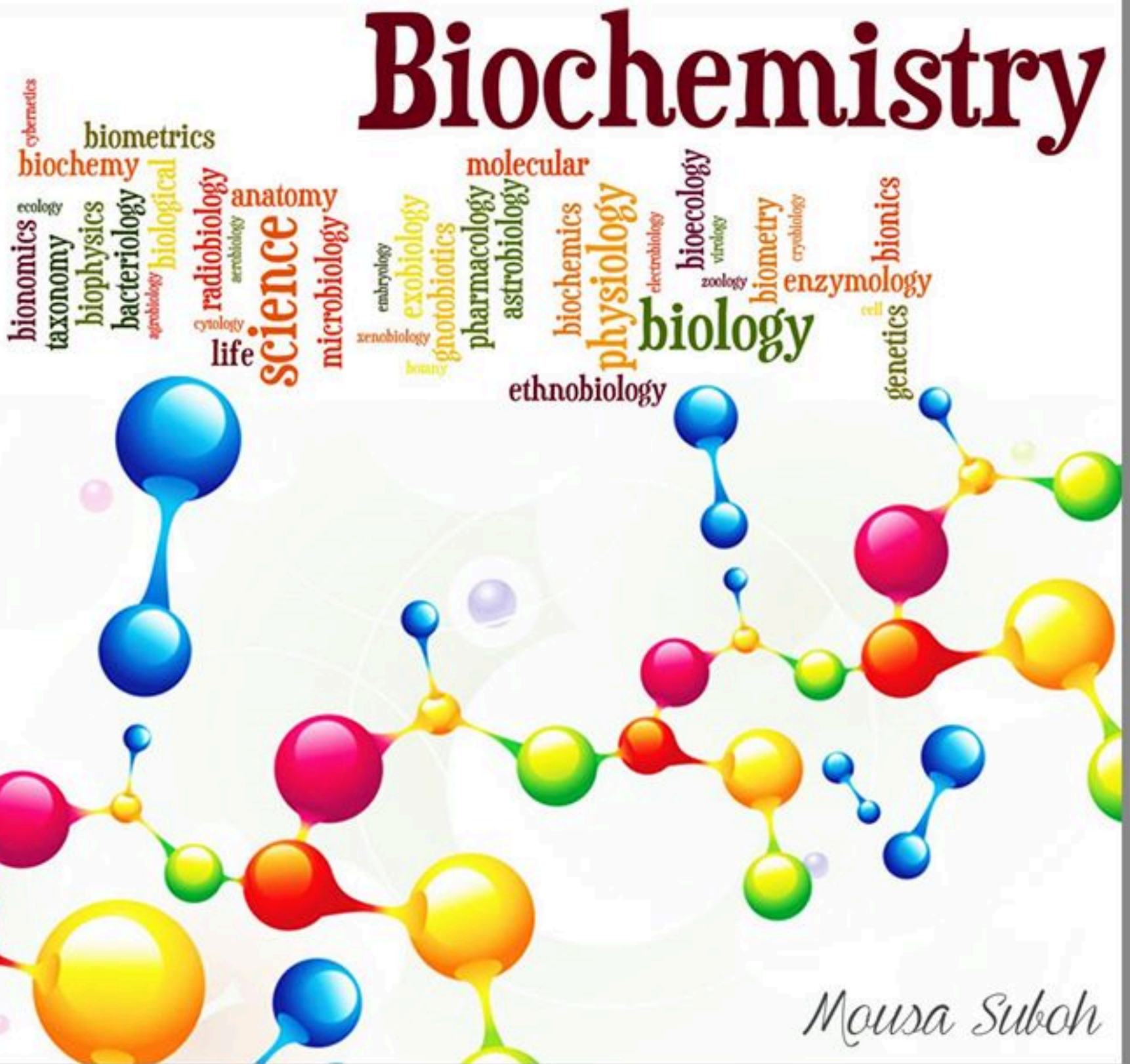
Slide : 2-Lipids part (1)

Dr. Name : Dr. Nafez Abo-Tarboosh

Sections : 4-5-6

■ Slide ☐ Sheet

Medical Committee
The University of Jordan



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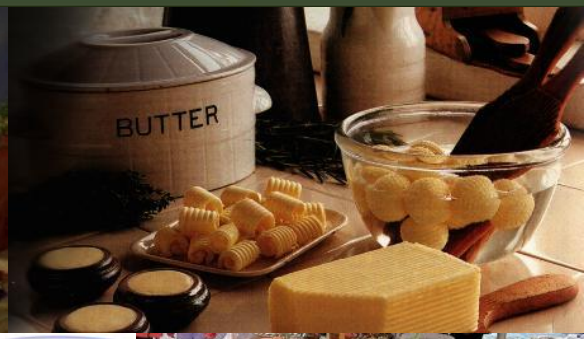
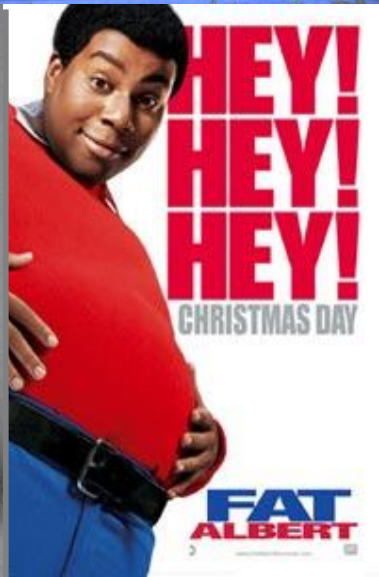
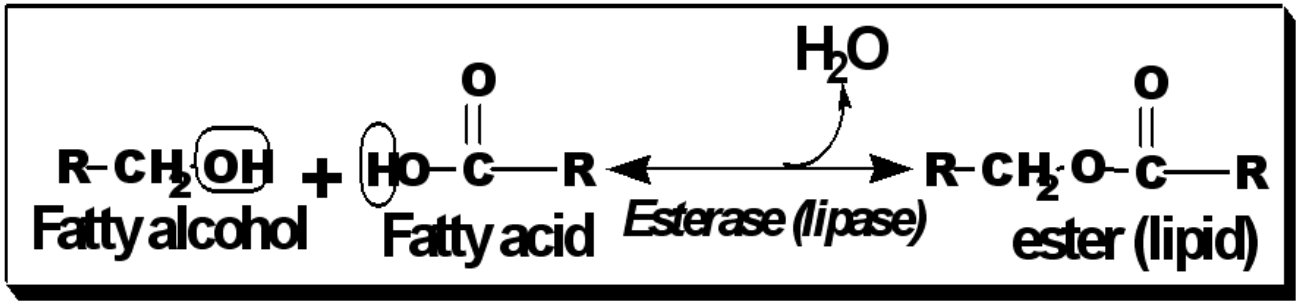
Lipids





Lipids – Definition & General Properties

- A heterogeneous class of naturally occurring organic compounds
- Formed mainly from alcohol & fatty acids combined together by ester linkage



- They are Amphipathic in nature
- Insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone)
- They are widely distributed in plants & animals

Lipids – function & biological importance

1) They are storable to unlimited amount (vs. carbohydrates)

2) They provide considerable amount of energy to the body (25% of body needs) & provide a high-energy value (more energy per gram vs. carbohydrates & proteins)

3) Supply the essential fatty acids (PUFAs)

4) Supply the body with fat-soluble vitamins (A, D, E & K)

5) They are important constituents of the nervous system

6) Structural (cell membrane): cholesterol & fatty acids

Lipids – function & biological importance

7) Stored lipids are in all human cells & acts as:
   A. A store of energy
   B. A pad for the internal organs
   C. A subcutaneous thermal insulator against loss of body heat

8) Combine with proteins "Lipoproteins"

9) Precursor for: adrenal cortical hormones, sex hormones, vitamin D_3 & bile acids

Classification of Lipids

- Lipids include:
  - ✓ Open Chain forms
    - Fatty acids, triacylglycerols, sphingolipids, phosphoacylglycerols, glycolipids,
    - Lipid-soluble vitamins
    - Prostaglandins, leukotrienes, & thromboxanes
  - ✓ Cyclic forms
    - Cholesterol, steroid hormones, & bile acids

- Lipids include:
  - ✓ Derived Lipids (glycerol & sphingosine)
  - ✓ Simple lipids (Fats, oils, & Waxes)
  - ✓ Compound, conjugated, or complex lipids
  - ✓ Cyclic lipids (steroids)
  - ✓ Lipid-associating substances (vitamins)

- Lipids include:
  - ✓ Storage Lipids
  - ✓ Structural Lipids in Membranes
  - ✓ Lipids as Signals, Cofactors & Pigments

Classification of Lipids

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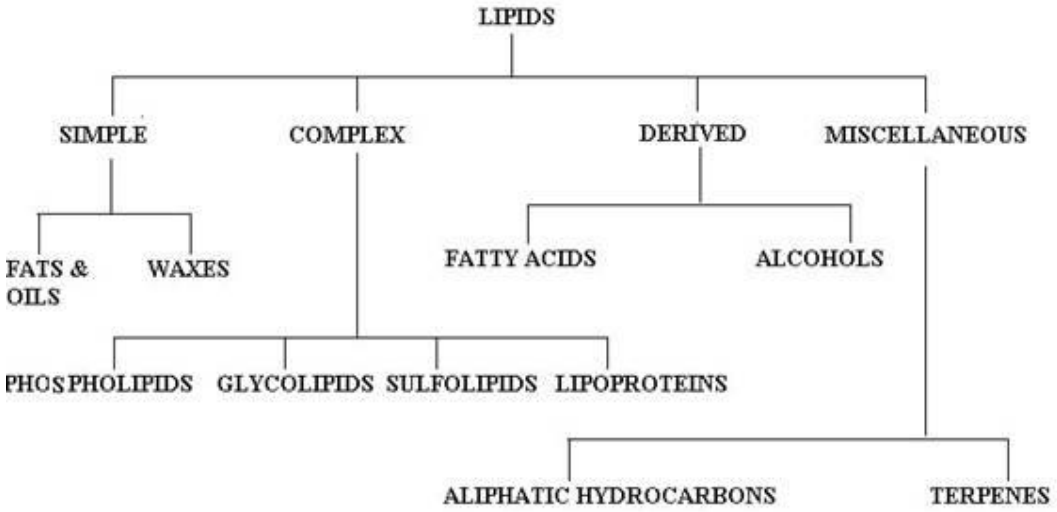
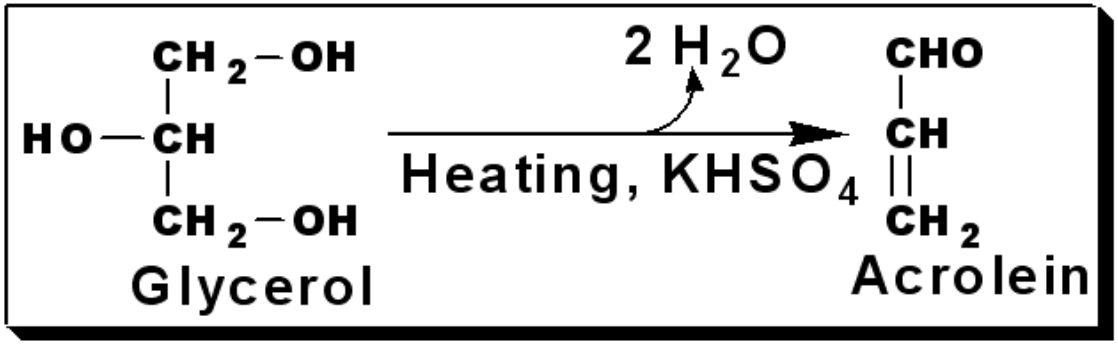
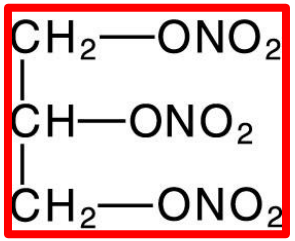


Fatty alcohols - Glycerol

- Trihydroxylic alcohol
- Popular name: glycerin
- Synthesized from glucose
- Properties:





Trinitroglycerin

1) Colorless viscous oily liquid with sweet taste
2) On heating with sulfuric acid or $KHSO_4$ (dehydration) it gives acrolein that has a bad odor (detection)
3) Combines with three molecules of nitric acid to form trinitroglycerin that is used as a vasodilator

Glycerol

4) Nutritive value (glucose)

5) In structure of phospholipids

6) On esterification with fatty acids it gives:

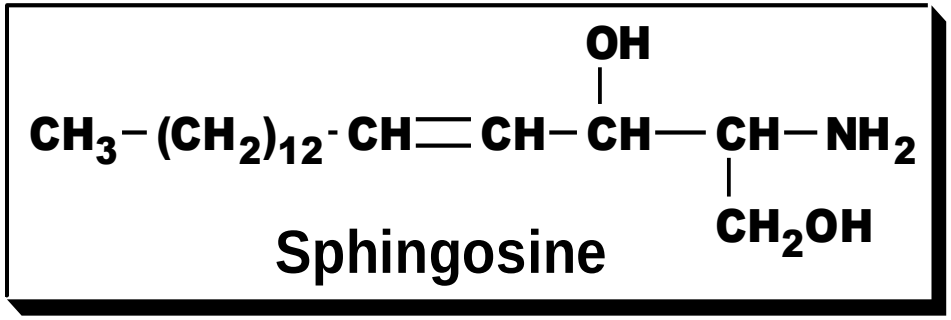
   A. Monoglyceride or monoacyl-glycerol

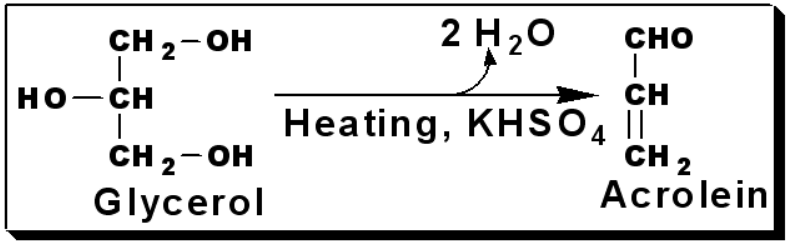
   B. Diglyceride or diacyl-glycerol

   C. Triglyceride or triacyl-glycerol

Fatty alcohols - Sphingosine

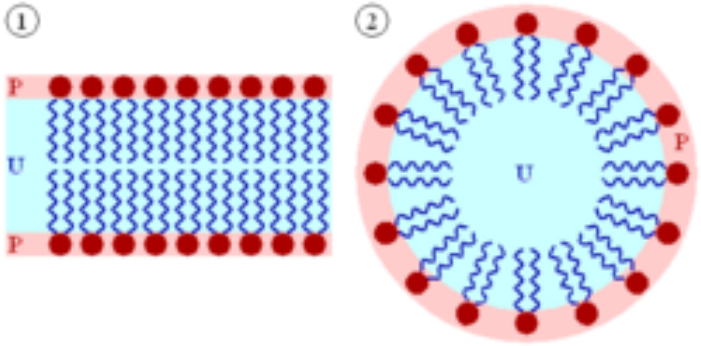
- It is the fatty alcohol present in sphingolipids
- It is synthesized in the body from serine & palmitic acid
- Tests negative with acrolein test



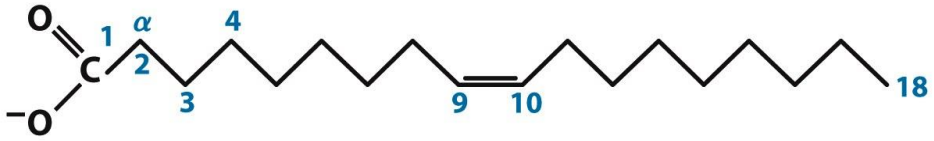


Fatty Acids

- Aliphatic mono-carboxylic acids
- Obtained from hydrolysis

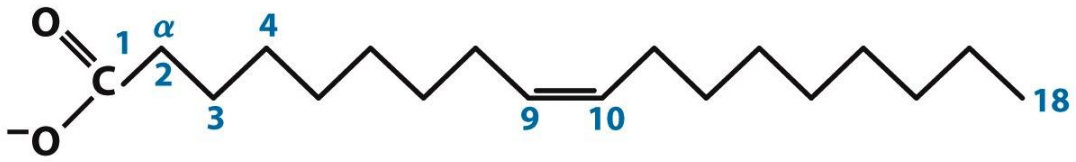


- Formula: $R\text{-}(CH_2)_n\text{-}COOH$
  - "n": mostly even (2-36)
- Mostly straight chain (a few exceptions are branched)
- Amphipathic molecules (bilayers & micelles)
- Saturated vs. unsaturated

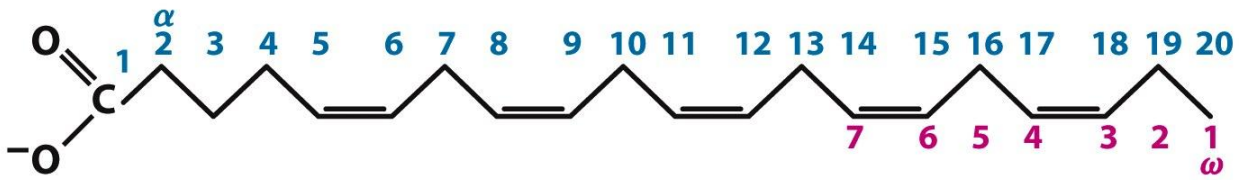


Fatty Acid Structure

- Saturated fatty acids N:o
- Unsaturated Fatty acids: cis isomer predominates; trans is rare
- Double bonds specified by (Δ^n)

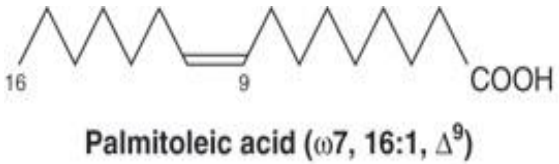


(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid

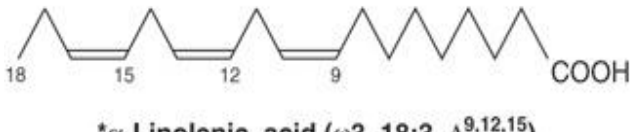


(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), an omega-3 fatty acid

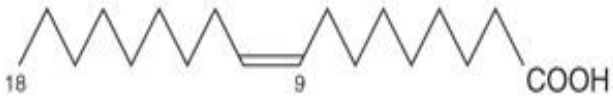
Common Fatty Acids



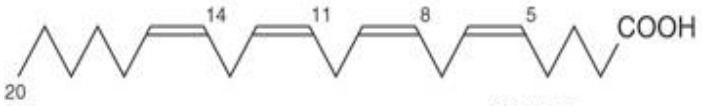
Palmitoleic acid (ω7, 16:1, Δ^9)



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

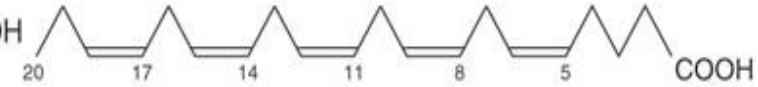


Oleic acid (ω9, 18:1, Δ^9)



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

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

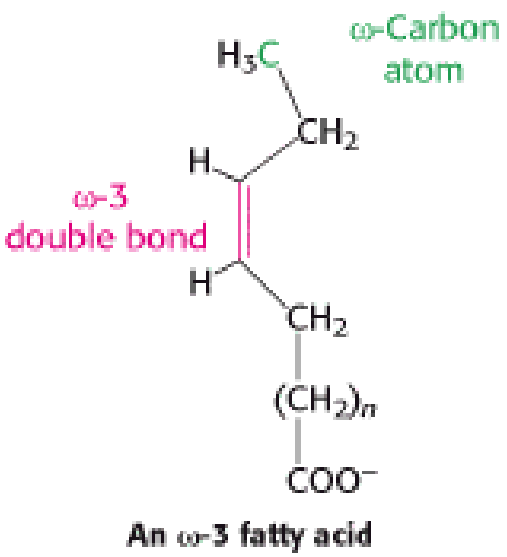


Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

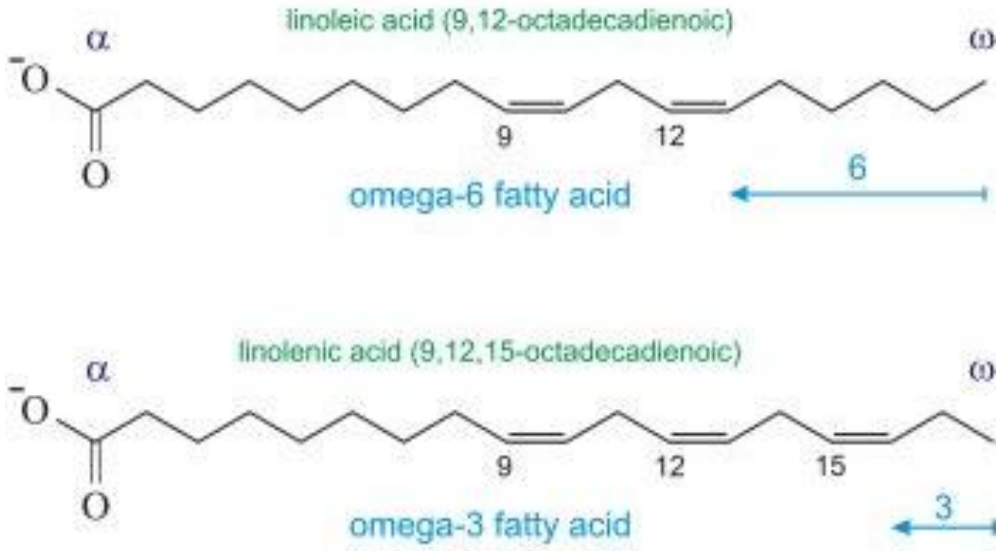
No. of carbons	No. of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	n-Octadecanoate	$CH_3(CH2)_{16}COO^-$
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH=CH(CH_2)_7COO^-$
18	2	Linoleate	cis,cis-Δ^9,Δ^{12}-Octadecadienoate	$CH_3(CH_2)_2(CH=CHCH_2)_2(CH_2)_6COO^-$
18	3	Linolenate	all-cis-$\Delta^9,\Delta^{12},\Delta^{15}$-Octadecatrienoate	$CH_3CH_2(CH=CHCH_2)_3(CH_2)_6COO^-$
20	4	Arachidonate	all-cis-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-Eicosatetraenoate	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COO^-$

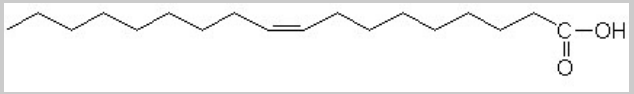
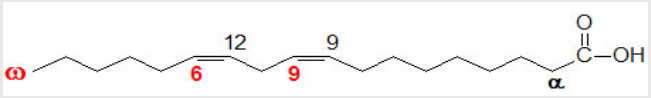
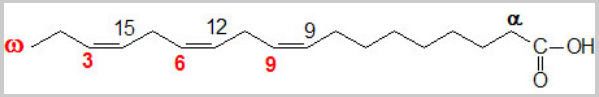
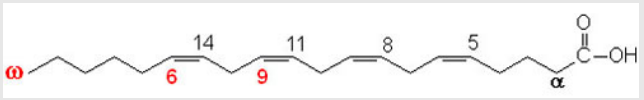
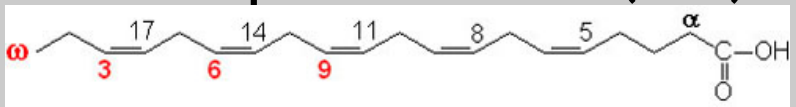
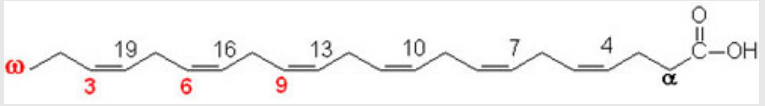
Another way of naming

- (ω)-C: distal methyl C as #1



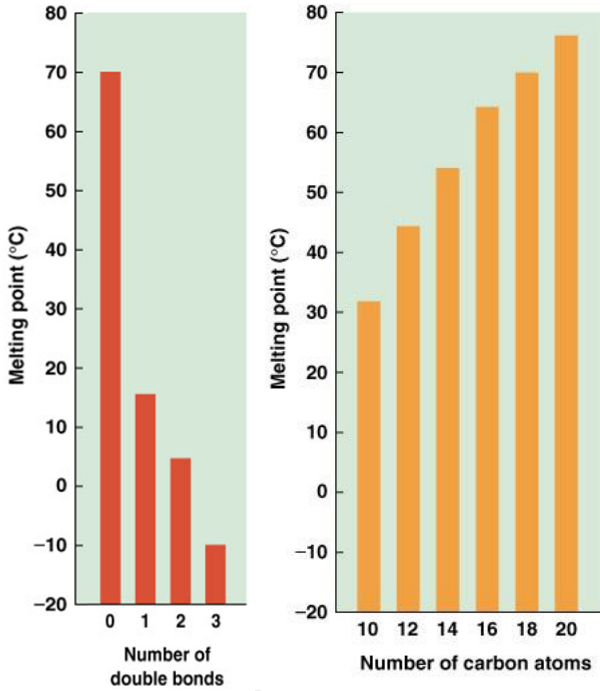
An ω-3 fatty acid



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)

Fatty Acids - Physical Properties

- Solubility
  - ✓ Longer chains
    - ○ The more hydrophobic, the less soluble
  - ✓ Double bonds increase solubility



- Melting points
  - ✓ Depend on chain length & saturation
  - ✓ Double bonds lead to low melting temps

Typical Naturally Occurring Saturated Fatty Acids

Acid	Number of Carbon Atoms	Formula	Melting Point (°C)
Lauric	12	$CH_3(CH_2)_{10}CO_2H$	44
Myristic	14	$CH_3(CH_2)_{12}CO_2H$	58
Palmitic	16	$CH_3(CH_2)_{14}CO_2H$	63
Stearic	18	$CH_3(CH_2)_{16}CO_2H$	71
Arachidic	20	$CH_3(CH_2)_{18}CO_2H$	77

Typical Naturally Occurring Unsaturated Fatty Acids

Acid	Number of Carbon Atoms	Degree of Unsaturation*	Formula	Melting Point (°C)
Palmitoleic	16	16:1—Δ^9	$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	−0.5
Oleic	18	18:1—Δ^9	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	16
Linoleic	18	18:2—$\Delta^{9,12}$	$CH_3(CH_2)_4CH{=}CH(CH_2)CH{=}CH(CH_2)_7CO_2H$	−5
Linolenic	18	18:3—$\Delta^{9,12,15}$	$CH_3(CH_2CH{=}CH)_3(CH_2)_7CO_2H$	−11
Arachidonic	20	20:4—$\Delta^{5,8,11,14}$	$CH_3(CH_2)_4CH{=}CH(CH_2)_4(CH_2)_2CO_2H$	−50

Classification - Double Bonds

1) **Saturated Fatty Acids**
   - A. **No double bonds**
   - B. **Solid at room temperature (short chained?)**
   - C. **Even or odd numbered**
   - D. **The following molecular formula, $C_nH_{2n+1}COOH$**
   - E. **They are either:**
     - i. **Short chain F.A. (1-6 carbons)**
     - ii. **Medium-chain F.A. (7-10 carbons)**
     - iii. **Long chain F.A.(more the 10 carbon)**

Saturated fatty acids

Short & Medium chain F.A.

SHORT CHAIN F.A.

- They are liquid in nature
- Water-soluble
- Volatile at room temperature
- Examples: acetic, butyric, & caproic acids

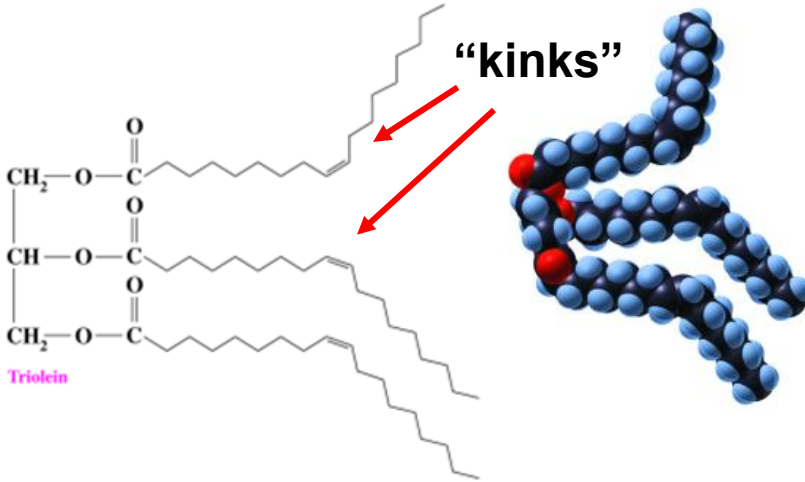
Acetic F.A. (2C) CH_3-COOH
Butyric F.A. (4C) CH_3-$(CH_2)_2$-COOH
Caproic F.A. (6C) CH_3-$(CH_2)_4$-COOH

MEDIUM-CHAIN F.A.

- Solids at room temperature
- Water-soluble
- Non-volatile at room temperature
- Examples: caprylic & capric F.A.

Caprylic (8 C) CH_3-$(CH_2)_6$-COOH
Capric (10 C) CH_3-$(CH_2)_8$-COOH

Long-chain & Unsaturated F.A.



LONG CHAIN

- Occur in <u>hydrogenated oils</u>, animal fats, butter & coconut & palm oils
- <u>Non-volatile & water-insoluble</u>

- Examples: <u>palmitic, stearic</u>, & lignoceric F.A.

Palmitic (16C) $CH_3-(CH_2)_{14}-COOH$
Stearic (18 C) $CH_3-(CH_2)_{16}-COOH$
Lignoceric (24C) $CH_3-(CH_2)_{22}-COOH$

2. UNSATURATED

- <u>Monounsaturated:</u>
  - One double bonds
  - Formula (C_nH_{2n-1} COOH)
- <u>Polyunsaturated:</u>
  - More than one double bond
  - (C_nH_{2n-} more than 1 COOH)
- <u>Do not pack closely (Cis)</u>

Monounsaturated fatty acids

1) **Palmitoleic acid (16):** $CH_3\text{-}(CH_2)_5CH = CH\text{-}(CH_2)_7\text{–}COOH$
- It is found in all fats
- It is C16:1Δ^9, (16 C_s & one double bond at $C_{9\text{-}10}$)

2) **Oleic acid (18):**
- Is the most common fatty acid in natural fats
- It is C18:1Δ^9

$$CH_3\text{-}(CH_2)_7\text{-}\ CH{=}CH\ –\ (CH_2)_7\text{-}COOH$$

3) **Nervonic acid:** (Unsaturated lignoceric acid)
- It is found in cerebrosides
- It is C24:1Δ^{15}

$$CH_3\ –\ (CH_2)_7\ CH{=}\ CH\ –\ (CH_2)_{13}\text{-}\ COOH$$

Polyunsaturated fatty acids
"Essential fatty acids"

1-Linoleic (18;2):

- $C18:2\Delta^{9,12}$ $CH_3\text{-}(CH_2)_4\text{-}CH = CH\text{-}CH_2\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}COOH$
- It is the most important since other fatty acids can be synthesized from it in the body. ω6

2-Linolenic acid (18;3):

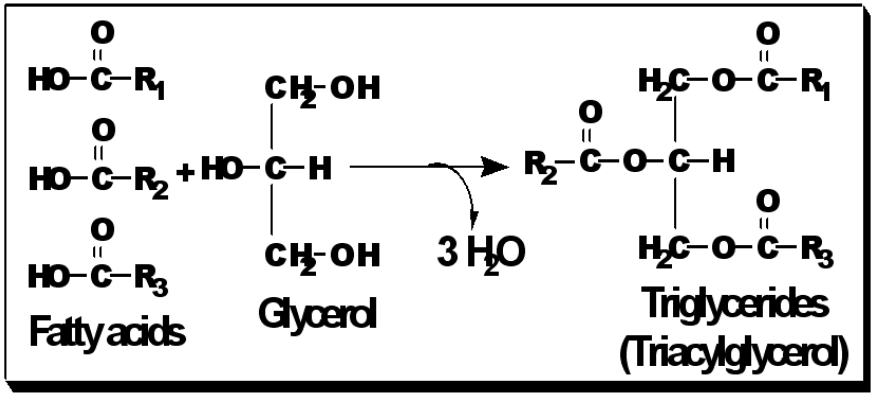
- $C18:3\Delta^{9,12,15}$ $CH_3\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}(CH_2)_7\text{-}COOH$
- In corn, peanut, olive, cottonseed & soybean oils. ω3

3-Arachidonic acid (20;4):

- $C20:4\Delta^{5,8,11,14}$ $CH_3\text{-}(CH_2)_4\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}(CH_2)_3\text{-}COOH$
- It is an important component of phospholipids in animal & in peanut oil from which prostaglandins are synthesized

Simple Lipids
A. Neutral Fats & oils (Triacylglycerols)

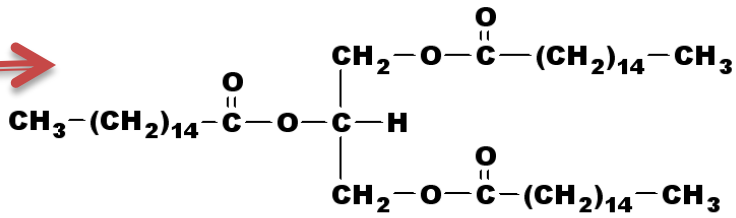
1. **Esters of glycerol with F.A**
   - ✓ Commonest: palmitic, stearic & oleic
2. **Uncharged** due to absence of ionizable groups in it
3. **Most abundant lipids in nature**



No. of carbons	No. of double bonds	Common name	Systematic name	Formula
16	0	Palmitate	n-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	n-Octadecanoate	$CH_3(CH_2)_{16}COO^-$
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^-$

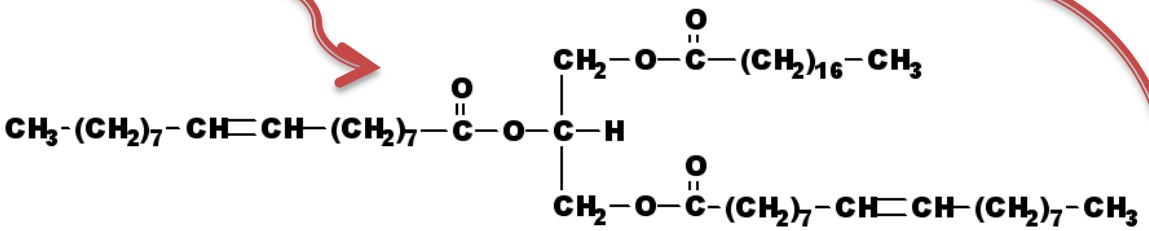
Simple Lipids
A. Neutral Fats & oils (Triacylglycerols)

4. Either;
   a) Simple: same type, e.g., tripalmitin

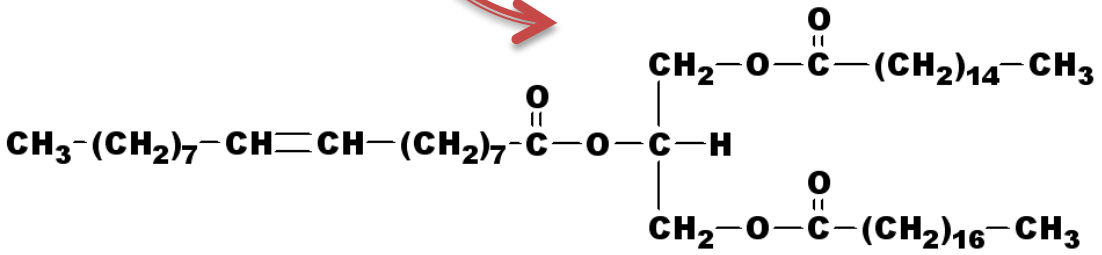


Tripalmitin
(simple triacylglycerol)

   b) Mixed: of different types, e.g., stearo-diolein & palmito-oleo-stearin



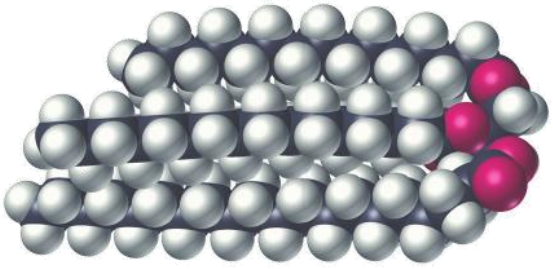
1-Stearo-2,3-diolein
(mixed triacylglycerol)



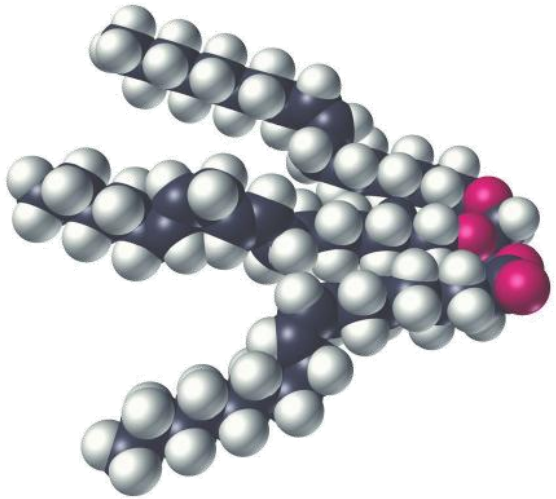
1-palmito-2-oleo-3-stearin
(mixed triacylglycerol)

Physical properties of fat & oils

1. Freshly prepared are colorless, odorless & tasteless (the yellow color is due to carotene pigments)
2. Fats have specific gravity less than 1
3. Fats are insoluble in water (organic solvents as ether & benzene)
4. Room temperature: Oils (liquid) vs. fats (solids)



A fat

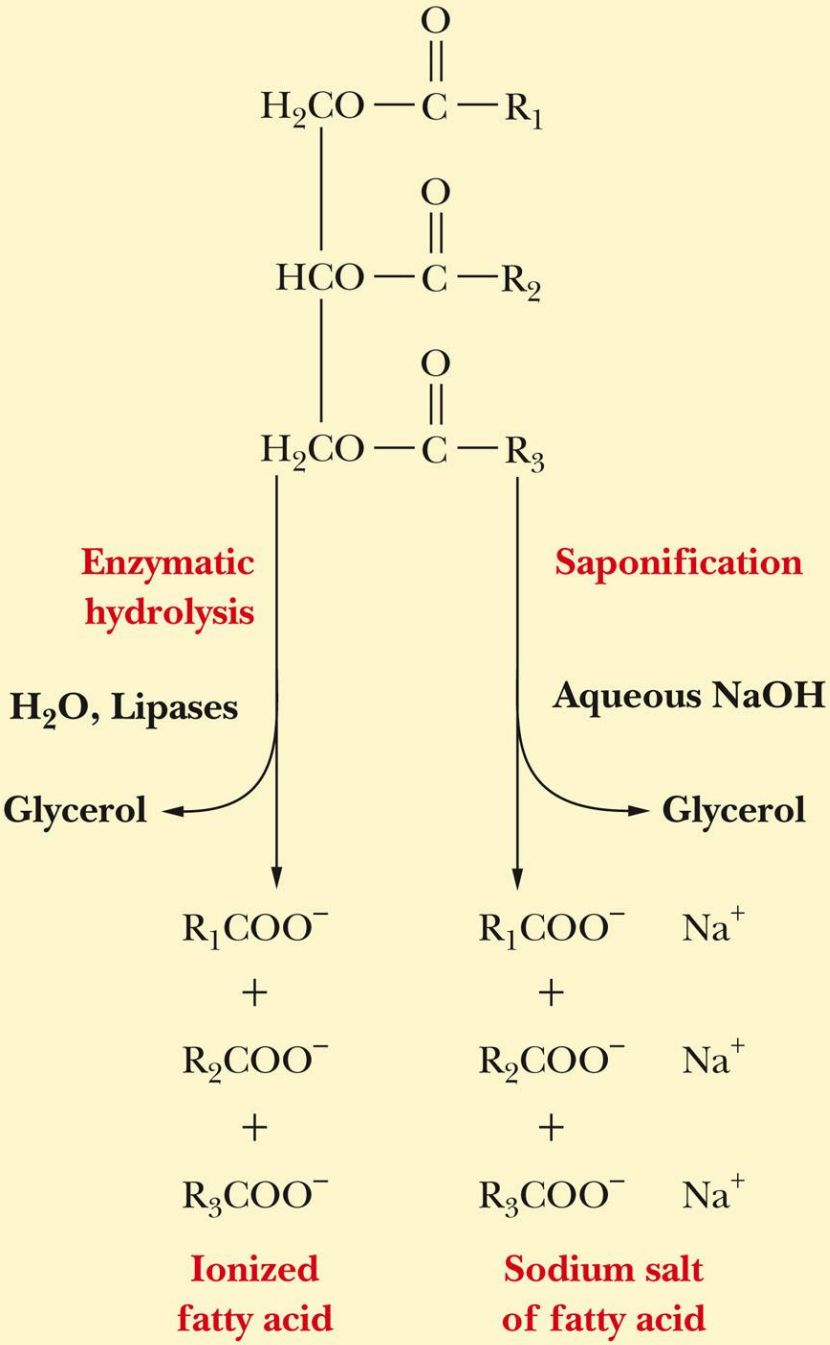


An oil

Chemical Properties of fats & oils (Reactions)

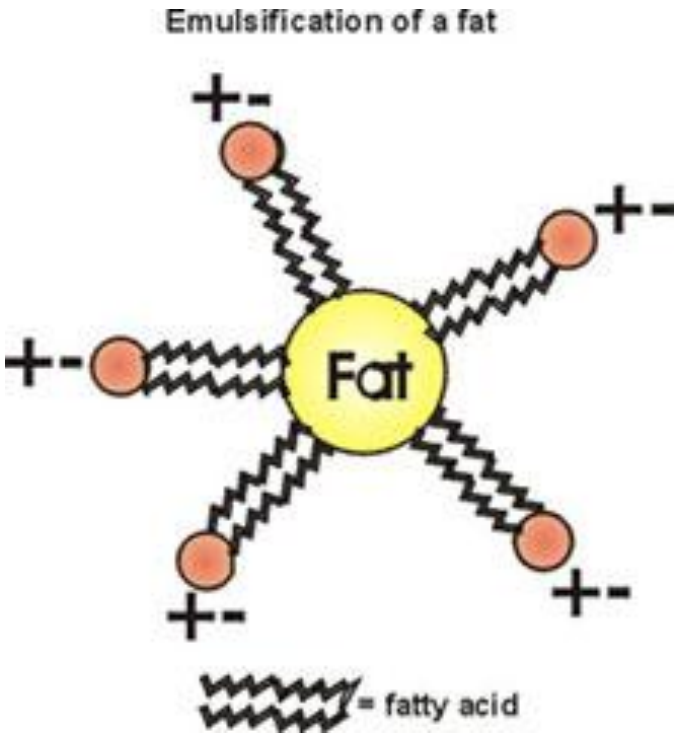
A. Hydrolysis :
   - Steam, acid, enzyme (e.g., lipase of pancreas)

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



Emulsification

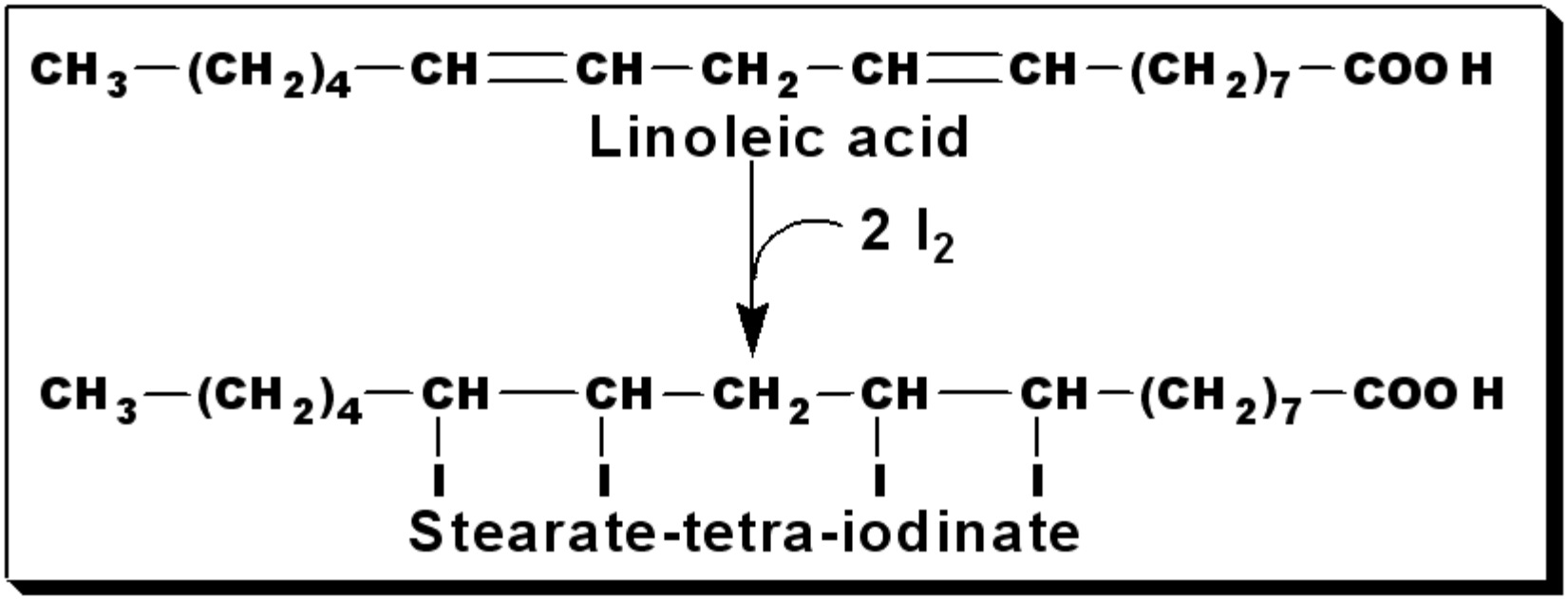
- Because of their amphipathic nature, the act as emulsifying agents, that is substances that can surround nonpolar molecules and keep them in suspension in water



Chemical Properties of fats & oils

C. **Halogenation: added to unsaturated F.A (e.g., iodination)**

- ✓ **Used to determine the <u>degree of unsaturation</u> of the fat or oil that determines its biological value**

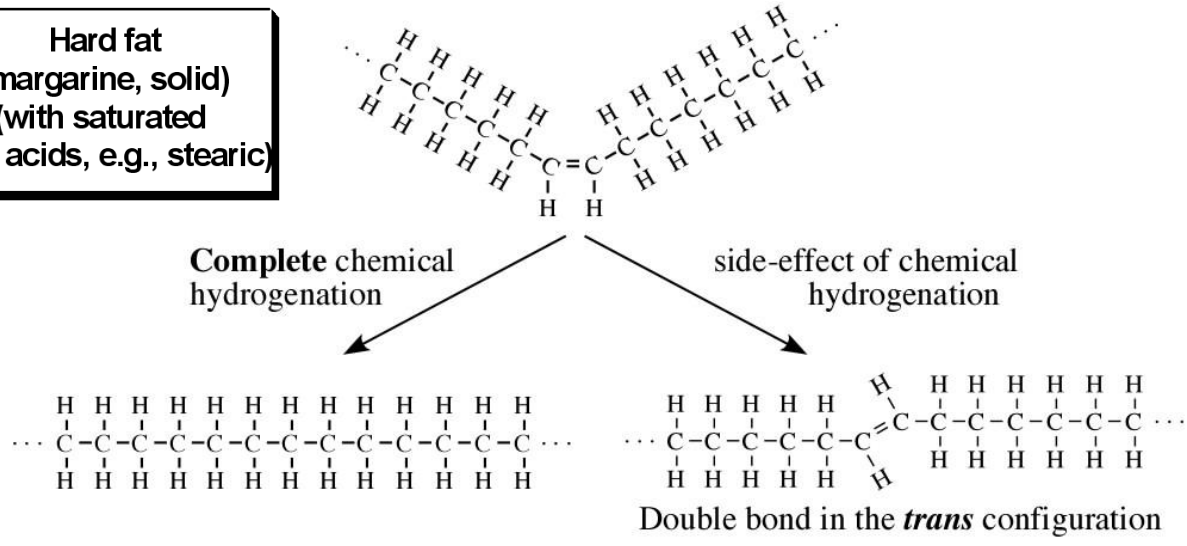


Chemical Properties of fats & oils

D. Hydrogenation or hardening of oils:

- ✓ Addition reaction (unsaturated F.A)
- ✓ Done under high pressure of hydrogen
- ✓ The basis of hardening oils (margarine manufacturing)
- ✓ Hydrogenation converts cis-double bonds to trans

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

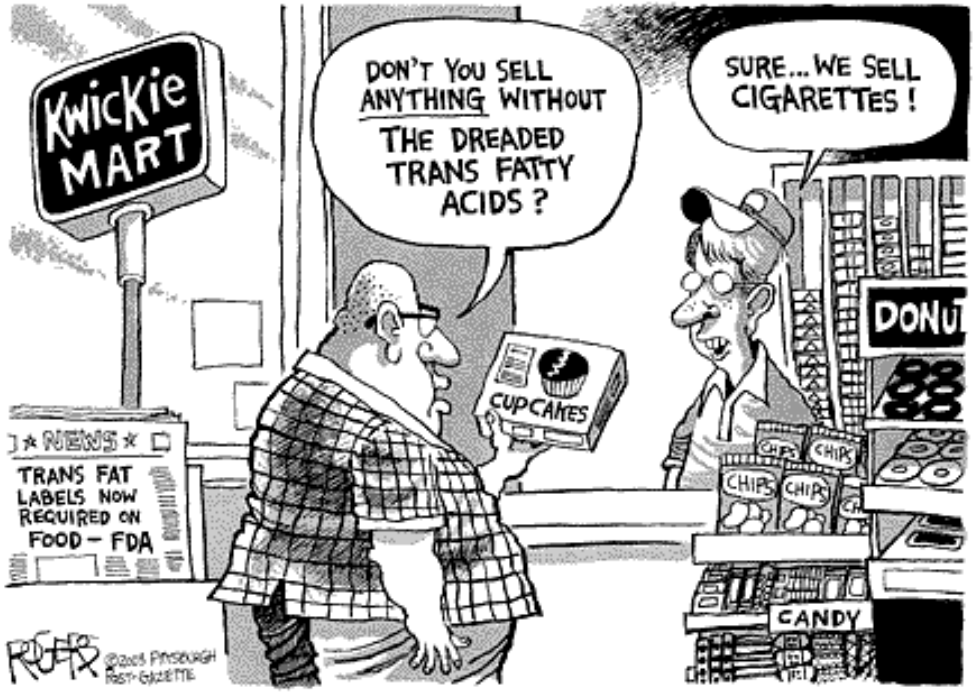


Chemical Properties of fats & oils

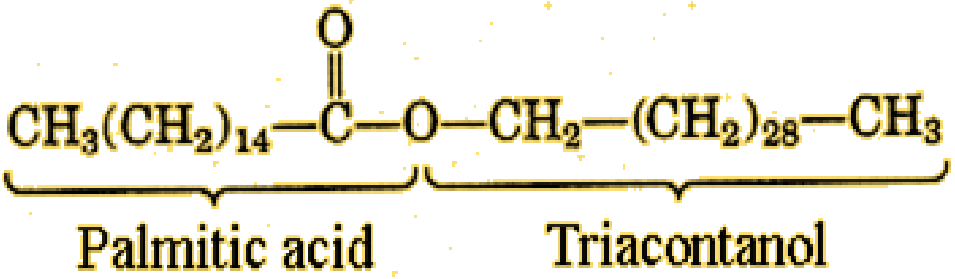
D. Hydrogenation or hardening of oils:

- ✓ Chemists invented partial hydrogenation
  - ✓ Converts some, but not all, double bonds into single bonds
  - ✓ Called (trans fat): elevated risk of coronary heart disease (CHD)

- ✓ Advantages: more pleasant, easily stored & transported, less liable to oxidation
- ✓ Disadvantages: lack of fat-soluble vitamins (ADEK) & essential fatty acids



Simple Lipids
B. Waxes



1. Solid simple lipids
2. Contains a monohydric alcohol (C16 ~ C30), (higher molecular weight than glycerol) esterified to long-chain fatty acids (C14 ~ C36). Examples: palmitoyl alcohol
3. Insoluble in water & Negative to acrolein test
4. Are not easily hydrolyzed (fats) & are indigestible by lipases (nutritional value)
5. Coatings: prevent loss of water by leaves of plants

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

Differences between neutral lipids & waxes

Property	Waxes	Neutral lipids
1.Digestibility	Indigestible (not hydrolyzed by lipase)	Digestible (hydrolyzed by lipase)
2-Type of alcohol	Long-chain monohydric alcohol + one fatty acid	Glycerol (trihydric) + 3 F.A
3-Type of F.A	Mainly palmitic or stearic acid	Long & short chain F.A
4-Acrolein test	Negative	Positive
5-Nature at room temperature	Hard solid	Soft solid or liquid
6-Saponification	Nonsaponifiable	Saponifiable
7-Nutritive value	No nutritive value	Nutritive
8-Example:	Bees wax	Butter & vegetable oils

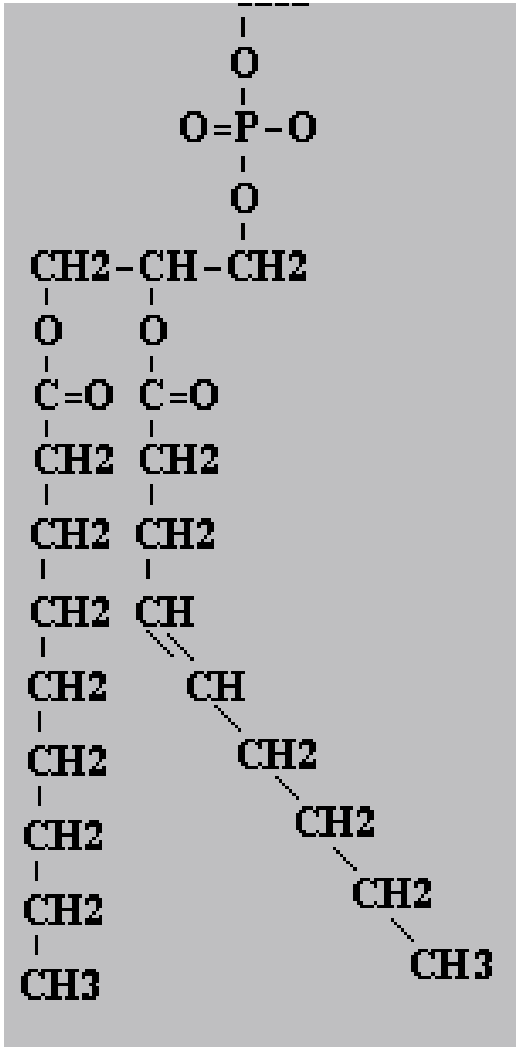
Compound (conjugated) Lipids

- They are lipids that contain additional substances, e.g., sulfur, phosphorus, amino group, carbohydrate, or proteins beside fatty acid & alcohol
- Classified into the following types according to the nature of the additional group

1. Phospholipids
2. Glycolipids
3. Lipoproteins
4. Sulfolipids & amino lipids

1. Phospholipids (phosphatides)

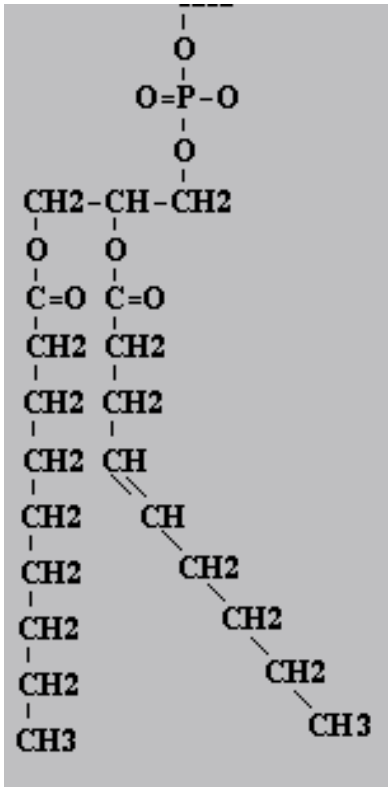
1. Contain phosphoric acid group
2. Every animal & plant cell:
   - ✓ Membranes of cells & subcellular organelles
3. Important role in signal transduction across membranes
4. Snake venom hydrolyses membrane phospholipids
5. A source of polyunsaturated F.A



1. Phospholipids (phosphatides)

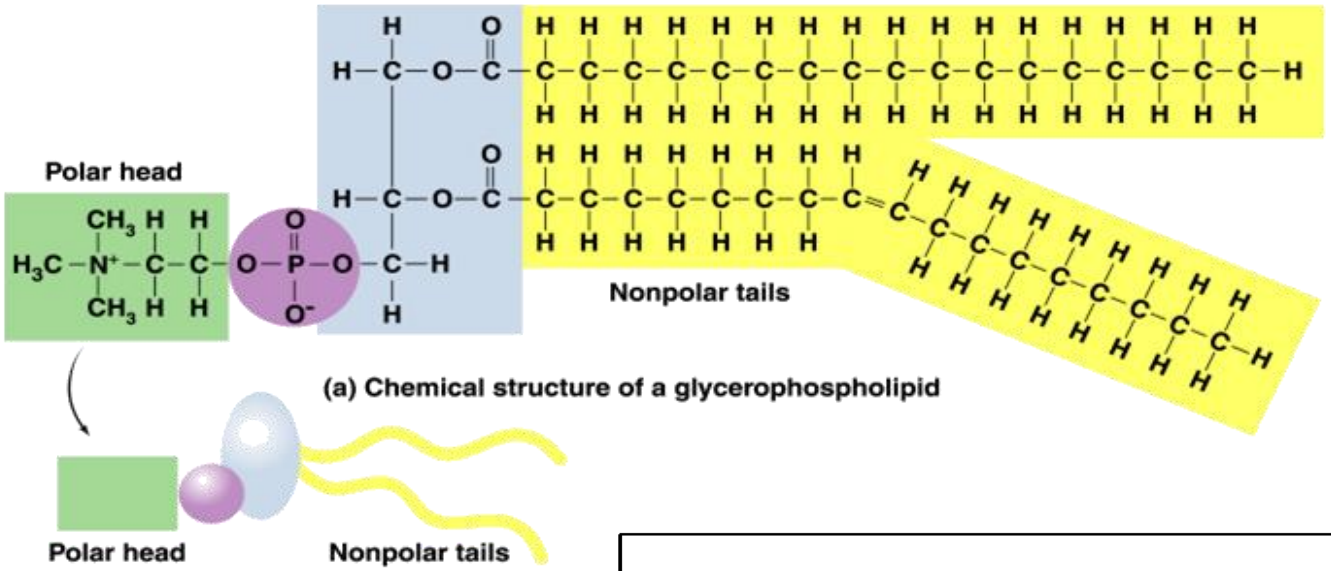
- **Structure**:

1. **Fatty acids (saturated & unsaturated)**
2. **Fatty alcohols (glycerol & sphingosine)**
3. **Phosphoric acid**
4. **Nitrogenous base (choline, Ser, Thr, or ethanolamine)**



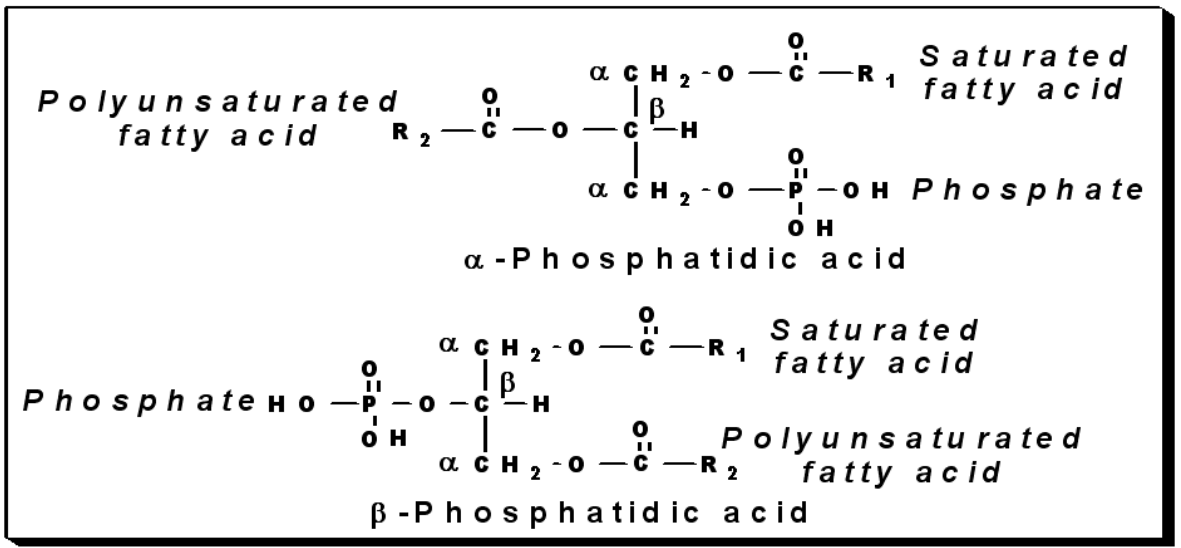
- **Classification: according to the type of the alcohol**
  - **Glycerophospholipids**
    - ✓ **Phosphatidic acids**
    - ✓ **Lecithins**
    - ✓ **Cephalins**
    - ✓ **Plasmalogens**
    - ✓ **Inositides**
    - ✓ **Cardiolipin**
  - **Sphingophospholipids: sphingosine as an alcohol**

Glycerophospholipids - Phosphatidic acids



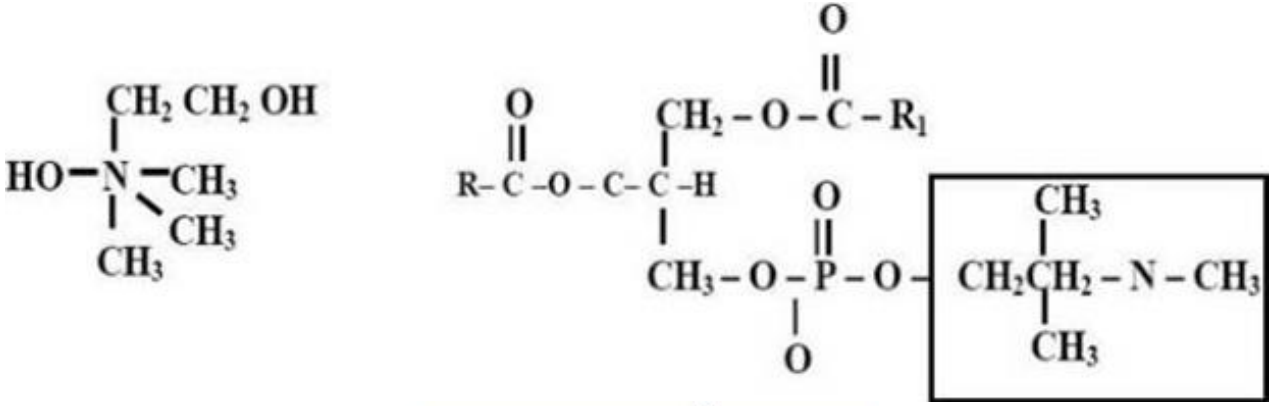
Nitrogenous base

H

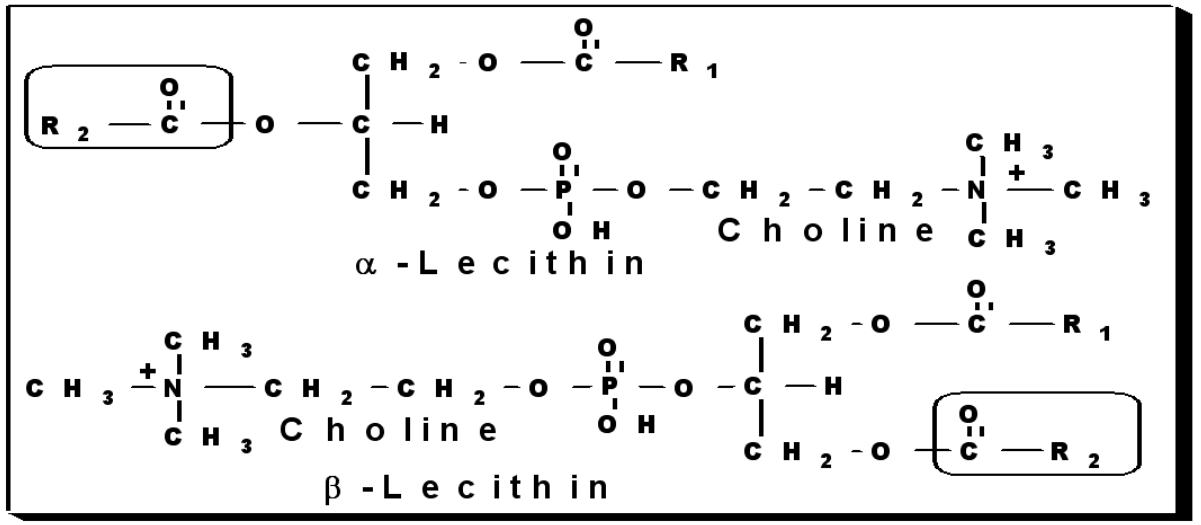


Glycerophospholipids - Lecithins

- Choline as a nitrogenous base
- Most abundant membrane lipid



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

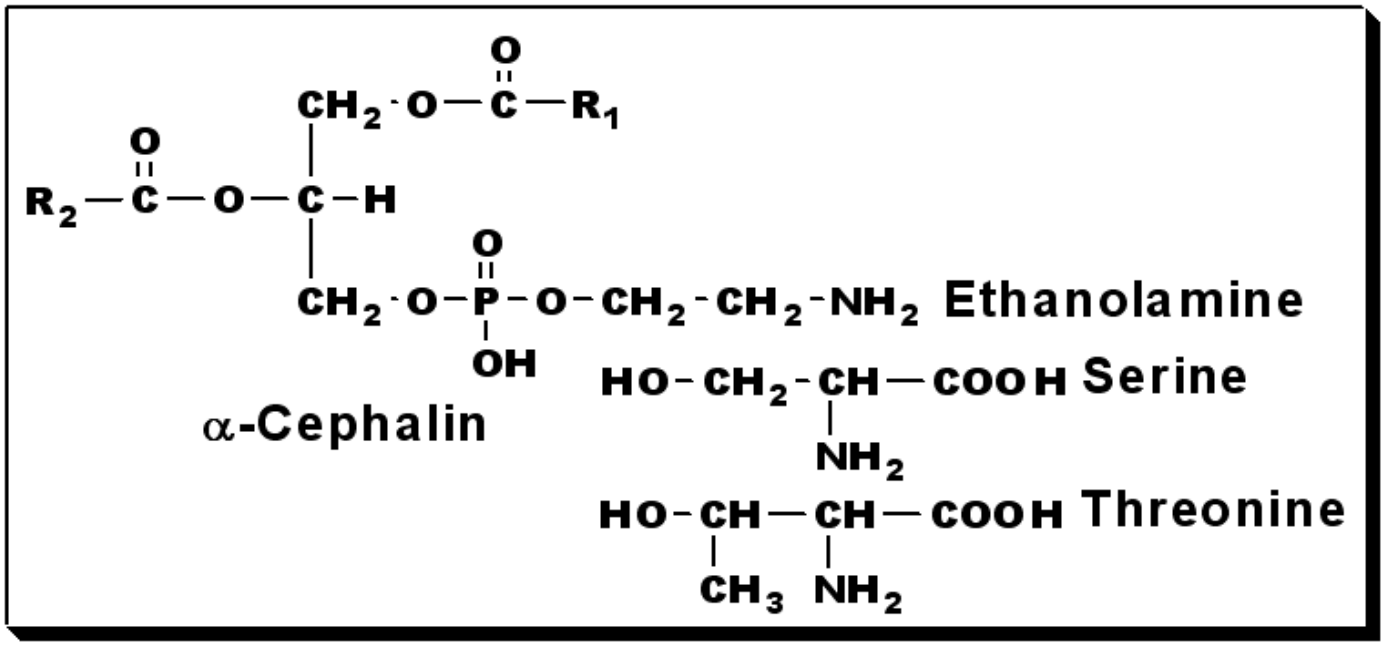


Glycerophospholipids - Lecithins

- **Snake venom: <u>lecithinase hydrolyzes PUFAs</u> converting lecithin into lysolecithin (hemolysis of RBCs)**

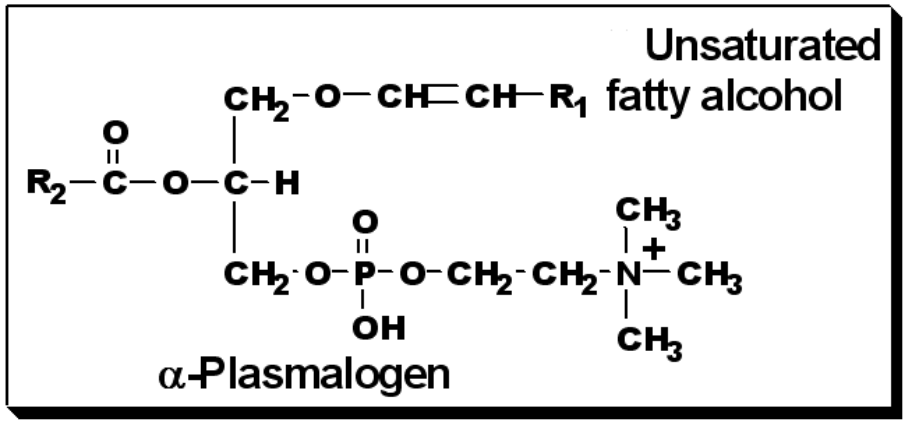
Glycerophospholipids - Cephalins or Kephalins

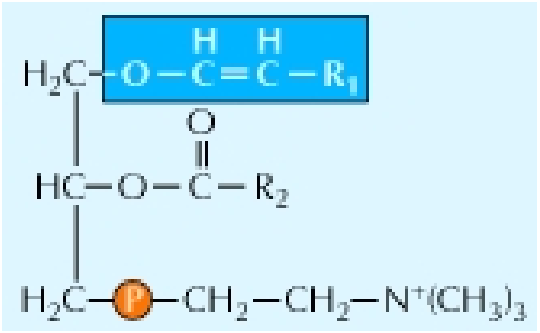
- Choline is replaced by ethanolamine, serine or threonine
- Occur in association with lecithins in tissues
- Isolated from the brain (Kephale = head)

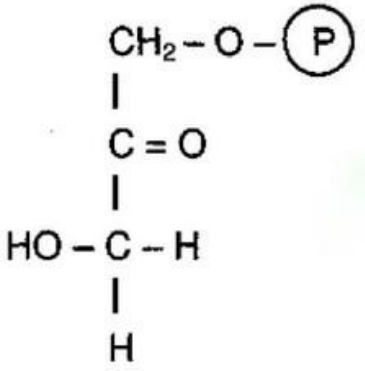


Glycerophospholipids - Plasmalogens

- Found in the cell membrane phospholipids of brain, muscle, liver, & semen
- They have a protective role against ROS
- Structure:
  - Precursor: Dihydroxyacetone phosphate
  - Unsaturated fatty alcohol at C1 connected by ether bond
  - In mammals: at C3; phosphate + ethanolamine or choline

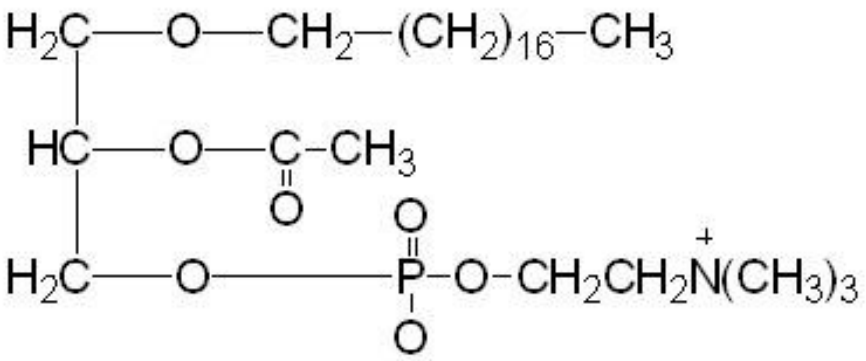






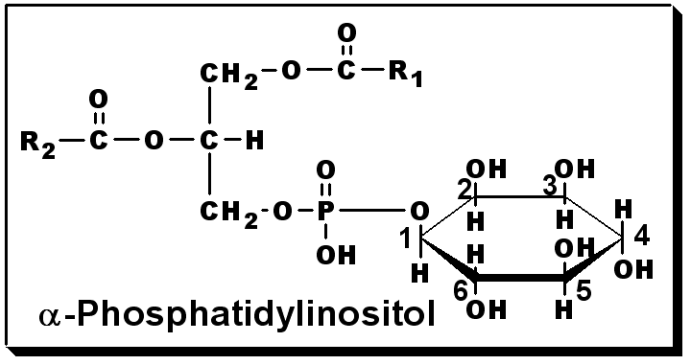
Major classes of plasmalogens

- Ethanolamine plasmalogen (myelin cells-nervous tissues)
- Choline plasmalogen (cardiac tissue)
  - Platelet activating factor
- Serine plasmalogens (retina)



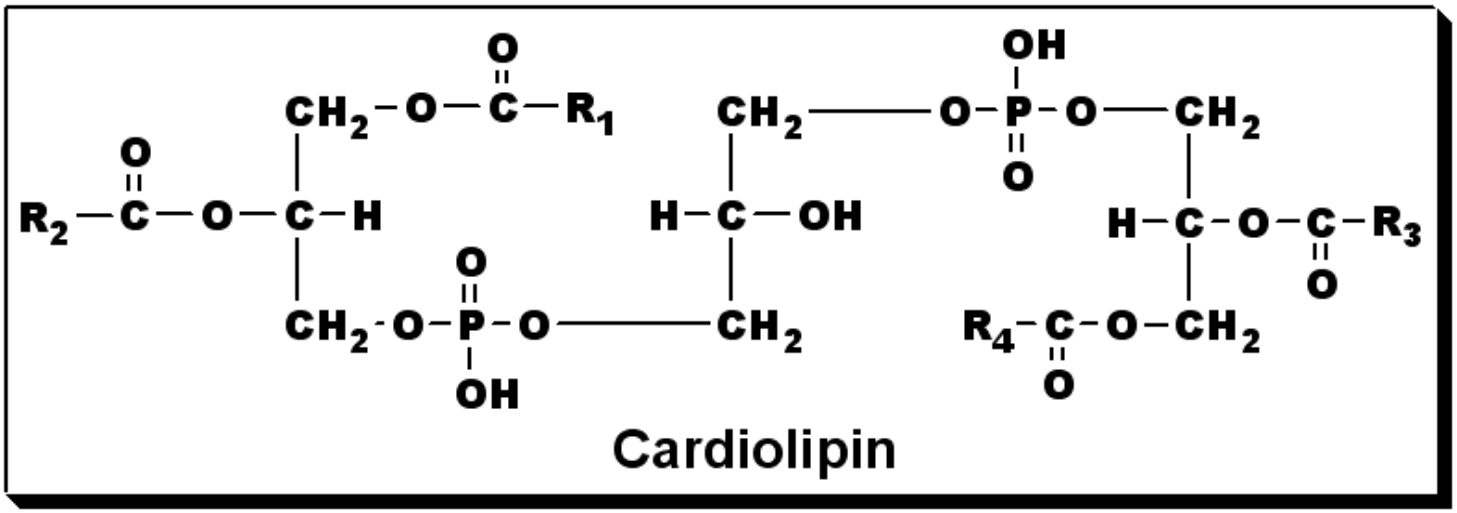
Glycerophospholipids - Inositides

- Phosphatidyl inositol
- Nitrogenous base: cyclic sugar alcohol (inositol)
- Structure: glycerol, saturated F.A, unsaturated F.A, phosphoric acid & inositol
- Source: Brain tissues
- Function:
  - Major component of cell membrane
  - Second messenger during signal transduction
  - On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5-diphosphate produces diacyl-glycerol (DAG) & inositol-triphosphate (IP_3); which liberates calcium



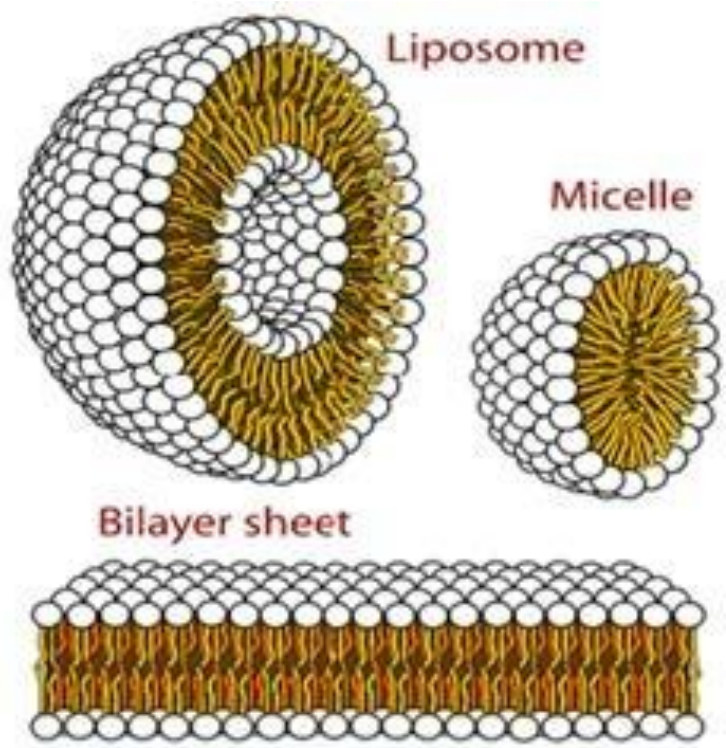
Glycerophospholipids - Cardiolipins

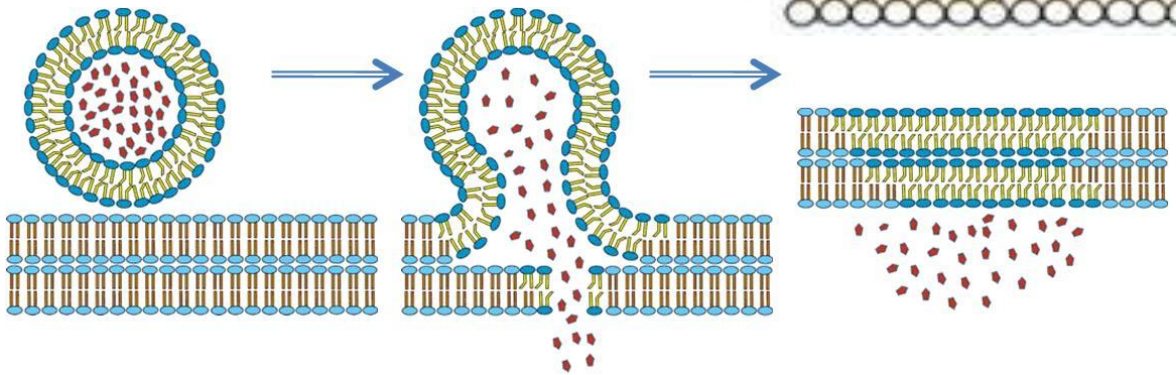
- <u>Diphosphatidyl-glycerol</u>
- Structure: 3 molecules of glycerol, 4 fatty acids & 2 phosphate groups
- Found in the inner membrane of mitochondria
- Initially isolated from heart muscle (cardio)



The different structures of phospholipids

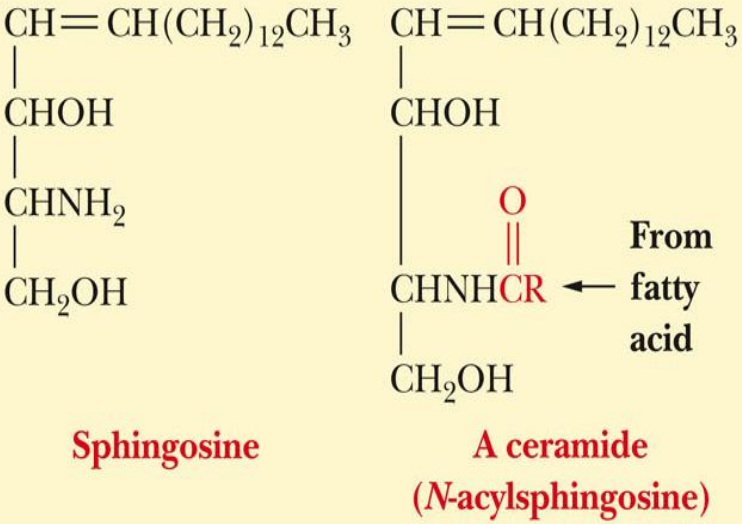
- **Uses of liposomes: delivery**

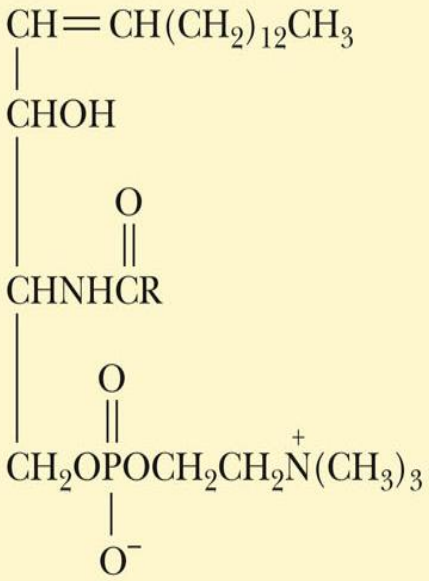




Sphingophospholipids – Sphingomyelins & Ceramides

- Sphingomyelins: found in large amounts in brain & nerves
- Structure:
  - Sphingosine as the alcohol
  - Two nitrogenous bases: sphingosine itself & choline (C1)
  - One long-chain fatty acid
  - Phosphoric acid
- Ceramides: the amino group of sphingosine is attached to a F.A by an amide linkage
  - Found in spleen, liver & RBCs

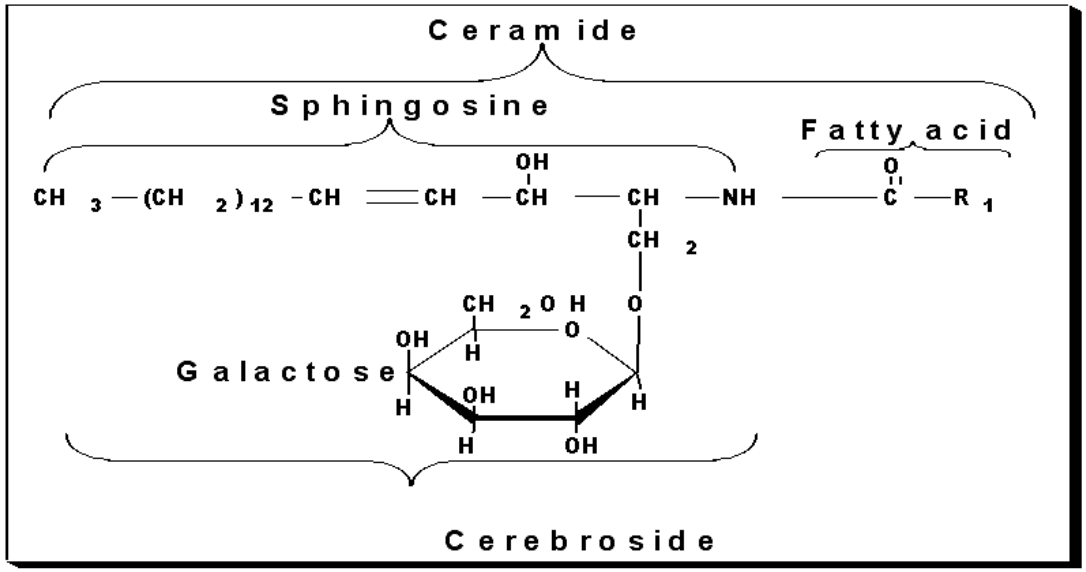


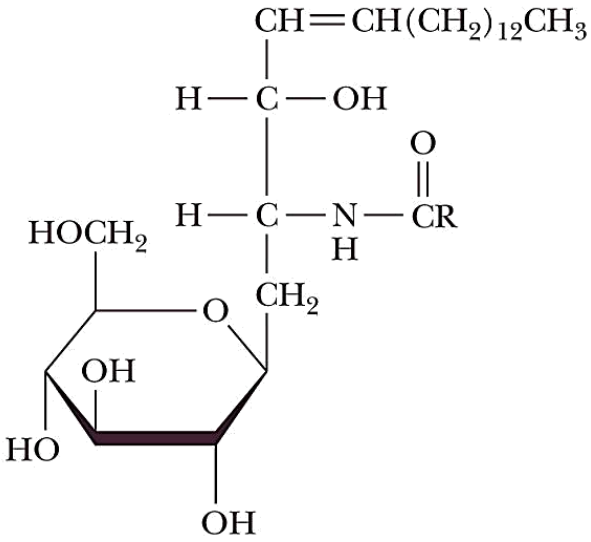


2. Glycolipids

- Contain carbohydrate residues
- Sphingosine as the alcohol
- Contains a very long-chain fatty acid
- They are present in cerebral tissue (cerebrosides)
- Classification: number & nature of carbohydrate present;

1) Cerebrosides: have one galactose or glucose molecule. Myelin sheath of nerves & white matter of the brain

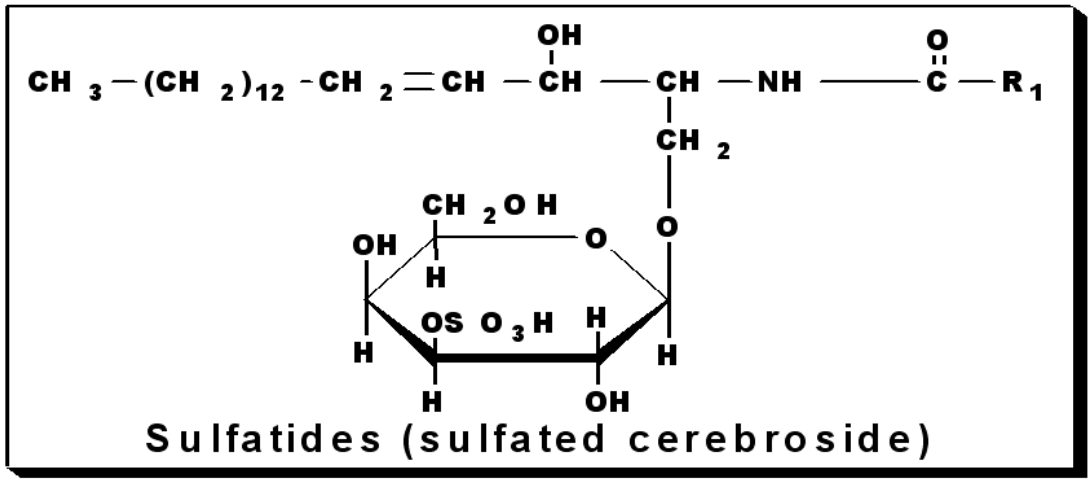




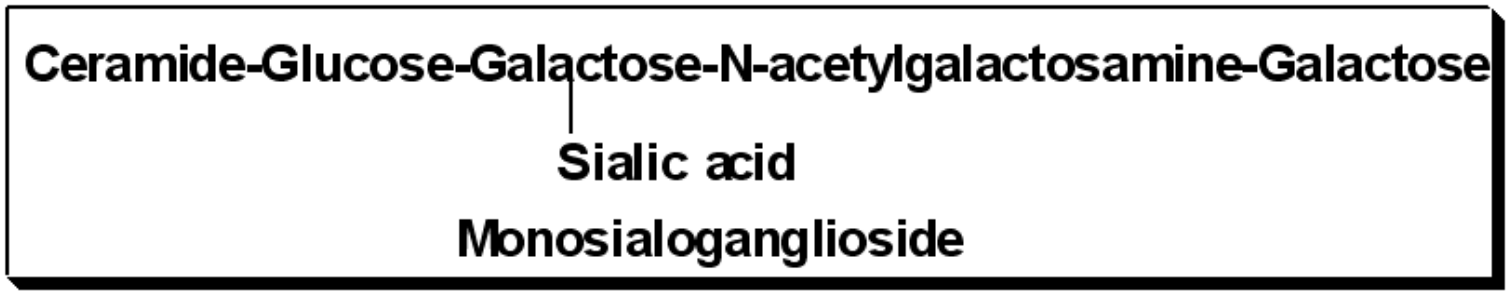
A Glucocerebroside

2. Glycolipids

2) Sulfatides: galacto-cerebrosides with sulfate on the sugar (sulfated cerebrosides).
   - ✓ Abundant in brain myelin



3) Gangliosides: have several sugar & sugaramine residues. Brain, ganglion cells, & RBCs. Receptor for cholera toxin in the human intestine



Sphingolipids & blood groups