogenated by treatment with H2 gas in the presence of Nickel.
- The hydrogenation of oils is used to prepare commercial cooking fats like margarine, banaspati ghee etc.

**Hardening** is the process of converting oils to fats by catalytic hydrogenation of double bonds. **Margarine** is made by hydrogenating oils.

Vegetable oils, which are highly unsaturated, are converted into solid vegetable fats, such as Crisco, by catalytically hydrogenating some or all of the double bonds. This process, called **hardening**, is illustrated by the hydrogenation of glyceryl trioleate to glyceryl tristearate.




(15.2)

**Margarine** is made by hydrogenating cottonseed, soybean, peanut, or corn oil until the desired butter-like consistency is obtained. The product may be churned with milk and artificially colored to mimic butter's flavor and appearance.

Hydrogenation of corn oil, and other vegetable oils, provides margarine.

# HALOGENATION

- Unsaturated glycerides of fats react with halogens (Chlorine, Bromine, Iodine, Iodine chloride & Iodine bromide) and produces a saturated halogenated glyceride.
- Like hydrogenation, one atom of halogens is added to each side of the double bond.

**Iodine number:**

- Since the quantity of halogens absorbed by the glycerides of a fat can be measured accurately, it is possible to calculate the relative unsaturation of fats.
- Iodine number is thus defined as "**percent of iodine absorbed by the fat**" OR **the grams of iodine absorbed by 100 grams of fats**. Iodine number gives information about the number of unsaturated bonds present in fats.

# ACETYLATION

- Acetylation occurs when there is presence of hydroxylated fatty acids in fats and gives rise to corresponding esters.
- It is the reaction of fats with acetic anhydride & other acetylating agents; where –OH group is replaced by –O—CO—$CH_3$.
- **Acetyl Number:** is "**milligram of KOH required to combine with acetic acid liberated by saponification of one gram of acetylated fats**". It indicates the amount of hydroxylated fatty acids present in fats.

# OXIDATION

- Oxidation of unsaturated fatty acids at double bond yields a variety of products, depending upon the oxidizing agents and conditions employed.
- Ozones & oxygen may add to double bond to form **Ozonides & Peroxides** respectively.
- Auto oxidation due to exposure of air & light (e. g. in linseed oil) makes hard film over the surface of oils.

## Rancidity

- Rancidity is the term used to represent the deterioration of fats and oils resulting in an unpleasant taste. Fats containing unsaturated fatty acids are more susceptible to rancidity.
- unpleasant odour & taste developed by most natural fats upon ageing
- Rancidity occurs when fats and oils are exposed to air, moisture, light, bacteria etc.
- Two main causes for rancidity: hydrolysis and oxidation of fats. So rancidity is also of two types—
  - Hydrolytic rancidity
  - Oxidative rancidity

# Hydrolytic Rancidity

- Hydrolytic rancidity occurs due to partial hydrolysis of triacylglycerols by bacterial enzymes.
- Triglycerides are hydrolyzed in to free fatty acids and glycerols or mono or diglycerides.
- Fatty acids of low molecular weight ($C_4$ to $C_{10}$) give bad odour. This type of rancidity is hastened by the presence of some lipolytic enzymes in fats.

# Oxidative Rancidity

- Oxidative rancidity is due to oxidation of unsaturated fatty acids due to various oxidative processes.
- Again this type of rancidity is divided into two categories depending on the product formed.
  - **Aldehydic Rancidity**—

    Oxidation of unsaturated glycerides at double bonds may form peroxides which then decompose to form aldehydes of objectionable odour & taste. This process increases by exposure to light.
  - **Ketonic Rancidity**—

    Keto acids are formed after beta oxidation of free fatty acids obtained after hydrolysis of glycerides. $CO_2$ is released from these keto acids and causes rancidity.

# Acid Number

- It indicates the number of free fatty acids present in a fat. Acid number is defined as "**milligram of KOH required to neutralize the free fatty acids present in one gram of fat**".
- Acid number is helpful in determining the rancidity due to free fatty acid.

# Reichert-Meissel Number

- It is also known as RM number, RM value or volatile fatty acid number. RM value represents "**the millilitres of decinormal (1/10N) alkali required to neutralize the volatile fatty acids obtained from 5 gram of fats**".

# Polenske Value

- The Polenske number indicates about the non volatile fatty acids present in a fat. It represents "**the millilitres of decinormal alkali required to neutralize water insoluble fatty acids not volatile with steam distillation obtained from 5 grams of fats**".

# Test to Check Purity of Fats and Oils

- **Acid number:**
- In normal circumstances refined oils should be free from any free fatty acids.
- Oils, on decomposition due to chemical or bacterial contamination-yield free fatty acids.
- Therefore, oils with increased acid number are unsafe for human consumption
- **Saponification number:**
- Saponification number is a measure of the average molecular size of the fatty acids present
- The value is higher for fats containing short chain fatty acids.

# Test to Check Purity of Fats and Oils

- **Iodine number:**
- Iodine number is useful to know the relative unsaturation of fats, and is directly proportional to the content of unsaturated fatty acids.
- Thus lower is the iodine number, less is the degree of unsaturation.

- Determination of iodine number will help to know the degree of adulteration of a given oil.

# Test to Check Purity of Fats and Oils

- **Reichert-Meissl (RM) number:**
- RM number is useful in testing the purity of butter since it contains a good concentration of volatile fatty acids (butyric acid, caproic acid and caprylic acid).
- Butter has a RM number in the range 25-30, while it is less than 1 for most other edible oils.
- Thus any adulteration of butter can be easily tested by this sensitive RM number .

# Major differences in fats and oils

| Fats | Oils |
|---|---|
| Solid at room temperature | Liquid at room temperature |
| Have relatively less molecular weight fatty acids | Have higher fatty acids |
| Have more saturated glycerides | Have less glycerides of saturated fatty acids |
| Have higher saponification number as the fatty acids are of less MW | Have lesser saponification number |
| Iodine number is less | Iodine number is more |

# WAXES

**have long chain high molecular weight alcohols in place of glycerol**

Esters of FA with higher molecular weight monohydric alcohols

**EXAMPLES**

- ✓ Lanolin
- ✓ Beeswax
- ✓ Whale sperm oil

# COMPLEX LIPIDS

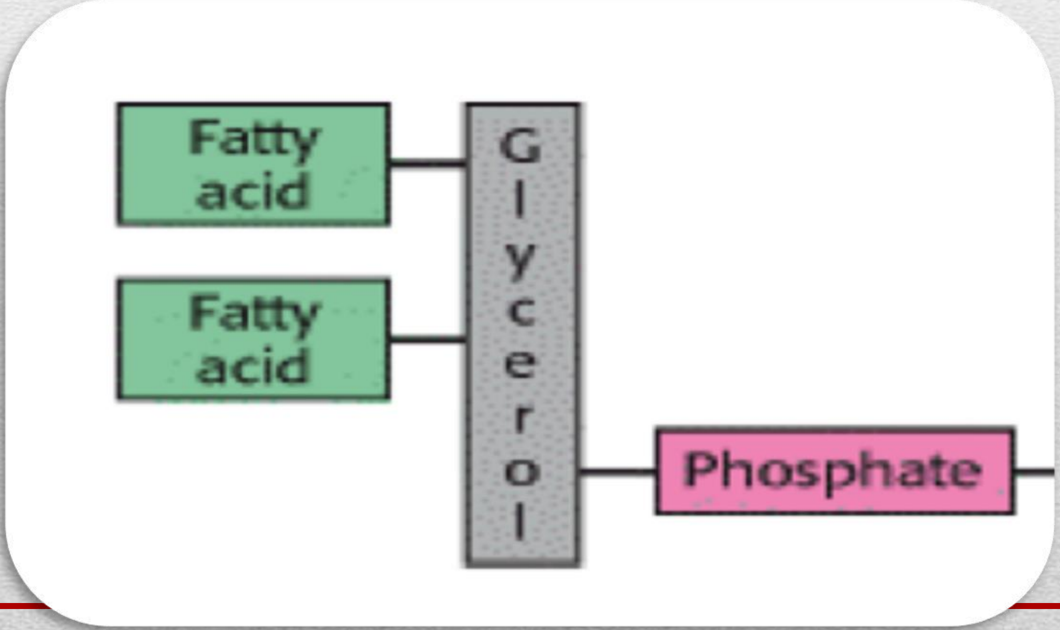
**These are esters of FA with alcohol containing additional[prosthetic] groups.**

Subclassified according to the type of prosthetic group

- Phospholipids
- Glycolipids
- Lipoproteins

# PHOSPHOLIPIDS

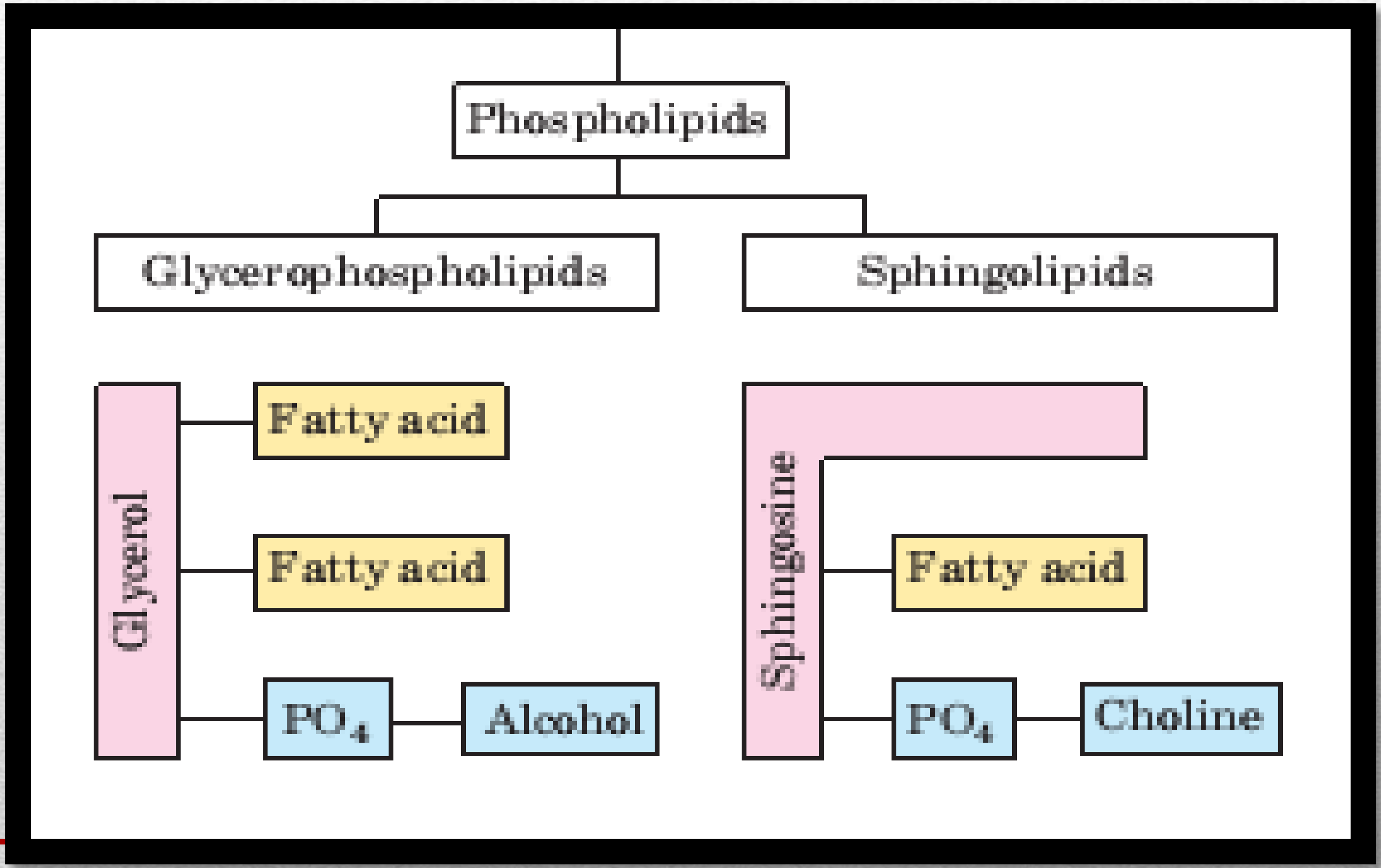
FA + ALCOHOL + PHOSPHORIC ACID




They frequently have nitrogen containing bases

# PHOSPHOLIPIDS

Phospholipids may be classified on the basis of the type of alcohol present



## A. Glycerophospholipids

## B. Spingophospholipids

### ALCOHOL IS GLYCEROL

- ✓ Phosphatidylcholine
- ✓ Phosphatidyl ethanolamine
- ✓ Phosphatidyl serine
- ✓ Phosphatidyl inositol
- ✓ Plasmalogens
- ✓ Cardiolipins

### ALCOHOL IS SPINGOSINE

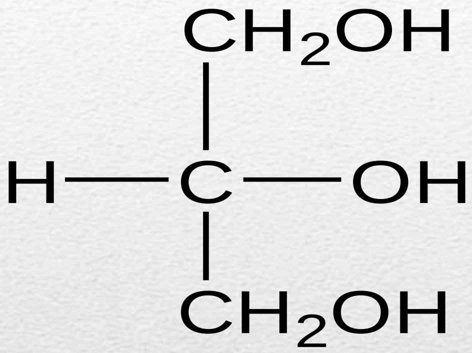
- ✓ Spingomyelins

# Glycerophospholipids

**Glycerophospholipids** (phosphoglycerides), are common constituents of cellular membranes.

They have a **glycerol** backbone.

Hydroxyls at **C1** & **C2** are esterified to **fatty acids**.

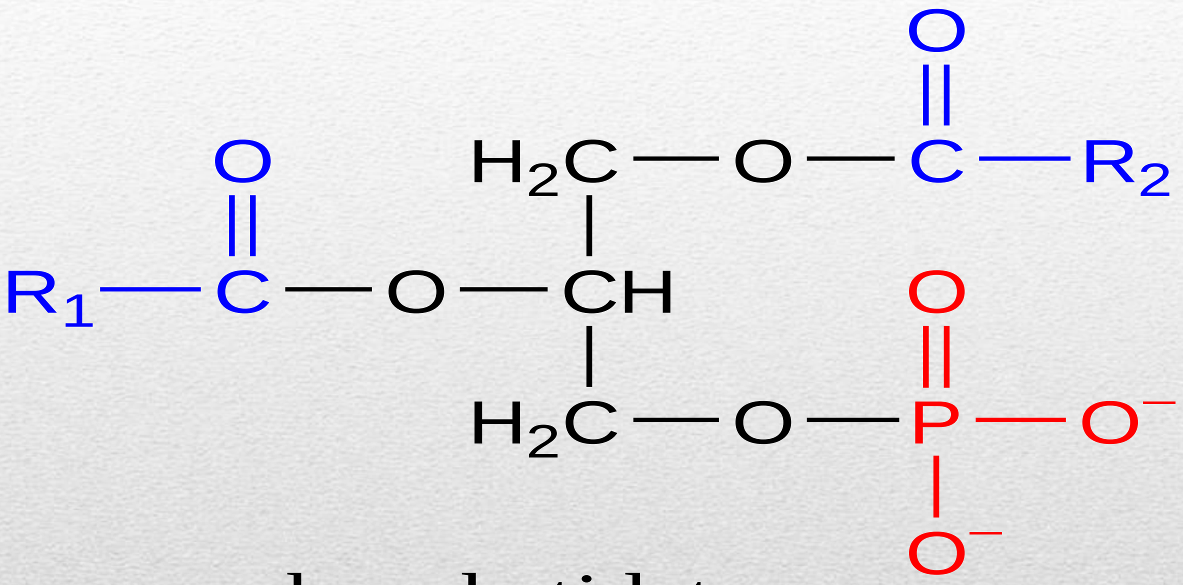



glycerol

An **ester** forms when a hydroxyl reacts with a carboxylic acid, with loss of $H_2O$.

Formation of an ester:

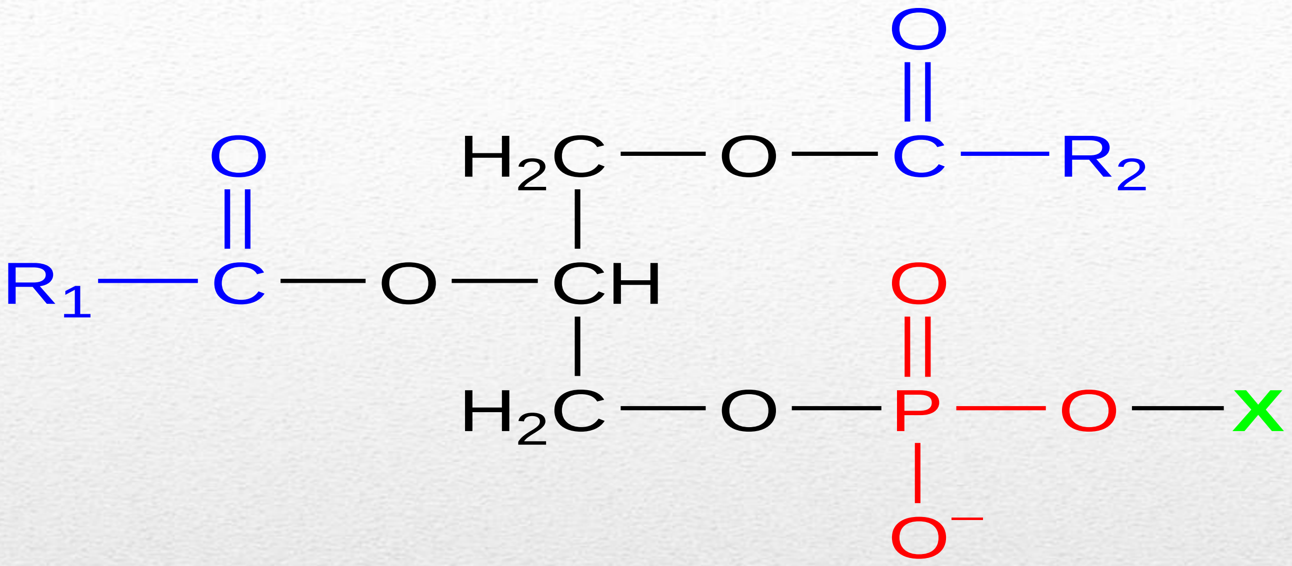
# Phosphatidate




phosphatidate

In **phosphatidate**:

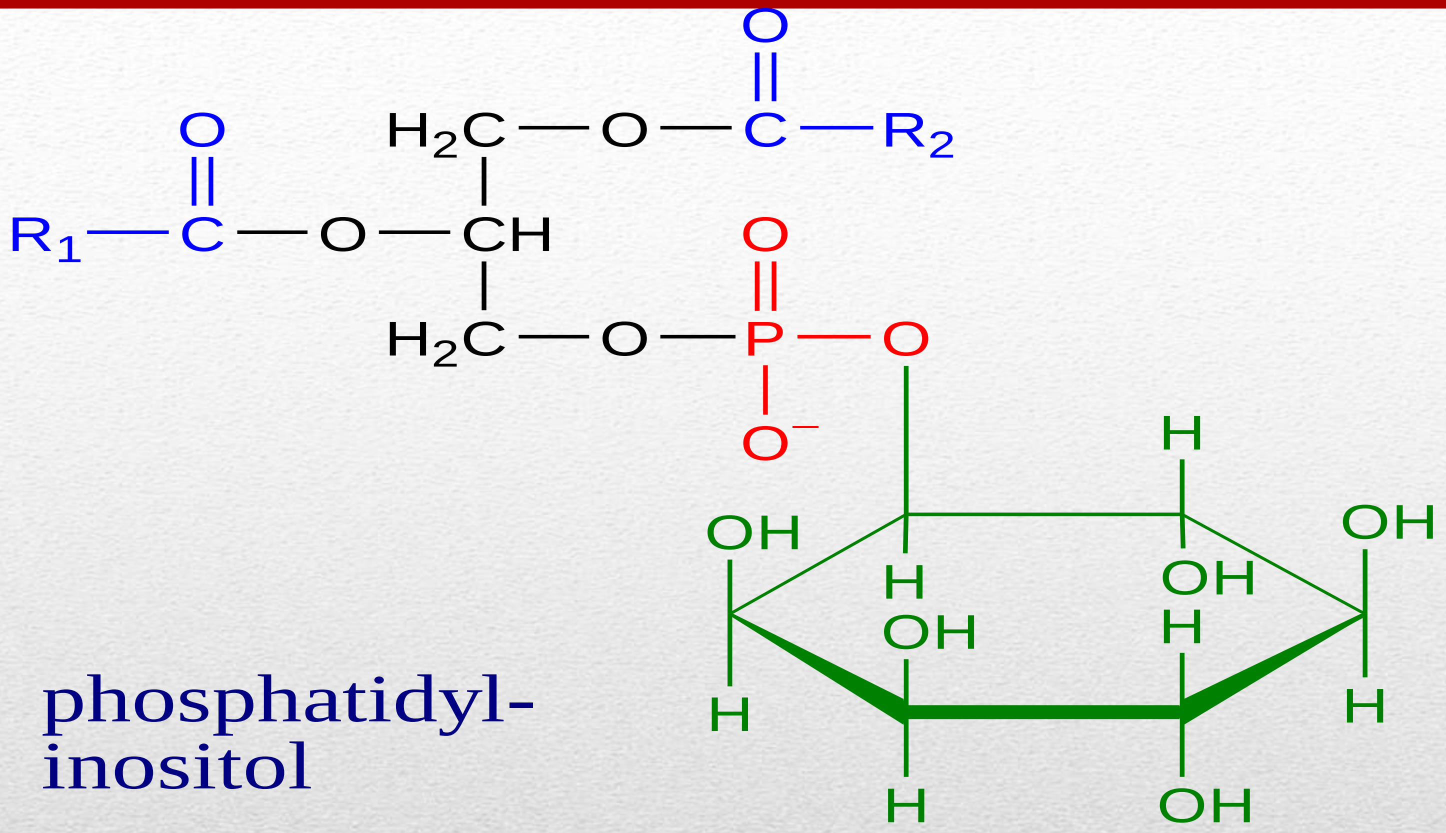
- **fatty acids** are esterified to hydroxyls on **C1** & **C2**
- the **C3** hydroxyl is esterified to **$P_i$**.



glycerophospholipid

In most **glycerophospholipids** (phosphoglycerides),
$P_i$ is in turn esterified to **OH** of a **polar head group** (**X**): e.g., **serine, choline, ethanolamine, glycerol, or inositol**.

The 2 fatty acids tend to be non-identical. They may differ in length and/or the presence/absence of double bonds.

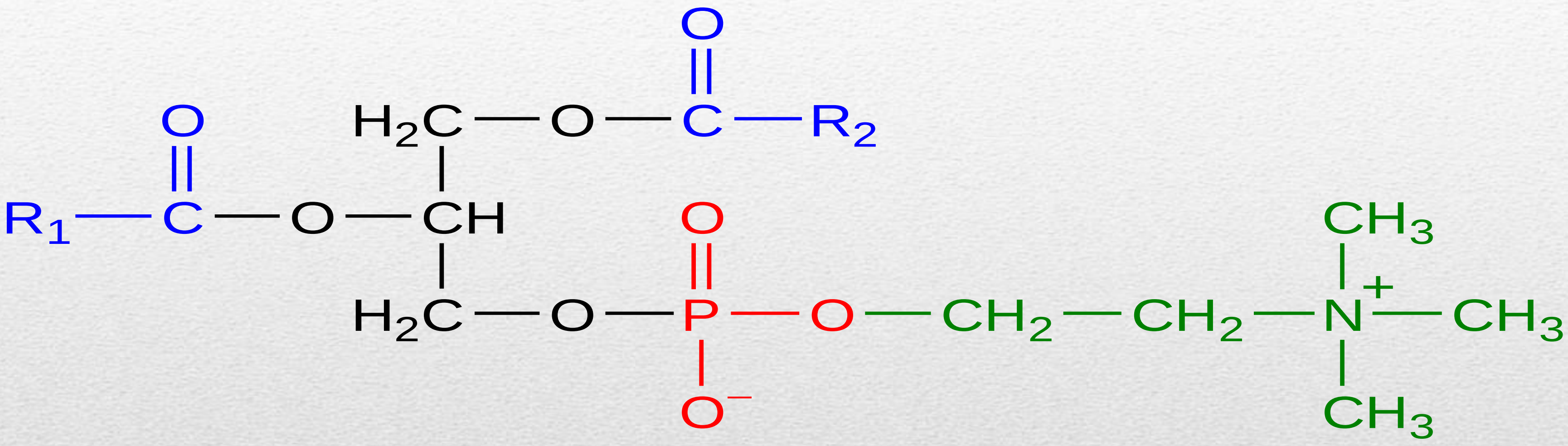



phosphatidyl-
inositol

**Phosphatidylinositol**, with inositol as polar head group, is one glycerophospholipid.

In addition to being a membrane lipid, phosphatidylinositol has roles in cell signaling.

# LECITHIN




phosphatidylcholine

**Phosphatidylcholine**, with choline as polar head group, is another glycerophospholipid.

It is a common membrane lipid.

# CEPHALIN

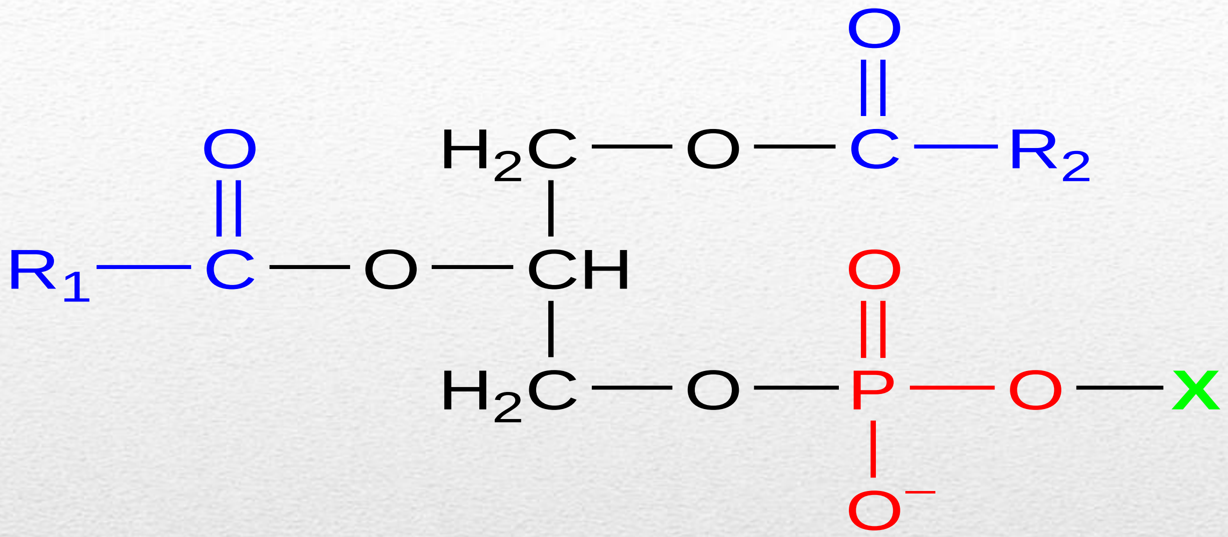
- It contains ethanolamine ($-CH_2-CH_2-N^+H_3$) as head group, thus also known as **phosphatidyl ethanolamine**.

# Phosphatidyl Serine

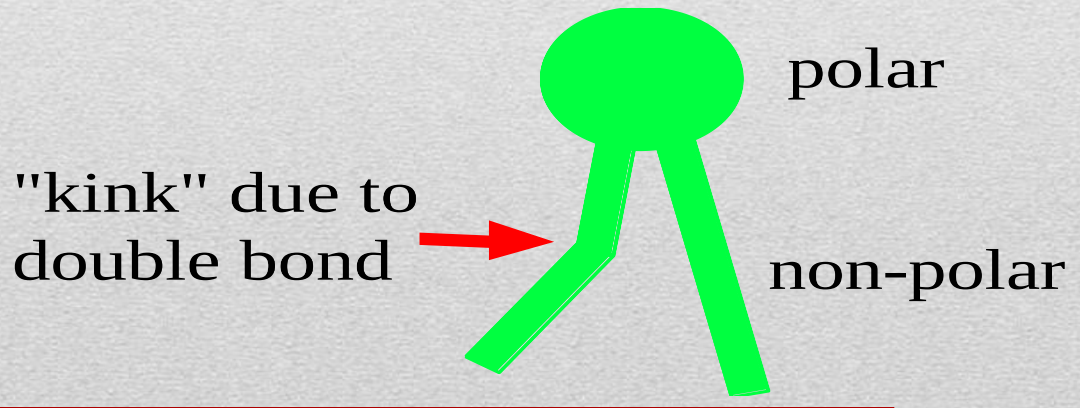
- the head group is serine ($-CH_2-CH.COO^{-}-N^{+}H_3$).
- It plays a key role in **cell cycle signaling**, specifically in relationship to apoptosis.
- It also has a role in blood clotting.

Each glycerophospholipid includes

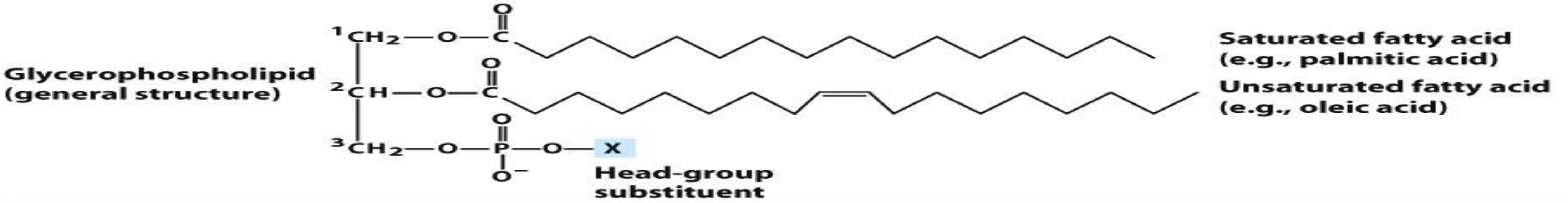
- a **polar** region: **glycerol**, **carbonyl O** of fatty acids, **$P_i$**, & the polar head group (**X**)
- **non-polar** hydrocarbon tails of fatty acids (**$R_1$**, **$R_2$**).

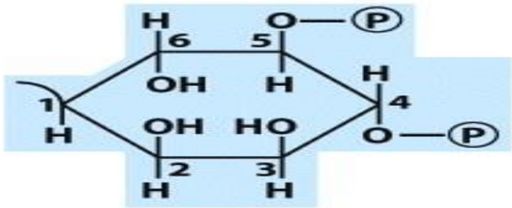
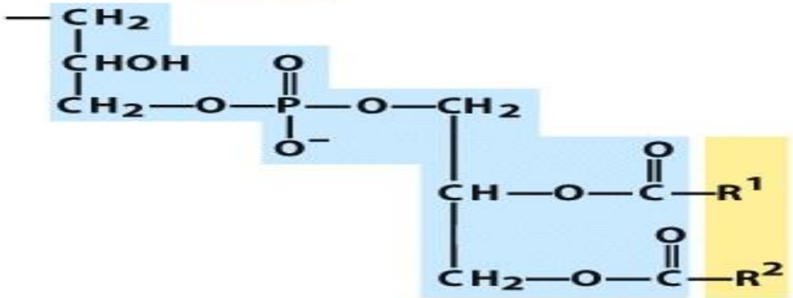


glycerophospholipid



# Structure of phospholipids

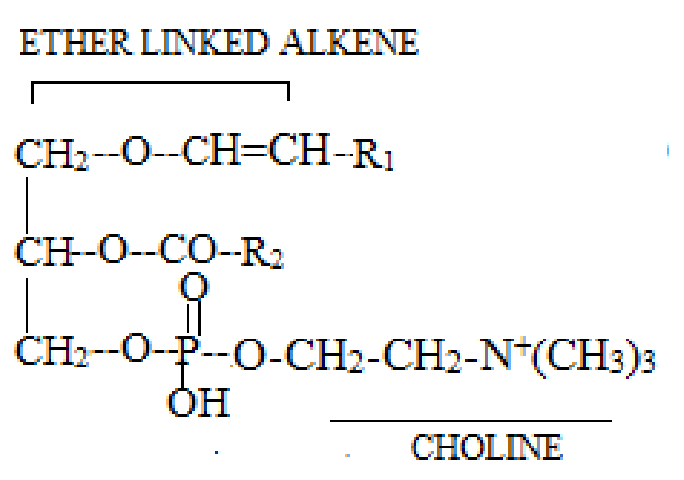



| Name of glycerophospholipid | Name of X | Formula of X | Net charge (at pH 7) |
|---|---|---|---|
| Phosphatidic acid | — | — H | − 1 |
| Phosphatidylethanolamine | Ethanolamine | $—CH_2—CH_2—\overset{+}{N}H_3$ | 0 |
| Phosphatidylcholine | Choline | $—CH_2—CH_2—\overset{+}{N}(CH_3)_3$ | 0 |
| Phosphatidylserine | Serine | $—CH_2—CH(COO^-)—\overset{+}{N}H_3$ | − 1 |
| Phosphatidylglycerol | Glycerol | $—CH_2—CH(OH)—CH_2—OH$ | − 1 |
| Phosphatidylinositol 4,5-bisphosphate | *myo*-Inositol 4,5-bisphosphate |  | − 4 |
| Cardiolipin | Phosphatidyl-glycerol |  | − 2 |

# ETHER LINKED PHOSPHOLIPIDS

- in which one of the two acyl chains is attached to glycerol in ether linkage rather than usual ester linkage
- Two types:
  - Plasmalogens
  - Platelet Activating Factor (PAF)

# Plasmalogens

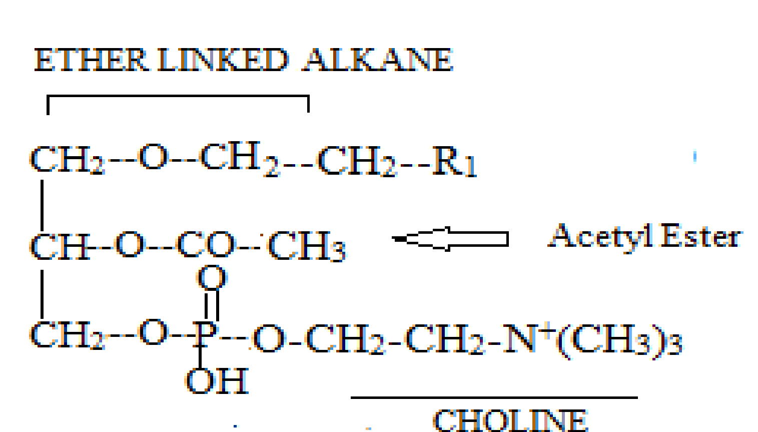



- They have an **alkene** attached in ether linka rol with a fatty acid.
- Part of membranes,
- They also function as antioxidants.
- As antioxidants, they have protective effects against oxidative stress.
- The antioxidant activity comes from the **enol ether double bond** being targeted by a variety of reactive oxygen species

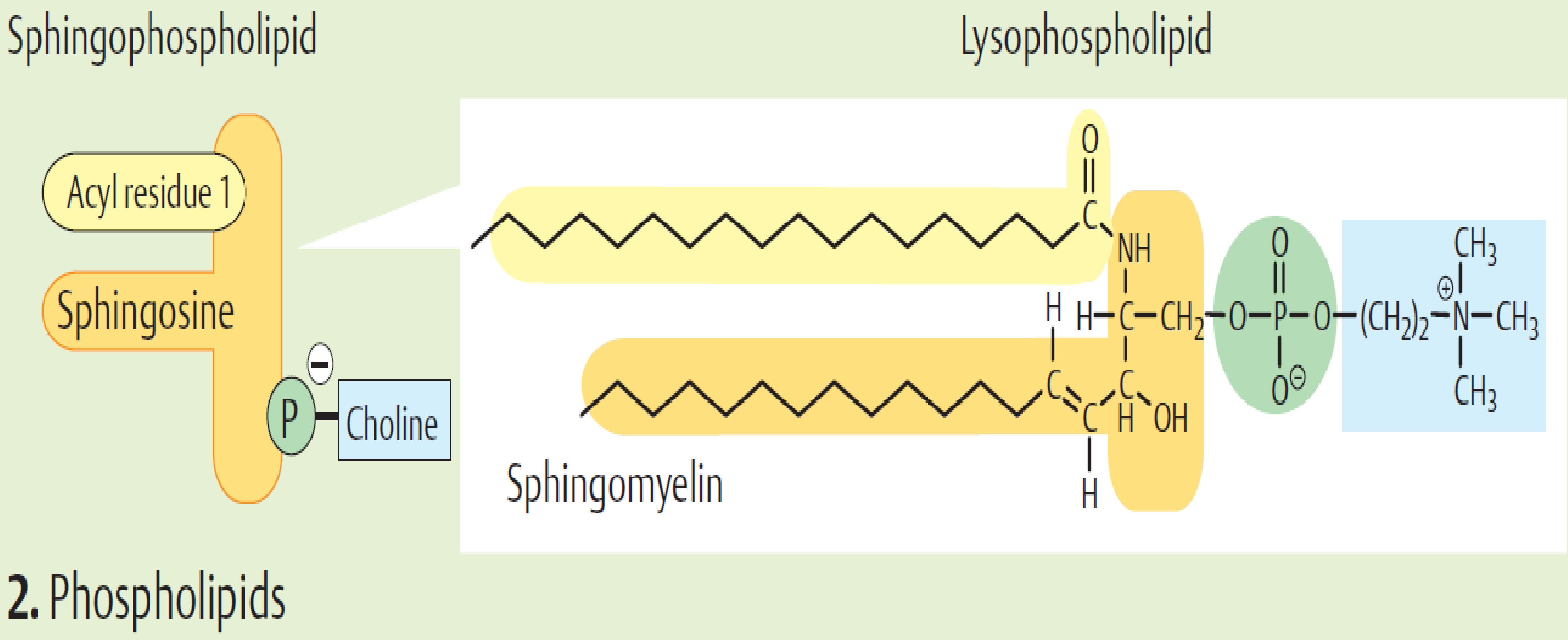
# PAF

- They have an **alkane** attached in ether linkage at first position of glycerol with a fatty acid and at second position.
- They essentially have an acetyl ester.
- Choline is also present as nitrogenous base.
- functions as a mediator of hypersensitivity, acute inflammatory reactions and anaphylactic shock.
- Synthesized in response to the formation of antigen-IgE complexes on the surfaces of basophils, neutrophils, eosinophils, macrophages and monocytes.
- The synthesis and release of PAF from cells leads to platelet aggregation and the release of serotonin from platelets.
- Serotonin is a vasoconstrictor and thus help in blood clotting.
- Also exert a variety of effects on liver, smooth muscles, heart,

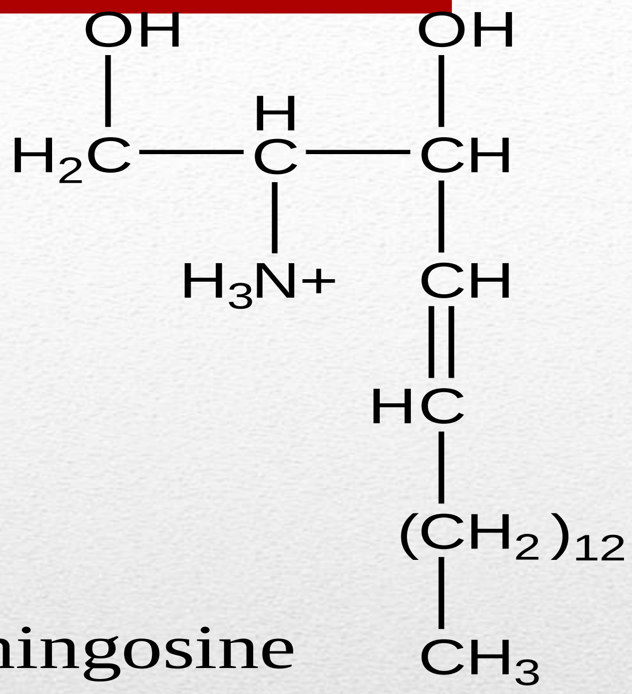
uterus and lung tissues, playing important role in inflammation & allergic response.



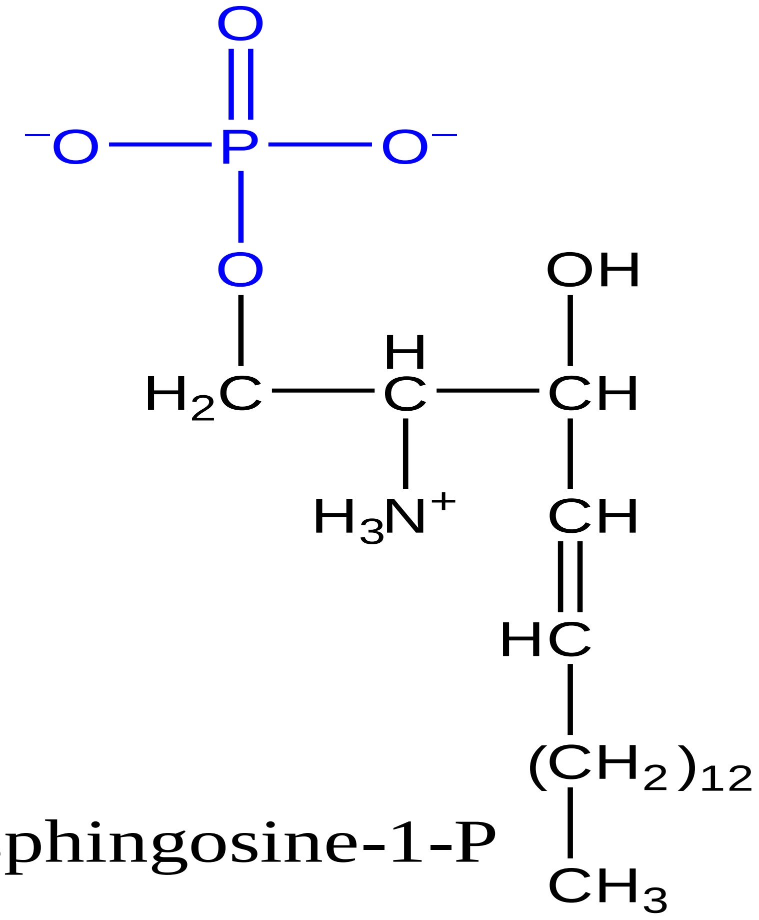
# SPHINGOPHOSPHOLIPID



**Sphingolipids** are derivatives of the lipid **sphingosine**, which has a long hydrocarbon tail, and a polar domain that includes an amino group.




sphingosine



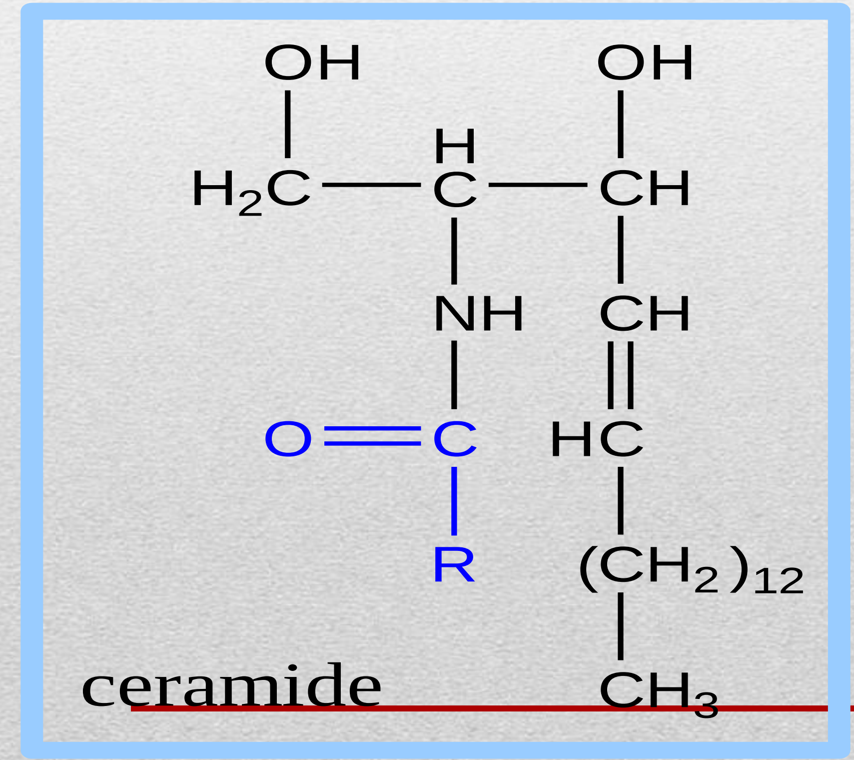

sphingosine-1-P

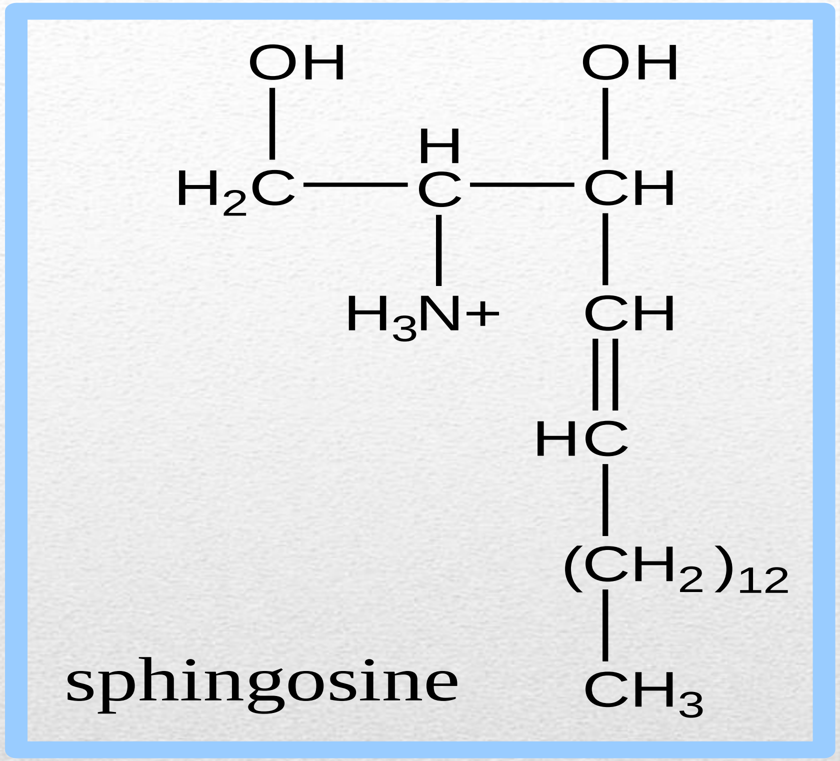
Sphingosine may be reversibly phosphorylated to produce the **signal** molecule **sphingosine-1-phosphate**.

Other derivatives of sphingosine are commonly found as constituents of biological membranes.

## Ceramide

The amino group of sphingosine can form an amide bond with a **fatty acid** carboxyl, to yield a **ceramide**.



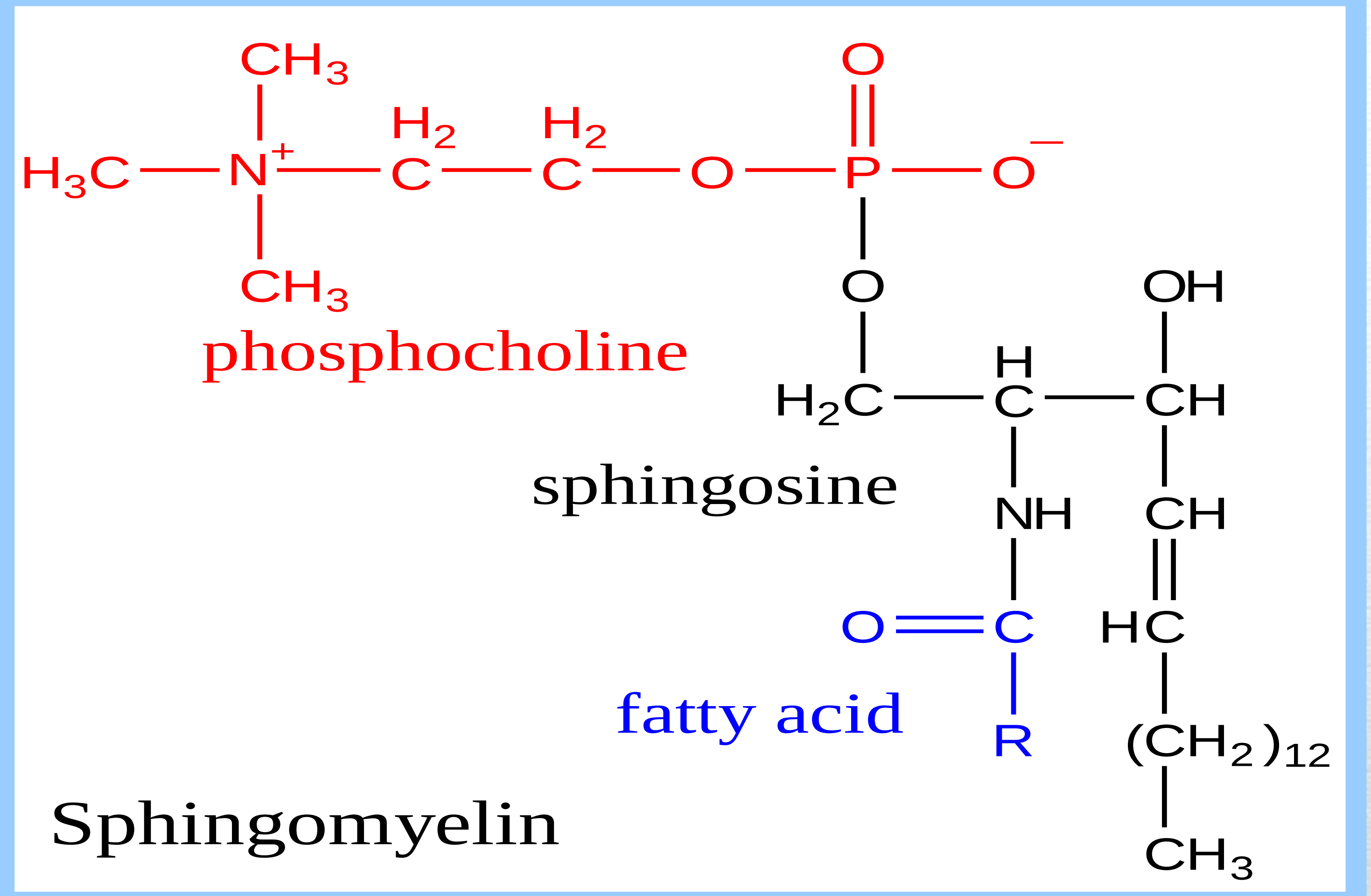




In the more complex sphingolipids, a **polar "head group"** is connected to the terminal hydroxyl of the sphingosine moiety of the ceramide.

## Sphingomyelin

**Sphingomyelin** has a phosphocholine or phosphethanolamine head group.

Sphingomyelins are common constituent of plasma membranes.




Sphingomyelin, with a phosphocholine head group, is similar in size and shape to the glycerophospholipid phosphatidyl choline.

# Functions of phospholipids

- In association with proteins phospholipids form the structural components of membranes and regulate membrane permeability.

- Phospholipids participate in the absorption of fat from the intestine.

- Essential for the synthesis of different lipoproteins, and thus participate in the transport of lipids.

- Accumulation of fat in liver (fatty liver) can be prevented by phospholipids, hence they are regarded as lipotropic factors.

- Arachidonic acid, an unsaturated fatty acid liberated from phospholipids, serves as a precursor for the synthesis of eicosanoids (prostaglandins, prostacyclins, thromboxanes etc.).

# Functions of phospholipids

- Phospholipids participate in the reverse cholesterol transport and thus help in the removal of cholesterol from the body.

- Phospholipids act as surfactants (agent lowering surface tension).

- Cephalins,an important group of phospholipids participatin blood clotting.

- Phospholipids( phosphatidyl inositoal ) involved in signal transmission across membranes.

# GLYCOLIPIDS

FA + ALCOHOL[SPINGOSINE] +CARBOHYDRATE WITH NITROGEN BASE

- They do not contain phosphate group

Example

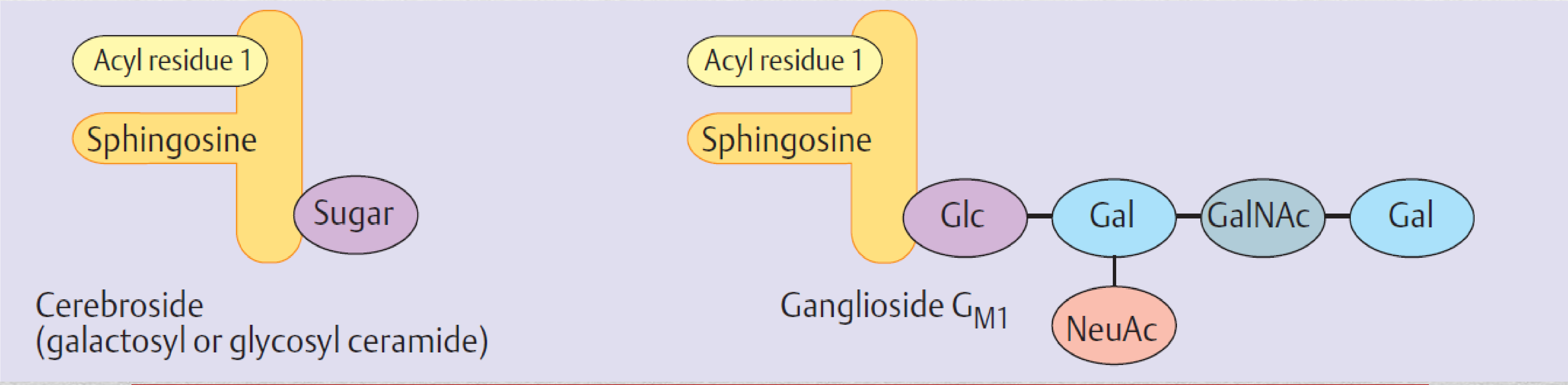
- ✓Cerebrosides
- ✓Gangliosides

## Cerebroside

- The head group in these cases is either galactose or glucose.

## Ganglioside

- They have oligosaccharides and one or more residues of N- Acetyl Neuraminic Acid (Sialic acid).
- They are present in ganglions of nervous tissue.



# LIPOPROTEINS

Lipid with prosthetic group PROTEIN

- ✓Chylomicrons
- ✓Very low density lipoprotein (VLDL)
- ✓Intermediate density lipoprotein (IDL)
- ✓Low density lipoprotein (LDL)
- ✓High density lipoprotein (HDL)

# Lipo proteins

- Formed by combination of proteins with lipids.
- Blood lipoproteins are present in plasma and are used for the **transport** of lipids as lipoprotein complexes.
- These complexes contain triacylglycerol lipid droplets and cholesteryl esters surrounded by the polar phospholipids and **proteins identified as apolipoproteins**.
- These lipid-protein complexes vary in their content of lipid and protein. They are categorized based on their density as—
  - Chylomicrons
  - Very Low Density Lipoprotein (VLDL)
  - Intermediate Density Lipoproteins (IDL)
  - Low Density Lipoproteins (LDL)
  - High Density Lipoproteins (HDL)

# Chylomicrons

- are assembled in the intestinal mucosa as a means to transport dietary cholesterol and triacylglycerols to the rest of the body.
- are the molecules formed to **mobilize dietary (exogenous) lipids**.
- Predominant lipids of chylomicrons are triacylglycerols (TG).
- The apolipoproteins include apoB-48 and apoA-I, -A-II and IV.

# Very Low Density Lipoproteins (VLDLs)

- The dietary excess of fat and carbohydrate is converted to triacylglycerols in the liver.
- These triacylglycerols are packaged into VLDLs and released into the circulation for delivery to the various tissues
- VLDLs are, therefore, the molecules formed to **transport endogenously derived triacylglycerols** to extra-hepatic tissues.
- VLDLs also contain **some cholesterol** and cholesteryl esters
- Apoproteins in VLDL include: apoB-100, apoC-I, apoC-II, apoC-III and apoE.

# Intermediate Density Lipoproteins (IDLs)

- IDLs are formed when triacylglycerols are removed from VLDLs.
- The fate of IDLs is either conversion to LDLs or direct uptake by the liver.
- Conversion of IDLs to LDLs occurs as more triacylglycerols are removed.
- The liver takes up IDLs after they have interacted with the LDL receptor to form a complex, which is endocytosed by the cell.

# Low Density Lipoproteins (LDLs)

- Cholesterol synthesized by the liver can be transported to extra-hepatic tissues if packaged in VLDLs. In the circulation VLDLs are converted to LDLs through the action of lipoprotein lipase.
- LDLs are the **primary plasma carriers of cholesterol** for delivery to all tissues.
- The exclusive apolipoprotein of LDLs is apoB-100.

# High Density Lipoproteins (HDLs)

- HDLs are synthesized in the liver and small intestine.
- HDLs acquire cholesterol by extracting it from cell surface membranes.
- **Cholesterol-rich HDLs return to the liver**, where they are endocytosed.
- This process has the effect of lowering the level of intracellular cholesterol, since the cholesterol stored within cells as cholesteryl esters will be mobilized to replace the cholesterol removed from the plasma membrane.
- The primary apoproteins of HDLs are apoA-I, apoC-I, apoC-II and apoE.
- In fact, a major function of HDLs is to act as circulating stores of apoC-I, apoC-II and apoE.

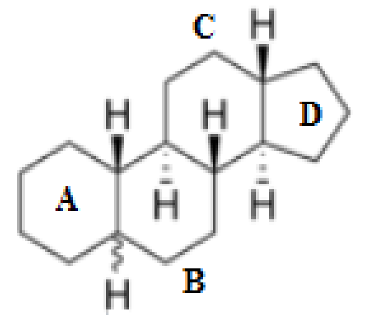
# DERIVED LIPIDS

**These are the derivatives obtained on the hydrolysis of group 1 and group 2 lipids which possess the characteristics of lipids.**

Example

- STEROLS
- BILE ACIDS
- STEROID
- VITAMIN
- EICOSANOIDS

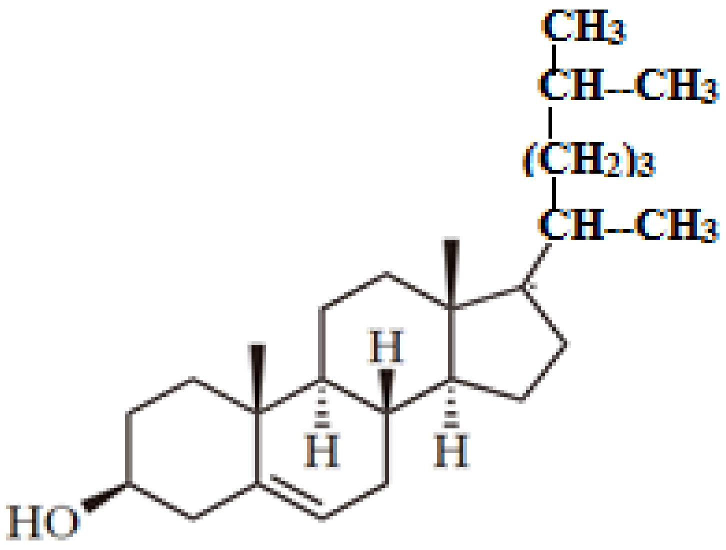
# STEROLS



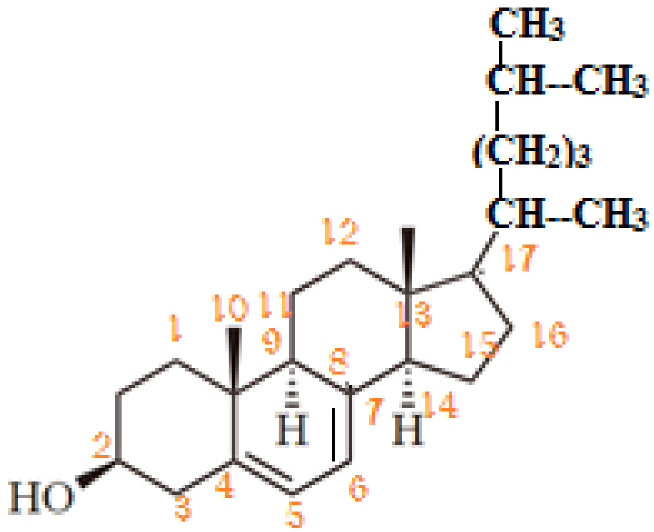

- Sterine + ol; Greek, sterine means solid, so sterols = “solid alcohol”.
- are **structural lipids** present in most eukaryotic cells.
- The sterols and steroids have a common feature of having a phenanthrene nucleus attached to a cyclopentane ring which then collectively called as **cyclopentano perhydrophenanthrene ring** or simply as steroid nucleus.
- composed of 17 carbon atoms in C—C bonds forming 4 fused rings in a three-dimensional shape.
- The three cyclohexane rings (A, B, and C) form the skeleton of a perhydro derivative of phenanthrene.

# CHOLESTEROL & 7 dehydrocholesterol

- Chole + sterol = “solid bile alcohol”
- Present in all animal tissues and accompanied by 7 dehydrocholesterol.
- Is amphipathic with a polar head group (the OH at C-3) and a non polar hydrocarbon body.
- The hydrocarbon side chain is attached at C-17 of steroid nucleus.




**CHOLESTEROL**




**7-DEHYDO CHOLESTEROL**

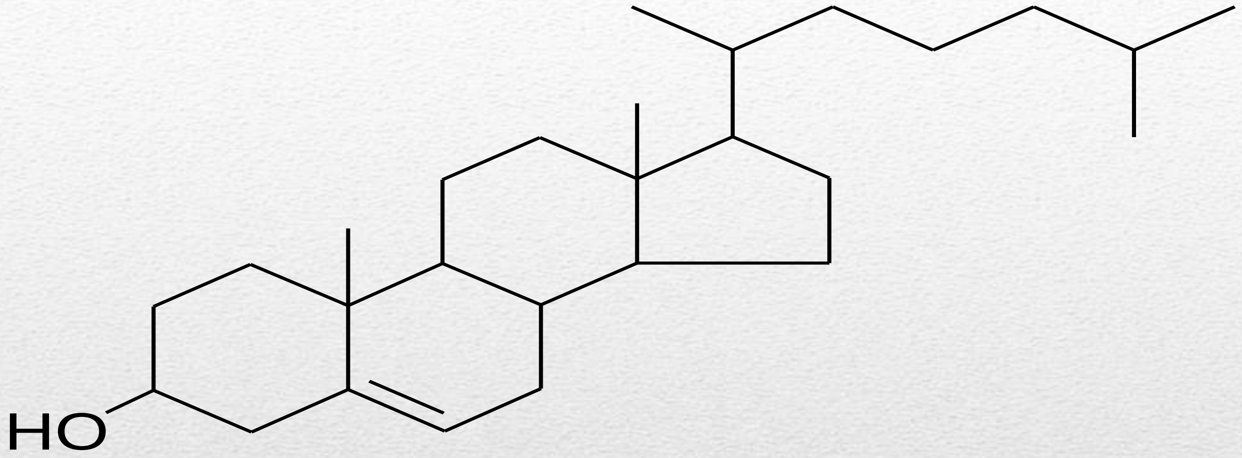
## Cholesterol

- Cholesterol being poor conductor of electricity serves as an insulator against electric discharge.
- In brain thus is found abundantly.
- Main component of animal cell membrane
- Essential to maintain membrane structural **integrity and fluidity**.
- Thus animal cells do not need to build cell walls like plants and most bacteria.
- Within the cell membrane, cholesterol also functions in **intracellular transport, cell signaling and nerve conduction**.

## 7-Dehydrocholesterol

- functions as cholesterol precursor.
- **Provitamin-$D_3$**: Converted to vitamin $D_3$ (cholecalciferol) in the skin by UV irradiation.

**Cholesterol**, an important constituent of cell membranes, has a **rigid** ring system and a short branched hydrocarbon tail.




Cholesterol

Cholesterol is largely **hydrophobic**.

But it has one polar group, a **hydroxyl**, making it **amphipathic**.

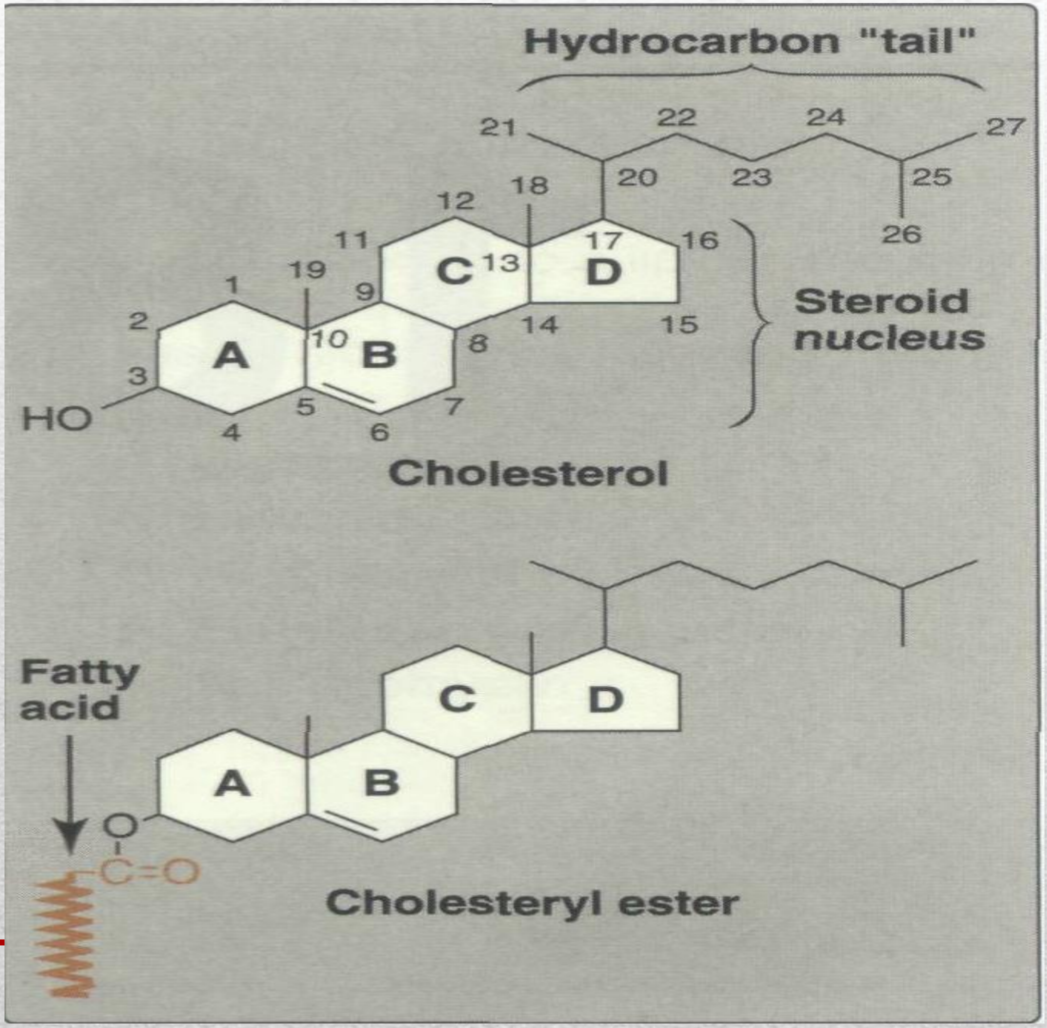
# Structural features of cholesterol (Chol) and cholesteryl esters (Chol-esters)

*Cholesterol*

- Four fused hydrocarbon rings (A, B, C, and D, called the "steroid nucleus"
- C8 branched hydrocarbon chain attached to C17
- Hydroxyl group at C-3
- Double bond between C-5 and C-6
- Sterols: Steroids with 8 to 10 C in sides chain and hydroxyl group at C-3
- Cholesterol does not occur in plants

*Cholesteryl esters*

- Most plasma cholesterol is in an esterified form.
- More hydrophobic than Chol
- Not in membranes



**Cholesterol** inserts into bilayer membranes with its hydroxyl group oriented toward the aqueous phase & its hydrophobic ring system adjacent to fatty acid chains of phospholipids.

The **OH** group of cholesterol forms hydrogen bonds with polar phospholipid head groups.

## **Two strategies** by which phase changes of membrane lipids are avoided:

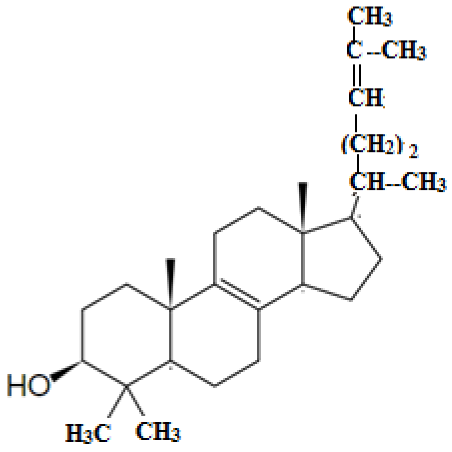
- **Cholesterol** is abundant in membranes, such as plasma membranes, that include many lipids with long-chain saturated fatty acids.

  In the absence of cholesterol, such membranes would crystallize at physiological temperatures.

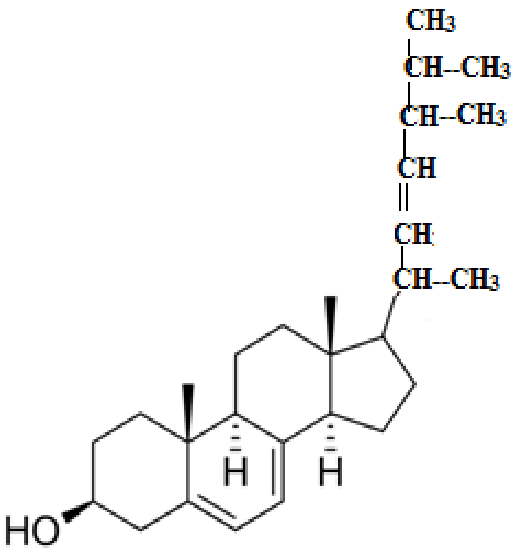
- The inner mitochondrial membrane lacks cholesterol, but includes many phospholipids whose fatty acids have one or more **double bonds**, which **lower the melting point** to below physiological temperature.

- **Lanosterol** is present in wools and it is considered to be the main compound from which all animal and fungal sterols are derived.

- **Ergosterol** is found in cell membranes of fungi and protozoa and serves almost the same functions as of cholesterol in animal cells. Ergosterol is a provitamin form of vitamin $D_2$ (ergocalciferol or calciferol).



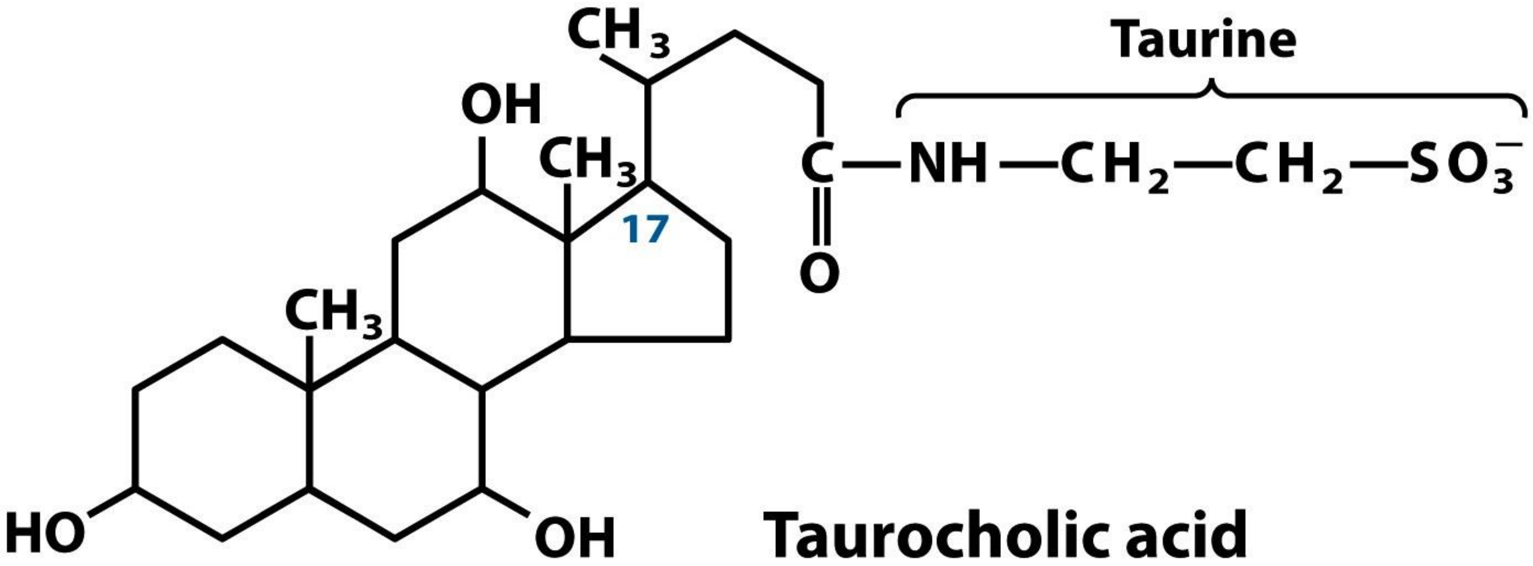
LANOSTEROL



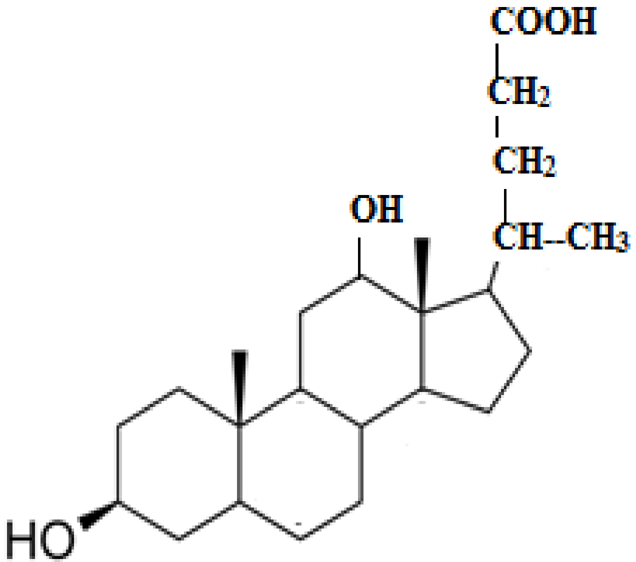
ERGOSTEROL

# BILE ACIDS

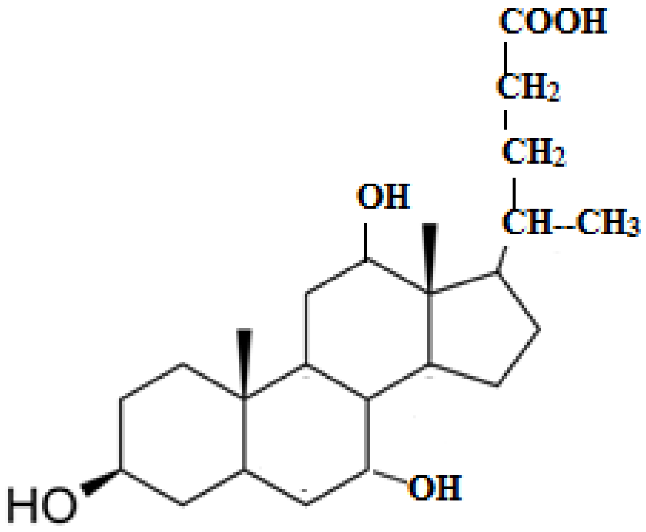
- are polar derivative of cholesterols & act as detergents in the intestine, thus helping in fat digestion
- Bile salts or bile acids constitute the major pathway for the excretion of cholesterol in mammals.
- They have **5 carbon side chain** at C-17 of steroid nucleus that terminate in –COOH.
- The carboxyl group may combine with glycine and taurine to make glycocholic and taurocholic acid.



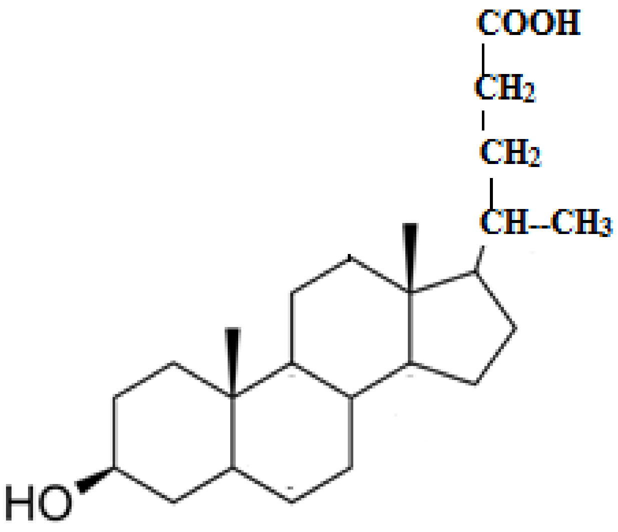

**Taurocholic acid**
**( a bile acid)**




DEOXYCHOLIC ACID




CHOLIC ACID




LITHOCHOLIC ACID

# STEROIDS

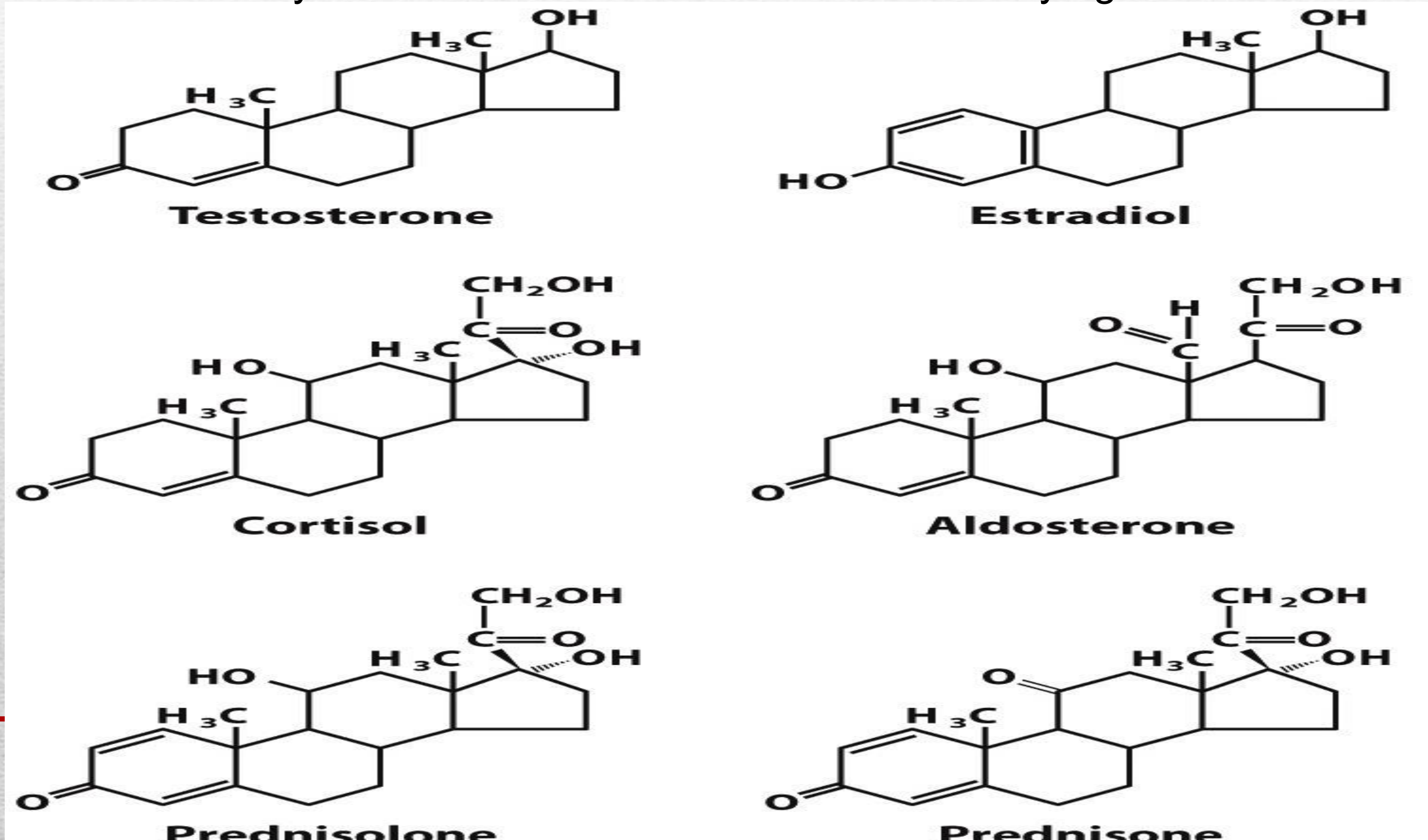
- are oxidized derivative of sterols.
- Have steroid nucleus but lack the alkyl chain attached to C-17
- Mostly act as hormone.
- They all are derived from cholesterol.
- Steroid hormones can be grouped into two classes:
  - **Corticosteroids** and
  - **Sex steroids**.
- Within these two classes are five types according to the receptors to which they bind; and they are: glucocorticoids, mineralocorticoids (corticosteroids), androgens, estrogens, and progestogens (sex steroids).

Testosterone, the male sex hormone, is produced in the testes.

Estradiol, one of the female sex hormones, is produced in the ovaries and placenta.

Cortisol and aldosterone are hormones synthesized in the cortex of the adrenal gland; they regulate glucose metabolism and salt excretion.

Prednisolone and prednisone are synthetic steroids used as antiinflammatory agents.



# VITAMIN D

- derived from 7-dehydrocholesterol by the action of the UV component of sunlight on the skin.
- UV light brings **photolysis of 7- dehydrocholesterol between C-9 and -10**, leading to a rearrangement of the double bonds of the molecule to form previtamin D3.
- This molecule spontaneously isomerizes to form **vitamin D3** (**cholecalciferol**).
- Subsequent hydroxylation reactions take place in the liver and kidneys to produce 1,25- dihydroxycholecalcerol (1,25(OH)D3), the active hormone.
- In the same manner, the ergosterol also breaks open the ring to form calciferol or vitamin D2.

# EICOSANOIDS

- Derived from 20 carbon polyunsaturated fatty acid, arachidonic acid (20:4) or from eicosopentaenoic acid (20:5); they are termed as eicosanoids (eicosa/ icosa =20).
- The major source of arachidonic acid is through its release from cellular stores.
- Within the cell, it resides predominantly at the C-2 position of membrane phospholipids and is released from there upon the activation of phospholipase $A_2$.
- The immediate dietary precursor of arachidonate is linoleic acid, whereas α-linolenic acid is precursor of eicosapentaenoate.

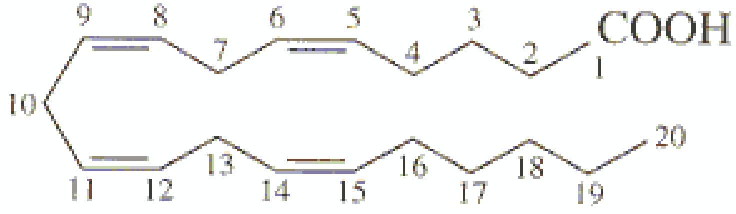
# EICOSANOIDS

- The eicosanoids are **paracrine hormone**.
- The eicosanoids produce a wide range of biological effects on inflammatory responses, on the intensity and duration of pain and fever, and on reproductive function.
- They also play important roles in inhibiting gastric acid secretion, regulating blood pressure through vasodilation or constriction, and inhibiting or activating platelet aggregation and thrombosis.
- 3 classes:
  - **Prostaglandins (PG)**
  - **Thromboxanes (TX)**
  - **Leukotrienes (LT)**

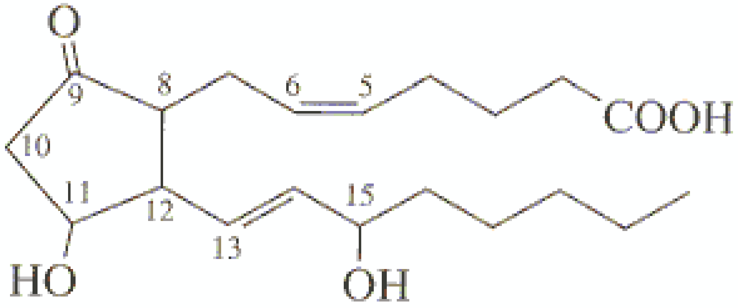
# Functions of the Eicosanoids

Eicosanoids participate in many processes in the body:

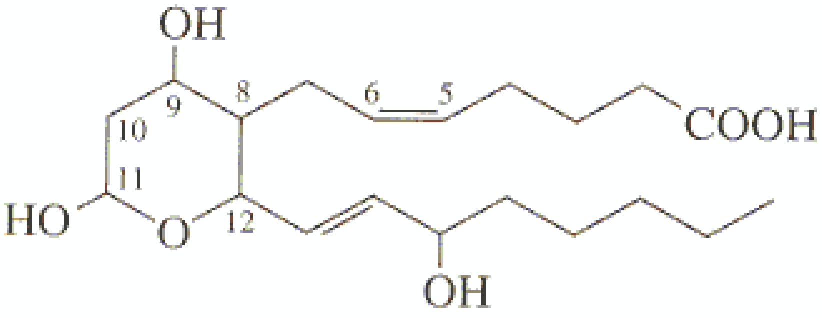
- Inflammatory response that occurs after infection or injury with symptoms such as pain, swelling, and fever. An exaggerated or inappropriate expression of the normal inflammatory response may occur in individuals who have allergic or hypersensitivity reactions
- Contraction of smooth muscles (particularly in the intestine and uterus)
- Increase in the excretion of water and sodium by the kidney
- Regulation of blood pressure
- Regulation of bronchoconstriction and bronchodilation (modulators)



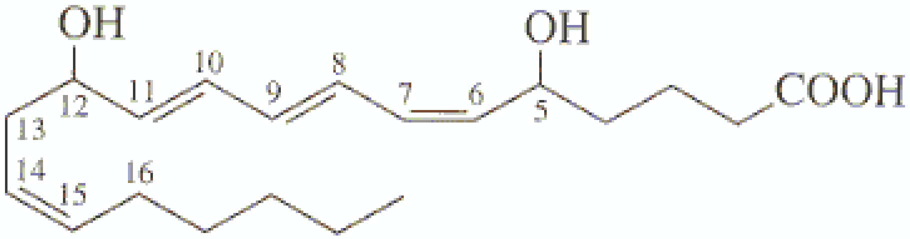

**(a) Arachidonic acid**




**(b) Prostaglandin $E_2$**

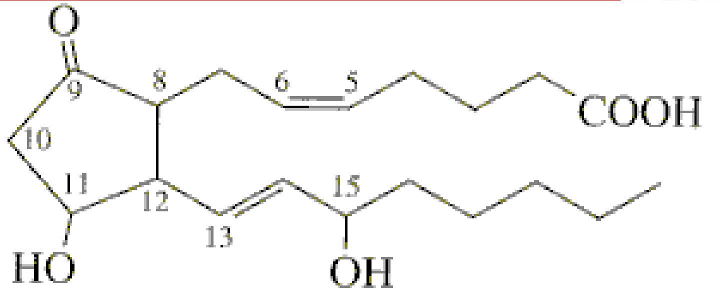



**(c) Thromboxane $B_2$**




**(d) Leukotriene $B_4$**

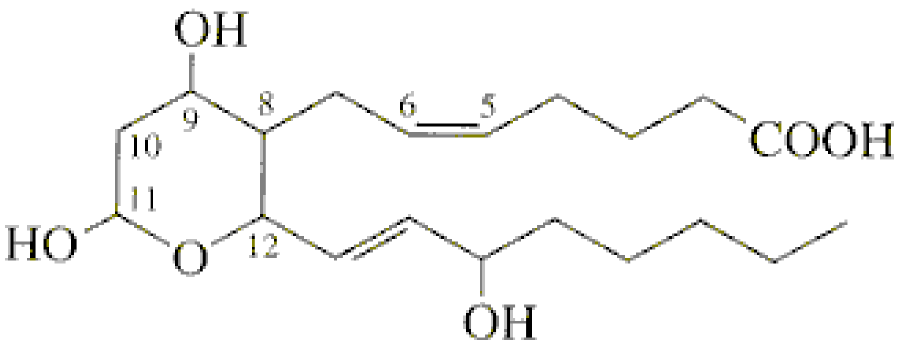
# Prostaglandins (PG)



(b) Prostaglandin $E_2$

- act in many tissues by regulating the synthesis of cAMP which is the intracellular messanger molecule
- Prostaglandins are grouped into two categories, depending on their solubility.
- **PGEs** are ether soluble, where as **PGFs** are phosphate buffer (Fosfat in Sweedish) soluble.
- All PGs show at least some activity in lowering blood pressure and inducing the smooth muscles to contract.
- PGs in another group elevate the body temperature (producing fever) and cause inflammation and pain.

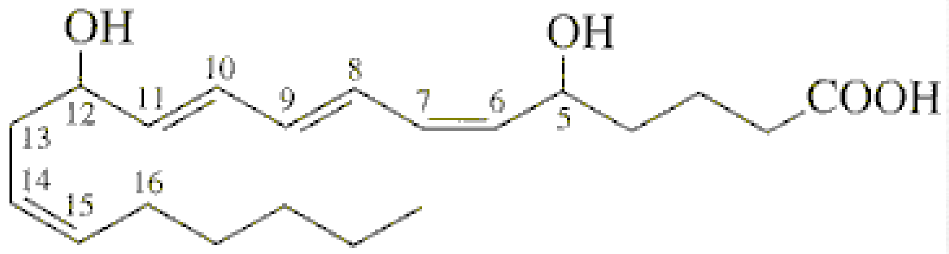
# THROMBOXANES (TX)




(c) Thromboxane $B_2$

- They have a six membered ring containing an ether. They are produced by platelets (Thrombocytes) and act in the formation of blood clots and the reduction of blood flow to the site of a clot.

# LEUKOTRIENES (LT)




(d) Leukotriene $B_4$

- They contain **3 consecutive double bonds**.
- They are powerful biological signals e.g. leukotriene D4 derived from leukotriene A4 induces contraction of muscle lining the airways of lung.
- Overproduction of leukotrienes thus causes asthamatic attacks and leukotriene synthesis is one target in antihistaminic drugs.

# Functions of Eicosanoids

| EICOSANOID | Cell | FUNCTIONS |
|---|---|---|
| $PGD_2$ | Mast cells | Inhibits platelet and leukocyte aggregation, decreases T-cell proliferation and lymphocyte migration and secretion of IL-1α and IL-2; induces vasodilation and production of cAMP |
| $PGE_2$ | Kidney, Spleen, Heart | Increases vasodilation and cAMP production, enhancement of the effects of bradykinin and histamine, induction of uterine contractions and of platelet aggregation, maintaining the open passageway of the fetal ductus arteriosus; decreases T-cell proliferation and lymphocyte migration and secretion of IL-1α and IL-2 |
| $PGF_{2\alpha}$ | Kidney, Spleen, Heart | Increases vasoconstriction, bronchoconstriction and smooth muscle contraction |
| $PGH_2$ | | Precursor to thromboxanes $A_2$and $B_2$, induction of platelet aggregation and vasoconstriction |
| $PGI_2$ | Heart, vascular endothelial cells | Inhibits platelet and leukocyte aggregation, decreases T-cell proliferation and lymphocyte migration and secretion of IL-1α and IL-2; induces vasodilation and production of cAMP |

# Functions of Eicosanoids

| EICOSANOID | Cell | FUNCTIONS |
|---|---|---|
| $TXA_2$ | Platelets | Induces platelet aggregation, vasoconstriction, lymphocyte proliferation and bronchoconstriction |
| $TXB_2$ | Platelets | Induces vasoconstriction |
| $LTB_4$ | Monocytes, Basophils, Neutrophils, Eosinophils, Mast cells, Epithelial cells | Induces leukocyte chemotaxis and aggregation, vascular permeability, T-cell proliferation and secretion of INF-γ, IL-1 and IL-2 |
| $LTC_4$ | Monocytes alveolar macrophages basophils, eosinophils, mast & epithelial cells | Component of SRS-A, microvascular vasoconstrictor, vascular permeability and bronchoconstriction and secretion of INF-γ |
| $LTD_4$ | Monocytes and alveolar macrophages, eosinophils, mast cells, epithelial cells | Predominant component of SRS-A, microvascular vasoconstrictor, vascular permeability and bronchoconstriction and secretion of INF-γ |
| $LTE_4$ | Mast cells and Basophils | Component of SRS-A (slow-reactive substance of anaphylaxis), microvascular vasoconstrictor and bronchoconstriction |