University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Introduction to

BIOCHEMISTRY

Lecture #: (.....7.....)

■ Sheet ☐ Slides ☐ Other

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Lipids

The last lecture about lipids

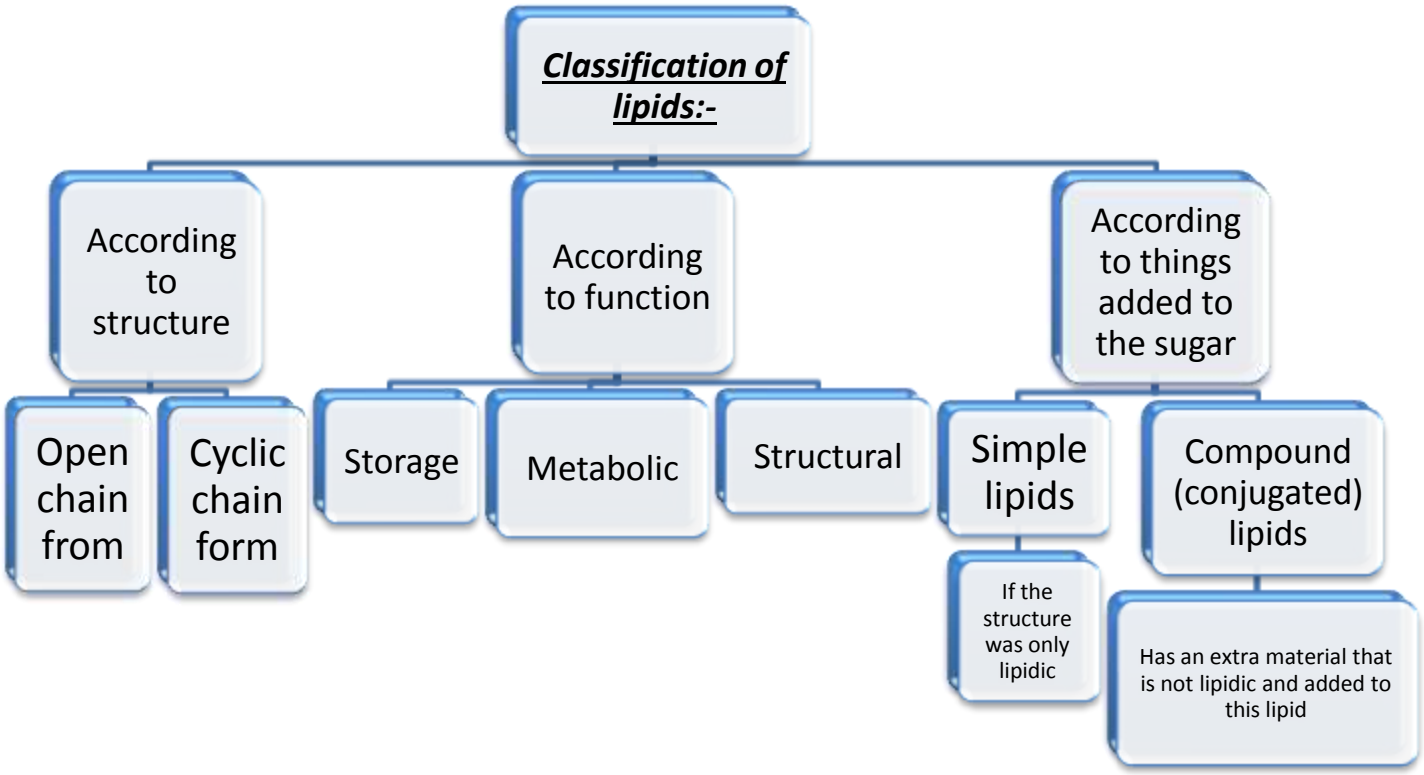
Just to refresh your memory:-

What are lipids?

Alcohol+fatty acid, estrefication between them gives me lipids.

What are alcohols?

Hydrocarbon compounds containing one or more hydroxyl group (which is the functional group).



- Fatty alcohols that make lipids are either glycerol

What is glycerol?

3 carbon unit molecule alcoholic at each one - it has 3 hydroxyl groups.
Second fatty alcohol= sphingosine (palmatic acid) connected to serine which is an amino acid that contains nitrogen (amine group), carboxylic group, alpha carbon, hydrogen and R group.

- Acrolein test you should be familiar with it, which is the dehydration of

glycerol in the presence of heat and sulfuric acid or KHSO4

Glycerol or any material that contains glycerol

↓ dehydration

Acrolein

• So acrolein test is used to detect the presence of glycerol or glycerol derivatives in a sample.

<u>What are fatty acids?</u>

Carboxylic acid molecules that contain a hydrocarbon tail which varies in its length (short-medium-long) and (saturated or unsaturated).

• Physical properties of fatty acids especially with respect to solubility and melting points.

• Solubility increases with increase in degree of saturation and vise versa.

(high saturation,,,,,,,,,,high solubility)

• Saturated fatty acids can be (short-medium-long)

-Short chain saturated fatty acid: Acetic F.A. (2C)
-Long chain :

Palmitic acid (16C) /saturated.

Stearic acid (18 C) /saturated.

You have to memorize the molecular formula of the Palmitic F.A. and Stearic F.A.

Check the slides ☺

• Unsaturated fatty acids may contain:-

One double bond (monounsaturated) or more than on double bond (poly unsaturated).

-monounsaturated fatty acids:- Oleic acid (18C) 1 double bond on carbon no. 9

- Polyunsaturated fatty acids are essential fatty acids.(2 pure essential and 1 conditionally essential)

Pure essential (linoleic, linolenic) …… each one contains 18C

↓ 2 double bonds ↓ 3 double bonds

Conditionally essential (arachidonic) …… 20C, 4 double bonds and you can make it in the body from linoleic acid.

Tip:- always the intervals of double bonds is by 3 meaning if the first double bond is on carbon 9 then the second one is on carbon 12 and the third is on carbon 15 and so on……. Just +3.

Simple lipids:-

• Structures made of lipids only (a fatty acid with glycerol only)

A. **Triacylglycerol** = glycerol + 3 fatty acids.
   » If the 3 fatty acids are of the same type we call it **triacylglycerol simple.**

   » If the 3 fatty acids are of the same type we call it **triacylglycerol mixed.**

- ***Chemical reactions that triacylglycerol can undergo?***

1- Hydrolysis (acidic or enzyme)
Gives me glycerol+ 3 fatty acids (ionizable)

2- Saponification: alkaline hydrolysis in an alkaline medium
This is a special type of hydrolysis, it gives me the salt.

3- Halogination
This reaction is used to detect if you have any unsaturated fatty acids in the solution and if you have it how much is the degree of unsaturation.

4- Hydrogenation
It's bad it gives you more pleasant taste though it's bad for health for different reasons we talked about before.

5- Oxidation (Rancidty)
When we say (السمنة أو الزبدة بتهوي)it means it can be oxidized with atmospheric oxygen. Oxidation of triacylglycerols is BAD!!!

B. **Waxes**

• Solid simple lipids containing a monohydric alcohol.
• In waxes fatty acids alcohol bond not to glycerol but instead to a long chain alcohol + long chain fatty acid.
• They are not very useful-it doesn't breakdown nor can be digested.

Differences between neutral lipids (triacylglycerols) and waxes

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Compound lipids:-

• Something else other than a lipid added to the lipidic structure so as it will be functioning.

• Classification according to the type of residue attached to the lipid:-

1. Phospholipids (phosphate, phosphoric acid, phosphorus group)
2. Glycolipids (carbohydrates)
3. Lipoproteins (protein)
4. Sulfolipids & amino lipids (sulfite or amino group)

1- Phospholipids

Compound phospholipids can be classified according to the alcohol molity inside them to:-

• Sphingophospholipids:
sphingosine as an alcohol

• Glycerophospholipids

Can be sub-classified also to different molecules according to the presence of a nitrogenous base attached to the structure or not and if there is…. What type is it?

- **Phosphatidic acids** (No nitrogenous base)
- **Lecithins** (Contain choline attached to phosphate)
- **Cephalins** (choline is replaced by ethanolamine, serine or threonine amino acids)
- **Plasmalogens** (different that of carbon no. 1 the fatty acid is unsaturated alcohol and the present bond is ether not ester)
- **Inositides** (second messengers, when its broken down it gives me two 2nd messengers which are inisitoltriphosphate IP3 and diacylglycerol DAG)
- **Cardiolipin** (3 glycerol units connected to each other by 2 phosphoric acids, connecting the middle glycerol with carbon no. 1 and carbon no. 3 with the peripheral ones)

So cardiolipins = 3 glycerol molecules + 2 phosphoric acids + 4 fatty acids

Sphingophospholipids:-

• Sphingosine is the alcohol not glycerol.

Sphingosine = palmetic acid connected with serine.

Serine has a nitrogen molecules.
-If the nitrogen is attached to the fatty acid and there is no more any other modification we call it (Ceramides)
-If the nitrogen is attached to the fatty acid and there is modification on the carbon of the serein with phosphoric acid we call it (Sphingomyelins)

• Sphingomyelins is found in myelin sheeth and nervous system.

2- Glycolipids

• Sphingosine attached to a fatty acid
• Sphingosine on tyrosine residues on the serine residue at the side chain where a monosaccharide or a carbohydrate is attached.
If this carbohydrate was a glucose or a galactose we call it (Cerebrosides)

Cerebrosides = sphingosine attached to a fatty acid and modified by a glucose or galactose residue. If a sulfate group was found attached to them we call them (Sulfatides)

• If more than one monosaccharide, oligosaccharide for example we call it (Gangliosides) found in Brain, ganglion cells, & RBCs.

Gngliosides = usually distinguished by having sialic acid (n-acetyluramicacid) as a modification on that oligosaccharide.

3- Lipoproteins

• A structure of lipids and proteins (Lipids attached to proteins)
• The proteins are called apolipoproteins, they are of different types.
• The lipid part is composed of either phospholipids or triacylglycerol or cholesterol.
• We can classify lipoproteins according to their function into:-
1- Structural
Found in membrane, surfactant in lung and in eye in the visual site promoted to the rhodopsin protein.
2- Transport
Found in blood plasma

We all know the LDL and HDL…….

So what is the difference between them?

Simply, they differ in their densities.

How to compare their densities?

• The density is increasing with the protein content and decreasing with the lipid content.

So HDL »» lipoproteins with high percentage of proteins

LDL »» low percentage of proteins

Types of lipoproteins according to their density:-

1- **Chylomicrons:**
Has the lowest density, contains the lowest percentage of proteins andthe highest percentage of lipids.
Lipids…….elongated proteins…….globular
Meaning as long as the lipidic structure is increasing the diameter is increasing and the density is decreasing and vise versa.
So chylomicrons have the largest diameter and the lowest density and the main lipid part is triacylglycerol.

2- **Very low-density lipoproteins (VLDL):**
The main lipidic structure is triacylglycerol. The diameter is smaller because the lipidic part is smaller; the protein content reaches 10%.

3- **Low-density lipoproteins (LDL):**
The protein content reaches 20%, the lipidic structure is formed of 60% cholesterol and 40% phospholipids, this indicates very high amount of cholesterol and that's why LDLs are bad for your health, and it can get oxidized.

4- High-density lipoproteins (HDL) or alpha-Lipoproteins:

High percentage of proteins 50%, the lipidic structure is formed of 40% cholesterol and 60% fatty acids, this indicates low amount of cholesterol and that's why HDLs are good for your health. Act as cholesterol scavengers (why?) because it contains less amount of cholesterol so it can catch/attract more cholesterol from the blood and by that it lowers cholesterol percentage in blood.

- Increase in HDLs -> decrease in liability of atherosclerosis disease
- Increase in LDLs -> increase in liability of atherosclerosis disease

- High amount of LDL -> problems in blood circulation-> problems in heart.
- High amount of HDL -> less problems in blood circulation ->less problems in heart.
    - HDL is higher in females than males.

<u>Steroids: Cholesterol, Bile Salts, and Steroid Hormones</u>

- Steroids are structures of 4 rings, 3 of them are hexagonal and 1 is pentagonal.
- 4 ringed structure derived from essential fatty acids usually arachidonic acid (20C, 4 double bonds, conditionally essential)
- Usually steroids are found with association with fats (triacyglycerols)
- By hydrolysis steroids are separated from fats.
- They are derivatives of cholesterol.
- Cholesterol is one of the steroids, composed of 4 rings, 3 of them are hexagonal and 1 is pentagonal.
- Types of steroids:-

1. Sterols

2. Adrenal cortical hormones

3. Male and female sex hormones (testosterone- estradiol- progesterone) they are derivatives of arachidonic acid.

4. Vitamin D group

5. Bile acids

- Cholesterol is the most important steroid in the animal tissue, contains a free hydroxyl group or esterified to a fatty acid (ester linkage to a fatty acid linoleic, oleic, palmitic acids or other F.A)
- Cholesterol is found in most tissues and most cells but its percentage differs from one tissue to another.

Adrenal cortex….10% brain…..2%

- Cholesterol in membrane …… maintains fluidity of membrane (how?)

Cholesterol is formed of rings of hydrocarbon constitution,all hydrophobic, no hydrophilic structures plus the ring structure which doesn't have the ability to move

freely less than the aliphatic ones, phospholipids have fatty acids that move in a way or another in the membrane giving it fluidity, once you put cholesterol in between the phospholipids it makes hydrophobic interaction with the fatty acids found in phospholipids so the number of bonds between them increases making this fatty acid elongated, preventing its movement keeping it in its pale due to the bonds that are initiated with the cholesterol so it induces more rigidity to this membrane.

Where do we get the cholesterol from?

We synthesis it inside the body from acetylcholine, it doesn't exist it plants so we can't get it from plants, however we can get it from animal sources (butter, milk, etc)

Chemical properties of cholesterol:-

It is very important to know that cholesterol can me oxidized into 7-Dehydrocholesterol, which in turn can be oxidized by ultra violet sun light
Into vitamin 3 derivative, which goes to the kidney and gets mature to a full form vitamin D3 which is used by dihydrocholesterol.

Bile acids

• Cholesterol related, having the same structure 4 rings, 3 of them are hexagonal and 1 is pentagonal.
• There are 2 types of them:-

1- Cholic acid 2- Chenodeoxycholic acid/deoxycholic acid
Whats the difference between them? One of them is oxy and the other Is deoxy.

Cholic acid:-

3 hydroxyl groups in the structure of the ring.

Deoxycholic acid:-

Misses one oxygen [so -> di-oxy]

• Both cholic acid and deoxycholic acid can be modified by attachment of glycine residue.
Glycine (the smallest amino acid containing an amine group, carboxylic group, carbon connected to 2 hydrogens)
Cholic acid + glycine = glycocholic acid
Deoxycholic acid + glycine = glycodeoxycholic acid
• They can react with Na or K or any positively charged ion to give bile salts.
• Bile acids are found in gall bladder in the form of salts.

What are bile salts?

Cholesterol related material, secreted by liver then migrate and kept within the gall bladder and then they are secreted upon eating.

- **The function of bile acids is that:-**
  1- They make Emulsification of lipids during digestion.
  2- Activation of pancreatic lipase to be able to hidrolyse triacylglycerol.
  3- Help digestion & absorption of fat-soluble vitamins to get use of them.
  4- Solubilization of cholesterol in bile & prevent gallstone formation.
  5- Choleretic action (stimulate their own secretion)

Eicosanoids

• Signaling molecules brought from oxidation of essential fatty acids mainly arachidonic acids.
• Important as signaling molecules in body and have wide range of function.
Arachidonic acid = omega 6 fatty acid
Omega 3 fatty acids are also essential and can give arise to eicosanoids. however the most common fatty acid that gives eicosanoids is the arachidonic acid.

• The half life time for these eicosanoids is too short (differs from one to another but varies between 10sen-5min) **what does that mean?**

When a material has a short half- life time it doesn't affect the strength of its effect but it affects the place of effect, having a short half-life t means that the cell that produces it affects only its self and the cell neighboring (small place affected) then it will undergo degradation.

• So eicosanoids have a Paracrine or autocrine function. (Why?)

Paracrine: affects neighbouring area
Autocrine: affects the same area it's secreted from.
Endocrine: affects areas far from the place it was secreted like hormones.

• They are synthesized throughout the body in different parts depending on their type:-
» some of them are very tissue specific secreted in a special place.

However most of the places in the body do produce eicosanoids of different types.

- Mostly their degradation/metabolism occurs in lungs.
- **Families of eicosanoids:**
  - ✓ Prostaglandins
  - ✓ Prostacyclins
  - ✓ Thromboxanes
  - ✓ Lipoxins
  - ✓ Leukotrienes

- ***Eicosanoids functions:-***

*Induction of inflammation (bronchoconstriction & dilation)
Because they have different types, their reactions might be opposite from each other.
Example:-

- Prostaglandin….. Some of it dilates alveoli in lungs and some constrict alveoli in lungs.
- They induce bleeding and at the same time clotting. (but it is not the same molecule that causes bleeding causes clotting, they have huge number of subtypes)
- Prostaglandins I, G, E, F each one having different function.

*** Mediation of pain signals**
Makes you feel the pain, so when we take medicines , like: Aspirin, brufin, vulturine , which stops the formation of eicosanoids it stops pain.
*** Induction of fever**
*** Smooth muscle contraction**
(Including uterus contraction, induces labor, giving birth)
*** Smooth muscle relaxation (muscles of lungs)**
*** Protection of stomach lining (protect cells from enzymes like pepsine)**
Some pain killers that we take like aspirin may affect the stomach because it blocks the function of eicosanoinds there.
*** Stimulation of platelet aggregation**
*** Inhibition of platelet aggregation**
*** Sodium and water retention from the kidneys**

How metabolism of eicosanoids occurs?

Membrane lipids containing polyunsaturated fatty acids, part of them is arachidonic acid, steroids in general cortisol, cortisone.

• Cortisol: is the magic medicine it works as anti inflammatory drug stopping all inflammatory responses in the body so the body relaxes (why?)
Because steroids contradict (stops) the action of phospholipase 2 which stops membrane lipids from transforming into arachidonic acid.

What does arachidonic acid have to do with inflammation?

By two pathways it gives inflammatory molecules that cause inflammatory processes (prostaglandins, troposins, leukotriens and different eicosanoids subclasses)

Who is responsible of the inflammation process (pain, fever)?

Eicosanoids, so if we stop their formation through steroids the inflammatory process will end.

What are these pathways?

1- Lypoxygenase
2- Cyclo- oxygenase

Non steroidal anti inflammatory drugs (brufen, aspirin) they stop the function of cyclo-oxygenase -> the arachidonic acid won't change into Prostaglandins and thromboxanes which cause pain and fever
That's why they are used as anti biotic to decrease the fever and analgesic [painkiller] and they might affect on the stomach.
How Acetylsalicyte (aspirin) work?
Gives the acetyl group to the cyclo-oxygenase, then it will linked to cyclo-oxygenase on a specific serine residue -> it becomes inactive enzyme and do not produce Prostaglandins and thromboxanes.

♦ **Theraputic uses:**

1- Induction of labor at full term. [9 months, 63-64 weeks]
2- Therapeutic abortion الإجهاض
3- Maintenance of ductus arteriosus
   the pulmonary artery goes to the lungs, but In the embryo the lungs are not functioned yet, so the pulmonary artery is connected to the aorta through ductus arteriosus , so the blood goes directly to the aorta -> to the whole body of the embryo
   -At normal conditions the ductus arterious closes after labor but sometimes congenitally it doesn't close (this will affect the oxygenation process in the blood). So before the surgery for closing this ductus arteriosus we give eicosanoids as they inhibit the platelet aggregation (as platelets are small in size so they may clot) so these eicosanoids will induce bleeding (no aggregation) then you can start the surgery .
4- Treatment of peptic ulcer because the protect the lining of the stomach
5- Erectile dysfunction