❖ Lipids

- **Lipids:** are a **heterogeneous** class of naturally occurring organic compounds that share some properties based on structural similarities, **mainly a dominance of nonpolar groups (Hydrophobic)**
  - They are **Macromolecules** (but **not polymers**), widely distributed in animals and plants
  - They are highly heterogeneous → they don't share a certain functional group → they only share the dominance of non-polar group (hydrophobic)

- They are **amphipathic** in nature, and some of the are completely non-polar (hydrophobic)
  - **Amphipathic:** Molecules have polar (hydrophilic) and non-polar (hydrophobic) groups

- They are mainly **water-insoluble**, but they are **soluble in fat or organic solvents** (ether, chloroform, benzene, acetone) → due to the non-polar group which make the hydrophobic

- **Lipids are classified into:**

Simple Lipids	Complex lipids	Derived lipids	Miscellaneous
Fats	⇨ Membrane lipids	Fatty acids	⇨ Other lipids
Oils	Glycerides	Alcohol	Aliphatic Hydrocarbons
Waxes	Glycerophospholipids	Eicosanoids	Terenes
	Sphingolipids	**Cyclic lipids**	
	Glycolipids	Steroids	
	Lipoproteins		
	Sulfolipids		

- **Lipids functions:**

Storage & energy source
- It is the main function of lipids, and they can store large amount of energy, due to:
  - long Hydrocarbon chains
  - Water-insolubility (no enlargement in size)
- Used when there is depletion in carbohydrates
- Stored in the **adipose** tissue mainly in the form of **triacylglycerol**

Structural
- They are main components of **cell membrane** which separate different compartments
- They organize the **movement** of molecules btw the compartments (inside and outside the cell)
  - Such as keeping lysosomal enzymes inside the lysosomes

Signalling
- Many **hormones & ligands** are composed of lipids → which can bind to receptors on the surface of the cell or inside it

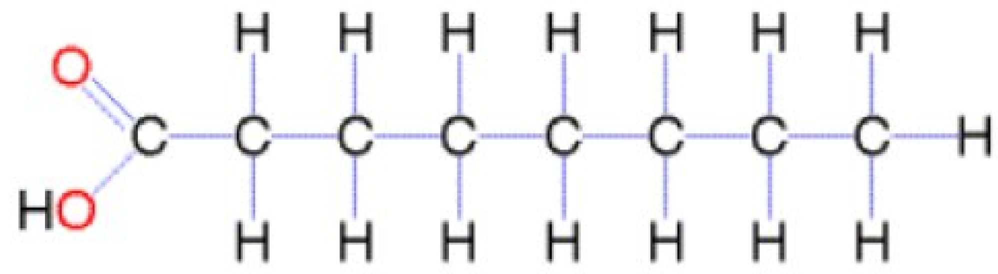
Precursors of other molecules
- They can be found in:
  - **Hormones** like sex hormones
  - **Lipid soluble vitamins** (A, D, E, K)
  - **Cofactors** → participate in reactions

Shock absorbance & protect organs
Protect essential organs from being traumatized such as kidney (which is covered by lipids)

Thermal insulator
Keep the temperature of the body in normal ranges especially at low temperatures

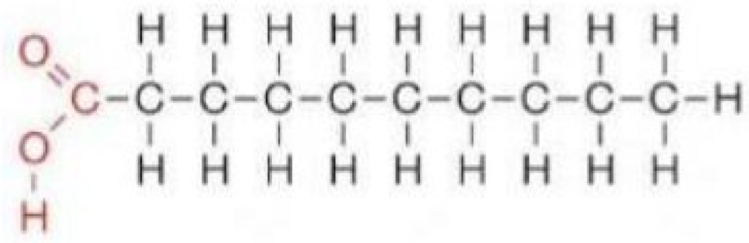
- **Fatty Acids:** **Mono-carboxylic** acids with long hydrocarbon chain (**Aliphatic**)
  - Formula → **$R-(CH_2)_n-COOH$**
  - The length normally ranges from **12-24 C (**physiological**)** and the most **abundant** lengths **16-18 C**

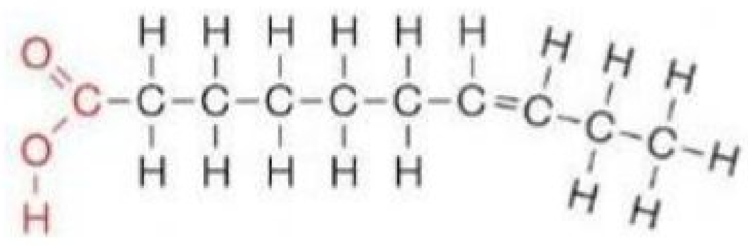
- Fatty acids are **Amphipathic** molecules
    - ➢ Carboxyl group → polar / Hydrocarbon chain → non-polar



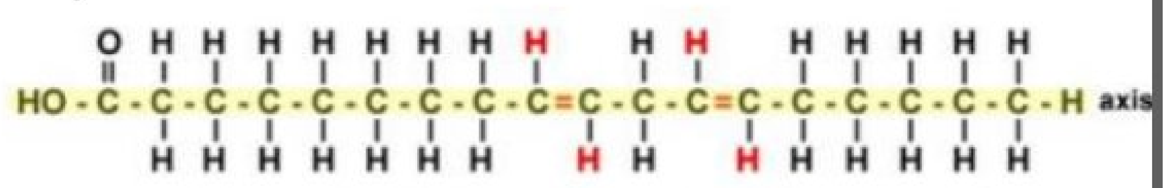
- <u>**Functions of fatty acids:**</u>
  1) **Building blocks for other lipids** (such as triacylglycerol)
  2) **Modifications of many proteins** (lipoproteins)
  3) **Important fuel molecules** → can be broken into smaller molecules (such as acetyl CoA) used to provide energy
  4) **Derivatives of important cellular molecules** (such as phospholipids & sphingolipids)

- <u>**Fatty acids can be classified according to saturation into:**</u>
    - ➢ **Saturated:** All the bonds between carbons (C – C) are **single bonds**
    - ➢ **Unsaturated:** Have 1 or more **double bond** between carbons
        - ✓ **Mono-unsaturated:** Contains only **1 double bond**
        - ✓ **Poly-unsaturated:** Contains **2 or more double bonds**

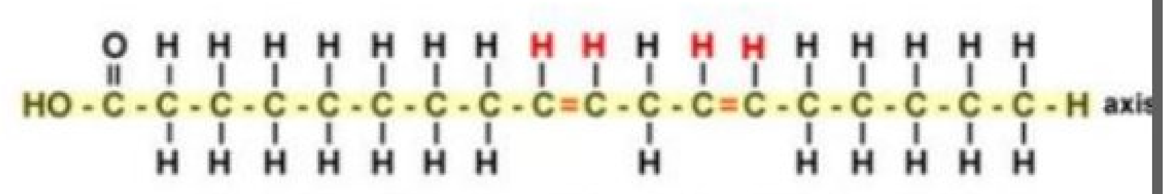




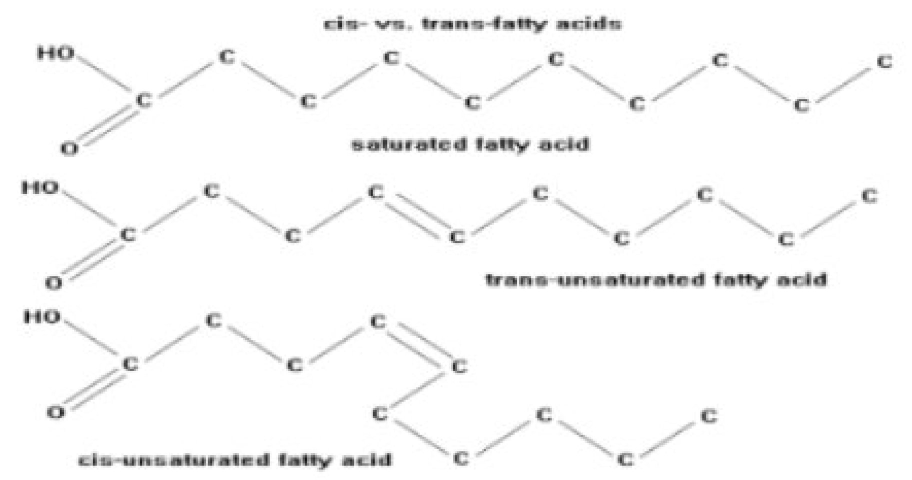
- Unsaturated fatty acids can be either in the **Cis or Trans** form (isomer):
    - ➢ **Cis:** The **same orientation** of H atoms of the carbons forming the double bond → producing a **Kink (bend)** to avoid the steric hindrance between 2 H atoms
    - ➢ **Trans:** The **opposite orientation** of H atoms of the carbons forming the double bond → there is **no kink**
- <u>Cis isomers are more abundant (predominant) than trans</u>



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



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



- Membrane fluidity depends on the saturation of fatty acids (lipids):
    - ➢ **Saturated & Trans** unsaturated fatty acids → have no kinks → chains are parallel → forming hydrophobic interactions → can be <u>packed easily</u> → **more rigidity** → **less membrane fluidity**
        - ✓ They can cause <u>atherosclerosis & increase blood pressure</u> due to their accumulation on the walls of blood vessels
    - ➢ **Cis** unsaturated fatty acids → have kinks → reducing hydrophobic interactions → so it can't be packed easily → **less rigidity** → **more membrane fluidity**

- <u>**The properties of fatty acids (such as melting point and water solubility) depend on:**</u>
  1) **Chain length** ➔ the number of carbons forming the chain
      - ➢ **Longer chains** → more non-covalent interactions (Hydrophobic & Van der Waals) between chains → more energy needed to break them → **higher melting point**
      - ➢ **Longer hydrocarbon chain** → more non-polar & hydrophobic → **decrease water solubility**
  2) **Saturation** ➔ The number of double bonds
      - ➢ **More double bonds** → unsaturated (mainly cis which is more abundant naturally) → causes kinks → less non-covalent interactions → less energy needed to break them → **less melting point**

- **Saturated fatty acids can be:**
  - **Short Chain F.A.** → **liquid** in nature, water soluble, **volatile** at room temperature (RT)
    - ✓ About 1-5 carbons in length, examples: **Acetic, Butyric, Caproic FA**
  - **Medium Chain F.A.** → **solid** at RT, water soluble, **non**-volatile at RT
    - ✓ About 6-12 carbons in length, examples: **Caprylic, Capric FA**
  - **Long & Very Long Chain F.A.** → **solid** at RT, water insoluble, **non**-volatile at RT
    - ✓ Long → About 13-20 carbons in length, examples: **Palmitic, Stearic FA**
    - ✓ Very long → About 20-24 carbons in length

- Short and medium chain FA are water soluble → because of the dominance of the **carboxyl** group

- **There are many Ways to Name a Fatty Acid:**

A) Systematic Way:

- gives us the whole information about a FA (Number of carbons, double bonds number and location)
- FA ends with -oic acid
  - **Number of Carbons (Mono-, Di-,…)**, for example:
    - ✓ 3 Carbons: Tri-
    - ✓ 16 Carbons: Hexadeca-

1 = Mono	5 = Penta	9 = Nona
2 = Di	6 = Hexa	10 = Deca
3 = Tri	7 = Hepta	20 = Eico
4 = Tetra	8 = Octa	22 = Doco

  - **Saturation:**
    - **Saturated** → single bonds → Alkane → **-ane + -oic = -anoic** suffix
      - ✓ Saturated, 16 carbons: **Hexadecanoic acid** or **n-Hexadecanoic acid**
    - **Unsaturated** → double bonds → Alkene → **-ene + -oic = -enoic** suffix
      - ✓ Unsaturated with 1 double bond, 16 C: **Hexadecenoic acid**
      - ✓ Unsaturated with 2 double bonds, 16 C: **Hexadecadienoic acid**

  - **The Location & type of double bonds:**
    - Cis/trans-Δ^n → n = the number of the carbon that has a double bond
      - ✓ Cis with 1 double bond between carbon 5 & 6, 16C: **Cis-Δ^5 Hexadecaenoic**

  - **Designation of Carbons & bonds:**
    - Number of carbons: Number of double bonds
      - ✓ 18:0 → 18 C with no double bonds (saturated)
      - ✓ 18: 3 → 18 C with 3 double bonds (poly-unsaturated)

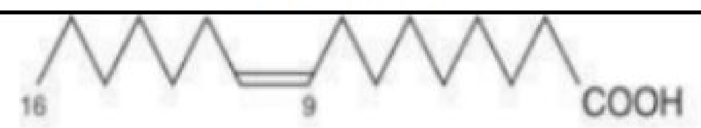
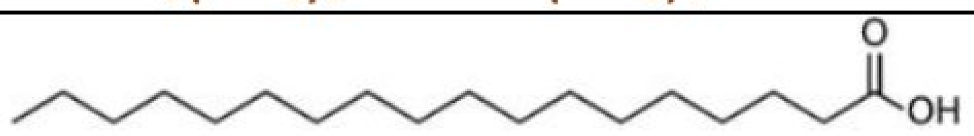
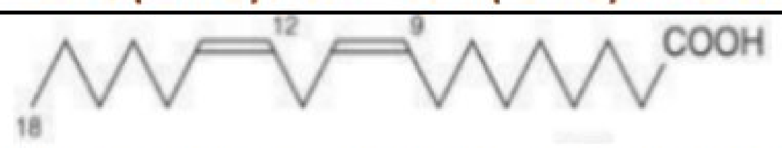
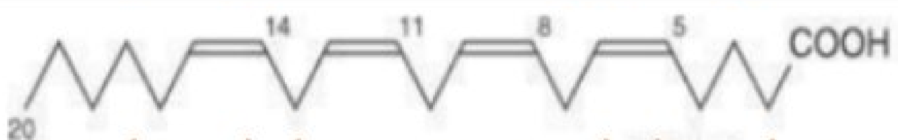
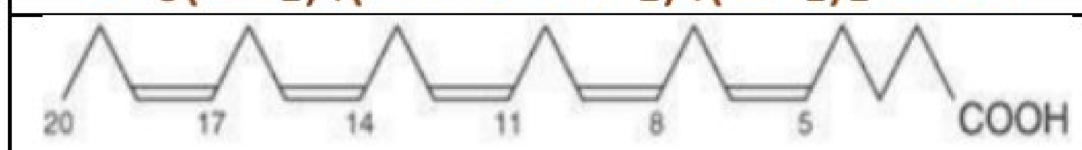
> **Note:**
> **Counting starts from the carboxyl group (Alpha carbon)**

B) Common Names

- For example: **Δ^9 Hexadecenoic acid is called Palmitoleic acid**

C) Omega classification

- We use omega (ω) to indicate the location of the double bond
  - If there are many double bonds → ω indicates the **location only for the last one**
  - We **start counting from the last carbon** (the hydrocarbon end, not the carboxyl end)
  - FAs with the same ω classification → has **properties, characteristics and function in common**

Structure & Formula	Systematic Name / Omega	Common Name	C : Double
 $CH_3(CH2)_{12}COOH$	n-Tetradecanoic Acid	Myristic Acid	14 : 0
 $CH_3(CH_2)_{14}COOH$	n-Hexadecanoic Acid	Palmitic Acid	16 : 0
 $CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	Δ^9 -Hexadecenoic acid / ω 7	Palmitoleic Acid	16 : 1
 $CH_3(CH_2)_{16}COOH$	n-Octadecanoic Acid	Stearic Acid	18 : 0
 $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	Δ^9 -Octadecenoic acid / ω 9	Oleic Acid	18 : 1
 $CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_5COOH$	$\Delta^{9,12}$ -Octadecadienoic acid ω 6	Linoleic Acid	18 : 2
 $CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	$\Delta^{9,12,15}$ -Octadecatrienoic acid ω 3	Alpha-Linolenic Acid (ALA)	18 : 3
 $CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	$\Delta^{5,8,11,14}$ -Eicosatetraenoic acid ω 6	Arachidonic Acid	20 : 4
 $CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	$\Delta^{5,8,11,14,17}$ -Eicosapentaenoic acid / ω 3	Eicosapentaenoic Acid (EPA)	20 : 5
 $CH_3CH_2(CH{=}CHCH_2)_6CH_2COOH$	$\Delta^{4,7,10,13,16,19}$ -Docosahexaenoic Acid / ω 3	Docosahexaenoic Acid (DHA)	22 : 6

- **Notes:**
  - FA has 2 ends → Carboxylic end (The first carbon and called Alpha carbon), and Hydrocarbon end (the last carbon and called omega carbon)
  - **Linoleic acid is the precursor of Arachidonic acid**
  - **Alpha-linolenic acid (ALA) is the precursor of EPA & DHA**
  - EPA & DHA are **fish oil**
  - FA can donate the H atom in the carboxyl group (COOH) forming a conjugate base (COO^-) which ends with the suffix **-ate**
    - ✓ Example: Oleic acid → Oleate

❖ Omega Fatty acids

- **Omega 3 FAs:**
  - Such as **ALA → produces EPA → Producing DHA**
  - Used to reduce inflammatory reactions by:
    - ✓ **Reducing the conversion of Arachidonic acid into eicosanoids** (they are important in the inflammatory response)
    - ✓ Promoting the **synthesis of Anti-inflammatory** molecules

Inflammation:
It is a response to any change in the cells or body (such as infection by bacteria, trauma, burn...), causes:
Redness, swelling, pain, high temperature in the area of inflammation

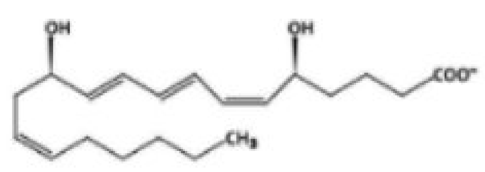
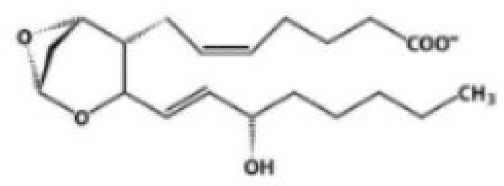
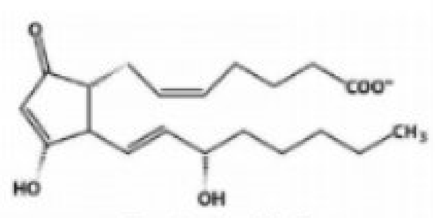
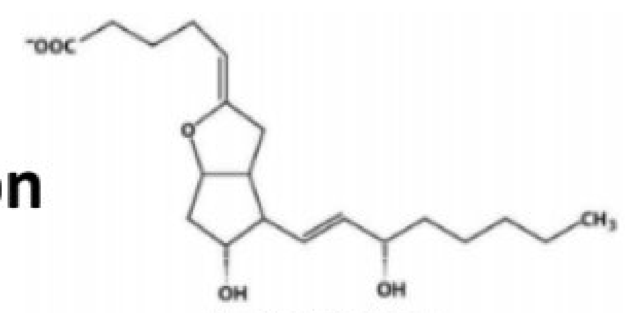
- **Omega 6 FAs:**
  - Such as Linoleic acid & **Arachidonic Acid**
  - Arachidonic acid is a precursor of eicosanoids (important role in the inflammatory response):
    - ✓ Stimulates **platelets & leukocytes** activation

- ✓ Signals **pain** & induces **bronchoconstriction**
- ✓ Regulate **gastric secretion**

- **Omega 9 FAs:**
  - ➢ Such as **Oleic acid** which **reduces cholesterol** in the blood circulation

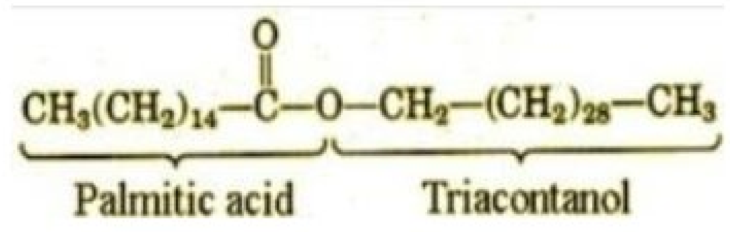
______ ______ ______ ______ ______ ______ ______

- ## Arachidonic Acid:
  - ➢ It is **all cis- $\Delta^{5,8,11,14}$ -Eicosatetraenoic acid** → polyunsaturated FA (20:4)
  - ➢ Can be cut from the tails of phospholipids or diacylglycerol
  - ➢ **Arachidonate** can be used to produce different types of **Eicosanoids**, by 2 pathways:
    - ✓ **Linear pathway**
      - o By **lipoxygenase** producing → **leukotrienes**
    - ✓ Cyclic pathway
      - o By **PGH2 synthase** producing → **Prostaglandin H2**, which can be used by:
        - ➔ **Thromboxane synthase** producing → **Thromboxane**
        - ➔ **Prostacyclin synthase** producing → **prostacyclin**

Leukotrienes	Thromboxanes
o (20:4) o **linear structure** o 3 of the double bonds are conjugated o Causes **constriction** of smooth muscles especially in the **respiratory** tract (causing **asthma**) 	o (20:2) o **Cyclic** o Have 2 ethers o **Platelet aggregation** o Cause **constriction** of smooth muscles in the **blood vessels**  Thromboxane A_2 (TXA_2)
Prostaglandins	**Prostacyclins**
o (20:3) o **Cyclic** (5 membered ring) o **Inhibit platelet aggregation** (blood clotting) o Inflammation & fever  Prostaglandin E_2	o (20:2) o **Cyclic** (**2 rings**) o **Inhibit platelet aggregation** o **Vasodilator**  Prostacyclin (PGI_2)

- **Aspirin:**
  - ➢ A drug reduces fever, inflammations & blood clotting by **inhibiting 2 types of COX enzymes**
    - ✓ **Inhibits Cyclooxygenase (COX) 1** → **inhibiting Thromboxane** production → **inhibit platelet aggregation**
    - ✓ **Inhibits Cyclooxygenase 2** → **inhibiting Prostaglandins** production → reducing inflammation (Anti-inflammatory & Anti-Pyretic)
- **Note:**
- Cyclooxygenase enzymes have 3 forms (1,2 & 3)
- **COX-1** is important for many **homeostatic functions** (such as homeostasis in GI tract, renal tract, platelet functions & Macrophages differentiation)
- **COX-2 is** important for **inflammation**
  - ➢ So, **aspirin inhibits COX-2** (desirable to reduce inflammation), and inhibits **COX-1** (undesirable causing side effects)
  - ➢ **Celebrex inhibits only COX-2** → but is prescribed with a strong warning of side effects (on the heart)

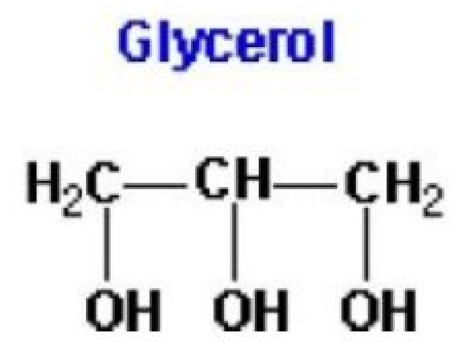
❖ Waxes

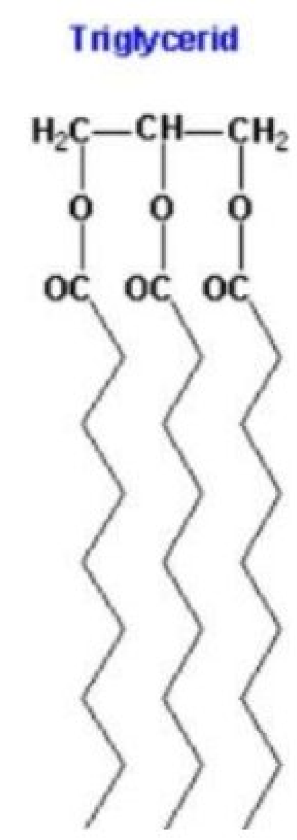


- Simple solid lipids containing a **monohydric alcohol + Long chain FAs**
  - ➢ The monohydric alcohol has only 1 OH group with a **high molecular weight** with <u>16-30</u> Carbons
  - ➢ LCFA → <u>14-36 Carbons</u> such as palmitoyl alcohol
  - ➢ Both groups are linked together by **ester linkage**
- They are **water insoluble**, **Negative acrolein test** (a test of the presence of glycerin or fats)
- Are **not easily hydrolyzed** & are **indigestible by lipases**
- They are **very resistant to rancidity** (oxidation or hydrolysis of fats and oils)
- They have **no nutritional value**
- They present in the **coatings** that prevent → the loss of water from leaves of plants, wetting of feathers and fast deterioration of fruits

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

❖ Complex lipids





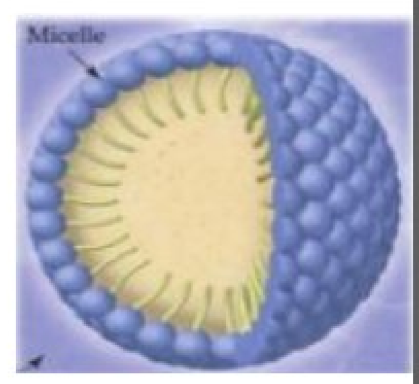
- **Triacylglycerol (TAGs):**
  - ➢ They are triglycerides, and they are **storage lipids**
  - ➢ Triacylglycerol → consists of **Glycerol** + **3 Fatty Acids**
  - ➢ Each carbon in the glycerol is attached to a FA by **ester linkage**
  - ➢ The 3 fatty acids can be all similar or different (in length & saturation)
  - ➢ If the 3 FA are similar → it is a **simple triglyceride** such as tristearin (3 stearic acids)
  - ➢ If the 3 FA are not similar → it is a **mixed triglyceride**

- **Vegetable oils** consist mostly of **unsaturated** fatty acids → mainly cis → kinks → less non-covalent interactions → **more fluid** → **liquid** fats (oils)
- **Animal Fats** consist mostly of **saturated** fatty acids → no kinks → more non-covalent interactions → **less fluid** → **solid** fats
  - ➢ Both of them consist of a mixture of different TAGs

- <u>**We can break TAGs by:**</u>

Hydrolysis	Saponification
• Can be hydrolysed by **steam, acids and enzymes** (such as <u>lipases of pancreas</u>) • In the body, lipases break TAG releasing **glycerol** + 3 Fatty acids which release their proton forming **FA in the ionized form ($RCOO^-$)**	• **Alkaline hydrolysis** (by adding alkaline solution such as NaOH) • Releasing **Glycerol** + **soaps [salts of FAs] (RCOONa)** • Soaps causes the **easy mixing (emulsification) of oily materials** with water or hydrophilic compounds

- When soap is mixed with water → a spherical cluster of lipids is formed called **micelle,** where:
  - ➢ The **nonpolar Hydrocarbon chains, grease & dirts** cluster together **inside the micelle** forming a nonpolar microenvironment away from water (hydrophilic environment)
  - ➢ The **hydrophilic ionic** heads are exposed (on the surface) and **interact with water**



- **Hydrogenation:** Adding H atoms to the **double bond forming a single bond** (converting **unsaturated to saturated**) forming Hydrogenated oils
  - If a vegetable oil converted into **Hydrogenated oils** → more non-covalent interactions → more packed → less fluid → **more solid**
- Poly-unsaturated fats and oils can be **<u>partially</u> hydrogenated** → converting **some double bonds** (not all of them) into **single bonds** & generates **trans fats**
  - **Trans fat** consumption has risks on health → primarily the elevated risk of **CHD (coronary heart disease)**
  - Margarine has only 2 thirds of the double bonds of the starting vegetable oil hydrogenated, so it becomes remains soft in the refrigerator and melts on warm temperatures

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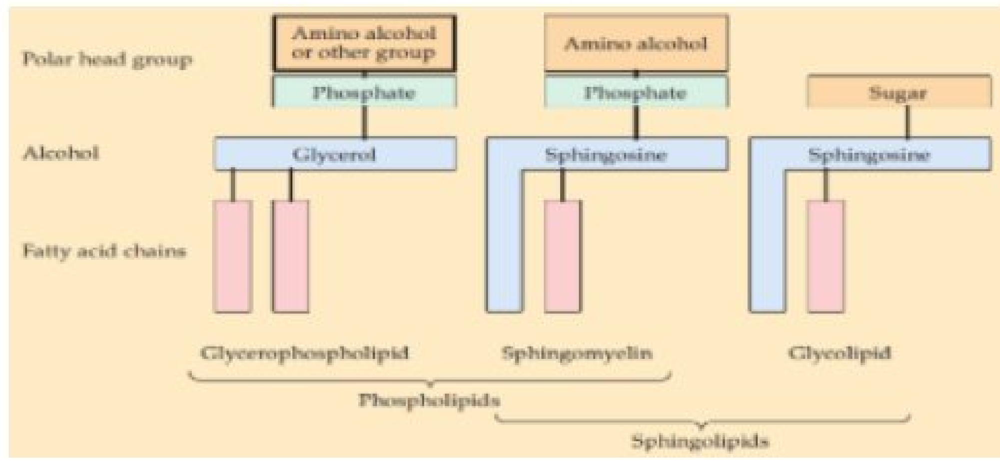
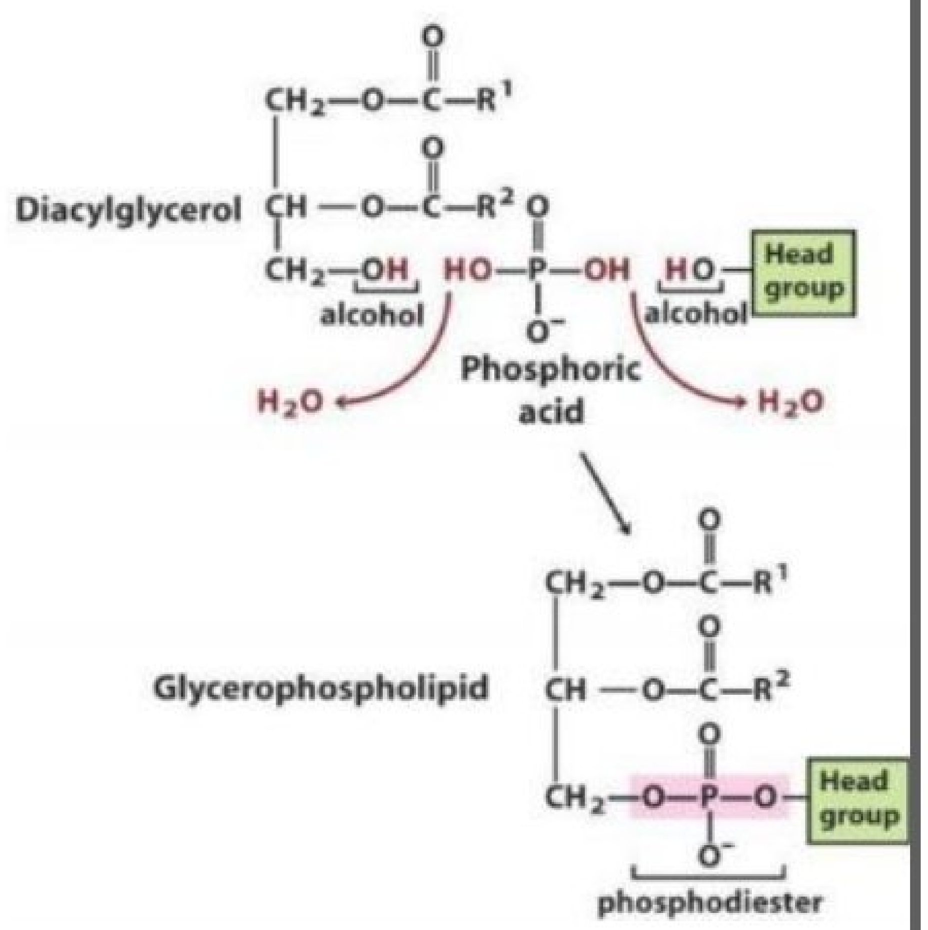
❖ Membrane lipids



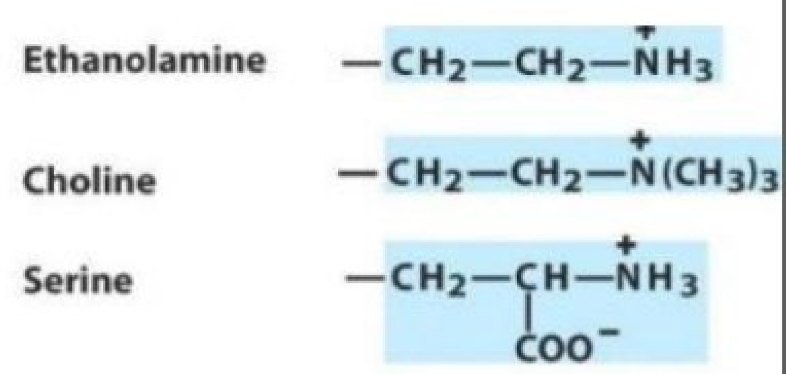
- Cell membrane are made up mainly from 2 types of lipids:
  1) **Phosholipids:** The <u>most abundant</u>, and contain a **phosphate** group (such as glycerophospholipids, sphingomylein)
  2) **Sphingolipids:** Contain **sphingosine** (a large bent molecule)
- **Animal** cell membranes → contain **cholesterol**

❖ Glycerophospholipids



- Contain a Glycerol (3 carbons each one has OH group)
  - 2 carbon of glycerol bind to FA chains (**2 FAs**) by **ester bonds** (diacylglycerol DAG) → making the **hydrophobic tails**
  - The 3rd carbon bind to a **phosphate group** which binds to **another polar** group → making the **hydrophilic head (polar head)**
    - ✓ The phosphate group is bound to the glycerol & the polar group by **ester bonds** (forming phosphodiester)
    - ✓ The addition of phosphate & the polar head is done by dehydration reaction

- It can be divided into many sub-types according to the type of the polar group bound to phosphate:
  - Phosphate + H → **Phosphatidic acid** → H is not a polar group (the father of glycerophospholipids)
  - Phosphate + choline → **phosphatidylcholine** (Lecithins) → <u>the most abundant membrane lipid</u>
  - Phosphate + inositol → **phosphatidylinositol**
  - Phosphate + Ethanolamine → **phosphatidylethanolamine**
  - Phosphate + serine → **phosphatidylserine**
    - ✓ The head group → contain a **negative** region (phosphate) & a **positive** region

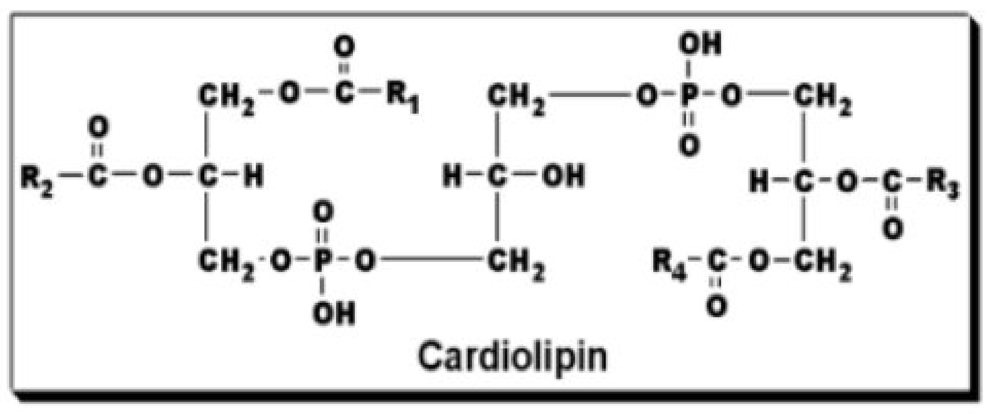


- Phosphatidylethanolamine & phosphatidylserine are called **Cephalins** → abundant in the brain (Cepha)
- Inositol is very close to sugars in terms of structure
- **Phosphatidylinositol** has an important role in **signaling** → it is cleaved by **phospholipase C** in the **IP3 & DAG** signaling pathway
- Also there are many other types of glycerophospholipids such as **cardiolipin, Plasmalogens**

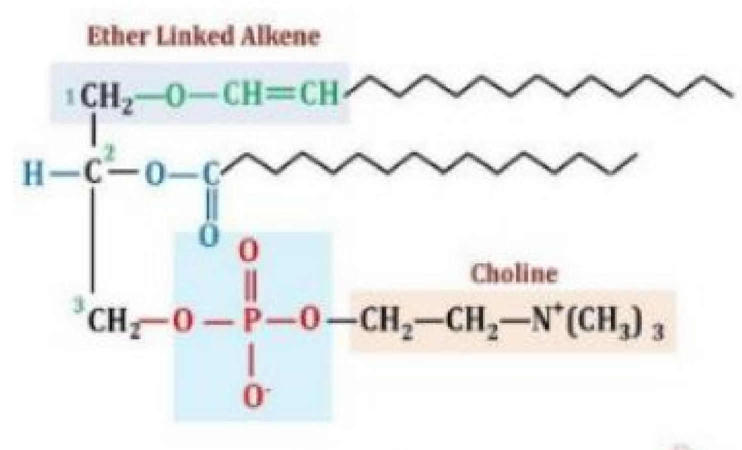
- ## **Lecithins:**
- **phosphatidylcholine**
- They can be used as **Emulsification agents** (Emulsifiers) → due to their amphipathic nature so the can surround the nonpolar molecules (and attach to them by their hydrophobic tails) keeping them in suspension in water (hydrophilic heads interact with water) → we can benefit from that in snacks (such as chocolate & cake…)

- Snake venom contains **lecithinase** → which causes the break down (hydrolysis) of poly-unsaturated fatty acids in **lecithin and convert it into lysolecithin** → **disrupting the plasma membrane** because phosphatidylcholine is the most abundant lipid in membranes → causing **RBCs hemolysis**

- ## **Cardiolipins:**
- **Di-phosphatidyl glycerol**
- Found mainly in the **inner membrane of the mitochondria**
- Called cardio because it has firstly isolated from the heart muscle
- It consists of **3 Glycerols + 4 FAs + 2 phosphate**


Cardiolipin

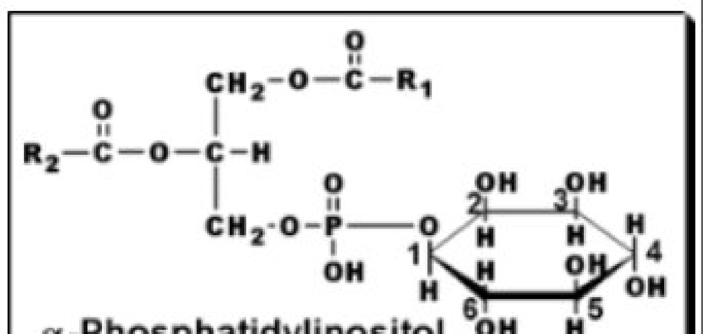
- ## **Plasmalogens:**
- Found in the cell membrane of **brain, muscle, liver, semen**
- Protect theses tissues **against reactive oxygen species** (which are hurmful)
- Precursor → **Dihydroxyacetone**
- It consists of a Glycerol molecule bound to:
  - **Unsaturated Fatty alcohol** on carbon 1 → by **ether bond**
  - **Fatty acid** on carbon 2 → ester bond
  - On carbon 3 there are a **phosphate + a polar group** such as ethanolamine and choline



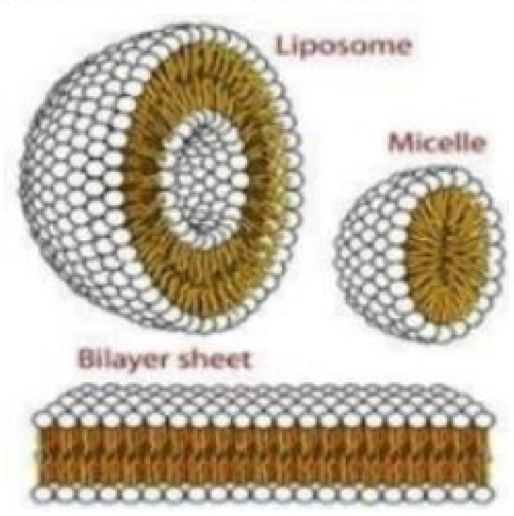
Plasmalogen

- It has many classes according to the polar group it has:
  - **Ethanolamine plasmalogen** → in the myelin sheath (nervous system)
  - **Choline plasmalogen** → in the cardiac tissue and act as **platelet activation factor**
  - **Serine plasmalogen**

- ## **Inositides (phosphatidylinositol):**
- Inositol is a **nitrogenous base (cyclic sugar alcohol)** → similar but not a sugar
- Consists of Glycerol + 2 FAs (saturated, unsaturated) + phosphoric acid + inositol
- Found in the **brain**
- Functions:
  - A major component in the **cell membrane**
  - **Signaling** → in IP3 & DAG second messenger system
    - ✓ Phospholipase C hydrolyze Phosphatidylinositol bisphosphate (PIP2) into DAG & IP3 (Inositol triphosphate) → which liberates calcium from ER


α-Phosphatidylinositol

- Lipids are arranged in the cell membrane in a bilayer where the hydrophobic tails are hidden inside & the hydrophilic heads are exposed to the aqueous solutions (cytosol & ECM)
- **Liposome:** A round membranous structure consist of a **lipid bilayer** similar to that in the cell membrane (can fuse into it) → can be used to **deliver drugs** to a specific tissue (cells)

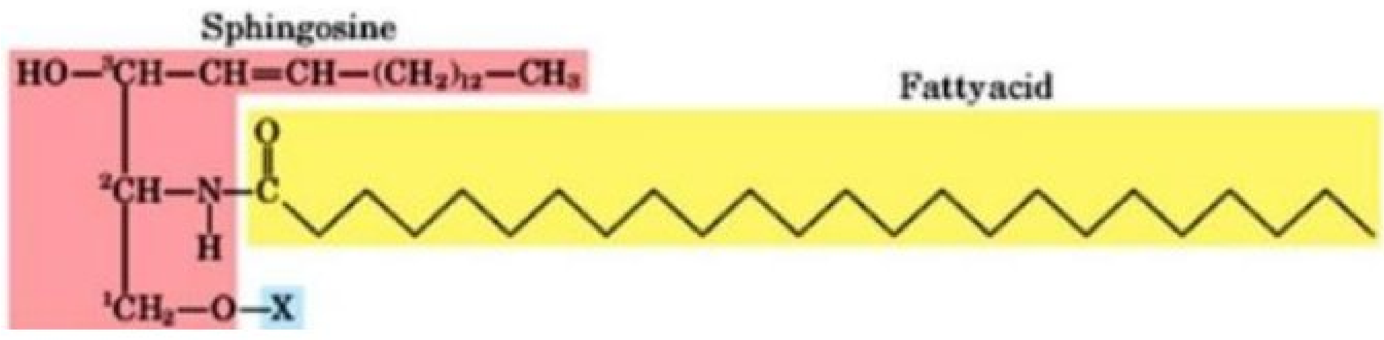


- **Micelle:** A round membranous structure consist of a **single layer** of lipids where the hydrophobic tails protrudes inside the micelle

Amphipathic lipids move:
1) **Lateral movement**
2) **Rotate around itself**
3) **Flipflop** (between different sheets)

❖ Sphingolipids

- Found in the cell membrane of all eukaryotes, it is **highest in the CNS**
- The core of sphingolipids is **sphingosine** (long-chain amino alcohol)
  - ➢ **Sphingosine:** 18 carbon molecule, the first carbon has OH and the second carbon has amino group and the rest is a hydrocarbon chain (carbon 4 has a double bond producing **a kink in the molecule**)
  - ➢ 3rd carbon binds to a molecule (polar)
  - ➢ 2nd carbon binds to a FA by **amide bond**

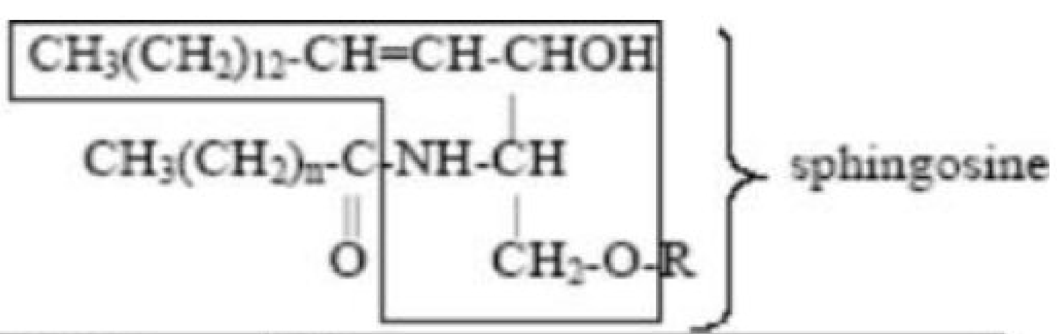


- ## Ceramide:
- The father of sphingolipids (the simplest) → consists of **sphingosine + FA (on C-2) + H (on C-3)**

- ## Types of sphingolipids:

Sphingomyelins

- They are considered as **phospholipids**
- The major component of the **coating around nerve fibers (myelin sheath)**
  - o Act as **electrical insulator** (doesn't transmit electricity → increasing the velocity of transmission → faster action potential)
- C1 attach to **phosphate + a polar group** (mainly choline)
- If the there is a **disorder (problem) in the structure of Sphingomyelin** → distortion of myelin sheath → causing **multiple sclerosis disease** → causing delayed action potential
- Symptoms differ according to the nerve affected and their function (vision, balance...)
- Usually affects young females



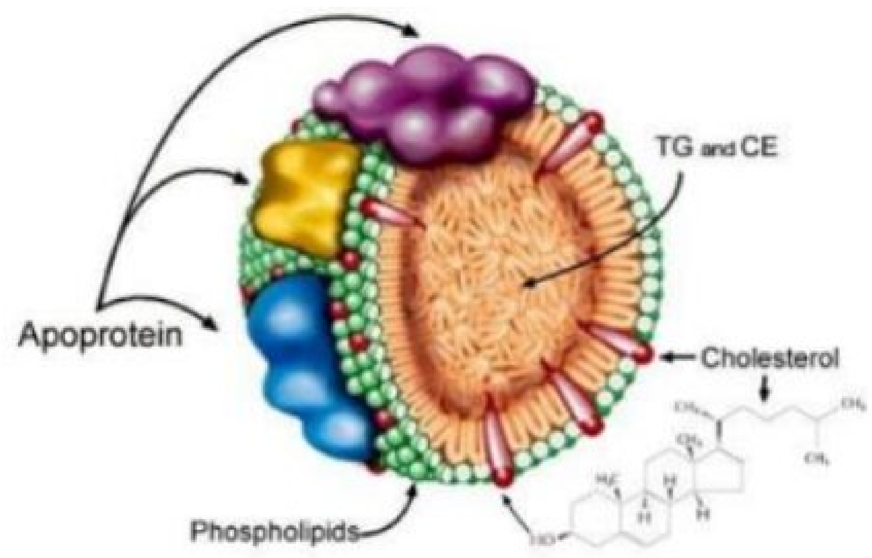
	Sphingolipid type	R group
	Ceramide	H
	Sphingomyelin	phosphocholine
	Cerebroside	monosaccharide (galactose or glucose)
glycolipids	Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
	Ganglioside	three or more sugars including at least one sialic acid

Glycosphingolipids (glycolipids)

- C1 attach to **carbohydrates**
- Glycolipids on the cell surface act as receptors in cell recognition (pathogens, blood types) & chemical messengers
- There are 3 types of glycolipids:
  - o **Cerebrosides:** contain a single Hexose (monosaccharide)
    - ➢ The simplest glycolipid
    - ➢ glucocerebroside & galactocerebrosides
  - o **Globosides:** attached to **2 or more sugars**
  - o **Gangliosides: 3 or more sugars**
    - ➢ Globosides & Gangliosides are more complex
    - ➢ Sugar can be glu, gal, galNAc...
    - ➢ **Gangliosides must contain sialic acid**
- Gangliosides present **mostly in ganglia**, and it is targeted by **cholera toxin** in the intestines affecting the nervous system
- **Blood types** depend on the sequence of sugars of glycolipids on the surface of RBCs:
  - ➢ 5-main sugars → **Glu, Gala, GalNAc, Gala, Fuc (fucose)** → **O** type
  - ➢ Addition of **GalNAc** → **A** type
  - ➢ Addition of **Gal** → **B** type

- ## Sulfatides:
- **Synthesized from galactocerebrosides** → by the modification of galactose by adding sulfate group to carbon number 3
- Abundant in the **brain myelin**

- ## Lipoproteins:
- Consist of **lipids + proteins** → used to **transport lipids**
  - Lipids are mainly hydrophobic molecules → so they can't move in hydrophilic or aqueous solutions (such as plasma of the blood)
  - So they are transported using lipoproteins

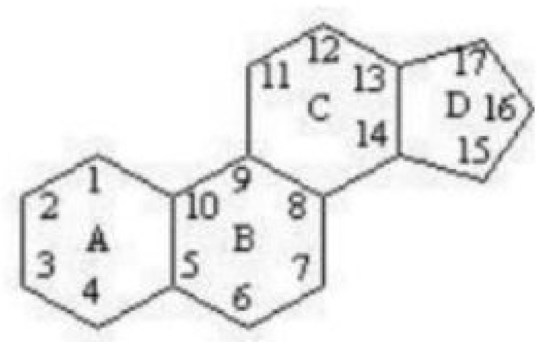


- Lipoproteins consist of proteins with lipids inside it (such as **Cholesterol, Cholesterol esters, phospholipids & triacylglycerides**)

- There are many types of lipoproteins according to the percentage & density of proteins forming them:
  - **HDL (High density lipoproteins)** → The highest protein & least lipid content, the smallest in size
  - **LDL (Low density lipoproteins)**
  - **IDL (Intermediate density lipoproteins)**
  - **VLDL (Very Low density lipoproteins)**
  - **Chylomicrons** → The least protein & highest lipid content, the largest in size

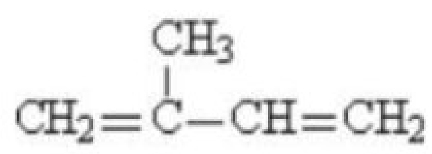
- HDL have the highest density → highest proteins → least lipids → smallest size
- Chylomicrons have the lowest density → least proteins → highest lipids → largest size
- **The smallest is HDL → then LDL → IDL → VLDL → Chylomicrons (the largest)**
- **Note:**
  - **HDL** is used to transport lipids **toward the liver** to be consumed forming bile acids, vitamin D (so they are good)
  - **LDL** is used to transport lipids **toward the tissues** to be stored (so they are bad)

- ## Steroids:
- Lipids that share the presence of the **nucleus** (4 fused rings) which is composed of:
  - **3 six-membered rings (A,B,C) + a five-membered ring (D)** fused together
  - They can have an additional side chain



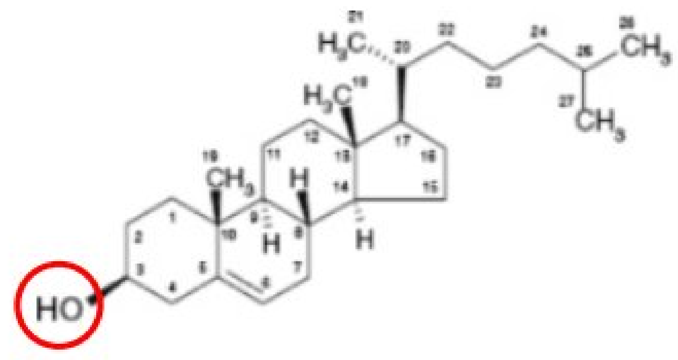
Steroid nucleus

- The precursor of steroids is **isoprene** (composed of 5 carbons)



Isoprene

- The most common steroid is **cholesterol** → which is **amphipathic**
  - Has a polar OH group on carbon 3 + the rest of the molecule is non-polar



- Cholesterol is used to produce:
  - Hormones (**sex hormones** → androgen, estrogen, progestins)
  - Vitamins (such as **vitamin D**)
  - **Bile acids** → contributes in the intestinal absorption of fats (act as emulsifiers)

- Also cholesterol present in the **cell membrane** of animal cells

- ## Cholesterol ester:
- Modified cholesterol with a **FA added to the OH** group forming ester

- They are important in **transporting cholesterol inside lipoproteins** (mainly HDL) → transporting the largest amount of cholesterol and lipids
  - It is used because inside the HDL there is a high concentration of cholesterol and we are moving it **against concentration gradient** → so we use another form (cholesterol ester) to transport more and more of cholesterol and packing HDL with more lipids

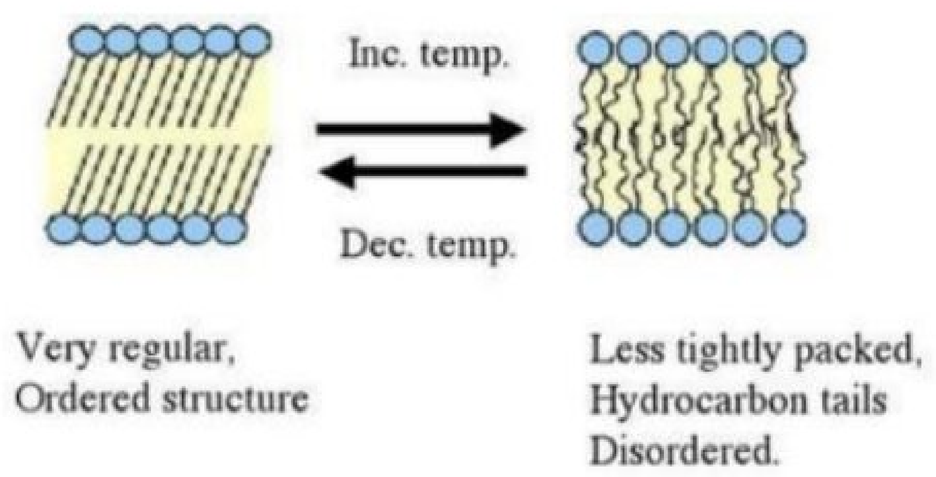
- **Atherosclerosis:**
  - A disease caused by the accumulation of lipids (such as LDLs) on the walls of the blood vessels
    - ✓ Causing the walls thicker and **narrowing of blood vessels** → making it hard for RBCs to move (RBCs contain hemoglobin which is important for transporting oxygen to cells → important for energy)
    - ✓ And also making the **flexibility of the blood vessels less**

❖ Cell membrane

- The membranes is composed of 45% lipids, 45% proteins & 10% carbohydrates exciting side by side
- Membranes are a **bilayer** of lipids with proteins (inserted or attached to it)
- **Fluid mosaic model** → a model describes the membrane
  - fluid → the components are not stable (moving) / mosaic → composed of different molecules

- Lipid components in the cell membrane → phospholipids, sphingolipids & cholesterol
  - The outer leaflet is rich of Phosphatidylcholine, sphingomyelin & glycoproteins
    - ✓ Important for **cell recognition**
  - The inner leaflet is rich of Phosphatidylethanolamine, phosphatidylserine & Phosphatidylinositol
    - ✓ Important for **signaling**
  - Cholesterol is distributed in both leaflets
- Lipids are distributed differently in different types of cells, animal, eukaryotes & prokaryotes

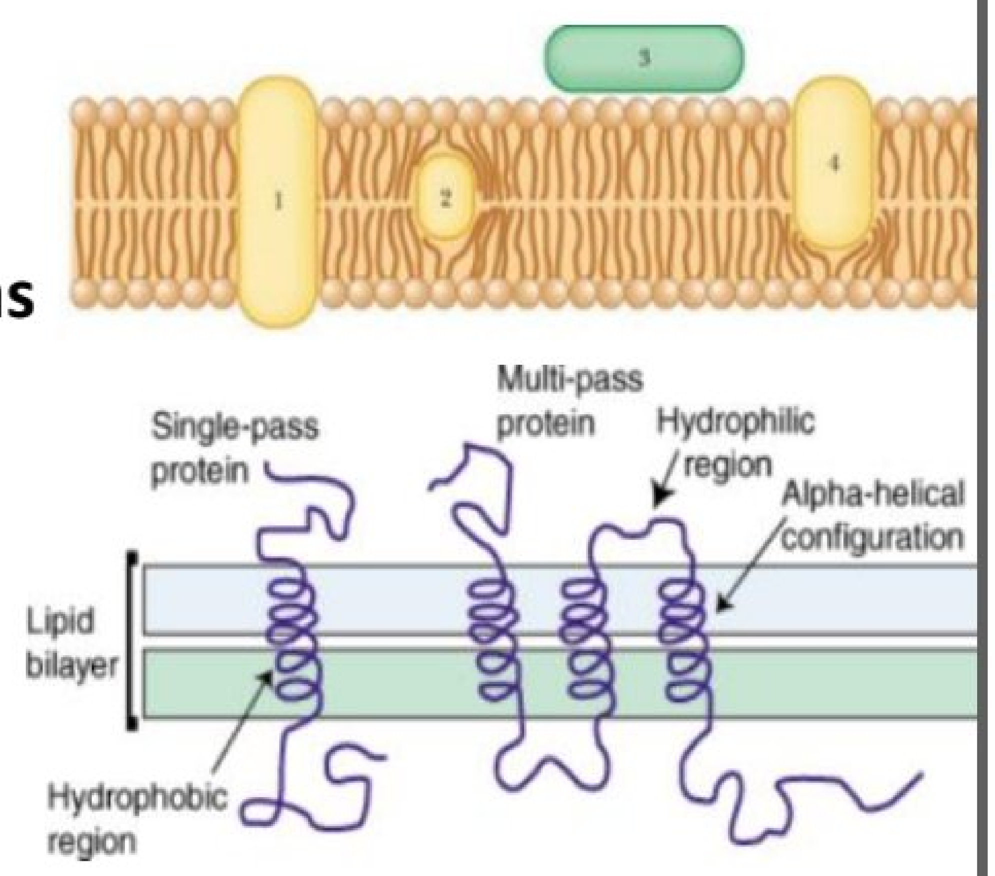
- Temperature affects the fluidity of the membrane:
  - As **temperature increases** → lipids move faster with more energy → less rigid → **more fluidity**
  - As **temperature decreases** → lipids move slower with less energy → more rigid → **less fluidity**



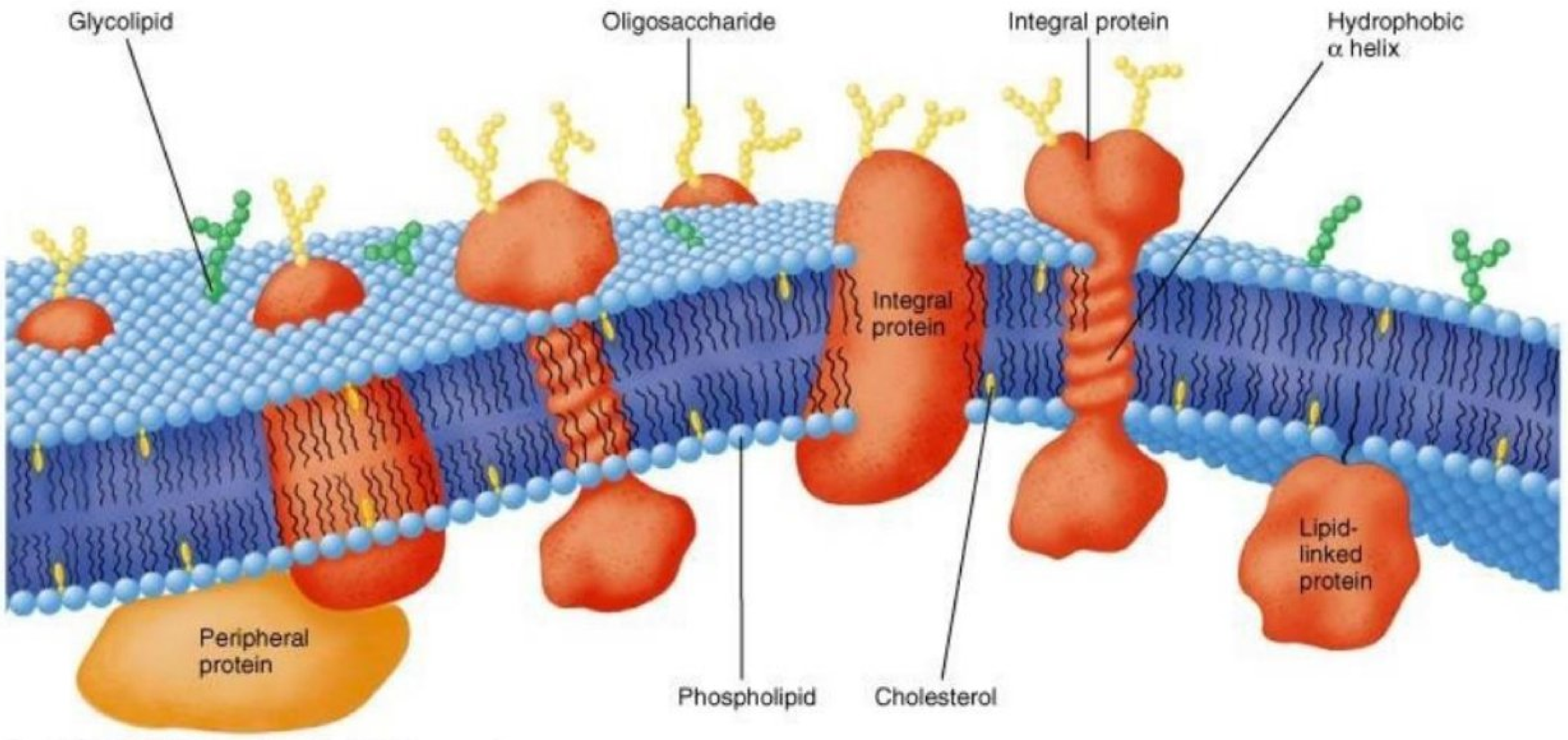
- The fluidity of membranes depends on:
  - **The saturation of fatty acids**
  - **Cholesterol** → **stabilizing & regulating the fluidity**
  - Cholesterol is rigid and form non-covalent interactions (hydrophobic, van der waals) with FAs
    - ✓ At **high temperature** → decreasing the mobility of FAs making membrane **less fluid**
    - ✓ At **low temperature** → interferes with close packing of FAs in the crystal state making **less solid**
  - Also **temperature** affects the fluidity

- **Membrane proteins:**
- There are many types of membrane proteins → Integral, Peripheral & Lipid anchored proteins

- ## Integral Membrane proteins:
- **Pass through the bilayer** of the membrane
- They are inserted (anchored) into the membrane via **hydrophobic regions**
- They are formed of a-helix and B-sheets
- Usually the inserted region in the bilayer is a-helix → and they can have only **1 a-helix** inserted (single-pass protein) or **multiple** (multi-pass)
- They can act as **channels and carriers**



- ## Peripheral Membrane proteins:
- They **don't penetrate** the hydrophobic core of the membrane → don't have hydrophobic regions (amino acids)
- Associated to the surface of the membrane or integral proteins by <u>**non-covalent interactions**</u>
  - **Not strongly** attached so can be removed <u>without disrupting</u> the membrane structure
  - They can be **detached easily** (such as treatment with mild detergents)
- The difference between Peripheral & lipid anchored proteins is:
  - **Peripheral** → attached to the membrane via **non-covalent bonds**
  - **Lipid anchored** → attached to the membrane via **covalent bonds**



- Functions of the membrane:
  - **Transport:** The membrane is an impermeable barrier so it uses proteins (channels & carriers)
  - **Signaling:** using protein receptors and other small molecules (can be lipids)
  - **Catalysis:** catalyzing reactions such as enzyme-linked receptors