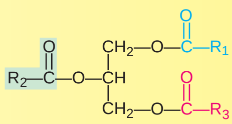
Chapter 3 Lipids



The fat speaks :

"With water, I say, 'Touch me not';
To the tongue, I am tasteful;
Within limits, I am dutiful;
In excess, I am dangerous!"

Lipids (*Greek*: lipos–fat) are of great importance to the body as the chief concentrated storage form of energy, besides their role in cellular structure and various other biochemical functions. As such, lipids are a ***heterogeneous group*** of compounds and, therefore, it is difficult to define them precisely.

Lipids may be regarded as organic substances relatively insoluble in water, soluble in organic solvents (alcohol, ether etc.), actually or potentially related to fatty acids and utilized by the living cells.

Unlike the polysaccharides, proteins and nucleic acids, lipids are not polymers. Further, lipids are mostly small molecules.

Classification of lipids

Lipids are broadly classified (modified from Bloor) into simple, complex, derived and miscellaneous lipids, which are further subdivided into different groups

1. **Simple lipids :** ***Esters of fatty acids*** with alcohols. These are mainly of two types

(a) **Fats and oils** (triacylglycerols) **:** These are esters of fatty acids with glycerol. The ***difference*** between fat and oil is only ***physical***. Thus, oil is a liquid while fat is a solid at room temperature.

(b) **Waxes :** Esters of fatty acids (usually long chain) with alcohols other than glycerol. These alcohols may be aliphatic or alicyclic. Cetyl alcohol is most commonly found in waxes. Waxes are used in the preparation of candles, lubricants, cosmotics, ointments, polishes etc.

2. **Complex (or compound) lipids :** These are esters of fatty acids with alcohols containing ***additional groups*** such as phosphate, nitrogenous base, carbohydrate, protein etc. They are further divided as follows

(a) **Phospholipids :** They contain phosphoric acid and frequently a nitrogenous base. This is in addition to alcohol and fatty acids.

(i) **Glycerophospholipids :** These phospholipids contain glycerol as the alcohol e.g., lecithin, cephalin.

(ii) **Sphingophospholipids :** Sphingosine is the alcohol in this group of phospholipids e.g., sphingomyelin.

(b) **Glycolipids :** These lipids contain a fatty acid, carbohydrate and nitrogenous base. The alcohol is sphingosine, hence they are also called as glycosphingolipids. Glycerol and phosphate are absent e.g., cerebrosides, gangliosides.

(c) **Lipoproteins :** Macromolecular complexes of lipids with proteins.

(d) **Other complex lipids :** Sulfolipids, aminolipids and lipopolysaccharides are among the other complex lipids.

3. **Derived lipids :** These are the derivatives obtained on the hydrolysis of group 1 and group 2 lipids which possess the characteristics of lipids. These include glycerol and other alcohols, fatty acids, mono- and diacylglycerols, lipid (fat) soluble vitamins, steroid hormones, hydrocarbons and ketone bodies.

4. **Miscellaneous lipids :** These include a large number of compounds possessing the characteristics of lipids e.g., carotenoids, squalene, hydrocarbons such as pentacosane (in bees wax), terpenes etc.

NEUTRAL LIPIDS : The lipids which are uncharged are referred to as neutral lipids. These are mono-, di-, and triacylglycerols, cholesterol and cholesteryl esters.

Functions of lipids

Lipids perform several important functions

1. They are the concentrated fuel reserve of the body (triacylglycerols).

2. Lipids are the constituents of membrane structure and regulate the membrane permeability (phospholipids and cholesterol).

3. They serve as a source of fat soluble vitamins (A, D, E and K).

4. Lipids are important as cellular metabolic regulators (steroid hormones and prostaglandins).

5. Lipids protect the internal organs, serve as insulating materials and give shape and smooth appearance to the body.

FATTY ACIDS

Fatty acids are ***carboxylic acids with hydrocarbon side chain***. They are the simplest form of lipids.

Occurrence

Fatty acids mainly occur in the esterified form as major constituents of various lipids. They are also present as free (unesterified) fatty acids. Fatty acids of animal orgin are much simpler in structure in contrast to those of plant origin which often contain groups such as epoxy, keto, hydroxy and cyclopentane rings.

Even and odd carbon fatty acids

Most of the fatty acids that occur in natural lipids are of even carbons (usually 14C – 20C). This is due to the fact that biosynthesis of fatty acids mainly occurs with the sequential addition of 2 carbon units. ***Palmitic acid (16C) and stearic acid (18C) are the most common***. Among the odd chain fatty acids, propionic acid (3C) and valeric acid (5C) are well known.

Saturated and unsaturated fatty acids

Saturated fatty acids do not contain double bonds, while unsaturated fatty acids contain one or more double bonds. Both saturated and unsaturated fatty acids almost equally occur in the natural lipids. Fatty acids with one double bond are monounsaturated, and those with 2 or more double bonds are collectively known as ***polyunsaturated fatty acids (PUFA)***.

Nomenclature of fatty acids

The naming of a fatty acid (systematic name) is based on the hydrocarbon from which it is derived. The saturated fatty acids end with a suffix ***-anoic*** (e.g., octanoic acid) while the unsaturated fatty acids end with a suffix ***-enoic*** (e.g., octadecanoic acid). In addition to systematic names, fatty acids have common names which are more widely used (***Table 3.1***).

Numbering of carbon atoms : It starts from the carboxyl carbon which is taken as number 1. The carbons adjacent to this (carboxyl C) are 2, 3, 4 and so on or alternately α, β, γ and so on. The terminal carbon containing methyl group is known omega (ω) carbon. Starting from the methyl end, the carbon atoms in a fatty acid are numbered as omega 1, 2, 3 etc. The numbering of carbon atoms in two different ways is given below

$$\underset{\omega_1}{\overset{7}{CH_3}}-\underset{\omega_2}{\overset{6}{CH_2}}-\underset{\omega_3}{\overset{5}{CH_2}}-\underset{\omega_4}{\overset{4}{CH_2}}-\underset{\omega_5}{\overset{3}{CH_2}}-\underset{\omega_6}{\overset{2}{CH_2}}-\overset{1}{COOH}$$

Length of hydrocarbon chain of fatty acids

Depending on the length of carbon chains, fatty acids are categorized into 3 groups—***short chain*** with less than 6 carbons; ***medium chain*** with 8 to 14 carbons and ***long chain*** with 16 to 24 carbons.

Shorthand representation of fatty acids

Instead of writing the full structures, biochemists employ shorthand notations (by numbers) to represent fatty acids. The general rule is that the total number of carbon atoms are written first, followed by the number of double bonds and finally the (first carbon) position of

TABLE 3.1 Selected examples of biochemically important fatty acids

Common Name	Systematic name	Abbreviation*	Structure
I. Saturated fatty acids			
Acetic acid	Ethanoic acid	2 : 0	CH_3COOH
Propionic acid	n-Propanoic acid	3 : 0	CH_3CH_2COOH
Butyric acid	n-Butanoic acid	4 : 0	$CH_3(CH_2)_2COOH$
Valeric acid	n-Pentanoic acid	5 : 0	$CH_3(CH_2)_3COOH$
Caproic acid	n-Hexanoic acid	6 : 0	$CH_3(CH_2)_4COOH$
Caprylic acid	n-Octanoic acid	8 : 0	$CH_3(CH_2)_6COOH$
Capric acid	n-Decanoic acid	10 : 0	$CH_3(CH_2)_8COOH$
Lauric acid	n-Dodecanoic acid	12 : 0	$CH_3(CH_2)_{10}COOH$
Myristic acid	n-Tetradecanoic acid	14 : 0	$CH_3(CH_2)_{12}COOH$
Palmitic acid	n-Hexadecanoic acid	16 : 0	$CH_3(CH_2)_{14}COOH$
Stearic acid	n-Octadecanoic acid	18 : 0	$CH_3(CH_2)_{16}COOH$
Arachidic acid	n-Eicosanoic acid	20 : 0	$CH_3(CH_2)_{18}COOH$
Behenic acid	n-Docosanoic acid	22 : 0	$CH_3(CH_2)_{20}COOH$
Lignoceric acid	n-Tetracosanoic acid	24 : 0	$CH_3(CH_2)_{22}COOH$
II. Unsaturated fatty acids			
Palmitoleic acid	*cis*-9-Hexadecenoic acid	16 : 1; 9	$CH_3(CH_2)_5CH = CH(CH_2)_7COOH$
Oleic acid	*cis*-9-Octadecenoic acid	18 : 1; 9	$CH_3(CH_2)_7CH = CH(CH_2)_7COOH$
Linoleic acid**	*cis, cis*-9,12–Octadeca-dienoic acid	18 : 2; 9, 12	$CH_3(CH_2)_4CH = CHCH_2CH = CH(CH_2)_7COOH$
Linolenic acid**	All *cis*–9,12,15–Octa-decatrienoic acid	18 : 3; 9, 12, 15	$CH_3CH_2CH = CHCH_2CH = CHCH_2CH = CH(CH_2)_7COOH$
Arachidonic acid	All *cis*–5,8,11,14–Eicosatetraenoic acid	20 : 4; 5, 8, 11, 14	$CH_3(CH_2)_4CH = CHCH_2CH = CHCH_2CH = CHCH_2CH = CH(CH_2)_3COOH$

* *Total number of carbon atoms, followed by the number of double bonds and the first carbon position of the double bond(s).*

** *Essential fatty acids.*

double bonds, starting from the carboxyl end. Thus, saturated fatty acid, palmitic acid is written as 16 : 0, oleic acid as 18 : 1; 9, arachidonic acid as 20 : 4; 5, 8, 11, 14.

There are other conventions of representing the double bonds. Δ^9 indicates that the double bond is between 9 and 10 of the fatty acid. ω 9 represents the double bond position (9 and 10) from the ω end. Naturally occurring unsaturated fatty acids belong to ω 9, ω 6 and ω 3 series.

- ***ω 3 series*** Linolenic acid (18 : 3; 9, 12, 15)
- ***ω 6 series*** Linoleic acid (18 : 2; 9, 12) and arachidonic acid (20 : 4; 5, 8, 11, 14)
- ***ω 9 series*** Oleic acid (18 : 1; 9)

The biochemically important saturated and unsaturated fatty acids are given in the ***Table 3.1***.

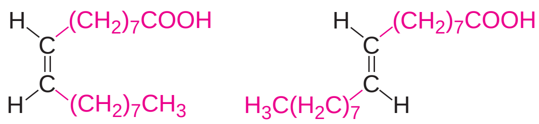
ESSENTIAL FATTY ACIDS

The fatty acids that cannot be synthesized by the body and, therefore, ***should be supplied in the diet*** are known as essential fatty acids (EFA). Chemically, they are ***polyunsaturated fatty acids***, namely ***linoleic acid*** (18 : 2; 9, 12) and ***linolenic acid*** (18 : 3; 9, 12, 15). ***Arachidonic acid*** (20 : 4; 5, 8, 11, 14) becomes essential, if its precursor linoleic acid is not provided in the diet in sufficient amounts. The structures of EFA are given in the ***Table 3.1***.

Biochemical basis for essentiality : Linoleic acid and linolenic acid are essential since humans lack the enzymes that can introduce double bonds beyond carbons 9 to 10.

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. (***Chapter 23***). They are also needed for the synthesis of another important group of compounds, namely ***eicosanoids*** (***Chapter 32***).

Deficiency of EFA : The deficiency of EFA results in ***phrynoderma*** or ***toad skin***, characterized by the presence of horny eruptions on the posterior and lateral parts of limbs, on the back and buttocks, loss of hair and poor wound healing.



Oleic acid (*cis* form) **Elaidic acid** (*trans* form)

Fig. 3.1 : *Cis-trans isomerism in unsaturated fatty acids.*

Isomerism in unsaturated fatty acids

Unsaturated fatty acids exhibit ***geometric isomerism*** depending on the orientation of the groups around the double bond axis.

If the atoms or acyl groups are present on the same side of the double bond, it is a ***cis configuration***. On the other hand, if the groups occur on the opposite side, it is a ***trans configuration***. Thus oleic acid is a *cis* isomer while elaidic acid is a *trans* isomer, as depicted in ***Fig.3.1***. *Cis* isomers are less stable than *trans* isomers. Most of the naturally occurring unsaturated fatty acids exist as *cis* isomers.

In the *cis* isomeric form, there is a molecular binding at the double bond. Thus, oleic acid exists in an L-shape while elaidic acid is a straight chain. Increase in the number of double bonds will cause more bends (kinks) and arachidonic acid with 4 double bonds will have a U-shape. It is believed that *cis* isomers of fatty acids with their characteristic bonds will compactly pack the membrane structure.

Hydroxy fatty acids : Some of the fatty acids are hydroxylated. β-Hydroxybutyric acid, one of the ketone bodies produced in metabolism, is a simple example of hydroxy fatty acids. Cerebronic acid and recinoleic acid are long chain hydroxy fatty acids.

Cyclic fatty acids : Fatty acids with cyclic structures are rather rare e.g., ***chaulmoogric acid*** found in chaulmoogra oil (used in leprosy treatment) contains cyclopentenyl ring.

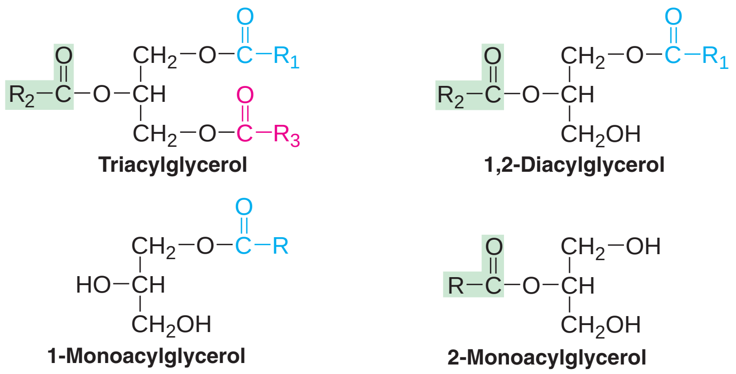


Fig. 3.2 : *General structures of acylglycerols*
(For palmitoyl R = $C_{15}H_{31}$; for stearoyl R = $C_{17}H_{35}$; For linoleoyl R = $C_{17}H_{31}$)

Eicosanoids : These compounds are related to eicosapolyenoic fatty acids and include prostaglandins, prostacyclins, leukotrienes and thromboxanes. They are discussed together (***Chapter 32***).

TRIACYLGLYCEROLS

Triacylglycerols (***formerly triglycerides***) are the esters of glycerol with fatty acids. The fats and oils that are widely distributed in both plants and animals are chemically triacylglycerols. They are insoluble in water and non-polar in character and commonly known as ***neutral fats***.

Fats as stored fuel : Triacylglycerols are the most abundant group of lipids that primarily function as fuel reserves of animals. The fat reserve of normal humans (men 20%, women 25% by weight) is sufficient to meet the body's caloric requirements for 2-3 months.

Fats primarily occur in adipose tissue : Adipocytes of adipose tissue—predominantly found in the subcutaneous layer and in the abdominal cavity—are specialized for storage of triacylglycerols. The fat is stored in the form of globules dispersed in the entire cytoplasm. And surprisingly, triacylglycerols are not the structural components of biological membranes.

Structures of acylglycerols : Monoacylglycerols, diacylglycerols and triacylglycerols, respectively consisting of one, two and three molecules of fatty acids esterified to a molecule of glycerol, are known (***Fig.3.2***). Among these, triacylglycerols are the most important biochemically.

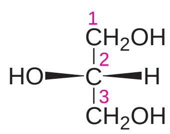
Simple triacylglycerols contain the same type of fatty acid residue at all the three carbons e.g., tristearoyl glycerol or tristearin.

Mixed triacylglycerols are more common. They contain ***2 or 3 different types of fatty acid*** residues. In general, fatty acid attached to C_1 is saturated, that attached to C_2 is unsaturated while that on C_3 can be either. Triacylglycerols are named according to placement of acyl radical on glycerol e.g., 1,3-palmitoyl 2-linoleoyl glycerol.

Triacylglycerols of plants, in general, have higher content of unsaturated fatty acids compared to that of animals.

Stereospecific numbering of glycerol

The structure of glycerol gives an impression that carbons 1 and 3 are identical. This is not true in a 3-dimensional structure. In order to represent the carbon atoms of glycerol in an unambiguous manner, biochemists adopt a ***s***tereospecific ***n***umbering (***sn***) and prefix glycerol with ***sn***.



sn-**Glycerol**

It should be noted that C_1 and C_3 are different. Cells possess enzymes that can distinguish these two carbons. Thus glycerokinase phosphorylates *sn*-3 (and not *sn*-1) glycerol to give *sn*-glycerol 3-phosphate.

PROPERTIES OF TRIACYLGLYCEROLS

A few important properties of triacylglycerols, which have biochemical relevance, are discussed below

1. **Hydrolysis :** Triacylglycerols undergo stepwise enzymatic hydrolysis to finally liberate free fatty acids and glycerol. The process of hydrolysis, catalysed by ***lipases*** is important for digestion of fat in the gastrointestinal tract and fat mobilization from the adipose tissues.

2. **Saponification :** The hydrolysis of triacylglycerols by alkali to produce glycerol and soaps is known as saponification.

Triacylglycerol + 3 NaOH ⟶
Glycerol + 3 R-COONa (soaps)

3. **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.

Rancidity occurs when fats and oils are exposed to air, moisture, light, bacteria etc. ***Hydrolytic rancidity*** occurs due to partial hydrolysis of triacylglycerols by bacterial enzymes. Oxidative rancidity is due to oxidation of unsaturated fatty acids. This results in the formation of unpleasant products such as dicarboxylic acids, aldehydes, ketones etc. Rancid fats and oils are unsuitable for human consumption.

Antioxidants : The substances which can prevent the occurrence of oxidative rancidity are known as antioxidants. Trace amounts of antioxidants such as tocopherols (vitamin E), hydroquinone, gallic acid and α-naphthol are added to the commercial preparations of fats and oils to prevent rancidity. Propyl gallate, butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are the antioxidants used in food preservation.

4. **Lipid peroxidation *in vivo* :** In the living cells, lipids undergo oxidation to produce peroxides and free radicals which can damage the tissue. The free radicals are believed to cause inflammatory diseases, ageing, cancer, atherosclerosis etc. It is fortunate that the cells possess antioxidants such as vitamin E, urate and superoxide dismutase to prevent *in vivo* lipid peroxidation (***Chapter 34***).

Tests to check purity of fats and oils

Adulteration of fats and oils is increasing day by day. Several tests are employed in the laboratory to check the purity of fats and oils. Some of them are discussed hereunder

Iodine number : It is defined as the ***grams*** (number) ***of iodine absorbed by 100 g of fat*** or ***oil***. 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. The iodine numbers of common oils/fats are given below.

Fat/oil	*Iodine number*
Coconut oil	7 — 10
Butter	25 — 28
Palm oil	45 — 55
Olive oil	80 — 85
Groundnut oil	85 — 100
Cottonseed oil	100 — 110
Sunflower oil	125 — 135
Linseed oil	175 — 200

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

Saponification number : It is defined as the ***mg*** (number) ***of KOH required to hydrolyse (saponify) one gram of fat or oil***. 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. The saponification numbers of a few fats and oils are given below

Human fat : 195–200
Butter : 230–240
Coconut oil : 250–260

Reichert-Meissl (RM) number : It is defined as the number of ml 0.1 N KOH required to completely neutralize the soluble volatile fatty acids distilled from 5 g fat. 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). This is in contrast to other fats and oils which have a negligible amount of volatile fatty acids. 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.

Acid number : It is defined as the number of mg of KOH required to completely neutralize free fatty acids present in one gram fat or oil. 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.

PHOSPHOLIPIDS

These are complex or ***compound lipids*** containing ***phosphoric acid***, in addition to fatty acids, nitrogenous base and alcohol (***Fig.3.3***).

There are two classes of phospholipids

1. Glycerophospholipids (or phosphoglycerides) that contain glycerol as the alcohol.
2. Sphingophospholipids (or sphingomyelins) that contain sphingosine as the alcohol.

Glycerophospholipids

Glycerophospholipids are the major lipids that occur in biological membranes. They consist of glycerol 3-phosphate esterified at its C_1 and C_2 with fatty acids. Usually, C_1 contains a saturated fatty acid while C_2 contains an unsaturated fatty acid.

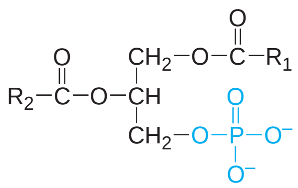
1. **Phosphatidic acid :** This is the simplest phospholipid. It does not occur in good concentration in the tissues. Basically, phosphatidic acid is an intermediate in the synthesis of triacylglycerols and phospholipids.

The other glycerophospholipids containing different nitrogenous bases or other groups may be regarded as the derivatives of phosphatidic acid.

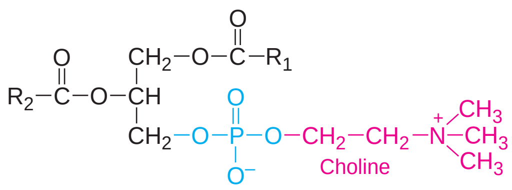
2. **Lecithins** (***phosphatidylcholine***)**:** These are the most abundant group of phospholipids in the cell membranes. Chemically, lecithin (*Greek* : lecithos—egg yolk) is a phosphatidic acid with choline as the base. Phosphatidylcholines represent the ***storage form of body's choline***.

BIOMEDICAL / CLINICAL CONCEPTS

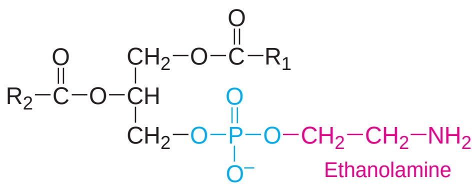
- *Lipids are important to the body as constituents of membranes, source of fat soluble (A, D, E and K) vitamins and metabolic regulators (steroid hormones and prostaglandins).*
- *Triacylglycerols (fats) primarily stored in the adipose tissue are concentrated fuel reserves of the body. Fats found in the subcutaneous tissue and around certain organs serve as thermal insulators.*
- *The unsaturated fatty acids–linoleic and linolenic acid—are essential to humans, the deficiency of which causes phrynoderma or toad skin.*
- *The cyclic fatty acid, namely chaulmoogric acid,is employed in the treatment of leprosy.*
- *Fats and oils on exposure to air, moisture, bacteria etc. undergo rancidity (deterioration). This can be prevented by the addition of certain antioxidants (vitamin E, hydroquinone, gallic acid).*
- *In food preservation, antioxidants—namely propyl gallate, butylated hydroxyanisole and butylated hydroxytoluene—are commonly used.*



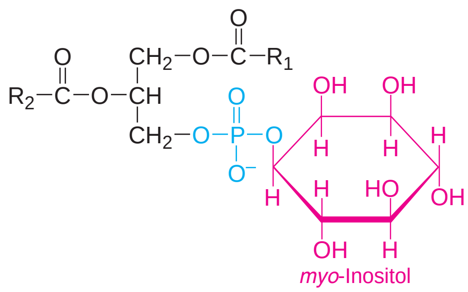
(1) **Phosphatidic acid**



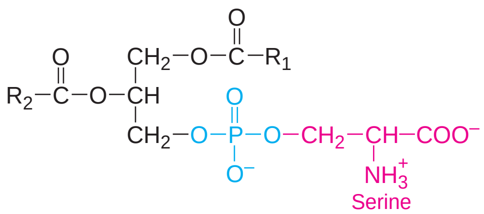
(2) **Lecithin** (phosphatidylcholine)



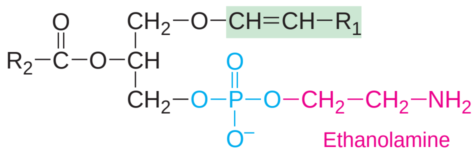
(3) **Cephalin** (phosphatidylethanolamine)



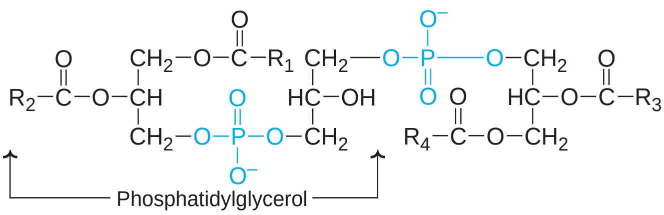
(4) **Phosphatidylinositol**



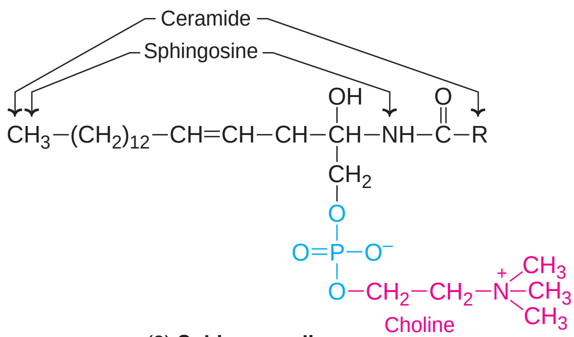
(5) **Phosphatidylserine**



(6) **Plasmalogen** (phosphatidalethanolamine)



(7) **Cardiolipin** (diphosphatidylglycerol)



(8) **Sphingomyelin**

Fig. 3.3 : *Structures of phospholipids.*

(a) **Dipalmitoyl lecithin** is an important phosphatidylcholine found in lungs. It is a surface active agent and prevents the adherence of inner surface of the lungs due to surface tension. Respiratory distress syndrome in infants is a disorder characterized by the absence of dipalmitoyl lecithin.

(b) **Lysolecithin** is formed by removal of the fatty acid either at C_1 or C_2 of lecithin.

3. **Cephalins** (***phosphatidylethanolamine***) **:** Ethanolamine is the nitrogenous base present in cephalins. Thus, lecithin and cephalin differ with regard to the base.

4. **Phosphatidylinositol :** The steroisomer *myo*-inositol is attached to phosphatidic acid to give phosphatidylinositol(PI). This is an important component of cell membranes. The action of certain hormones (e.g. oxytocin, vasopressin) is mediated through PI.

5. **Phosphatidylserine :** The amino acid serine is present in this group of glycerophospholipids. Phosphatidylthreonine is also found in certain tissues.

6. **Plasmalogens :** When a fatty acid is attached by an ***ether*** linkage at C_1 of glycerol in the glycerophospholipids, the resultant compound is plasmalogen. Phosphati***dal***-ethanolamine is the most important which is similar in structure to phosphati***dyl***ethanolamine but for the ether linkage (in place of ester). An unsaturated fatty acid occurs at C_1. Choline, inositol and serine may substitute ethanolamine to give other plasmalogens.

7. **Cardiolipin :** It is so named as it was first isolated from heart muscle. Structurally, a cardiolipin consists of two molecules of phosphatidic acid held by an additional glycerol through phosphate groups. It is an important component of inner mitochondrial membrane and essential for mitrochondrial function. Decreased cardiolipin levels may result in mitochondrial dysfunction, aging, hypothyroidism, cardioskeletal myopathy (Barth syndrome). Cardiolipin is the only phosphoglyceride that possesses ***antigenic properties***.

Sphingomyelins

Sphingosine is an amino alcohol present in sphingomyelins (sphingophospholipids). They do not contain glycerol at all. Sphingosine is attached by an amide linkage to a fatty acid to produce ***ceramide***. The alcohol group of sphingosine is bound to phosphorylcholine in sphingomyelin structure (***Fig.3.3***). Sphingomyelins are important constituents of myelin and are found in good quantity in brain and nervous tissues.

Ceramide, acts as a second ***messenger*** (signaling molecule) by regulating programmed cell death (apoptosis), cell cycle and cell differentiation. A ceramide containing a 30-carbon fatty acid is a major component of skin, and it ***regulates skin's water permeability***.

Functions of phospholipids

Phospholipids constitute an important group of compound lipids that perform a wide variety of functions

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

2. Phospholipids (lecithin, cephalin and cardiolipin) in the mitochondria maintain the conformation of electron transport chain components, and thus cellular respiration.

3. Phospholipids participate in the ***absorption of fat*** from the intestine.

4. Phospholipids are essential for the synthesis of different lipoproteins, and thus participate in the ***transport of lipids***.

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

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

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

8. Phospholipids act as surfactants (agents lowering surface tension). For instance, dipalmitoyl phosphatidylcholine is an important

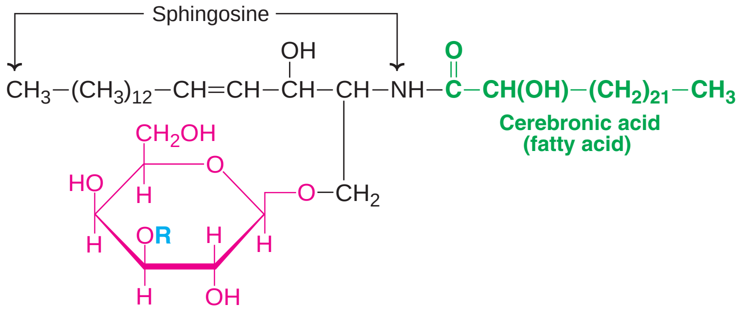


Fig. 3.4 : *Structure of galactosylceramide (R = H). For sulfagalactosylceramide R is a sulfatide* (R = SO_4^{2-}).

lung surfactant. ***Respiratory distress syndrome*** in infants is associated with insufficient production of this surfactant.

9. Cephalins, an important group of phospholipids participate in blood clotting.

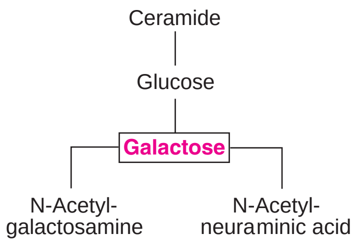
10. Phosphatidylinositol is the source of second messengers—inositol triphosphate and diacylglyceol, that are involved in the action of some horomones.

GLYCOLIPIDS

Glycolipids (***glycosphingolipids***) are important constituents of cell membrane and nervous tissues (particularly the brain). ***Cerebrosides*** are the simplest form of glycolipids. They contain a ceramide (sphingosine attached to a fatty acid) and one or more sugars. Galactocerebroside (galactosylceramide) and glucocerebroside are the most important glycolipids. The structure of galactosylceramide is given in ***Fig.3.4***. It contains the fatty acid cerebronic acid. Sulfagalactosylceramide is the ***sulfatide*** derived from galactosylceramide.

Gangliosides : These are predominantly found in ganglions and are the most complex form of glycosphingolipids. They are the derivatives of cerebrosides and contain one or more molecules of N-acetylneuraminic acid (NANA), the most important sialic acid. The structure of NANA is given in carbohydrate chemistry (***Refer Fig.2.11***).

The most important gangliosides present in the brain are GM_1, GM_2, GD, and GT, (***G*** represents ***g***anglioside while ***M***, ***D*** and ***T*** indicate ***m***ono-, ***d***i- or ***t***ri- sialic acid residues, and the number denotes the carbohydrate sequence attached to the ceramide). The ganglioside, GM_2 that accumulates in Tay-Sachs disease is represented next (outline structure).



LIPOPROTEINS

Lipoproteins are molecular complexes of lipids with proteins. They are the transport vehicles for lipids in the circulation. There are five types of lipoproteins, namely ***chylomicrons, very low density lipoproteins (VLDL), low density lipoproteins (LDL), high density lipoproteins (HDL) and free fatty acid-albumin complexes***. Their structure, separation, metabolism and diseases are discussed together (***Chapter 14***).

STEROIDS

Steroids are the compounds containing a cyclic steroid nucleus (or ring) namely ***cyclopentanoperhydrophenanthrene (CPPP)***. It consists of a phenanthrene nucleus (rings A, B and C) to which a cyclopentane ring (D) is attached.

The structure and numbering of CPPP are shown in ***Fig.3.5***. The steroid nucleus represents saturated carbons, unless specifically shown as

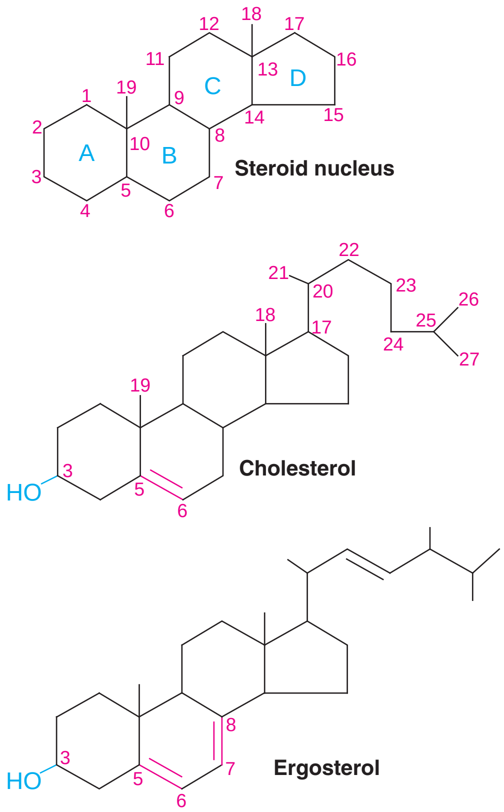


Fig. 3.5 : Structures of steroids (A, B, C—Perhydro-phenanthrene; D-Cyclopentane).

double bonds. The methyl side chains (19 & 18) attached to carbons 10 & 13 are shown as single bonds. At carbon 17, steroids usually contain a side chain.

There are several steroids in the biological system. These include ***cholesterol, bile acids, vitamin D, sex hormones, adrenocortical hormones***, sitosterols, cardiac glycosides and alkaloids. If the steroid contains one or more hydroxyl groups it is commonly known as ***sterol*** (means solid alcohol).

CHOLESTEROL

Cholesterol, ***exclusively found in animals***, is the most abundant animal sterol. It is widely distributed in all cells and is a major component of cell membranes and lipoproteins. Cholesterol (*Greek* : chole–bile) was first isolated from bile. Cholesterol literally means 'solid alcohol from bile.'

Structure and occurrence

The structure of cholesterol ($C_{27}H_{46}O$) is depicted in ***Fig.3.5***. It has one hydroxyl group at C_3 and a double bond between C_5 and C_6. An 8 carbon aliphatic side chain is attached to C_{17}. Cholesterol contains a total of 5 methyl groups.

Due to the presence of an –OH group, cholesterol is weakly amphiphilic. As a structural component of plasma membranes, cholesterol is an important determinant of membrane permeability properties. The occurrence of cholesterol is much higher in the membranes of sub-cellular organelles.

Cholesterol is found in association with fatty acids to form cholesteryl esters (esterification occurs at the OH group of C_3).

Properties and reactions : Cholesterol is an yellowish crystalline solid. The crystals, under the microscope, show a notched (⏍) appearance. Cholesterol is insoluble in water and soluble in organic solvents such as chloroform, benzene, ether etc.

Several reactions given by cholesterol are useful for its qualitative identification and quantitative estimation. These include Salkowski's test, Liebermann-Burchard reaction and Zak's test.

Functions of cholesterol : Cholesterol is a poor conductor of heat and electricity, since it has a high dielectric constant. It is present in abundance in nervous tissues. It appears that cholesterol functions as an insulating cover for the transmission of electrical impulses in the nervous tissue. Cholesterol performs several other biochemical functions which include its role in membrane structure and function, in the synthesis of bile acids, hormones (sex and cortical) and vitamin D (for details, ***Refer Chapters 7*** and ***19***).

ERGOSTEROL

Ergosterol occurs in plants. It is also found as a structural constituent of membranes in yeast and fungi. Ergosterol (***Fig.3.5***) is an important precursor for vitamin D. When exposed to light,

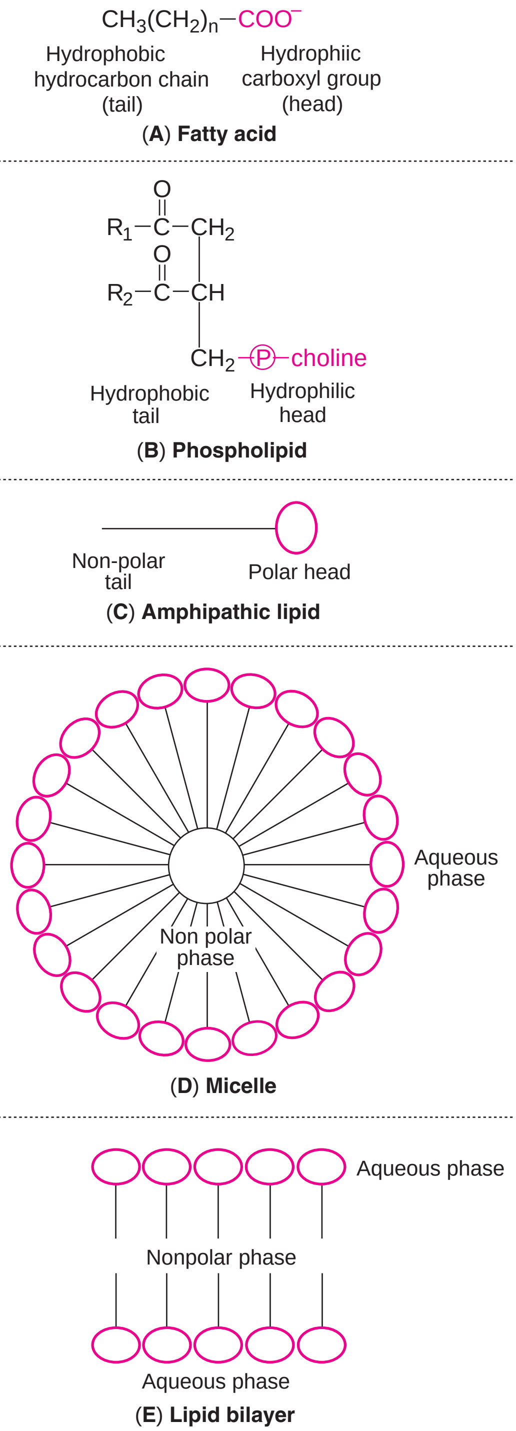


***Fig. 3.6 :** Summary of amphipathic lipids in the formation of micelle and lipid bilayer.*

the ring B of ergosterol opens and it is converted to ergocalciferol, a compound containing vitamin D activity.

The other sterols present in plant cells include ***stigmasterol*** and ***β-sitosterol***.

AMPHIPATHIC LIPIDS

As per definition, lipids are insoluble (hydrophobic) in water. This is primarily due to the predominant presence of hydrocarbon groups. However, some of the lipids possess polar or hydrophilic groups which tend to be soluble in water. Molecules which contain both hydrophobic and hydrophilic groups are known as ***amphipathic*** (*Greek* : amphi-both, pathos—passion).

Examples of amphipathic lipids : Among the lipids, ***fatty acids, phospholipids***, sphingolipids, ***bile salts*** and ***cholesterol*** (to some extent) are amphipathic in nature.

Phospholipids have a hydrophilic head (phosphate group attached to choline, ethanolamine, inositol etc.) and a long hydrophobic tail. The general structure of an amphipathic lipid may be represented as a polar or hydrophilic head with a non-polar or hydrophobic tail (***Fig.3.6***).

Fatty acids contain a hydrocarbon chain with a carboxyl (COO^-) group at physiological pH. The carboxyl group is polar in nature with affinity to water (hydrophilic) while hydrocarbon chain of fatty acid is hydrophobic.

Orientation of amphipathic lipids : When the amphipathic lipids are mixed in water (aqueous phase), the polar groups (heads) orient themselves towards aqueous phase while the non-polar (tails) orient towards the opposite directions. This leads to the formation of ***micelles*** (***Fig.3.6***).

Micelles are primarily molecular aggregates of amphipathic lipids. Micelle formation, facilitated by bile salts, is very important for lipid digestion and absorption (***Chapter 8***).

BIOMEDICAL / CLINICAL CONCEPTS

- *The phospholipid–dipalmitoyl lecithin—prevents the adherence of inner surface of the lungs, the absence of which is associated with respiratory distress syndrome in infants.*
- *Cephalins participate in blood clotting.*
- *The action of certain hormones is mediated through phosphatidylinositol.*
- *Phospholipids are important for the synthesis and transport of lipoproteins and reverse transport of cholesterol.*
- *Cholesterol is essential for the synthesis of bile acids, hormones (sex and cortical) and vitamin D.*
- *Lipoproteins occur in the membrane structure, besides serving as a means of transport vehicles for lipids.*
- *Lipids are associated with certain disorders—obesity, atherosclerosis, and diabetes mellitus.*
- *Liposomes are used for administration of a variety of therapeutic substances (drugs, proteins, nucleic acids) in order to target specific organs or tissues.*

Membrane bilayers

In case of biological membranes, a bilayer of lipids is formed orienting the polar heads to the outer aqueous phase on either side and the nonpolar tails into the interior (***Fig.3.6***). The formation of a lipid bilayer is the basis of membrane structure.

Liposomes : They are produced when amphipathic lipids in aqueous medium are subjected to ***sonification***. They have intermittent aqueous phases in the lipid bilayer. Liposomes, in combination with tissue specific antigens, are used as carriers of drugs to target tissues.

Emulsions : These are produced when nonpolar lipids (e.g. triacylglycerols) are mixed with water. The particles are larger in size and stabilized by emulsifying agents (usually amphipathic lipids), such as bile salts and phospholipids.

SOAPS AND DETERGENTS

Soaps are sodium or potassium salts of fatty acids. They are produced by saponification of fats. Sodium soaps are hard that result in bar soaps. Soaps serve as cleansing agents since they can emulsify oils and remove the dirt.

Detergents

Detergents are synthetic cleansing agents e.g. sodium lauryl sulfate. Detergents are superior in their cleansing action compared to soaps, and are used in washing clothes, and in tooth paste.

SUMMARY

1. *Lipids are the organic substances relatively insoluble in water, soluble in organic solvents (alcohol, ether), actually or potentially related to fatty acids and are utilized by the body.*

2. *Lipids are classified into simple (fats and oils), complex (phospholipids, glycolipids), derived (fatty acids, steriod hormones) and miscellaneous (carotenoids).*

3. *Fatty acids are the major constituents of various lipids. Saturated and unsaturated fatty acids almost equally occur in natural lipids. The polyunsaturated fatty acids (PUFA) namely linoleic acid and linolenic acid are the essential fatty acids that need to be supplied in the diet.*

4. *Triacylglycerols (simply fats) are the esters of glycerol with fatty acids. They are found in adipose tissue and primarily function as fuel reserve of animals. Several tests (iodine number, RM number) are employed in the laboratory to test the purity of fats and oils.*

5. *Phospholipids are complex lipids containing phosphoric acid. Glycerophospholipids contain glycerol as the alcohol and these include lecithin, cephalin, phosphatidylinositol, plasmalogen and cardiolipin.*

6. *Sphingophospholipids (sphingomyelins) contain sphingosine as the alcohol in place of glycerol (in glycerophospholipids). Phospholipids are the major constituents of plasma membranes.*

7. *Cerebrosides are the simplest form of glycolipids which occur in the membranes of nervous tissue. Gangliosides are predominantly found in the ganglions. They contain one or more molecules of N-acetylneuraminic acid (NANA).*

8. *Steroids contain the ring cyclopentanoperhydrophenanthrene. The steroids of biological importance include cholesterol, bile acids, vitamin D, sex hormones and cortical hormones. A steroid containing one or more hydroxyl groups is known as sterol.*

9. *Cholesterol is the most abundant animal sterol. It contains one hydroxyl group (at C_3), a double bond (C_5–C_6) and an eight carbon side chain attached to C_{17}. Cholesterol is a constituent of membrane structure and is involved in the synthesis of bile acids, hormones (sex and cortical) and vitamin D.*

10. *The lipids that possess both hydrophobic (non -polar) and hydrophilic (polar) groups are known as amphipathic. These include fatty acids, phospholipids, sphingolipids and bile salts. Amphipathic lipids are important constituents in the bilayers of the biological membranes.*