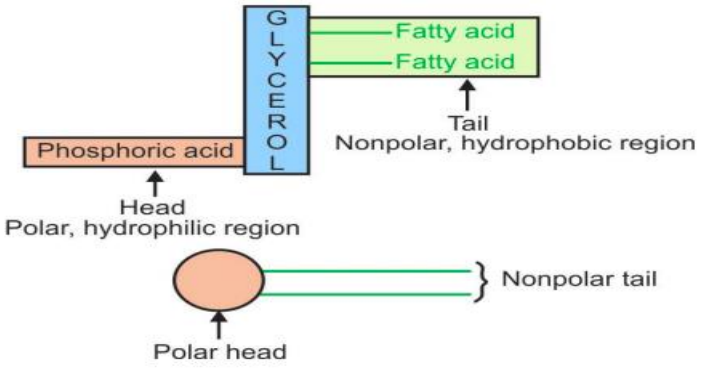
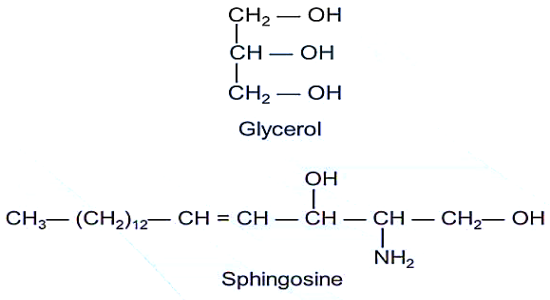
Phospholipids metabolism

Introduction

- Phospholipids (PLs) are complex lipids because they contain phosphate group as additional group together with an alcohol and fatty acids.
- Phospholipids are amphipathic have polar part and non-polar part



- There are two classes of phospholipids
  - Glycerophospholipids (containing glycerol as the alcohol)
  - Sphingophospholipids (containing sphingosine as the alcohol)

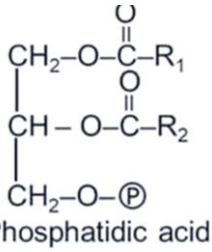


1- Glycerophospholipids

- Major lipids that occur in biological membranes
- Consist of glycerol-3-phosphate esterified at its C1 and C2 with fatty acids

Examples:

1) Phosphatidyl choline (lecithin)
2) Phosphatidyl serine (cephaline)
3) Phosphatidyl inositol.
4) Diphosphatidyl glycerol (cardiolipin).

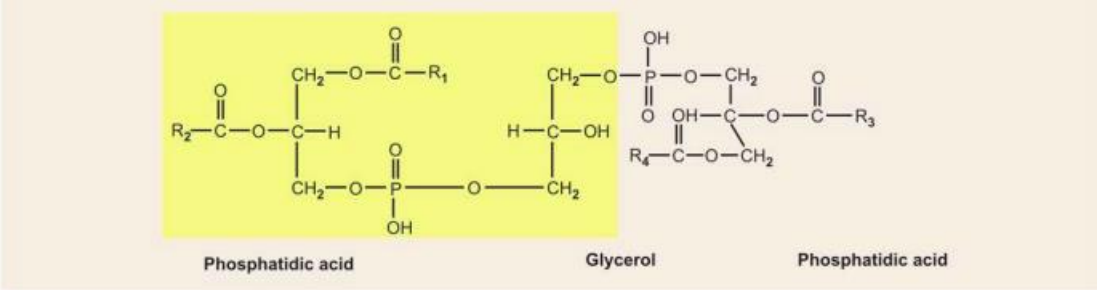


Cardiolipin (Diphosphatidylglycerol)

- Two molecules of phosphatidic acid esterified through their phosphate groups with a molecule of glycerol are called **cardiolipin**

- Cardiolipin is a major lipid of mitochondrial membrane and is necessary for optimum function of the electron transport process.

- This is important in some autoimmune diseases.



Functions of glycerophospholipids

A. Formation of biologic membranes:

- Glycerophospholipids spontaneously form bilayers, the phospholipids are arranged in bilayers with the polar head groups oriented towards the extracellular side and the cytoplasmic side with a hydrophobic core.

B. Assembly of Lipoproteins: Phospholipids are a part in the formation of chylomicrons that are exported from intestinal cells to the liver.

C. Role in solubilization of cholesterol in Bile:

- The relative concentration of cholesterol in the bile favors its precipitation and so the formation of gallstones; it is referred to as lithogenic bile. Bile salts and phospholipids in the bile play a significant role in keeping the cholesterol in solution by forming mixed micelles.

D. Role as second messengers:

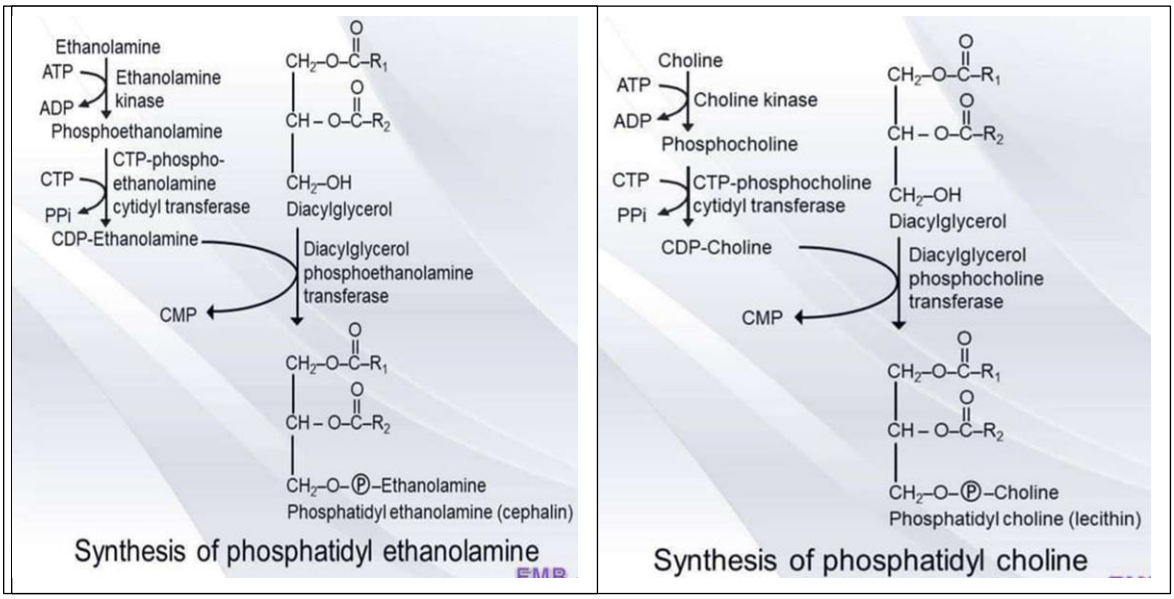
- Phosphatidylinositol acts as a second messenger for the activity of certain hormones.

E. Special functions:

- In mitochondria, cardiolipin is necessary for optimum function of the electron transport process.

Biosynthesis of Phospholipids

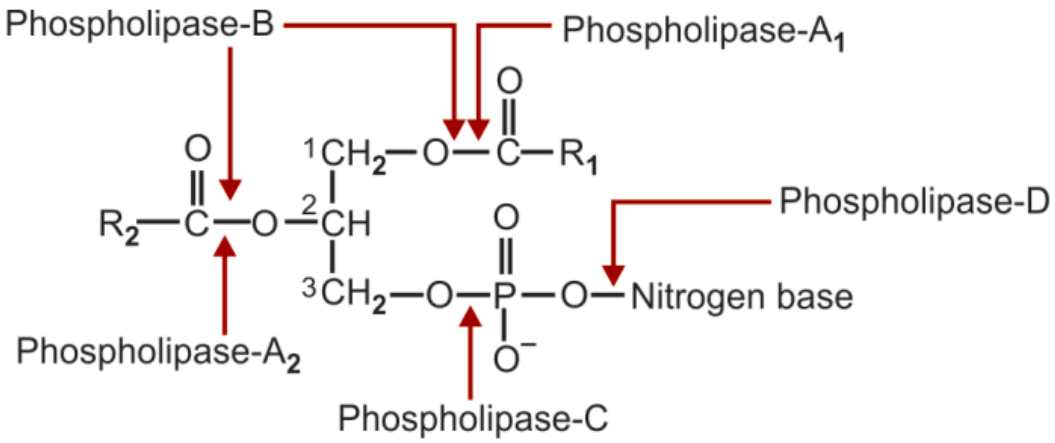
- **The biosynthesis of** phosphatidylcholine and phosphatidylethanolamine also involves the conversion of phosphatidate to 1,2-diacylglycerol.
- Before the next step, however, choline or ethanolamine must first be activated by phosphorylation by ATP and then linked to CDP.
- The resulting CDP-choline or CDP-ethanolamine reacts with 1,2-diacylglycerol to form either phosphatidylcholine or phosphatidylethanolamine, respectively
- In the case of phosphatidylinositol formation, it is phosphatidate that is linked to CDP, forming CDP-diacylglycerol, which is then linked to inositol by phosphatidylinositol synthase.



Degradation of glycerophospholipids

- Phospholipases that are located in cell membranes or in lysosomes can degrade glycerophospholipids.
- Glycerophospholipids are hydrolyzed by phospholipase
- Several specific phospholipases have been isolated which are designated as A1, A2 (B), C and D.
- Each phospholipase acts on specific bond

-The bonds hydrolyzed by phospholipases A1, A2 or B, C and D are shown in the figure below (See Figure).



2- Phosphosphingolipids

Sphingolipids

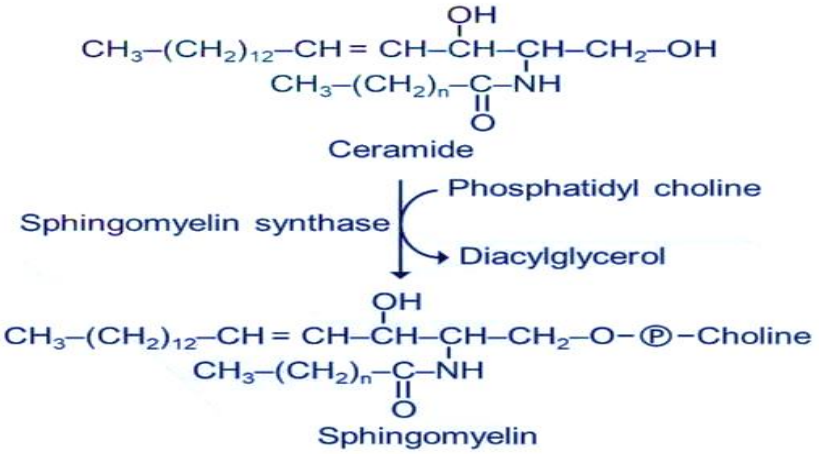
- They are another group of lipids found in biological membranes especially in the nervous system.
- There are three types of sphingolipids which are sphingomyelin, cerebrosides and gangliosides.
- Location of a sphingolipid: About 6 percent of the membrane lipids of grey matter cells in the brain are gangliosides.

- Types of sphingolipids and their hydrophilic groups :
- Sphingomyelin: contains phosphorylcholine So, it is a phospholipid and also a sphingolipid.
- Cerebrosides: contain galactose or glucose. So they are glycolipids and also sphingolipids.
- Gangliosides: contain branched oligosaccharide chains terminating in a 9-carbon sugar which is sialic acid (N-acetylneuraminic acid, NANA)

- **Synthesis of phosphosphingolipids**

- 1) Sphingomyelins is synthesis from ceramide and phosphatidyl choline

- Sphingomyelins are amphipathic; they are present in cell membranes of the nervous system.

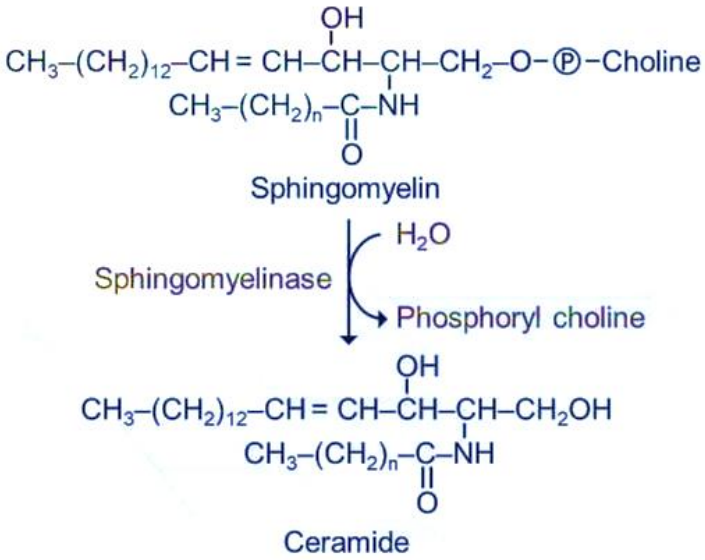


Biosynthesis of ceramide:

In all sphingolipids, a long chain acyl-CoA reacts with sphingosine to form ceramide

Degradation of Sphingomyelin

- The sphingomyelins are hydrolyzed by the lysosomal enzyme, sphingomyelinase to a ceramide and a phosphorylcholine.
- The ceramide, so formed, is further hydrolyzed by another lysosomal enzyme, ceramidase, into sphingosine and free fatty acid.



Metabolism of Glycolipids

- Glycolipids mean sugar containing lipids.
- Glycolipids contain the alcohol sphingosine.
- The amino group of sphingosine is esterified by a fatty acid.
- One or more sugar units are attached to the hydroxyl group of sphingosine.
- Glycolipids are widely distributed in every tissue of the body, particularly in nervous tissue such as brain.

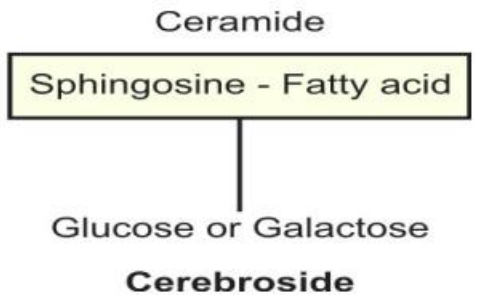
- Classification of Glycolipids

- Two main types of glycolipids have been distinguished:

1. Cerebrosides
2. Gangliosides.

Cerebrosides (Ceramide + Monosaccharides)

- Cerebroside is the simplest glycolipid in which there is only one sugar residue, either glucose or galactose linked to ceramide and named as glucocerebroside and galactocerebroside respectively.



- Gangliosides: (Cerebroside + Oligosaccharides + N-acetylneuraminic acid, NANA)

- Gangliosides are complex glycolipids, derived from glucocerebroside.

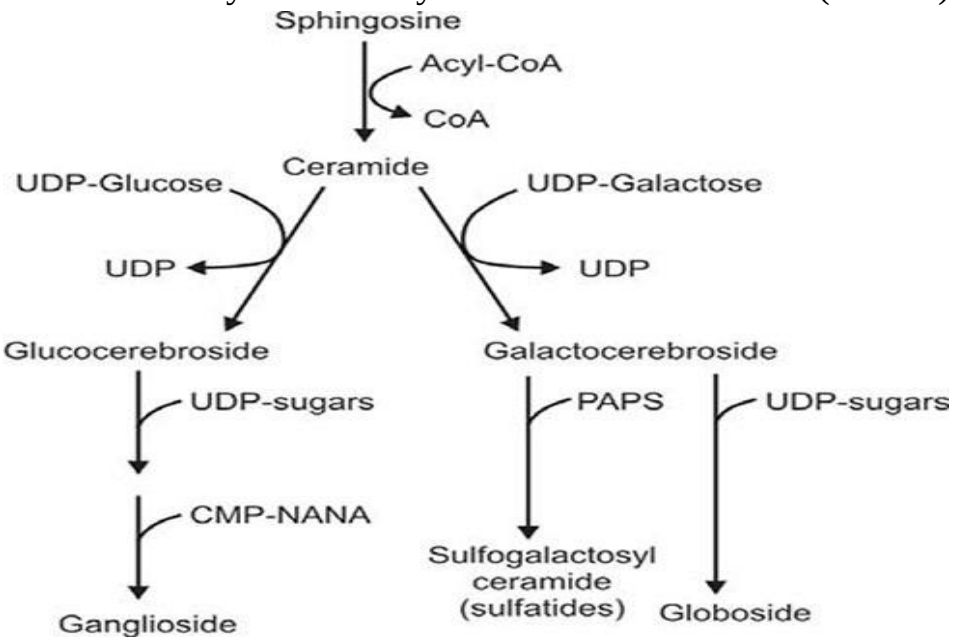
- Ganglioside contains oligosaccharides and one or more molecules of sialic acid, which is usually N-acetylneuraminic acid (NANA) attached to ceramide.

- **Functions of Glycolipids**

1- Glycolipids are important constituents of the nervous tissue such as the brain and are present in outer leaflet of all cell membranes.
2- They play a role in the regulation of cellular interactions, growth and development.
3- Glycolipids serve as cell surface receptors for certain hormones and a number of drugs. They also serve as receptors for cholera and tetanus toxins.
4- Glycolipids are antigenic and they have been identified as a source of blood group antigens.

Biosynthesis of Glycolipids

- **Cerebroside** is the simplest glycolipid in which there is only one sugar residue, either glucose or galactose linked to ceramide and named as glucocerebroside and galactocerebroside respectively.
- A ceramide reacts with UDP-glucose or UDPgalactose to form glucocerebroside or galactocerebroside respectively.
- **Gangliosides** are the more complex glycolipids, contain a branched chain oligosaccharide of as many as seven sugar residues.
- Gangliosides are produced from ceramide by the addition of activated sugar, e.g. UDP-glucose, UDP-galactose and sialic acid usually N-acetylneuraminic acid (NANA)



Sphingolipidoses

1. Niemann-Pick disease

- Sphingomyelin can be hydrolyzed by the lysosomal enzyme **sphingomyelinase** to a ceramide and a phosphorylcholine.
- The ceramide so formed is further hydrolyzed by another lysosomal enzyme ceramidase into a sphingosine and a free fatty acid.
- In Niemann-Pick disease, there is a deficiency of **sphingomyelinase.**

As a result, **sphingomyelins accumulate** in liver, brain and spleen. The clinical findings are:

– Enlarged liver and spleen

– Mental retardation and death may occur in early childhood.

2. **Gaucher's disease**

- The **inherited deficiency β-glucosidase** impairs the hydrolysis of glucocerebrosides, which results in accumulation of **glucocerebrosides** in brain, liver, spleen, and bone marrow.

• This disorder is associated with mental retardation and enlargement of liver and spleen.

3. **Farber's disease**

5- The **inherited deficiency of enzyme ceramidase** impairs the hydrolysis of **ceramides** which results in accumulation of ceramides in the body tissue.

• The symptoms include **skeletal deformities**, and mental retardation. The disease is fatal and death occurs in early childhood.

REFRANCES

1. Harper's Biochemistry. Lange, USA.

2. Lippincott Illustrated Reviews: Biochemistry, 7e. Denise R. Ferrier

3. Text book of medical biochemistry. Chtterjea MN. India. Latest edition.