Biosynthesis Of Membrane Phospholipids

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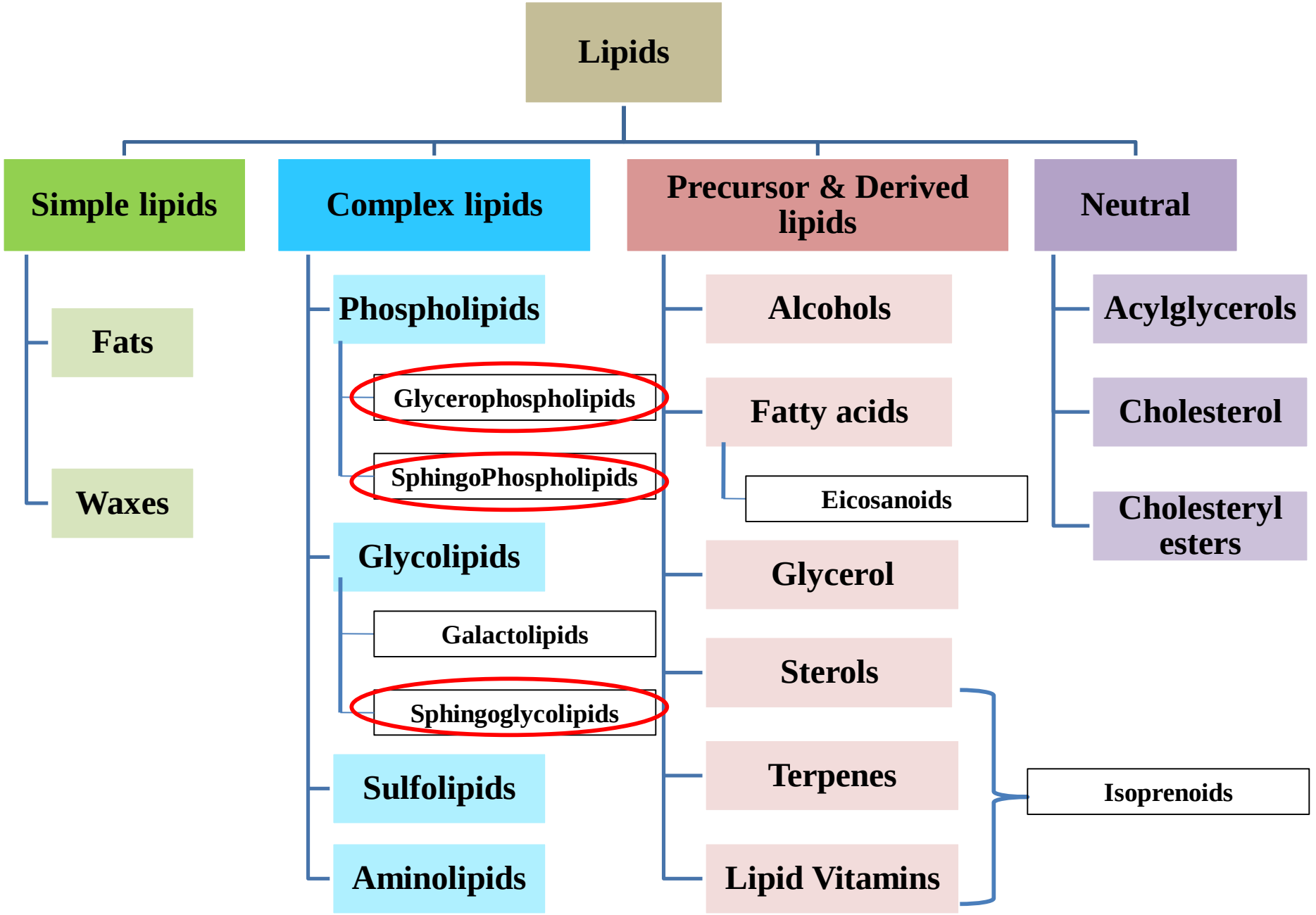
Phospholipids

- They are complex or conjugate lipids containing phosphoric acid, in addition to Fatty acid, Nitrogenous base & Alcohol.
- Many different phospholipid species can be constructed by combining various fatty acids and polar head groups with the glycerol or sphingosine backbone.
- In eukaryotic cells, phospholipid synthesis occurs primarily on the surfaces of the smooth endoplasmic reticulum and the mitochondrial inner membrane.

Phospholipids

- Some newly formed phospholipids remain at the site of synthesis, but most are destined for other cellular locations.
- They are transported in vesicles to their final destination.
- Two major classes of membrane phospholipids:
  1) Glycerophospholipids
  2) Sphingolipids


Lipids
Simple lipids
Complex lipids
Precursor & Derived lipids
Neutral
Fats
Waxes
Phospholipids
Glycerophospholipids
SphingoPhospholipids
Glycolipids
Galactolipids
Sphingoglycolipids
Sulfolipids
Aminolipids
Alcohols
Fatty acids
Eicosanoids
Glycerol
Sterols
Terpenes
Lipid Vitamins
Isoprenoids
Acylglycerols
Cholesterol
Cholesteryl esters

Assembly Of Phospholipids

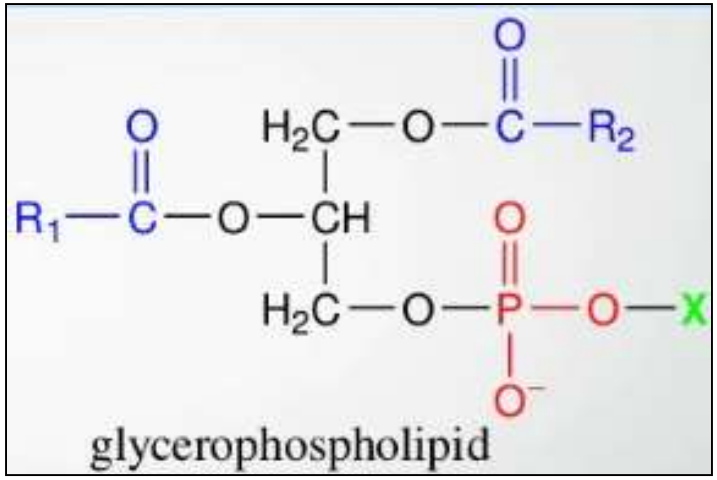
- All the biosynthetic pathways follow a few basic patterns. In general, **the assembly of phospholipids from simple precursors requires**-

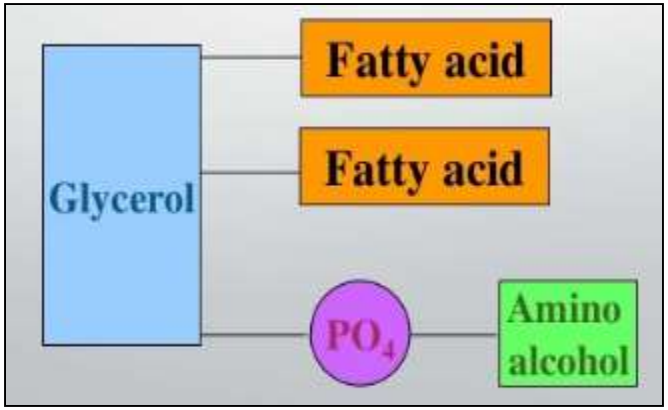
1) Synthesis of the backbone molecule (glycerol or sphingosine)
2) Attachment of fatty acid(s) to the backbone through an ester or amide linkage
3) Addition of a hydrophilic head group to the backbone through a phosphodiester linkage
4) Alteration or exchange of the head group to yield the final phospholipid product.

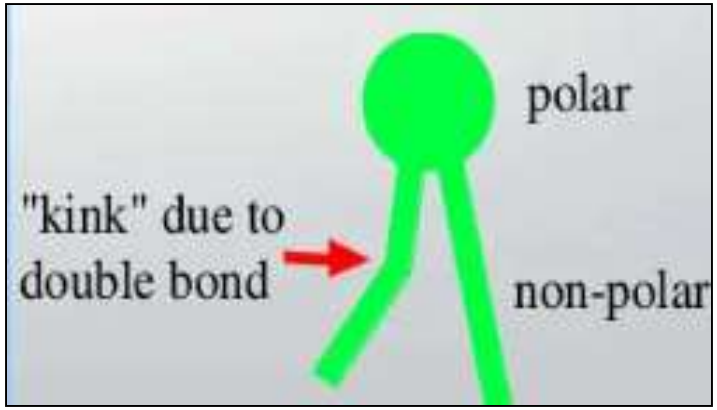
Gycerophospholipids

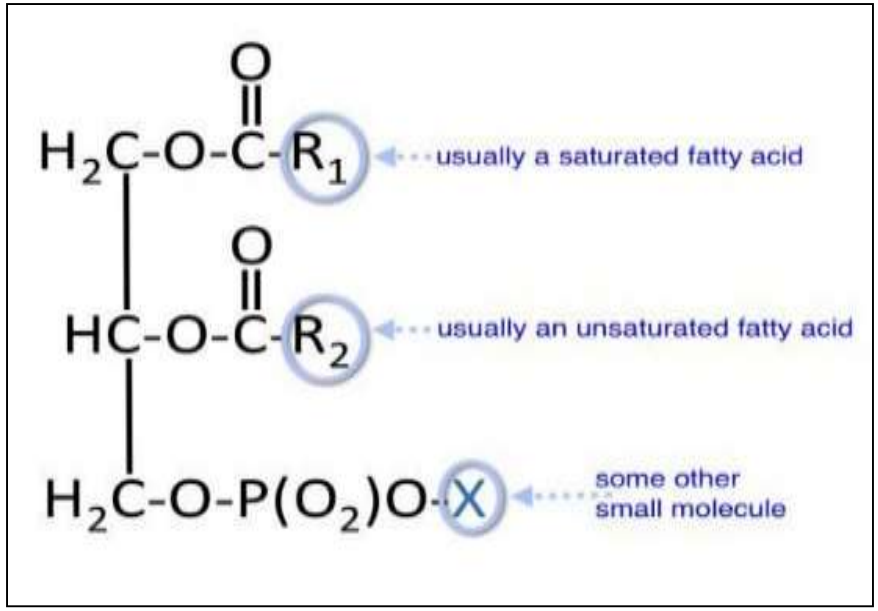
- Glycerophospholipids are the main class of phospholipids.
- They are the main lipid component of cell membranes, and are important in the cell's semipermeability.
- They also interact with triacylglycerols and cholesterol to increase their solubility in the blood.
- These abilities of glycerophospholipids are due to their **amphipathic nature**, with a polar head group and nonpolar tails.
- Each glycerophospholipid includes
  1) **polar region:** glycerol, carbonyl O of fatty acids, Pi, & the polar head group (X)
  2) **non-polar** hydrocarbon tails of fatty acids (R1, R2).

Gycerophospholipids

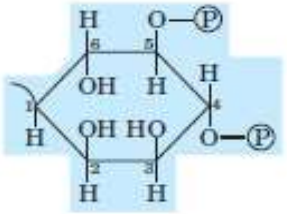
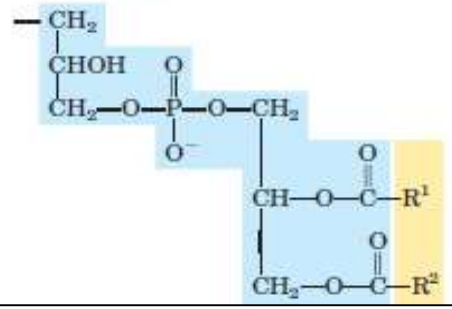








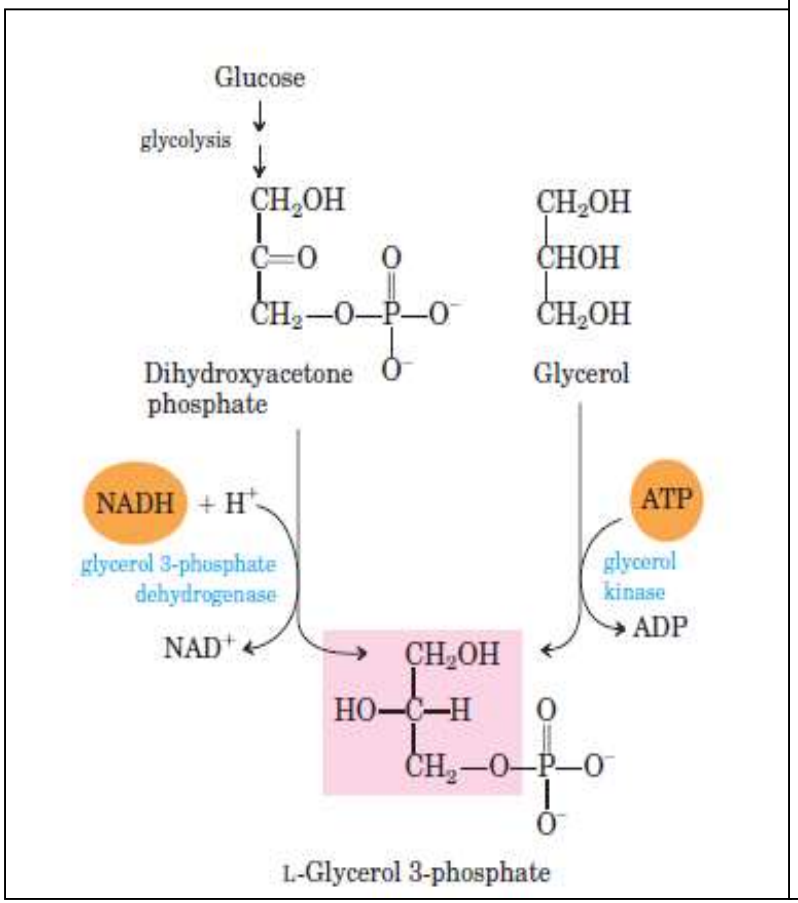
Glycerophospholipids

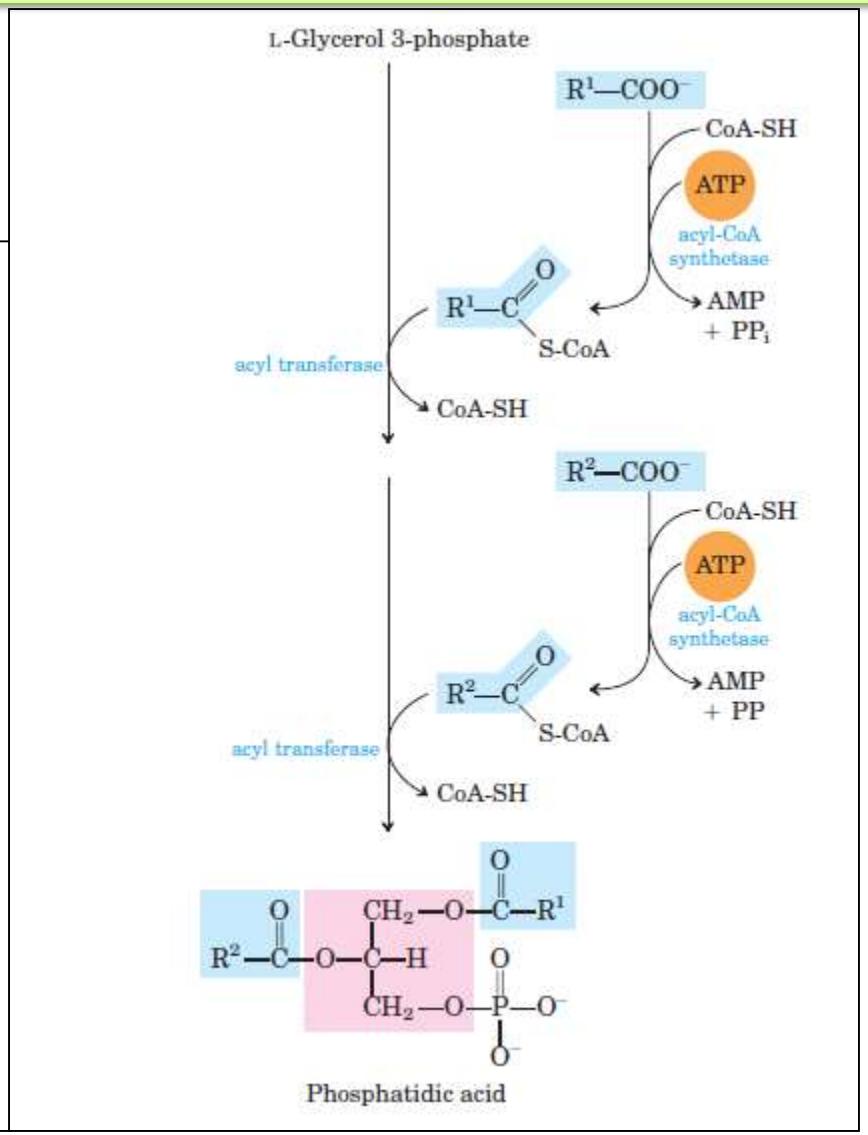
Name of glycerophospholipid	Name of X	Formula of X
Phosphatidic acid	—	—H
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Phosphatidylserine	Serine	$-CH_2-\underset{\displaystyle COO^-}{\underset{\vert}{CH}}-\overset{+}{N}H_3$
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{\displaystyle OH}{\underset{\vert}{CH}}-CH_2-OH$
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate	
Cardiolipin	Phosphatidyl-glycerol	

Biosynthesis of Glycerophospholipid

- Cells Have Two Strategies for Attaching Phospholipid Head Groups
- The **first step** where two fatty acyl groups are esterified to C-1 and C-2 of L-glycerol 3-phosphate to form phosphatidic acid.
- Commonly but not invariably, the fatty acid at C-1 is saturated and that at C-2 is unsaturated.

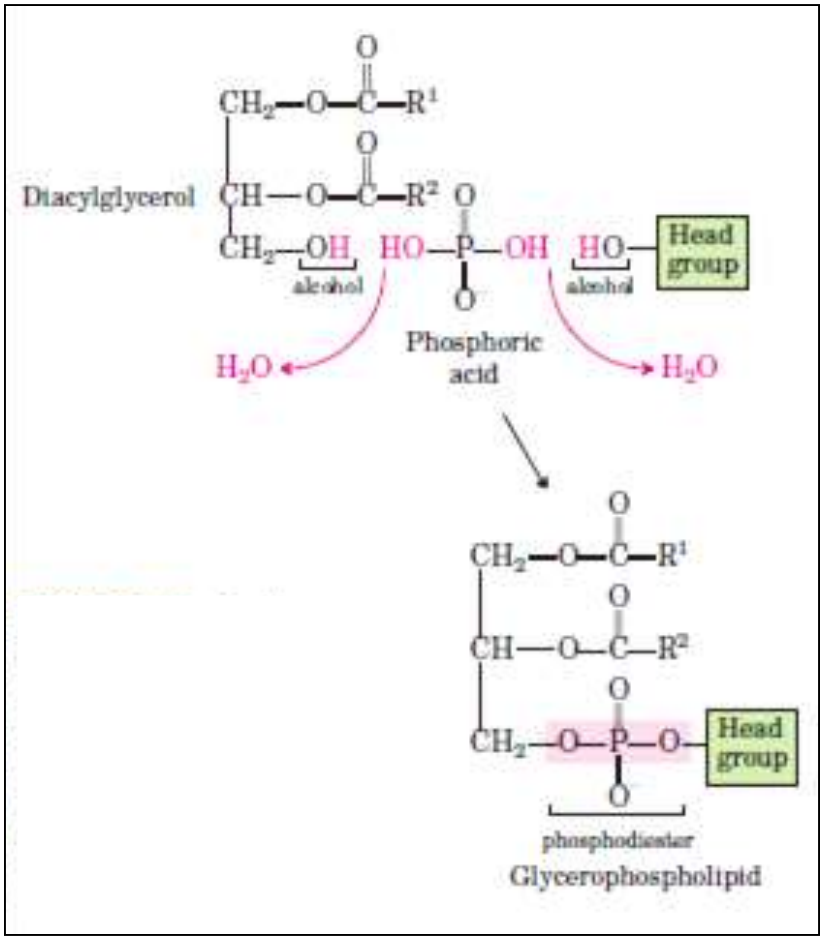
Biosynthesis of Glycerophospholipid





Biosynthesis of Glycerophospholipid

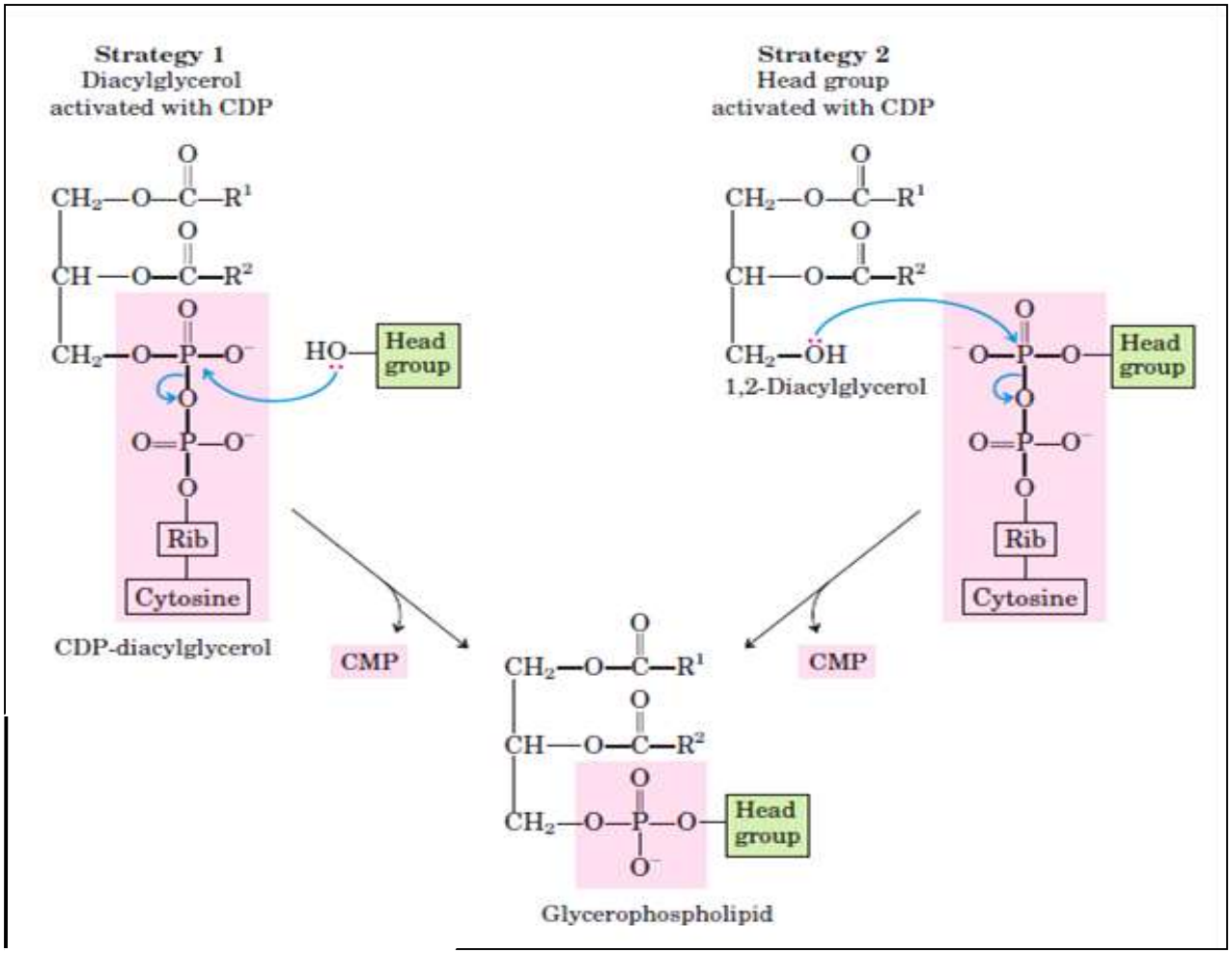
- A second route to phosphatidic acid is the phosphorylation of a diacylglycerol by a specific kinase.
- The polar head group of glycerophospholipids is attached through a phosphodiester bond, in which each of two alcohol hydroxyls (one on the polar head group and one on C-3 of glycerol) forms an ester bond with phosphoric acid.



Biosynthesis of Glycerophospholipid

- In the biosynthetic process, one of the hydroxyls is first activated by attachment of a nucleotide, cytidine diphosphate (CDP).
- Cytidine monophosphate (CMP) is then displaced in a nucleophilic attack by the other hydroxyl.
- The CDP is attached either to the diacylglycerol, forming the activated phosphatidic acid CDP-diacylglycerol (strategy 1), or to the hydroxyl of the head group (strategy 2).
- Eukaryotic cells employ both strategies, whereas prokaryotes use only the first.

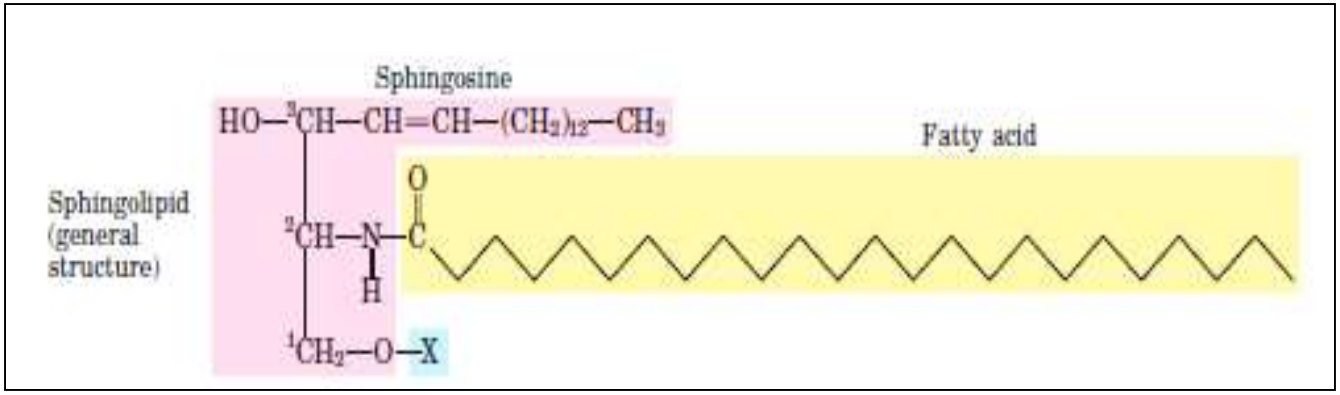
Biosynthesis of Glycerophospholipid

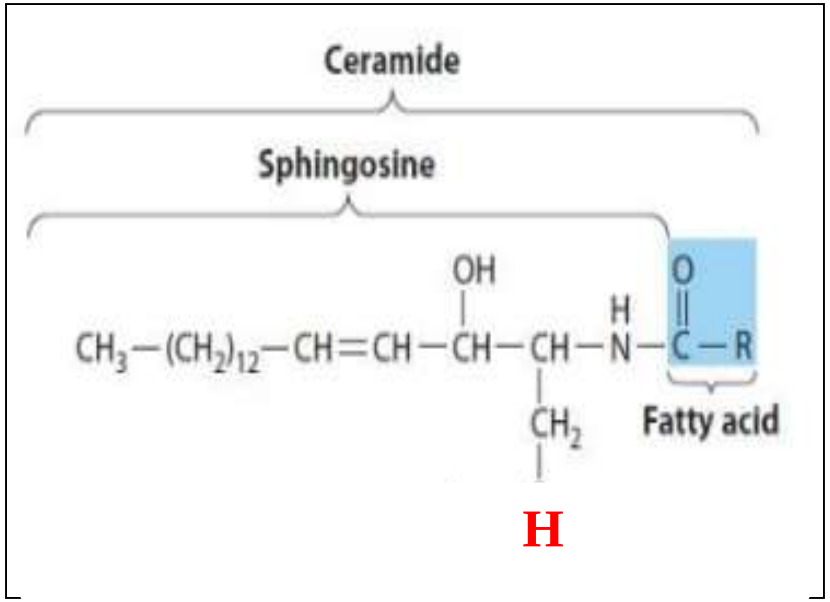


Sphingolipids

- Sphingolipids are the fourth large class of membrane lipids
- They have a polar head group and two non-polar tails.
- Sphingolipids are **composed of** :
  - one molecule of the long-chain amino alcohol (sphingosine)
  - one molecule of a long-chain fatty acid
  - a polar head group that is joined by a glycosidic linkage in some cases and by a phosphodiester in others.
- **Ceramide** is the structural parent of all sphingolipids.

Sphingolipids





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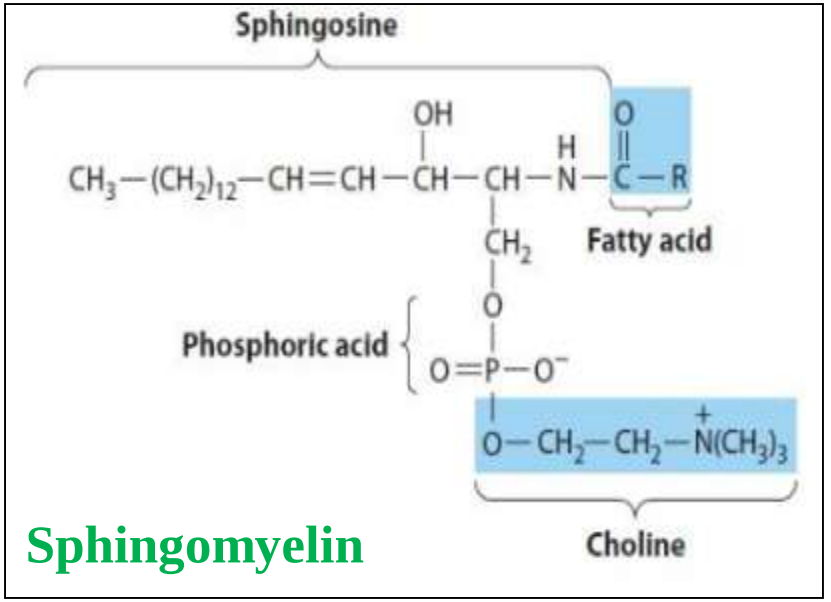
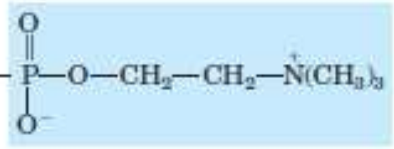
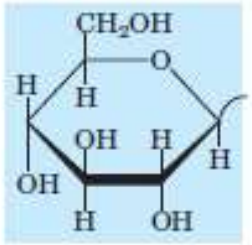
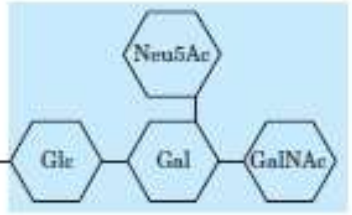


Sphingomyelin

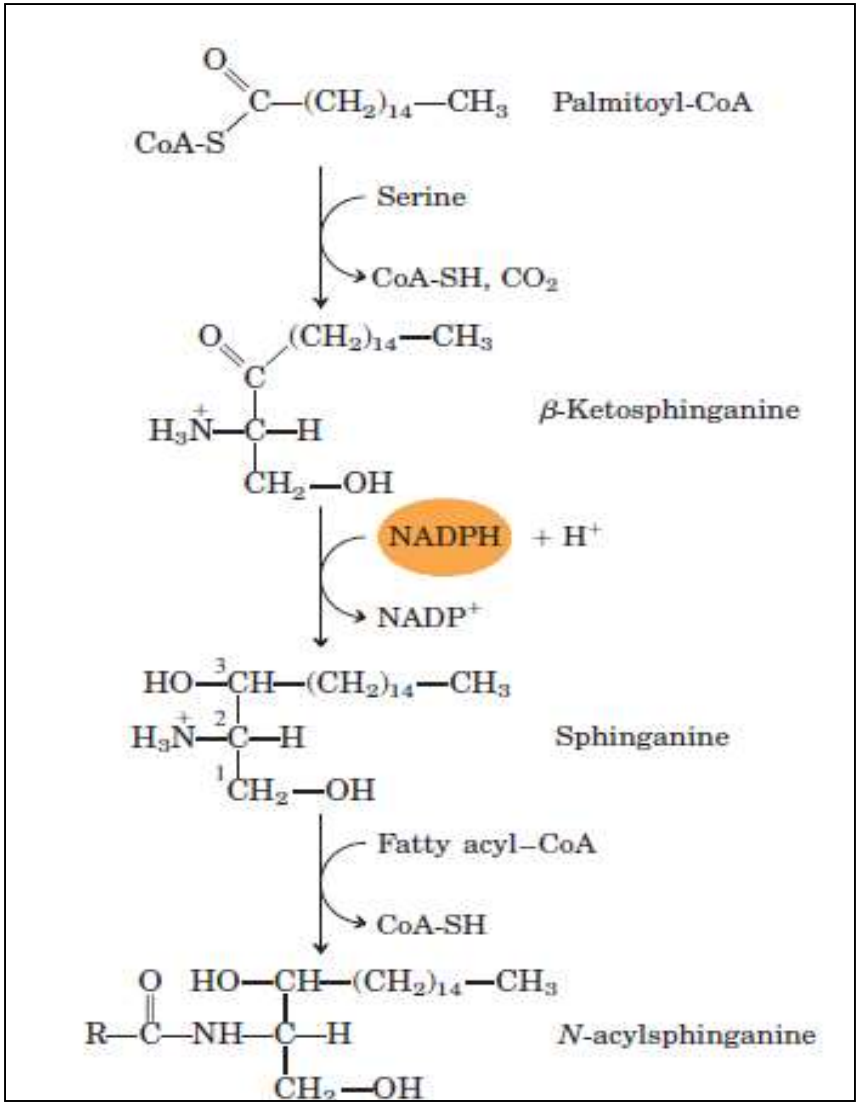
Sphingolipids

Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Biosynthesis of sphingolipids

- Condensation of palmitoyl-CoA and serine
- Condensation is followed by reduction with NADPH yields sphinganine.
- Sphinganine is then acylated to N-acylsphinganine.
- N-acylsphinganine is also known as ceramide.

Biosynthesis of sphingolipids



THANK YOU