Biochemistry

Pavel Pestryakov

Novosibirsk State University
Institute of chemical biology and fundamental medicine, SB RAS

+7(913)892-3045
Pavel.pestryakov@niboch.nsc.ru

LIPIDS

According to Bloom LIPIDS characteristics:

- ***They are insoluble in water.***
- ***Solubility in one or more organic solvents, such as ether, chloroform, benzene, acetone, etc, so called fat solvents.***
- Some relationship to the fatty acids as esters either actual or potential.
- Possibility of utilization by living organisms.

Classification (chemical)

1. Simple lipids. They are esters of **fatty acids** with **glycerol** or other higher alcohols.

2. Compound lipids. They are **fatty acids** esterified with alcohol; but in addition they contain other groups. Depending on these extra groups, they are subclassified.
    a. Phospholipids, containing phosphoric acid.
    b. Non-phosphorylated lipids.

3. Derived lipids. They are compounds which are derived from lipids or precursors of lipids, e.g. fatty acids, steroids, cholesterol.

4. Lipids complexed to other compounds.

LIPIDS Structure - FATTY ACIDS – DERIVED LIPIDS

1. Lipid component
2. Derived lipid

Fatty acids are aliphatic carboxylic acids and have the general formula, R—CO—OH, where COOH (carboxylic group) represents the functional group. Obtained by fat hydrolysis.

SATURATED (-anoic)

Common name	No carbon atoms	Chemical nature	Occurrence
A. Even chain Saturated fatty acids			
Acetic	2	Saturated; small chain	Vinegar
Butyric	4	do	Butter
Caproic	6	do	Butter
Capric	10	do	Coconut oil
Lauric	12	do	Coconut oil
Myristic	**14**	**do**	**Coconut oil**
Palmitic	**16**	**Saturated; long chain**	**Body fat**
Stearic	**18**	**do**	**do**
Arachidic	20	do	Peanut oil (Arachis oil)
B. Odd-chain fatty acids			
Propionic	3	Saturated; Odd chain	Metabolism

Acetic acid $CH_3—COOH$
Butyric acid $CH_3(CH_2)_2—COOH$
Palmitic acid $CH_3—(CH_2)_{14}—COOH$
Stearic acid $CH_3—(CH_2)_{16}—COOH$

Acetic (C=2) and butyric (C=4) are involved in the basics of metabolic intermediates.
Palmitic (C=16) and stearic (C=18) – most abundant in body fat.

Most of natural lipids consist even FA.
Odd FA can be found in microbiota and milk.

Short chain <7
Long chain >15
Very long >23

LIPIDS Structure - FATTY ACIDS

UNSATURATED (-enoic)

Common name	No carbon atoms	Chemical nature	Occurrence
C Even chain Unsaturated fatty acids			
Palmitoleic	16	Monounsaturated (ω7)	Body fat
Oleic	**18**	**do (ω 9)**	**do**
Erucic	22	do (ω 9)	Mustard oil
Nervonic	24	do (ω 9)	Brain lipids
Linoleic	**18**	**2 double bonds (ω 6)**	**Vegetable oils**
Linolenic	**18**	**3 double bonds (ω 3)**	**do**
Arachidonic	**20**	**4 double bonds (ω 6)**	**Vegetable oils**
Timnodonic	20	eicosa pentaenoic (ω 3)	Fish oils, brain
Clupanodonic	22	docosa pentaenoic (ω 3)	Fish oils, brain
Cervonic	22	docosa hexaenoic (ω 3)	Fish oils, brain

Each animal species will have characteristic pattern of fatty acid composition. Thus human **body fat** contains 50% oleic acid, 25% palmitic acid 10% linoleic and 5% stearic acid.

Internal classification:

- ***Monounsaturated***
- ***Polyunsaturated***

Polyunsaturated linoleic and linolenic are ESSENTIAL (EFA)
Polyunsaturated arachidonic can be synthesized if essential FA are in diet.

Linoleic (C_{18}) Δ9, 12 **(two double bonds)** (ω6 family)

$CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$

18 ω6 12 9 1

Linolenic (C_{18}) Δ9, 12, 15 **(three double bonds)** (ω3 family)

$CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$

18 ω3 15 12 9 1

Arachidonic (C_{20}) Δ5, 8, 11, 14 **(four double bonds)** (ω6 family)

$CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-(CH_2)_3-COOH$

20 ω6 14 11 8 5 1

W (omega) – numbers from methyl end, not from carboxylic (w3 w6 w9)

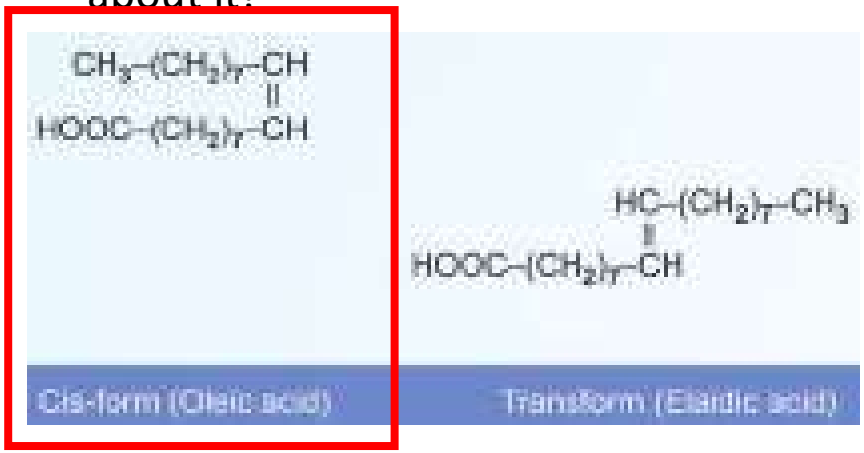
LIPIDS Structure - FATTY ACIDS

UNSATURATED (-enoic)

Common name	No carbon atoms	Chemical nature	Occurrence
C. Even chain, Unsaturated fatty acids			
Palmitoleic	16	Monounsaturated (ω7)	Body fat
Oleic	**18**	**do (ω 9)**	**do**
Erucic	22	do (ω 9)	Mustard oil
Nervonic	24	do (ω 9)	Brain lipids
Linoleic	**18**	**2 double bonds (ω 6)**	**Vegetable oils**
Linolenic	**18**	**3 double bonds (ω 3)**	**do**
Arachidonic	**20**	**4 double bonds (ω 6)**	**Vegetable oils**
Timnodonic	20	eicosa pentaenoic (ω 3)	Fish oils, brain
Clupanodonic	22	docosa pentaenoic (ω 3)	Fish oils, brain
Cervonic	22	docosa hexaenoic (ω 3)	Fish oils, brain

Name	Saturated fatty acids(%)	Mono-unsaturated fatty acids(%)	PUFA (%)
Coconut oil	(*)86	12	2
Sunflower oil	12	24	64
Palm oil	42	52	6

Since we have double bond in the structure – there should be isomers about it!



Natural – CIS- (some little TRANS- during the metabolism)

??? Healthy = cis-, unhealthy = trans-

POSSIBLE HEALTH ISSUES:
Trans fatty acids adversely affect multiple risk factors, including plasma lipids and lipoproteins, systemic inflammation, endothelial dysfunction, insulin resistance.

LIPIDS Structure - FATTY ACIDS

Common name	No carbon atoms	Chemical nature	Occurrence
BRANCHED			
D. Branched fatty acids			
Iso valeric acid	5	Branched	Metabolic intermediate
MODIFIED			
E. Hydroxy fatty acids			
Cerebronic acid	24	Hydroxy acid	Brain lipids

F. methyl fatty acids

G. Cyclic fatty acids

- Chaulmoogric acid - from chaulmoogra seeds,
- Hydnocarpic acid

Both of them have been used earlier for long time for treatment of leprosy.

LIPIDS PROPERTIES - FATTY ACIDS

Since we have double bond in the structure – there should be chemistry about it!

1. Hydrogenation of unsaturated – usually solidifies oil

$$\text{Linolenic} \xrightarrow{(+)2H} \text{Linoleic} \xrightarrow{(+)2H} \text{Oleic} \xrightarrow{(+)2H} \text{Stearic}$$

2. Halogenation of unsaturated

Oleic acid + I_2 → Di-iodo oleic acid

The number of halogen atoms taken up will depend on the number of double bonds and is an index of the degree of unsaturation. (See iodine number, under triglycerides).

3. Melting point

long chain saturated FA – solids at 25

unsaturated – stay longer as liquids

The more unsaturated – the more thermoliquids

4. Salt formation (Na/K salts - soaps)

$$CH_3—COOH + NaOH \rightarrow CH_3—COONa + H_2O$$

Ca/Mg soaps - insoluble

5. Oxidation

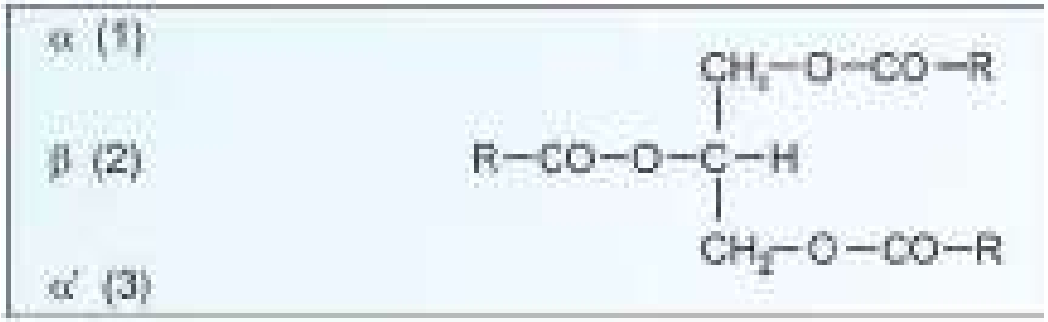
ENERGY in the body – partially by oxidation of FA

autooxidation of unsaturated FA

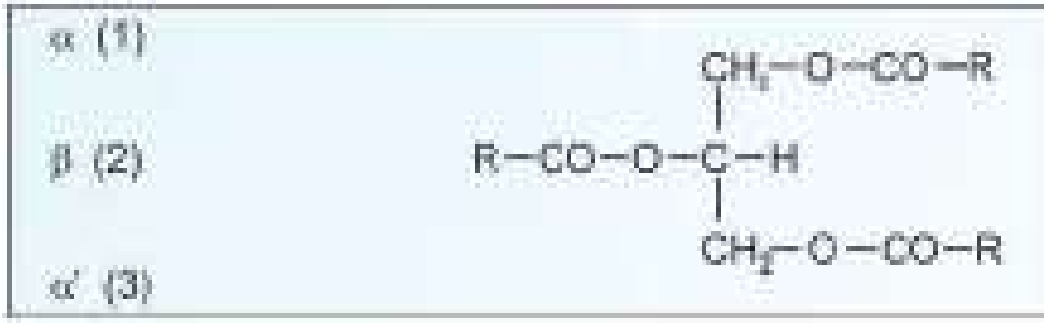
5. Esterification with alcohol

!! Mono-, di-, tri-gliceride

Triglycerids – neutral FAT



SIMPLE LIPIDS – NEUTRAL FAT – triglycerides – triacyl glycerols



Glycerol esters with FA

i. Naturally occurring fats and oils are mixtures of triglycerides.

ii. If all the three hydroxyl groups of the glycerol are esterified to the same fatty acid, a **simple triacyl glycerol** is formed.

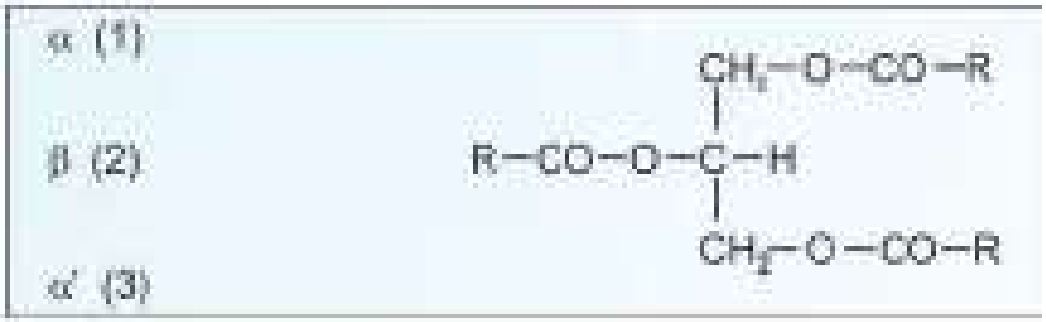
iii. A **mixed triglyceride** is formed, when different fatty acids are esterified to the hydroxyl groups of glycerol.

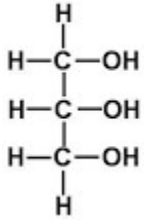
iv. *Generally two hydroxyl groups are esterified to similar fatty acid and the third with a different* one, e.g. 1, 3-dipalmitoyl-2-olein; 1-palmitoyl-2, 3-distearin, etc. When a unsaturated FA is present, it is commonly esterified to the 2nd or β carbon atom.

SIMPLE LIPIDS – WAXES = higher FA + big monohydroxy-alcohols

Long straight chains (60-100); Secretion of insects, leafes, plants; Uses in osmetics, polishes. (cetyl alcohol ($C_{16}H_{33}OH$), cholesterol, VitA/Vit D)

SIMPLE LIPIDS – NEUTRAL FAT – triglycerides – triacyl glycerols





Glycerol esters with FA

STRUCTURE -

i. Naturally occurring fats and oils are mixtures of triglycerides.

ii. If all the three hydroxyl groups of the glycerol are esterified to the same fatty acid, a **simple triacyl glycerol** is formed.

iii. A **mixed triglyceride** is formed, when different fatty acids are esterified to the hydroxyl groups of glycerol.

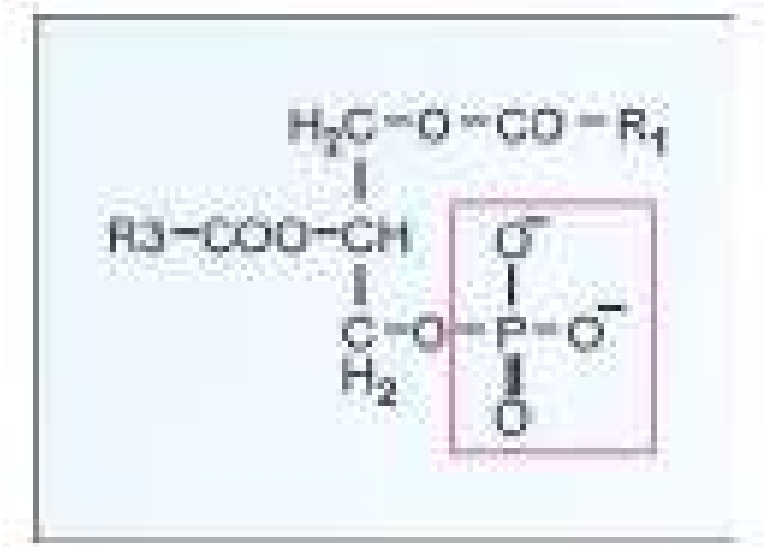
iv. *Generally two hydroxyl groups are esterified to similar fatty acid and the third with a different* one, e.g. 1, 3-dipalmitoyl-2-olein; 1-palmitoyl-2, 3-distearin, etc. When a unsaturated FA is present, it is commonly esterified to the 2nd or β carbon atom.

PROPERTIES -

1. insoluble in water – OIL (unsaturated/short chains) or FAT (saturated long chain)
2. Serves as Energy storage (adipose tissue – approx 10 kg triglycerides per 70 kg male)
3. Can be hydrolysed by lipases (sequentially to glycerol and 3 FA)
4. Can be hydrolysed by alkali – saponification (to glycerol and soaps). Saponification number can give an idea about average molecular weight of FA in fat

COMPOUND LIPIDS – Phospholipids

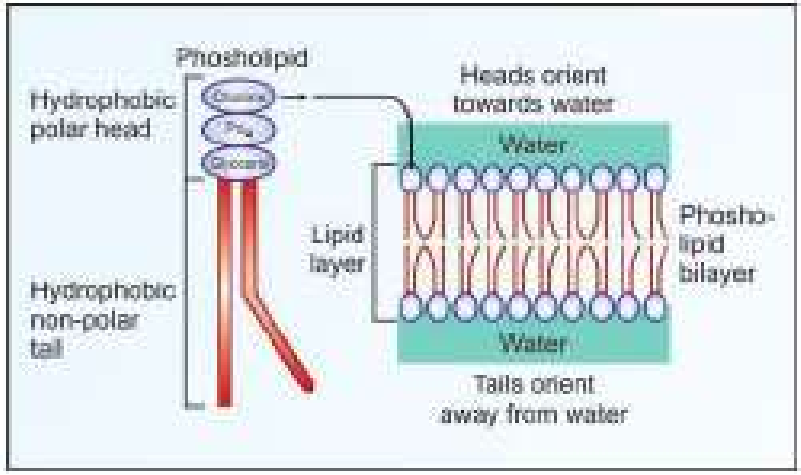
Simplest – phosphatidic acid =
glycerol + 2 FA at C1 and C2 + $PO4^{2-}$ at C3

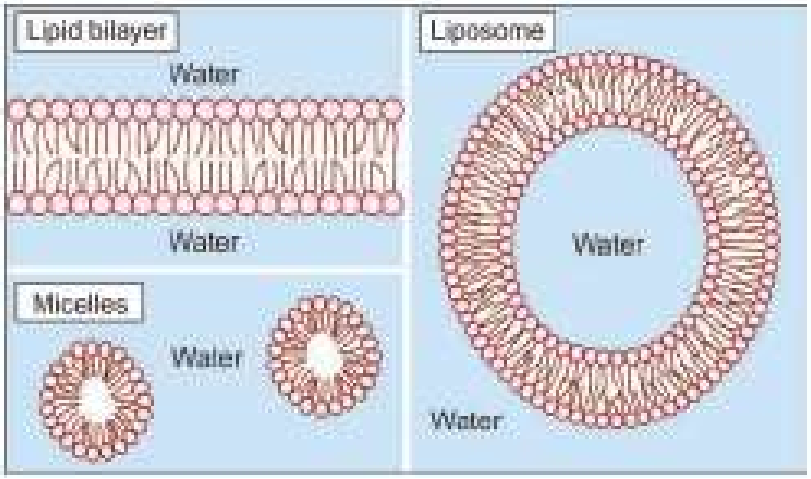


Liposomes and drug delivery

Membranes (layers are formed) C>6

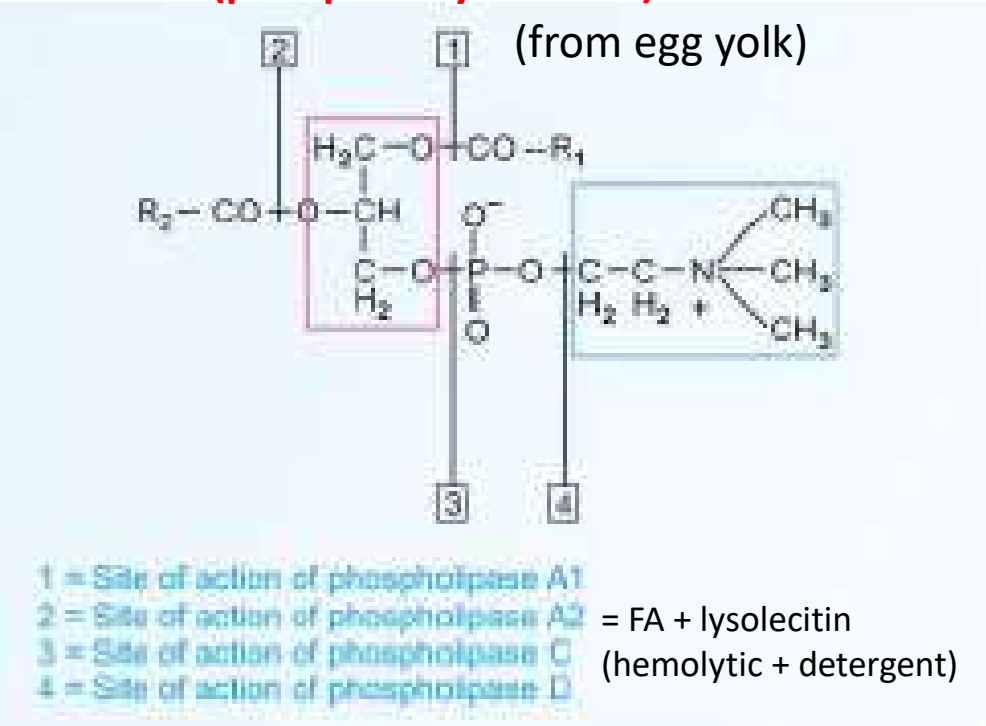
Since we have asymmetric atom – there should be stereoisomers.
natural PL – belongs to L-





COMPLEX LIPIDS – Phospholipids –

1. Lecitin (phosphatidyl choline)



= FA + lysolecitin
(hemolytic + detergent)

Glycerol + 2 FA + Phosphate + Choline
(usually R2 – polyunsaturated)

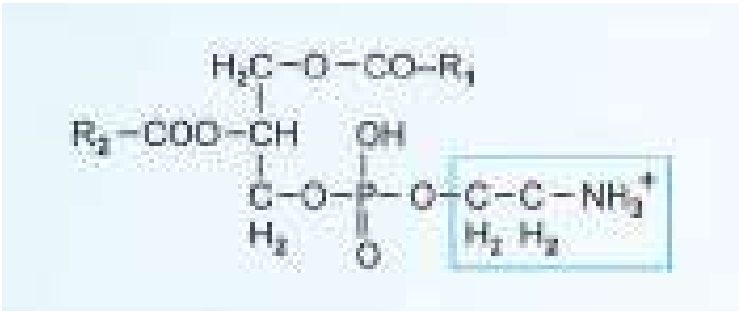
NITROGEN-CONTAINING PHOSPHOLIPID

CWITTERIONIC nature (pI 6.7)

Is digested by phospholipases (venoms)

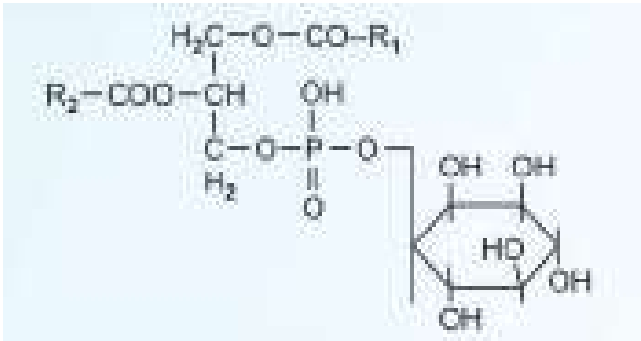
Important biological property –
Lung surfactant (dipalmitoyl lecithin, phosphatidyl glycerol, cholesterol and surfactant proteins A, B and C)

1. Cephalin (phosphatidyl ethanolamine)



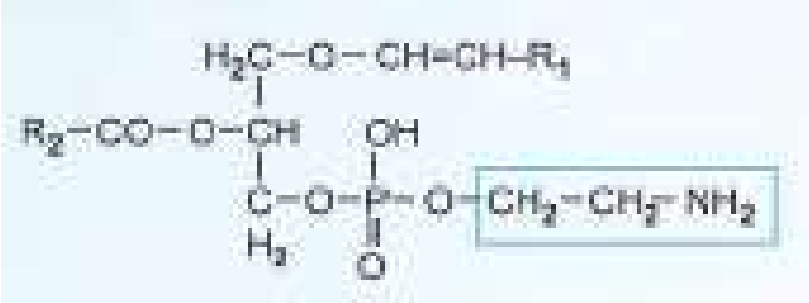
Important biological property in biomembranes

1. phosphatidyl inositol



COMPLEX LIPIDS – Phospholipids –

2. Plasmalogens



Glycerol + at C1 a-b unsaturated alcohol + FA at C2 + phosphate at C3 + (ethanolamine or choline) at phosphate
Biomembranes of brain and muscle

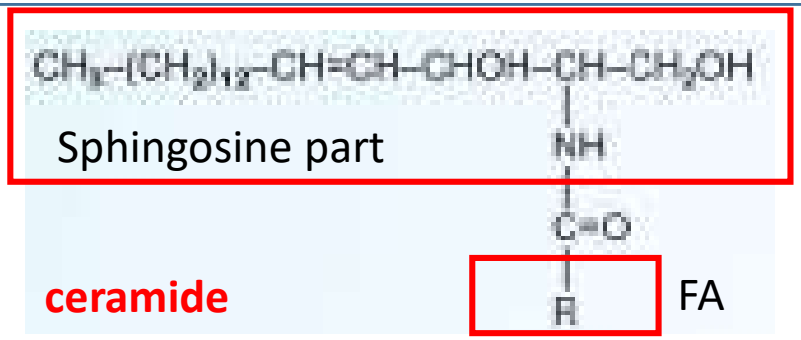
3. Phosphatidyl glycerol (cardiolipin)

Phosphatidic acid + Glycerol + phosphatidic acid
Mitochondrial membrane! Low amount of cardiolipin = mt dysfunction == heart failure, hypothyroidism, myopathies.

COMPLEX LIPIDS

4. SPHINGOLIPIDS:

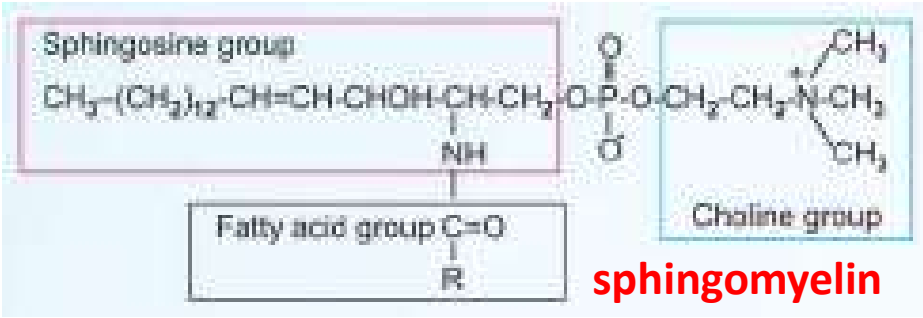
- **phosphosphingosides**
- **glycosphingolipids**
- **sulfatides**



Common part - sphingosine + FA to form ceramide

Phosphosphingosides

Sphingosine + FA + phosphate + …



(biomembranes, especially nervous system!!)
Variety, depending on FA

NON-phosphorylated – Sulfolipids (sulfatides)

Sphingosine + FA + oligosugar + $SO4^{2-}$ groups
Membranes of nervous tissue

Accumulation of SF in CNS under some conditions – lipid storage diseases(inborn)

NON-phosphorylated - glycosphingolipids

Sphingosine + FA + mono-sugar

Ceramide + Glucose → Gluco cerebroside
Ceramide + Galactose→ Galacto cerebroside

Large amounts in nervous system

Sphingosine + FA + oligo-sugar/oligo -aminosugar = globosides

Ceramide + Galactose + Glucose → Lactosyl ceramide

Erythrocyte membrane

Sphingosine + FA + oligo-sugar that contain sialic acid = **gangliosides**
Stability of nerve fibers –
Autoantibodies to some gangliosides
Destroys peripheral motor nerves

LIPIDS Function

1. Storage form of **energy** (triglycerides)
2. **Structural** components of biomembranes (phospholipids and cholesterol)
3. Metabolic **regulators** (steroid hormones and prostaglandins)
4. Act as **surfactants**, detergents and emulsifying agents (amphipathic lipids)
5. Act as **electric insulators** in neurons
6. Provide **insulation** against changes in external temperature (subcutaneous fat)
7. Give **shape** and contour to the **body**
8. Protect internal organs by providing a **cushioning** effect (pads of fat - kidneys)
9. Help in **absorption of fat soluble** vitamins (A, D, E and K)
10. **Improve taste** and palatability of food.
11. Involved in metabolism – breakdown products are used to build other biomolecules

MEDICAL IMPORTANCE

1. Excessive fat deposits cause obesity. Truncal obesity is a risk factor for heart attack.
2. Abnormality in cholesterol and lipoprotein metabolism leads to atherosclerosis and cardiovascular diseases.
3. In diabetes mellitus, the metabolisms of fatty acids and lipoproteins are deranged, leading to ketosis.

STEROIDS

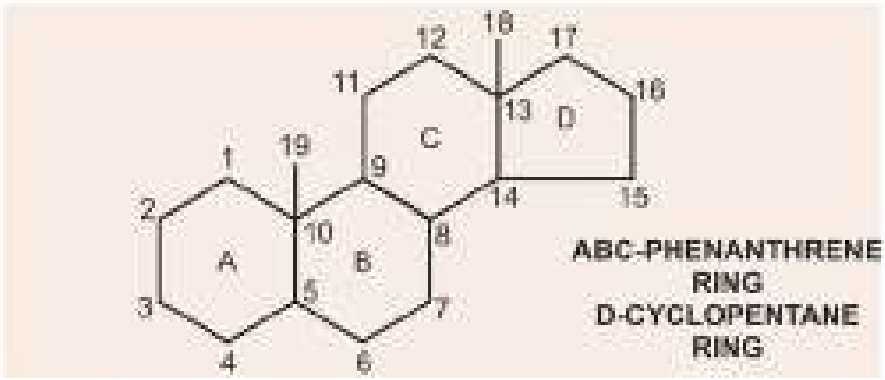


Fig. 4.3: Cyclopentanoperhydrophenanthrene nucleus

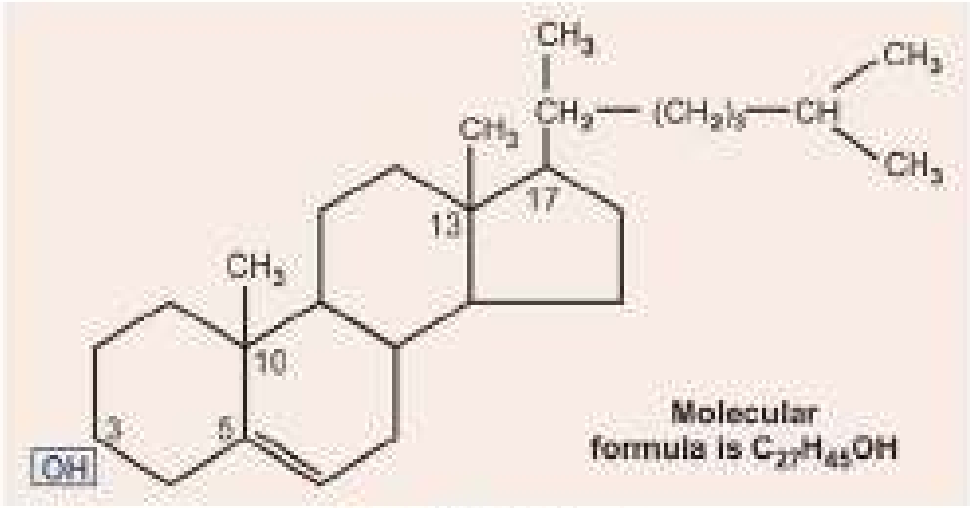


Fig. 4.4: Cholesterol

Literature biochemistry

1. Lehninger Principles of Biochemistry (Nelson D.L., Cox M.M.)
2. Principles and Techiniques of Biochemistry and Molecular Biology (Wilson K., Walker J.)