

PHOSPHOLIPID COMPOUNDS OF PHYSIOLOGICAL IMPORTANCE



BIOCHEMISTRY433@HOTMAIL.COM



RESPIRATORY BLOCK



OBJECTIVES:

- Selected members of phospholipids
- Physiological importance of phospholipids
- Phospholipases:
 - Phospholipases A1, A2, C and D
 - Lysosomal phospholipase:
Sphingomyelinase

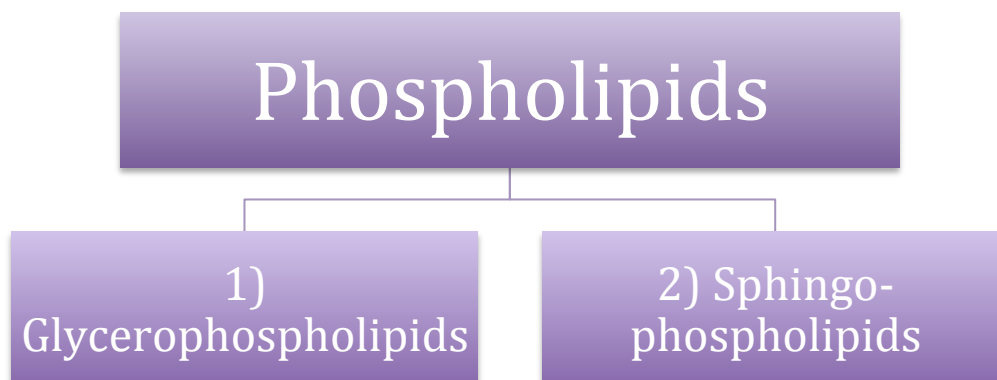
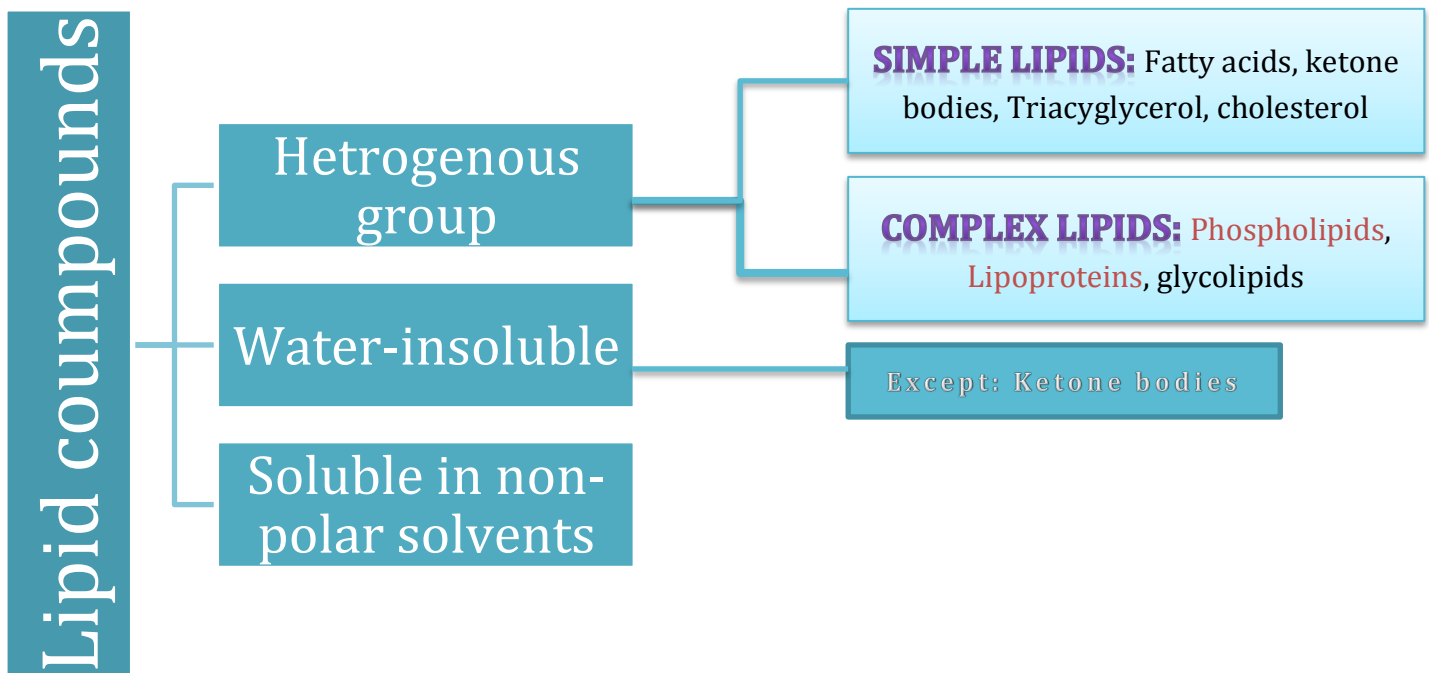
Functions of Phospholipids

Non-membrane-bound

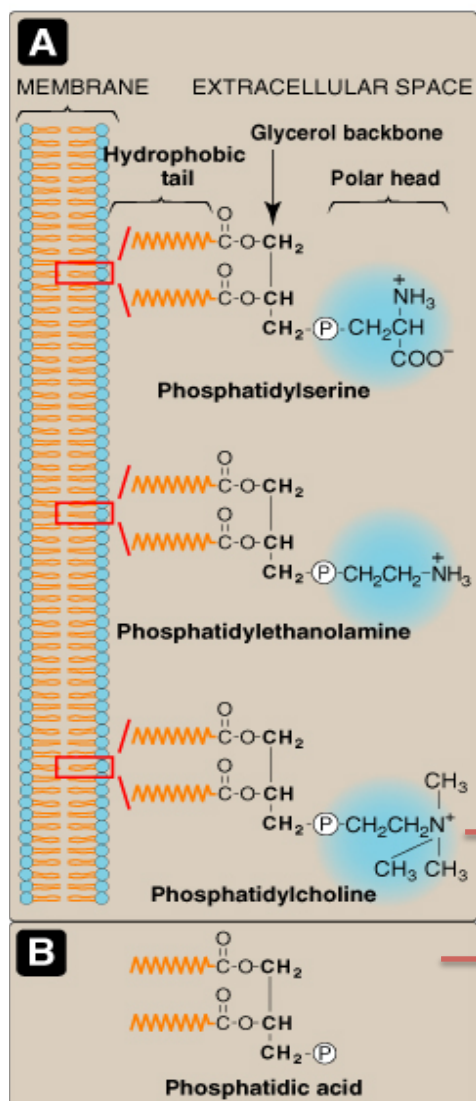
- Easy **re-inflation** of alveoli by air (surfactant)
- **Coat of lipoprotein**
- **Detergent effect**: essential component of bile, solubilize cholesterol, preventing gall stones, emulsifying lipids, helping lipid digestion

Membrane-bound

- **Anchoring**: gives amphipathic function, when protein (hydrophilic) wants to bind to a membrane (hydrophobic) it can't, phospholipids do this job
- **Predominant lipid of cell membrane**
- **Signaling: source** of IP3 and DAG (will be discussed)
- **Myelin sheath**: insulator and speeds up transmission



1) Glycerophospholipids



We will discuss:

- 1- Phosphatidylcholine (Lecithin) e.g., Surfactant (Dipalmitoylecithin)
- 2- Phosphatidylinositol (Signaling and anchoring molecule)

Parent Compound (found in all glycerophospholipids compound) **Phosphatidic acid**

1. Dipalmitoylecithin (Lung surfactant)

- **Synthesis and secretion:** by granular pneumocytes
Major lipid component (65%) of lung surfactant (Remaining 35%: Other phospholipids, cholesterol & proteins)
- Surfactant decreases surface tension of fluid layer, lining of alveoli, reducing the pressure needed for their inflation by air, and preventing alveolar collapse (atelectasis)

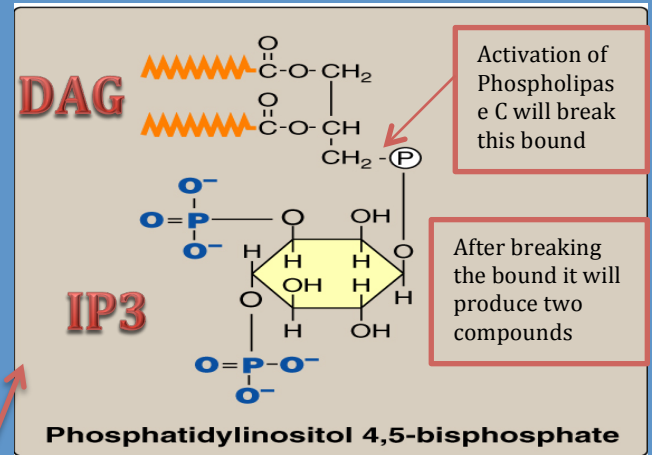
Congenital Respiratory distress syndrome (RDS)

- Insufficient production of lung surfactant (especially in pre-term babies) leads to neonatal death
- Pre-natal diagnosis by: Lecithin/sphingomyelin (L/S) ratio in amniotic fluid
- Ratio of 2 or above indicates lung maturity and no RDS (i.e., shift from sphingomyelin to lecithin synthesis by pneumocytes that normally occurs by 32 weeks of gestation)
- Prevention: Glucocorticoids to the pregnant mother with low L/S ratio shortly before delivery
- Treatment: Intratracheal administration of surfactant to pre-term infants with RDS

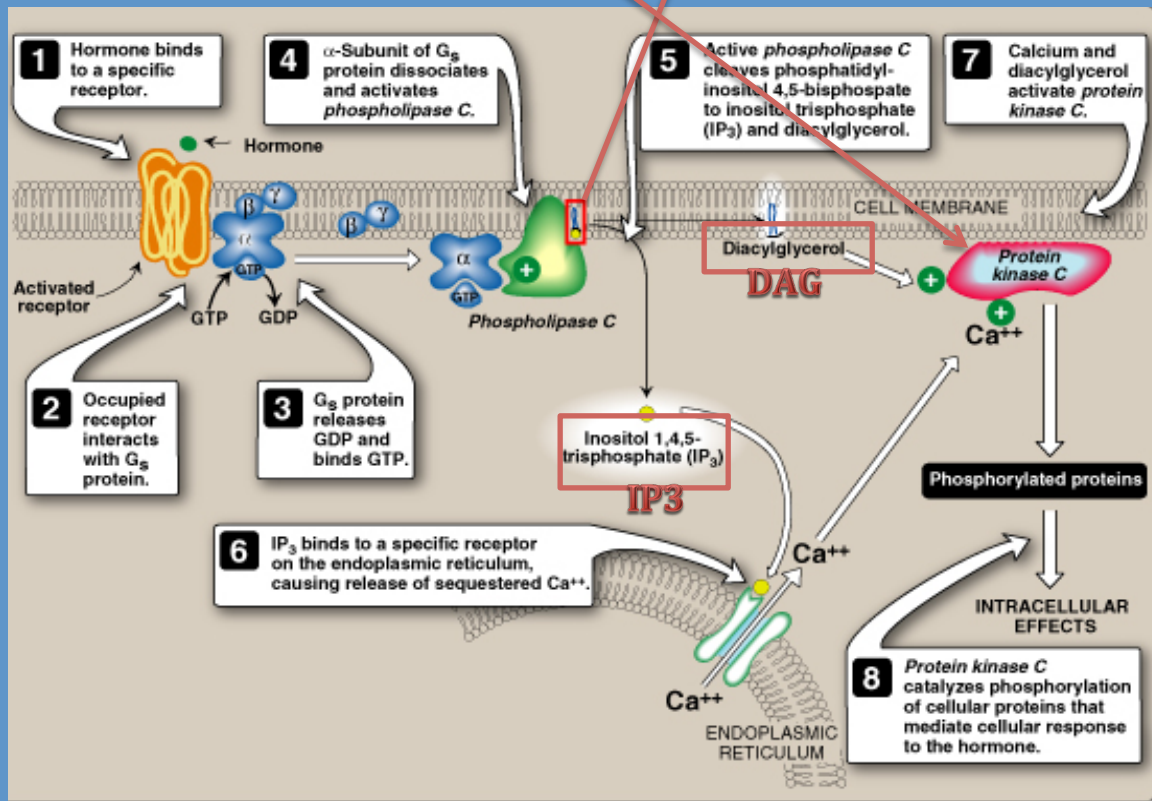
2. Phosphatidylinositol 4,5 biphosphate (PI)

It has 2 functions: signaling and anchoring

- **Signal:** Hormones or neurotransmitters e.g., Acetylcholine, antidiuretic hormone (V1-receptor) and catecholamines (α_1 actions)
- **Receptor:** G-protein coupled receptor
- **Effects:**
 - 1) Activation of phospholipase C
 - 2) Hydrolysis of phosphatidylinositol 4,5-bisphosphate
 - 3) Production of IP₃ (Ca²⁺) and DAG
 - 4) Activation of **protein kinase C** Phosphorylation of cellular proteins
- **Response:** Biological responses to hormones



So, how DAG and IP₃ will transfer the signal?



PI- PROTEIN ANCHORING

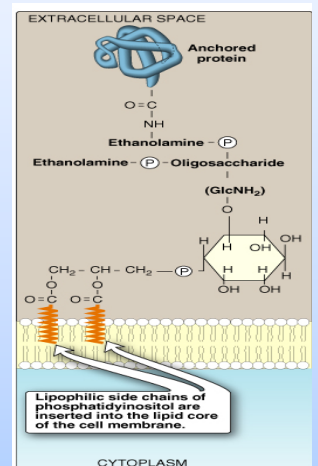
Anchoring of proteins to membranes via Carbohydrate Phosphatidylinositol Bridge

Examples of anchored proteins:

1. Alkaline phosphatase (to the surface of small intestine)

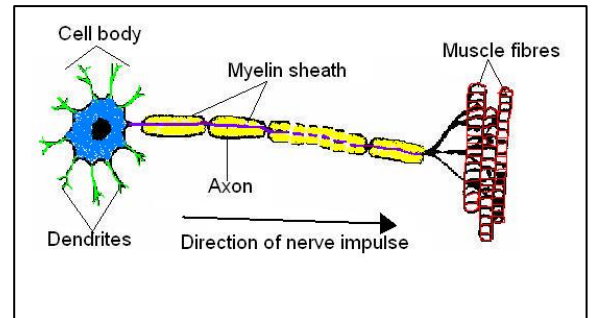
2. Acetylcholine esterase

(to postsynaptic membrane) These proteins can be cleaved from their attachment to the membranes by phospholipase C



2) Sphingo-phospholipids group

- Ceramide is the parent of sphingolipid component.
- Ceramide + phosphocholine = sphingomyelin
- Structure of myelin:
 - 80% Lipids (glycolipids mainly + sphingomyelin)
 - 20% proteins
- Myelin sheath insulates the nerve axon to avoid signal leakage and greatly speeds up the transmission of impulses along axons.
- Sphingosine has long chain unsaturated amino alcohol.



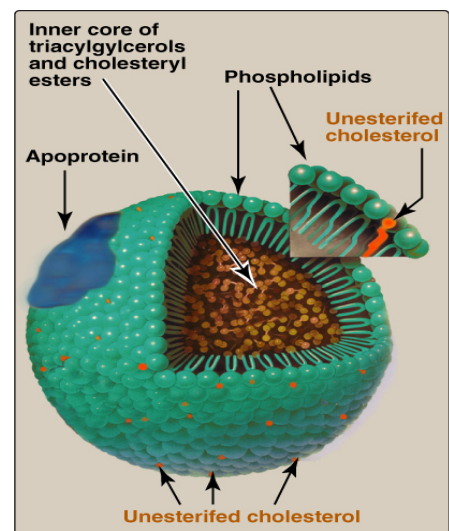
Lipoprotein

Inner part (core):

- According to the type of lipoproteins
- Different lipid components in various combinations
- Hydrophobic

Outer (coat):

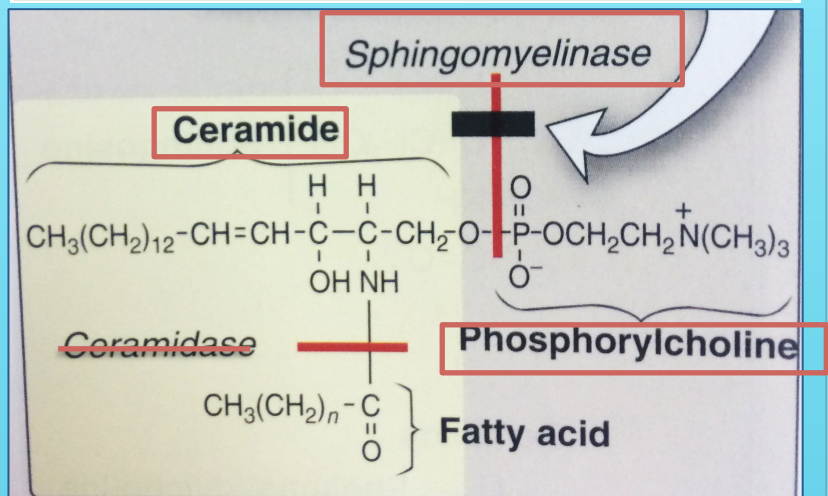
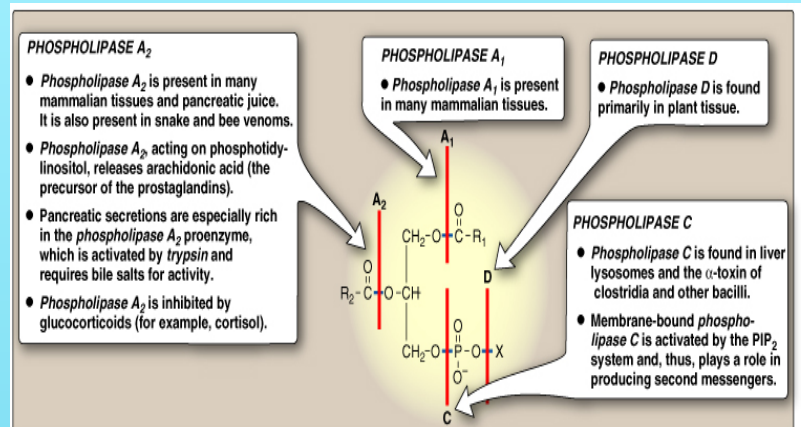
- Apoproteins or apolipoproteins
- Phospholipids
- Free cholesterol



PHOSPHOLIPASES

(1) For glycerophospholipids:
Phospholipases A₁, A₂, C and D (D in plants)
Present in all tissues and pancreatic juice
Present in snake venoms and bacterial toxins

(2) Sphingomyeline is degraded by sphingomyelinase, a lysosomal enzyme that hydrolytically removes phosphorylcholine, leaving a ceramide.
Sphingomyeline + sphingomyelinase = phosphorylcholine + ceramide



Function of Phospholipase:

(1) Degradation of phospholipids

- Production of second messengers
- Digestion of phospholipids by pancreatic juice
- Pathogenic bacteria degrade phospholipids of membranes and causing spread of infection

(2) Remodeling of phospholipids:

- Specific phospholipase removes fatty acid from phospholipid
- Replacement of fatty acid by alternative fatty acid using fatty acyl CoA transferase e.g., Binding of 2 palmitic acids in: Dipalmitoylphosphatidylcholine (DPPC) Binding of arachidonic to carbon 2 of phosphatidylinositol or phosphatidylcholine.

Q1) Diabetic 35 week pregnant patient came to your clinic and you predicted that she will deliver prematurely which one of these test will make us sure that the baby has normal surfactant level:

- a- manteaux test
- b- lecithin/sphingomeylin ratio more than "2"
- c- RAST test
- d- E.M.G test

Q2) which one of the following enzymes is used in surfactant remodeling:

- A- phospholipase A1
- B- phospholipase A2
- C- phospholipase D
- D- ANS(1+2)

Q3) phospholipids is transported in the circulation in the form of:

- A- phospholipase A1
- B- phospholipase A2
- C- lipoprotein
- D- phospholipase c

Q4)The MAIN component of lung surfactant is:

- A- cholesterol
- B- proteins
- C- Carbohydrates.
- D- dipalmitoylecithin

Q5) lung surfactant are made of:

- A- non membrane bound phospholipid
- B- membrane bound phospholipid
- C- phospholipase D
- D- phospholipase A2

Q6) All lipid compounds are lipid soluble except:

- A- Ketone bodies
- B- cholesterol
- C- fatty acids
- D- triacylglycerol

Q7) 28 week pregnant lady was going to deliver her baby, which one of these you should give her to prevent the low surfactant percentage:

- A- VIT.D
- B- Adrenalin
- C- Intra tracheal administration of surfactant
- D- Glucocorticoids

Q8) The main component of myelin sheath is:

- A- phosphatidic acid
- B- Ceramide
- C- lacithin
- D- glycolipid

Q9) phosphatidylinositol system will lead to the activation of:

- A- Protein kinase A
- B- Protein kinase C
- C- Protein kinase D
- D- Protein kinase F

Q10) Hydrolysis of phosphatidylinositol 4,5-bisphosphate by phospholipase c will lead to the production of:

- A- IP3
- B- DAG
- C- NAD-H
- D- Ans (1+2)

Q11) The anchor proteins can be cleaved from their attachment to the membranes by:

- A- Phospholipase C
- B- Phospholipase A2
- C- Phospholipase A1
- D- Phospholipase D

Q12) phospholipase A2 is inhibited by:

- A- Trypsin
- B- Glucocorticoids
- C- fructose 1,6-bisphosphatase
- D- Bacteria

Q13) phospholipase A2 is activated by:

- A- Trypsin
- B- Glucocorticoids
- C- Lysosomes
- D- Bacteria

Ans: 1-B. 2-D. 3-C. 4-D. 5-A. 6-A. 7-D. 8-D. 9-B. 10-D. 11-A. 12-B. 13-A

GOOD LUCK

Sara alDokhayel

Maha AlRajhi

Layan AlTaweel

Maram AlAqil

Amjad AlBatili

Lamees alMezaini

Ghada AlHindi

Ahmed AlHussien

Ahmed AlQhtani

Mojahed Otef

Ahmed Alzoman

Meshal AlOhali

Ziyad AlAjlan

You can contact us at:
Biochemistry433@hotmail.com