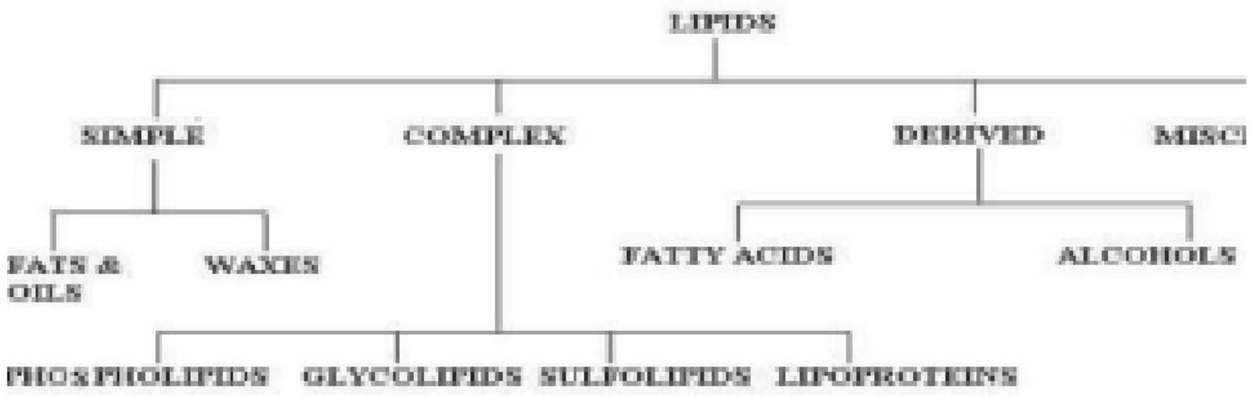
MED-HUB

BIOCHEMISTRY

LIPIDS

Lipids:

- Lipids are a heterogeneous class of naturally occurring organic compounds, they are hydrophobic.
- Many of them are amphipathic.
- Classes:



- Lipid Functions:
  1. They are a major source of energy.
  2. They are storable to unlimited amount.
  3. Structural components (cell membranes).
  4. Precursors of hormone and vitamins.
  5. Work as shock absorbers and thermal insulator.

❖ Why we store energy in a form of lipids rather than carbohydrates? because:

1. lipids are water insoluble so they won't attract water molecules to the adipose tissue but if we stored energy in carbohydrates which are highly polar so they will attract the water molecules.

2. (1)g of fat has (9) calories but (1) g of carbohydrates has (4) calories so it's much larger in terms of amount.

We have:

1.Fatty acids:

- Aliphatic mono carboxylic acids.
- Its non-polar even if it has a polar group but the presence of the long hydrocarbon chain that is non polar will dominate and make the whole molecule non polar and insoluble in water.

- Functions of F.A:
  1. Building block of other lipids.
  2. Important fuel molecules.
  3. Used for modifying proteins such as lipoproteins.
  4. Derivatives of important cellular molecules.

- Types of fatty acids:
  1. Saturated fatty acids are those with all of C-C bonds being single.
  2. Unsaturated fatty acids are those with one or more double bonds between carbons:
     - Monounsaturated fatty acids.
     - Polyunsaturated fatty acids.

- Properties of lipids are melting point and solubility, and they depend on two things:

  1. Chain length: ⇧ number of carbons→⇧ melting point.
  2. Degree of saturation: ⇧ double bonds→⇩decrease the melting point.

- Naming of F.A:

The first way:

1. First of all we start with mentioning the number of carbons in fatty acids.
2. we need to add to the name if it has one double bond, two, or three.
3. followed by the suffix (OIC).

EX: if we have a F.A made of 18 carbon and have one double bond the name of it is: = octadecenoic acid.

if we have a F.A made of 18 carbon and have two double bond the name of it is: = octadecadienoic acid.

The second way:

In this system we count the carbons from the end of the molecule not from the carboxyl group and we take the first double bond.

Numerical Symbol	Common Name and Structure	Comments
18:1$^{\Delta 9}$	Oleic acid 	Omega-9 monounsaturated
18:2$^{\Delta 9,12}$	Linoleic acid 	Omega-6 polyunsaturated
18:3$^{\Delta 9,12,15}$	α-Linolenic acid (ALA) 	Omega-3 polyunsaturated
20:4$^{\Delta 5,8,11,14}$	Arachidonicacid 	Omega-6 polyunsaturated
20:5$^{\Delta 5,8,11,14,17}$	Eicosapentaenoic acid (EPA) 	Omega-3 polyunsaturated (fish oils)
22:6$^{\Delta 4,7,10,13,16,19}$	Docosahexaenoicacid (DHA) 	Omega-3 polyunsaturated (fish oils)

REQUIRED

Omega fatty acids:

1. Omega-3 fatty acids:

- They reduce inflammatory reactions by:
  A. Reducing conversion of arachidonic acid into eicosanoids.
  B. Promoting synthesis of anti-inflammatory molecules.

2. Omega-6 fatty acids:

- Stimulates platelet and leukocyte activation.
- Signals pain.
- Induces bronchoconstriction.
- Regulates gastric section.

3. Omega-9 fatty acid:

- Reduces cholesterol in the circulation.

- Derived acids from fatty acids:

1. Prostaglandins:

Functions:

- Inhibition of platelet aggregation.
- Blood clotting.

2. Leukotrienes:

- It contains (4) double bonds, (3) of these double bonds are conjugated, that's why it's called leukotrienes.
- They constrict the smooth muscles.

3. Thromboxane:

Functions:

- Constriction of smooth muscles.
- Induces platelet aggregation.

4. Prostacyclin:

Functions:

- An inhibitor of platelet aggregation.
- A vasodilator.

❖ From what we derive these derived acids?

- Form arachidonic Acid which can be converted to the other molecules (like prostaglandins, etc) by the activity of enzyme called cyclooxygenases (COX).

- And we have COX1, COX2, COX3.
- There are two major pathway arachidonic acid can take depending on which enzyme is used:
  1. First pathway: arachidonic acid is converted into thromboxane by COX1.
  2. Second pathway: arachidonic acid is converted into prostaglandins by COX2.

- There are inhibitors for this enzyme (COX):
  1. Aspirin: inhibits platelet aggregation as well as blood clotting, so, it reduces heart disease.

  HOW?

by inhibiting the enzymes (cyclooxygenases) that convert arachidonic acid to these molecules, cyclooxygenase (1) converts arachidonic acid to thromboxane and cyclooxygenase (2) converts it to prostaglandins so by inhibiting these two enzymes you reduce inflammation, reduce fever and you can inhibit platelet aggregation and reducing heart attacks.

2. Celebrex.

- Fatty acids reactions:
  1. Enzymatic hydrolysis: There is an enzyme called (pancreatic lipase) that can break triglycerides using water, producing three fatty acids molecules and glycerol.

  2. Saponification: since lipids have ester linkages, they can be cleaved back into a salt of fatty acid and alcohol (glycerol) by reacting with water and a base (such as an aqueous solution of NAOH).

  3. Hydrogenation: two hydrogen atoms are added across C-C double bond, resulting in a hydrogen-saturated.

- Waxes:
  - They are molecules that results from the Reaction between a fatty acid (C14~C36) by its carboxylic head with a monohydric alcohol (C16~C30) by Esterification reaction forming an Ester bond.
  - They have zero nutritional value as we cannot digest them.
  - They are highly insoluble in water, negative to acrolein test which tests for the presence of glycerin and fats.
  - They have a long half-life.

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Membrane lipids:

- Membrane lipids are classified into two major types:

1. Phospholipids (phosphoacylglycerols) they contain phosphate group.
   - ➢ Made of glycerol molecule (that has 3 OH groups).
   - ➢ The first two carbons are connected to fatty acids and the third carbon is attached to a phosphate group.
   - ➢ Different head groups are linked to the phosphate group to make different types of phosphoacylglycerols like:

1. Lecithin (Phosphatidylcholine):
   - ➢ Its head group is: choline → $-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
   - ➢ exists a lot in the plasma membrane of RBCs.
   - ➢ Lecithinase the enzyme that hydrolyzes polyunsaturated fatty acids and converting lecithin into lysolecithin which found in the snake venom.
   - ➢ Act as emulsifying agents.

2. Cardiolipins:
   - ➢ It is composed of a glycerol molecule connecting two glycerophospholipids.
   - ➢ Found in the inner mitochondrial membrane.
   - ➢ Structure: (3) molecules of glycerol, (4) fatty acids & (2) phosphate groups.

3. Plasmalogens:
   - ➢ They have a protective role against reactive oxygen species.
   - ➢ Precursor of the backbone: Dihydroxyacetone phosphate.
     - At C1: Unsaturated fatty alcohol connected by ether bond.

- At C2: Fatty acid connected by ester bond.

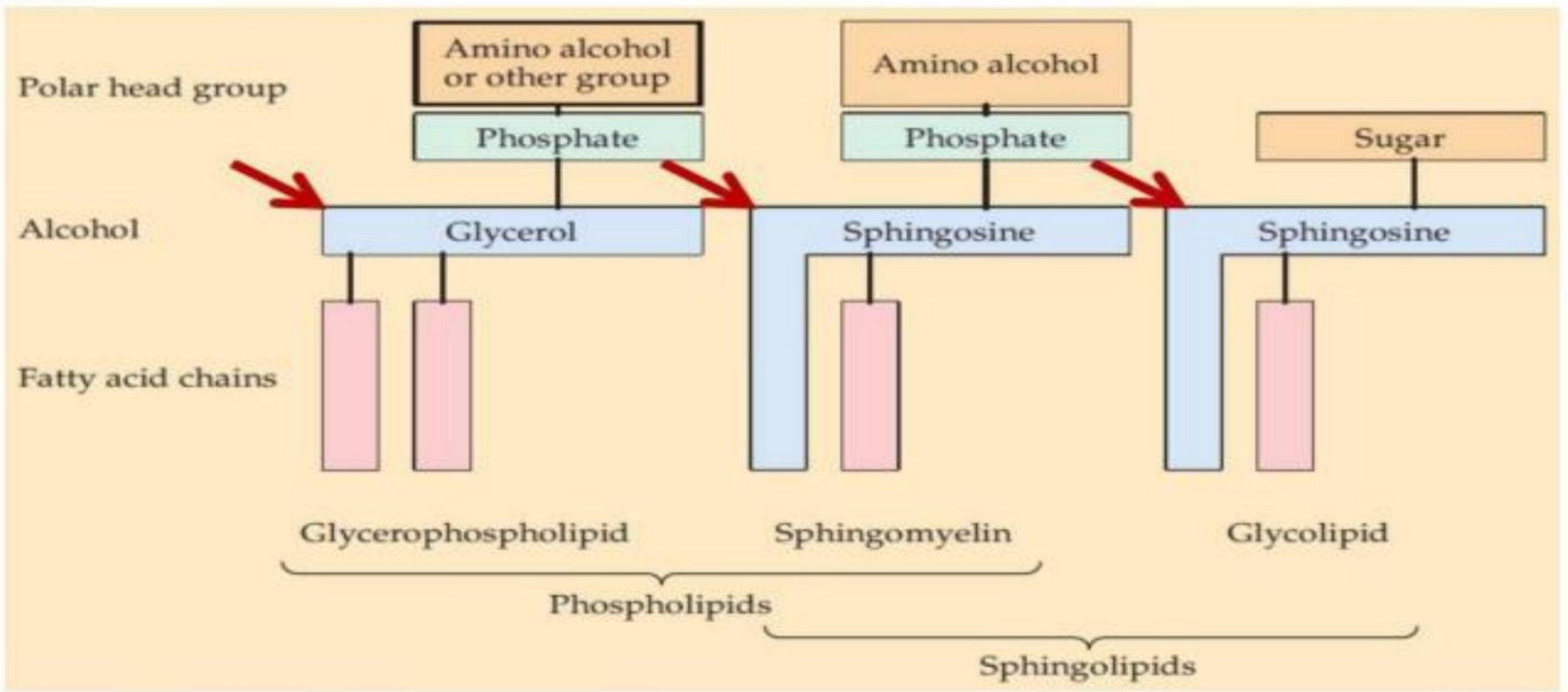
➢ Choline plasmalogen: which is a class of plasmalogens and act as platelet activating factor.

4. Inositides:

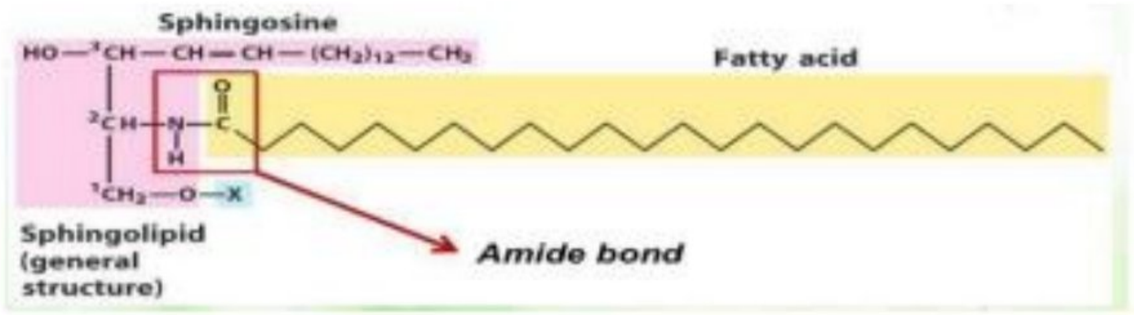
➢ Structure: glycerol, saturated FA, unsaturated FA, phosphoric acid & inositol.
➢ Source: Brain tissues.
➢ Functions:
   1. Major component of cell membrane.
   2. Second messenger during signal transduction.

NOTE: The difference between the micelle structure and the liposome is that the micelle is made only of one layer of amphipathic molecule with the core being hydrophobic (fatty acids) and the outer surface is polar. While the liposome has a hydrophilic core and can be formed from a lipid bilayer.

THE CLASSIFICATION OF LIPIDS



2. Sphingolipids (contain sphingosine backbone).
   - The core of sphingolipids is the long-chain amino alcohol, sphingosine.
   - Sphingolipids consist of one fatty acid, whereas the bent structure of the sphingosine, a long-chain (18c) amino alcohol with a double bound, acts as the second tail. Sphingosine acts also as a connecting region joining hydrophobic tails with X group.



   - Types of sphingolipids depends on what is linked to the (O) like the (X) in the photo above:
     1. Ceramide:
        - The simplest sphingolipid.
        - the precursor of all other sphingolipids.
        - The group attached to C1 is (O) in ceramide.
     2. Sphingomyelin:
        - Is a sphingolipid that is a major component of the coating around nerve fibers.
        - The group attached to C1 is a phosphocholine.
     3. Glycosphingolipids (Glycolipids):
        - The group attached to C1 is carbohydrate.
        - Can function in immune and cell recognition like (ABO blood groups) and act as chemical messengers.

- There are three types of glycolipids according to the type of sugar attached:

Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

- Sulfatides: Cerebroside-derived molecules, specifically derived from Galactocerebroside.

Lipoproteins:

- Lipoproteins are a sub-group of lipid molecules in which they contain high amounts of proteins along with different types of lipids being a component of this structure.
- We have different types of lipoproteins and they differ from each other in the Lipid/Protein ratio and the component of them:

NOTE: As lipid content increases, the Lipid/Protein ratio increases and the density (density of proteins) decreases in a given volume.

1. Chylomicron: is important for absorbing lipid molecules through the Intestinal tract, the larger lipoprotein, have smaller density and a high ratio of Lipids/Proteins.
2. High density lipoproteins (HDLs): transport lipid molecules to Liver to produce important substances such as Vitamin D and Bile acids, which is why it is commonly known as Good Cholesterol.

3. Low density lipoproteins (LDLs): transport lipid molecules to cells where they are usually stored, leading to accumulation of these fat molecules (Obesity and other health problems) and for that reason, they are known as Bad Cholesterol.

Steroids:

- Steroids are another class of lipid molecules that share the presence of a structure known as Steroid Nucleus, which has 3 six-membered rings fused together along with a five-membered ring.
- The addition of different functional groups to their terminal five-membered ring will create several different steroid molecules, for example: Cholesterol.

  - Cholesterol: is the most common type of steroids in animal cells, in which there is a hydrocarbon side chain attached to the last ring as well as an OH- group attached to carbon (3) of the first six-membered ring making the molecule Amphipathic.
  - Cholesterol is important for synthesizing other molecules like:
    1. Hormones: such as androgen, estrogens (estradioal), progestins.
    2. Some vitamins such as vitamin D.
    3. Bile (steroid) acids.
  - Cholesterol esters (CE): are compounds in which a fatty acid is attached at the (OH-) group of Carbon 3 (modified esters).
  - CE represent an inactive form of Cholesterol and thus are used to transport Cholesterol within lipoproteins, specifically in HDLs.

Cell membrane:

- The contents of the Plasma membrane are distributed as the following:
  - The outer leaflet contains:
    1. Phosphatidylcholine.
    2. Sphingomyelin.
    3. Glycolipids.
    4. Cholesterol.
  - The inner leaflet contains:
    1. Phosphatidylethanolamine.
    2. phosphatidylserine.
    3. phosphatidylinositol (signaling).
    4. Cholesterol.
- Membrane fluidity and Fatty acids:

  1.Saturated fatty acyl chains:

  Saturated ⇒ linear and exposed surface ⇒ more non-covalent interactions ⇒ more rigidity.

  2. Unsaturated fatty acyl chains:

  Unsaturated ⇒ kinked structure-less space ⇒ less non-covalent interactions ⇒ more fluidity.

- Membrane fluidity and temperature:

  When there is an increase in temperature, Phospholipid molecules gain more kinetic energy causing a disruption in their interactions as they move faster and away from each other, leading to a decrease in membrane rigidity and vice versa.
- Membrane fluidity and Cholesterol:
  - Cholesterol acts as a fluidity buffer, makes a membrane less solid at low temperatures and more solid at high temperatures.

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