Lecture : 12 1 , 2 , 3

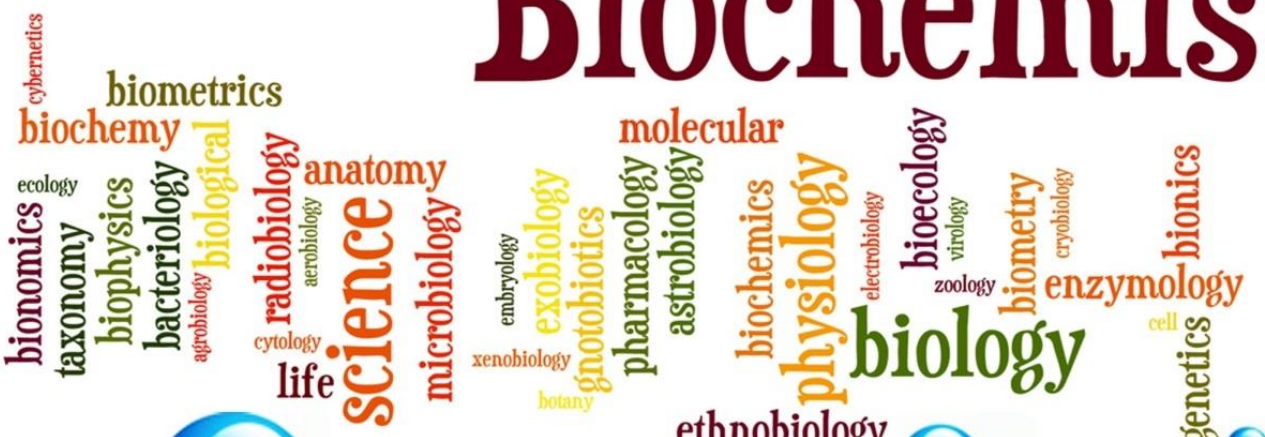
Dr. Name : Mamoun Ahram

Done By : Nouf Khalifeh

☐ Slide ■ Sheet

Medical Committee
The University of Jordan

Biochemistry



Mousa Suboh

Lipids

Reference: Campbell and Farrell's Biochemistry, Chapter 8

What are lipids?

Lipids are a heterogeneous class of organic compounds.

Lipids are not related to each other so its hard to put them in one class of molecules rather they are classified together because they share very important property that is they are hydrophobic molecules.

Macromolecules are classified into 4 types:

1-carbohydrates

2-proteins

3-lipids

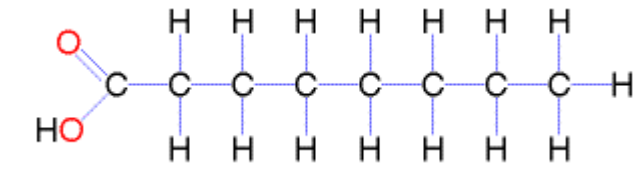
4-nucleic acids

Carbohydrates, proteins, and nucleic acids are polymers (made of repeated monomers).

Lipids are not polymers although they are macromolecules because they don't have the repeated units (monomers).

Lipids features:

1-they are amphipathic, it means when you look at the whole molecule you can divide it into two parts: hydrophobic(non polar part)& hydrophilic(polar part)



Polar part | Non polar part

2-They are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone)

3- they are widely distributed in plants and animals but they are different from each other and they are also found in prokaryotes

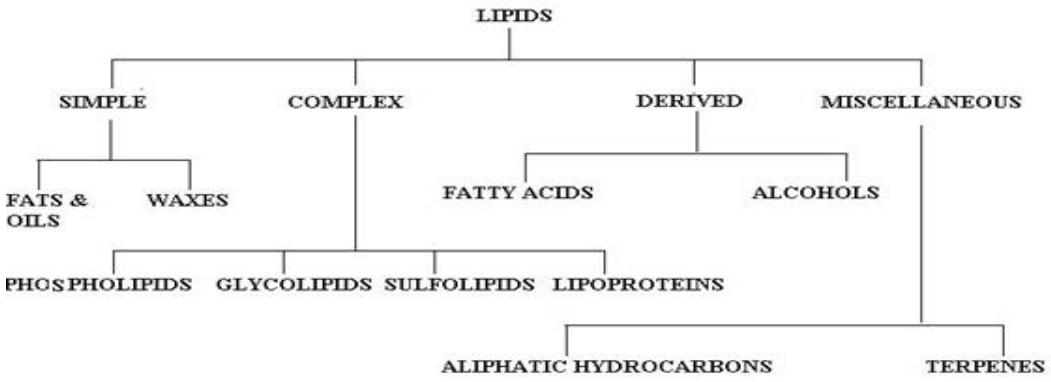
Lipids classes:

1-simple lipids (fats, oils, and waxes).

2-complex lipids when they are conjugated with other parts (glycerides, glycerophospholipids, sphingolipids, glycolipids, lipoproteins).

3-Derived lipids (fatty acids, alcohols, eicosanoids).

4-Cyclic lipids (steroids).



Lipid functions:

storage lipids they are source of energy-1

2-structural lipids they exist in plasma membrane & organelles membranes like the mitochondria ,Golgi apparatus .

3-signaling molecules or cofactors.

Lipids are the main source of energy, they produce energy more than carbohydrate.

1g of fat produces 9kcal while1g of carbohydrate produce 4kcal.

Lipids are stored in unlimited amounts but for example glycogen is stored in liver so the amount of glycogen stored will be limited.

Example: during a fasting day after 6-7 hours all the glycogen in the liver will be gone but the fat does not get completely removed from the body.

4- Precursors of hormone and vitamins.

5- Shock absorbers and thermal insulator.

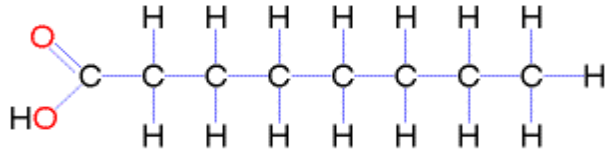
Thermal insulator: simply keeps you warm.

Shock absorber: they create a pad to cushion our internal organs (liver, stomach…etc).

Fatty acids (the basic lipid molecule) :-

They are aliphatic mono-carboxylic acids, (they end with a carboxylic group).

*they are amphipathic molecules, (they contain two parts: polar (small), non-polar (large))



polar	Non-polar

Formula of fatty acids:- R-(CH2)n-COOH

Fatty acids have different lengths:

Physiological: (12-24) carbons fatty acids

Abundant in our body: (16-18) carbons fatty acids

Note: we can have other sizes as well.

They have different degrees of unsaturation, (different number of double bonds) the more double bonds the more unsaturated the molecule is.

Fatty acids functions:

1-Fatty acids are building blocks of other lipids (phospholipids, sphingolipids, triglyceride, cholesterol esters…etc).

2-modification of many proteins (lipoproteins) and sugars (glycolipids).

3-Important fuel molecules as a source of energy

4-we can use them to synthesis important cellular molecules.

Types of fatty acids:

Saturated fatty acids, they have no double bonds.

*short chain has (2-6) carbons.

*medium chain has (7-10) carbons.

*long chain has (more than 10 carbons).

Unsaturated fatty acids

*monounsaturated (one double bond).

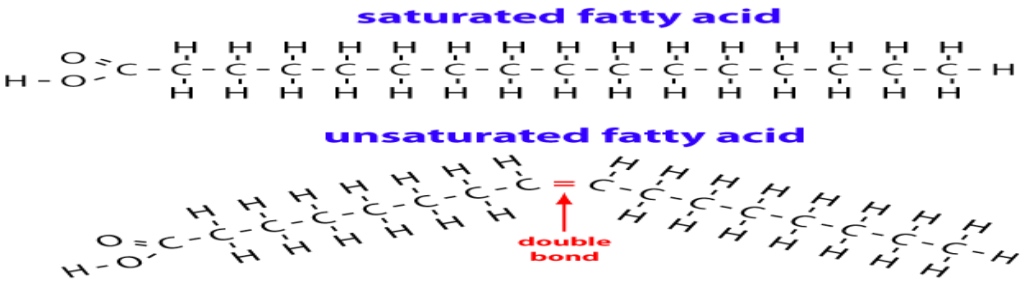
*polyunsaturated (more than one double bond) .

These are some of the most important fatty acids they contain 18 carbons:

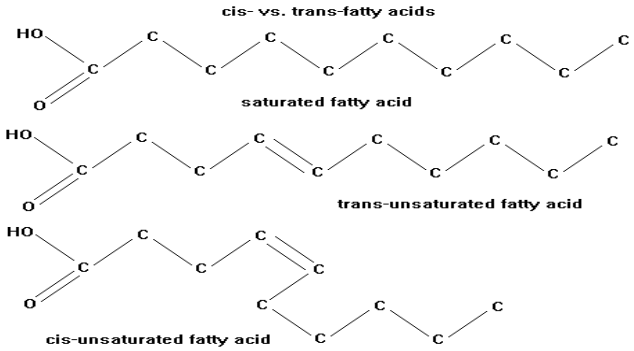
1-steric acid (or sterate at physiological PH) saturated fatty acid.

2-oleic acid (it's the fatty acid that makeup olive oil), monounsaturated fatty acid.

3-linoleic acid (it has two double bonds) polyunsaturated fatty acid.



 # most of these double bonds in the unsaturated fatty acid are in the cis orientation (physiologically cis isomer predominates but trans configuration is rare).



*Notice that the trans configuration doesn't differ from the saturated form.

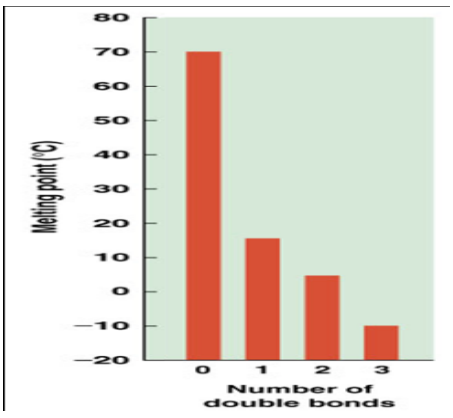
* Notice that the cis configuration makes a kink in the structure of the fatty acid .

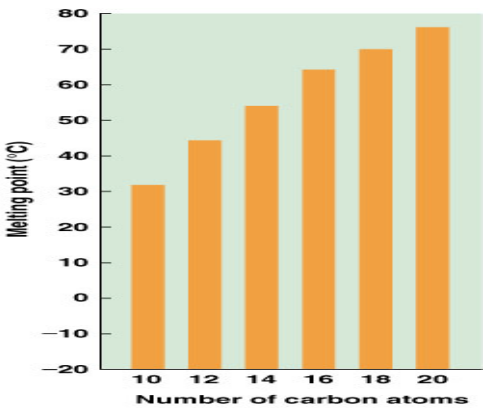
Properties of fatty acids:

The properties of fatty acids (melting point and solubility) are dependent on chain length (carbon atoms number) and degree of saturation.

*the longer the fatty acid is the higher the melting point.
*the more double bonds presented in the fatty acid, the lower the melting point.
Example: oleic fatty acid (olive oil) if you keep it in a temperature around 10-15 degrees it becomes solid because olive oil contains a double bond which decrease the melting point of the fatty acid

Notice in the figure below that the effect of double bond is more than the effect of the number of the carbon atoms on the melting point. (that also make huge difference physiologically).





Comparison between long, medium, and short chain fatty acids:

Long chain F.A	Medium chain F.A	Short chain F.A
Solid at room temperature.	Solid at room temperature.	They are liquid in nature.
Water- insoluble (the longer the chain the more hydrophobic the molecules becomes).	Water-soluble.	Water -soluble because there is an obvious effect of the carboxylic group on solubility.
Non-volatile at room temperature.	Non-volatile at room temperature.	Volatile at room temperature.
Examples: palmitic, stearic, & lignoceric F.A.	Examples: caprylic & capric F.A.	Examples: acetic, butyric, & caproic acids.
Occur in hydrogenated oils, animal fats, butter & coconut & palm oils,(products seen in kitchen).		

Greek number prefix:

Number	prefix	Number	prefix	Number	prefix
1	Mono -	5	Penta -	9	Nona-
2	Di -	6	Hexa -	10	Deca -
3	Tri -	7	Hepta -	20	Eico -
4	Tetra -	8	Octa -		

Naming of fatty acids:

Fatty acids are organic molecules that contains carboxylic group, so we change the alkane name to carboxylic name.

Example:

If we have an 18 carbon fatty acid.

Name: octadecane (alkane), (octa and deca) is octadecanoic acid (carboxylic acid).

*one double bond: octadecenoic acid.

*Two double bonds: octadecadienoic acid.

*Three double bonds: octadecatrienoic acid.

Designation of carbons and bonds:

*18:0 = an 18 carbon fatty acid with no double bonds.

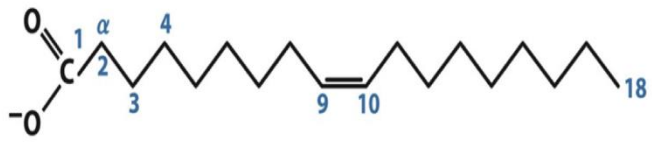
Steric acid (18:0); palmitic acid (16:0)

*18:2 = an 18 carbon fatty acid with 2 double bonds like Linoleic acid

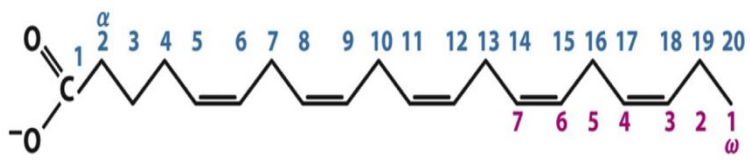
Note: the names of fatty acids that the dr. repeats you should memorize them.

Designation of location of bonds:

Δ^n: The position of a double bond.
cis-Δ^9 : a cis double bond between Carbon no. 9 and 10.
trans- $\Delta^{2,9}$: a trans double bond between carbon no.2 and 3 and between 9 and 10.
trans-Δ^2: a trans double bond between Carbon no. 2 and 3.



(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid

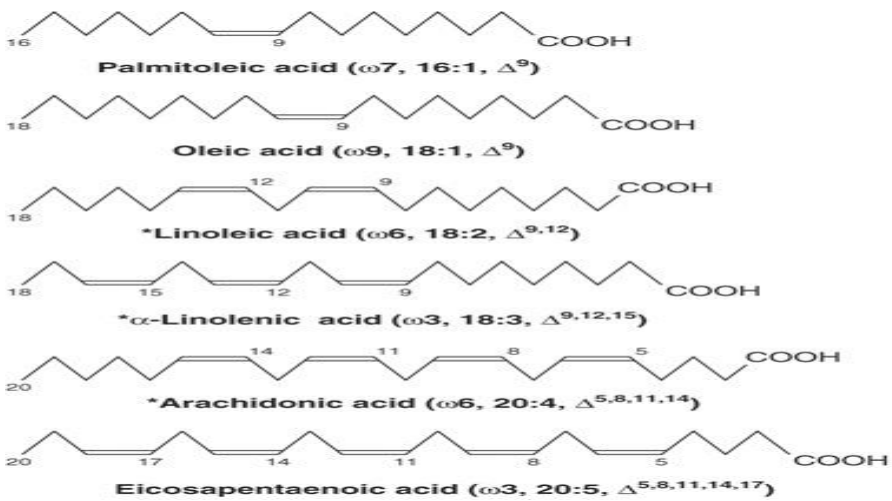


(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), an omega-3 fatty acid

Note: carbon no.1 is the carboxylic group, so you start counting from there.

Examples:

You should memorize these



No. of carbons	No. of double bonds	Common name	Systematic name	formula
14	0	Myristate	n-Tetradecanoate	CH3(CH2)12COO-
16	0	Palmitate	n-Hexadecanoate	CH3 (CH2) 14COO-
18	0	Stearate	n-Octadecanoate	CH3(CH2) 16COO-
18	1	Oleate	cis-Δ9-Octadecenoate	CH3(CH2) 7CH=CH(CH2) 7COO-
18	2	Linoleate	cis,cis-Δ9,Δ12-Octadecadienoate	CH3(CH2) 2(CH=CHCH2) 2(CH2) 6COO-
18	3	Linolenate	all-cis-Δ9,Δ12,Δ15-Octadecatrienoate	CH3CH2(CH=CHCH2) 3(CH2) 6COO-
20	4	Arachidonate	all-cis-Δ5,Δ8,Δ11,Δ14-Eicosatetraenoate	CH3 (CH2) 4(CH=CHCH2) 4(CH2) 2COO

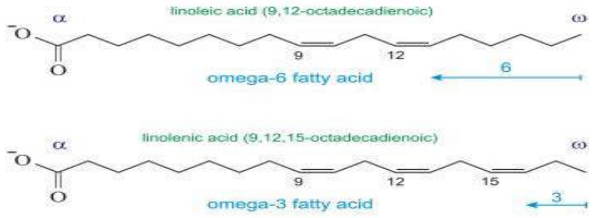
Note: the dr. said that we should know the common names and the the no. of carbons and double bonds, but he didn't mention the systematic name or the formula so I'm not sure if we should memorize them or not!!!?

Another way of naming:

if you went to a pharmacy you may have seen the vitamins and the supplements and the omega 3,6,and 9.

Omega 3,6,9 are actually fatty acids, so what do we mean by omega 3,6,9 ??

In this way of naming fatty acids we start counting from the methyl group at the other end of the fatty acid not from the carboxylic group.



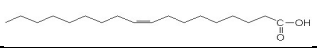
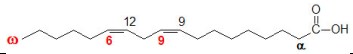
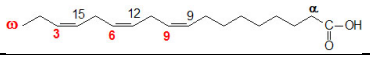
These are the omega carbons (the other end of the fatty acid) we have to start counting from here to reach the first double bond, we don't care for the other double bonds if they exist in the molecule.

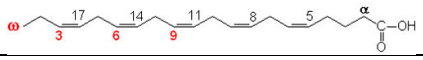
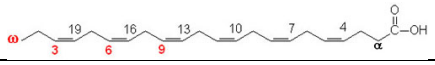
Note: when we name a fatty acid as an omega fatty acid, it means it's a fatty acid that has at least one double bond.

- This system is not really a detailed naming system; it doesn't give us a lot of information except that there is a double bond that exist at carbon no. 3 or 6 or 9.

Linoleic acid: precursor of arachidonates.
Linolenic acid: precursor of EPA and DHA.

Home work: look at oleic acid and tell if it has a double bond, and how can we designate oleic acid using the omega naming system??

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
$20:4^{\Delta 5,8,11,14}$	Arachidonic acid 	Omega-6 polyunsaturated

$20:5^{\Delta 5,8,11,14,17}$	Eicosapentaenoic acid (EPA) 	Omega-3 polyunsaturated (fish oils)
$22:6^{\Delta 4,7,10,13,16,19}$	Docosahexaenoic acid (DHA) 	Omega-3 polyunsaturated (fish oils)

These fatty acids can be used to chemically derive other important molecules from them.

Arachidonate is a very important fatty acid; its 20 carbon fatty acid, that's why we call it eicosanoid, it has 4 double bonds. (please refer to the structure in slide #19)

We can get arachidonic acid from the membrane.

From arachidonic acid we can generate a number of molecules:

1- Leukotriens
2- Prostacyclins
3- Prostaglandin
4- Thromboxanes

These molecules are collectively known as eicosanoids (they are all 20 carbon fatty acids).

Eicosanoids and their functions:

Prostaglandins:

- Inhibition of platelets aggregation; platelets are involved in blood clotting
  It controls the process of blood clotting.

Leukotrienes:

- They are involved in constricting smooth muscles
- They are involved in asthma (constriction of blood vessels and smooth muscles)
  They are a target of therapy for asthma.

Thromboxanes:

- Constriction of smooth muscles.
- Induce platelets aggregation.
  (the opposite of prostaglandins; the one with higher concentration will show the effect according to homeostasis).

Prostacyclins:

- Inhibition of platelets aggregation.
- A vasodilator (release the tension of smooth muscles).

Notice the names:

Prosta: because when they where first discovered, they where discovered as products of prostate gland.

Cyclins: because they contain two cycles.

Leuko: because they where discovered first as products of leukocytes (immune cells).

Triens: because their structure has 3 double bonds.

Thromboxanes: because they where discovered as important mediator for blood clotting.

Aspirin and heart :

Aspirin is very good for the heart because what aspirin does , Thromboxanes activates platelets and they induce platelets aggregation, Platelets aggregation causes heart diseases (atherosclerosis).

What aspirin does is that it inhibits platelets aggregation by inhibiting the enzyme that produces Thromboxanes, so the body will produce less Thromboxanes.

Aspirin is a small drug its called saliycylic acid, it acytilates the enzyme so it makes the enzyme inactive, this leads to inhibition of production of

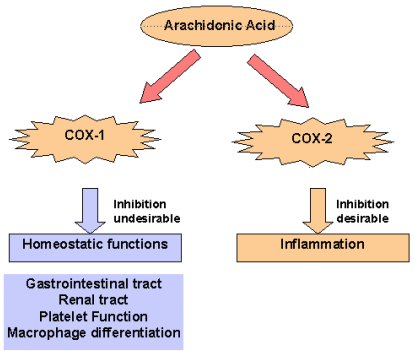
prostaglandins which leads to inhibit Thromboxanes production. (refer to the figure in slide #22).

That's why doctors tell old peoples to take baby aspirin, because it wouldn't cause bleeding , because when you take a lot of aspirin it may cause stomachache because its an acid so it induces gastric secretion and it may cause bleeding so when they take baby aspirin they can take it daily or weekly it depends on the person.

Aspirin is anti-inflammatory and fever reducing because it inhibits the synthesis of prostaglandins.

In brief:

Asprin targets the enzyme known as cyclooxygenase; we have two types of enzymes cox1 and cox2, aspirin inhibits both of them when both of them are inhibited usually the person will have harsh side effects (stomach pain, ulcer..), because of that they have manufactured another drug which is celebrex its found in pharmacies now .



Celebrex inhibits cox2 only so the patient will not have any of these undesirable effects but it prevents inflammation only.

Note that this drug is not suitable for persons who have heart diseases because it may cause heart failure.