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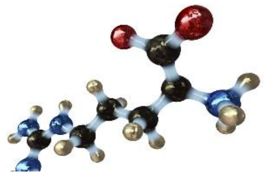


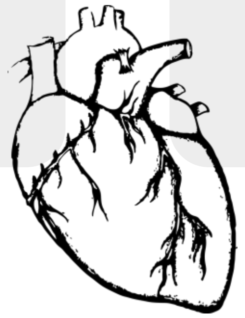
BioChemistry

﴿وَلَقَدْ خَلَقْنَا ٱلْإِنسَٰنَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِۦ نَفْسُهُۥ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ ٱلْوَرِيدِ﴾

MID | Lecture 9

Lipids pt.1 &2

Written by : Muhannad Barhoom
Nezar Alsabatin
Ahmad Mohy



Reviewed by : Yamen Aljarrah

Color coding used in the modified:

- *Black: the original slides*
- *Navy Blue: the doctor's explanation/words*
- *Gray: additional information and explanation*
- *Red: important information*

Lipids

Prof. Mamoun Ahram

Lipids

They aren't uniform (unequal distribution)

- Lipids are a heterogeneous class of naturally occurring organic compounds that share some properties based on structural similarities, mainly a dominance of nonpolar groups.

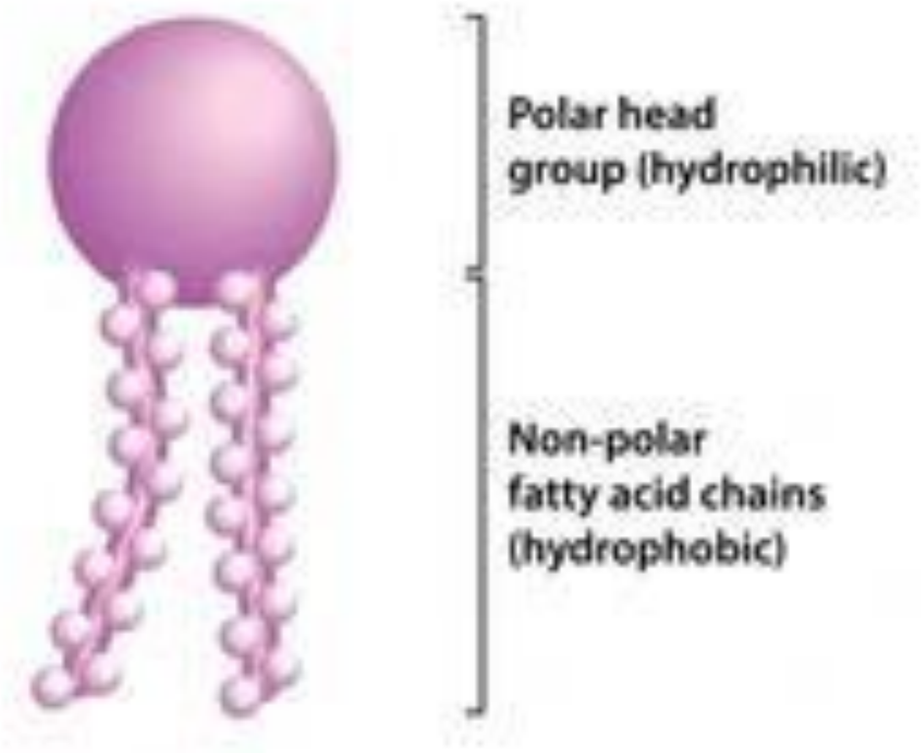
Even though these molecules aren't uniform ,what makes them belong to the class of lipids is that all of them are hydrophobic(lipophilic).

- They are Amphipathic.

This Molecule has two parts hydrophillic (water, loving)and hydrophobic (water hating).
They do not have to be in the same size.Maybe the hydrophillic part is smaller than the hydrophobic one But you can still differentiate between them

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

Macromolecules:
1-proteins: polymers made from amino acids.
2-Sugars are polymers made from monosccharide residues.
3-Nucleic acids are polymers made from neucleotides.
4-lipids aren't considered polymers because there aren't repeating units of a substance to be considered a polymer, though it's still a macromolecule.

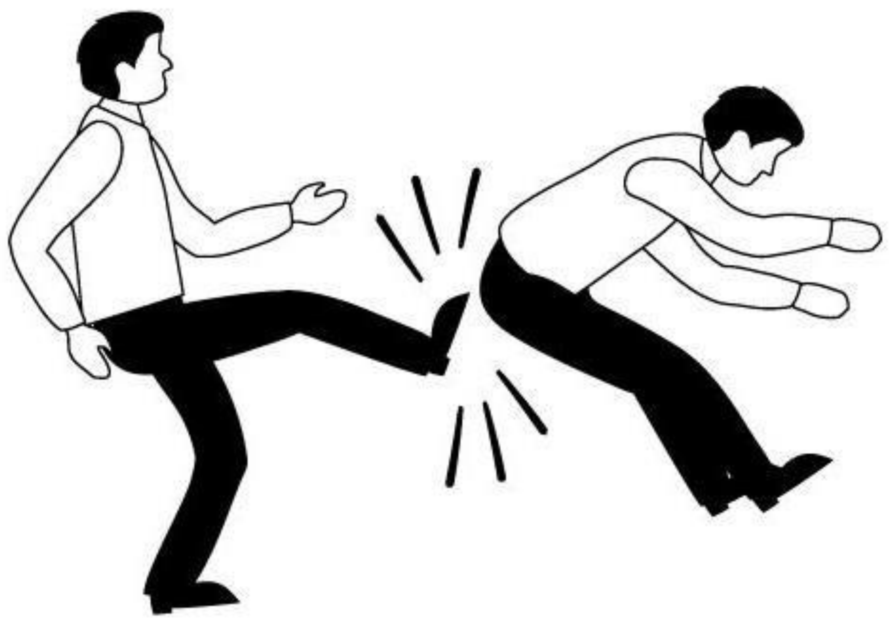


Lipid Functions

We can store more energy in a lipid Molecules, then sugar molecules And this is because lipid molecules are more reduced , meaning they have more electrons . Unlike sugar molecules Which have oxygen that decreases the number of effective electrons.

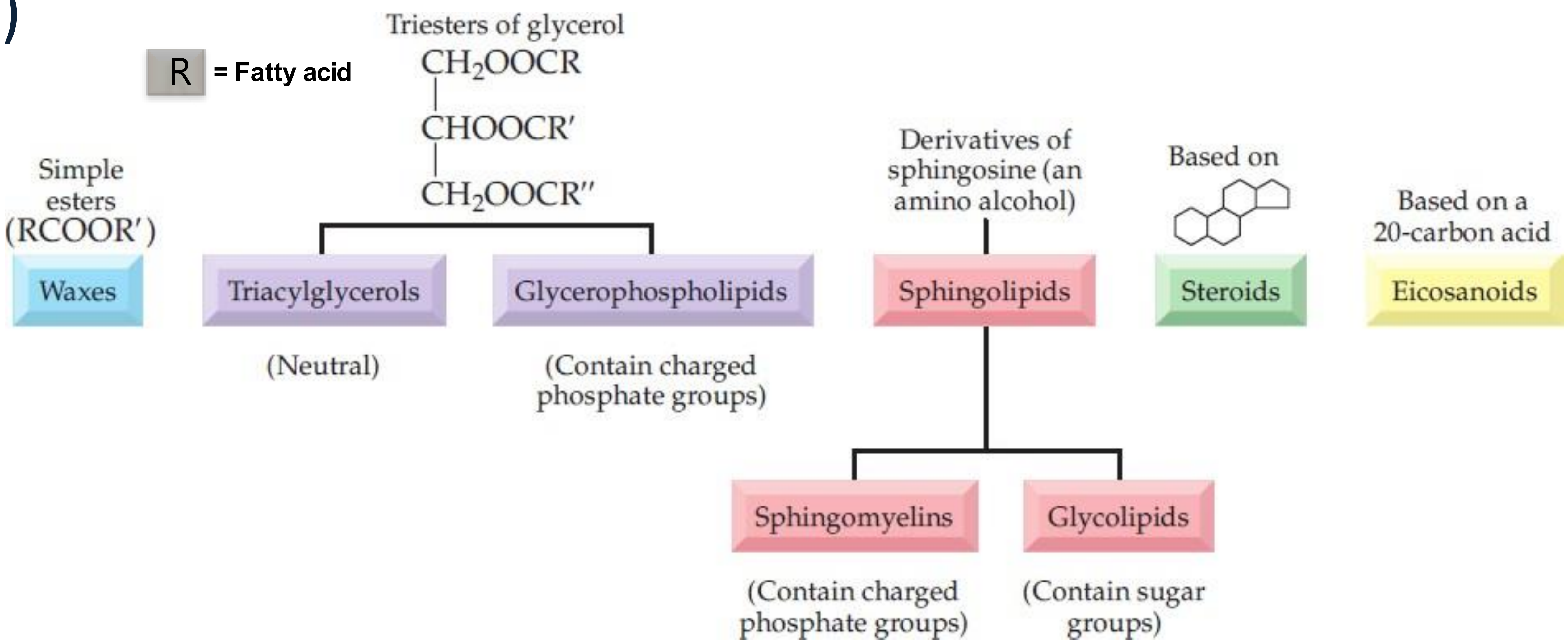
- Lipids include:
  - Storage lipids for energy purpose
    - They are storable to unlimited amounts (vs. carbohydrates)
    - They provide a considerable amount of energy to the body (25% of body needs) &
    - provide a high-energy value (more energy per gram vs. carbohydrates & proteins)
  - Structural lipids in membranes
- Signaling molecules, hormone precursors, cofactors, & pigments Shock absorbers and thermal insulators

They protect internal organs



Classes

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



Fatty acids

Nearly present in all of lipids

Chain of carbon and hydrogen

1 Terminal -COOH

- Aliphatic mono-carboxylic acids
- Formula: R-(CH_2)n-COOH
- Lengths Including the carbon on the carboxylic group
  - Physiological (12-24)
  - Abundant (16 and 18) The most abundant.
- Degree of unsaturation Number of double bonds in the hydrocarbon chain.
- Amphipathic molecules

They differ in the degree of saturation

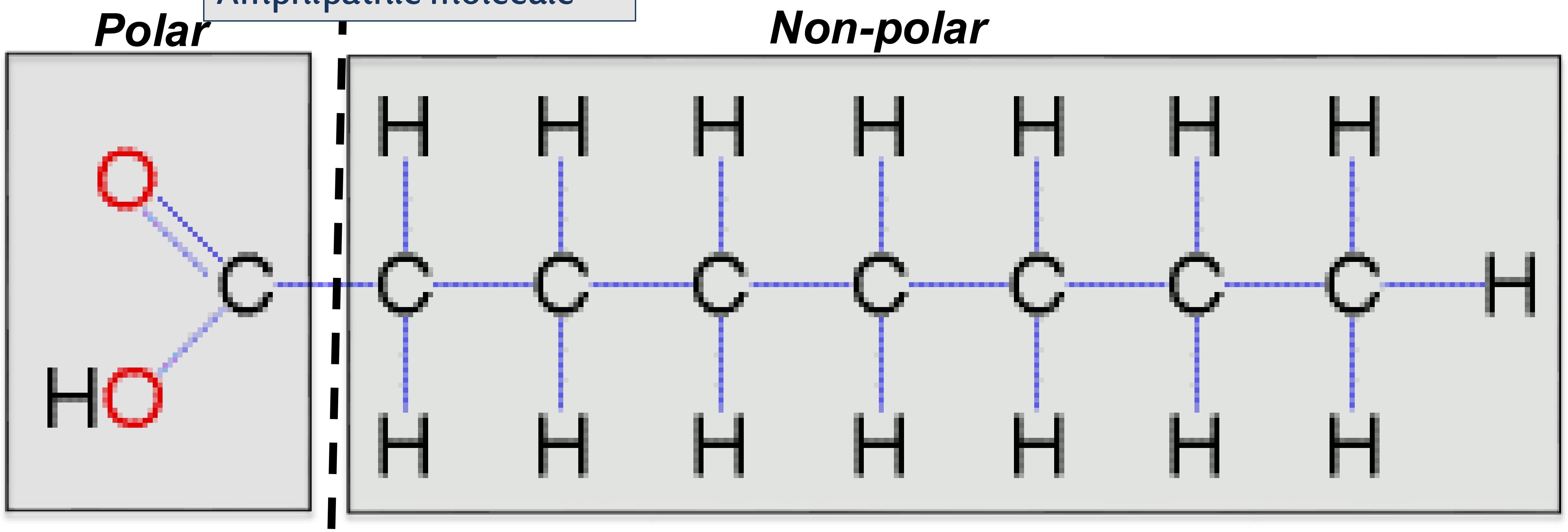
Functions:

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

Saturated molecule means it has the maximum number of hydrogen atoms bound to carbons.

Unsaturated molecule means that we can add more hydrogen to it due to the presence of double bonds.

Amphipathic molecule

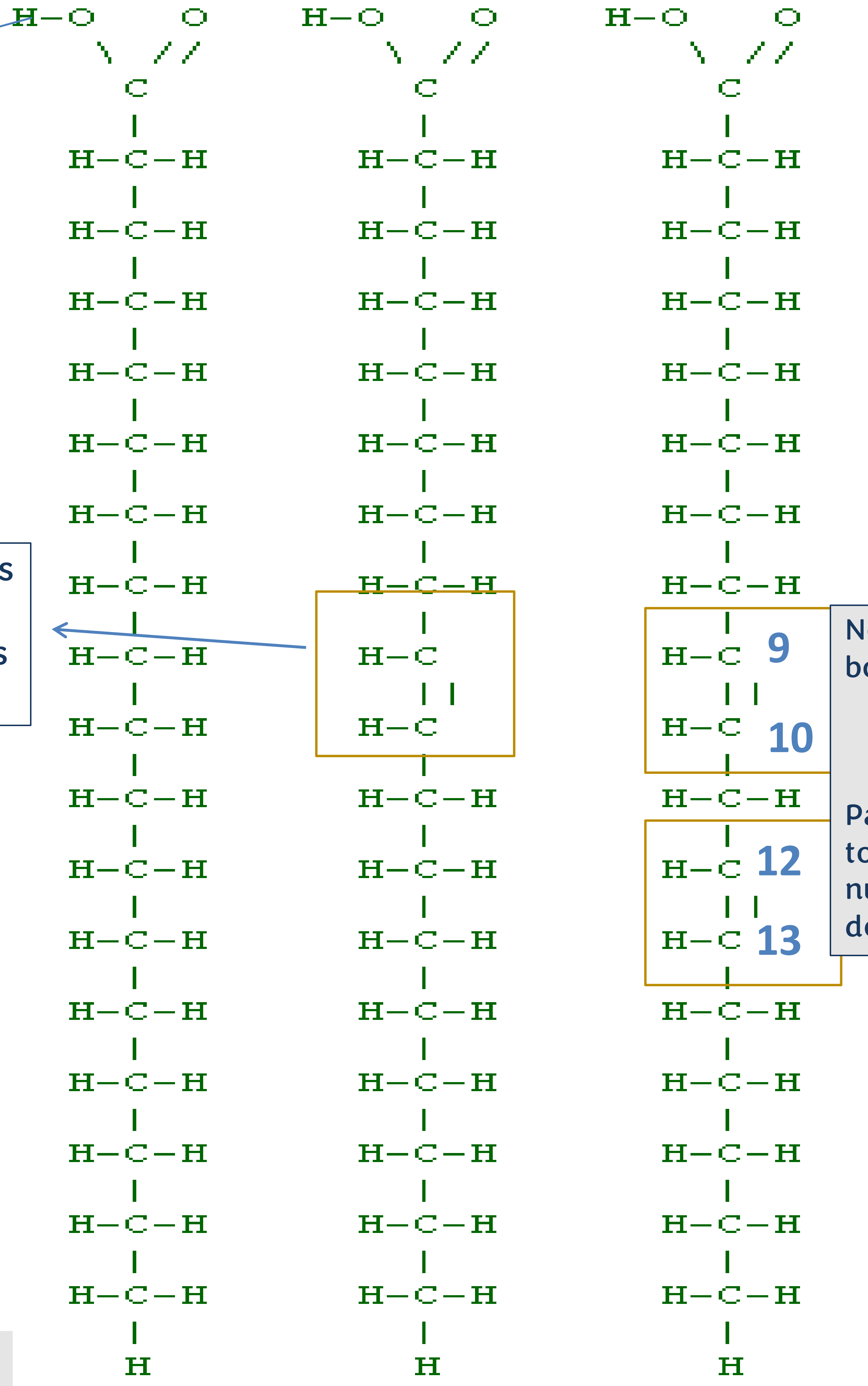


Types of fatty acids

- 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.

If unprotonated we call it sterate

The double bonds in oleic acid is between carbons 9 and 10.



Stearic Acid

Oleic Acid

Linoleic Acid

Notice that all bonds are cis

Pay attention to the numbering of double bonds

-Stearic acid: saturated, 18 carbons long and no double bonds.

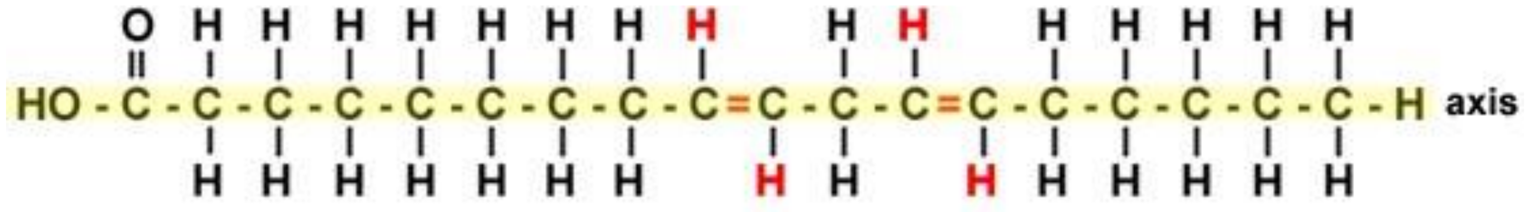
-Oleic acid: monounsaturated , 18 carbons long , one double bond.

-Linoleic acid : polyunsaturated , 18 carbons long and 2 double bonds.

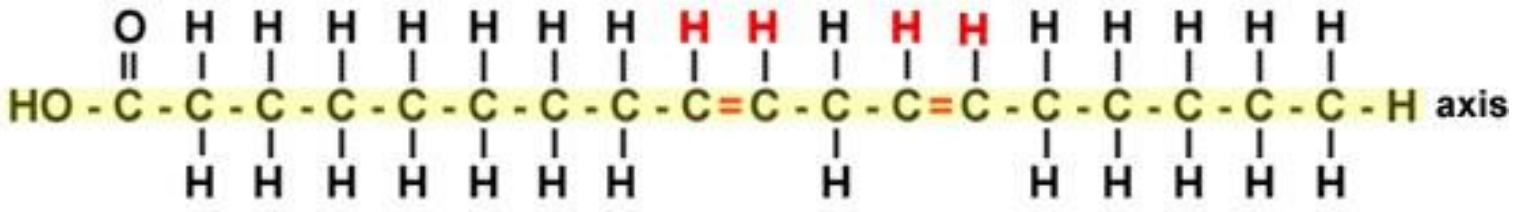
You should know the structure and the name of the fatty acids in this slide !!

Cis vs. trans bonds

In the opposite direction



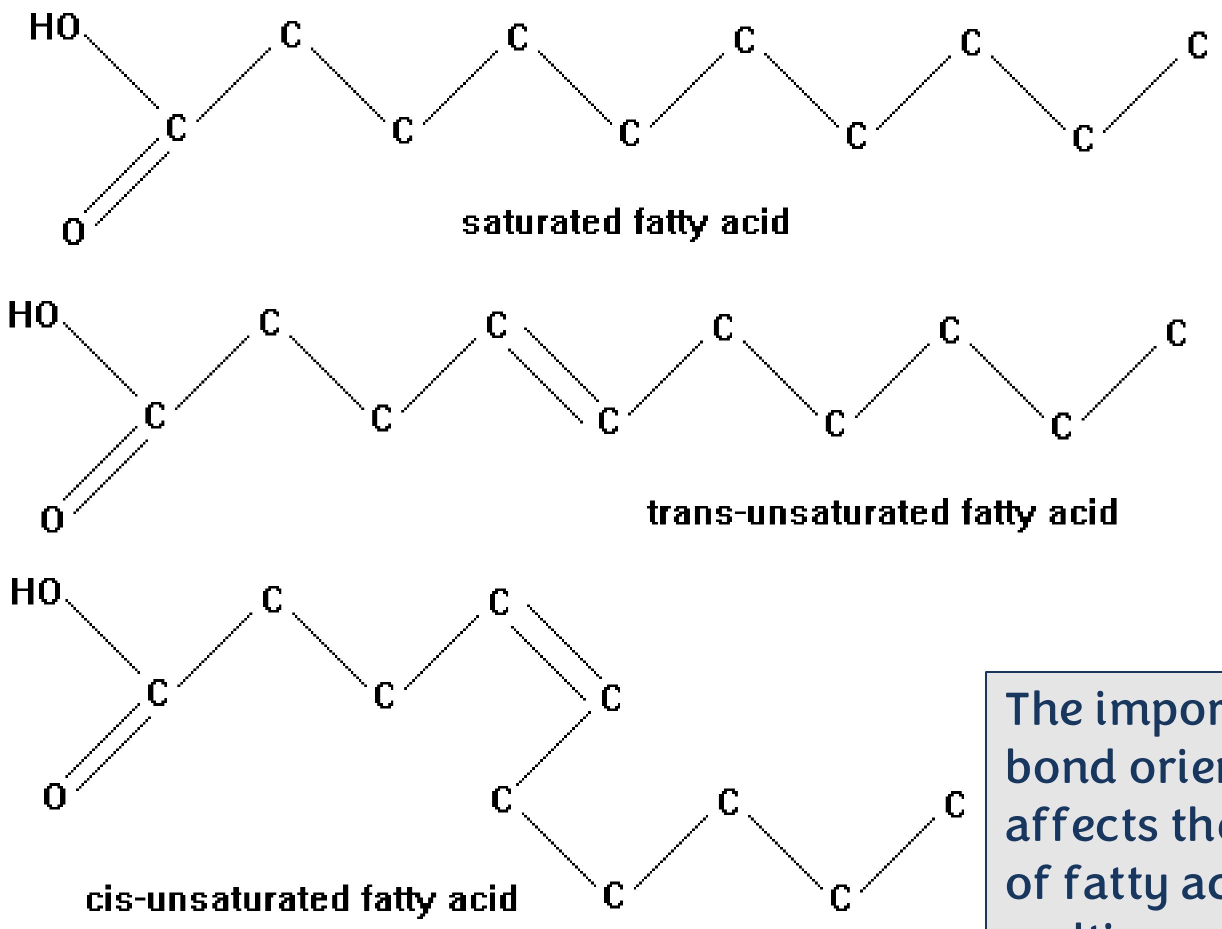
linoleic acid: *trans* configuration (*trans* isomer)

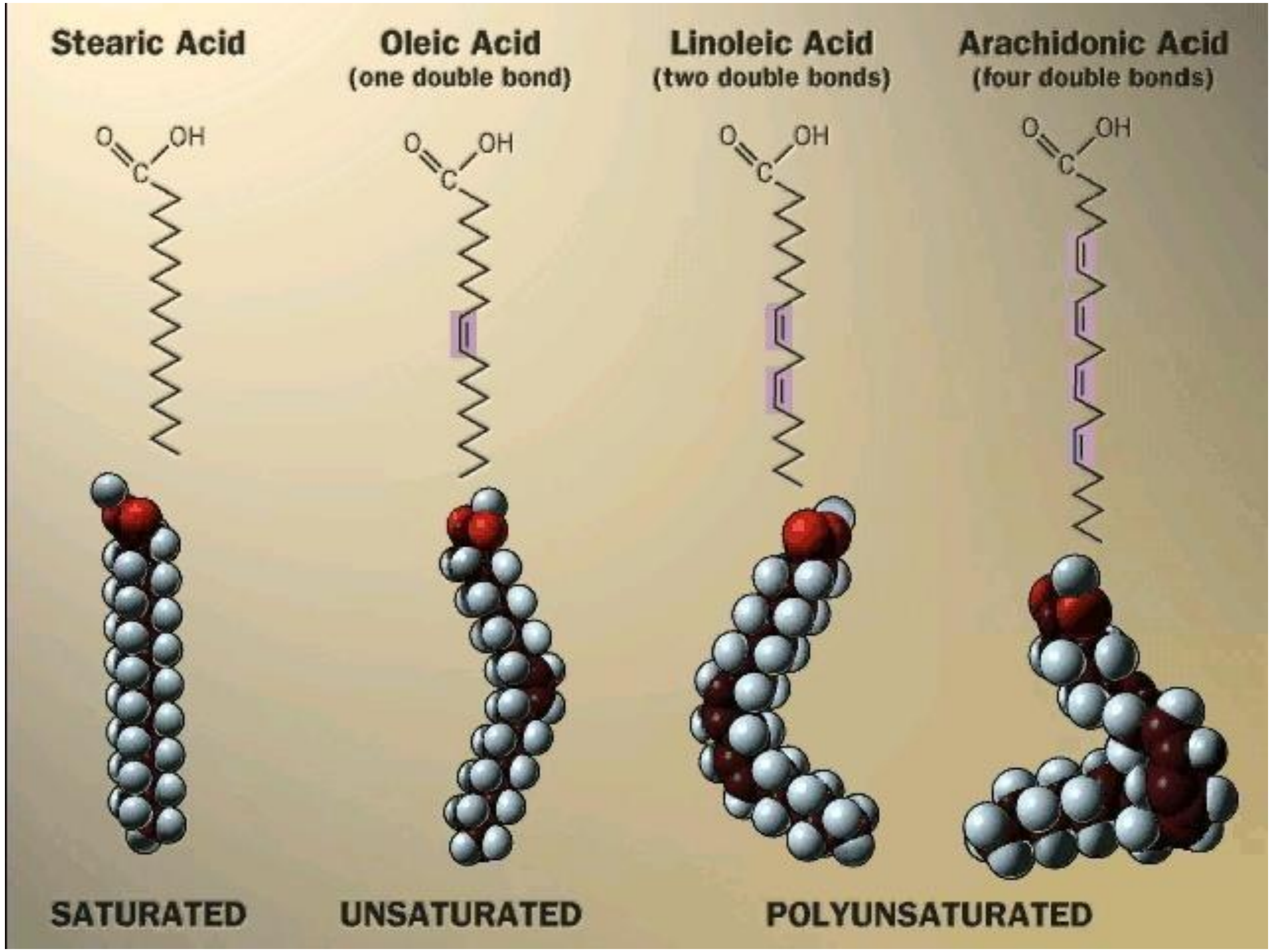


linoleic acid: *cis* configuration (*cis* isomer)

In the same direction

cis- vs. trans-fatty acids





The importance of the double bond orientation is that it affects the physical properties of fatty acids especially the melting point.

Physiologically: Important

- **cis isomer predominates**
- **trans is rare**

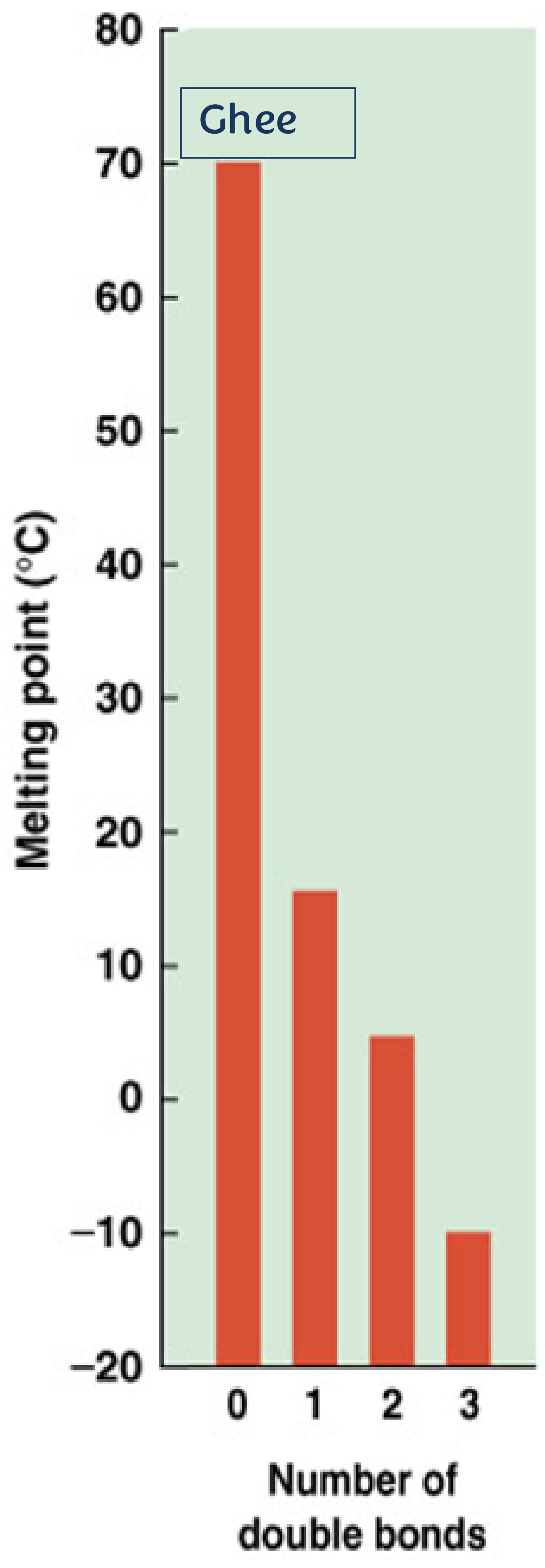
The more double bonds the molecule has, the kinkier it appears

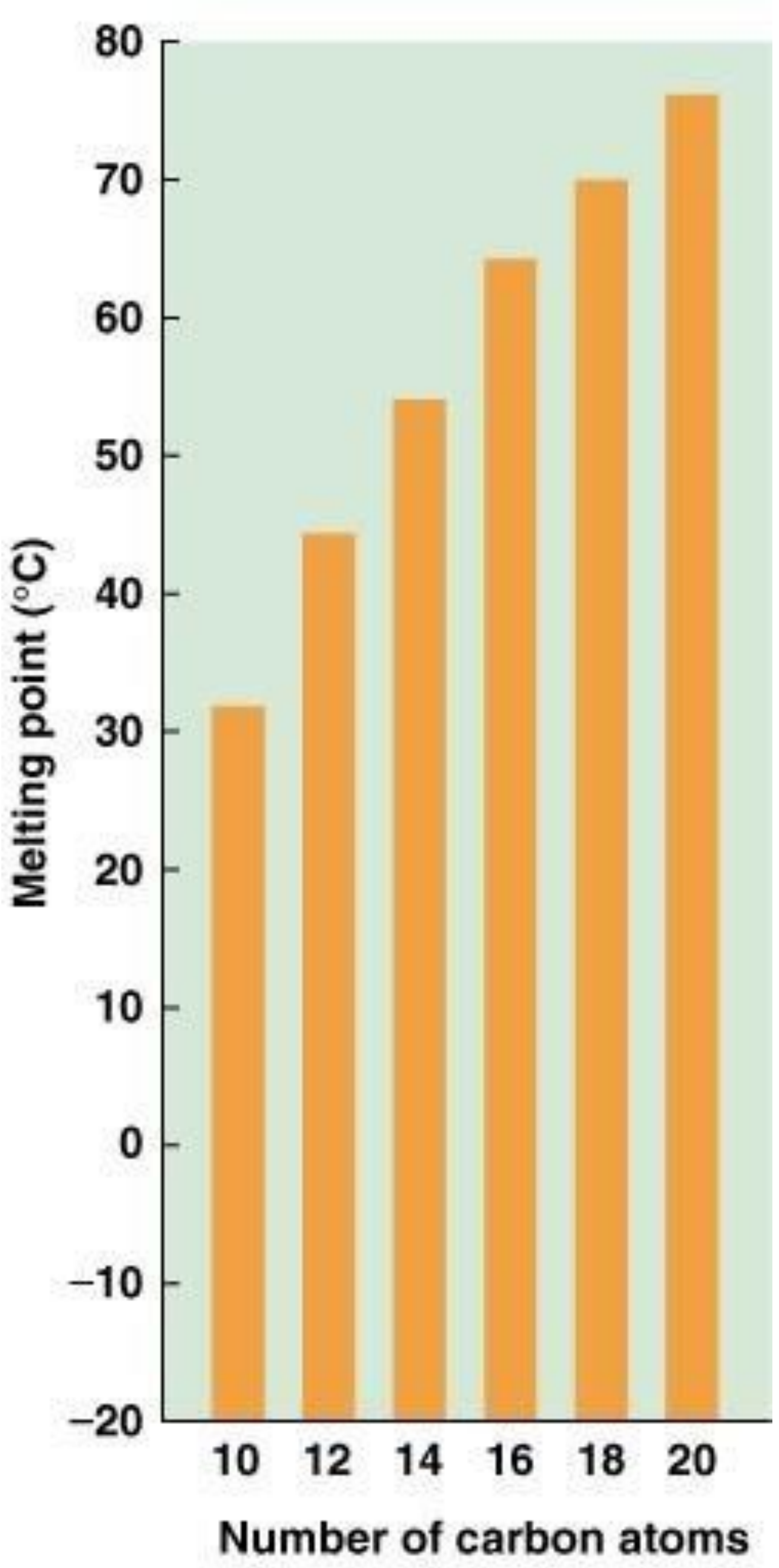
Properties of fatty acids

- When the number of carbons(the chain length) increases the melting point increases.
- When the number of double bonds increases(the degree of saturation decreases) the melting point decreases.

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

Ghee (السمنة) is solid at room temperature because it is saturated, while olive oil is liquid in summer and solid in winter because it's unsaturated (it contains oleic acid).





Properties of saturated fatty acids

In all of these types c1 is the carbon in carboxyl group.

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 That's why we can smell Vinegar, volatile = متطاير	Non-volatile at RT	Non-volatile
Acetic and butyric acids	Caprylic, caproic, & capric acids	Palmitic and stearic acids

In Vinegar

In butter

"Capri" is a Latin word describing goats , Goats' milk contain medium chain Fatty acids

Palm oil

Nutmeg

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-	22	Docosa

Naming of a fatty acid

- Alkane to oic
  - 8 + 10 = 18
  - Octadecane (octa and deca) is octadecanoic acid
    - One double bond = octadec<u>en</u>oic acid
    - Two double bonds = octadeca<u>die</u>noic 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

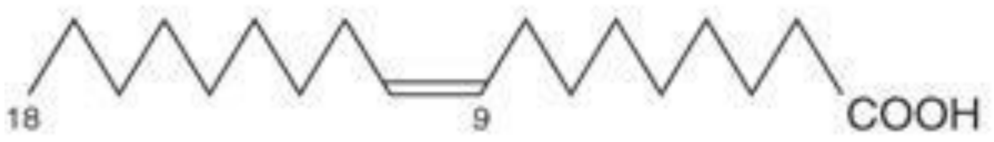
Notice that between each two double bonds there are three carbons and this has to do with the working mechanism of the enzyme which forms these bonds

To differentiate between linoleic acid and **<u>linolenic</u>** acid you can say that: since **<u>linolenic</u>** has one more letter so it has one more double bond....which means:
Linoleic has 2 Double bonds
Linolenic has 3 Double bonds

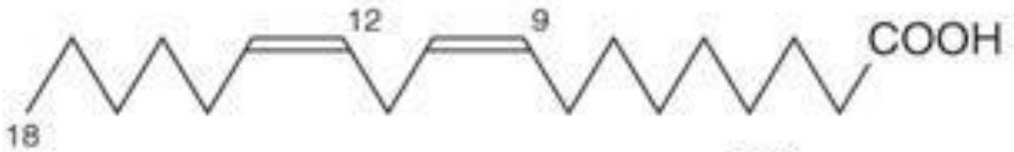
Linoleic and linolenic acids are essential acids. This means that we can't produce them and we have to take them from food.

You should know the names and structure....

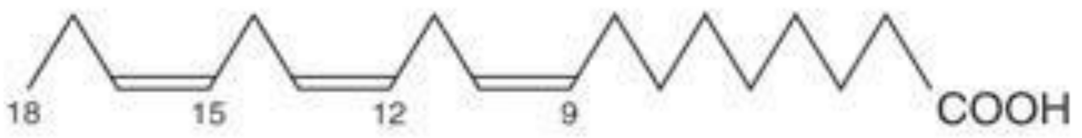
Palmitoleic acid (ω7, 16:1, Δ^9)



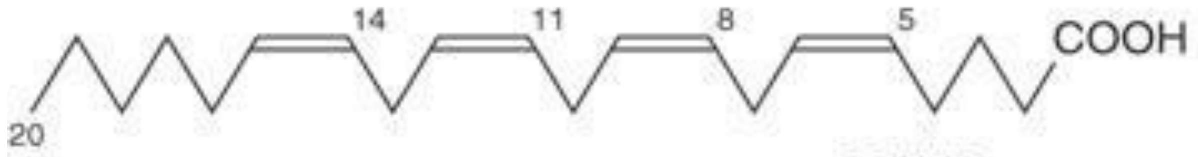
Oleic acid (ω9, 18:1, Δ^9)



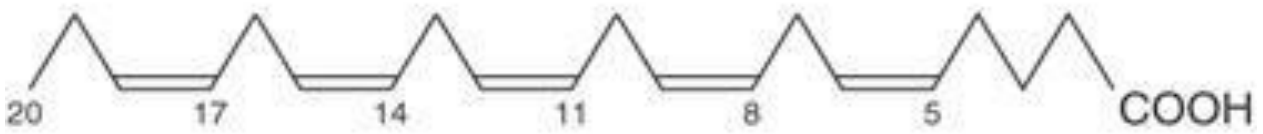
*Linoleic acid (ω6, 18:2, $\Delta^{9,12}$)



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



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



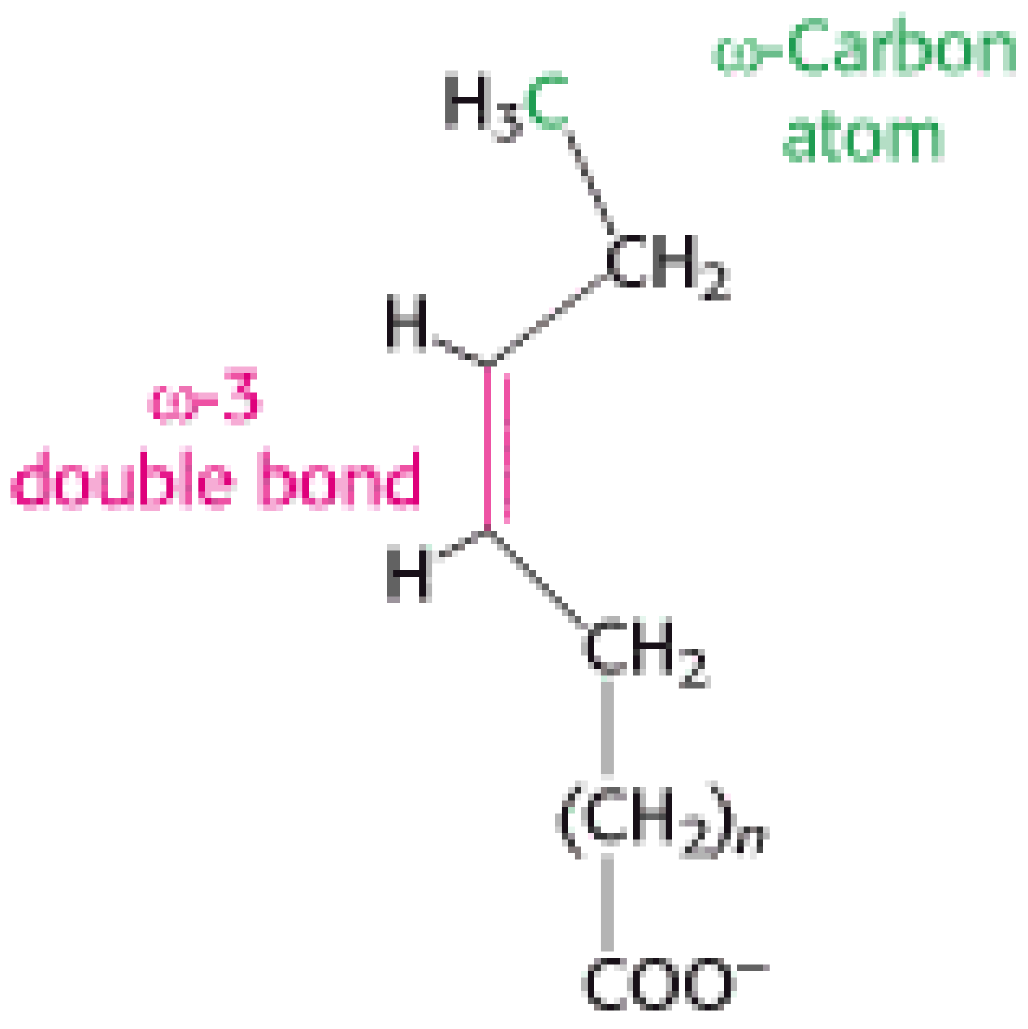
Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

Commonly known as EPA

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-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	$CH_3(CH_2)_4\ (CH=CHCH_2)_4(CH_2)_2\ COO$-

Another way of naming

- (ω)-C: distal methyl C as #1



An ω-3 fatty acid

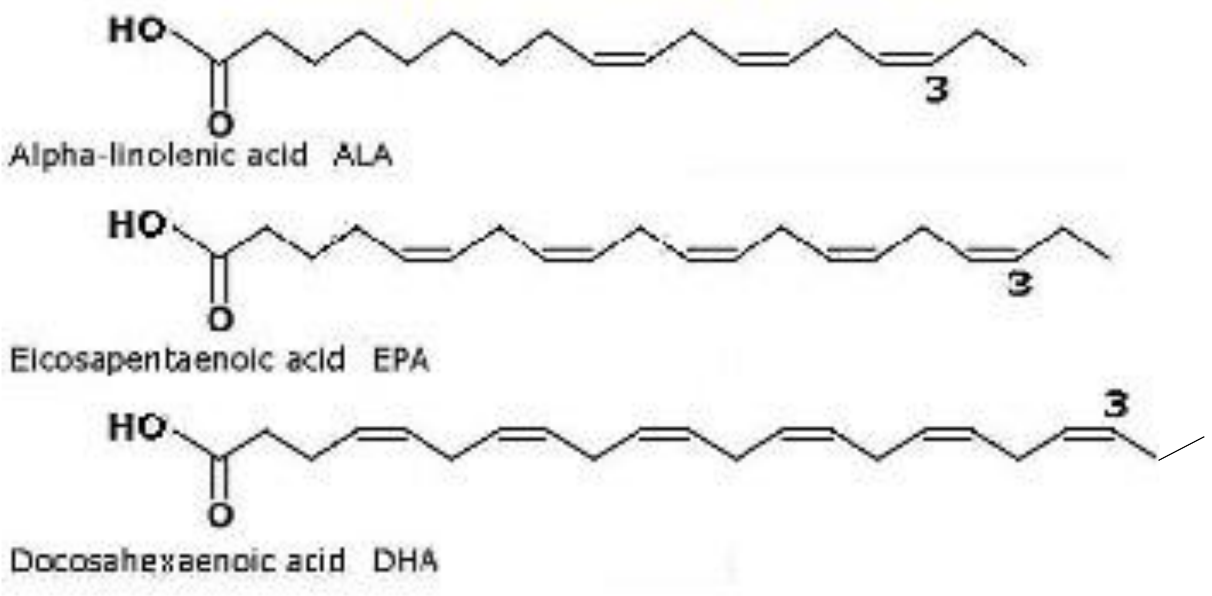
Per softgel

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

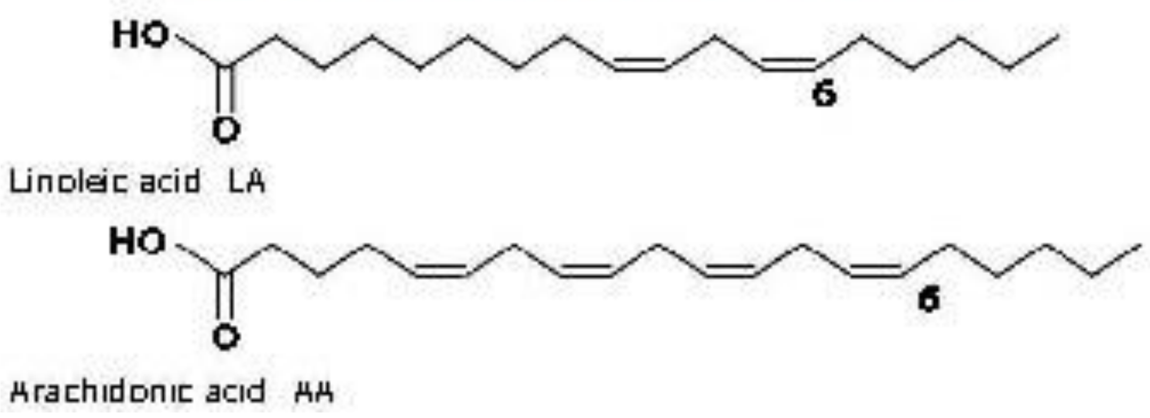
Why omega?
Because it is the last letter in Greek so we name the last carbon in the fatty acid (methyl group) omega carbon and we designate the location of the double bond with respect to it.
The problem with this way of naming is that it doesn't show how many double bonds the fatty acids has.

ω3 means there's **at least** one double bond in the fatty acid and it's on the the 3rd carbon **STARTING THE COUNTING FROM THE ω CARBON**

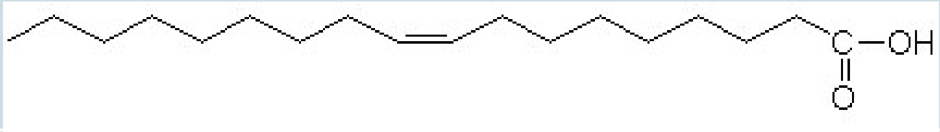
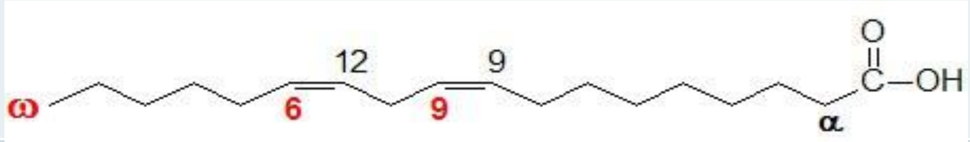
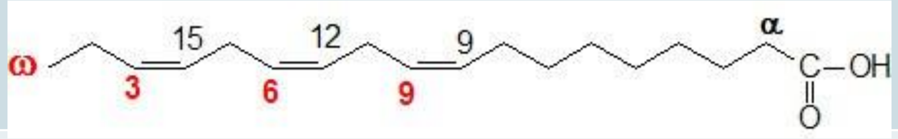
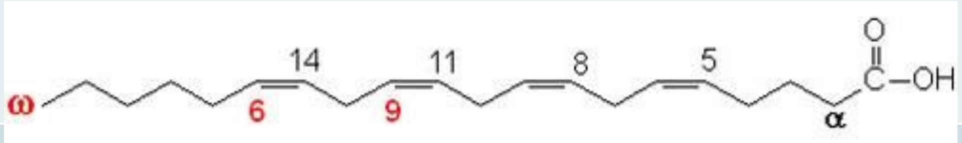
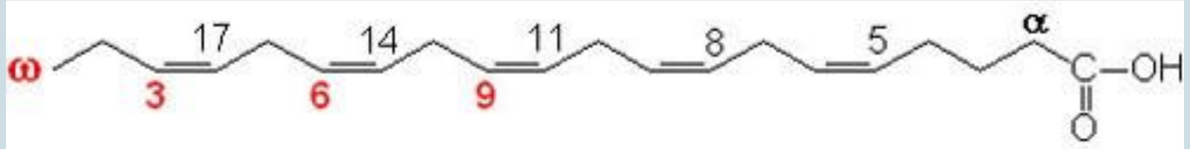
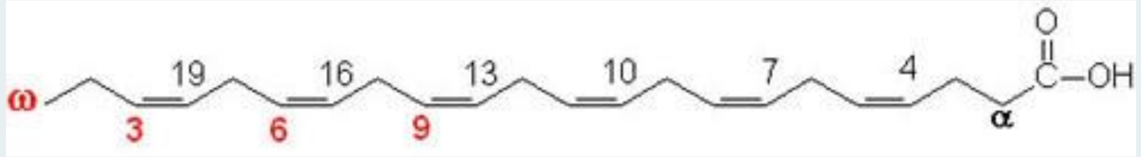
Omega-3 fatty acids



Omega-6 fatty acids



- **Essential FAs:**
  - **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)

Note: it's good to take ω3 and ω9 fatty acids but it's not that important to take ω6

You have to know everything here......

Derived fatty acids: Waxes & Eicosanoids

Waxes:

- Made of 2 parts because it's the outcome of a reaction of a fatty acid and a hydrocarbon alcohol. The carboxylic group reacts with the hydroxyl group which will result in 2 hydrocarbon chains that are connected with an ester group.
- It is hydrophobic (lipophilic, soluble in organic solvents).

Waxes

$$\underbrace{CH_3(CH_2)_{14}-\overset{\displaystyle O}{\overset{\|}{C}}}_{\text{Palmitic acid}}-\underbrace{O-CH_2-(CH_2)_{28}-CH_3}_{\text{Triacontanol}}$$

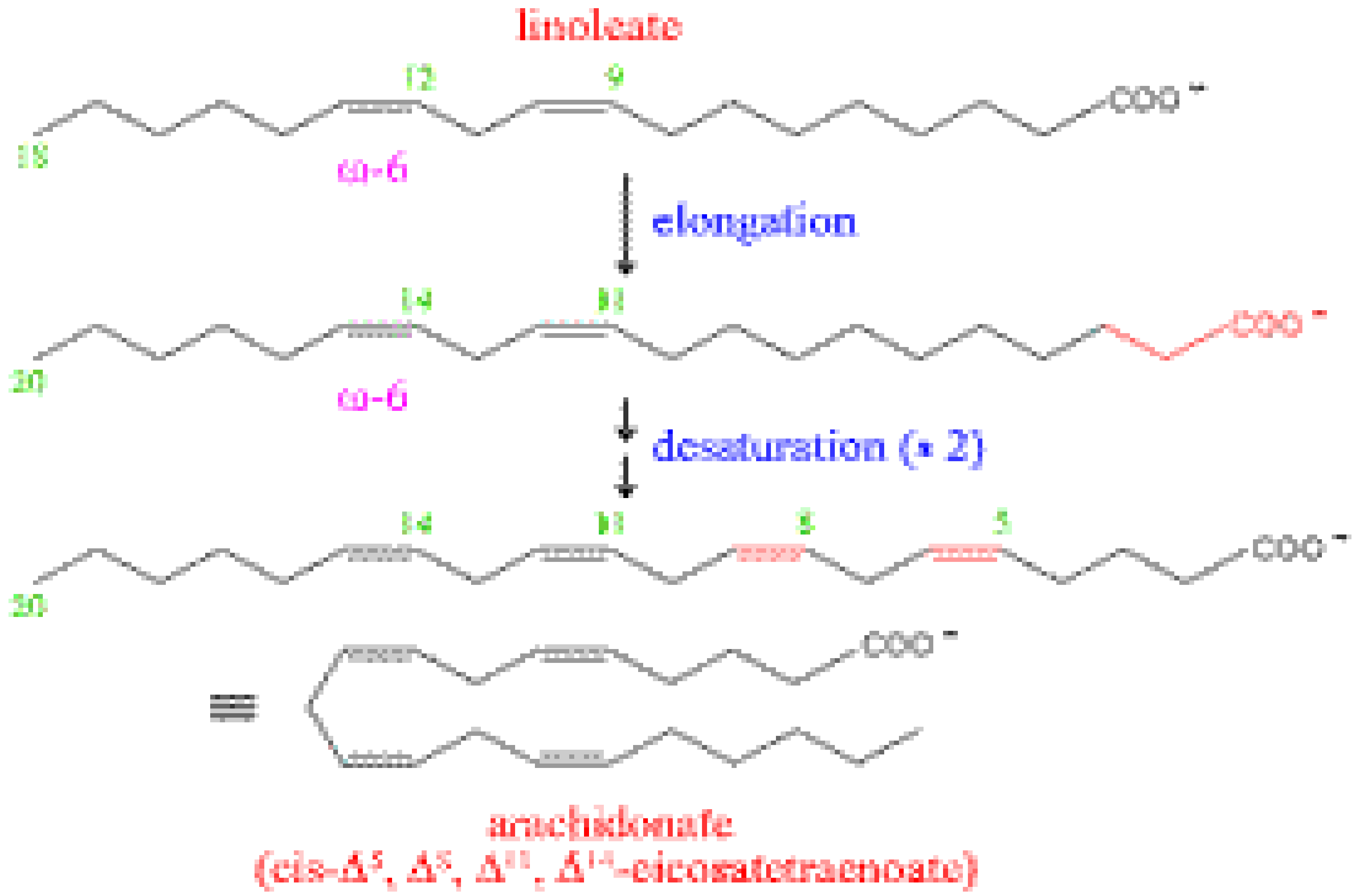
- Solid simple lipids containing a monohydric alcohol (C16 ~ C30, higher molecular weight than glycerol) esterified to long-chain fatty acids (C14 ~ C36).
  - Example: palmitoyl alcohol
- Insoluble in water
- Not easily hydrolyzed (fats) & indigestible
- Very resistant to rancidity
- No nutritional value
- External coating of plant leaves that prevent loss of water

Type	Structural Formula	Source	Uses
Beeswax	$CH_3(CH_2)_{14}-\overset{\displaystyle O}{\overset{\|}{C}}-O-(CH_2)_{29}CH_3$	Honeycomb	Candles, shoe polish, wax paper
Carnauba wax	$CH_3(CH_2)_{24}-\overset{\displaystyle O}{\overset{\|}{C}}-O-(CH_2)_{29}CH_3$	Brazilian palm tree	Waxes for furniture, cars, floors, shoes
Jojoba wax	$CH_3(CH_2)_{18}-\overset{\displaystyle O}{\overset{\|}{C}}-O-(CH_2)_{19}CH_3$	Jojoba	Candles, soaps, cosmetics

Do not memorize the structures but study them

Arachidonate

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



Very important to know the steps of producing arachidonate (cis, eicosatetraeonate, Δ5, 8, 11, 14)

Eicosanoids

Active lipids in our bodies. They are very important physiologically and pathologically

- "eicosa" is Greek for "20"
- **Eicosanoids** are active lipids that function as "local hormones"
- They are derived from the 20-carbon arachidonate.
- They consist primarily of:
  - the prostaglandins (including prostacyclins) and thromboxanes, which are synthesized by cyclooxygenases
  - leukotrienes and lipoxins, which are synthesized from lipooxygenases.

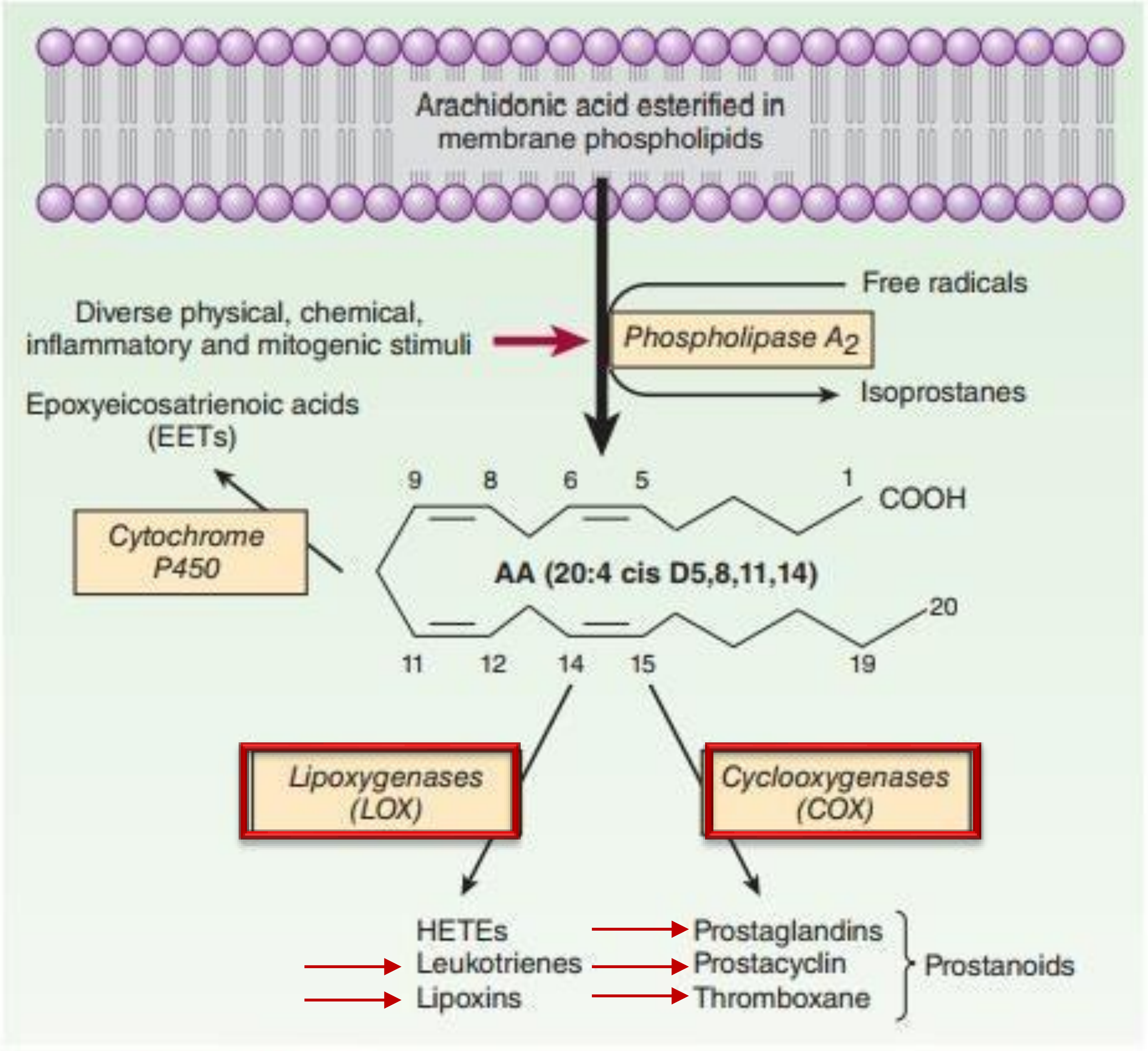


FIGURE 18–1 Pathways of arachidonic acid (AA) release and metabolism.

Arachidonic acid is an essential molecule, because it's precursor is linoleate, and linoleate is an essential fatty acid.

- Arachidonic acid is stored in cell membrane, then it's released from there and get converted into eicosanoids and they could be classified to:

A.Prostaglandins (it's was named prostaglandins because scientists first discovered that it was secreted from the prostrate gland in males).

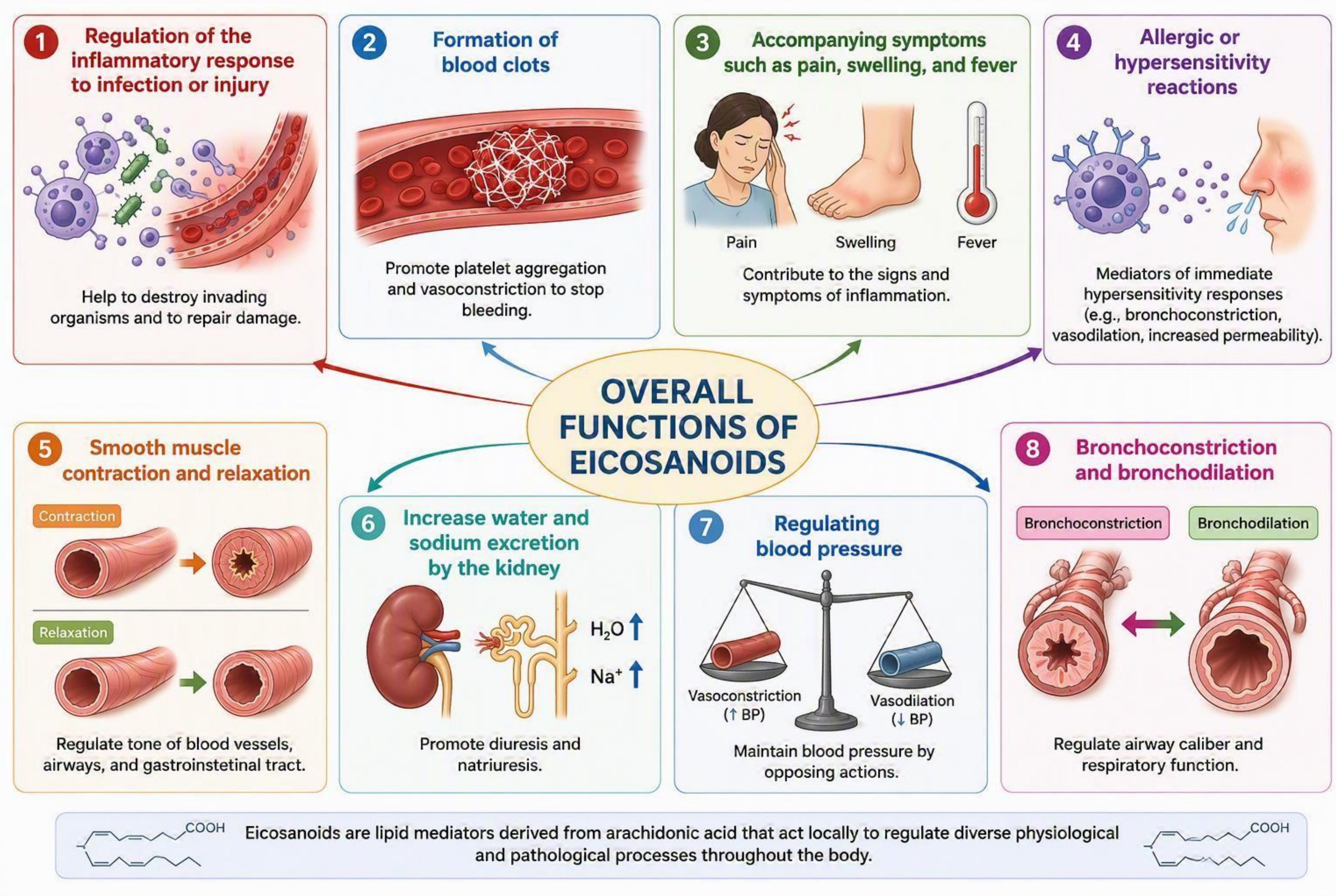
B.Leukotrienes (it's named because it was first discovered that they are secreted from leukocytes, and they have a structure called a triene, so it's named leuokotrienes).

Overall functions

- Regulation of the inflammatory response to infection or injury (mosquitos bite induce the release of eicosanoids)
  - to destroy invading organisms and to repair damage
- Formation of blood clots (blood cells travel in a relatively high pace and they could damage blood vessels, so eicosanoids mediate the process of repairing damaged vessels)
- Accompanying symptoms such as pain, swelling, and fever
- Allergic or hypersensitivity reactions (such symptoms are caused during a huge release of eicosanoids as a result of the entry of bacteria or pathogens).
- Smooth muscle contraction of vessels (to slow down blood flow) and relaxation (happens after smooth muscle contraction to dilate vessels and promote clearance of them).
- Increase water and sodium excretion by the kidney
  - regulating blood pressure.
- Bronchoconstriction and bronchodilation

Extra note the professor provided in the lecture (not related to the previous topic):

A new study says that as a result of global contamination and the increasing CO_2 levels in the atmosphere , it's causing the bicarbonate ion levels to rise in our body by 7% , so our physiology is because of this change.


1 Regulation of the inflammatory response to infection or injury
Help to destroy invading organisms and to repair damage.
2 Formation of blood clots
Promote platelet aggregation and vasoconstriction to stop bleeding.
3 Accompanying symptoms such as pain, swelling, and fever
Pain
Swelling
Fever
Contribute to the signs and symptoms of inflammation.
4 Allergic or hypersensitivity reactions
Mediators of immediate hypersensitivity responses (e.g., bronchoconstriction, vasodilation, increased permeability).
OVERALL FUNCTIONS OF EICOSANOIDS
5 Smooth muscle contraction and relaxation
Contraction
Relaxation
Regulate tone of blood vessels, airways, and gastroinstetinal tract.
6 Increase water and sodium excretion by the kidney
H2O ↑
Na+ ↑
Promote diuresis and natriuresis.
7 Regulating blood pressure
Vasoconstriction (↑ BP)
Vasodilation (↓ BP)
Maintain blood pressure by opposing actions.
8 Bronchoconstriction and bronchodilation
Bronchoconstriction
Bronchodilation
Regulate airway caliber and respiratory function.
COOH
Eicosanoids are lipid mediators derived from arachidonic acid that act locally to regulate diverse physiological and pathological processes throughout the body.
COOH

Eicosanoids and their functions

Don't memorize the structures

They control cellular function in response to injury

- Prostaglandins (20 carbons, Eicosanoids, internal 5-carbon ring)
  - Induction of inflammation
  - **Inhibition** of platelet aggregation
    - Inhibition of blood clotting

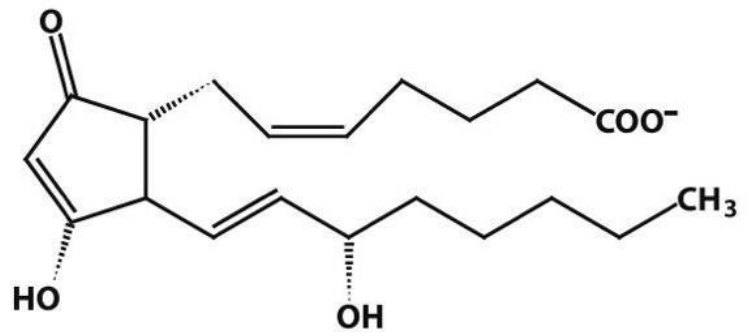
Chemical groups can be added to the ring.

- Thromboxanes (20 carbons, internal 6-carbon ring with oxygen)
  - Constriction of smooth muscles
  - **Induction** of platelet aggregation

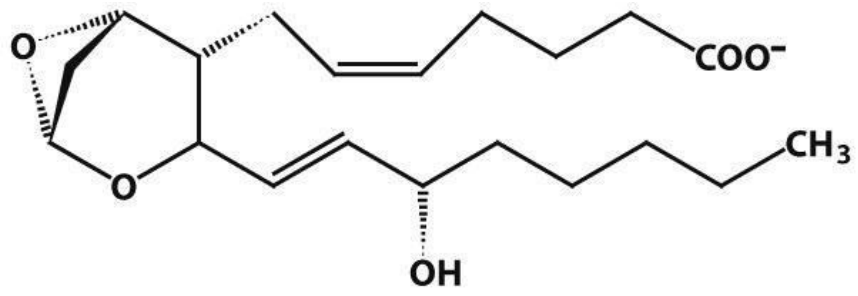
Thromboxanes came from thrombocites which are platelets.

- Leukotrienes (20 carbons, 4 double bonds, 3 are conjugated (a triene))
  - Constriction of smooth muscles
    - Asthma **Bronchoconstriction**
- Lipoxins
  - Inhibitors of inflammation

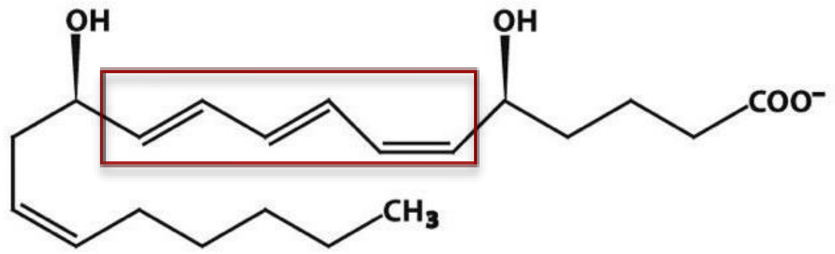
Neither memorize the specific functions nor the structures



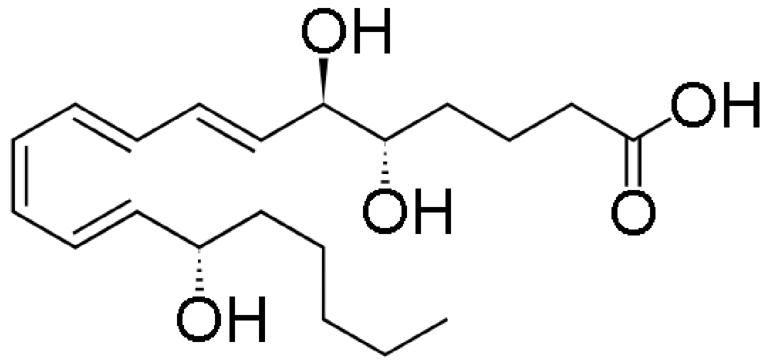
Prostaglandin E_2



Thromboxane A_2 (TXA_2)



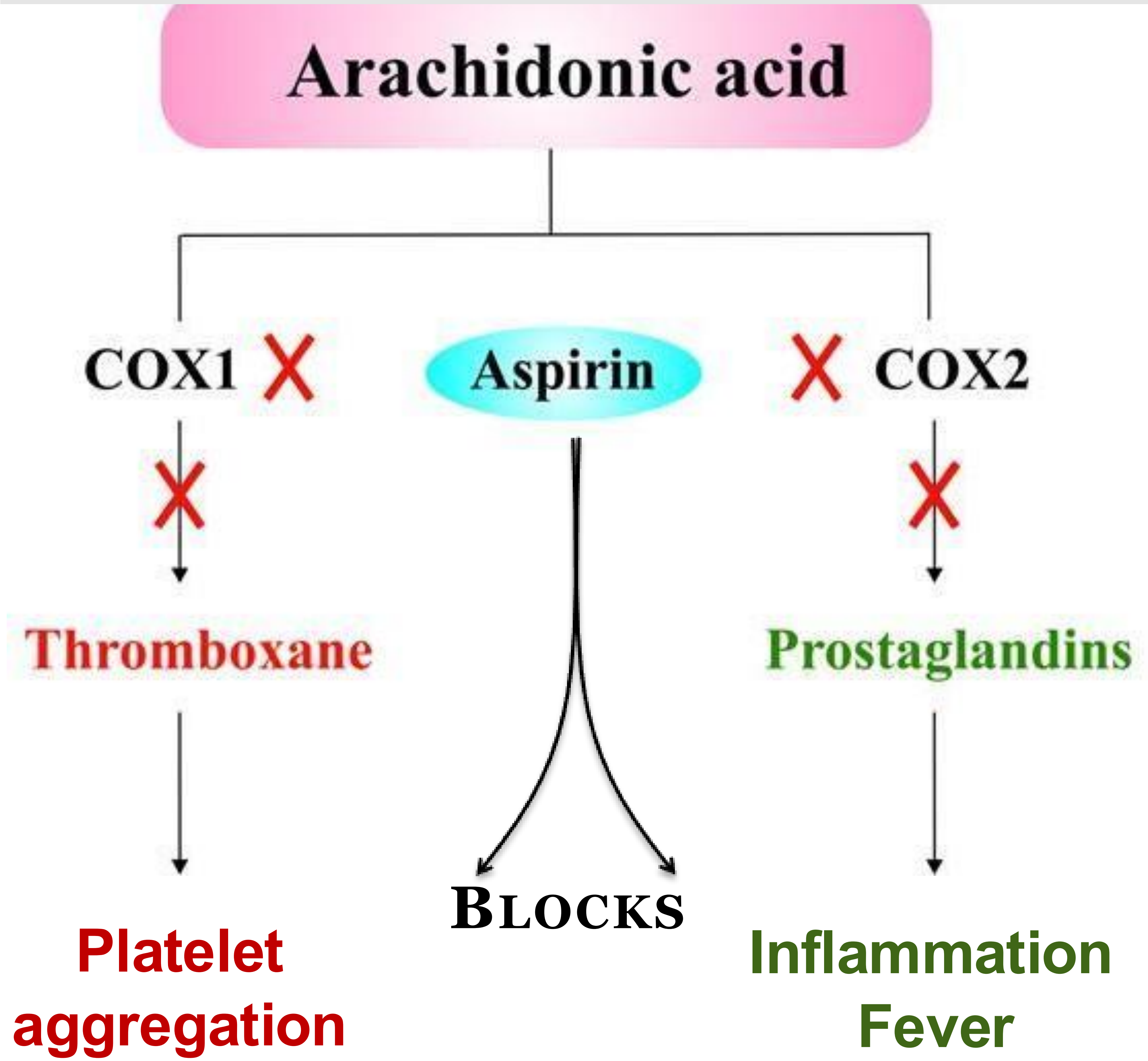
Leukotriene B_4



Lipoxins

Aspirin is good

It inhibits cyclooxygenase enzymes, so arachidonic acid doesn't transform to eicosanoids (prostaglandins and thromboxanes).



No blood clotting therefore no heart attacks

COX: Cyclooxygenase

Some fascinating drugs discovered in the last 100 years:

1. Penicillin (the first antibiotic.)

2.Statins (reduce cholesterol levels and have an effect on cancer).

3.Metformin (reduces sugar blood levels and have effect on cancer).

4.GLPs (lowers weight.)

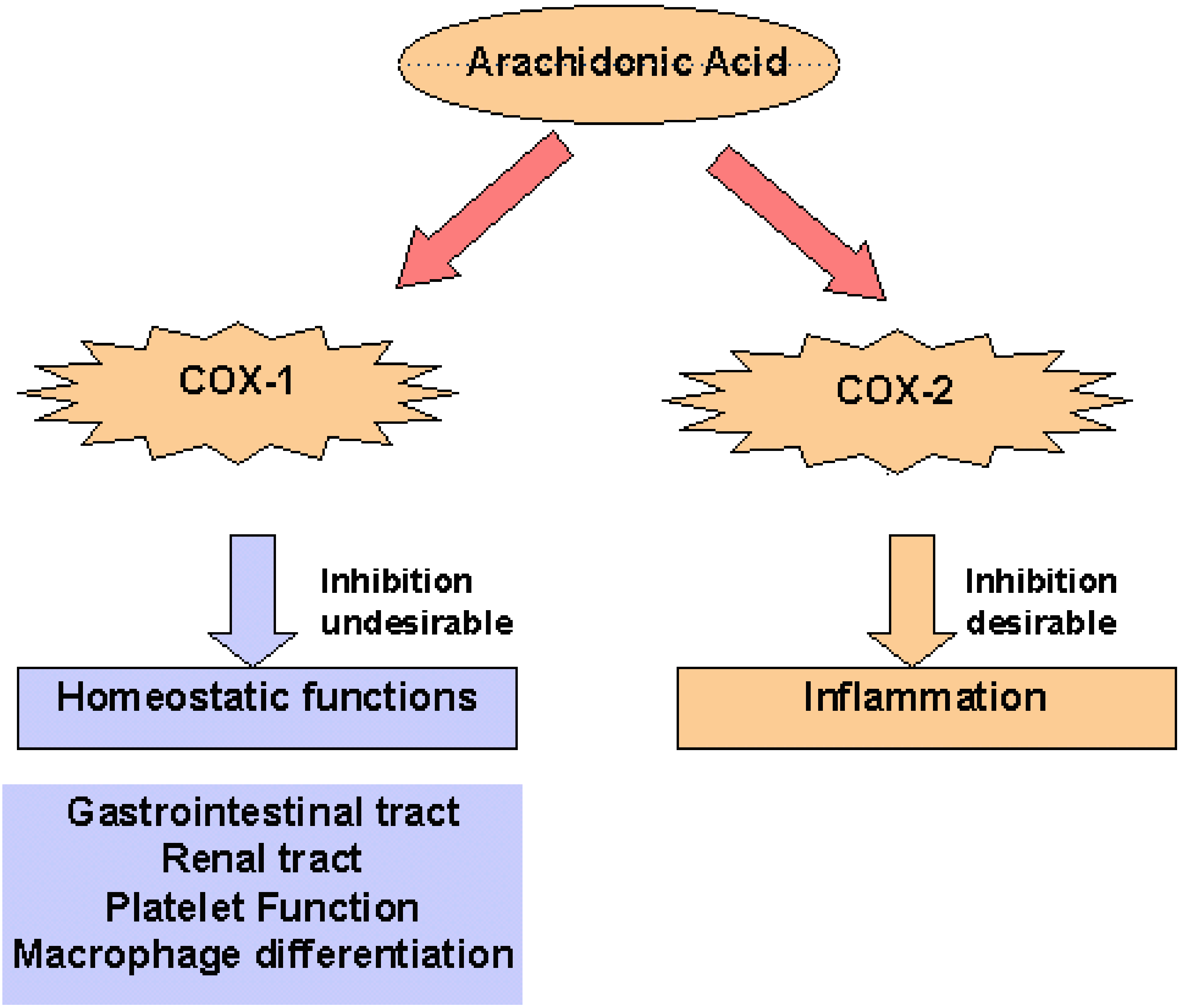
5. Aspirin (reduces pain, fever, inflammation, etc…)

- Aspirin stops platelet aggregation which results in stopping blood clots and preventing heart attacks , but it would result in excessive bleeding because there is no clotting for blood and this is really dangerous for old people. So, **baby aspirin** is prescribed to stop blood clotting which prevents heart attacks, while also preventing bleeding as it doesn't stop blood clotting completely.

- People who have a sensitive stomach and suffer with ulcers are not allowed to take aspirin, because it will damage the stomach because it inhibits CoX1 (inhibiting this stops blood clotting which is essential in the case of ulcers.) and aspirin blocks both CoX1 and CoX2, so a new drug was produced in order to inhibit CoX2 only (selective). With this drug, we could stop the inflammation by inhibiting CoX2 and not harming the GI system (stomach).

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.

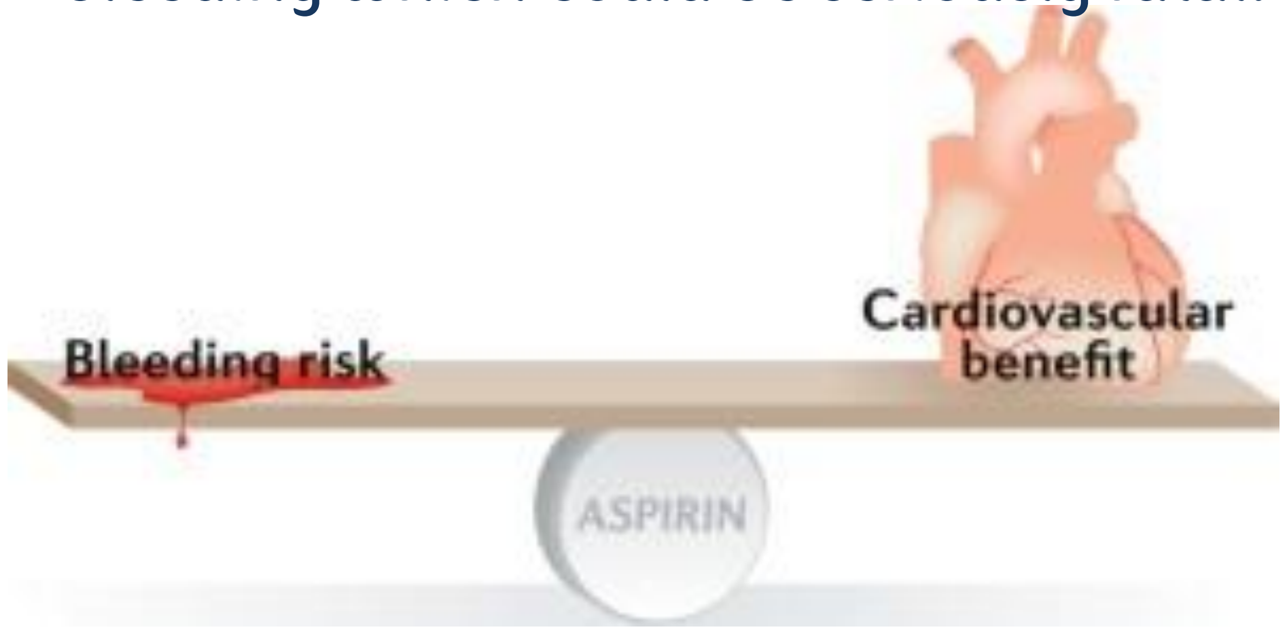


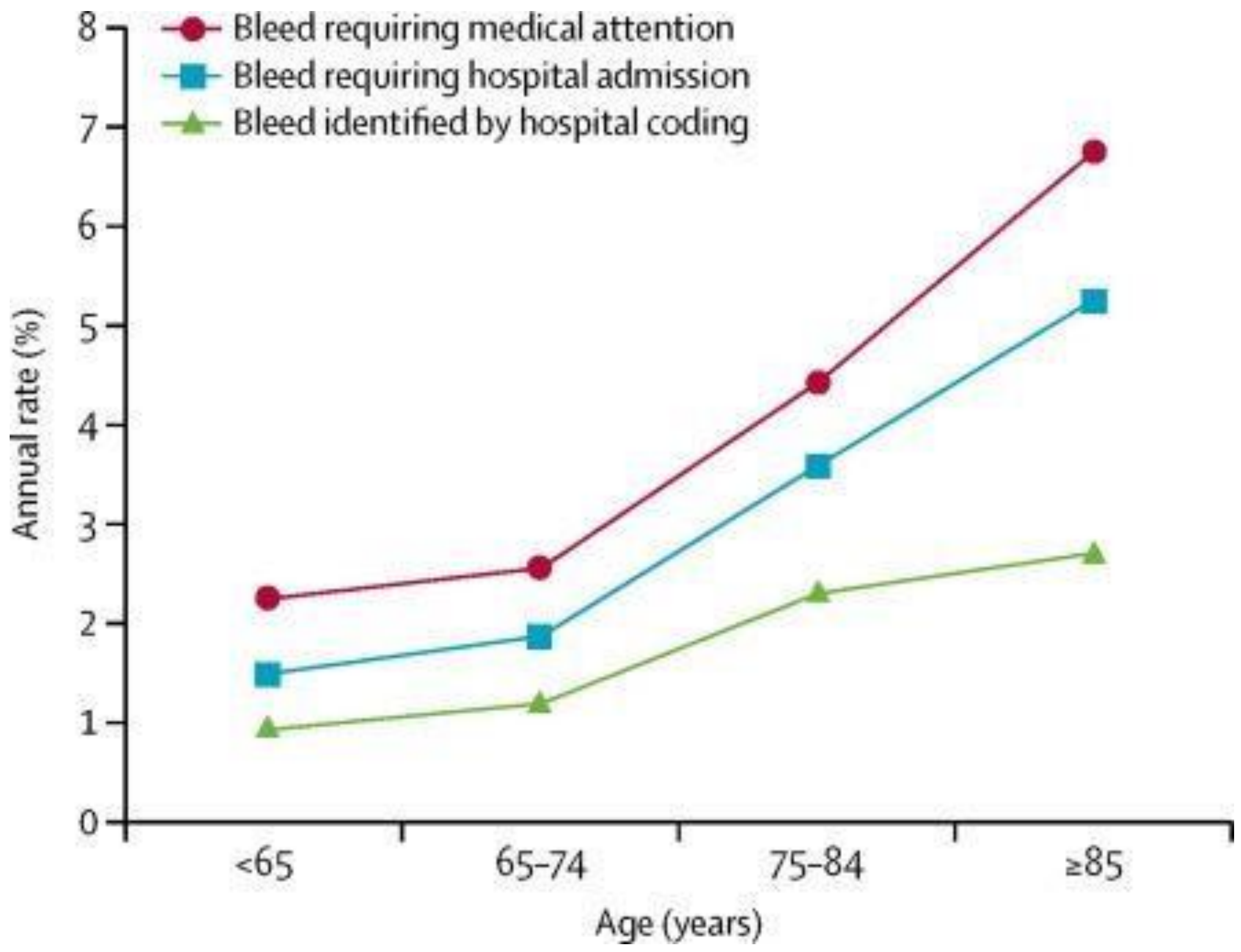
Aspirin can be bad

Cardiovascular disease vs. bleeding

- Aspirin also causes excessive bleeding among the elderly.

Elder people are advised not to take aspirin because of the excessive bleeding which could be seriously fatal.





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.

The text underlined is important .

Celebrex Reduces pain and inflammation

- A newer generation of drugs targets COX2.
  - Be cautious with Celebrex
  - Vioxx (from the same family) was withdrawn from the market
    - caused heart failure

In 2004, vioxx was introduced in the market and it had a massive success, but it was withdrawn from the market when it was discovered that it leads to heart attacks.

Celebrex could cause heart attacks for people with a history of heart problems.

Cardiovascular Risk

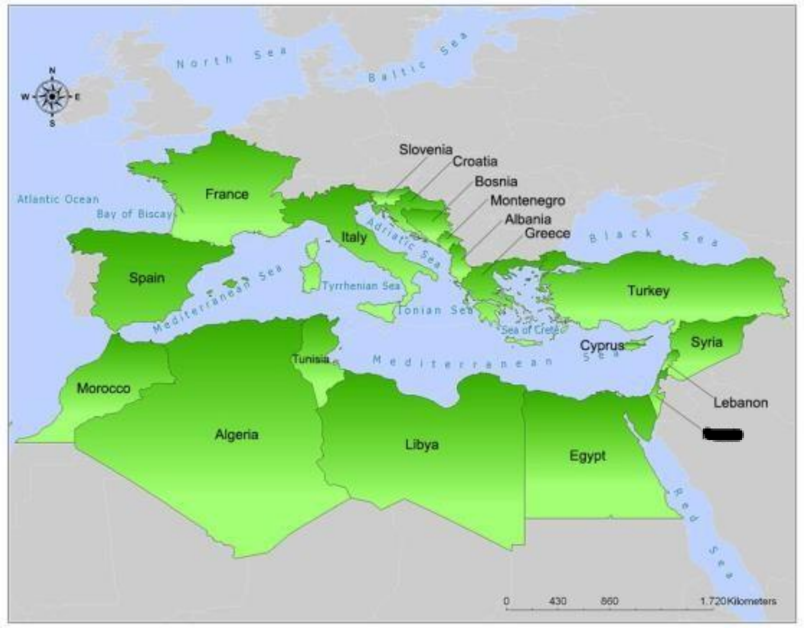
- CELEBREX may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may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

Celecoxib is the drug's name while celebrex is just the commercial name

Omega fatty acids

- Omega-3 fatty acids
  - α-linolenic acid → eicosapentaenoic acid (EPA) → docosahexaenoic acid (DHA)
    - They reduce inflammatory reactions.
- Omega-6 fatty acids: Arachidonic acid
- Omega-9 fatty acids
  - Oleic acid (very healthy)
    - It reduces cholesterol in the circulation.

Healthy mediterranean food



Quiz!

Good luck!

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

Reference Used:

Prof. Mamoun Ahram recorded lecture

[“lipids pt.1”] & [“lipids pt.2”]

Extra References for the Reader to Use:

Marks’ Basic Medical Biochemistry (6th edition)

اللَّهُمَّ يَا مُسَهِّلَ كُلِّ صَعْبٍ، وَيَا مُيَسِّرَ كُلَّ أَمْرٍ، يَا رَبَّ الْقُدْرَةِ وَالْقُوَّةِ، يَسِّرْ لِي أُمُورِي، وَافْتَحْ لِي أَبْوَابَ التَّوْفِيقِ وَالرَّحْمَةِ.اللَّهُمَّ اجْعَلْ لِي مِنْ كُلِّ هَمَّ فَرَجًا، وَمِنْ كُلِّ ضِيقٍ مخْرَجًا، وَمِنْ كُلِّ عُسْرٍ يُسْرًا، وَاخْتِمْ لِي بِالْخَيْرِ فِي كُلِّ طريق.اللَّهُمَّ وَفِّقْنِي لِمَا تُحِبُّهُ وَتَرْضَاهُ، وَسَدِّدْ خُطَايَ ،وَأَلْهِمْنِي رُشْدِي، وَاجْعَلِ النُّورَ فِي طَرِيقِي، وَالْبَرَكَةَ فِي أَيَّامِي، وَالرِّضَا فِي قَلْبِي. يا رَبِّ يَسِّرْ وَلَا تُعَسرْ، وَتَمِّمْ بِالْخَيْرِ، وَاجْعَلْ عَوَاقِبَ أُمُورِنَا إِلَى كل خَيْر. 💙💙