Lipids

Summer 2023

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.

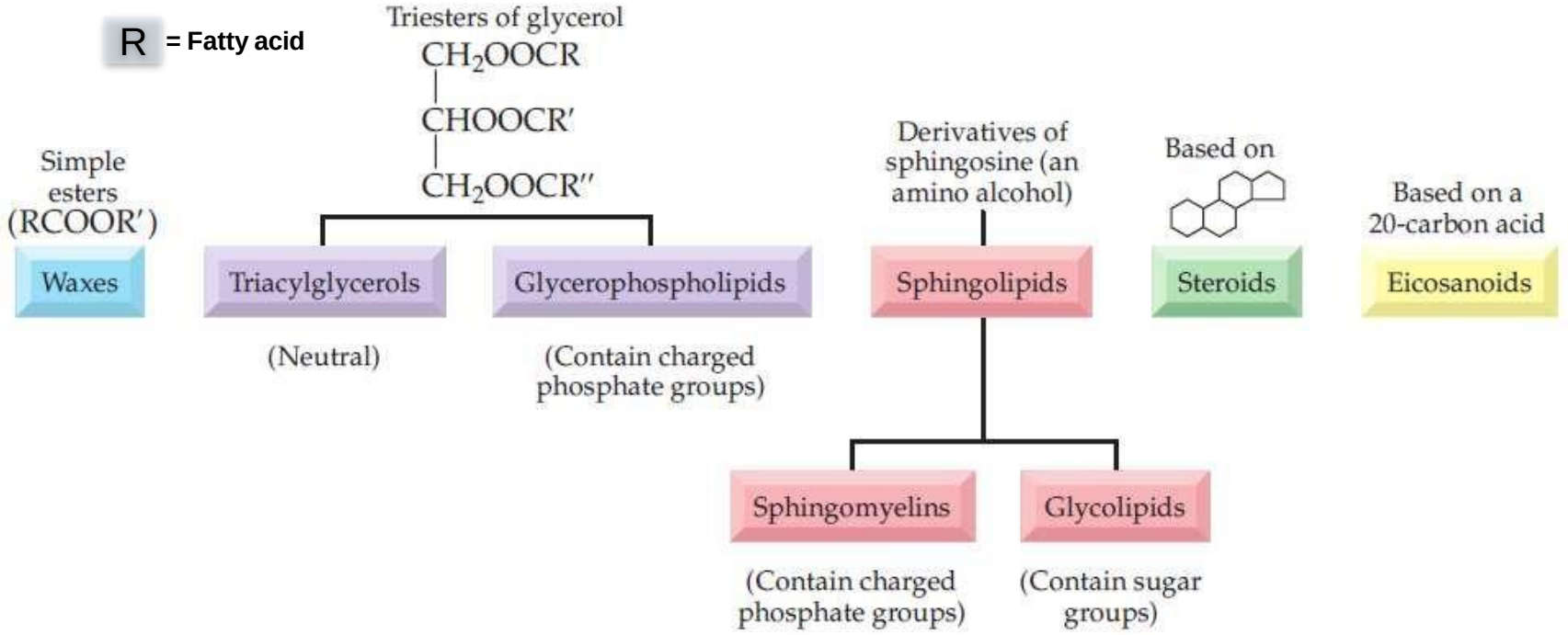
- They are Amphipathic in nature.
- They are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).
- They are widely distributed in plants & animals.

- Adipose tissue protects organs, especially superficial organs like the kidneys. Also, they're found in the heart (but not as much as the kidneys because the heart is protected by the thoracic cage)

Lipids are insoluble while carbohydrates are soluble.
If we want to store the same amount of carbohydrates and lipids, lipids won't attract water molecules while carbohydrates will, this makes them occupy a larger volume.

Classes

- Simple lipids (fats, oils, and waxes)
- Complex lipids (glycerides , glycerophospholipids, sphingolipids, glycolipids, lipoproteins)
- Derived lipids (fatty acids, alcohols, eicosanoids) Eicosanoids are inflammatory mediators, derivative of one of the fatty acids.
- Cyclic lipids (steroids) **Like cholesterol**



Lipid Functions

- Lipids include:
  - Storage lipids
  - Structural lipids in membranes
  - Lipids as signals, cofactors & pigments
- A major source of energy
  - They are storable to unlimited amounts (vs. carbohydrates)
  - They provide a considerable amount of energy to the body (25% of body needs) & provide a high-energy value (more energy per gram vs. carbohydrates & proteins)
- Structural components (cell membranes)
- Precursors of hormones and vitamins Such as :Steroid hormones, sex hormones and aldosterone
- Shock absorbers and thermal insulators

The body stores energy in the form of lipids not carbohydrates, why?
because it gives us more energy
#1 gram lipids = 9 kcal
#1 gram carbohydrates = 4 kcal
On average, for a person weighing 70 kg he will have at least 15 kg lipids.

- Triacylglycerols are the storage form of lipids in adipocytes

- Lipids also give shape for the body
- Structural components (cell membranes)

--> The membrane acts as a barrier for compartmentalization to regulate different biological functions.

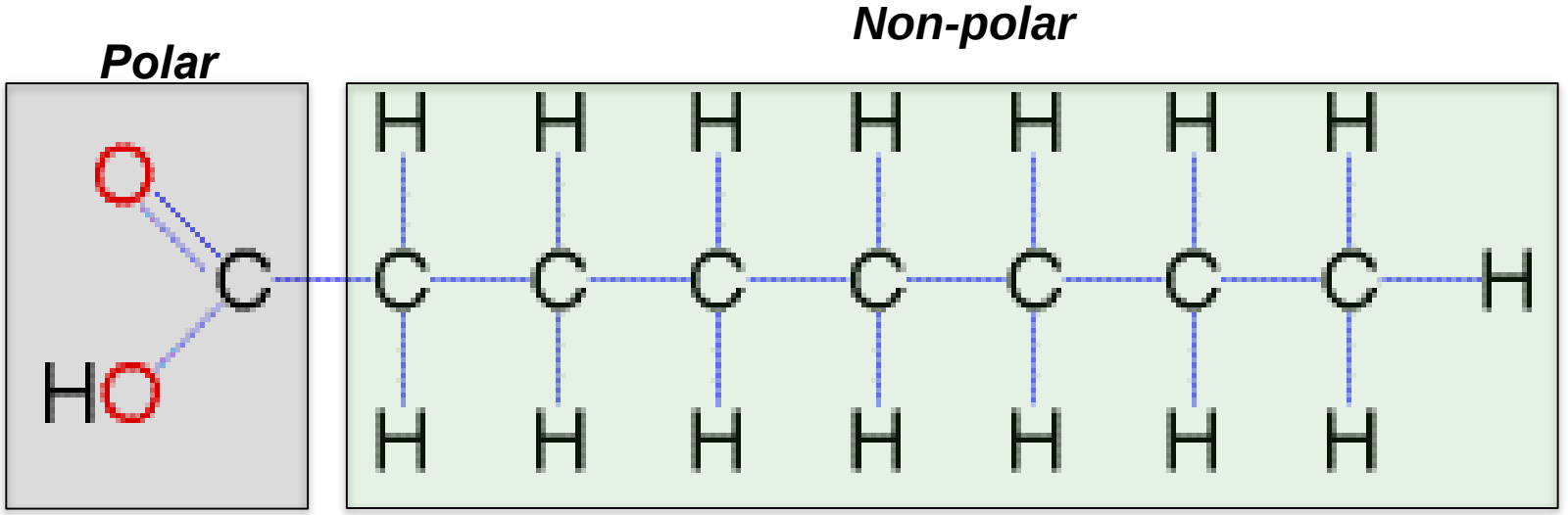
Fatty acids

- Aliphatic mono-carboxylic acids
- Formula: R-(CH_2)n-COOH
- Lengths
  - Physiological (12-24)
  - Abundant (16 and 18)
- Degree of unsaturation
- Amphipathic molecules

Functions:

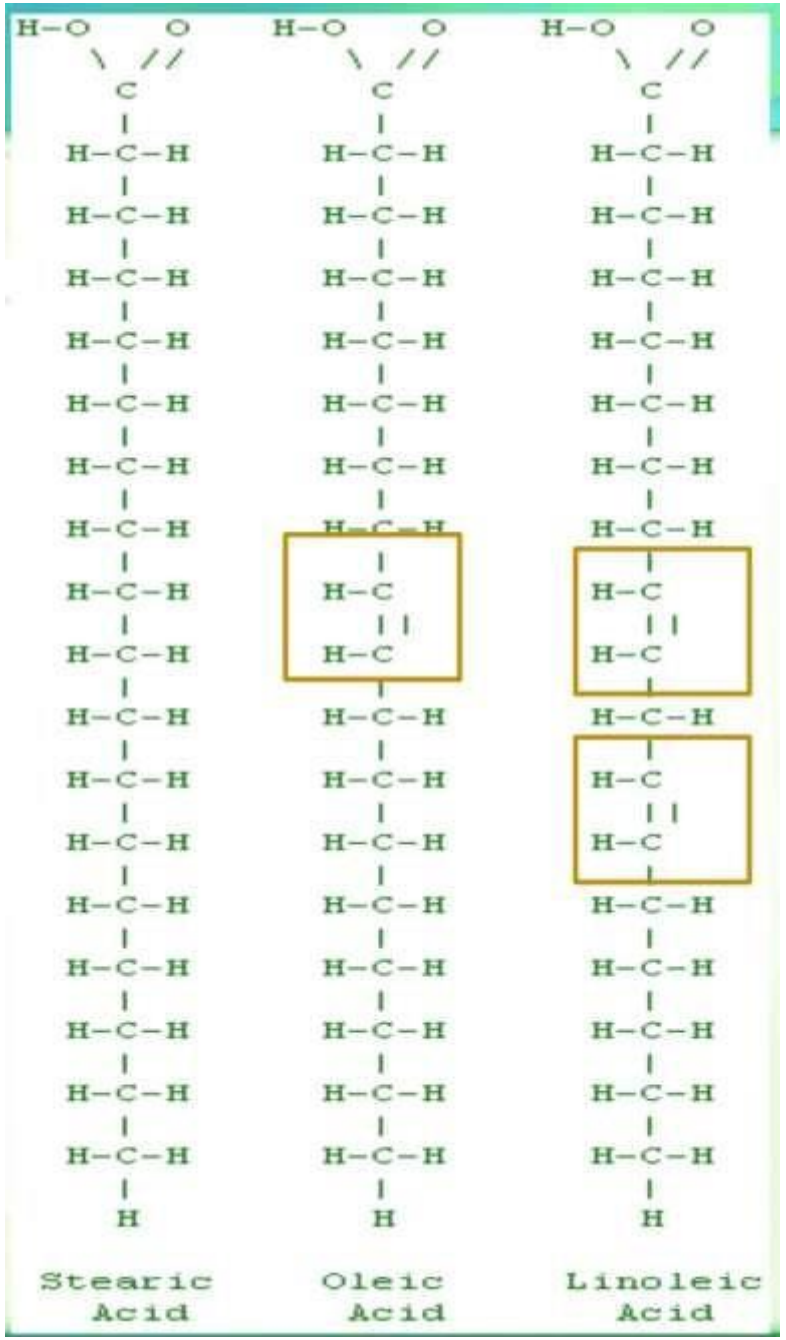
- **Building blocks of other lipids**
- **Modification of many proteins (lipoproteins)**
- **Important fuel molecules**
- **Derivatives of important cellular molecules**

But most of the chain is non-polar.



Types of fatty acids

- Saturated fatty acids are those with all of the 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.



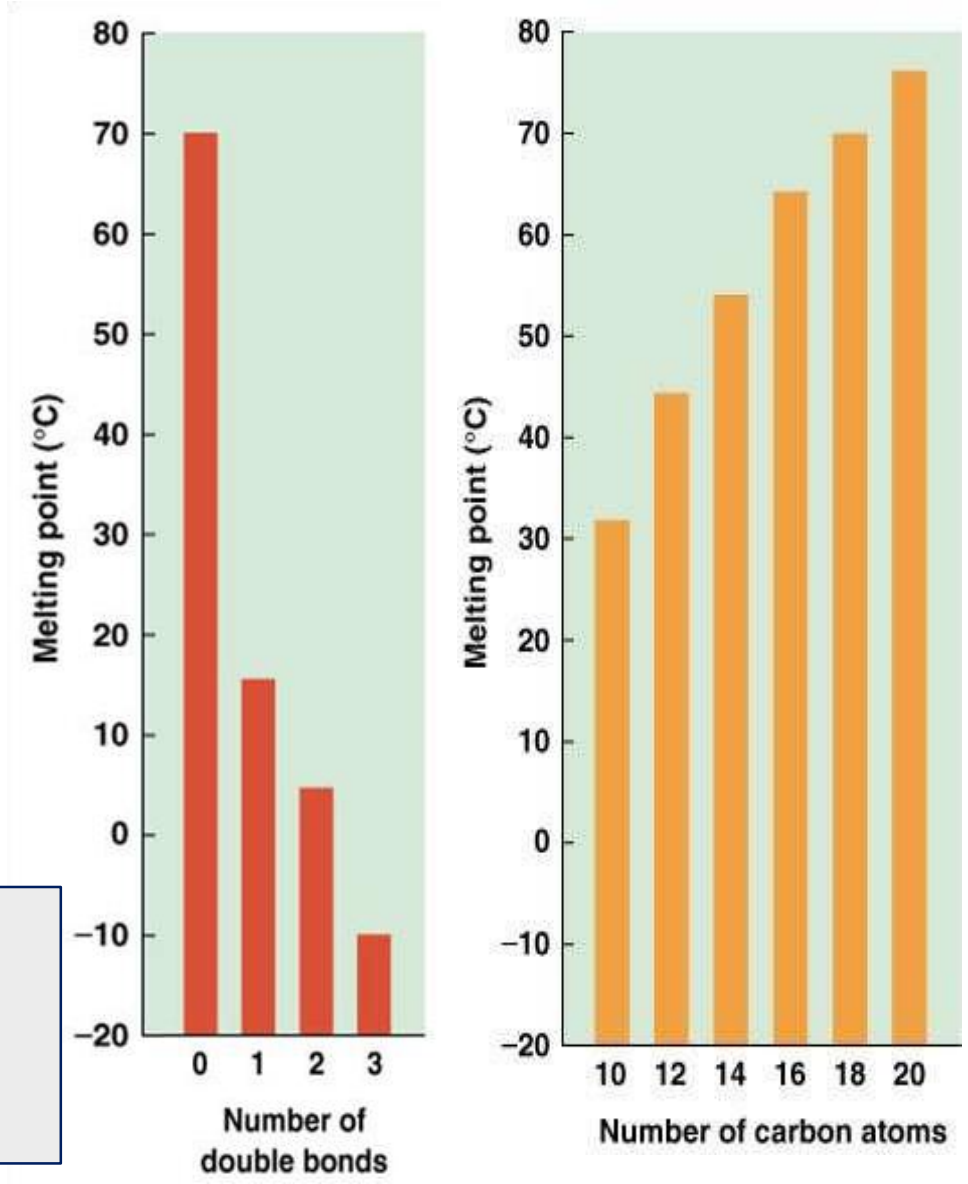
- Fatty acids are carboxylic acids with long R chains.
- Mostly, the number of carbons in the chain are even numbers, ex: (8,10,12)
- In fatty acids chains, there are hydrocarbon chain (non-polar side) and carboxylic group (polar side).
- Saturated and unsaturated molecules will differ in structure and in some physical properties.
- Fatty acids are considered the building or the structural unit of phospholipids.
- Another use for fatty acids is making eicosanoids inflammatory mediator which works during inflammation and fasting conditions.

Properties of fatty acids

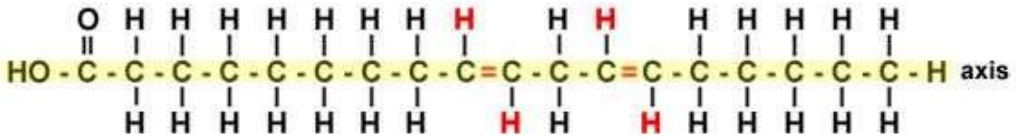
- The properties of fatty acids (melting point) are dependent on chain length and degree of saturation.
- As chain length increases, melting point increases
- As saturation increases (less double bonds) melting point increases
- Double bonds introduce kinks (bending) in the structure causing the melting point to decreases

More carbon molecules will make more non-covalent interactions (ex: hydrophobic interactions).

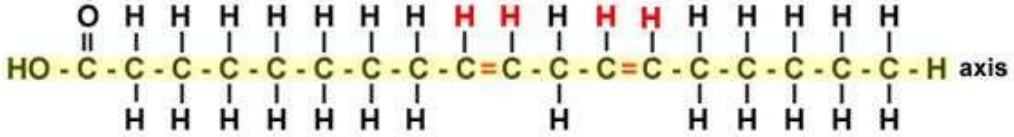
- **Increasing the number of carbons increases the melting point.**
- **Increasing the number of double bonds decreases the melting point.**



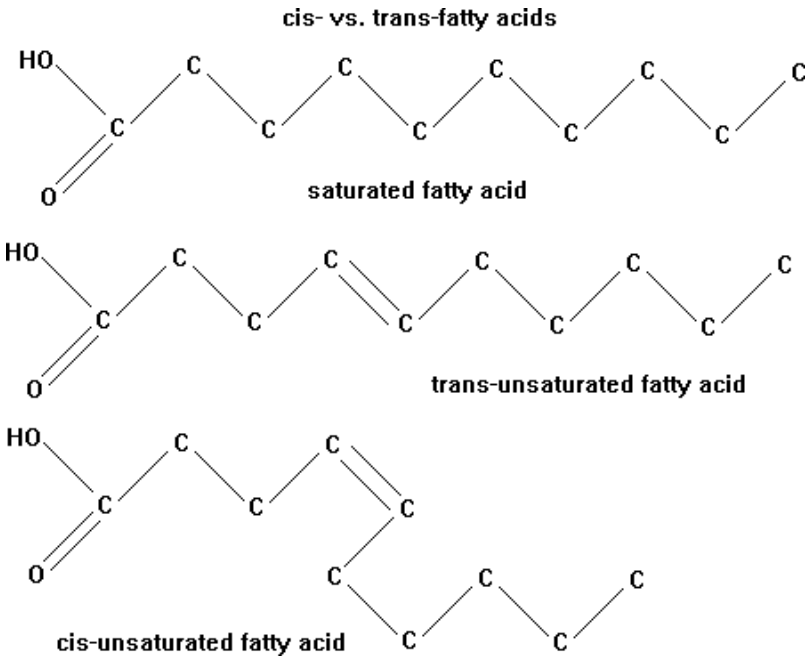
Cis vs. trans bonds

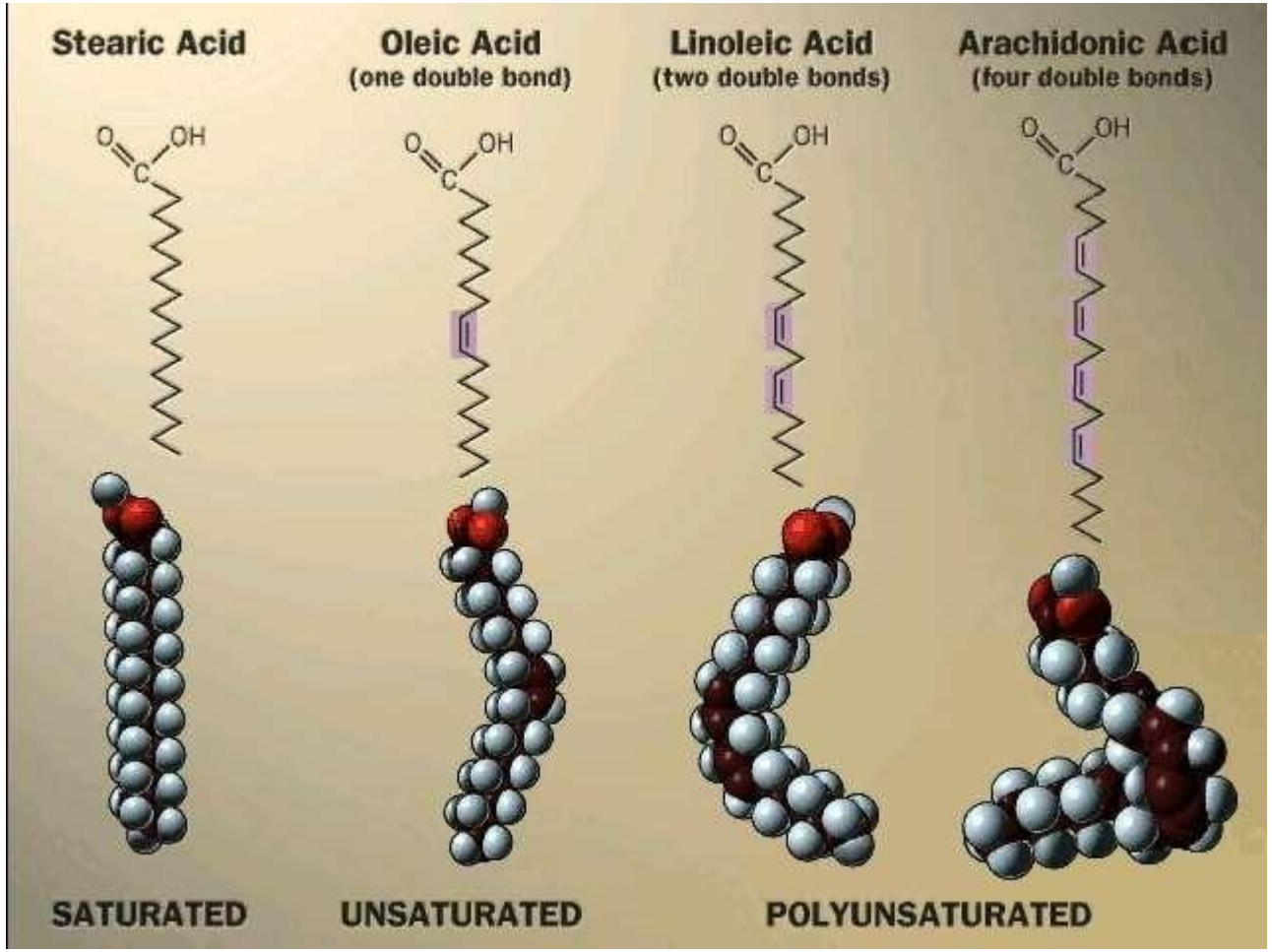


linoleic acid: *trans* configuration (*trans* isomer)



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





Physiologically:

—> cis isomer is more present

—> trans is rare

- The double bond causes a kink in the structure of the unsaturated fatty acid. which effects on its physical properties like its melting point, because these kinks increase the distance between carbon atoms that decreases the noncovalent interactions and making them easier to break.(less heat is needed to break them)
- Generally, oils contain more double bonds than fats and that's why they are in liquid state.
- In cis isomers, the two hydrogen atoms are next to each other. This causes kinks; to give the hydrogen atoms more space.
- In trans isomers, the hydrogens are already far away from each other, so they take a confirmation that's almost very similar to saturated fatty acids.
- Margarine is an example of trans fatty acid.

Properties of saturated fatty acids

Short chain F.A. (2-4)	Medium-chain F.A. (6-10)	Long chain F.A. (12-20)
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

- short chains the effect of carboxylic group is more dominant
- very long chains exist in nervous system

-These are prefixes used to name fatty acids ,similar to how the naming works in Organic chemistry(start numbering form the carbon that has the functional group)

mono means 1 carbon in the chain
di means 2
Octa means 8, and so on

notes for systematic (IUPAC) naming :

1 Count number of carbons in the chain including the carboxyl group

2 Check how many double bonds are present and note its location relative to the carboxyl group (carboxyl carbon is number 1 always)

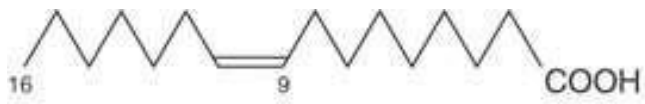
Number	prefix	Number	prefix	Number	prefix
1	Mono-	5	Penta-	9	Nona-
2	Di-	6	Hexa-	10	Deca-
3	Tri-	7	Hepta-	20	Eico-
4	Tetra-	8	Octa-		

Naming of a fatty acid

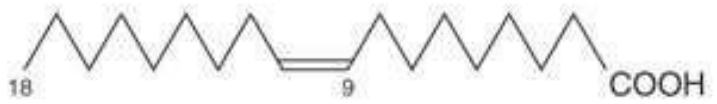
saturated(no double bond)

8 + 10 =18 C

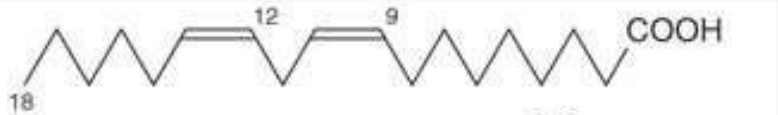
- Alkane to oic
  - Octadecane (octa and deca) is octadecanoic acid
    - One double bond = octadecenoic acid
    - Two double bonds = octadecadienoic acid
    - Three double bonds = octadecatrienoic acid
- Designation of carbons and bonds
  - 18:0 = a C18 fatty acid with no double bonds
    - stearic acid (18:0); palmitic acid (16:0)
  - 18:2 = two double bonds (linoleic acid)
- Designation of the location of bonds
  - Δn: The position of a double bond
    - cis-Δ9: a cis double bond between C 9 and 10
    - trans-Δ2: a trans double bond between C 2 and 3



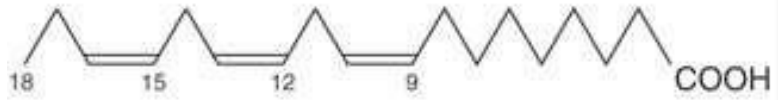
Palmitoleic acid (ω7, 16:1, Δ^9)



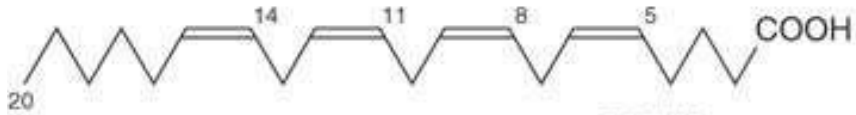
Oleic acid (ω9, 18:1, Δ^9)



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



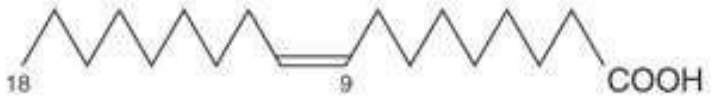
*α-Linolenic acid (ω3, 18:3, $\Delta^{9,12,15}$)



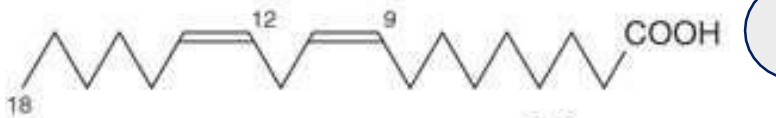
*Arachidonic acid (ω6, 20:4, $\Delta^{5,8,11,14}$)

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

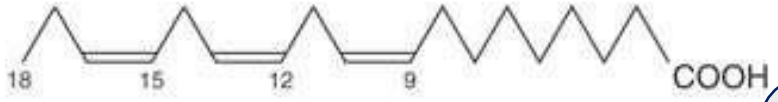
Palmitoleic acid (ω7, 16:1, Δ^9)



Oleic acid (ω9, 18:1, Δ^9)



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

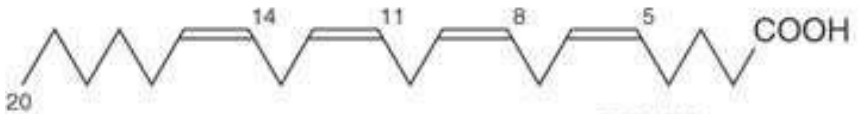


*α-Linolenic acid (ω3, 18:3, $\Delta^{9,12,15}$)

1

2

-These are Essential Fatty acids ,meaning that they can only be obtained from food, and can't be synthesized in the body.



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

-precursor to eicosanoids ,can be found in lard(from pigs),and can be synthesized by the body.

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

-Memorize the names with their descriptions

1

1- Number of carbons: 18 Number of double bonds: 2
The location of the double bond between : carbon 9 and 10 carbon no. 12 and 13

2

2- Number of carbons: 18
Number of double bonds: 3
The location of the double bond
is between carbon no. 9 and 10 carbon no. 12 and 13 carbon no. 15 and 16

The Most founded fatty acids

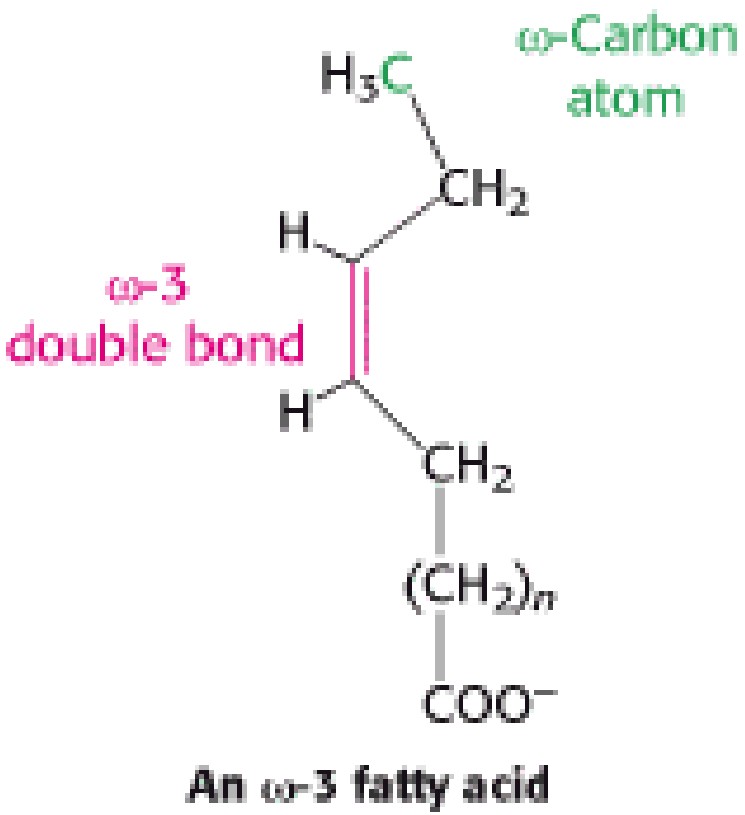
Number of carbons	Number of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	n-Octadecanoate	$CH_3(CH2)_{16}COO^-$
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH=CH(CH_2)_7COO^-$
18	2	Linoleate	cis,cis-Δ^9,Δ^{12}-Octadecadienoate	$CH_3(CH_2)_4CH=CHCH_2CH(CH_2)_7COO^-$
18	3	Linolenate	all-cis-$\Delta^9,\Delta^{12},\Delta^{15}$-Octadecatrienoate	$CH_3CH_2(CH=CHCH_2)_3(CH_2)_6COO^-$
20	4	Arachidonate	all-cis-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-Eicosatetraenoate	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COO^-$

-know the common names of fatty acids!!
The doctor said memorize the structure and try to name them if you are given the structure only

Another way of naming : Omega

(Begin counting from the opposite side to the carboxyl group to the first double bond you find)

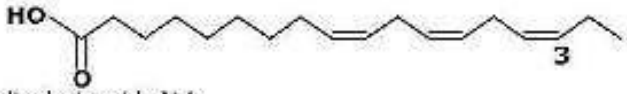
- (ω)-C: distal methyl C as #1



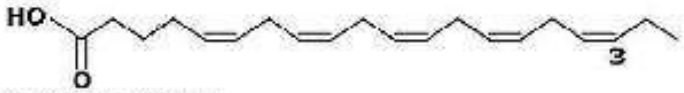
An ω-3 fatty acid

Per softgel		
Organic Flaxseed Oil (Linseed Oil)		400mg
Pure Fish Oil		400mg
Starflower Oil (Borage Oil)		400mg
typically providing:		
Alpha Linolenic Acid (ALA)	Omega-3	200mg
Docosahexaenoic Acid (DHA)	Omega-3	48mg
Eicosapentaenoic Acid (EPA)	Omega-3	72mg
Gamma Linolenic Acid (GLA)	Omega-6	88mg
Linoleic Acid (LA)	Omega-6	204mg
Oleic Acid	Omega-9	168mg

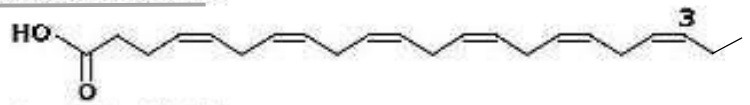
Omega-3 fatty acids



Alpha-linolenic acid ALA

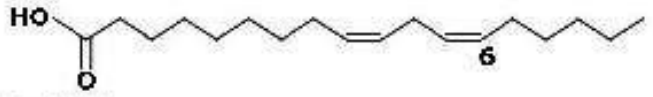


Eicosapentaenoic acid EPA

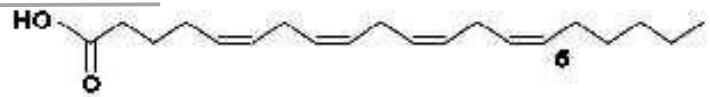


Docosahexaenoic acid DHA

Omega-6 fatty acids



Linoleic acid LA



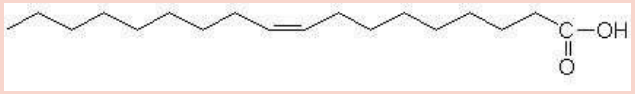
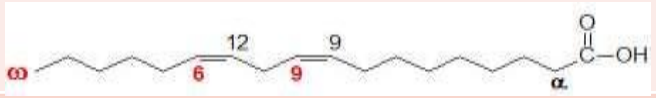
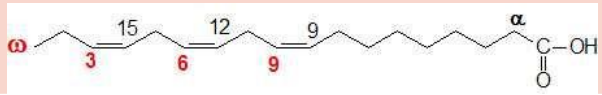
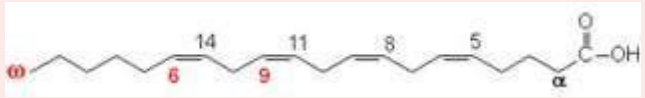
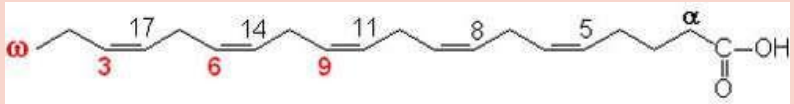
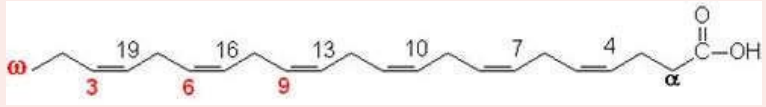
Arachidonic acid AA

- **Linoleic acid: precursor of arachidonates**
- **Linolenic acid: precursor of EPA and DHA**

-this type of naming is used because each type has similar functions;omega-3 fatty acids all have similar functions to each other ,they are very useful l to the brain/CNS

Naming with (omega): Start counting from the other side of the carboxylic group until you reach the double bond. this naming doesn't give information about the number of double bonds. Then why do we use this naming style? Because molecules that have the same name (omega 3 for example) are found to have similar functions.

- Linoleic acid and Linolenic acid are very important acids that must be a part in our diets .

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)

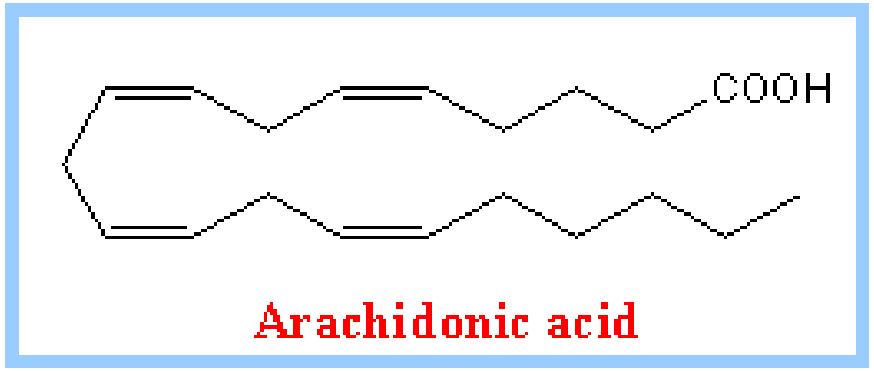
Derived fatty acids: Eicosanoids

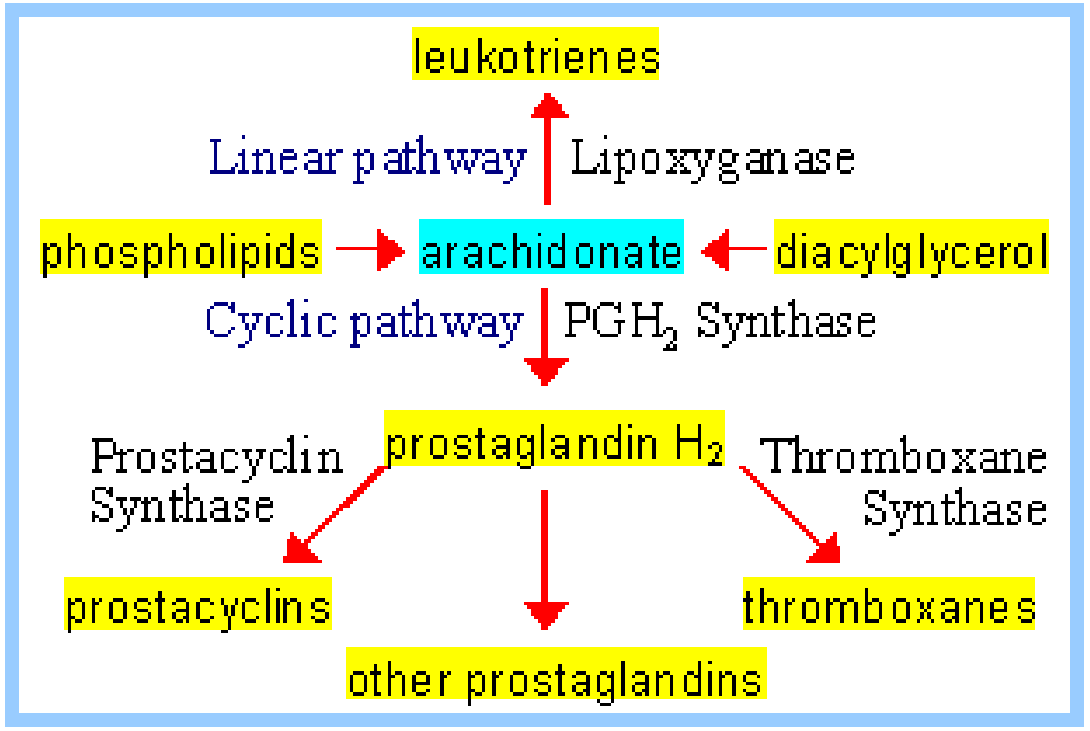
(Eicosanoids derived from arachidonic acid that's poly unsaturated fatty acid)

Arachidonate

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

There are different pathways(cyclic pathway and linear pathway)for Arachidonate occur as a result of many modifications(like adding functional groups or formation of cycles) without removing or adding more C

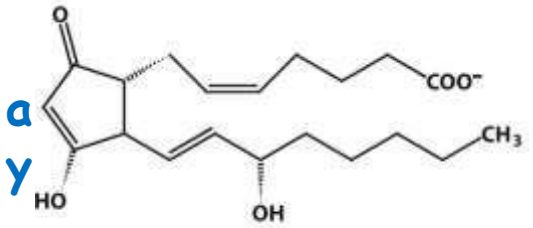




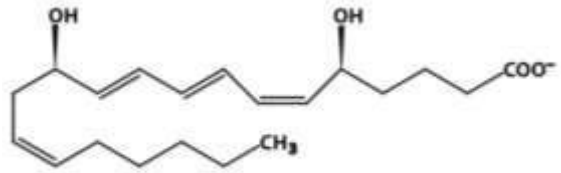
Eicosanoids and their functions

They control cellular function in response to injury

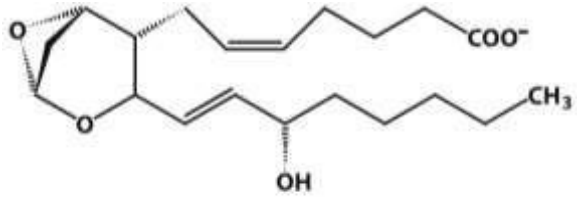
- Prostaglandins. they were discovered first in prostate ➔ cyclic pathway
  - Induction of inflammation
  - Inhibition of platelet aggregation blood coagulation
    - Inhibition of blood clotting
- Leukotrienes they were discovered first in white blood cells ➔ linear pathway
- Leukotrienes : 3 conjugated double bonds
  - Constriction of smooth muscles
    - Asthma Asthma drugs inhibit Leukotrienes to dilate the muscle
- Thromboxanes mostly in blood vessels
  - Constriction of smooth muscles
  - Induction of platelet aggregation
- Prostacyclins. relaxation of smooth muscles
  - An inhibitor of platelet aggregation
  - Induction of vasodilation



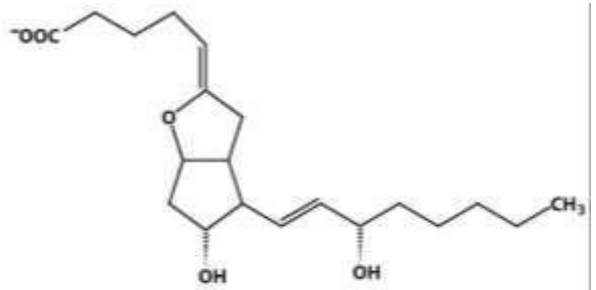
Prostaglandin E_2



Leukotriene B_4



Thromboxane A_2 (TXA_2) Cyclic ether



Prostacyclin (PGI_2)

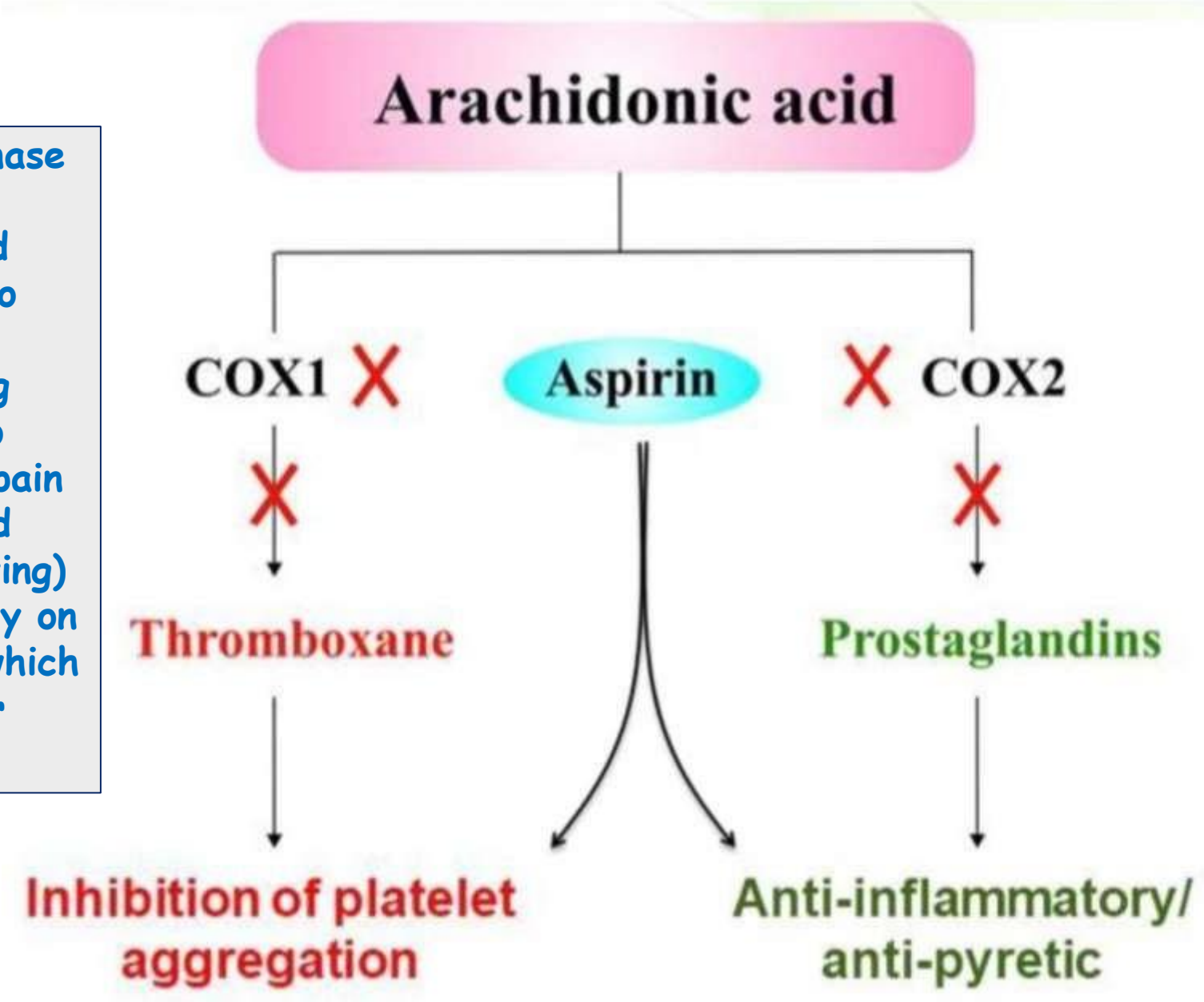
More than one cycle

Eicosanoids and their functions

They control cellular function in response to injury

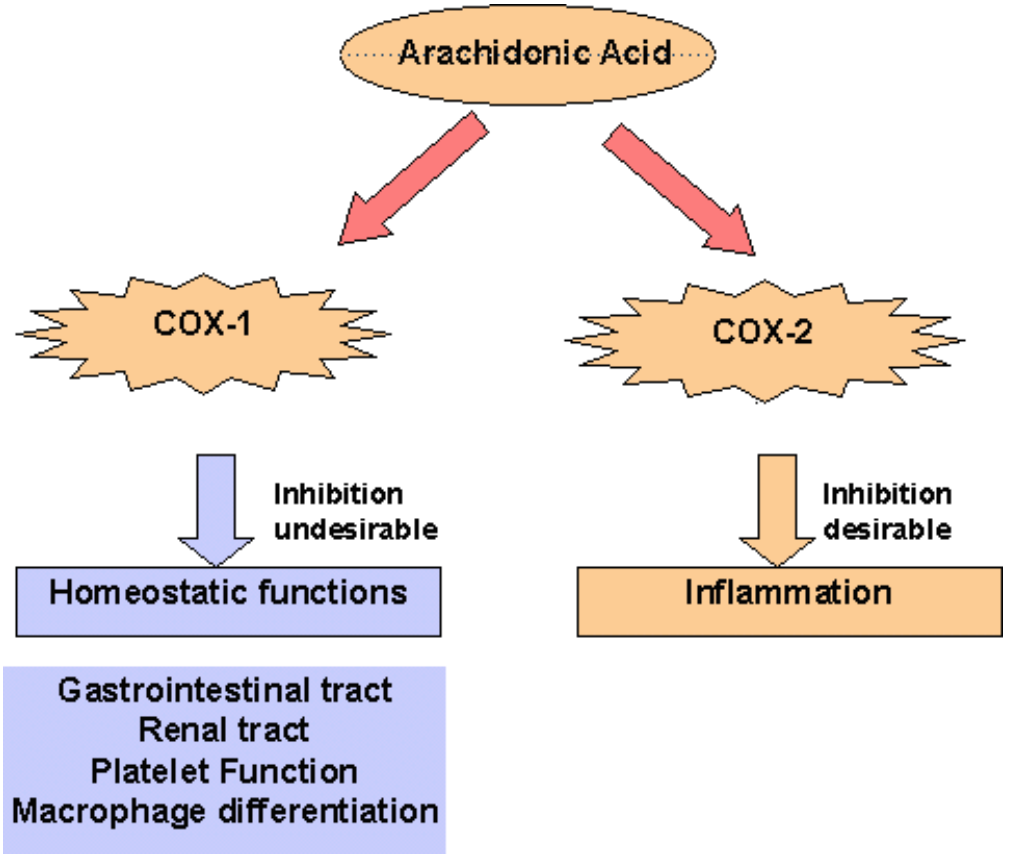
(inflammatory mediators) Inflammation increases blood flow and permiability of the blood vessels . As a result redness , swelling (edema) , heat and pain occur.

COX : cyclooxygenase
Aspirin acts as inhibitor COX1 and COX2 enzymes , so aspirin is anti-inflammatory drug that can be use to reduce fever and pain also prevents blood aggregation (clotting)
Aspirin can act only on COX1 and COX2 which leads to stop their functions too



Targets of Aspirin

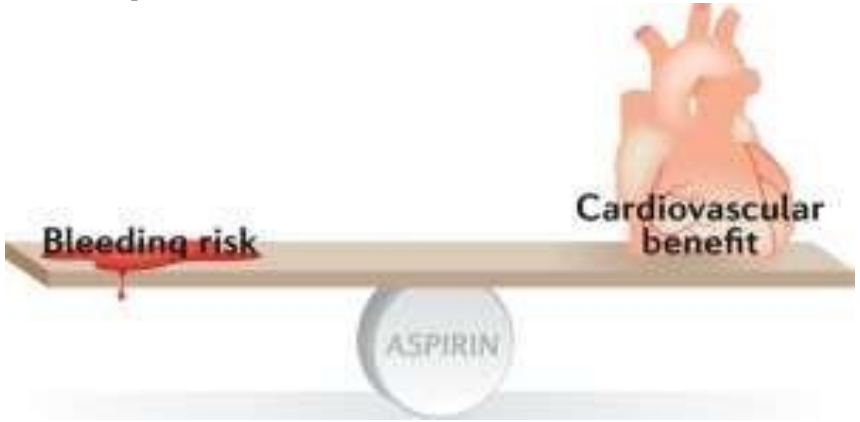
- Cyclooxygenase is present in three forms in cells, COX-1, COX-2, and COX-3.
- Aspirin targets both, but COX-2 should only be the target.

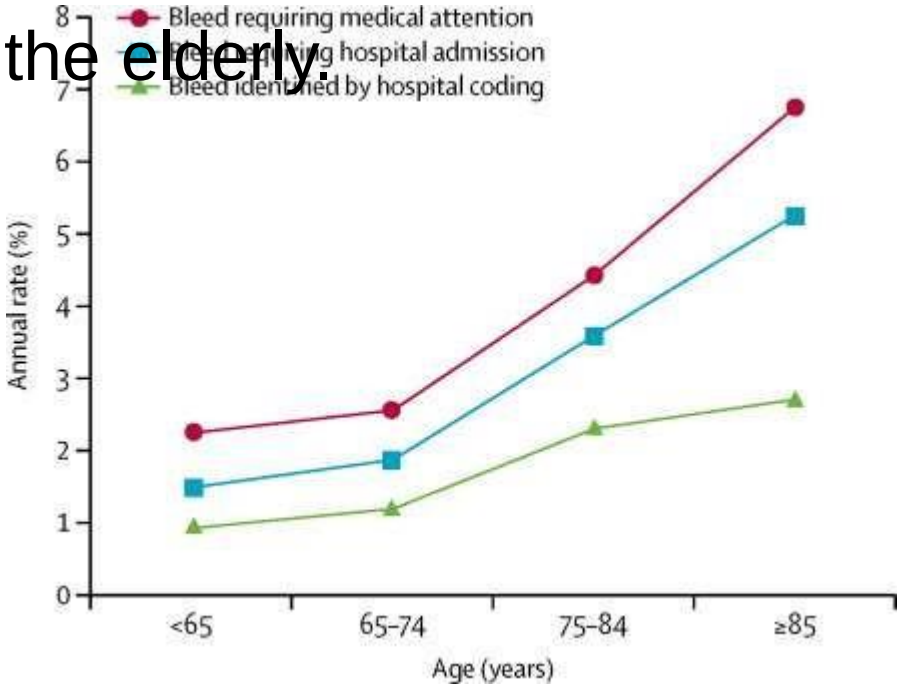


Why the inhibition of COX2 is desirable ? To reduce inflammation and it's symptoms

Aspirin is bad Cardiovascular disease vs. bleeding

- Aspirin also causes excessive bleeding among the elderly.





Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events: a population-based cohort study

Linxin Li*, Olivia C Geraghty*, Ziyah Mehta, Peter M Rothwell, on behalf of the Oxford Vascular Study

Interpretation In patients receiving aspirin-based antiplatelet treatment without routine PPI use, the long-term risk of major bleeding is higher and more sustained in older patients in practice than in the younger patients in previous trials, with a substantial risk of disabling or fatal upper gastrointestinal bleeding. Given that half of the major bleeds in patients aged 75 years or older were upper gastrointestinal, the estimated NNT for routine PPI use to prevent such bleeds is low, and co-prescription should be encouraged.

Celebrex

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

Cardiovascular Risk

- CELEBREX may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See **WARNINGS** and **CLINICAL TRIALS**).

- CELEBREX is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see **WARNINGS**).