Lecture : 13

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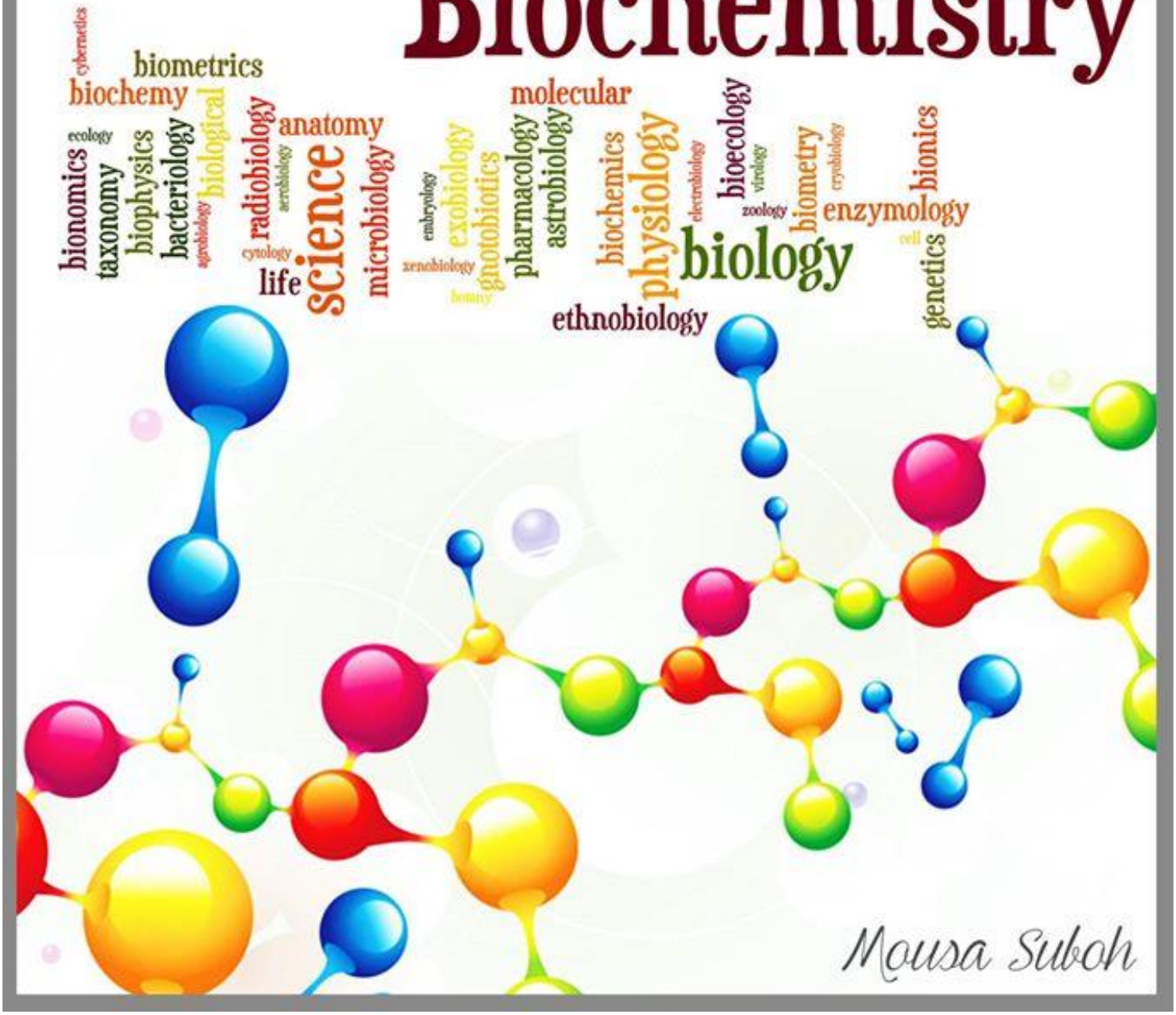
☐ Slide ■ Sheet

Medical Committee
The University of Jordan

Biochemistry



Lipids (2)

- To get the best of this sheet **PLEASE** study it side by side with the doctor's slides.

- In this lecture the doctor continued talking about Eicosanoids.

- Derived Fatty Acids: Eicosanoids

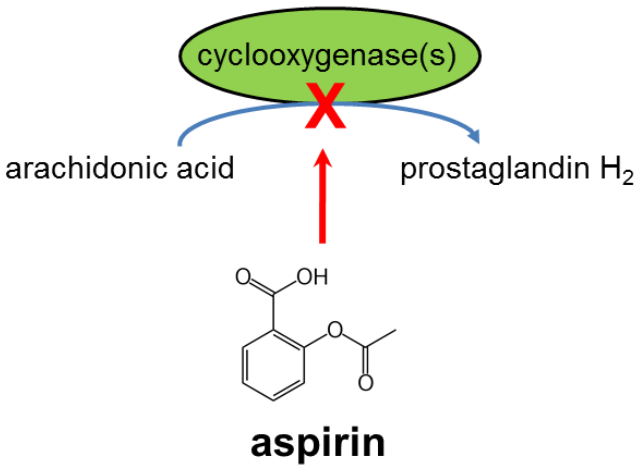
Slide 20

Thromboxane A2 is an eicosanoid that induces the aggregation of platelets; therefore, high levels of thromboxane A2 leads to heart attacks. Old people are advised to take baby aspirin regularly since it blocks the synthesis of thromboxane A2 by inhibiting cyclooxygenase (an enzyme) and causes reduction in the rate of heart attacks.

Slide 21

How does aspirin work?

Aspirin blocks the synthesis of prostaglandins that induce inflammation (pain) and fever therefore taking aspirin will reduce inflammation and fever symptoms relieving pain. It blocks the synthesis of prostaglandins by inhibiting cyclooxygenases which convert arachidonic acid to prostaglandins, and from prostaglandins we get thromboxanes. Aspirin is a salicylic acid and it modifies cyclooxygenase by adding acetyl group to it so it gets inhibited.



Slide 22

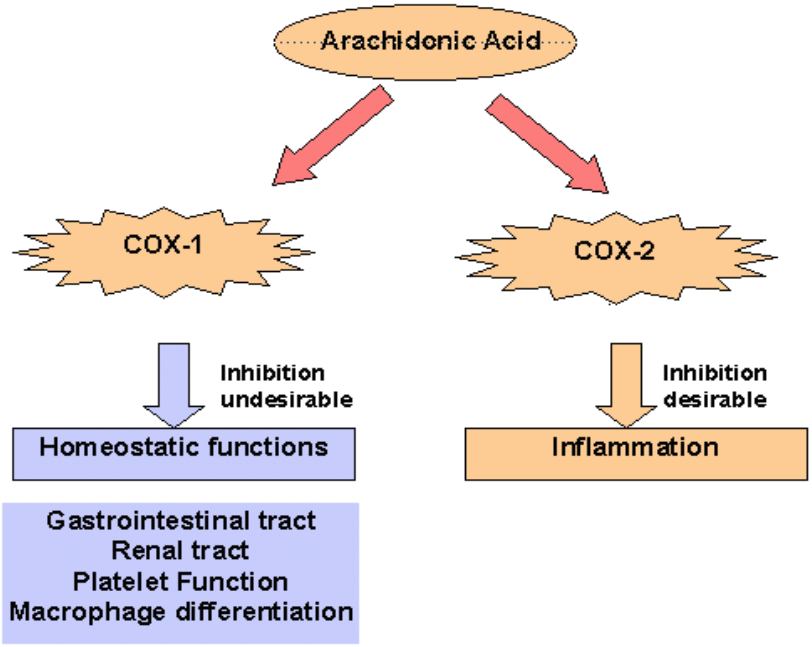
Note that cyclooxygenase has two forms: cyclooxygenase 1 & cyclooxygenase 2 and both of them are inhibited by aspirin. Cyclooxygenase 1 if inhibited causes some side effects such as stomach pain and ulcers, that's why before the prescription of aspirin, the patient is asked about having stomach problems, if he experience stomach problems, he mustn't be given aspirin.

Meanwhile cyclooxygenase 2 is the one responsible of causing inflammation.

Slide 23

Celebrex is a drug that is more specific for cyclooxygenase 2 (doesn't affect cyclooxygenase 1) so it won't affect the stomach but it inhibits cyclooxygenase 2 reducing inflammation and pain. When it was first released it was noticed that it causes higher rates of heart attack, so it was removed from the markets and an agreement was reached to add a label on the drug that says "people with heart problems should not take Celebrex".

Doctor didn't say anything about how does Celebrex affect the heart he just mentioned so.



Slide 24

Omega- 3 fatty acids include: α-linolenic acid, eicosapentaenoic acid EPA, docosahexanoic acid DHA. Those reduce inflammation and they have a positive effect on the body. That's why people are advised to take omega -3 fatty acids; they motivate the brain and the thinking process.

Omega- 9 fatty acids include: oleic acid (olive oil) that reduces cholesterol in the circulation. And that's why people in the Mediterranean region (Spain ,Italy ,north Africa ...) all have lower rates of heart attacks because their food is largely dependent on olive oil .

Omega-6 fatty acids are precursors of arachidonic acid that stimulates platelet and leukocyte activation, signals pain, regulates gastric secretion and induces bronchoconstriction.

Complex Lipids:

Slide 26

Complex lipids are larger structures contain fatty acids.

They all have fatty acids but they differ between each other by either the backbone or in the R groups/molecules that replace one of the fatty acids (at least one fatty acid must be there).

So there are

1. Triglycerides also known as triacylglycerols. (3 fatty acids and a backbone of glycerol)(Storage lipids , neutral).

2. Phospholipids (contains phosphate) subtypes are: (They differ in the backbone)

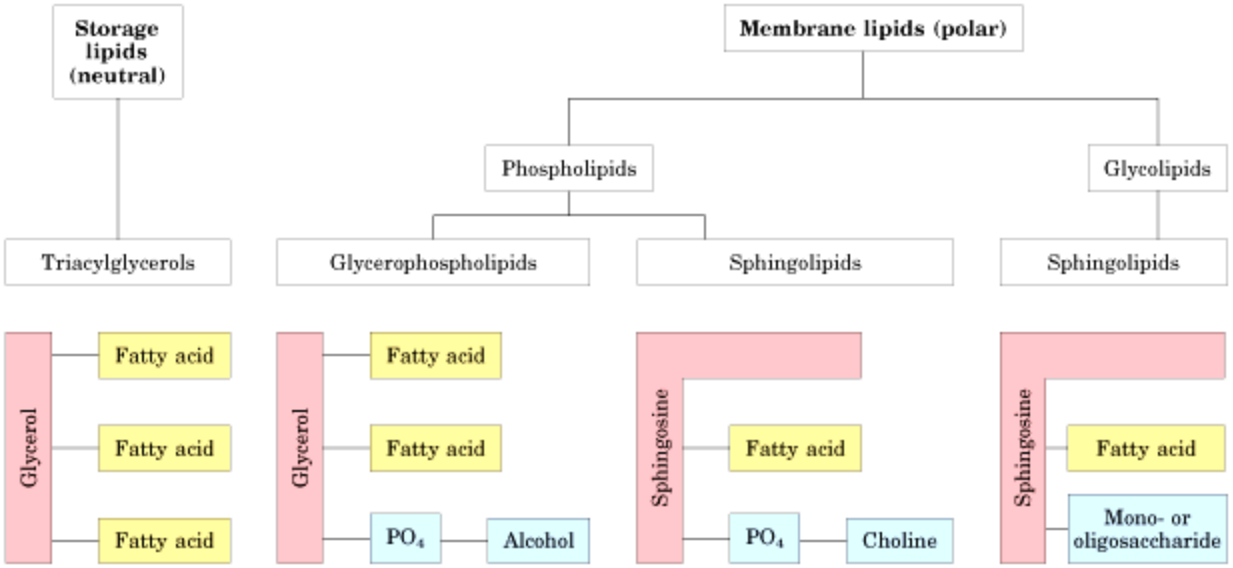
   A. Glycerophospholipids.

   B. Sphingolipids.

3. Glyclolipds which are another type of sphingolipids but instead of phosphate they have mono or oligosaccharide.

- Number 2 & 3 are membrane lipids.

- Note that sphingolipids are found in phospholipids and glycolipids.



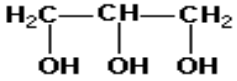
Slide 27

Triglycerides are the main storage material of lipids in our body, excess fat/fatty acids/lipids are stored as triglycerides in adipose tissues .The components of triglycerides are

1. Glycerol (alcohol molecule also called fatty alcohol).

2 .Fatty acids

Glycerol



You can have monoglyceride with only one fatty acid attached to the hydroxyl group, or diglyceride with two fatty acids , or triglycerides with 3 fatty acids attached to three hydroxyl groups.

The linkage of fatty acid to the alcohol group results in the formation of an ester bond (ester linkage).

Carboxyl group + hydroxyl group -→ ester molecule

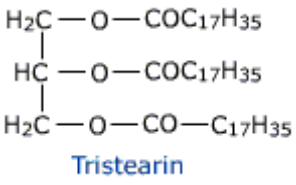
Slide 28

We can have simple triglycerides where the same fatty acid molecule is repeated, or a mixed triglyceride where we have 3 different fatty acids of different length and degree of unsaturation.

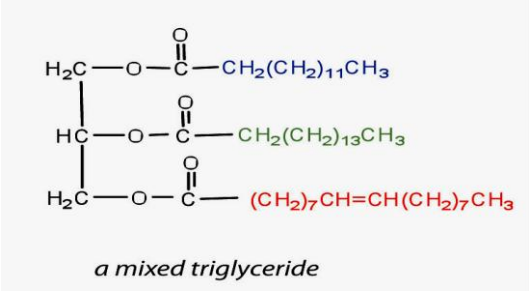
The types of fatty acids will affect the solubility and the physical properties of the triglycyrides.

So when we have unsaturated fatty acid (at least one) it will make the triglyceride liquid in nature.

If we have three saturated fatty acids, this will make the triglyceride solid in nature (room temperature).



simple triglyceride



Slide 29

What make unsaturated triglyceride liquid in nature and saturated triglyceride solid in nature?

Because saturated fatty acids are long straight chains and can be packed to each other when you have three of them (high van der Waals and hydrophobic interactions) while unsaturated fatty acids have kinks because of the Cis double bond therefore the three chains will be separated from each other so its hydrophobicity will be less than that's of saturated fatty acids (low van der Waals interactions).

Triglycerides that are saturated are mainly present in animal cells whereas those that are unsaturated are mainly found in plants. (سمنة و زيت)

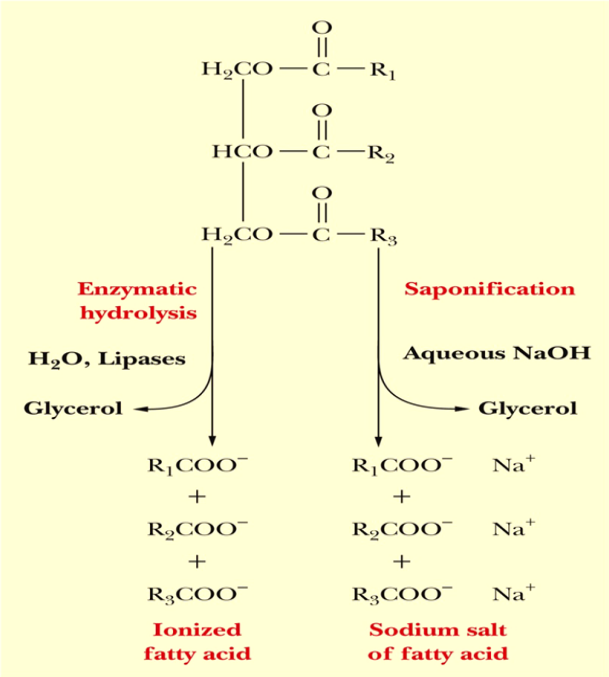
Slide 30

You can separate the fatty acids in a triglyceride by different manners one of them is enzymatic, by the use of the enzyme lipase which degrades lipids , so we will get a glycerol molecule with three separated fatty acid chains.

-Whenever you have an enzyme for example, Lipase: breaks lipids, Esterase: breaks ester bond, Peptidase or protinase: breaks proteins, Saccharidase: breaks saccharides and so on.

Another method of separating fatty acid chains from glycerol is called saponification (the production of soap). So adding an alkaline(NaOH) to a triglyceride molecule will result in

separating the fatty acids from the glycerol , fatty acids in this case will be obtained as salts (sodium salts of these fatty acids). This is the basis of soaps.



Slide 31

How soap works?

Soap is amphipathic ; contains hydrophobic(uncharged) and hydrophilic(charged carbonate groups) regions. Grease is mainly hydrophobic, so when you wash your hands with soap and water, you will have a mixing of the fatty acid salts with the grease and these fatty acids will form a spherical structure called micelle that has a charged head outside and uncharged tail inside and this will lead to a charged dipole interaction with water molecules. The micelle is hydrophobic from the inside so that grease (dirt) can be dissolved in due to hydrophobic interactions, and since the micelle structure is already dissolved in water it is then can be washed away leaving your hands clean :D. -By the way if grease were hydrophilic then it doesn't need soap to be dissolved in, it already can be dissolved in water😂☺.

*Remember that soap which is a salt dissolves in water and the Na+ doesn't remain connected to the carbonate group that's why it leaves the fatty acid charged.

Slide 32

Hydrogenation:

A reaction that happens to unsaturated fatty acids, saturated fatty acids can't undergo hydrogenation. It causes the removal of double bonds and creates single bonds instead by adding 2 hydrogen atoms per each double bond, in other meaning it converts unsaturated fatty acid into saturated fatty acid .

This hydrogenation process is used in the food industry, to turn plants oil (unsaturated) to the saturated form. The doctor states that the reason for the hydrogenation of oil plant is that because animal fat (saturated) tastes better, last longer and they have better cooking properties compared to oils!! However, the hydrogenation that occurs is incomplete meaning that you will still have unsaturated fatty acid but instead of having many unsaturated bonds u will have a fewer number, which makes it more solid.

Slide 34

An example of hydrogenation product is Margarine which is used instead of butter .It is softer than butter because it was converted from liquid form to the solid form by incomplete hydrogenation. Therefore, it is easier to spread over a slice of bread and it tastes better .

Slide 33

A problem concerning the hydrogenation process is that the incomplete hydrogenation which is used in industry results in the removal of some double bonds and causing other double bond to change their cis configuration to the Trans configuration so whenever you have incomplete hydrogenation you have conversion of cis to Trans and this is known as Trans fats. And the fatty acids that have trans double bonds look exactly the same as the fully saturated fatty acids

Slide 34again: P

Products containing trans-fat have the amount of trans-fat submitted on the product , because trans-fat is associated with coronary heart disease ,heart attacks , deposition of cholesterol in arteries and several health risks.

Trans-fat can also occur in oil that is boiled over and over again in restaurants converting unsaturated fat to trans-fat that's why it is unhealthy eating fast food because restaurants might use the same oil over a long period, so be careful when choosing the place you buy falafel from: D.

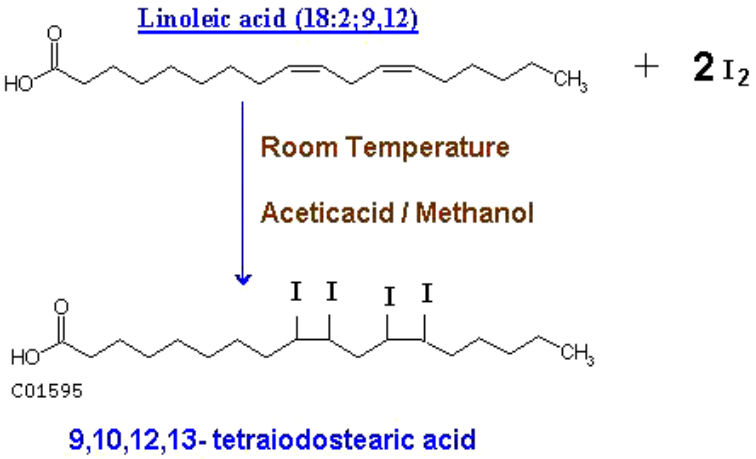
What is the problem with trans-fat?

The problem is that trans-fat can't be digested so it stays in our system and gets deposited in the arteries, because the body can't remove it. .

Slide 35

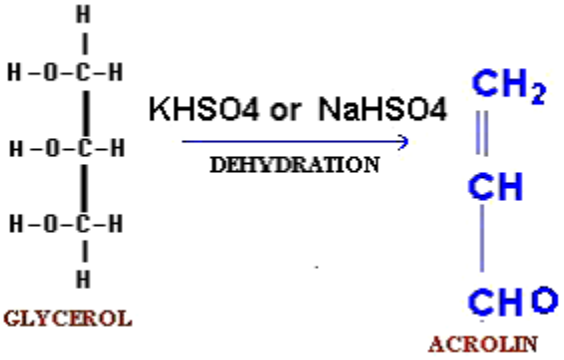
Other reactions of fatty acids are halogenation (adding a halogen atom F, Cl, Br,I).

For an example we can add iodine (the addition of it by a halogenation reaction), this is used to measure the number of double bonds (degree of unsaturation) by measuring the amount of iodine that has reacted.



Slide 36

Acrolin test is a test where fats are heated in the presence of dehydrating agents, resulting in a product known as acrolin and this acrolin can be detected using different methodologies and can be used to tell us if a sample has a triacylglycerols or not(just a detection method).



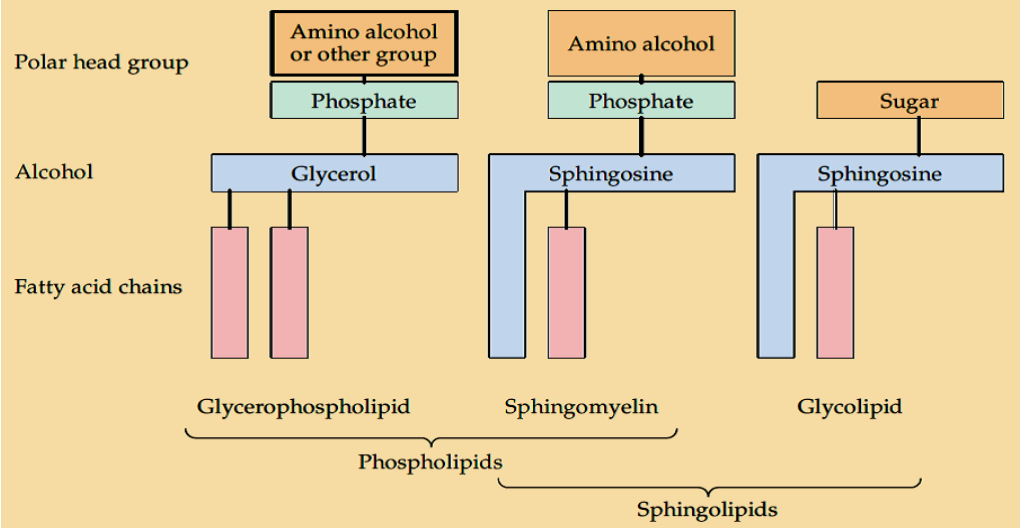
Slide 37

Another type of complex lipids is waxes. Waxes are highly hydrophobic products composed of a reaction between fatty acid and a long chain of alcohol (alcohol and acid forms an ester group).Overall, the whole molecule is highly hydrophobic and they are insoluble in water. Also they are negative to acrolin test , not easy hydrolysed, indigestible by lipase (no nutritional value), have resistant to rancidity. They include beeswax ,that we see in bees' products, candles and hair wax.

Slide 38

Membrane lipids: they are complex lipids used as structural molecules in the cell membrane and they include glycerophospholipids, sphingomyelin, and glycolipid. The most prevalent class is glycerophospholipids.

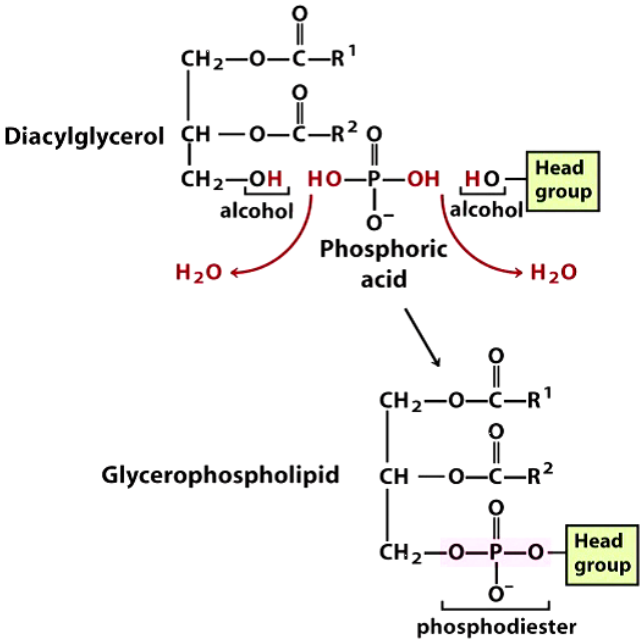
Note that sphingomyelin and glycerophospholipids both contains a phosphate group that why the are categorized as phospholipids, sphingomyelin and glycolipid both contain a Sphingosine back bone that why are categorized as Sphingolipids.



Slide 39

Glycerophospholipids (phosphoacylglycerols) are part of the phospholipids group. They contain a glycerol backbone, attached to it 2 fatty acids on carbon number 1, 2 ,and carbon number 3 is attached to a phosphate group. Such molecule that contains glycerol , 2 fatty acids , and a phosphate group is called phosphatidic acid.From this phosphatidic acid you can generate different type of phospholipids.

There are also different type of phospholipids that contains Sphingosine backbone, called sphingolipids that can also have a phosphate group attached to it.



Slide 40

There are different types of glycerophospholipids depending on the group attached to the phosphate:

1. Phosphatidic acids that contains a phosphate group connected to a hydrogen that is ionized at physiological pH.

2.Phosphatidylcholine also called (lecithins), these are the most abundant membrane lipids, found in the ingredients of ice cream. Lecithins are used in these products as an emulsification agents which are amphipathic that dissolve fat in them. They can also dissiolve in water keeping fat away from water - just like the idea of micelles. So whenever you mix lecithins or phospholipids in fat droplets they will surround the fat droplets by hydrophobic interactions between fat and the fatty acid chains of phospholipids, and the phospholipids heads will be exposed to water and that's why fatty molecules can dissolve in water. That's why lecithins are used in the ice-cream so the fat molecules can be dissolved in water. Leicithins are also used in mayonnaise. (slide 42) .

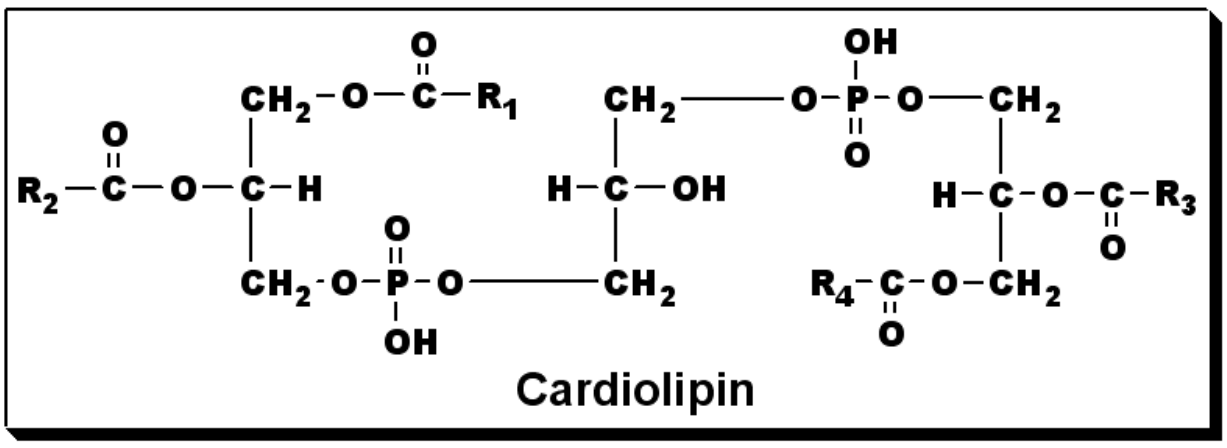
Phosphatidylcholine **Choline** $-CH_2-CH_2-\overset{+}{N}(CH_3)_3$

Snake venom contains an enzyme called lacithinase that degrades phosphatidylcholine in the plasma membrane of red blood cells and whenever you have the degradation of phospholipids in cells you will have hemolysis which will eventually cause death. Slide 41

3. Phosphatidyl inositol: is a small molecule present in the intracellular surface of cells and it is one of those molecules that send messages from outside the cell to the inside (remember the silly example about the door bell , the child and his mother :P)

4. Cephalins includes phosphotidylethanolamine and phosphotidleserine , phosphotidylethanolamine is present on the outside surface of the cell membrane , in phosphatidylserine you have the conjugation of serine amino acid to the phosphate group.

5. Cardiolipin is a diphosphatidylglycerol glycerol they are composed of three glycerol molecules that are connected to each other mainly found in the heart muscle and it makes up the membrane of the mitochondria . Slide 44



6. Plasmalogens, they are different from glycerophospholipids because plasmalogins are derivatives of another sugar molecule which is dihydroxy acetone whereas the other glycerophospholipids are derivatives of glyceraldehyde.

Plasmalogens are mainly found in cell membrane of different tissue such as brain, muscles,liver and semen.

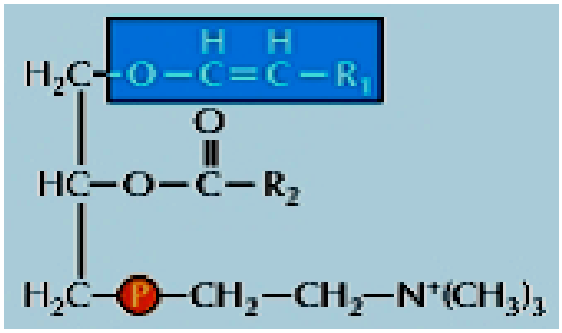
They have a protective role against reactive oxygen species.

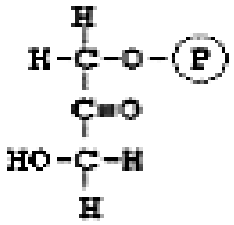
Notice the structure difference between plasmalogens and the other types of glycerophospholipds:

1. The precursor is different.

2. Unsaturated fatty alcohol at C-1 connected by ether bond rather than ester bond also this fatty is alkene (unsaturated) and not alkane.

3. In mammal s the phosphate group at C-3 is connected to ethanolamine or choline. **Slide 44**





Dihydroxyacetone phosphate

Major classes of plasmalogens include:

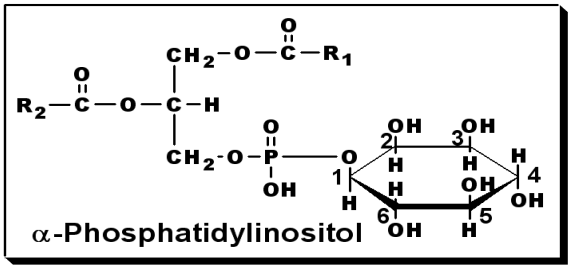
1.Ethanolamine: plasmalogen which is mainly present in nervous tissue.

2.Cholin: plasmalogen mainly found in cardiac tissues.

3. Serine plasmalogens. **Slide 45**

slide 46

Inositides contain phosphatidyl inositol with a sugar molecule which is attached to the phosphate.It is mainly present in the brain tissue, and they are a major component of cell membrane and they are signalling molecules .The way they send a signal is that by degrading them we can have 2 molecules which are diacyl-glycerol (DAG) and inositoltriphosphate (IP3) both of which can liberate calcium ions.



α-Phosphatidylinositol

Slide 47

There are different types of lipids structures. We already talked about one of them the micelles.

There are 2 other types the liposome and the bilayer sheet.

The bilayer sheet is the basis of the plasma membrane .

The liposomes are spherical structures just like micelle the difference is that the inside and the outside of it are hydrophilic so that it can be used for delivery purposes.

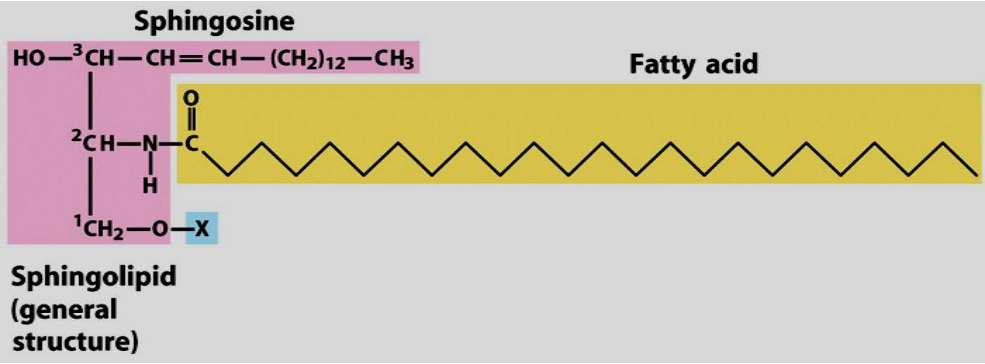
Liposomes can be used for drug delivery. If you have a drug with unwanted side effects on the body and you only want to deliver it to a specific tissue to avoid those side effects, packaging the drug in liposome will solve this issue by integrating with specific cells' plasma membrane and fusing with the it releasing the drug inside the cell.

Slide 48

Another type of membrane phospholipids is sphingolipids which differ from glycerophospholipids in having a sphingosine backbone rather than a glycerol backbone .sphingosine has an alkene linked to it

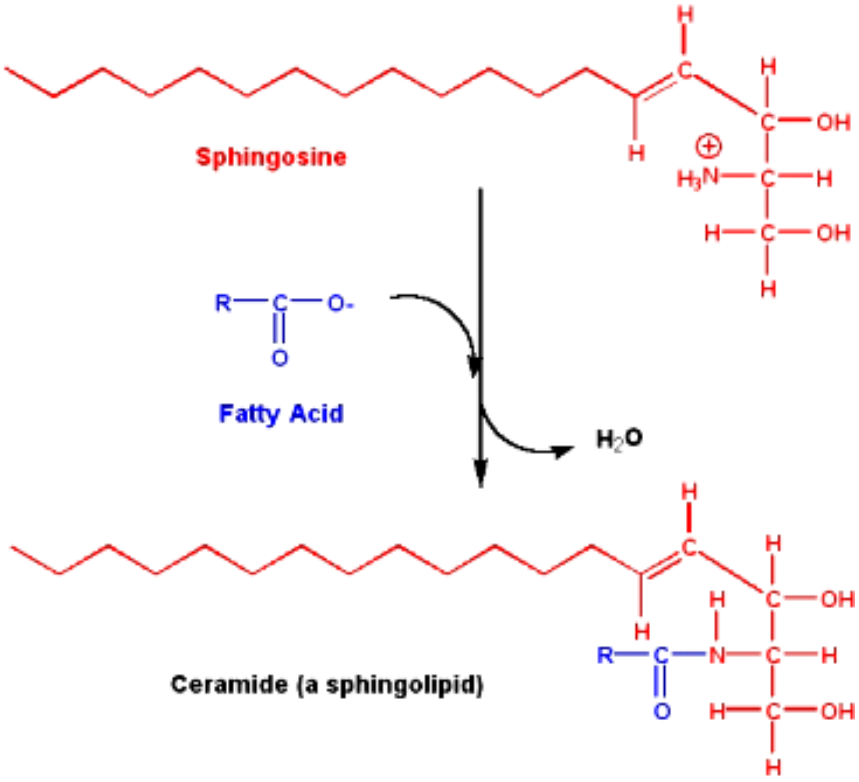
Notice the different between the structure of sphingosine and plasmalogins , plasmalogins have an ether group connected to the first carbon then you have an alkene chain , but here you only have an alkene group as a part of the large sphingosine backbone.

In carbon number 2 you have a fatty acid usually palmatic acid, and to carbon number 1 you can have an R or X group and it is different from one sphingolipids to another.



Slide 49

The basic form of sphingolipids is ceramide which has the R group is hydrogen, and from ceramide you can have the different type of sphingolipids .


Sphingosine
Fatty Acid
H_2O
Ceramide (a sphingolipid)