Fatty Acids:

- Aliphatic monocarboxylic acid
- Formula $R-(CH_2)_n COOH$
- Vary in unsaturated level [saturated fats are rich in electrons cuz they're reduced]
- Vary in length
  - → physiological range [12-24]
  - → Abundant [16-18]
- Amphipathic molecule [hydrophilic + hydrophobic]

- Functions
  - → Building blocks for other lipids
  - → Fuel molecules
  - → derivatives of cellular molecules
  - → modification of proteins [lipoprotein]

- Classification depending on saturation
  - → Saturated → all C-C bonds are single
  - → Unsaturated
    - → monounsaturated → it has one double bond between its carbons
    - → polyunsaturated → it has two or more bond between its carbons

Unsaturated
- → trans → opposite direction $H-C=C-H$ [physiologically they're rare]
- → cis
  - → same direction $\overset{H}{C}=\overset{H}{C}$ [" " " predominates]
  - → It has a Kink

double bonds number ↑ Kinks ↑

- Melting point depends on
  - → chain length [increasing carbon atoms number increase the interactions ∗ more surface area to interact with]
  - → saturation degree [Saturated > monounsaturated > polyunsaturated]

Tight packing → high melting point

Kinks → loose packing → low melting point.

- Saturated fatty acids
  - → Short F.A [2-4]
    - → liquid in nature
    - → volatile at RT
    - → Water soluble [the hydrophilic portion is dominant]
    - → Acetic acid [vinegar], butyric acid [butter]
  - → Medium F.A [6-10]
    - → Solid at RT
    - → non-volatile at RT
    - → water soluble
    - → capric, caprylic, caproic acids [Goat's Milk]
  - → Long F.A [12-20]
    - → Solid at RT
    - → non-volatile
    - → water insoluble
    - → Palmitic acid [palm oil], stearic acid

- Unsaturated F.A
  - → palmitoleic acid hexadecenoic acid, w7, 16:1, Δ^{9}
  - → oleic acid Octadecenoic acid, w9, 18:1, Δ^{9}
  - → Lenoleic acid Octadecadienoic acid, w6, 18:2, $\Delta^{9,12}$
  - → Lenolenic acid Octadecatrienoic acid, w3, 18:3, $\Delta^{9,12,15}$
  - → Arachidonic acid Ecosatetraenoic acid, w6, 20:4, $\Delta^{5,8,11,14}$
  - → Ecosapentaenoic acid, w3, 20:5, $\Delta^{5,8,11,14,17}$

- Saturated acid: Myrestic acid : Tetradecanoic acid

- The last methyl group is called ω [omega], we conseder it the 1st carbon in naming in the Omega style

Examples
- → ω3
  - → linolenic acid
  - → EPA, Ecosapentaenoic acid 20:5
  - → DHA, Docsahexaenoic acid 22:6, $\Delta^{4,7,10,13,16,19}$
- → ω6
  - → Linoleic acid
  - → Arachidonic acid

∗ Linoleic acid and Linolenic acid are Essential F.A [From diet only]

Linoleic acid is precursor of Arachidonates

Linolenic acid is precursor of DHA, EPA

Derived fatty acid

- Wax :
  - Solid simple lipids
  - It is formed by → Monohydric alcohol [molecular weight higher than glycerol [16-30] , ex. palmitoyl alcohol
    → long chain fatty acid [14-36]
  - Water insoluble [hydrophobic]
  - Not easily hydrolyzed , indigenstible
  - Very resistant to rancidity
  - No nutritional value
  - External coating layer on plants leaves to prevent water loss

- Linoleic acid $\xrightarrow[\text{2. De unsaturation}]{\text{1. Elongation}}$ Arachidonic acid

- Arachidonic is stored in the membrane and Phospholipase A_2 change smth
  Arachidonic $\xrightarrow{\text{enzymes}}$ Ecosanoids [local hormones]
  - → Cyclooxygenase
    - → Prostaglandins [including prostacyclins]
      prostate cuz it was thought that prostate gland produced them
    - → Thromboxanes
  - → lipooxygenase
    - → Leukotriens [Leuko from Leukocytes [white blood cell]]
    - → Lipoxins

- Ecosanoids Functions
  - → Regulation of the inflammatory reaction response to infection or injury
    [destroying invading organisms and repair damage → blood- cell friction
    → infection by bacterea or virus
  - → Accompanying symptoms : fever, pain, swelling
  - → Formation of Blood clots
  - → Smooth muscles constriction and relaxation
  - → Bronchodilation and Bronchoconstriction
  - → Increase water and sodium excretion by the kidneys
    regulating blood pressure
  - → Allergic or hypersensitivity reaction
    - → bronchoconstriction
    - → Vaso dilation
    - → increasing the permeability

- Specific Functions

Prostaglandins [20 carbon with internal 5 carbon ring] → Induction of inflammation
→ Inhibition of platlet aggregation

Thromboxanes [20 carbon with internal 6 carbon ring] → Induction of platlet aggregation [No blood clots]
→ Constriction of smooth muscles

Leukotriens [20 carbon , with 4 double bonds , 3 of them are conjugated] → Constriction of Smooth muscles [Asthma]

Lipoxins → Inhibition of Inflammation

- Cyclooxygenase 1 → Thromboxanes → Platlet aggregation
  Cyclooxygenase 2 → Prostaglandins → Inflammation , fever
  > Aspirin blocks both. and inhibits heart failure , heart attack , etc...

- Aspirin causes GI ulcers [extra; COX1 produces a layer that protects the stomach and GI tract from the acids , etc.. and Aspirin prevents the COX1 production . As a consequence the acids with their enzymes will irritate the tissues leading to ulcers]

Extra Notes : From the doctor
- Penicillin is the first antibiotic discovered
- Statin related to cholestrol and cancer therapy
- Glucofage + Metformin for diabetic and prediabetic patients
  + It is good for people over 45 years
- GLPA related to weight loss ex. Wegovi , Ozempic , etc

- In humans there are 3 forms of the COX , COX1 , COX2 , COX3
  Aspirin prevents both , even though it should prevents only COX2

COX1 → Homeostatic function such as : GI and Renal tracts , platlet aggregation , Macrophages differentiation
COX2 → Inflammation

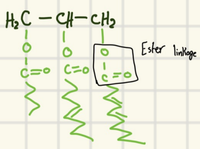
- Aspirin is good but it can cause excessive bleeding especially for elderly
- Celebrex (Celecoxib) → blocks COX2 only, but it can cause heart failure, etc.
- Vioxx was from the same family but it was withdrawn from the market cuz it caused heart failure

- Omega 3 → linolenic acid; → EPA, DHA → reduces inflammatory reaction

- Omega 6 → linoleic acid, Arachidonic
- Omega 9 → Oleic acid → reduces cholestrol in circulation

Triacyglecerol

- Storage lipid consist of glycerol and 3 fatty acids.
- It forms adipose tissue and it is found also in liver



Glycerol + 1 fatty acid = Monoglyceride
Glycerol + 2 fatty acid = Di glyceride
Glycerol + 3 fatty acid = Triglyceride

Simple Triacylglycerol: identical fatty acids
Mixed Triglyceride: different fatty acids

- Vegetable oils consist almost mainly of unsaturated fatty acids → Kinks → low melting point → liquid
- Animal fats have high percentage of saturated fatty acids → Tightly packed → high melting point → solid

Saponification:

- hydrolysis under alkaline condition [Alkaline hydrolysis]
- hydrolysis agents → steam, acid [chemical reagents]; → Enzyme example [lipase of pancereas], [bilogical reagents]
- produces salts of fatty acids, release the glycerol.
- The product [Soup] cause emulsification of oily Materials.

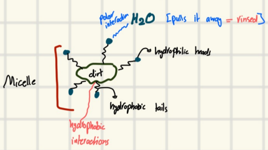
Triacylglycerol [oils] $\xrightarrow[\text{hydrolysis}]{\text{Alkaline}}$ Soup [This rxn is called Saponification]

- we react the oil with strong base (NaOH) to produce $\boxed{RCOONa}$ fatty acid salt

How Soup works?

- Hydrophobic tails clusters together [oriented inside] to create a nonpolar microenvironment and the hydrophilic heads [The COO^- part of the fatty acid] interacts with water.

- The resulting spherical clusters are called Micelles
- Dirt and grease will be trapped in the hydrophobic interaction [micelles] and the whole complex can easily be rinsed away
  [the water pulls away the hydrophilic hea with its micelles together]



Trans Fat

Hydrogenation: C-C double bonds in vegetable oils [unsaturated fats] can be hydrogenated in order to yield saturated fats

alkene $\xrightarrow[Pd]{H_2}$ alkane

- Even though animal fats are unhealthy compared to vegetable oil, but it's healthier than trans fats, they have some benefits → better cooking properties; → better taste

- Companies use method to convert unsaturated vegetable oil to Solid form by Partial hydrogenating them

- Partial hydrogenation converts some of the double bonds, NOT All, to single bonds generating Trans Fats

- Trans Fat is loved by industrial companies for
  - Its appealing taste
  - It has longer shelf life than [cis, or saturated fatty acids]

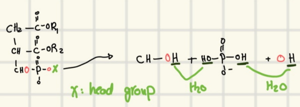
Why is it bad for health → Our body can't handle it cuz it's a foreign molecules and it accumulates in the blood vessels which will cause an elevation risk of the coronary heart diseases.
[It also increases the LDL [bad cholestrol level] and decrease the HDL [Good Cholestrol] level which will lead generally to increase the cholestrol in the blood vessels, furthermore, it will accumulate and leads to many abnormal conditions in the vessels] extra

- Example on Trans Fat : - Margarine
  * only about 2/3 of the C-C double bonds in starting material is hydrogenated.
  * It will be soft in the fridge, and can melt on a warm toast easily.

Membrane lipids

- Membrane lipids
  - → Phospholipids
    - → Glycerophospholipids [Most abundant type]
    - → phospho sphingolipid
  - → Glycolipids
    - → sphingolipids
    - → glyceroglycolipids
  - → Steroids → Cholestrol

- Phosphoacylglycerol

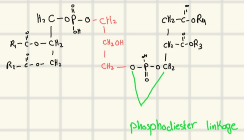


- Head Groups
  - → H → Phosphotidic acid [unprotonated = phosphotidate]
  - → $CH_2-CH_2-N(CH_3)_3$ [Choline] → Phosphotidylcholine [Lecithin]
    - → - Most abudant in Membrane
    - → - Snake's venom has an enzyme called [lecithinase] or [phopholipase A_2] It hydrolyze the [poly unsaturated fatty acids] and it converts Lecithin → Lysolecithin
      Causes hemolysis of RBCs [mainly the membrane of them leading them to die]
  - → $CH_2-CH_2-\overset{+}{N}H_3$ [ethanolamine] → phosphotidylethanolamine
  - → $CH_2-CH(COO^-)-\overset{+}{N}H_3$ [Serine] → Phosphotidyl serine [abundant in the brain]

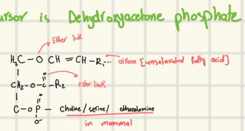
  phosphotidylethanolamine and Phosphotidyl serine → Cephalins

- Lecithin is found in [icecream, chocolate, mayonose, etc..] because It can act as an emulsifying agents ; meaning their amphipathic nature can allow them to surround non polar molecules and Keeps them in suspension in water. [dissolving fats in water]

- Cardiolipins : - It's type of phosphoacylglycerol
  - Found in the inner membrane of mitochondria [crestea]
  - Initially It was isolated from heart muscle [Cardiolipins]
  - Diphosphotidyl - glycerol
  - 4 fatty acids, 3 glycerol, 2 phosphate groups

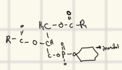


- Plasmologins : - Type of glycerophospholipids
  - Found in cell membrane fraction of
    - → brain, liver
    - → muscle, semen
  - They have protective role against reactive oxygen species
  - Its precursor is Dehydroxyacetone phosphate
  - structure:



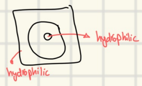
  - Types
    - → Ethanol amine Plasmologin → myelin in nervous tissue
    - → Choline plasmologin → Cardiac tissue [platlet activation factor]
    - → Serine plasmologin

- Phosphotidyl inositol : - Cyclic sugar alcohol [inositol]
  - Source: from the brain
  - Structure: Glycerol, unsaturated F.A , saturated F.A, Phosphoric acid and inositol

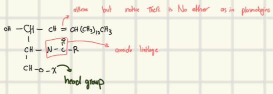


- Function → major component in cell membrane
→ Signalling molecules produced upon hydrolysis [It is broken into active signaling Molecules]

- Structure of Phospholipids
  - → Liposome [used to deliver drugs to the cells, endocytosis]
  - → micelle [as in Soap; emulsification]
  - → bilayer sheet [as in cell membrane]

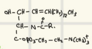


- Sphingolipids : - Found in the plasma membrane of all eukaryotic
  - Is highest in the centeral nervous system
  - The core is the long chain of amino alcohol, sphingosine

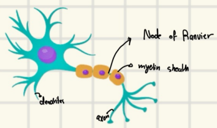


- Types of sphingolipids
  - → Ceramide [the head group would be H]
    - It's the simplest sphingolipid
  - → Sphingomyelin [the head group is phosphocholine]
    - It's the major component of the coating around nerve fiber
      It's hydrophobic to prevent the electrons from escaping
    - The only phosphosphingolipid
  - → Glycosphingolipid [Glycolipids]

- Myelin
  - composed of sphingomyelin



  - Multiple sclerosis; immune cells attack the myelin and damage it.



Glycolipids

- Glycolipids their backbone either
  - → Glycerol → Phosphotidyl-inositol
  - → sphingosine
    - → Cerebroside
    - → Globoside
    - → Ganglioside

    in nervous tissue

- sphingosine can attach carbohydrates on C_1; And they're called Glycolipid
- Glycolipids are in the cell membrane acting as cell surface receptor [Pathogens] and chemical messenger.

- Glycolipids
  - → Cerebroside → simplest glycolipid; one hexose sugar [glucose, galactose] is attached to the sphingosin by O-glycosidic linkage.
    galactocerebroside
  - → Globoside → two or more sugars [glucose, galactose, N-acetylglucosamine]
  - → Ganglioside
    - → three or more sugars including at least One sialic acid [neuraminic acid]
    - → They can bind to cholera toxins in the intestines and it facilitates its endocytosis to the cell [causing excessive diarrhea]

- Sulfatides : - They are synthesized from galactocerebroside with attachment of $[SO_4]^{-2}$ on C_3 [it gives it a -ve charge]
  - abundant in the brain myelin

- Sphingolipids can serve as intercellular communication and as antigenic determinant of the ABO blood groups.

- Some are used as receptors by Viruses' or bacteral toxins.
- The sugar sequence of the ABO antigen can bind to
  - → protein [glycoprotein]
  - → sphingosine [glycolipid, specifically [globoside]

- lipoprotein
  - → large structure, [micelles] having glycerophospholipids and proteins
  - → Function: transport different types of lipids [phospholipid, cholestrol, cholestrol ester, triacylglycerol] in the blood plasma
  - → Types
    - → Chylomicrons
    - → VLDL
    - → LDL
    - → IDL
    - → HDL

* They differ in Density, size, proteins attached to it [affecting its role]

Density depends on **Proteins** / Lipids

Density ↑ size ↓

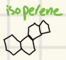
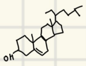
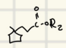
* When consumed fats reaches intestine ; it'll get hydrolyzed and packaged into Chylomicrons. [absorption pathway, exogenous, dietary lipids]
  - As Chylomicrons flow in the blood endothelial enzymes will drag the fatty acids to tissues to be metabolized, an chylomicrons are left carrying Cholestrol to the liver.

Endogenous

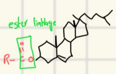
* Liver packages [cholestrol, fatty acids, lipids, etc] in VLDL ; and as it flows in the blood the fatty acids from the triacylglycerol are removed, leaving Cholestrol and increasing the density ↑ [$\frac{\text{protein}}{\text{lipid}\downarrow}$] , so it'll be converted into LDL ; which will deliver Cholestrol from the liver to peripheral tissues.

- Liver also releases HDL ; which transports Cholestrol from the peripheral tissues to the liver

- Liver main function
  - Storing Molecules [glucose, cholestrol, triacylglycero, etc]
  - Detoxification

- Steroids :
  - Its precursor isoperene $CH_2=CH-\overset{CH_3}{\overset{|}{C}}=CH_2$
  - Its nucleus  17 carbons
  - Most common example: Cholestrol
    - structure 
    - 27 carbon, 4 rings < 3 hexo, 1 pento , chemical group
    - amphipathic [OH polar]
    - Cholestrol Test involves
      - LDL (bad cholestrol)
      - HDL [Good Cholestrol]
      - Free cholestrol
    - Products
      - Hormones
        - Estrogen, Progestrone , Estradiol , Progestins , Testosterone [Sex hormones]
        - glucocorticoids ; Cortisol
      - Vitamin D [2extra double bonds at the 2n ring]
      - Bile acids
        - attached R at the 3d ring  and $COOR_2$ at 4th one 
        - intestinal absorption of fat
        - secreted by Galbladder
        - emulsifying agents [cuz they're amphipathic] ; they can surround droplets of fat in a **hydrophilic** environment in intestines
        - People without **Galbladder** can't hydrolyze fats well

- Cholestrol can bind to a fatty acid at [OH on C_3] becoming a Cholestrol ester; it becomes more hydrophobic and it loses its amphipathic feature.



It's a way of **storing** fatty acids.

- Bad Cholestrol LDL can accumulate in the blood vessels causing → narrow blood vessel → closure

Atheroscolorosis

Cell Membrane

- The plasma membrane is called fluid mosaic model
- 45 % lipids, 45% proteins , **10% carbohydrates**
- They exist side by side without forming other intermediate.

- Phospholipids
  - outer layer
    - phosphotidyl choline [lecithin]
    - Glycolipids < cell communication, cell recognition
    - sphongomyelin
  - inner layer
    - phosphotidyl serine
    - phospholidylethanolamine
    - phosphotidyl - inositol [signalling Molecule]

- Cholestrol is found in both layers.
  It is related to mammals (↳ animals) X [prokaryots, plants, etc..]
  It's distirbuted EQUALLY

But **Phospholipid Distribution** isn't uniform since each layer has different types.

- Saturated fatty acids have straight tails allow them to closely packed to each other [rigid membrane]
- Unsaturated fatty acids have Kinks due to the double bonds ; preventing tight packaging + increase Fluidity.

- Cholestrol + cis unsaturated fatty acids prevents tight packing of hydrophobic chains ; let the membrane lipids and proteins to move laterally in the plane of the leaflet → dynamic membrane [for signaling]

- Cholestrol can also stabilize the fluidic membrane by increasing hydrophobic interactions between fatty acids and cholestrol ring structure.

Unsaturated levels differ between nations
- Africa saturated ↑
- Eskimo unsaturated ↑ Their diet depends on fish [omega 3]