Membrane Lipid Metabolism

See online here

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.

\[
\begin{align*}
X = -H & \quad \text{Phosphatidic Acid} \\
X = -\text{CH}_2-\text{CH}-\text{COOH} & \quad \text{Phosphatidylserine} \\
& \quad \quad \quad \text{NH}_2 \\
X = -\text{CH}_2-\text{CH}_2-^+ & \quad \text{Phosphatidylethanolamine} \\
X = -\text{CH}_2-\text{CH}_2-N(\text{CH}_3)_3 & \quad \text{Phosphatidylcholine} \\
\end{align*}
\]

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.

![Diagram of ceramide synthesis](image)

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


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

**Legal Note:** Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our legal information page.