11

BIOCHEMISTRY

faculty of medicine - JU2017

Sheet ○ Slides

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Sphingolipids :

Complex lipids which are really important and found in the plasma membranes of all eukaryotic cells, and is highest (abundant) in the cells of the central nervous system.

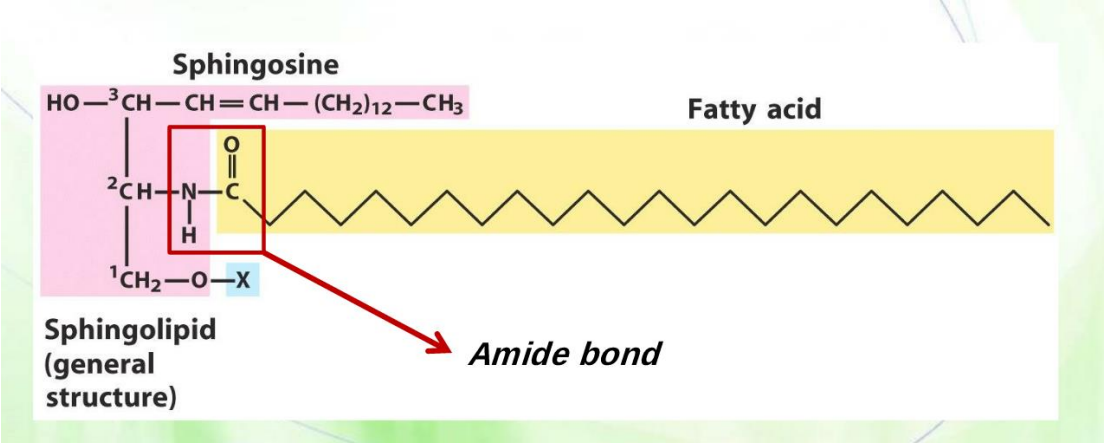
Structure :

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

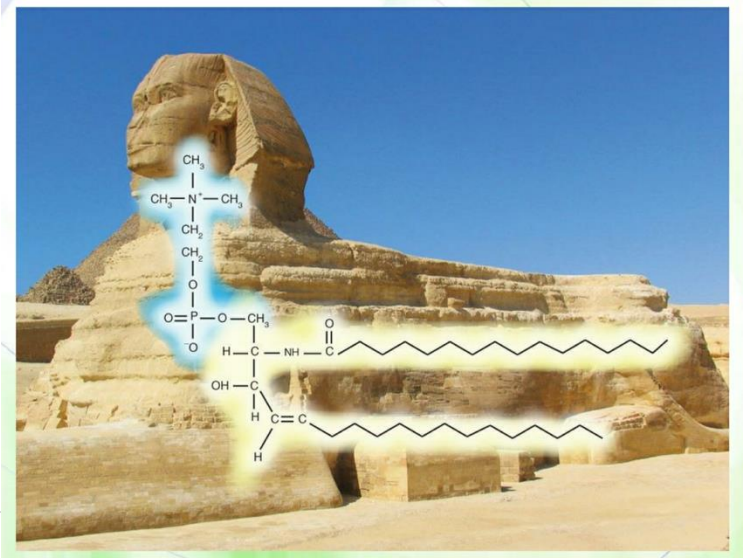
Sphingolipids are made of a backbone (in pink) called sphingosine. A fatty acid chain is attached to this backbone, there is also an oxygen with head group that can be any type to differentiate sphingolipids from each other.

Sphingosines also have a long hydrocarbon chain with an alkene group, plasmalogens have an alkene group too, so how to distinguish between them?

From the nitrogen group (amide bond) at the end of the fatty acid chain in sphingolipids which is NOT found in plasmalogens .



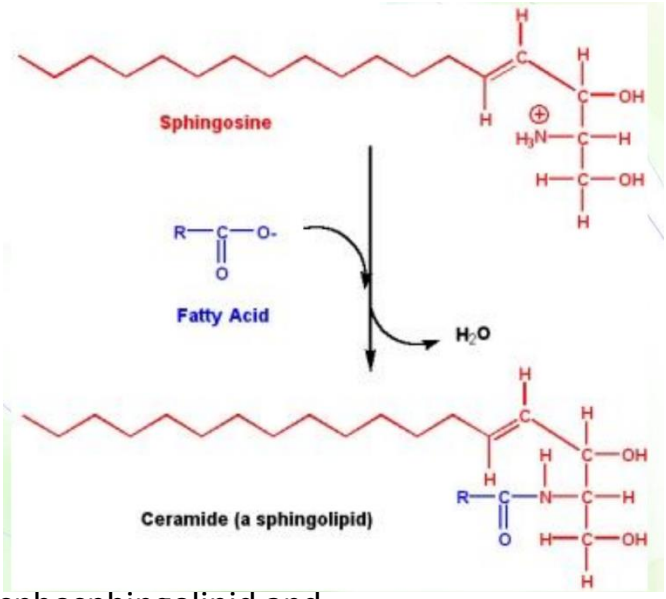
The name of sphingolipids came from sphinges (not because they have the same structure but because when sphingolipids were discovered, they were called mysterious lipids, and that's why they were given the name of sphingolipids).



We've said before that the simplest phospholipid is: phosphatidate (phosphatidic acid)

The simplest sphingolipid is: Ceramide

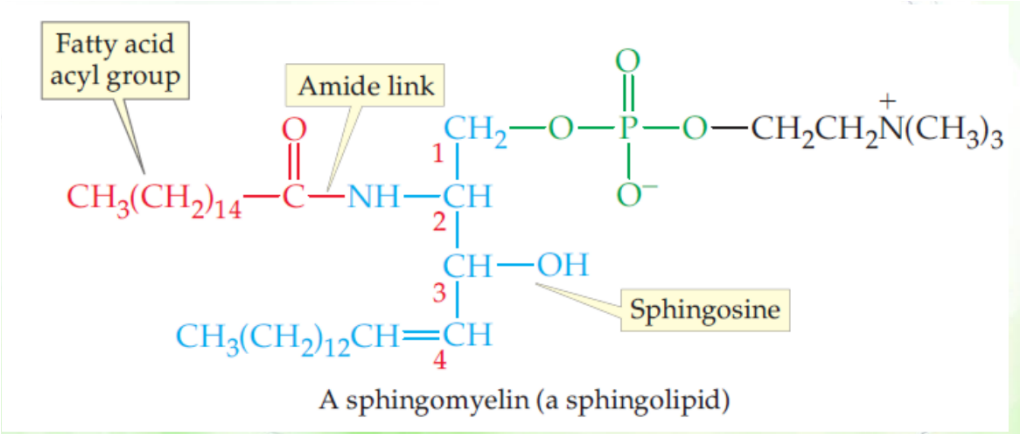
Note: on the head group, we can put different groups and according to that we will have different types of sphingolipids that can be divided into 2 classes:



1.**Phosphosphingolipid** (phosphate group as a head group, we have only one example which is sphingomyelin.
<< we must be able to distinguish between phosphosphingolipid and glycerophospholipid because both contain phosphate group>>
2.**Glycosphingolipid (Glycolipids)**

Sphingomyelin:

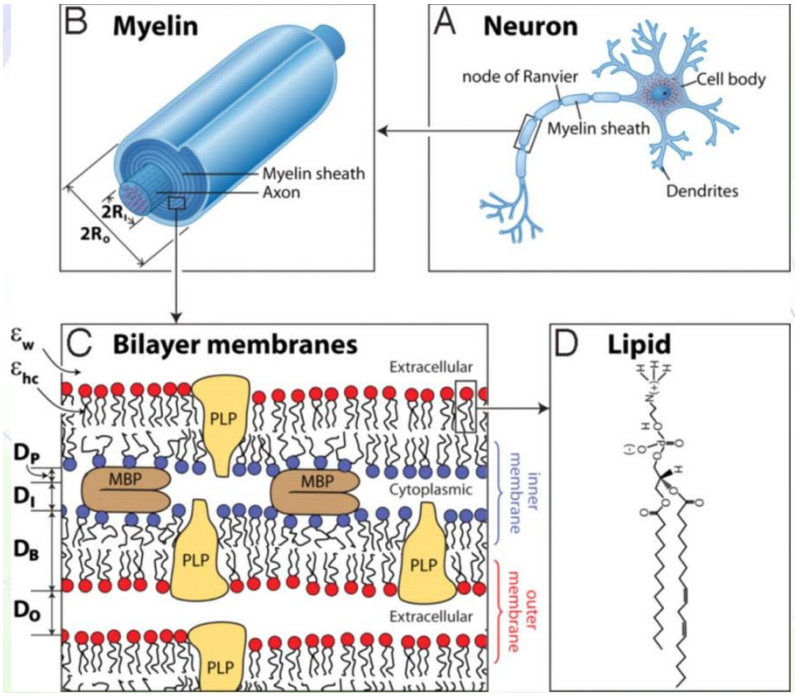
Sphingolipid that is found mainly in the CNS as a major component of the coating around the nerve fibers (axons).
The group attached to C1 is phosphate + choline (phosphocholine).



Myelin sheath provides protection and it is made of layers of lipid structures which are the sphingomyelin.

- Multiple sclerosis (تصلب لويحي متعدد) :

Auto immune disease in which immune cells attack the myelin sheath. This causes a disruption in the transmission of impulses throughout the body. This could be fatal for the patient if left untreated.



Glycolipids :

Sphingolipids can also contain carbohydrates attached to C1 and these are known as glycolipids.

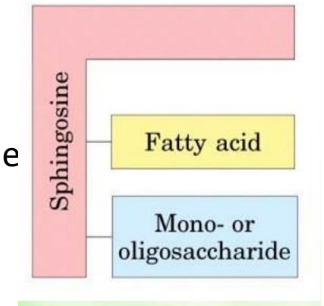
Glycolipids are present on the cell membranes (respectively outside), and act as cell surface receptors that can function in cell recognition. ex: (pathogens) and chemical messengers

Note: Sugars are located on the outside of the cells, except one type (mentioned earlier) >> phosphatidylinositol that functions in signaling.

The type of the sugar molecule determines the type of the glycolipid, we have 3 types:

Cerebrosides
Globosides
Gangliosides

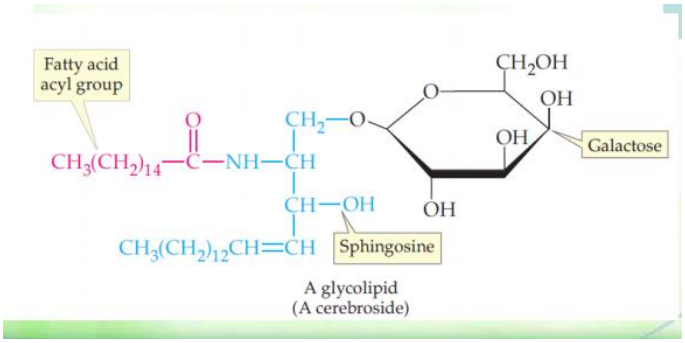
Their name indicates that they are found abundantly in the CNS .

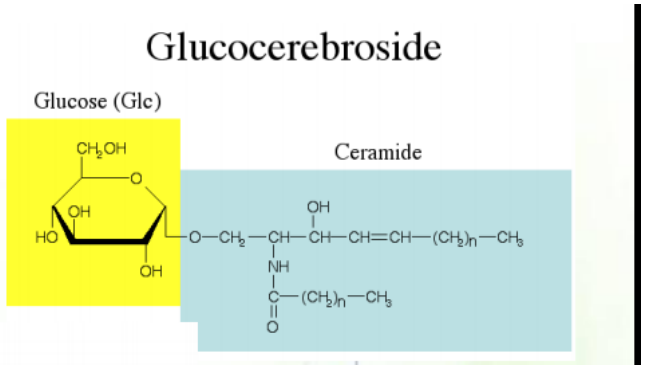


• Cerebrosides: the simplest glycolipid, contain a monosachride (one molecule)
single hexose (galactose or glucose).

Galactocerebroside Glucocerebroside

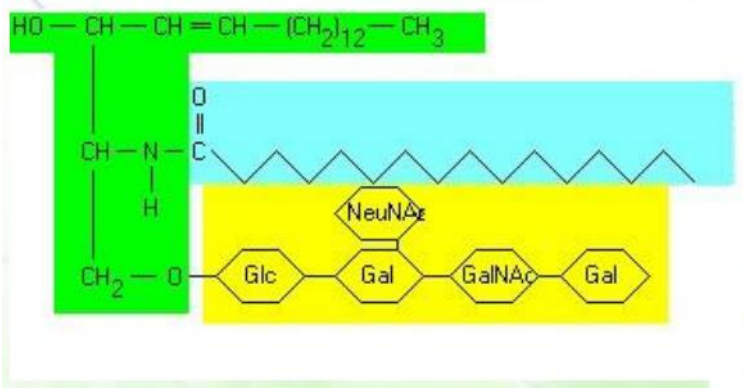
To distinguish between them we look at carbon number 4 of the sugar molecule .

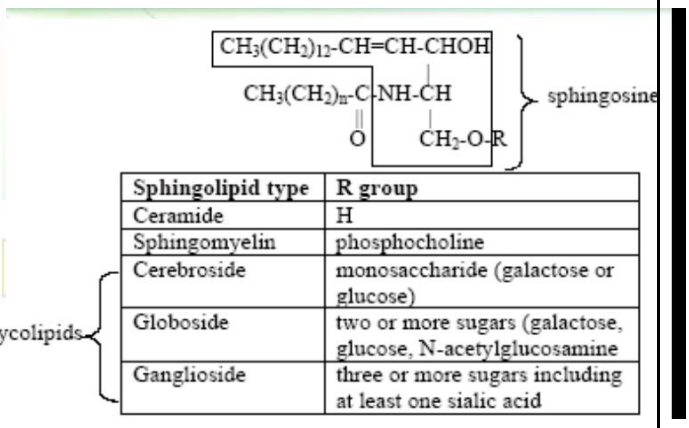




• Globosides and Gangliosides are more complex glycolipids containing a group of sugar molecules (2 or more) . Both contain glucose, galactose, and N-acetylgalactosamine, but **gangliosides must also contain sialic acid as one of the sugar molecules.**

Gangliosides are targeted by cholera toxin in the human intestine .





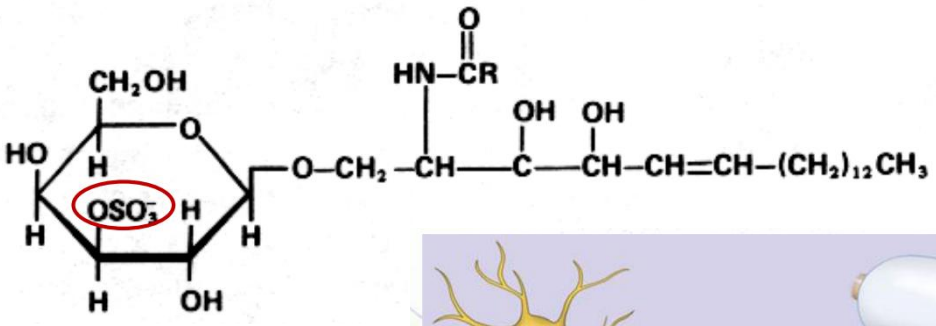
Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine
Ganglioside	three or more sugars including at least one sialic acid

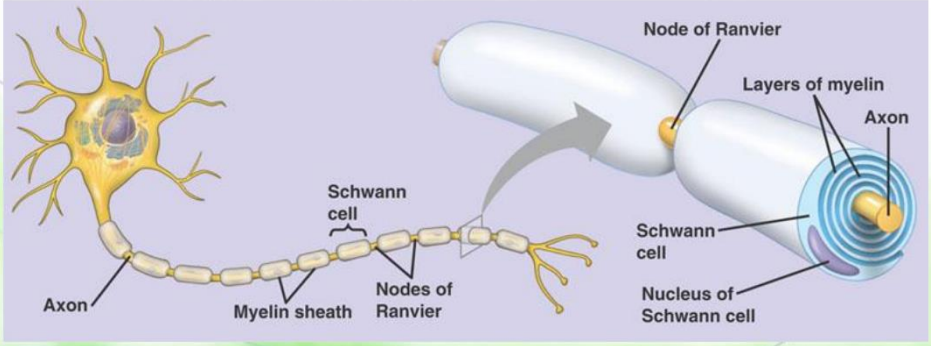
glycolipids

Remember : simplest sphingolipid >> ceramide

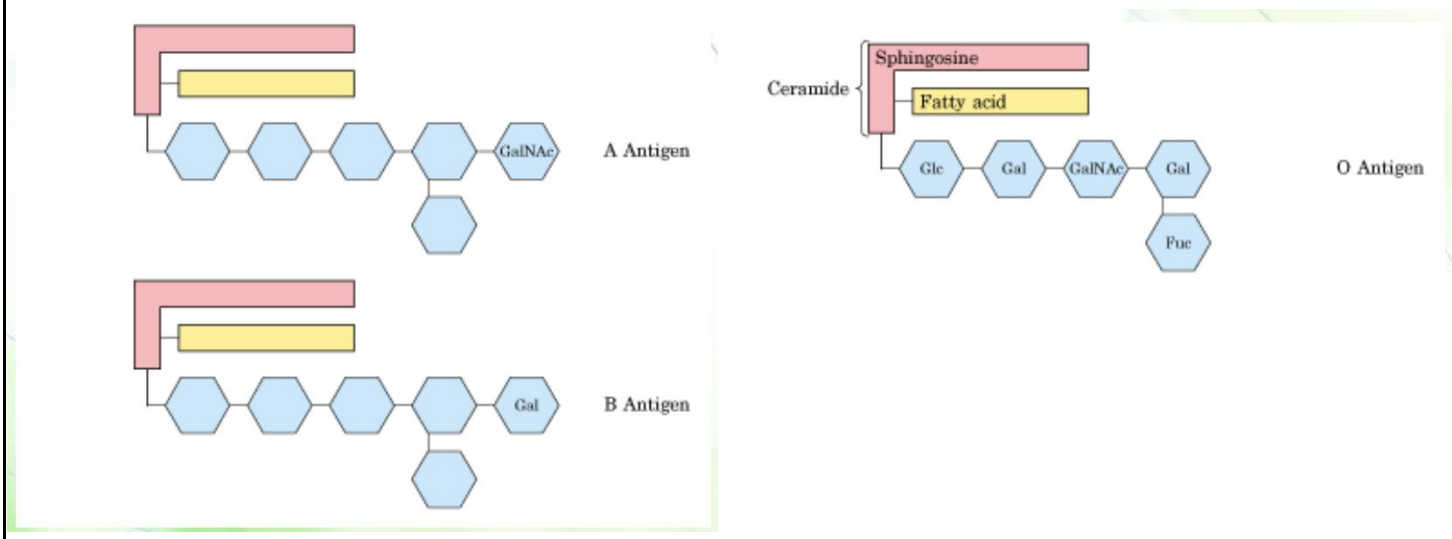
Simplest phosphosphingolipid >> sphingomyelin

If we modify galactocerebroside (by adding sulfate group) → it will now be called Sulfatides, it is also abundant in brain myelin.





Sphingolipids and blood groups: Blood typing (A,B,AB,O) differ from each other according to the sugar molecules which are found on the plasma membrane and attached to sphingolipid (Globoside).



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Lipoproteins :

Combination of proteins + lipids

It's good to take a blood test once during your early adult stage,which is because of genetic disease in lipid metabolism (problem in lipoproteins) >> increasing lipids in blood that may lead to strokes or heart attacks.

Function (purpose) of lipoproteins: Transport different types of lipids (cholesterol ,cholesterol esters , phospholipids & triacylglycerols) in blood plasma .

** intestinal cells absorb lipids, then they are packaged in lipoproteins that carry them in the blood to the liver which they are then carried by another type of lipoprotein in the blood to peripheral tissues (during this step their shape changes from type to type).
** if the peripheral tissues don't need them → they will be carried back to the liver through lipoproteins to get rid of them.
We have different types of lipoproteins, each has its own function and its own source of synthesis such as intestinal cells , liver cells (mainly) , ….
☞Lipoproteins have different purposes according to transport:

Good cholesterol: type of lipoprotein that rescues the body from cholesterol ,it is found in peripheral tissues to transports the cholesterol back to the liver to get it out of our system .

Bad cholesterol: type of lipoprotein that carry lipids to peripheral tissues and it's the one that accumulates in blood causing a heart attack.

** Lipoproteins differ in the type of lipids that they carry, some of them mainly carry triglycerides while others mainly carry cholesterol .

** They have also different sizes (large & small).

** They differ in the lipid to protein ratio (some has high lipid content relative to proteins, others have high protein content relative to lipid) .

(As lipid content increases, the density decreases / as protein content increases, the density increases)

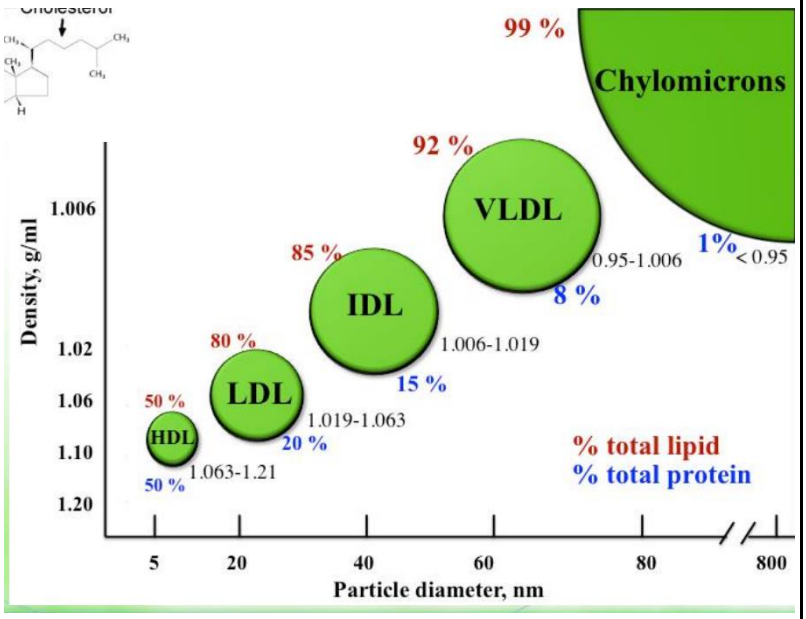
We said that there are three types of lipid structures:

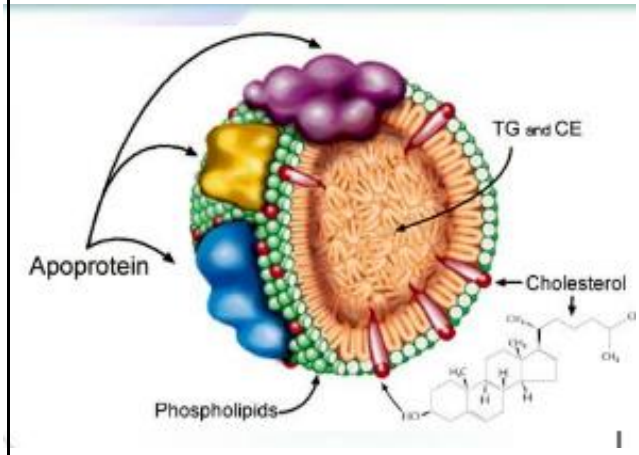
Micelle

Liposome

Lipid bilayer

→Lipoproteins look like micelle (inside we have lipid molecules)





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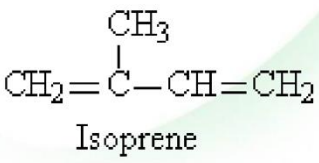
Cholesterol is 27 carbon molecule (it has a steroid nucleus (4 rings) = 17 carbon) AND a carbon chain of 10 carbons .

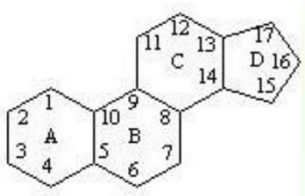
Steroid nucleus made from Isoprenes (5 carbon molecules).

The precursor



Isoprene

The nucleus

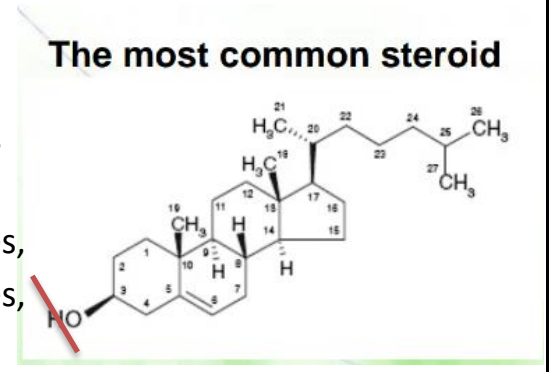


Steroid nucleus

From its structure, cholesterol is amphipathic because of the hydroxyl group , and the rest of the molecule is hydrophobic (non polar).

We can draw a line dividing it into polar and non polar parts.

**Cholesterol is really important , many products are derived from it :

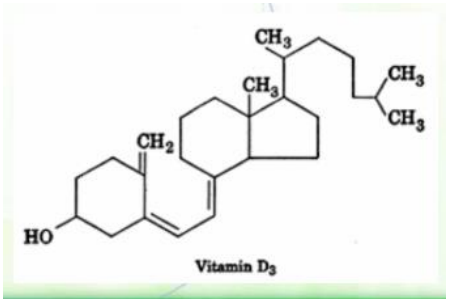


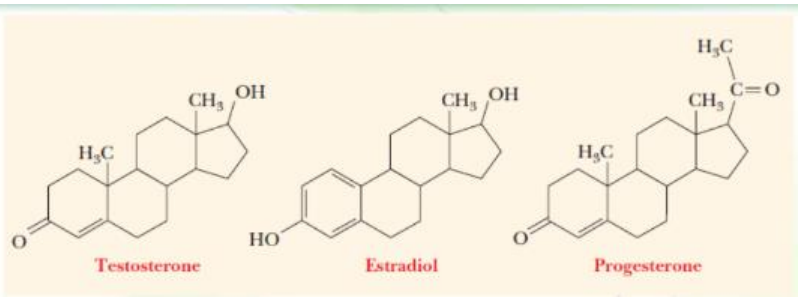
1)**Steroid hormones** such as sex hormones (androgens, estrogens, progestins).

{estrogen is a female hormone but is also found in males, androgen is a male hormone but is also found in females, the difference is in the concentration (amount).

2)**Some vitamins such as vitamin D** (isoprenids → cholestreol → vitamin D)

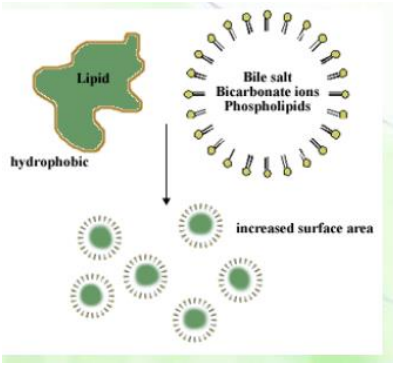
(vitamins A,E,K are made directly from isoprenoids).



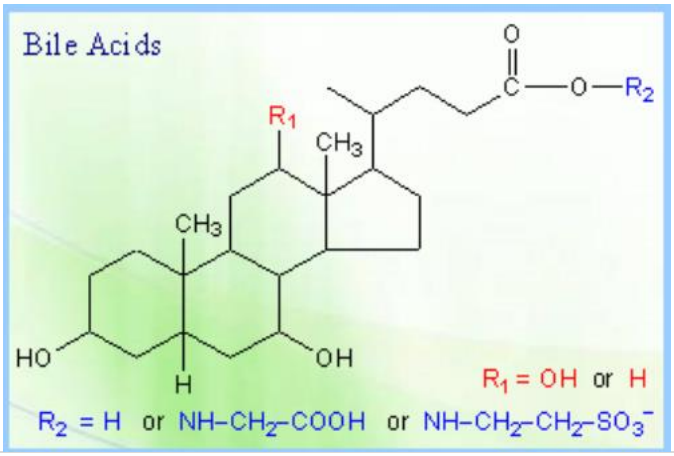


3)**Cholesterol is the source (precursor) of bile acids** which is the yellow material made by the gallbladder.

Bile acids break lipid drops into droplets that will be surrounded by bile acids (bile acids allow fat (lipid droplets) to be absorbed by intestinal cells then they will be carried by lipoproteins to the liver as we've said earlier.



**from the structure of bile acid its also amphipathic , we have different polar groups distributed in the molecule (in the 3D structure we can draw a line), the upper part is hydrophobic and the lower one is the polar groups.

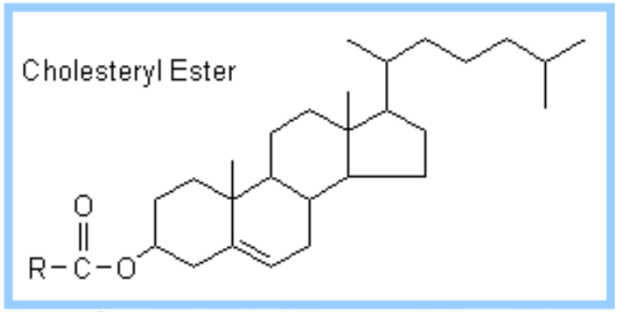


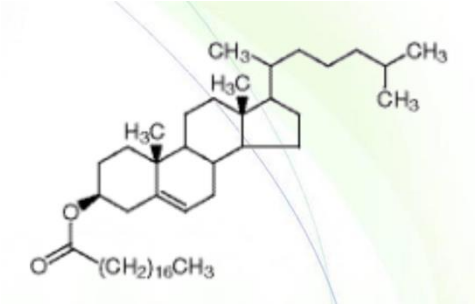
** Fatty acids in the body are mainly in the form of triacylglycerol .

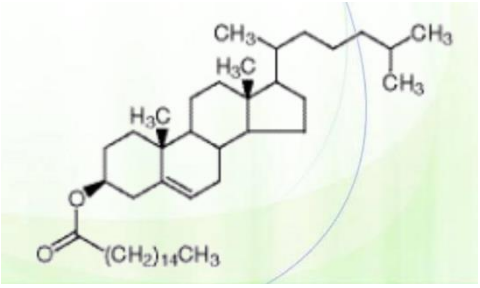
Cholesterol with a fatty acid chain attached to hydroxyl group (-OH) of C3 is called **cholesterol ester.

(different fatty acid chains can be attached to cholesterol).

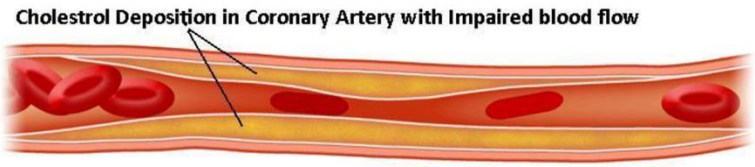
-Name the molecules ??







**Cholesterol is associated with atherosclerosis (deposition of fat in blood vessels) which causes closure of these vessels and leads to heart attacks and strokes , especially bad cholesterol .



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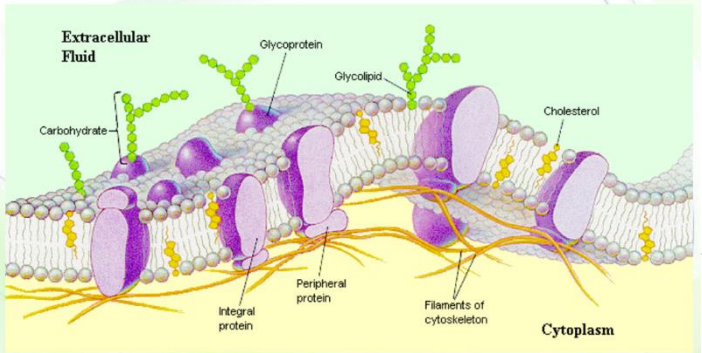
**Plasma membrane is a bilayer sheet structure of lipids, it is made of 2 layers (2 leaflets : outer exposed to the outside and inner exposed to the inside).

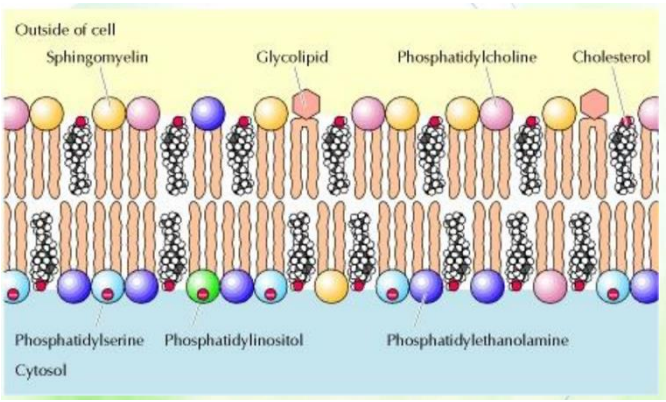
**Plasma membrane is composed of (components) : 45% phospholipids , 45% proteins of different types associated (imbedded) within the lipid bilayer and 10% carbohydrates (sugars) to the outside of the cell.

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



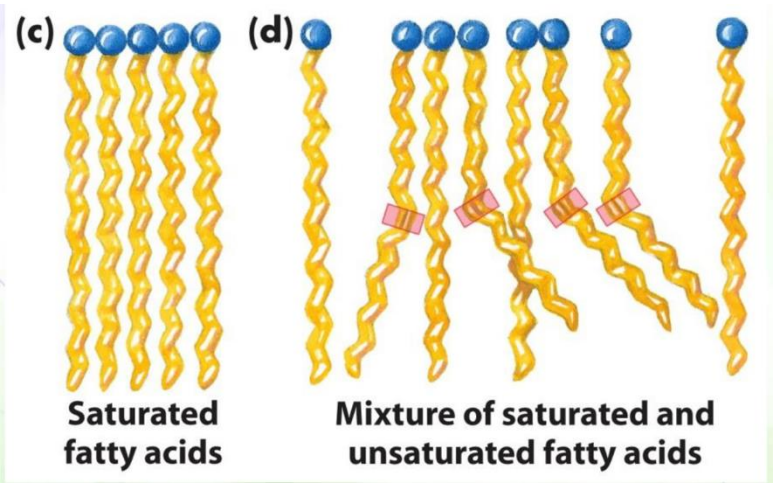
**Phospholipids of the outer leaflet of the bilayer sheet differ from the inner leaflet .
Outer : phosphatidylcholine, sphingomyelin and glycolipids (for cell recognition).
Inner : phosphatidylethanolamine, phosphatidylserine and phosphatidylinositol (for signaling).
**Cholesterol is also found and important in the plasma membrane, it is almost equally distributed in both leaflets (unlike phospholipids that are distributed unequally).

**Only animals and human cells have cholesterol within their membrane, plant cells have no cholesterol but a structure similar to it, bacteria cells also have no cholesterol.



-**Note**: the Predominant lipids in the bilayer sheet are glycerophospholipid.

**The type of fatty acids are important for membranes because fatty acids determine the fluidity of the membrane (if the membrane is flexible or not).
**Fluidity is important because proteins are signaling molecules which are not stuck in one place (they can move) inside the membrane.
☞So the more fluidic the membrane → the more free the molecules can move (This is important in signaling , membranes that need high signaling must be fluidic) .
Ex: Visual cells in the eye (visualization process is continuous because the membranes are fluidic so signaling molecules move freely).
☞ Saturated fatty acid → membrane is rigid (because they are packed).
Unsaturated fatty acid → membrane is flexible (free).

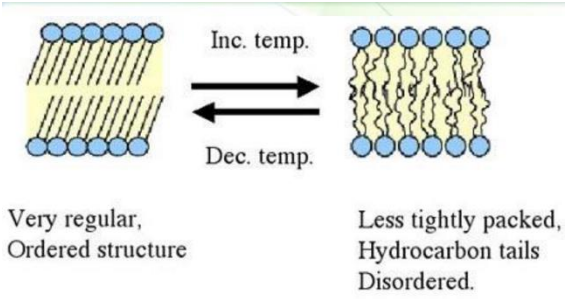


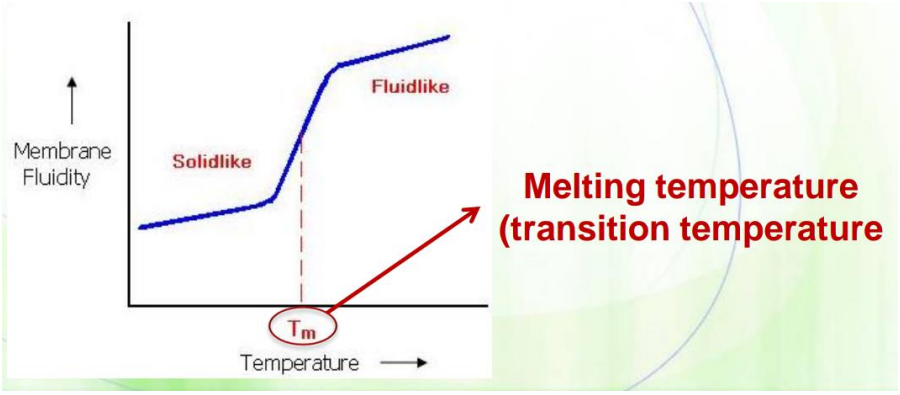
**Temperature also affects the fluidity of the membrane :

Low temperature → Solid like structure.

High temperature → Fluid like structure with movable fatty acids.

**If we increase the temperature → higher Kinetic energy → fatty acids start to collide with each other → plasma membrane can be disturbed.





-How can plasma membrane can be protected from that ??

By cholesterol, which is beneficial in both low and high temperatures, the presence of cholesterol stabilizes the extended straight-chain arrangement of saturated fatty acids by van der Waals interactions.

At low temperature it makes the membrane a little bit fluidic (less solid) ,why?

Because cholesterol molecules are found between fatty acids, so they increase the spaces between them.

At high temperature it makes the membrane more solid (it prevents the membrane from collapsing) ,why?

Because as we said at high temperature there is kinetic energy so fatty acid chains collide with each other, so cholesterol molecules prevent them from that, in turn preventing the membrane from collapsing (being disturbed).

**Cholesterol and hydroxyl groups interact with phospholipids and hydrophobic structures to make hydrophobic interactions with fatty acids.