Biologically important lipids

Lecture

Dentistry 1st year

Introduction

- Lipids are biological substances with hydrophobic character (i.e. they are insoluble or relatively insoluble in water but soluble in nonpolar solvents).

- The lipids are present in the body mainly in the adipose tissue as energy reserve, but their most important role is the formation of biomembranes. They are also involved in cell signaling.

Classification of lipids

- Lipids are classified as simple or complex.

Simple lipids

- Esters of fatty acids with various alcohols

  - Fats: esters of fatty acids with glycerol

    Liquid fats are also known as (natural) oils (sunflower, olive, soya etc.)

  - Waxes: esters of long-chain fatty acids + monohydroxyl alcohol [long CH_3-$(CH_2)_n$-CH_2OH chain].

Complex lipids

- Esters containing other groups than alcohol and fatty acid residue
  - Phospholipids: lipids containing in addition to fatty acid and alcohol residues a phosphoric acid residue.
    - They frequently have in addition to glycerol also another alcohol bonded to phosphoric acid- GLYCEROPHOSPHOLIPID.
    - Instead of glycerol an long chain amino alcohol sphingosine (sphingenine) may be present which result in formation of SPHINGOPHOSPHOLIPIDS

Complex lipids (cont.)

- Glycolipids (glycosphingolipids) are lipids containing fatty acid residue, sphingosine, and a saccharide (sugar) residue(s).

Precursor and lipid relate substances

Main categories of precursors and lipid related substances

- Fatty acids (nonesterified)
- Long chain alcohols
- Steroids
- Lipid soluble vitamins
- Lipid soluble hormones

Biologically important lipids

Fatty acids

Fatty acids (FA) are naturally occuring monocarboxylic acids.

The characteristics of FA:

- The total numer of carbons in fatty acids is even number.
- They have a carbon chain that is unbranched.
- Double bond, when present in the carbon chain is in a *cis* configuration.

Classification of fatty acids

- According to the length of the carbon chain

• Short chain fatty acids – SCFA	< 6 C
• Medium chain fatty acids – MCFA	6 – 12 C
• Long chain fatty acids – LCFA	14 – 20 C
• Very long chain fatty acids – LCFA	> 20 C

Classification of fatty acids

- According to saturation of carbon chain
  - Saturated
  - Unsaturated

Fatty acids

A) Saturated fatty acids (no double bonds)

Common name	No of C	Present in	Characteristics
Butyric	4	Small amounts in some fats (especially butter). Formed by carbohydrate fermentation by rumen organism.	Present mainly in milk fat, Easily digestible In free form often unpleasent odour
Valeric	5		
Caproic	6		
Caprylic	8	Small amounts in fats of plant origin	
Capric	10		
Lauric	12	Coconut oil, cinnamon, nutmeg, palm kernel	
Myristic	14		
Palmitic	16	Common in all animal and plant fats	Solid at room temperature Present in animal and plant fat Heavy for digestion
Stearic	18		
Arachidic	20	Peanut (arachis) oil	
Behenic	22	Different seeds	
Lignoceric	24	Cerebrosides, peanut oil	

Fatty acids

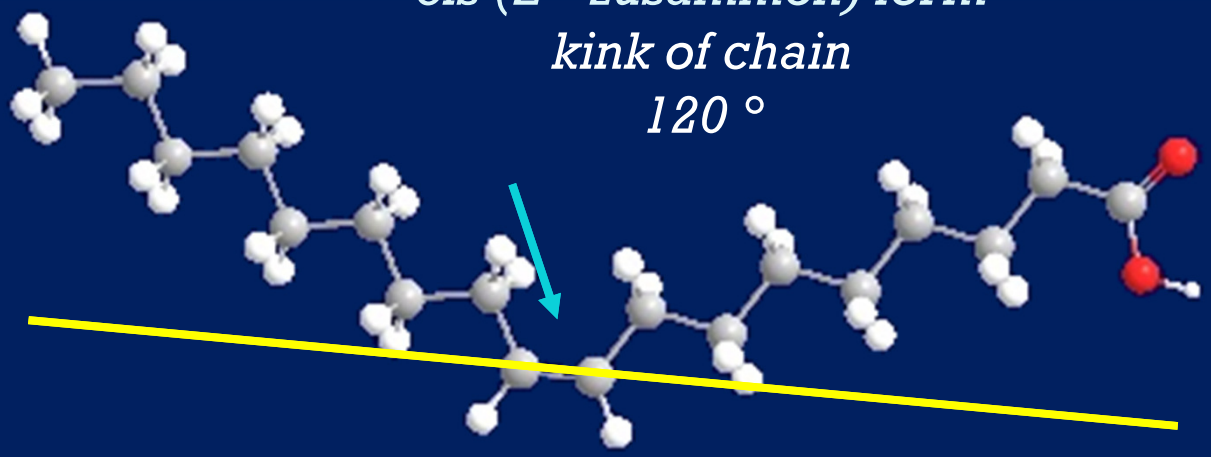
B) Unsaturated fatty acids (one or more double bonds)

- Monounsaturated fatty acids (MUFA)
- Polyunsaturated fatty acids (PUFA)

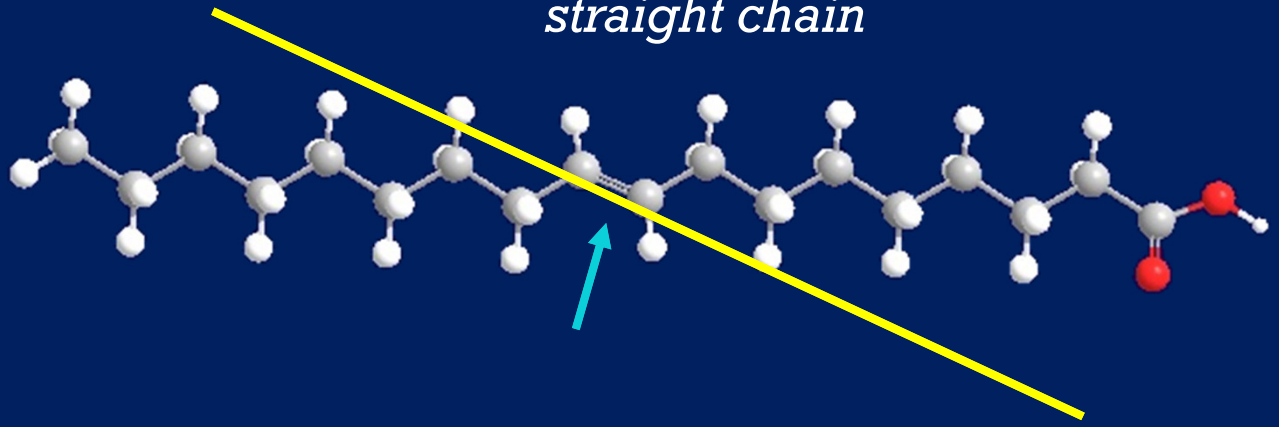
- *Cis* isomers
- *Trans* isomers

Cis and *trans* unsaturated fatty acids

cis (Z - zusammen) form
kink of chain
120 °



Trans (E - entgegen) form
straight chain



Cis and *trans* unsaturated fatty acids

- Most of the naturally occuring fatty acids is in the *cis* form; small amounts of the *trans* unsaturated fatty acids are present in ruminant fats, i.e. butter and suet.
- A lot of *trans* unsaturated fatty acids is formed as a by-product during the „hardening“ of plant oils (saturation of double bonds by hydrogenation).
- Higher amount of *trans* unsaturated fatty acids in food increases risk of some diseases, e.g. atherosclerosis.

Unsaturated fatty acids

Shorthand notation of FA structure

Example – linoleic acid

18:2;9,12

First number – the number of carbon atoms

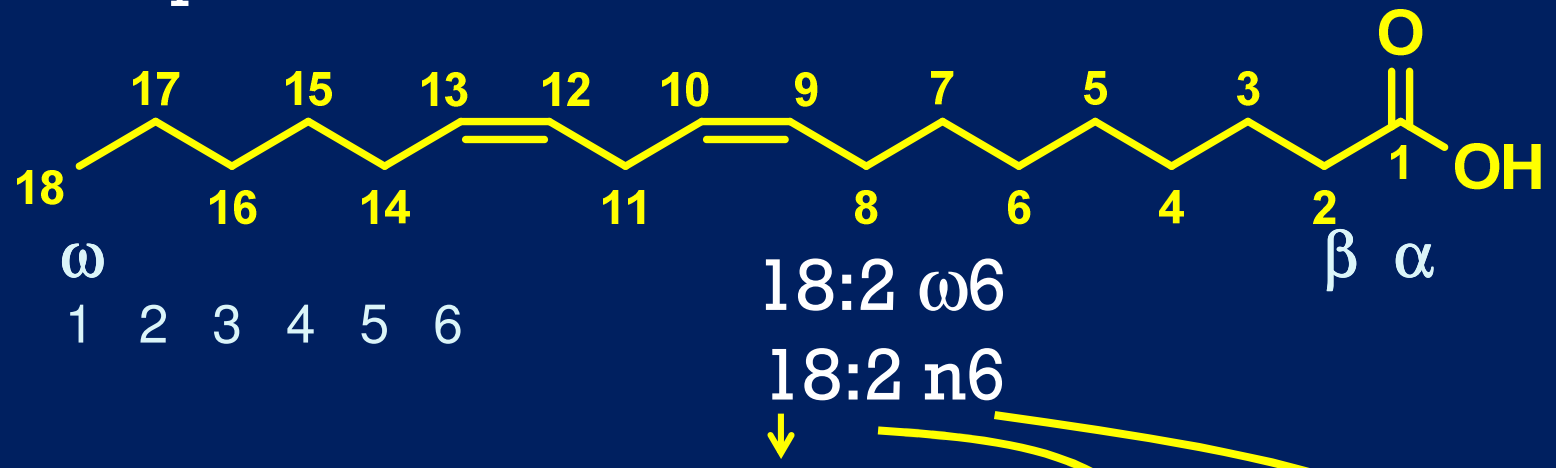
Second number after colon – the number of double bonds

Numbers after the semicolon – the position of double bonds
(Carbon numbering starts from carboxyl group)

Unsaturated fatty acids

Shorthand notation of FA structure – ω system

Example – linoleic acid



18:2 ω6

18:2 n6

First number – the number of carbon atoms

Second number after colon – the number of double bonds

Numbers after the semicolon – the position of double bonds
(Carbon numbering starts from methyl end ω or n- last carbon)

Unsaturated fatty acids - monoenoic

Common name	Systematic name		Serie	
Palmitooleic	*cis*-9 hexadecenoic	16:1;9	ω 7	all fats
Oleic	*cis*-9-octadecenoic	18:1;9	ω 9	most common FA in nature
Elaidic	*trans*-9-octadecenoic	18:1;9	ω 9	hydrogenated and ruminant fats
Erucic	*cis*-13-docosenoic	22:1;13	ω 9	rape & mustard seed oil, toxic in high content

Monounsaturated fatty acid MUFA

Unsaturated fatty acids - polyunsaturated

Common name	Systematic name		Serie
Linoleic	all-cis-9,12-octadecadienoic	18:2;9,12	ω6
	many plant oils – corn, soybean etc *essential FA*		
γ-linolenic	all-*cis*-6,9,12-octadecatrienoic	18:3;6,9,12	ω6
	some plants (evening primrose), minor in animal		
α-linolenic	all-*cis*-9,12,15-octadecatrienoic	18:3;9,12,15	ω3
	high in lin seed!! (flax seed) prevents some diseases *essential FA*		
Arachidonic	all-cis-5,8,11,14 eicosatetraenoic	20:4; 5,8,11,14	ω6
	animal fats and peanut oil important component of phospholipids		

Unsaturated fatty acids - polyunsaturated

Common name	Systematic name		Serie
Timnodonic EPA	all-cis-5,8,11,14,17-eicosapentaenoic	20:5;5,8,11,14,17	ω3
	Fish oils!!! (cod liver etc.)		
Clupanodonic	all-cis-7,10,13,16,19-docosapentaenoic	22:5;7,10,13,16,19	ω3
	Fish oils!!! Brain phospholipids		
Cervonic DHA	all-cis-4,7,10,13,16,19-docosahexaenoic	22:6;4,7,10,13,16,19	ω3
	Fish oils!!! Brain phospholipids		

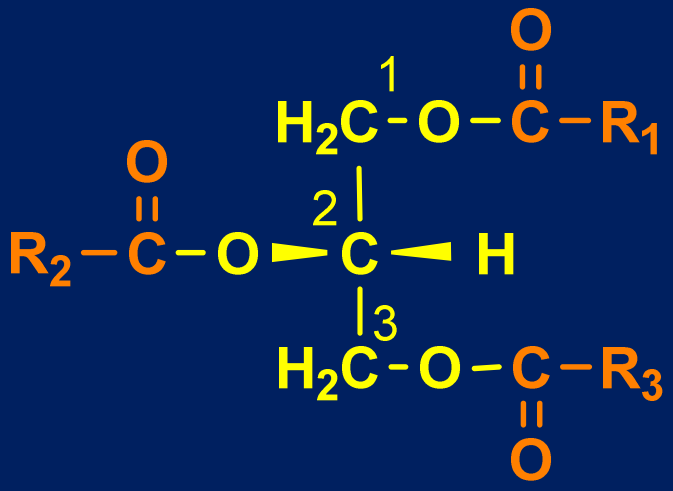
- The polyunsaturated fatty especially of the ω3 series are very important part of nutrition, also called vitamin F.
- The deficiency of „vitamin F“ is an important factor in many so called „civilisation disease“ as atheroslerosis, arthritis and probably some immunodeficiency diseases.

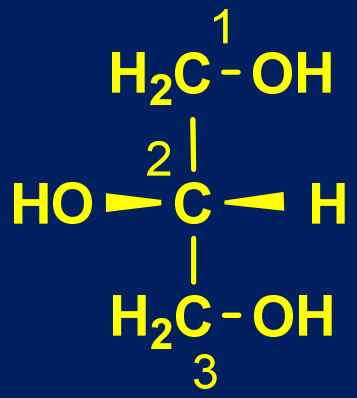
Eicosanoids

- These substances are derived from polyenoic 20 C fatty acids (greek *eicosa* = 20).
- This family of substances is biologically very active and includes the prostanoids (prostaglandin, prostacyclin and thromboxanes), leucotrienes and lipoxines.
- The precursor is usually the arachidonic acid.

Triacylglycerols

- Triacylglycerols (TAG) are the main storage forms of fatty acids.
- They are composed of glycerol esterified to three fatty acids.

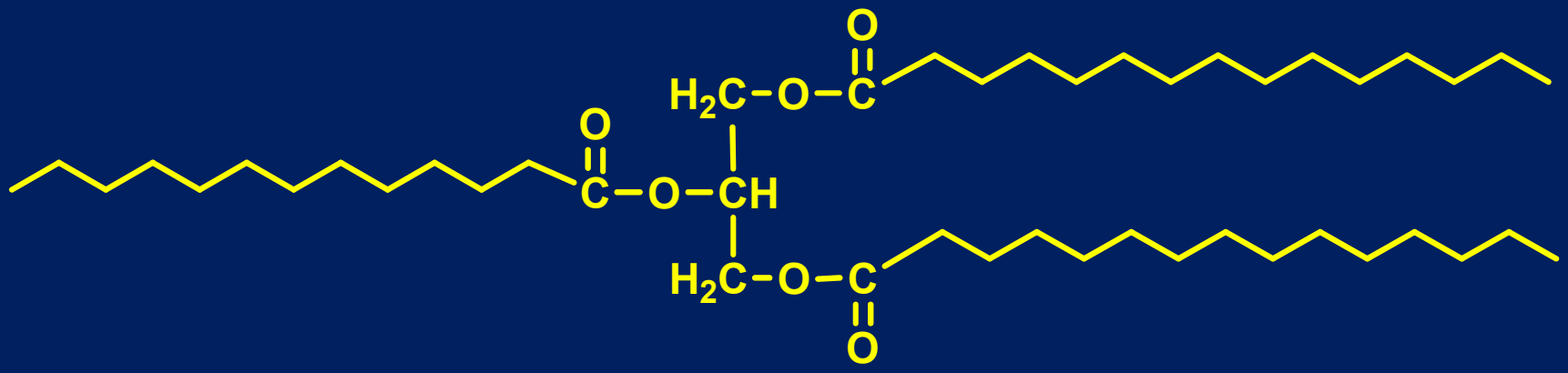




- The residues R_1, R_2 and R_3 are usually not identical in TAG.
- The carbons of glycerol differ from each other and are discriminated by enzymes.

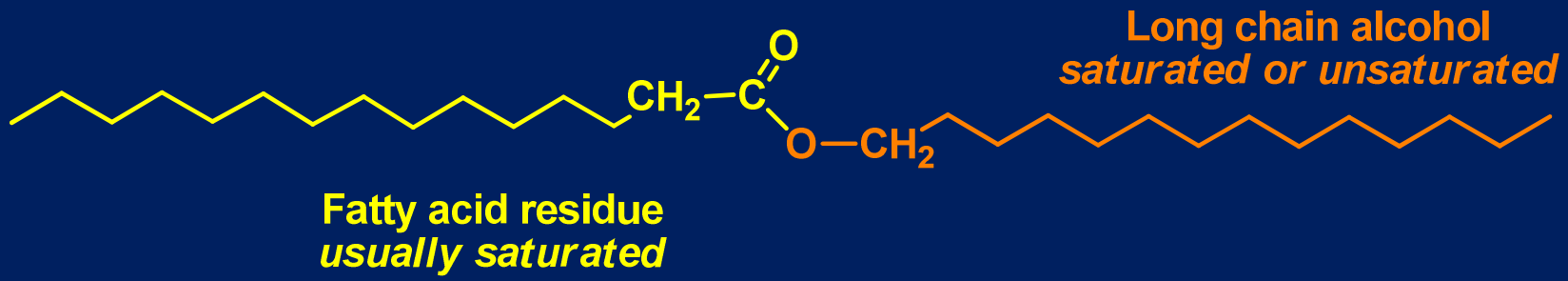
Triacylglycerols

- They are insoluble in water. They are not present in the biomembranes.



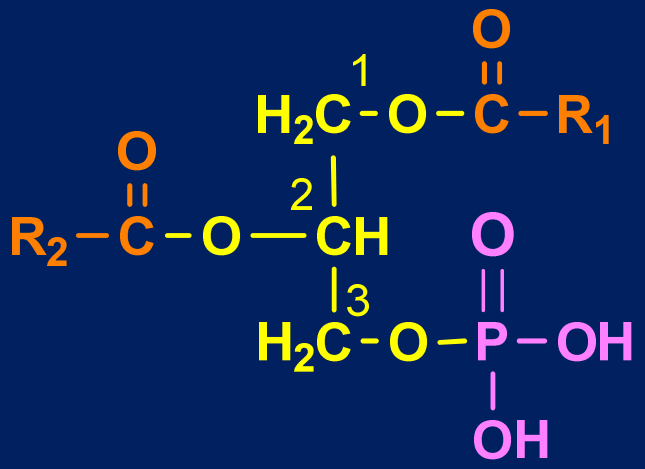
Waxes

- Esters of fatty acids and long chain alcohols
- Very hydrophobic



Phospholipids

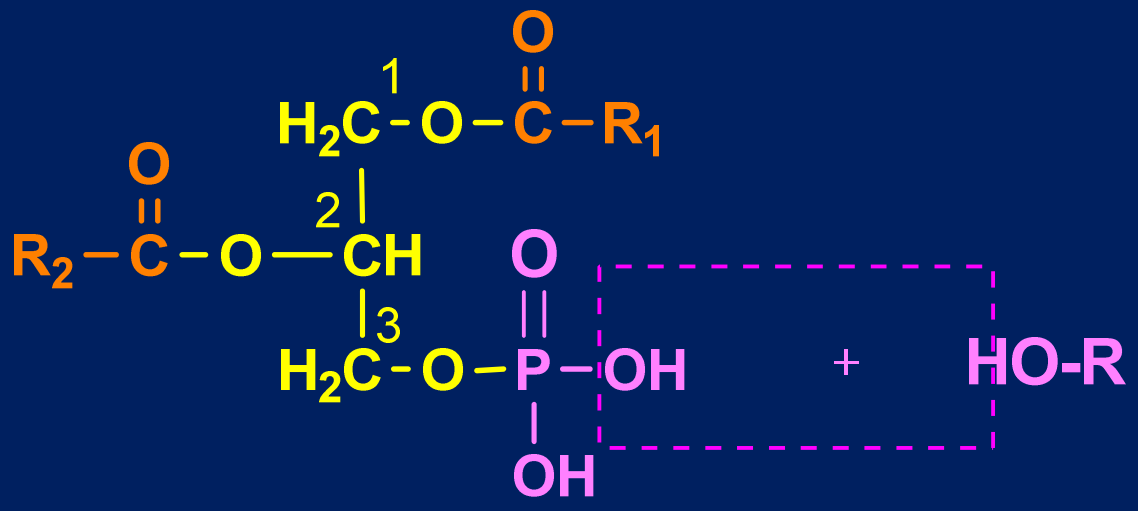
- Phospholipis are the main constituents of biomembranes.
- Glycerol-based phospholipids are called glycerophospholipids.
- The basis of their structure is phosphatidic acid – 1,2-diacylglycerol with a phosphate group attached to C3.



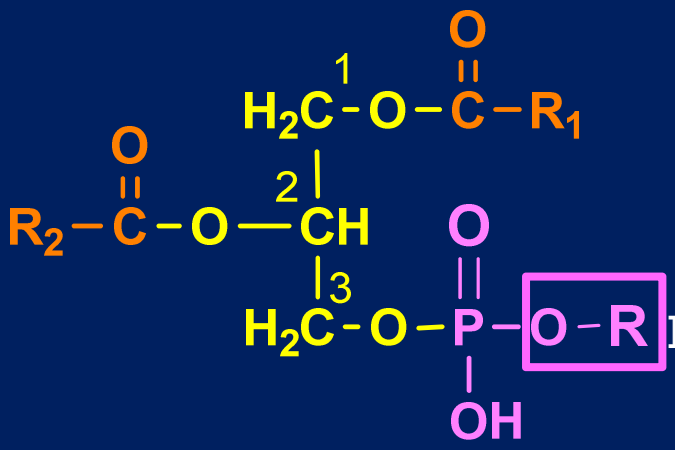
Phospholipids

- The phosphate group reacts with OH groups of alcohols.

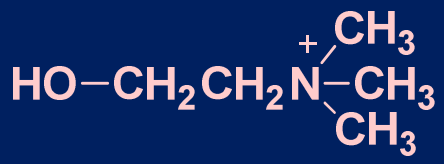
Phosphatidyl – R (residue)



Phospholipids

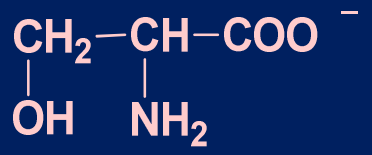


Phosphatidylcholine
(lecithine)

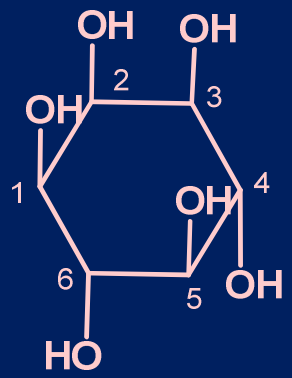


Phosphatidylethanolamine
(cephaline)

Phosphatidylserine



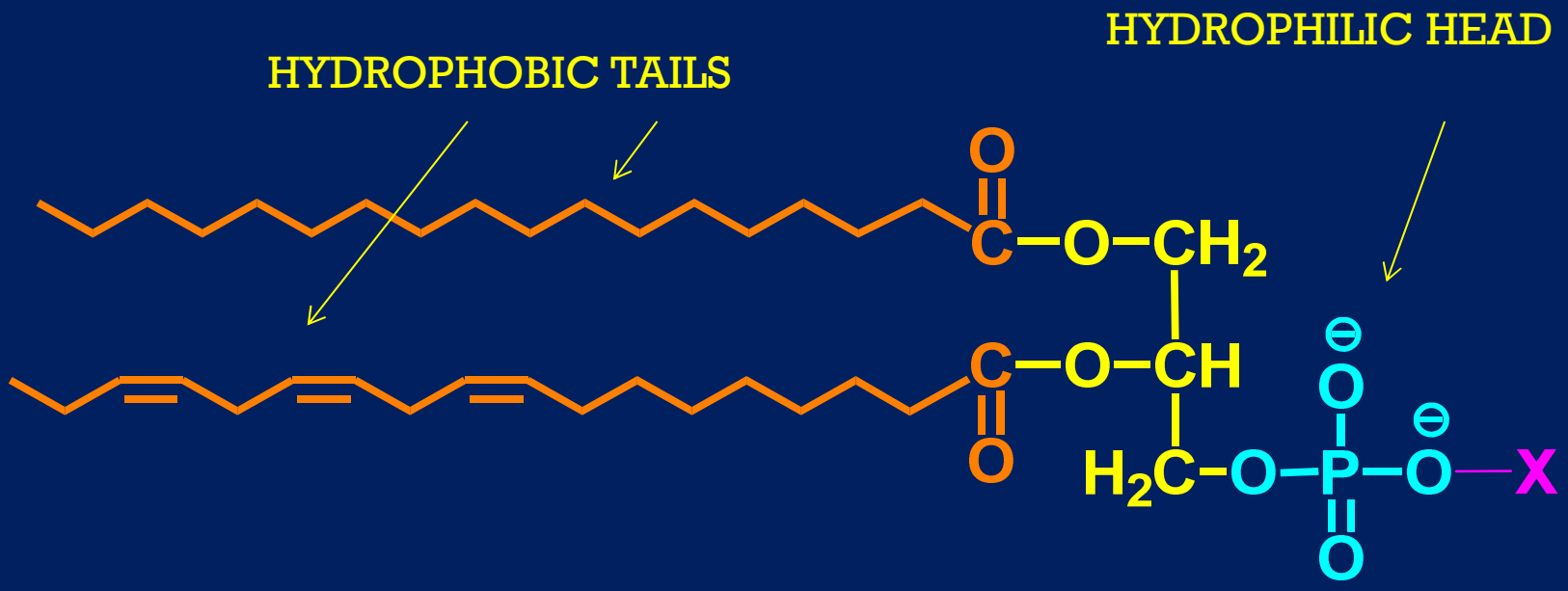
Phosphatidylinositol



In membrane usually present as phosphatidylinositol 4,5-bisphosphate

Phospholipids

- Glycerophospholipids have a hydrophobic portion, the nonpolar fatty acid residues and a hydrophilic portion, the polar head group. They are amphiphilic.



Phospholipids

Cardiolipin

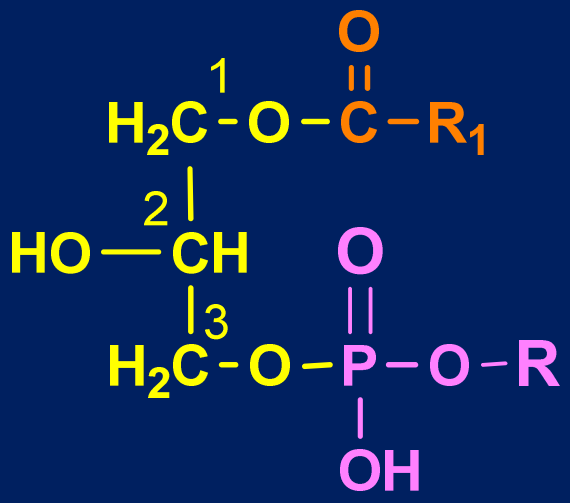
- When two phosphatidic acids are bound to a glycerol molecule a phospholipide named diphosphatidylglycerol originates.

- Cardiolipin is present mainly in mitochondria and was first isolated from heart tissue, which has high number of mitochondria in their cells (cardiolipin means lipid from heart).

Phospholipids

Lysophospholipids

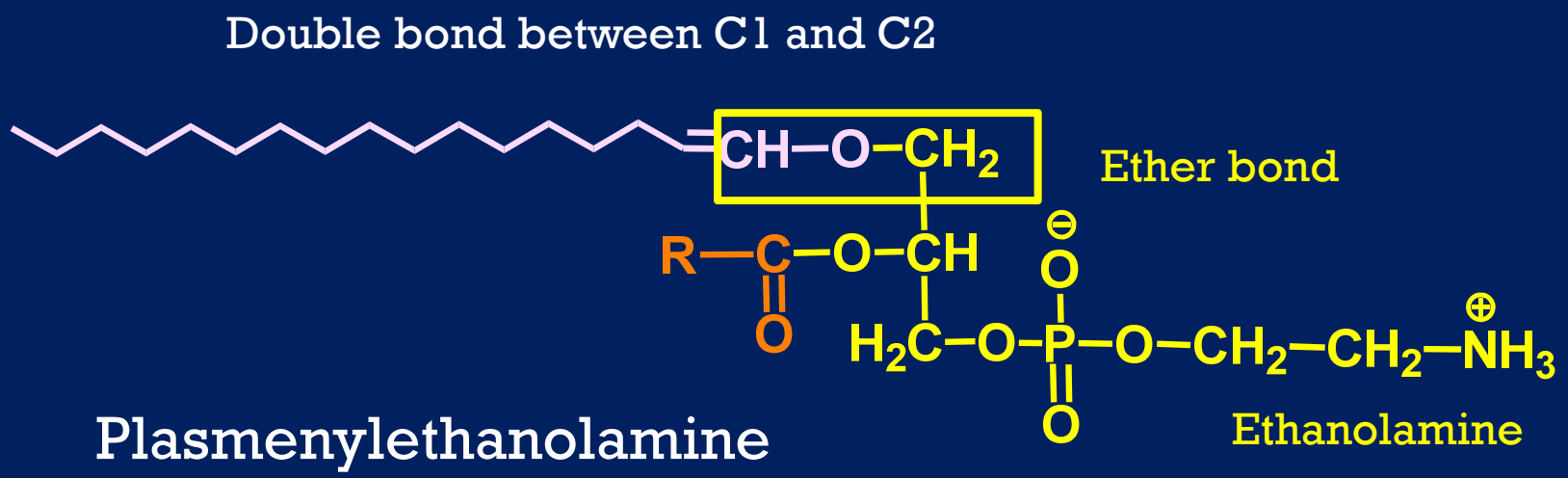
- Phosphoacylglycerols containing only one acyl-radical (one fatty acid residue + phosphoric acid)



Phospholipids

Plasmalogens

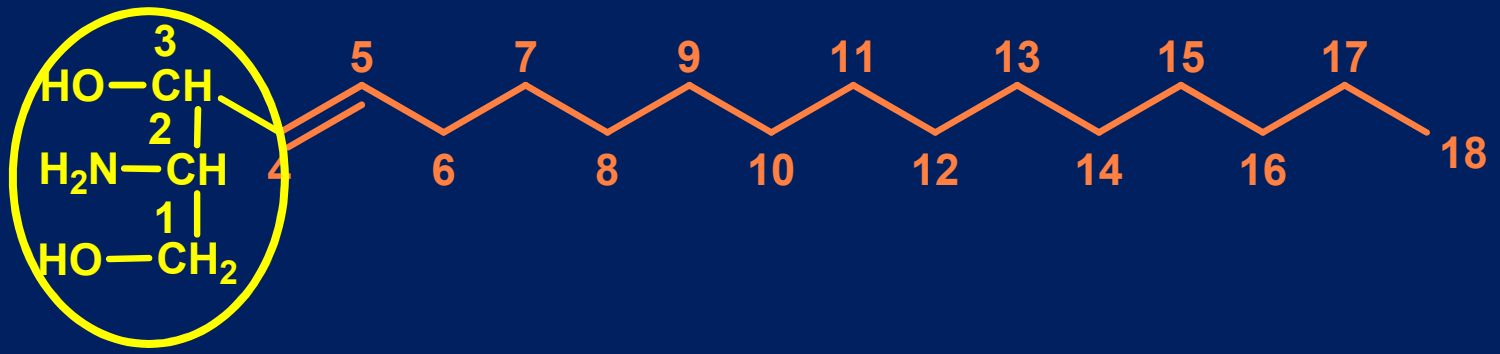
- They occur mainly in brain and muscle.
- They have on the first (sn-1) carbon an ether bond instead of the ester (present mainly in mitochondria).



Plasmenylethanolamine

Sphingolipids

- Sphingolipids are found in biological membranes.
- Sphingolipids do not contain glycerol.
- The main alcohol in their molecule is sphingosine (instead of glycerol) – an amino alcohol with unsaturated alkyl side chain.

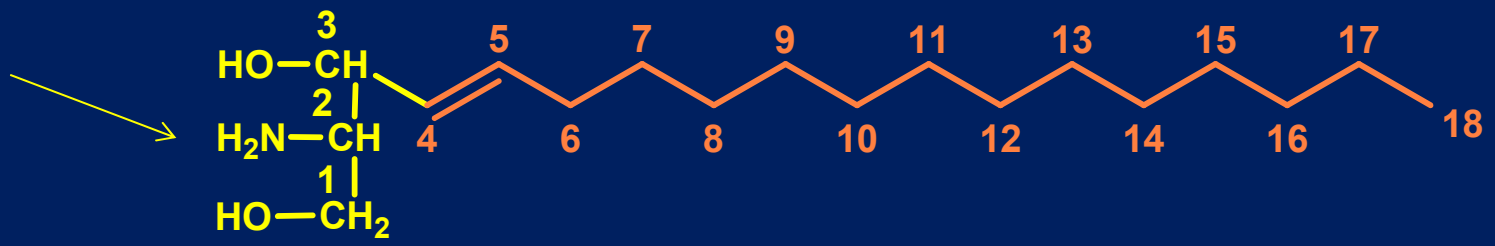


- In sphingolipids the first three carbon atoms at the polar end of sphingosine are analogical to the three carbon atoms of glycerol in glycerophospholipids.

Sphingolipids

- Lipids derived from sphingosine:
  - Ceramides
  - Sphingomyelins
  - Glycolipides

A fatty acid mtached via amide linkage to C2 NH_2 group

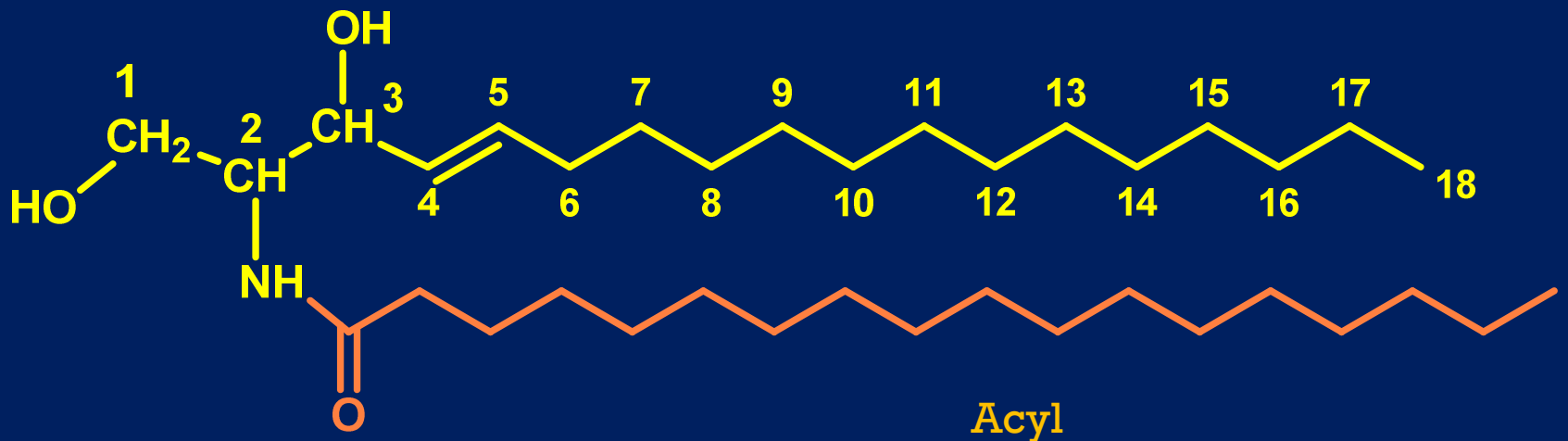


A head groups can be attached to the C1 hydroxyl group

Ceramides

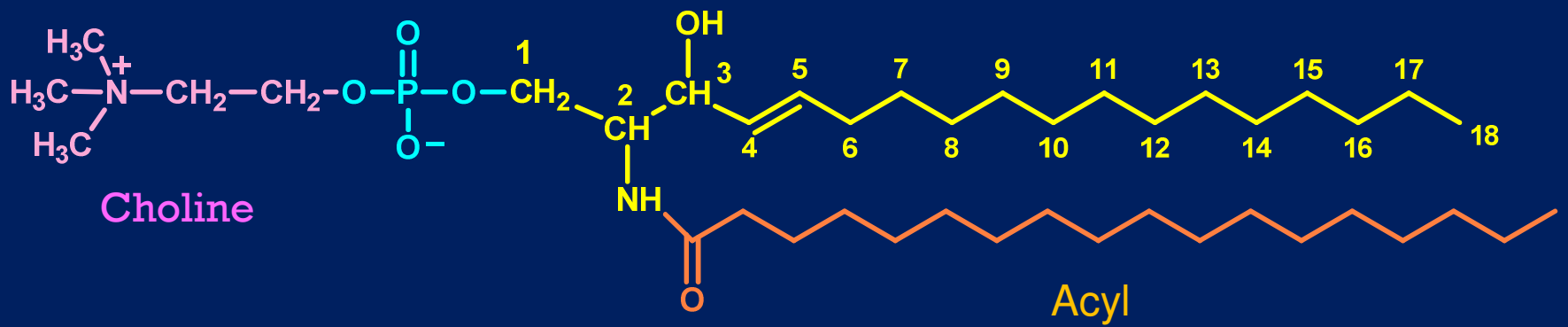
Ceramides

- sphingosin forms an amide bond to a fatty acid.
- precursor of sphingolipids



Sphingomyeline

- In the sphingomyelins the amino group of sphingosine is bonded to a fatty acid by an amide linkage and the primary alcohol group of sphingosin is esterified with phosphoric acid. The phosphoric acid residue also forms a second ester linkage with a cholin.



- Sphingomyelins are important structural components of the myelin sheath.

Glycolipids

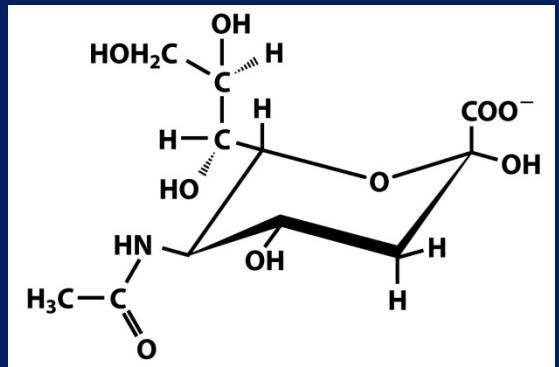
- Glycolipids contain both fatty acid and a carbohydrate component (s) attached to a sphingosine molecule.

Example

- Galactosylceramide (R = -H) – the simple representative of glycolipids
- Sulphogalactosylceramide (R = - SO_3H)

Glycolipids

- Gangliosides
  - Glycolipides with longer and/or branched oligosacharide chain often contain one or more molecule of sialic acid (in human neuraminic acid, an acetylated aminosugar derivate acid)



N-Acetylneuraminic acid (a sialic acid) (Neu5Ac)

Steroids

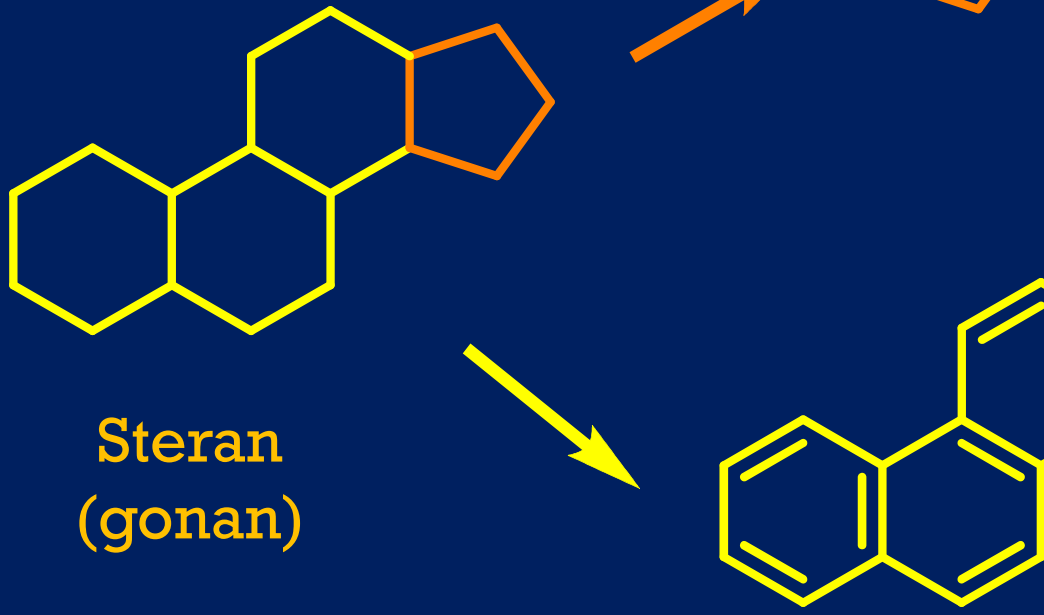
Steran (gonan) is a molecular core structure common to all of the steroids. It consists of four saturated rings.

Steran
(gonan)

Steroids

Cyclopentanoperhydrophenantren (CPPP)

- CPPP is the basic structure from which all steroids can be derived by adding the side chains

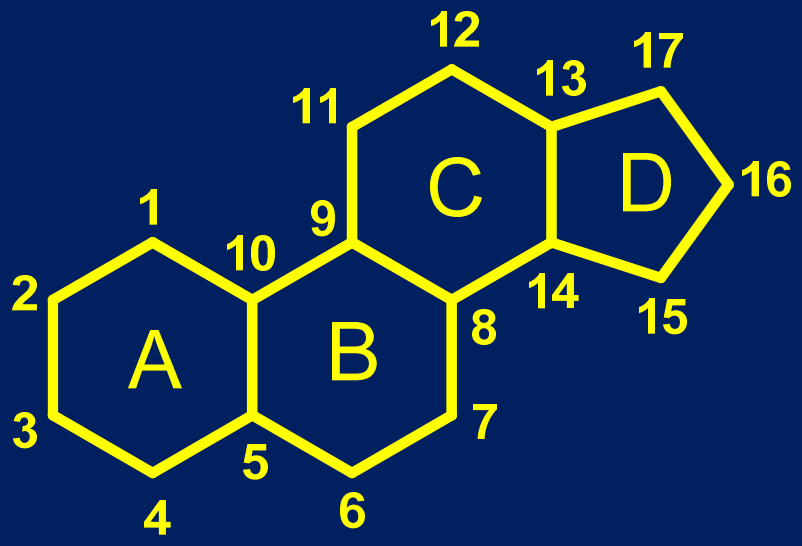


Cyklopentan
(five membered ring)

Steran
(gonan)

Phenantren
(three six membered rings)

Steroids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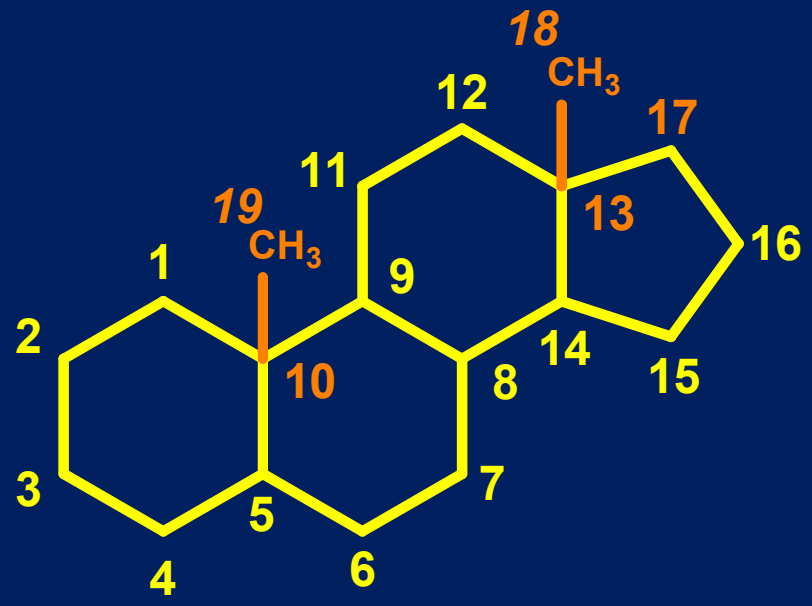
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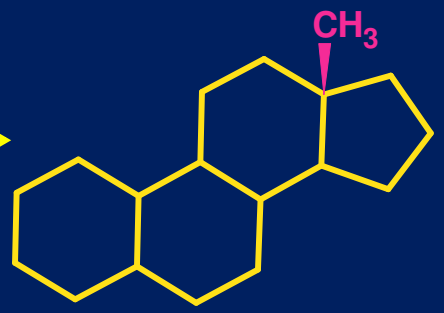
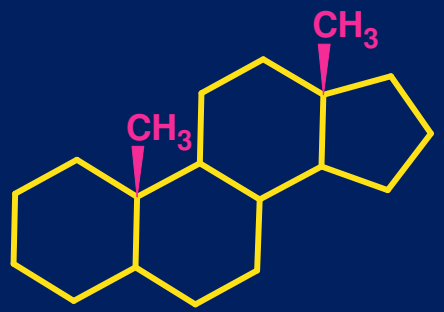
Steroids

The nomenclature originates from **sterane.**
By adding side chains we can get:

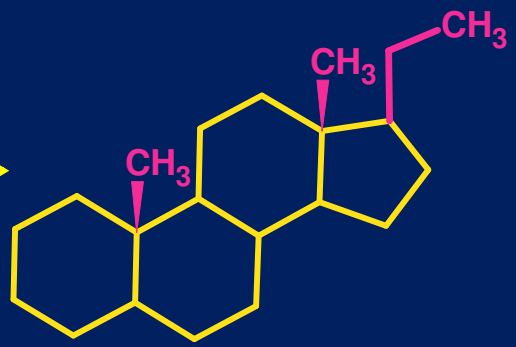
- Estrane (C18)



- Androstane (C19)

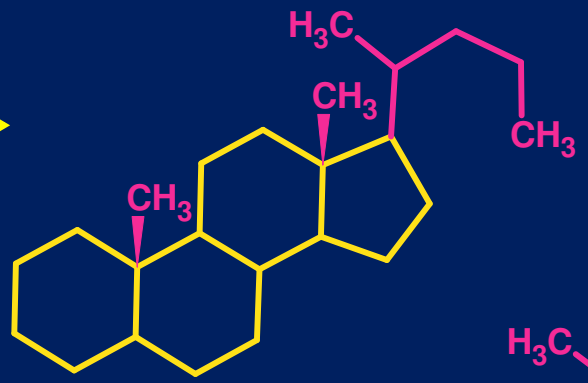


- Pregnane (C21)

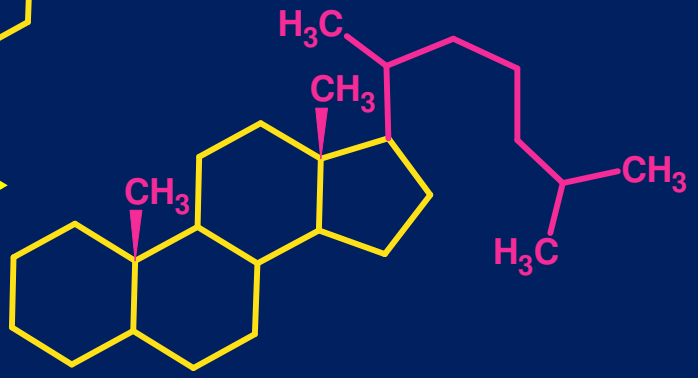


Steroids

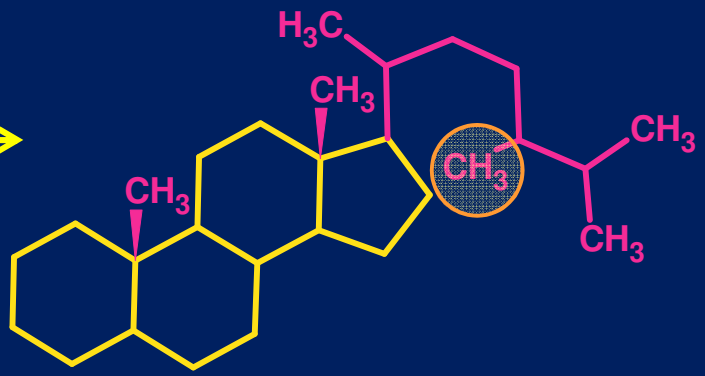
- Cholane (C24)



- Cholestane (C27)



- Ergostane (C28)
  - Ergosterol is a plant steroid



Cholesterol

Cholesterol is
amphiphilic molecule:

- steran structure largely hydrophobic
- one polar OH group

5-cholesten-3β-ol

Cholesterol

Biological role of cholesterol

- The most common steroid in animal.
- Moderate the fluidity of eukaryotic *cell membranes*
- It is a precursor of all *steroid hormones*
- The *bile acids* are derived from cholesterol.
- *Cholecalciferol* is also derived from cholesterol

  (vitamin D_3 is necessary for calcium absorption in the gut).