LIPIDS

INTRODUCTION TO BIOCHEMISTRY

R. MAITI

LECTURER IN PHARMACY

LIPIDS

- Diverse hydrophobic molecules which are insoluble in water (and other polar solvents) and soluble in non-polar molecules like ether and chloroform
- Made of C,H,O
- No general formula.
- C:O ratio is very high in C
- Lipids are either compounds that yield fatty acids on hydrolysis and complex alcohols that can combine with fatty acids to form esters.

CLASSIFICATION OF LIPIDS

Glycerol Esters:

- Triglycerides, diglycerides, and monoglycerides (acyleglycerol).
- Phosphglycerides.

Sphingosine Derivatives:

- Sphingomyellin.
- Glycosphingolipids.

Terpenes (Isoprene Polymers):

- Vitamin A.
- Vitamin E.
- Vitamin K.

Sterol Derivatives:

- *Cholesterol and Cholesterol esters.*
- *Steroid hormones.*
- *Bile acids*
- *Vitamin D.*

Fatty Acids

RCOOH is a general chemical formula for a *fatty acid* where R is alkyl chain.

Fatty acid chain lengths vary and commonly are classified according to the number of carbon atom present.

The defined groups of fatty acids are:-

- Short chain (2 to 4 carbon atoms).
- Medium chain (6to 10 carbon atoms).
- Long chain (12 to 26carbon atoms).

Those of importance in human nutrition and metabolism are of the long chain class containing

Fatty Acids

Fatty acids are classified further according to their degree of saturation:

- Saturated Fatty acids have no double bonds between carbon atoms.
- Monounsaturated Fatty acids contain one double bond .
- Polyunsaturated Fatty acids contain more than one double bond .

The double bonds in polyunsaturated fatty acids of both animals and plant origin are usually three carbon atoms apart.

Fatty Acids

The labeling of the carbon atoms in Fatty acids can be either from the carboxyl terminal (Δ- numbering system), or methyl terminal (ɳ- or ɯ-numbering system). And etc…

For example Linoleic acid which contain 18 carbons and two unsaturated bonds between carbons 9 and 10 and between carbons 12 and 13, can be written as ($C_{18}:2_{9-}^{12}$).

By use of the (ɳ- or ɯ-numbering system) the linoleic acid would be abbreviated to ($C_{18}:2_{n-6}$) in which only the first carbon forming the unsaturated pair is written.

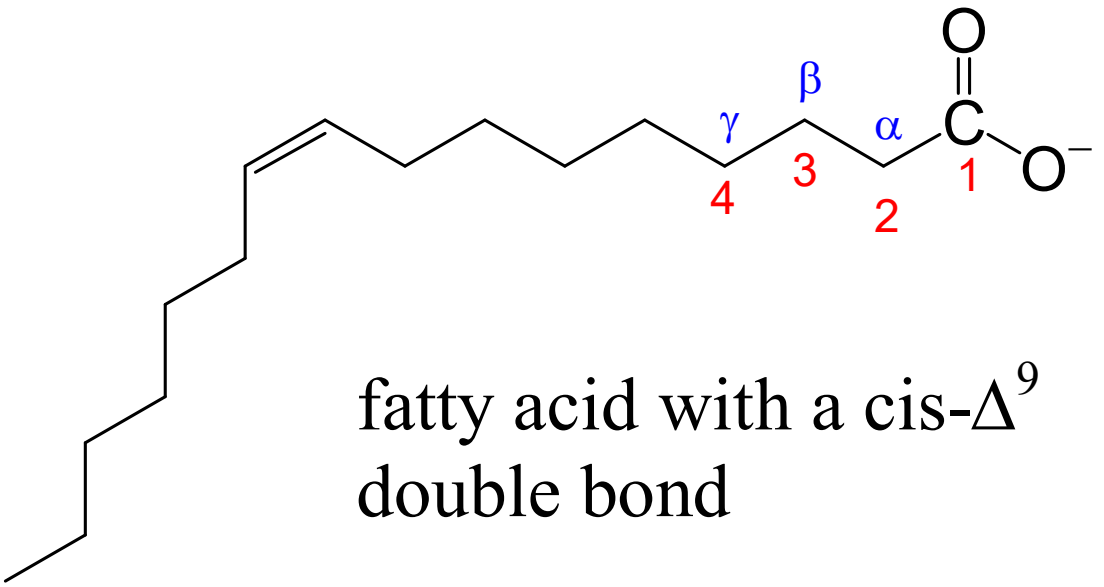
Fatty Acids

- **Lipids are non-polar** (hydrophobic) compounds, soluble in organic solvents.
- Most membrane lipids are **amphipathic**, having a **non-polar** end and a **polar** end.
- **Fatty acids** consist of a hydrocarbon chain with a carboxylic acid at one end.
- A 16-C fatty acid: $CH_3(CH_2)_{14}\text{-}COO^-$

  Non-polar **polar**
- A 16-C fatty acid with one cis double bond between C atoms 9-10 may be represented as **16:1 cis Δ^9**.

Double bonds in fatty acids usually have the **cis** configuration.

Most naturally occurring fatty acids have an **even number** of carbon atoms.



fatty acid with a cis-Δ^9 double bond

Some fatty acids and their common names:

14:0 myristic acid; 16:0 palmitic acid; 18:0 stearic acid;

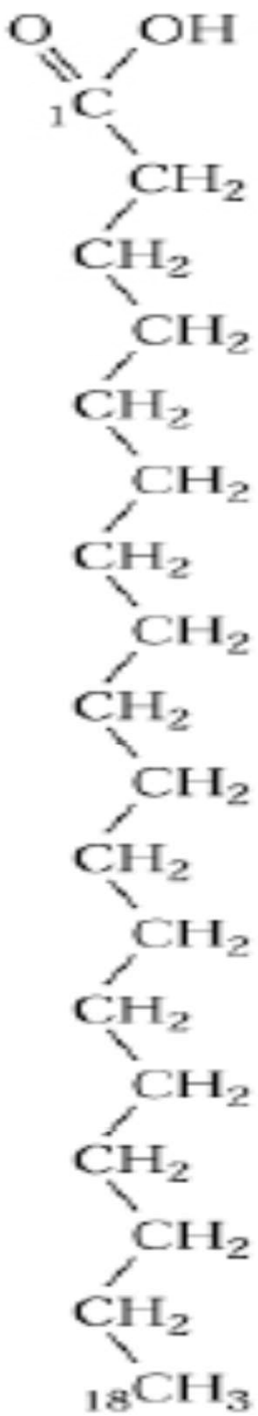
18:1 cisΔ^9 oleic acid

18:2 cis$\Delta^{9,12}$ linoleic acid

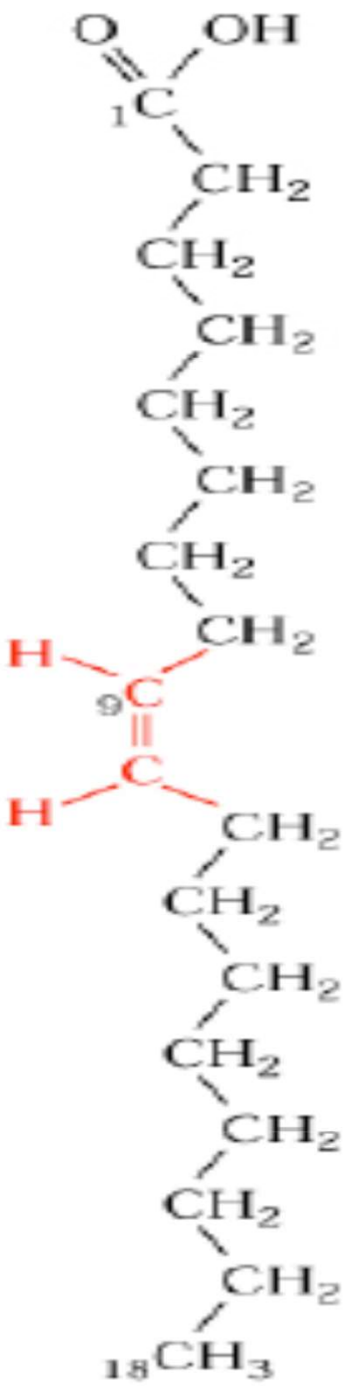
18:3 cis$\Delta^{9,12,15}$ linonenic acid (an omega-3)

20:4 cis$\Delta^{5,8,11,14}$ arachidonic acid

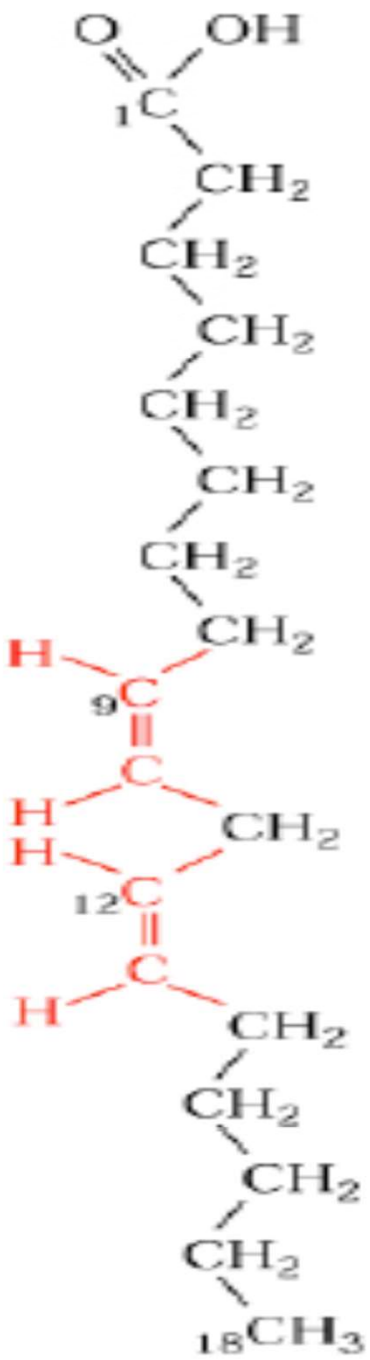
20:5 cis$\Delta^{5,8,11,14,17}$ eicosapentaenoic acid (an omega-3)



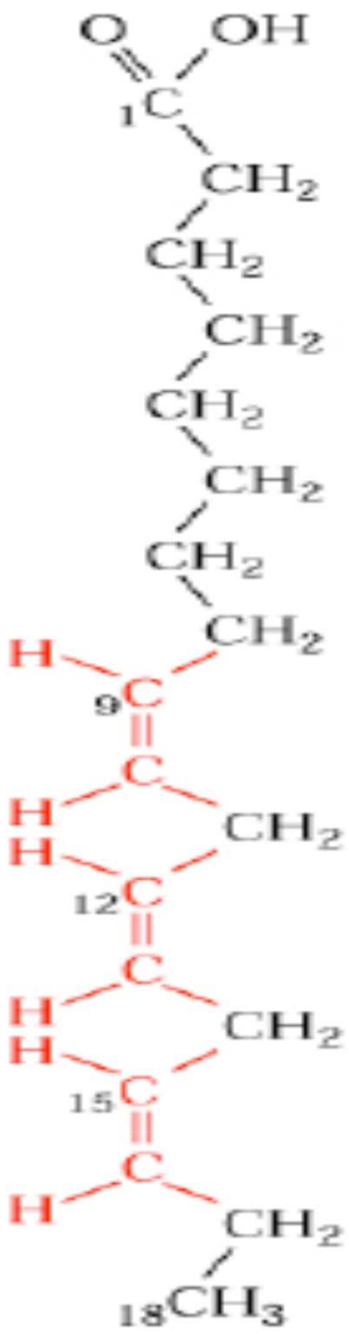
Stearic acid



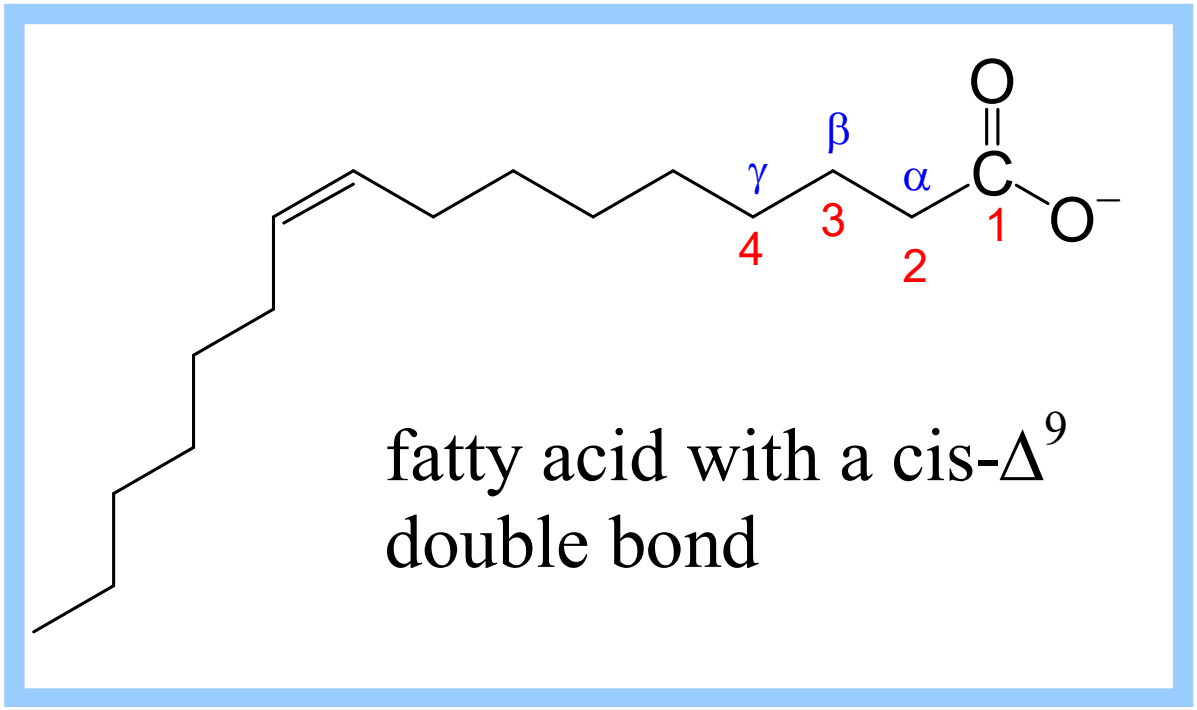
Oleic acid



Linoleic acid



α-Linolenic acid



There is free rotation about **C-C** bonds in the fatty acid hydrocarbon, except where there is a double bond.

Each cis double bond causes a **kink** in the chain.

Rotation about other **C-C** bonds would permit a more linear structure than shown, but there would be a kink.

Fatty Acids

Humans can synthesize most fatty acids, including saturated, monounsaturated, and some polyunsaturated fats.

However , some fatty acids cannot be synthesized like linolenic acid which is found only in plants.

Because it is not synthesized but is vital for **health**, **growth**, and **development**, it is termed essential fatty acid.

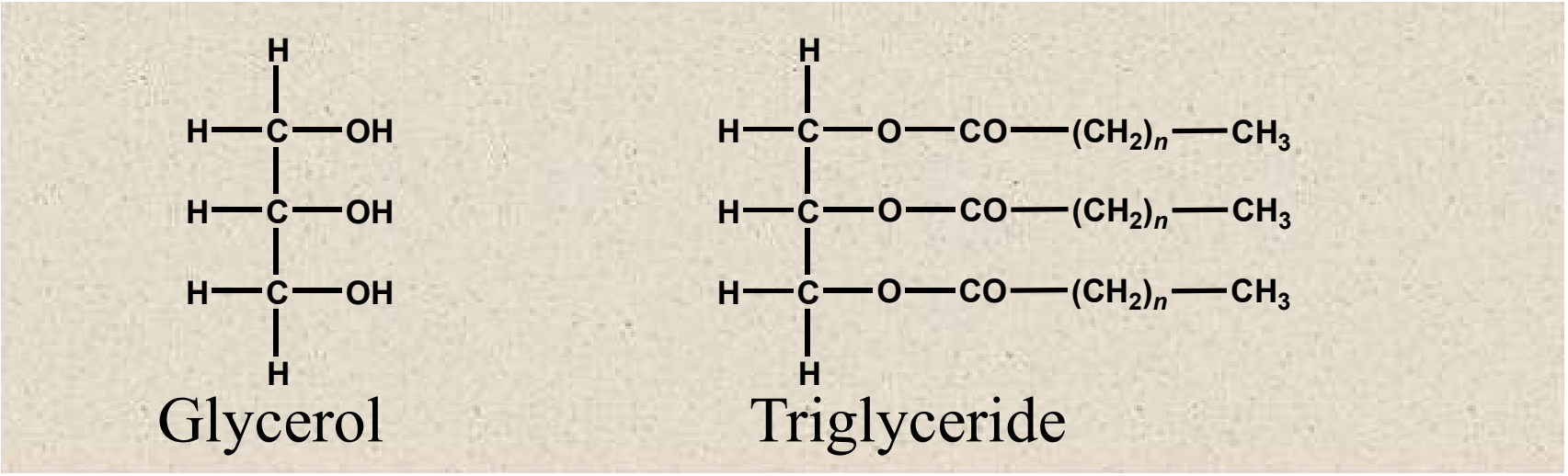
(required for the biosynthesis of prostaglandin).

Clinical importance of fatty acids

- Fecal fatty acids are sometimes measured to detect malabsorptive and pancreatic disorders—the test is mostly considered obsolete.
- Serum free fatty acids help distinguish between hyperinsulinemic hypoglycemia (FFA normal) and disorders of fatty acid oxidation (FFA elevated and negative ketones)

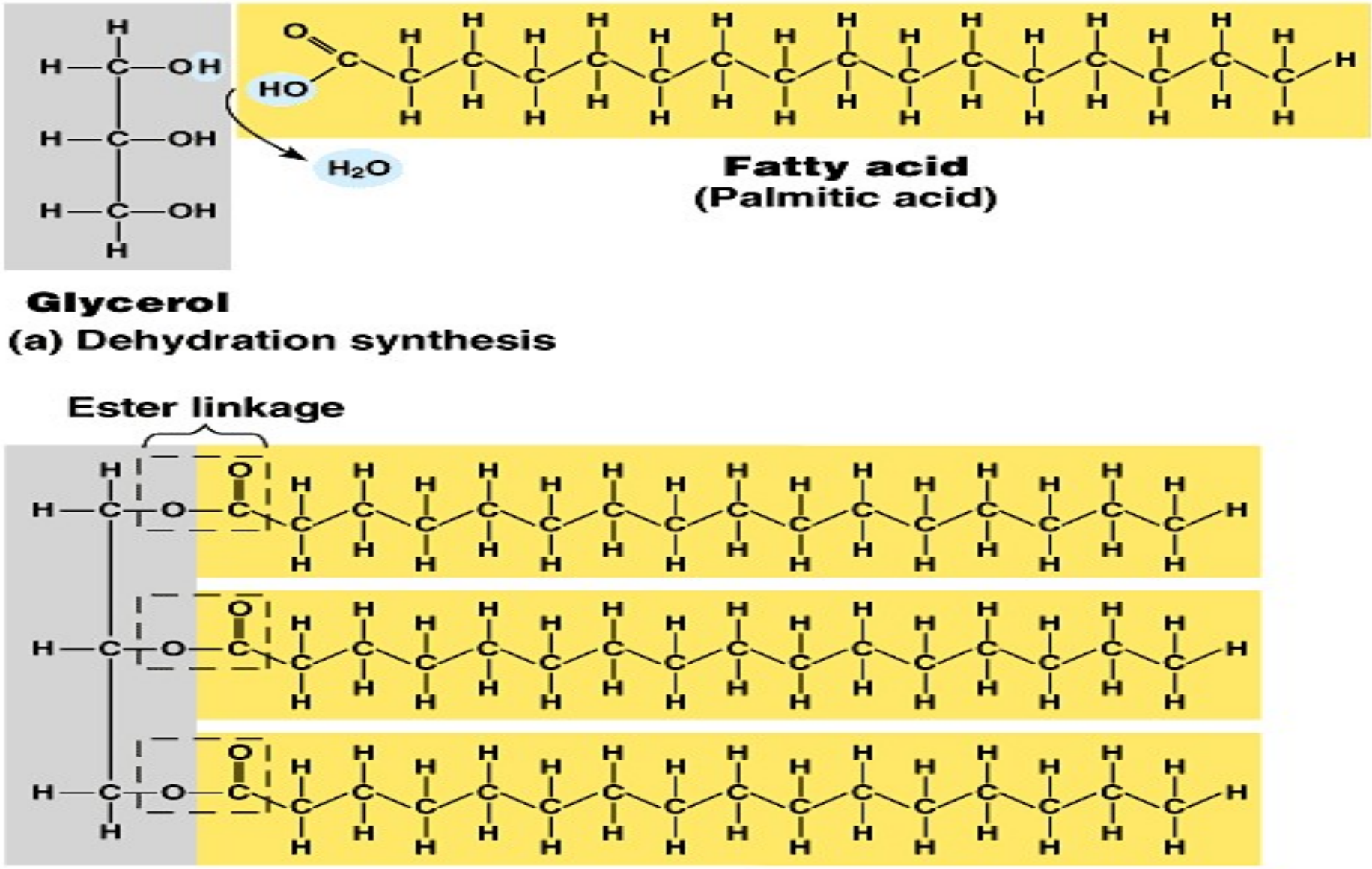
Glycerol esters (acylglycerols)

- Glycerol is a three-carbon alcohol that contains a hydroxyl group on each of its carbon atom.
- Each hydroxyl can be esterified with a fatty acid.



- The class of acyglycerol (glyceride) is determind by the number of fatty acyle groups present; (monoglycerides,diglycerides and triglycerides)

Triglyceride



Triglycerides

- Triglycerides from plants tend to have large amount of C_{18}:2 or linoleic residues and are liquid at room temperature (RT).
- Triglycerides from animals especially ruminants, tend to have C_{12}:0 through C_{18}:0 fatty-acid residues (saturated fats) and are solid at RT.

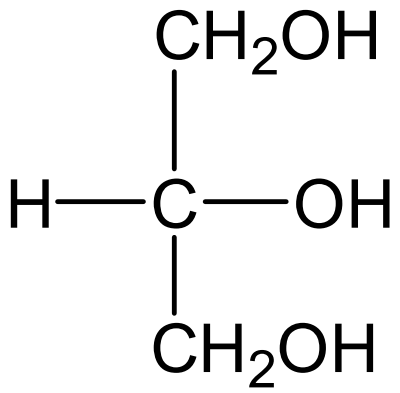
- Some plant triglyceride, such as coconut oil, are highly saturated and may be solid at RT.

Glycerophospholipids

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

They have a **glycerol** backbone.

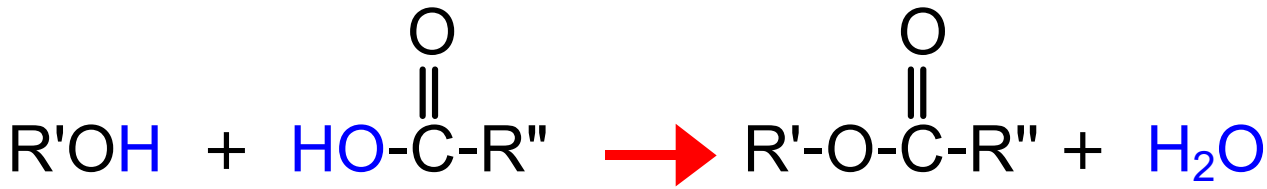
Hydroxyls at **C1** & **C2** are esterified to **fatty acids**.



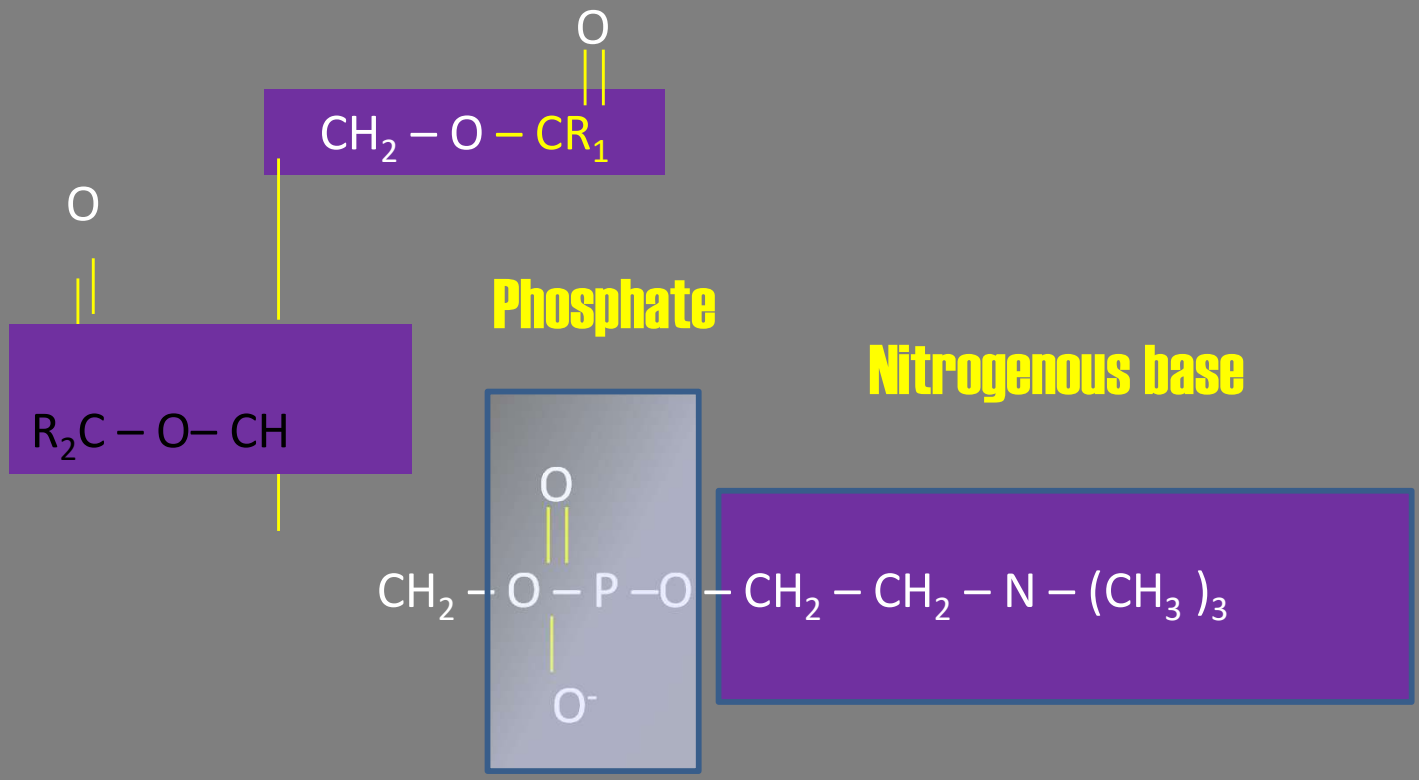
glycerol

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

Formation of an ester:



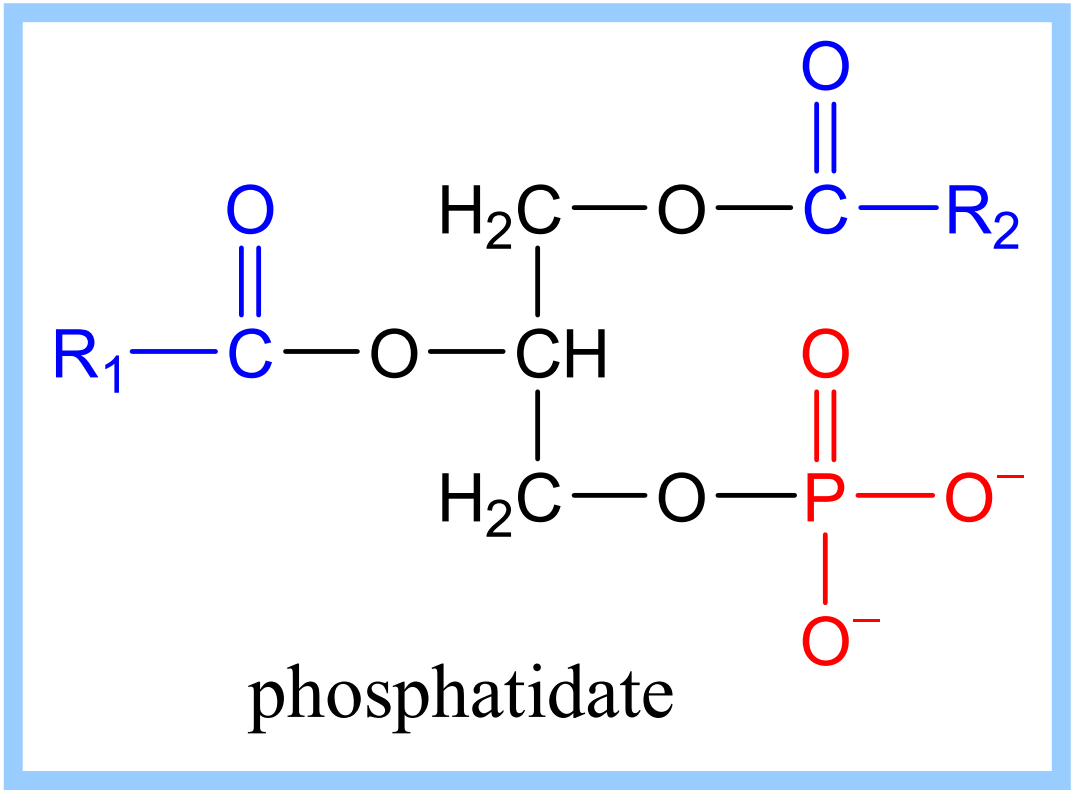
PHOSPHOLIPID



PHOSPHOLIPID

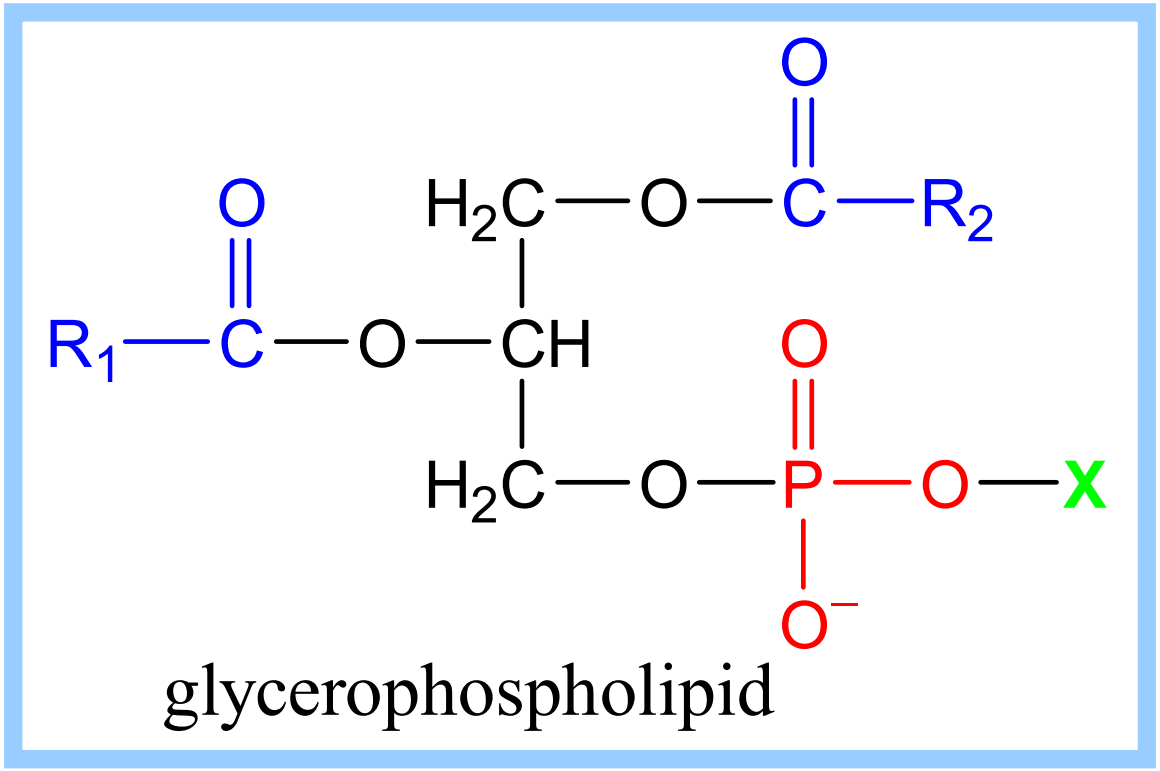
- Phospholipids are complex lipids, resembling triglycerides, but containing phosphate and a nitrogenous base in place of one of the fatty acids.
- They are important components of cell membranes and lipoproteins, maintaining the solubility of non-polar lipids and cholesterol.

Phosphatidate



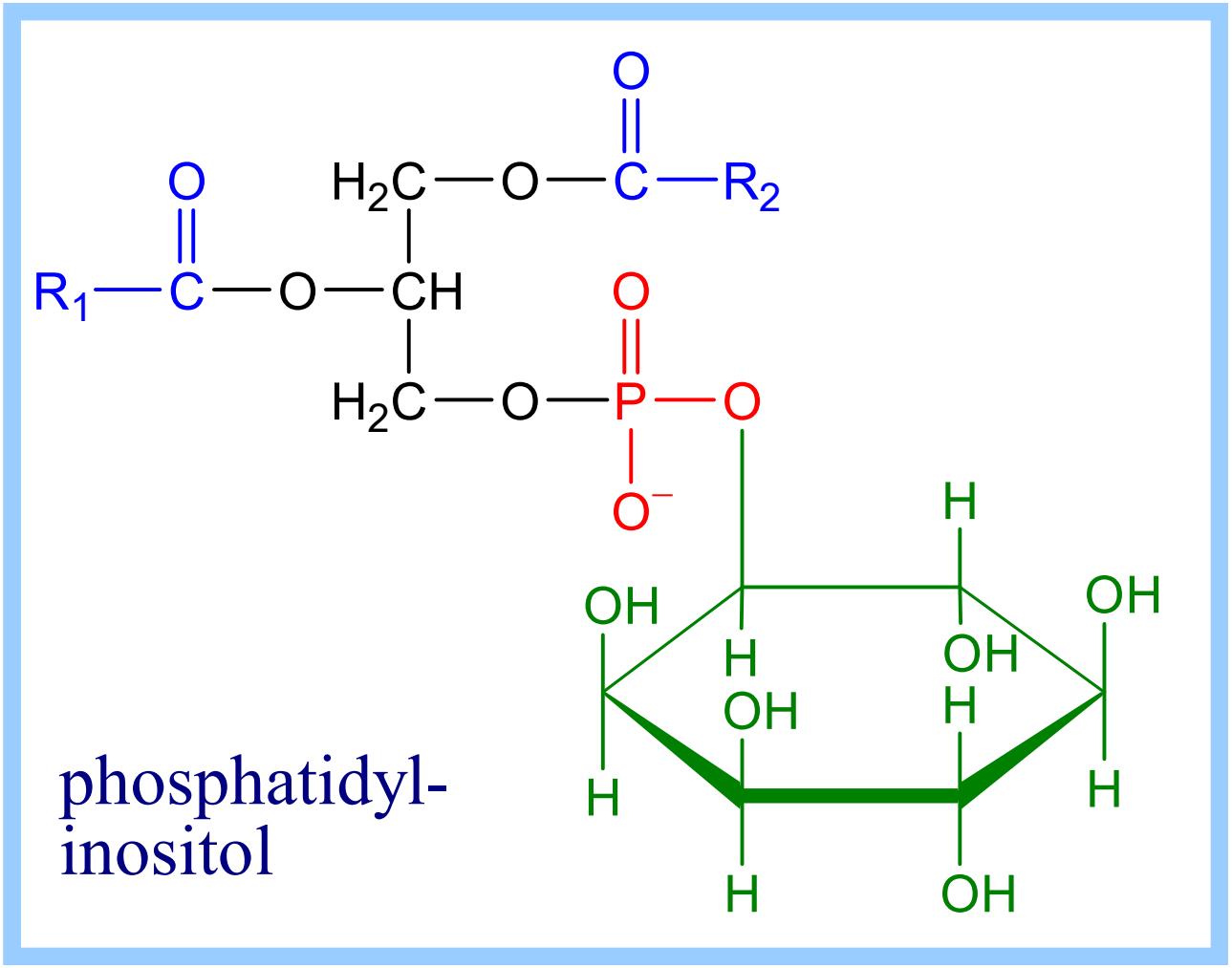
In **phosphatidate**:

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



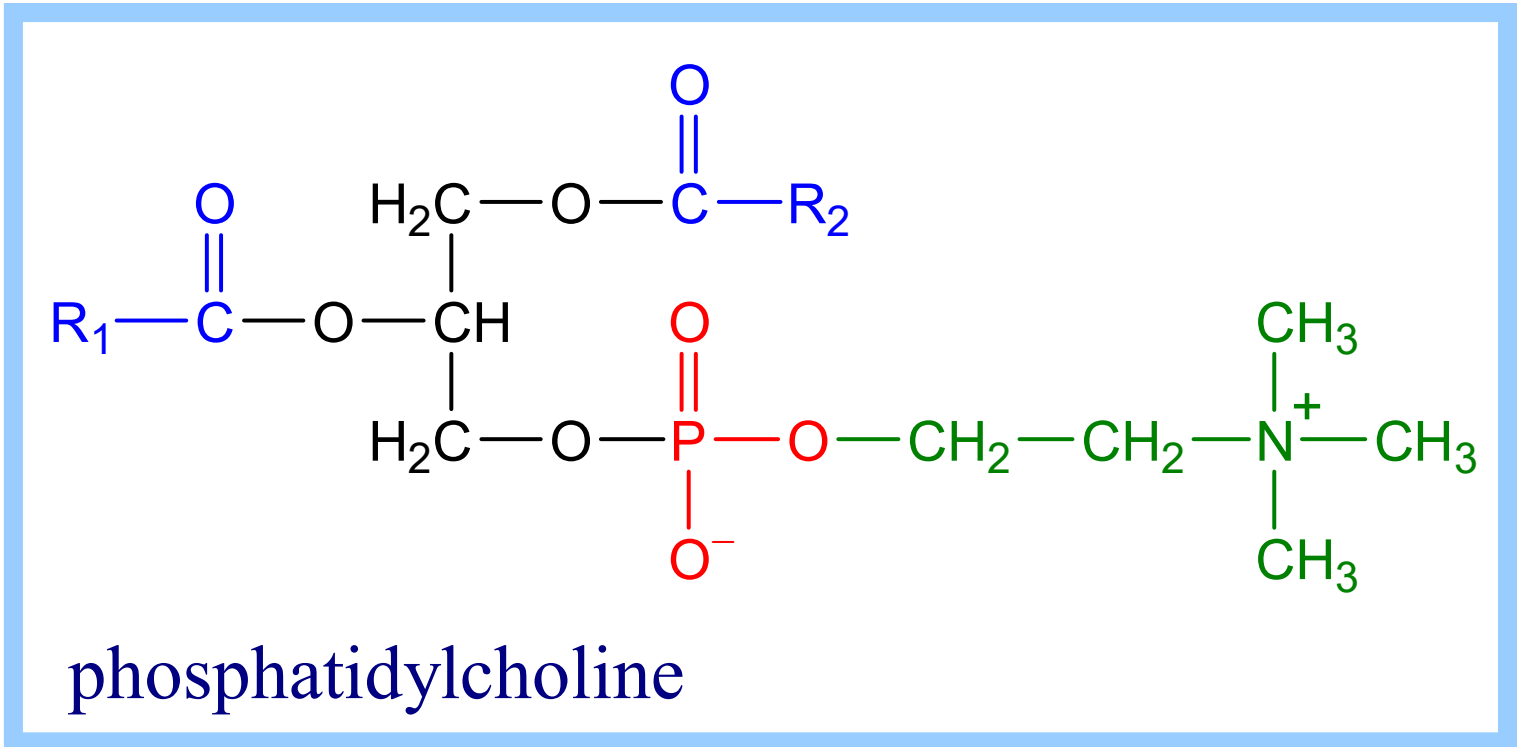
In most **glycerophospholipids** (phosphoglycerides), **P_i** is in turn esterified to **OH** of a **polar head group** (**X**): e.g., **serine, choline, ethanolamine, glycerol, inositol**.

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



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

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

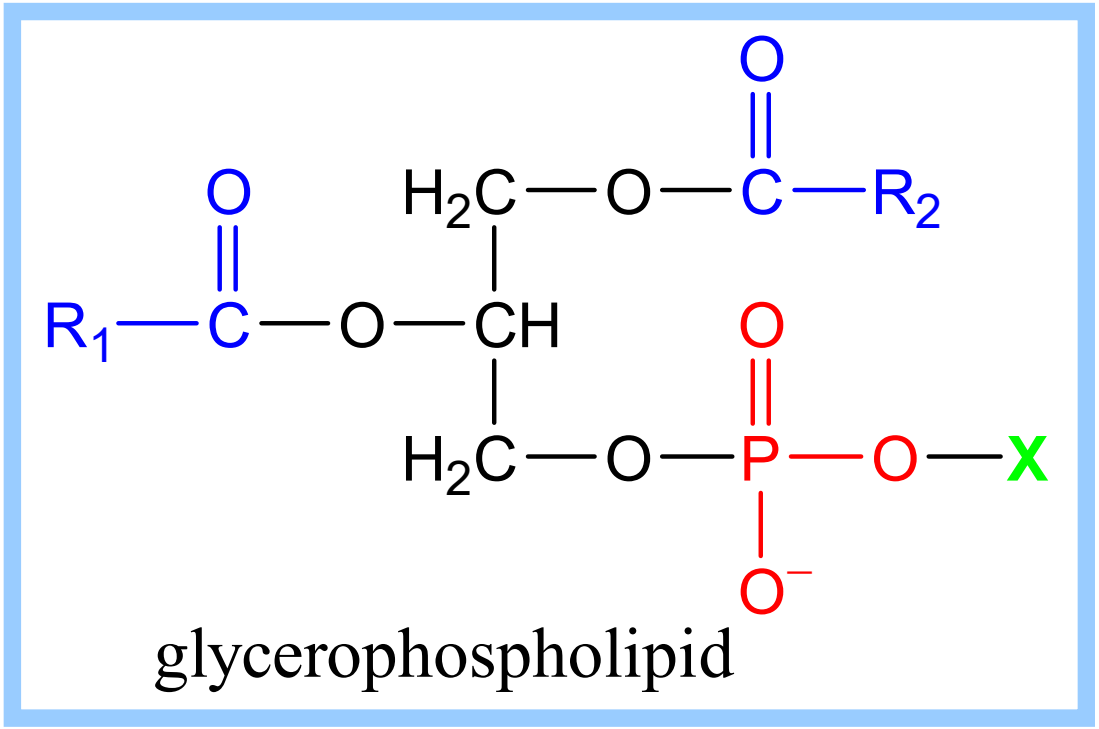


Phosphatidylcholine, with choline as polar head group, is another glycerophospholipid.

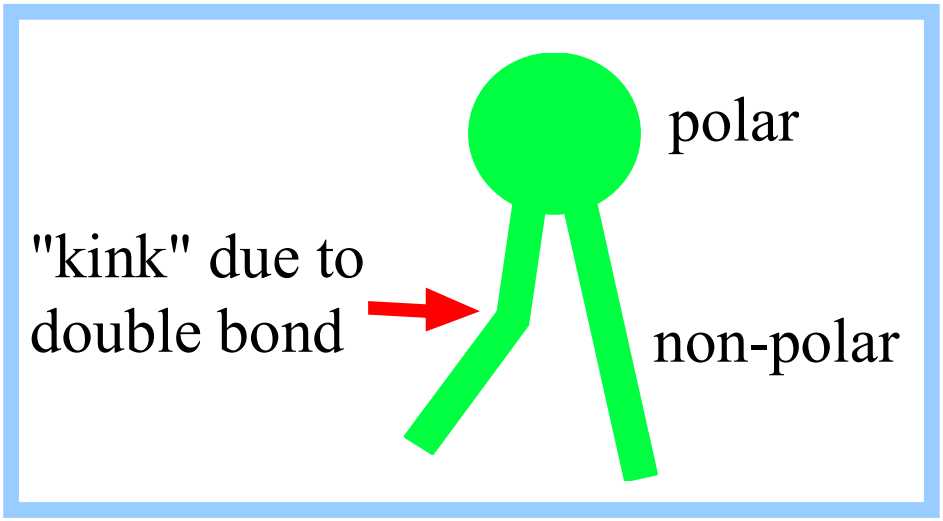
It is a common membrane lipid.

Each glycerophospholipid includes

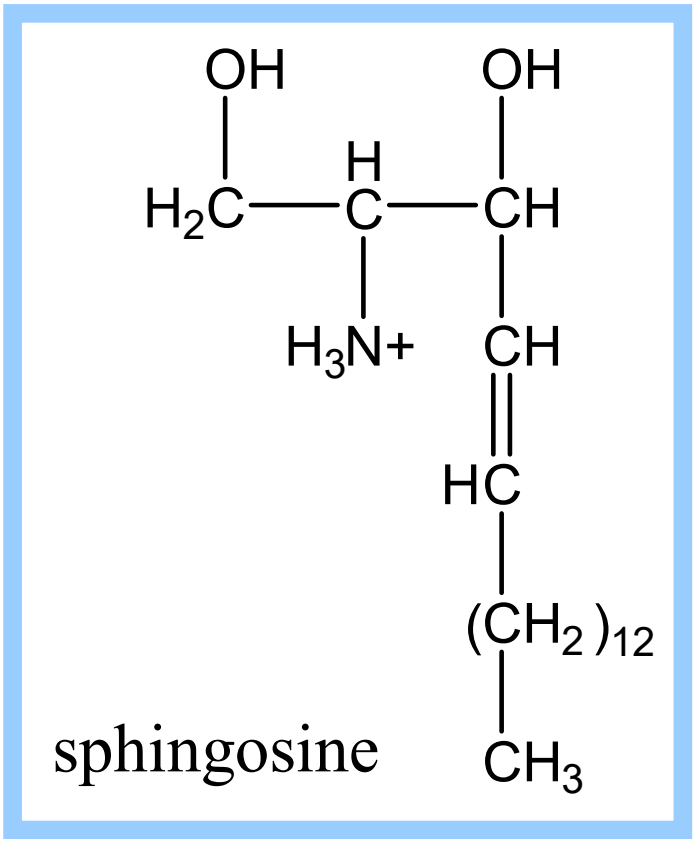
- a **polar** region: **glycerol**, **carbonyl O** of fatty acids, P_i, & the polar head group (**X**)
- **non-polar** hydrocarbon tails of fatty acids (R_1, R_2).



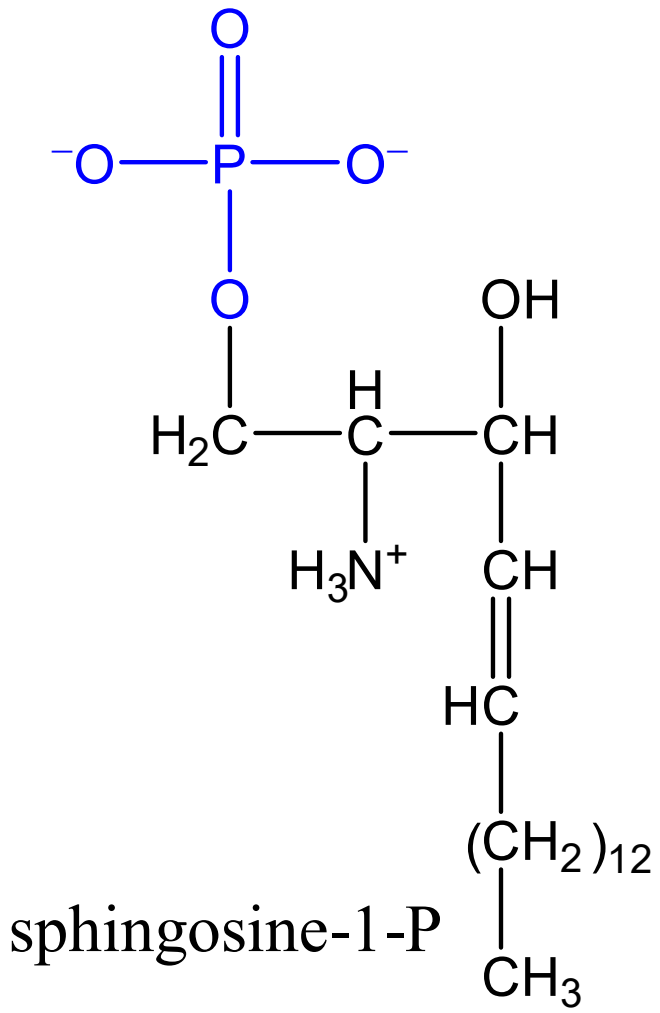
glycerophospholipid



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



sphingosine

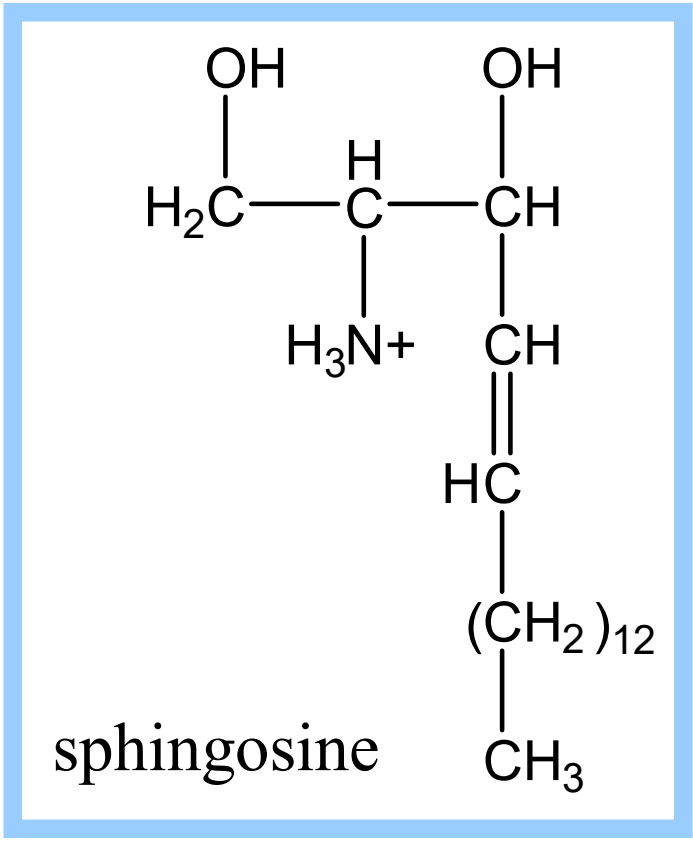


sphingosine-1-P

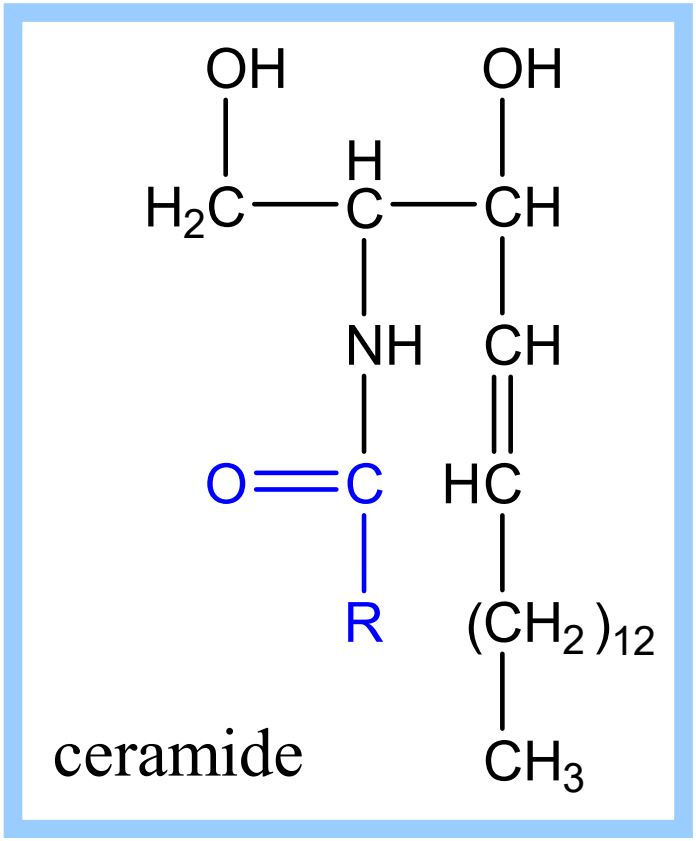
Sphingosine may be reversibly phosphorylated to produce the **signal** molecule **sphingosine-1-phosphate**.

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

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



sphingosine

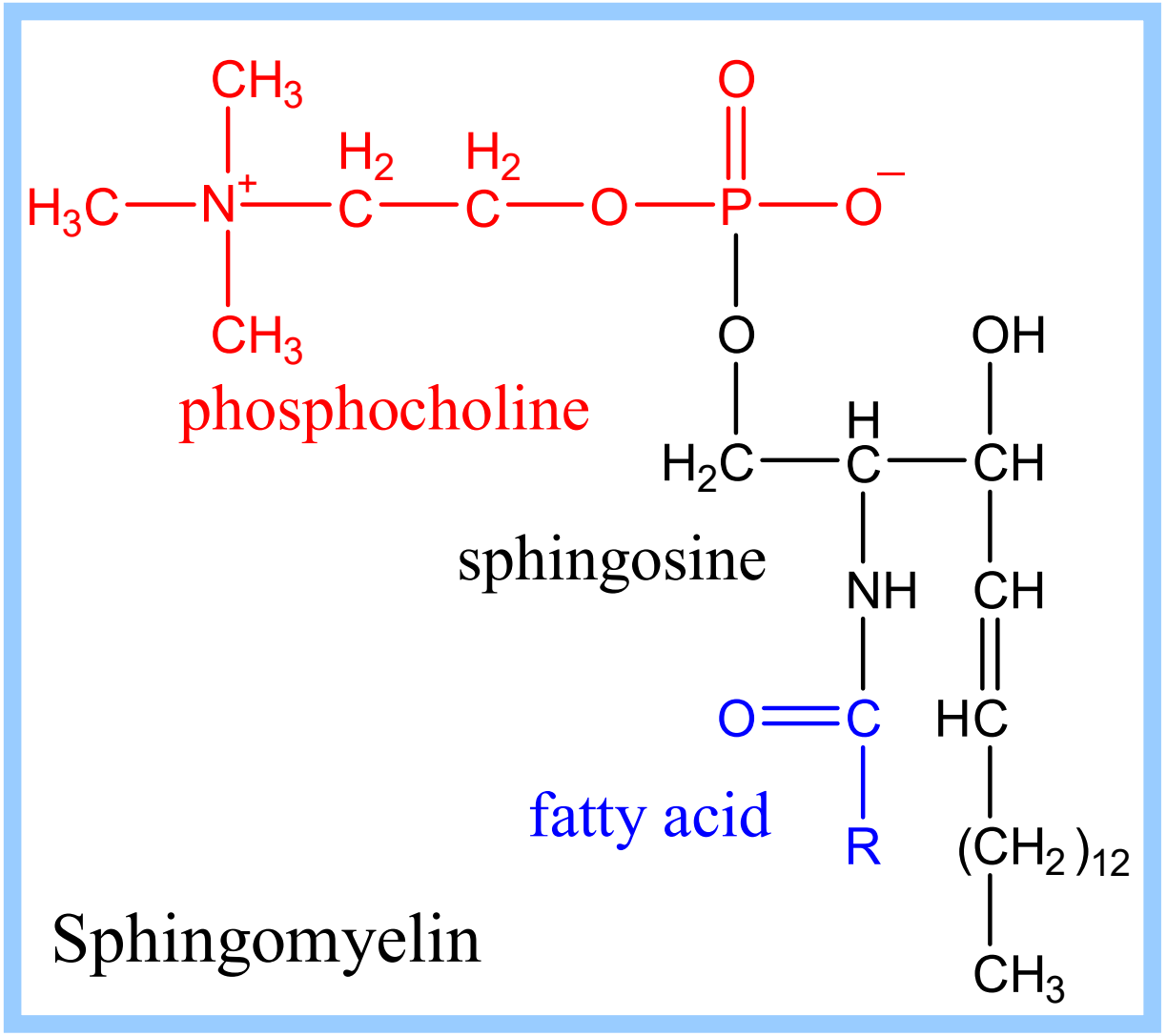


ceramide

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

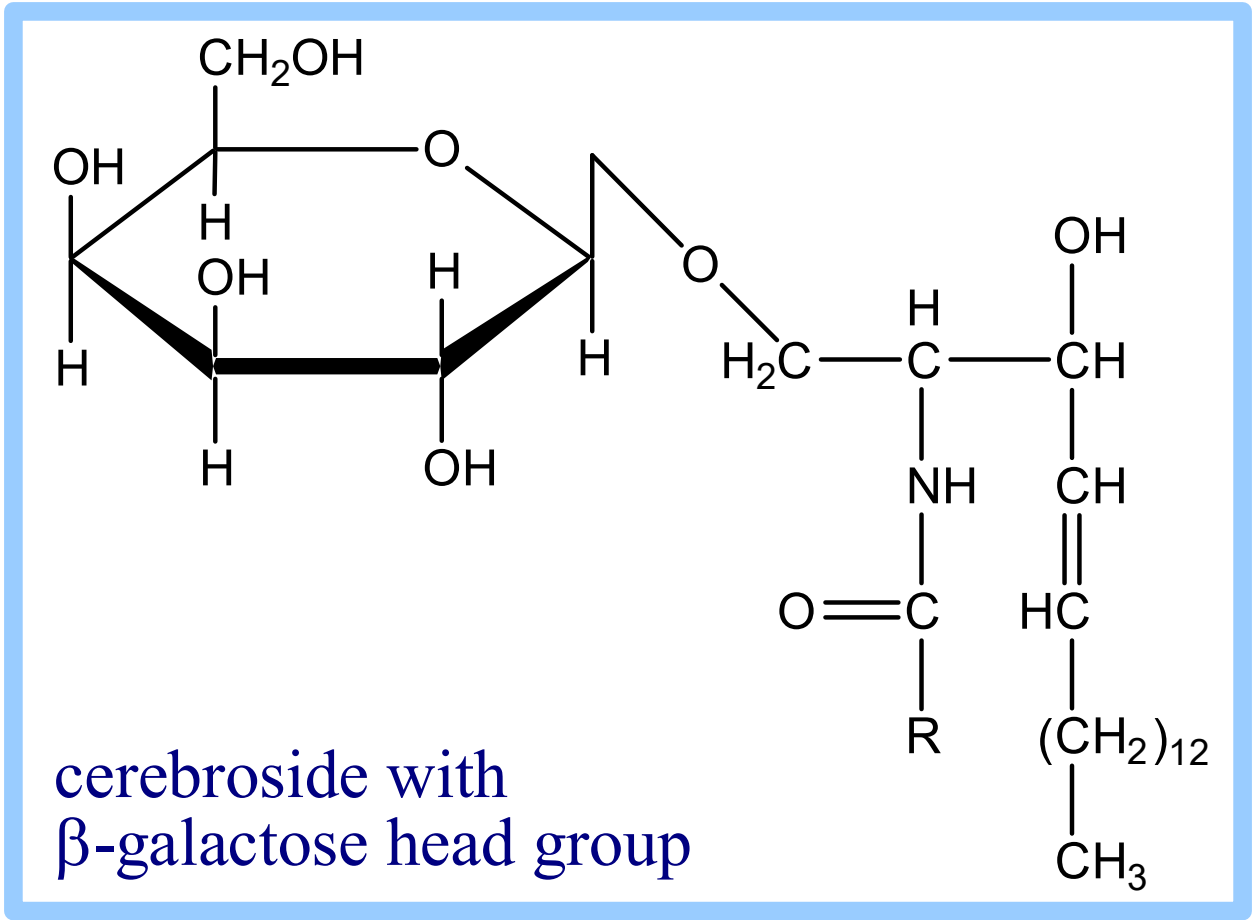
Sphingomyelin has a phosphocholine or phosphethanolamine head group.

Sphingomyelins are common constituent of plasma membranes



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

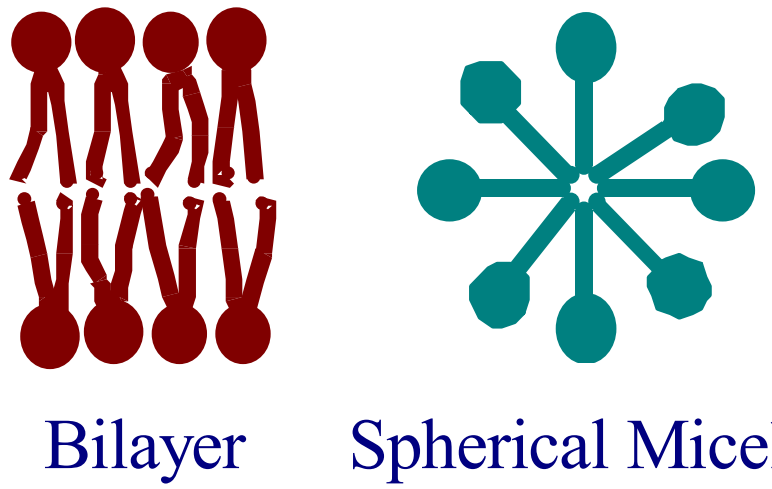
A **cerebroside** is a sphingolipid (ceramide) with a **monosaccharide** such as glucose or galactose as polar head group.



A **ganglioside** is a ceramide with a polar head group that is a **complex oligosaccharide**, including the acidic sugar derivative sialic acid.

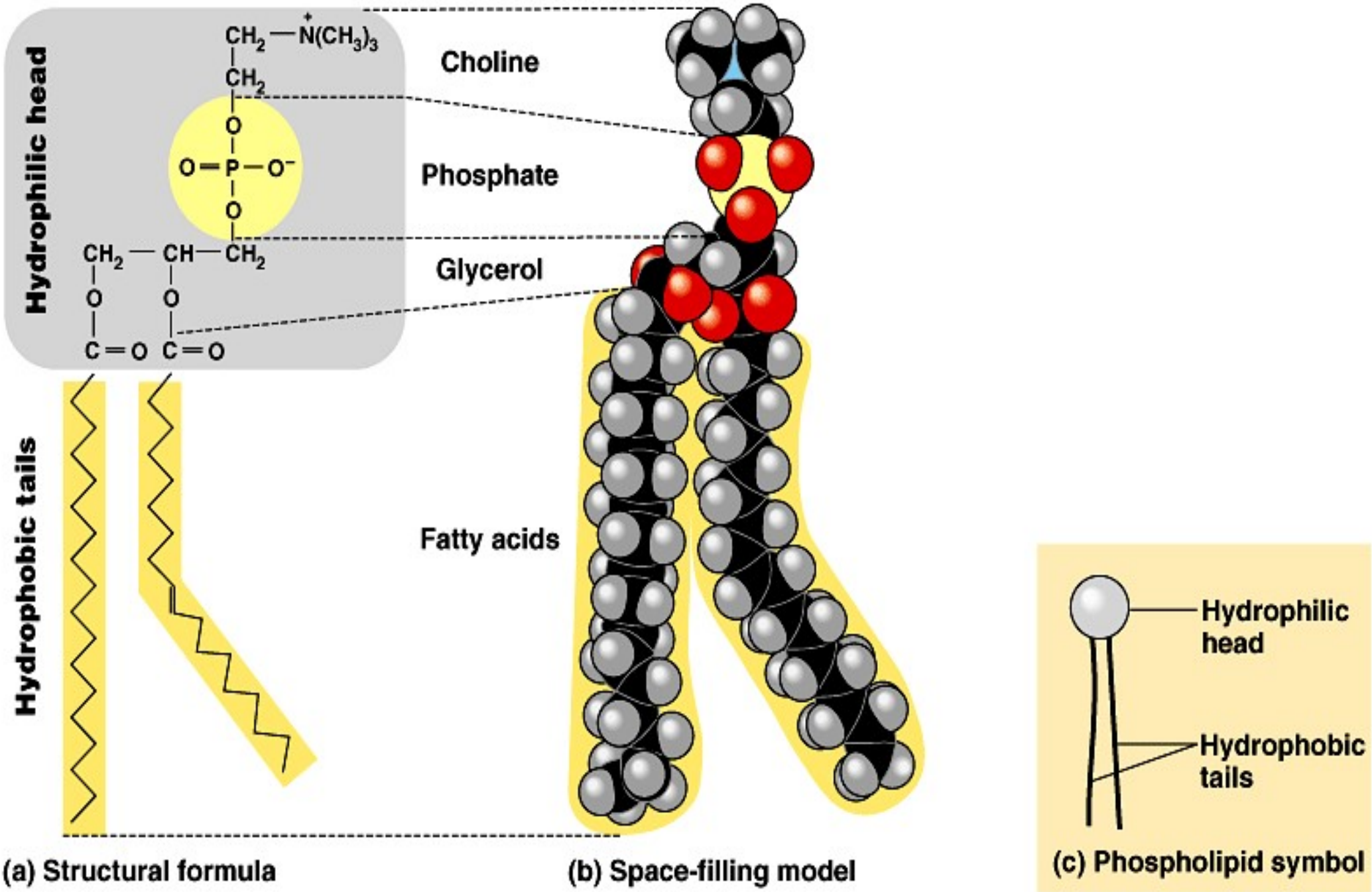
Cerebrosides and gangliosides, collectively called **glycosphingolipids**, are commonly found in the outer leaflet of the plasma membrane bilayer, with their sugar chains extending out from the cell surface.

Amphipathic lipids in association with water form complexes in which polar regions are in contact with water and hydrophobic regions away from water.



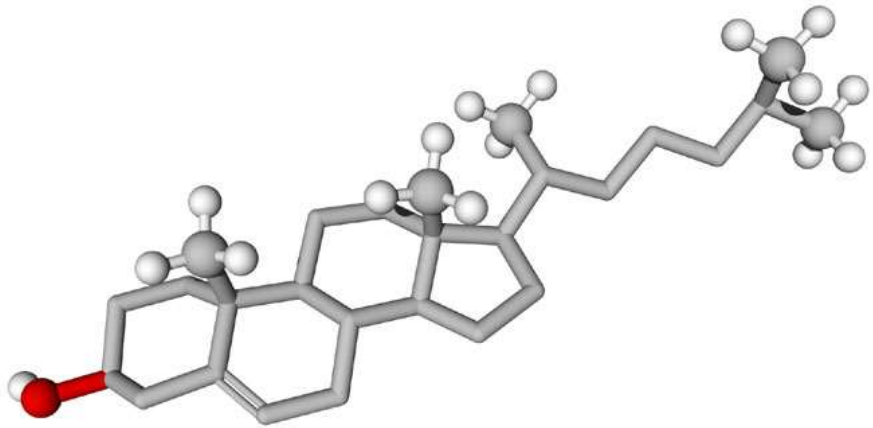
Depending on the lipid, possible molecular arrangements:

- Various **micelle** structures. E.g., a spherical micelle is a stable configuration for amphipathic lipids with a **conical** shape, such as **fatty acids.**
- A **bilayer**. This is the most stable configuration for amphipathic lipids with a **cylindrical** shape, such as **phospholipids**.

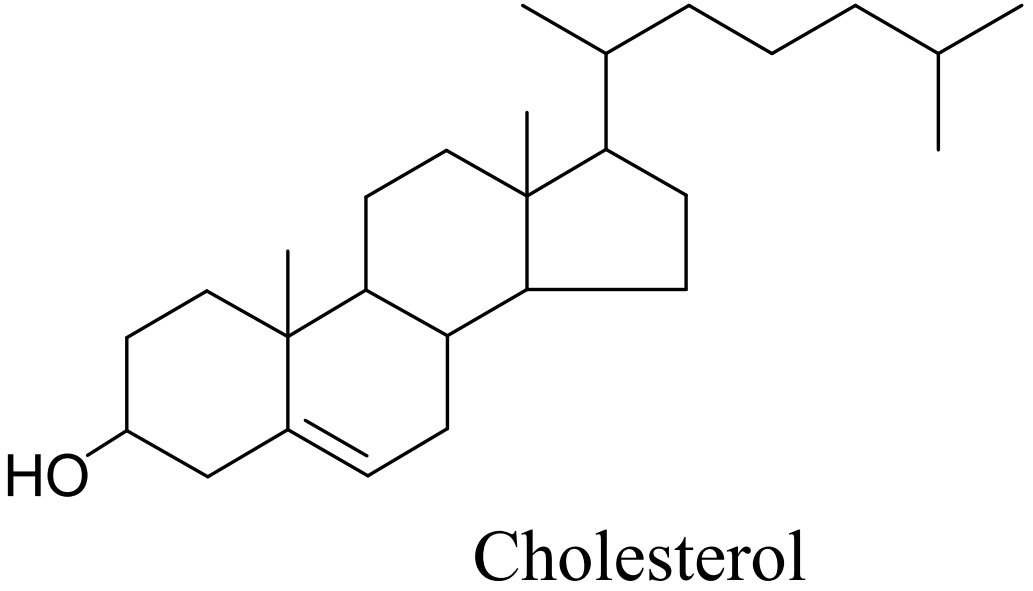


Steroids

- Characterized by a backbone of four fused carbon rings.
- Differ in the functional groups attached to the rings.
- Examples:
  - cholesterol
  - sex hormones

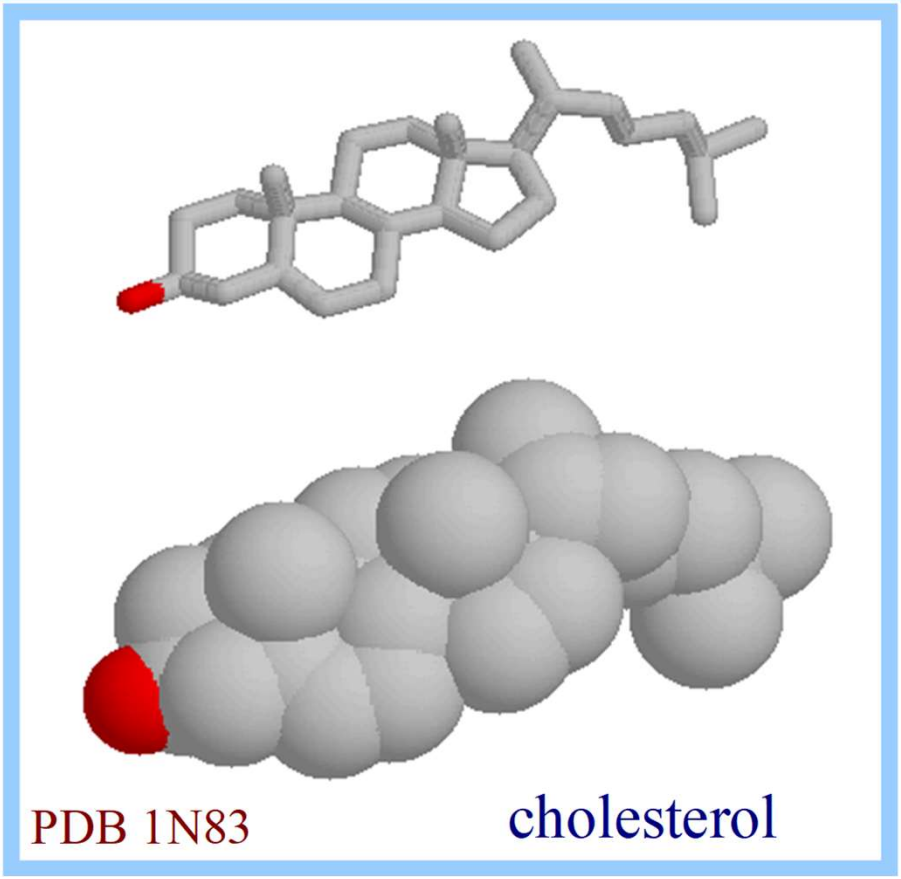


Cholesterol, an important constituent of cell membranes, has a **rigid** ring system and a short branched hydrocarbon tail.



Cholesterol is largely **hydrophobic**.

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



Role of Cholesterol

- Keeps the lipids in membrane from aggregrating: Keeps the membrane intact as a bilayer
- Precursor to Bile Acids
  - Act as detergents to dissolve dietary fats
  - Fats can be broken better by enzymes
- Precursor to steroid hormones that regulate gene expression
- Precursor to Vitamin D

Lipoproteins

Lipids must be transported to the various tissues to accomplish their metabolic functions. Because of their insolubility, they are transported in plasma in macromolecular complexes called Lipoproteins.

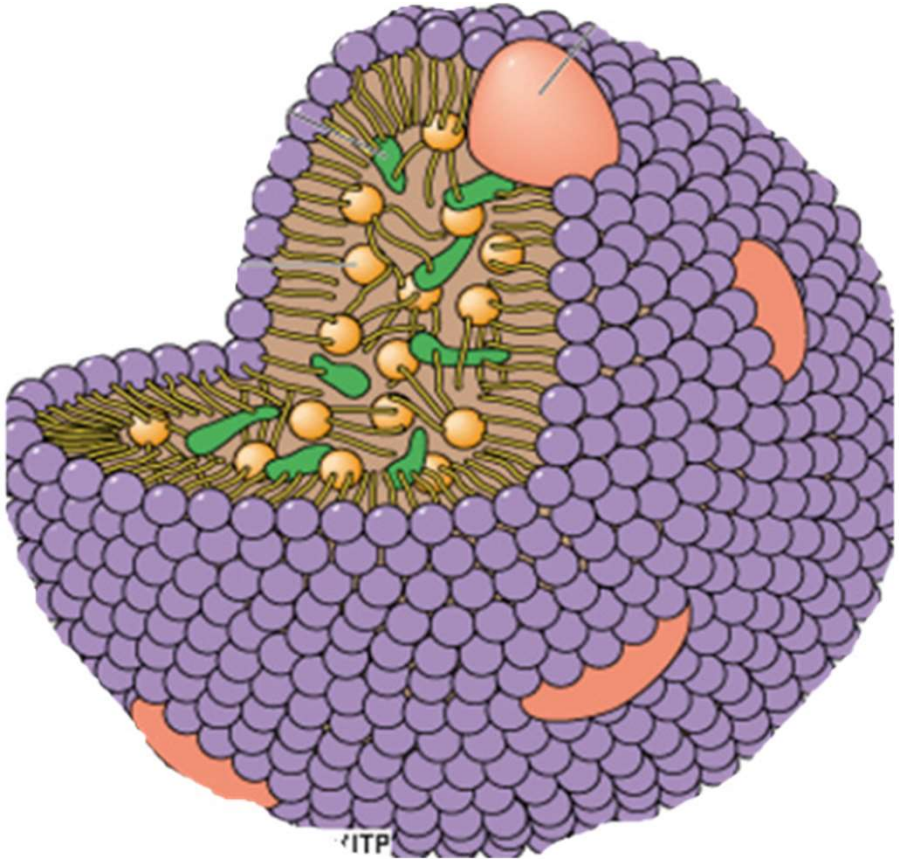
Chemistry:

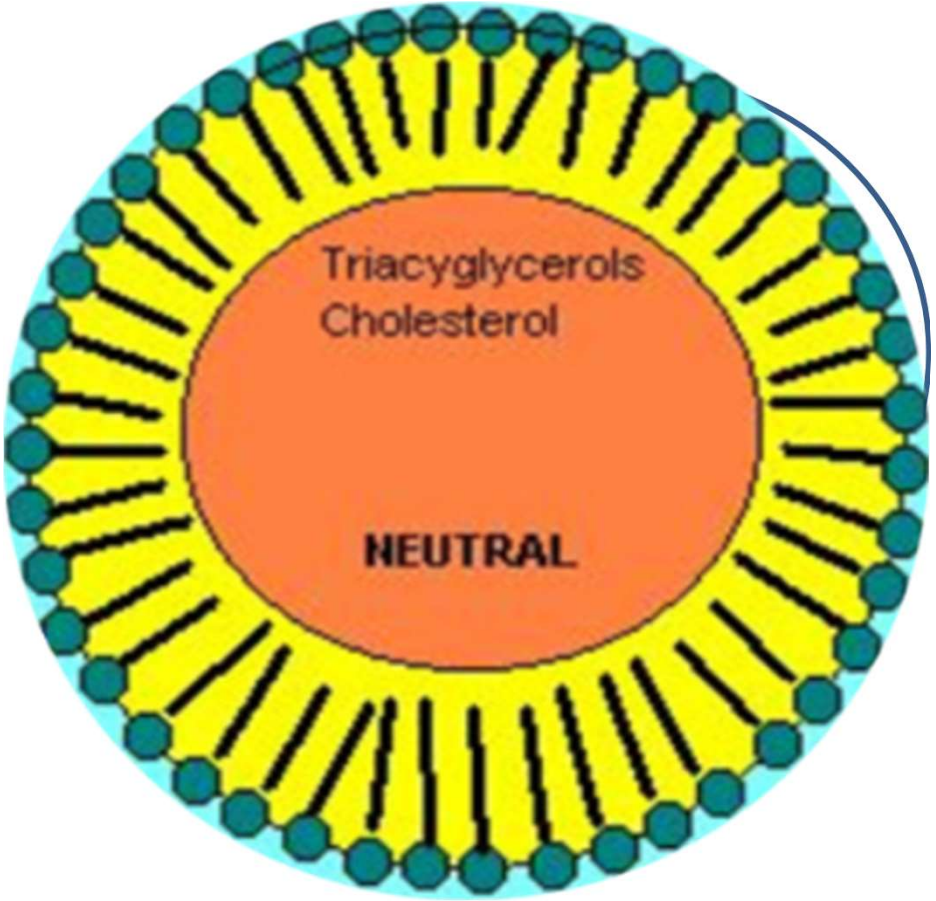
Lipoproteins are spherical particles with non polar lipids (triglycerides and cholesterol esters) in their core and more polar lipids (phospholipids and free cholesterol) oriented near the surface.

They also contain one or more specific proteins called *apolipoproteins,* that are located on their surface.

Lipoproteins

Lipoprotein: Glycerol part on outside; FA and cholesterol on inside





Spherical Lipoprotein

Classification of Lipoproteins

- Lipoproteins are classified by their density which, in turn, reflects size. The greater the lipid/protein ratio in the complex, the larger it is and the lower its density.
- There are five main classes of lipoproteins.

***Triglyceride-rich* particles include :**

- Chylomicrons, which transport exogenous lipid from the intestine to all the cells.
- VLDL (very low density lipoproteins), which transport endogenous lipid from the liver to cells;.
- IDL (intermediate density lipoproteins), which are usually undetectable in normal plasma. It is normally a transient intermediate lipoprotein formed during the conversion of VLDL to LDL.
- It contains both cholesterol and endogenous triglycerides.

Classification of Lipoproteins

- LDL (low density lipoproteins):

  formed from VLDL, transport cholesterol to cells.

- HDL (high density lipoproteins):

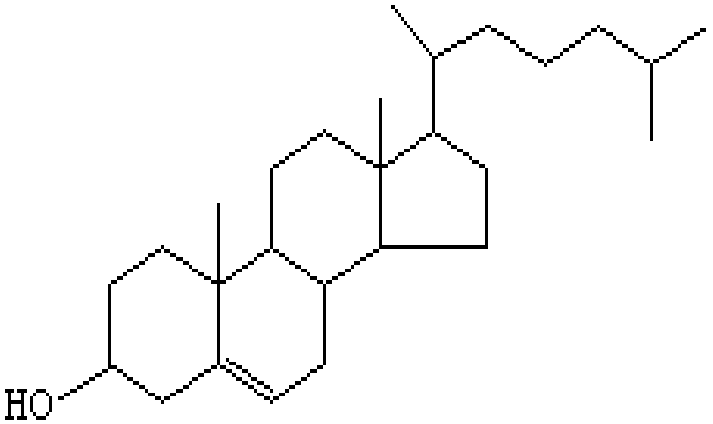
  These are involved in the transport of cholesterol from the cells to the liver.

LDL and ***HDL*** are two smaller lipoproteins contain mostly cholesterol.

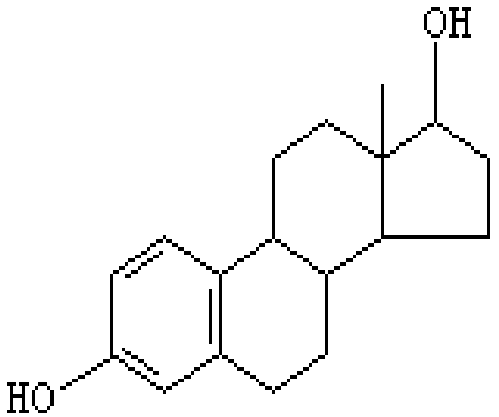
Ratio of LDL to HDL

- LDL cholesterol of less than 100 mg/dL is the optimal level. Less than 130 mg/dL is near optimal for most people.
- A high LDL level (more than 160 mg/dL or 130 mg/dL or above if you have two or more risk factors for cardiovascular disease) reflects an increased risk of heart disease
- Low HDL cholesterol levels [less than 40 mg/dL] is thought to increase the risk for heart disease.

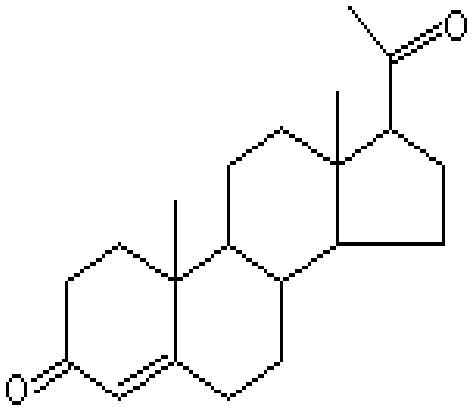
Steroid hormones



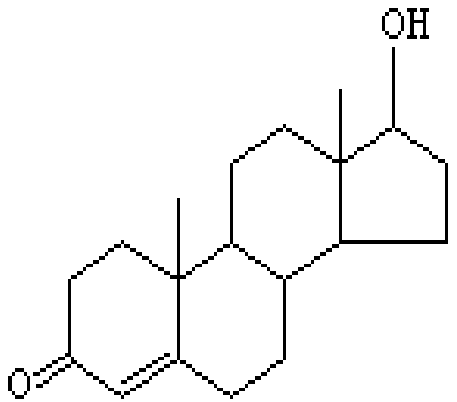
Cholesterol (34)



Oestrogen (35)



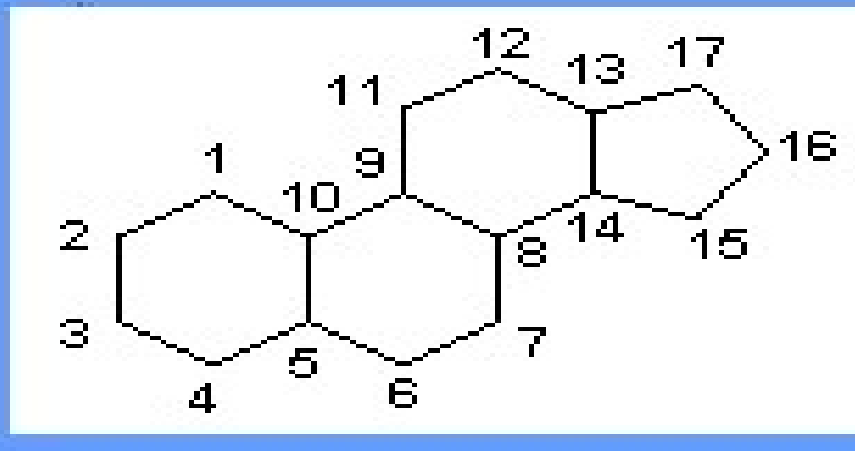
Progesterone (36)

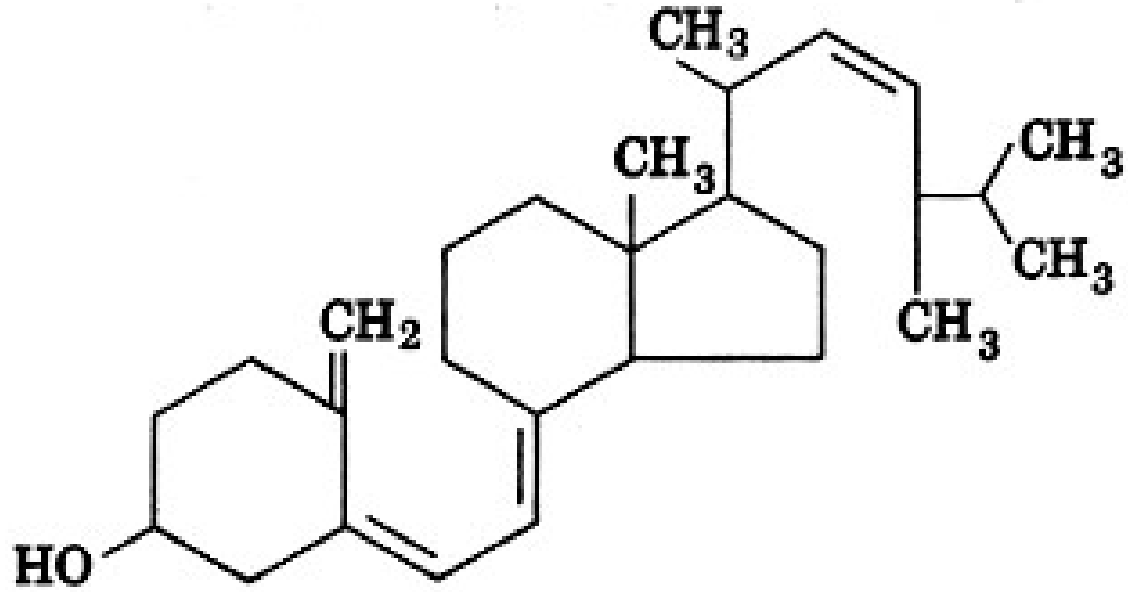


Testosterone (37)

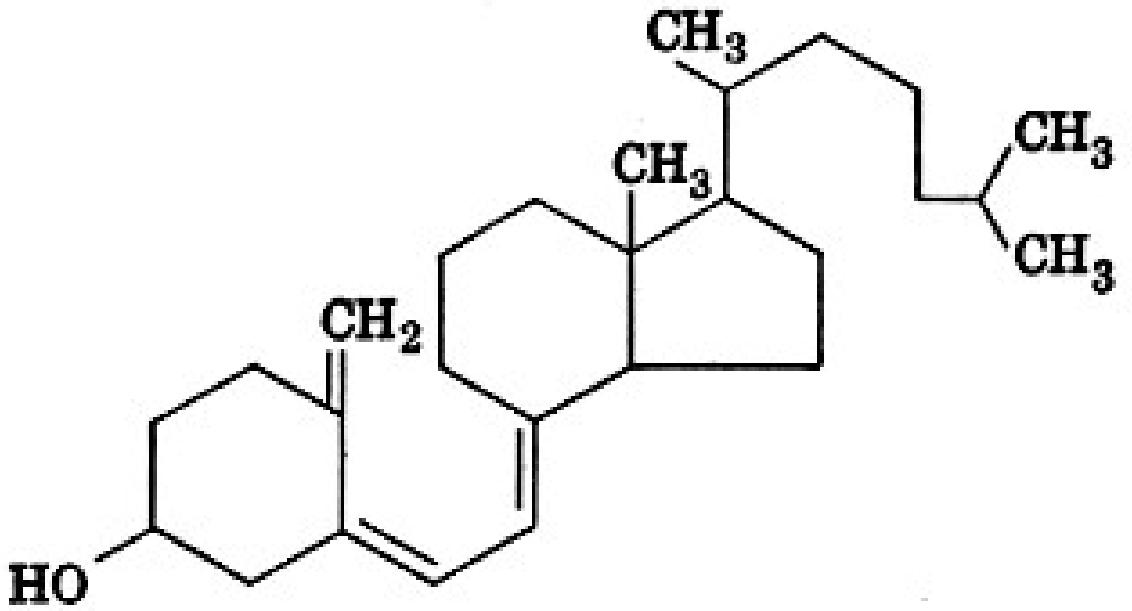
Bile Salt

sodium glycoholate





Vitamin D_2 (calciferol)

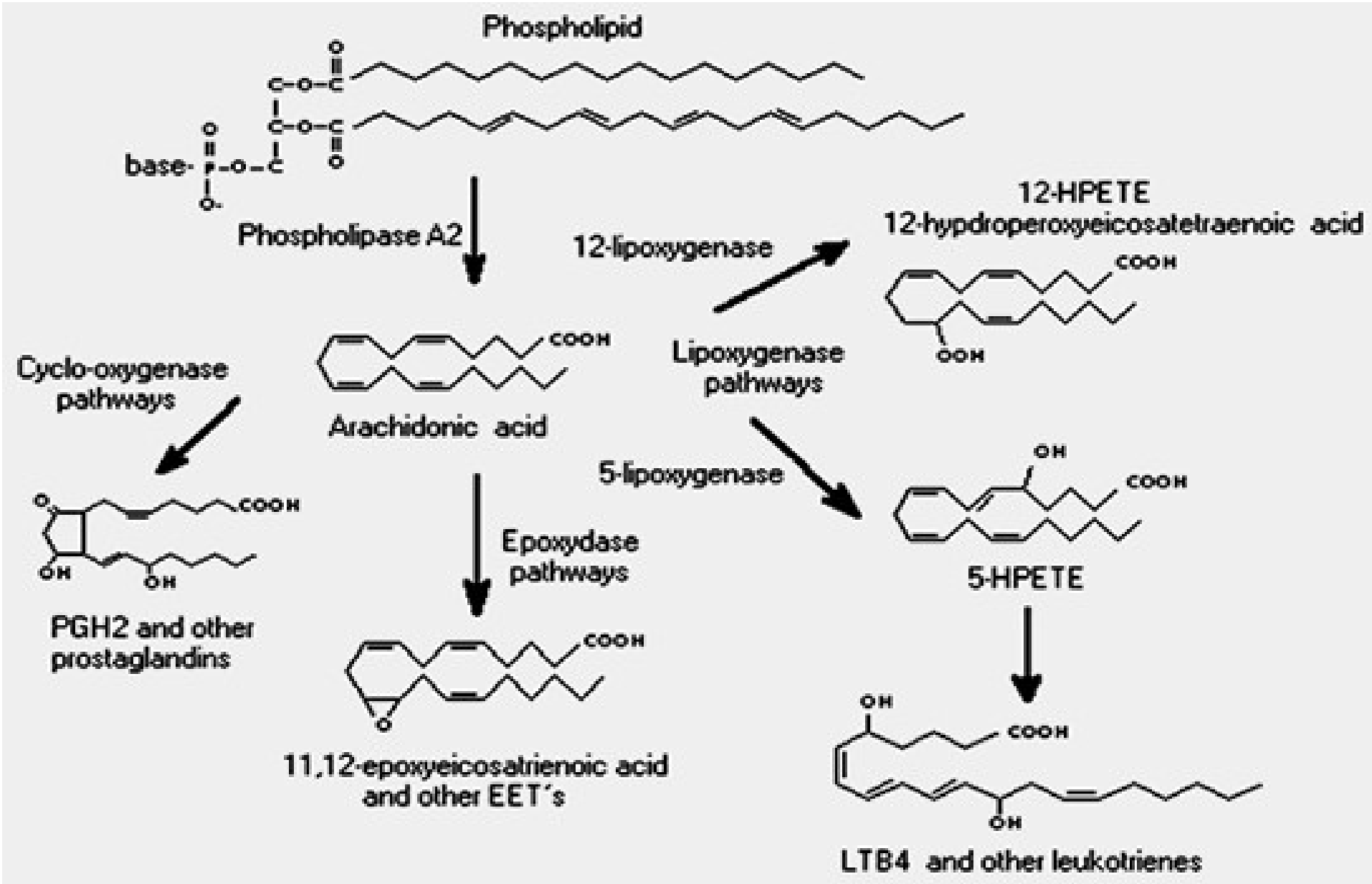


Vitamin D_3

Eicosanoids

- Prostaglandins: different types
  - Some stimulate contraction of smooth muscle during menstruation and labor
  - Others produce fever and inflammation and pain
- Thromboxanes: act in the formation of blood clot
- Leukotrienes: induces contraction of the muscle lining the lungs
  - overproduction leads to asthma

Eicosanoids/Leukotrienes



NAMASKAR

THE END