LIPIDS:

INTRODUCTION:

-Lipids [macromolecules but NOT polymers] **are** a heterogeneous class of naturally occurring organic compounds that share some properties based on structural similarities, mainly a dominance of nonpolar groups.

-They are *amphipathic* in nature.

-They are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).

-They are widely distributed in plants & animals.

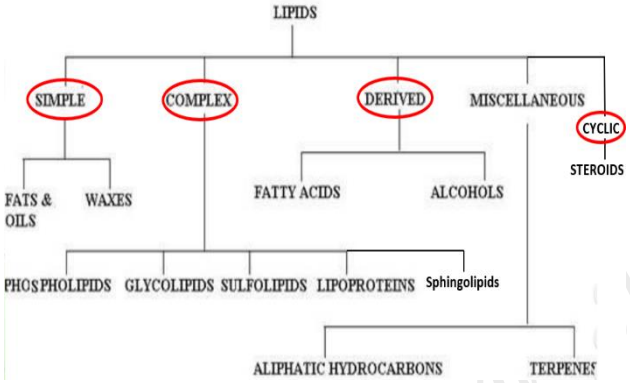
FUNCTIONS:

- Storage lipids
- Structural lipids in membranes
- Lipids as signals, cofactors & pigments
- They are a major source of energy

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

- Structural components (cell membranes)
- Precursors of hormone and vitamins
- Shock absorbers
- Thermal insulator

CALSSIFICATION:



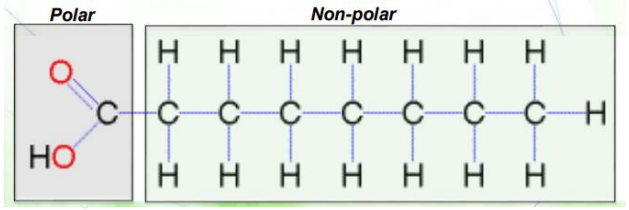
DERIVED LIPIDS:

***Fatty Acids:**

-Aliphatic (دهني) mono-carboxylic acids

-Formula: $R\text{-}(CH_2)_n\text{-}COOH$

-Amphipathic molecules



-Functions:

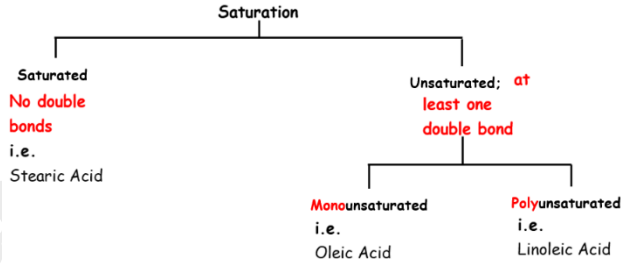
- Building blocks of other lipids
- Modification of many proteins (lipoproteins)
- Important fuel molecules
- Derivatives of important cellular molecules

-Lengths:

Physiological (12-24)

Abundant (16 and 18)

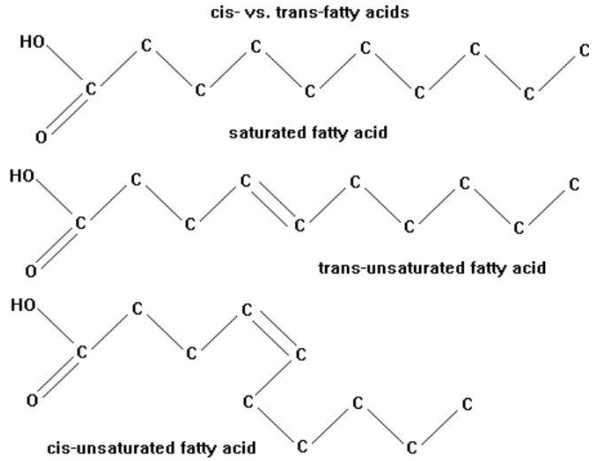
-Degree of Saturation:



NOTE:

Fatty Acid	No. of Carbons	Double Bond(s)
Stearic acid	18	0
Oleic acid	18	1; at C-9
Linoleic acid	18	2: at C-9 + C-12

-Cis-Trans Isomerism:



NOTE:

The **cis-form** takes more space than the **trans-form**

-Properties of Fatty Acids:

Examples are melting point and solubility, which are **dependent on:**

-Degree of Saturation [more significant]

-Chain Length

Short chain F.A.	Medium-chain F.A.	Long chain F.A.
They are liquid in nature	Solids at room temperature	Solids at room temperature
Water-soluble	Water-soluble	Water-insoluble
Volatile at RT	Non-volatile at RT	Non-volatile
Acetic, butyric, caproic	Caprylic & capric F.A.	Palmitic and stearic F.A

◊ Naming Fatty Acids:

RECALL:

Number	prefix	Number	prefix	Number	prefix
1	Mono-	5	Penta-	9	Nona-
2	Di-	6	Hexa-	10	Deca-
3	Tri-	7	Hepta-	20	Eico-
4	Tetra-	8	Octa-		

NOTE: 11 – 19; they have compound names, **i.e.**:

14 = 4 + 10 = Tetradeca

18 = 8 + 10 = Octadeca

Formula: No. of C - a of deca (Depending on **no. of double bonds**) **0** = a **1** = e **2** = die **3** = trie - noic acid

Description of a Fatty Acid:

(ω#, #: #, $\Delta^{\#,\#,\#,\dots}$), where;

ω# = رقم أول كربونة عليها رابطة ثنائية بعد بدء التعداد من الكربونة الأبعد عن المجموعة الوظيفية باعتبار تلك الكربونة هي الرقم 1

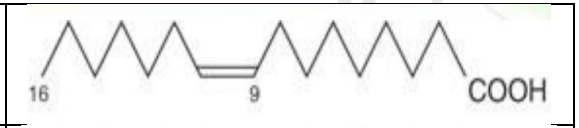
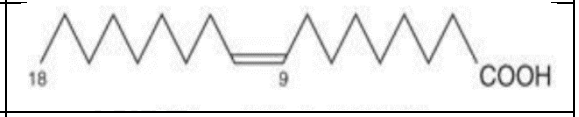
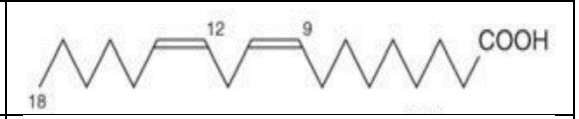
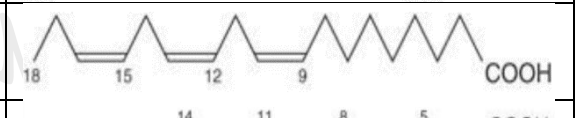
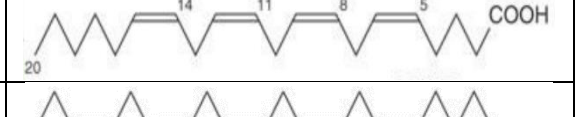
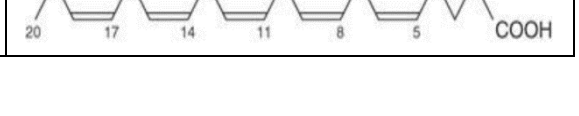
= عدد الكربونات في الجزيء

= عدد الروابط الثنائية في الجزيء

= رقم الكربونة التي تحمل الرابطة الثنائية

Exercises:

Name Each Molecule and Describe it too:

1	
2	
3	
4	
5	
6	

Answer:

No.	Systematic Name	Description
1	Hexadecenoic acid	(ω7, 16:1, Δ^9)
2	Octadecenoic acid	(ω9, 18:1, Δ^9)
3	Octadecadienoic acid	(ω6, 18:2, $\Delta^{9,12}$)
4	Octadecatrienoic acid	(ω3, 18:3, $\Delta^{9,12,15}$)
5	Eicotetrenoic acid	(ω6, 20:4, $\Delta^{5,8,11,14}$)
6	Eicopentenoic acid	(ω3, 20:5, $\Delta^{5,8,11,14,17}$)

Common Names:

1	Palmitoleic Acid
2	Oleic Acid
3	Linoleic Acid
4	Linolenic Acid
5	Arachidonic Acid
6	Eicosapentaenoic Acid

NOTE:

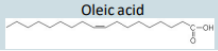
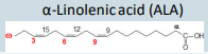
Linoleic acid: precursor of **arachidonates**

Linolenic acid: precursor of **EPA** and **DHA**

-Some Common Fatty Acids:

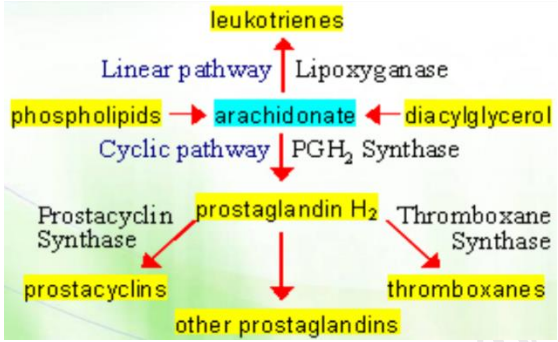
Number of carbons	Number of double bonds	Common name	Systematic name	Formula
14	0	Myristate	n-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	n-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	n-Octadecanoate	$CH_3(CH2)_{16}COO^-$
18	1	Oleate	cis-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH=CH(CH_2)_7COO^-$
18	2	Linoleate	cis,cis-Δ^9,Δ^{12}-Octadecadienoate	$CH_3(CH_2)_4CH=CHCH_2CH(CH_2)_7COOH$
18	3	Linolenate	all-cis-$\Delta^9,\Delta^{12},\Delta^{15}$-Octadecatrienoate	$CH_3CH_2(CH=CHCH_2)_3(CH_2)_6COOH$
20	4	Arachidonate	all-cis-$\Delta^5,\Delta^8,\Delta^{11},\Delta^{14}$-Eicosatetraenoate	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2COOH$

-Some Common Fatty Acids (In the Omega- Naming):

Numerical Symbol	Common Name and Structure	Comments
$18:1^{\Delta9}$	Oleic acid 	Omega-9 monounsaturated
$18:2^{\Delta9,12}$	Linoleic acid 	Omega-6 polyunsaturated
$18:3^{\Delta9,12,15}$	α-Linolenic acid (ALA) 	Omega-3 polyunsaturated
$20:4^{\Delta5,8,11,14}$	Arachidonic acid 	Omega-6 polyunsaturated
$20:5^{\Delta5,8,11,14,17}$	Eicosapentaenoic acid (EPA) 	Omega-3 polyunsaturated (fish oils)
$22:6^{\Delta4,7,10,13,16,19}$	Docosahexaenoic acid (DHA) 	Omega-3 polyunsaturated (fish oils)

◊ Eicosanoids:

-Derived from Arachidonic Acid

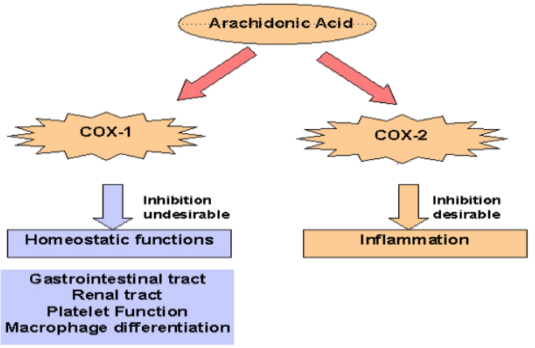


-Eicosanoids and their Functions:

Eicosanoid	Function(s)
Prostaglandins	• Induction of inflammation • Inhibition of platelet aggregation, thus; inhibition of blood clotting
Prostacyclin	• An inhibitor of platelet aggregation • A vasodilator
Thromboxane	• Induction of platelet aggregation • Constriction of smooth muscles
Leukotrienes	• Constriction of smooth muscles, thus; induction of asthma

-Aspirin:

A medication that targets both COX 1 and COX 2. **RECALL:**



Thus, no inflammation but with *side effects*.
The Aim is to target COX 2 only, **HOW?**
By using **Celebrex** [Celecoxib capsules]
(With a strong warning of side effects on the label)

-Omega Fatty Acids:

Molecule	Function(s)
Omega-3 fatty acids; **α-linolenic Acid → Eicosapentaenoic Acid (EPA) → Docosahexaenoic Acid (DHA)**	• They reduce inflammatory reactions by: -Reducing conversion of arachidonic acid into eicosanoids -Promoting synthesis of anti-inflammatory molecules

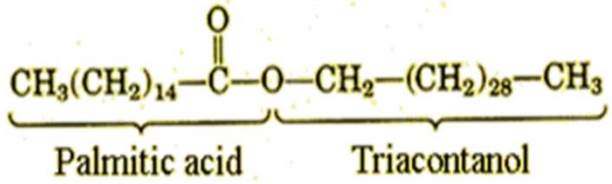
Omega-6 fatty acids; Arachidonic Acid	• Stimulates platelet and leukocyte activation • Signals pain • Induces bronchoconstriction • Regulates gastric secretion
Omega-9 fatty acids; Oleic Acid	• Reduces cholesterol in the circulation

SIMPLE LIPIDS:

***Waxes:**

A monohydric alcohol (C16 ~ C30 -higher molecular weight than glycerol-) esterified to long-chain fatty acids (C14 ~ C36).

i.e. Palmitoyl alcohol



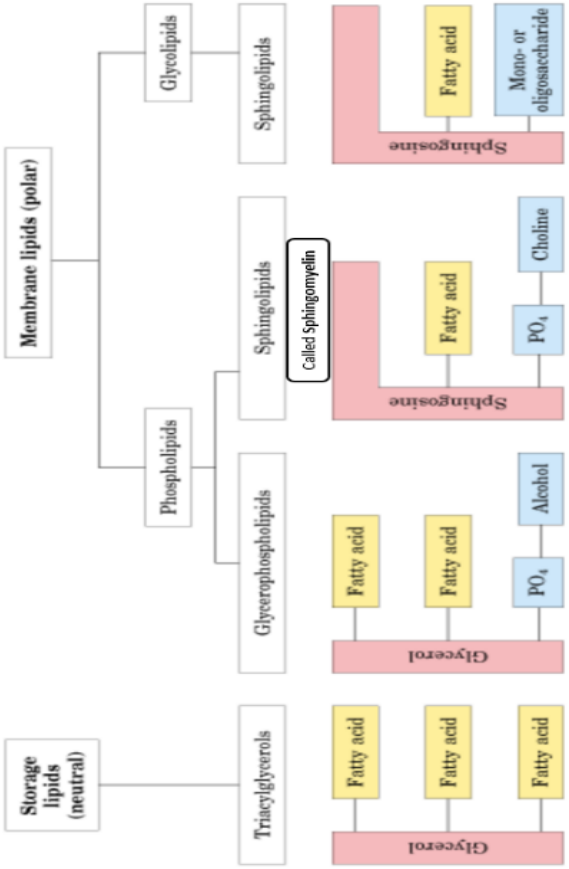
Other Examples:

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

-Features of Waxes:

- Insoluble in water
- Are not easily hydrolyzed (fats) & are indigestible by lipases
- Are very resistant to rancidity (نخر)
- Are of no nutritional value
- Coatings that prevent loss of water by leaves of plants

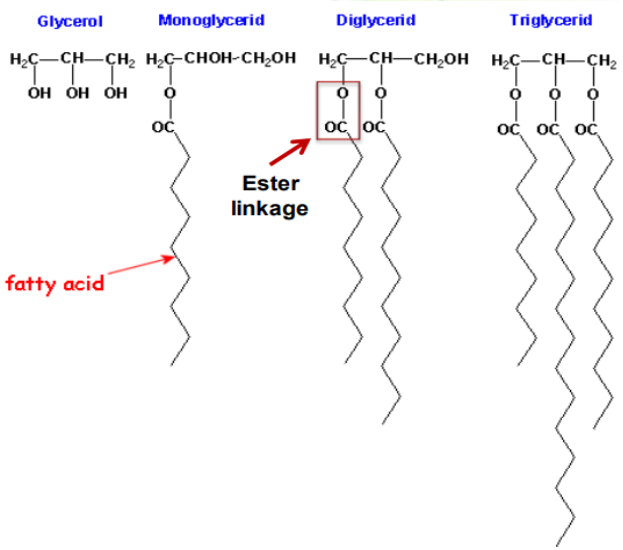
COMPLEX LIPIDS:



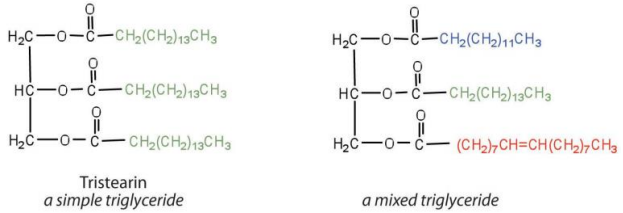
***Storage Lipids:**

◊ Triglycerides:

-Classification *According to* Number of Fatty Acids Attached to the Glycerol Backbone:



-Classification *According to* What Fatty Acids are Attached to the Glycerol Backbone:



Tristearin
a simple triglyceride

a mixed triglyceride

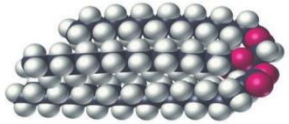
NOTE: In a *mixed* Triglyceride, differences in fatty acids are:

- Length
- Degree of Saturation

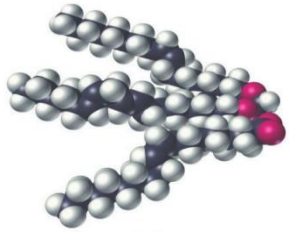
-Solid vs. Liquid Fats:

Vegetable oils consist almost entirely of unsaturated fatty acids, whereas **animal fats** contain a much larger percentage of saturated fatty acids.

This is the primary reason for the different melting points of fats and oils.

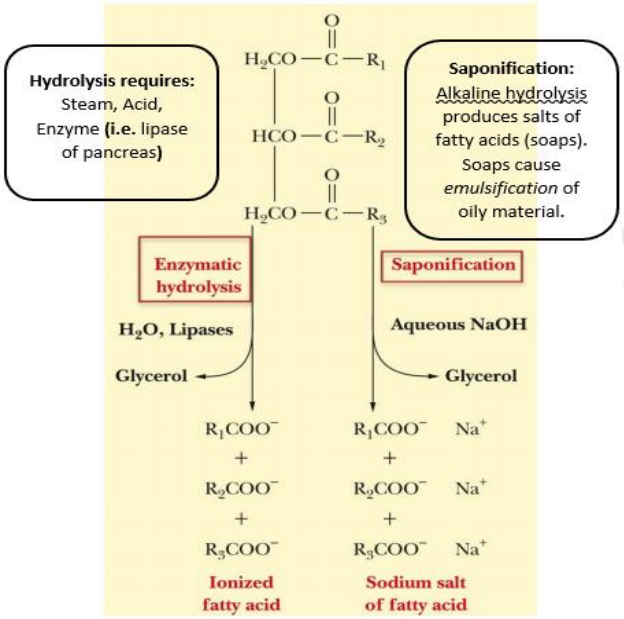


A fat

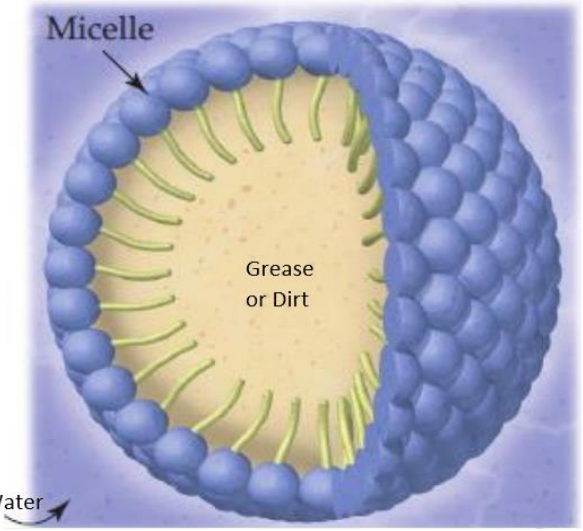


An oil

-Saponification; A Reaction of Triglycerides:

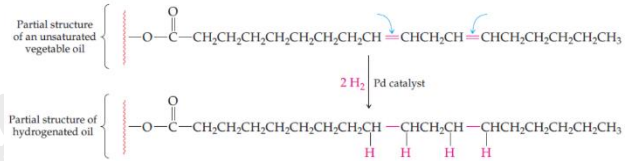


-Using a Soap; the Formation of Micelles:

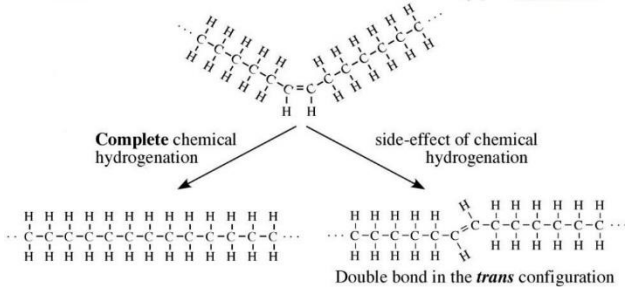


-Hydrogenation:

The process of saturating the unsaturated fatty acids. [Alkene → Alkane]



- Partial hydrogenation converts some, but not all, double bonds into single bonds generating (trans fats).



The primary health risk identified for trans-fat consumption is an elevated risk of Coronary Heart Disease (CHD). Atherosclerosis may also occur.

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

Nutrition Facts

Serv Size 1 Tbsp (14g)
Servings: About 24
Calories 80
Calories from Fat 80

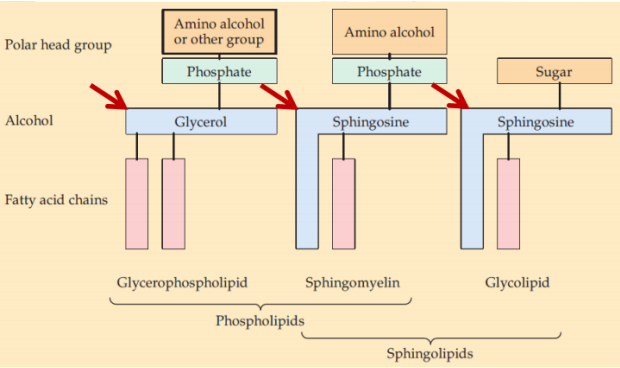
Amount/Serving	% DV*	Amount/Serving	% DV*
Total Fat 8g	**12%**	**Cholesterol** 0mg	**0%**
Sat Fat 2.5g	**13%**	**Sodium** 85mg	**4%**
Trans Fat 0g		**Total Carb** 0g	**0%**
Polyunsat Fat 3g		Sugars 0g	
Monounsat Fat 2.5g		**Protein** 0g	

Vitamin A 15% • Vitamin D 15%
Vitamin B6 35% • Vitamin B12 20% • Vitamin E 15%
Not a significant source of dietary fiber, Vitamin C, Calcium and Iron

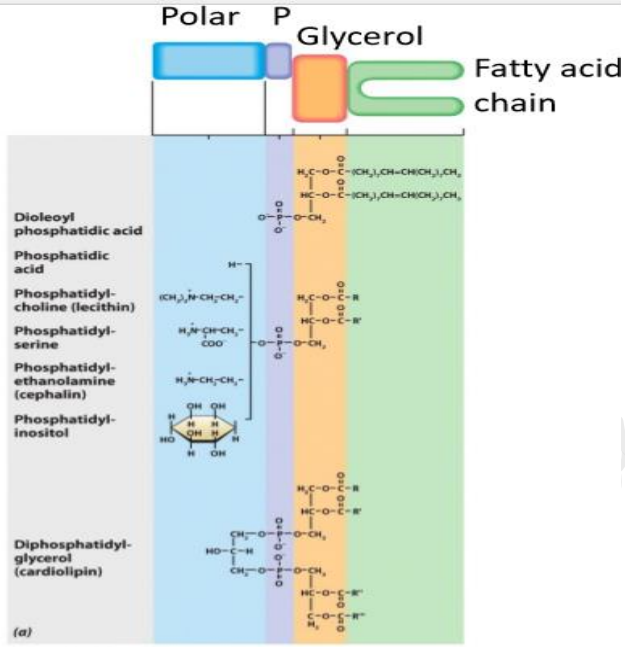
*Percent Daily Values (DV) are based on a 2,000 calorie diet.

INGREDIENTS: Natural Oil Blend (palm fruit, soybean, fish, canola and olive oils), water, plant sterols; contains less than 2% of salt, sorbitan esters of fatty acids, monoglycerides of vegetable fatty acids, natural and artificial flavors, TBHQ (to preserve freshness), potassium sorbate, lactic acid, soy lecithin, vitamin B12, vitamin E acetate,vitamin B6, beta carotene (color), vitamin A palmitate, calcium disodium EDTA, Vitamin D3.

***Membrane Lipids:**



◊ **Phospholipids; Glycerophospholipids (Phosphoacylglycerols):**
[The most prevalent class of membrane lipids**]**



NOTE: Simplest = Phosphoric Acid

-Classification of Glycerophospholipids:

Phosphatidic acids;
-The simplest (basic) glycerophospholipid

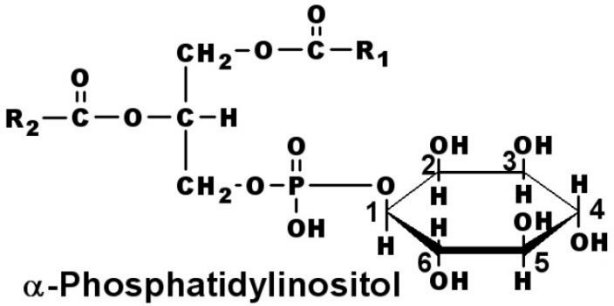
Phosphatidylcholine (lecithin);
-Most abundant membrane lipid
-Used in Food Production
-Snake venom contain *lecithinase*, which hydrolyzes polyunsaturated fatty acids and converting lecithin into *lysolecithin*; thus, hemolysis of RBCs
-Because of their amphipathic nature, they act as ***emulsifying agents***, that is substances that can surround nonpolar molecules and keep them in suspension in water.

https://www.youtube.com/watch?v=7I8GXmpKrVg

Cephalins:
- **Phosphatidylethanolamine**
- **Phosphatidylserine;**

-Abundant in brain

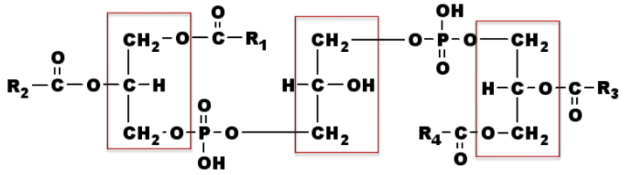
Inositides (Phosphatidylinositol);
-**Found in** brain tissue **[**Concentrated on the cytosolic side of cells**]**
-**Structure:** Glycerol, saturated FA, unsaturated FA, phosphoric acid, & inositol
Nitrogenous base: cyclic sugar alcohol (inositol)



-**Functions:**
- Major component of cell membrane
- Sends messages across cell membranes
- Second messenger during signal transduction **[**On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5- diphosphate produces diacyl-glycerol (DAG) & inositol triphosphate (IP3); which liberates calcium**]**

Cardiolipin;
-Di-phosphatidyl-glycerol
-**Found in** the inner membrane of mitochondria
-Initially **isolated from** heart muscle (cardio)

-**Structure:** 3 molecules of glycerol, 4 fatty acids & 2 phosphate groups



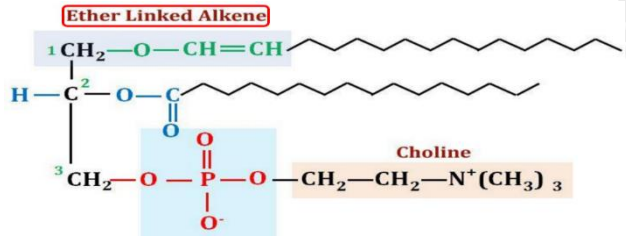
Plasmalogens;

-They are found in the cell membrane phospholipids fraction of brain, muscle, liver and semen.

-They have a protective role against **reactive oxygen species** (**i.e.** Oxygen radicals, H_2O_2)

-**Structure:**

Precursor: Dihydroxyacetone phosphate + Unsaturated fatty alcohol at C1 connected by ether bond. In mammals, at C3, phosphate + ethanolamine or choline



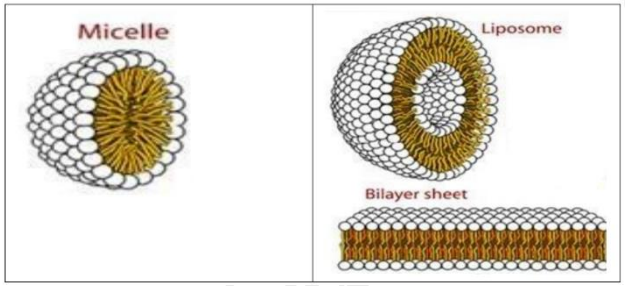
-**Major classes of Plasmalogens:**

Ethanolamine plasmalogen (myelin-nervous tissues)

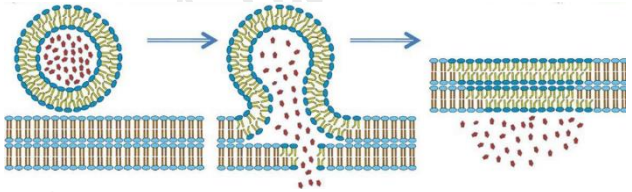
Choline plasmalogen (cardiac tissue); Platelet activating factor

Serine plasmalogens

-The Different Structures of Phospholipids:



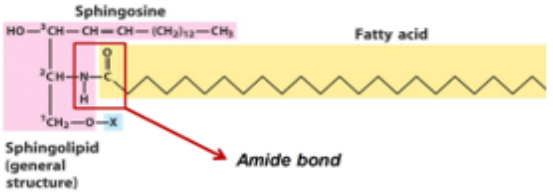
•**Uses of Liposomes: Delivery**



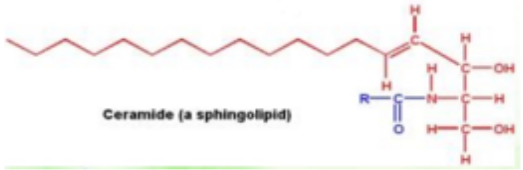
Introduction to Sphingolipids:

Found in the plasma membranes of all eukaryotic cells **and is highest in** the cells of the central nervous system.

The core of sphingolipids is the long-chain amino alcohol, sphingosine.



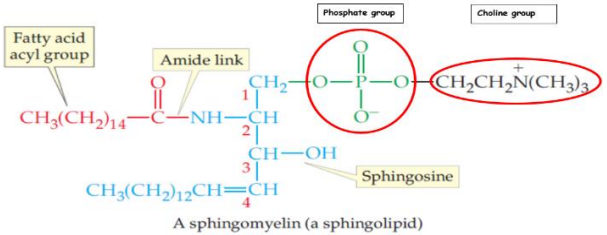
The simplest sphingolipid is Ceramide.



◊ **Phospholipids; Sphingomyelin (A Type of Sphingolipids):**

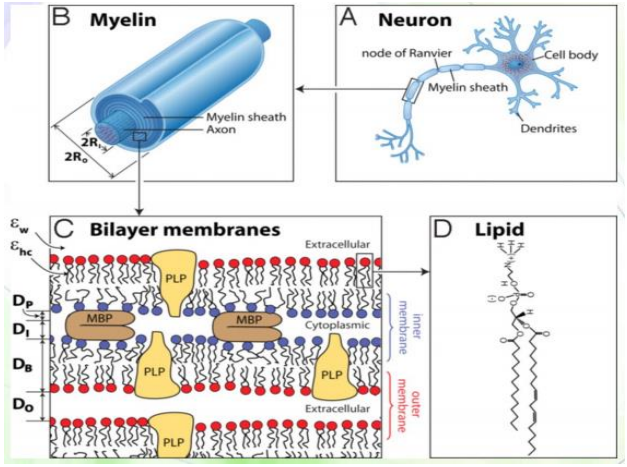
-A major component of the coating around nerve fibers

-The group attached to C1 is a phosphocholine.



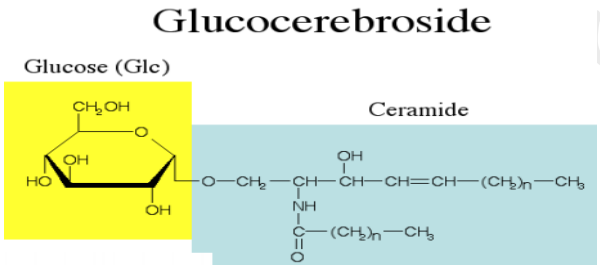
A sphingomyelin (a sphingolipid)

-Zooming into the Myelin:

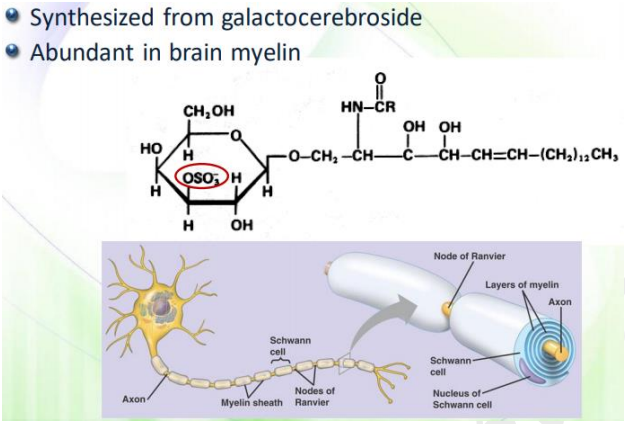


◊ **Glycolipids; Sphingolipids:**
Sphingolipids containing carbohydrates attached at C-1.
-Found on cell membranes **and act as** cell surface receptors that can function in cell recognition (**i.e.** Pathogens) and chemical messengers

-Types of Glycolipids:
•**Cerebrosides:** the simplest glycolipids, contain a single hexose (galactose or glucose).

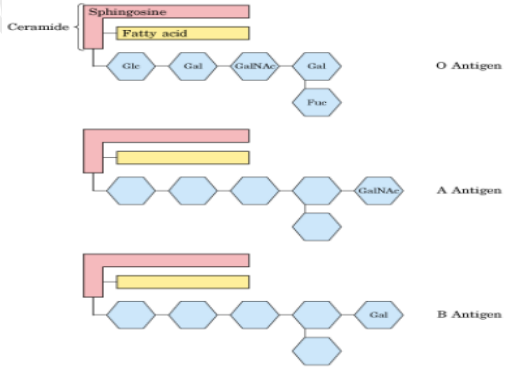


(Sulfides: Galactocerebroside Derivative)
- Synthesized from galactocerebroside
- Abundant in brain myelin



•**Globosides** & •**Gangliosides** are more complex glycolipids.
Both contain glucose, galactose, and N-acetyl galactosamine, but **gangliosides** must also contain sialic acid.
NOTE:
Gangliosides are targeted by **cholera toxin** in the human intestine.

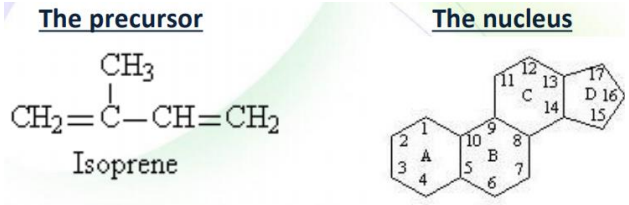
-As proteins do, sphingolipids affect blood groups.



WRAP UP [Sphingolipids]:

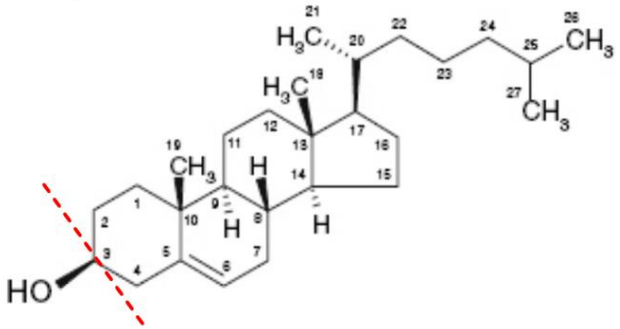
Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

CYCLIC LIPIDS: STEROIDS
***Structure:**



NOTE: The steroid nucleus is composed of 17 carbons **within** 4 rings.

***The Common Steroid: Cholesterol**
-Composed of 27 carbons.



[Amphipathic]

-Products of Cholesterol:

- Hormones

i.e. Sex hormones (Androgens, Estrogens, Progestins)

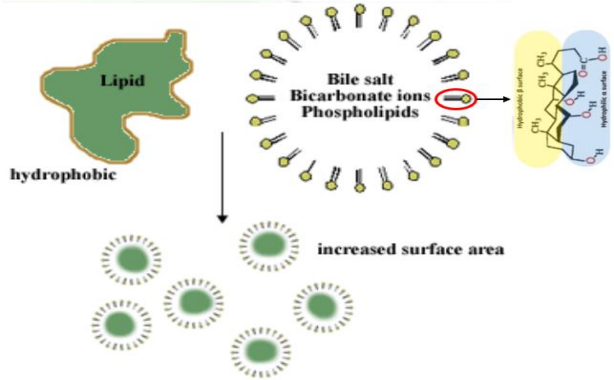
- Some vitamins such as vitamin D

Vitamins A, D, E, and K are made from **isoprenoids**

Vitamin D -*in specific*- is made from **cholesterol**

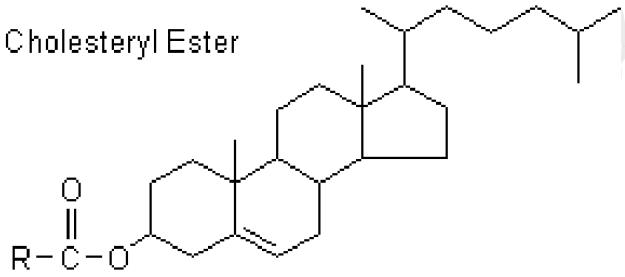
- Bile acids (**for** intestinal absorption of fat)

HOW??



-Cholesterol Esters:

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

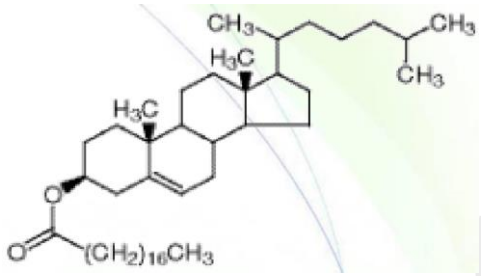


Exercise:

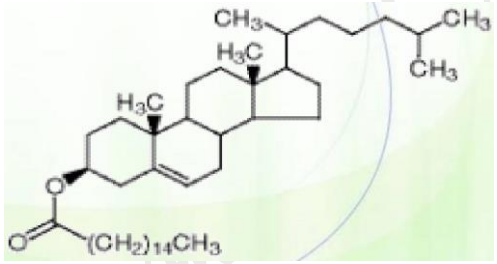
Name Each of the Following Molecules.

[Strategy:

Cholesterol + (Acid Name -~~ic~~)-ate**]**



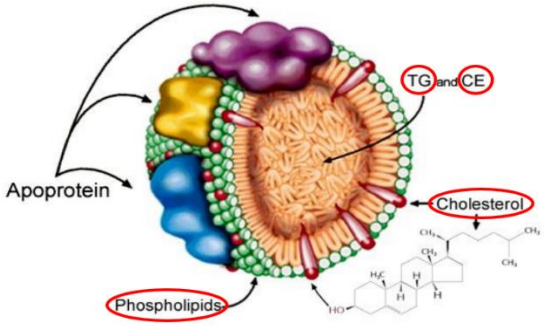
Answer: Cholesterol Stearate



Answer: Cholesterol Palmitate

***Lipids Transporting:**

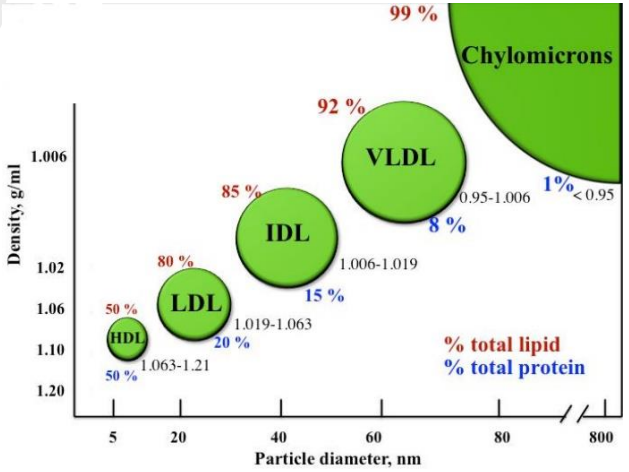
-By a lipoprotein (micelle structured molecule)



-Function:

Transport of different types of lipids (cholesterol, cholesterol esters [CE], phospholipids & triacylglycerols [TG]) in blood plasma.

-Different Types of Lipoproteins:



NOTE:

As lipid content increases, the density decreases

As protein content increases, the density increases

- **The Dark Side of LDL:**

LDL can accumulate in blood vessels causing **atherosclerosis**, thus, **heart attacks**.

CELL MEMBRANE:

***Introduction:**

-The hypothesized model is the fluid mosaic model

-Components: 45% lipid, 45% protein and 10% carbohydrate

[They exist side by side without forming some other substance of intermediate nature**]**

***Composition:**

-The two leaflets of the membrane *differ* from each other in the composition.

The outer leaflet: phosphatidylcholine, sphingomyelin and glycolipids (cell recognition)

The inner leaflet: phosphatidylethanolamine, phosphatidylserine and phosphatidylinositol (signaling)

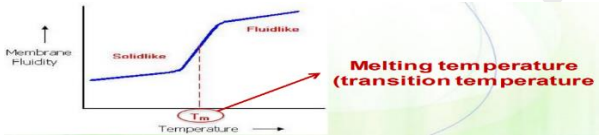
***Fluidity:**

◊ Degree of Saturation

More saturated phospholipids, less fluidity and vice versa.

◊ Temperature

Higher temperature, more fluidity and vice versa.



◊ Cholesterol

[In animal cells only. Plant cells have another steroid. Prokaryotic cells have non**]**

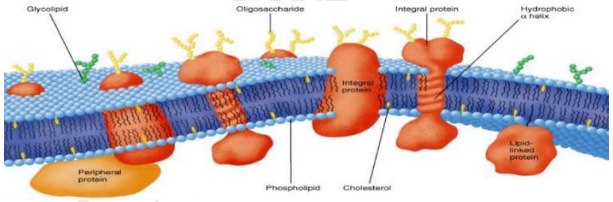
-It stabilizes the extended straight-chain arrangement of saturated fatty acids by *Van der Waals interactions*.

-Cholesterol makes a membrane less solid at low temperatures (**It** interferes with close packing of fatty acid tails in the crystal state)

and

more solid at high temperatures (**It** decreases the mobility of hydrocarbon tails of phospholipids)

***Membrane Proteins:**



Peripheral proteins:

They are associated with the exterior of membranes (or *loosely* with the phosphate head of a phospholipid) **via** noncovalent interactions

Integral membrane proteins:

They are anchored into membrane via hydrophobic regions

Lipid-anchored:

They are associated via a lipid group

◊ Peripheral Membrane Proteins:

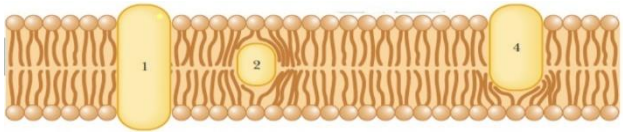
They are associated with membranes but do not penetrate the hydrophobic core of the membrane.

Often associated with integral membrane proteins.

They are not strongly bound to the membrane and can be removed without disrupting the membrane structure (treatment with mild detergent)

◊ Integral Membrane Proteins:

Can be associated with the lipid bilayer in several ways;



The membrane integral domains are:

1. Single or multiple
2. α-helix or β-sheet

Some can form channels.

-Functions:

Transport:

Membranes are impermeable barrier.

Proteins can be carriers or channels

Signaling:

Protein receptors and small molecules (some can be lipids themselves)

Catalysis:

Enzyme-linked receptors

Q-BANK FROM PAST PAPERS:

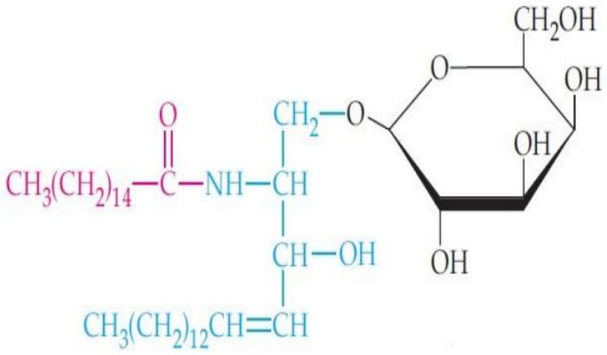
1) Lecithin is a designation of:

A) Phosphatidylinositol
B) Phosphatidylserine
C) Cardiolipin
D) Phosphatidylcholine
E) Plasmalogen

2) Which of the following is false regarding vLDL?

A) It transports dietary TG to the liver
B) Its diameter is larger than HDL
C) It contains cholesterol
D) All of the above are false
E) None of the above is false

3) What is the following molecule?

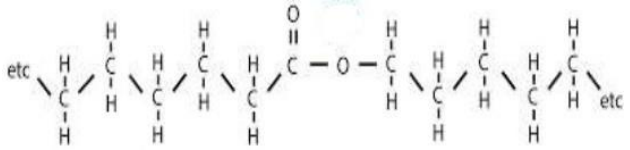


A) Glucocerebroside
B) Ceramide
C) Galactocerebroside
D) Sphingomyelin
E) Globoside

4) Which of the following is correct regarding integral proteins?

A) They can be affected by mild detergents
B) They contain a hydrophobic region embedded in the membrane
C) They are exposed from the extracellular side only
D) All of the above are correct
E) None of the above is correct

5) Which of the following is false regarding this molecule?



A) Humans are unable to digest it and it is useless
B) Insoluble in water
C) Made of two fatty acids
D) Has no nutritional value
E) The ester group is the only hydrophilic part of it

6) Aspirin works through inhibition of the production of:

A) Prostaglandins
B) Prostacyclin
C) Thromboxane
D) Leukotrienes
E) All Eicosanoids

7) What's true about the structure of the following fatty acid?

A) Palmitate
B) Precursor for eicosanoids
C) Trans fatty acid
D) Cis-delta 9 hexadecenoic acid
E) More than one of the above

8) Which one of the following common in all sphingolipid?

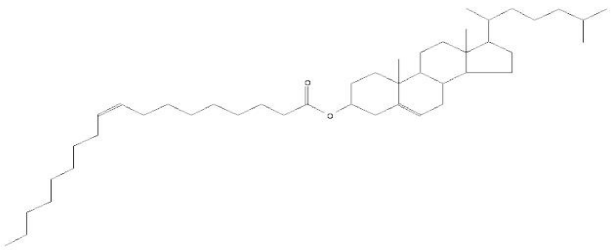
A) Glycerol
B) Phosphate
C) N-acetylgalactoamine
D) Ceramide
E) More than one of the above

9) Fatty acid 16:1, Δ^9 is the structure of:

A) Stearic acid
B) Oleic acid
C) Oleinoic acid
D) Mystiric acid
E) Palmitoleic acid

10) After you test a patient, it turns out that the material surrounding her nerves is destroyed. This material is:
A) Phosphatidylinositol
B) Cerebrosides
C) Sphingomyelins
D) Glycoproteins
E) Cephalin

11) The name of the following structure is:



A) Cholesteryl oleate
B) Cholesteryl palmitate
C) Cholesteryl stearate
D) Cholesteryl laurate
E) None of the above

12) The following membrane lipid is a major component of the inner mitochondrial membrane:
A) Lecithin
B) Cephalin
C) Cardiolipin
D) Glycolipids
E) Phosphatidylinositol

13) Gangliosides contain all the following EXCEPT:
A) Fatty acid
B) Phosphate
C) Ceramide
D) Hexose
E) N-acetyl neuraminic acid (Sialic acid)

14) All sphingolipids have in common:
A) Ceramide
B) Phosphorylcholine
C) N-acetylneuraminic acid
D) Glycerol
E) Phosphate

15) Arrange the following fatty acids according to their melting point starting from the largest to the smallest (oleic acid, linoleic acid, palmitic acid and palmitoleic acid):
A) palmitic acid, oleic acid, palmitoleic acid and linoleic acid
B) palmitic acid, palmitoleic acid, oleic acid and linoleic acid
C) linoleic acid, palmitoleic acid, palmitic acid and oleic acid
D) linoleic acid, palmitoleic acid, oleic acid and palmitic acid
E) oleic acid, linoleic acid, palmitoleic acid, and palmitic acid

16) All of the following are from cholesterol except:
A) Testosterone
B) Vitamin D
C) Thromboxane
D) Estradiol
E) None of the above

17) Regarding the COX isoenzymes. All are true except:
A) COX-1 is present in all tissues
B) COX-2 is inducible by inflammatory stimuli
C) Aspirin inhibits COX-1 and COX-2
D) All of the above
E) None of the above

→ Answers:

Q. No.	Ans.	Q. No.	Ans.
1	D	10	C
2	A	11	A
3	A	12	C
4	B	13	B
5	C	14	A
6	A	15	A
7	D	16	C
8	D	17	E
9	E		

Done by: Abdullah Al-Jaouni