

## GUTS Lecture Syllabus for Lipid Structure and Nomenclature

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### **Learning Objectives**

After completing the GUTS lecture and associated self-assessment questions you should:

- Be able to list some of the functions of lipids in metabolism.
- Be able to explain how the hydrophobic nature and amphipathicity of lipids influences their functions and their disposition in cell membranes
- Understand the structural classification of lipids
- Be able to describe the key structural features of a: fatty acid, triglyceride, phospholipid, glycolipid, sphingomyelin, cerebroside, and sulfatide.
- Understand the structural and functional differences between unsaturated fatty acids, saturated fatty acids, cis and trans fatty acids.


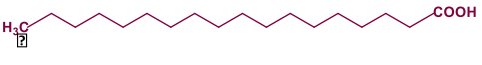

Lipids are very heterogeneous. The property shared by all lipids is that they are composed mostly of carbon and hydrogen and thus are hydrophobic. While phosphate, carboxylate, amine, alcohol and other hydrophilic groups may be added, the core structure of each lipid consists of long hydrocarbon chains or rings that are hydrophobic in character. This property affects all of the functions of lipids.

Although we tend to think of lipids as fats, and therefore potentially bad for us, we could not live without them. Fats can be utilized as energy sources when we eat them or stored for later metabolic need. During strenuous exercise, during fasting or starvation, and even overnight while we sleep, our carbohydrate stores are depleted and most cells in our bodies switch to using lipids as an energy source. If these lipids are not available, serious metabolic disorders result. Lipids also provide thermal insulation to keep us warm and physical padding, especially on the balls of our feet; loss of these fat pads is a significant cause of foot pain as one ages. You have all heard that lipids are the major components of cell membranes and so are responsible for establishing a special protected environment inside of cells there the reactions essential to life can occur. Functions of lipids that may be unfamiliar to you are that certain lipids are important signaling molecules within cells; many vitamins are synthesized from lipids; and lipids and their derivatives are required for the adsorption of fats and other hydrophobic materials from our diets as well as for elimination of hydrophobic molecules as waste material.

When studying lipids it is sometimes difficult to remember how these important molecules are related to one another. I find that a structure-based classification of lipids is easiest to follow and that is the organizing principle of this lecture. Structurally, most lipids that you will encounter in medicine will fall into one of three classes: those derived from glycerol and fatty acids (the triglycerides and phospholipids); those lipids containing fatty acids added to molecules other than glycerol; and cholesterol and its derivatives. Let's look first at the fatty acids.

## I. Fatty Acids

Fatty acids are long-chain hydrocarbons that contain a carboxylic group at one end of the molecule and a methyl group at the other end. Fatty acids differ from one another in the length of the hydrocarbon chain, the presence or absence of double bonds in the chain, the location of these double bonds, and the orientation of functional groups around the double bonds. Most fatty acids in humans contain an even number of carbon atoms and from 12 – 20 carbon atoms in a chain. When naming fatty acids, the carboxyl carbon is designated C1 and the final carbon in the chain is designated the omega carbon.

Formula	Common Name	Structure
$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$	Palmitic Acid	
$\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$	Stearic Acid	
$\text{CH}_3(\text{CH}_2)_{18}\text{COOH}$	Arachidic Acid	

By convention, fatty acids are often drawn as zig-zag stick figures as shown above. The top and bottom of each stick is assumed to have a C bound and the line linking the top and bottom indicates the C-C bond. Hydrogens are usually not shown but rather carbons are assumed to be fully reduced unless indicated otherwise. This means that, for any carbon atom in a fatty acid, unless a functional group is shown attached you should assume that the carbon has the maximum permissible number of hydrogens bound.

The fatty acids shown in this figure contain only single carbon-carbon bonds and the maximum number of hydrogen atoms. These are termed saturated fatty acids. The names shown for these fatty acids are their common names and are the ones you will most likely encounter in your studies. You should remember the three shown here. Palmitic and Stearic acids are among the most common fatty acids found in nature. Arachidic acid is the precursor of arachidonic acid, which is important in signaling, inflammation, and vasodilation.

Other fatty acids contain one or more double bonds. Fatty acids with one double bond are called monounsaturated fatty acids, while fatty acids with more than one double bond are called polyunsaturated fatty acids. There is substantial evidence that the type and amount of fatty acids in our diets can have a significant effect on health. Food manufacturers in the U.S. are now required to label many of their products to indicate the percentage and amounts of monounsaturated fatty acids (1 double bond) and polyunsaturated fatty acids (more than one double bond).

A second important distinction for these fatty acids is whether the groups attached to the carbons in a double bond are in the cis- or trans-configuration. The cis-double bond produces a kink in the fatty acid chain, which turns out to be a good thing because this helps maintain fluidity of membranes. Trans-double bonds do not produce this kink which allows the fatty acids to pack tightly in membranes. This increases the rigidity of the membrane, which is not a desirable effect.

- **Unsaturated fatty acids** have one or more double bonds in the hydrocarbon chain.
  - Monounsaturated have one double bond. Ex., Oleic acid (18 carbons)  

$$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$$
  - Polyunsaturated have > one double bond. Ex., Linoleic acid (18 carbons)  

$$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2(\text{CH}_2)_6\text{COOH}$$
- Double bonds are rigid and do not allow rotation of attached groups around the bond. Groups attached to carbon atoms in double bonds can be either is **cis- or trans-configuration**.
 

$$\begin{array}{c} \text{H}_3\text{C}(\text{H}_2\text{C})_6\text{H}_2\text{C} \\ | \\ \text{C}=\text{C} \\ | \quad | \\ \text{H} \quad \text{H} \end{array}$$

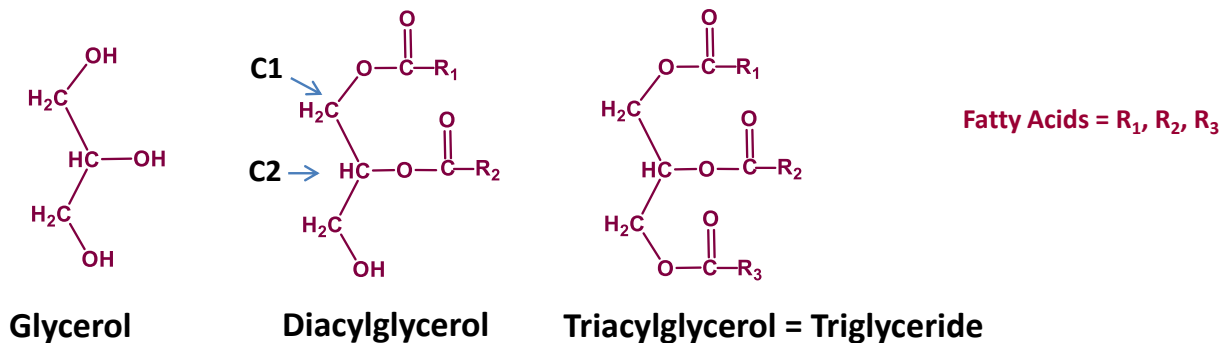
**cis-configuration**

$$\begin{array}{c} \text{H}_3\text{C}(\text{H}_2\text{C})_6\text{H}_2\text{C} \\ | \\ \text{C}=\text{C} \\ | \quad | \\ \text{H} \quad \text{CH}_2(\text{CH})_6\text{COOH} \end{array}$$

**trans-configuration**

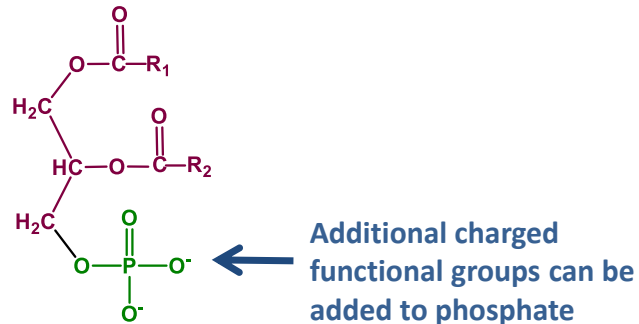
## II. Triglycerides and Phosphatidic Acid.

In cells, fatty acids are often linked to glycerol, a naturally occurring product of metabolism. Diacylglycerols carry two fatty acids esterified to glycerol, one at C1 and the other at C2, whereas triacylglycerols contain an additional fatty acid esterified at C3. (See the figure below.) The fatty acids carried at positions C1 and C2 are often different from one another; usually the fatty acid at C1 is saturated, the one at C2 is usually unsaturated, and, in triglycerides, the fatty acid at C3 can be either saturated or unsaturated. Diacylglycerols play an important role in signaling within cells. Triglycerides are the storage form for fat; lipid droplets that you will see in adipose tissue in pathology are formed entirely of triacylglycerides.



Phospholipids are derived from phosphatidic acid, which is structurally similar to diacylglycerol except that C3 bears a phosphate group instead of a fatty acid. Thus phospholipids are amphipathic (“two-

natured) in that the phosphate and glycerol part of the phospholipid is hydrophilic while the long hydrocarbon tails of the fatty acids are hydrophobic. Phospholipids are the most abundant of the lipid molecules found in cell membranes. Here they form bilayers with the charged head groups facing the exterior of the cell and the cytoplasm; the hydrophobic tails face one another in the bilayer. In many cases the phosphate group bears additional functional groups such as serine, choline, ethanolamine, or inositol. These groups add more charge to the head group and may also serve as recognition sites for proteins and other cellular molecules.

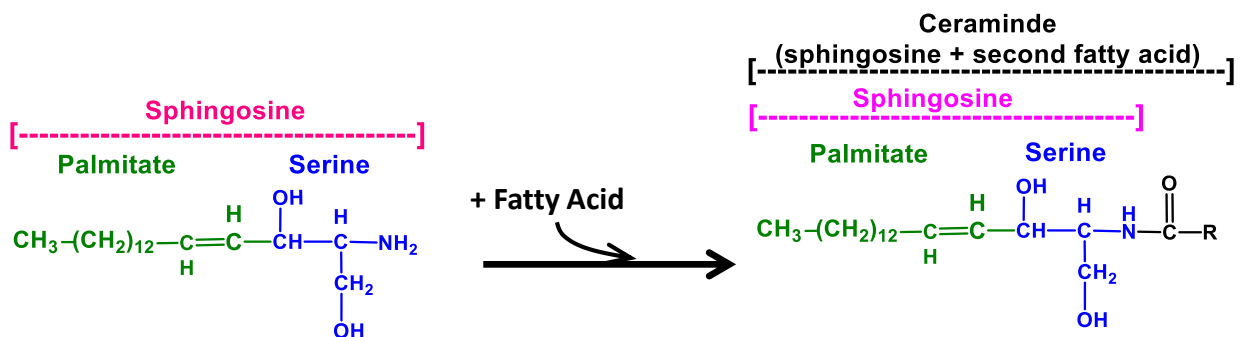


**Phosphatidic Acid**

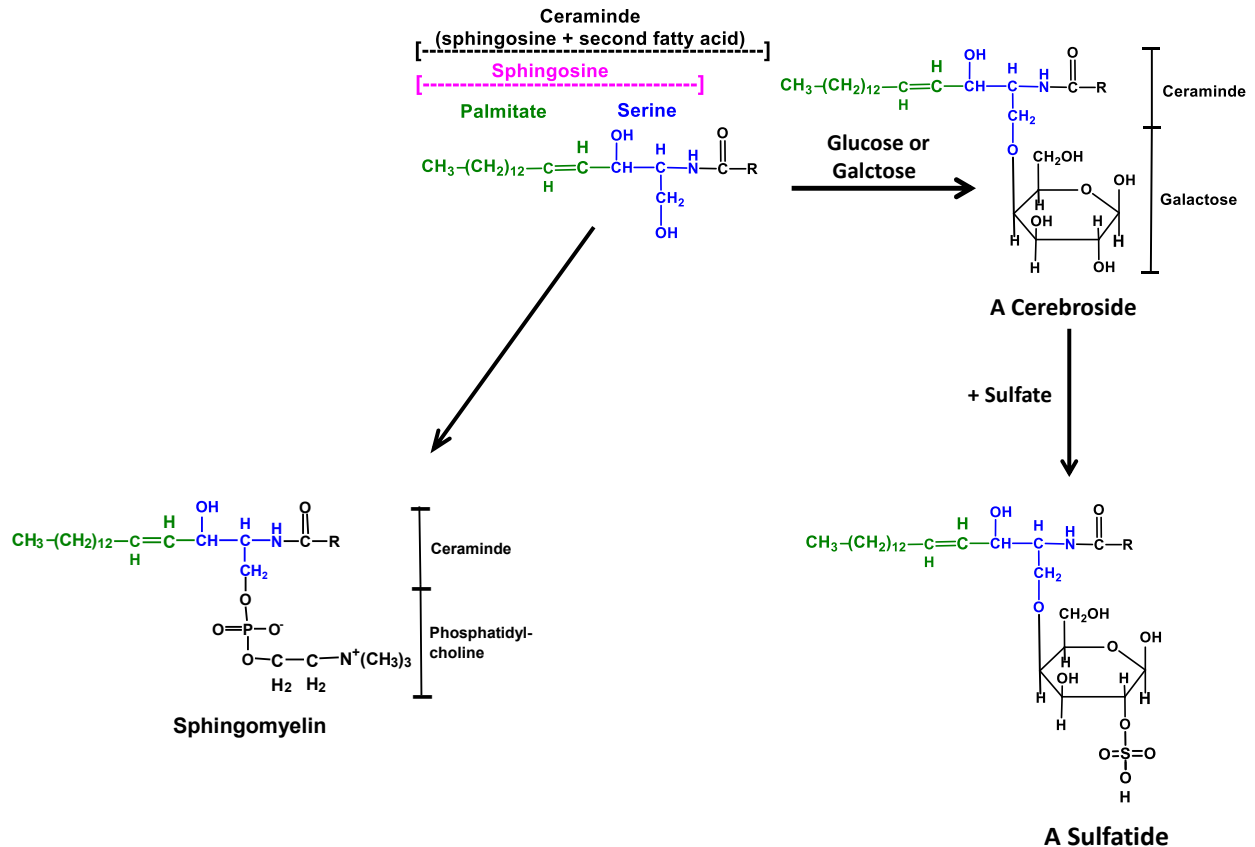
### III. Complex Lipids.

Complex Lipids form a large class of molecules in which fatty acids are bound to molecules other than glycerol. This is a HUGE group of molecules and the figure shows just a few of the more important types.

In sphingolipids the glycerol backbone seen in phospholipids is replaced by a molecule called sphingosine. Sphingosine is composed of the fatty acid palmitate linked to the amino acid serine. In sphingolipids, the amino group of serine is always bound to another fatty acid (indicated as R) to form the molecule ceramide.



Addition of different molecules to the remaining –OH groups of serine defines the name and resulting characteristics of the sphingolipid. For example, addition of a single glucose or galactose to the -OH of serine produces a cerebroside, a type of glycolipid; among other functions cerebroside cover nerve axons and enable fast and efficient conduction of nerve impulses.

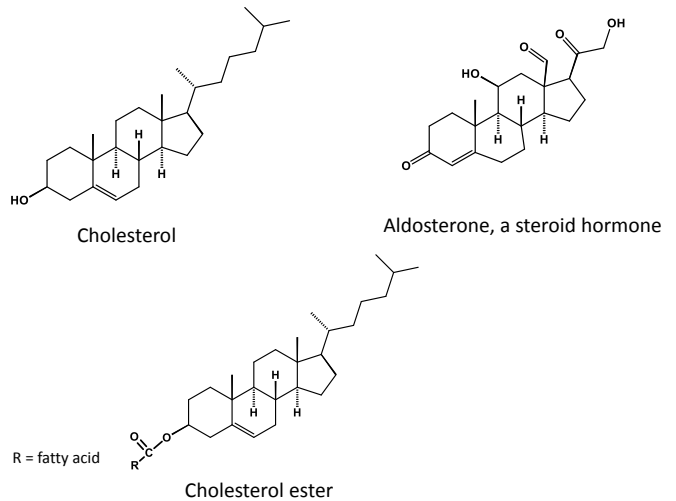


Sulfatides are similar to cerebroside but contain a sulfate group attached to galactose; in addition to being found in high concentrations in the nervous system, sulfatides have been implicated in both blood clotting and in breakdown of clots, and as adhesion molecules that recruit immune cells to inflamed tissue. Sphingomyelins are produced by addition of phosphatidylcholine to ceramide. These important lipids are found in most cell membranes and make up to 20% of total phospholipid in many biological membranes.

#### IV. Cholesterol

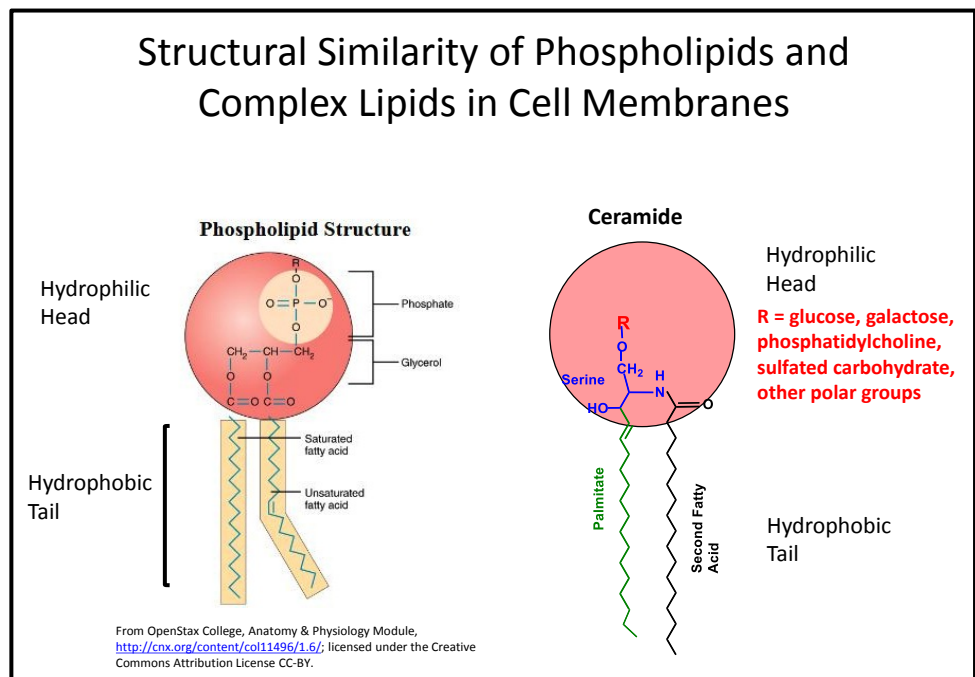
The final complex lipid in this GUTS lecture is cholesterol. Cholesterol is the primary precursor for a variety of important molecules including steroid hormones and vitamin D. We take in cholesterol in our diet and our liver also makes cholesterol from acetylCoA, an important intermediate in glucose metabolism and in fatty acid metabolism. Cholesterol is found only in eukaryotic cells where it plays an important role in modulating the fluidity of membranes.

Cholesterol is made of 4 rings. There is only one double bond and only one hydroxyl group in the entire structure. As a result the molecule is very hydrophobic and tends to be found in association with other lipids or with hydrophobic portions of proteins. Mostly cholesterol is found in membranes. The ring structure of cholesterol is rigid, and thus its presence in cell membranes tends to make them less fluid; this is not a good thing when it happens in the cells of your circulatory system. When outside of membranes cholesterol is usually bonded via the hydroxyl group to a long-chain fatty acid; this structure is called a cholesterol ester and it is even more hydrophobic than cholesterol. Cholesterol esters are transported through the bloodstream as part of large protein-lipid complexes.



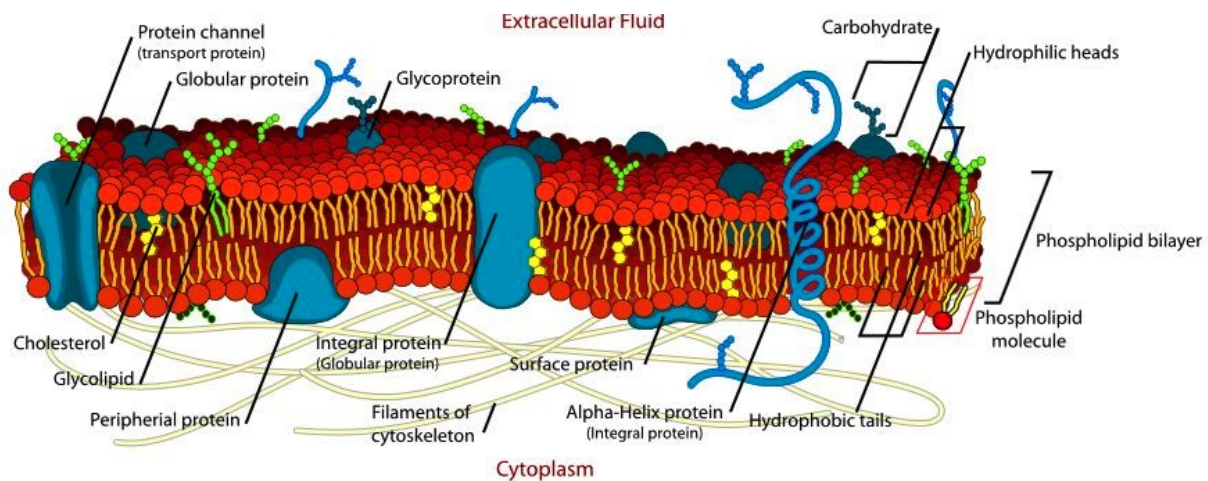
## V. Lipids in Membranes

Phospholipids, glycolipids and sphingolipids are all components of membranes. Although their backbones may be either glycerol or serine, the fatty acids linked to them form long hydrophobic tails that protrude into (indeed are part of) the lipid bilayer that forms membranes. The hydrophilic functional groups attached to glycerol or to serine (in ceramide) lie on the surfaces of the bilayer, where they are exposed to water.



Cholesterol on the other hand has only a single polar group, the hydroxyl group. In cell membranes only the hydroxyl group of cholesterol is found on the surface of the membrane. The rest of the molecule is buried deep in the hydrophobic portion of the bilayer where it interacts with the hydrophobic tails of phospholipids, and of ceramide derivatives. As you examine the next slide, look for the cholesterol (its yellow) deep in the lipid bilayer.

The figure below shows the relative positions of some of the molecules mentioned in this lecture. Note the phospholipid bilayer, with the polar head groups on the surface of each side of the bilayer and the hydrocarbon tails of extending into the hydrophobic core. Several glycolipids are visible (green) with their two fatty acids extending into the core and their hydrophilic serine and attached carbohydrate on the surface of the bilayer. Cholesterol (yellow) is buried deep in the hydrophobic portion of the bilayer with its single -OH group in the polar region of the bilayer. In addition to the lipids shown here, there are a variety of proteins found in membranes. Some of these proteins extend all the way through the bilayer and so will have hydrophobic amino acids in the regions making contact with the bilayer and hydrophilic amino acids on the extracellular and intracellular surfaces.



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