Lipids

Summer 2023

Lipids

*Lipids have suitable shape for storage energy and they have high amount of energy

- 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.

*Lipids are water insoluble (hydrophobic)

*Lipids are thermo insulation

Classes

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

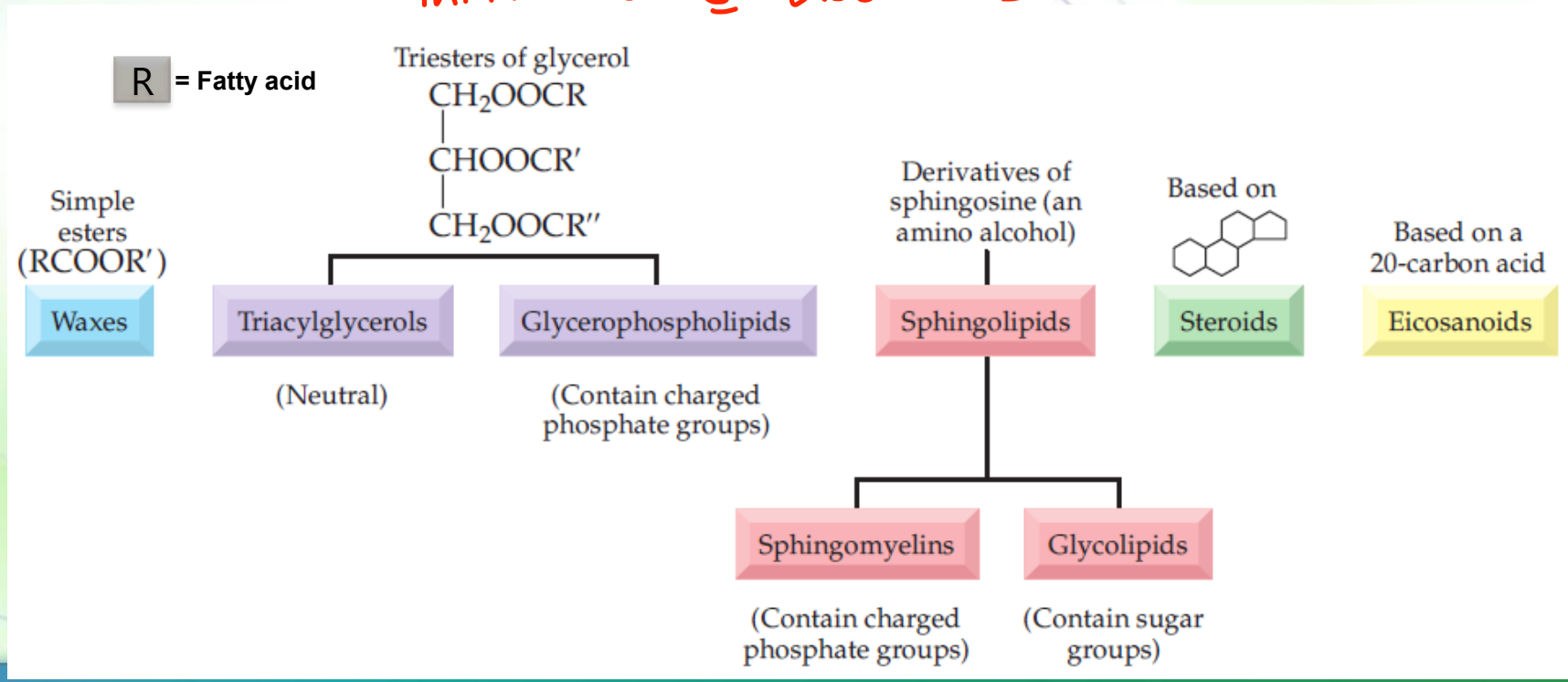
solid Liquid

membrane Lipid

derived From Fatty acid, they act ar inFlammatory mediator

*مش شرط يكون في inFFlammation في bacteria

4 Fused ring



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
- Shock absorbers and thermal insulators

* Aldosterone is a lipid molecule

Fatty acids

- Aliphatic mono-carboxylic acids with a long R chain
- Formula: R-(CH_2)n-COOH *mostly it has even number of carbon
- Lengths
  - Physiological (12-24)
  - Abundant (16 and 18) most common
- Degree of unsaturation
- Amphipathic molecules

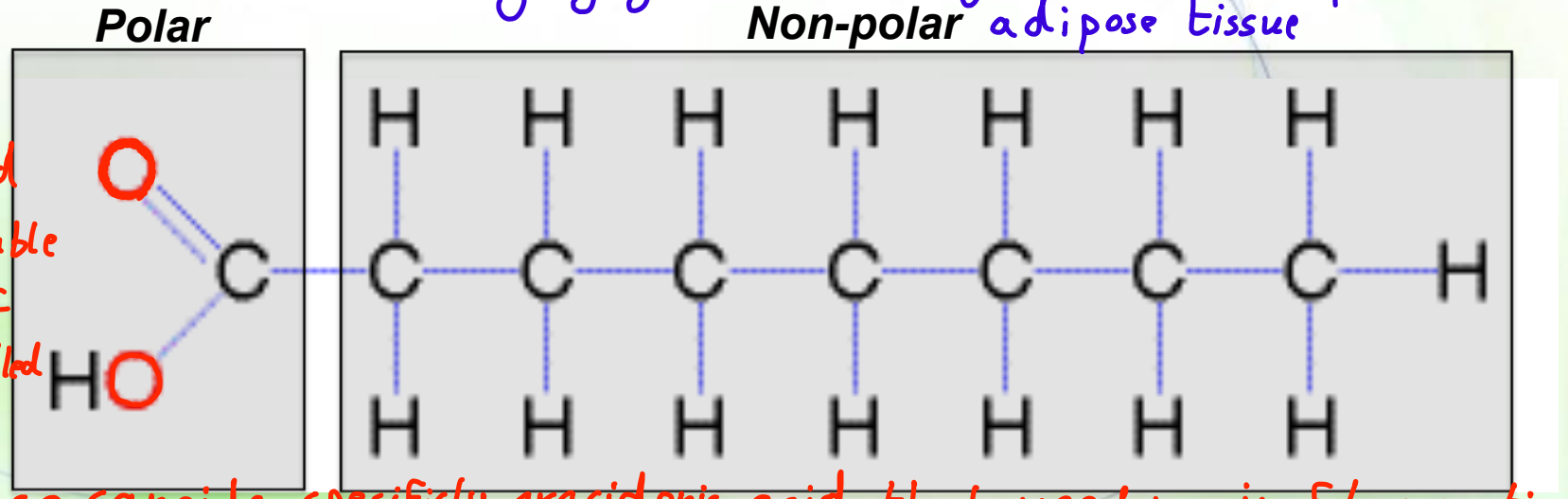
Functions:

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

*triacylglycerol is a storage form of lipid in adipose tissue

*Most of this molecule is non-polar

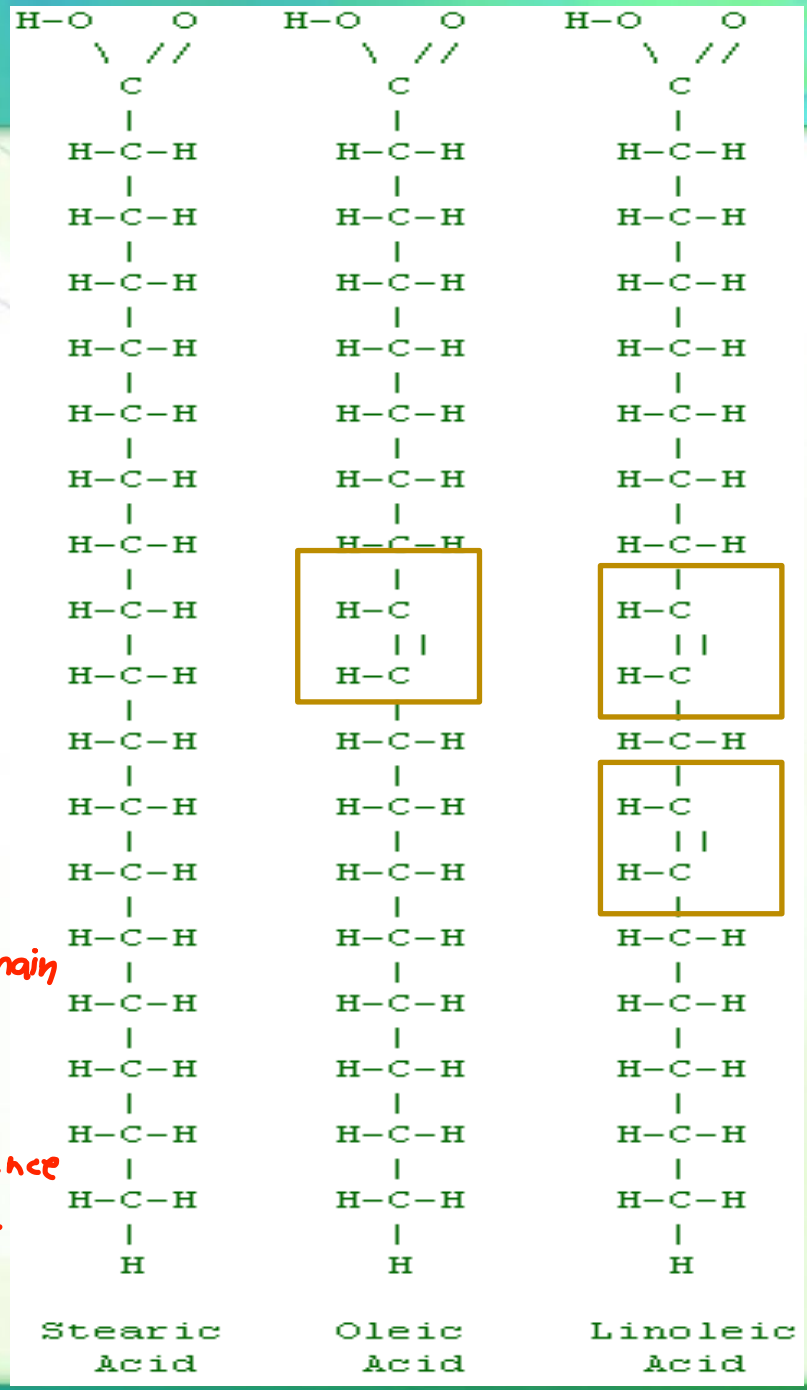
*The chain might be saturated or unsaturated, if it has one double bond it called monounsaturated and if it has more than one double bond it called poly unsaturated



*Fatty acids manufactor eicosanoids, spesificly aracidonic acid that used in in Flammation

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.

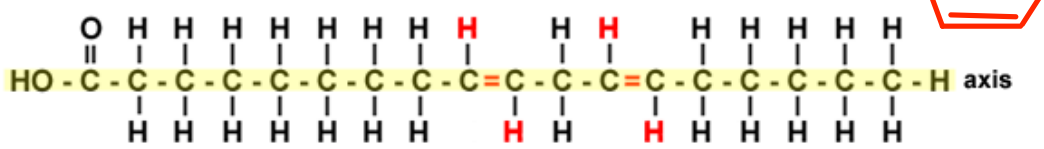


*Double bond make a kink in Fatty acid chain, so we can't make compaction between Fatty acids make them away From each other make more distance between them that decrease non-covalent interaction that make it easy to break, so melting point, poiling point Lesser

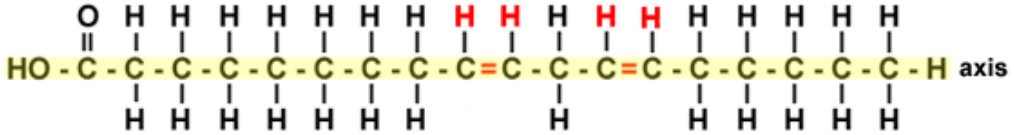
Cis vs. trans bonds

* Oil has more double bond than another lipids

cis trans

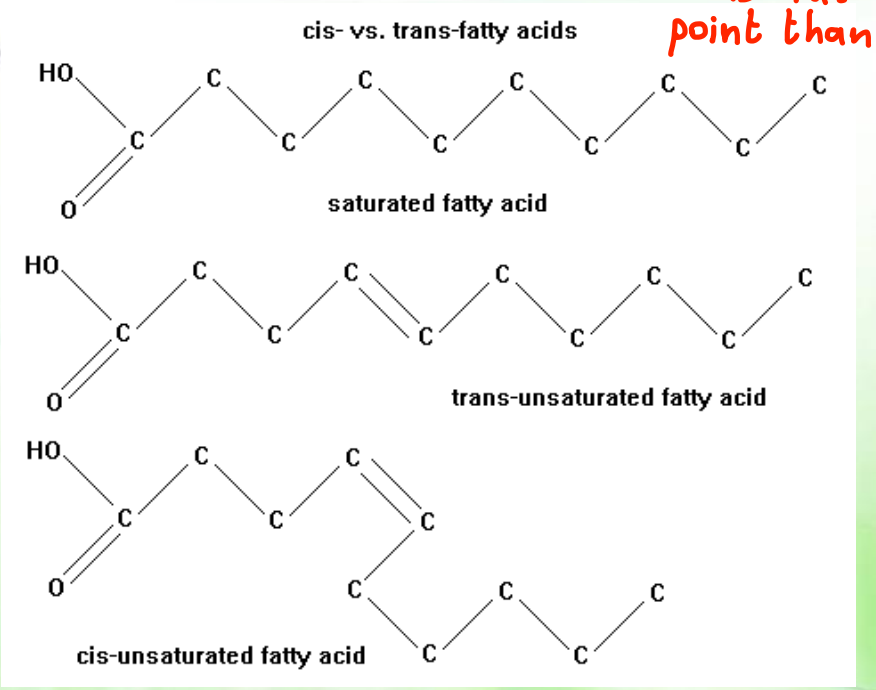


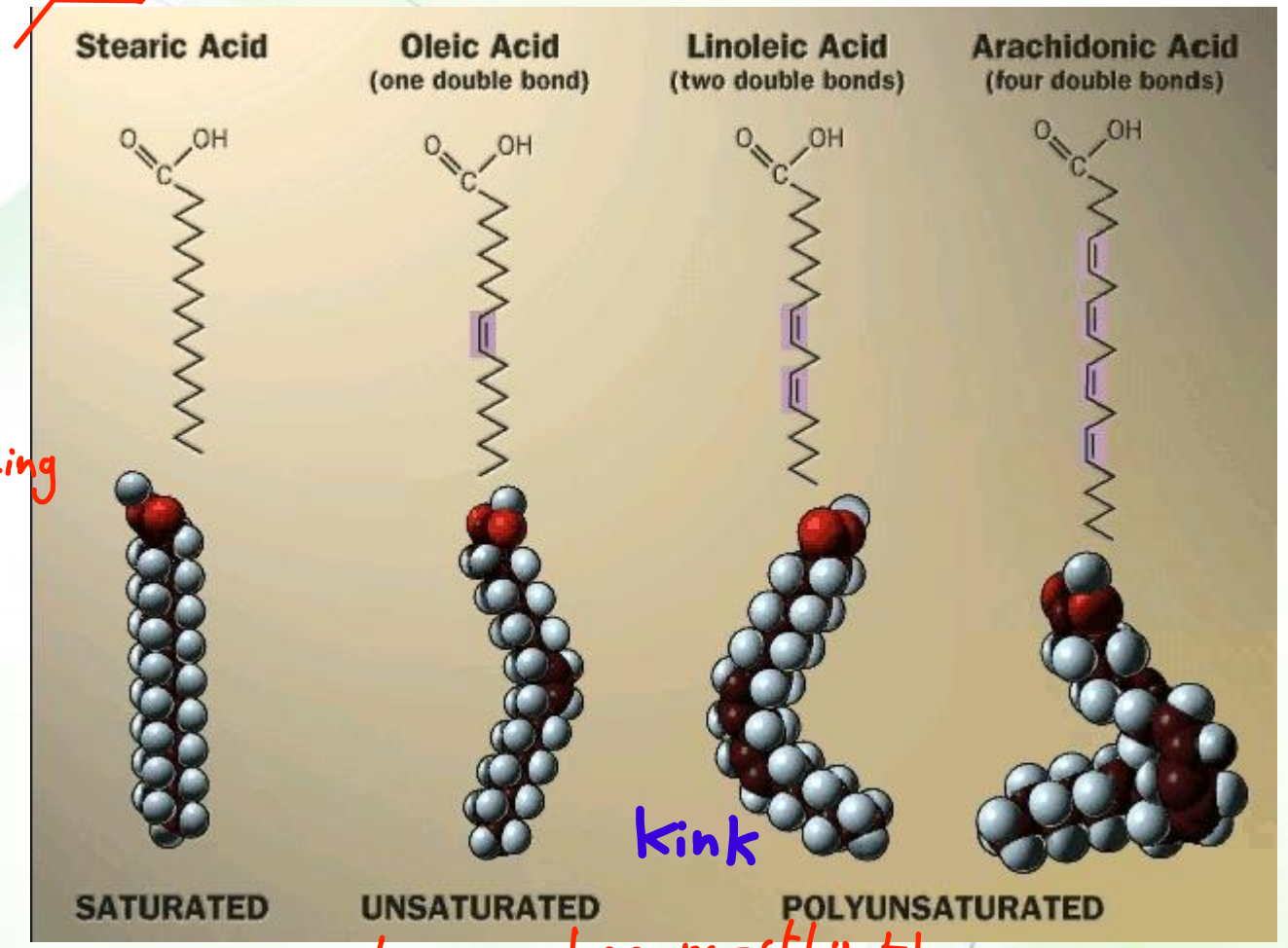
linoleic acid: *trans* configuration (*trans* isomer)



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

tras has higher poiling point than cis





Physiologically:

cis isomer predominates

trans is rare

* trans has mostly the same configration of saturated because they are away from each other

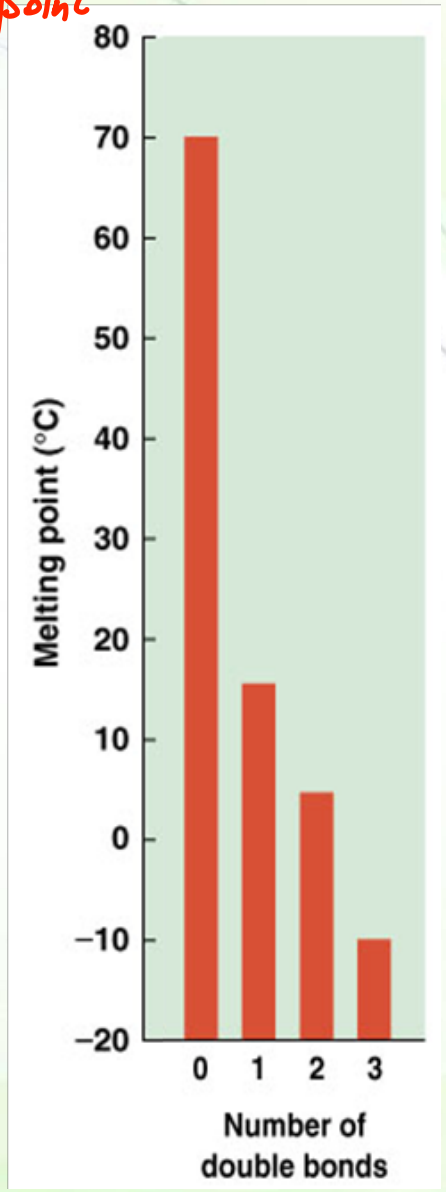
Properties of fatty acids

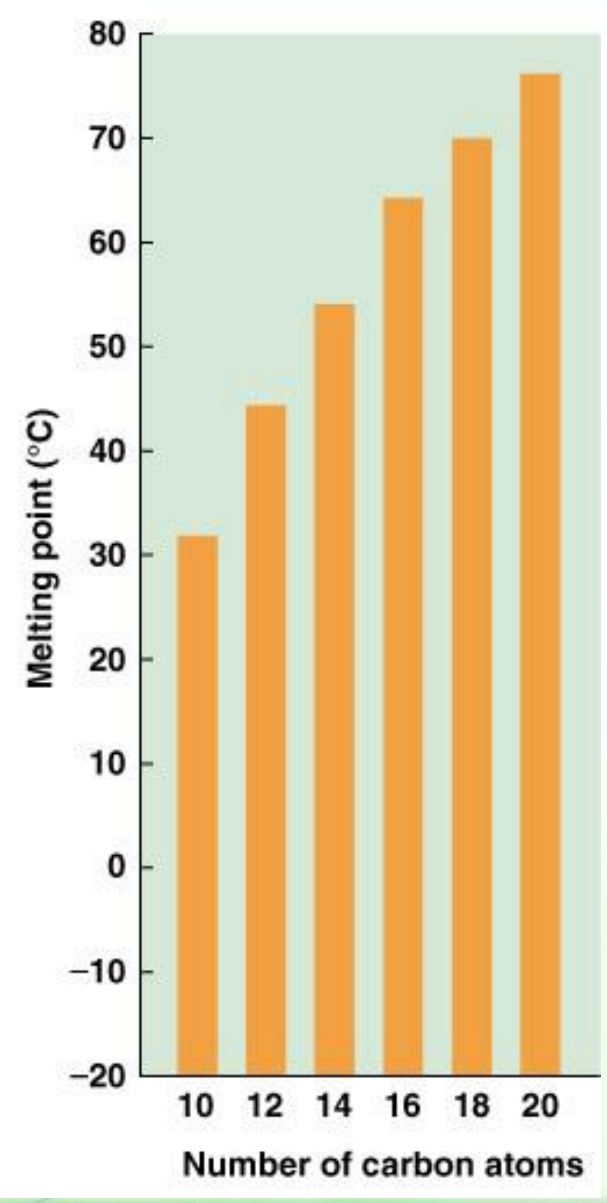
* Double bond effect in boiling and melting point in present or absent and how many they have, and the number of carbons

melting point $\propto$ # of carbons

$$\text{melting point} \propto \frac{1}{\#\text{double bonds}}$$

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





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 (Lower than short chain)	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 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-		

Naming of a fatty acid

* تسمية المركبات بتكون زي تسمية الأرقام باللغة العربية
الثامنة عشر (octadecane)

- 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
  - has zero double bond
  - 18:0 = a C18 fatty acid with no double bonds
    - saturated
    - stearic acid (18:0); palmitic acid (16:0)
  - has two double bond
  - 18:2 = two double bonds (linoleic acid)
    - unsaturated
- Designation of the location of bonds
  - Δn: The position of a double bond
    - more common ← 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)

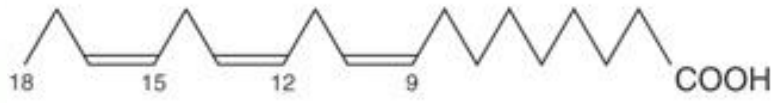
Oleic acid (ω9, 18:1, Δ^9)

First double bond

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

essintial Fatty acid

The body can't manufactor it, so we have to obtain it From diet



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

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

precursor of Eicosanoid

مش مطلوب

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

(EPA)

* When I start naming, First I will look to Fatty acid how many carbon it has, then how many double bond are present and there Location
* We start numbering From carboxylic acid to the end of chain

Octa decanoic acid :- Fatty acid with 18 carbon and no double bond

Octadecenoic acid :- Fatty acid with 18 carbon and 1 double bond

Octadecadienoic acid :- Fatty acid with 18 carbon and 2 double bond

* In omega, we start numbering From the opposite site

Name it in your own

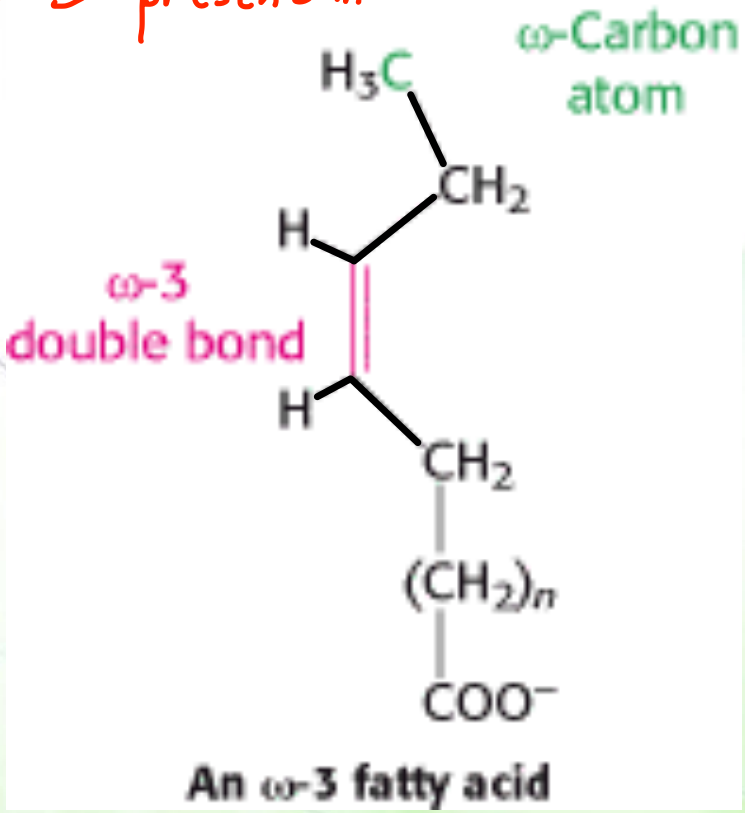
Number of carbons	Number of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	n-Octadecanoate	$CH_3(CH2)_{16}COO^-$
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH=CH(CH_2)_7COO^-$
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	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COO^-$

ate because it has Low pka, so it Lose H^+

Another way of naming

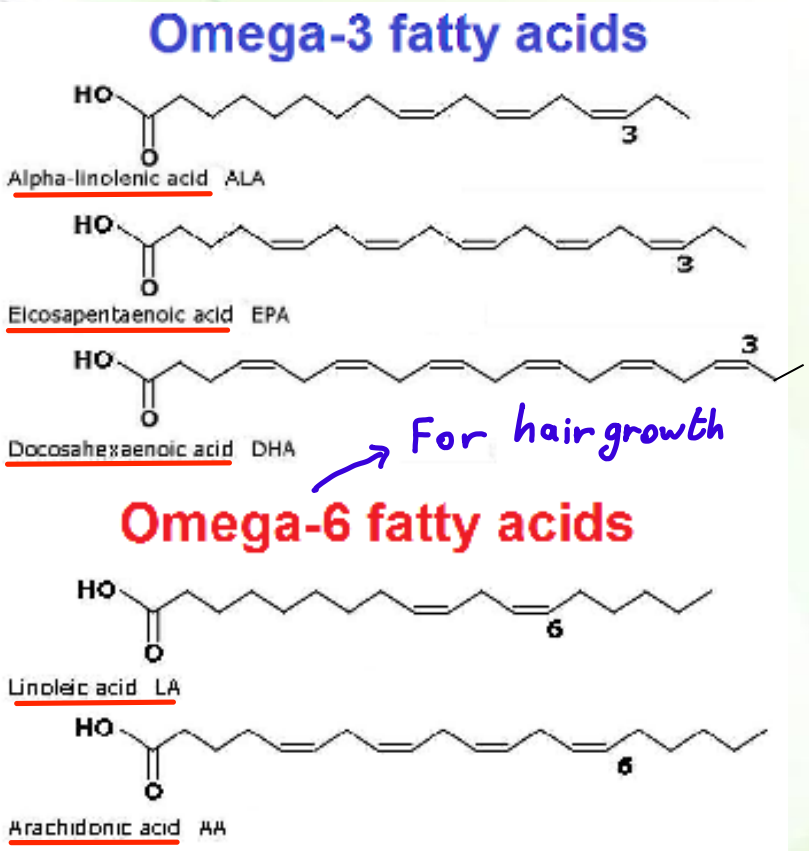
- (ω)-C: distal methyl C as #1

ω-3 present in CNS

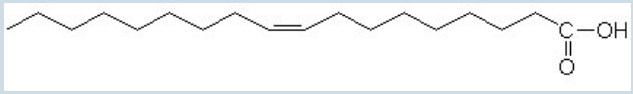
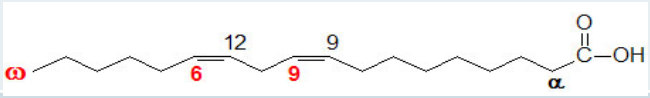
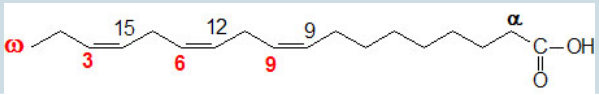
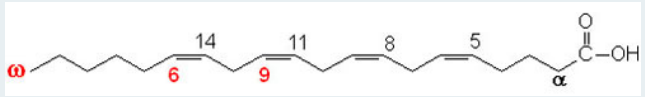
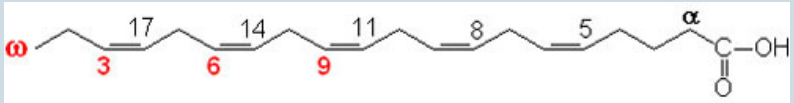
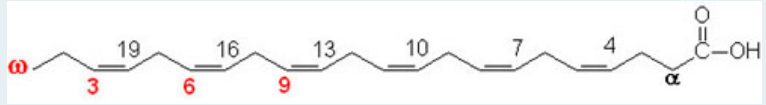


An ω-3 fatty acid

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



- **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)

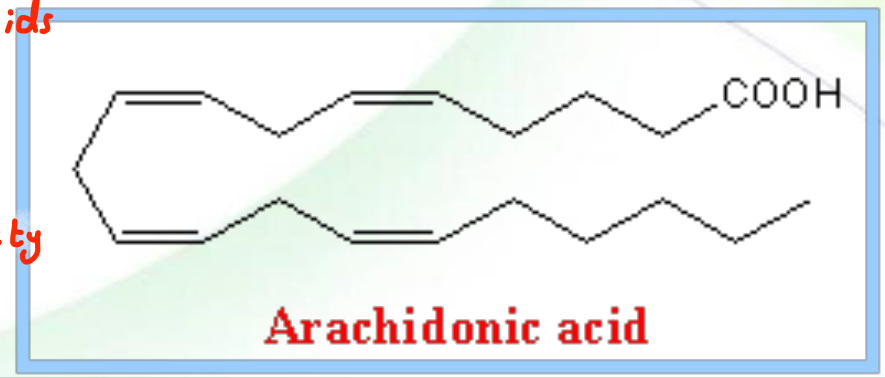
Derived fatty acids: Eicosanoids

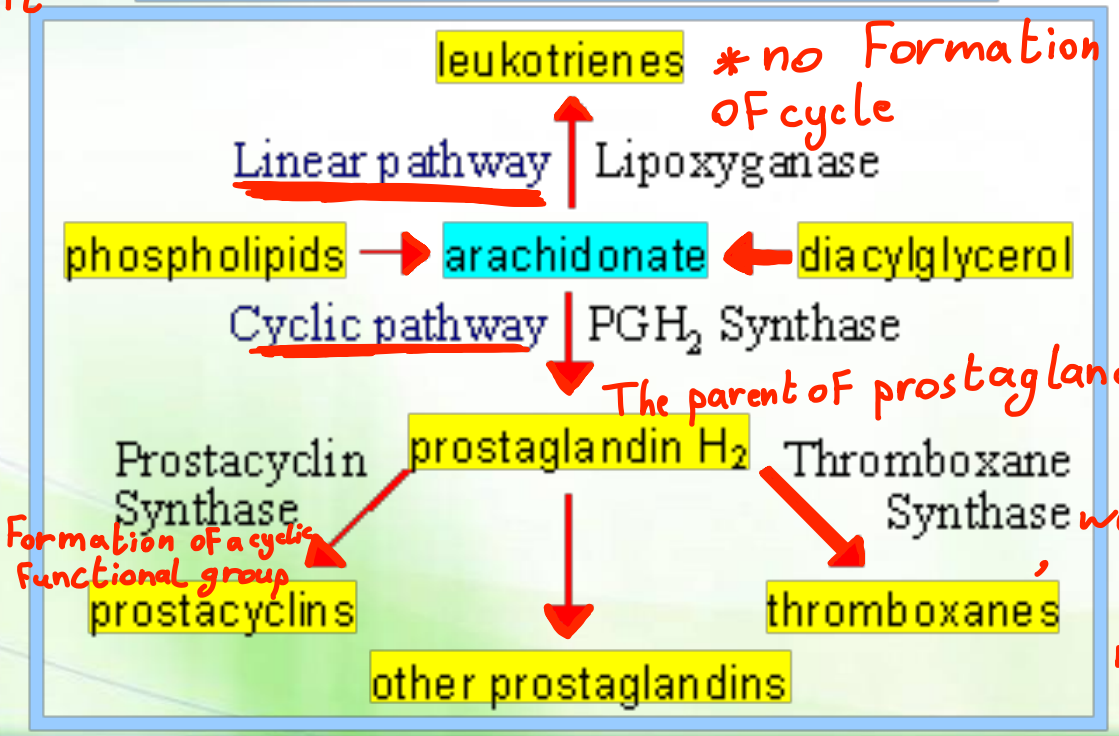
* Eicosanoids derived From Arachidic acid

Arachidonate

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

* It is poly unsaturated Fatty acids with 20 carbon and 4 double bond
* our human body can make it
* when we make it, we separate Fatty acids From tails oF phospholipid and go to the area where we make it





* no Formation oF cycle
* Modification:- Formation of a cyclic and add Functional group
The parent oF prostaglandins

* All oF them are inFlammatory mediator
* The symptoms oF inFlammation are :-
1-redness 2-swelling (edema) 5-increase blood Flow 3-pain 4-heat because we increase permeability oF blood vessel in that's side, leakage oF molecules like leukocytes and White blood cells (WBC) to the inFlammation site

Eicosanoids and their functions

*different molecule that can be derived from arachidonic acid like

They control cellular function in response to injury

- Prostaglandins (because they discovered in prostate)
  - Induction of inflammation
  - Inhibition of platelet aggregation
  - Inhibition of blood clotting (تخثر الدم)
- Leukotrienes (Leukocyte:- white blood cells) (They are discovered in WBC)
  - Constriction of smooth muscles
    - Asthma :- Chronic inflammatory disease
- Thromboxanes
  - Constriction of smooth muscles (more in blood vessels)
  - Induction of platelet aggregation
- Prostacyclins
  - An inhibitor of platelet aggregation
  - Induction of vasodilation

* It discovered in another site, but it still has the same name

*This five membered ring is a charactaristics of all prostaglandin مش مطلوب باقي المجموعات بالشكل

(introduction to blood coagulation)

* It has 4 double bond, but it called triene because it has 3 conjugate bond

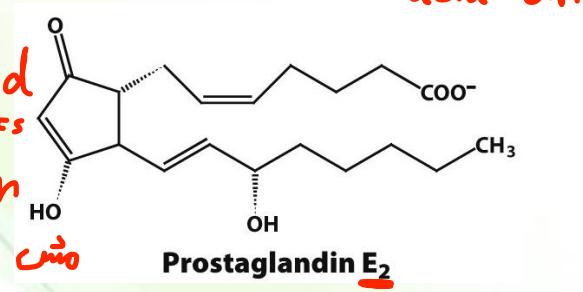
* there are effect in airways

* They are made in cyclic pathway, so they have acycles

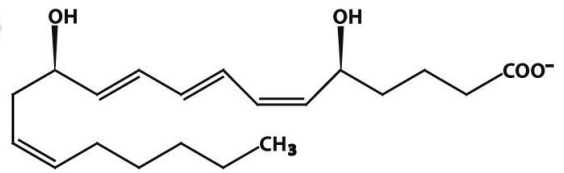
* they have more than one cycle

* opposite from prostaglandins

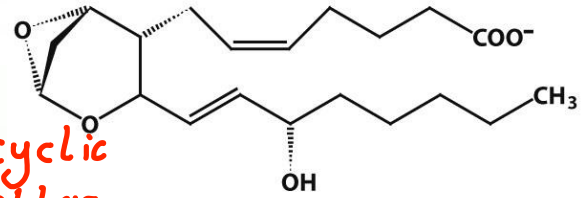
* Relaxation of smooth mucsles



Prostaglandin E_2

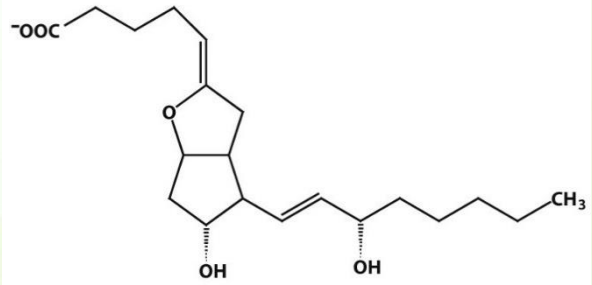


Leukotriene B_4



cyclic ether

Thromboxane A_2 (TXA_2)

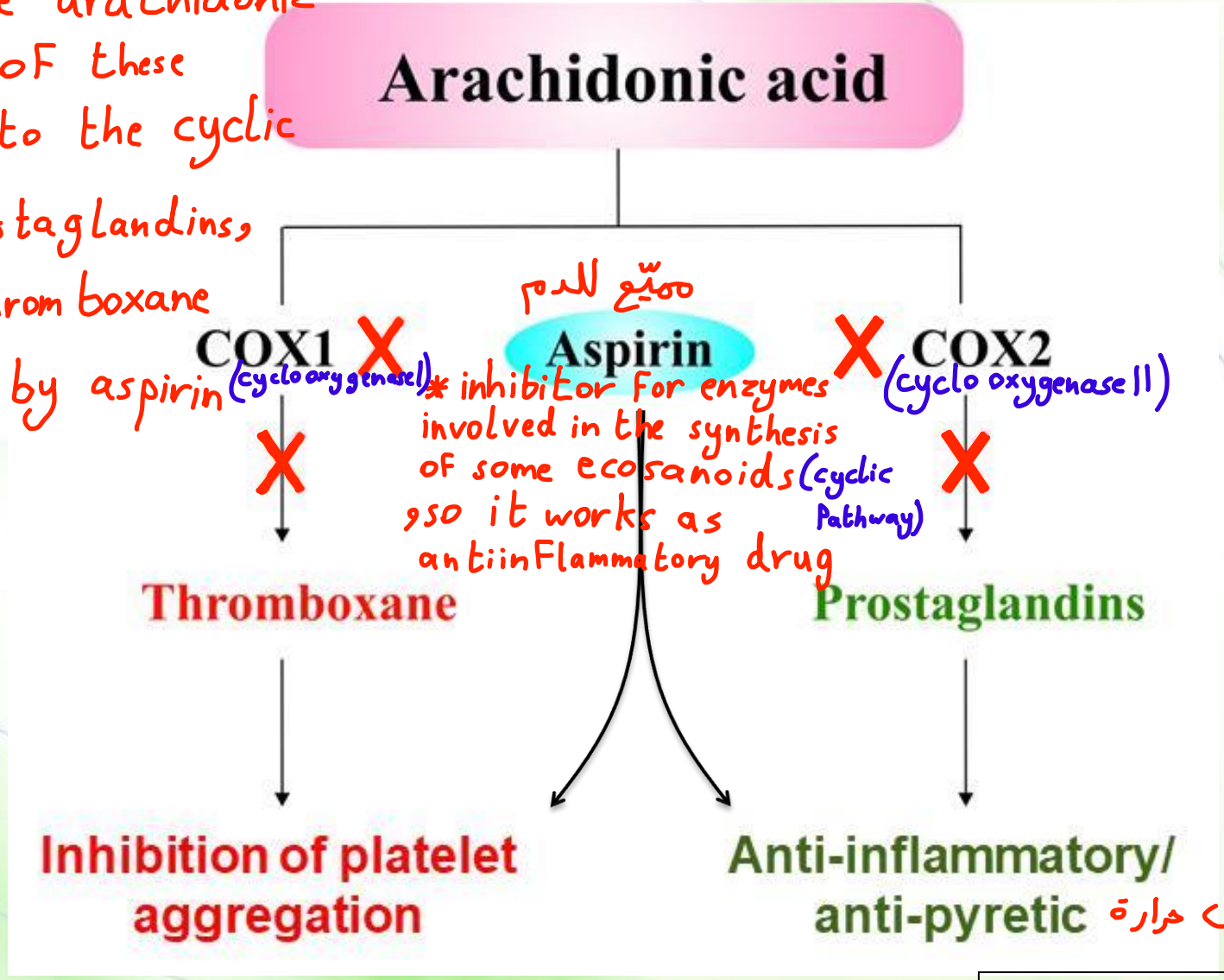


Prostacyclin (PGI_2)

*When the bleed occur The First speed responce of the body to stop this because in any bleed there is loss of blood and Fluid and it may kill the person if it is very large because it make hypovolemic shock is bring platelet and close the injury by it, but it close the injury temporarily, so this introduction and it will be continued by Formation of blood cloot and repair the tissue

Aspirin is good

* The process of use arachidonic acids in synthesis of these molecules that go to the cyclic pathways like prostaglandins, Prostacyclin and thromboxane can be inhibitioned by aspirin

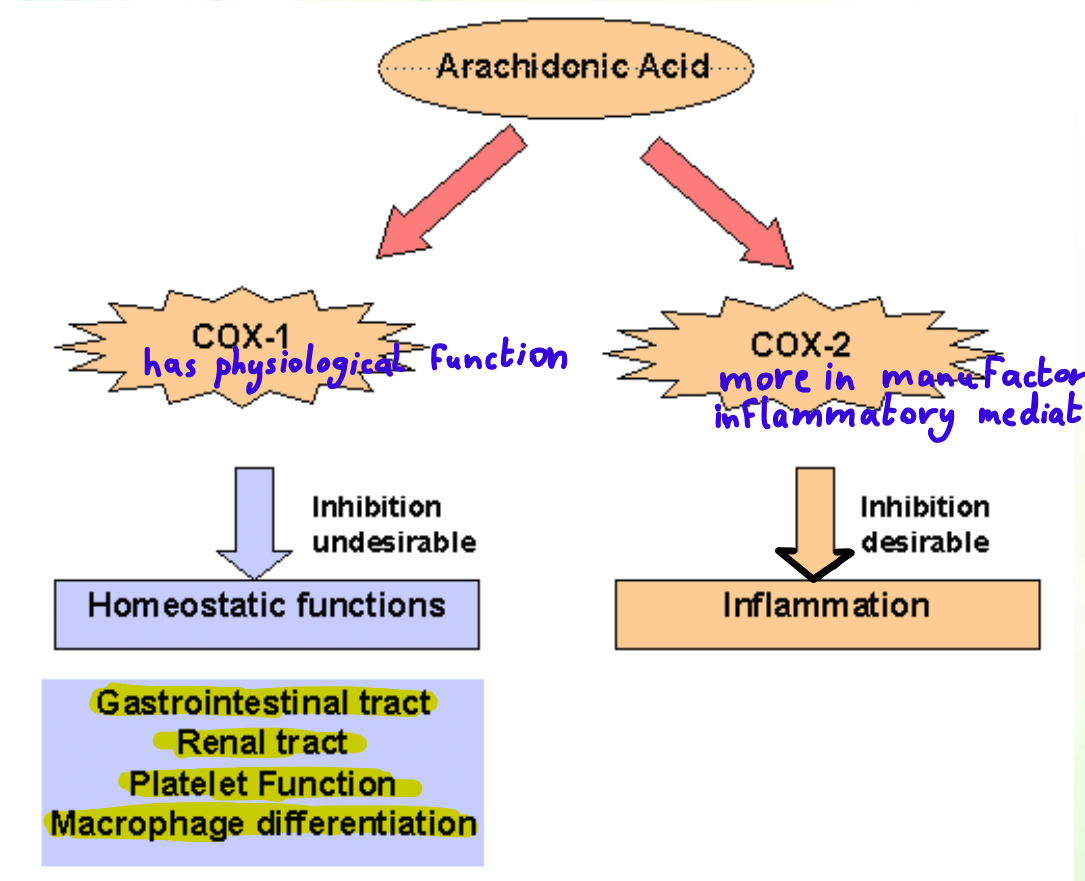


COX: Cyclooxygenase

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.

major Form

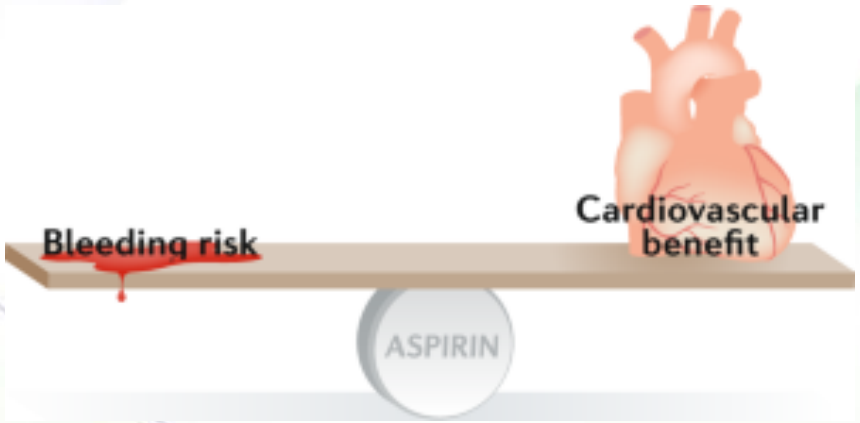


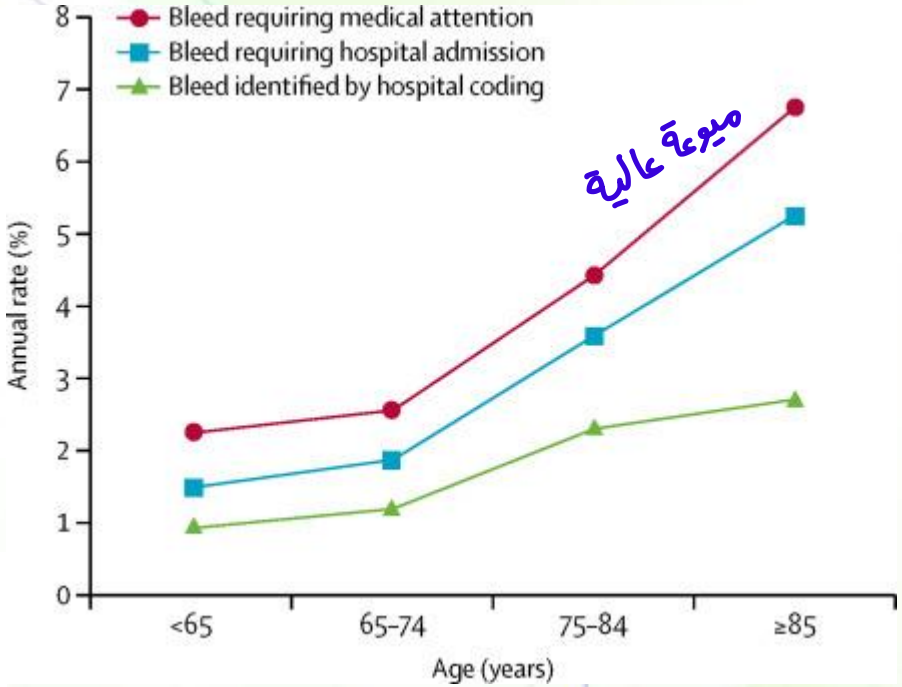
Aspirin is bad

يمنع تخثر الدم

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

* It is like aspirin, but it effect only on COX II
* It is selective, it target COX2 and inhibition it, but it has cardiovascular side effect

- 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

* It is the First double bond From the other side

- Omega-3 fatty acids ↓ inFlammation
  - examples:- α-linolenic acid → eicosapentaenoic acid (EPA) → docosahexaenoic acid (DHA)
    - They reduce inflammatory reactions by:
      - Reducing conversion of arachidonic acid into eicosanoids
      - Promoting the synthesis of anti-inflammatory molecules

* Increase of inFlammation is dangerous because it may cause cancer at long age

- Omega-6 fatty acids:
  - Arachidonic acid ↑ inFlammation
    - stimulates platelet and leukocyte activation,
    - signals pain,
    - Induces bronchoconstriction,
    - regulates gastric secretion

* Fatty acid with the same omega have the same Features

- Omega-9 fatty acids
  - Oleic acid
    - Reduces cholesterol in the circulation

Why is linoleic acid essential?

* Mostly very long Fatty acids >20 present in CNS or nervous system

1. It serves as a precursor of arachidonic acid. ← neuronal Fatty acids
2. It covalently binds another fatty acid attached to cerebrosides (to be discussed) in the skin, forming an unusual lipid (acylglucosylceramide) that helps to make the skin impermeable to water.
   ↳ Linoleic acid + cerebroside

   This function of linoleic acid may help to explain the red, scaly dermatitis and other skin problems associated with a dietary deficiency of essential fatty acids.
3. It is the precursor of important neuronal fatty acids.

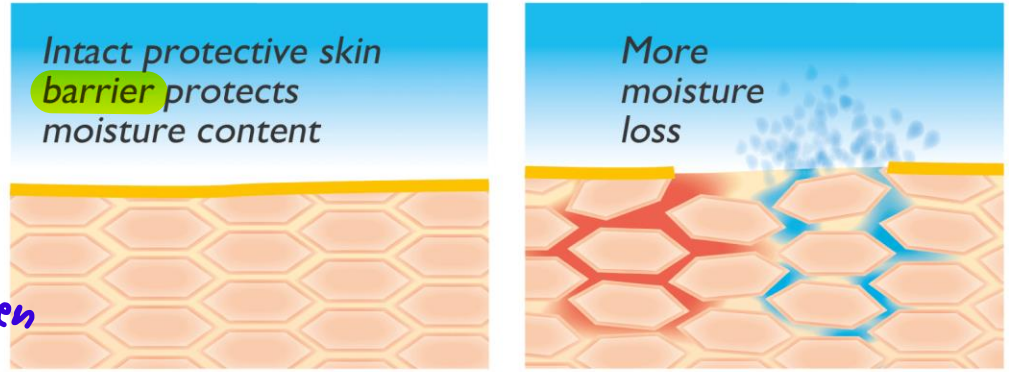
* The skin has Lipid molecules in it, so it prevent water From enter to the body easily.

* IF the skin doesn't have lipid molecules, it will be an exhibition of rips and wounds which is open the skin and lose the Function as a barrier

تعرض للتمزقات

difference between

- essential Fatty acid → can't be synthesized in the body
- non-essetial Fatty acid → can be synthesized in the body

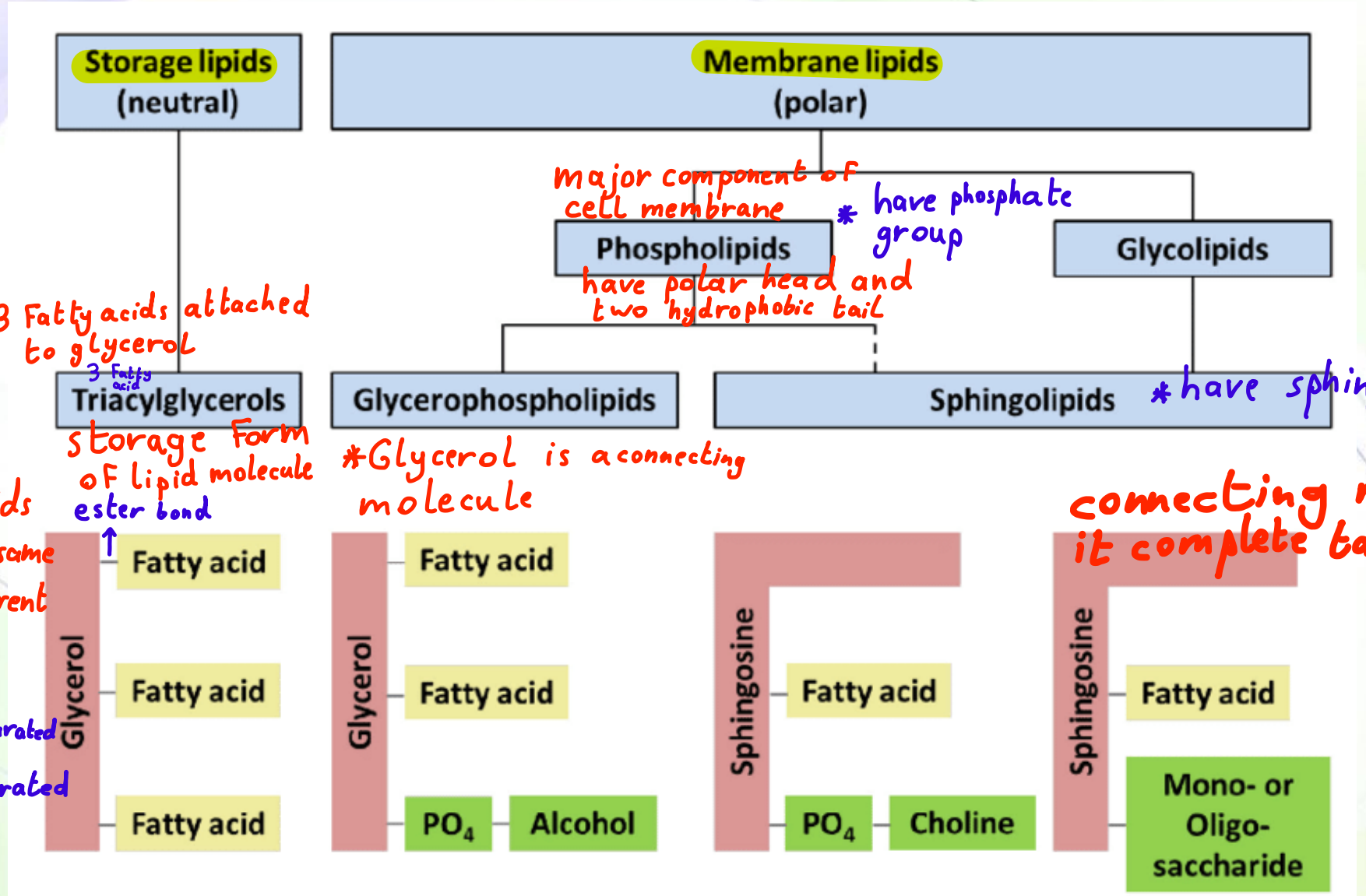


Intact protective skin barrier with linoleic acid rich lipids

Loss of lipids results in break-down in skin barrier function. The skin loses a large amount of water and dries out.

only obtained From Food

Complex lipids


Storage lipids
(neutral)
Membrane lipids
(polar)
major component of cell membrane
* have phosphate group
Phospholipids
Glycolipids
have polar head and two hydrophobic tail
3 Fatty acids attached to glycerol
3 Fatty acid
Triacylglycerols
Glycerophospholipids
Sphingolipids
* have sphingosine
storage form of lipid molecule
ester bond
*Glycerol is a connecting molecule
* Fatty acids could be the same type or different saturated or unsaturated
* oil ↑unsaturated
Fat ↓unsaturated
*
Glycerol
Fatty acid
Fatty acid
Fatty acid
Glycerol
Fatty acid
Fatty acid
PO4
Alcohol
Sphingosine
Fatty acid
PO4
Choline
connecting region it complete tails
Sphingosine
Fatty acid
Mono- or Oligo-saccharide

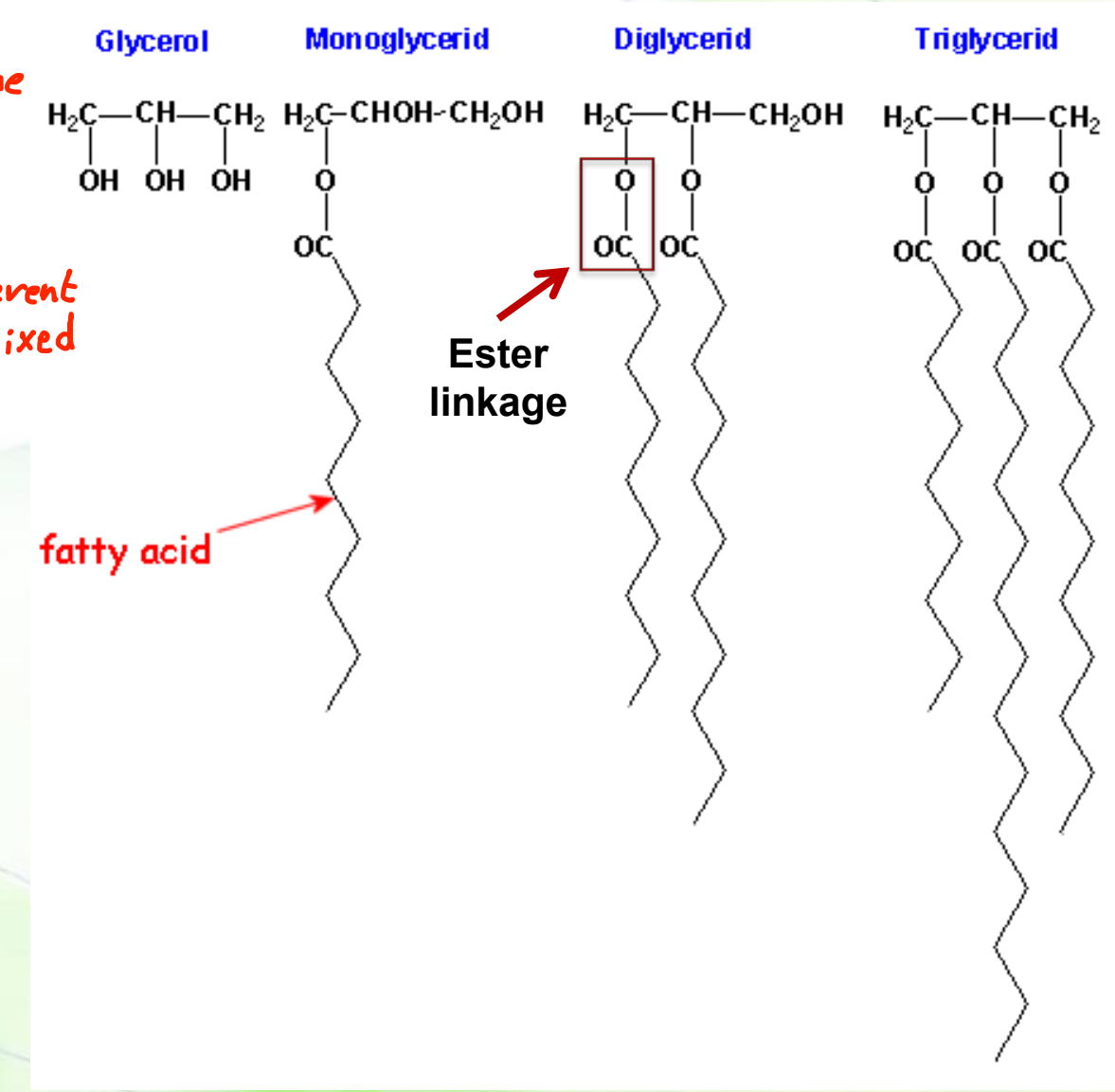
Triglycerides

الدهون الثلاثية (Triacylglycerol)

(old name)

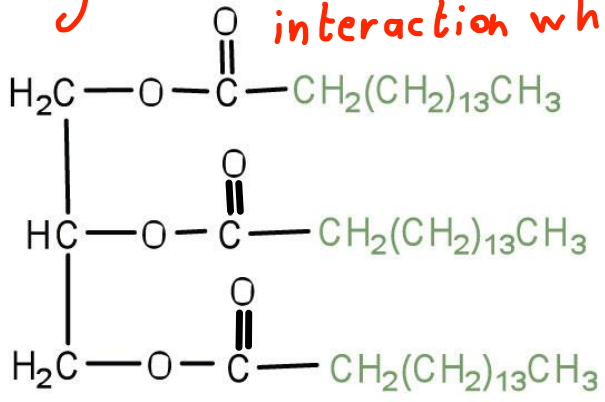
* IF the TAG has the same Fatty acid, it called simple TAG

* IF the TAG has different Fatty acids, it called mixed TAG

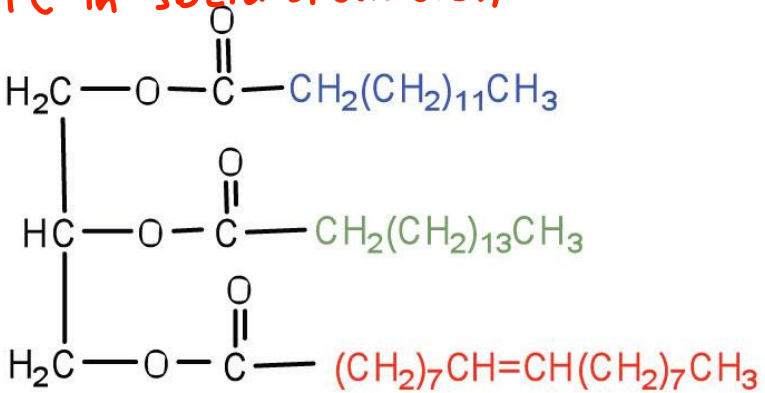


Types of glycerides

* once we have unsaturated fatty acids, we are going to have kink, so it will be wider which decrease non-covalent interactions between TAG which make it more liquid
* In Fats it has high amount of saturated TAG, so it form large number of hydrophobic interaction which make it in solid situation



Tristearin
a simple triglyceride



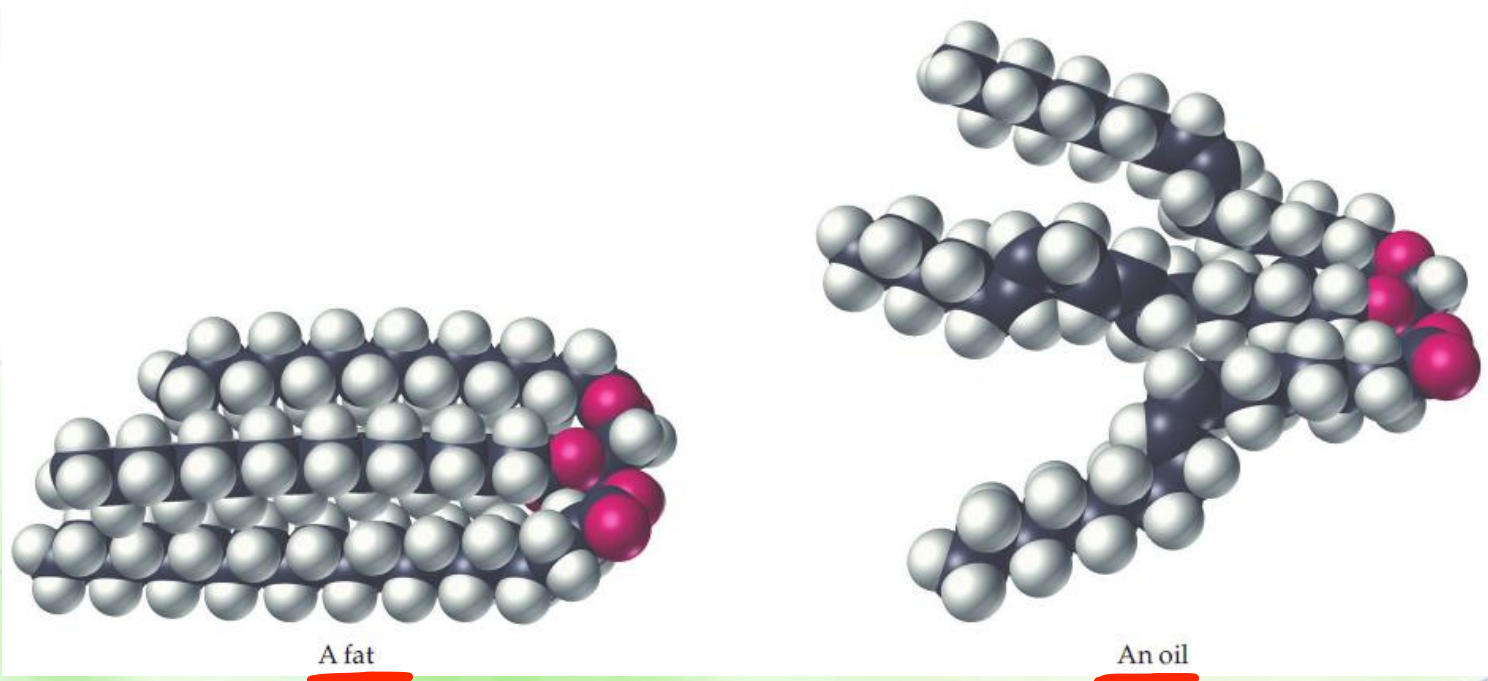
a mixed triglyceride

How soluble will a triglyceride be if fatty acids are unsaturated?

* number of carbons affect in solubility, but saturated and unsaturated has no effect on, but it affect in melting point

Solid vs. liquid fats

- Vegetable oils consist almost entirely of unsaturated fatty acids, whereas animal fats contain a much larger percentage of saturated fatty acids.
  - This is the primary reason for the different melting points of fats and oils.



Saponification

add H_2O

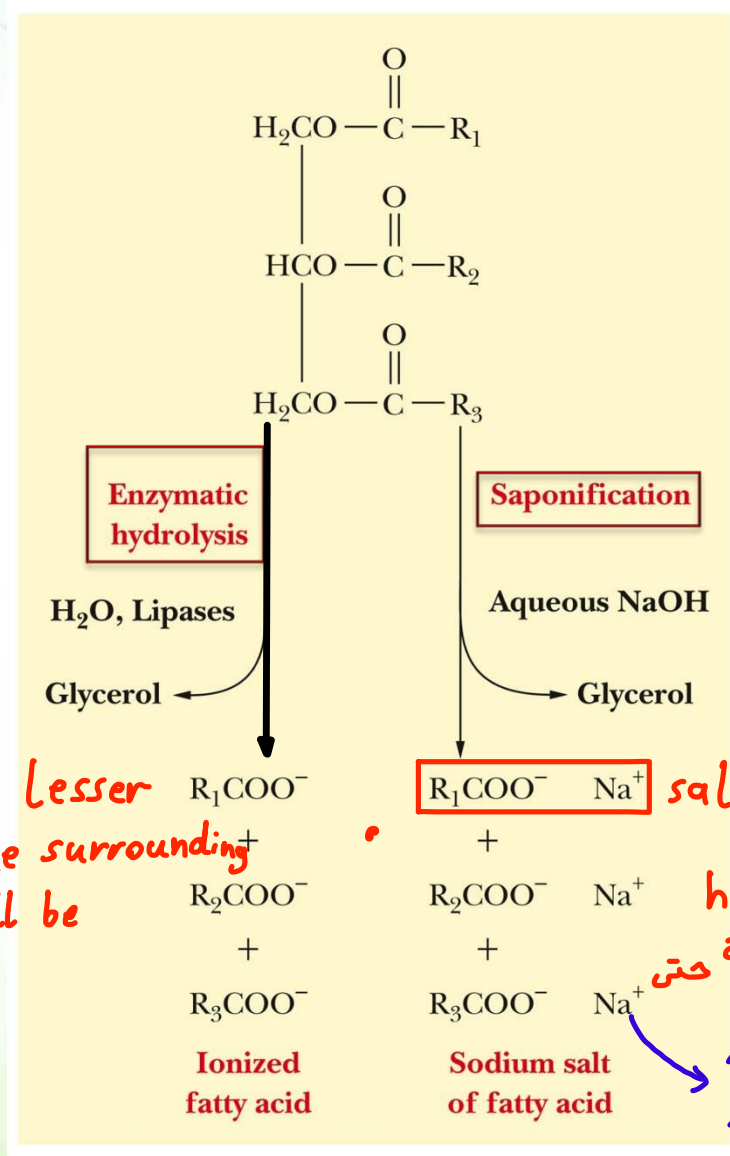
- **Hydrolysis**: steam, acid, enzyme (e.g., lipase of pancreas)

تفاعل تصبن الصابون

- **Saponification**: Alkaline hydrolysis produces salts of fatty acids (soaps). Soaps cause emulsification of oily material.

* TAG react with a base which make the base to react with carboxylic acid and produce a salt, water and glycerol

* we take the triacyl glycerol and react it release all the fatty acids, a reaction occurs with the alkaline group like NaOH



pka is lesser than the surrounding, so it will be ionized

salt (amphipathic molecule has polar head and non-polar tail)

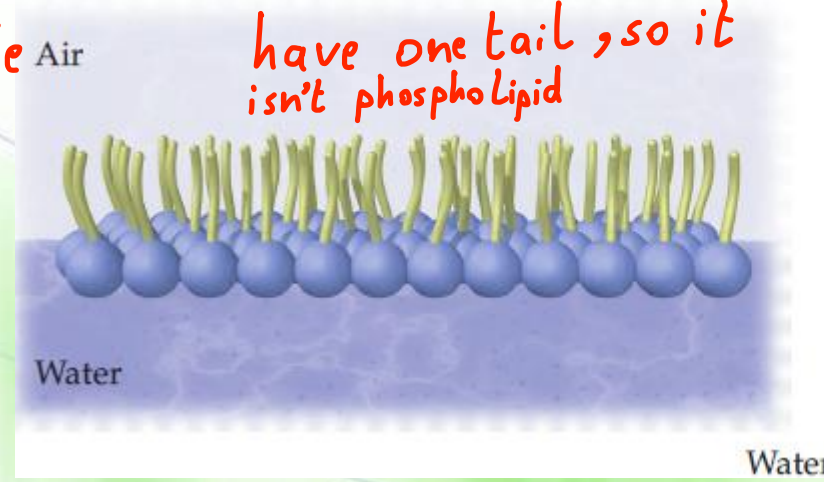
الذرات تبقى مشحونة حتى لو ارتبطت مع بعضها

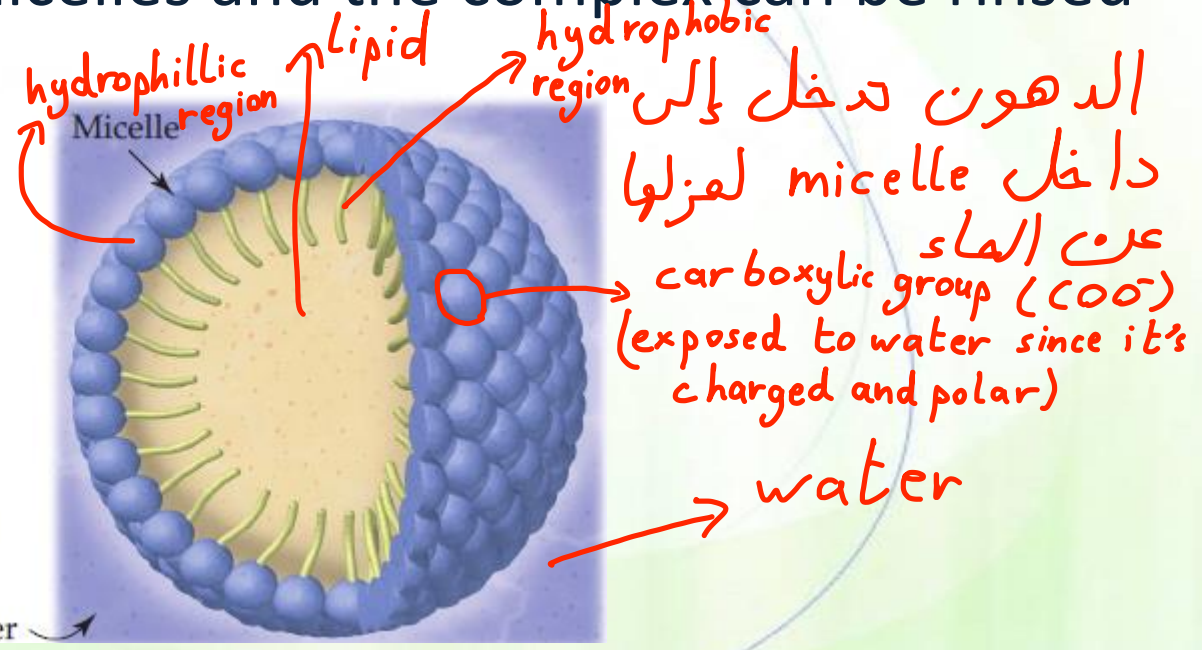
↑ charge
↑ polarity
* more effecient removal of Fats

How does soap work?

- When mixed with water, the hydrophobic hydrocarbon tails cluster together to create a nonpolar microenvironment and the hydrophilic ionic heads interact with water.
- The resulting spherical clusters are called micelles.
- Grease and dirt are trapped inside micelles and the complex can be rinsed away.

* one bubble doesn't represent one micelle ,it present a lot of micelles





* because it's amphipathic (hydrocarbon chain is hydrophobic while the polar is hydrophilic)
Let's say you are try to wash your hand From oil or grase, chain of Fatty acid will surround them and once we wash the soup with water, it interacts with the polar heads of Fatty acids, removing the oil or grease

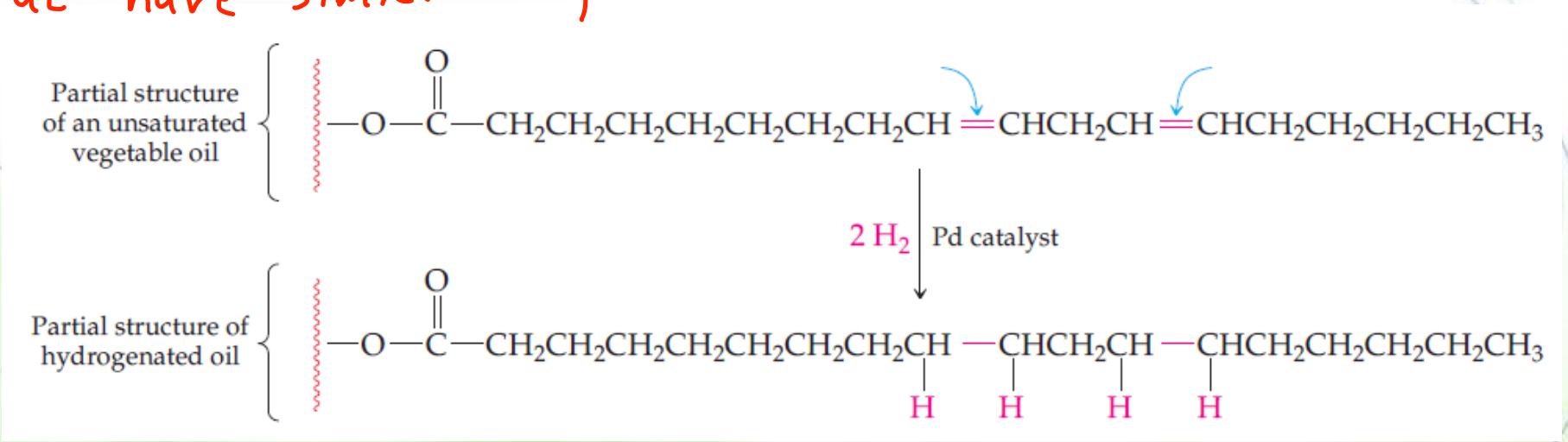
Hydrogenation الهدرجة

(add H_2) unsaturated → saturated

- The carbon-carbon double bonds in vegetable oils can be hydrogenated to yield saturated fats in the same way that any alkene can react with hydrogen to yield an alkane.

* When we add H_2 to lipid has double bonds, it transform it to saturated, but not all double will be saturated, only some of them and other will transform to trans configration

* trans Fat have similar shape to saturated Fat



Trans fat

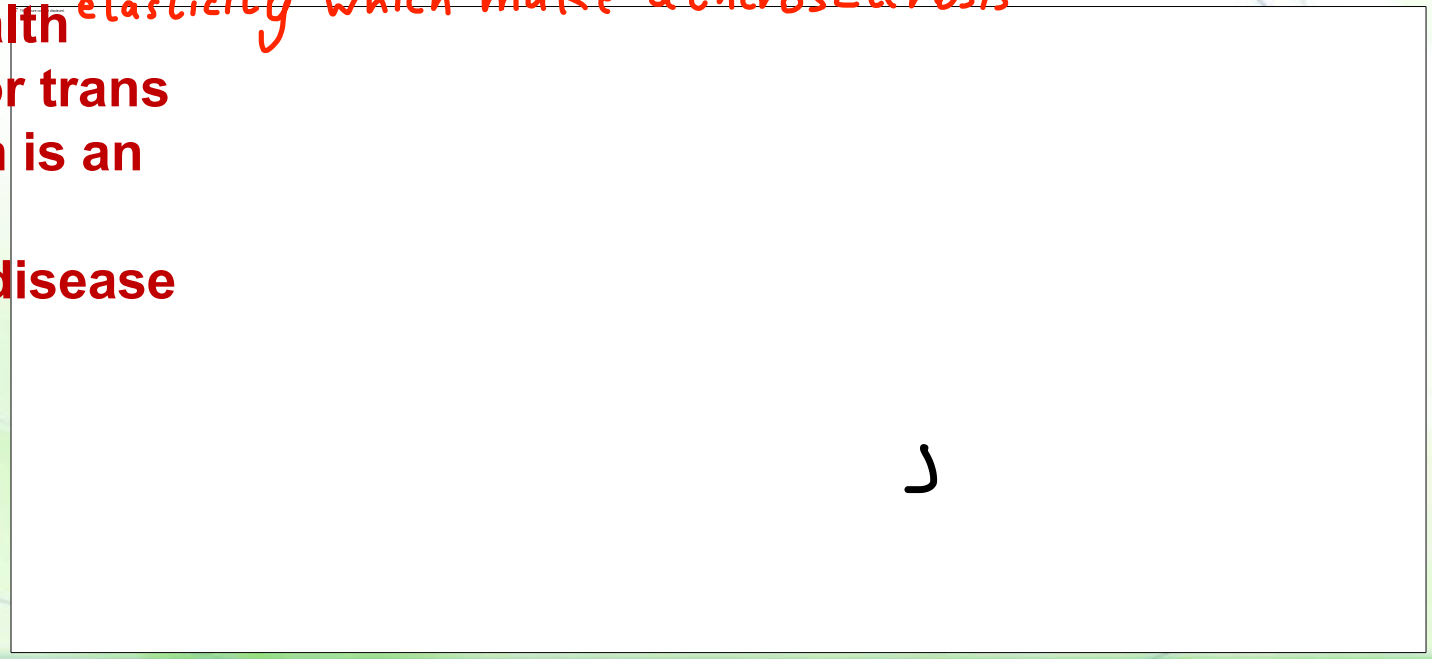
* It has side effect in health, spicifically to cardiovascular system

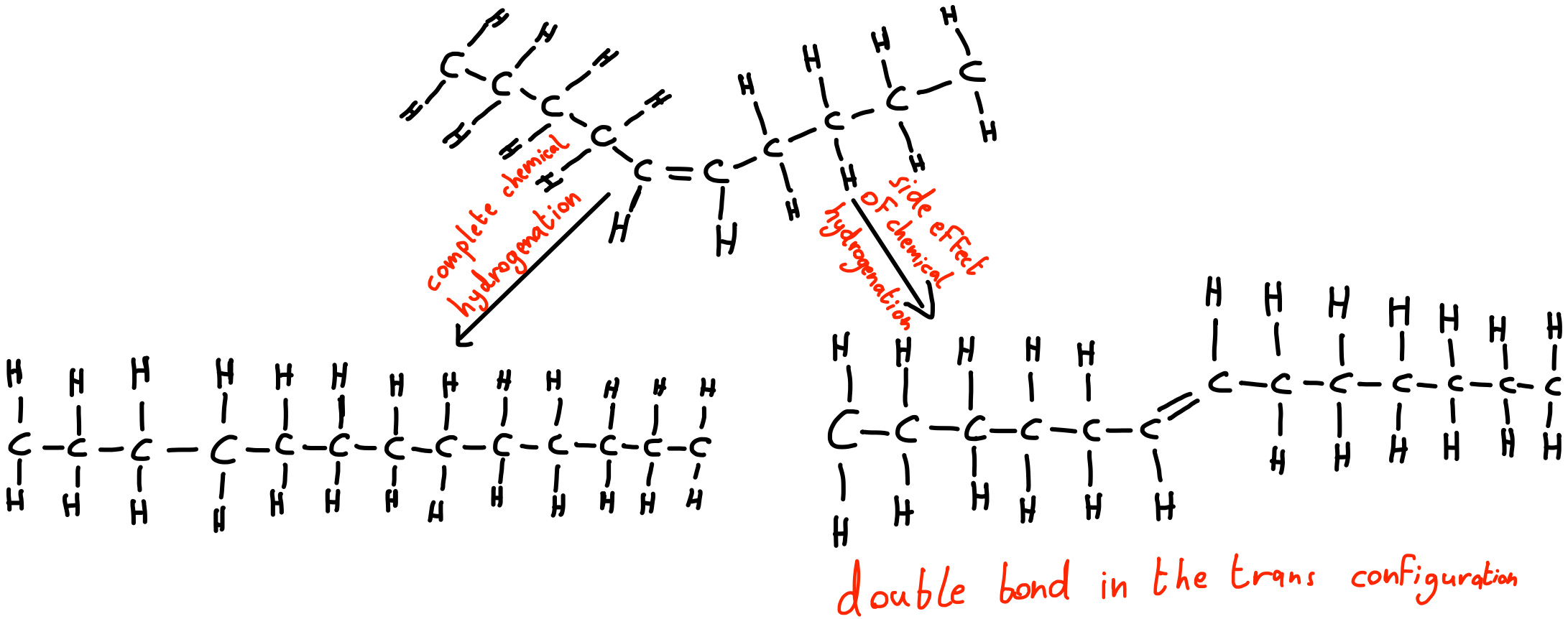
- Although the animal fat is unhealthy, it has better cooking properties and better taste.
- Therefore, chemists invented a method of converting unsaturated oil into solid form by partially hydrogenating it.
- Partial hydrogenation converts some, but not all, double bonds into single bonds generating (trans fats).

* high concentration, make perciptation

* when trans Fat accumulate, it will be rigid, so it perciptate in blood vessel make it narrow and increase rigidity which make it loss their elasticity which make atherosclerosis

The primary health risk identified for trans fat consumption is an elevated risk of coronary heart disease (CHD).





double bond in the trans configuration

Example: margarine

* Butters come only From animals not plants

- In margarine, only about two-thirds of the double bonds present in the starting vegetable oil are hydrogenated, so that the margarine remains soft in the refrigerator and melts on warm toast.

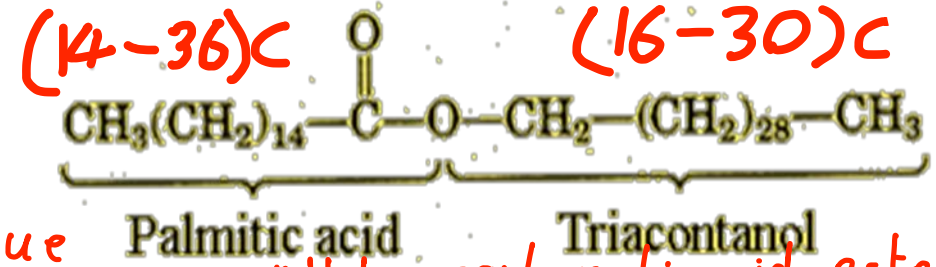
Nutrition Facts

Serving Size 1 Tbsp (14g)
Servings Per Container 32

Amount Per Serving	
Calories 100	Calories from Fat 100
	% Daily Value*
Total Fat 11g	17%
Saturated Fat 2g ←	10%
Trans Fat 3g ←	
Cholesterol 0mg	→ 0%

Waxes

(14-36)C (16-30)C



* very hydrophobic
* there is no nutritional value
* It has carboxylic acid ester

- Solid simple lipids containing a monohydric alcohol (C16 ~ C30, higher molecular weight than glycerol) esterified to long-chain fatty acids (C14 ~ C36). Examples: palmitoyl alcohol
- Insoluble in water
- Are not easily hydrolyzed (fats) & are indigestible by lipases
- Are very resistant to rancidity
- Are of no nutritional value
- Coatings that prevent loss of water by leaves of plants

Like ducks which have wax in their skin prevent it from absorb water and sinking

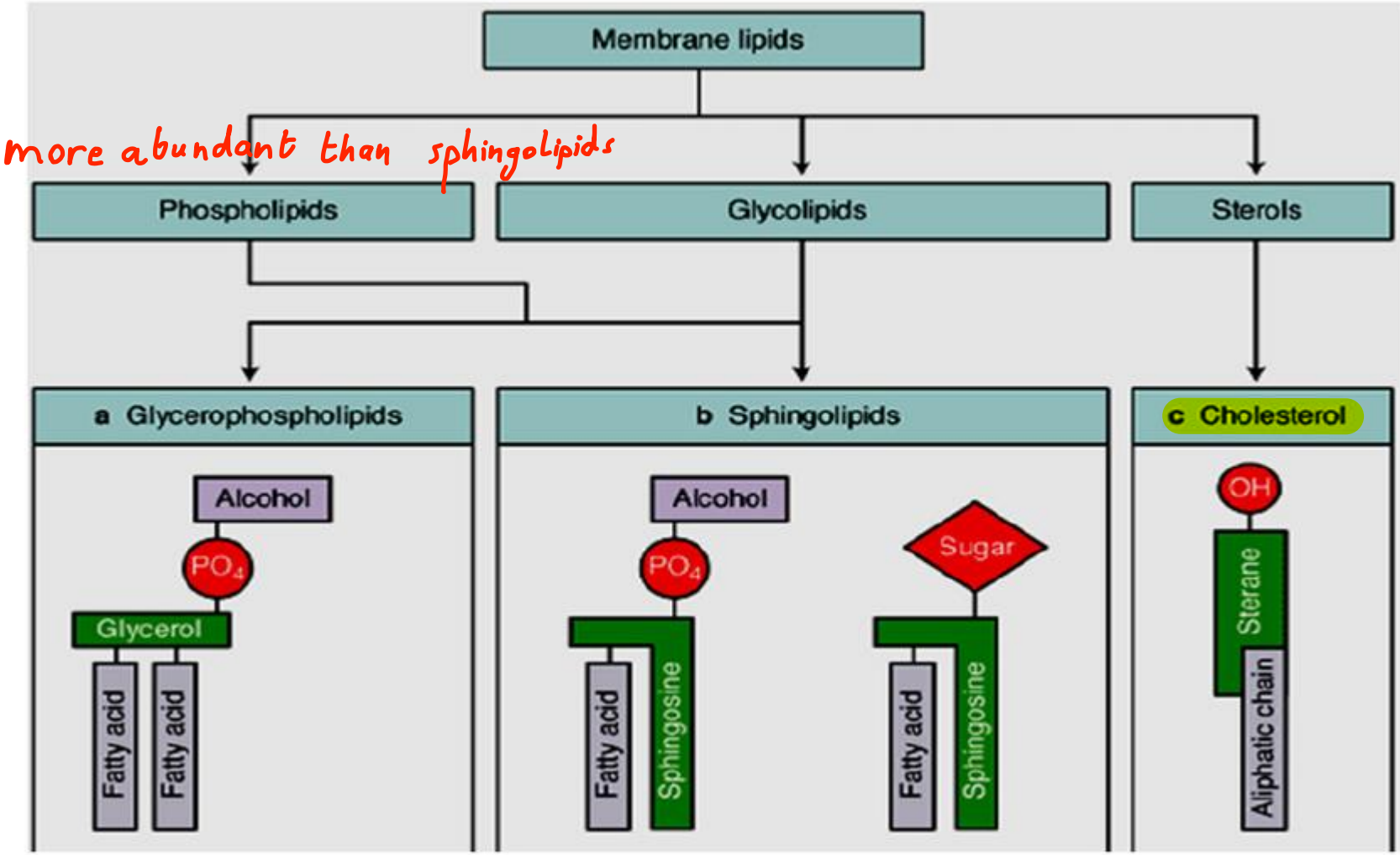
تغليف

don't memorize the table

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

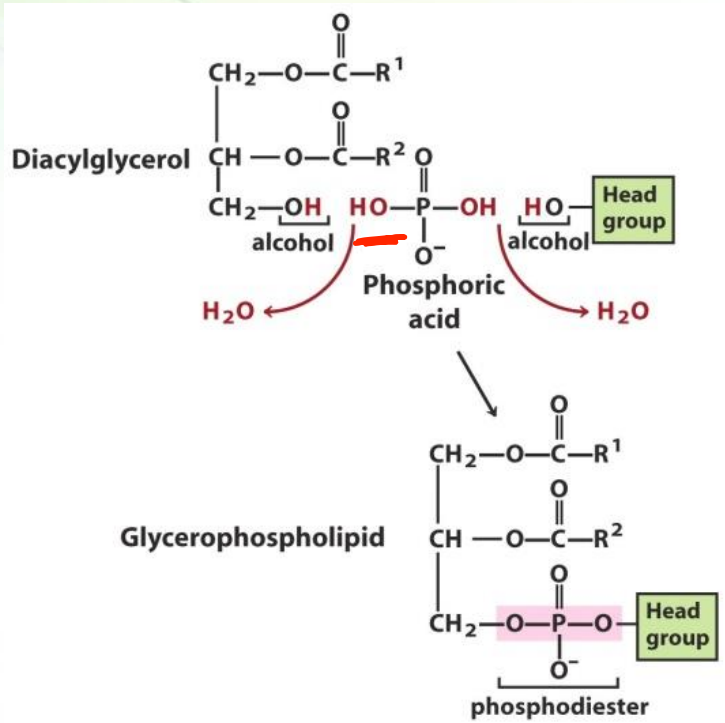
Membrane lipids

The most prevalent class of lipids in membranes is the <u>glycerophospholipids</u>



Phospholipids (phosphoacylglycerols)

- Phosphatidic acids
- Phosphatidylcholine (lecithin)
  - Most abundant membrane lipid
- Cephalins
  - Phosphatidylethanolamine
  - Phosphatidylserine
    - abundant in brain
- Phosphatidylinositol * highly polar molecule
  - sends messages across cell membranes
- Cardiolipin
- Plasmalogens



Phosphatidic acid	—	— H
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$
most abundant type, Phosphatidylcholine (Lecithin)	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Phosphatidylserine	amino acid Serine	$-CH_2-\underset{\displaystyle COO^-}{CH}-\overset{+}{N}H_3$

has two Functional groups make it very high polar at physiological condition

Glycerophospholipids - Lecithins

* It is used as emulsifier in Food industry like cake and chocolate
مستحلب

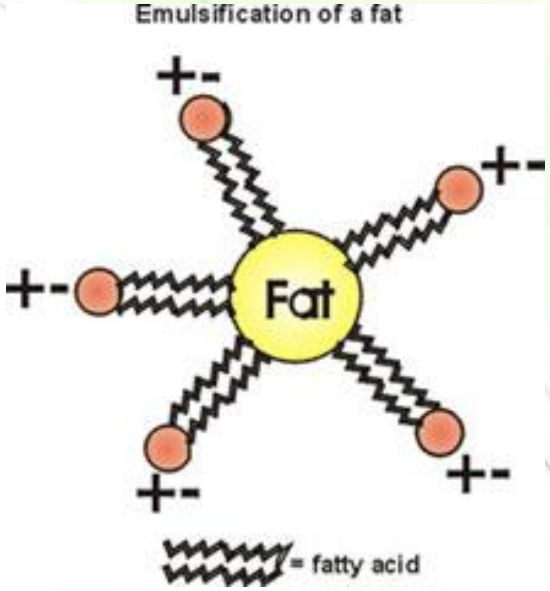
- Snake venom (سمّ) contain lecithinase, which hydrolyzes polyunsaturated fatty acids and converting lecithin into lysolecithin (just one Fatty acid not two)
  - hemolysis of RBCs, so it loss their Function

Phosphatidylcholine **Choline** $-CH_2-CH_2-\overset{+}{N}(CH_3)_3$

Emulsification

amphipathic molecule

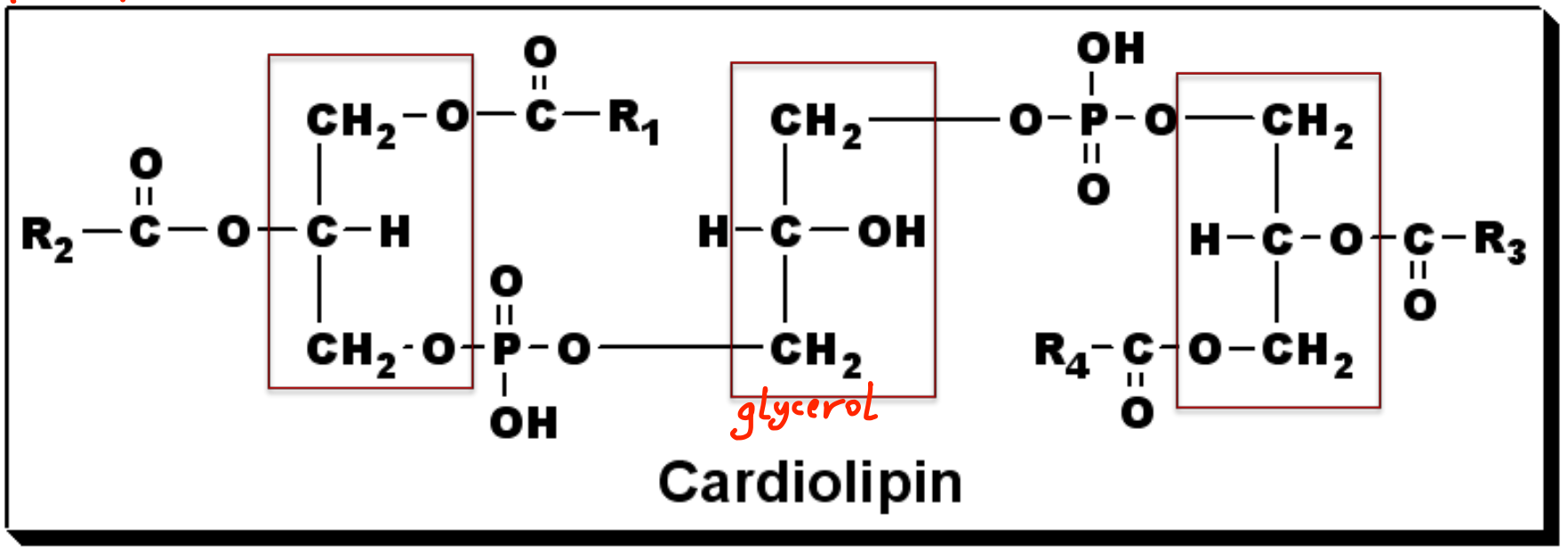
- Because of their amphipathic nature, they act as emulsifying agents, that is substances that can surround nonpolar molecules and keep them in suspension in water.



Glycerophospholipids - Cardiolipins

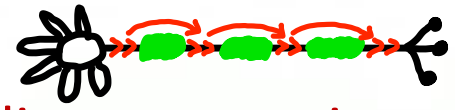
- Diphosphatidyl-glycerol
- Found in the inner membrane of mitochondria
- Initially isolated from heart muscle (cardio)
- Structure: 3 molecules of glycerol, 4 fatty acids & 2 phosphate groups

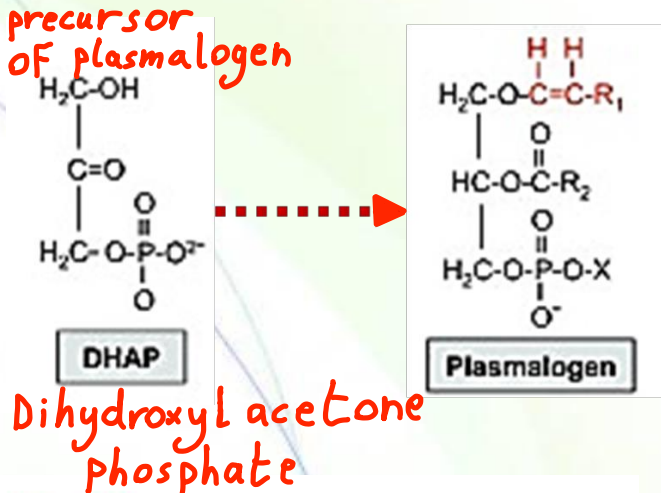
* Two phospholipids attach to each other through glycerol in between

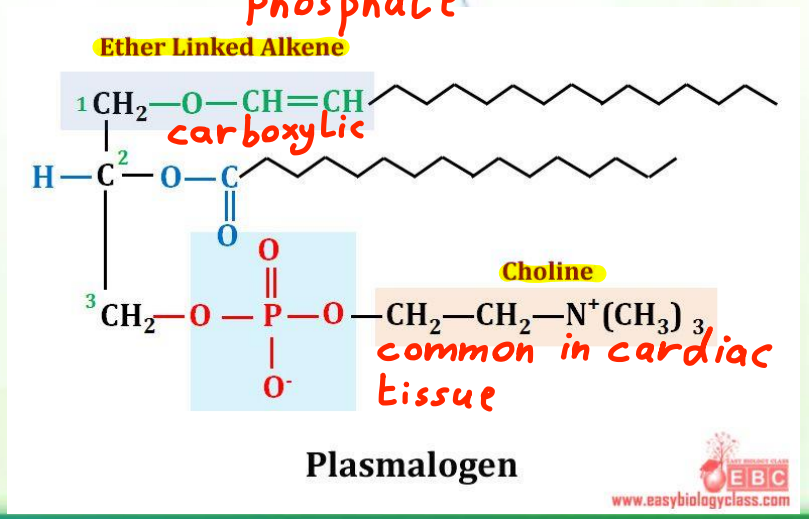


Plasmalogens

- They are found in the cell membrane phospholipids fraction of brain & muscle, liver, and semen.
- They have a protective role against reactive oxygen species
- Structure:
  - Precursor: Dihydroxyacetone phosphate
  - Unsaturated fatty alcohol at C1 connected by ether bond
  - In mammals: at C3; phosphate + ethanolamine or choline
- Major classes of plasmalogens
  - Ethanolamine plasmalogen (myelin-nervous tissues)
  - Choline plasmalogen (cardiac tissue)
    - Platelet activating factor
  - Serine plasmalogens

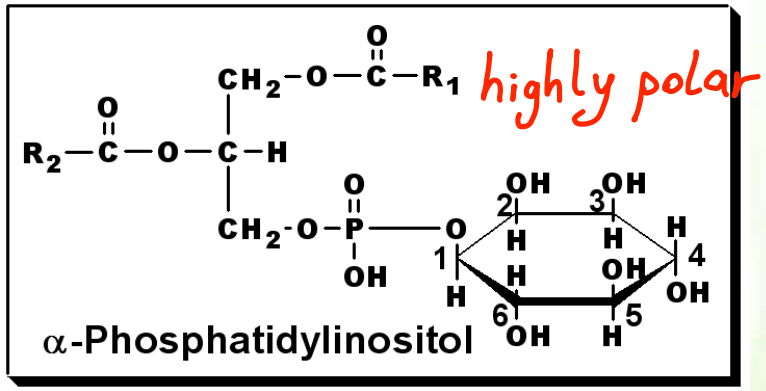






Glycerophospholipids - Inositides

- Phosphatidyl inositol — poly alcohol ring structure
- Nitrogenous base: cyclic sugar alcohol (inositol)
- Structure: glycerol, saturated FA, unsaturated FA, phosphoric acid, & inositol
- Source: Brain tissues

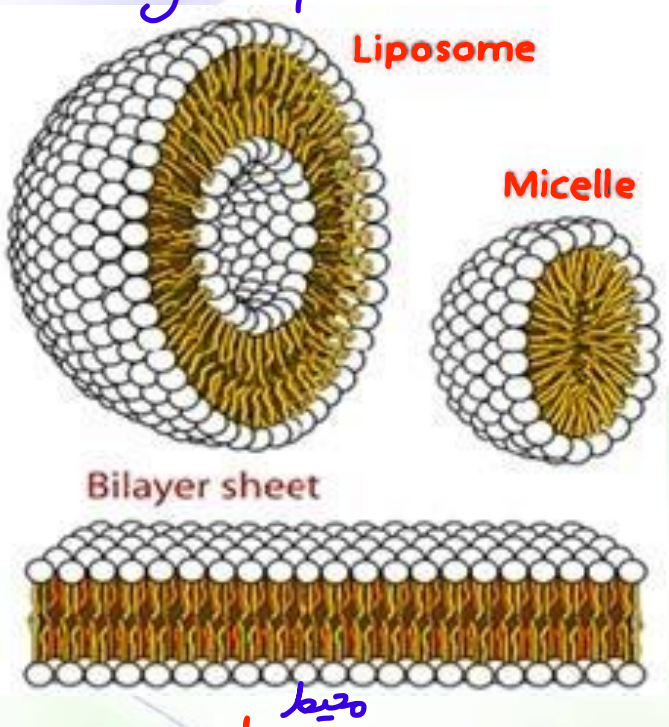


- Functions: * The major Function is in signaling
  - Major component of cell membrane
  - Second messenger during signal transduction
  - On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5-diphosphate (PIP_2) produces diacyl-glycerol (DAG) & inositol-triphosphate (IP3); which liberates calcium

It is polar, so it doesn't stay attached to the membrane, so it act as a second messenger

The different structures of phospholipids

hydrophillic in inside

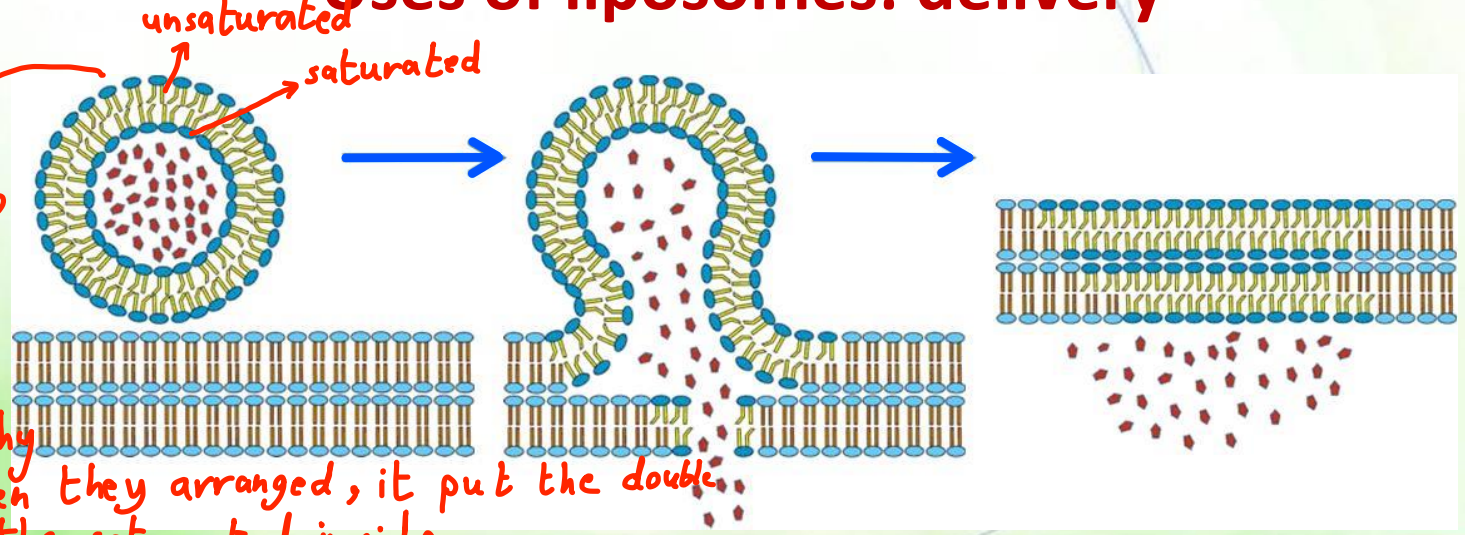


hydrophobic in inside

* Phospholipids are differ in charge, volume and the tails, so this make a divercity in glycerophospho lipid and make a differnce in volume and this will show in vesicle when it budding From plasma membrane, the vesicle is Look like a ball, so it contain two leaFlet it similar to Liposome which is outside the body, it is made in labrotary, we put a drug or vaccine inside it

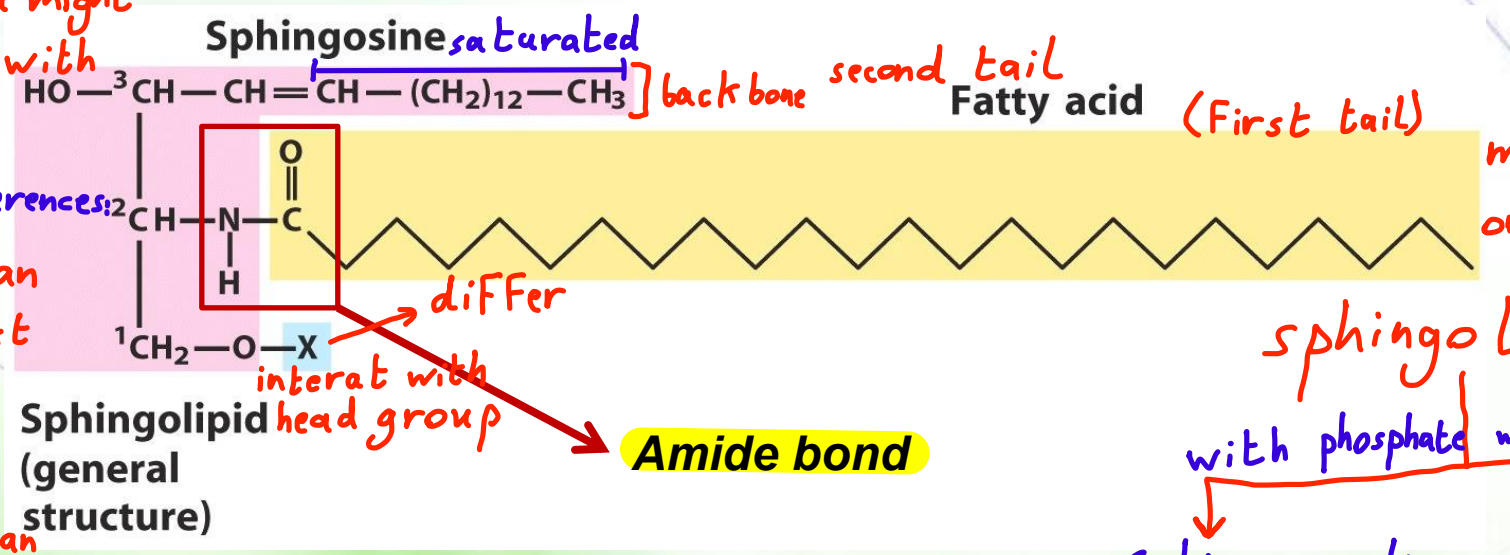
The edge From inside is very smaller than outside, but the ratio is 1:1, so when the viscle budding, they arranged and they move all the time that's why we call it Fluid mosaic model, so when they arranged, it put the double bond which make a kink outside and the saturated inside

Uses of liposomes: delivery



Sphingolipids

- Sphingolipids are found in the plasma membranes of all eukaryotic cells and is highest in the cells of the central nervous system
- The core of sphingolipids is the long-chain amino alcohol, sphingosine



* because of the presence of an alkene group, you might confuse sphingolipids with plasmalogens but there are two differences:
① plasmalogen contain an ether group and it's last carbon is attached to a phosphate group
② in plasmalogen we have an ester group on carbon number 2 while we have an amide bond in sphingolipids

sphingo lipid
with phosphate → Sphingomyelin
without phosphate → Glycolipid

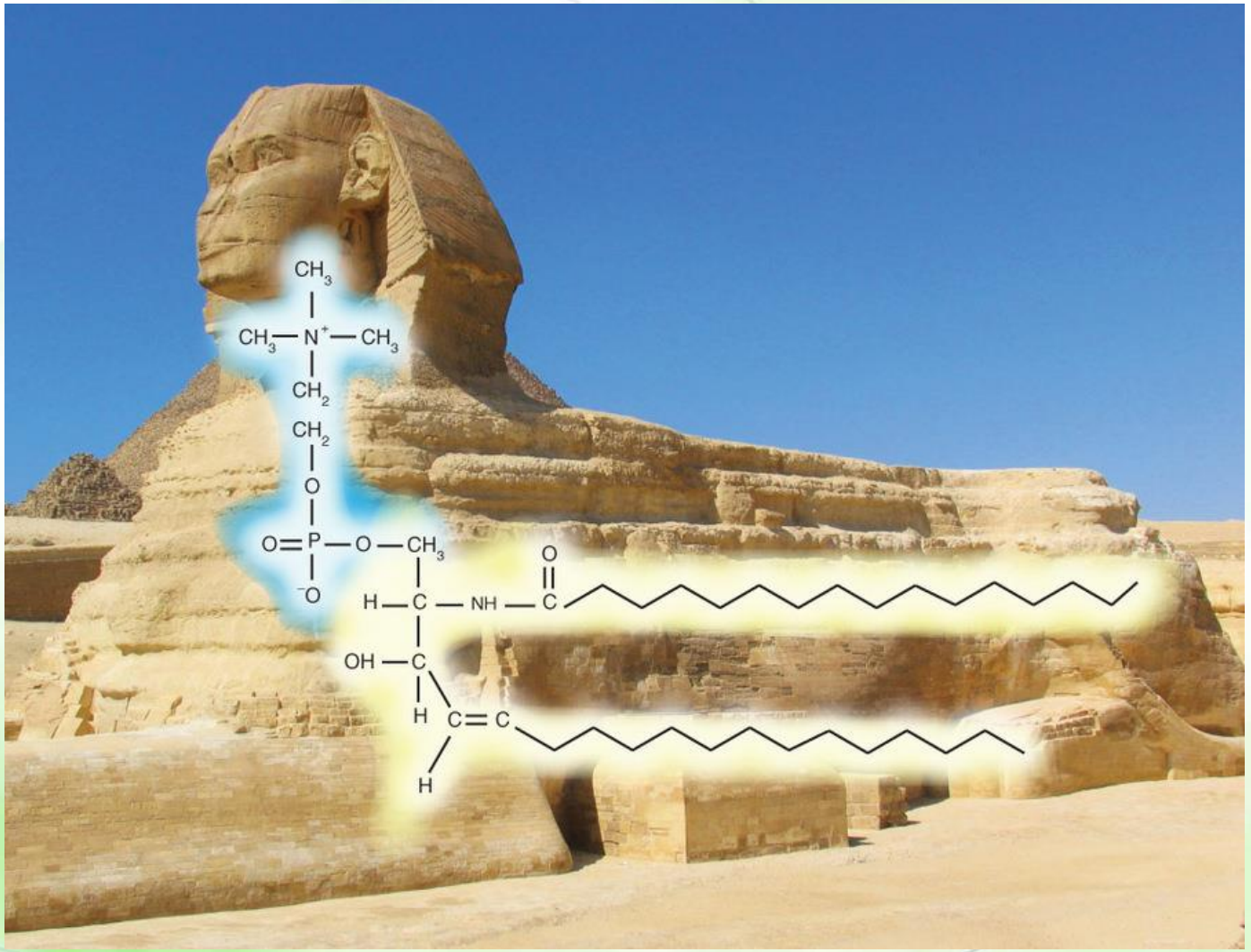
Mysterious lipids

مش مطلوب

***Sph*ynx → *sph*ingolipids**

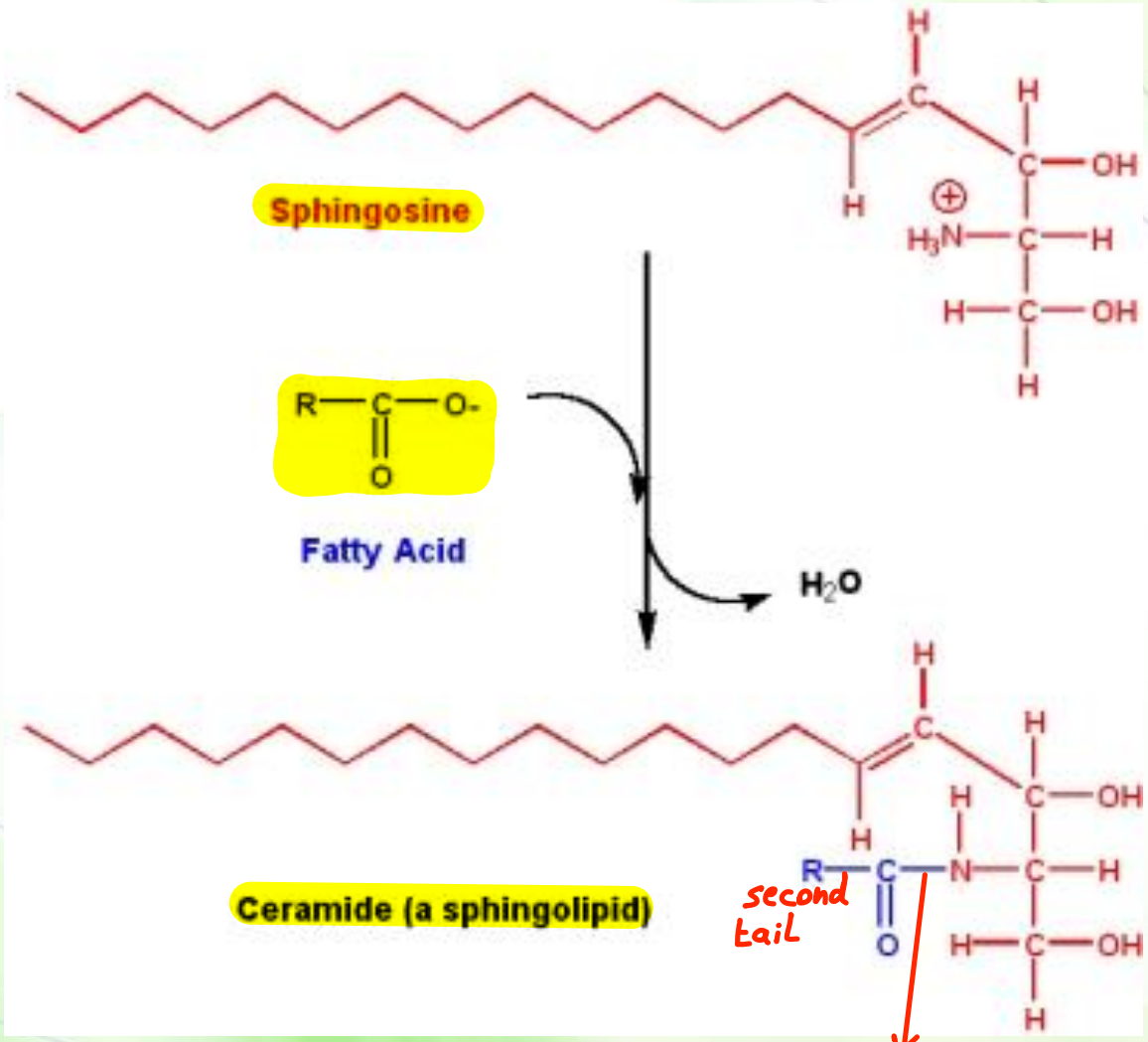
Trivia

Named for the Sphinx of Thebes, who killed passersby that could not solve her riddles



Ceramide

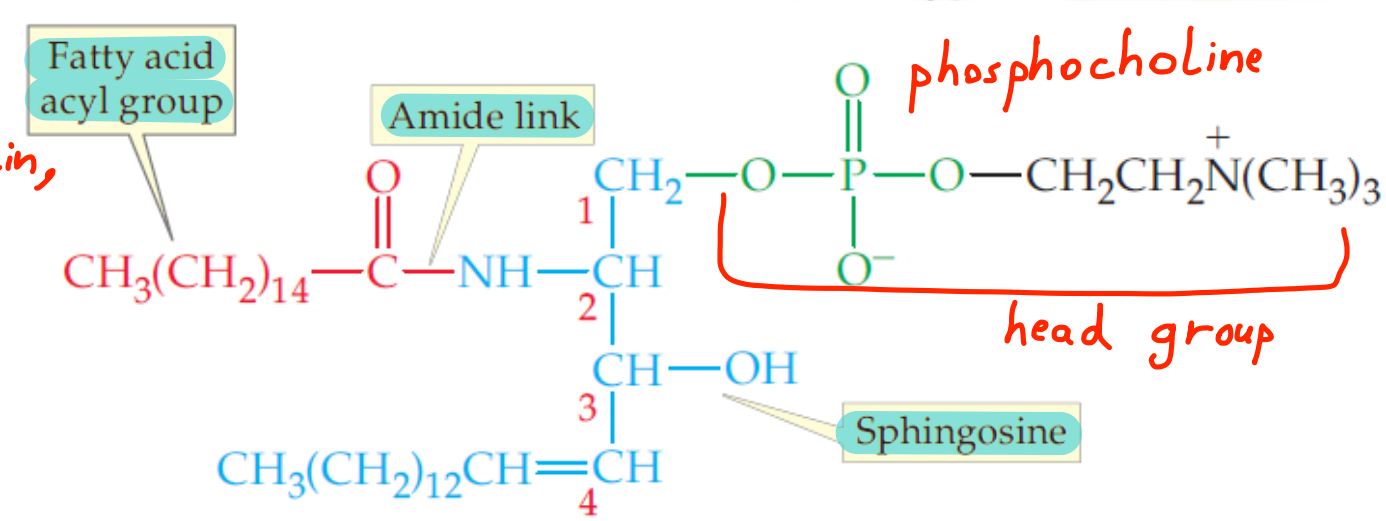
* It is the parent molecule like phosphatdic acid in glycerophospholipids



Types of sphingolipids

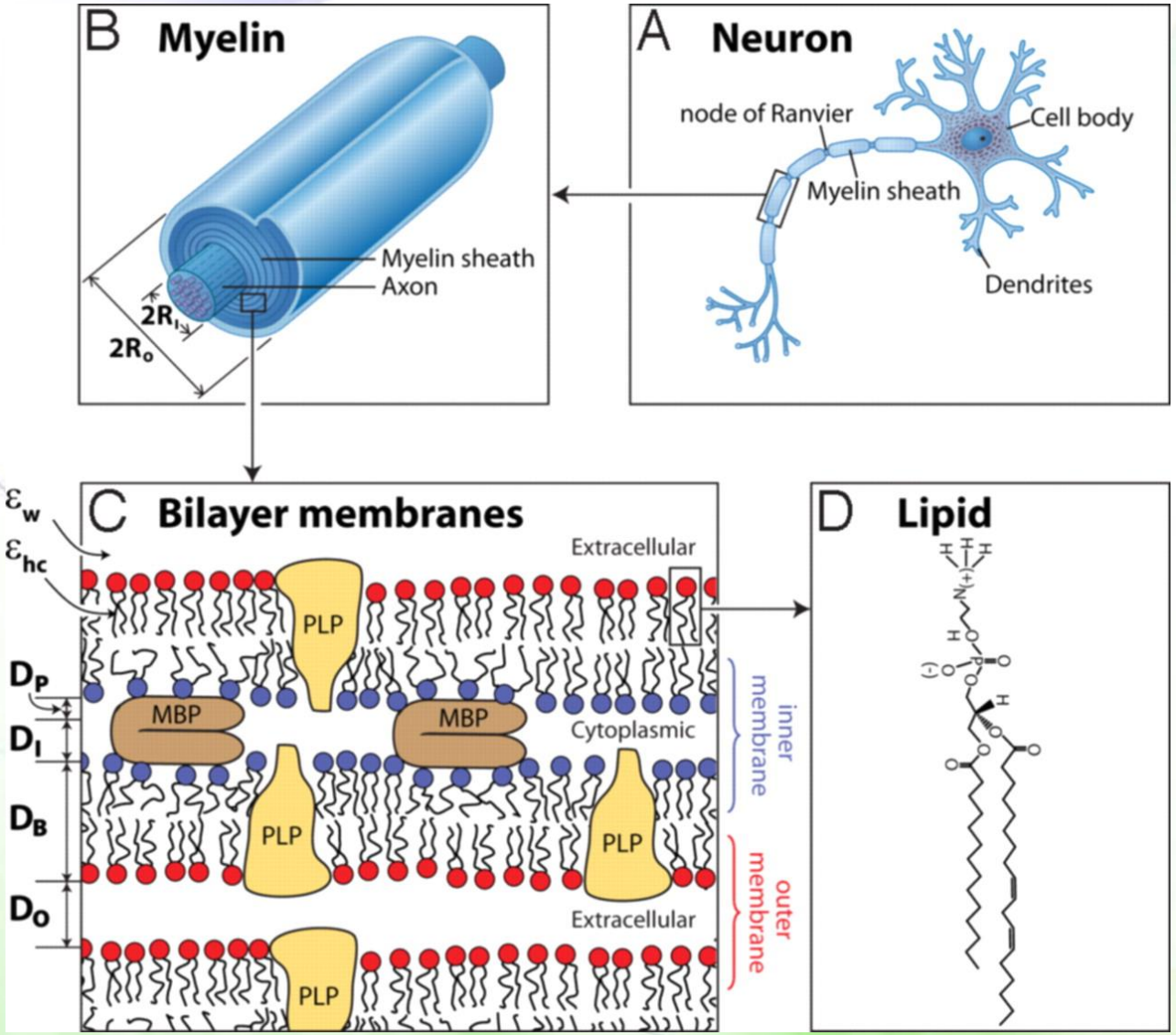
- The sphingolipids are divided into two subcategories:
  - Sphingomyelin
    - It is a sphingolipid that is a major component of the coating around nerve fibers.
    - The group attached to C1 is a phosphocholine
  - Glycosphingolipid (or glycolipids)

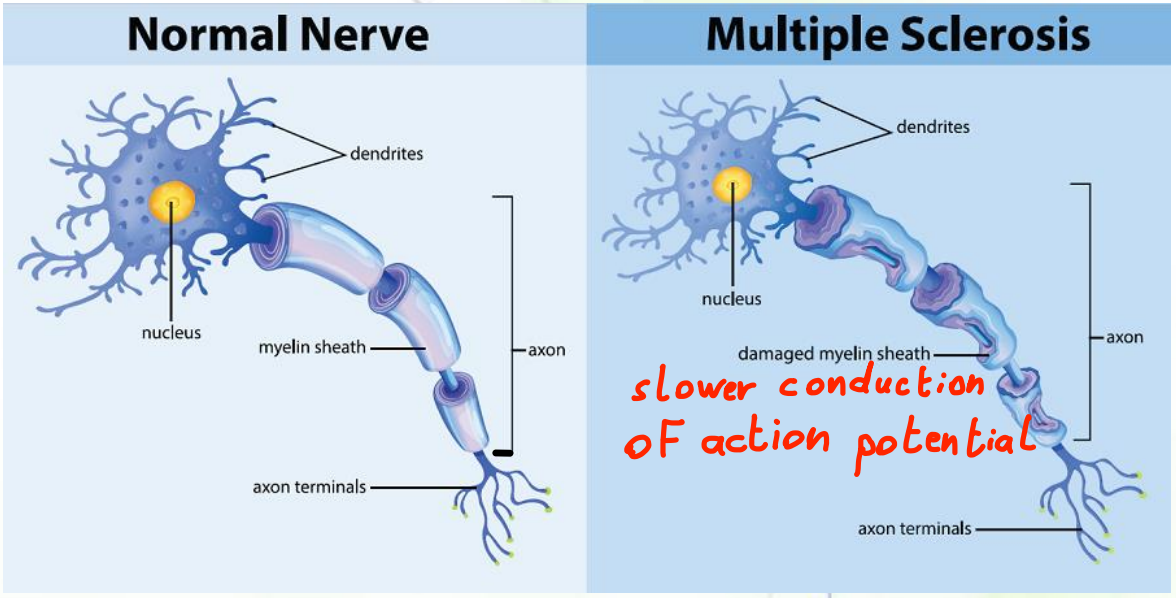
* It is the major component of myelin sheath
* If we have disorder in sphingomyelin, It will cause multiple sclerosis (MS)
* MS is an immune disease
* It is more common in Females and young age
* It isn't inherted disease



A sphingomyelin (a sphingolipid)

Zooming into the myelin

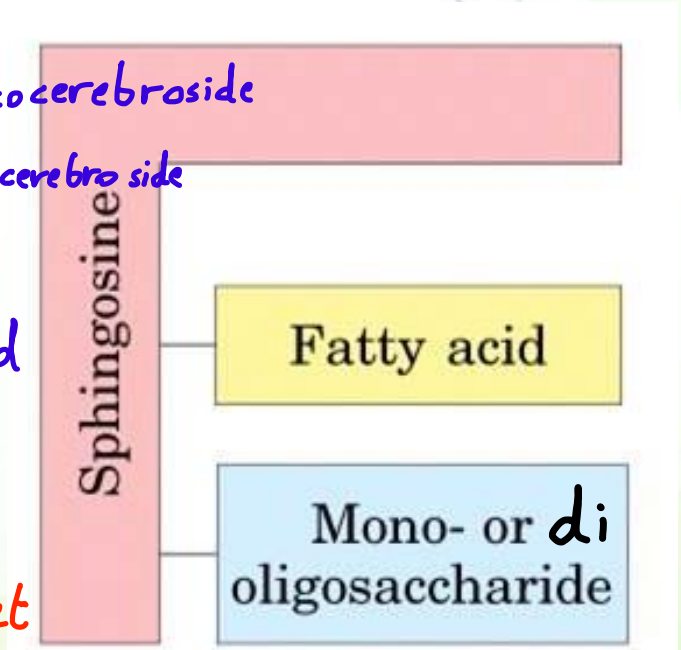




Glycolipids (sphingolipid)

* have a sugar in their head group
* They are present outside the cell to cell recognition and cell-cell interaction

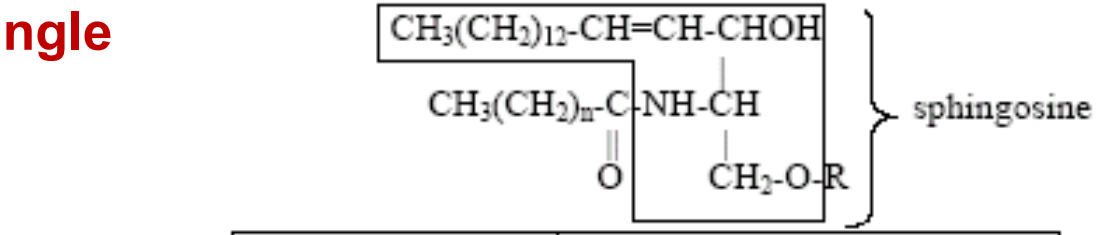
- Sphingolipids can also contain carbohydrates attached at C-1 and these are known as glycolipids
- Glycolipids are present on cell membranes and act as cell surface receptors that can function in cell recognition (e.g., pathogens) and chemical messengers
- There are three types of glycolipids
  - Cerebrosides (in cerebrum in nervous system) (mono/ IF it has glucose it called glucocerebroside / IF it has galactose it called galactocerebroside)
  - Globosides (di/oligo)
  - Gangliosides (in ganglia which is a group of cell bodies outside the CNS) (oligo, but it has common sugar called sialic acid (N-acetylneuramic acid) in all gangliosides)



* Glycolipid is very big, so it is better to be in outer leaflet

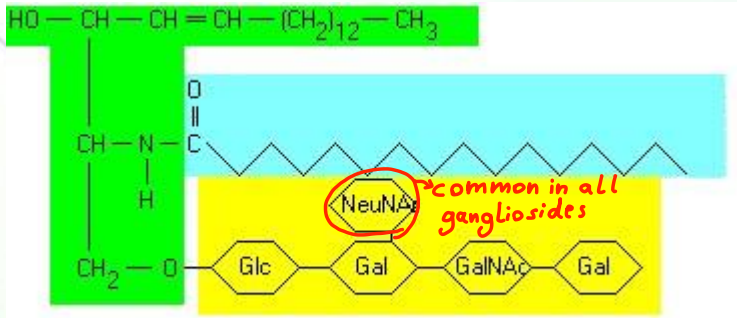
Glycolipids

- **Cerebrosides: the simplest glycolipids, contain a single hexose (galactose or glucose).**
- **Globosides and gangliosides are more complex glycolipids.**
- **Both contain glucose, galactose, and N-acetylgalactosamine, but gangliosides must also contain sialic acid.**

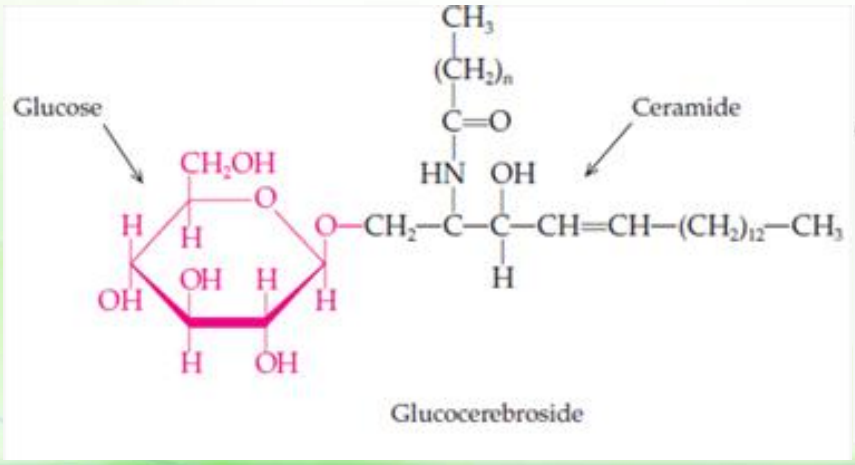


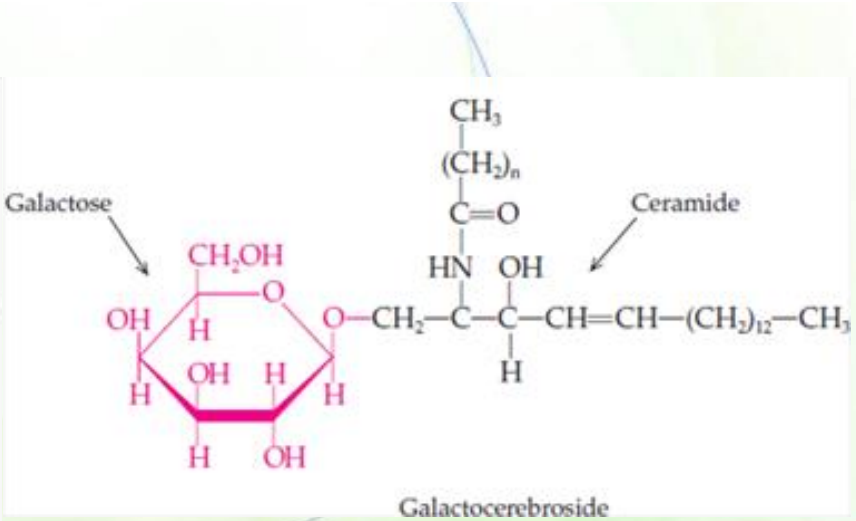
Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

glycolipids



Gangliosides are bound by cholera toxin in the human intestine facilitating its endocytosis into the cells.

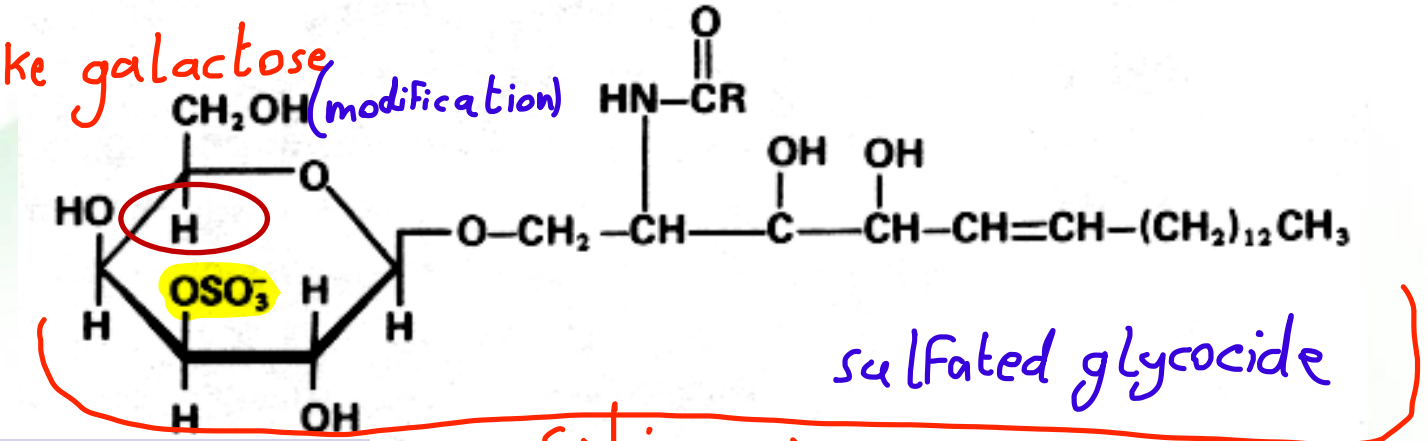




Sulfatides

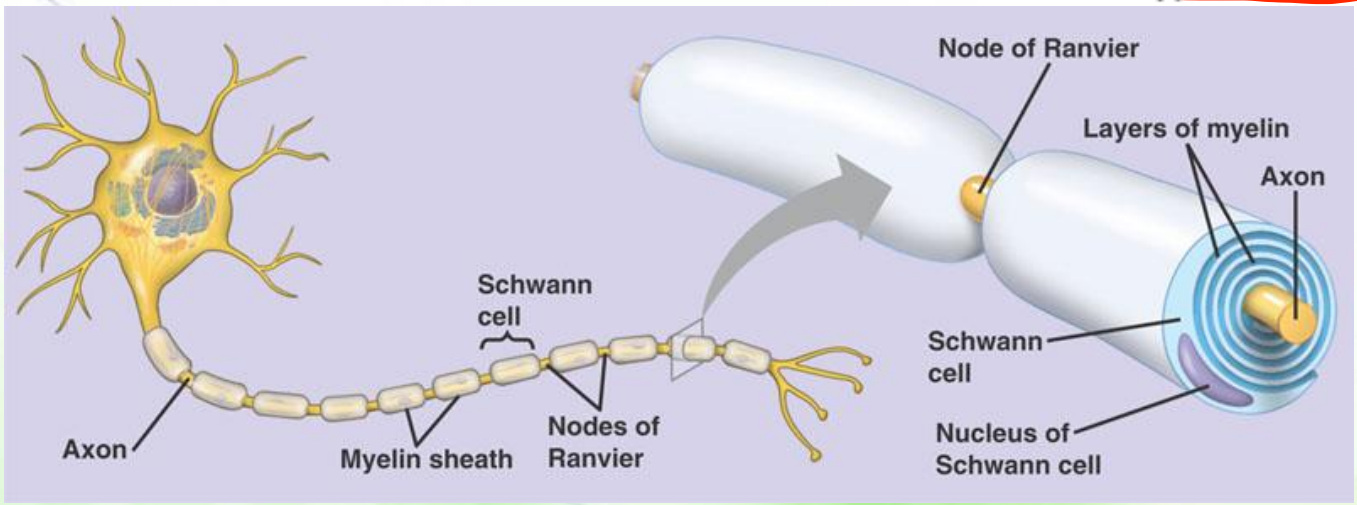
- Synthesized from galactocerebroside
- Abundant in brain myelin (myelin sheath)

Like galactose (modification)



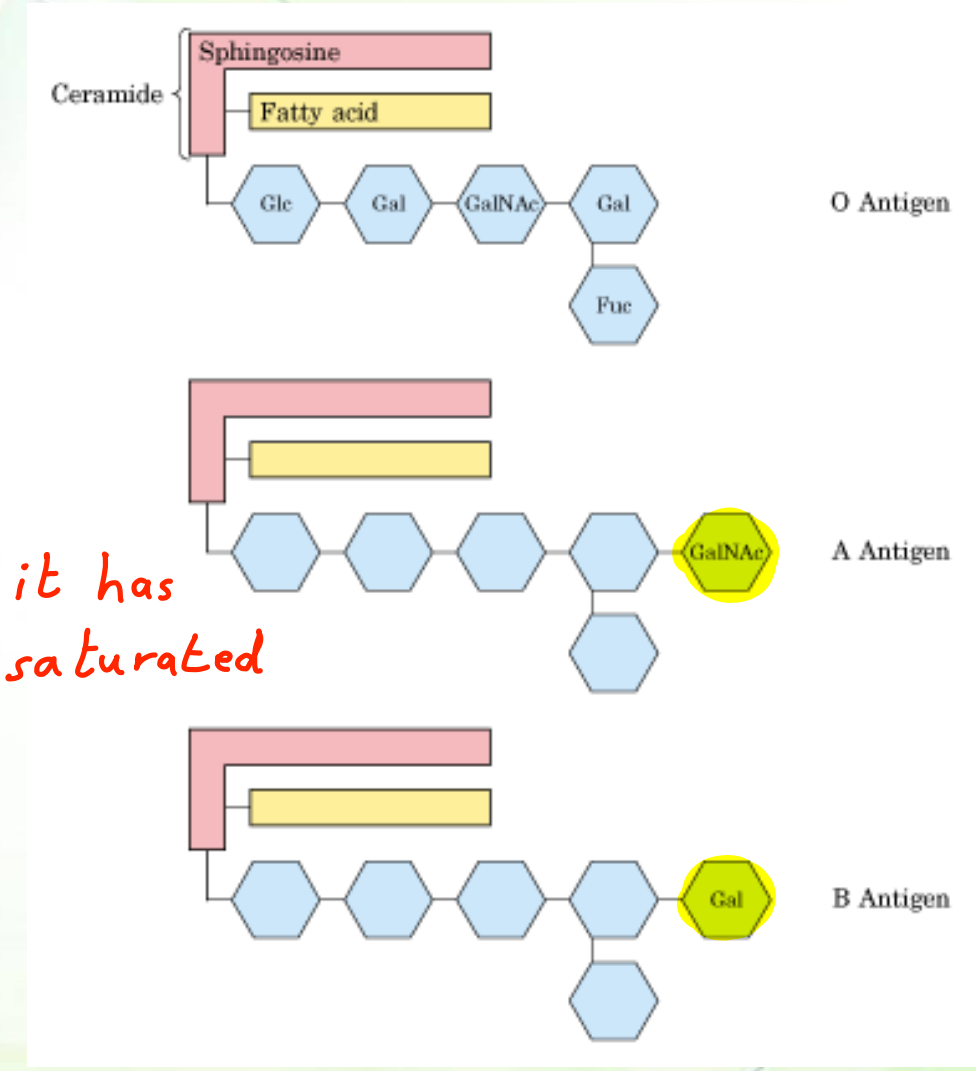
sulfated glycocide

Sphingosine



Sphingolipids and blood groups

- Sphingolipids serve in intercellular communication and as the antigenic determinants of the ABO blood groups.
- Some are used as receptors by viruses and bacterial toxins.

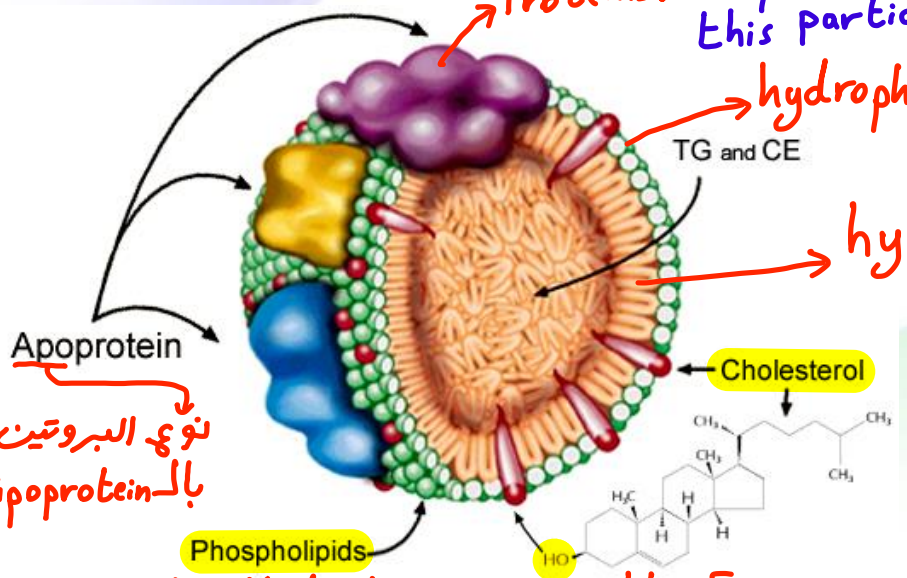


* The double bond present in the First of chain, so it has a kink in the start of him, so it consider as saturated which give rigidity to the molecule

* It Found in Lipid raFt

Lipoproteins

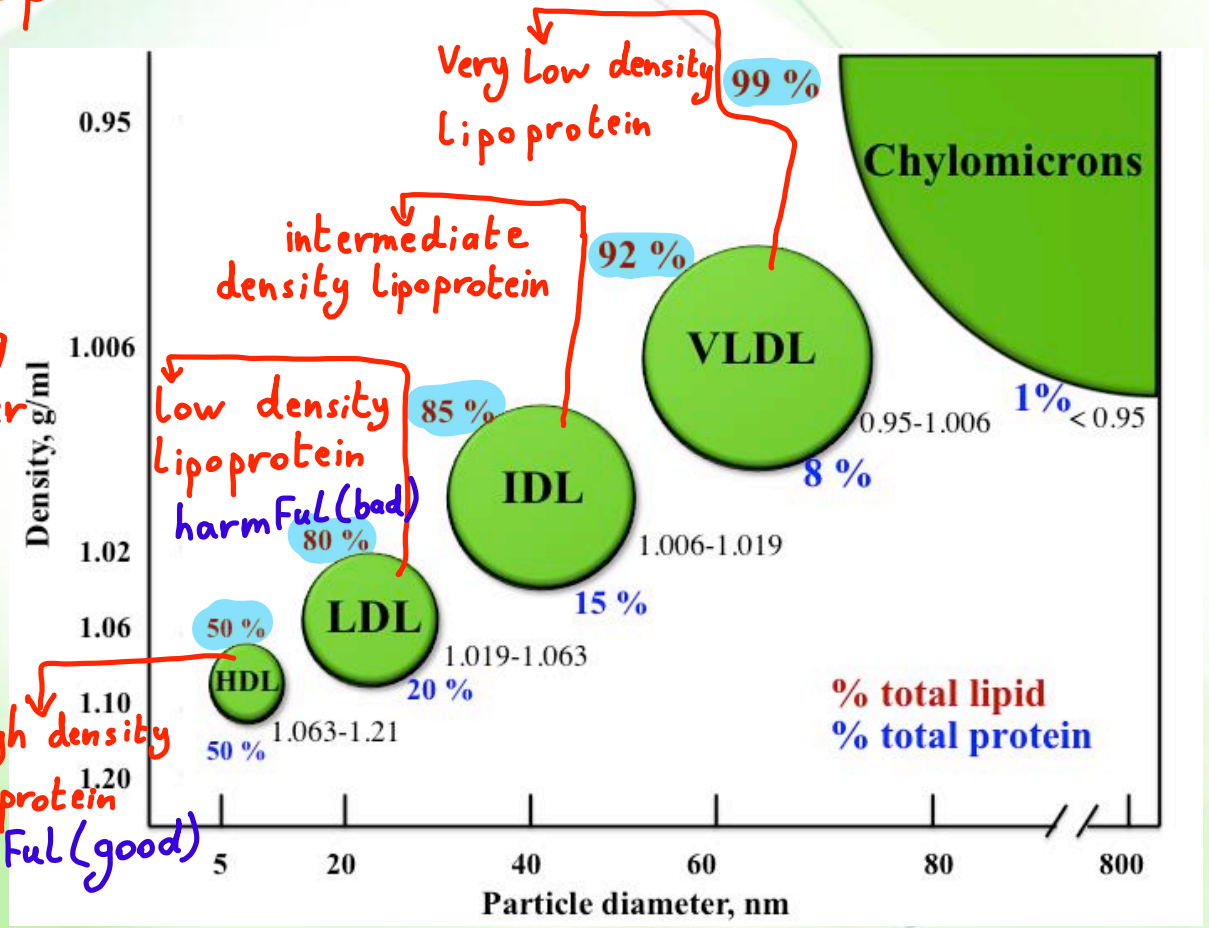
* Can Facilitate lipid movement



Function: transport of different types of lipids (cholesterol, cholesterol esters, phospholipids & triacylglycerols) in blood plasma.

* a particle that it is responsible For moving Lipid molecule From one side to another because Lipids are hydrophobic molecule and we need to move them in blood and cells ,so we have a large structure of a lipoprotein to transport them

As lipid content increases, the density decreases



* They differ in their composition (How much is Fat and how much is protein), the type of Fat, Function, density and the direction of movement

* HDL is the best because it has high content of proteins

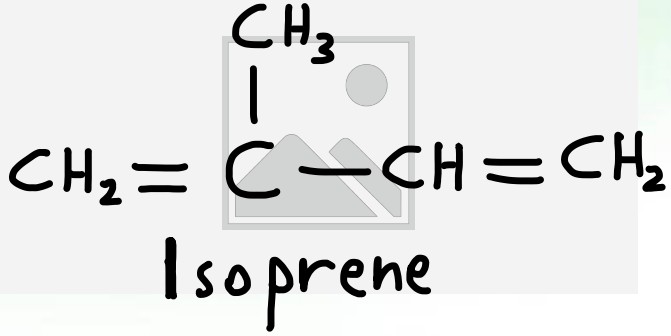
* Chylomicrons is responsible For moving Lipid molecule From intestinal cells after absorption to the Lympth, then to the venous cell

* LDL is responsible For move Cholestrol spiciFically From the Liver to the cells, so iF we have a large amount of LDL, it will accumulate in blood vessels

* HDL is responsible For move cholestrol From cells to the liver, that's why it is useFul

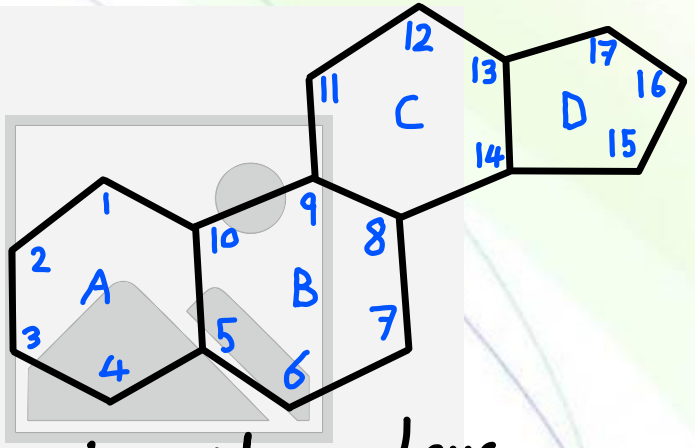
Steroids

The precursor



Isoprene

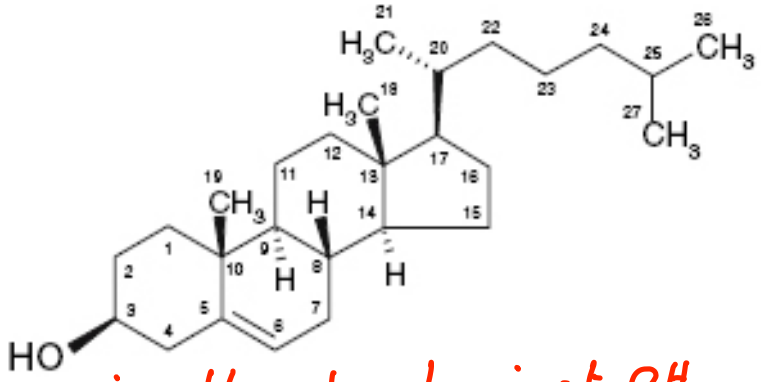
The nucleus



steroid nucleus

* 4 Fused ring

The most common steroid



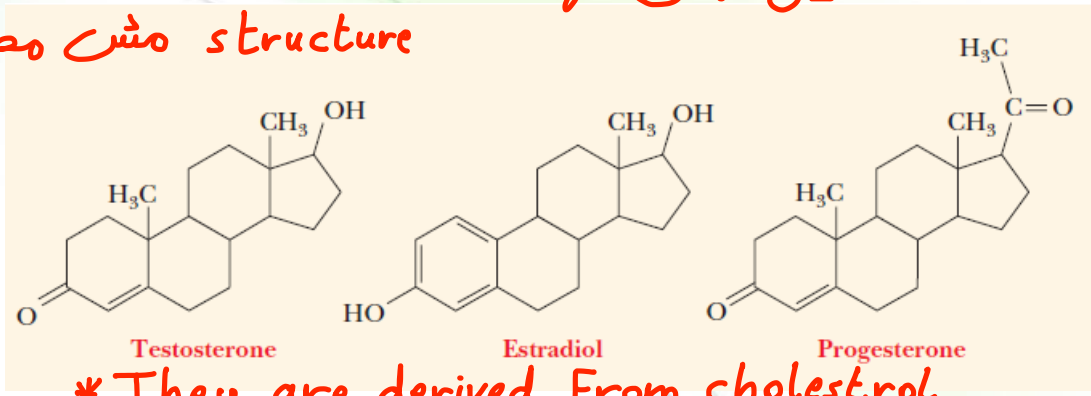
in all molecule just OH are polar

Products of cholesterol

- Hormones
  - Sex hormones (androgens,. estrogens, progestins)
- Vitamin D
- Bile acids (intestinal absorption of fat)

التفاصيل مش مهمة

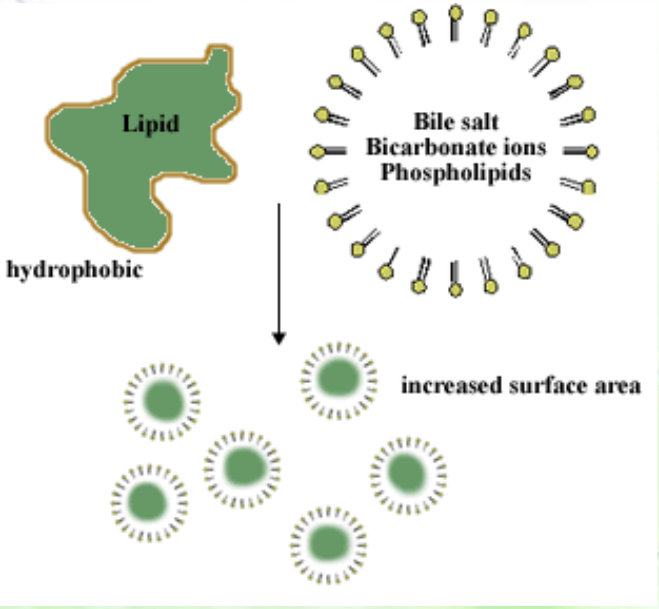
مش مطلوب structure



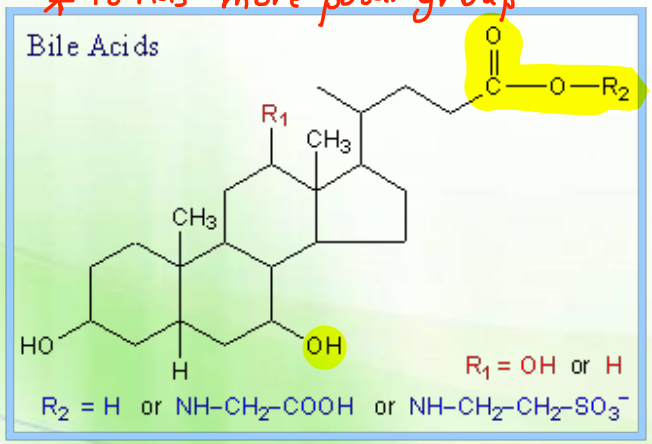
* It used to make another hormones like cortisol and aldosterone

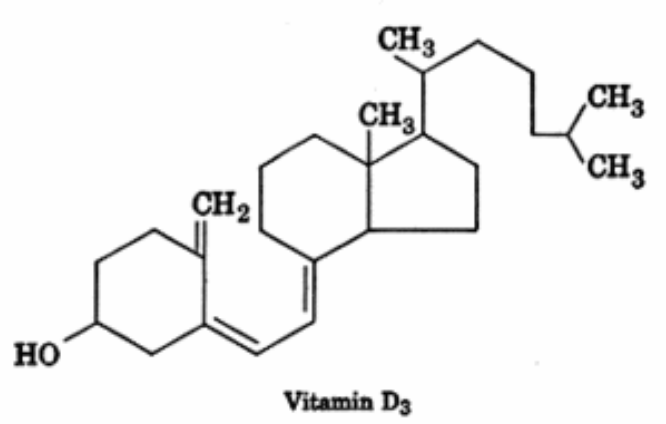
* They are derived From cholestrol

in liver



* It has more polar group

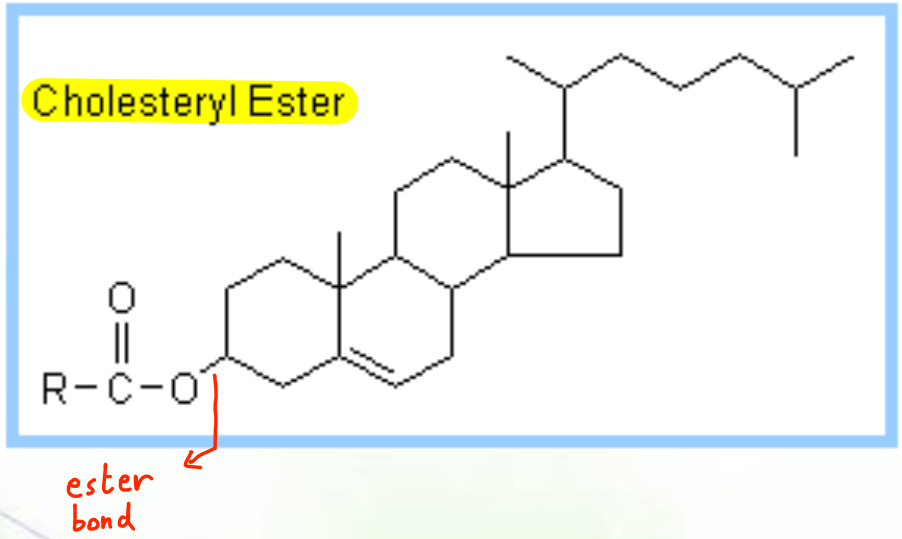


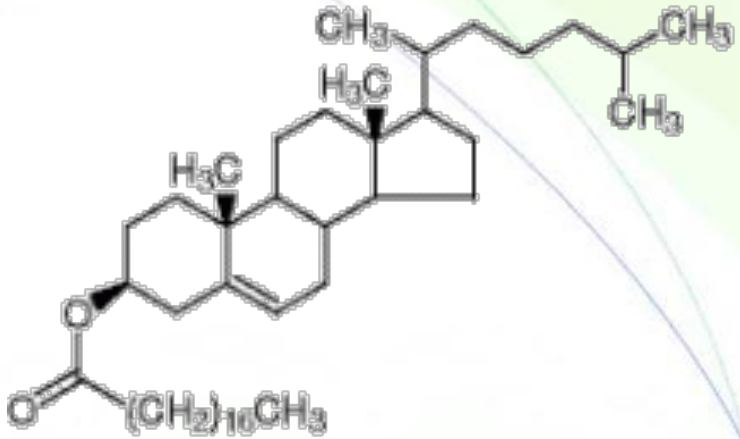


Cholesterol esters

- A cholesterol with a fatty acid attached at (-OH) of C3

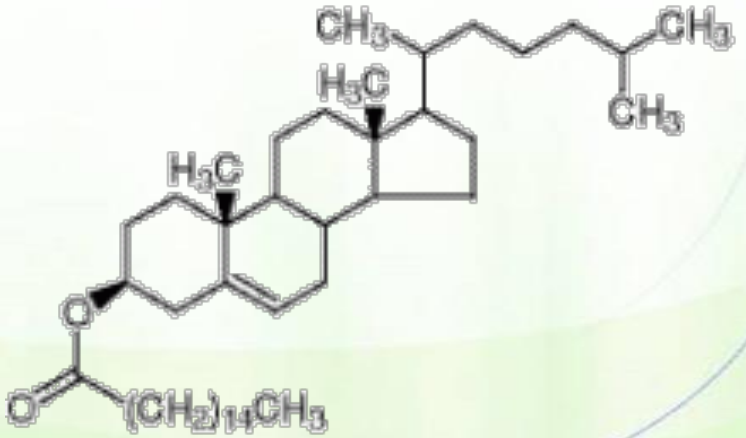
* It is important in loaded cholestrol in HDL which make it load more cholestrol





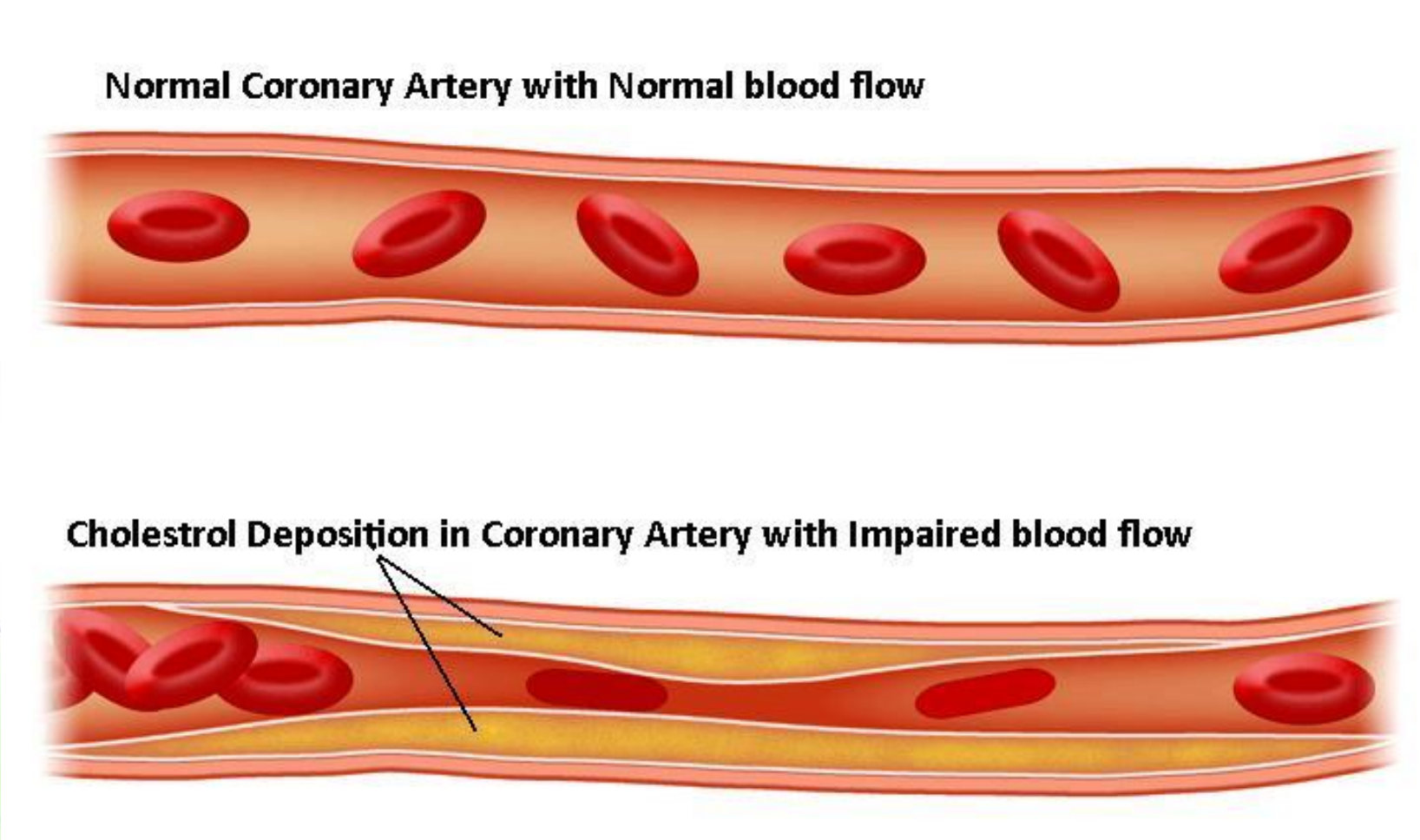
Name the molecules?

Cholestrol palmetate



Atherosclerosis

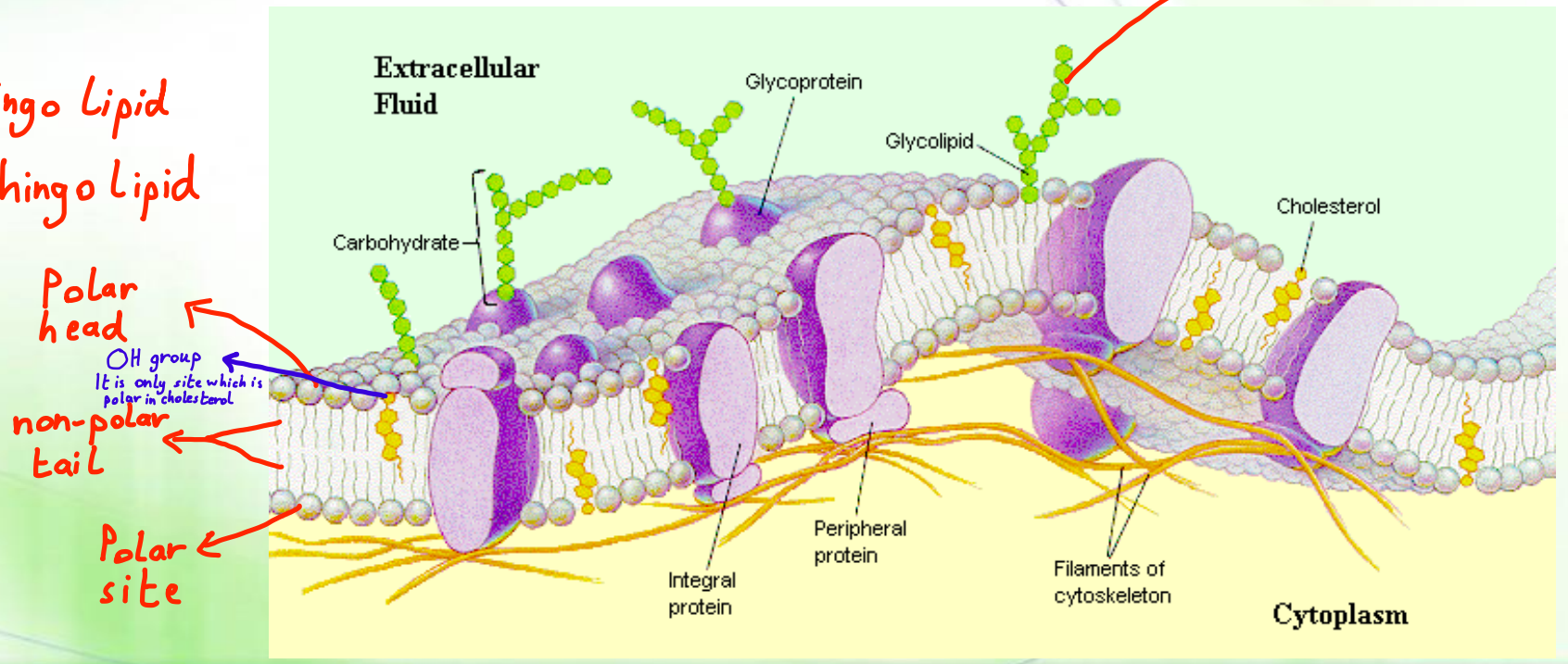
* IF cholesterol accumulate in blood vessel it make it more rigid and less Flexible that's prevent RBC's From move



Cell membranes

- The membrane is hypothesized in a model known as the fluid mosaic model.
- Components: 45% lipid, 45% protein and 10% carbohydrate
- They exist side by side without forming some other substance of intermediate nature.

* every one phospho or sphingo lipid matched with one phospho or sphingo lipid the ratio is 1:1, but they are distributed unequally



Phospholipids

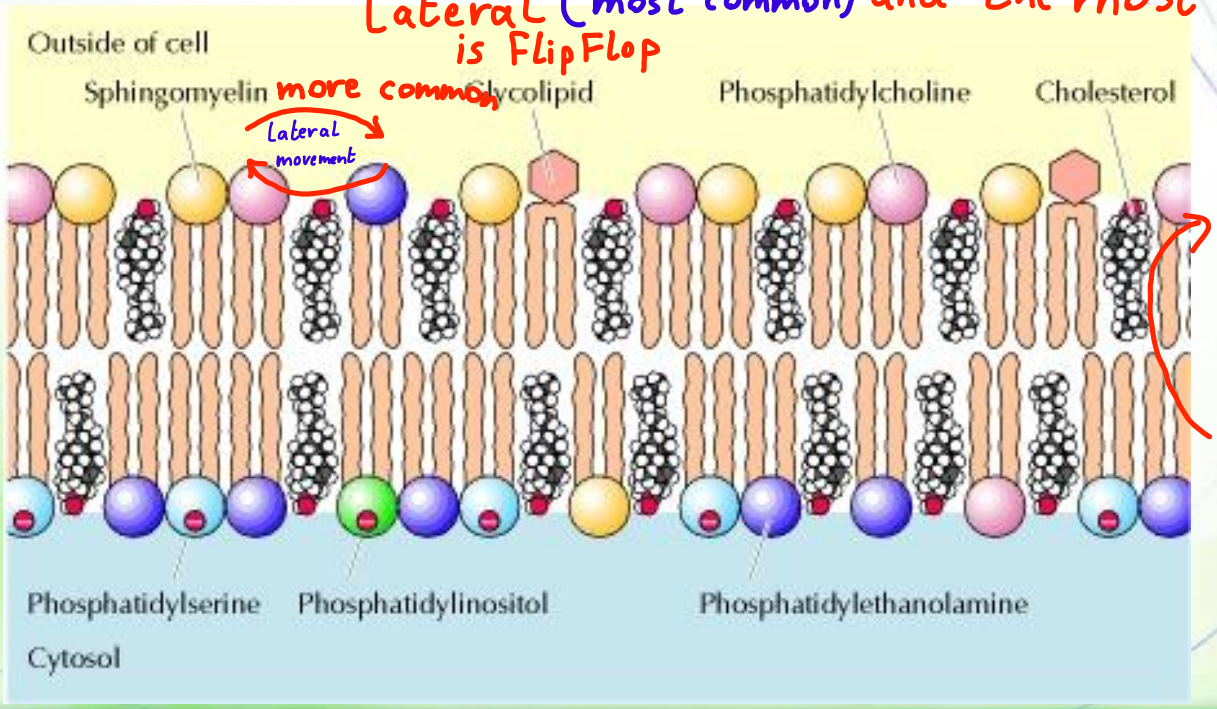
* they have different distribution among two leaflet depending mostly on Function

- The outer: phosphatidylcholine, sphingomyelin, and glycolipids (cell recognition)
  - The most abundant phospholipid
  - major component of myelin sheath
  - we have small amount of this molecule in inner leaflet
- The inner: phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol (signaling)
  - we have small amount of this molecule in outer leaflet

Cholesterol is distributed in both leaflets

✓ Animal cells vs.
? plant cells vs.
✗ prokaryotic cells

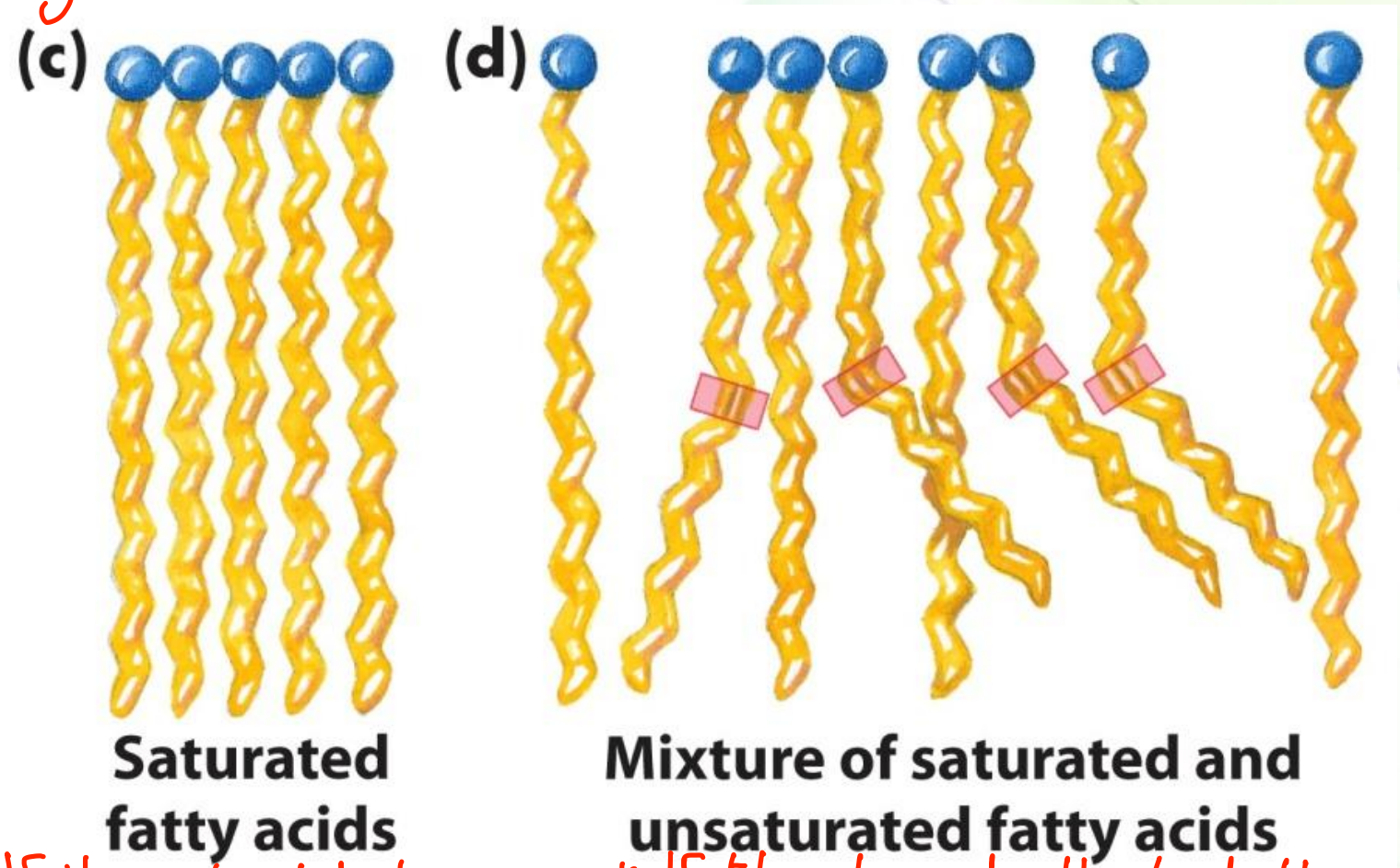
* phosphe and sphingo lipid are dynamic molecules Lateral (most common) and the most scarce movement is FlipFlop



* Flip Flop movement needs energy to occur

Fatty acids and membrane fluidity

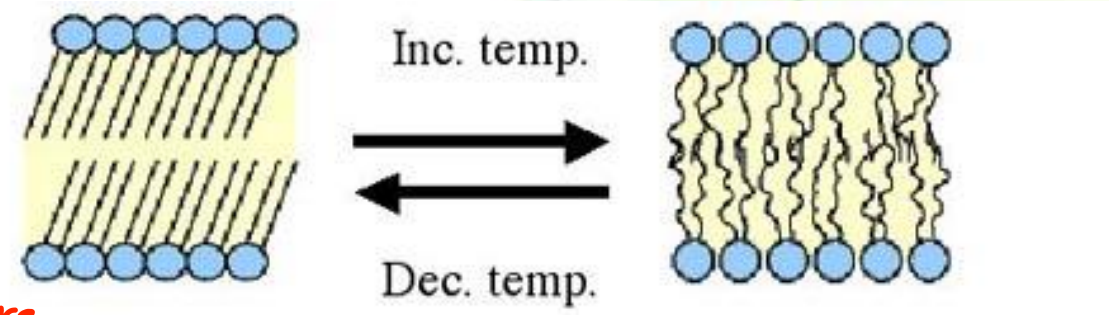
* Fatty acids affect in membrane Fluidity through their Fatty acid



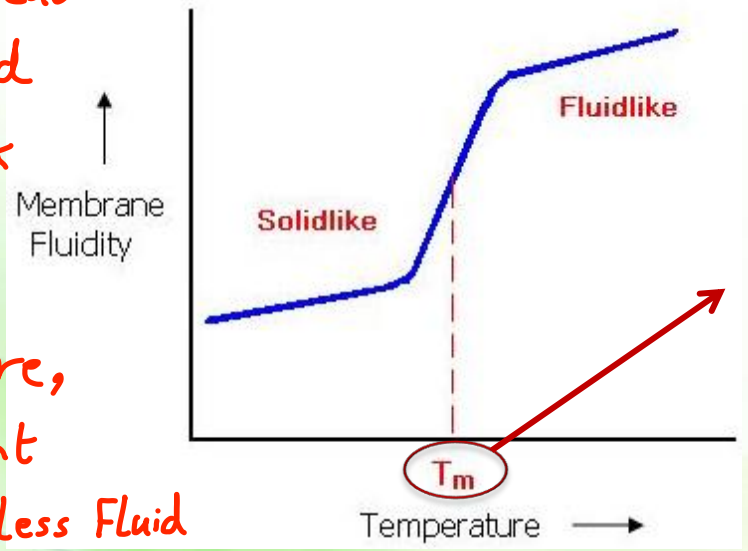
* If it is saturated, it will be straight line, compacted and rigid because they make more hydrophobic interaction

* If they have double bonds, they will have kinks, so they will be wider and increase Fluidity of the membrane

Membrane fluidity and temperature



* another Factor effect in Fluidity is the temperature , but it not make Fluctuation in human body , but it make in test tube in industry as we make Liposome which work as delivery of drug. IF we put a heat to them , they get this energy and make kinetic energy , then break non-covalent interaction and become more Fluid
* IF we decrease the temperature, they loss energy , then their movement decrease and more compacted and less Fluid



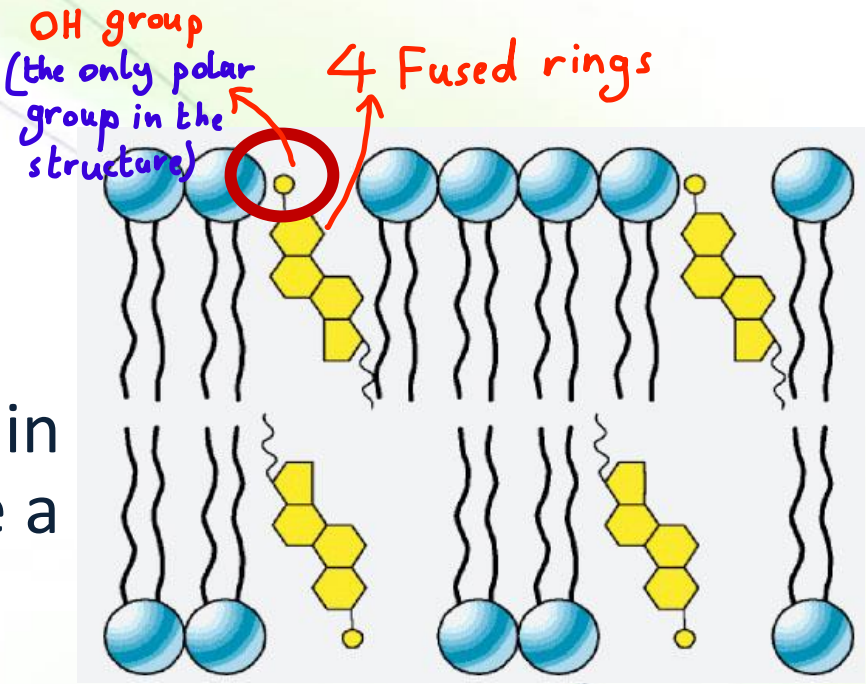
Melting temperature (transition temperature

Cholesterol and membrane fluidity

* Cholesterol has a large number of carbons that can Form hydrophobic interactions and the structure of cholesterol is very rigid, this will increase rigidity and decrease Fluidity

- The presence of cholesterol and the cis unsaturated fatty acids in the membrane prevent the hydrophobic chains from packing too closely together, allowing free membrane proteins and lipid molecules to move laterally in the plane of the leaflet making the membrane a dynamic environment.
- Cholesterol can also stabilize very fluid membranes by increasing interactions between the fatty acids of phospholipids through hydrophobic interactions with the cholesterol ring structure.

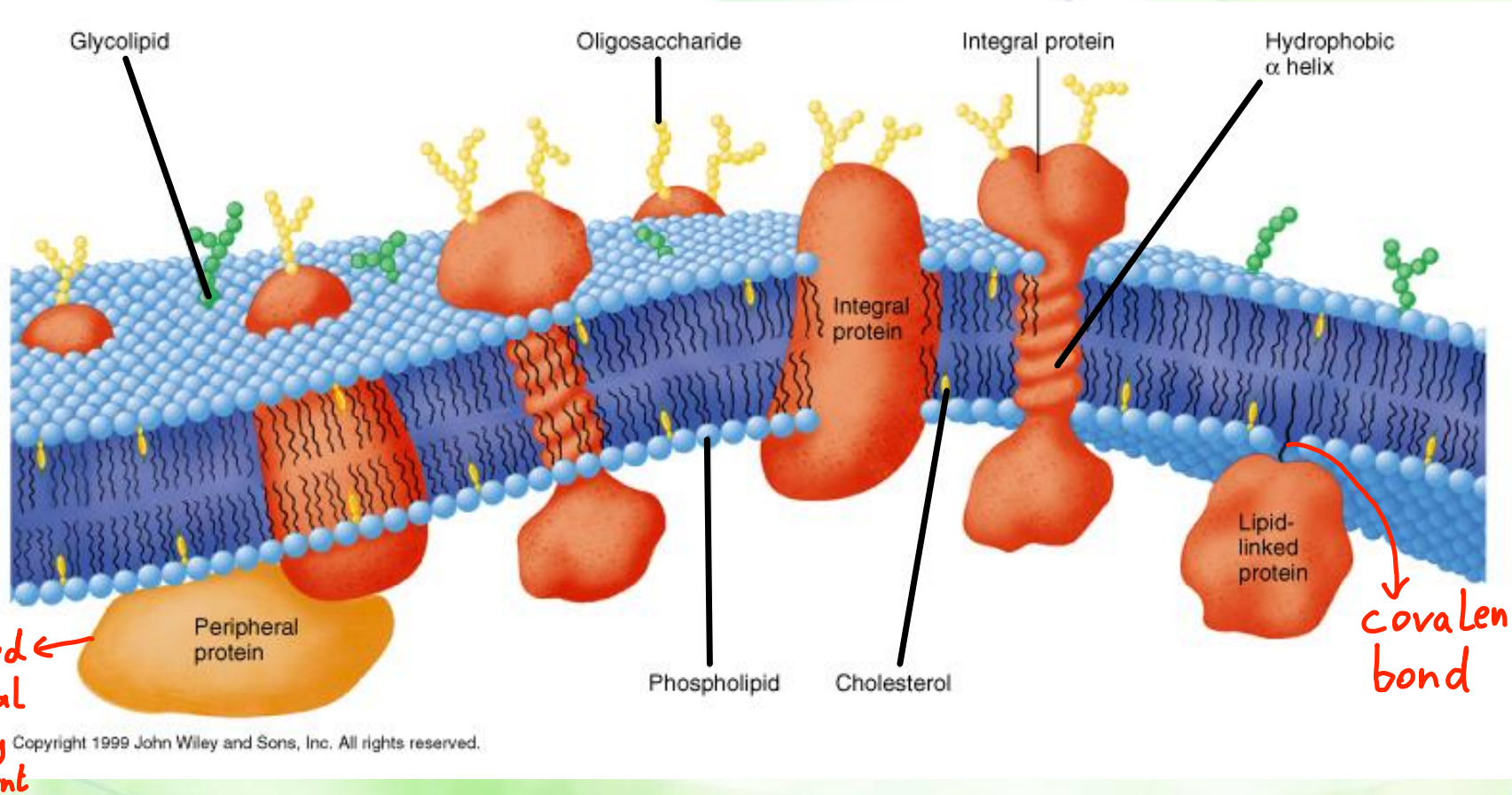
* they contribute to viral infections and immune diseases



* Cholesterol are abundant in lipid raFt

* Increase the concentration of Cholesterol will increase rigidity and decrease Fluidity

Membrane proteins



Types of membrane proteins

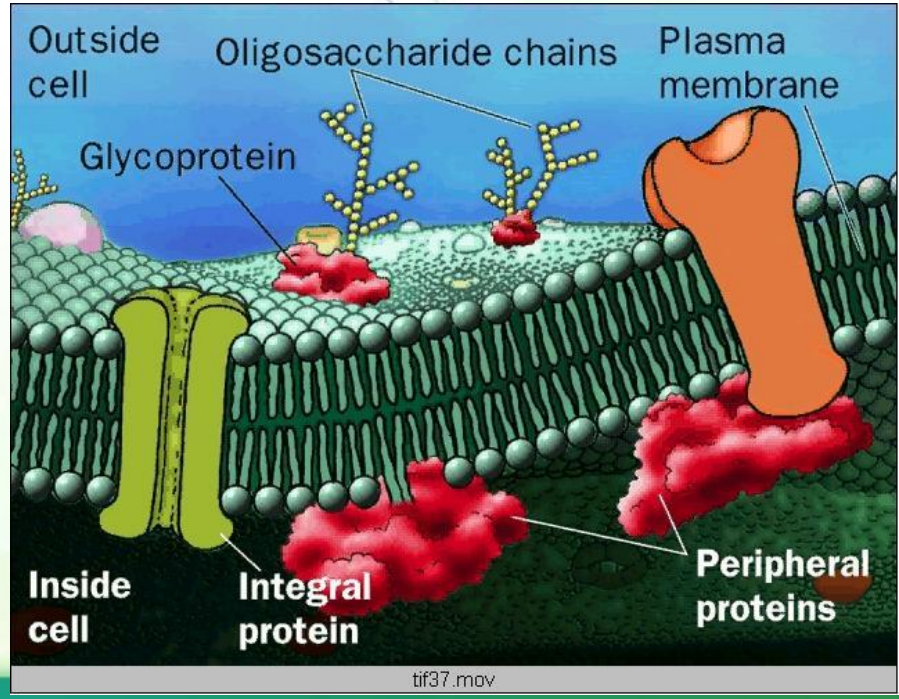
- Peripheral proteins:
  - are associated with the exterior of membranes via noncovalent interactions
- Integral membrane proteins: (spanning the membrane)
  - anchored into membrane via hydrophobic regions
- Lipid-anchored: (covalent interaction with plasma membrane)
  - associated via a lipid group

Peripheral membrane proteins

- They are associated with membranes but do not penetrate the hydrophobic core of the membrane.
  - They can be associated with integral membrane proteins.
- They are not strongly bound to the membrane and can be removed without disrupting the membrane structure.
  - Treatment with mild detergent

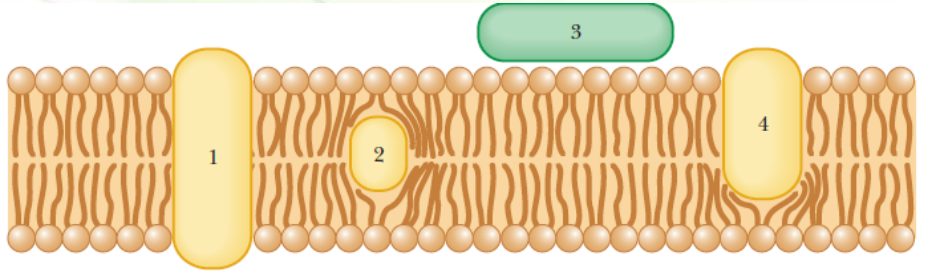
used to insulate particles

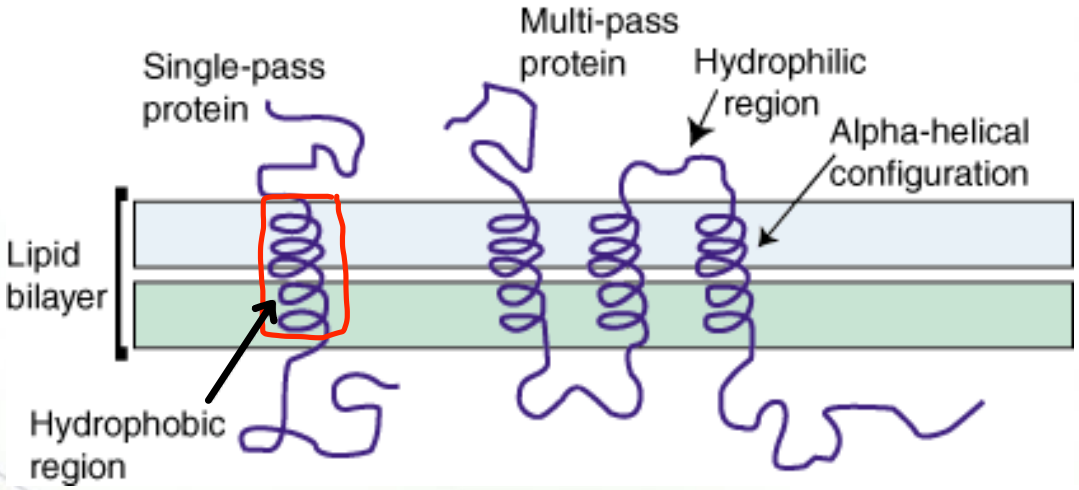
* It is easy to isolate peripheral proteins which are attracted by non-covalent interaction because it expose to detergent



Integral membrane proteins

The integral membrane proteins can be associated with the lipid bilayer in several ways.



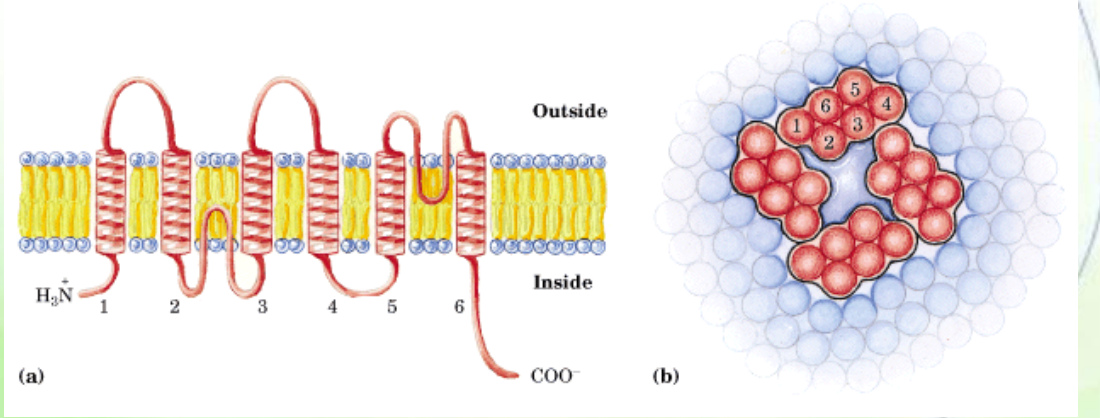


The membrane integral domains are:

1. Single or multiple

2. α-helix (human) or β-sheet (bacteria)

Some can form channels.



* It is very hard to isolate integral membrane protein because the center region is hydrophobic

Structure-Function of Membranes

- Transport:
  - Membranes are impermeable barrier
  - Proteins can be carriers or channels
- Signaling
  - Protein receptors and small molecules (some can be lipids themselves)
- Catalysis
  - Enzyme-linked receptors

* protein has more diversity than lipid and carb

* protein has more diversity than lipids and carbs