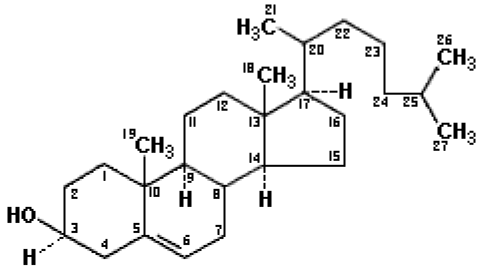
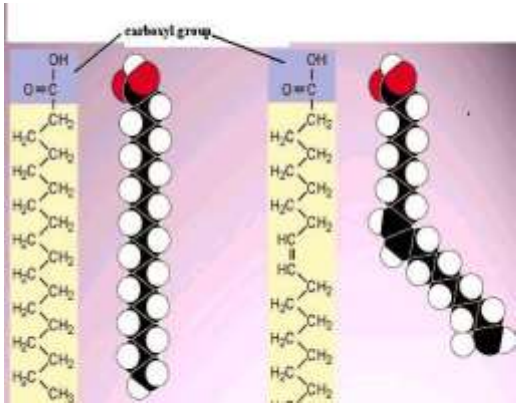
Lipid Chemistry





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Lipids

- The lipids are a heterogeneous group of compounds, including fats, oils, steroids, waxes, and related compounds, that are related more by their physical than by their chemical properties.

- They have the common property of being
- (1) relatively **insoluble in water** and (2) **soluble in nonpolar solvents** such as ether and chloroform.

Functions of lipids

- **Storage** form of energy
- Important dietary components because of their **high energy value** and also because of the fat-soluble vitamins and the essential fatty acids contained in the fat of natural foods.
- Structural components of biomembranes
- Serve as **thermal insulators** in the subcutaneous tissues and around certain organs
- Nonpolar lipids act as electrical insulators, allowing rapid propagation of depolarization waves along **myelinated nerves**

Functions of lipids(Contd.)

- Provide **shape and contour** to the body
- Act as **metabolic regulators**
- Combinations of lipid and protein (lipoproteins) are important cellular constituents, occurring both in the cell **membrane** and in the mitochondria, and serving also as the means of **transporting lipids** in the blood.

Clinical significance of lipids

Following diseases are associated with abnormal chemistry or metabolism of lipids-

- Obesity
- Atherosclerosis
- Diabetes Mellitus
- Hyperlipoproteinemia
- Fatty liver
- Lipid storage diseases

Classification of Lipids

Simple lipids: Esters of fatty acids with various alcohols.

a. **Fats**: Esters of fatty acids with glycerol. **Oils** are fats in the liquid state.

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

Classification of Lipids(Contd.)

2. **Complex lipids**: Esters of fatty acids containing groups in addition to an alcohol and a fatty acid.

a. **Phospholipids**: Lipids containing, in addition to fatty acids and an alcohol, a phosphoric acid residue. They frequently have nitrogen-containing bases and other substituents, eg, in **glycerophospholipids** the alcohol is glycerol and in **sphingophospholipids** the alcohol is sphingosine.

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

c. **Other complex lipids**: Lipids such as sulfolipids and aminolipids. Lipoproteins may also be placed in this category.

Classification of Lipids(Contd.)

3) Precursor and derived lipids: These include-

- fatty acids
- glycerol
- steroids
- other alcohols
- fatty aldehyde
- ketone bodies
- hydrocarbons, lipid-soluble vitamins, and hormones.

Fatty Acids

- Fatty acids are aliphatic carboxylic acids
- Have the general formula R-(CH2)n-COOH
- They occur mainly as esters in natural fats and oils but do occur in the unesterified form as **free fatty acids,** a transport form found in the plasma.
- Fatty acids that occur in natural fats are usually straight-chain derivatives containing an even number of carbon atoms.
- The chain may be **saturated** (containing no double bonds) or **unsaturated** (containing one or more double bonds).

Classification of Fatty Acids

Fatty acids can be classified in many ways-

1) According to nature of the hydrophobic chain-

a) Saturated
b) Unsaturated
c) Branched chain fatty acids
d) Substituted Fatty acids

Saturated fatty acids do not contain double bonds, while unsaturated fatty acids contain double bonds

Saturated Fatty Acids

- Saturated fatty acids may be envisaged as based on acetic acid (CH_3 —COOH) as the first member of the series in which —CH_2 — is progressively added between the terminal CH_3 — and —COOH groups.
- Fatty acids in biological systems usually contain an even number of carbon atoms, typically between 14 and 24. The 16- and 18-carbon fatty acids are most common.
- The hydrocarbon chain is almost invariably unbranched in animal fatty acids. A few branched-chain fatty acids have also been isolated from both plant and animal sources.

Saturated Fatty Acids

Number of C atoms	Common Name	Systemic Name	Formula
2	Acetic acid	Ethanoic acid	CH3COOH
4	Butyric acid	Butanoic acid	$CH_3(CH_2)_2COOH$
6	Caproic acid	Hexanoic acid	$CH_3(CH_2)_4COOH$
8	Caprylic acid	Octanoic acid	$CH_3(CH_2)_6COOH$
10	Capric acid	Decanoic acid	$CH_3(CH_2)_8COOH$
12	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$
14	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$
16	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$
18	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$
20	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$
22	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$

Unsaturated fatty Acids

Unsaturated fatty acids may further be divided as follows-

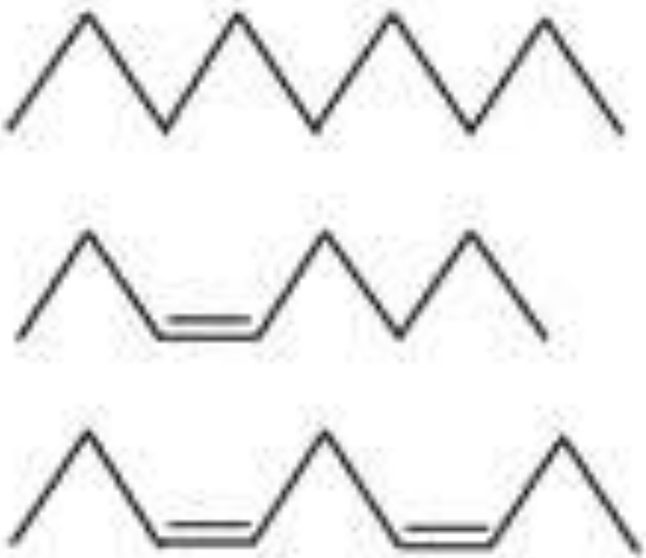
(1) **Monounsaturated** (monoethenoid, monoenoic) acids, containing one double bond.

(2) **Polyunsaturated** (polyethenoid, polyenoic) acids, containing two or more double bonds.

The configuration of the double bonds in most unsaturated fatty acids is cis.

The double bonds in polyunsaturated fatty acids are separated by at least one methylene group.

TYPES OF FATTY ACIDS
(according to the number of double bonds)



Saturated (No bond)

Monounsaturated (1 bond)

Polyunsaturated (>1 bond)

Nomenclature of Fatty acids

- The systematic name for a fatty acid is derived from the name of its parent hydrocarbon by the substitution of *oic*

  for the final *e.*
- For example, the C18 saturated fatty acid is called *octadecanoic acid* because the parent hydrocarbon is octadecane.
- A C18 fatty acid with one double bond is called octadec*enoic* acid; with two double bonds, octadeca*dienoic* acid; and with three double bonds, octadeca*trienoic* acid.
- The notation 18:0 denotes a C18 fatty acid with no double bonds, whereas 18:2 signifies that there are two double bonds.

Nomenclature of Fatty acids(Contd.)

Carbon atoms are numbered from the carboxyl carbon (carbon No. 1). The carbon atoms adjacent to the carboxyl carbon (Nos. 2, 3, and 4) are also known as the α ,β , and γ carbons, respectively, and the terminal methyl carbon is known as theω or n-carbon. The position of a double bond is represented by the symbol Δfollowed by a superscript number.

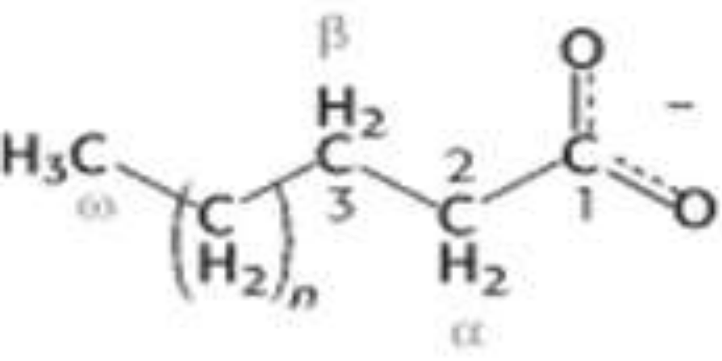
eg, Δ 9 indicates a double bond between carbons 9 and 10 of the fatty acid;

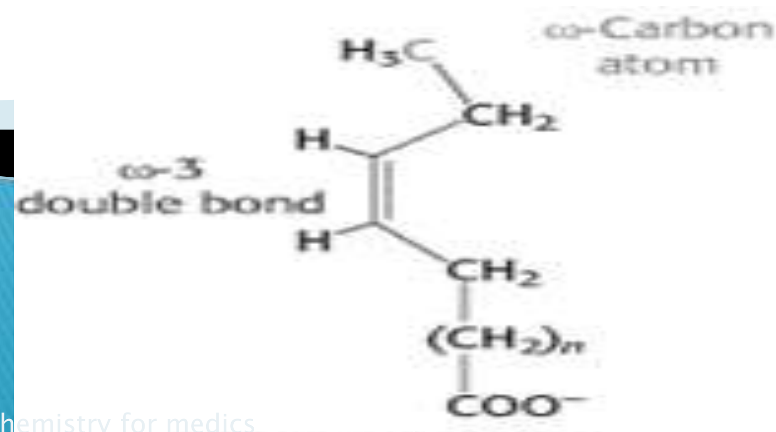
Nomenclature of Fatty acids(Contd.)

Alternatively, the position of a double bond can be denoted by counting from the distal end, with the ω-carbon atom (the methyl carbon) as number 1.

ω9 indicates a double bond on the ninth carbon counting from the ω-carbon.

In animals, additional double bonds are introduced only between the existing double bond (eg, 9, 6, or 3) and the carboxyl carbon, leading to three series of fatty acids known as the ω9, ω6, and ω3 families, respectively.





An ω-3 fatty acid

Unsaturated Fatty Acids

S.No.	Number of C atoms, number and location of double bonds	Family	Common Name	Systemic Name
[A]	**Monoenoic acids (one double bond)**			
1.	16:1;9	ω 7	Palmitoleic acid	*cis*–9–Hexadecenoic
2.	18:1;9	ω 9	Oleic Acid	*cis*–9–Octadecenoic
3.	18:1;9	ω 9	Elaidic acid	*trans* 9–Octadecanoic
[B]	**Dienoic acids (two double bonds)**			
1.	18:2;9,12	ω 6	Linoleic acid	all–*cis*–9,12–Octadecadieno

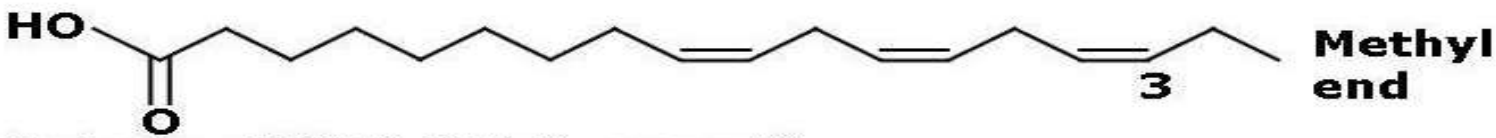
Unsaturated Fatty Acids(Contd.)

S.No.	Number of C atoms, number and location of double bonds	Family	Common Name	Systemic Name
[c]	**Trienoic acids (three double bonds)**			
1.	18:3;6,9,12	ω 6	Y- Linolenic acid	all-*cis*-6,9,12-Octadecatrienoic
2.	18:3;9,12,15	ω 3	α-Linolenic	all-*cis*-9,12,15Octadecatrienoic
[D]	**Tetraenoic acid(Four double bonds)**			
	20:4;5,8,11,	ω6	Arachidonic	all-*cis*-

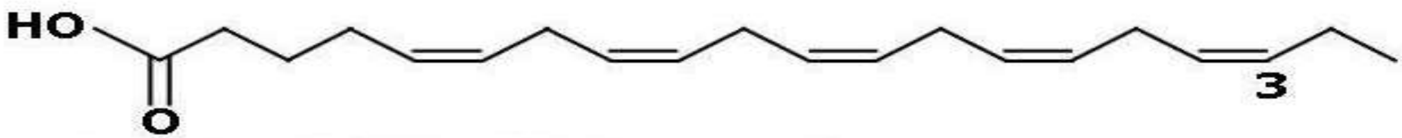
Unsaturated Fatty Acids(Contd.)

S.No.	Number of C atoms, number and location of double bonds	Family	Common Name	Systemic Name
[E]	**Pentaenoic acids (Five double bonds)**			
1.	20:5;5,8,11,14,17	ω 3	Timnodonic acid	all–*cis*–5,8,11,14,17–Eicosapentaenoic
[F]	**Hexaenoic acid(Four double bonds)**			
	22:6;4,7,10,13,16,19	ω3	Cervonic acid	all–*cis*–4,7,10,13,16,19–

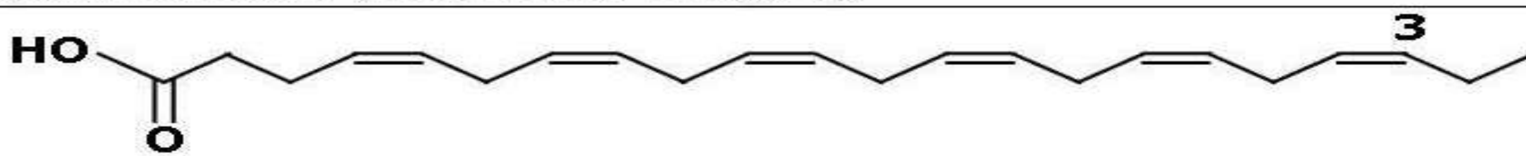
Omega 3 and Omega 6 fatty acids



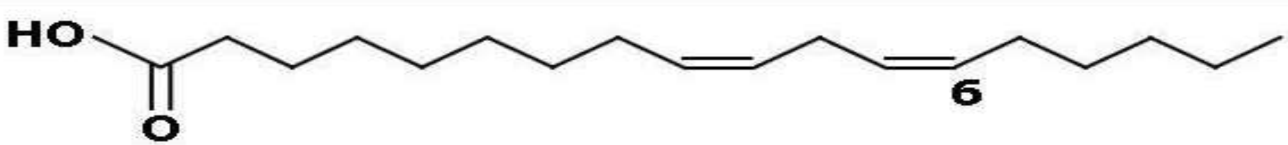
Alpha-linolenic acid (ALA, C18:3, omega-3)



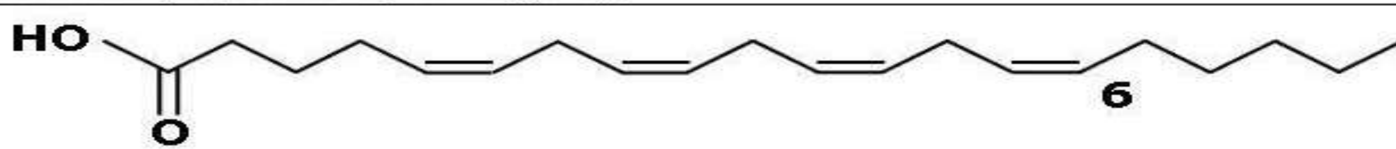
Eicosapentaenoic acid (EPA, C20:5, omega-3)



Docosahexaenoic acid (DHA, C22:6, omega-3)



Linoleic acid (LA, C18:2, omega-6)



Arachidonic acid (AA, C20:4, omega-6)

Cis and Trans-Isomers in unsaturated fatty acids

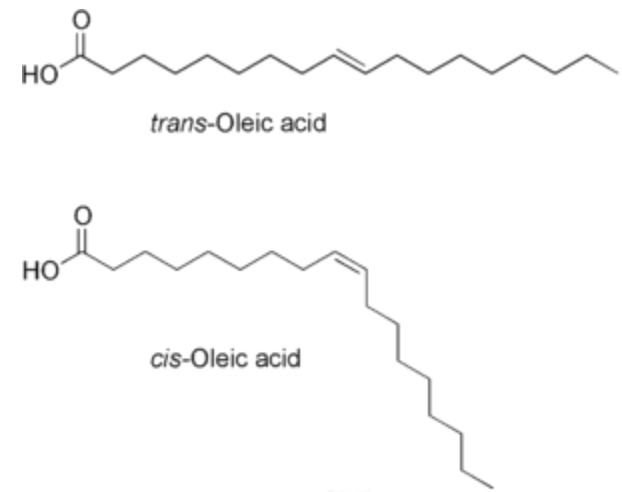
- Depending upon the orientation of the radicals around the axis of the double bond-
- Cis- If the radicals are on the same side of the double bond
- Trans- If the radicals are on the opposite side
- Oleic acid and Elaidic acid have the same formula but Oleic acid is cis while Elaidic acid is Trans Fatty acid

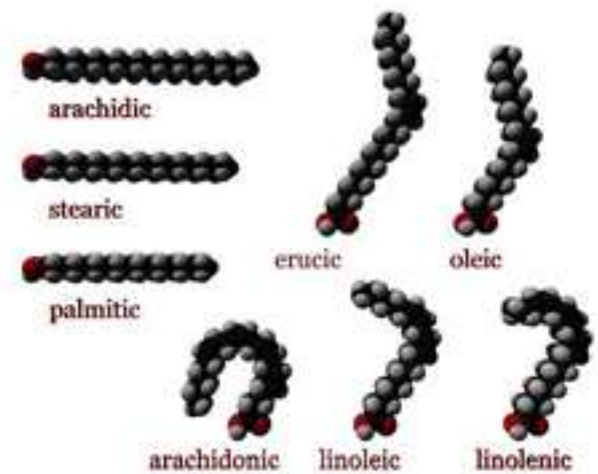
Cis and Trans-Isomers in unsaturated fatty acids

The hydrocarbon chains in saturated fatty acids are, fairly straight and can pack closely together, making these fats solid at room temperature.

Oils, mostly from plant sources, have some double bonds between some of the carbons in the hydrocarbon tail, causing bends or **“kinks”** in the shape of the molecules.

Increase in the number of *cis* double bonds in a fatty acid leads to a variety of possible spatial configurations of the molecule—eg, Arachidonic acid, with four *cis* double bonds, has "kinks" or a U shape.





Significance of unsaturated fatty acids

- Because of the kinks in the hydrocarbon tails, unsaturated fats can't pack as closely together, making them liquid at room temperature.

- The membrane lipids, which must be fluid at all environmental temperatures, are more unsaturated than storage lipids.
- Lipids in tissues that are subject to cooling, eg, in hibernators or in the extremities of animals, are more unsaturated.
- At higher temperatures, some bonds rotate, causing chain shortening, which explains why biomembranes become thinner with increases in temperature.

- The carbon chains of saturated fatty acids form a zigzag pattern when extended, as at low temperatures.

Trans Fatty acids

- *Trans* fatty acids are present in certain foods, arising as a by-product of the saturation of fatty acids during hydrogenation, or "hardening," of natural oils in the manufacture of margarine.
- An additional small contribution comes from the ingestion of ruminant fat that contains *trans* fatty acids arising from the action of microorganisms in the rumen.
- Naturally-occurring unsaturated vegetable oils have almost all cis bonds, but using oil for frying causes some of the cis bonds to convert to trans bonds.

c)Branched Chain Fatty acids

- Phytanic acid present in butter
- Sebum also contains branched chain fatty acids

- There may be even or odd chain fatty acids.
- Even chain fatty acids are predominantly present.

d) Cyclic fatty acids-

- Chaulmoogric acid and Hydnocarpic acid

e) Substituted fatty acids

- Cerebronic acid- OH fatty acid

2)Classification of fatty acids based on length of hydrophobic chain

- Short chain–with 2–6 carbon atoms
- Medium chain– with 8–14 carbon atoms
- Long chain– with 16–18 carbon atoms
- Very long chain fatty acids– with 20 or more carbon atoms

Biological Importance of fatty acids-

1-Fatty acids are the **building blocks of dietary fats.** The human body stores such fats in the form of **triglycerides**.

2)- Fatty acids are also **required for the formation of membrane lipids such as phospholipids and glycolipids.**

3) -They are required for the **esterificaton of cholesterol** to form cholesteryl esters.

4) They **act as fuel molecules** and are oxidized to produce energy.

Essential fatty acids

- Polyunsaturated fatty acids such as **Linoleic and Linolenic acids** are essential for normal life functions. They are therefore characterized as essential fatty acids.
- **Arachidonic acid** is considered as semi essential fatty acid since it can be synthesized from Linoleic acid .
- Essential polyunsaturated fatty acids can be classified as belonging to one of two "families", the omega-6 family or the omega-3 family.
- Fatty acids belonging to these two families differ not only in their chemistry, but also in their natural occurrence and biological functions.

Significance of essential fatty acids

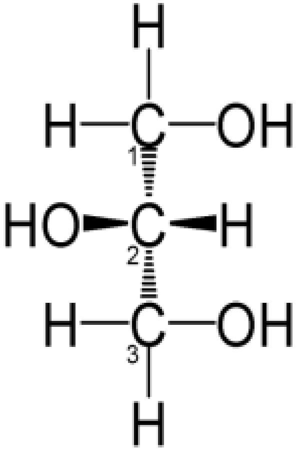
- Components of cell membranes, structural elements of gonads and mitochondrial membrane
- Required for brain growth and development
- Precursors of Eicosanoids
- Play important role in vision
- They have a cardio protective role- Lower serum cholesterol and increase HDL levels
- Prevent fatty liver formation
- Deficiencies of essential polyunsaturated fatty acids may cause a wide variety of symptoms, including retarded growth in children, reduced fertility and pathologic changes in the skin.

Glycerol-Structure and significance

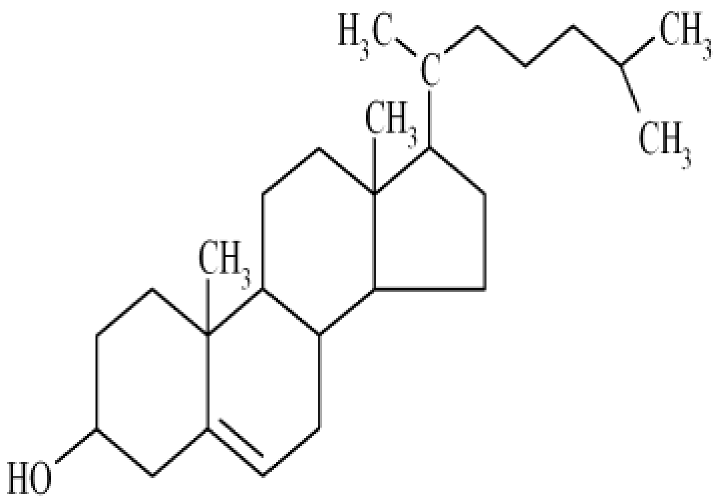
- Also called 'Glycerin'.
- Trihydric alcohol as it contains three hydroxyl groups
- Can be obtained from diet, from lipolysis of fats in adipose tissue and from glycolysis.
- Can be utilized for the synthesis of triacylglycerols, phospholipids, glucose or can be oxidized to provide energy
- Used as a solvent in the preparation of drugs and cosmetics
- Nitroglycerine is used as a vasodilator

Glycerol- Structure

- To number the carbon atoms of glycerol unambiguously, the -*sn* (stereochemical numbering) system is used.
- Carbons 1 and 3 of glycerol are not identical when viewed in three dimensions.
- Enzymes readily distinguish between them and are nearly always specific for one or the other carbon; eg, glycerol is always phosphorylated on *sn*-3 by glycerol kinase to give glycerol 3-phosphate and not glycerol 1-phosphate.



Cholesterol- Chemistry



- Most important sterol in human body
- Molecular formula- $C_{27}H_{45}$ OH
- Possesses a cyclo pentano perhydrophenatherene ring nucleus
- Has an -OH group at C3
- A double bond between C5 and C6
- Two- CH3 groups at C10 and C13
- An eight carbon side chain attached to C17

Forms of Cholesterol

- Cholesterol occurs both as free form or in ester form

- **In cholesteryl ester,** the hydroxyl group on position 3 is esterified with a long-chain fatty acid.

- Cholesterol esters are formed by the transfer of acyl group by **Acyl transferases-(LCAT and ACAT)**

- In plasma, both forms are transported in lipoproteins

- Plasma **low-density lipoprotein (LDL) is the vehicle of uptake of cholesterol and cholesteryl ester into many tissues.**

- Free cholesterol is removed from tissues by plasma high-density lipoprotein (HDL) and transported to the liver, where it is eliminated from the body either unchanged or after conversion to bile acids in the process known as **reverse cholesterol transport**

- A sum total of free and ester cholesterol in serum is called serum total cholesterol

Significance of Cholesterol

- Cholesterol is widely distributed in all cells of the body but particularly in **nervous tissue.**
- It is a **major constituent of the plasma membrane and of plasma lipoproteins**.
- It is synthesized in many tissues from acetyl-CoA and is the **precursor of all other steroids in the body, including corticosteroids, sex hormones, bile acids, and vitamin D.**
- Cholesterol is a major constituent of **gallstones.**
- Its chief role in pathologic processes is as a factor in the genesis of **atherosclerosis** of vital arteries, causing cerebrovascular, coronary, and peripheral vascular disease.

Normal serum level and Variations

- Normal level of serum total cholesterol ranges between **150-220 mg/dL**
- **Physiological variations-**
- Low at the time of birth, increases with advancing age.
- The level is increased during pregnancy
- **Pathological Variations-**
- **a) Low cholesterol (Hypocholesterolemia)-**
- Thyrotoxicosis, anemia, hemolytic jaundice, wasting diseases and malabsorption syndrome.

Pathological variations of serum Total Cholesterol (Contd.)

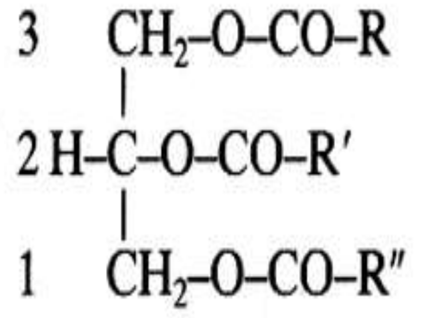
B) Hypercholesterolemia-

- Nephrotic syndrome
- Diabetes Mellitus
- Obstructive Jaundice
- Myxoedema
- Xanthomatous biliary cirrhosis
- Hypopituitarism
- Familial Hypercholesterolemia
- Idiopathic

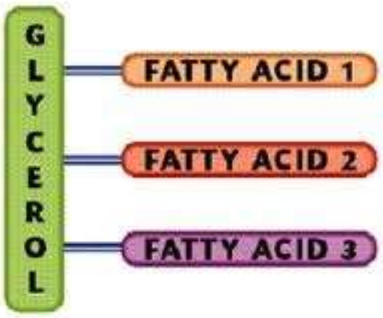
Other sterols of biological Importance

- 7- dehydrocholesterol- also called as Provitamin D3 (Precursor of vitamin D)
- Ergo sterol-plant sterol (First isolated from Ergot- Fungus of Rye)
- Stigmasterol and Sitosterol- Plant sterols
- Coprosterol (Coprostanol)- Reduced products of cholesterol- found in feces
- Other steroids- Bile acids, adrenocortical hormones, gonadal hormones, D vitamins and Cardiac glycosides.

Simple Lipids



sn-1,2,3-tri-*O*-acyl glycerol



- **Neutral fats or Triacyl Glycerides-**
- The triacylglycerols are esters of the trihydric alcohol, glycerol and fatty acids.
- Mono- and Diacylglycerol, wherein one or two fatty acids are esterified with glycerol, are also found in the tissues.
- Naturally occurring fats and oils are mixtures of triglycerides.
- If all the OH groups are esterified to same fatty acids- It is **Simple Triglyceride**
- If different fatty acids are esterified- it is known as **Mixed triglyceride.**
- **Polyunsaturated fatty acid is esterified at 2nd position.**

Properties of triglycerides

- Colourless, odourless and tasteless
- Insoluble in water
- Specific gravity is less than 1.0, consequently all fats float in water
- Oils are liquids at 20^0C, they contain higher proportion of Unsaturated fatty acids
- Fats are solid at room temperature and contain saturated long chain fatty acids
- Triglycerides are the storage form of energy in adipose tissue
- Triglycerides in the body are hydrolyzed by **Lipases**

Lipases

- Lipases are enzymes which catalyze hydrolysis of triglycerides yielding fatty acids and glycerol
- Lipases are present in following places-
- Lingual Lipase-In saliva
- Gastric lipase- in gastric juice
- Pancreatic lipase -in pancreatic juice
- Intestinal lipase- in intestinal epithelial cells
- Hormone sensitive lipase - in adipose tissue

Properties of triglycerides(Cotd.)

- **Saponification**–When the triglycerides are hydrolyzed by alkali the process is known as Saponification.

- **Rancidity**–Fats and oils have a tendency to become rancid.
- Rancidity refers to the appearance of unpleasant taste and smell of fats.
- **Hydrolytic rancidity** is due to partial hydrolysis of triglycerides due to traces of lipases present in the given fat
- **Oxidative rancidity** is due to partial oxidation of unsaturated fatty acids with the resultant formation of epoxides and peroxides by free radicals.
- Preserving the fats with antioxidants can prevent rancidity

Waxes

- They are esters of higher fatty acids with higher mono hydroxy aliphatic alcohols(e.g. Cetyl alcohol)
- Have very long straight chain of 60-100 carbon atoms
- They can take up water without getting dissolved in it
- Used as bases for the preparation of cosmetics, ointments, polishes, lubricants and candles.
- In nature, they are found on the surface of plants and insects.

Identification of fats and oils

Lipid index	Details	Significance
Saponification number	Number of mg of KOH required to saponify the free and combined fatty acids in 1G. of a given fat	Indicates molecular weight and is inversely proportional to it.
Iodine number	Number of grams of iodine absorbed by 100 gm of fat	It is a measure of degree of unsaturation of a fat
Acid number	Number of mg of KOH required to neutralize the fatty acids in a gram of a fat	Indicates the degree of rancidity of a fat

Identification of fats and oils(Contd.)

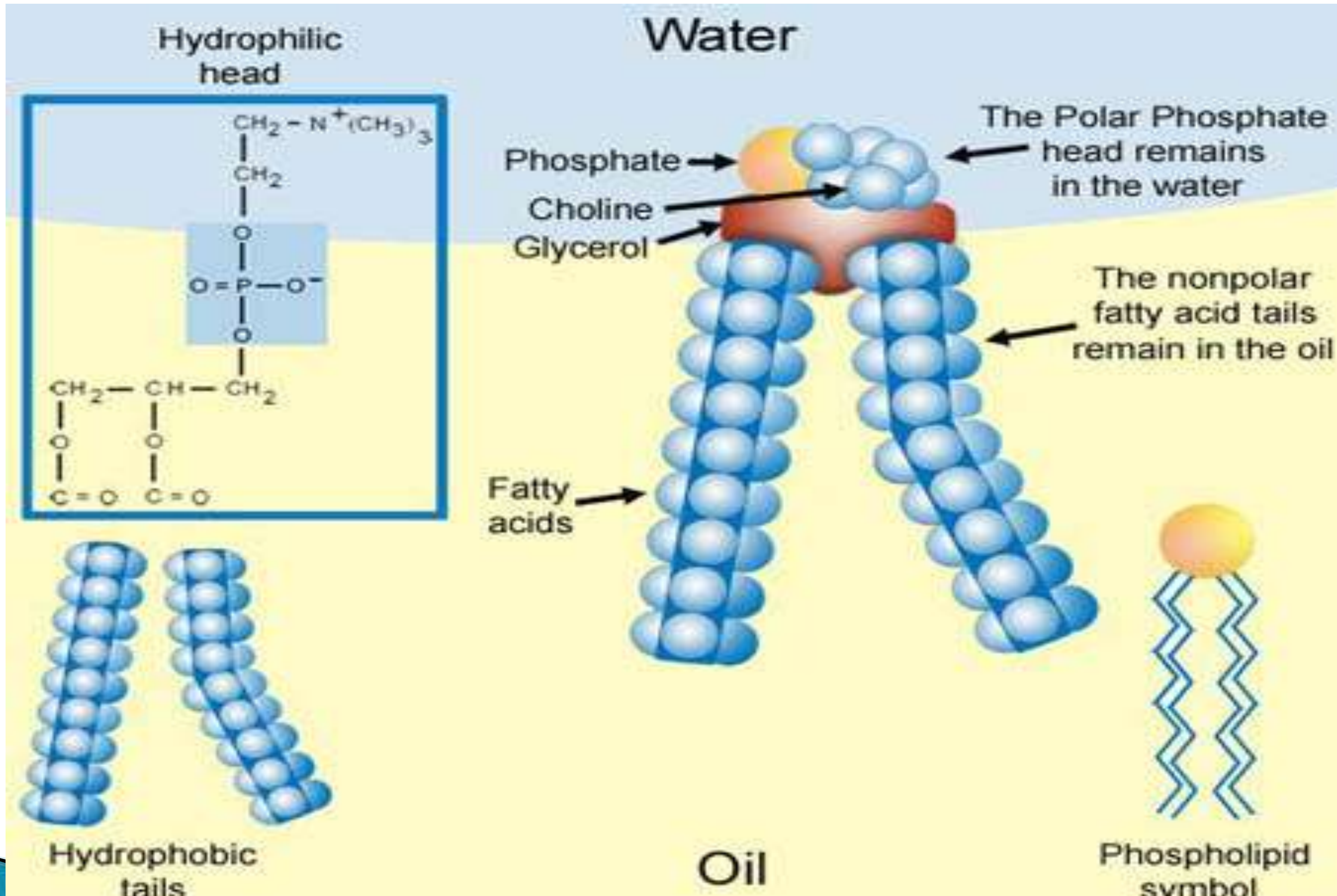
Lipid index	Details	Significance
Polenske number	Number of ml of 0.1 normal KOH required to neutralize the insoluble fatty acids from 5 gram of fat	Indicates the presence of non volatile fatty acids in a given fat
Reichert-Meissl Number	Number of ml of 0.1 N alkali required to neutralize the soluble fatty acids distilled from 5 G of fat	Measures the amount of volatile soluble fatty acids.
Acetyl Number	Number of mg of KOH required to neutralize the acetic acid obtained by saponification of 1G.of fat after it has been acetylated.	Measures the number of -OH groups present in a fatty acid

Compound Lipids

a)Phospholipids-

- Contain in addition to fatty acids and glycerol/or other alcohol, a phosphoric acid residue, nitrogen containing base and other substituents.
- Phospholipids may be regarded as derivatives of **phosphatidic acid** , in which the phosphate is esterified with the —OH of a suitable alcohol.
- They are amphipathic molecules containing a polar head and a hydrophobic portion

Phospholipids



Classification of phospholipids

Based on nature of alcohol-

1)Glycerophospholipids- Glycerol is the alcohol group.

Examples-

- Phosphatidyl choline
- Phosphatidyl ethanolamine
- Phosphatidyl serine
- Phosphatidyl inositol
- Phosphatidic acid
- Cardiolipin
- Plasmalogen
- Platelet activating factor
- Phosphatidyl Glycerol

2)Sphingophospholipids- Sphingol is the alcohol group

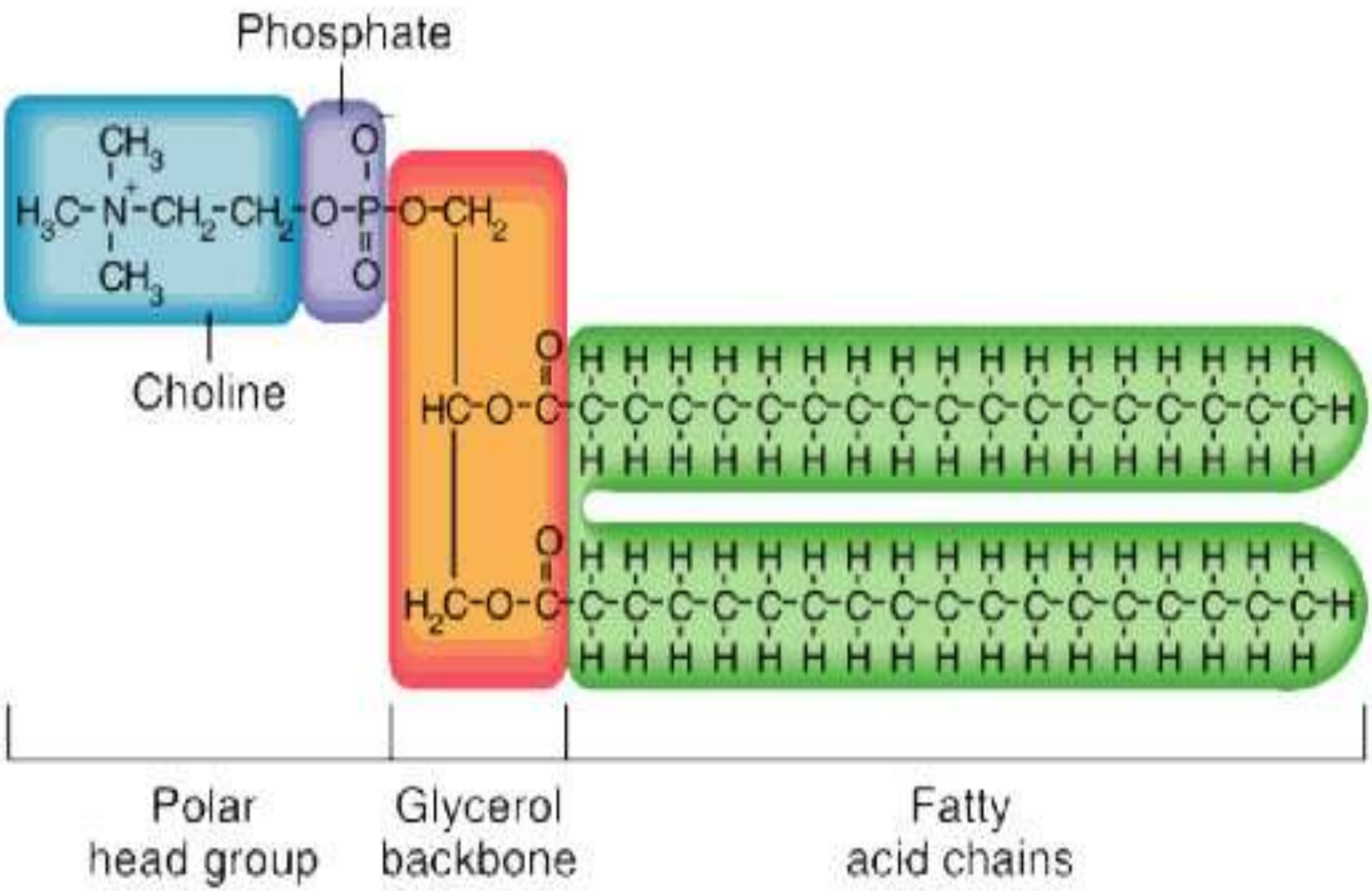
Example- Sphingomyelin

1)Glycerophospholipids

1) Phosphatidylcholines (Lecithins)

- Phosphoacylglycerols containing choline are the most abundant phospholipids of the cell membrane
- Are present a large proportion of the body's store of choline. Choline is important in nervous transmission, as acetylcholine, and as a store of labile methyl groups
- **Dipalmitoyl lecithin** is a very effective surface-active agent and a major constituent of the **surfactant** preventing adherence, due to surface tension, of the inner surfaces of the lungs. Its absence from the lungs of premature infants causes **respiratory distress syndrome.**

Structure of Phosphatidyl choline



Glycerophospholipids(Contd.)

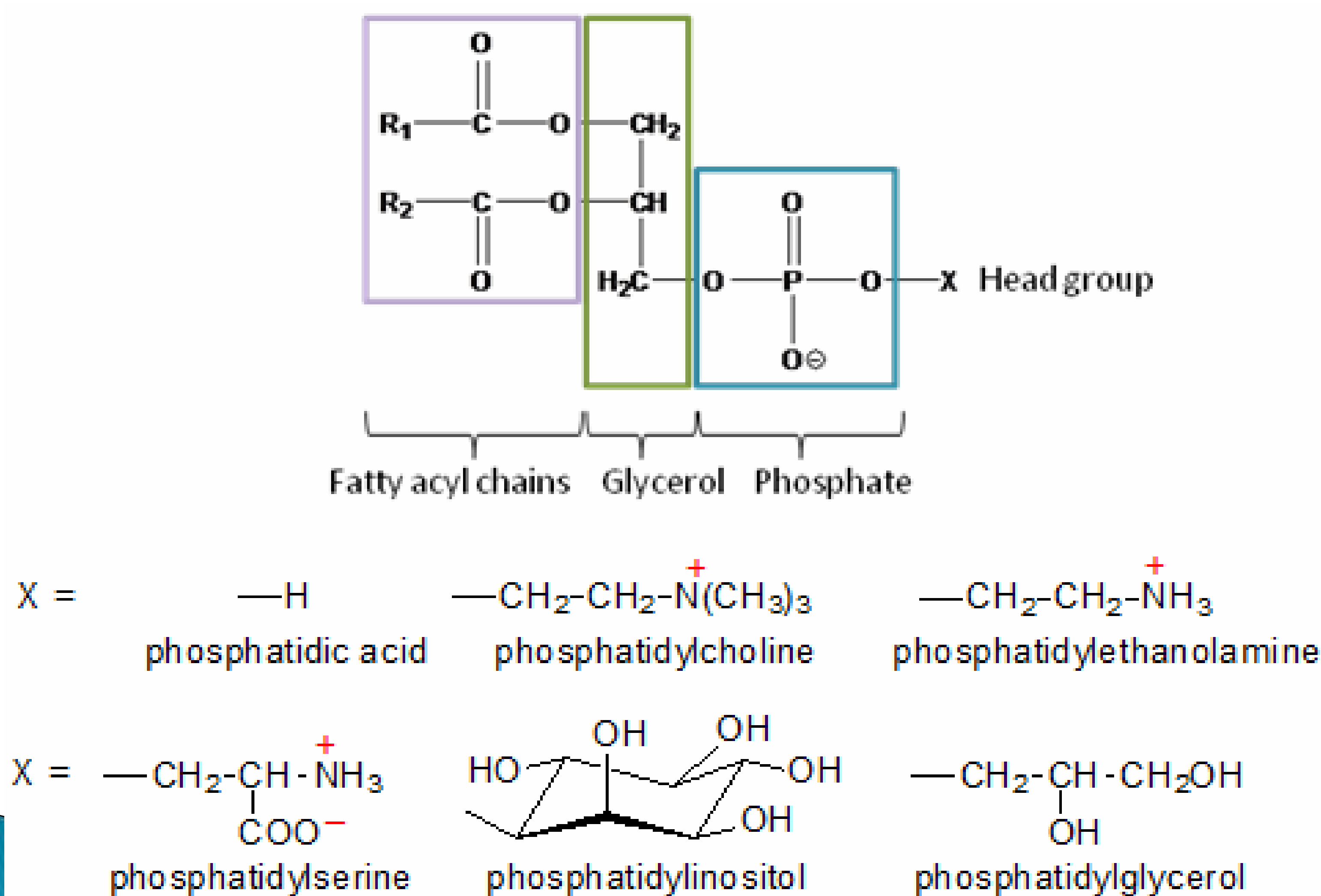
2) **Phosphatidyl ethanolamine (cephalin)-**

- Structurally similar to Lecithin with the exception that the base Ethanolamine replaces choline
- Brain and nervous tissue are rich in Cephalin

3) Phosphatidyl Serine-(found in most tissues) differ from phosphatidylcholine only in that serine replaces choline

4) Phosphatidylinositol -The inositol is present in **phosphatidylinositol** as the stereoisomer, myoinositol.**Phosphatidylinositol 4,5-bisphosphate** is an important constituent of cell membrane phospholipids; upon stimulation by a suitable hormone agonist, it is cleaved into **diacylglycerol** and **inositol trisphosphate,** both of which act as internal signals or second messengers.

Glycerophospholipid– structures



Glycerophospholipids(Contd.)

5) Cardiolipin –

- Abundantly found in mitochondrial membrane.
- This is the only phospholipid with antigenic properties.

6) Plasmalogens –

- constitute as much as 10% of the phospholipids of brain and muscle.
- Structurally, the plasmalogens resemble phosphatidylethanolamine but possess an ether link on the *sn*–1 carbon instead of the ester link found in acylglycerols.
- Typically, the alkyl radical is an unsaturated alcohol .
- In some instances, choline, serine, or inositol may be substituted for ethanolamine.

Glycerophospholipids(Contd.)

7) Platelet activating factor (PAF)-

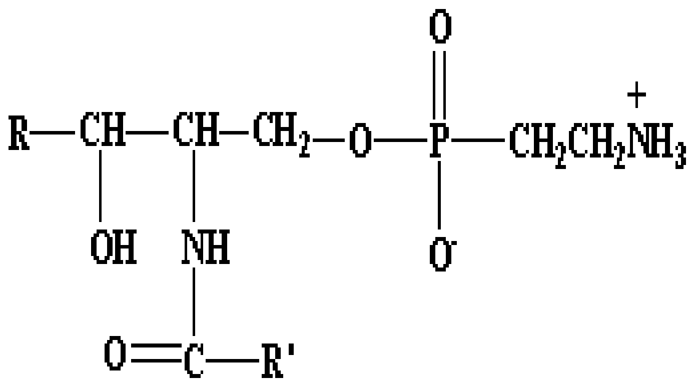
- Ether glycerophospholipid
- Contains an unsaturated alkyl group in an ether link to carbon -1
- An acetyl residue at carbon 2 of the glycerol backbone.
- Synthesized and released by various cell types
- PAF activates inflammatory cells and mediates hypersensitivity, acute inflammatory and anaphylactic reactions
- Causes platelets to aggregate and degranulate and neutrophils and alveolar macrophages to generate superoxide radicals

8) Phosphatidyl Glycerol-

- Formed by esterification of phosphatidic acid with glycerol
- Diphosphatidyl glycerol, cardiolipin is found in the mitochondrial membrane

2)Sphingophospholipids

- **Sphingomyelin-**
- Backbone is sphingosine (amino alcohol)
- A long chain fatty acid is attached to amino group of sphingosine to form Ceramide
- The alcohol group at carbon-1of sphingosine is esterified to phosphoryl choline, producing sphingomyelin
- Sphingomyelin is an important component of myelin of nerve fibers



Functions of Phosphipids

- Components of cell membrane, mitochondrial membrane and lipoproteins
- Participate in lipid absorption and transportation from intestine
- Play important role in blood coagulation
- Required for enzyme action- especially in mitochondrial electron transport chain
- Choline acts as a lipotropic agent
- Membrane phospholipids acts as source of Arachidonic acid
- Act as reservoir of second messenger- Phosphatidyl Inositol
- Act as cofactor for the activity of Lipoprotein lipase
- Phospholipids of myelin sheath provide insulation around the nerve fobers
- Dipalmitoyl lecithin acts as a surfactant

Lecithin Sphingomyelin ratio(L/S)

- L/S Ratio in amniotic fluid is used for the evaluation of fetal lung maturity
- Prior to 34 weeks gestation, lecithin and sphingomyelin concentrations are equal but afterwards there is marked increase in Lecithin concentration.
- A L/S ratio of> 2 or > 5 indicates adequate fetal lung maturity
- Delivery of a premature,low birth weight baby with low L/S ratio (1 or<1) predisposes the child to respiratory distress syndrome

2) Glycolipids(Glycosphingolipids)

- **Glycolipids** differ from sphingomyelins in that they do not contain phosphoric acid and the polar head function is provided by monosaccharide or oligosaccharide attached directly to ceramide by an O- glycosidic linkage.
- The number and type of carbohydrate moieties present, determine the type of glycosphingolipid. There are two types of Glycolipids-
- A) **Neutral glycosphingolipids**
- **B) Acidic glycosphingolipids**

a) Neutral Glycosphingolipids

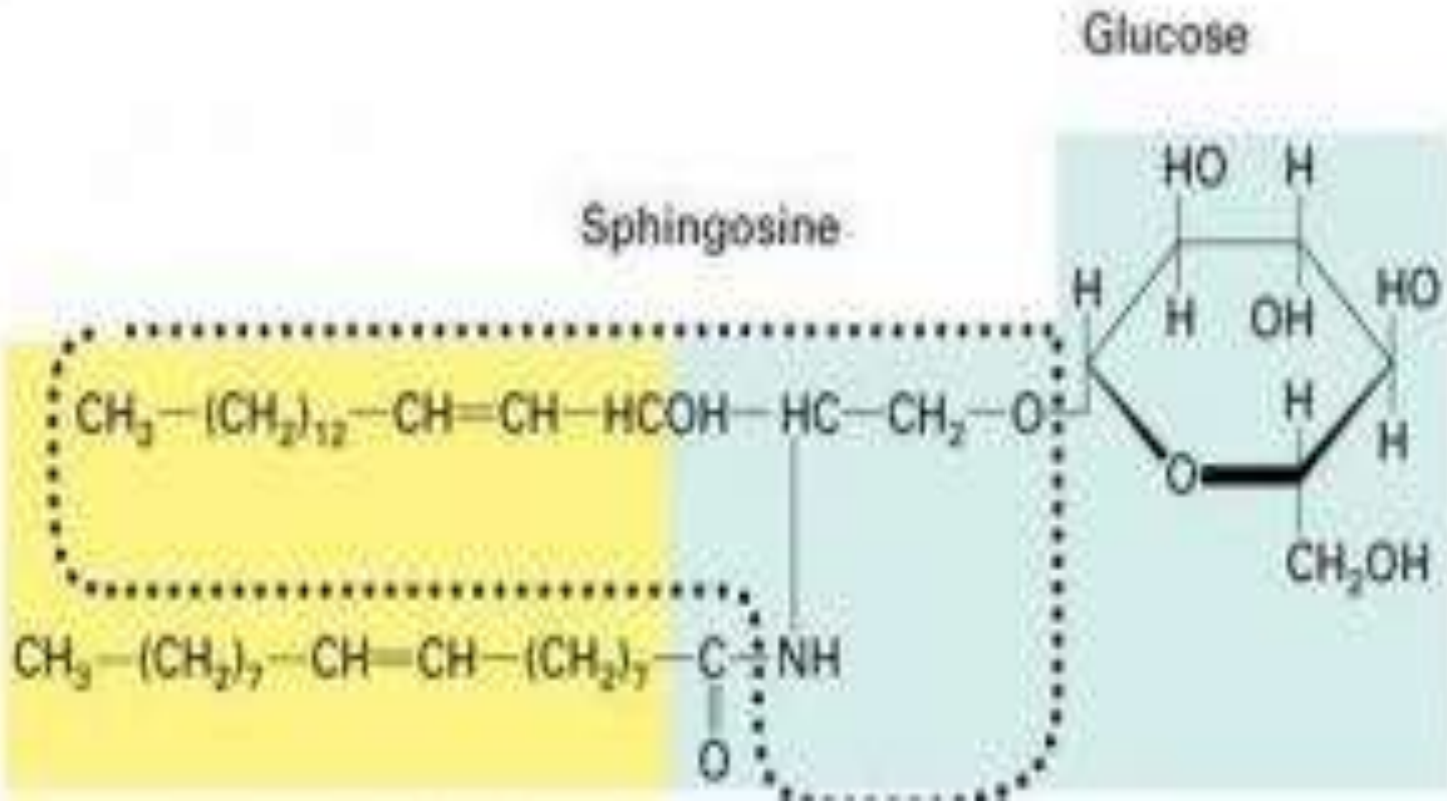
- **Cerebrosides**- These are ceramide monosaccharides, that contain either a molecule of galactose(Galactocerebroside)or glucose(Glucocerebroside)
- Found predominantly in the brain and nervous tissue with high concentration in myelin sheath
- Ceramide oligosaccharides (Globosides) are produced by attaching additional monosaccharides to Glucocerebroside.
- Lactosyl ceramide contains lactose (Galactose and Glucose attached to ceramide)

a) Neutral Glycosphingolipids

Cerebrosides (Contd.) – Individual cerebrosides are differentiated on the basis of kind of fatty acids in the molecule. Four types are commonly observed-

a) Kerasin- contains Lignoceric acid
b) Cerebron- Contains cerebronic acid
c) Nervon- contains Nervonic acid
d) Oxynervon- contains hydroxy derivative of nervonic acid

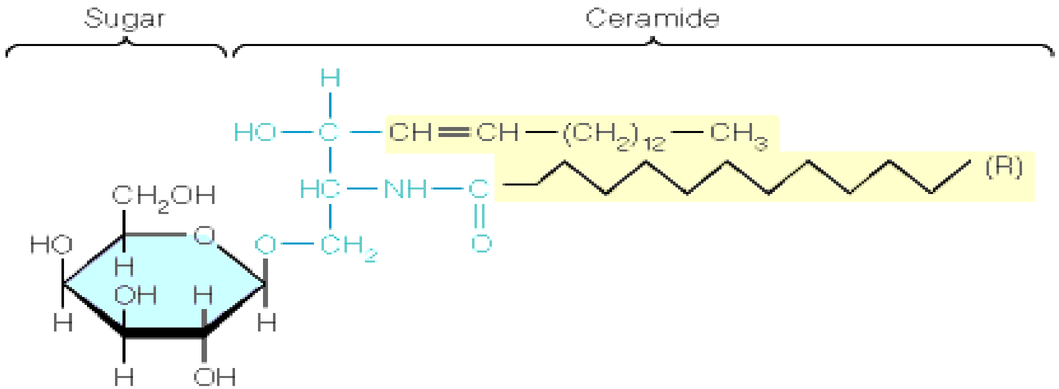
Structure- Glucosyl ceramide



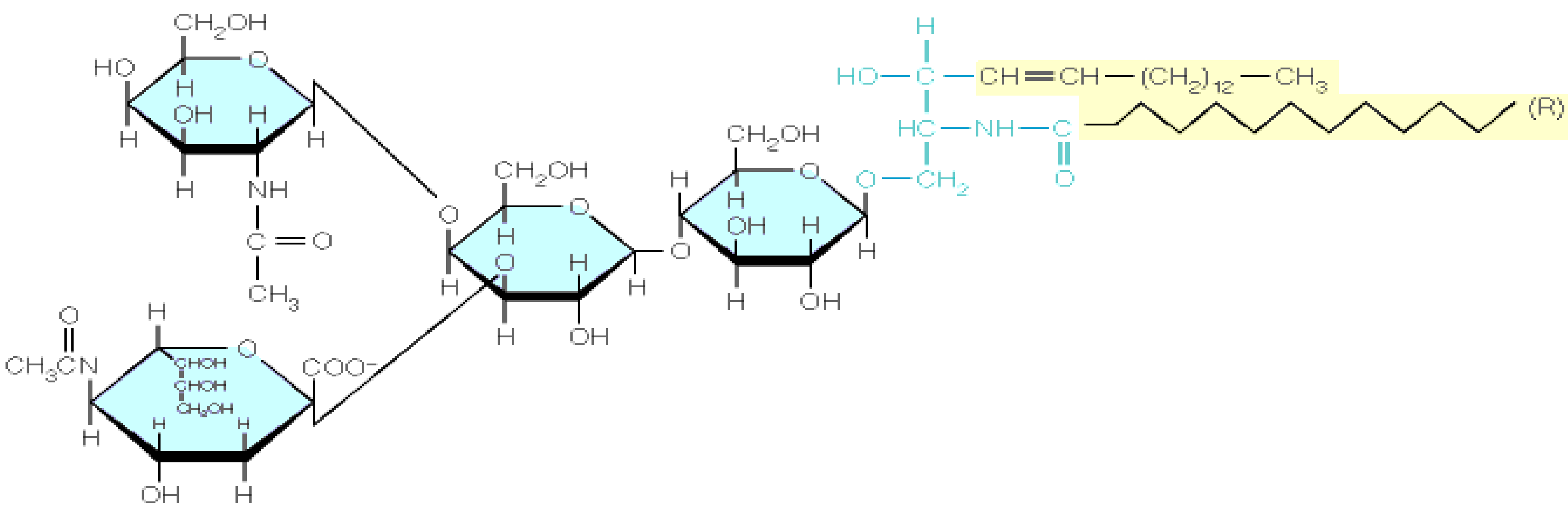
b) Acidic Glycosphingolipids (Gangliosides)

- They are negatively charged at physiological pH
- The negative charge is imparted by N- acetyl Neuraminic acid(Sialic acid)
- Brain gangliosides may contain up to four Sialic acid residues and based on that they are-GM, GD, GT and GQ, containing 1,2,3 or 4 Sialic acid residues
- Four important types of Gm series are-
- GM1, GM2 and GM3
- GM1 is complex of all

Glycolipids– Structures



(a) Galactosylceramide



(b) GalNAcβ(1→4)Galβ(1→4)Glcβ(1→1)ceramide
$\begin{pmatrix} 3 \\ \uparrow \\ \alpha 2 \end{pmatrix}$
Sia

Functions of Glycosphingolipids

- They occur particularly in the outer leaflet of the plasma membrane, where they contribute to **cell surface carbohydrates.**
- They act as cell surface receptors for various hormones, and growth factors
- Play important role in cellular interactions, growth and development
- They are source of blood group antigens and various embryonic antigens
- GM1 acts as a receptor for cholera toxin in human intestine

3) Sulfolipids(Sulfoglycosphigolipids)

- They are cerebrosides that contain sulfated galactosyl residues
- Negatively charged at physiological pH
- Found predominantly in nerve tissue and kidney
- Failure of degradation causes them to accumulate in nervous tissues

Lipid storage diseases(Sphingolipidosis)

Disease	Enzyme deficiency	Nature of lipid accumulated	Clinical Symptoms
Tay Sach's Disease	Hexosaminidase A	G_{M2} Ganglioside	Mental retardation, blindness, muscular weakness
Fabry's disease	α-Galactosidase	Globotriaosylceramide	Skin rash, kidney failure (full symptoms only in males; X-linked recessive).
Metachromatic leukodystrophy	Arylsulfatase A	Sulfogalactosylceramide	Mental retardation and Psychologic disturbances in adults; demyelination.

Lipid storage diseases(Sphingolipidosis)- contd.

Disease	Enzyme deficiency	Nature of lipid accumulated	Clinical symptoms
Krabbe's disease	β-Galactosidase	Galactosylceramide	Mental retardation; myelin almost absent.
Gaucher's disease	β -Glycosidase	Glucosyl ceramide	Enlarged liver and spleen, erosion of long bones, mental retardation in infants.
Niemann-Pick disease	Sphingomyelinase	Sphigomyelin	Enlarged liver and spleen, mental retardation; fatal in early life.
Farber's disease	Ceramidase	Ceramide	Hoarseness, dermatitis, skeletal deformation, mental retardation; fatal in early life

Amphipathic lipids

- Fatty acids, phospholipids, sphingolipids, bile salts, and, to a lesser extent, cholesterol contain polar groups. Therefore, part of the molecule is **hydrophobic,** or water-insoluble; and part is **hydrophilic,** or water-soluble. Such molecules are described as **amphipathic**
- They become oriented at oil:water interfaces with the polar group in the water phase and the nonpolar group in the oil phase.
- A bilayer of such amphipathic lipids is the basic structure in biologic membranes

Amphipathic lipids

- **Liposomes**–Liposomes may be formed by sonicating an amphipathic lipid in an aqueous medium.
- They consist of spheres of lipid bilayers that enclose part of the aqueous medium.
- Liposomes are of potential clinical use—particularly when combined with tissue-specific antibodies—as carriers of drugs in the circulation, targeted to specific organs, eg, in cancer therapy.
- In addition, they are used for gene transfer into vascular cells and as carriers for topical and transdermal delivery of drugs and cosmetics.

Amphipathic lipids

- **Emulsions** -are much larger particles,
- formed usually by nonpolar lipids in an aqueous medium.
- These are stabilized by emulsifying agents such as amphipathic lipids (eg, lecithin), which form a surface layer separating the main bulk of the nonpolar material from the aqueous phase .

Amphipathic lipids