# 10

# BIOCHEMISTRY
faculty of medicine - JU2017

ketone starch lipid protein amine carbohydrates isomers

◉ Sheet ○ Slides


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## A QUICK RECAP

# Eicosanoids

They are derived from **Arachidonic acid**, a fatty acid that contains 20 carbon atoms and four double bonds. They regulate a wide variety of physiological responses and pathological processes, and control important cellular processes.

Lipids Classified under the term of **Eicosanoids**:

- **Prostaglandins**
- **Leukotrienes**
- **Thromboxane**
- **Prostacyclins**

**They were discussed previously. For more information, see sheet 9.**

**Arachidonic Acid** can be converted into other compounds (such as prostaglandins and leukotrienes) by metabolism by an **enzyme** known as cyclooxygenases (**COX**). Cyclooxygenase is present in three forms in different tissues, $COX_1$, $COX_2$, and $COX_3$. There are two major pathways arachidonic can take depending on which enzyme is used;

**1st pathway:**

arachidonic acid is converted into **thromboxane** by $COX_1$, which in turn induces platelet aggregation.

**2nd pathway:**

arachidonic acid is converted into **prostaglandins** by $COX_2$, they can cause pain, fever and inflammation making the environment unhospitable for any pathogen invading the body, prostaglandins also inhibit platelet aggregation.

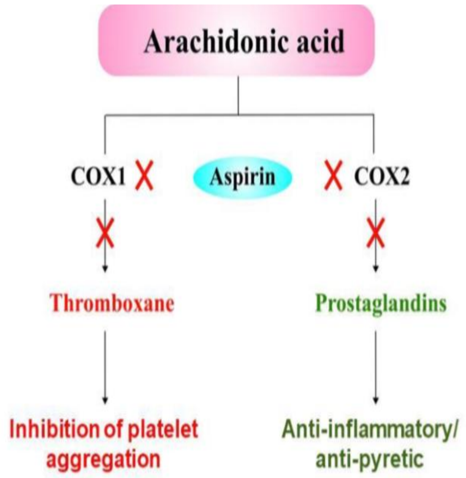
## Cyclooxygenases Inhibitors

1) **ASPIRIN**: a drug that is widely used for reducing body temperature and preventing inflammation process. As a side result it also inhibits platelet aggregation as well as blood clotting, so it reduces heart disease.

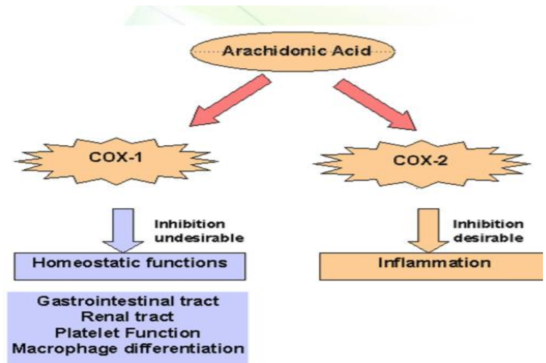
**Mechanism**: it was discovered that prostaglandins seem to be responsible for causing fever, inflammation and pain. ASPIRIN treats these symptoms by preventing the production of prostaglandins.
BUT what **ASPIRIN** really does is that it prevents COX from working, which in turn blocks prostaglandins production. **Aspirin** targets both, but $COX_2$ should only be targeted.

One of the prostaglandins that aspirin prevents from synthesizing is thromboxane, which is involved in activation of platelets to initiate aggregation and blood clotting. That means if you take aspirin daily it becomes harder for blood to clot. This is extremely useful in preventing diseases caused by blood clots such as heart attacks and stroke, that's why its recommended for older aged people who have a higher risk of suffering from those diseases.

As mentioned earlier, prostaglandins aren't just involved in inflammation and pain, using aspirin also stops other body functions as well as it decreases production of protective mucous in the stomach which means that stomach acid can burn through the stomach lining leading to gastric ulcers and internal bleeding since there is also less clotting occurring, this side effect becomes even more dangerous (because a clot is what stops the bleeding when you have a wound) therefore it's not recommended for people who have a tendency of developing gastric ulcers or have genetic problems with clotting and it is also not recommended for people who are treated with blood thinners or are prone to bleed easily.




2) **CELEBREX:** A new generation drug, but is prescribed with a strong warning of side effects on the label.
what is special about it is that **CELBREX** is a selective-inhibitor of $COX_2$ so that it doesn't affect aggregation and clotting of blood.
Celebrex isn't recommended for people who have heart problems as it increases heart rate leading to fatal results.




## OMEGA FATTY ACID

- **Omega-3 fatty acids:**

  α-linolenic acid→ eicosapentaenoic acid (EPA) → docosahexaenoic acid (DHA)

  **Functions:**
  - They reduce inflammatory reactions by:
    - Reducing conversion of arachidonic acid into eicosanoids,
    - Promoting synthesis of anti-inflammatory molecules.

*omega-3 is good for your memory, so TAKE IT DAILY!!!!(You can get omega 3 from fish and walnuts, or simply buy supplements)

- **Omega-6 fatty acids:**

The precursor is Linoleic acid, ω-6 has many functions such as:

- stimulates platelet and leukocyte activation,
- signals pain
- Induces bronchoconstriction,
- regulates gastric secretion.

NOTE **Linoleic and linolenic acids are both ESSETNTIAL FATTY ACIDS, our body can't synthesize them we take them from diet.**

- **Omega-9 fatty acids:**

They are derived from Oleic acid, they reduce cholesterol in the circulation. Mediterranean food is a great source of omega-9 due to the amount of olive oil used; Olive oil is a great source of Oleic acid.

## WAXES

Solid simple lipids containing a monohydric alcohol (C16 ~ C30, higher molecular weight than glycerol) esterified to long-chain fatty acids (C14 ~ C36).

Ex: Palmitoyl alcohol

$$CH_3(CH_2)_{14}-\overset{\overset{O}{\|}}{C}-O-CH_2-(CH_2)_{28}-CH_3$$

**A long chain fatty acid + A long hydrocarbon chain alcohol**

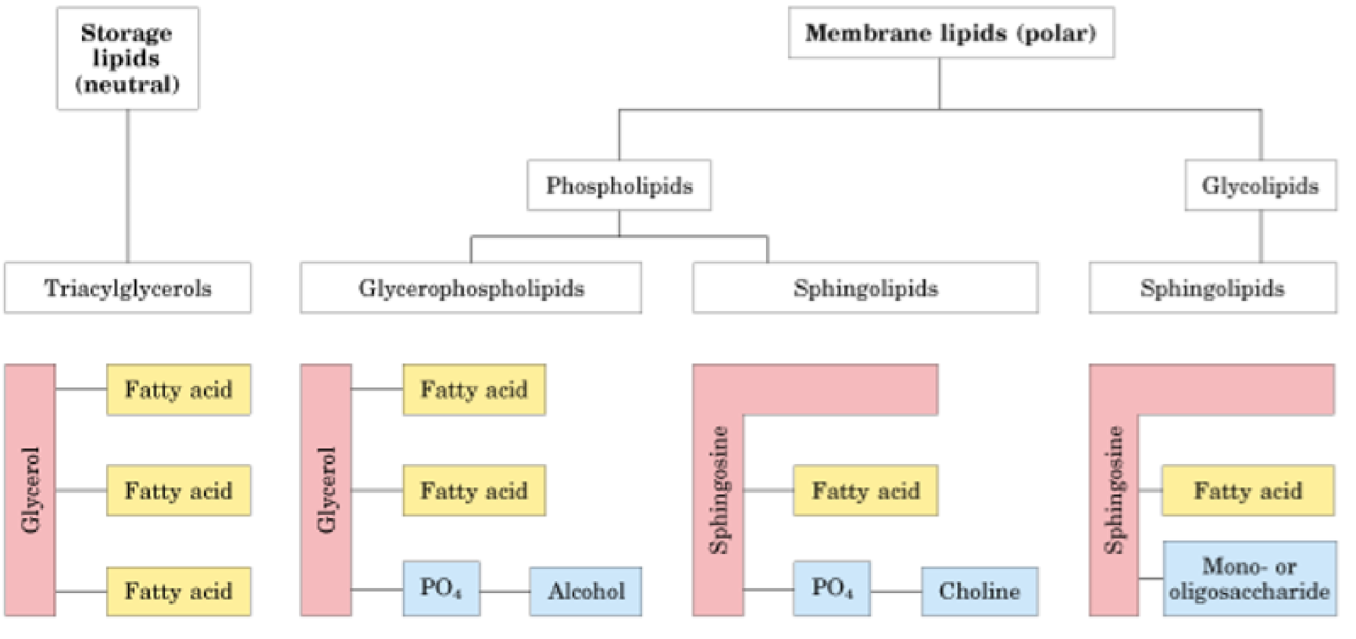
GIVES an ESTER, characterized by being quite hydrophobic (Insoluble in water)

**FEATURES:**

- Coatings that prevent loss of water by leaves of plants,
- Are of no nutritional value, because it's indigestible.
- Are not easily hydrolyzed (fats) & are indigestible by lipases,
- Are very resistant to rancidity (unpleasant odors ).

## COMPLEX LIPIDS

**Complex lipids** have in common two main parts **Backbone** and attached **functional groups.**
the **backbone** can be either glycerol or sphingosine.
**attached groups** can be phosphate, nitrogen base, carbohydrate …etc.




Another **classification** for complex lipids:

- **Triacylglycerols**
- **Glycerophospholipids**
- **Sphingolipids**; that could either be Sphingophospholipids or Glycolipids.

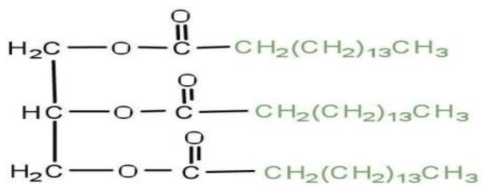
### 1) Triacylglycerol (Triglyceride)

In glycerol there are 3 hydroxyl groups each can be substituted/replaced with a fatty acid chain. So, we can get monoacylglycerol, diacylglycerol and triacylglycerol.

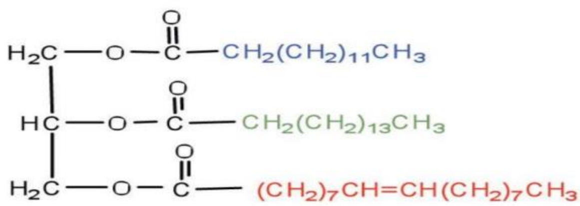
- In our bodies, we store fat in the form of triacylglycerol.

the fatty acid chains substituted for hydroxyl groups can be similar or different, they also can be saturated or not.

simple triacylglycerol → 3 similar fatty acids



mixed triacylglycerol → 3 different fatty acids

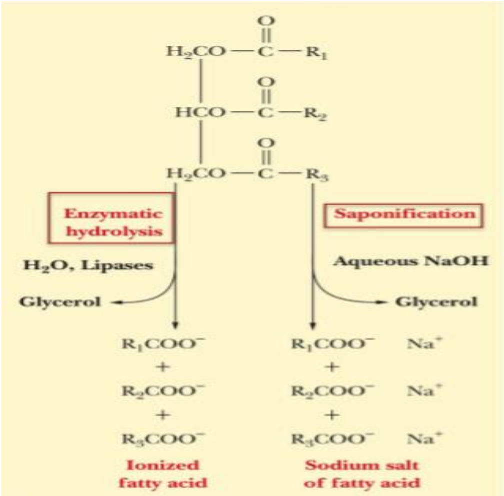


- **Solid vs liquid fats:**

depends mainly on the saturation of the fatty acid chains from which triacylglycerol is formed, since double bonds cause kinks in the structure of fatty acids. This is the primary reason for the different melting points of fats and oils.

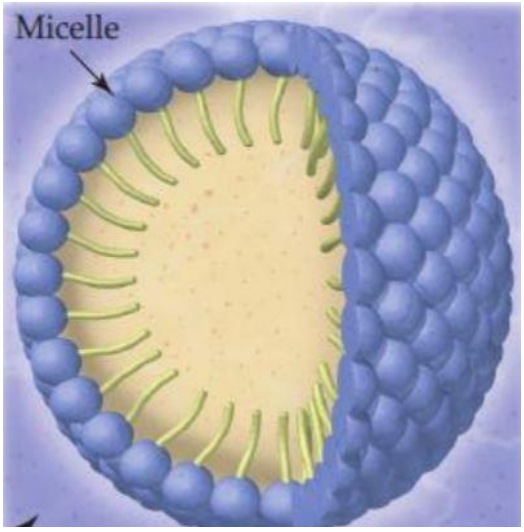
- So you can say that the fluidity of fat is inversely proportional to the saturation at the same temperature

*It is worth mentioning that vegetable oils consist almost entirely of unsaturated fatty acids, whereas animal fats contain a much larger percentage of saturated fatty acids.




- **Saponification (hydrolysis):**

since lipids have ester linkages, they can be cleaved back into a salt of fatty acid and an alcohol (glycerol) by reacting with water and a base (such as an aqueous solution of NaOH). It can be also cleaved in our bodies by certain enzymes (lipase of pancreas).




- **how does soap work?**

- When mixed with water, the hydrophobic hydrocarbon tails cluster together and orient inward to create a nonpolar microenvironment and the hydrophilic ionic heads interact with water.
- The resulting spherical clusters are called **Micelles**.
- Grease and dirt are trapped inside micelles and the complex can be rinsed away.

*Basically, soap causes emulsification of oily material.

- **Hydrogenation:**

In a hydrogenation reaction, two hydrogen atoms are added across C-C double bond, resulting in a hydrogen-saturated bond. So, chemists invented a method of converting unsaturated fat into a more solid form by partially hydrogenating it, but it was found that Partial hydrogenation converts some, but not all, double bonds into single bonds generating (**trans fats**). So, we will still have double bonds but in the trans form.

* The primary health risk identified for **trans-fat** consumption is an elevated risk of coronary heart disease (**CHD**) and heart attacks as it accumulates in our circulation without being digested because the double bonds aren't recognized by our body enzymes.

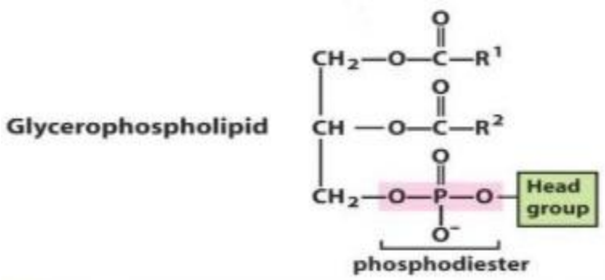
*The main reason behind using trans-fat is that it gives a longer shelf life and it tastes way better.

* In margarine, only about two-thirds of the double bonds present in the starting vegetable oil is hydrogenated, so that the margarine remains soft in the refrigerator and will melt on warm toast. Note that **Margarine has no trans-fat**.

## Membrane Lipids

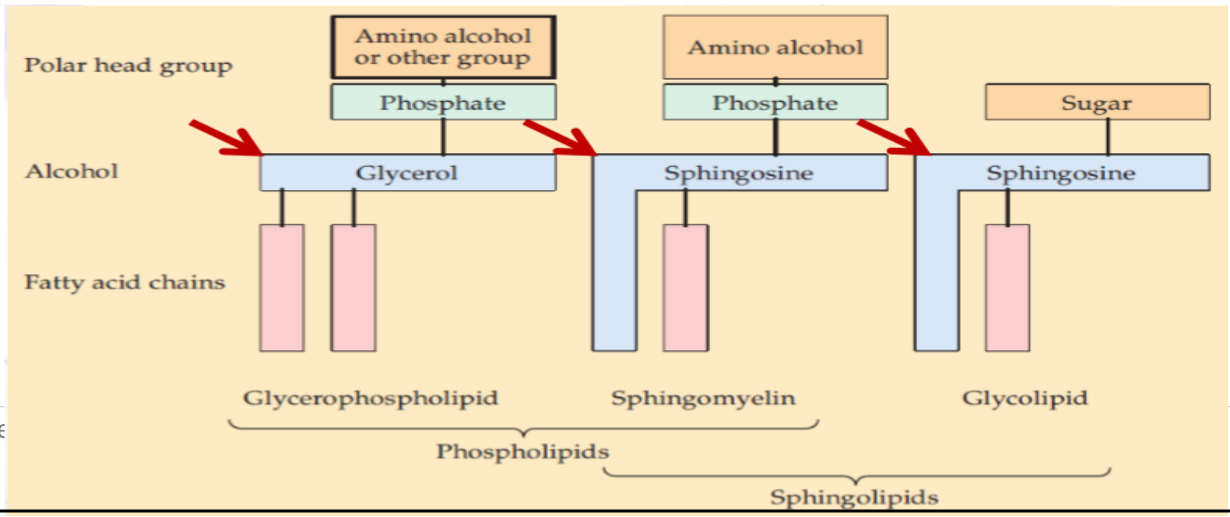
The most prevalent class of lipids in membranes is the **glycerophospholipids,** the least is **glycolipids.**
*The only sphingophospholipids present in plasma membrane is sphingomyelin.
*Membrane lipids are amphipathic.
*The existence of the lipid bilayer depends On hydrophobic interactions.

### 1) glycerophospholipids:




The common structure in **glycerophospholipids** is glycerol, two fatty acid and a phosphate group to which a head group is attached.

*head group can be either choline, serine or ethanolamine.
*the simplest form is **phosphatidic acid** in which the head group is just a hydrogen.



| | | |
|---|---|---|
| Phosphatidic acid | — | $-H$ |
| Phosphatidylethanolamine | Ethanolamine | $-CH_2-CH_2-\overset{+}{N}H_3$ |
| Phosphatidylcholine | Choline | $-CH_2-CH_2-\overset{+}{N}(CH_3)_3$ |
| Phosphatidylserine | Serine | $-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$ |

## * Classification of Glycerophospholipids

- **phosphatidylcholine (Lecithins) :**

  * most abundant membrane lipid
  * it was found that phosphatidylcholine is the target of snake venom. This venom contains lecithinase, which hydrolyzes polyunsaturated fatty acids and converting lecithin into lysolecithin. [causing hemolysis of RBCs]

- **phosphatidic acid:**

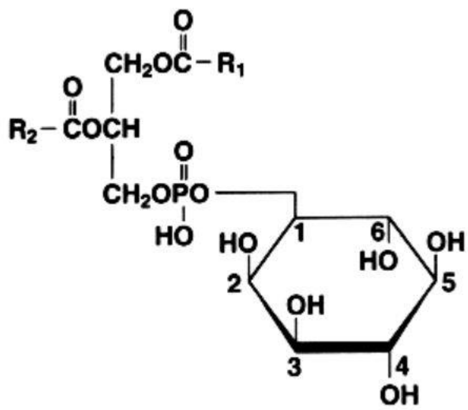
  The simplest glycerophospholipid, has 2 fatty acids and a phosphate group.

- **Cephalins:**

  Phosphatidylethanolamine and phosphatidylserine (abundant in brain)

- **Phosphatidylinositol:**

  *Sends messages across cell membranes
  *The head group is a sugar molecule.
  *Nitrogenous base: cyclic sugar alcohol (inositol).
  *Structure: glycerol, saturated FA, unsaturated FA, phosphoric acid, & inositol.
  *Source: Brain tissues
  *Note that it is not in the membrane but it is attached to it and works as a Signaling molecule

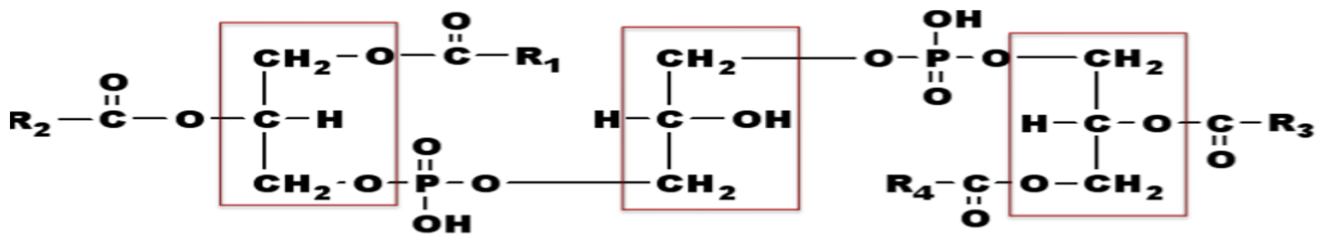



- Functions:
  - Major component of cell membrane
  - Second messenger during signal transduction
  - On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5diphosphate produces diacyl-glycerol (DAG) & inositol triphosphate (IP3); which liberates calcium

- **Cardiolipins:**

 * From the name is related to the heart; abundant in the heart muscle.
 * Diphosphatidyl-glycerol
 * Found in the inner membrane of mitochondria
 * Initially isolated (when it was first discovered in early 1940s ) from heart muscle (cardio)
 * Structure: 3 molecules of glycerol, 4 fatty acids & 2 phosphate groups

* The following picture shows the structure of cardiolipin which you must know and you must also have enough knowledge to be able to distinguish different glycerophospholipids from each other



- **Plasmalogens**

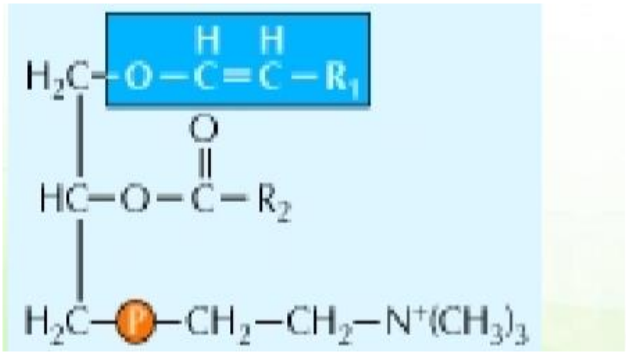
 * they are found in the cell membrane phospholipids fraction of brain & muscle, liver, and semen.
 * they have a protective role against reactive oxygen species
 * Structure:

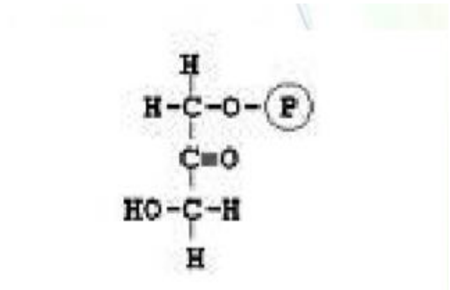
 Precursor: Dihydroxyacetone phosphate. (simplest ketose)

 Unsaturated fatty alcohol at C1 connected by ether bond.

 In mammals: at C3; phosphate + ethanolamine or choline.

The picture below, shows a Choline plasmalogens, notice the double bond on C1



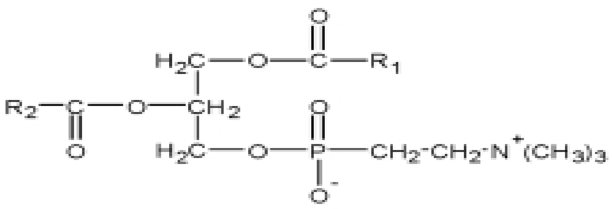


Dihydroxyacetone phosphate

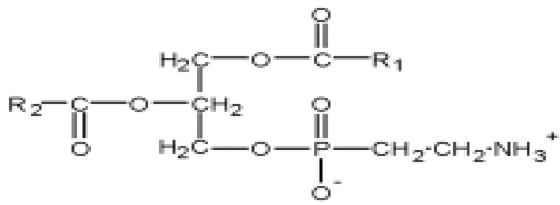
- Major classes of Plasmalogens:

**1-**Ethanolamine plasmalogen (myelin-nervous tissues)
**2-** Choline plasmalogen (cardiac tissue)
    *Platelet activating factor
**3-** Serine plasmalogens (serine is an amino acid

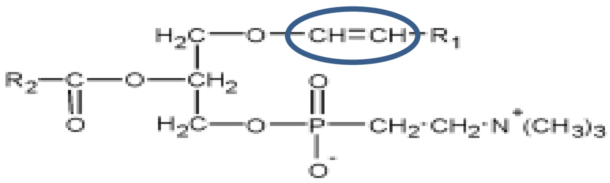
*The following picture shows the difference between plasmalogens and other phospholipids, the main difference is the presence of a double bond adjacent to the oxygen of C1 of the glycerol molecule.



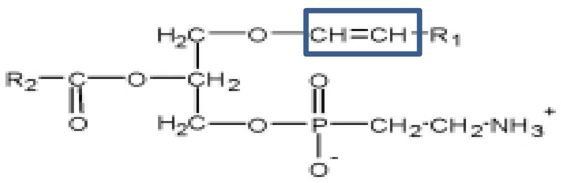
phosphatidyl-choline



phosphatidyl-ethanolamine



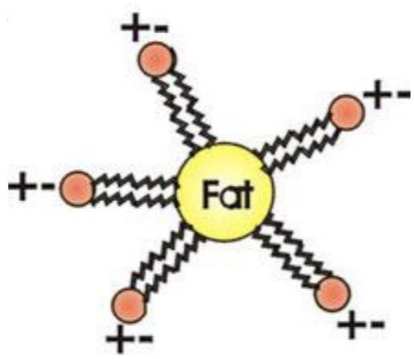
choline-plasmalogen



ethanolamine-plasmalogen

- **Emulsification:**

A process by which we can dissolve hydrophobic material (such as fat) in an aqueous environment or when being mixed with water using an emulsifying (agent) such as lecithin Because of their amphipathic nature.



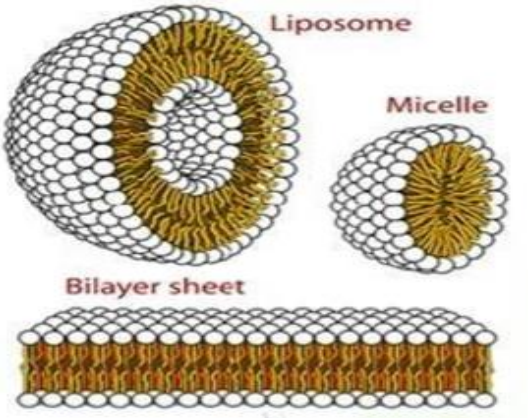

***Emulsifying agent:*** A substance that can surround nonpolar molecules (fat) and keep them in suspension in water.Therefore fat and water molecules can mix together more easily.

* So, what really happens is that when fat is mixed with water, as mentioned earlier, it’s broken up into smaller droplets and then fat becomes surrounded by hydrophobic fatty

acid chains of lecithin, with its phosphate hydrophilic heads exposed to the watery or aqueous environment.

* The same thing happens in our bodies but it's the BILE acid which emulsifies the fat we consume instead of lecithin. So basically, Bile is the emulsifying agent in our body.

- Finally, the **<u>different structures of phospholipids</u>**.




The difference between a liposome and a micelle is the interior, the liposome has a hydrophilic interior, while the micelle has a hydrophobic one.

## Phospholipids role in therapeutics

sometimes it could be extremely hard to get a specific drug to enter the cell, or we want to apply gene therapy ( get DNA(which is very hydrophilic and charged) in the cell ) because of the hydrophobic lipid bilayer which makes up most of the plasma membrane, so the molecule that is destined to enter the cell ( which is polar or charged ) will be packed in a **liposome**( lipid balls which you can insert a molecule inside of it), then integration between the liposome and the plasma membrane occurs so the molecule enters the cell (endocytosis).

Best of luck

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