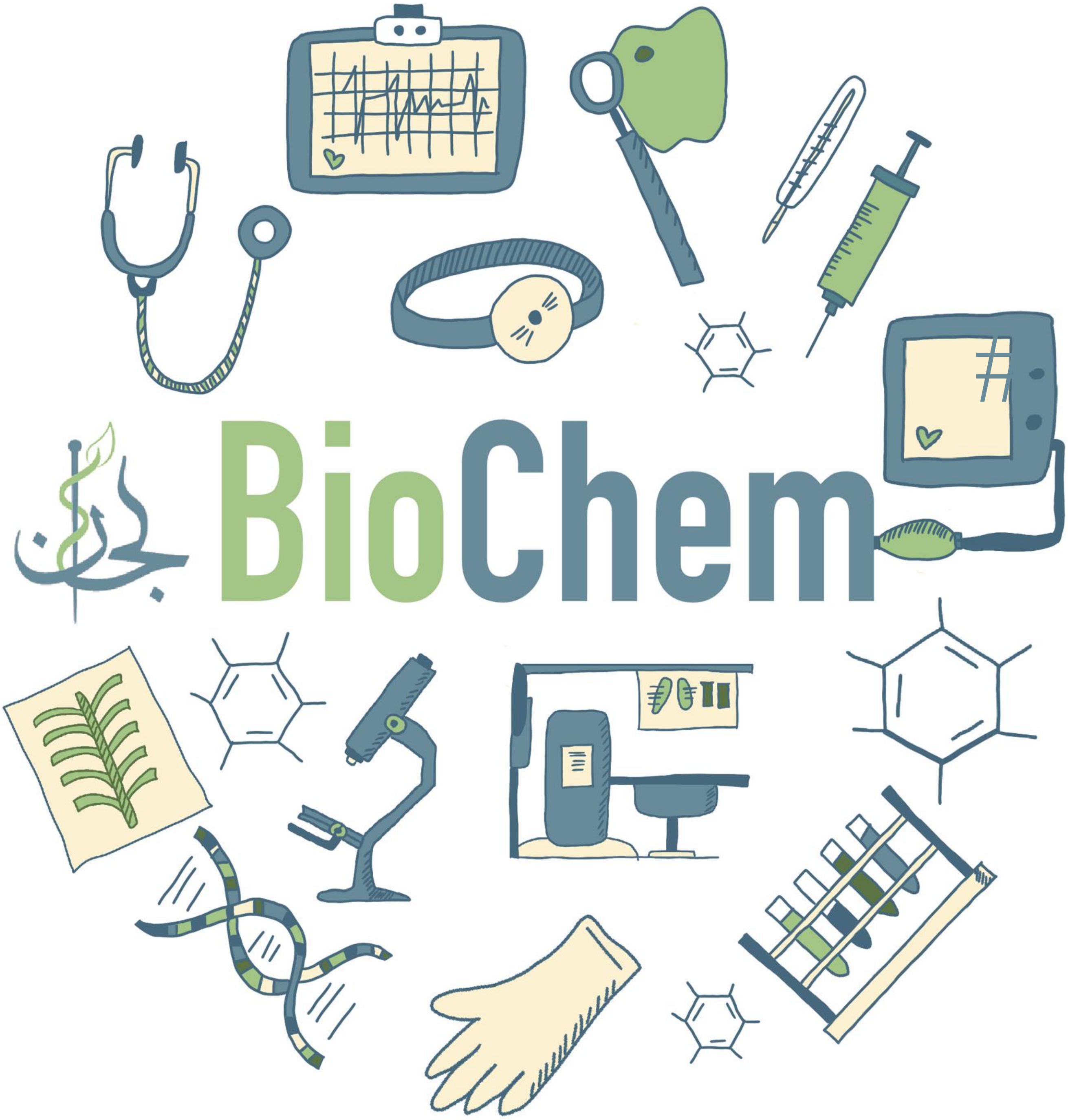


Writer: Roa’a Oriqat

Science: Hani shihadeh

Grammar: Noor Arman

Doctor: Mamoun Ahram

❖ Lipids :-

- Lipids are a heterogeneous class of naturally occurring organic compounds that share some properties based on structural similarities, mainly a dominance of nonpolar groups.
    - ➢ There is a difference between lipids and the other molecules that we have discussed before.
    - ➢ Nucleic acids are made of monomers (nucleotides) connected to each other.
      Proteins are made of amino acids also linked covalently to each other.
      Sugar molecules, like glycogen, starch, cellulose, even Glycosaminoglycan, are made of repeated subunits.
      Whether monosaccharaides (as in glycogen and starch), or repetitive disaccharides (as in glycosaminoglycan).
      All of these molecules are polymers, whereas lipids are not.
    - ➢ Lipids are macromolecules, so they are large molecules in general.
- They are Amphipathic in nature:

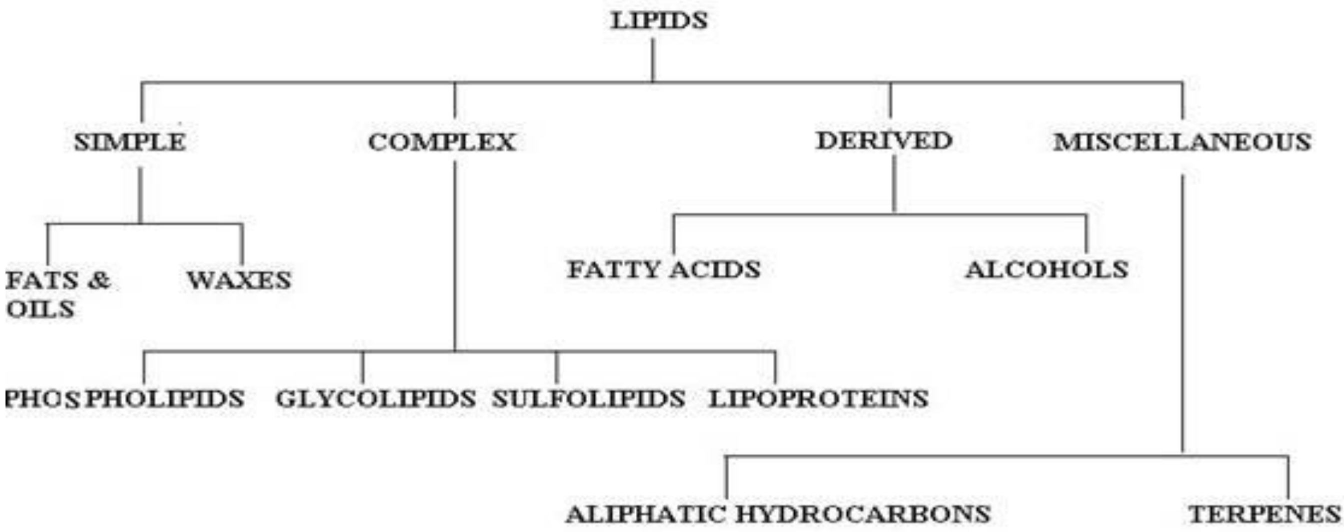
➢ Amphi means (dual), which means both, so they have two natures, a hydrophobic nature and a hydrophilic nature. Basically, the idea is that you can draw a line and say this part is hydrophobic and this part is hydrophilic

➢ In general, they are hydrophobic. As a result, they are **insoluble** in water.

- They are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).
- They are widely distributed in plants & animals.

** Classes:-

1. Simple lipids (fats, oils, and waxes)
2. Complex lipid = large lipids = lipid molecules (glycerides , glycerophospholipids, sphingolipids, glycolipids, lipoproteins, sulfolipids , phospholipids)
3. Derived lipids (fatty acids, alcohols, eicosanoids)
4. Cyclic lipids (steroids) :- a class of lipids that are all derived from cholesterol



❖ Lipid Functions :-

1. Storage lipids

➢ They are used for energy purposes, just like glycogen (in animals and humans) and starch (in plants).

2. Structural lipids in membranes

➢ The ones that make up membranes, plasma membranes, mitochondrial membranes (all types of membranes)

3. Lipids as signals, cofactors & pigments

➢ Lipids can function in signaling inside cells such as the phosphatidylinositol

- They are a major source of energy

They are storable to unlimited amount (vs. carbohydrates)

They provide considerable amount of energy to the body (25% of body needs) & provide a high-energy value (more energy per gram vs. carbohydrates & proteins)

➢ They are the major source of energy in cells, in our body. In fact, they can produce double the amount of energy compared to the same amount of carbohydrates, so they provide a lot of energy

- Structural components (cell membranes)
- Precursors of hormone and vitamins
- Shock absorbers thermal insulator

➢ They insulate our internal organs and protect them, they are thermal insulators as well (they provide us with heat). So that's the reason why if someone kicks you on the butt, you don't feel much pain because of the lipids. So the more lipids you have in a given area, the less pain you will feel there.

** Fatty Acids :-

Functions:

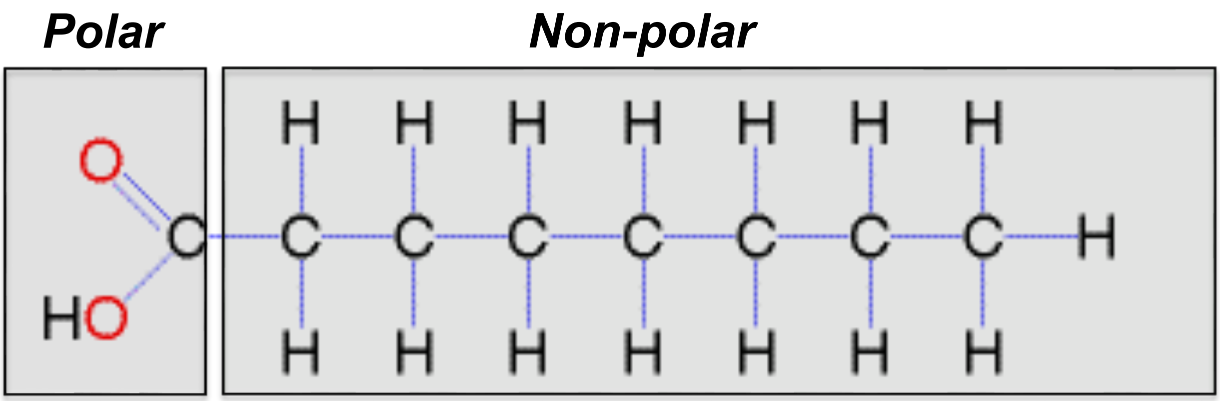
- **Building blocks of other lipids**
- **Modification of many proteins (lipoproteins)**
- **Important fuel molecules**
- **Derivatives of important cellular molecules**

- Aliphatic mono-carboxylic acids

➢ They are made of a hydrocarbon chain, (i.e. just Carbon and Hydrogen). Also, there is a carboxylic group at one end (that's why they are known as fatty acids)

- Amphipathic molecules

➢ They have two natures, a hydrophobic nature and a hydrophilic nature, so the idea is that you can draw a line and distinguish which part is hydrophobic and which part is hydrophilic.



- Chemical formula: **($R\text{-}(CH_2)_n\text{-}COOH$)**
- Lengths:-

➢ Physiological (12-24)

➢ Abundant (16 and 18)

- Degree of unsaturation

➢ Fatty acids can be saturated (meaning that they do not have any double bonds), or they can be unsaturated (meaning that they have at least one double-bond)

✓ Note:-

➢ There are no fatty acids with triple bonds, even in our body.

❖ Types of fatty acids

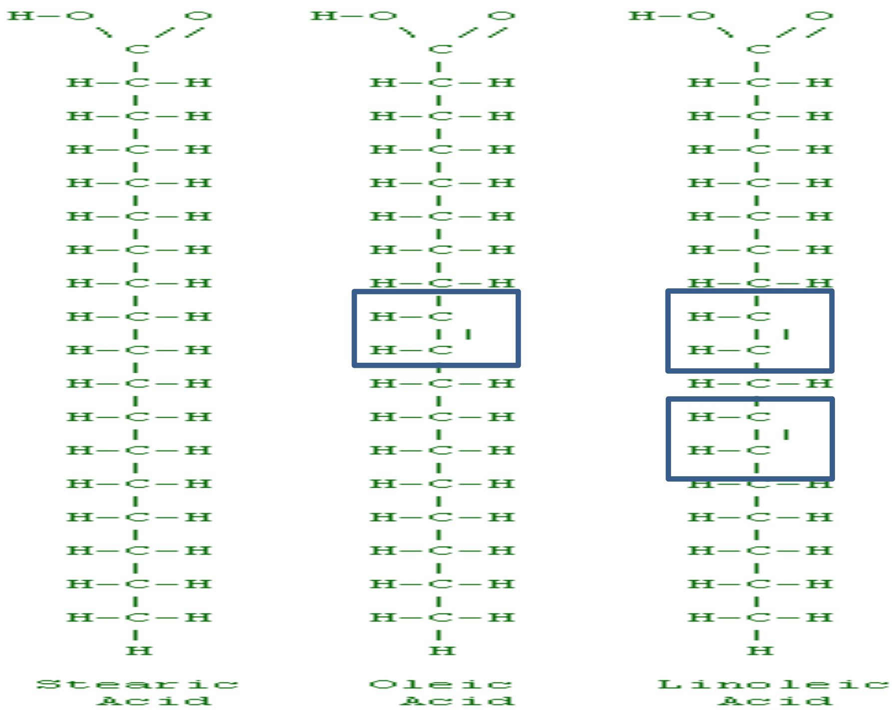
- Saturated fatty acids are those with all of C-C bonds being single.

- Unsaturated fatty acids are those with one or more double bonds between carbons

- Monounsaturated fatty acid: a fatty acid containing one double bond.
- Polyunsaturated fatty acids contain two or more double bonds.

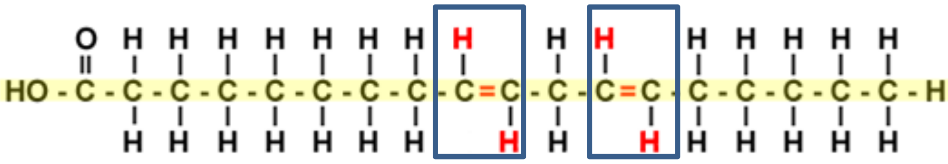
<u>Here is some information about the figure:-</u>

- Stearic Acid: - an 18 carbon fatty acid, with no double bond.
- Note that you start numbering from the carboxylic group.
- Oleic Acid :- a mono unsaturated fatty acid, which contains just one double bond (It is the same as olive oil)
- Linoleic acid. That's an important one. It is an 18 carbon fatty acid with two double bonds (we say that it is a polyunsaturated fatty acid, because it has more than one double bond)



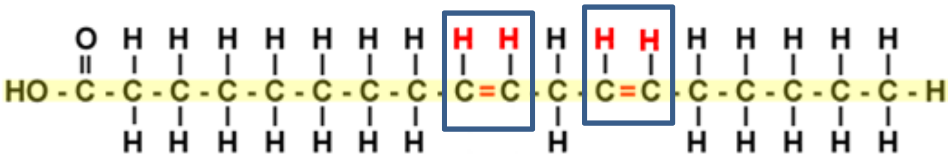
❖ Cis vs. trans bonds

- If we look at these double bonds, they can take either one of two forms. They can have a **trans configuration** or **Cis configuration**.
-



linoleic acid: *trans* configuration (*trans* isomer)

Both Hydrogens going in opposite directions, so this is a trans fatty acid



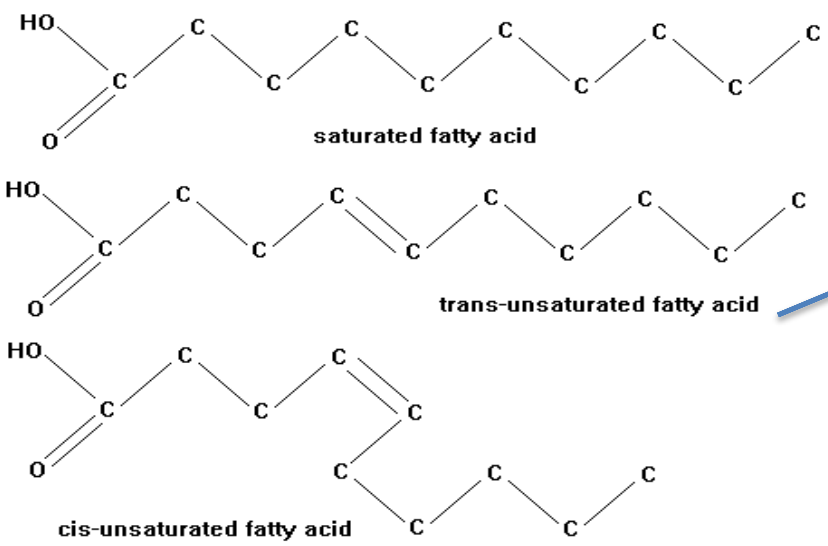
linoleic acid: *cis* configuration (*cis* isomer)

Both hydrogens going upward, (the same direction), so this is a cis fatty acid

cis isomer predominates; trans is rare

- Above is a simple drawing; it doesn't really reflect what it looks like in three dimensions.
  What we see here however, is a better illustration of what they look like in three dimensions.

cis- vs. trans-fatty acids



This is a saturated fatty acid (No double bond)

This is a mono unsaturated fatty acid with a Trans double bond

You have the bond going down, up, then down, then up

This is a mono unsaturated fatty acid with a cis double bond

you have the bond going up, down, up, down, up, down, down, down.

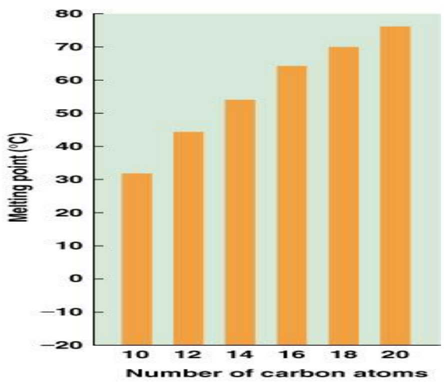
➢ Good note: - The cis fatty acid takes up a little more space than a trans fatty acid, even though both of them have double bonds.

❖ Properties of fatty acids

➢ Now, the question is what is the relationship between double bonds and physical properties, specifically melting point?
Also what is the relationship between the length of the hydrocarbon chain, (that is how many carbon atoms does a fatty acid have), and its melting point?

➢ Melting point of fatty acid: is the temperature at which it changes state from solid to liquid and vice versa

- The properties of fatty acids (melting point and solubility) are dependent on chain length and degree of saturation

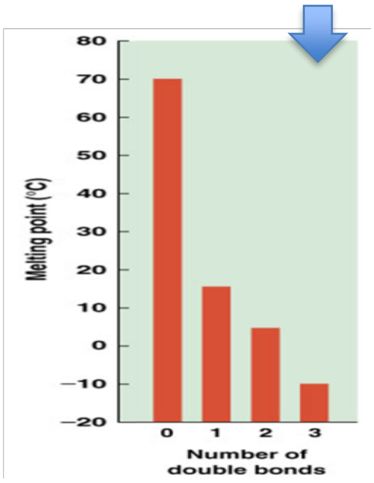


Let's look at the effect of the length of the hydrocarbon chain

A 10 carbon fatty acid is solid at a temperature of 30 and below, and it is liquid at 30 and above.

Now, note that the more carbons you add the higher the melting point is, so a 20 carbon fatty acid at a temperature of about 70 is still solid.

This figure represents the effects of adding double bond to an 18 carbons-fatty acid on a melting temperature



Now, look at the effect of double bonds: An 18 carbon fatty acid with no double bonds has the melting temperature of about 70. Introduction of just one double bond reduces the melting temperature to about 15. Introduction of another one reduces the melting point further more, so the effect of double bond is really more significant than the length of a fatty acid or hydrocarbon

➢ An 18 carbon fatty acid with one double bond is Oleic acid (Olive oil). It makes sense because if you have olive oil, it's in liquid form, but if you put it in the fridge or if you put it on the kitchen bench during winter time and it's cold, it solidifies.

❖ Properties of saturated fatty acids

These are the different classes of saturated fatty acids and these are their properties

Short chain F.A.	Medium-chain F.A.	Long chain F.A.
They are liquid in nature	Solids at room temperature	Solids at room temperature
Water-soluble	Water-soluble	Water-insoluble
Volatile at RT (متطاير)	Non-volatile at RT	Non-volatile
Acetic, butyric, caproic FA → (CH3COOH)	Caprylic & capric F.A.	Palmitic and stearic F.A

- Butyric Acid makes up butter (if you put butter at room temperature it becomes liquid, and that's why it melts really fast in your mouth when it warms up)
- Caproic fatty acid: - capri means goat, so in goat milk you have a lot of short chain fatty acids.
- Palmitic fatty acid is derived from palm tree.

❖ Greek number prefix

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

❖ Greek number prefix

- Alkane to oic
- Octadecane (octa and deca) is octadecanoic acid:

➢ We have an octadecane, meaning that we have octa is eight, deca is 10. That's an 18 carbon fatty acids, and we add a carboxylic group to it, so it becomes octadecanoic acid

- One double bond = octadecenoic acid
- Two double bonds = octadecadienoic acid
- Three double bonds = octadecatrienoic acid

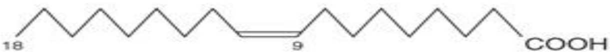
- Designation of carbons and bonds

- 18:0 = a C18 fatty acid with no double bonds
- stearic acid (18:0); palmitic acid (16:0)
- 18:2 = a C18 fatty acid with two double bonds (linoleic acid)

- Designation of location of bonds

- We can also use Δ^n (The position of a double bond)
- cis-Δ^9 :a cis double bond between C9 and C10
- trans-Δ^2:a trans double bond between C2 and C3

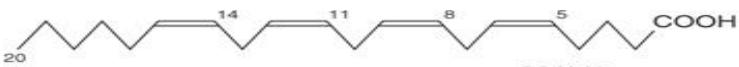
Palmitoleic acid (ω7, 16:1, Δ^9)



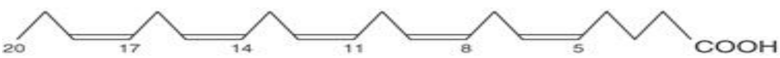
Oleic acid (ω9, 18:1, Δ^9)

*Linoleic acid (ω6, 18:2, $\Delta^{9,12}$)

*α-Linolenic acid (ω3, 18:3, $\Delta^{9,12,15}$)



*Arachidonic acid (ω6, 20:4, $\Delta^{5,8,11,14}$)



Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

These are some of the most common fatty acids that we will focus on.

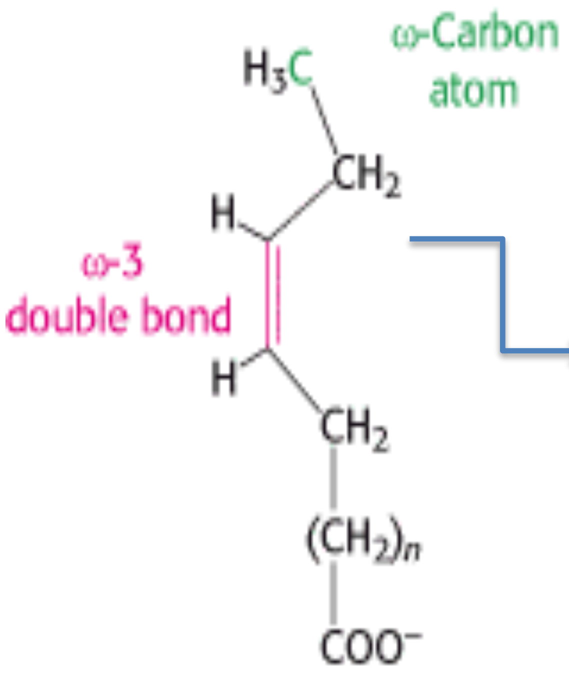
Oleic acid, Linoleic acid, Linolenic acid, Arachidonic acid

Common name not scientific name

Number of carbons	Number of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3\,(CH_2)_{14}COO$-
18	0	Stearate	n-Octadecanoate	$CH_3(CH2)_{16}COO$-
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO$-
18	2	Linoleate	cis,cis-Δ^9,Δ^{12}-Octadecadienoate	$CH_3(CH_2)_4CH{=}CHCH_2CH(CH_2)_7COOH$
18	3	Linolenate	all-cis-$\Delta^9,\Delta^{12},\Delta^{15}$-Octadecatrienoate	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$
20	4	Arachidonate	all-cis-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-Eicosatetraenoate	$CH_3(CH_2)_4\,(CH{=}CHCH_2)_4(CH_2)_2$ COOH

❖ Another way of naming :-

➢ There is an easier way of naming fatty acids, especially for those that contain double bonds, by saying this is an omega fatty acid, where Omega means that this fatty acid has a double bond and its followed by an indication, a number indicating where this double bond exists, except that we start counting from the other end, i.e. from the methyl group rather than from the carboxylic Group.

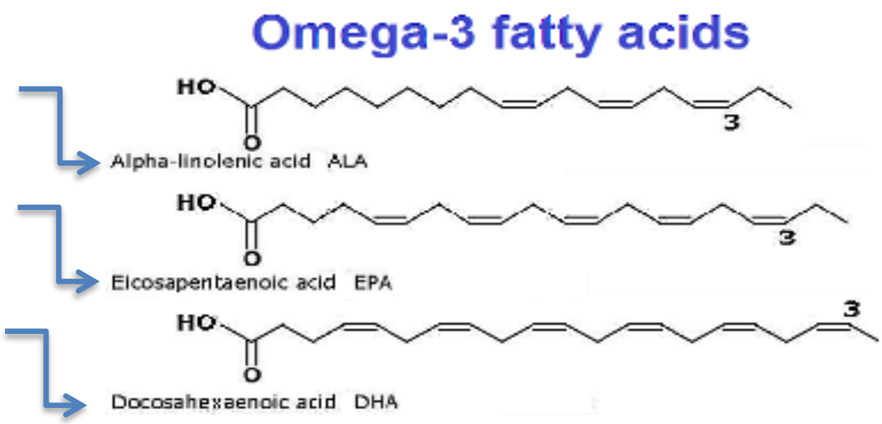


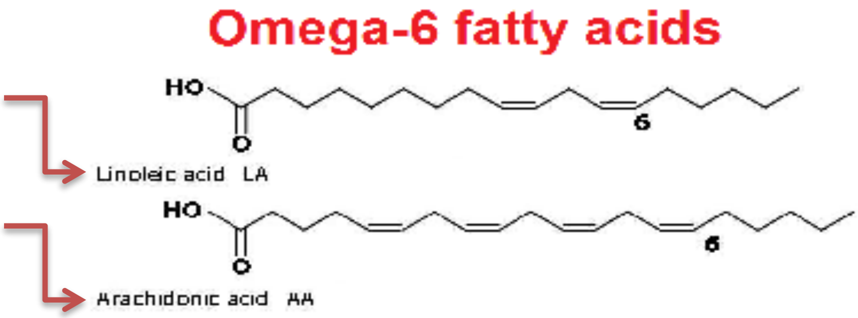
An ω-3 fatty acid

(ω)-C: distal methyl C as #1

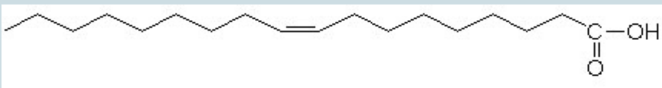
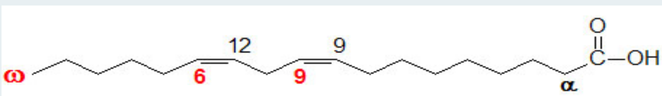
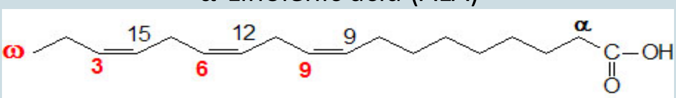
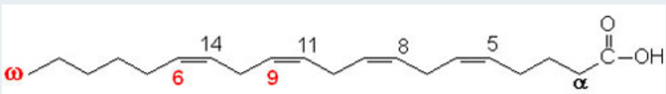
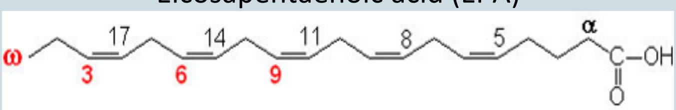
Here we have what we call an omega three fatty acid because there is a double bond carbon between carbon 3 and 4

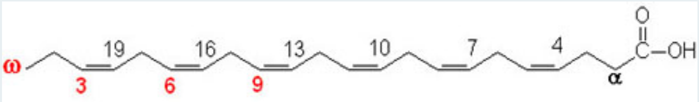
- <u>These are examples of other omega fatty acids :-</u>





- Linoleic and Linolenic fatty acids are essential fatty acids, meaning that we can't synthesize them and we have to get them from our diet
- **Linoleic acid: precursor of arachidonates**
- **Linolenic acid: precursor of EPA and DHA**

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)

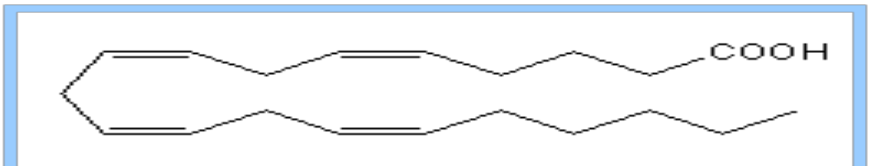
$22{:}6^{\Delta 4,7,10,13,16,19}$	Docosahexaenoic acid (DHA) 	Omega-3 polyunsaturated (fish oils)

❖ *Derived fatty acids: Eicosanoids*

This is an important class of fatty acids and these are all 20 carbon fatty acids

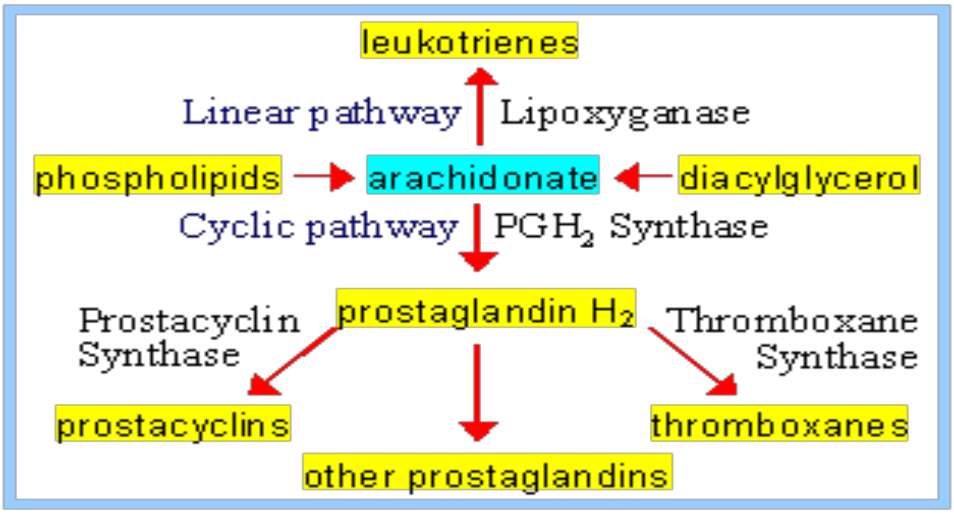
❖ Arachidona

all *cis*-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-eicosatetraenoate, $CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO^-$



Arachidonic acid

- ➢ Arachidonic acid, which is a 20 Carbon fatty acid, is a precursor for other important eicosanoids that are 20 carbon molecules, including leukotrienes, prostaglandins, prostacyclins, and thromboxanes.
- leukotrienes came from leukocytes (immune cells)
- prostaglandins were given the stem because they were first identified as molecules synthesized or found in prostate gland
- prostacyclins are found in prostate gland
- thromboxanes are related to thrombin, which is a protein involved in blood clotting, thrombus.
- ➢ All of these are enzymatically catalyzed, so arachidonic acid to leukotrienes or arachidonic acid to other molecules.

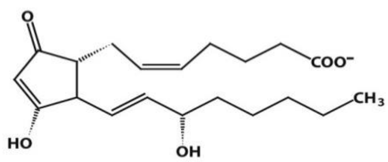


Eicosanoids and their functions

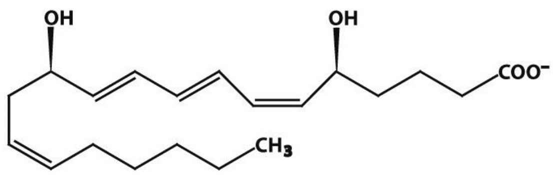
These are really important molecules physiologically as well as pathologically

- ✓ Prostaglandins
- Induction of inflammation
- Inhibition of platelet aggregation
- Inhibition of blood clotting
- ✓ Leukotrienes
- Constriction of smooth muscles
- ➢ They are associated with Asthma, so as a mode of treatment for asthmatic individuals, they may be given as inhibitors of production of leukotrienes.
- ✓ Thromboxanes
- Constriction of smooth muscles
- Induction of platelet aggregation, so they can induce blood clotting
- ✓ Prostacyclins
- An inhibitor of platelet aggregation
- A vasodilator, meaning that it expands blood vessels.

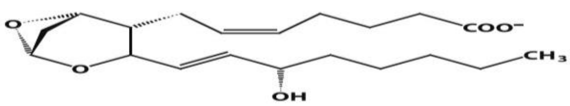
❖ Note that their functions are or may be contradictory to each other one way or another, but there is an important concept in our body known as homeostasis, which means there is a physiological balance, so our body balances out our response to effectors.



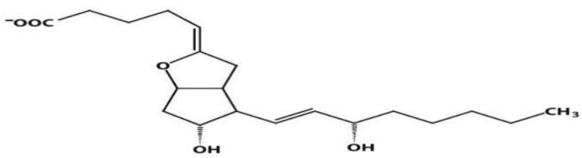
Prostaglandin E_2



Leukotriene B_4



Thromboxane A_2 (TXA_2)



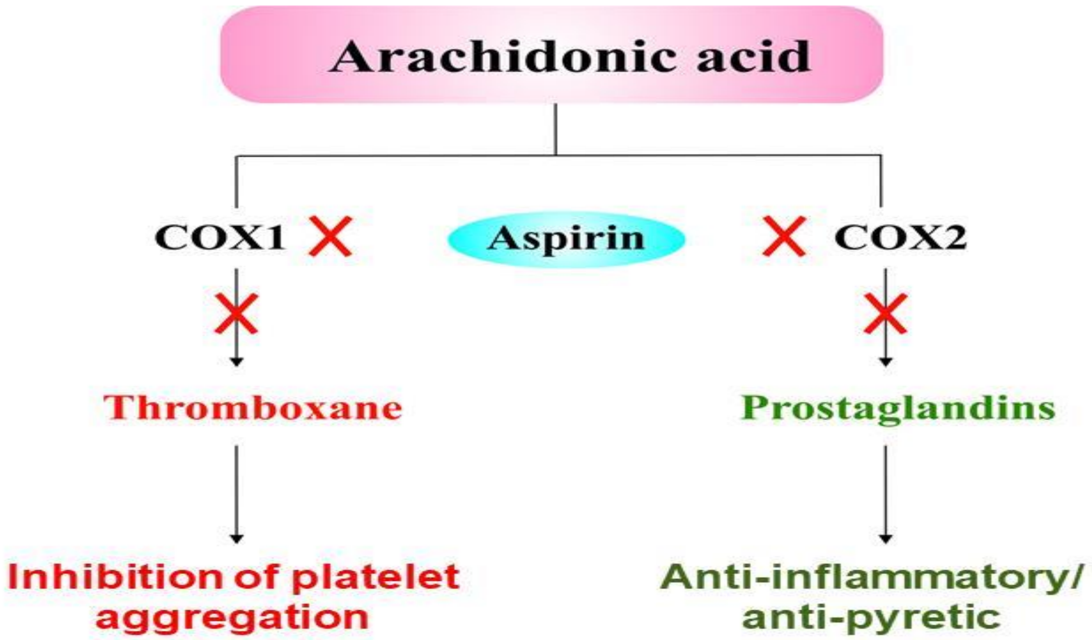
Prostacyclin (PGI_2)

Aspirin is good

- Arachidonic acid can be converted to thromboxane or prostaglandins.
- Aspirin was found to inhibit the production of both of these mediators or signaling molecules. As a result, aspirin is an anti-inflammatory medication and it is antipiretik, meaning that it reduces fever. It also inhibits platelet aggregation.
- It had been thought for years that aspirin is good for older people by reducing the incidence of heart attacks and companies made billions of dollars, only last year, there was a research article saying that this is not true, aspirin is not beneficial in that sense.

✓ How does aspirin do that?

- By inhibiting the enzymes that convert arachidonic acid to these components. These enzymes are known as Cyclooxygenase, and there are three isoforms. Specifically, we'll focus on two :
  - Cyclooxygenase 1: converts arachidonic acid to thromboxane.
  - Cyclooxygenase 2: converts arachidonic acid to prostaglandin.
    - So by inhibiting these two enzymes, you reduce inflammation, reduce fever, and you can inhibit platelet aggregation, reducing the rate of heart attacks.



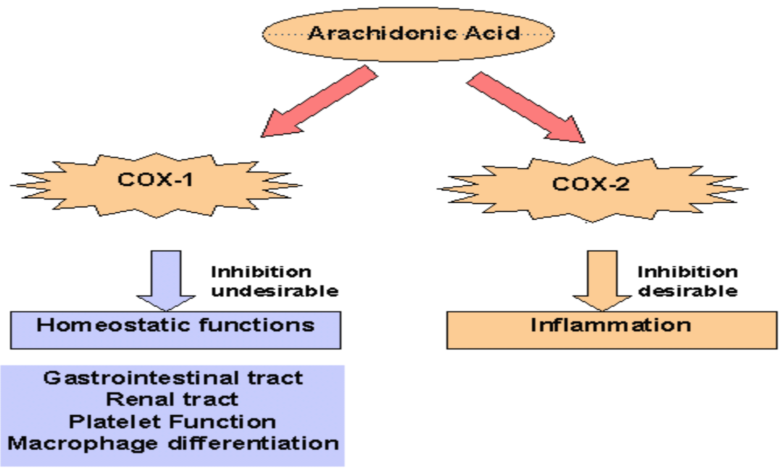
COX: Cyclooxygenase

Targets of Aspirin

- Cyclooxygenase is present in three forms in cells, COX-1, COX-2, and COX-3.
- Aspirin targets both, but COX-2 should only be targeted.

➢ It turns out that actually by inhibiting COX 1, there are undesirable effects that would appear. People with sensitive stomachs are not supposed to take aspirin, because it will affect their gastrointestinal tract specifically the stomachs, so people thought why don't we create a drug/medication that would only inhibit COX 2.

And that's the beauty of biochemistry. By understanding enzymes, their functions, and their structures, we can design better drugs.



Celebrex

- A new generation drug, Celebrex, targets COX2, but is prescribed with a strong warning of side effects on the label.

➢ There was a drug called Celebrex and the scientific name is celecoxib. That would inhibit only COX 2, but not COX 1, so it does not have bad effects on our stomach, but it reduces inflammation. It is a good medication, except that it may have bad effects on people with heart problems.

Omega fatty acids

- ✓ Omega-3 fatty acids
- α-linolenic acid → eicosapentaenoic acid (EPA) → docosahexaenoic acid (DHA)
  - ➢ They include EPA and DHA.
  - ➢ They are derived from linolenic acid (the molecule with 3 double bonds)
- They reduce inflammatory reactions by:

1- Reducing conversion of arachidonic acid into eicosanoids
2- Promoting synthesis of anti-inflammatory molecules

- ❖ It's good if you take pills or food that contains omega three fatty acids because it is good for your memory
- ❖ Tuna, salmon, and sardine are really great source for Omega three fatty acids

- ✓ Omega-6 fatty acids:
- Arachidonic acid
- ➢ Omega-6-fatty acids include arachidonic acid as well as linoleic acid, except that their effects are not really that good because they :-

1- stimulate platelet and leukocyte activation
2- signal pain
3- Induce bronchoconstriction
4- regulate gastric secretion

- ✓ Omega-9 fatty acids
- Oleic acid
- Reduces cholesterol in the circulation, and that's why they say that Mediterranean food is good overall because we use a lot of olive oil in our diet.

SHORT QUIZ

1) Which of the following statements concerning fatty acids is correct?

A) One is the precursor of prostaglandins.
B) Phosphatidic acid is a common one.
C) They all contain one or more double bonds.
D) They are a constituent of sterols.
E) They are strongly hydrophilic.

2) Which of the following molecules or substances contain, or are derived from, fatty acids?

A) Beeswax
B) Prostaglandins
C) Sphingolipids
D) Triacylglycerols
E) All of the above contain or are derived from fatty acids

3) An example of a glycerophospholipid that is involved in cell signaling is

A) arachidonic acid.
B) ceramide.
C) phosphatidylinositol.
D) testosterone.
E) vitamin A (retinol)

4) Circle the fatty acid in each pair that has the higher melting temperature.

(a) 18:1Δ9 18:2Δ9,12

(b) 18:0 18:1Δ9

(c) 18:0 16:0

5) Which of the following structures is a 20:2 (Δ4,9) fatty acid?

a) CH3(CH2)9CH = CH(CH2)3CH = CH(CH2)2COOH
b) CH3(CH2)2CH = CH(CH2)3CH = CH(CH2)9COOH
c) CH3(CH2)10CH = CH(CH2)3CH = CHCH2COOH
d) CH3CH2CH = CH(CH2)3CH = CH(CH2)10COOH

6)Which is a property of eicosanoids?

a) All eicosanoids contain three conjugated double bonds.
b) All eicosanoids contain arachidonic acid and sphingosine.
c) Prostaglandins and leukotrienes both contain a ring structure.
d) Thromboxanes and prostaglandins both contain a carboxyl group.

7) What is the proper designation for the unsaturated fatty acids in this lipid?

a) 18:2 (Δ9,12)
b) 18:2 (Δ6,9)
c) 17:2 (Δ9,12)
d) 17:2 (Δ5,8)

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CH2 – O – CH2 – (CH2)16CH3
 |           O
 |           ||
CH – O – C – (CH2)4CH=CHCH2CH=CH(CH2)7CH3
 |           O
 |           ||
CH2 – O – C – (CH2)4CH=CHCH2CH=CH(CH2)7CH3
```

ANSWERS

Q1	Q2	Q3	Q5	Q6	Q7
A	E	C	A	D	B

4A =18 :1 Δ9 4B = 18:0 4C = 18:0