Lipids

Summer 2023-2024

Lipids

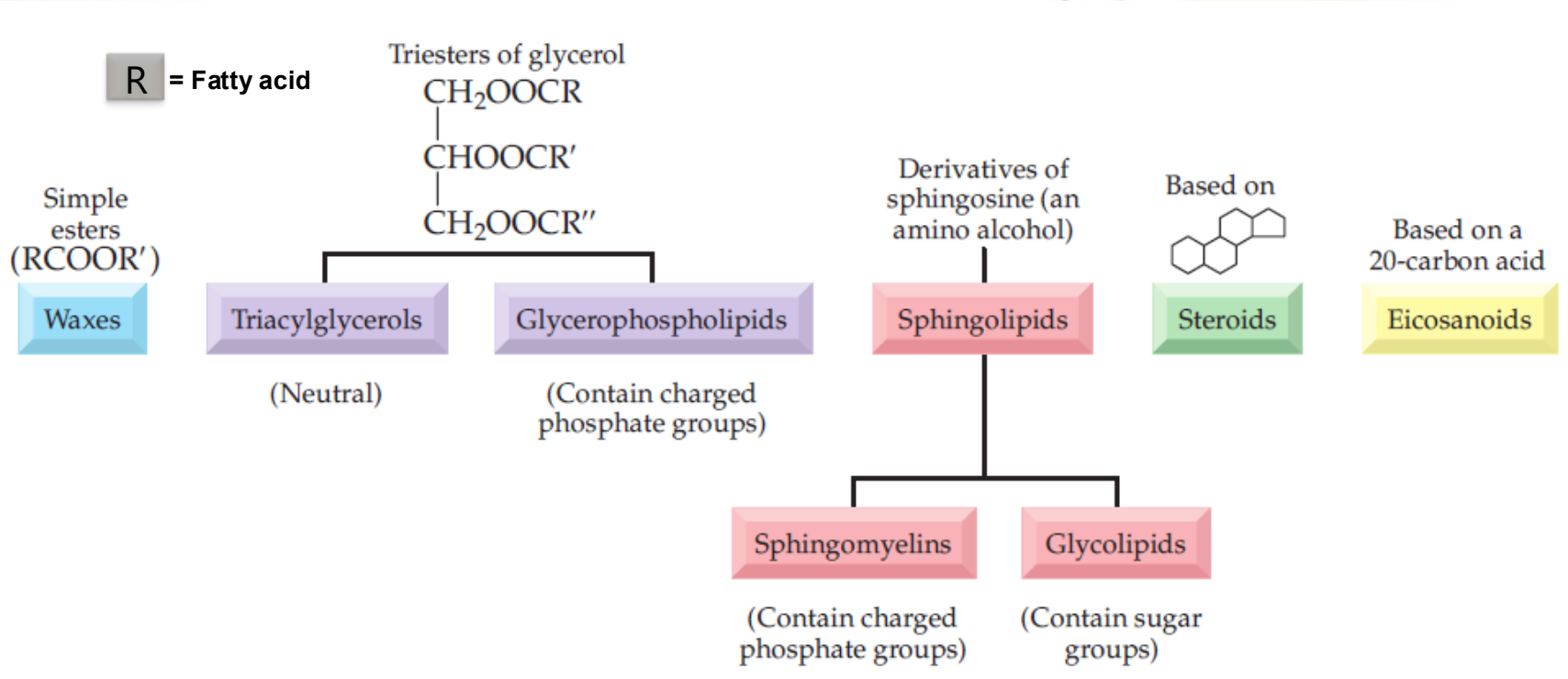
Macromolecules, not polymers

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

- They are Amphipathic. → polar + non polar parts (hydrocarbon chain)
- They are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).
- They are widely distributed in plants & animals.

Classes

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



Lipid Functions

- 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

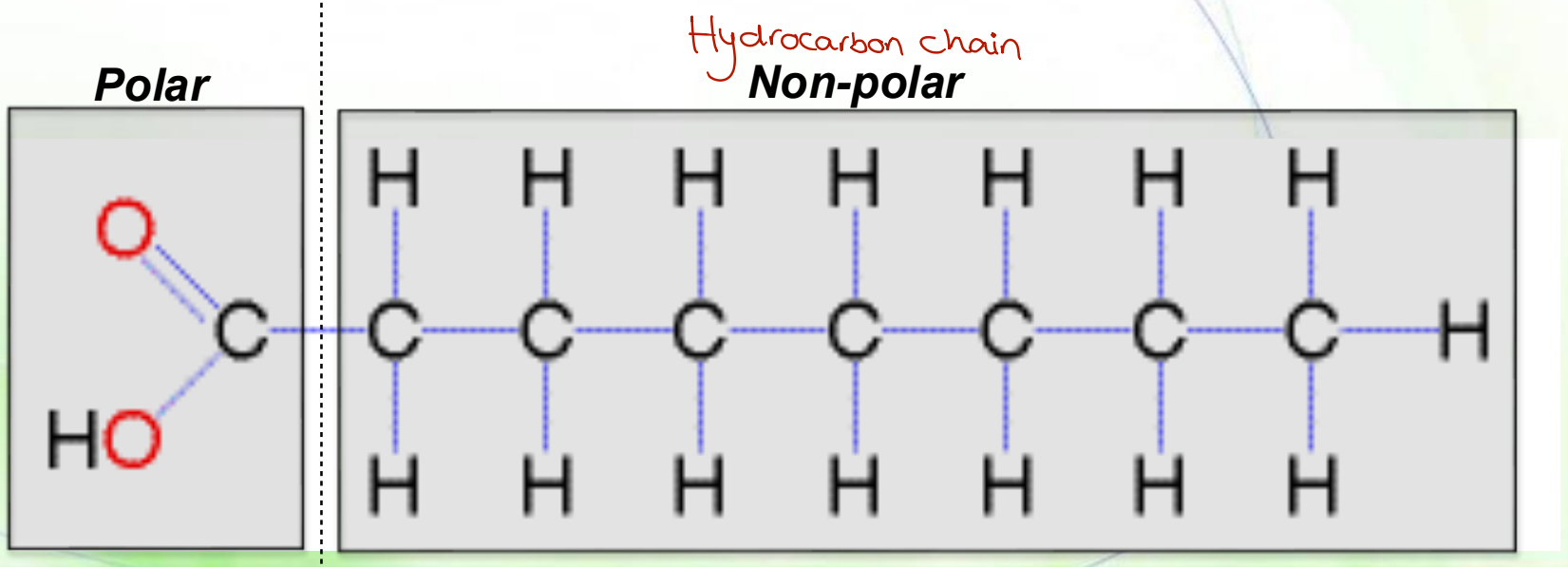
2x energy compared to Carbohydrates Since they are Saturated (have more Hydrogens compared to Oxygen)

Fatty acids

- Aliphatic mono-carboxylic acids
- Formula: R-(CH_2)n-COOH
- Lengths
  - Physiological (12-24) Physiologically relevant
  - Abundant (16 and 18) found most commonly in human
- Degree of unsaturation
- Amphipathic molecules

Functions:

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



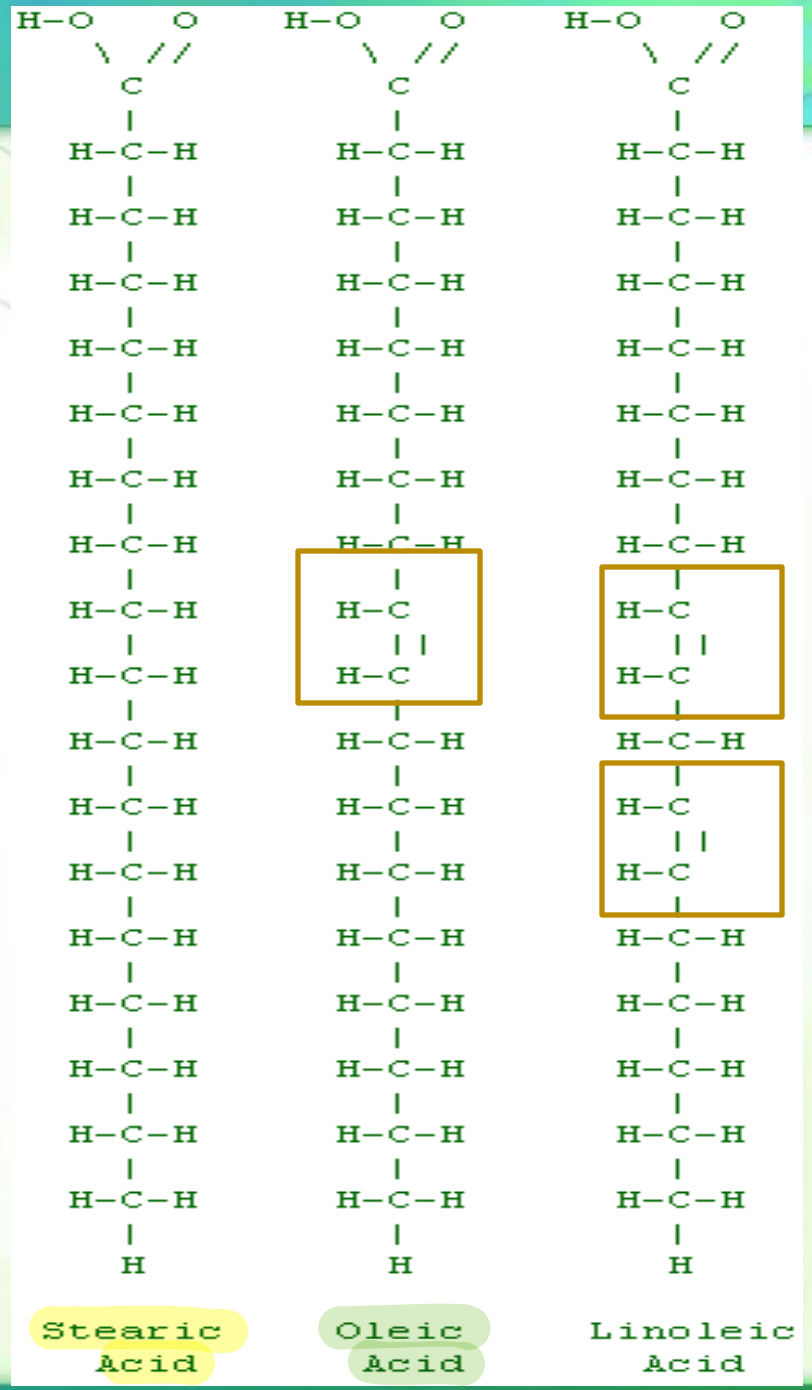
Types of fatty acids

- 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.

Stearic : Saturated fatty Acid

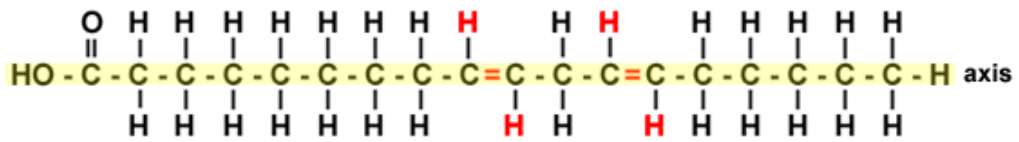
Oleic : Monounsaturated fatty acid

Linoleic : Polyunsaturated fatty acids

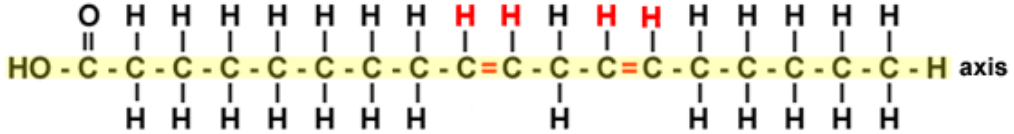


Cis vs. trans bonds

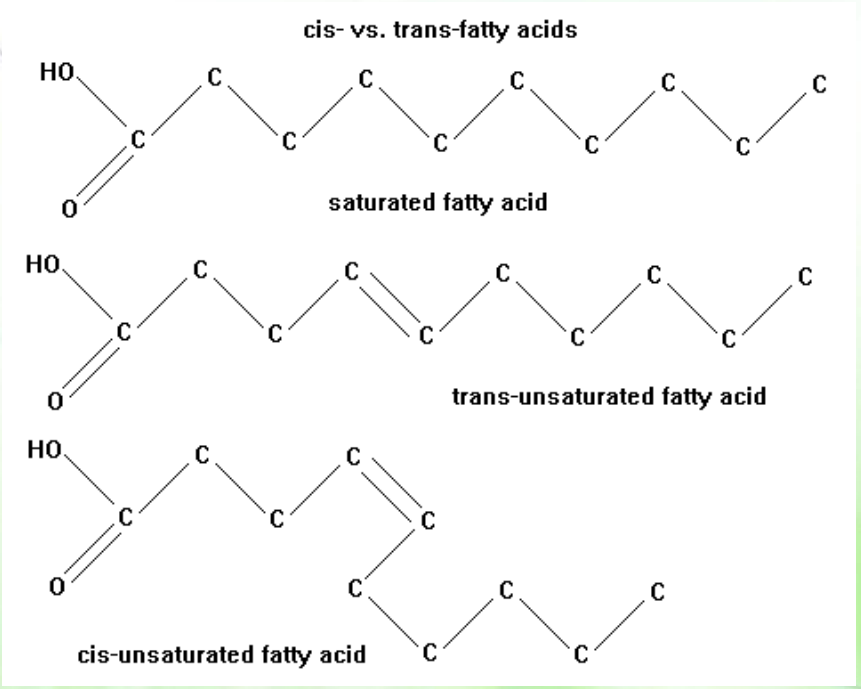
Presence of Double Bonds causes kinks (bending)



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



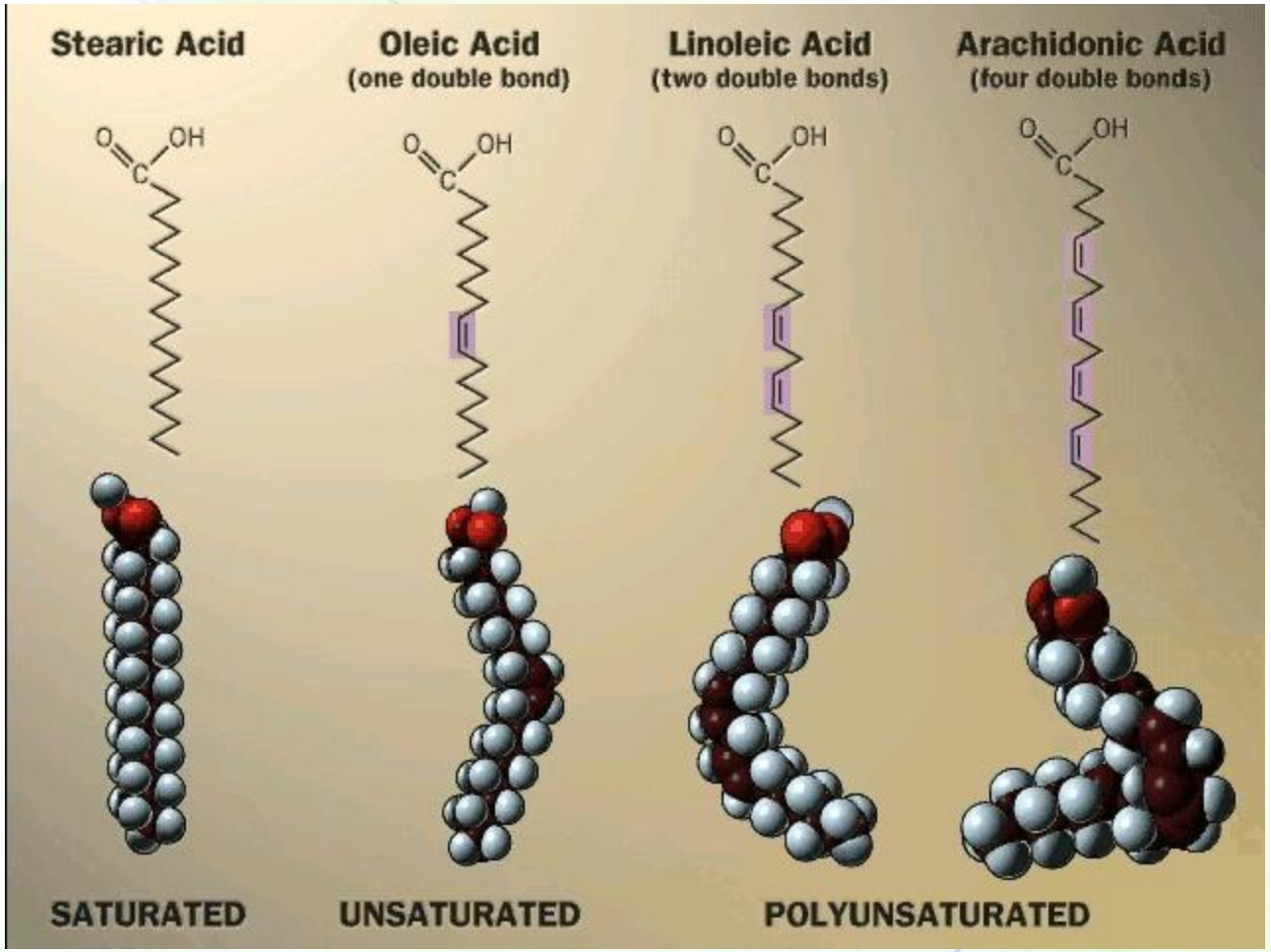
linoleic acid: *cis* configuration (*cis* isomer)



no kinks

Kinks

more kinks (bending)



Physiologically:

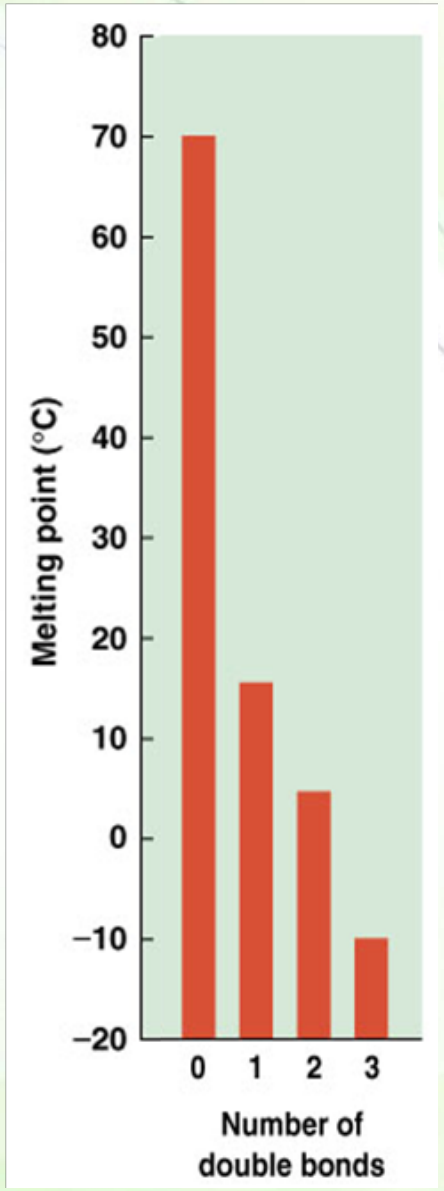
- **cis isomer predominates**
- **trans is rare**

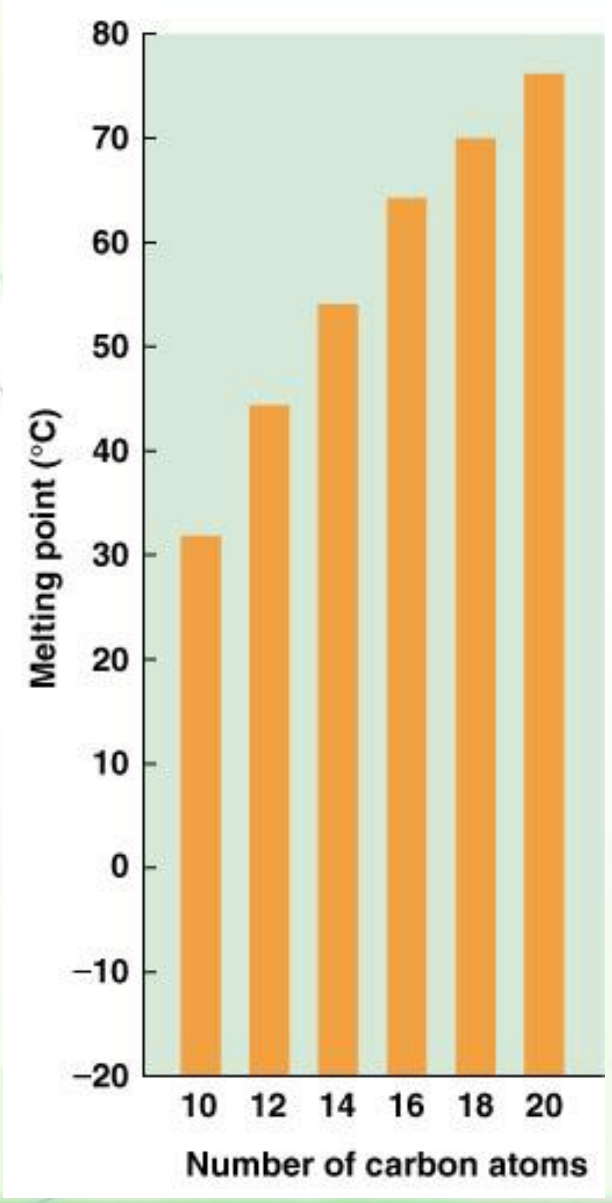
Properties of fatty acids

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

↑ Carbons ↑ BP, MP

↑ Double Bond ↓ BP, MP (big effect)





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 acids	Caprylic & capric acids	Palmitic and stearic acids

Very long chain (20+)

ethanoic (2 carbon) butanoic (4 carbon)

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-		

Look at total # of Carbons (including Carbon of Carboxyl Group, if found)

18 = 8 + 10

= Octa + Decane

= Octadecane (Alkane), Octadecanoic acid (Acid), octadecene (Alkene)

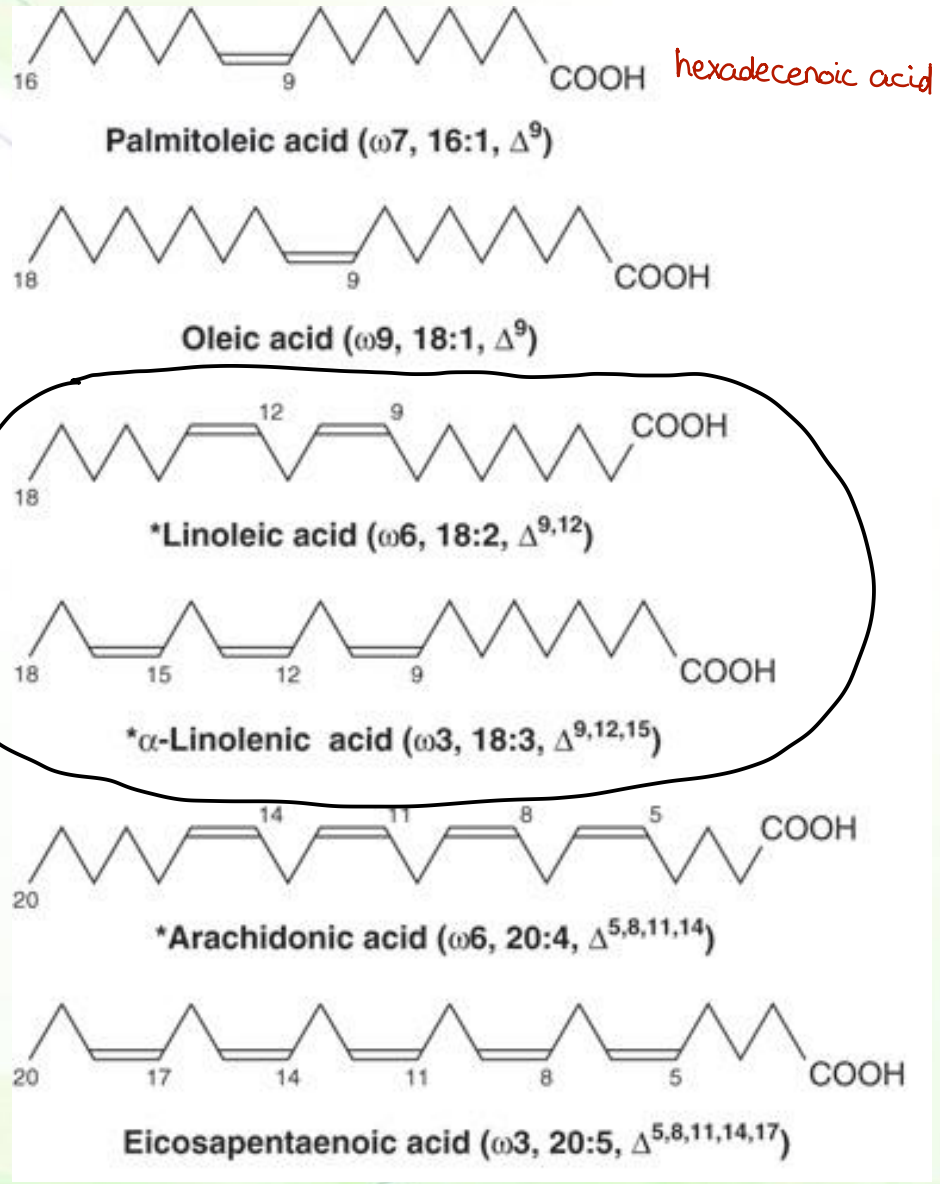
Naming of a fatty acid

how to differentiate b/w Linoleic & Linolenic ? Linolenic has more letters ⇒ more double bonds (3 vs 2)

Linoleic is what makes Arachidonic Acid

- 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

Double bonds always have 3 carbons b/w them. (Action of Enzymes)



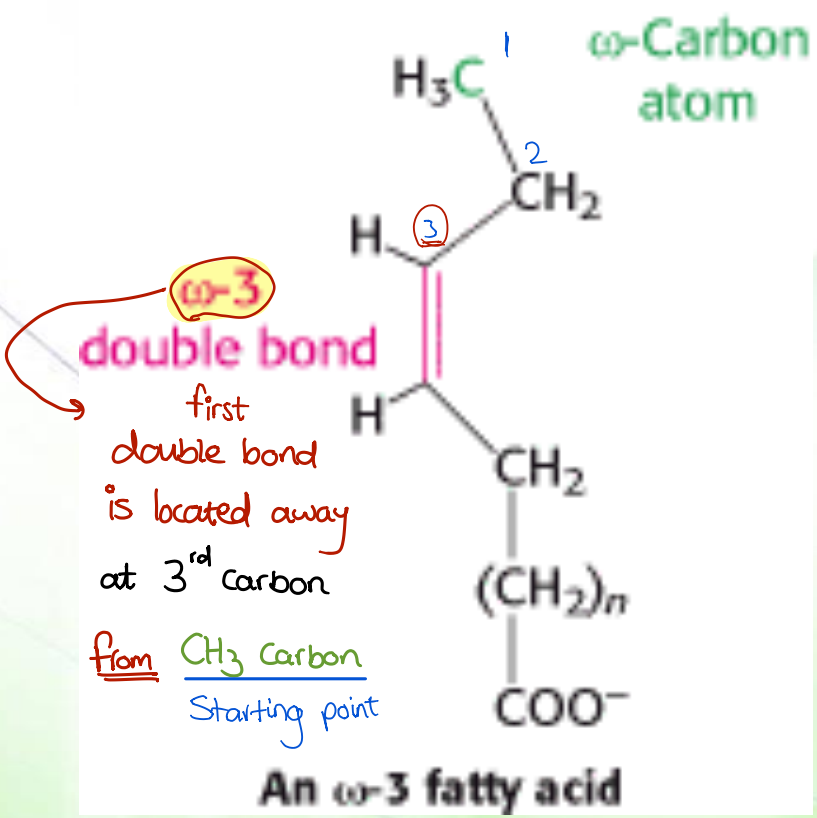
Memorize whole table 

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	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COO^-$

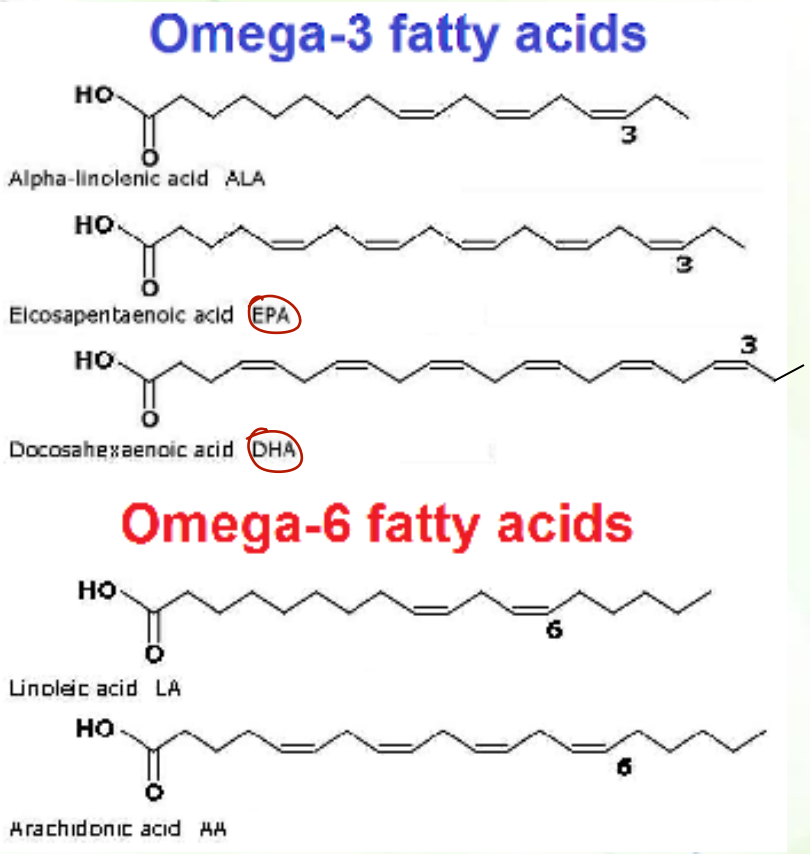
Another way of naming

- (ω)-C: distal methyl C as #1

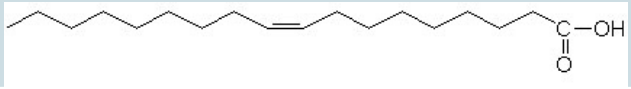
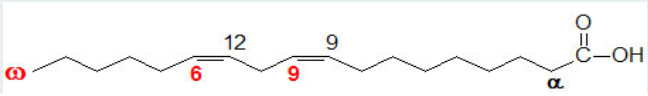
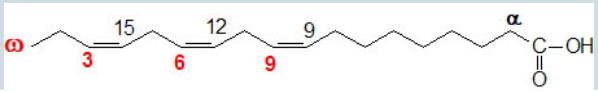
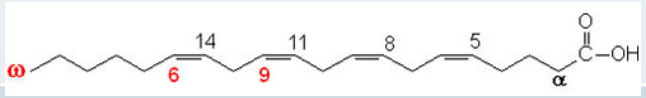
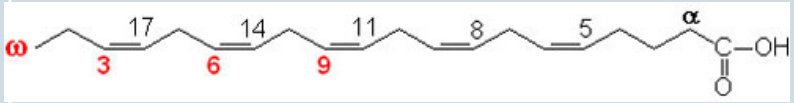
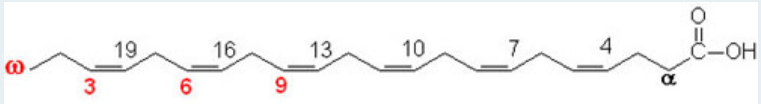
Last letter in greek Alphabet



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



- **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)

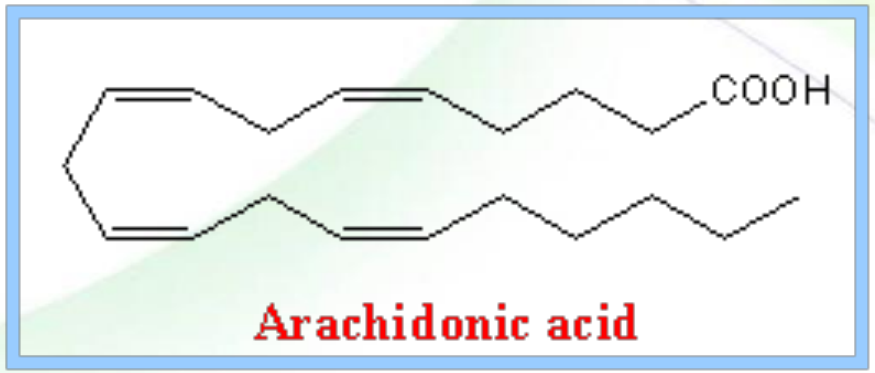
Derived fatty acids: Eicosanoids

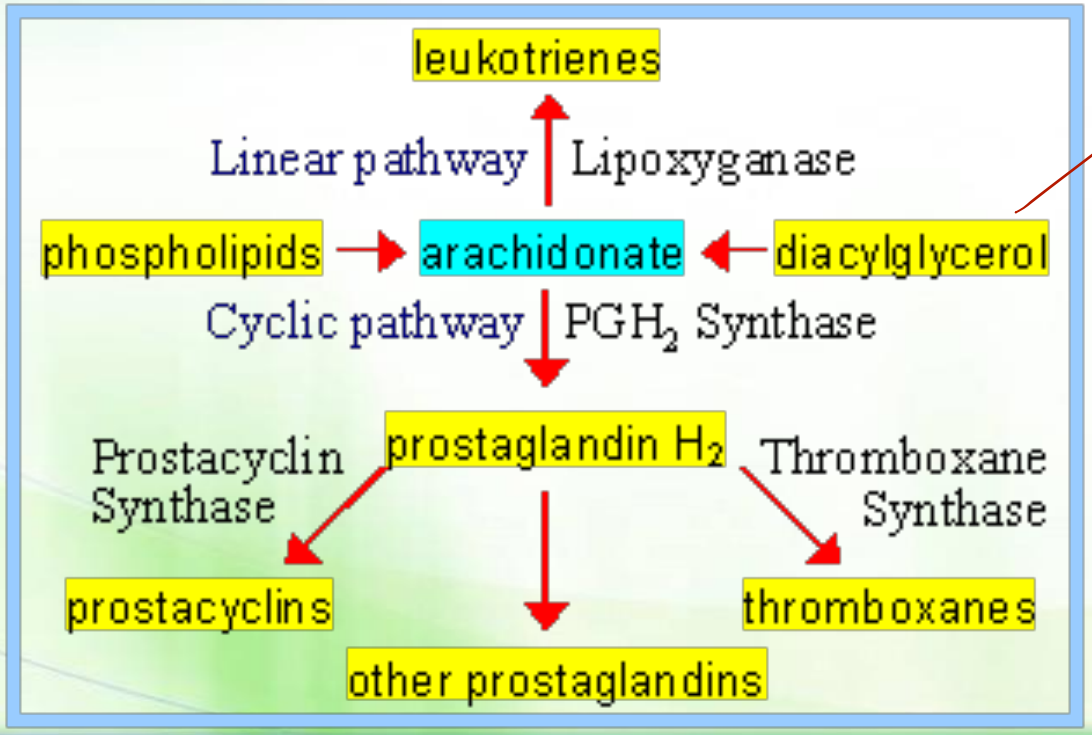
20 carbons ⟹ derived from Arachidonate

Inflammatory Response

Arachidonate

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





Eicosanoids and their functions

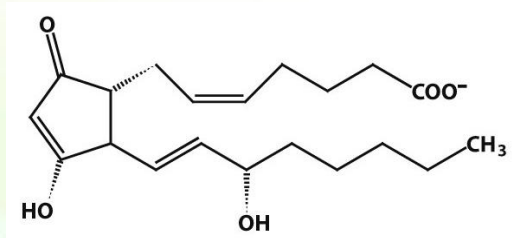
They control cellular function in response to injury

- Prostaglandins
  - Induction of inflammation
  - Inhibition of platelet aggregation
    - Inhibition of blood clotting
- Leukotrienes
  - Constriction of smooth muscles
    - Asthma
- Thromboxanes
  - Constriction of smooth muscles
  - Induction of platelet aggregation
- Prostacyclins
  - An inhibitor of platelet aggregation
  - Induction of vasodilation

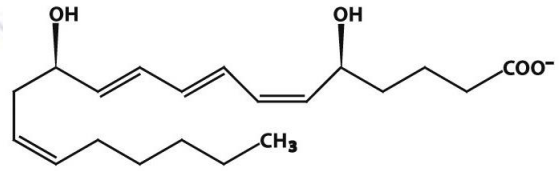
Clumping of platelets together for blood clotting

Neither memorize the specific functions nor the structures

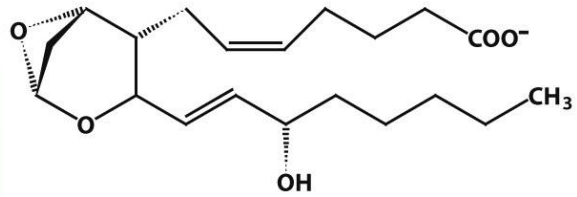
Just know that, in general, they regulate Inflammatory Response



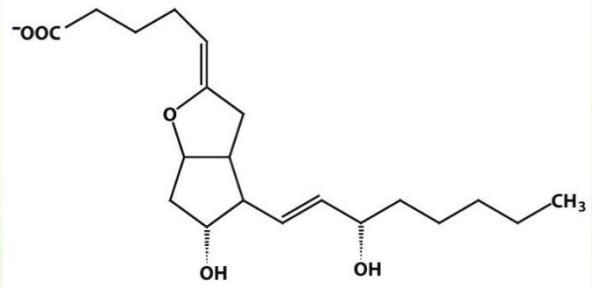
Prostaglandin E_2



Leukotriene B_4



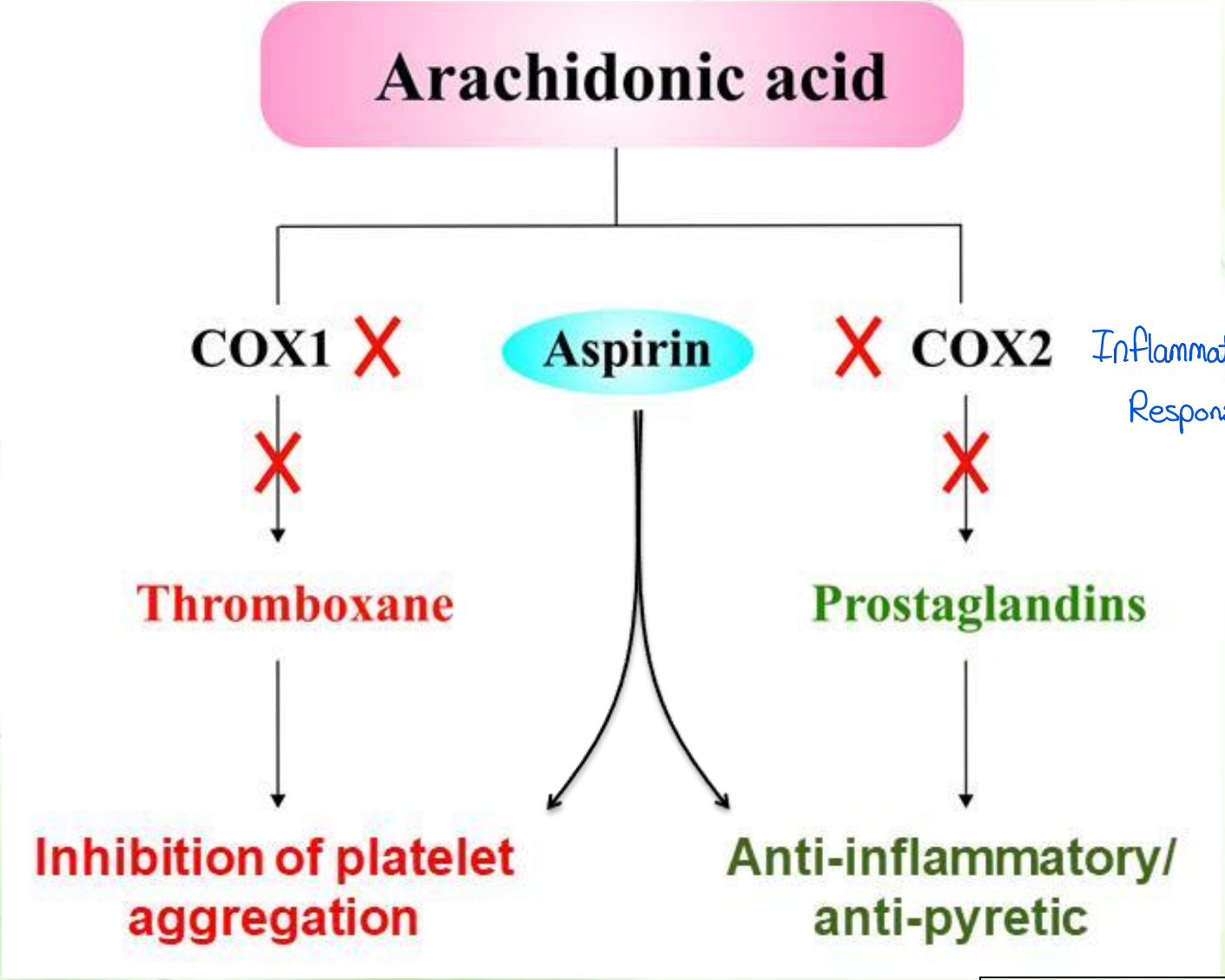
Thromboxane A_2 (TXA_2)



Prostacyclin (PGI_2)

Aspirin is good

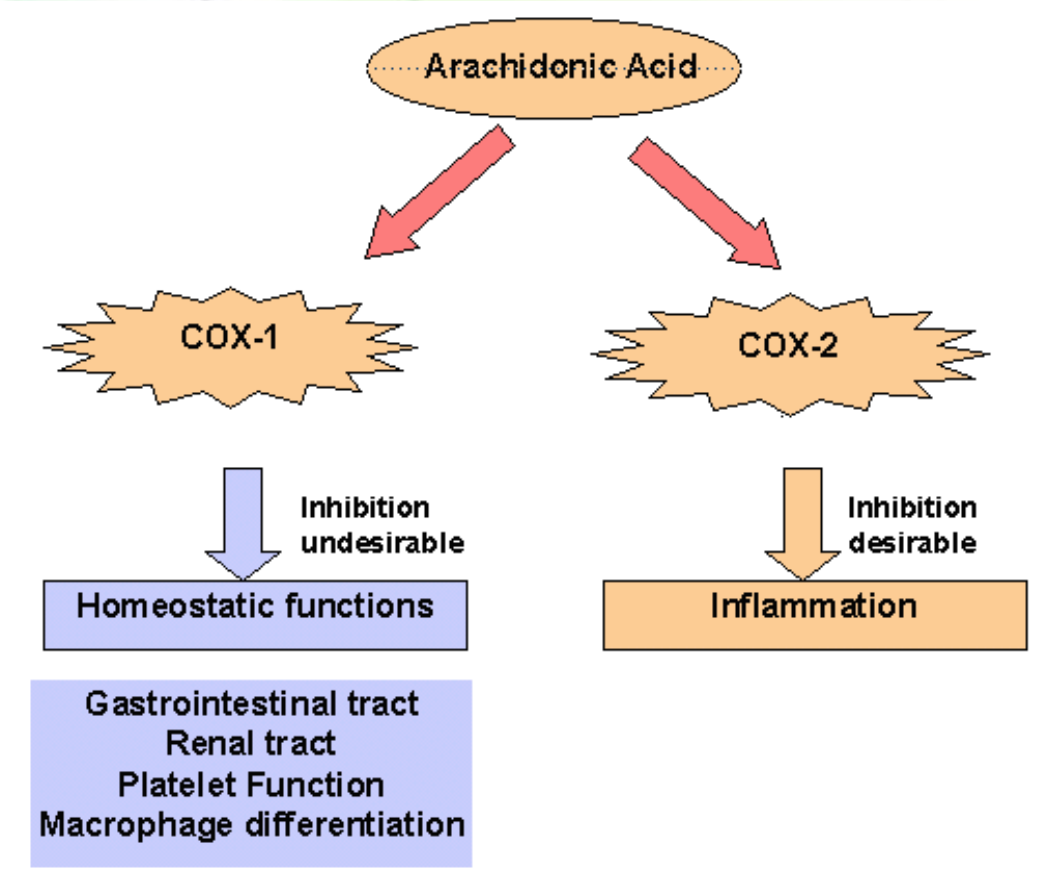
Aspirin also reduces risk of Heart Attack and Stroke.



COX: Cyclooxygenase

Targets of Aspirin

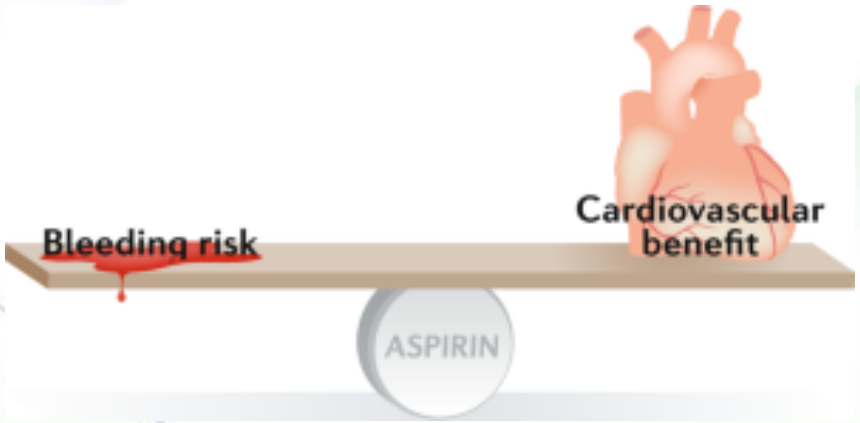
- Cyclooxygenase is present in three forms in cells, COX-1, COX-2, and COX-3.
- Aspirin targets both, but COX-2 should only be the target.

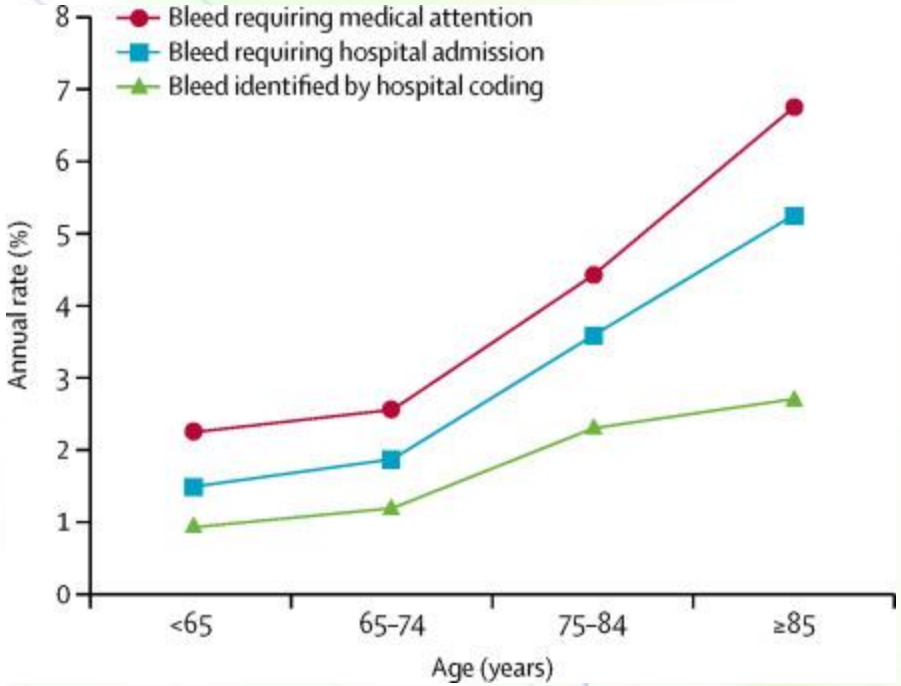


Aspirin can be bad

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 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**).

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
    - It reduces cholesterol in the circulation.

Healthy mediterranean food