LIPID CHEMISTRY

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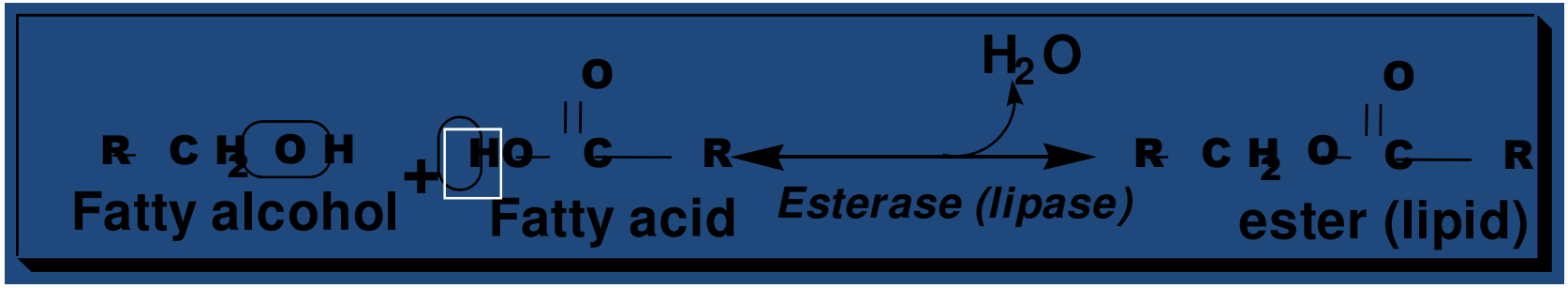
Introduction:

Definition: Lipids are organic compounds formed mainly from alcohol and fatty acids combined together by ester linkage.



General properties:

- Insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone, etc.).
- Include **fats, oils, waxes** and related compound.

Biological Importance of Lipids:

Lipids are important dietary constituents, because of the following reasons:

1. More palatable and storable to unlimited amount compared to carbohydrates.
2. High-energy value and provide more energy per gram than carbohydrates and proteins.
3. Supply the **Essential** fatty acids that cannot be synthesized by the body.
4. Supply the body with **fat-soluble vitamins** (A, D, E and K).
5. They are important constituents of the nervous system.

6. Essential constituent of **cell membrane** and nervous system.
7. Stored mainly in adipocytes. It is mainly triglycerides in nature and acts as:

I. A store of energy.
II. Protect the internal organs from outside shocks.
III. A subcutaneous thermal insulator against loss of body heat.

8. Lipoproteins, which are complex of lipids and proteins, are important cellular constituents.
9. Cholesterol enters in membrane structure and is used for synthesis of some hormones, vitamin D_3 and bile acids.
10. Pathology of disease like Obesity, atherosclerosis is related to lipids.

Classification of Lipids

Lipids are classified into:

I- Simple lipids: They are esters of fatty acids with fatty alcohol.

They are classified according to the alcohol present into:

Neutral fats: Esters of fatty acids with **glycerol** (triacylglycerols, or triglycerides).

Waxes: Esters of fatty acids with **long-chain alcohols** other than glycerol.

II- Compound or conjugated lipids: They are esters of fatty acids and alcohols in additions to other groups .They include the following types:

1. **Phospholipids (phosphatides):** phosphoric acid + a nitrogenous base + Alcohol. They are further classified according to the alcohol into lecithin, cephalin….ect.
2. **Glycolipids:**, carbohydrate + sphingosine, but not phosphoric acid nor glycerol.
3. **Lipoproteins:** composed of a lipid part + Proteins as plasma and membranous lipoproteins.
4. **Other compound lipids:** include:
   I. **Sulfolipids:** containing sulfur.
   II. **Aminolipids:** containing amino acids.

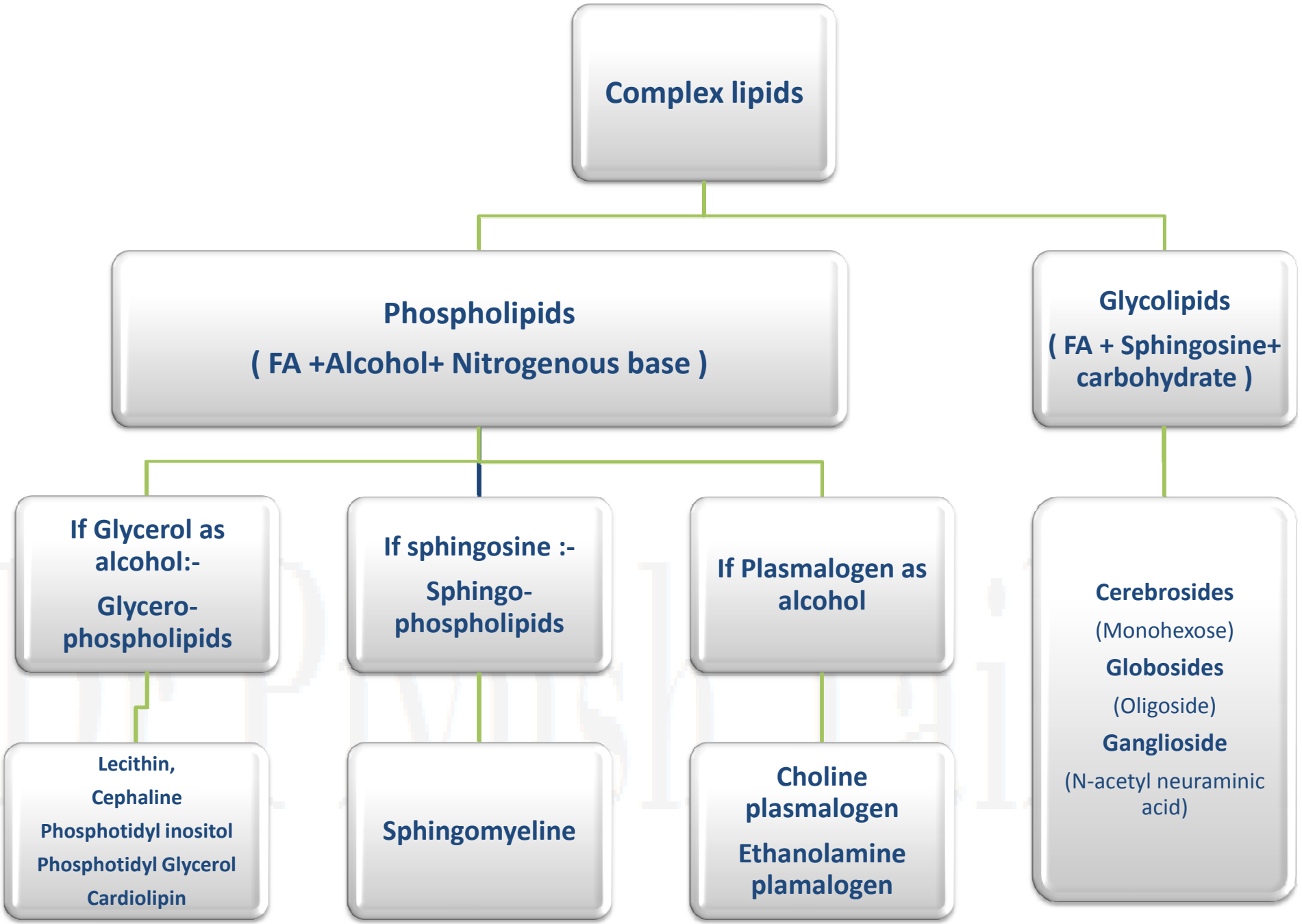
III- Derived Lipids:

Definition: They are products of hydrolysis of simple and compound lipids and/or their derivatives that still possess the general characteristics of lipids. They include:

1. Fatty acids, monoglycerides and aldehydes.
2. Alcohols including glycerol.
3. Sterols, steroids and hormonal derivatives of vit. D.
4. Eicosanoids (prostaglandins, leukotrienes and thromboxanes).
5. Ketone bodies.

IV- Lipid-associating substances:

Definition: They include fat-soluble vitamins (E and K), carotenoids, squalene and hydrocarbons.

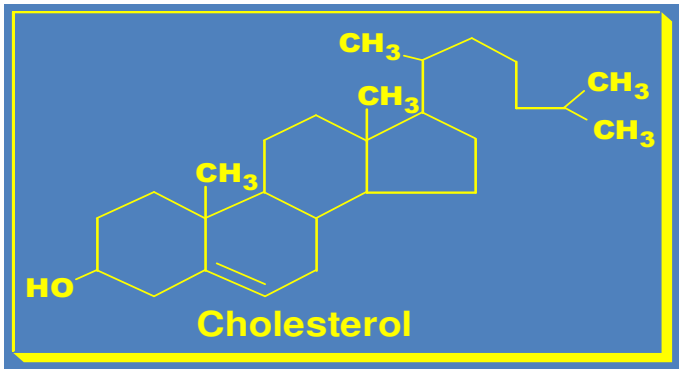

Complex lipids
Phospholipids
(FA +Alcohol+ Nitrogenous base)
Glycolipids
(FA + Sphingosine+ carbohydrate)
If Glycerol as alcohol:-
Glycero-phospholipids
If sphingosine :-
Sphingo-phospholipids
If Plasmalogen as alcohol
Cerebrosides
(Monohexose)
Globosides
(Oligoside)
Ganglioside
(N-acetyl neuraminic acid)
Lecithin,
Cephaline
Phosphotidyl inositol
Phosphotidyl Glycerol
Cardiolipin
Sphingomyeline
Choline plasmalogen
Ethanolamine plamalogen

Uses of Glycerol:

I. Glycerol enters in pharmaceutical and cosmetic preparations (hygroscopic).
II. Nitroglycerin is used as vasodilator especially for the coronary arteries, thus it is used in treatment of angina pectoris. Also, enters in explosives.
III. Glycerol is used in treatment of glaucoma (increased intraocular pressure).

Cholesterol

Structure:



Sources: It is synthesized in the body and is also taken in the diet (0.3 gm/day as in butter, milk, egg yolk, brain, meat and animal fat).

Importance: It enter in the structure of :

1. Steroid Vitamins e.g. Vitamin D
2. Steroid Hormones: e.g male and female sex hormones and corticosteroids
3. Bile salts which have important role in digestion and absorption of lipids.

Fatty Acids

Definition: Fatty acids are aliphatic mono-carboxylic acids.

1. They have the general formula R-$(CH_2)_n$-COOH
2. "n" is mostly an even number of carbon atoms (2-34) with a few exceptions that have an odd number or even zero in acetic acid.

Classification:

Fatty acids can be classified as follows:

I) <u>Saturated,</u> i.e., they contain no double bonds with 2-24 or more carbons. They have the following molecular formula, $C_nH_{2n+1}COOH$. Examples are butyric, palmitic and stearic acids.

Saturated Fatty Acids They are classified into:

A- Short chain: 2-6 carbon atoms

They are further classified into:

i) Volatile short-chain fatty acids:

ii) Non-volatile short-chain fatty acids:

B- Medium-chain fatty acids : 8 – 14 carbon atoms

C- Long-chain fatty acids: 16 or more carbon atoms

- Examples:

16 C Palmitic acid $CH_3\text{-}(CH_2)_{14}\text{-}COOH$

18 C Stearic acid $CH_3\text{-}(CH_2)_{16}\text{-}COOH$

II) Unsaturated,: They contain one or more double bonds

a) Monounsaturated, $C_nH_{2n-1}COOH$)

Examples:

- **Palmitoleic acid:** $CH_3-(CH_2)_5-CH=CH-(CH_2)_7-COOH$
- **Oleic acid:** $CH_3-(CH_2)_7-CH=CH-(CH_2)_7-COOH$
- **Nervonic acid:** $CH_3-(CH_2)_7-CH=CH-(CH_2)_{13}-COOH$

b) Polyunsaturated, (Essential fatty acids)

Definition: They are Polyunsaturated fatty acids (contain more than 1 double bond and called essential due to the following:

a) They can not be synthesized in the human body (due to lack of enzymes that can form more than one double bond)
b) Must be taken in adequate amounts in the diet.
c) They are required for normal growth and metabolism.

Functions OF PUFA :

1. Useful to prevent atherosclerosis.
2. Prostaglandin & eicosanoids are synthesized
3. They participate in structure of all cellular and subcellular membranes and the transporting plasma phospholipids.
4. Essential for skin integrity, normal growth and reproduction.
5. Important role in blood clotting.
6. Important in preventing and treating fatty liver.
7. Important role in health of the retina and vision.
8. They can be oxidized for energy production.

Deficiency: Their deficiency in the diet leads to nutritional deficiency disease. Its symptoms include:

1. Poor growth and health with susceptibility to infections, dermatitis,
2. Decreased capacity to reproduce,
3. Impaired transport of lipids, fatty liver,
4. Lowered resistance to stress.

Source: vegetable oils such as corn oil, peanut oil, olive oil, cottonseed oil, soybean oil and many other plant oils, cod liver oil and animal fats.

Examples:

- **Linoleic:** C18:2$\Delta^{9, 12}$.

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

- **Linolenic:** C18:3$\Delta^{9, 12,15}$.

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

- **Arachidonic acid:** C20:4$\Delta^{5, 8, 11, 14}$.

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

It is synthesized in the body from linoleic acid which in turn is metabolized into prostaglandins.

Physical Properties of fatty acids (FAs)

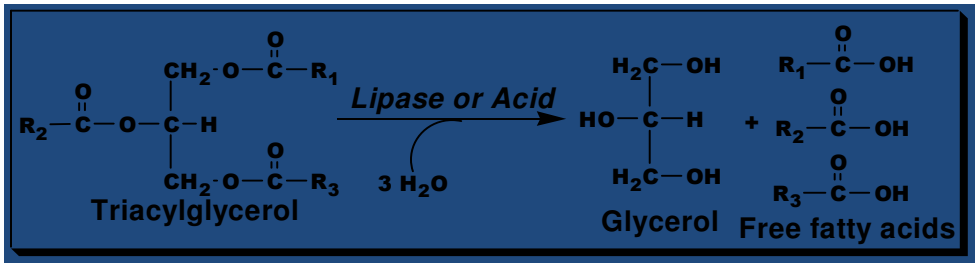
- Nonpolar = Poor solubility in water
- Melting points of FAs and triglycerides are strongly influenced by the length and degree of unsaturation of the hydrocarbon chain.
- At room temperature (25 degrees), saturated FAs from are semisolids (waxy) whereas unsaturated FAs of same lengths are oily liquids.
- **Melting Point increase with Length**
- **Melting Point decrease with Unsaturation**

Chemical Properties of fats and oils:

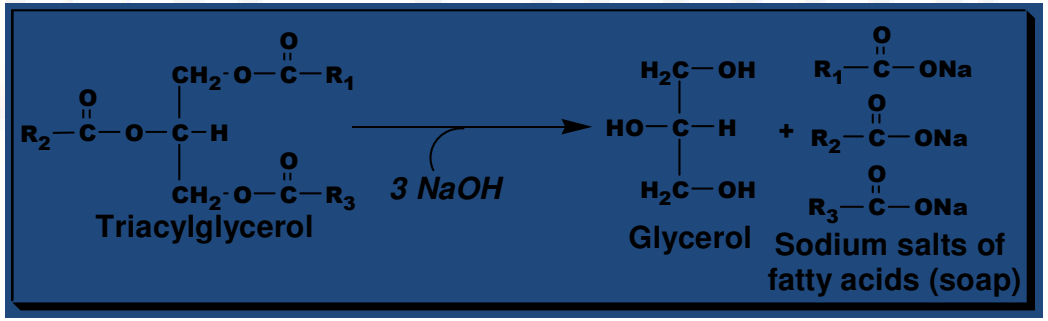
1- Hydrolysis:

Definition: hydrolysis of TG into their constituents (fatty acids and glycerol) by the action of super heated steam, acid, alkali or enzyme (e.g., lipase of pancreas).

1- Enzymatic and acid hydrolysis = glycerol and free fatty acids.



2- Alkaline hydrolysis produces glycerol and salts of fatty acids (**soap**). This is why alkaline hydrolysis of fats and oils is called **saponification**.



Types of Soaps:

1. Ordinary or hard soap are made by saponification of neutral fats by NaOH.
2. Green soap (or soft soap) is potassium soap.
3. useless insoluble soap is Calcium and magnesium soaps

Saponification number (or value):

Definition: It is the number of milligrams of KOH required to completely saponify one gram of fat.

Uses: Saponification number is used to

1- Study the natural characteristics of fats

2- Detect fat adulteration and selection of more suitable type of fat for soap manufacturing.

Iodine number (or value):

Definition: It is the number of gram - iodine absorbed by 100 grams of fat or oil.

Uses:

1- Measure for the degree of unsaturation of the fat, more the iodine number, the greater the unsaturation.

2- Used for the identification of the type of fat,

3-Detection of adulteration and determining the biological value of fat.

Examples: Saturated fatty acids have iodine number = 0, oleic acid = 90, linoleic acid = 181. Iodine number of olive oil is 79-88, cottonseed oil is 103-111, and linseed oil is 175-202.

3) Hydrogenation or hardening of oils:

Definition: It is a type of addition reactions accepting hydrogen at the double bonds of unsaturated fatty acids.

Method: The hydrogenation is done under high pressure of hydrogen and is catalyzed by finely divided nickel or copper and heat. It is the base of hardening of oils (margarine manufacturing), e.g., change of oleic acid of fats (liquid) into stearic acid (solid).

-It is advisable not to saturate all double bonds; otherwise margarine produced will be very hard, of very low biological value and difficult to digest.

Rancidity

Definition:

- It is a physico-chemical change in the natural properties of the fat leading to the development of unpleasant odour or taste or abnormal color particularly on aging after exposure to atmospheric oxygen, light, moisture, bacterial or fungal contamination and/or heat.

Types and causes of Rancidity:

1. Hydrolytic rancidity
2. Oxidative rancidity
3. Ketonic rancidity

1-Hydrolytic rancidity:
Due to hydrolysis of the fat
by lipase from bacterial contamination
at high temperature and moisture.
2-Oxidative Rancidity:
oxidation of fat or oil
Due to exposure to oxygen, light and/or heat
producing peroxide derivatives
that are toxic and have bad odor.
3-Ketonic Rancidity:
due to contamination with fungi
Moisture accelerates ketonic rancidity.

Prevention of rancidity is achieved by:

1. Avoidance of the causes (exposure to light, oxygen, moisture, high temperature and bacteria or fungal contamination).
2. By keeping fats or oils in well-closed containers in cold, dark and dry place.
3. Addition of anti-oxidants. The most common natural antioxidant is vitamin E.

Hazards of Rancid Fats:

1. The products of rancidity are toxic, i.e., causes food poisoning and cancer.
2. Rancidity destroys the fat-soluble vitamins (vitamins A, D, K and E).
3. Rancidity destroys the polyunsaturated essential fatty acids.
4. Rancidity causes economical loss because rancid fat is inedible(Unfit to eat).

B-Waxes

- Containing a monohydric alcohol (with a higher molecular weight than glycerol) esterified to long-chain fatty acids.
- Examples : palmitoyl alcohol, cholesterol, vitamin A or D.
- Properties of waxes:
  - Waxes are insoluble in water
  - soluble in fat solvents
- Not easily hydrolyzed as the fats
- Indigestible by lipases.
- Very resistant to rancidity.
- Thus they are of no nutritional value.

2-Compound Lipids

Definition:

- They are lipids that contain additional substances, e.g., sulfur, phosphorus, amino group, carbohydrate, or proteins beside fatty acid and alcohol.
- Compound or conjugated lipids are classified into the following types according to the nature of the additional group:

1. **Phospholipids**
2. **Glycolipids.**
3. **Lipoproteins**
4. **Sulfolipids and amino lipids.**

A-Phospholipids

Importance:

1. **Large amounts in the liver and brain as well as blood.**
2. **In membranes bounding cells and subcellular organelles**
3. **Transfer of substances through membranes**
4. **Essential for secretion and transport of plasma lipoprotein complexes. Thus, they are lipotropic agents that prevent fatty liver.**
5. **Myelin sheath of nerves is rich with phospholipids.**

5-Excretion of cholesterol in the bile.

6-Important function in blood clotting and platelet aggregation.

7-lung alveoli Surfactant that prevent its collapse.

8-Role in signal transduction across the cell membrane.

9-Phospholipase A2 in snake venom hydrolyses membrane phospholipids into hemolytic lysolecithin or lysocephalin.

10-Source of PUFA for synthesis of eicosanoids.

Snake bite cause severe haemolysis

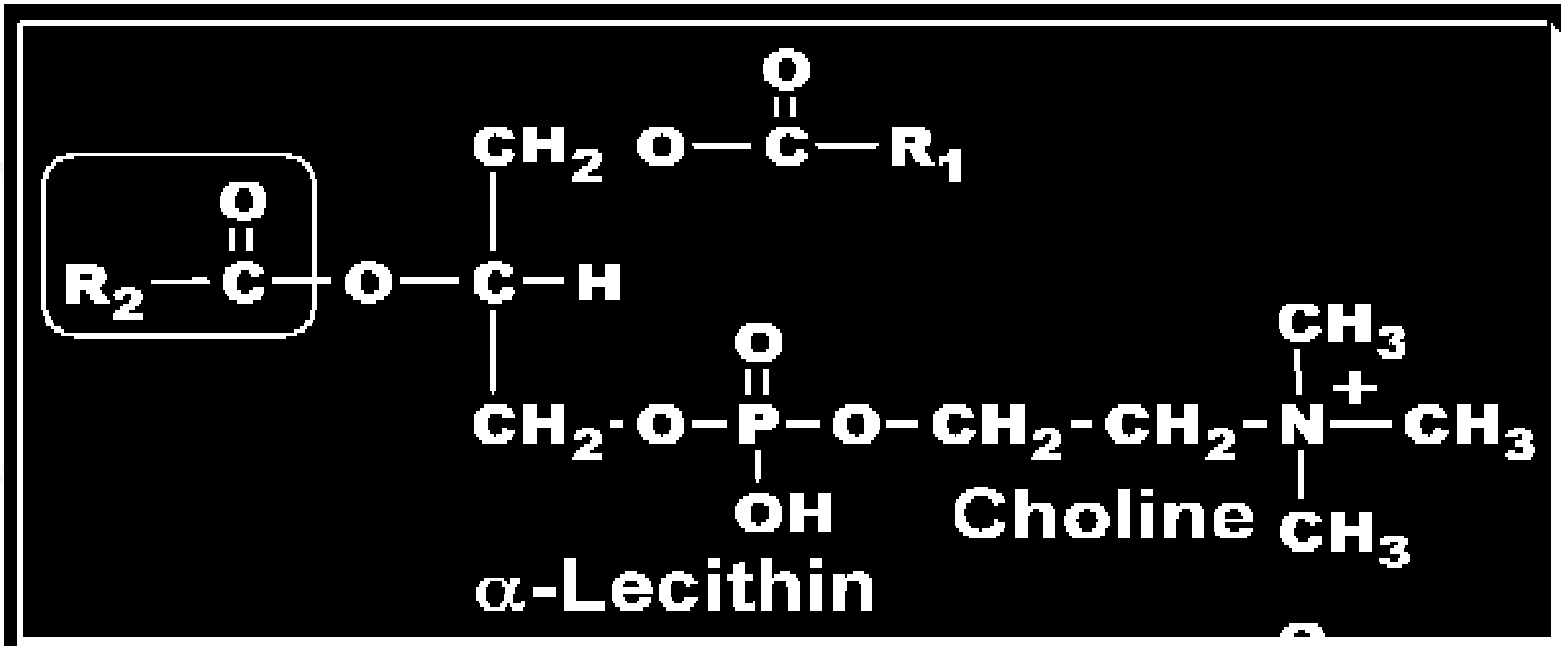
The venom contains lecithinase,

hydrolyzes the PUFA

converting lecithin into lysolecithin (detergent like action).

Lysolecithin causes hemolysis of RBCs.

cause anaphylactic shock as well as bleeding tency.



Lung surfactant

- Premature baby can suffer from ARDS(Acute Respiratory Distress Syndrome)
- Following are Lung surfactant
  - Dipalmitoyl-lecithin
  - Sphingomyelin
  - Apoproteins called apoprotein A, B, C, and D.
- It is produced by alveolar cells.
- It lowers alveolar surface tension and improves gas exchange besides activating macrophages to kill pathogens.
- It prevent collapse of the alveolie.
- In premature babies, this surfactant is deficient and they suffer from Respiratory Distress Syndrome.
- Glucocorticoids increase the synthesis of the surfactant complex and promote differentiation of lung cells.

6-Cardiolipins:

- **Definition**:
- **They are diphosphatidyl-glycerol.**
- **They are found in the inner membrane of mitochondria**
- **initially isolated from heart muscle (cardio).**
- **It is formed of 3 molecules of glycerol, 4 fatty acids and 2 phosphate groups.**
- **Function: Used in serological diagnosis of autoimmunity diseases.**

B-Glycolipids

- **Definition: They are lipids that contain carbohydrate residues with sphingosine as the alcohol and a very long-chain fatty acid (24 carbon series).**
- **They are present in cerebral tissue, therefore are called cerebrosides**
- **Classification: According to the number and nature of the carbohydrate residue(s) present in the glycolipids the following are**

1. **Cerebrosides. They have one galactose molecule (galactosides).**
2. **Sulfatides. They are cerebrosides with sulfate on the sugar (sulfated cerebrosides).**
3. **Gangliosides. They have several sugar and sugaramine residues.**

C-Lipoproteins

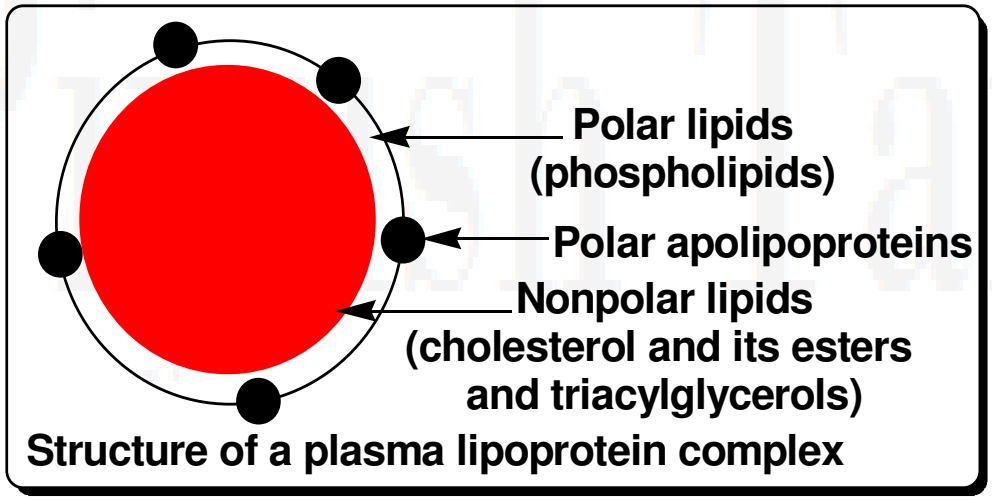
- **Definition: Lipoproteins are lipids combined with proteins in the tissues. The lipid component is phospholipid, cholesterol or triglycerides. The holding bonds are secondary bonds.**
- **They include:**

1. **Structural lipoproteins: These are widely distributed in tissues being present in cellular and subcellular membranes. In lung tissues acting as a surfactant in a complex of a protein and lecithin. In the eye, rhodopsin of rods is a lipoprotein complex.**

- **Transport lipoproteins:**
- **These are the forms present in blood plasma. They are composed of a protein called apolipoprotein and different types of lipids. (Cholesterol, cholesterol esters, phospholipids and triglycerides). As the lipid content increases, the density of plasma lipoproteins decreases**

- **Plasma lipoproteins can be separated by two methods:**

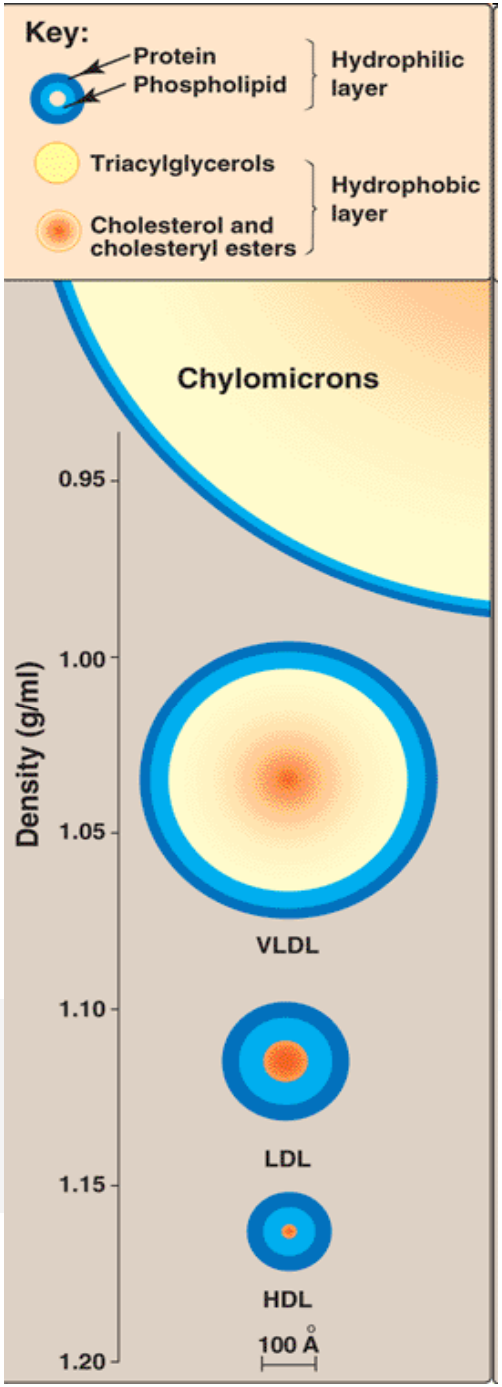
1. **Ultra-centrifugation: Using the rate of floatation in sodium chloride solution leading to their sequential separation into chylomicrons, very low density lipoproteins (VLDL or pre-β-lipoproteins), low density lipoproteins (LDL or β-lipoproteins), high density lipoproteins (HDL or α-lipoproteins) and albumin-free fatty acids complex.**
2. **Electrophoresis: is the migration of charged particles in an electric field either to the anode or to the cathode. It sequentially separates the lipoproteins into chylomicrons, pre-β-, β-, and α-lipoprotein and albumin-free fatty acids complex.**

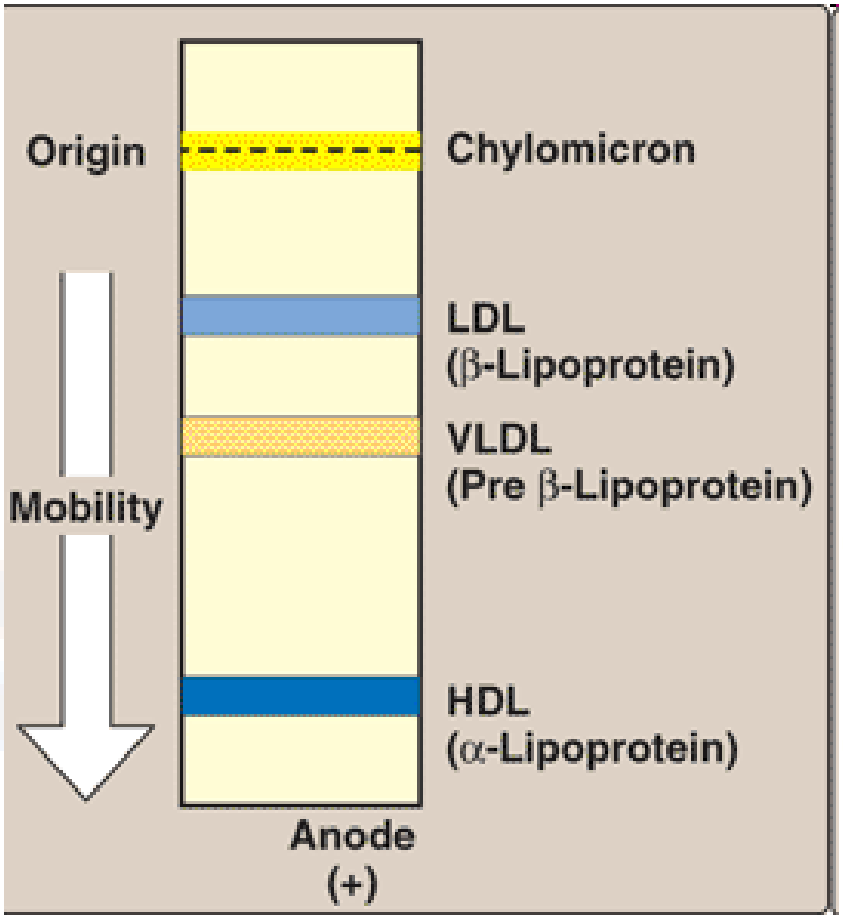


Structure of a plasma lipoprotein complex

Types of lipoproteins

- Chylomicrons
- VLDL - very low density lipoprotmedeins
- IDL – intermediate density lipoproteins
- LDL - low density lipoproteins
- HDL - high density lipoproteins
- Lp(a)- lipoprotein a
- Free fatty acid - albumin complexes


Key:
Protein
Phospholipid
Hydrophilic layer
Triacylglycerols
Cholesterol and cholesteryl esters
Hydrophobic layer
Chylomicrons
Density (g/ml)
0.95
1.00
1.05
1.10
1.15
1.20
VLDL
LDL
HDL
100 Å


Origin
Chylomicron
LDL
(β-Lipoprotein)
VLDL
(Pre β-Lipoprotein)
Mobility
HDL
(α-Lipoprotein)
Anode
(+)

a) Chylomicrons:

a) The largest diameter and the least density.

b) 1-2% protein only and 98-99% fat.

c) The main lipid fraction is triglycerides absorbed from the intestine and they contain small amounts of the absorbed cholesterol and phospholipids.

b) Very low-density lipoproteins (VLDL) or pre-β-lipoproteins:

Diameter is smaller than chylomicrons.

7-10% protein and 90-93% lipid.

The lipid content is mainly triglycerides formed in the liver. They contain phospholipid and cholesterol more than chylomicrons.

c) Low-density lipoproteins (LDL) or β-lipoproteins:

10-20% proteins in the form of apolipoprotein B. Their lipid content varies from 80-90%. They contain about 60% of total blood cholesterol and 40% of total blood phospholipids.

The liability to atherosclerosis increases.

d) High-density lipoproteins (HDL) or α-Lipoproteins:

35-55% proteins in the form of apolipoprotein A. 45-65% lipids formed of cholesterol (40% of total blood content) and phospholipids (60% of total blood content).

- They act as cholesterol scavengers, as their percentage increases, the liability to atherosclerosis decreases.
- Due to their high protein content they possess the highest density.

e) Albumin-free fatty acids complex: It is a proteolipid complex with 99% protein content associated with long-chain free fatty acids for transporting them.