Chapter 19 – Lipids

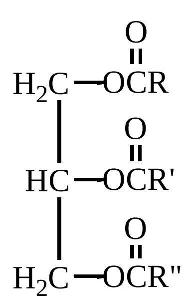
In the last chapter we looked at what constitutes the major energy source for most people. We now turn to a group of compounds that is not only a major portion of our diet, but also a major constituent of our own bodies. Lipids include fats, oils, and cholesterol, as well as other compounds that are less well known, but very important for the operation of our bodies.

19.1 What Lipids Are

Lipids are a class of compounds that are defined by how they are isolated, rather than by their composition. This makes them different from all of the other molecules we've seen so far. Until now, all molecule types were defined by functional groups. Lipids are molecules that can be extracted from plants and animals by low polarity solvents such as ether, chloroform, or even acetone. They are not appreciably soluble in water. Fats (and the fatty acids from which they are made) belong to this group, as do oils, waxes, and steroids. Other classes of molecules belong to this class, as we will see. We now explore a number of ways to classify lipids.

Hydrolyzable lipids are those that contain a functional group that will react with water. The functional group is usually an ester and the list of compounds includes neutral fats, waxes, phospholipids, and glycolipids. Nonhydrolyzable lipids lack such functional groups and include steroids and fat-soluble vitamins (e.g. A, D, E, and K).

Fats and oils are composed of triacylglycerols. These are compounds prepared by the union of glycerol (1,2,3-trihydroxypropane) and 3 fatty acids to form a triester. These are the neutral fats and a generic example is shown below.



The old name for these molecules was *triglycerides* and that name is still used by physicians in blood tests.

Complete hydrolysis of triacylglycerols yields three fatty acids and a glycerol molecule. Fatty acids are long chain carboxylic acids (typically 16 or more carbon atoms) which may or may not contain carbon-carbon double bonds. Fatty acids almost always contain an even number of carbon atoms and are usually unbranched. Oleic acid, $CH_3(CH_2)_{16}CO_2H$ is the most abundant fatty acid in nature. It is monounsaturated.

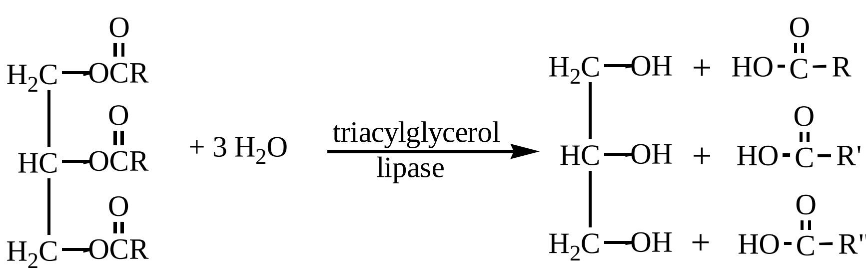
Those fatty acids with no carbon-carbon double bonds are called <u>saturated</u>, those with one double bond are <u>monounsaturated</u>, and those with two or more double bonds are called <u>polyunsaturated</u>. Typically each triacylglycerol contains 3 fatty acids. These fatty acids may be the same or different. Saturated fats are typically solids and are derived from animals, while unsaturated fats are liquids and usually extracted from plants. In all unsaturated fats the double bond assumes a *cis* geometry. This prevents the molecules from packing as efficiently as they do in saturated molecules and this causes the lower boiling points of unsaturated fats.

Fatty acids may also be classified as essential or nonessential. <u>Essential fatty acids</u> are those that our bodies cannot synthesize and must be obtained from our diets. <u>Nonessential fatty acids</u> are those that we can make in our bodies because we have the proper enzymes present.

Waxes are simple esters with very long hydrocarbon chains. In Chapter 15 you learned that short chain esters frequently generated pleasant odors (e.g. $CH_3(CH_2)_2CO_2CH_2CH_3$ = pineapple). One of the reasons they give a pleasant smell is that with short hydrocarbon chains they are slightly water-soluble so can be dispersed throughout fruits and vegetables and being small and lightweight they have high vapor pressures (evaporate readily). In contrast, the wax $CH_3(CH_2)_{24}CO_2(CH_2)_{29}CH_3$ (melissyl cerotate, a major component of beeswax) is a water-insoluble, solid at room temperature. The chain, including an ester oxygen, is 57 atoms long. For all intents and purposes, this material is no more water-soluble than any alkane. Lanolin is another wax. In plants, waxes cover the outside of fruits, vegetables, and leaves to prevent excessive loss of water and to protect against attack by parasites. In animals, waxes can make feathers water repellent or keep skin soft, among other things. Whale oil, $CH_3(CH_2)_{14}CO_2(CH_2)_{15}CH_3$ (cetyl palmitate) was once used as fuel, in oinments and cosmetics, and in candles. Its use has been banned since 1970. The first part of the compound name *cetyl* is derived from the biological order (*cetacia*) to which whales belong.

19.2 Chemical Properties of Triacylglycerols

As was mentioned in the previous section, hydrolysis of a triacylglycerol yields a glycerol molecule and 3 (usually different) fatty acid molecules. Unlike the acids used by chemists to accomplish such a task, the body employs the enzyme *triacylglycerol lipase* to catalyze the hydrolysis.



As you know, our bodies retain fat as an energy storage mechanism, not simply to deny us fun foods as we get older. When a fat molecule is hydrolyzed some of that energy is released. (The three new O-H bonds are stronger than the three C-O bonds that are broken. The difference in the bond strengths accounts for most of the energy released.)

When fats are ingested the body cleaves off one or two of the acid groups in the intestines.

This is because fat molecules are too large to pass through cell membranes. The monoacylglycerol (or diacylglycerol) and fatty acid then pass into the cell. Later the molecules are recombined into fat molecules. Fat molecules travel through the body by hitching a ride on proteins traveling in the bloodstream.

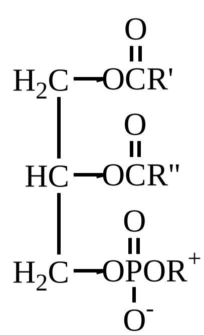
Soaps were discussed briefly in Chapter 15 (pp. 7 – 8 of the notes). The reaction of sodium hydroxide with fat molecules releases glycerol and the sodium salts of the fatty acids (RCO_2Na). No source I have found discussing the production of soap says that they are made from synthetic fatty acids. Although none explicitly says that they are made by the saponification and further processing of animal fat, it appears that that is how they are, in fact, made. My guess is that soap manufacturers are trying to avoid grossing out their customers.

By now, you have almost certainly seen the phrase “partially hydrogenated vegetable oil” in the ingredient list of some food. What does it mean? We learned in Chapter 12 that hydrogen could be added to alkenes (carbon-carbon double bonds) to make alkanes. This process is called <u>hydrogenation</u>. As we learned a short time ago, most vegetable oils contain very high percentages of unsaturated acids. By hydrogenating some (not all) of the C=C double bonds in the oil, its melting point slowly rises until it becomes a solid at room temperature. This is the major reason for making partially hydrogenated fats. Solid fats are easier to store and many people prefer the texture and convenience of solids. For example, “natural” peanut butter (or homemade stuff you can make yourself) will separate with time. When you open a bottle of natural peanut butter there will be a significant oil layer on top that must be stirred back in to soften it enough to spread on a piece of bread. Wait a day or two and the oil begins to come out again. Standard commercial brands remove some of the peanut oil, partially hydrogenate it, and then put it back. This prevents separation and helps maintain texture.

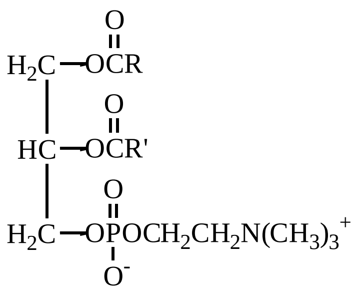
In terms of caloric content all fats are the same, 9.0 Calories per gram. Because they are liquids and won't form solid deposits in your veins and arteries, fats with very high percentages of monounsaturated and polyunsaturated fatty acids are healthier than those with high percentages of saturated fatty acids. Partially hydrogenated vegetable oil differs from animal fat only in that it lacks cholesterol.

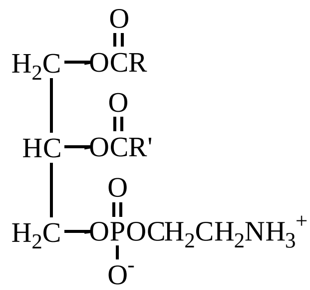
19.3 Phospholipids

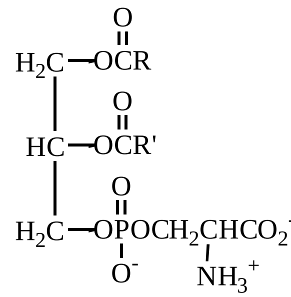
There are two classes of phospholipids. The first are the glycerophospholipids, which are themselves subdivided into two groups. The first group, phosphatides, is molecules composed of glycerol substituted with two fatty acid esters (just like in fats) and at the third position a phosphate unit connects to an alcohol. You will see that the picture I've drawn is different from that shown in your book (p. 557) in that this picture has charges on the "phospho" part of the molecule. This is because I have found no examples of neutral phospholipids. While they may well exist, they are clearly not among the most important examples of this class of compounds.



Three alcohols that form phosphatides are choline, ethanolamine, and serine. These compounds are important to the body and are transported as the following phosphatides. The enzymes either cut the molecule free when it is needed or convert it to some other necessary material. The phosphate group and the organic chain attached to it carry electrical charges. All three phosphatides are components of cell membranes.







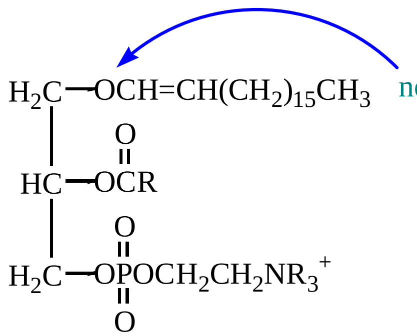
phosphatidylcholine phosphatidylethanolamine phosphatidylserine

lecithin cephalin

Choline is a water-soluble vitamin (as recognized by the *Food and Nutrition Board*, usually classified as a B vitamin) used to make complex lipids. Phosphatidylcholine is the principal phospholipid of cell membranes. It is also converted to acetyl choline ($CH_3CO_2CH_2CH_2N(CH_3)_3^+$), which is an important neurotransmitter (it carries electrical charges from one nerve cell to another). Choline helps break down homocysteine – a cardiovascular disease risk factor. A lack of this vitamin leads to fatty livers and/or hemorrhagic kidney disease.

Serine is the parent of a family of amino acids that also includes glycine and cysteine. Enzymes convert serine (as part of phosphatidylserine) to glycine and cysteine. Serine is also involved in the generation of ethanolamine, which is in turn converted to choline. Interestingly, phosphatidylethanolamine is deficient in Alzheimer's patients. They also act as a histamine blocker in the body.

The other subclass of glycerophospholipids are the <u>plasmalogens</u>. These differ from triacylglycerols by even more than the phosphatides. A generic plasmalogen would look like:

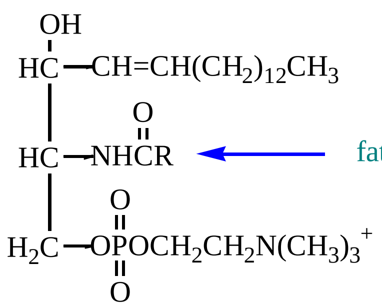


note the ether linkage and adjacent C=C double bond

R = H or CH_3

The compound with R = CH_3 is called platelet activating factor. It is a strong bronchoconstrictor. It also stimulates other cells to increase their functional and metabolic activities.

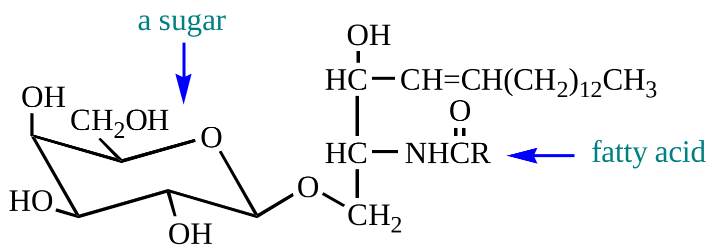
The second major class of phospholipids are the sphingolipids. Sphingolipids include the sphingomyelins and cerebrosides. Both are based on the molecule sphingosine. Sphingomyelins have the basic formula:



fatty acid, this is the only group that can vary

As the name suggests this lipid is affiliated with the myelin sheath surrounding the cells of the central nervous system. Sphingomyelins comprise about 25% of the lipids in the myelin sheath and their role is key to brain function and electrical transmission through our nervous system.

The other type of sphingolipids we are concerned with are cerebrosides, which are not phospholipids. These compounds are again based on attachments to a sphingosine molecule.

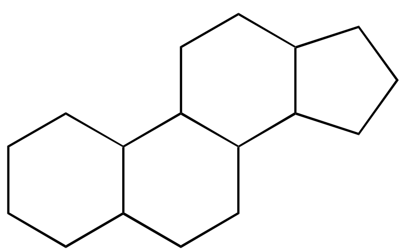


Not surprisingly, these molecules are called glycolipids (*cf*. glycosides are acetals of sugars). Most of these molecules incorporate β-D-galactose sugars. Cerebrosides are found most commonly in cell membranes in the brain. One cerebroside found outside the brain, a glucocerebroside, is found in the membranes of macrophages (cells that destroy foreign microorganisms).

Several disorders are associated with malfunctioning of sphingolipid metabolism. Probably the best known is Tay-Sachs disease, which strikes infants and is typically fatal by age 3. Niemann-Pick disease also strikes infants and is fatal early in life. Gaucher's disease and Fabry's disease strike later in life and are generally less devastating.

19.4 Steroids

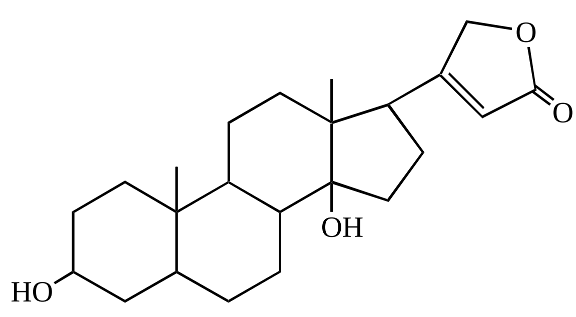
Steroids are nonhydrolyzable lipids. All steroids contain the following fused ring system:



Like other fats, these molecules have high molecular weights. Several important ones are pictured on pp. 559-61 of your textbook. Most have so few polar groups that they will have negligible water solubility. Cortisol, with two keto and 3 hydroxy groups is an exception having slight solubility in hot water. Your book does a nice job describing several steroids and you should read about them.

Your book calls bile salts "detergents" that aid in the digestion and absorption of various lipids and fatty acids. Why is the term *detergent* appropriate? If you didn't read the Interaction 19.4 on p. 556, now is a good time. Detergents belong to a class of molecules called *surfactants* for surface-active agents. They are molecules with a very polar end (typically an ionic group) and a long nonpolar segment. When placed in a polar environment (as both Tide® and bile are), the polar end associates well with water. The nonpolar tails will congregate together. While this is an oversimplification, you can think of these as forming a ball with the ionic groups forming the cover, and the organic (hydrophobic) tails pointing in towards the center. These structures are called micelles (see Figure 19.2 p. 562 of book for a representative picture). When one of these micelles comes into contact with fats, fatty acids, fat-soluble vitamins, etc. the fat is drawn into the center of the micelle for transport to the intestinal wall. At the wall, the hydrophobic groups can interact with cell membranes (which are themselves hydrophobic, *water avoiding*) in such a way as to allow the nutrient to pass into the intestinal cells. We will return to this at the end of the chapter.

The only steroids discussed in the text are animal steroids and, more specifically, ones found in humans. Steroids also occur in plants and the cardiac steroids form an important class. This might strike you as odd at first (it certainly did me) because plants don't have hearts. One member of this family is digitoxin, a powerful heart stimulant (shown below). It is somewhat



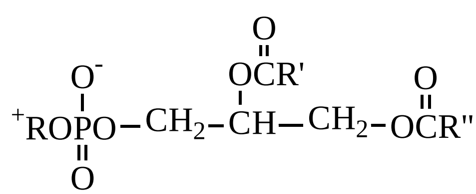
digitoxin

similar in composition to cholesterol and is used to treat congestive heart failure. Needless to say, too much of this steroid (like all steroids) is harmful, and is potentially fatal. Doses as low as 1 mg have a measurable effect on heart function. Digitoxin is extracted from the foxglove plant (*digitalis purpurea*).

19.5 Cell Membranes – Their Lipid Components

In several places in this section, you have been told that such-and-such compound is an important component of the membrane of some type of cell. We will now discuss the construction of a cell membrane and will end the chapter discussing why this is both marvelous and fascinating (at least to me).

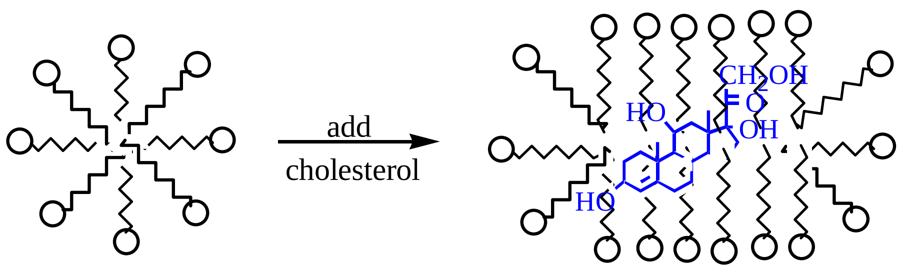
Consider a generic phospholipid.



The phosphate end is charged and will have strong attractive interactions with water (hydrophilic). The rest of the molecule will (except a minor dipolar interaction) interact very poorly with water (hydrophobic). When this substance is added to water it will undergo self-assembly to a larger structure. By that we mean the molecules will, all by themselves, associate and form a larger structure. This contrasts with adding acetic acid to water. If you added one million acetic acid molecules to a liter of water and stirred, what would happen? If we cut the liter in half we would expect to find 500,000 acetic acid molecules in each 500 mL. If we divided it into 1 mL samples we would expect each mL to have just about exactly 1000 acetic acid molecules. If we divided each mL into μL samples (1/1,000,000 L), we would expect almost all to have 1 acetic acid molecule (although some would have 2 and some 0 because of random motion). The point here is that when the vast majority of substances are added to a solvent they dissolve and randomly distribute.

If we added a substance that is completely insoluble in the solvent, we expect the layers to stay completely separate. Phospholipids are intermediate molecules, however. One part wants to go into solution, the other part resists it. The result is that the hydrophobic ends tend to congregate together and the hydrophilic ends do likewise, but that isn't quite enough. The natural shape for assembly is a sphere. This maximizes hydrophobic interactions on the inside and hydrophilic interactions on the surface. The result is the micelle shown in Figure 19.2 (p. 562).

As with detergents, molecules with little to no hydrophilic parts will be pulled into the micelle. Needless to say, this will cause the micelle to expand to accommodate the extra volume. The result is that the micelle will become ovate (oval shaped).



As more things are added, the oval becomes longer and flatter until it is essentially two layers. This is called a lipid bilayer and is the basic construction of the cell membranes. Thus, molecules like cholesterol help to stabilize the cell membrane by keeping the membrane flat. Figures 19.3 and 19.4 (p. 563) show this progression.

The cell membrane also includes proteins that assist in moving things into or through the cell membrane. We discuss them in the next chapter. Cell membranes are self-sealing for the same reason that they form in the first place. If something displaces some of the molecules in a cell membrane, intermolecular forces will push the hydrophilic and hydrophobic parts of each molecule back into place.

This brings us back to the first paragraph in this section. In all general chemistry courses we teach and learn that covalent and ionic bonds are quite strong and that intermolecular forces are relatively weak. Indeed, London forces (p. 161, 183 of your book) are generally thought of as being very weak. These forces are the ones operating between the tails in cell membranes. Ion-dipole forces and hydrogen bonding operate between the phosphate groups and water. Yet we have just seen that cell membranes are not one giant molecule stretching around the cell, but rather a large number of molecules only “loosely” associating. Thus the cumulative effect of intermolecular forces in this arrangement is so strong that it not only permits single cell creatures to exist, but also us. The cells in our bodies form from this aggregation of lipids and we too are held together by what we learn are only weak forces. This is truly something at which to marvel.

March 16, 2002