

Metabolism of Lipids (BCH303)

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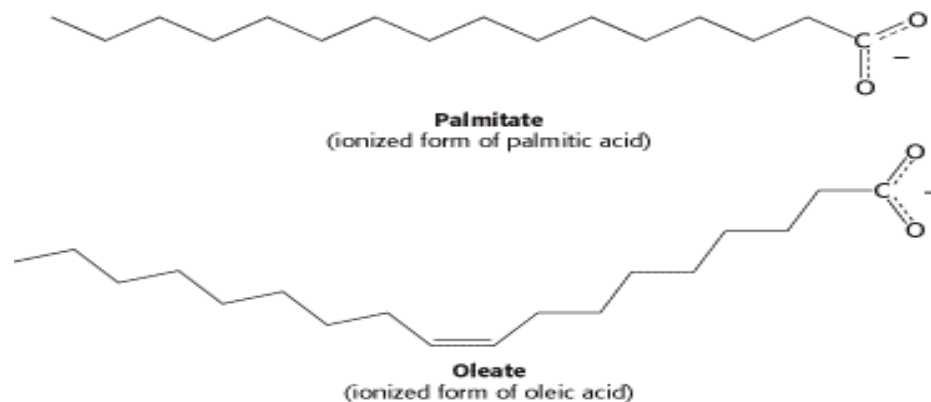
Lipids are a class of biological molecules defined by low solubility in water and high solubility in nonpolar solvents. As molecules that are largely hydrocarbon in nature, lipids represent highly reduced forms of carbon and, upon oxidation in metabolism, yield large amounts of energy. Lipids are thus the molecules of choice for metabolic energy storage.

The lipids found in biological systems are either **hydrophobic** (containing only nonpolar groups) or **amphipathic**, which means they possess both polar and nonpolar groups. The hydrophobic nature of lipid molecules allows membranes to act as effective barriers to more polar molecules.

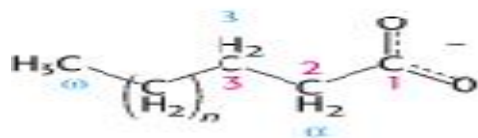
Fatty Acids

A **fatty acid** is composed of a long hydrocarbon chain (“tail”) and a terminal carboxyl group (or “head”). The carboxyl group is normally ionized under physiological conditions. Fatty acids occur in large amounts in biological systems, but rarely in the free, uncomplexed state. They typically are esterified to glycerol or other backbone structures. Most of the fatty acids found in nature have an even number of carbon atoms (usually 14 to 24). Certain marine organisms, however, contain substantial amounts of fatty acids with odd numbers of carbon atoms. Fatty acids are either **saturated** (all carbon-carbon bonds are single bonds) or **unsaturated** (with one or more double bonds in the hydrocarbon chain). If a fatty acid has a single double bond, it is said to be **monounsaturated**, and if it has more than one, **polyunsaturated**. Fatty acids can be named or described in at least three ways, as listed in the Table below.

The systematic name for a fatty acid is derived from the name of its parent hydrocarbon by the substitution of *oic* for the final *e*. For example, the C18 saturated fatty acid is called *octadecanoic acid* because the parent hydrocarbon is octadecane. A C18 fatty acid with one double bond is called *octadecenoic acid*; with two double bonds, *octadecadienoic acid*; and with three double bonds, *octadecatrienoic acid*. The notation 18:0 denotes a C18 fatty acid with no double bonds, whereas 18:2 signifies that there are two double bonds. The structures of the ionized forms of two common fatty acids palmitic acid (C16, saturated) and oleic acid (C18, monounsaturated) are shown in Figure below.



They are numbered starting at the carboxyl terminus, as shown in the margin. Carbon atoms 2 and 3 are often referred to as α and β , respectively. The methyl carbon atom at the distal end of the chain is called the ω -carbon atom.



Alternatively, the position of a double bond can be denoted by counting from the distal end, with the ω -carbon atom (the methyl carbon) as number 1. An ω -3 fatty acid, for example, has the structure shown in the margin.

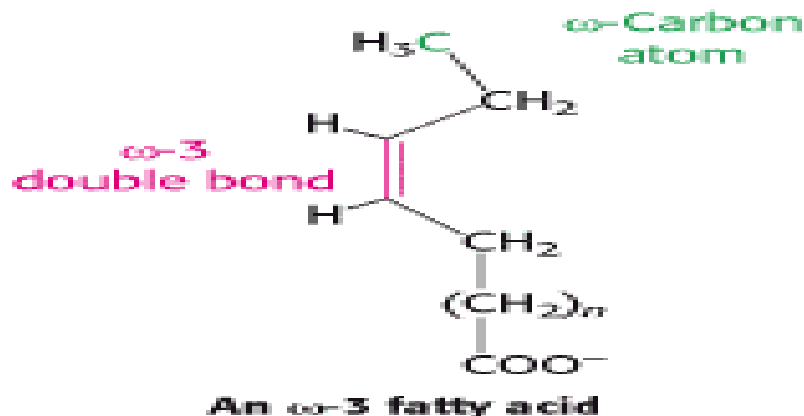


Table showing some Common Biological Fatty Acids

Number of Carbons	Common Name	Systematic Name	Symbol	Structure
Saturated fatty acids				
12	Lauric acid	Dodecanoic acid	12:0	$\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$
14	Myristic acid	Tetradecanoic acid	14:0	$\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$
16	Palmitic acid	Hexadecanoic acid	16:0	$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$
18	Stearic acid	Octadecanoic acid	18:0	$\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$
20	Arachidic acid	Eicosanoic acid	20:0	$\text{CH}_3(\text{CH}_2)_{18}\text{COOH}$
22	Behenic acid	Docosanoic acid	22:0	$\text{CH}_3(\text{CH}_2)_{20}\text{COOH}$
24	Lignoceric acid	Tetracosanoic acid	24:0	$\text{CH}_3(\text{CH}_2)_{22}\text{COOH}$
Unsaturated fatty acids (all double bonds are <i>cis</i>)				
16	Palmitoleic acid	9-Hexadecenoic acid	16:1	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$
18	Oleic acid	9-Octadecenoic acid	18:1	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$
18	Linoleic acid	9,12-Octadecadienoic acid	18:2	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_2(\text{CH}_2)_6\text{COOH}$
18	α -Linolenic acid	9,12,15-Octadecatrienoic acid	18:3	$\text{CH}_3\text{CH}_2(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_6\text{COOH}$
18	γ -Linolenic acid	6,9,12-Octadecatrienoic acid	18:3	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_3\text{COOH}$
20	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	20:4	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_4(\text{CH}_2)_2\text{COOH}$
24	Nervonic acid	15-Tetracosenoic acid	24:1	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_{13}\text{COOH}$

Unsaturated fatty acids are slightly more abundant in nature than saturated fatty acids, especially in higher plants. The most common unsaturated fatty acid is **oleic acid**, or 18:1(9), with the number in parentheses indicating that the double bond is between carbons 9 and 10. The number of double bonds in an unsaturated fatty acid varies typically from one to four, but, in the fatty acids found in most bacteria, this number rarely exceeds one.

The double bonds found in fatty acids are nearly always in the *cis* configuration. As shown in Figure below, this causes a bend or “kink” in the fatty acid chain. This bend has very important consequences for the structure of biological membranes. Saturated fatty acid chains can pack closely together to form ordered, rigid arrays under certain conditions, but unsaturated fatty acids prevent such close packing and produce flexible, fluid aggregates.

Some fatty acids are not synthesized by mammals and yet are necessary for normal growth and life. These *essential fatty acids* include **linoleic** and **γ -linolenic acids**. These must be obtained by mammals in their diet (specifically from plant sources). **Arachidonic acid**, which is not found in plants, can only be synthesized by mammals from linoleic acid. At least one function of the essential fatty acids is to serve as a precursor for the synthesis of **eicosanoids**, such as *prostaglandins*, a class of compounds that exert hormone-like effects in many physiological processes.

In addition to unsaturated fatty acids, several other modified fatty acids are found in nature. Microorganisms, for example, often contain branched-chain fatty acids, such as **tuberculostearic acid**. When these fatty acids are incorporated in membranes, the methyl group constitutes a local structural perturbation in a manner similar to the double bonds in unsaturated fatty acids. Some bacteria also synthesize fatty acids containing cyclic structures such as cyclopropane, cyclopropene, and even cyclopentane rings.

The properties of fatty acids and of lipids derived from them are markedly dependent on chain length and degree of saturation. Unsaturated fatty acids have lower melting points than saturated fatty acids of the same length. For example, the melting point of stearic acid is 69.6°C, whereas that of oleic acid (which contains one *cis* double bond) is 13.4°C. The melting points of polyunsaturated fatty acids of the C18 series are even lower. Chain length also affects the melting point, as illustrated by the fact that the melting temperature of palmitic acid (C16) is 6.5 degrees lower than that of stearic acid (C18). Thus, *short chain length and unsaturation enhance the fluidity of fatty acids and of their derivatives*

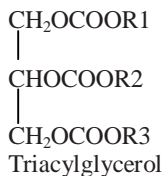
Fatty Acids in Food: Saturated Versus Unsaturated

Fats consumed in the modern human diet vary widely in their fatty acid compositions. The table below provides a brief summary. The incidence of cardiovascular disease is correlated with diets high in saturated fatty acids. By contrast, a diet that is relatively higher in unsaturated fatty acids (especially polyunsaturated fatty acids) may reduce the risk of heart attacks and strokes. Corn oil, abundant in the United States and high in (polyunsaturated) linoleic acid, is an attractive dietary choice. *Margarine* made from corn, safflower, or sunflower oils is much lower in saturated fatty acids than is butter, which is made from milk fat. However, margarine may present its own health risks. Its fatty acids contain *trans*-double bonds (introduced by the hydrogenation process), which may also contribute to cardiovascular disease. Although vegetable oils usually contain a higher proportion of unsaturated fatty acids than do animal oils and fats, several plant oils are actually high in saturated fats. Palm oil is low in polyunsaturated fatty acids and particularly high in (saturated) palmitic acid (whence the name *palmitic*). Coconut oil is particularly high in lauric and myristic acids (both saturated) and contains very few unsaturated fatty acids.

Some of the fatty acids found in the diets of developed nations (often 1 to 10 g of daily fatty acid intake) are *trans* fatty acids—fatty acids with one or more double bonds in the *trans* configuration. Some of these derive from dairy fat and ruminant meats, but the bulk are provided by partially hydrogenated vegetable or fish oils. Substantial evidence now exists to indicate that *trans* fatty acids may have deleterious health consequences. Numerous studies have shown that *trans* fatty acids raise plasma LDL cholesterol levels when exchanged for *cis*-unsaturated fatty acids in the diet and may also lower HDL cholesterol levels and raise triglyceride levels. The effects of *trans* fatty acids on LDL, HDL, and cholesterol levels are similar to those of saturated fatty acids, and diets aimed at reducing the risk of coronary heart disease should be low in both *trans* and saturated fatty acids.

Triacylglycerols

A significant number of the fatty acids in plants and animals exist in the form of **triacylglycerols** (also called **triglycerides**). Triacylglycerols are a major energy reserve and the principal neutral derivatives of glycerol found in animals. These molecules consist of a glycerol esterified with three fatty acids.



If all three fatty acid groups are the same, the molecule is called a simple triacylglycerol. Examples include **tristearoylglycerol** (common name *tristearin*) and **trioleoylglycerol** (*triolein*). Mixed triacylglycerols contain two or three different fatty acids. Triacylglycerols in animals are found primarily in the adipose tissue (body fat), which serves as a depot or storage site for lipids. Monoacylglycerols and diacylglycerols also exist, but are far less common than the triacylglycerols. Most natural plant and animal fat is composed of mixtures of simple and mixed triacylglycerols.

Acylglycerols can be hydrolyzed by heating with acid or base or by treatment with lipases. Hydrolysis with alkali is called **saponification** and yields salts of free fatty acids and glycerol. This is how **soap** (a metal salt of an acid derived from fat) was made by our ancestors. One method used potassium hydroxide (*potash*) leached from wood ashes to hydrolyze animal fat (mostly triacylglycerols).

(The tendency of such soaps to be precipitated by Mg and Ca ions in hard water makes them less useful than modern detergents.) When the fatty acids esterified at the first and third carbons of glycerol are different, the second carbon is asymmetric.

The various acylglycerols are normally soluble in benzene, chloroform, ether, and hot ethanol. Although triacylglycerols are insoluble in water, mono- and diacylglycerols readily form organized structures in water (discussed later), owing to the polarity of their free hydroxyl groups. Triacylglycerols are rich in highly reduced carbons and thus yield large amounts of energy in the oxidative reactions of metabolism. Complete oxidation of 1 g of triacylglycerols yields about 38 kJ of energy, whereas proteins and carbohydrates yield only about 17 kJ/g. Also, their hydrophobic nature allows them to aggregate in highly anhydrous forms, whereas polysaccharides and proteins are highly hydrated. For these reasons, triacylglycerols are the molecules of choice for energy storage in animals. Body fat (mainly triacylglycerols) also provides good insulation.