Biochemistry

carbohydrates isomers ketone starch lipid protein amine

◉ Sheet ○ Slides

Subject :	Biosynthesis of Glycerophospholipids
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Number :	24

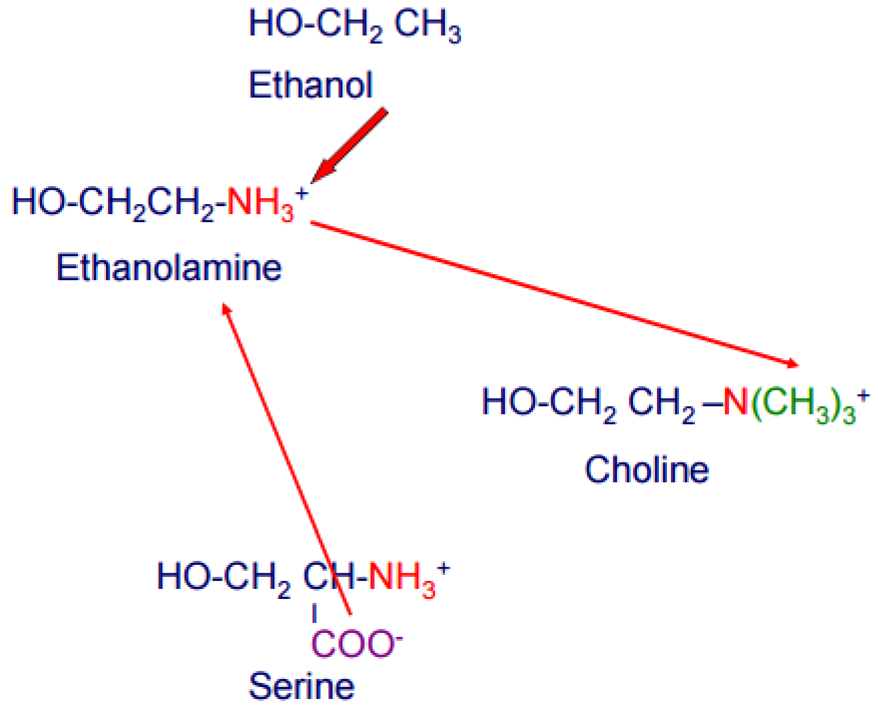
Introduction

Glycerophospholipids, phosphoglycerides or phosphoacylglycerols are very important molecules which serve many functions. In this sheet, we will discuss their structure, degradation, synthesis, remodeling and functions.

Structure of phosphoacylglycerols

In phosphoacylglycerols, glycerol is bound to two fatty acids by ester bonds. The last hydroxyl group of it is bound to a phosphate group, which forms two ester bonds;the first one is with glycerol and the second bond forms between the phosphate group and an alcohol. So, we can notice that two alcohols are found in a phosphoacylglycerol; glycerol and the phosphate-bound alcohol.

- Alcohols:
  To form a phosphoacylglycerol, phosphatidic acid[1] can form ester bond with these alcohols:
  1- Alcohols with amino group:
  Serine, ethanolamine and choline.



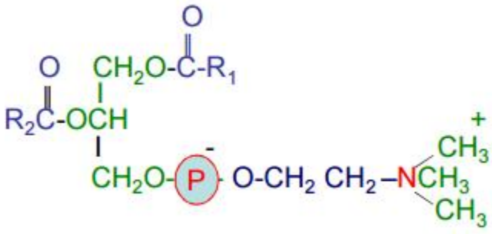
This figure[2] shows the relationship between the amino alcohols' structures. Ethanolamine differs from ethanol in the amino group. Serine "amino acid" has an additional carboxylic group to the structure of ethanolamine. Choline has addition 3 methyl groups to the structure of ethanolamine.

1: it is called phosphatidic acid when protonated, and phosphatidate when unprotonated

2: the figure does not represent the biochemical mechanism of the formation of the alcohols in the cells

Inositol "6-carbon alcohol; 6 hydroxyl groups**, it is not a sugar**" and glycerol.

- Phospatidylcholine[3]; an example



Phosphatidyl Choline (Lecithin)

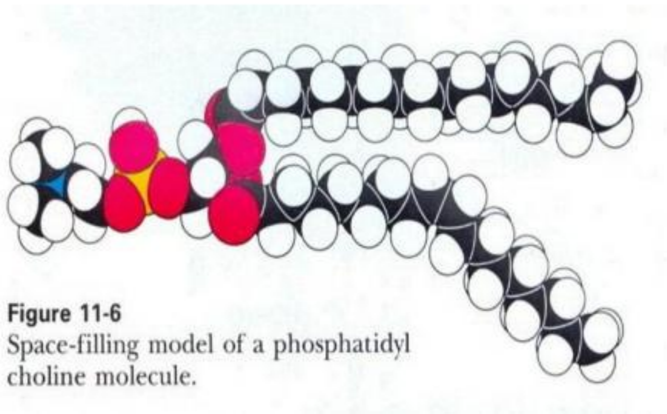
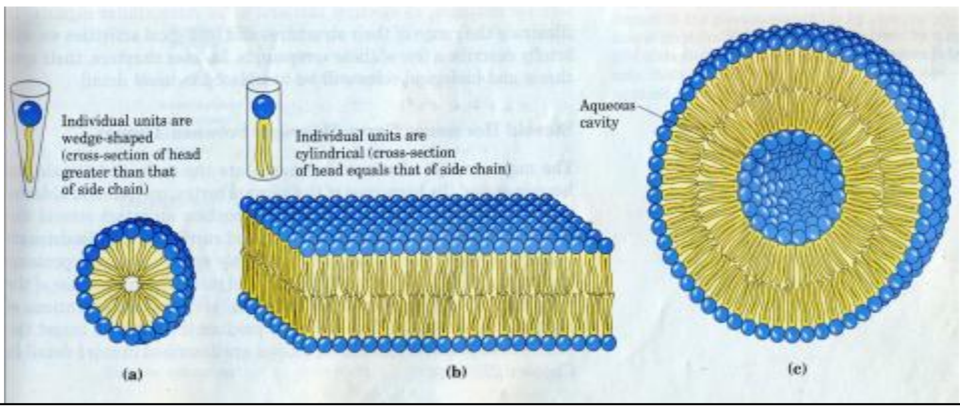


Figure 11-6
Space-filling model of a phosphatidyl choline molecule.

Phosphatidylcholine is commonly known as *lecithin*. Notice from the figures[4]that it has a negatively charged phosphate group, which is bound to a positively charged quaternary amine choline "hydrophilic head", in addition to the hydrophobic fatty acids "hydrophobic tails". This makes phospholipids *amphipathic* compounds; which when dissolved in water, the form **micelles** in order to minimize the contact between the hydrophobic tails and the polar molecules of water. Phospholipids form **cells' membranes** and can also form **liposomes** which have aqueous cavity inside.

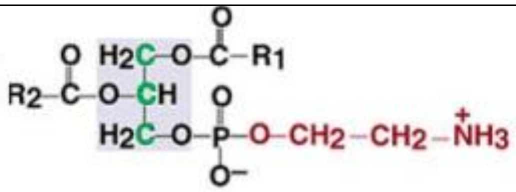
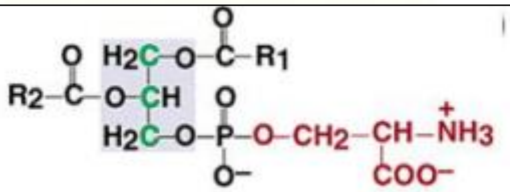
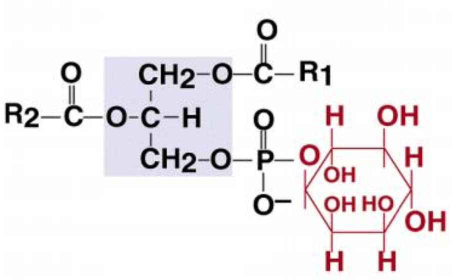
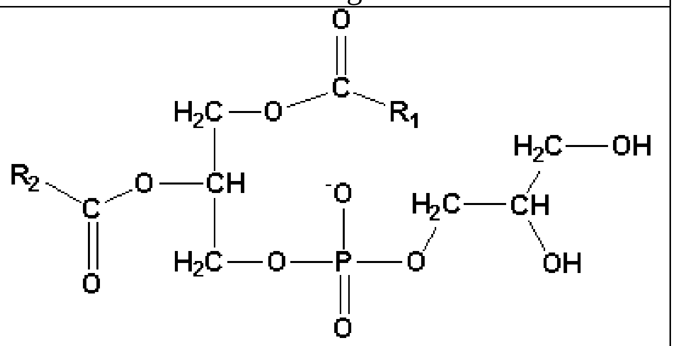
- Application

  Oil does not dissolve in water; instead, it forms distinct layer above the water surface. But when phospholipids are added to the solution, they will form micelles and integrate the nonpolar oil molecules into the interior of the micelles. This allows us to dissolve oils, butters and fatty acids in water. The resulted solution is a suspension which has a milky appearance, which is called *emulsion*, and phospholipids are called *emulsifiers*. Lecithin is used in food manufacturing "ex. Chocolates, powder milk …etc."



3: the name of PAGs is generally "phosphatidyl*alcohol*"

4: in order to understand the properties of a compound, scientists use space-filling models, which allow the three dimensional examination of the models.

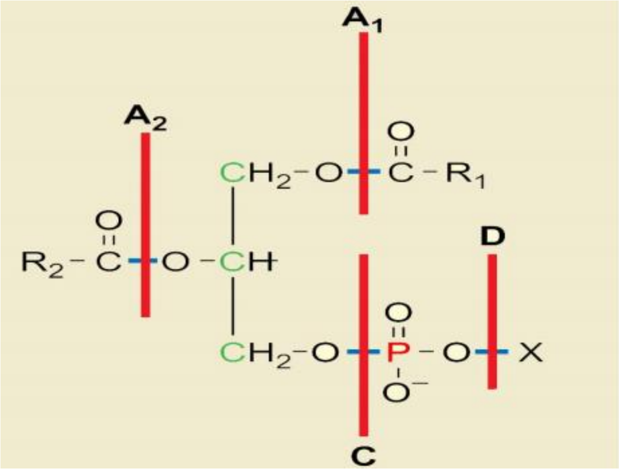
PAGs	Information
Phosphatidylethanolamine	
Phosphatidylserine	
Phosphatidylinositol	 Notice: inositol is not charged.
Phosphatidylglycerol	
cardiolipin	2 molecules of phosphatidic acid are connected by glycerol group. Not that important .

Degradation of phosphoacylglycerols

Phosphoacylglycerols have 4 ester bonds, each one has a different location and binds different molecules. So, to hydrolyze or esterify these bonds, specific enzyme will be needed to each bond. *Phospholipases* hydrolyze phosphoacylglycerol ester bonds in the following manner:

Phospholipase	substrate	Bond broken	products
A1	**INTACT** PHOSPHOACYL-GLYCEROLS ONLY	1st ester bond	FA + lysophosphoglyceride
A2		2nd ester bond	FA + lysophosphoglyceride
C		Ester bond between the phosphate group and glycerol	DAG + phosphorylated alcohol
D		Ester bond between the phosphate group and the alcohol	Phosphatidic acid + alcohol

5: make sure to be familiarized nomenclature. All these PAGs can participate in cell membrane formation.



- What about phospholipase B?
- This enzyme acts on *lysophosphoglyceride*, and hydrolyzes the ester bond between the glycerol and the remaining fatty acid.

- Pieces of information about the phospholipases:

- PLA2:

1- It is present in many mammalian tissues and pancreatic juice; it is also present in snake and bee venoms. This is behind the fact that victims of snake bite will have lyses of tissues.
2- Acting on phosphatidylinositol, releases arachidonic acid "precursor of prostaglandins; inflammatory mediators."
3- It is inhibited by glucocorticoids "ex. cortisol", with the result of anti-inflammatory effect.

- PLC:

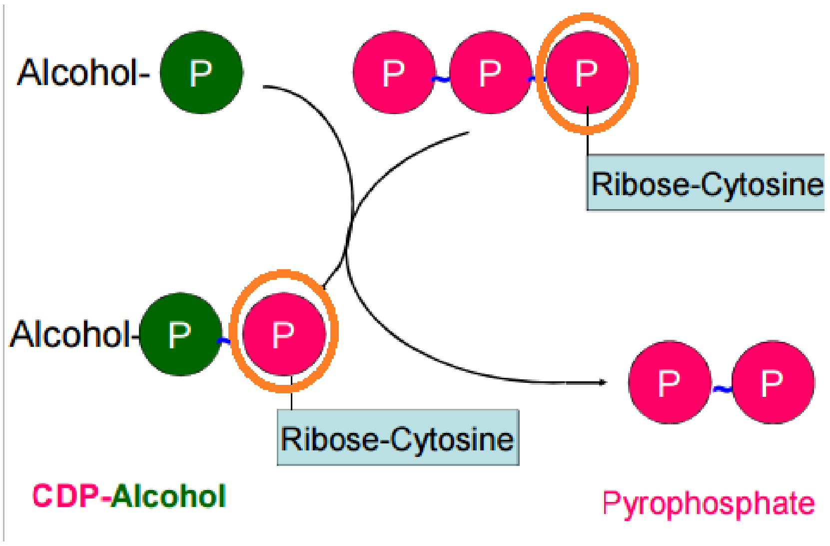
  Membrane-bound PLC is activated by PIP_2 system and, thus, plays a role in producing second messengers "produces DAG".

Synthesis of phosphoacylglycerols

Phosphatidic acid is a common intermediate between the biosynthesis of PAGs and TAGs. So, the same mechanism is used here to form pohosphatidic acid. The synthesis of phosphoacylglycerol has the following componnts: $alcohol_1$ "diacylglycerol", phosphate group and $alcohol_2$ "serine, inositol …etc."

Synthesis pathways usually require the activation of the components of synthesis.

- Formation of Activated Carrier



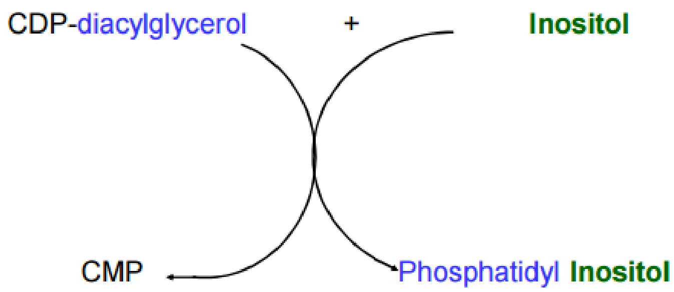
CTP + phosphorylated alcohol = CDP-alcohol + PPi

ΔG of the reaction is almost zero; it includes the breaking of a high energy bond "P-P in CTP", and the formation of a high energy bond "P-P in the CDP-alcohol". The hydrolysis of pyrophosphate by pyrophosphatase pushes the reaction into the forward direction. See the following examples:

- Transfer the activated alcohol to the other alcohol

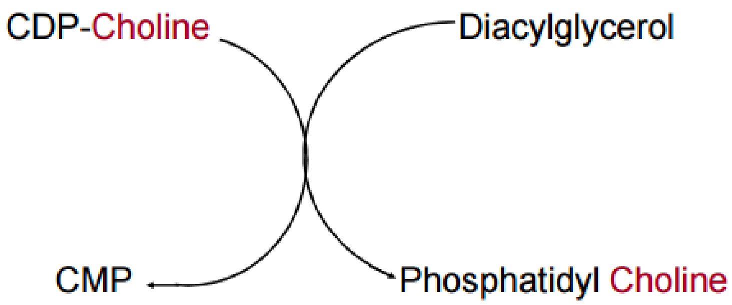
One of the alcohols is activated, and transferred to the other one. Two ways of transfer are:

1- Transfer ~(Phosphate-Alcohol$_1$) to Alcohol$_2$: the activated is phosphate-alcohol$_1$; includes inositol and glycerol (to make phosphatidylinositol/ phosphatidelglycerol).

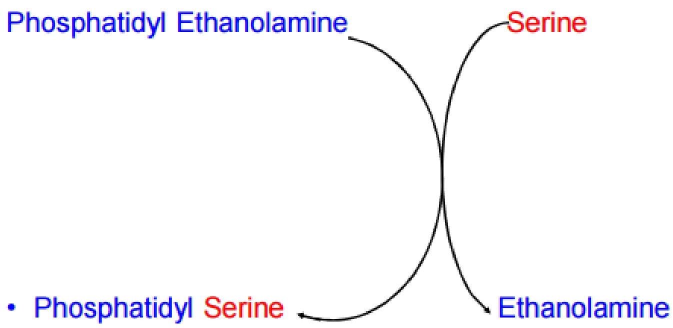


Notice: one of the two phosphates of CDP is incorporated in the PAG, and the other exits as CMP.

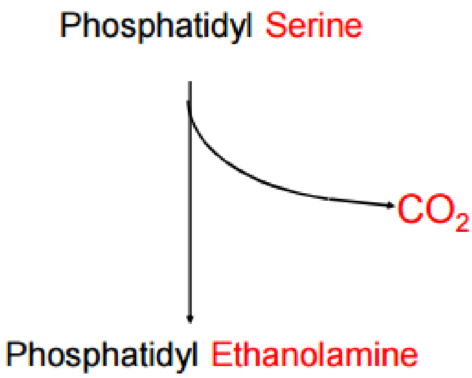
2- Transfer ~(Phosphate-Alcohol$_2$) to Alcohol$_1$: the activated is phosphate-alcohol$_2$; includes choline and ethanolamine.



- <u>The formation of phosphatidylserine:</u>
  This PAG is not produced by the previous methods, but by **exchange** of the polar head group. Carboxylation of ethanolamine to serine <u>does not occur</u>.



From phophatidylserine, phosphatidylethanolamine can be produced by decarboxylaion reaction. This reaction is irreversible. In order to get serine back into the compound, the exchange step must occur.



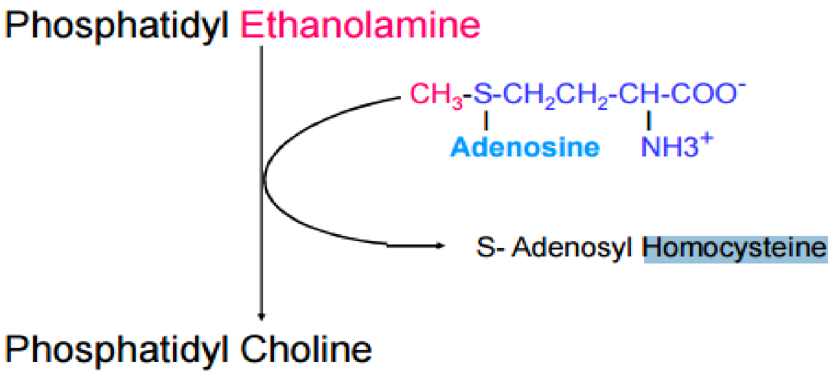
The net reaction of the exchange process and the decarboxylation is:

Serine >> Ethanolamine + CO_2

- <u>The formation of phosphatidylcholine:</u>

Phosphatidylcholine can be formed by transfer as mentioned previously, but this requires continuous supply of choline. Methylation of phosphatidyl ethanolamine does not require continuous supply of choline. The donor of methyl groups is S- adenosyl methionine (SAM), which contains methionine "amino acid with sulfur atom (thio) and methyl group (met)", which is bound to adenosine by the sulfur atom. The unusual thing about SAM structure is that the sulfur atom makes 3 bonds instead of 2; which leaves it **unstable** and results with the methyl group to be easily extracted. SAM is a

common methyl supplier in many methylation pathways "ex. Norepinephrine to epinephrine". SAM gives 1 methyl group at a time, so 3 SAM molecules are needed to make phaosphatidylcholine from phosphatidylethanolamine.
After transferring the methyl group, SAM becomes S-adenosylhomocysteine[6].



Remodeling

After the activity of PLA2, fatty acid on the second ester bond can be **changed**. Then another fatty acid can be added. This results with variety of phosphoacylglycerols.

Ether glycerophospholipids: (Ether = R-O-R')

- The ether bond cannot be hydrolyzed like ester bonds.
- They are present in cell membranes
- The platelet-activating factor has an ether bond, acetyl-chain (instead of long chain acyl group) and plays a role in activating platelets and thrombosis.

Functions of phosphoacylglycerols

1- Cell membranes
2- Source of arachidonic acid
3- Signaling molecules: platelet-activating factor is an important signaling molecule for platelets activation and aggregation.
4- Used as emulsifiers.

"If you can sit with your pain, listen to your pain and respect your pain-in time you will move through your pain."

6: homocysteine has 2 carbon atoms instead of 3 in cysteine.