
بسم الله الرحمن الرحيم

LIPID METABOLISM

Compound lipids metabolism

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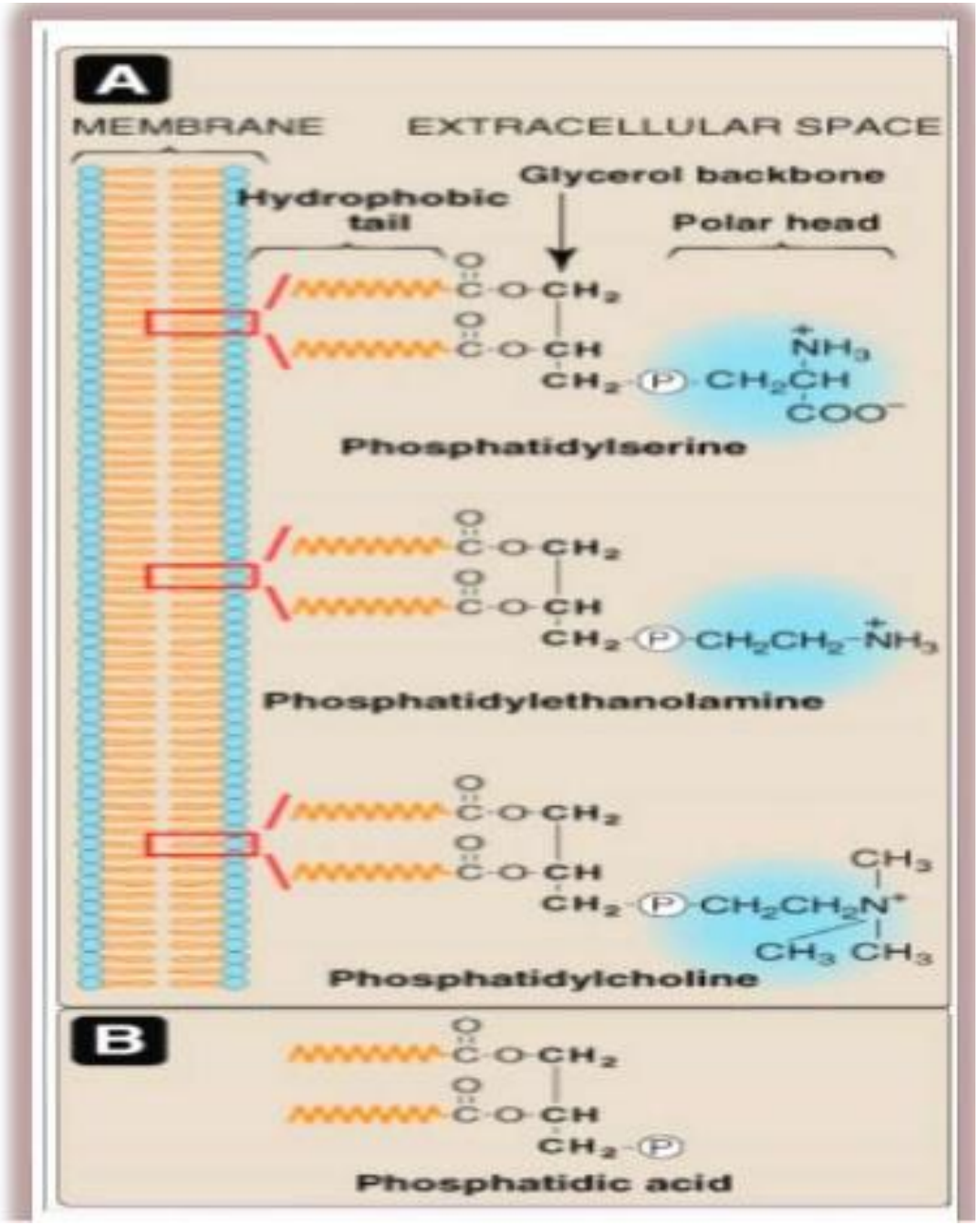
BY THE END OF THIS LESSON THE STUDENT WILL BE ABLE TO….

Inform Learner of Objectives

Know

- Phospholipids synthesis (compound lipids)
- Phospholipids degradation

Phosphilipids



- What are the three main steps in lecithin, cephalin, P serine and P Inasitol synthysis?

CLASSES OF PHOSPHOLIPIDS

- There are two classes of phospholipids:
- 1. Those that have glycerol as a backbone glycerophospholipids.

-Phosphtidylserine -Phosphtidylinasitol

- Phosphtidylcholine(lecithin) - Phosphtidylethanolamine(cephalin)

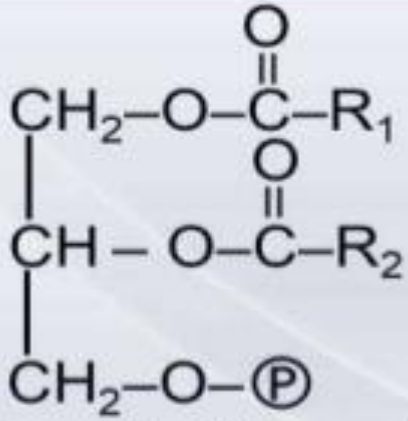
-Diphosphatidyl glycerol(cardiolipin) - plasmalogen

- 2.Those have sphingosine sphingophospholipids.

-Sphingomyelin

(i) Glycerophospholipid

Glycerophospholipids may be considered to be derivatives of phosphatidic acid

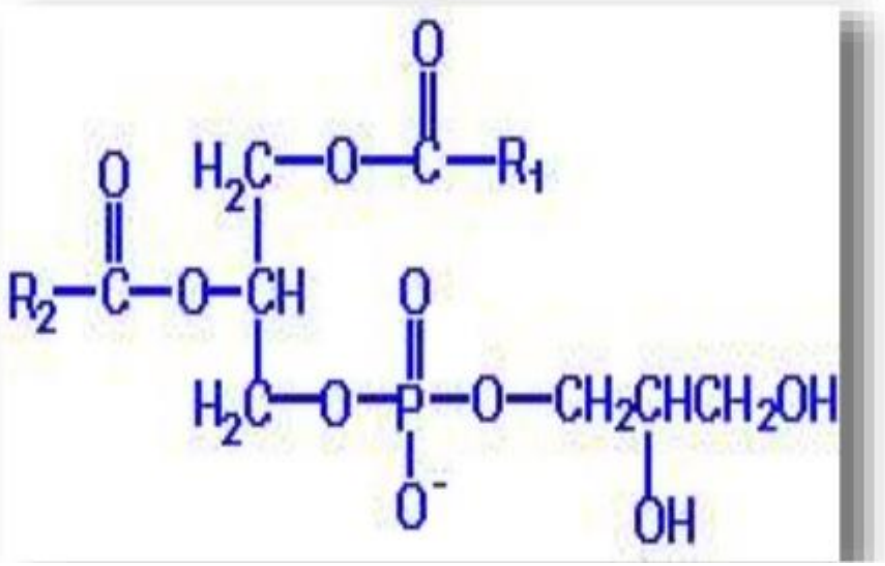


Phosphatidic acid

Phosphatidic acid is 1,2-Diacylglycerol-3-phosphate

synthesis of phosphatidyl glycerol and cardiolipin.

Phosphatidylglycerol



Synthesis of phosphatidyl glycerol & cardiolipin

- CDP-diacylglycerol combines with glycerol 3-phosphate to form phosphatidyl glycerol 3-phosphate, which forms phosphatidylglycerol.
- The phosphatidylglycerol combines with another molecule of phosphatidylglycerol to produce cardiolipin.
- Cardiolipin possess antigenic properties.

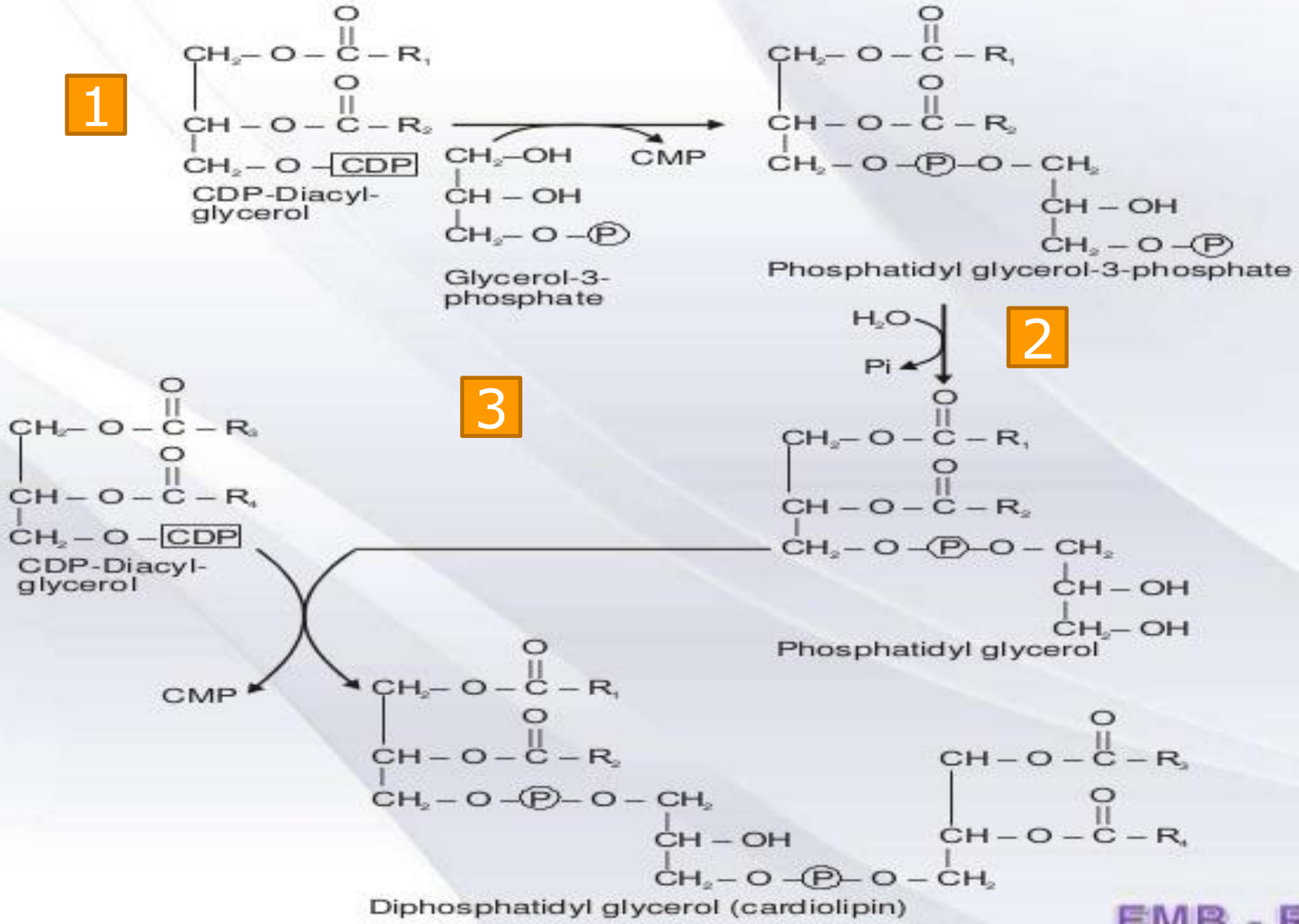
Synthesis of cardiolipin

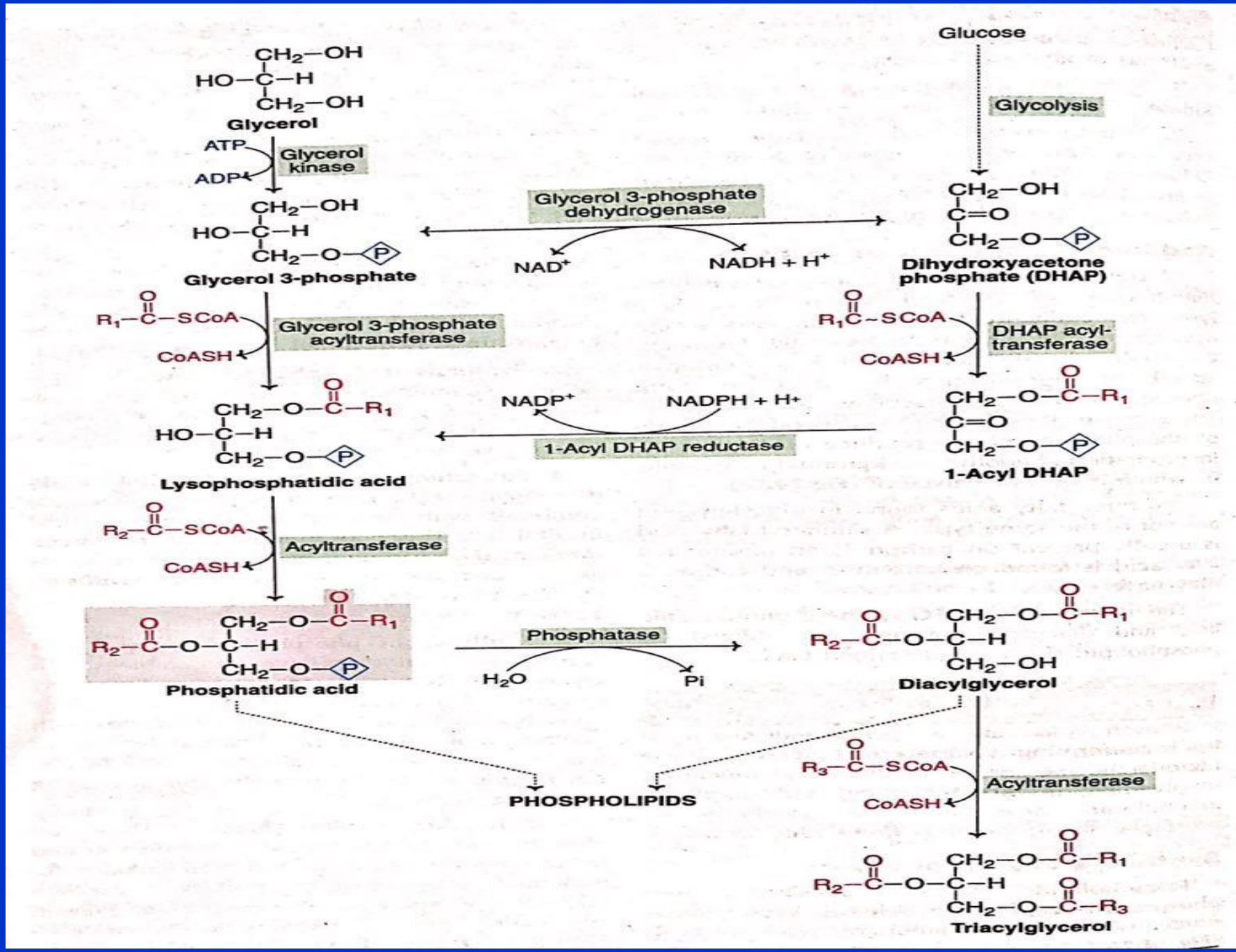
Cardiolipin is diphosphatidyl glycerol

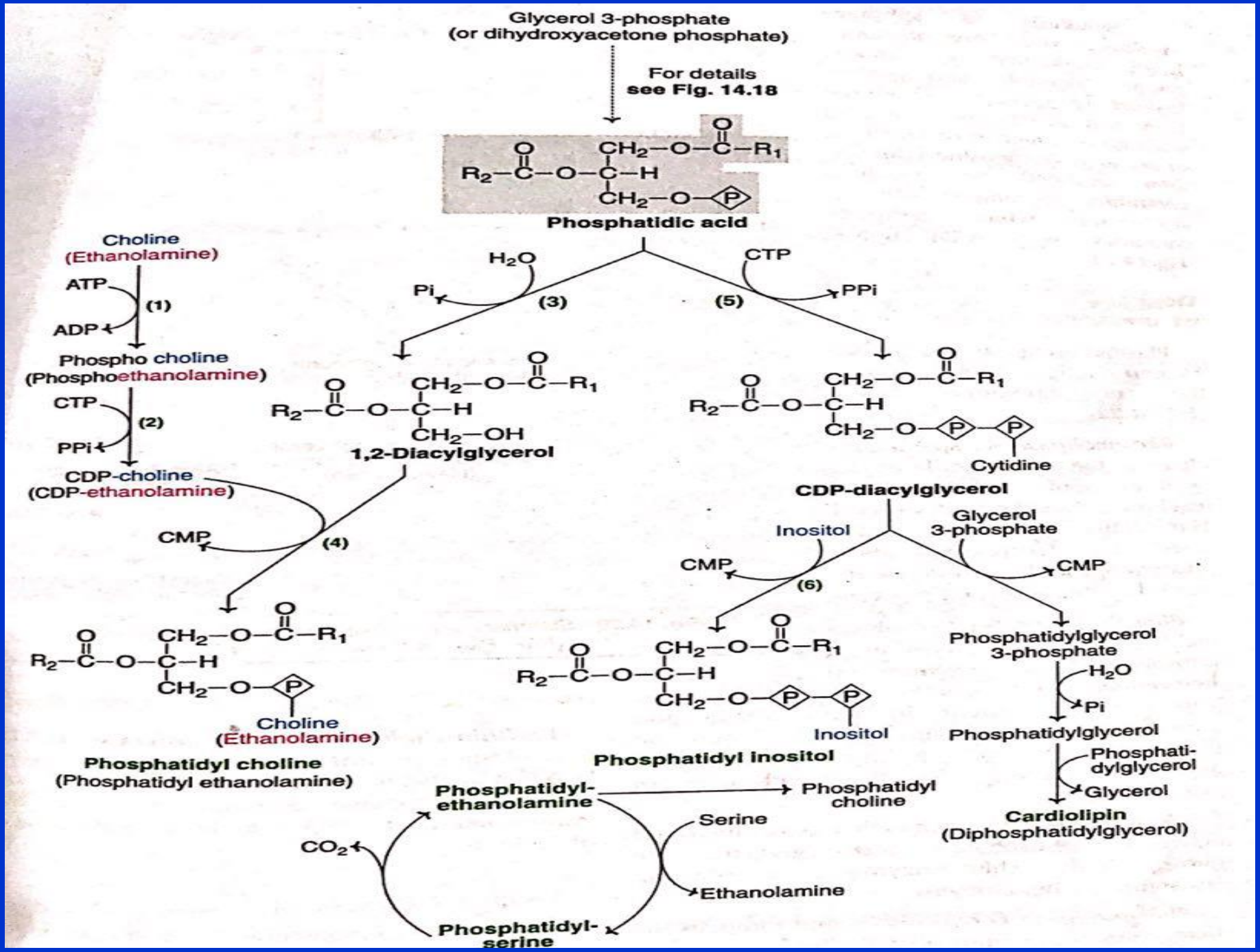
It is found only in mitochondria where it is synthesized from:

- Two molecules of CDP-diacylglycerol
- One molecule of glycerol-3-phosphate

Synthesis of cardiolipin




Glycerol
ATP
ADP
Glycerol kinase
Glycerol 3-phosphate
Glycerol 3-phosphate dehydrogenase
NAD+
NADH + H+
Glucose
Glycolysis
Dihydroxyacetone phosphate (DHAP)
CoASH
Glycerol 3-phosphate acyltransferase
DHAP acyl-transferase
Lysophosphatidic acid
NADP+
NADPH + H+
1-Acyl DHAP reductase
1-Acyl DHAP
Acyltransferase
Phosphatase
H2O
Pi
Phosphatidic acid
Diacylglycerol
PHOSPHOLIPIDS
Triacylglycerol


Glycerol 3-phosphate
(or dihydroxyacetone phosphate)
For details
see Fig. 14.18
Phosphatidic acid
Choline
(Ethanolamine)
ATP
(1)
ADP
Phospho choline
(Phosphoethanolamine)
CTP
(2)
PPi
CDP-choline
(CDP-ethanolamine)
CMP
(4)
Choline
(Ethanolamine)
Phosphatidyl choline
(Phosphatidyl ethanolamine)
H2O
Pi
(3)
1,2-Diacylglycerol
CTP
(5)
PPi
Cytidine
CDP-diacylglycerol
Inositol
CMP
(6)
Glycerol
3-phosphate
CMP
Inositol
Phosphatidyl inositol
Phosphatidylglycerol
3-phosphate
H2O
Pi
Phosphatidylglycerol
Phosphati-
dylglycerol
Glycerol
Cardiolipin
(Diphosphatidylglycerol)
Phosphatidyl-
ethanolamine
Phosphatidyl
choline
Serine
CO2
Ethanolamine
Phosphatidyl-
serine

synthesis of plasmalogen and PAF

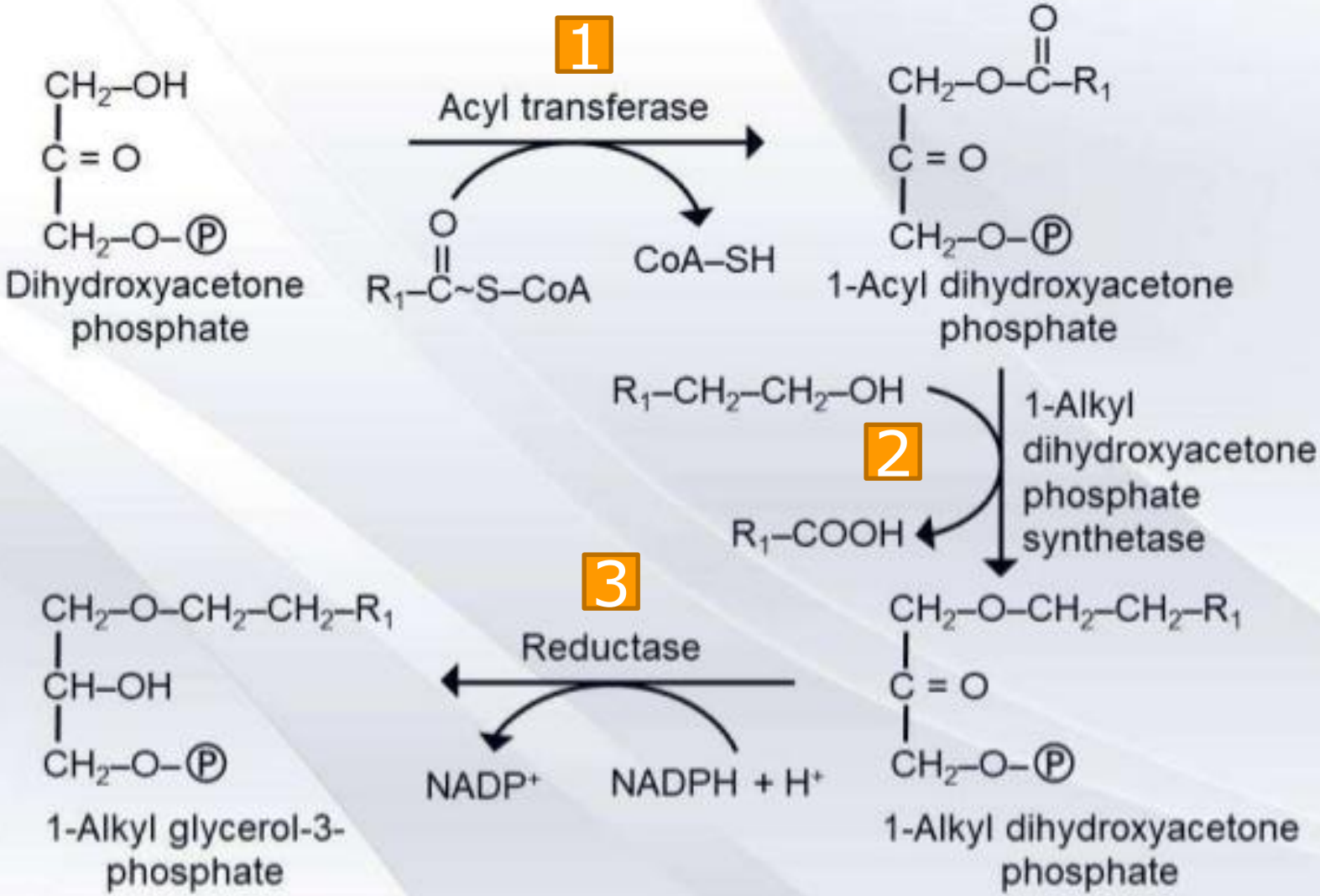
Plasmalogen:

- When the fatty acid at carbon 1 of a glycerophospholipid is replaced by an unsaturated alkyl group attached by an ether (rather than by an ester) linkage to the core glycerol molecule, an ether phosphoglyceride known as a plasmalogen is produced.

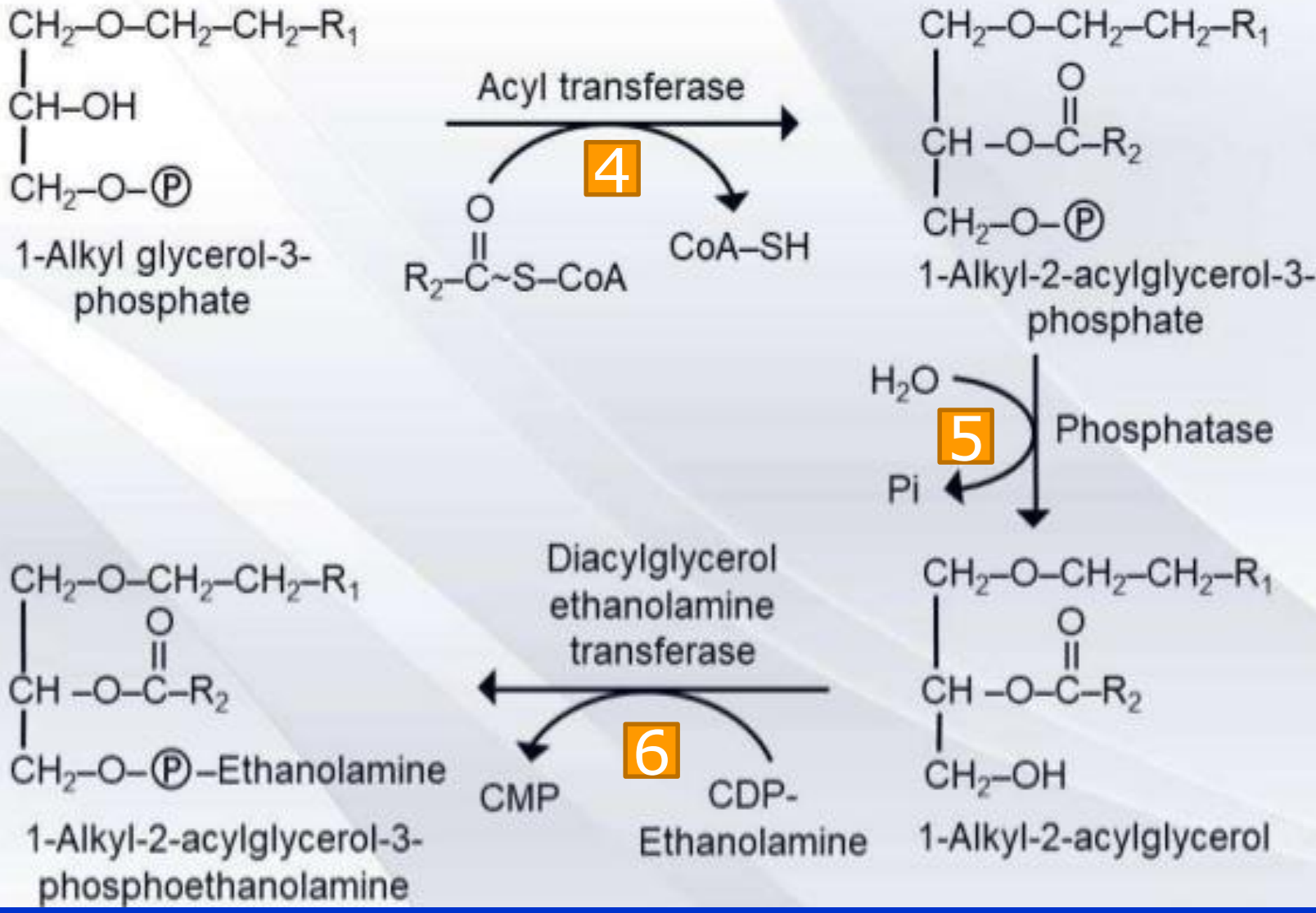
Formation of plasmalogens

- These are phospholipids with fatty acid at carbon 1 bound by an ether linkage instead of ester linkage.
- An important plasmalogen, 1-alkenyl 2-acetyl glycerol 3 –phosphocholine, causes blood platelet aggregation & is referred to as platelet activating factor (PAF).

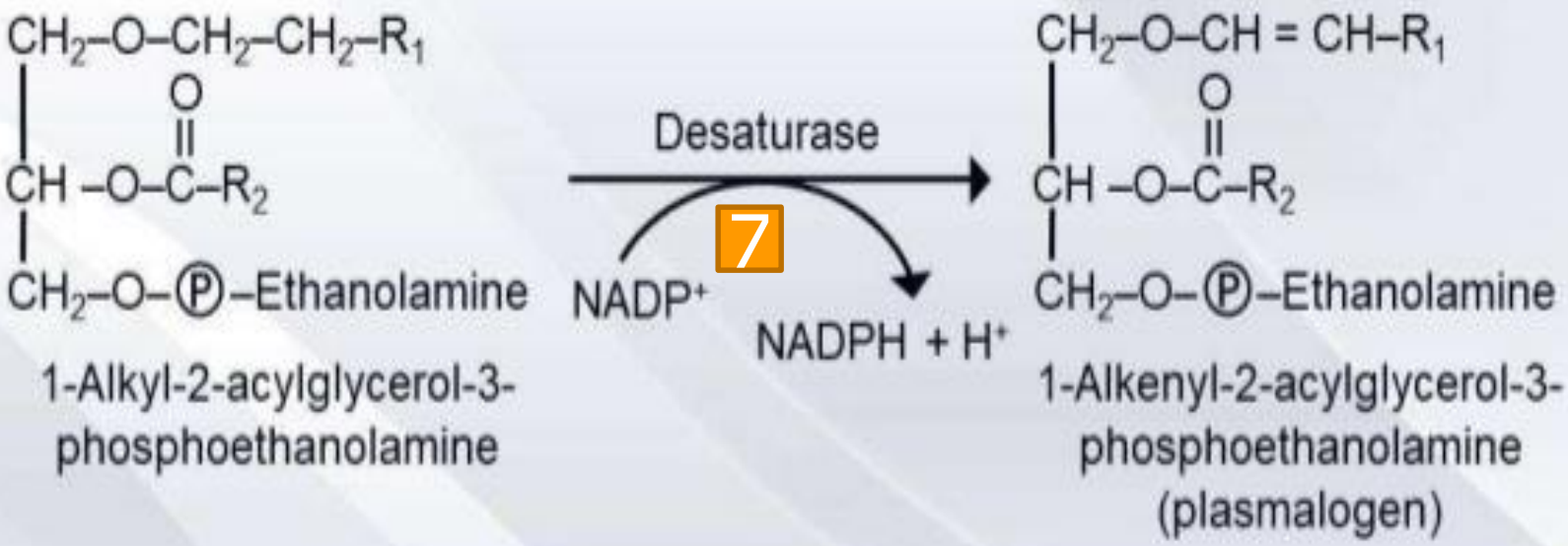
Synthesis of plasmalogen



Synthesis of plasmalogen



Synthesis of plasmalogen



Synthesis of plasmalogen

In some plasmalogens, ethanolamine is replaced by choline or serine

Ethanolamine plasmalogen is present in myelin

Choline plasmalogen is abundant in cardiac tissue

Serine plasmalogen is present in retina and white matter

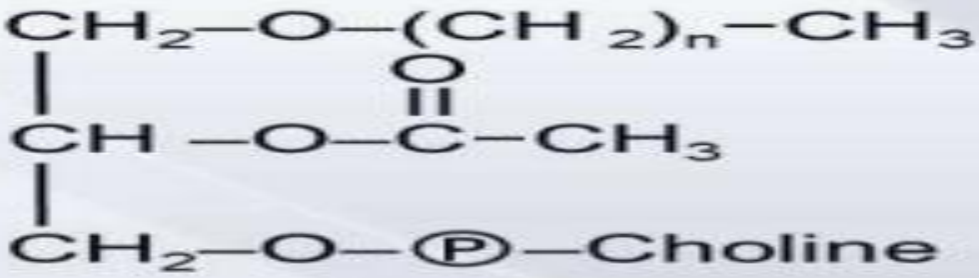
PAF

Platelet activating factor (PAF) is a specific type of plasmalogen

It has an alkyl group (generally 16-carbon) at position 1

The acyl group at position 2 is acetate

Phosphocholine is present at position 3



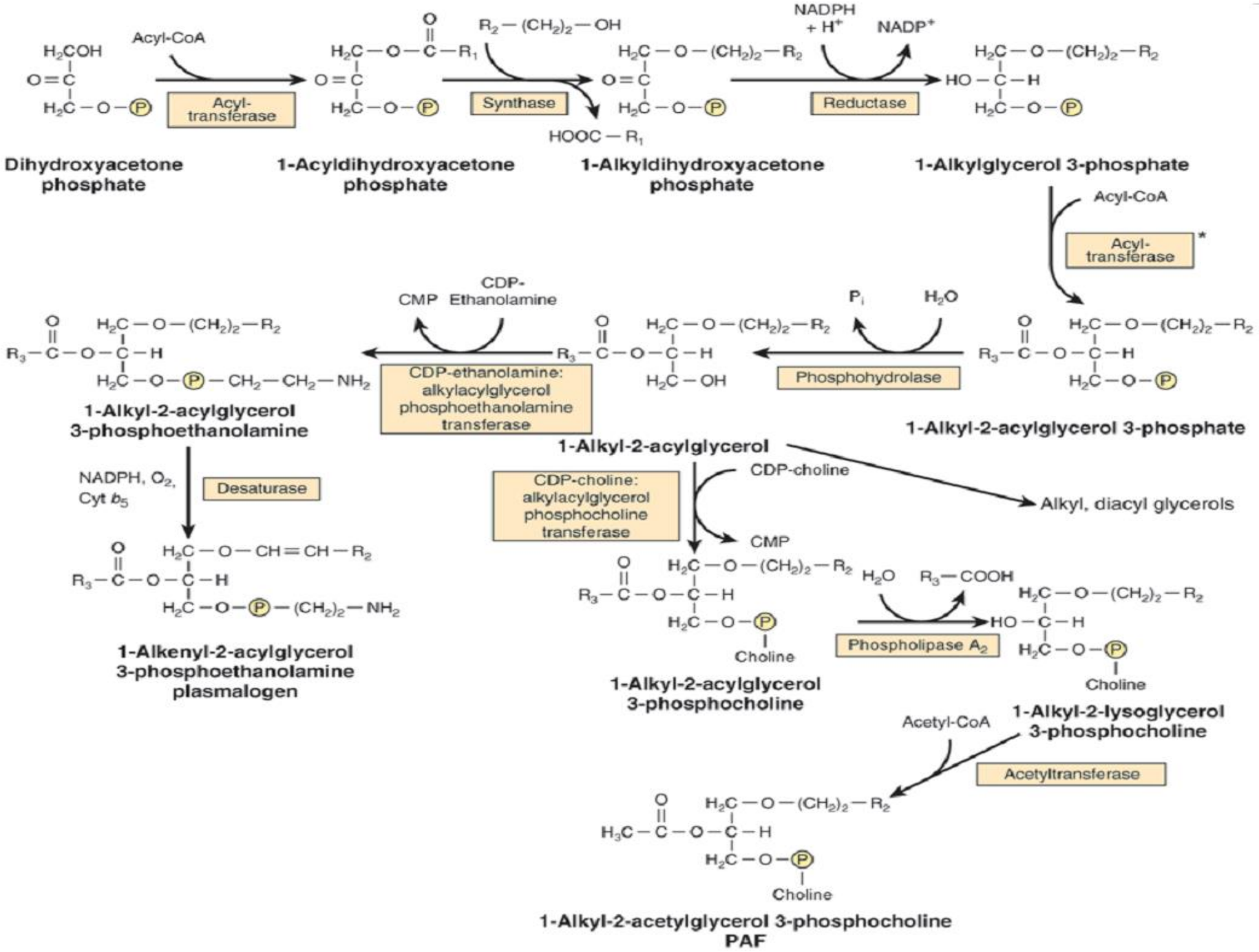
1-Alkyl-2-acetylglycerol-3-phosphocholine
(platelet activating factor)

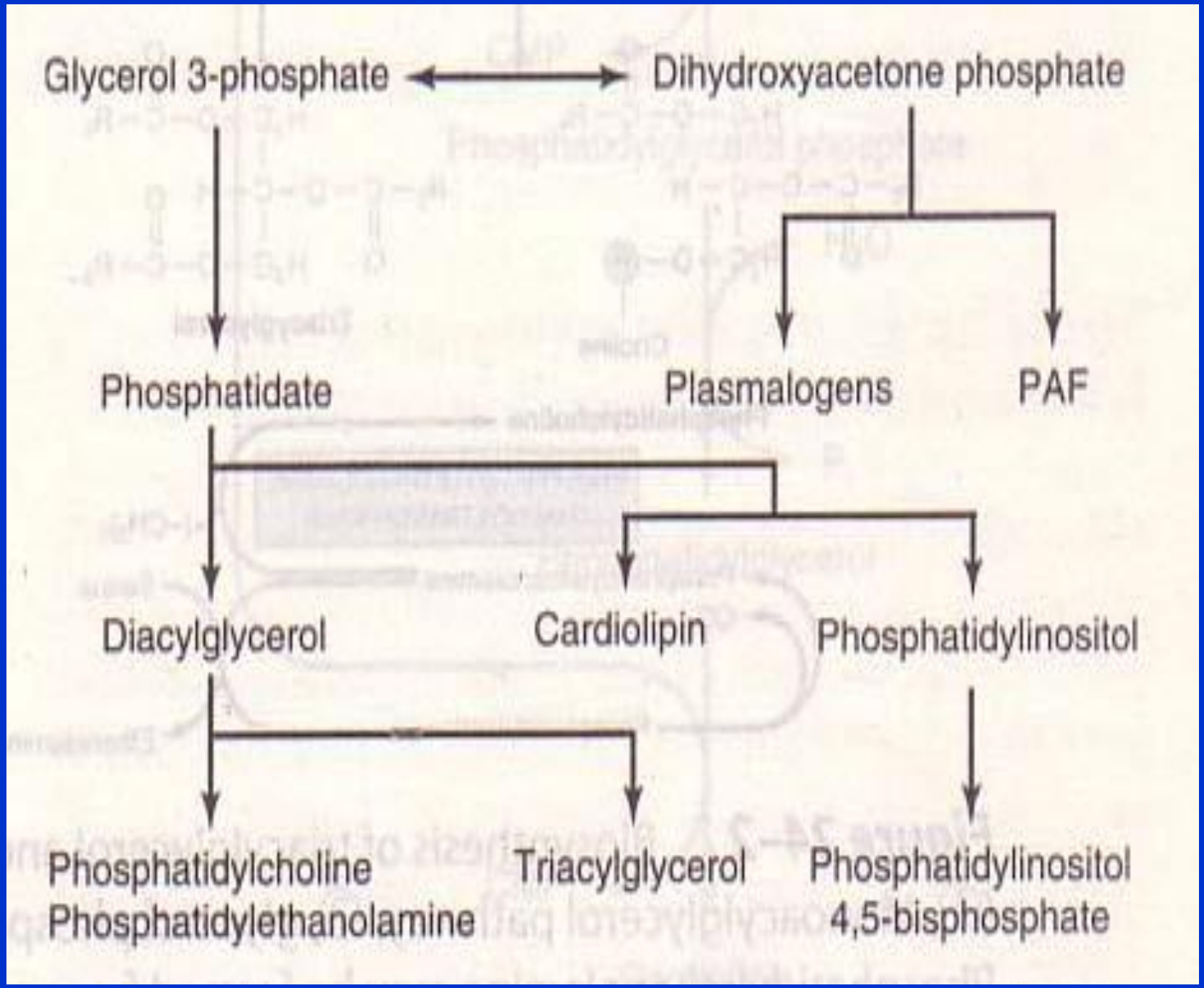
PAF is released by several types of cells in response to a variety of stimuli

It is a very powerful chemical mediator

It mediates inflammatory reaction, hypersensitivity and anaphylactic shock

PAF causes platelet aggregation, vasodilatation and bronchoconstriction


Acyl-CoA
Acyl-transferase
Dihydroxyacetone phosphate
1-Acyldihydroxyacetone phosphate
$R_2-(CH_2)_2-OH$
Synthase
$HOOC-R_1$
1-Alkyldihydroxyacetone phosphate
NADPH + H^+
$NADP^+$
Reductase
1-Alkylglycerol 3-phosphate
Acyl-CoA
Acyl-transferase
*
1-Alkyl-2-acylglycerol 3-phosphate
P_i
H_2O
Phosphohydrolase
1-Alkyl-2-acylglycerol
CDP-choline
Alkyl, diacyl glycerols
CDP-choline: alkylacylglycerol phosphocholine transferase
CMP
Choline
1-Alkyl-2-acylglycerol 3-phosphocholine
H_2O
R_3-COOH
Phospholipase A_2
Choline
1-Alkyl-2-lysoglycerol 3-phosphocholine
Acetyl-CoA
Acetyltransferase
1-Alkyl-2-acetylglycerol 3-phosphocholine
PAF
CDP-
CMP
Ethanolamine
CDP-ethanolamine: alkylacylglycerol phosphoethanolamine transferase
1-Alkyl-2-acylglycerol 3-phosphoethanolamine
NADPH, O_2, Cyt b_5
Desaturase
1-Alkenyl-2-acylglycerol 3-phosphoethanolamine plasmalogen


Glycerol 3-phosphate
Dihydroxyacetone phosphate
Phosphatidate
Plasmalogens
PAF
Diacylglycerol
Cardiolipin
Phosphatidylinositol
Phosphatidylcholine
Phosphatidylethanolamine
Triacylglycerol
Phosphatidylinositol
4,5-bisphosphate

Degradation of Phospholipids

Degradation of Phospholipids

- **Phospholipids are degraded by phospholipases which cleave the phosphodiester bonds.**
- **Four types of phospholipases.**
- **Phospholipase A_1**
- **Phospholipase A_2**
- **Phospholipase C**
- **Phospholipase D**

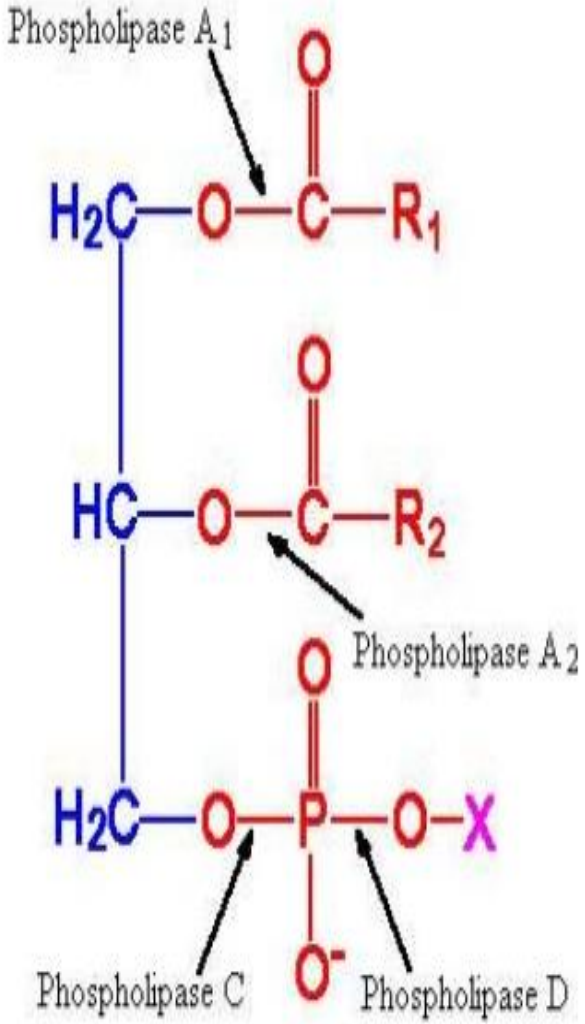
Degradation of Phospholipids

Phospholipase A_1:

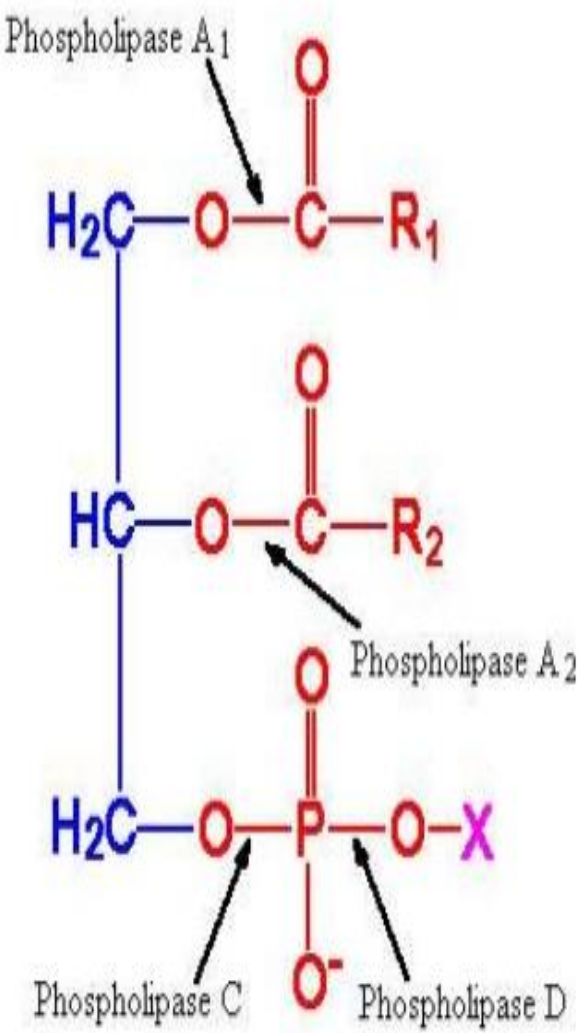
It specifically cleaves the fatty acid at C_1 position of phospholipids resulting in lysophospholipid.

These are further acted by lysophospholipase, phospholipase B to remove the second acyl group at C_2 position.

Degradation of phospholipids



Degradation of phospholipids

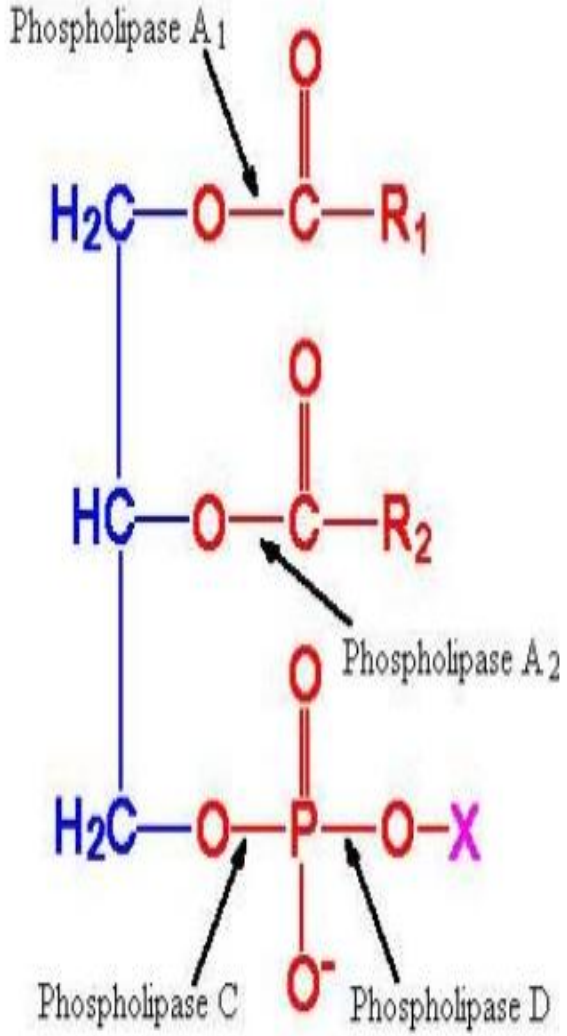


Phospholipase A_2 hydrolyses the fatty acid at C_2 position of phospholipids.

Snake venom & bee venom are rich sources of phospholipase A_2.

Phospholipase A_2 acts on phosphatidyl inositol to liberate arachidonic acid, the substrate for the synthesis of prostaglandins.

Degradation of phospholipids



Phospholipase C specifically cleaves the bond between phosphate & glycerol of phospholipids.

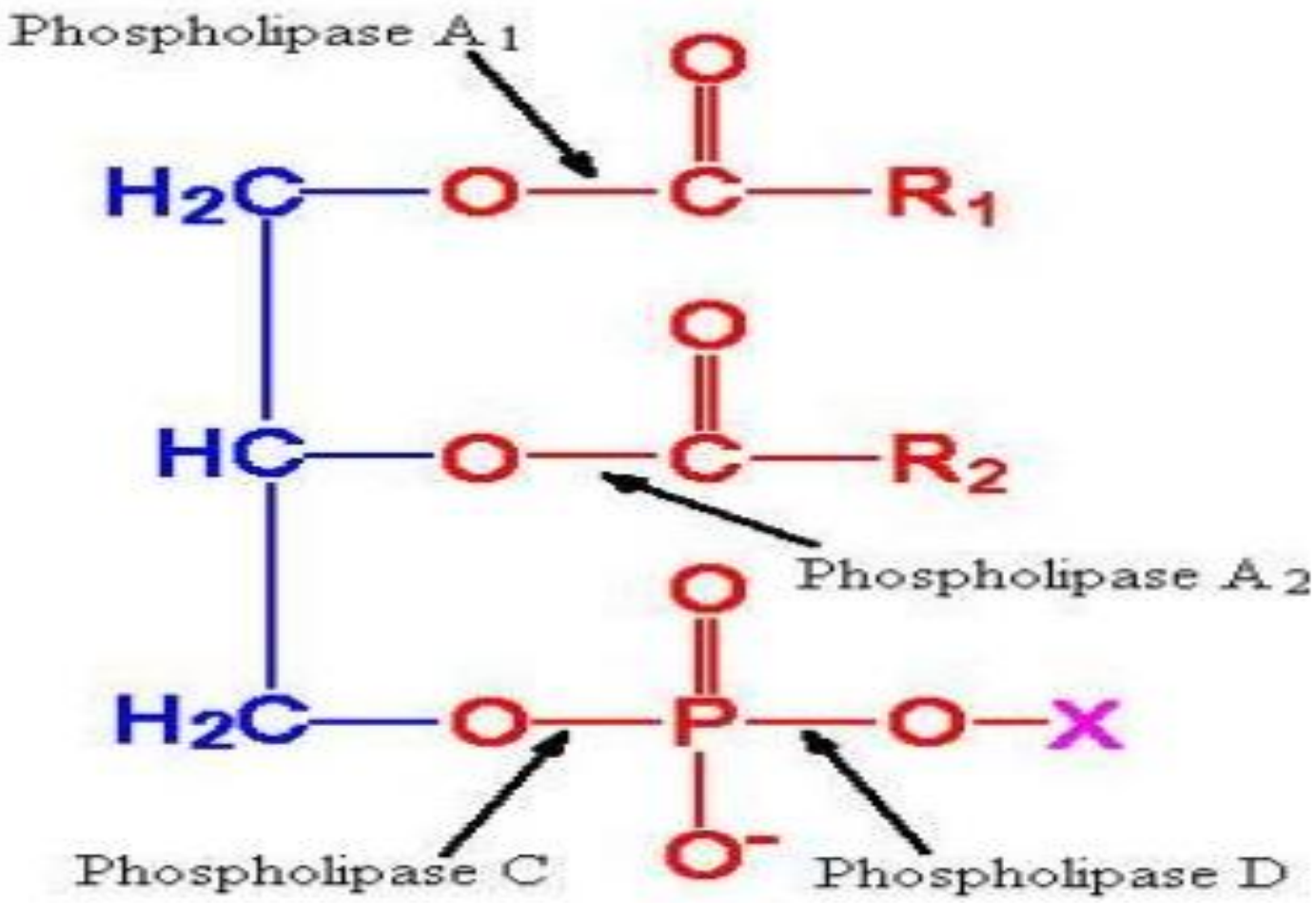
Phospholipase C is present in lysosomes of hepatocytes.

Phospholipase D hydrolyses & removes the nitrogenous base from phospholipids.

The degraded products of phospholipids enter the metabolic pool & utilized for various purposes.

ENZYMES INVOLVED

Degradation of phospholipids



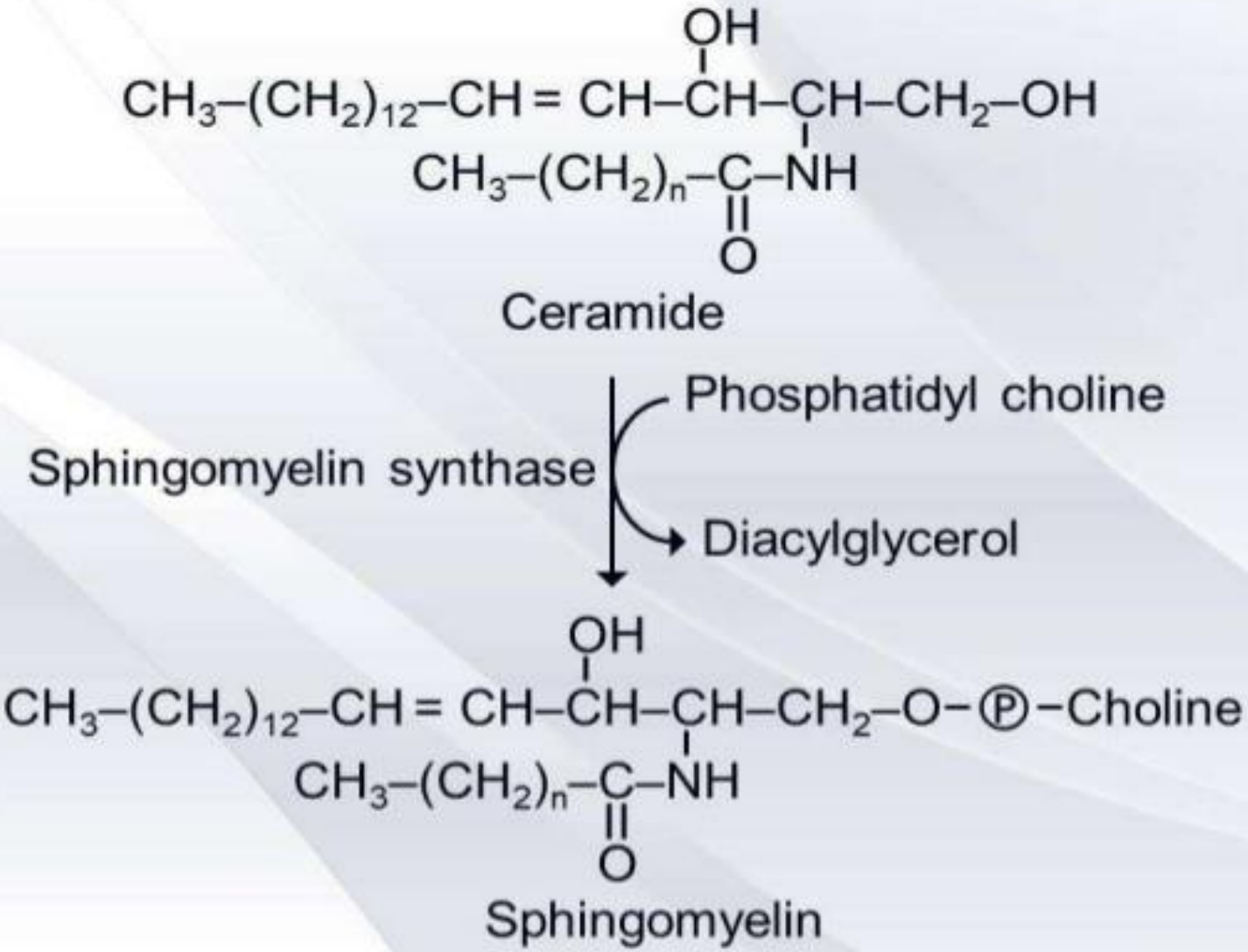
Synthesis of Sphingomyelin

Synthesis of sphingomyelin

Sphingomyelin is synthesized from ceramide and phosphatidyl choline

Ceramide is acyl sphingosine

SYNTHESIS OF SPHINGOMYELIN

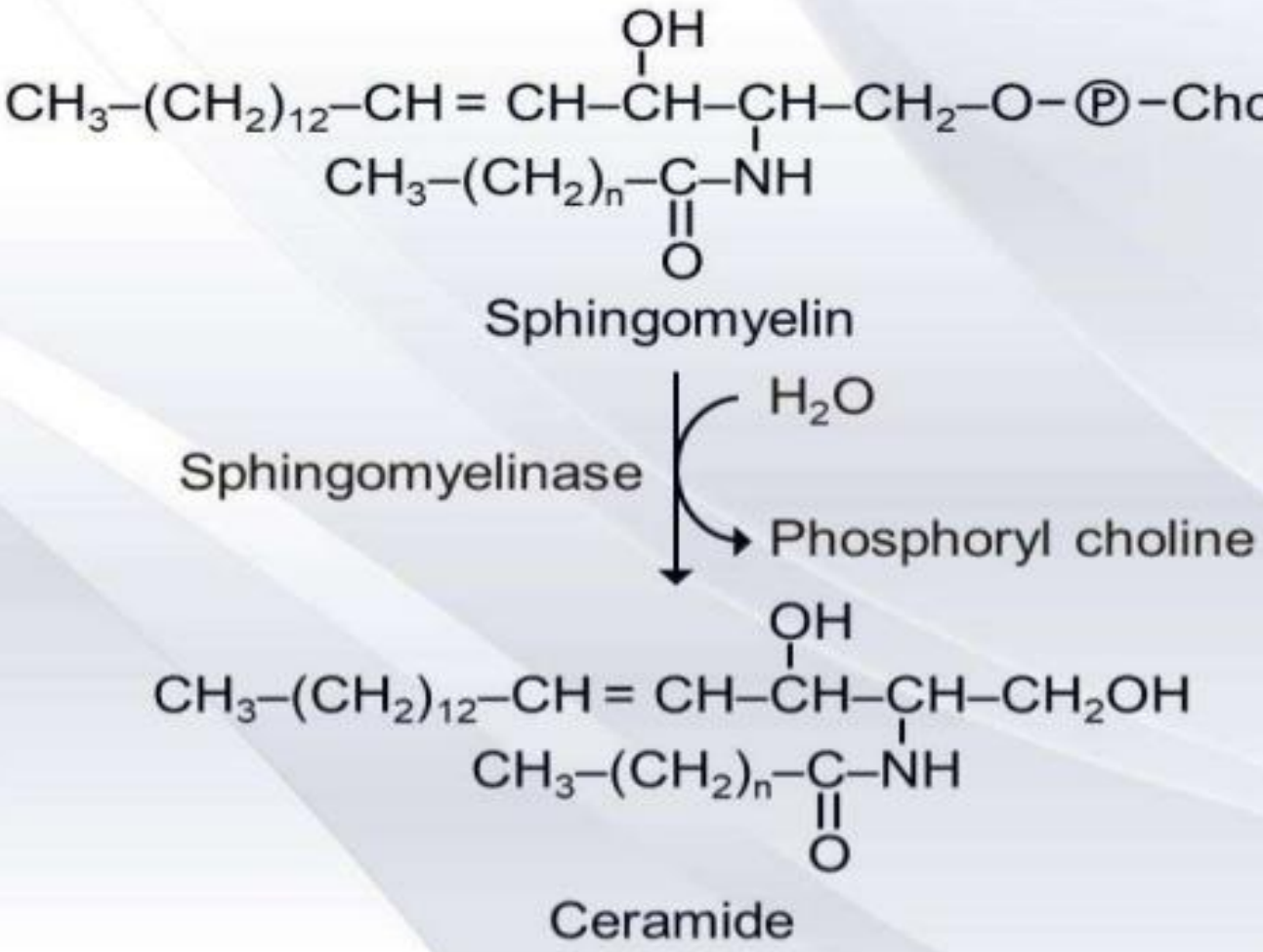


Catabolism of sphingomyelin

Sphingomyelin is catabolized by lysosomal sphingomyelinase

Sphingomyelin is hydrolysed into ceramide and phosphoryl choline

CATABOLISM OF SPHINGOMYELIN



Degradation of sphingomyelins

- **Sphingomyelinase of lysosomes hydrolyses sphingomyelins to ceramide & phosphoryl choline.**
- **Ceramide is further degraded to sphingosine & free fatty acid.**

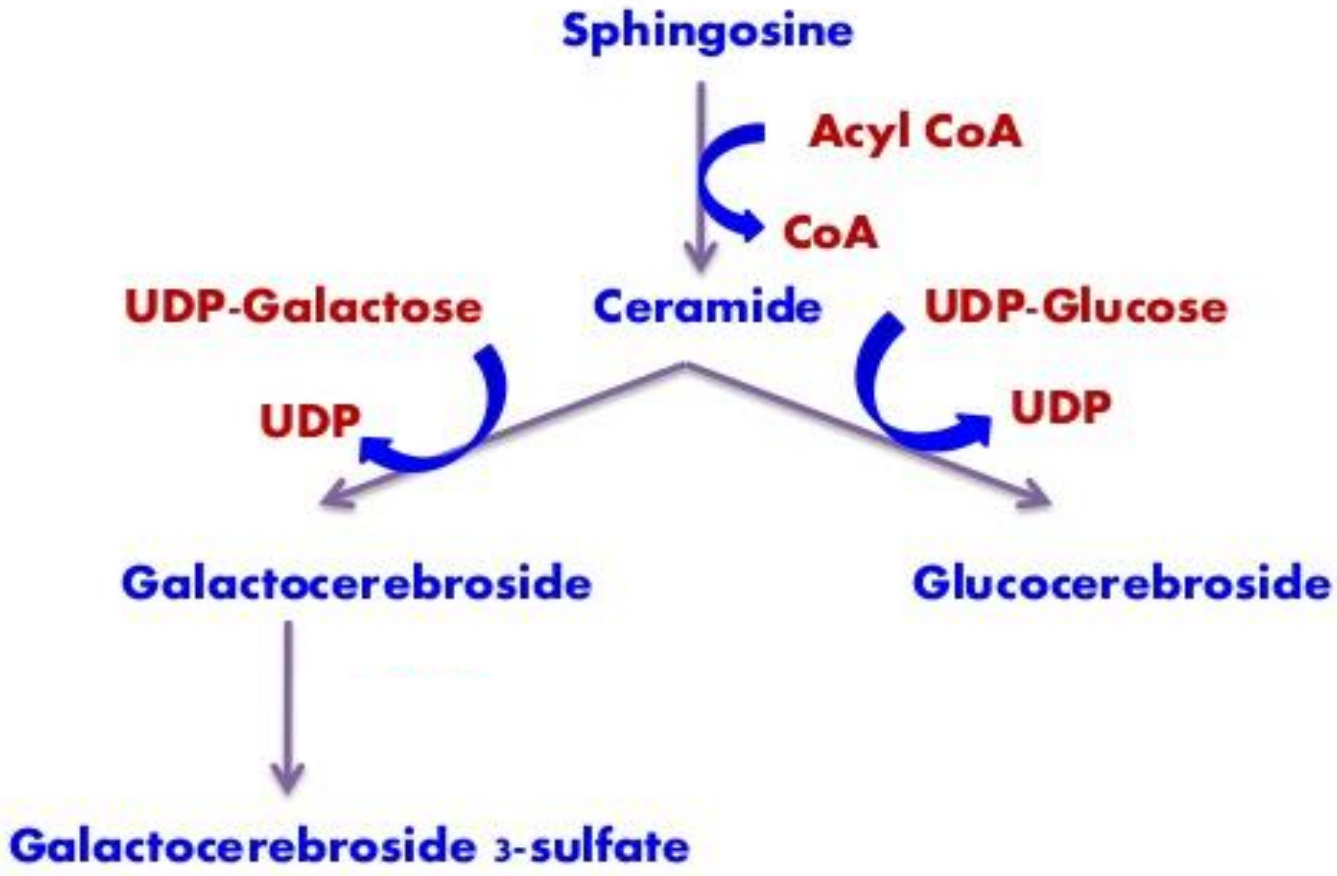
Action of sphingomyelinase & ceramidase on sphingomyelin

Metabolism of glycolipids

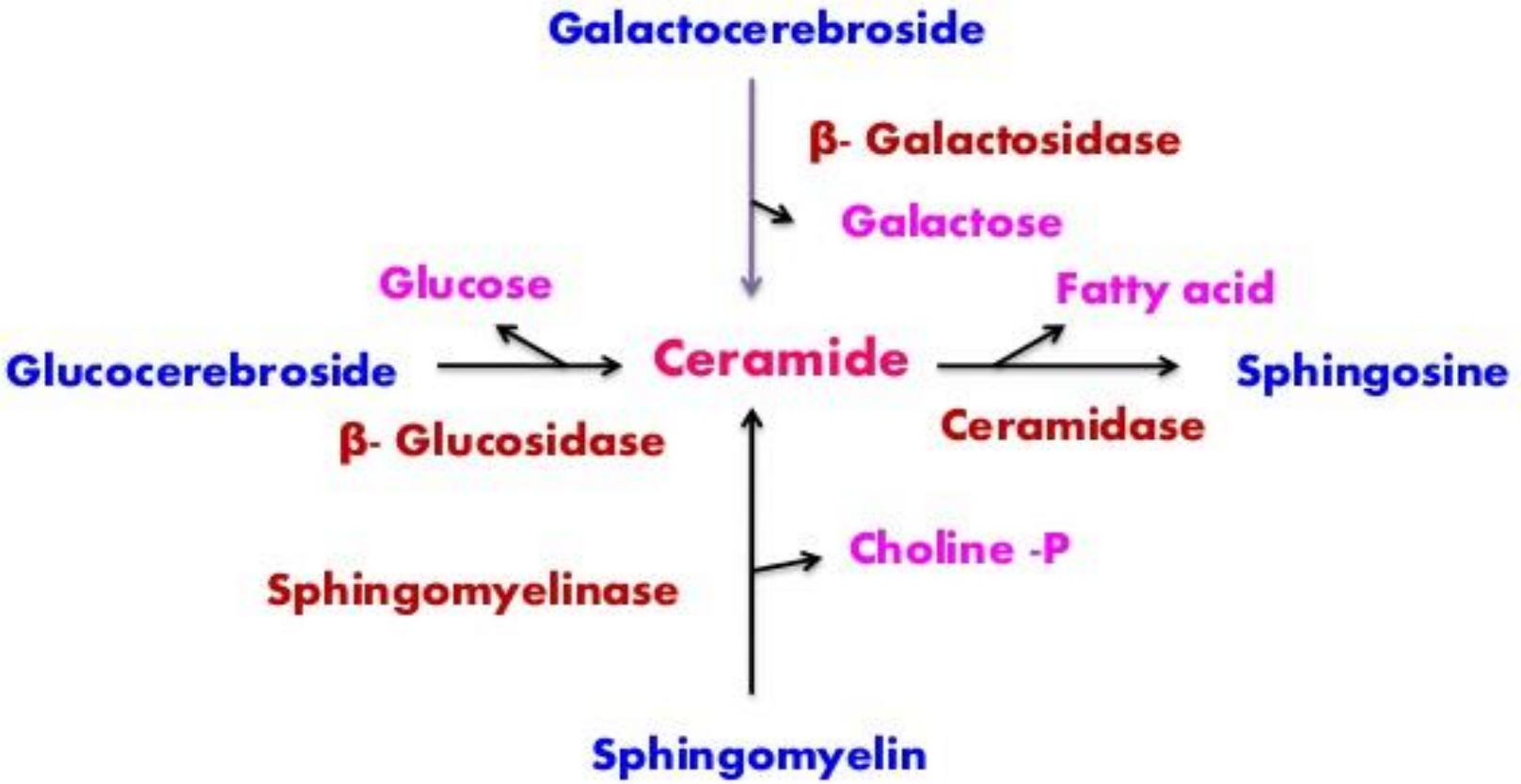
- Glycolipids are derivatives of ceramide (sphingosine bound to fatty acid), commonly called glycosphongolipids.
- The simplest form of glycosphingolipids are cerebrosides containing ceramide bound to monosaccharides.

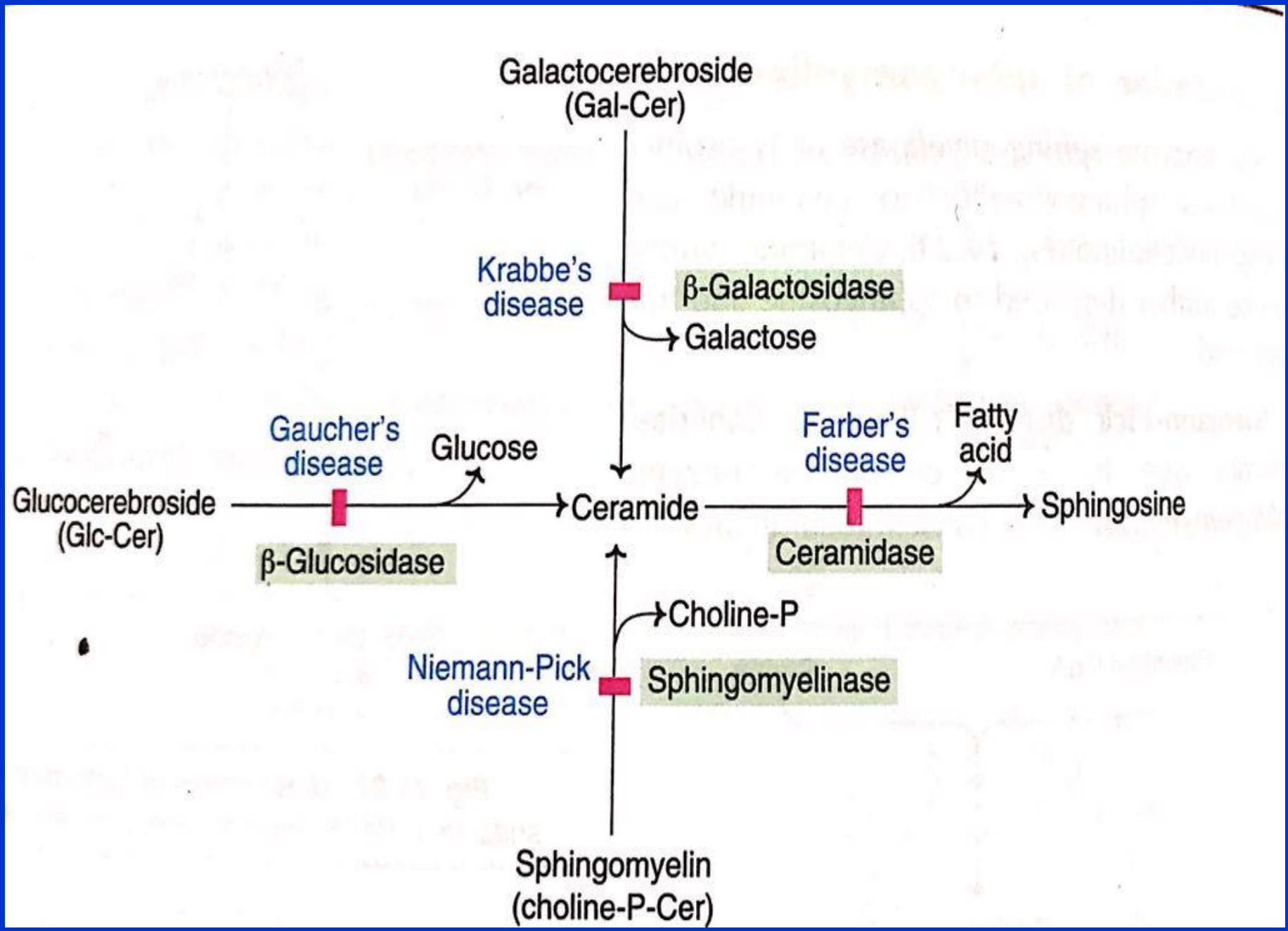
- Galactocerebroside (Gal-Cer) & glucocerebroside (Glu-Cer) are the common glycosphingolipids.
- Galactocerebroside is present in nervous tissue.
- Glucocerebroside is an intermediate in synthesis & degradation of glycosphingolipids

Biosynthesis of cerebrosides & sulfatides



Degradation of cerebrosides & sphingomyelins




Galactocerebroside
(Gal-Cer)
Krabbe's
disease
β-Galactosidase
Galactose
Gaucher's
disease
Glucose
Farber's
disease
Fatty
acid
Glucocerebroside
(Glc-Cer)
Ceramide
Sphingosine
β-Glucosidase
Ceramidase
Choline-P
Niemann-Pick
disease
Sphingomyelinase
Sphingomyelin
(choline-P-Cer)

Sphingomyelin lipidosis

Niemann Pick disease

Due to impaired degradation of sphingomyelin caused by deficiency of enzyme sphingomyelinase

- So sphingomyelin got accumulated in spleen, liver ,brain and bone marrow. It is a congenital disease.
- Autosomal recessive in nature
- There are 2 types: A and B
- Type A: more common present in 1/40000 population
- Type B: present in 1/80000 population
- More common in Jewish population

Niemann Pick disease :

Clinical manifestation

- Type A: there is progressive mental retardation, hepatosplenomegaly because of progressive accumulation of sphingomyelin. Children die within 2 years of life
- Type B: there is no involvement of brain but sphingomyelin is present in excessive amount in liver, spleen, and bone marrow. Death occurs within 20 years of life.

ANY QUESTION

- CHATTERJEA BIOCHEMISTRY
- LIPPINCOTT BIOCHEMISTRY
- HARPERS BIOCHEMISTRY
- SATYANARAYANA BIOCHEMI
- INTERNET

Thank you