LIPID CHEMISTRY

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Definitions of Lipids, Fatty acids, Saponifiable and Non-Saponifiable lipids, Saponification number and Iodine number

What are Lipids?

- **Lipids** are bio-molecules that are:
  - Hydrophobic in nature because of the high amount of Hydrocarbons in their structure,
  - Relatively insoluble in water but readily soluble in non-polar solvents such as Chloroform, Benzene and Ether,
  - Easily separated from other biological materials by extraction into organic solvents because of their hydrophobic properties,
  - Examples of lipids:
    - Fats, Oils, Steroids, Waxes, Fat-soluble Vitamins (Vitamins A, D, E and K),

What are fatty acids?

- Aliphatic Carboxylic Acids containing Long Hydrocarbon chains that may be Saturated or Unsaturated,
- Fatty acid has both Hydrophobic and Hydrophilic properties, thus are Amphipathic in nature,
- Fatty acid can be separated into two distinct parts:
  - Non-polar Hydrophobic Hydrocarbon Chain (Tail)
  - Polar (-COOH) group (Hydrophilic Head)
- Most naturally occurring fatty acids, obtained from hydrolysis of natural fats and oils contain **Even number of carbon atoms** because they are synthesized from Two-carbon units,
- Examples of fatty acids: Palmitic Acid, Oleic Acid, Arachidonic Acid, Linoleic Acid, Linolenic Acid, etc.

What are Saponifiable Lipids?

- Lipids that can be hydrolyzed either by Heat, Alkaline or Acid solutions,
- The hydrolyzed products usually include:
  - Fatty Acids (salts of fatty acids),
  - Glycerol, and in some cases other molecular components contained in the lipid,
- Examples:
  - Neutral fats,
  - Phospholipids,

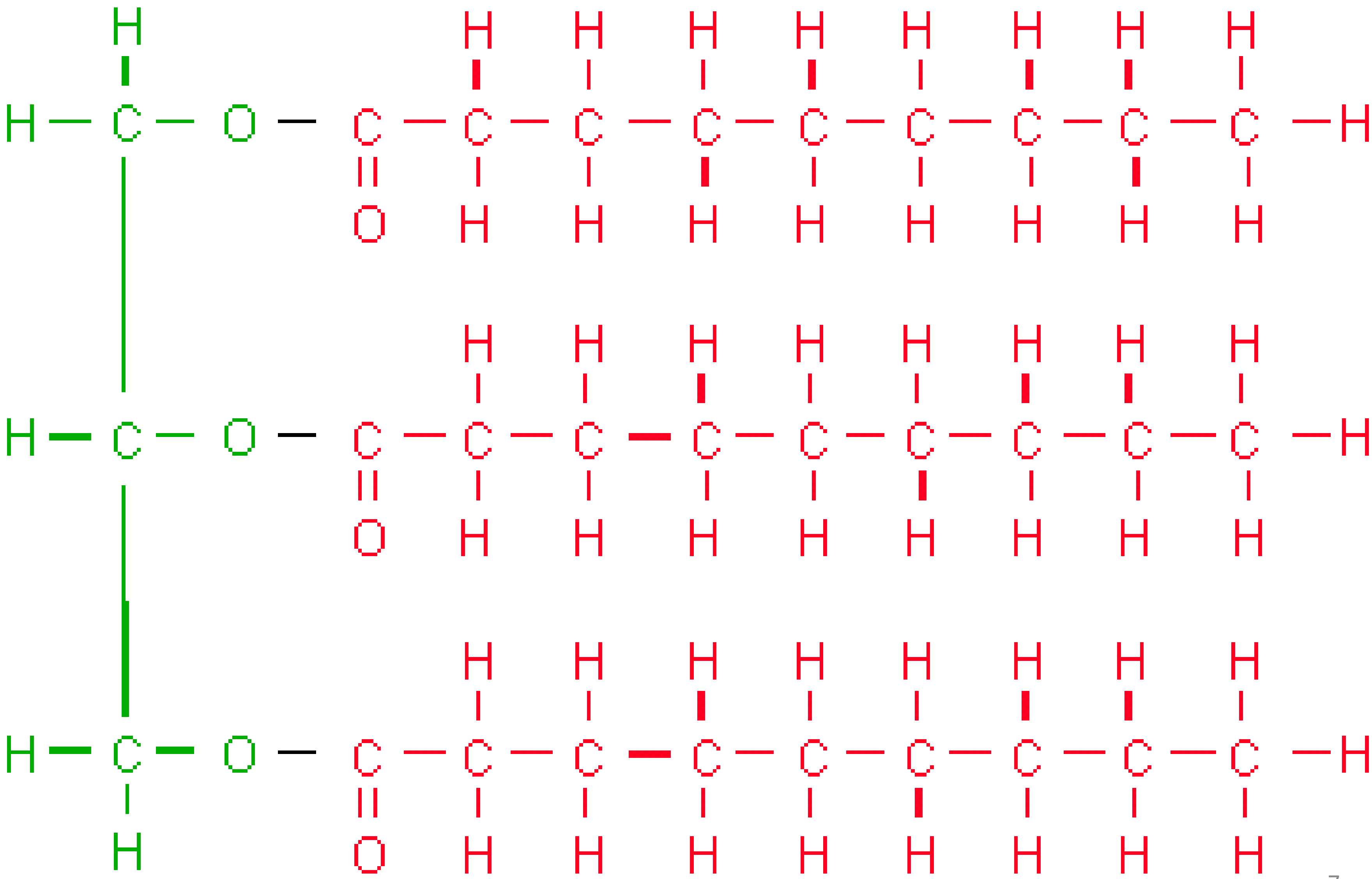
What are Non-Saponifiable Lipids?

- Non-Saponifiable lipids are those lipids that cannot be hydrolyzed,
- Examples:
  - Terpenes,
  - Steroids
  - Fat-soluble Vitamins

What is the Saponification Number of a Lipid?

- Saponification Number is the number of milligrams of KOH that is needed to Saponify one gram of Fat;
- Since each molecule of fat regardless of its size requires 3 molecules of KOH to Saponify it, the Saponification number also indicates the number of molecules of fat in one gram of fat;

Simple diagram to illustrate the structure of Fat



What is the Iodine Number of Fat?

- Iodine Number of fat is the number of grams of Iodine that is absorbed by 100 grams of Fat,
- It is a measure of the degree of un-saturation of the fatty acids in the structure of the Fat,

NOMENCLATURE OF SATURATED FATTY ACIDS

Systematic nomenclature of saturated fatty acids

- **IUPAC system** (Systematic name or Genevan system) and
- **Common names**
- **IUPAC or Systematic name** of a fatty acid is formed by replacing the ending **-e** with suffix **-oic acid** in the name of the Alkane with the same number of carbon atoms,
- Carboxyl Carbon is Carbon number one,
- Examples:
  - 16C fatty acid is: Hexadecan**oic acid** (from Hexadecan**e**)
  - 18C fatty acid is: Octadecan**oic acid** (from Octadecan**e**)

Common Names of Saturated fatty acids

- **Common names** of fatty acids are generally derived from either the Latin or Greek name of their source of origin,
- Greek letters or symbols **(α, β, γ, δ, ε,** etc.) can be used to number Carbon atoms in fatty acid molecules,
- Examples of Common names:
  - Palmitic acid from Latin - Palma (palm tree);
  - Arachidic acid from Greek - Arachne (spider), etc

IMPORTANT TO NOTE

- Nomenclature of fatty acids should not mix Greek letters or symbols with Systematic names of fatty acids, nor should numerals be mixed with Common names of fatty acids;
- Carboxyl Carbon in a fatty acid molecule is always considered as the First Carbon (C-1) in Systematic name, it has no corresponding Greek letter or symbol in Common name,
- In Systematic name:
  - Second Carbon atom (C-2) in Fatty Acid molecule corresponds to the α-Carbon in Common name,
  - Third Carbon atom (C-3) in Fatty Acid molecule corresponds to β-Carbon atom in Common name and so on,
- **Last or Terminal Carbon atom in a fatty acid molecule is considered as the ω-Carbon or the n-carbon atom,**

Common names, Systematic names and Short Hand Formula of some Saturated Fatty Acids

Common name	Systematic name	Short-hand structural formula
Valeric acid	Pentanoic acid	CH3(CH2)3COOH
Caproic acid	Hexanoic acid	CH3(CH2)4COOH
Caprylic acid	Octanoic acid	CH3(CH2)6COOH
Capric acid	Decanoic acid	CH3(CH2)8COOH
Lauric acid	Dodecanoic acid	CH3(CH2)10COOH
Myristic acid	Tetradecanoic acid	CH3(CH2)12COOH
Palmitic acid	Hexadecanoic acid	CH3(CH2)14COOH
Stearic acid	Octadecanoic acid	CH3(CH2)16COOH
Arachidic acid	Eicosanoic acid	CH3(CH2)18COOH
Behenic acid	Docosanoic acid	CH3(CH2)20COOH
Lignoceric acid	Tetracosanoic acid	CH3(CH2)22COOH

NOMENCLATURE OF UNSATURATED FATTY ACIDS

OMEGA-numbering and n-numbering systems:

- In all naturally occurring Unsaturated fatty acids the double bond is always in the **cis-configuration**,
- Nomenclature of Unsaturated fatty acids uses:
  - Systematic names
  - Common names
- Common names of Unsaturated fatty acids are derived from the Latin or Greek names of their source of origin;
- Replace ending **-e** with suffix **-enoic acid** in the name of the Alkyne with the same number of carbon atoms

SYSTEMATIC NOMENCLATURE OF UNSATURATED FATTY ACIDS

- Carboxyl Carbon is the First Carbon Atom (C-1)
- Systematic Nomenclature indicates:
  - **Number of Carbon atoms in the Fatty acid,**
  - **Number of Double bonds (unless it has only one double bond),**
  - **Position of the Double bonds,**
  - **Contain the suffix enoic,**
- The **delta (Δ) numbering system** is used to indicate the position of the double bond in fatty acids,

Examples for unsaturated fatty acids:

- Oleic acid, 18C with one double bond between C9 and C10;
  - Systematic name is: cis-Δ9-Octadecenoic acid;
- Linoleic acid, an 18C with two double bonds, between C9 and C10, and also between C12 and C13;
  - Systematic name is: cis-Δ9,12-Octadecadienoic acid,
- Systematic nomenclature can be used without delta sign,
  - Oleic acid is: cis-9-octadecenoic acid,
  - Linoleic acid is: cis-9, 12-octadecadienoic acid,
- **Shortened form of nomenclature can be used**:
  - Oleic acid it is: 18:1; 9;
    - It means 18C atoms, one double bond between C9 and C10,
  - Linoleic acid it is: 18:2;9,12;

Explain the Omega numbering system for unsaturated fatty acids

- **ω-numbering system** is used to indicate the position of a double bond by counting from the ω-Carbon;

Examples:

- **Oleic acid: ω 9, C18:1**
  - ω 9 means Oleic acid contains a double bond between C9 and C10 counting from the ω-carbon atom (i.e., from the last Carbon atom in the fatty acid molecule);
  - C18:1, means 18C atoms, one double bond;
- **Linoleic acid: ω 6, C18:2**
  - ω 6 means Linoleic acid contains a double bond between C6 and C7 counting from the ω-carbon atom,
  - C18:2, means 18C atoms, two double bonds, the first double bond is between C6 and C7 counting from the ω-carbon;

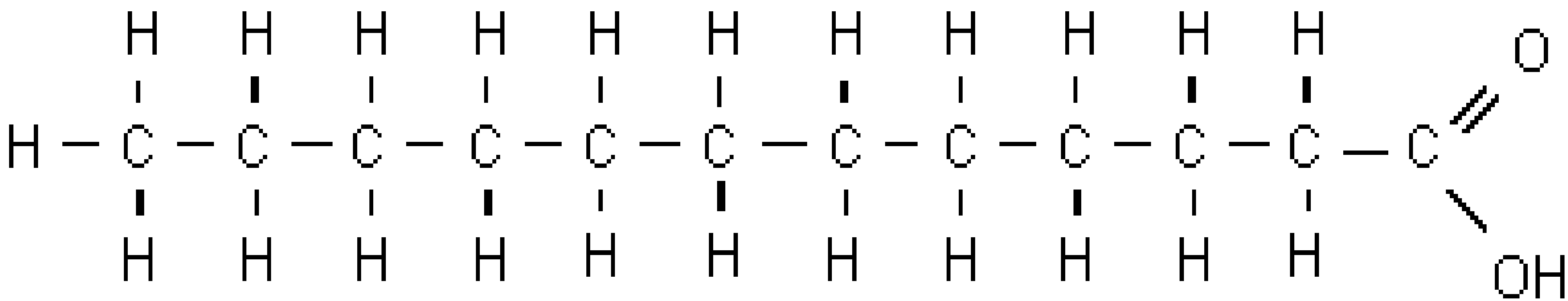
Omega Nomenclature

ω9 C18:1

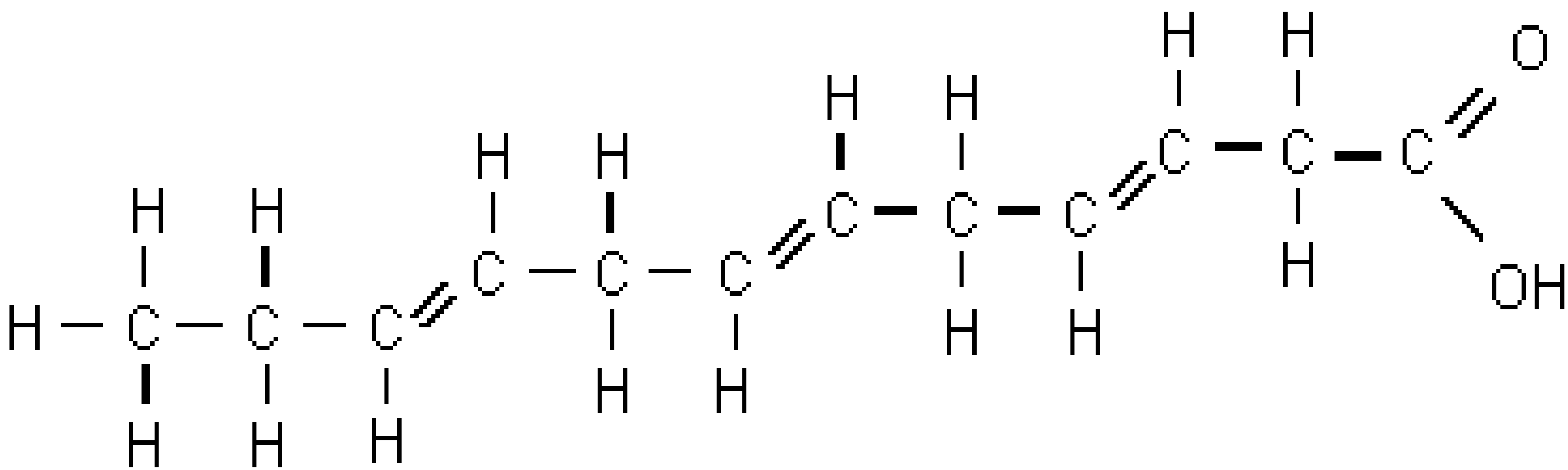
ω6 C18:2

ω3 C18:4

Schematic diagrams of Saturated and Unsaturated Fatty Acids



Saturated Fatty Acid



Unsaturated Fatty Acid

OMEGA NUMENCLATURE: IMPORTANT TO NOTE

- In Omega numbering system the position of the second double bond is not indicated;
- General principle is that in Polyunsaturated fatty acids, double bonds occur at every Third Carbon atom towards the Methyl end of the molecule:

- CH = CH - CH2 - CH = CH - CH2 - CH = CH -

- In other words, double bonds in Polyunsaturated fatty acids are **NOT** in the Conjugated form such as:

- CH = CH - CH = CH –

- Double bonds are separated by at least **Two single bonds**, not by just one single bond ,
- Thus, in Linoleic acid (ω 6, C18:2) the second double bond will be between C9 and C10 from the ω-carbon;

What are the groups of polyunsaturated fatty acids?

- Polyunsaturated fatty acids are grouped into Three series or families based on the Omega nomenclature. The groups are:

ω 9 or n-9 series:

- Fatty acids in which the first double bond is between C9 and C10 counting from the ω-carbon;
  - Examples: Oleic acid and Gondoic acid

ω 6 or n-6 series:

- Fatty acids in which the first double bond is between C6 and C7 counting from the ω-carbon;
  - Examples: Linoleic acid and Arachidonic acid

ω 3 or n-3 series:

- Fatty acids in which the first double bond is between C3 and C4 counting from the ω-carbon;
  - Examples: α-Linolenic acid and Timnodonic acid

Can polyunsaturated fatty acids be produced in mammalian tissues?

- Mammals can biosynthesize the ω 9 series of polyunsaturated fatty acids because of the presence of **Δ9-Desaturase** enzyme in liver and other tissues;
- The enzyme can introducing double bonds only between C-9 and the Carboxyl group;
- The **ω 6 series and ω 3 series** of polyunsaturated fatty acids **cannot be biosynthesized** by most animals including humans, because of lack of the Desaturase enzyme system capable of introducing double bonds beyond C-9 (carbon atom number 9 counting from the Carboxyl carbon);

Systematic names & Shortened names of some unsaturated fatty acids

Common names	Systematic names (all-cis-)	Shortened names
Palmitoleic acid	9-Hexadecenoic acid	16:1;9
Oleic acid	9-Octadecenoic acid	18:1;9
Vaccenic acid	11-Octadecenoic acid	18:1;11
Linoleic acid	9,12-Octadecadienoic acid	18:2;9,12
γ-Linolenic acid	6,9,12-Octadecatrienoic acid	18:3;6,9,12
α-Linolenic acid	9,12,15-Octadecatrienoic acid	18:3;9,12,15
Gondoic acid	11-Eicosenic acid	20:1;11
Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	20:4;5,8,11,14
Timnodonic acid	5,8,11,14,17-Eicosapentaenoic acid (EPA)	20:5;5,8,11,14,17
Erucic acid	13-Docosenoic acid	22:1;13
Clupanodonic acid	7,10,13,16,19-Docosapentaenoic acid	22:5;7,10,13,16,19
Cervonic acid	4,7,10,13,16,19-Docosahexaenoic acid (DHA)	22:6;4,7,10,13,16,19
Nervonic acid	15-Tetracosenoic acid	24:1;15

What are the essential fatty acids?

- ESSENTIAL FATTY ACIDS are **Unsaturated** fatty acids that **cannot** be biosynthesized in tissues of some animals including humans, thus they must be obtained in the diet. Examples:
  - **Linoleic acid (18:2;9,12) and**
  - **α-Linolenic acid (18:3;9,12,15)**
- Most of the essential fatty acids are members of the ω 6 and ω 3 series;
- Some animals including humans can biosynthesize **Arachidonic acid** from Linoleic acid obtained in the diet;
- Thus, **Linoleic acid** is called **True Essential Fatty Acid;**

State some of the physical properties of fatty acids

- Fatty acids are Amphipathic, because of the Hydrophobic tail and Hydrophilic (–COOH) head,
- The longer the Hydrocarbon chain the higher the melting point of the fatty acid,
- The greater the number of double bonds in the fatty acid the lower the melting point of the fatty acid,
- Unsaturated fatty acids have substantially lower melting points than saturated fatty acids,
- Example, melting point of:
  - Stearic acid (18:0) is 70o C
  - Oleic acid (18:1;9) is 13o C,
  - Linoleic acid (18:2;9,12) is -11o C.

CLASSIFICATION OF LIPIDS:
What are the major classes of lipids?

Lipids can be separated into 3 major classes:

- **Simple lipids**: Esters that fatty acids form with various alcohols;
- Simple lipids are made up of:
  - Fats,
  - Oils,
  - Waxes
- Fats and oils are esters of Fatty Acids and Glycerol;
- Waxes are esters of fatty acids and higher molecular weight monohydric alcohols,

- **Complex lipids**: Esters made up of Fatty Acids, Alcohol and other chemical compounds,
- Complex lipids are made up of:
  - Phospholipids,
  - Glycolipids,
  - Glycosphingolipids,
  - Sulfolipids,
  - Aminolipids
  - Lipolipids,

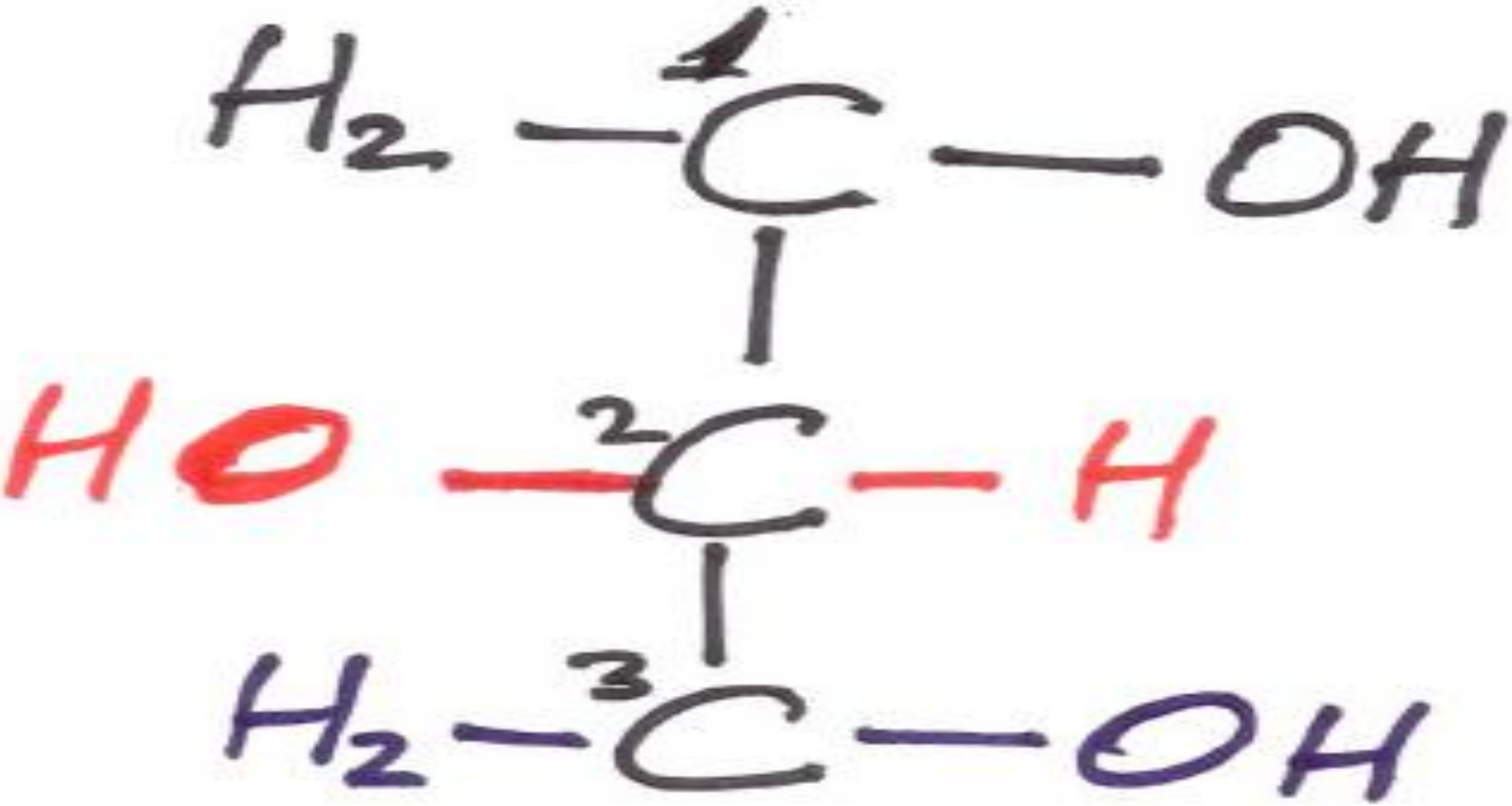
- **Precursor and derived lipids**:
- They include the following:
  - Fatty acids,
  - Glycerol,
  - Steroids,
  - Sterols,
  - Fatty Aldehyde,
  - Ketone bodies,
  - Hydrocarbons,
  - Lipid-soluble vitamins
  - Hormones

Simple Lipids:
What is the stereospecific (sn-) numbering system?

- Triacylglycerols (Triglycerides or Neutral Fats) are Tri-esters of Glycerol and 3 Fatty acids,
- General structure of a Triacylglycerol contains 3 Fatty Acyl groups linked by ester bonds to Glycerol (Propane-1, 2, 3-triol),
- If the fatty acyl groups that are esterified to C-1 and C-3 of the glycerol molecule are different, then the C-2 of the Glycerol molecule is asymmetric (Chiral center),

- Fatty Acyl group esterified to C-2 is written to the left of C-2 in a Fisher projection formula to designate the L-configuration of naturally occurring Triacylglycerols,
- Spatial arrangements of the -OH groups in C-1 and C-2 of Glycerol molecule are not identical,
- Therefore, the 3 carbon atoms in a Glycerol molecule are usually designated either by:
- **Stereospecific numbering** system (**sn-,** 1, 2, 3) or by
- An older numbering system that uses the symbols α, β and α ‘

Sterospecific numbering of Glycerol

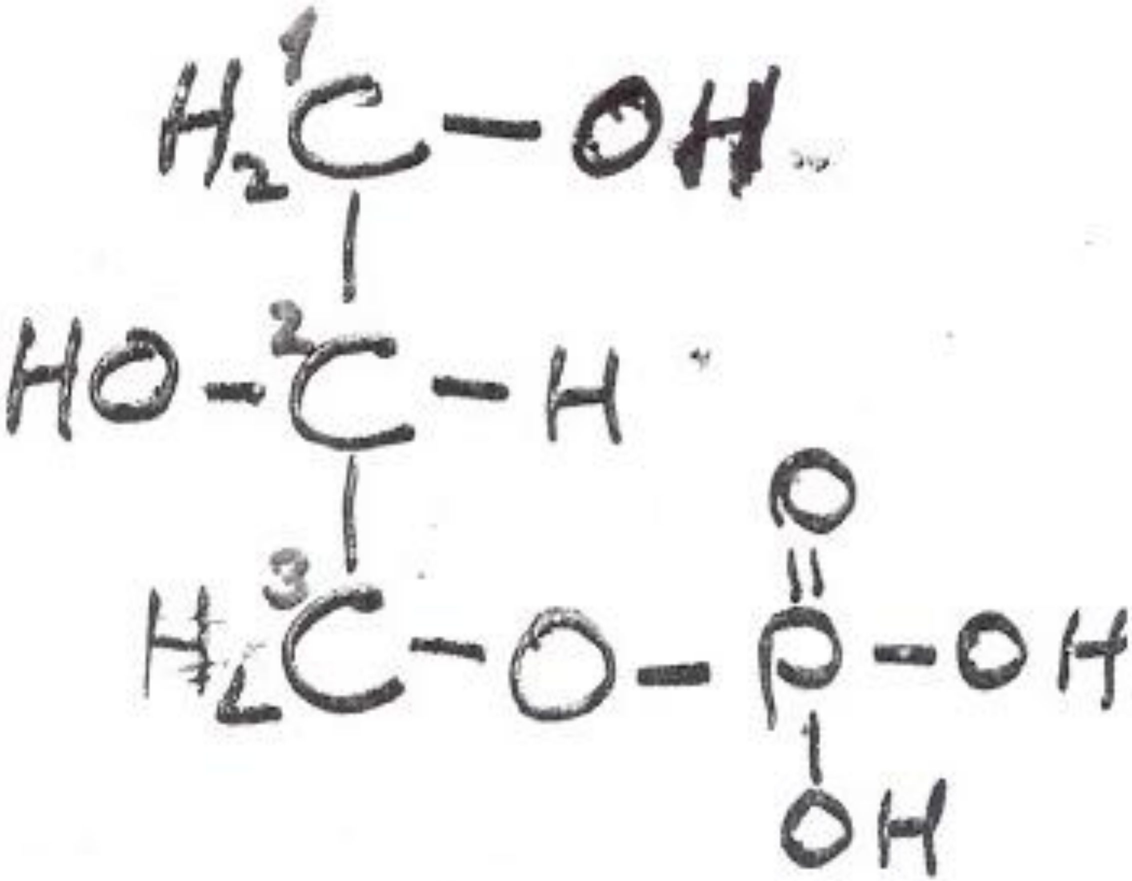


Sn - GLYCEROL

Why is the stereospecific (sn-) numbering system of Glycerol important?

- -sn- numbering of Glycerol is significant because some enzymes can readily distinguish sn-3 Carbon from sn-1 Carbon in Glycerol,
- Example: Glycerol kinase catalyzes the addition of a Phosphate group to -OH on sn-3 Carbon of Glycerol to produce Glycerol-3-Phosphate and not Glycerol-1-Phosphate,

Sn-Glycerol-3-Phosphate

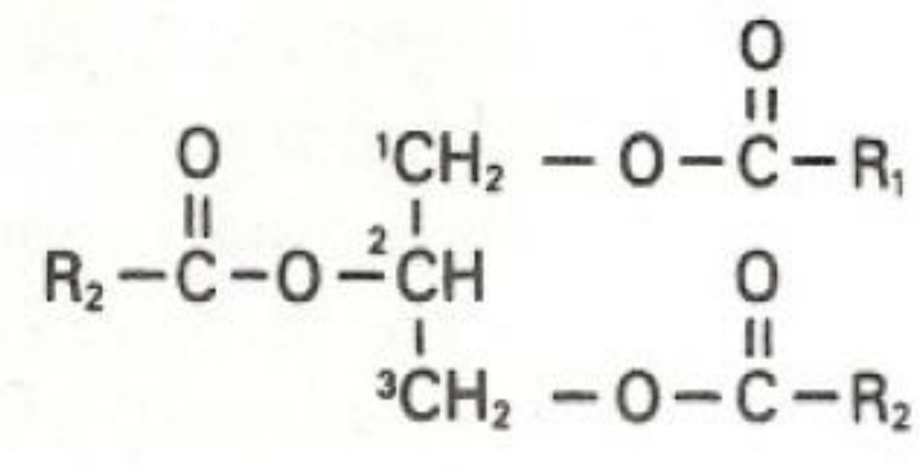


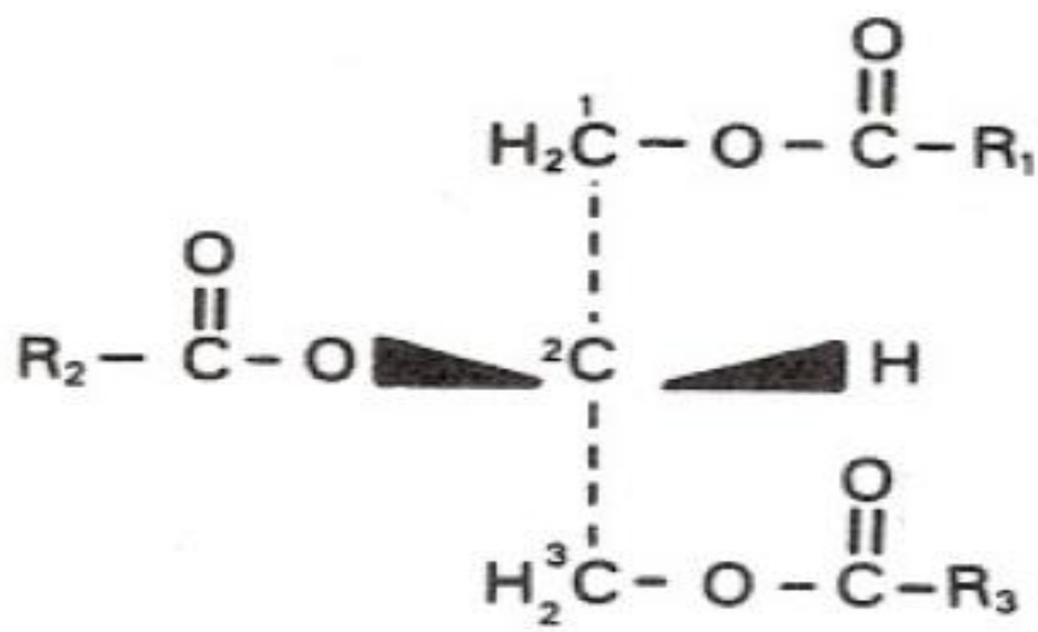
Sn-GLYCEROL-3-PHOSPHATE

Why are Simple Triacylglycerols different from Mixed Triacylglycerols?

- Triacylglycerol that contains identical fatty acyl groups that are esterified to the three-ester positions of Glycerol is called a **Simple Triacylglycerol**;
- Eexample,
- Triolein (Tri-oleoyl-glycerol) contains three molecules of Oleic acid residues esterified to a molecule of Glycerol,
- Tri-stearin (Tri-stearoyl-glycerol) contains three Stearic acid residues esterified to a molecule of glycerol,

Diagrams of Simple Tri-acyl-glycerols





- **Mixed Triacylglycerols** contain two or three different types of fatty acid residues esterified to a molecule of Glycerol,
- Such compounds are named according to the placement of the fatty acid residues on the glycerol molecule,
- Examples:
- 1-palmitoleoyl-2-linoleoyl-3-stearoyl-glycerol;
- 1,3-dipalmitoleoylstearoyl-glycerol.

How are Fats different from Oils?

- Fats and Oils are called Neutral fats,
- They are complex mixtures of simple and mixed Triacylglycerols, whose composition of fatty acid residues varies with the organism that produced them
- Fats are solid or semi-solid at room temperature;
- Oils are liquid at room temperature,
- Triacylglycerols in oils contain mainly unsaturated fatty acids
- Triacylglycerols in fats contain mainly saturated fatty acid,
- Melting points of unsaturated fatty acids are lower than those for saturated fatty acids,

COMPLEX LIPIDS

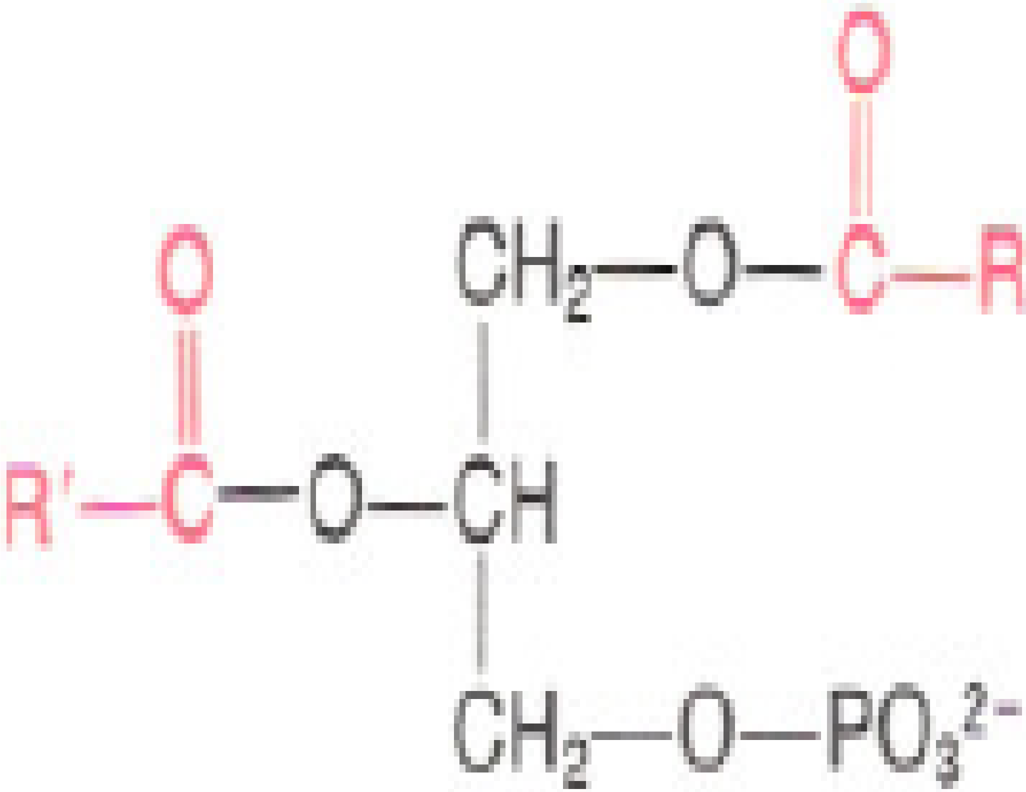
What are Phospholipids (give examples)?

- Phospholipids: Lipids containing Phosphate; eg:
  - **Phospho-Glycerides,**
  - **Sphingosine (e.g., Sphingomyelin),**
- Major lipids in cellular membranes of Glandular organs, Blood plasma, Egg yolk and Seeds of legumes,
- Phospho-glyceride (Glycero-phospho-lipids or Phospho-acyl-glycerol) are major components of the Biological Membranes,

Give the general structure of Phospholipids

- General structure of Phosphoglyceride (**see diagram**)
- Phosphoglyceride is made up of:
  - sn-3-Phosphorylated Glycerol (sn-Glycerol-3-Phosphate) esterified at C-1 , C-2 with Fatty acids;
  - A Third ester bond is formed between the Phosphate group at sn-C-3 and a Polar Alcohol ("X");
- Phosphoglycerides are Amphipathic they contain:
- Two non-polar aliphatic hydrophobic chains ("Tails") and
- Polar hydrophilic (Phosphoryl-X group) ("Head").,
  - Saturated fatty acid r with either 16C or 18C are esterified to sn-C-1 of Glycerol; while sn-C-2 in Glycerol is esterified unsaturated fatty acid that contains between 16C to 20C;

Diagram of Phosphoglyceride



Phosphatidic acid

Diagram of Phospholipid

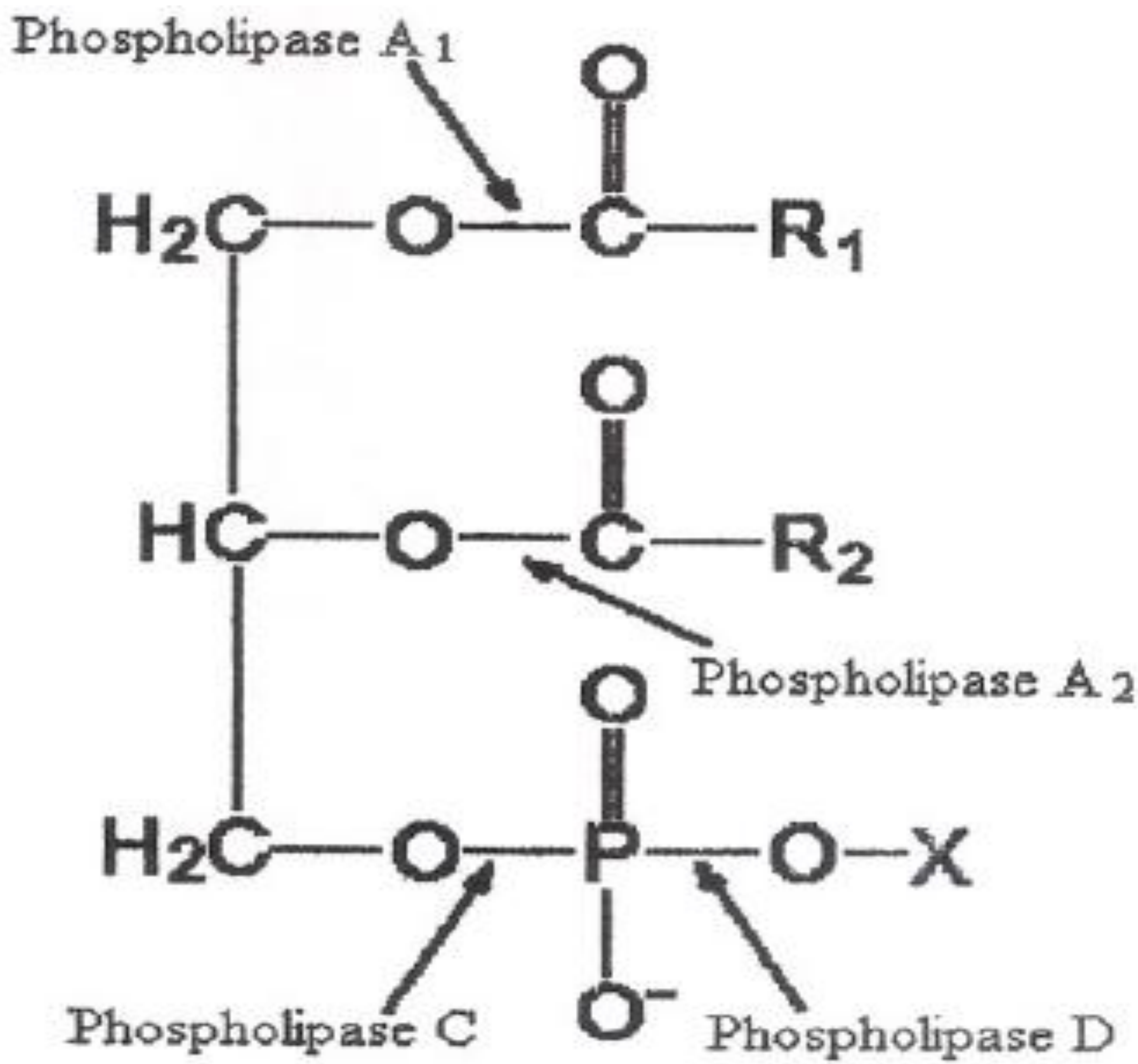
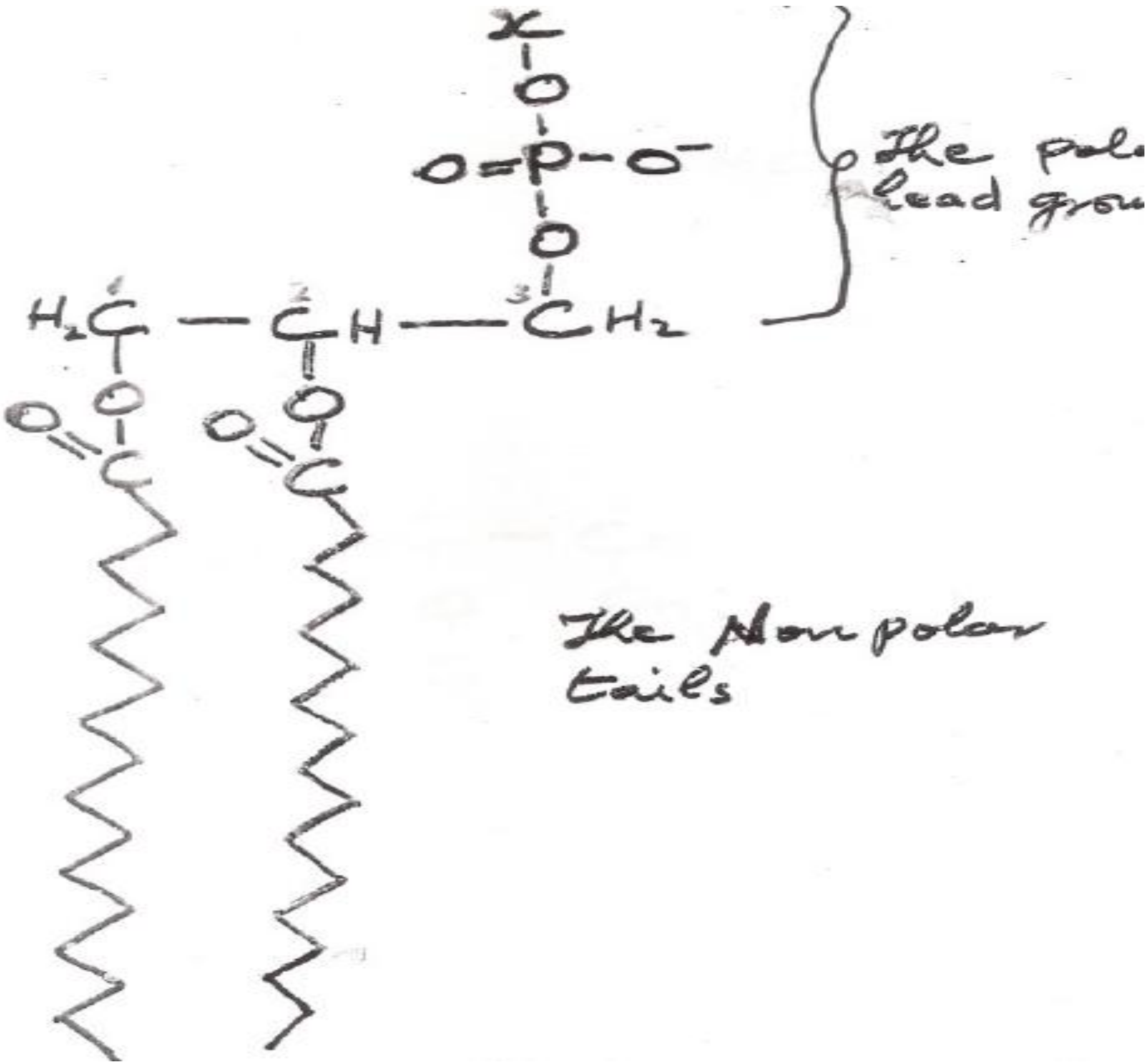


Diagram of Phosphoglyceride



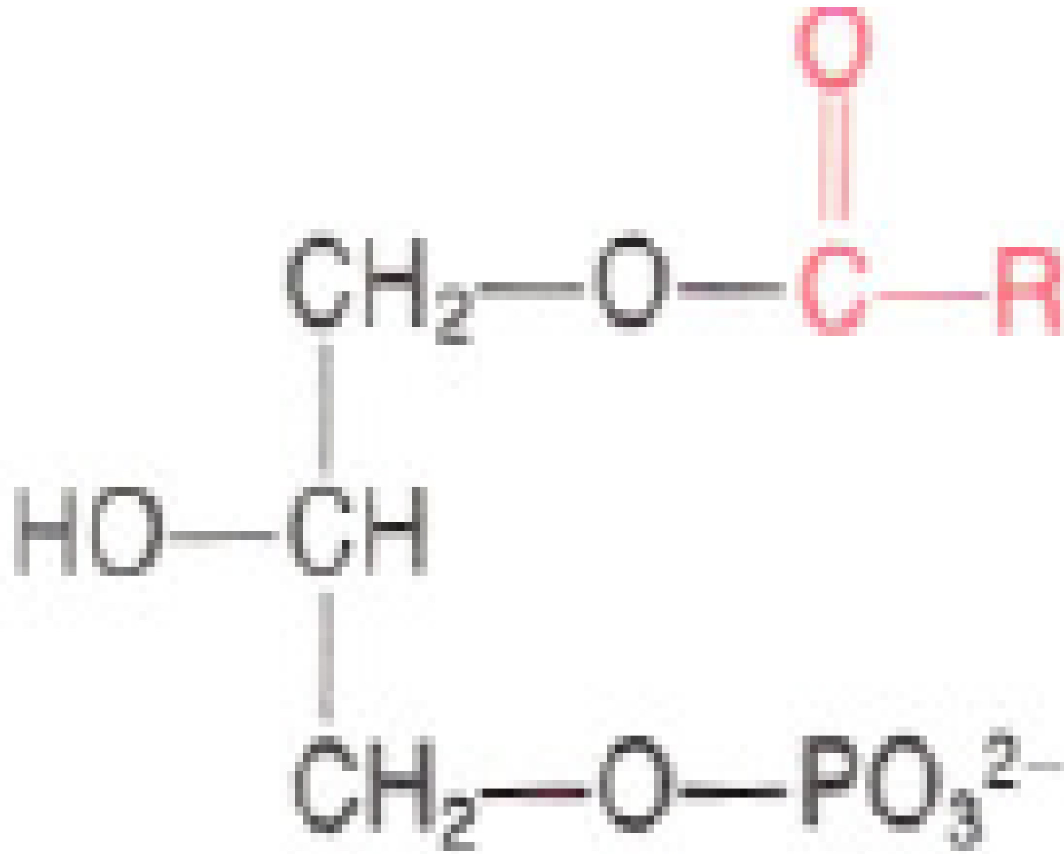
Structures and names of some Phosphoglycerides and their corresponding polar alcohol groups;
Phosphatidic acid: simplest Phosphoglyceride with "X" = -H

Phosphoglyceride (Glycerophospholipid)	**Polar alcohol group ("X")**
Phosphatidic acid	-H
Phosphatidylethanolamine (Cephaline)	Ethanolamine
Phosphatidylcholine (Lecithin)	Choline
Phosphatidylserine	Serine
Phosphatidylinositol	Myo-inositol
Phosphatidylglycerol	Glycerol

What are Lysophospholipids?

- **Lysophospholipids** are Glycerophospholipids that contain only one fatty Acyl residue in their molecule,
- Example: **Lecithin** (**Phosphatidylcholine**) contains 2 Fatty Acyl residues in its molecule, while Lysolecithin contains only One Fatty Acyl residue,

Diagram of Lyso-phospholipid



Lysophosphatidic acid

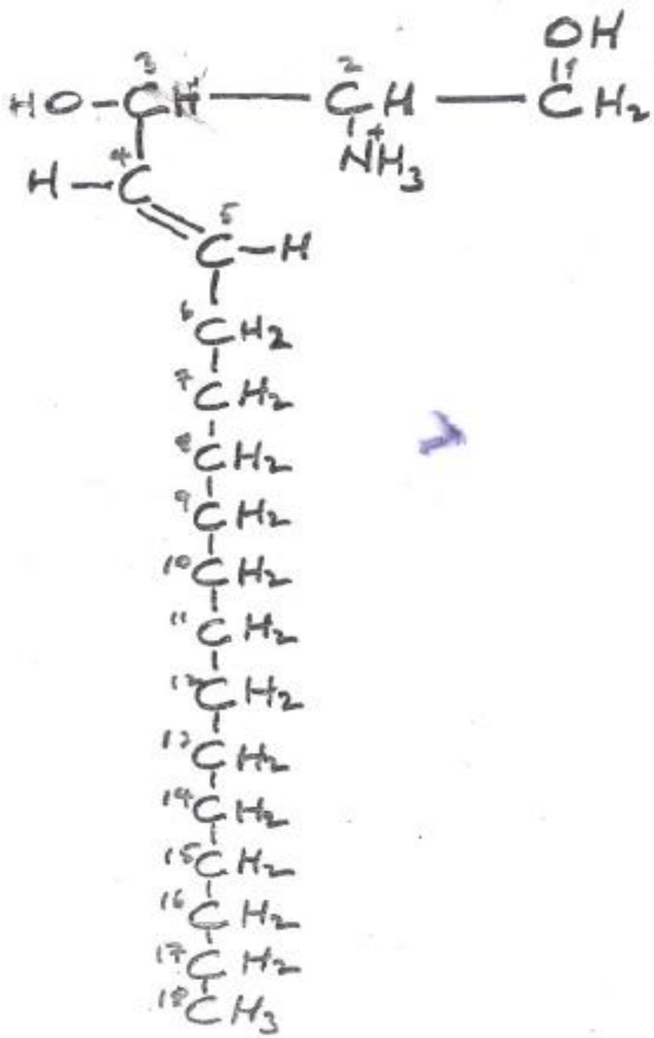
What is Plasmalogen?

- **Plasmalogens** are Glycerophospholipids (Phosphoglycerides)
- They are structurally different from other Glycerophospholipids,
- The sn-1-C of Glycerol is linked by Ether bond to a **cis-α, β -Unsaturated Alcohol** instead of a saturated fatty acid as in other Glycerophospholipids,
- Plasmalogen: Polar alcohol (Head) group "X" can either be Ethanolamine, Choline or Serine,

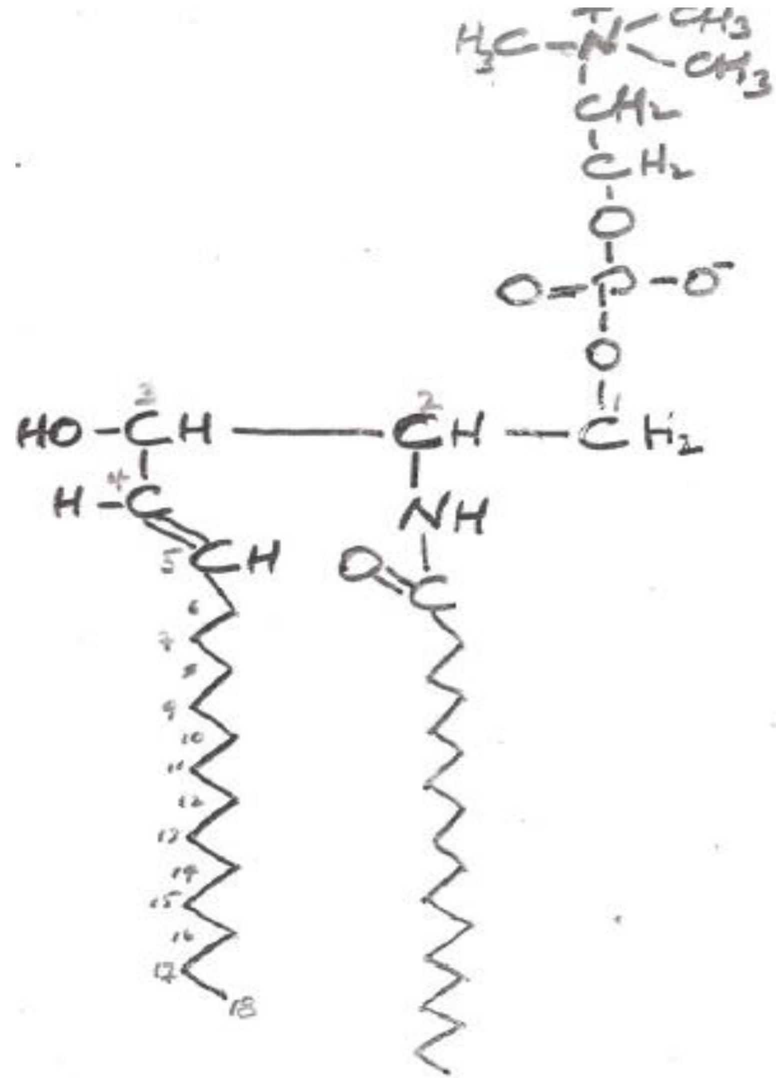
What is Sphingolipid

- All Sphingolipids are derived from **Sphingosine**,
- Different types of Sphingolipids are:
  - Sphingomyelin, (which are the only Sphingolipid that contain phosphate and have no sugar moiety),
  - Glycosphingolipids.
- **Sphingosine** (**also called 4-Sphingenine**) is an 18 carbon unsaturated amino alcohol (a diol),

Diagram of Sphingosine & Sphingomyelin



SPHINGOSINE

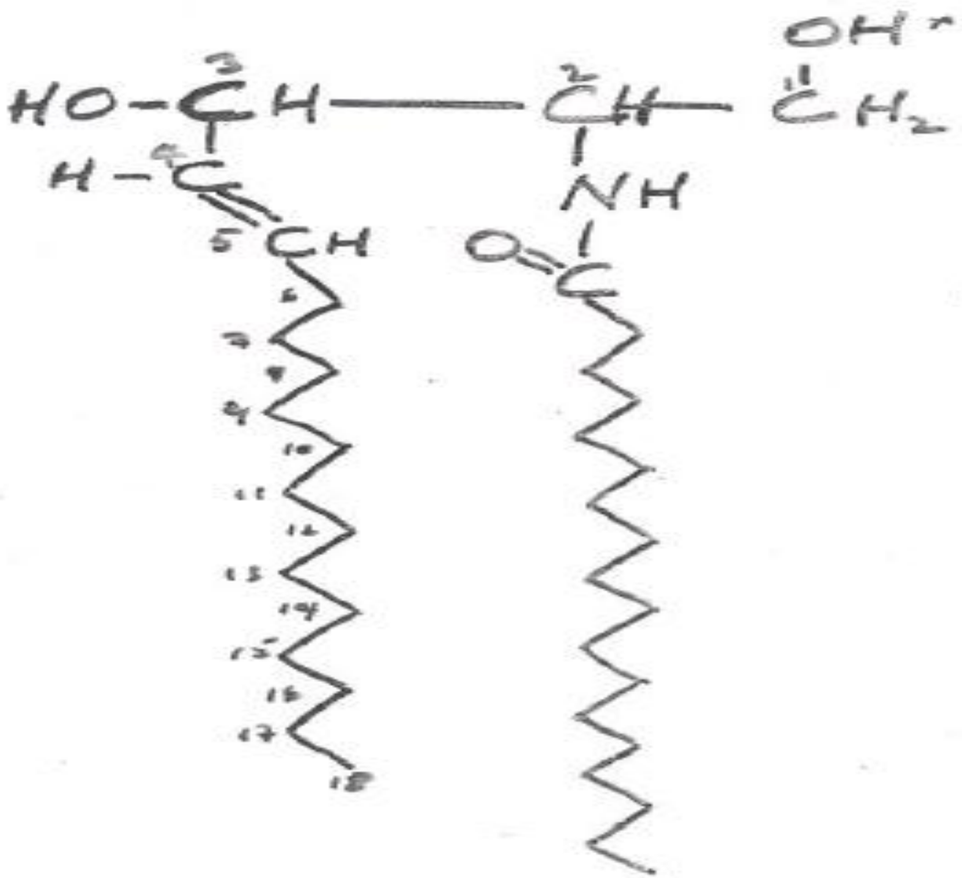


SPHINGOMYELIN

What is Ceremide?

- **Ceramide:** Compound formed when a fatty acid molecule is linked to -NH2 group in Sphingosine via amide bond,
- Ceramides are the N-fatty acyl derivatives of Sphingosine,
- Ceramides form the core structure of naturally occurring Sphingolipids,

Diagram of Ceramide



GENERAL STRUCTURE OF A CERAMIDE

EICOSANOIDS

- Eicosanoids are a group of compounds derived from metabolism of Eicosapolyenoic fatty acids (Polyunsaturated fatty acids with 20 Carbons). Examples:
  - **Prostanoids,**
  - **Leukotrienes (LTs) and**
  - **Lipoxins (LXs)**
- **Prostanoids** are a group of compounds that include:
  - **Prostaglandins (PGs),**
  - **Prostacyclins (PGIs) and**
  - **Thromboxanes (TXs)**

Diagram of Cholesterol