Membrane Lipid Metabolism

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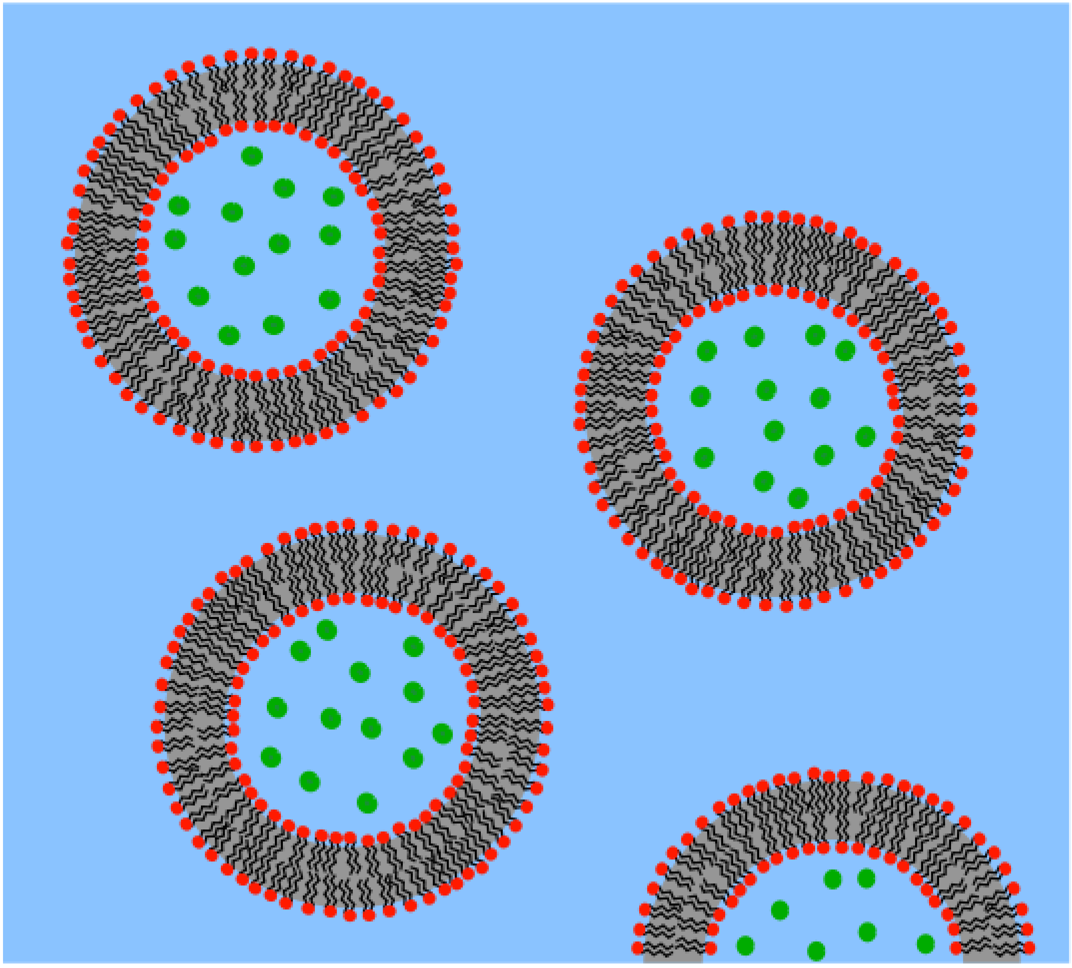
Lipids are a large and diverse group of naturally occurring organic compounds that have relatively very low solubility in water and higher solubility in non-polar organic solvents. Different types of lipid molecules include fatty acids, fats, oils, waxes, phospholipids, eicosanoids, steroids etc. The focus of this article is on two types of lipids, namely glycerophospholipids and sphingolipids. Specifically, the article emphasizes the synthesis of these two types of lipids.

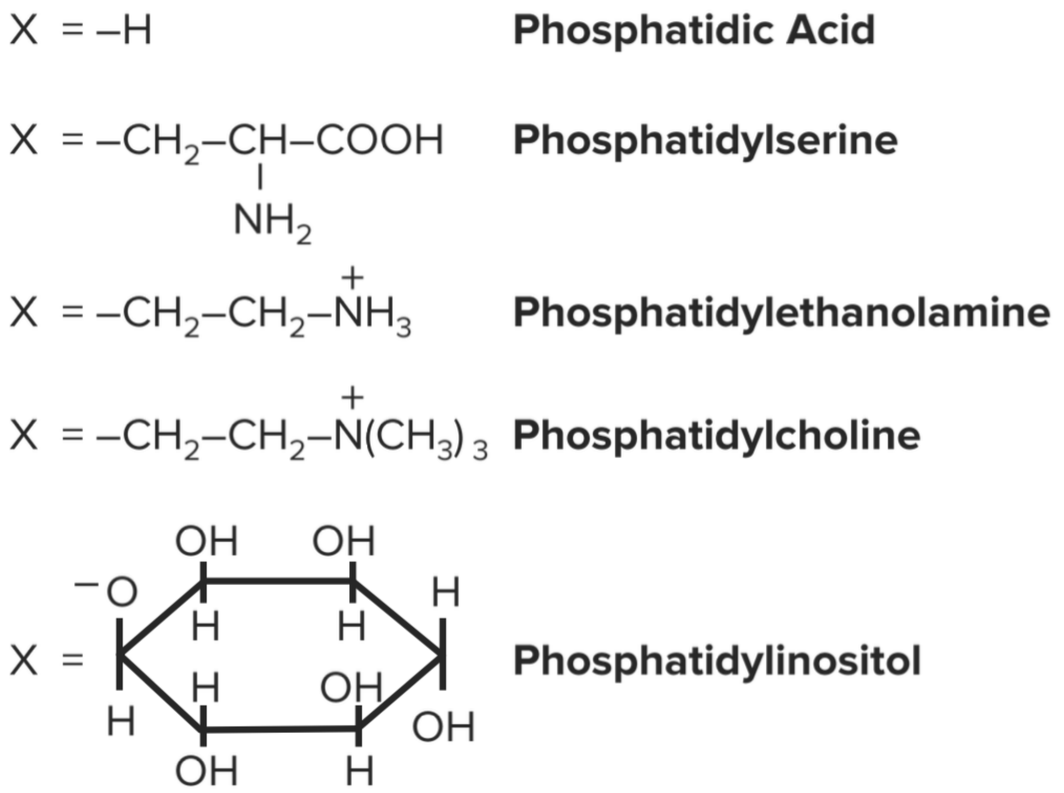


Glycerophospholipid

Glycerophospholipids, also called **phosphoglycerides**, are glycerol-bases phospholipids that serve as the **main components of biological membranes**. These molecules play key roles as suppliers of the first and secondary messengers in molecular recognition and signal transduction.

Glycerophospholipid molecules are **derivatives of triacylglycerol** where a phosphate group replaces one fatty acid group. The general structural components of glycerophospholipids include fatty acid groups, glycerol, and a phospho group.

Depending on the X-group, different types of glycerophospholipids are produced. The figure shows the different types of phospholipids produced depending on the X-group.



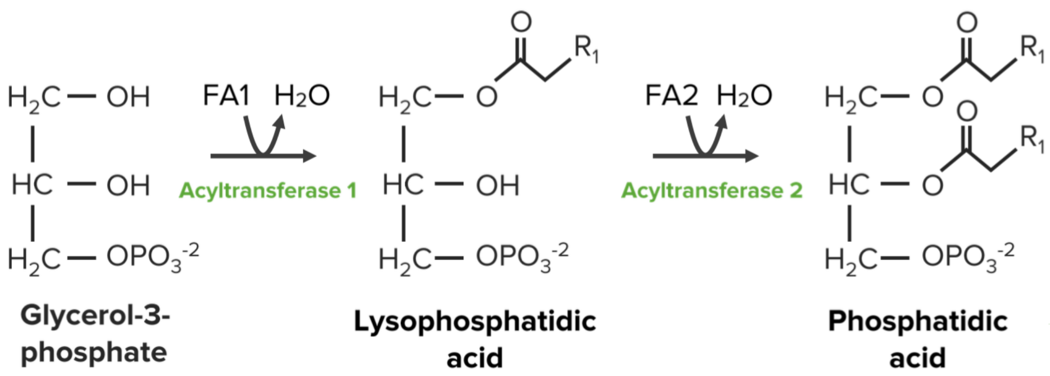
Synthesis of Glycerophospholipids

Most of the synthesis of glycerophospholipids occurs in the liver and kidneys**;** however, almost all of the tissues in the human body are capable of synthesizing this type of lipid. The synthesis is localized on the **membranes of the endoplasmic reticulum**.

There are **three major steps** in the synthesis of glycerophospholipids. The first part is to **form the glycerol backbone**. The next step is to **attach the fatty acids** to the glycerol backbone by forming ester linkages. The polar head group is then added by **forming a phosphodiester linkage**.

The initial steps in the synthesis are similar to those of the triacylglycerol synthesis where glycerol-3-phosphate undergoes two steps of fatty acid esterification in the presence of acyltransferases to produce phosphatidic acid or phosphatidate. Then, the phosphatidate can undergo **hydrolysis** in the presence of the hydrolase enzyme to produce 1,2-Diacylglycerol. Synthesis of glycerophospholipids will then proceed via two possible mechanisms of the addition of the head group either from phosphatidate or from 1,2-Diacylglycerol.

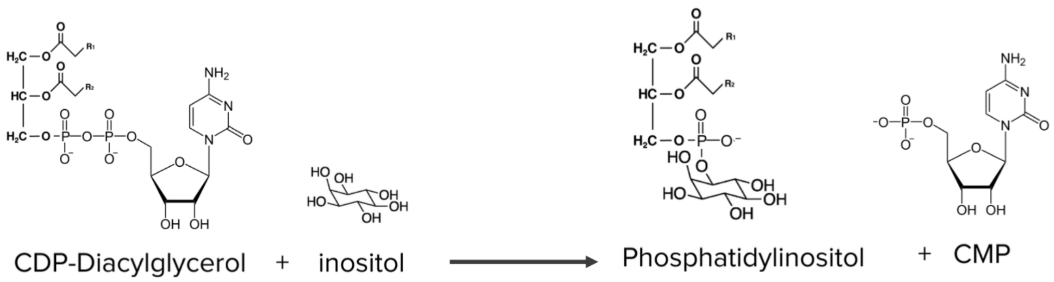
The following diagram shows the synthesis of phosphatidate.



In both mechanisms, the reaction is driven by **cytidine triphosphate (CTP)**. The first mechanism involves **phosphatidate** being **activated by CTP to produce CDP-diacylglycerol** that can accept the head group.

This mechanism is primarily used in the synthesis of **phosphatidyl inositol** or **cardiolipin**. The second mechanism, on the other hand, involves **diacylglycerol** accepting CDP-activated **choline** or **ethanolamine**. This mechanism is used primarily in the synthesis of phosphatidylcholine and phosphatidylethanolamine.

In the first mechanism, **phosphatidic acid** or **phosphatidate** is reacted with CTP to produce a more reactive intermediate in the form of CDP-diacylglycerol. The **CDP-Diacylglycerol** can then react to **free inositol** to produce **phosphatidylinositol**. When the CDP-Diacylglycerol is reacted with glycerol phosphate, **phosphatidylglycerol** will be synthesized.



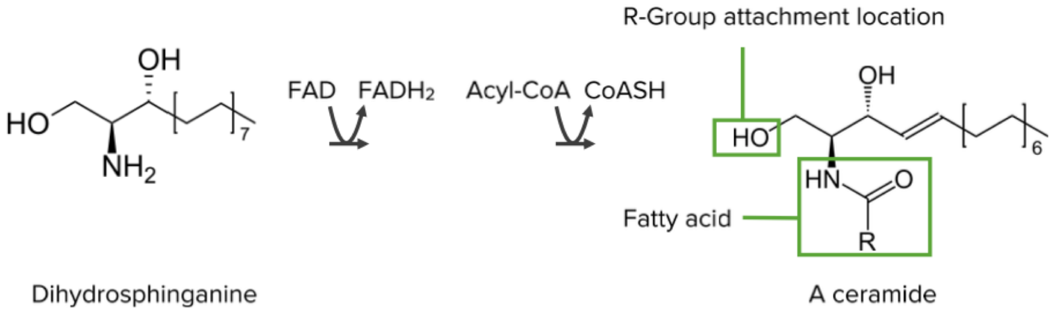
The second mechanism proceeds by producing first activated **cholines** or **ethanolamines** that can react with **diacylglycerol** to produce different **glycerophospholipids**. Activation of choline occurs in two steps:

First, **choline molecules** are **phosphorylated by ATP** to produce **choline phosphate molecules**. The choline phosphate then reacts with CTP to produce **CDP-choline**. The CDP-choline, when reacted with **1,2-diacylglycerol**, produces **phosphatidylcholine**. The biosynthesis of **phosphatidylethanolamine** proceeds similar to that of biosynthesis of phosphatidylcholine. Choline, in this case, is just replaced with ethanolamine.

Sphingolipids

Sphingolipids are a class of lipids containing a **sphingoid base backbone**. Sphingoid bases are **aliphatic amino alcohols** that include **sphingosine**. These lipids are also called **glycosylceramides** and play important roles in **signal transmission** and **cell recognition**. This type of lipids is particularly present in **nerve tissues** which is why disorders of sphingolipid metabolism have a great impact on the proper functioning of neural tissues.

The **De novo sphingolipid synthesis** starts with the production of **3-keto-dihydrosphingosine** by the enzyme **serine palmitoyltransferase**. The substrates used for this reaction are **serine** and **Palmitoyl-CoA**. When these two compounds combine and are reduced further, a **dihydrosphingosine** is formed. Using a **(dihydro)-ceramide synthase**, **dihydrosphingosine** is acylated to form dihydroceramide. The dihydroceramide is later desaturated to form **ceramide**. The synthesis of ceramide is depicted in the diagram below.



Depending on the R on the ceramide group, a different type of sphingolipid is produced. When the R group is a **phosphocholine** or a **phosphoethanolamine**, **sphingomyelin** is produced. If R is a **simple sugar**, a **cerebroside** is produced. A **more complex sugar** as an R group produces a **ganglioside**.

References

Voet, D. & Voet, J.G. (2011). Biochemistry. 4th ed. New York: J. Wiley and Sons.

Reece, J. B., & Campbell, N. A. (2011). Campbell biology. Boston: Benjamin Cummings / Pearson.

Lipid metabolism II – Phospholipids and glycolipids Eicosanoids Cholesterol and bile acids via Masaryk University (is.muni.cz)

Notes