LIPID CHEMISTRY

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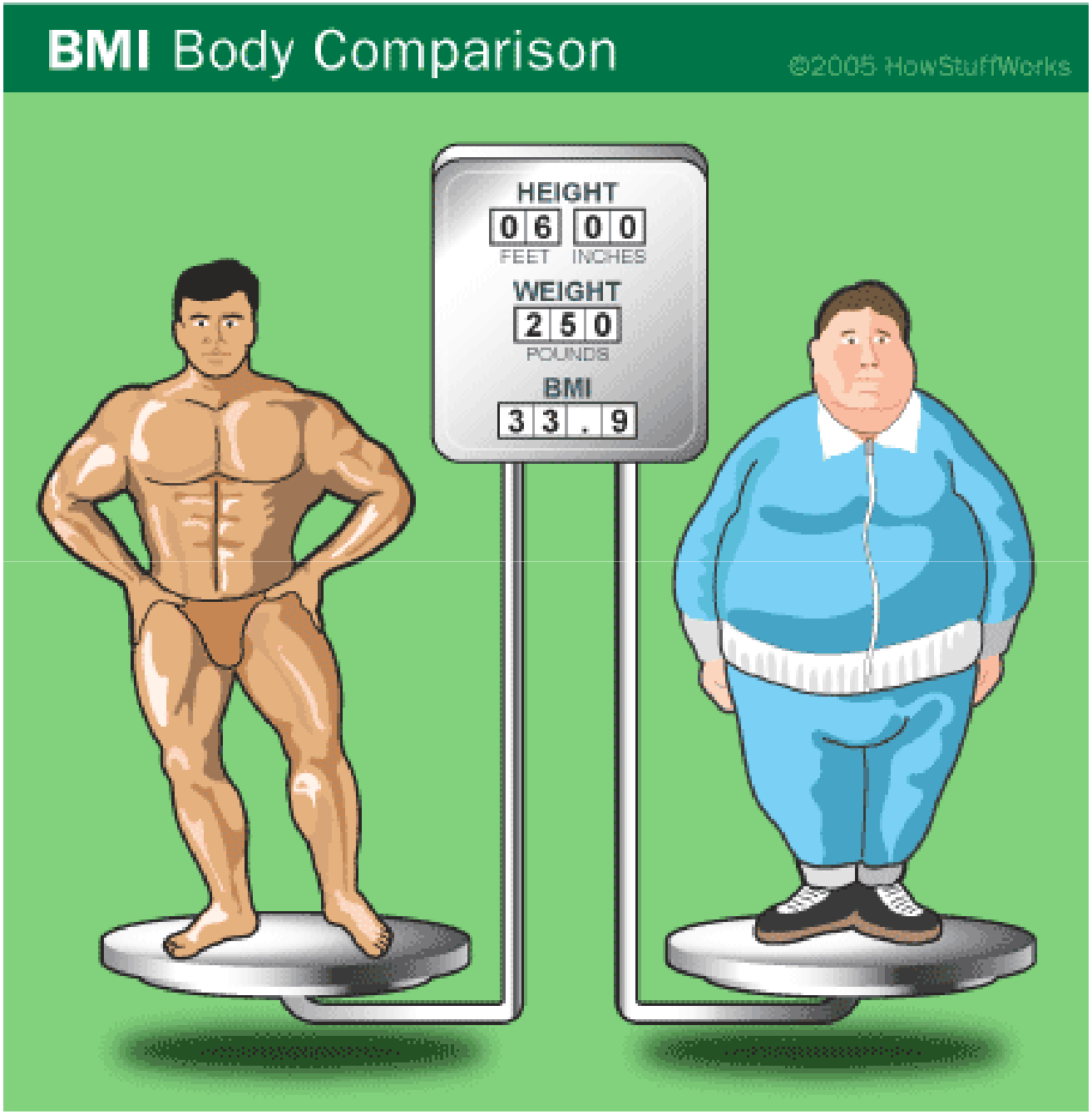
Competency BI4.1

- Describe and discuss main classes of lipids
  - Essential/Non-essential fatty acids
  - Cholesterol and hormonal steroids
  - Triglycerides
  - Major phospholipids and sphingolipids

relevant to human system and their major functions


fotolia
#205093419

WHO CLASSIFICATION OF WEIGHT STATUS	
WEIGHT STATUS	**BODY MASS INDEX (BMI), kg/m^2**
Underweight	<18.5
Normal range	18.5 – 24.9
Overweight	25.0 – 29.9
Obese	≥ 30
Obese class I	30.0 – 34.9
Obese class II	35.0 – 39.9
Obese class III	≥ 40


BMI Body Comparison
©2005 HowStuffWorks
HEIGHT
0 6
FEET
0 0
INCHES
WEIGHT
2 5 0
POUNDS
BMI
3 3 . 9

Clipper Method

What measure require for this transformation ?

- Is fat require in food?
- What type of fat is require?
- Why require?


Del Monte
EXTRA
VIRGIN
OLIVE
OIL


Amul
Pure Ghee


Cod-liver Oil Capsules
Kelp®
BEST CHOICE NUTRITION
PURE VITAMIN RICH
COD-LIVER OIL
VITAMIN A
Contains
VITAMIN D
EPA
DHA
Cod-liver Oil Capsules
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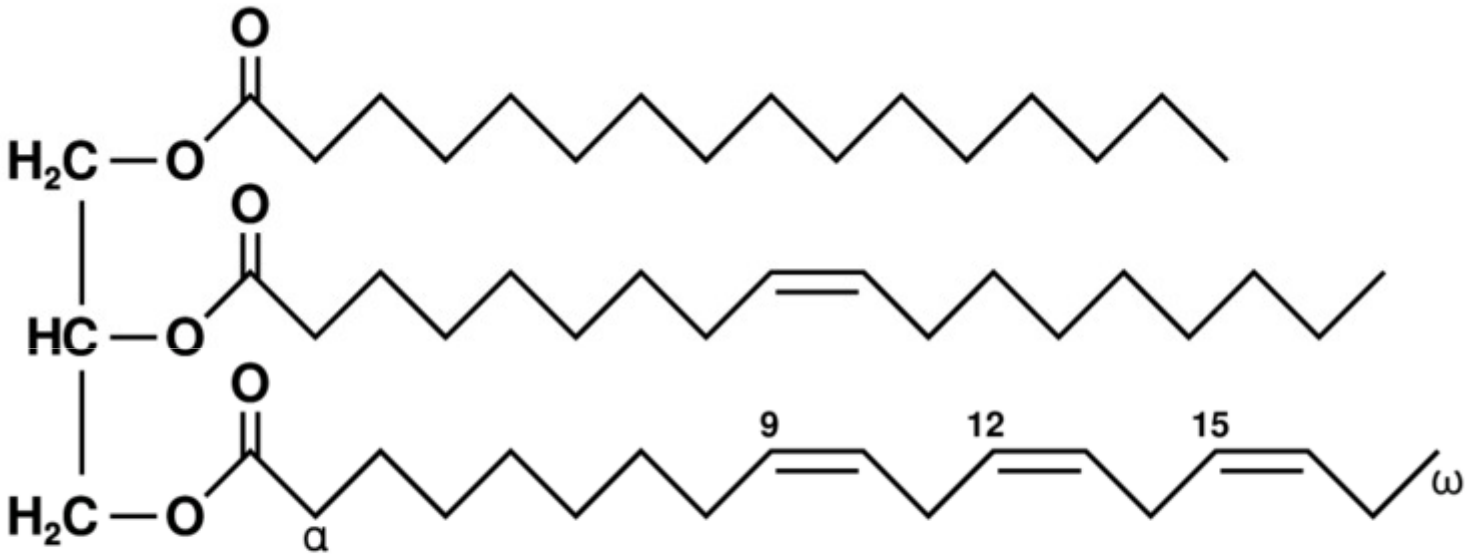
EPA
DHA

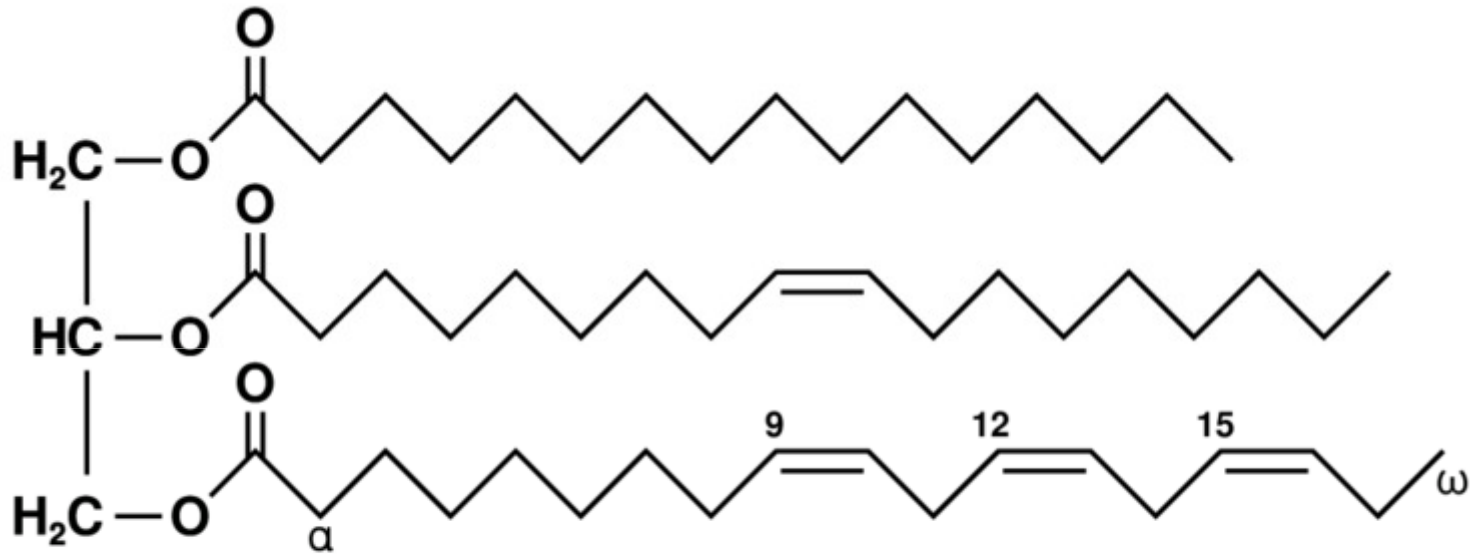
VADA PAV



Glycerol

Fatty Acid

Triglyceride



Glycerol

Fatty Acid

Triglyceride

- Stored mainly in adipocytes.
- A store of energy.
- Protect the internal organs from outside shocks.
- Subcutaneous thermal insulator

Biological Importance of Lipids:

1. More palatable food
2. Storable to unlimited amount compared to carbohydrates.
3. High-energy value
4. Supply **Essential fatty acids**.
5. Supply **fat-soluble vitamins** (A, D, E and K).
6. Important constituents of the nervous system.
7. Constituent of cell membrane and nervous system.
8. Cholesterol
    1. In membrane structure
    2. Synthesis of some hormones
    3. Synthesis of vitamin D3 and bile acids.

Classification of Lipid

I- Simple lipids:

Fatty acids + Alcohol.

Classified according to the alcohol present into:

Neutral fats:

Fatty acids + **Glycerol**

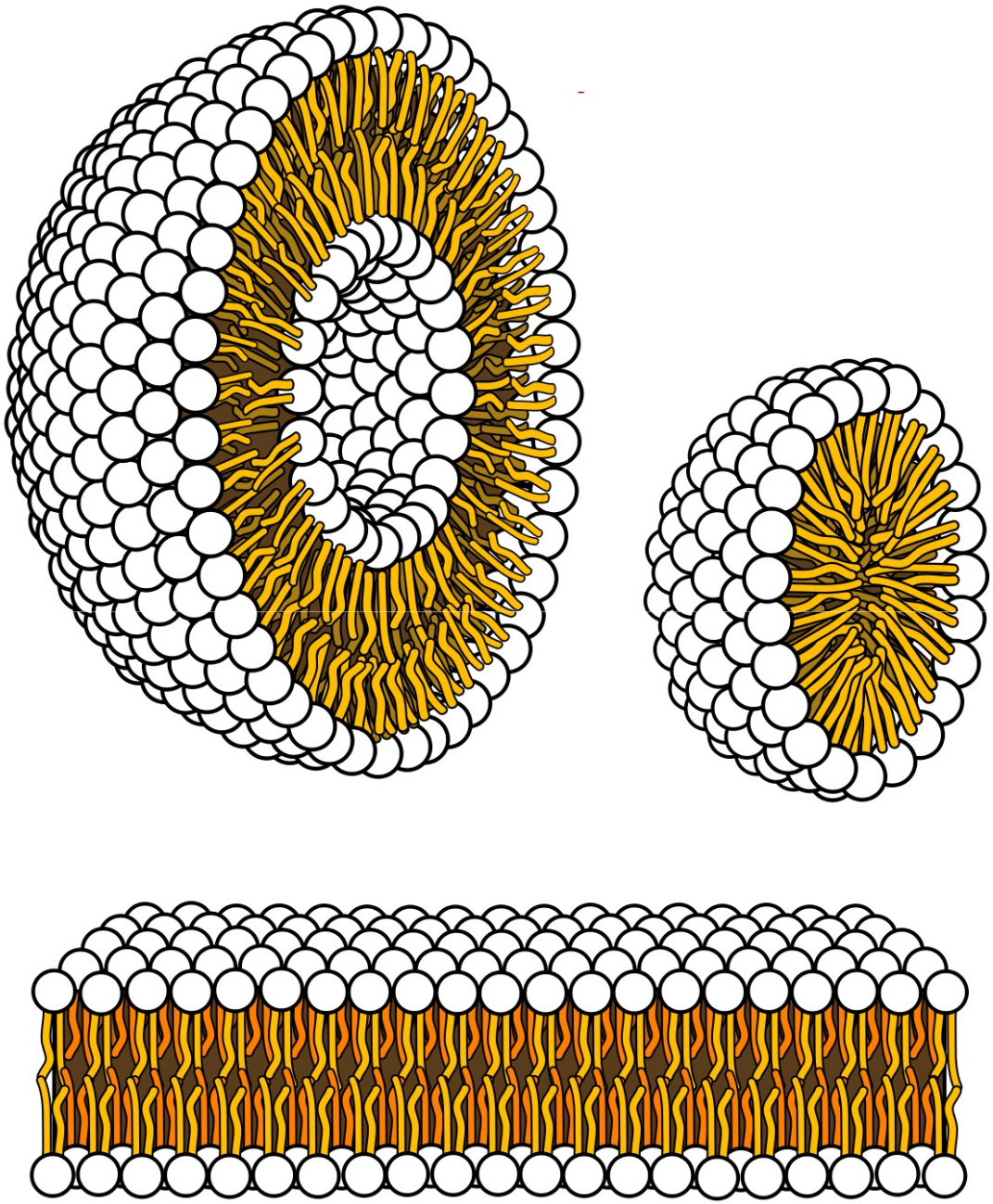
e.g. Triacylglycerols - Triglycerides

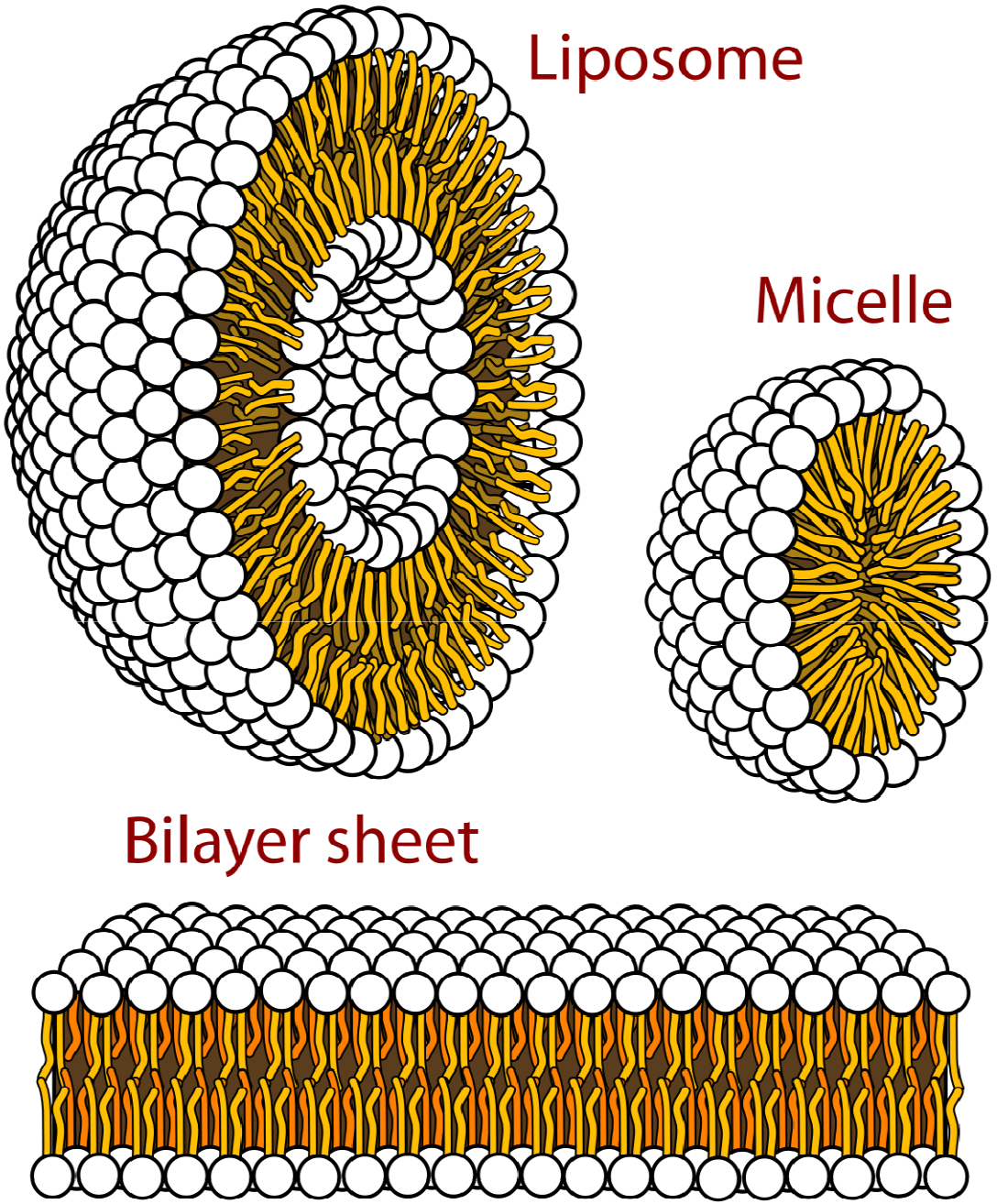
Waxes:

Fatty acids + **long-chain alcohols** other than glycerol.

e.g. Waxe

Grooming




Liposome
Micelle
Bilayer sheet

II- Compound or conjugated lipids

Fatty acids + alcohols + other groups .

1. **Phospholipids (phosphatides):**

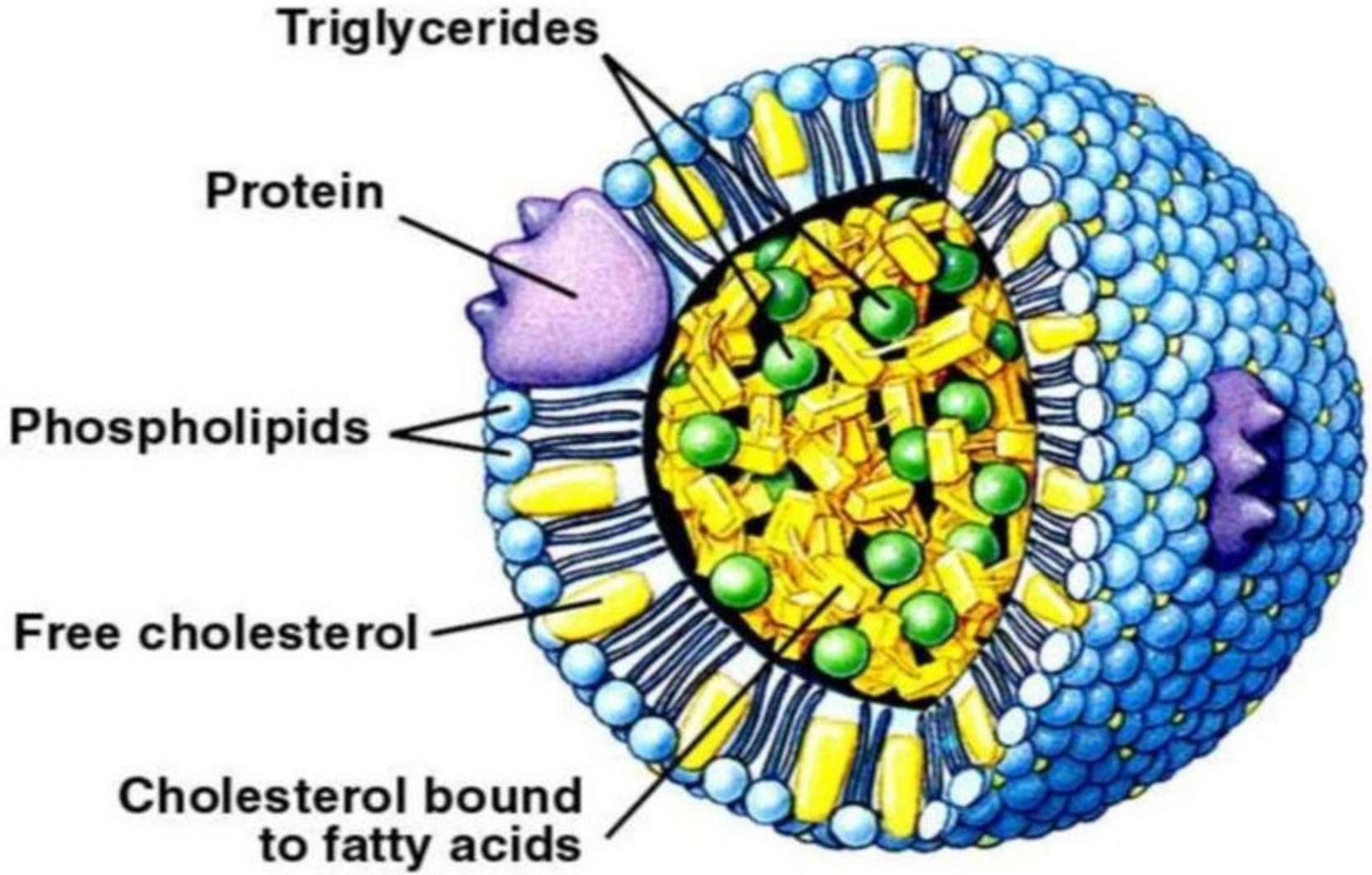
   FA + Alcohol + Phosphoric acid + Nitrogenous base

   1. Cephaline (Ethalonamine)
   2. Lecithine (Choline)
   3. Phosphotidylserine (Serine)

2. **Glycolipids:**

   Carbohydrate + Sphingosine

   (No Phosphoric acid No Glycerol)


Triglycerides
Protein
Phospholipids
Free cholesterol
Cholesterol bound
to fatty acids

3. **Lipoproteins:**

   Lipid part + Proteins

4. **Other compound lipids:** include:

   I. **Sulfolipids:** containing sulfur.

   II. **Aminolipids:** containing amino acids.

III- Derived Lipids:

Products of hydrolysis of simple and compound lipids and/or their derivatives

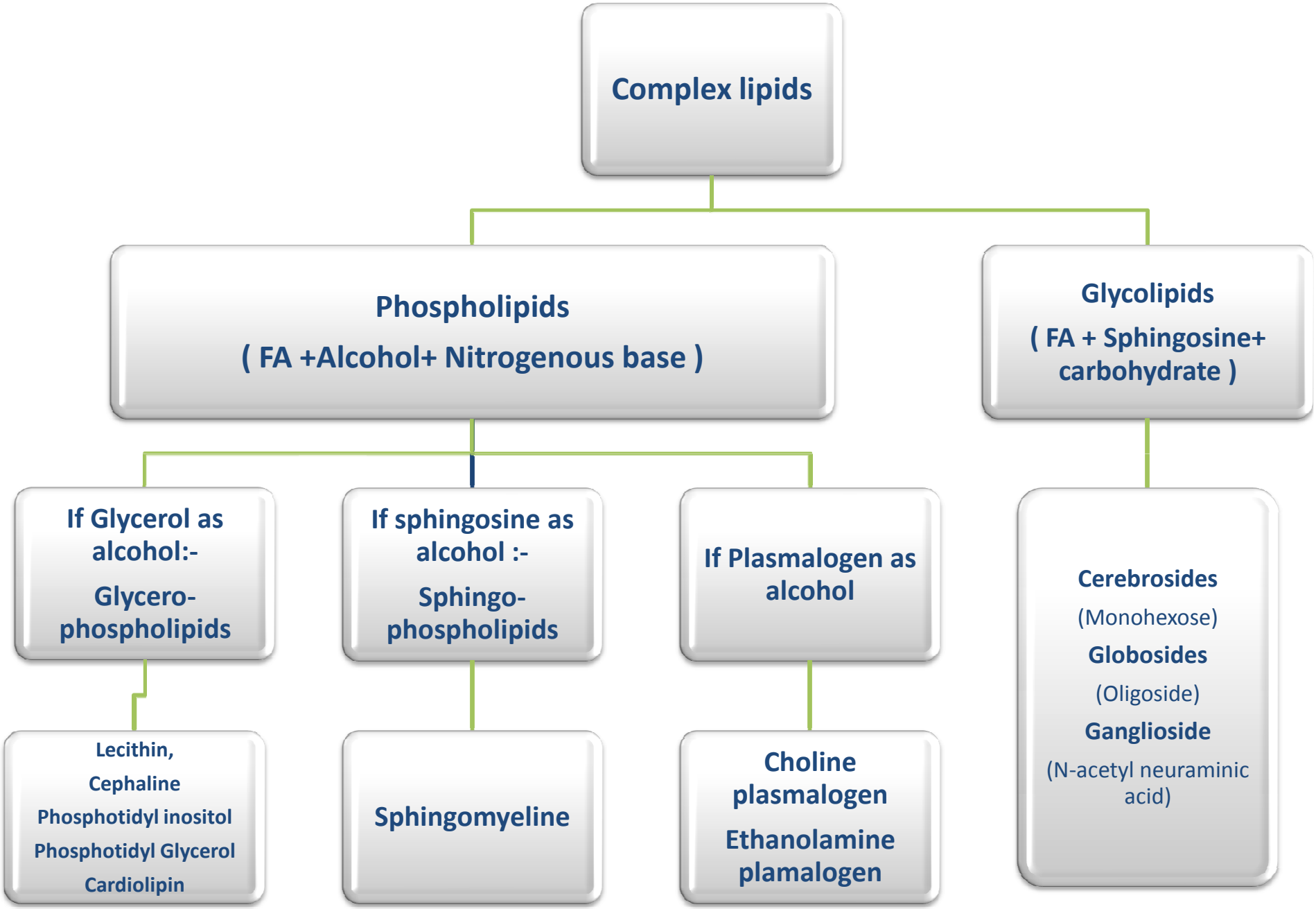
1. Fatty acids, Monoglycerides and aldehydes.
2. Alcohols including glycerol.
3. Sterols, steroids and hormonal derivatives of vit. D.
4. Eicosanoids
   Prostaglandins - Leukotrienes - Thromboxanes
5. Ketone bodies.

IV- Lipid-associating substances:

Fat-soluble vitamins (E and K)

Carotenoids

Squalene

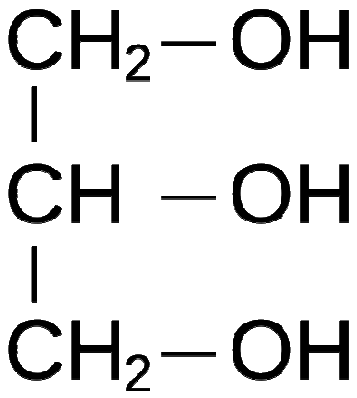

Complex lipids
Phospholipids
(FA +Alcohol+ Nitrogenous base)
Glycolipids
(FA + Sphingosine+ carbohydrate)
If Glycerol as alcohol:-
Glycero-phospholipids
If sphingosine as alcohol :-
Sphingo-phospholipids
If Plasmalogen as alcohol
Cerebrosides
(Monohexose)
Globosides
(Oligoside)
Ganglioside
(N-acetyl neuraminic acid)
Lecithin,
Cephaline
Phosphotidyl inositol
Phosphotidyl Glycerol
Cardiolipin
Sphingomyeline
Choline plasmalogen
Ethanolamine plamalogen

Alcohols

Include: Glycerol, Cholesterol, higher alcohols etc.

1. Glycerol:

Structure:



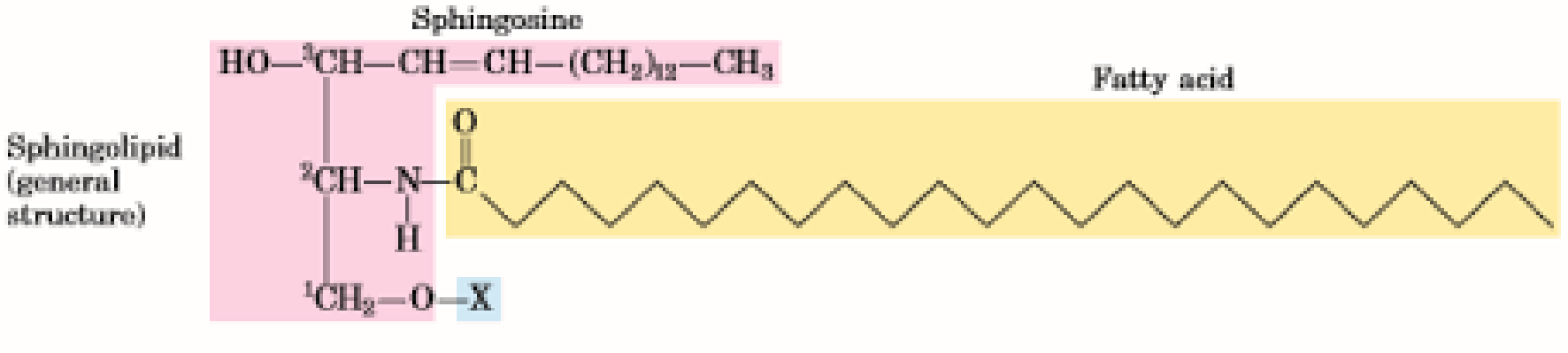
Properties:

- Colorless & Viscous oily
- Sweet taste.
- Soluble in water and alcohols
- Monoglyceride or monoacyl-glycerol= glycerol + 1 fatty acid .
- Diglyceride or diacyl-glycerol= glycero+ 2 fatty acids.
- Triglyceride or triacyl-glycerol = glycerol + 3 fatty acids.

Uses of Glycerol:

I. Glycerol enters in pharmaceutical and cosmetic preparations (hygroscopic).
II. Glycerol is used in treatment of glaucoma (increased intraocular pressure).

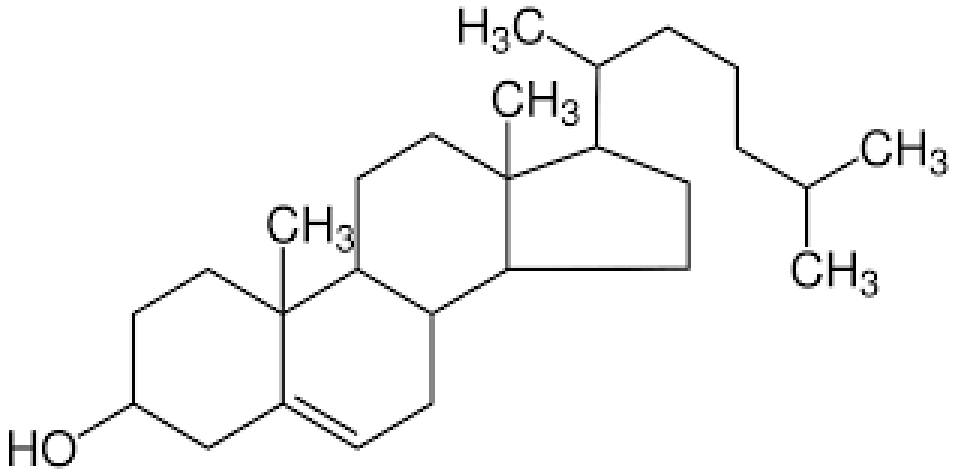
2- Sphingosine:



Importance:

- Sphingomyelin
- Glyco-lipids
- **Ceramide (Spingosine + FA)**

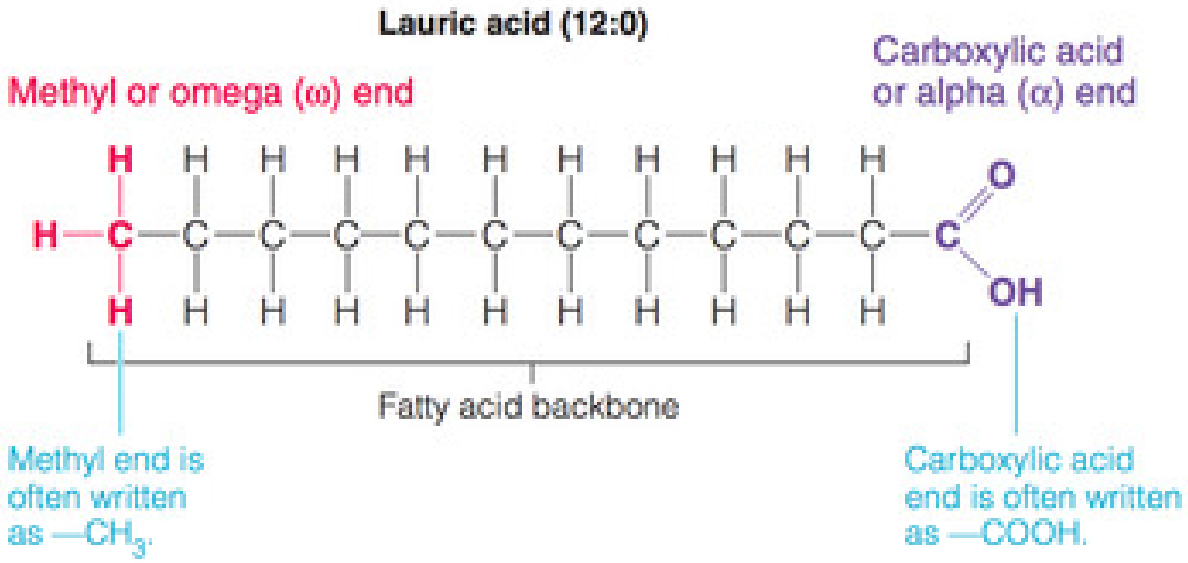
3- Cholesterol



Importance: It enter in the structure of :

- Steroid Vitamins e.g. Vitamin D
- Steroid Hormones: e.g male and female sex hormones and corticosteroids
- For synthesis of Bile salts which have important role in digestion and absorption of lipids.

Fatty Acids



Classification:

Fatty acids can be classified as follows:

I) **Saturated,**

No double bonds

2-24 or more carbons.

$C_nH_{2n+1}COOH$.

Saturated Fatty Acids They are classified into:

A- Short chain:

2-6 carbon atoms

Examples: acetic, butyric, caproic acids.

B- Medium-chain fatty acids :

8 – 14 carbon atoms

Examples: Lauric acid

C- Long-chain fatty acids:

16 or more carbon atoms

Examples:

16 C Palmitic acid CH3-(CH2)14-COOH

18 C Stearic acid CH3-(CH2)16-COOH

II) Unsaturated,: They contain one or more double bonds

a) Monounsaturated, $C_nH_{2n-1}COOH$

Examples:

- **Palmitoleic acid:** $CH_3\text{-}(CH_2)_5\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}COOH$
- **Oleic acid:** $CH_3\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}COOH$
- **Nervonic acid:** $CH_3\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}(CH_2)_{13}\text{-}COOH$

b) Polyunsaturated, (Essential fatty acids)

contain more than 1 double bond

Essential fatty acid due to the following:

- Can not be synthesized in the human body
- Due to lack of enzymes

Essential Fatty Acid

- **Linoleic: C18:2$\Delta^{9,12}$ (ω6)**

CH3-(CH2)4-CH=CH-CH2-CH=CH-(CH2)7-COOH

- **Linolenic: C18:3$\Delta^{9,12,15}$ (ω3)**

CH3-CH2-CH=CH-CH2-CH=CH-CH2-CH=CH-(CH2)7-COOH

- **Arachidonic acid: C20:4$\Delta^{5,8,11,14}$ (ω6)**

CH3-(CH2)4-CH=CH-CH2-CH=CH-CH2-CH=CH-CH2-CH=CH-(CH2)3-COOH

- Linoleic acid and Linolenic acid are PUFA
- Linoleic acid – 2 double bond
- Linolenic acid – 3 double bond
- Humans have carbon 9, 6, 5 and 4 desaturases,
- Can convert in saturated fatty acid it into unsaturated fatty acid.
- Lack to introduce double bonds after 10th carbon from carboxyl ,towards the ω-end (methyl end) of the chain.
- Linoleic acid is the precursor of arachidonic acid for formation of prostaglandin , leukotrienes and thromboxone synthesis (Eicosanoids synthesis).

Functions:

- Prostaglandin & eicosanoids are synthesized
- Neurotrasmittter
- Useful to prevent atherosclerosis.
- Participate in structure of all cellular and subcellular membranes.
- Essential for skin integrity, normal growth and reproduction.
- Important role in blood clotting.
- They can be oxidized for energy production.

III- Hydroxy fatty acids

-They contain one or more hydroxyl groups,

Examples:

•Oxynervonic (24:1Δ^{15}, hydroxy at C_2),

•Crebronic (24: hydroxy at C_2)

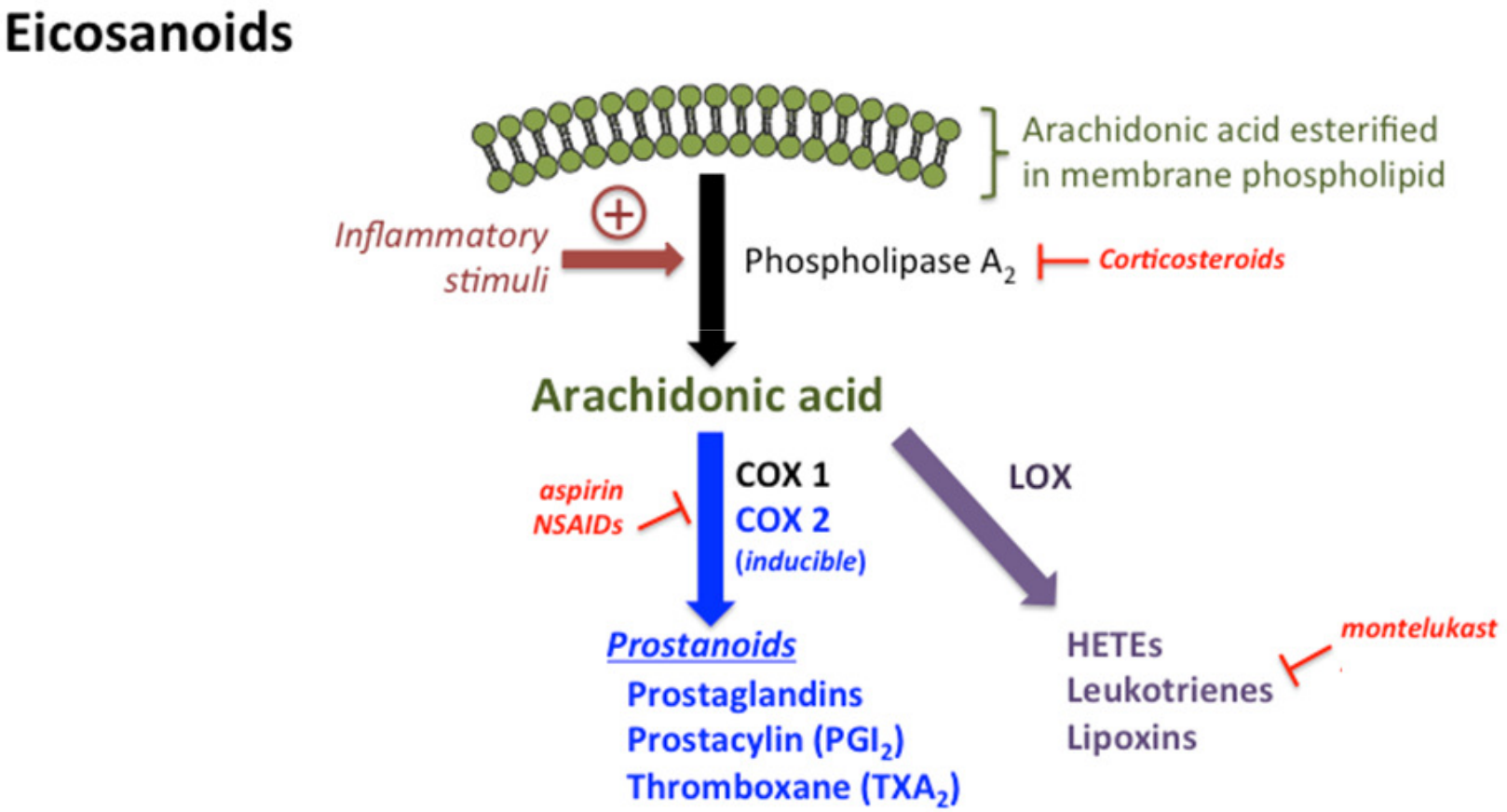
IV- Branched chain fatty acids:

There are fatty acids with branched chains

Examples:

• **Phytanic acid** that is a by-product of chlorophyll catabolism in human and animal that is present in butter. If it is not oxidized in the body it will be toxic.

Eicosanoid


Eicosanoids
Arachidonic acid esterified in membrane phospholipid
Inflammatory stimuli
Phospholipase A2
Corticosteroids
Arachidonic acid
aspirin NSAIDs
COX 1
COX 2
(inducible)
LOX
Prostanoids
Prostaglandins
Prostacylin (PGI2)
Thromboxane (TXA2)
HETEs
Leukotrienes
Lipoxins
montelukast

Cyclo-oxygenase (COX)

COX-1

- Found in the kidney, stomach and platelets.
- Play physiological role
- Protection of gastric mucosa
- Decrease gastric acid secretion
- Maintain normal functions of the kidney through prostaglandins.

COX-2

- located in macrophages, leukocytes and fibroblasts.
- **Induce** from inflammatory mediator = Synthesis prostaglandins
- Responsible for pain and inflammation.

Eicosanoid & NSAID

- Aspirin (NSAID) ,non-selectively inhibit COX enzyme.
- Inhibit both COX-1 & COX-2
- Decrease Prostaglanding = Reduce inflammation
- Decrease Thromboxone = Reduce platelet aggregation.
- Because of COX-2 inhibition=Anti-inflammatory effect occur
- Because of COX-1 inhibition = Anti-platelet effect occur
- Simultaneously , because of COX-1 inhibition ,
  - Decrease protection to gastric mucosa
  - Increase gastric acid secretion.
  - Increase chances of peptic ulcer.

Eicosanoid & NSAID

- **For Anti-inflammatory action**
- Aspirin inhibit COX-2 enzyme of endothelial cell.
- Endothelial cell has short life span of 1 day.
- In Short time = New Endothelial cell synthesis
  = New COX enzyme.
- Newly synthesized cell & COX enzyme
  = Over come the inhibition of aspirin.
- So Anti inflammatory action remain for short period.

- **Endothelial cell has nucleus, does it make any difference in action ???????**

Eicosanoid & NSAID

- **For Antiplatelet action**
- Aspirin act on platelet cell's COX-1 enzyme .
- Platelet cell has life span of 5-7 days.
- Inhibition of COX enzyme remains for longer time compare to endothelial cell
- Anti-platelet action remains for long time.

- **Platelet does not have nucleus, does it make any difference in action ???????**

Question to Face

- Anti inflammatory action of aspirin is reversible , but anti platelet action is irreversible
- The inhibition of COX-1 can be overcome in endothelial cells but not in platelets while patient is taking low dose aspirin.
- Aspirin has short anti-inflammatory action while longer anti-platelet action.
- When high dose of aspirin (NSAID) is use as anti-inflammatory, most commonly , it cause peptic ulcer.

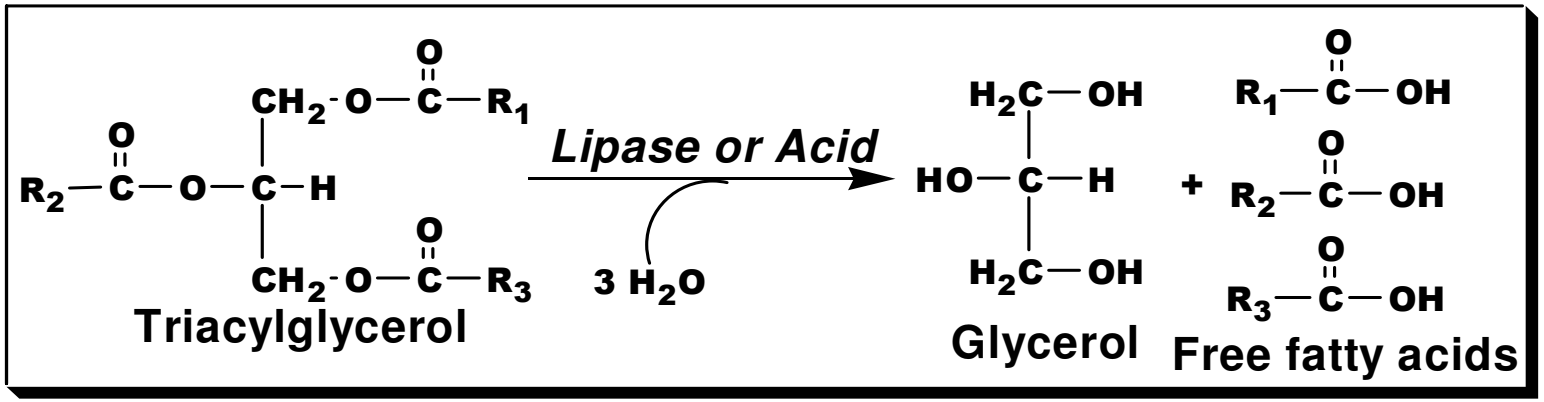
Physical Properties of fatty acids

- Nonpolar = Poor solubility in water
- Melting points of FAs is depend on
  - Length of Fatty acid chain
  - Degree of unsaturation
- **Melting Point increase with Length**
- **Melting Point decrease with Unsaturation**

Chemical Properties of fats and oils:

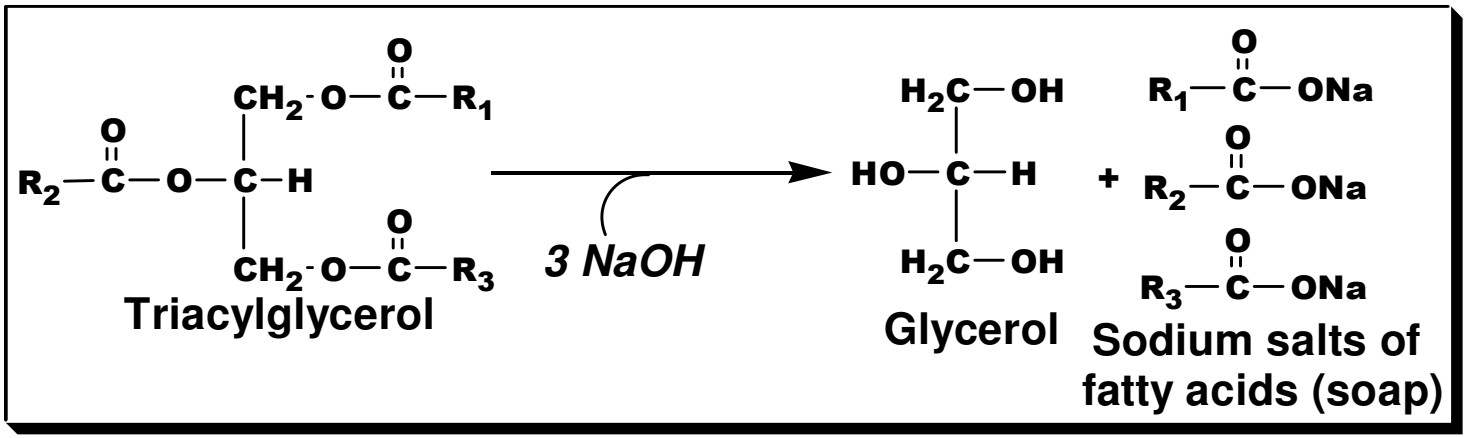
1- Hydrolysis:

1- Enzymatic and acid hydrolysis = Lipase



2- Alkaline hydrolysis =glycerol + salts of fatty acids (**soap**).

saponification.



Types of Soaps:

1. Hard soap = Saponification of neutral fats by NaOH.
2. Soft soap = Potassium soap.
3. Insoluble soap is Calcium and magnesium soaps

Saponification number (or value):

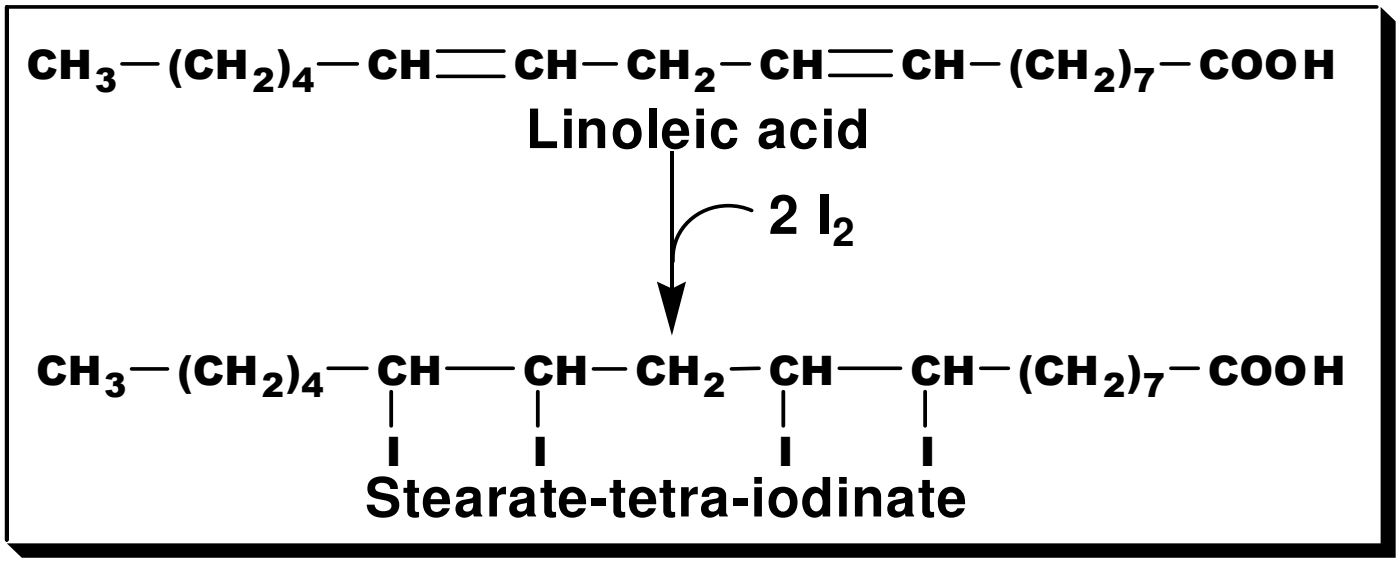
Definition:

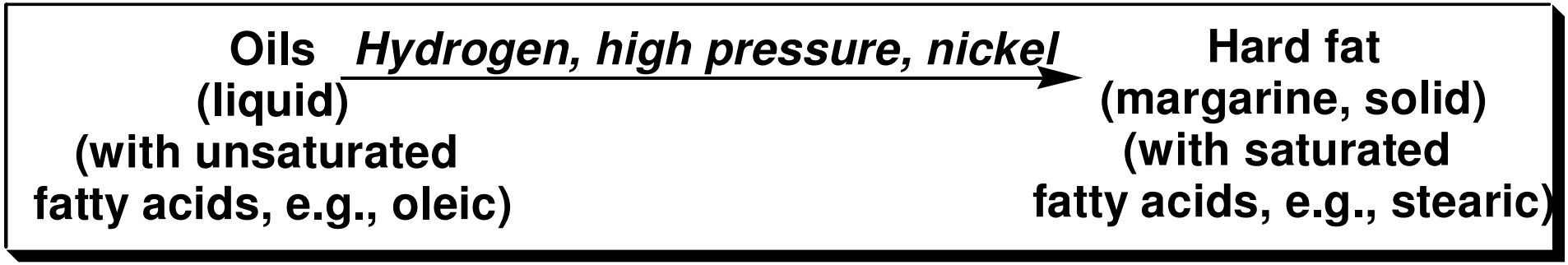
Number of milligrams of KOH required to completely saponify one gram of fat.

2. Halogenation:

Iodine Number = number of gram of iodine absorbed by 100 grams of fat.

Addition of halogens (e.g., hydrogen or iodine)
In unsaturated fatty acids at the double bonds.
Important determine the degree of unsaturation




Oils
(liquid)
(with unsaturated
fatty acids, e.g., oleic)
Hydrogen, high pressure, nickel
Hard fat
(margarine, solid)
(with saturated
fatty acids, e.g., stearic)

Rancidity

Definition:

- Physico-chemical change in the fat
- Leading to the development of
  - ✓ Unpleasant odour
  - ✓ Unpleasant taste or
  - ✓ Abnormal color
- Because of
  - ✓ Exposure to atmospheric oxygen
  - ✓ Light
  - ✓ Moisture
  - ✓ Bacterial or fungal contamination
  - ✓ Heat.

Types and causes of Rancidity:

1. Hydrolytic rancidity
2. Oxidative rancidity
3. Ketonic rancidity

1 Hydrolytic rancidity:

- Occur due ti bacterial lipase
- Occur at high temperature and moisture.
- Liberation of free fatty acids and glycerol

2 Oxidative Rancidity:

- Catalyzed by exposure to oxygen, light ,heat
- Producing peroxide derivatives
- E.g. peroxides, aldehydes, ketones & dicarboxylic acids
- That are toxic and have bad odor.

3 Ketonic Rancidity:

- Due to the contamination with fungi
- Moisture accelerates ketonic rancidity.
- Ketones ,fatty aldehydes and fatty alcohols are formed.

Prevention of rancidity is achieved by:

1. Avoidance of the causes
   - Exposure to light, oxygen, moisture, high temperature and bacteria or fungal contamination.
2. Keeping fats in well-closed containers in cold, dark and dry place.
3. Addition of anti-oxidants.
   - Vitamin E

Hazards of Rancid Fats:

1. Can causes food poisoning and cancer.
2. Destroys the fat-soluble vitamins
   - (vitamins A, D, K and E).
3. Destroys the polyunsaturated essential fatty acids.
   - Convert Cis toTrans form
4. Economical loss
   - Because it is unfit to eat.

Waxes

- Containing a Long Chain Alcohol (with a higher molecular weight than glycerol)
- E.g. Palmitoyl alcohol, cholesterol, vitamin A or D.
- Esterified to long-chain fatty acids.
- Properties of waxes:
  - Waxes are insoluble in water
  - soluble in fat solvents
- Not easily hydrolyzed
- Not digestible by lipases.
- Very resistant to rancidity.
- No nutritional value.

Compound Lipids

1. Phospholipids
2. Glycolipids.
3. Lipoproteins
4. Sulfolipids
5. Amino lipids.

Phospholipids

Importance:

1. Cells and subcellular organelles membrane
2. Transfer of substances through membranes is controlled by properties of phospholipids.
3. Important components of the lipoprotein
4. They are lipotropic agents that prevent fatty liver.
5. Myelin sheath of nerves is rich with phospholipids.
6. Important in digestion and absorption of lipids and excretion of cholesterol in the bile.
7. Important in blood clotting and platelet aggregation.
8. Provide lung surfactants & prevent its collapse.
9. Important role in signal transduction across the cell membrane.
10. They are source of polyunsaturated fatty acids for synthesis of eicosanoids.

Classification of Phospholipids

A-**Glycerophospholipids:** **They are regarded as derivatives of phosphatidic acids that are the simplest type of phospholipids and include:**

1. **Phosphatidic acids.**
2. **Lecithins**
3. **Cephalins.**
4. **Plasmalogens.**
5. **Inositides.**
6. **Cardiolipin.**

B-Sphingophospholipids:

1. **Sphingomyelins**

Snake Venom Poisoning (Snake Bite)

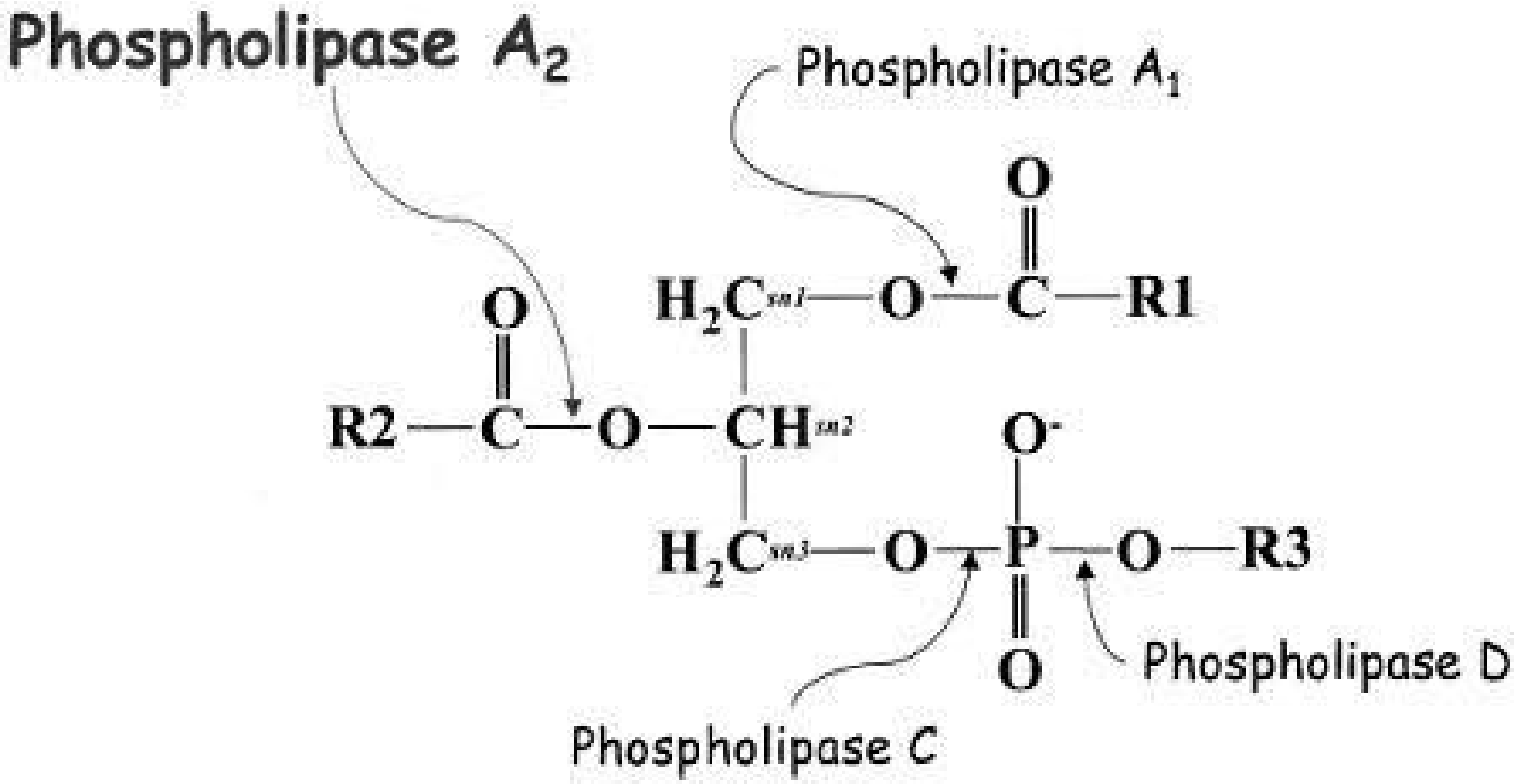
With Lipid

With Enzyme

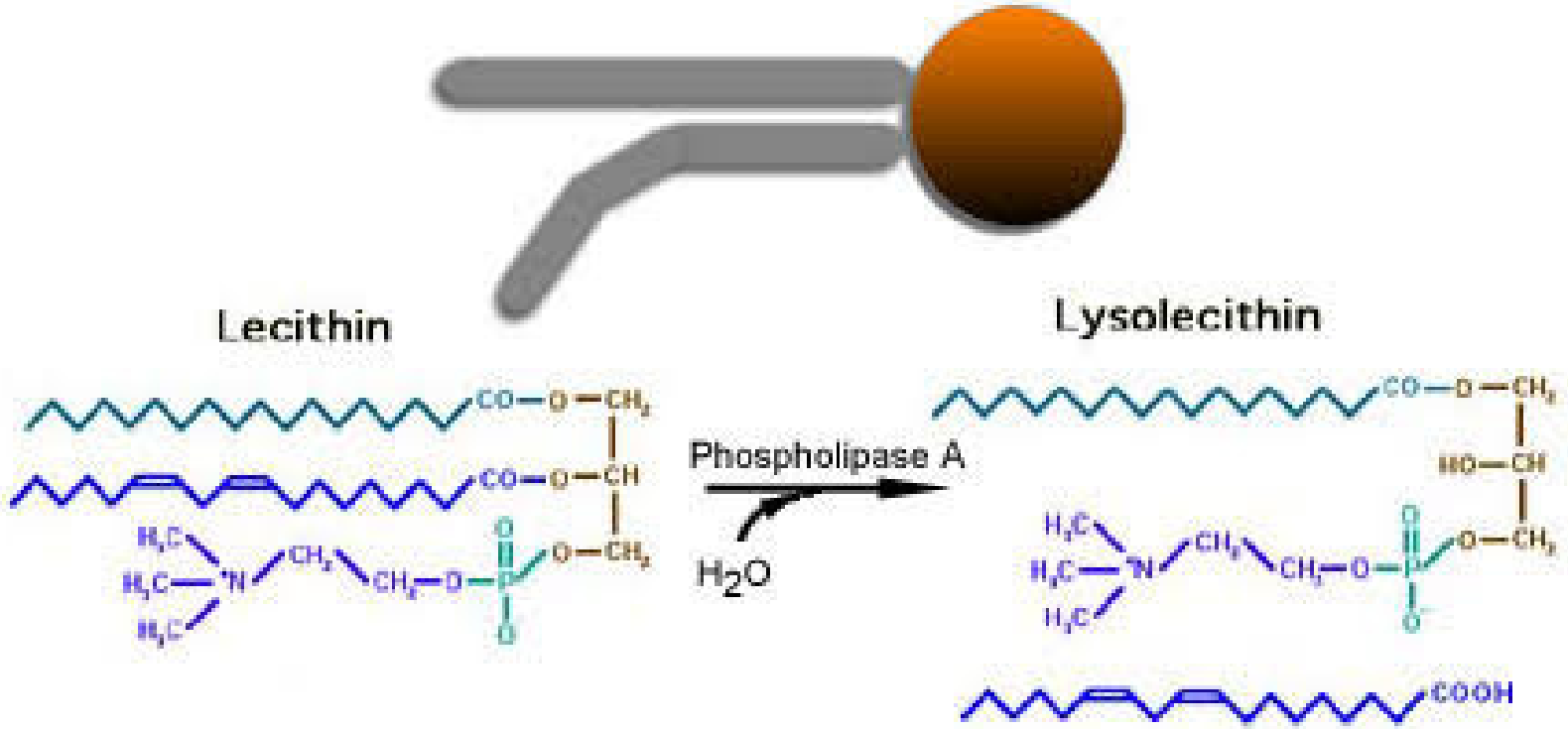
Snake Venom

- **Hydrolytic enzymes**
  - All Digestive hydrolases
    - Amylase , Lipase , Hyalunonidase , Collagenase
  - Phospholipases
  - Thrombin-like pro-coagulant
  - Kallikrein-like serine proteases
- **Neuro toxins** = Ach receptors at neuromuscular junctions.
  - α-Bungarotoxin
  - α-Cobratoxin
- **Phosphodiesterases** = lower the blood pressure.
- **Phospholipase A2**
  - causes hemolysis by lysing the phospholipid cell membranes of red blood cells
- **Fasciculins** - inhibit Ach-esterase

Phospholipase

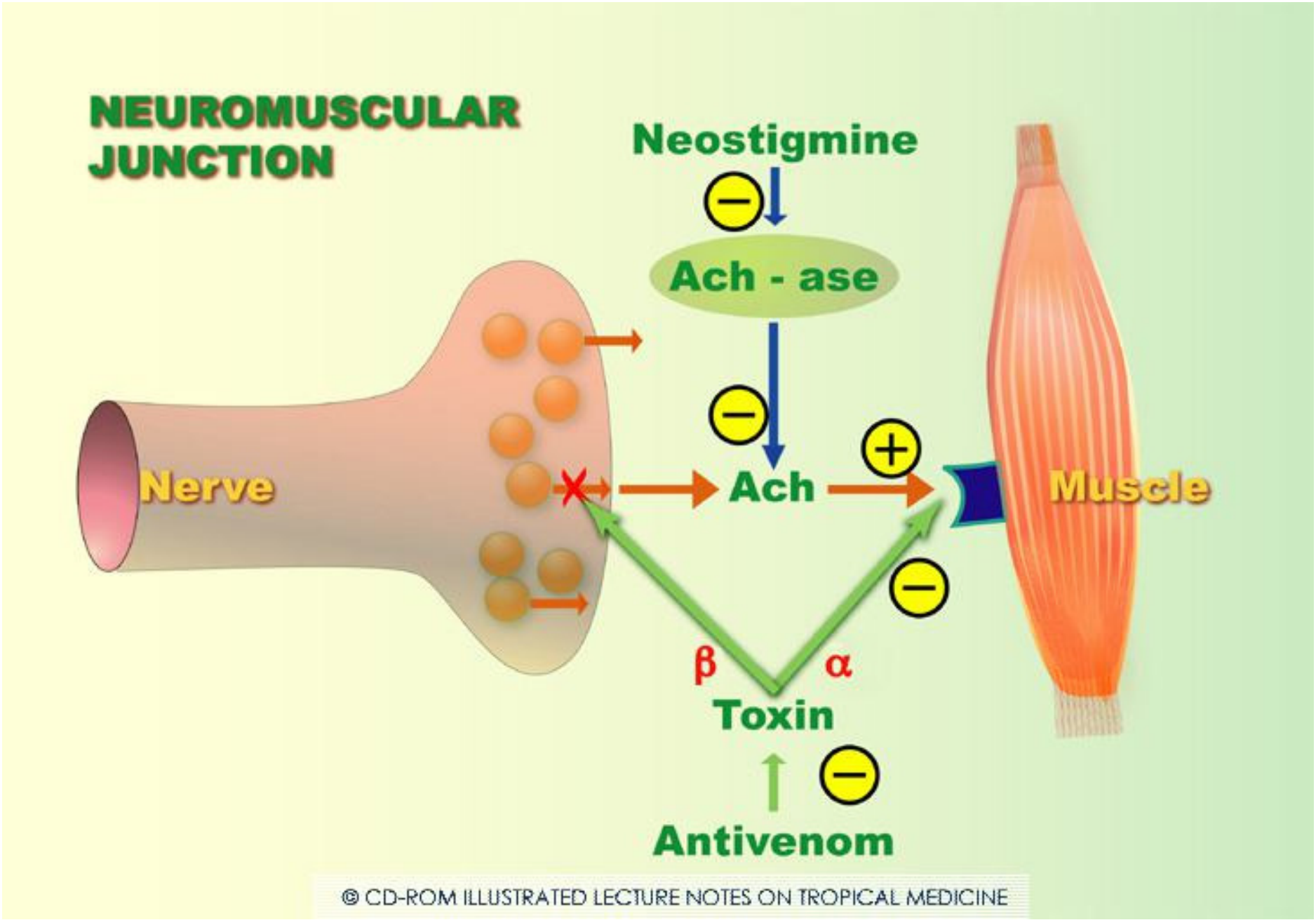


Phospholipase A2 Act on “Lecithine”



Snake bite causes severe hemolysis

- Snake venom contains hydrolase type of enzyme called phospholipase A2 (Lecithinase)
- Phospollipase A2 causes lysis of lecithine (phospholipid) of the cell memebrane of RBC.
- Phospholipid (of cell membrane)→ Lysolecithin + Fattyacid.
- This Lysolecithin work like surfactant.
- So RBC are damaged and leading to severe hemolysis of RBC.


NEUROMUSCULAR JUNCTION
Neostigmine
Ach - ase
Nerve
Ach
Muscle
β
α
Toxin
Antivenom
© CD-ROM ILLUSTRATED LECTURE NOTES ON TROPICAL MEDICINE

Investigation in Snake Bite

- To know effect on Coagulation
- To know effect of Neurotoxicity

Investigation in Snake Bite

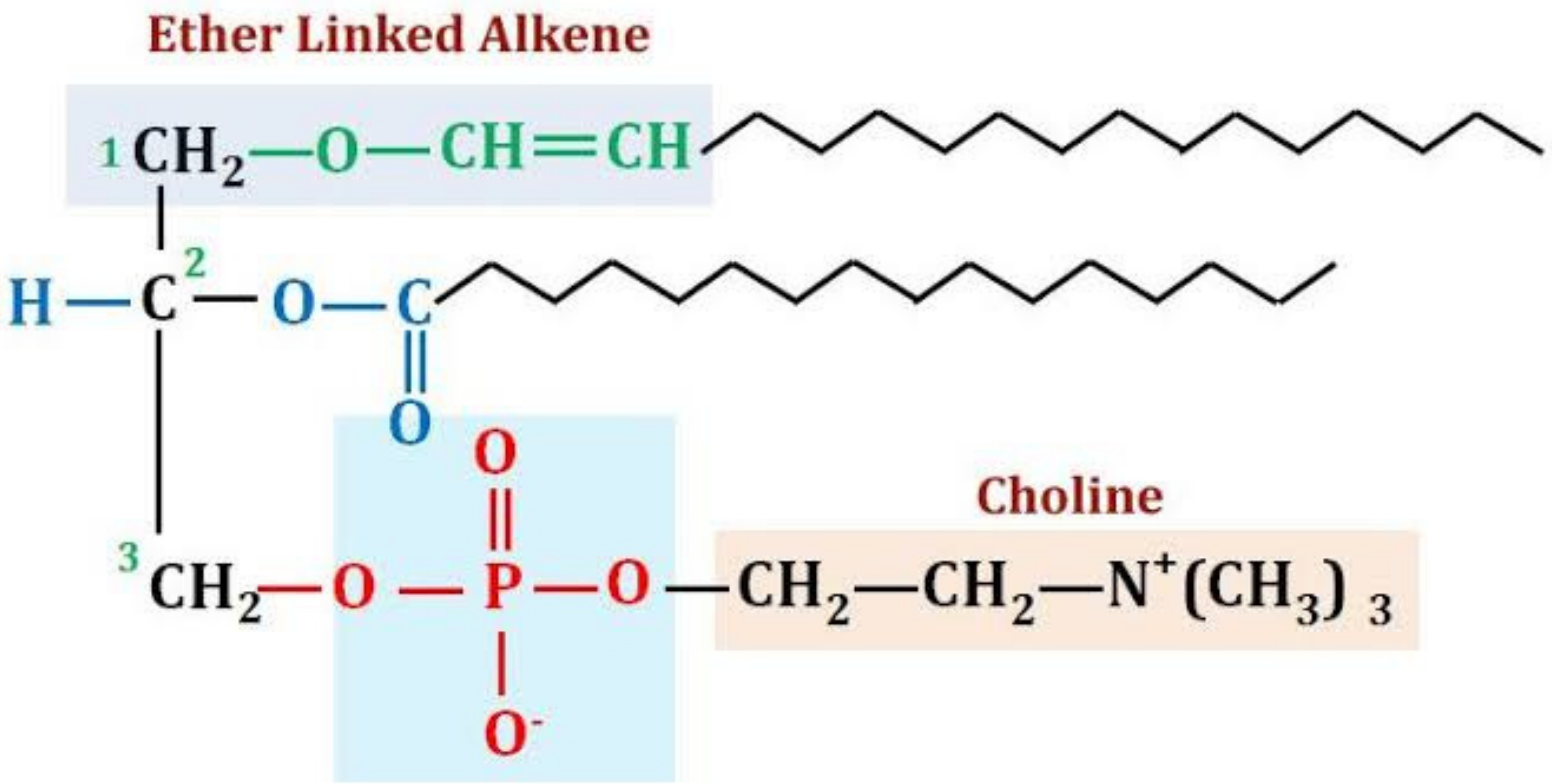
- To know effect on Coagulation
  - Bleeding time
  - Clotting time
- To know effect of Neurotoxicity
  - Acetyl-cholinesterase
  - Pseudoacetyl-cholinesterase ????????

Where is lipid here?

Phospholipid as Lung surfactant

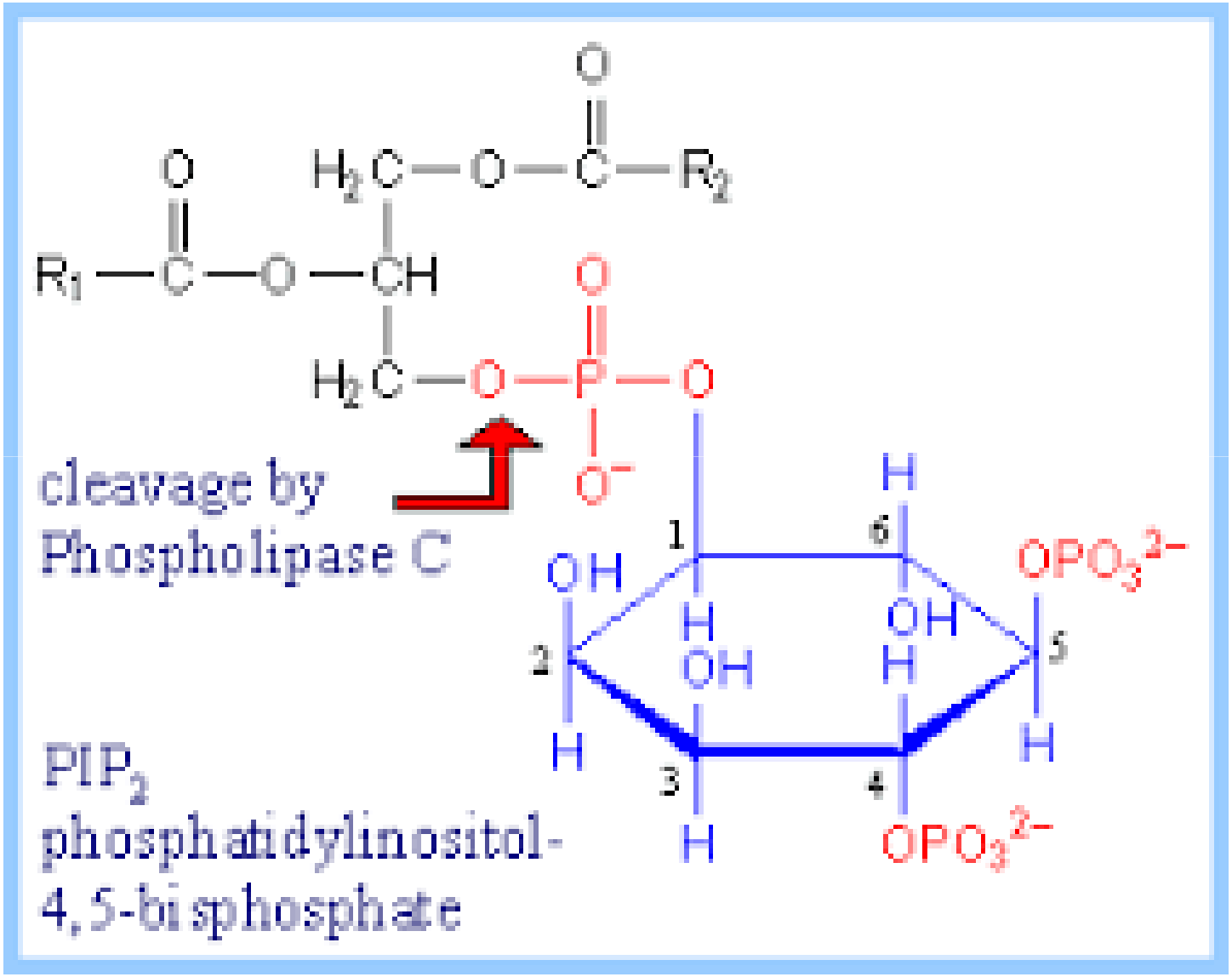
- Following are Lung surfactant
  - Dipalmitoyl-lecithin
  - Sphingomyelin
  - Apoproteins called apoprotein A, B, C, and D.
- It is produced by alveolar cells.
- It lowers alveolar surface tension and improves gas exchange besides activating macrophages to kill pathogens.
- It prevent collapse of the alveoli.
- In premature babies, this surfactant is deficient and they suffer from Respiratory Distress Syndrome.
- Glucocorticoids increase the synthesis of the surfactant complex and promote differentiation of lung cells.

Plasmalogen

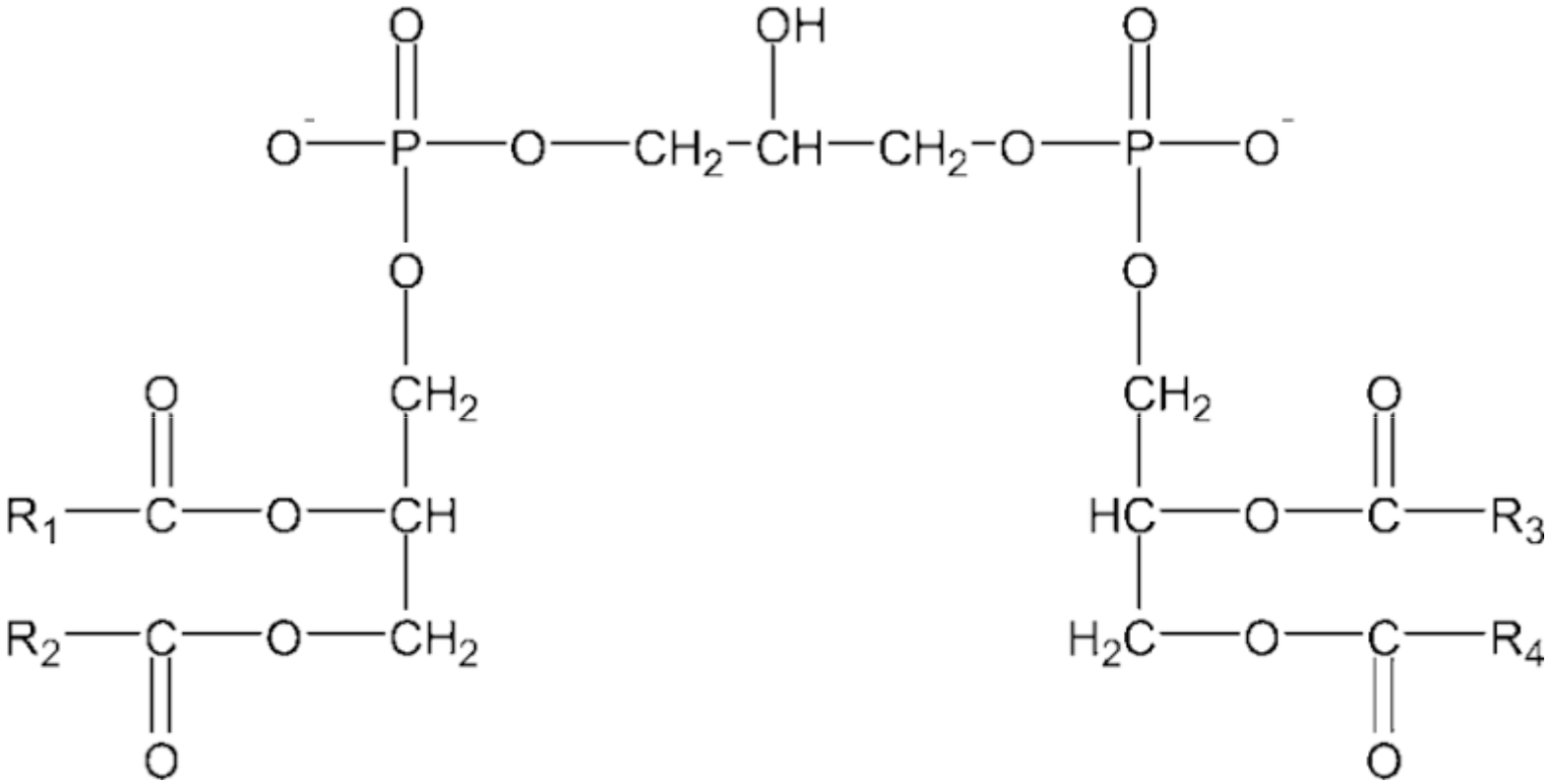


Plasmalogen

Phosphatidyl inositol



Cardiolipin



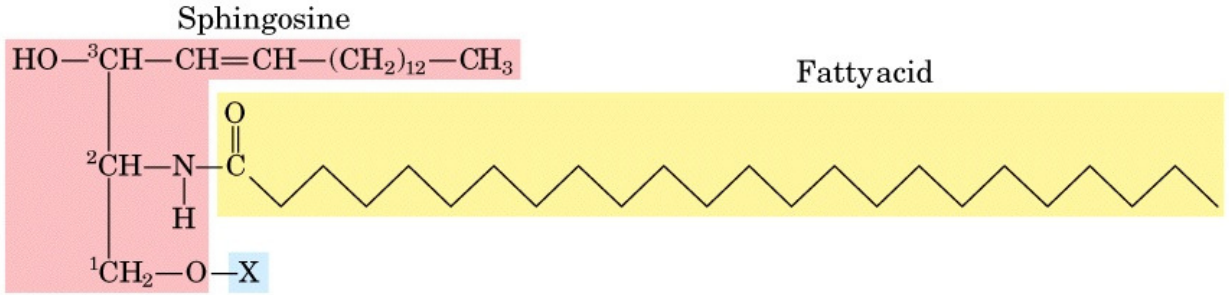
B-Sphingophospholipids

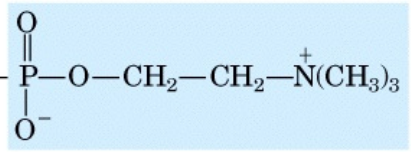
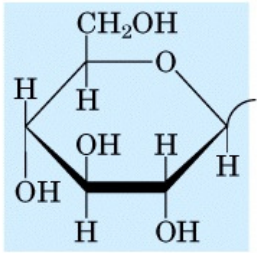
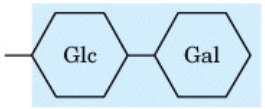
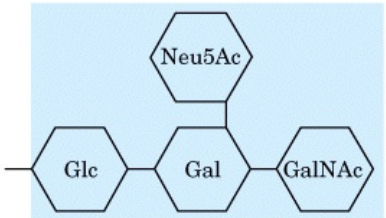
1-Sphingomyelins

- Found in large amounts in brain and nerves.
- In smaller amounts in lung, spleen, kidney, liver & blood.
- Structure:
- Sphingosine = long Chain Amino alcohol , Unsaturated
- Sphingosine = As alcohol, instead of glycerol.
- Sphingosine contain two nitrogenous bases: sphingosine itself and choline.
- To the amino group of sphingosine the fatty acid is attached by an amide linkage.

Sphingolipid

Sphingolipid (general structure)



Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

B-Glycolipids

Sphingosine (alcohol) + Very long-chain fatty acid + Carbohydrate

They are present in cerebral tissue = Cerebrosides

Classification:

According to the number and nature of the carbohydrate

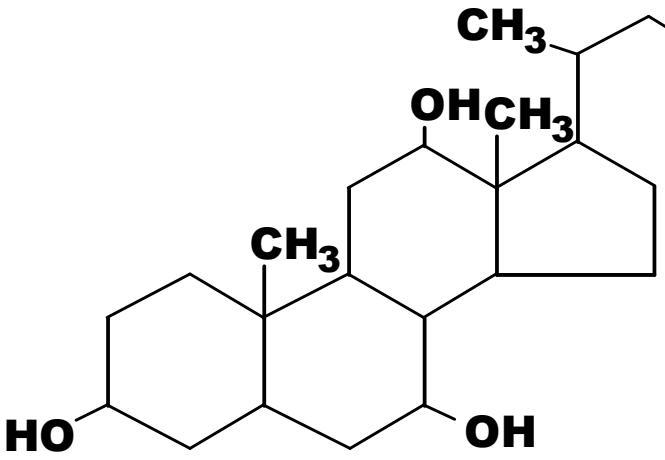
1. **Cerebrosides. = One galactose molecule (galactosides).**
2. **Sulfatides. = With sulfate on the sugar (sulfated cerebrosides).**
3. **Gangliosides = Several sugar and sugaramine residues.**

Bile acids

- Produced from oxidation of cholesterol in the liver producing
  - Cholic and Chenodeoxycholic acids
- Conjugated with glycine or taurine to produce
  - Glycocholic
  - Glycochenodeoxycholic
  - Taurocholic
  - Taurochenodeoxycholic acids.
- They react with sodium or potassium to produce bile salts.

Their function is as follows:

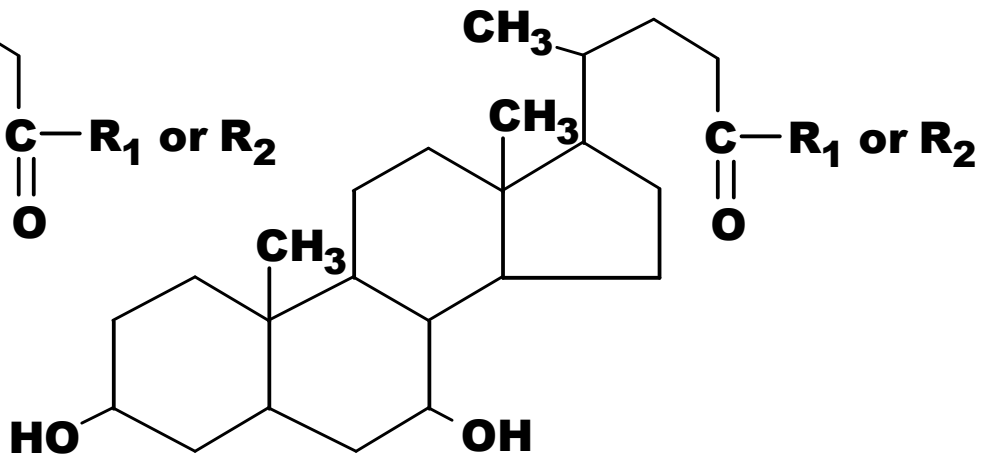
1. Emulsification of lipids during digestion.
    1. Help in digestion lipid.
2. Provide alkaline pH
    1. Activation of pancreatic lipase.
3. Help absorption of fat-soluble vitamins.
4. Solubilizing cholesterol in bile and prevent gall stone formation.
5. Cholesterol excretion – directly in form of bile acid/salt.



Sodium-tauro or
glyco-cholate

R_1 $H_2N-CH_2-COO^-Na^+$

Sodium glycate



Sodium-tauro or
glyco-chenodeoxycholate

R_2 $H_2N-(CH_2)_2-SO_3^-Na^+$

Sodium taurate