8

BIOCHEMISTRY

Faculty of medicine – JU2018

◉ Sheet ○ Slides

DONE BY

Anas Zayad &Mohammad Hatamleh

CONTRIBUTED IN THE SCIENTIFIC CORRECTION

Anas Zaqut

CONTRIBUTED IN THE GRAMMATICAL CORRECTION

Anas Zaqut

DOCTOR

Dr.Mamoun

Lipids

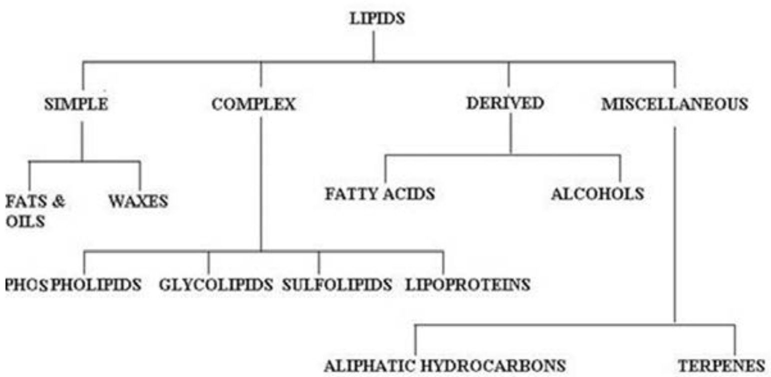
We have four macromolecules: Carbohydrates, proteins, nucleic acids and lipids. The first three are polymers which means they are made up of smaller subunits called monomers. Carbohydrates are made up of monosaccharides. Proteins are made up of amino acids. Nucleic acids are made up of nucleotides. Lipids are significant in the fact that they are not polymers. Lipids are a heterogeneous class of naturally occurring organic compounds that share some properties based on structural similarities, mainly a dominance of nonpolar group.

Lipids have a few distinguishing features:

- Lipids are amphipathic. This means that they have both hydrophobic and hydrophilic domains which are recognizable.
- Lipids are insoluble in water, but they are soluble in fat or organic solvent (ether, chloroform, benzene, and acetone).
- Lipids are found in both plants and animals.

There are different classes for lipids

- Simple lipids (fats, oils and waxes)
- Complex lipids (glycerides, glycerophospholipids, sphingolipids, glycolipids, lipoproteins).
- Derived fats (eicosanoids, fatty acids, and alcohol).
- Cyclic lipids (steroids).



We don't need to memorize the flowchart just be familiar with it

Lipid functions

Lipids have multiple functions:

- Storage lipids are used as a means for the production of energy. Lipids produce more energy than carbohydrates, this is because they are highly saturated and highly reduced and carry high amounts of energy within their bonds. Whenever we are in need of energy, fatty acids could be released to different organs and they can be used for the production of energy (lipids provide 25% of the bodily needs).
- There are also structural lipids, a good example of this is the cell membrane because the cell membrane is primarily made up of lipids (phospholipid and cholesterol).
- They can also be used as signals, cofactors, and pigments.
- Another function of lipids is that it keeps you warm, people with higher percentages of subcutaneous fat stay warmer than people who have lesser percentages of subcutaneous fat.
- It also acts as a great shock absorber; all of our internal organs are layered by a layer of fat that protects the organ. Also, if you were to get kicked in the buttocks you wouldn't feel it as much as if you were kicked in a different area this is because the Buttocks region contains a lot of subcutaneous fat.
- Precursor of hormones and vitamin.

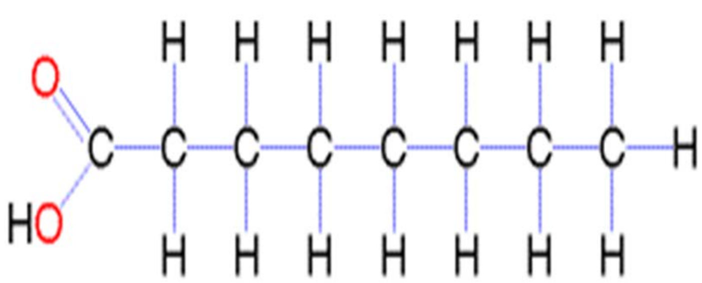
Fatty Acids

Fatty acids is aliphatic mono-carboxylic acid. Fatty acids are the most basic form of lipids. It has a basic formula of $R-(CH_2)_n-COOH$. Fatty acids are amphipathic. The hydrophobic part is a nonpolar hydrocarbon chain whereas the hydrophilic part is a polar carboxylic acid head. The physiological length of fatty acids are 12 to 24 carbons, however the majority of fatty acids are 16 to 18 carbons in length. Fatty acids differ in the degree of unsaturation.

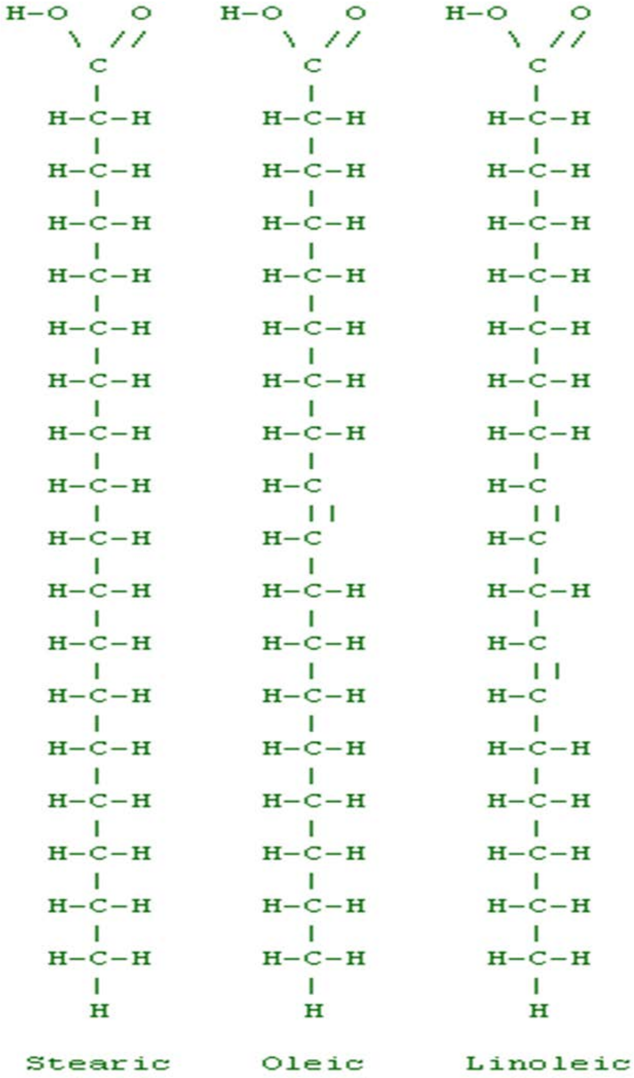
Functions:

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

Polar ***non-polar***



Note: In our body we don't have fatty acids with triple bond.



We have to memorize the name and structure for each one

<u>**Types of fatty acids:**</u>

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

Unsaturated fatty acids: are those with one or more double bonds between carbons, they can be either:

- Monounsaturated fatty acids: a fatty acid containing one double bond.
- polyunsaturated fatty acids: a fatty acid containing more than one double bond.

Notes about the diagram:

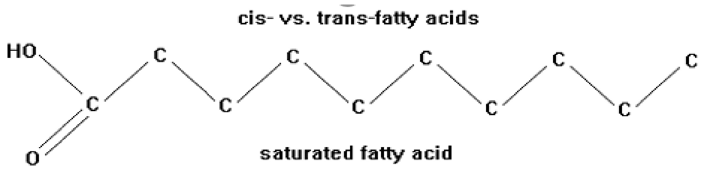
Seatric acid: contains 18 carbon and it is fully saturated.

Oleic acid: monounsaturated fatty acid and exists in oil.

Linoleic acid: polyunsaturated

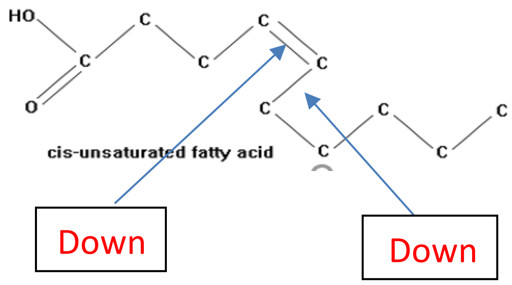
cis vs trans bonds

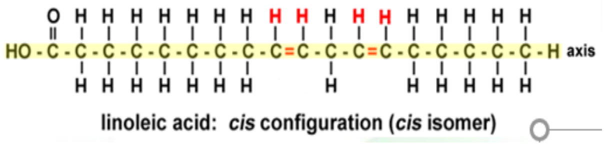
1. When the fatty acid is saturated all bonds are oriented in trans configuration (which means that the carbon atoms are oriented up and down relative to each other as detailed in the diagram below).



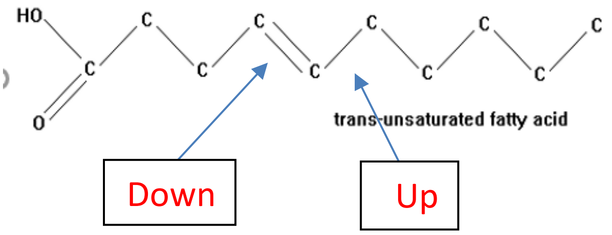
2.Double bonds have 2 possible configurations:

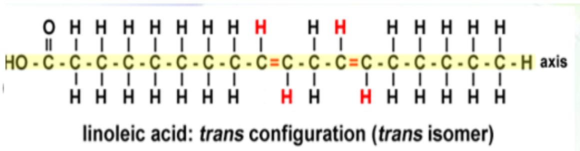
a) Cis configuration: cis configuration creates a kink in which the carbon atoms go in the same direction relative to each other (up, up or down, down) as shown below. Cis configuration predominates.





b) Trans configuration: trans configuration does not create a kink in the carbon chain, so the carbons are configured in the same opposite direction relative to each other. (up, down). Trans configuration is rare

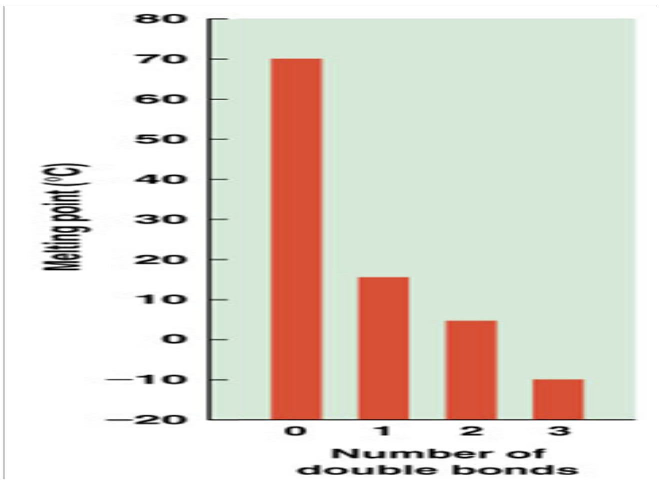




properties of fatty acids:

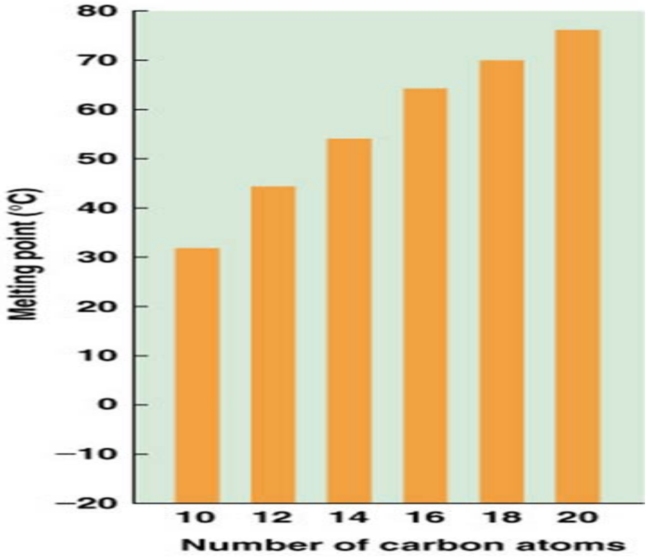
melting point and solubility are dependent on two very important factors:

1. Degree of saturation and melting point are directly proportional, for example when one double bond is added melting point decreases substantially.



Notes this diagram that melting point dropped from 70 C to 15 C when adding single double bond

2. The number of carbons is directly proportional to the melting point, and inversely proportional with solubility, so when the number of carbons in the hydrocarbon chain increases the melting point linearly increases, while the solubility decreases.



Pay attention to the fact that the effect of number of carbons is less apparent than double bond

properties of **saturated fatty acid:**

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	Non-volatile at RT	Non-volatile
Acetic, butyric, caproic FA	Caprylic & capric F.A.	Palmitic and stearic F. A

Greek number:

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-		

Nomenclature of fatty acids:

1. We start counting the carbon atoms starting from carboxylic group.
2. We take the prefix of the **alkane** and add the suffix -**oic,** because it is a carboxylic group, and we add the word acid at the end.
3. If a double bond exists in the carbon chain then we replace the "**ane**" with an "**ene**", because it is now considered an alkene.
4. If we have more than one double bond then we add **di**, **tri**, etc. (this is placed before the suffix – "**enoic**") based on the amount of double bond within the hydrocarbon chain.

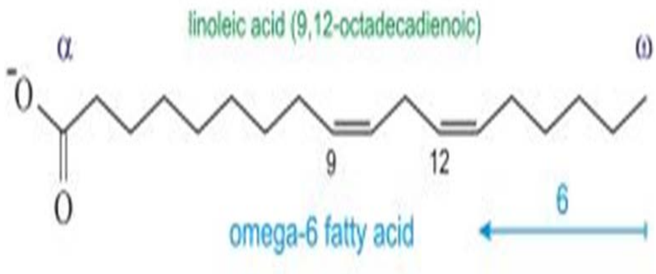
Note: This take us back to the IUPAC rules that we became familiar with during the second semester.

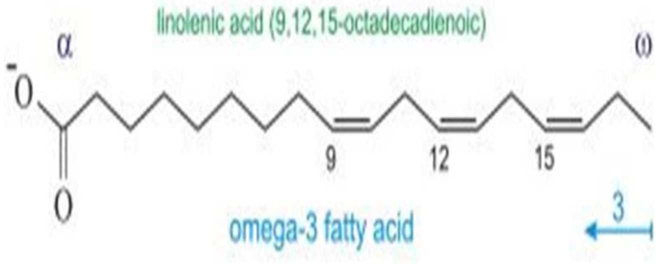
- For example, stearic acid has 18 carbon atoms, so it is systematic name would be octadecanoic acid.
- If we add one double bond then the fatty acid chain would be called octadecenoic acid
- If another double is added then the name changes once again to octadecadienoic acid.

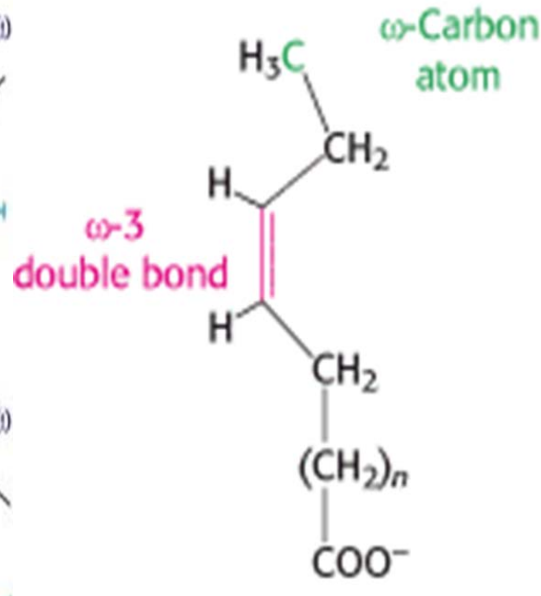
Another ways of naming

1. Designation of carbons and bonds, 18:0 the 18 designates the amount of carbon atoms in the fatty acid chain and the 0 designates the amount of double bonds. This fatty acid has 18 carbons and no double bonds so it is stearic acid.
2. The second method is the designation of location of the bonds Δ^n.
   Δ^n this symbol means that the double bond occurs between carbon number (n) and carbon number (n+1).
   cis-Δ^9: the double bond has a cis configuration which occurs between the ninth and tenth carbon atoms.
   trans-Δ^2: a trans double bond between C 2 and 3

3. ω-system(omega-system) : The ω-carbon is the last carbon in the hydrocarbon chain. We count only the nearest doubly bound carbon to the most distal carbon (the ω-carbon) at methyl end.
   Example:
   ω-3 fatty acid: fatty acid has a double bond at third carbon starting the numbering from methyl group.
   - Note: the carboxylic carbon is designated by the (α) symbol.







An ω-3 fatty acid

Palmitoleic acid (ω7, 16:1, Δ^9)

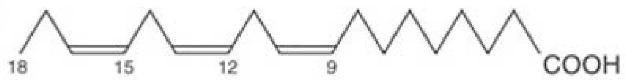
Hexadecenoic acid

Oleic acid (ω9, 18:1, Δ^9)

Octadecenoic acid

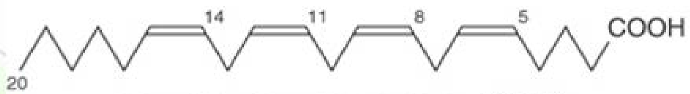
*Linoleic acid (ω6, 18:2, $\Delta^{9,12}$)

Octadecadienoic acid



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

Octadecatrienoic acid



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

Eicosatetraenoic acid

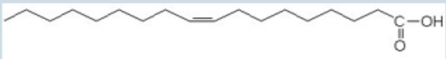
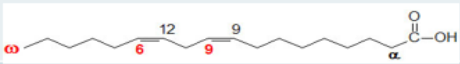
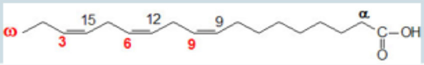
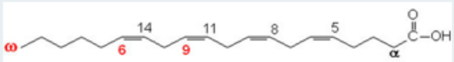
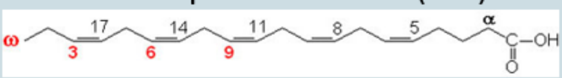
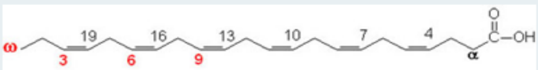
Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

Eicosapentaenoic acid

- We need to know the structures and names of previous fatty acids except the first and last one.
- Do not forget the structure of stearic acid (page 3)

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	$CH_3(CH_2)_2(CH{=}CHCH_2)_2(CH_2)_6COO$-
18	3	Linolenate	all-cis-Δ^9,Δ^{12},Δ^{15}-Octadecatrienoate	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COO$-
20	4	Arachidonate	all-cis-Δ^5,Δ^8,Δ^{11},Δ^{14}-Eicosatetraenoate	$CH_3\,(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO$-

(These 2 tables are for memorizing)

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)

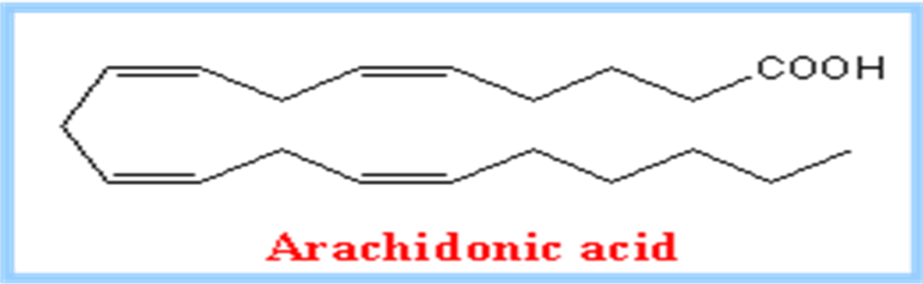
Some information about previous fatty acids:

1. Oleic acid: exits in olive oil.

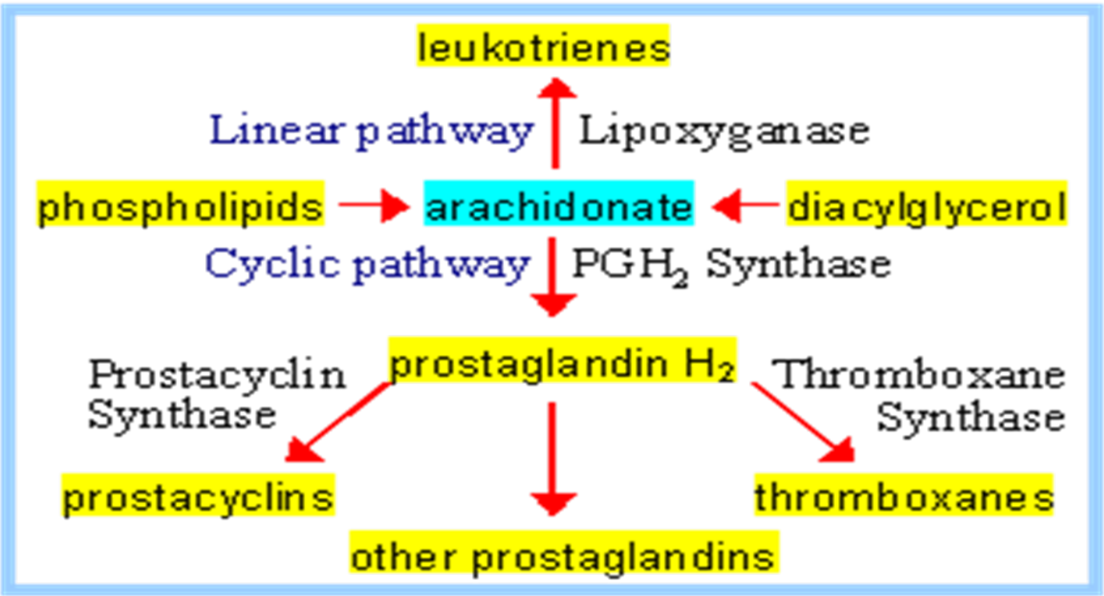
2. Arachidonic acid: important for production of eicosanoids.
3. Linolenic and linoleic fatty acids: they are essential fatty acids meaning we can not synthesize them, we have to take them from food, and they are important for production of arachidonic acid.
   Linolenic acid is also used as a precursor for EPA and DHA.

Derivative of fatty acids:

- **Eicosanoids:** as we established previously the Arachidonic acid is the precursor for all eicosanoids, which is any fatty acids with 20 carbons atoms.
- Systematic name of arachidonic is:
  cis-Δ^5,Δ^8,Δ^{11},Δ^{14}-eicosatetraenoate, $CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO^-$



Pathways for production of eicosanoids:



- From arachidonic acid we produce leukotrienes and prostaglandins (prostacyclin, other prostaglandins and thromboxane)

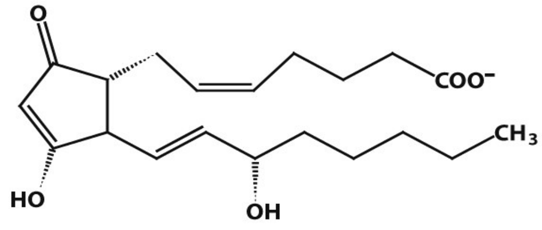
Eicosanoids and their function:

- **Prostaglandins**

- Inhibition of platelet aggregation

(Blood clotting)

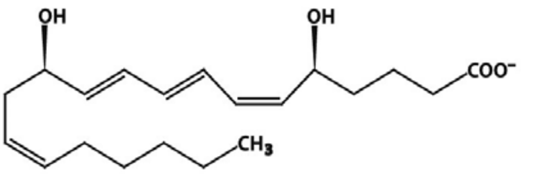
- It was first identified in prostate gland



Prostaglandin E_2

- **Leukotrienes**

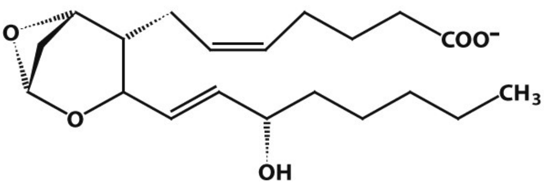
- Constriction of smooth muscles
- Asthma
- It was identified in leucocytes (WBCS)



Leukotriene B_4

- **Thromboxanes**

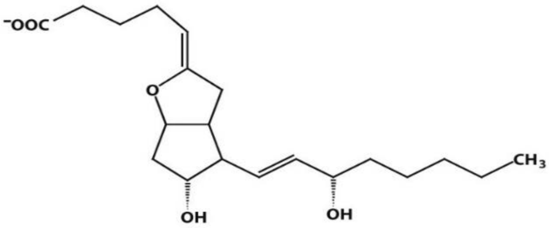
- Constriction of smooth muscles
- Platelet aggregation



Thromboxane A_2 (TXA_2)

- **Prostacyclins**

- An inhibitor of platelet aggregation
- A vasodilator



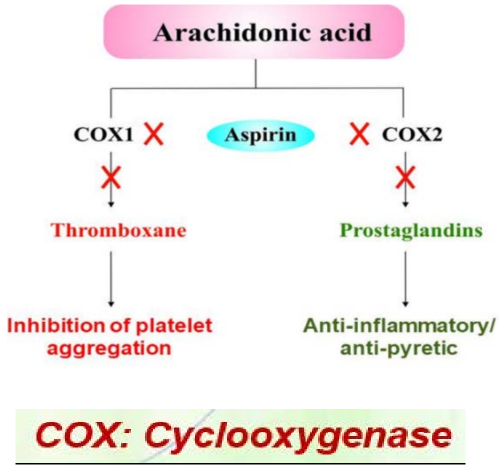
Prostacyclin (PGI_2)

[(Notice that different eicosanoids have different functions, the same eicosanoid (prostaglandins for example) also can have two opposite functions. That's because:
1) there are different types of prostaglandins
2) it also depends on the amount of prostaglandins secreted and where they're being secreted. -> we're talking about homeostasis (keeping a balance)]

Aspirin:

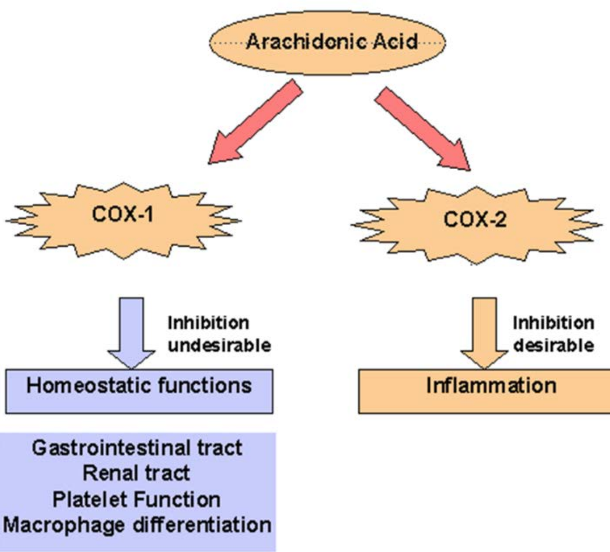
- Cyclooxygenase is present in three forms in cells, COX-1, COX-2, and COX-3.
- Aspirin targets both COX-1 and COX-2.

One of the prostaglandins that aspirin prevents from being synthesized is thromboxane, which is involved in platelet aggregation and blood clotting. This means if you take aspirin daily, it reduces the chance of blood aggregation (formation of blood clots). This is helps preventing diseases caused by blood clots and reduces your chances of getting diseases such as heart attacks and stroke, that's why its recommended for elderly people, who are at higher risk of suffering from those diseases, to take a pill daily.



As mentioned earlier, prostaglandins aren't just involved in inflammation and pain, using aspirin also stops other body functions. For example, it decreases production of the protective mucous which lines the stomach cavity. This results in stomach acid burning through the stomach lining leading to the formation of gastric ulcers and internal bleeding occurring, and as established earlier aspirin is a blood thinner, so this becomes even more dangerous, because a clot is what stops the bleeding when you have a wound. Therefore, it is not recommended for people who have a tendency for developing gastric ulcers, have genetic problems with clotting ,for people who are taking with blood thinner medication, or are prone to bleed easily.

- CELEBREX: A new drug developed by pharmaceutical companies, but is prescribed with a strong warning of side effects on the label. CELBREX is special in the fact that it is a selective-inhibitor of COX2. This means it does not influence the blood aggregation. Celebrex isn't recommended for people who have heart problems as it increases heart rate leading to myocardial infarction.



Omega fatty acids

•Omega-3-fatty acids:

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

(26 carbons fatty acid)

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 Arachidonic acid, ω-6 has many functions such as:

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

•Omega-9 fatty acids(oleic acid):

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.

The End