WHAT IS A LIPID?

Definitions

Although lipid analysts tend to have a firm understanding of what is meant by the term "**lipid**", there is no widely accepted definition. General textbooks usually describe lipids in woolly terms as a group of naturally occurring compounds, which have in common a ready solubility in such organic solvents as hydrocarbons, chloroform, benzene, ethers and alcohols. They include a diverse range of compounds, like fatty acids and their derivatives, carotenoids, terpenes, steroids and bile acids. It should be apparent that many of these compounds have little by way of structure or function to relate them. In fact, a definition of this kind is positively misleading, since many of the substances that are now widely regarded as lipids may be almost as soluble in water as in organic solvents.

Although the international bodies that usually decide such matters have shirked the task, a more specific definition of lipids than one based simply on solubility is necessary, and most scientist active in this field would happily restrict the use of "lipid" to fatty acids and their naturally occurring derivatives (esters or amides). The definition could be stretched to include compounds related closely to fatty acid derivatives through biosynthetic pathways (*e.g.* prostanoids, aliphatic ethers or alcohols) or by their biochemical or functional properties (*e.g.* cholesterol). My definition is -

"Lipids are fatty acids and their derivatives, and substances related biosynthetically or functionally to these compounds."

This treats cholesterol (and plant sterols) as a lipid, and could be interpreted to include bile acids, tocopherols and certain other compounds. It also enables classification of such compounds as gangliosides as lipids, although they are more soluble in water than in organic solvents. However, it does not include such natural substances as steroidal hormones, petroleum products, some fat-soluble vitamins, carotenoids or simple terpenes, except in rare circumstances.

If "lipids" are defined in this way, **fatty acids** must be defined also. They are compounds synthesised in nature *via* condensation of malonyl coenzyme A units by a fatty acid synthase complex. They usually contain even numbers of carbon atoms in straight chains (commonly C_{14} to C_{24}), and may be saturated or unsaturated, and can contain a variety of substituent groups.

Fahy *et al.* (*J. Lipid Res*., **46**, 839-862 (2005)) have developed a classification system for lipids that holds promise (see our page on **Nomenclature**). While their definition of a lipid is too broad for my taste, it is based on sound scientific principles, i.e.

> "Lipids are hydrophobic or amphipathic small molecules that may originate entirely or in part by carbanion-based condensations of thioesters (fatty acids, polyketides, etc.) and/or by carbocation-based condensations of isoprene units (prenols, sterols, etc.). "

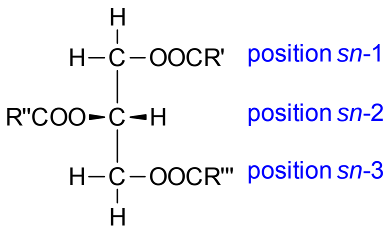
The most common lipid classes in nature consist of fatty acids linked by an ester bond to the trihydric alcohol - glycerol, or to other alcohols such as cholesterol, or by amide bonds to sphingoid bases, or on occasion to other amines. In addition, they may contain alkyl moieties other than fatty acids, phosphoric acid, organic bases, carbohydrates and many more components, which can be released by various hydrolytic procedures.

A further subdivision into two broad classes is convenient for chromatography purposes especially. **Simple** lipids are defined as those that on hydrolysis yield at most two types of primary product per mole; **complex** lipids yield three or more primary hydrolysis products per mole. Alternatively, the terms "neutral" and "polar" lipids respectively are used to define these groups, but are less exact.

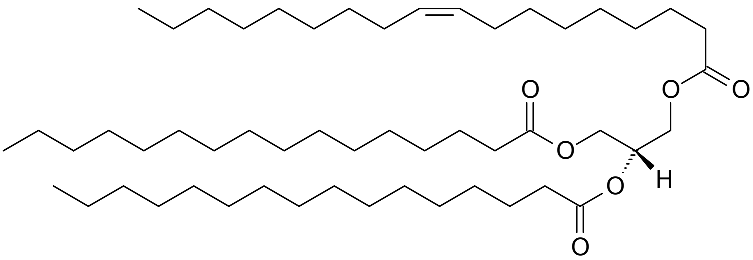
The complex lipids for many purposes are best considered in terms of either the **glycerophospholipids** (or simply if less accurately as **phospholipids**), which contain a polar phosphorus moiety and a glycerol backbone, or the **glycolipids** (both glycoglycerolipids and glycosphingolipids), which contain a polar carbohydrate moiety, since these are more easily analysed separately. The picture is further complicated by the existence of phosphoglycolipids and sphingophospholipids (e.g. sphingomyelin).

Simple Lipids

Triacylglycerols: Nearly all the commercially important fats and oils of animal and plant origin consist almost exclusively of the simple lipid class triacylglycerols (termed "triglycerides" in the older literature). They consist of a glycerol moiety with each hydroxyl group esterified to a fatty acid. In nature, they are synthesised by enzyme systems, which determine that a centre of asymmetry is created about carbon-2 of the glycerol backbone, so they exist in enantiomeric forms, *i.e.* with different fatty acids in each position.



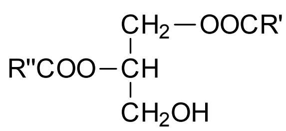
Fischer projection of a triacyl-*sn*-glycerol



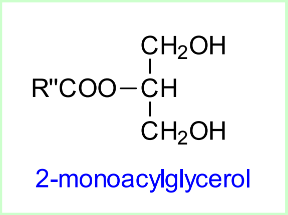
1,2-dihexadecanoyl-3-(9*Z*-octadecenyl)-*sn*-glycerol

A *stereospecific numbering* system has been recommended to describe these forms. In a Fischer projection of a natural L-glycerol derivative, the secondary hydroxyl group is shown to the left of C-2; the carbon atom above this then becomes C-1 and that below is C-3. The prefix "*sn*" is placed before the stem name of the compound, when the stereochemistry is defined. Their primary biological function is to serve as a store of energy. As an example, the single molecular species 1,2-dihexadecanoyl-3-(9*Z*-octadecenoyl)-*sn*-glycerol is illustrated.

Diacylglycerols (less accurately termed "diglycerides") and monoacylglycerols ("monoglycerides") contain two moles and one mole of fatty acids per mole of glycerol, respectively, and exist in various isomeric forms. They are sometimes termed collectively "partial glycerides". Although they are rarely present at greater than trace levels in fresh animal and plant tissues, synthetic materials have importance in commerce. However, 1,2-diacyl-*sn*-glycerols are key intermediates in the biosynthesis of triacylglycerols and other lipids, and they are vital cellular messengers, generated on hydrolysis of phosphatidylinositol and related lipids by a specific phospholipase C (see below).



1,2-/2,3-diacylglycerol

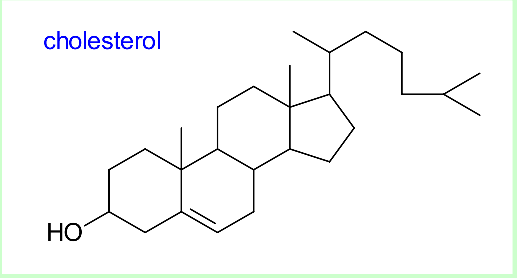


2-Monoacyl-*sn*-glycerols (are formed as intermediates or end-products of the enzymatic hydrolysis of triacylglycerols; these and other positional isomers are powerful surfactants. 2-Arachidonoylglycerol has important biological properties (as an endocannabinoid).

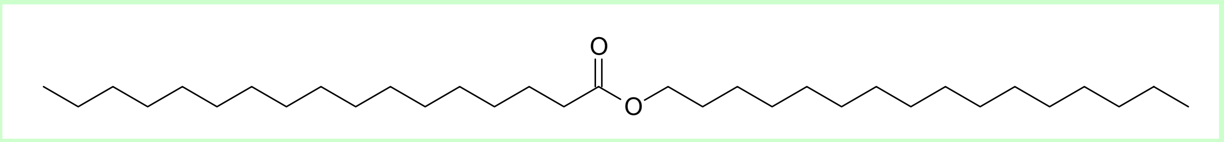
Acyl migration occurs rapidly in partial glycerides at room temperature, but especially on heating, in alcoholic solvents or in the presence of acid or base, so special procedures are required for their isolation or analysis if the stereochemistry is to be retained. Synthetic 1-/3-monoacylglycerols are important in commerce as surfactants

Sterols and sterol esters: Cholesterol is by far the most common member of a group of steroids in animal tissues; it has a tetracyclic ring system with a double bond in one of the rings and one free hydroxyl group. It is found both in the free state, where it has an essential role in maintaining membrane fluidity, and in esterified form, i.e. as cholesterol esters. Other sterols are present in free and esterified form in animal tissues, but at trace levels only.

In plants, cholesterol is rarely present in other than small amounts, but such 'phytosterols' as sitosterol, stigmasterol, avenasterol, campesterol and brassicasterol, and their fatty acid esters are usually found, and they perform a similar function. Hopanoids are related lipids produced by some bacterial species.

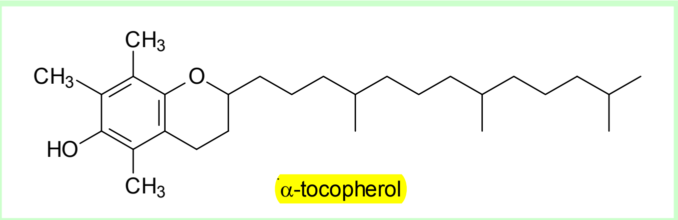


Waxes: In their most common form, ***wax esters*** consist of fatty acids esterified to long-chain alcohols with similar chain-lengths. The latter tend to be saturated or have one double bond only. Such compounds are found in animal, plant and microbial tissues and they have a variety of functions, such as acting as energy stores, waterproofing and lubrication.



In some tissues, such as skin, avian preen glands or plant leaf surfaces, the wax components can be much more complicated in their structures and compositions. They can contain aliphatic diols, free alcohols, hydrocarbons (*e.g*. squalene), aldehydes and ketones.

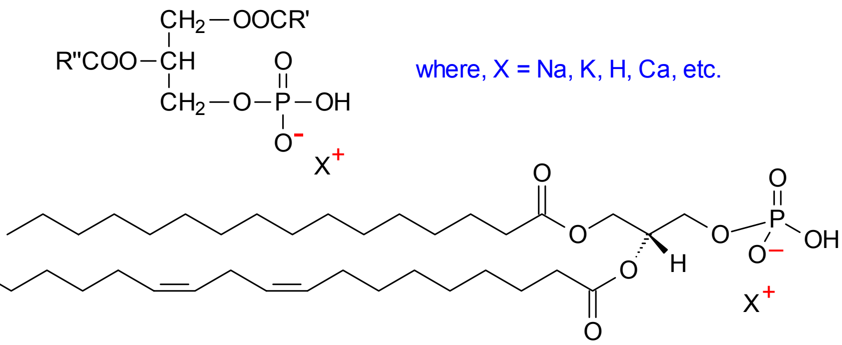
Tocopherols are substituted benzopyranols (methyl tocols) that occur in vegetable oils. Different forms (α, β, γ and δ) are recognized according to the number or position of methyl groups on the aromatic ring. α-Tocopherol (with the greatest Vitamin E activity) illustrated is an important natural antioxidant. Tocotrienols have similar ring structures but with three double bonds in the chain.



Free (unesterified) fatty acids are minor constituents of living tissues but are of biological importance as precursors of lipids, as an energy source and as cellular messengers.

Glycerophospholipids

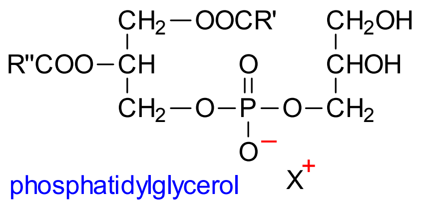
Phosphatidic acid or 1,2-diacyl-*sn*-glycerol-3-phosphate is found in trace amounts only in tissues under normal circumstances, but it has great metabolic importance as a biosynthetic precursor of all other glycerolipids. It is strongly acidic and is usually isolated as a mixed salt. One specific isomer is illustrated as an example.



1-hexadecanoyl, 2-(9*Z*,12*Z*-octadecadienoyl)-*sn*-glycero-3-phosphate
(phosphatidic acid)

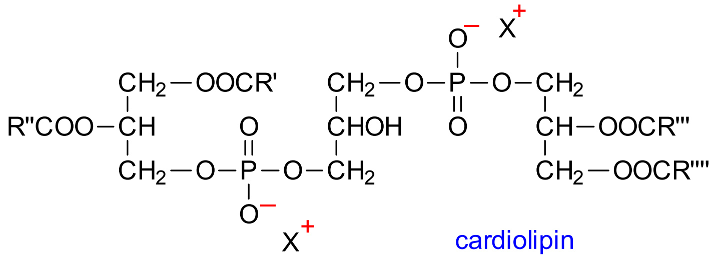
Lysophosphatidic acid with one mole of fatty acid per mole of lipid (in position *sn*-1) is a marker for ovarian cancer, and is a key cellular messenger.

Phosphatidylglycerol or 1,2-diacyl-*sn*-glycerol-3-phosphoryl-1'-*sn*-glycerol tends to be a trace constituent of most tissues, but it is often the main component of bacterial membranes. It has important functions in lung surfactant, where its physical properties are significant, and in plant chloroplasts, where it appears to have an essential role in photosynthesis. Also, it is the biosynthetic precursor of cardiolipin. In some bacterial species, the 3'-hydroxyl of the phosphatidylglycerol moiety is linked to an amino acid (lysine, ornithine or alanine) to form an *O*-aminoacylphosphatidylglycerol or 'lipoamino acid'.



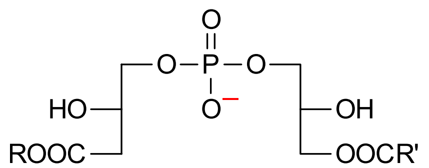
phosphatidylglycerol

Cardiolipin (diphosphatidylglycerol or more precisely 1,3-*bis*(*sn*-3'-phosphatidyl)-*sn*-glycerol) is a unique phospholipid with in essence a dimeric structure, having four acyl groups and potentially carrying two negative charges (and is thus an acidic lipid). It is an important constituent of mitochondrial lipids especially, so heart muscle is a rich source. Amongst other functions, it plays a key role in modifying the activities of the enzymes concerned with oxidative phosphorylation.



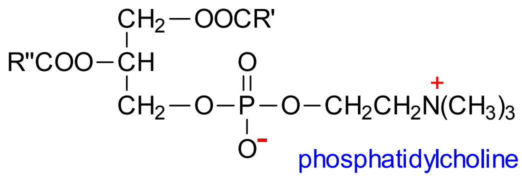
cardiolipin

Lysobisphosphatidic acid or bis(monoacylglycerol)-phosphate is an interesting lipid as its stereochemical configuration differs from that of all other animal glycero-phospholipids in that the phosphodiester moiety is linked to positions *sn*-1 and *sn*-1’ of glycerol, rather than to position *sn*-3, to which the fatty acids are esterified (some think that position *sn*-2 is more likely for the latter). It is usually a rather minor component of animal tissues, but is enriched in the lysosomes of liver and appears to be a marker for this organelle. The glycerophosphate backbone is particularly stable, presumably because of the unusual stereochemistry.



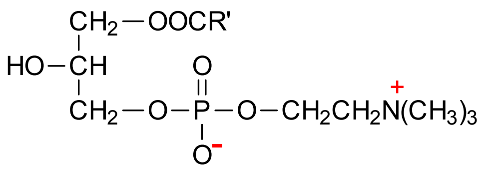
lysobisphosphatidic acid

Phosphatidylcholine or 1,2-diacyl-*sn*-glycerol-3-phosphorylcholine (or "lecithin", although the term is now used more frequently for the mixed phospholipid by-products of seed oil refining) is usually the most abundant lipid in the membranes of animal tissues, and it is often a major lipid component of plant membranes, but only rarely of bacteria. Together with the other choline-containing phospholipid, sphingomyelin, it is a key structural component and constitutes much of the lipid in the external monolayer of the plasma membrane of animal cells especially.



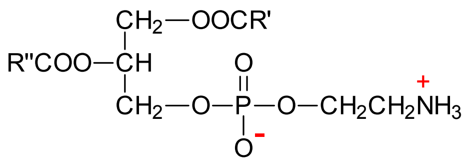
phosphatidylcholine

Lysophosphatidylcholine, which contains only one fatty acid moiety in each molecule, generally in position *sn*-1, is sometimes present as a minor component of tissues. It is a powerful surfactant and is more soluble in water than most other lipids.



lysophosphatidylcholine

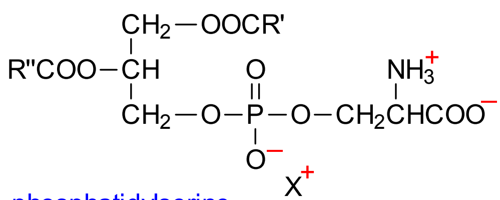
Phosphatidylethanolamine (once given the trivial name "cephalin") is usually the second most abundant phospholipid class in animal and plant tissues, and can be the major lipid class in microorganisms. As part of an important cellular process, the amine group can be methylated enzymically to yield first phosphatidyl-*N*-monomethylethanolamine and then phosphatidyl-*N,N*-dimethyl-ethanolamine, but these never accumulate in significant amounts; the eventual product is phosphatidylcholine.



phosphatidylethanolamine

N-Acyl-phosphatidylethanolamine is a minor component of some plant tissues, especially cereals, and it is occasionally found in animal tissues, where it is the precursor of some biologically active amides. Lysophosphatidylethanolamine contains only one mole of fatty acid per mole of lipid.

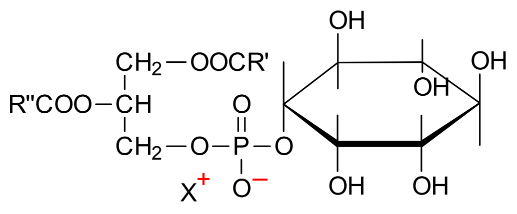
Phosphatidylserine is a weakly acidic lipid that is present in most tissues of animals and plants and is found also in microorganisms. It is located entirely on the inner monolayer surface of the plasma membrane and other cellular membranes. Phosphatidylserine is an essential cofactor for the activation of protein kinase C, and it is involved in many other biological processes, including blood coagulation and apoptosis (programmed cell death).



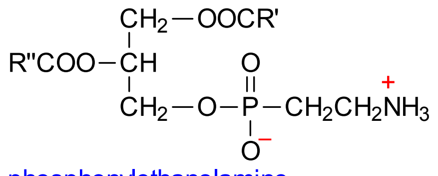
phosphatidylserine

N-Acylphosphatidylserine has been detected in some animal tissues.

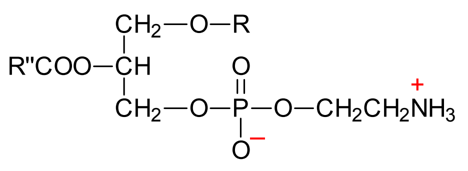
Phosphatidylinositol, containing the optically inactive form of inositol, *myo*-inositol, is a common constituent of animal, plant and microbial lipids. In animal tissues especially, it may be accompanied by small amounts of phosphatidyl-inositol 4-phosphate and phosphatidylinositol 4,5-bisphosphate ('poly-phosphoinositides'). These compounds have a rapid rate of metabolism in animal cells, and are converted to metabolites such as diacylglycerols and inositol phosphates, which are important in regulating vital processes. For example, diacylglycerols regulate the activity of a group of enzymes known as protein kinase C, which in turn control many key cellular functions, including differentiation, proliferation, metabolism and apoptosis. In addition, phosphatidylinositol is the primary source of the arachidonate used for eicosanoid synthesis in animals, and it is known to be the anchor that can link a variety of proteins to the external leaflet of the plasma membrane via a glycosyl bridge (glycosyl-phosphatidylinositol(GPI)-anchored proteins).

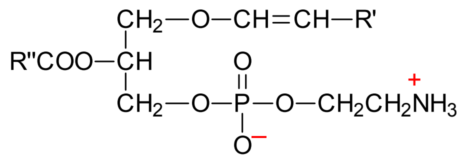

phosphatidylinositol

Phosphonolipids are lipids with a phosphonic acid moiety esterified to glycerol, i.e. with a carbon-phosphorus bond that is not hydrolysed easily by chemical reagents. For example, phosphonylethanolamine is found mainly in marine invertebrates and in protozoa. A ceramide analogue is often found in the same organisms (see below).


phosphonylethanolamine

Ether lipids: Many glycerolipids, but mainly phospholipids, and those of animal and microbial origin especially, contain aliphatic residues linked either by an ether bond or a vinyl ether bond to position 1 of *L*-glycerol. When a lipid contains a vinyl ether bond, the generic term "plasmalogen" is often used. They can be abundant in the phospholipids of animals and microorganisms, and especially in the phosphatidylethanolamine fraction. In this instance, it has been recommended that they should be termed "plasmenylethanolamine" and "plasmanylethanolamine", respectively.

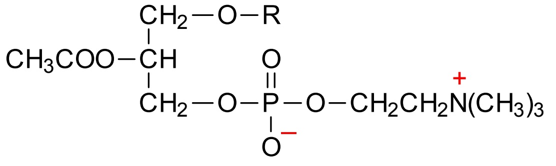

plasmanylethanolamine


plasmenylethanolamine

On hydrolysis of glycerolipids containing an alkyl ether bond, 1-alkylglycerols are released that can be isolated for analysis. Similarly, when plasmalogens are hydrolysed under basic conditions, 1-alkenylglycerols are released. Aldehydes are formed on acidic hydrolysis. With both groups of compound, the aliphatic residues generally have a chain-length of 16 or 18, and they are saturated or may contain one additional double bond, that is remote from the ether linkage.

1-Alkyl-2,3-diacyl-*sn*-glycerols, analogues of triacylglycerols, tend to be present in trace amounts only in animal tissues, but can be major constituents of certain fish oils. Related compounds containing a 1-alk-1'-enyl moiety ('neutral plasmalogens') are occasionally present also.

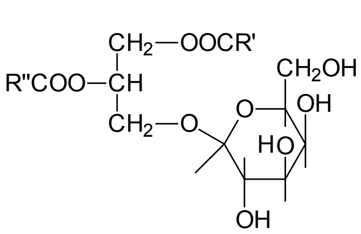
"**Platelet-activating factor**" or 1-alkyl-2-acetyl-*sn*-glycerophosphorylcholine is an ether-containing phospholipid that is presently being studied intensively because it can exert profound


platelet-activating factor

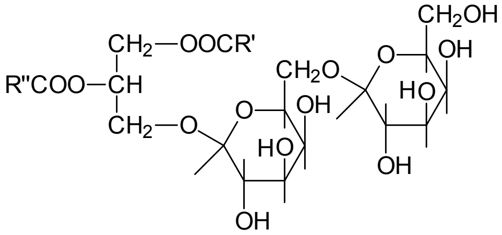
biological effects at minute concentrations. For example, it effects aggregation of platelets at concentrations as low as 10^{-11} M, and it induces a hypertensive response at very low levels. Also, it is a mediator of inflammation and has messenger functions.

Glycoglycerolipids

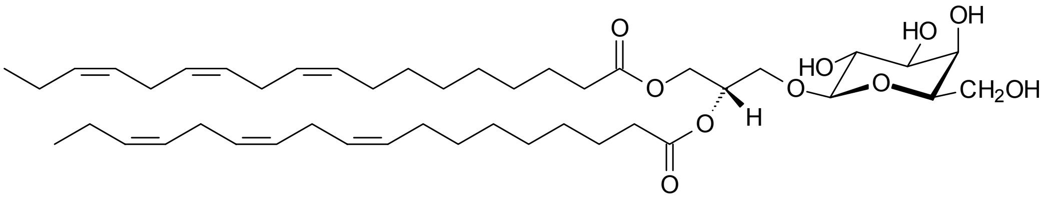
In plants, especially the photosynthetic tissues, a substantial proportion of the lipids consists of 1,2-diacyl-*sn*-glycerols joined by a glycosidic linkage at position *sn*-3 to a carbohydrate moiety. The main components are the **mono- and digalactosyldiacylglycerols**, but related compounds have been found with up to four galactose units, or in which one or more of these is replaced by glucose moieties. It is clear that these have an important role in photosynthesis, but many of the details have still to be worked out. In addition, a 6-*O*-acyl-monogalactosyldiacylglycerol is occasionally a component of plant tissues.



monogalactosyldiacylglycerol

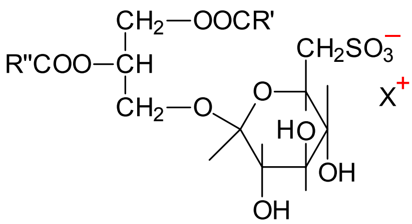


digalactosyldiacylglycerol



1,2-di-(9*Z*,12*Z*,15*Z*)-octadecatrienoyl-3-*O*-β-*D*-galactosyl-*sn*-glycerol

A related unique plant glycolipid is **sulfoquinovosyl-diacylglycerol** or the "plant sulfolipid". It contains a sulfonic acid residue linked by a carbon-sulfur bond to the 6-deoxyglucose moiety of a monoglycosyldiacylglycerol and is found exclusively in the chloroplasts.



sulfoquinovosyldiacylglycerol

Monogalactosyldiacylglycerols are not solely plant lipids as they have been found in small amounts in brain and nervous tissue in some animal species. A range of complex glyceroglycolipids have also been characterised from intestinal tract and lung tissue. They exist in both diacyl and alkyl acyl forms. Such compounds are destroyed by some of the methods used in the isolation of glycosphingolipids, so they may be more widespread than has been thought.

A complex glyco-glycero-sulfolipid, termed "**seminolipid**", of which the main component is 1-*O*-hexadecyl-2-*O*-hexadecanoyl-3-*O*-(3'-sulfo-β-D-galactopyranosyl)-*sn*-glycerol, is the principal glycolipid in testis and sperm.

A further range of highly complex glycolipids occur in bacteria and other micro-organisms. These include acylated sugars that do not contain glycerol.

Sphingomyelin and Glycosphingolipids

Sphingolipids consist of long-chain bases, linked by an amide bond to a fatty acid and via the terminal hydroxyl group to complex carbohydrate or phosphorus-containing moieties.

$CH_3(CH_2)_{12}CH{=}CH.CHOH.CHNH_2.CH_2OH$
trans
sphingosine

Long-chain bases (sphingoids or sphingoid bases) are the characteristic structural unit of sphingolipids. They are long-chain (12 to 22 carbon atoms) aliphatic amines, containing two or three hydroxyl groups, and often a distinctive *trans*-double bond in position 4. The commonest or most abundant of these in animal tissues is **sphingosine** ((2*S*,3*R*,4*E*)-2-amino-4-octadecen-1,3-diol). More than 60 long-chain bases have been found in animals, plants and microorganisms, and many of these may occur in a single tissue, but almost always as part of a complex lipid as opposed to in the free form. The aliphatic chains can be saturated, monounsaturated and diunsaturated, with double bonds of either the *cis* or *trans* configuration, and they may sometimes have methyl substituents. In addition, saturated and monoenoic straight- and branched-chain trihydroxy bases are found. The aliphatic moiety is similar in its physical properties to that of a fatty acid.

$CH_3(CH_2)_{13}.CHOH.CHOH.CHNH_2.CH_2OH$
phytosphingosine

Phytosphingosine or ((2*S*,3S,4*R*)-2-amino-octadecanetriol) is the most common long-chain base of plant origin. For shorthand purposes, a nomenclature similar to that for fatty acids can be used, *i.e.* the chain-length and number of double bonds are denoted in the same manner with the prefix "d" or "t" to designate di- and trihydroxy bases respectively. Thus, sphingosine is d18:1 and phytosphingosine is t18:0.

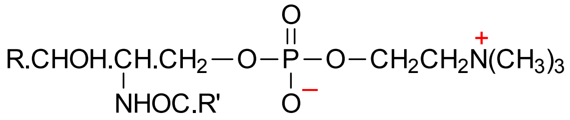
$R.CHOH.CH.CH_2OH$
$\quad\quad\quad |$
$\quad\quad NHOC.R'$
ceramide

Ceramides contain fatty acids linked by an amide bond to the amine group of a long-chain base. In general, they are present at low levels only in tissues, but they are key intermediates in the biosynthesis of the complex sphingolipids. In addition, they have important functions in cellular signalling, and especially in the regulation of apoptosis, and cell differentiation, transformation and proliferation.

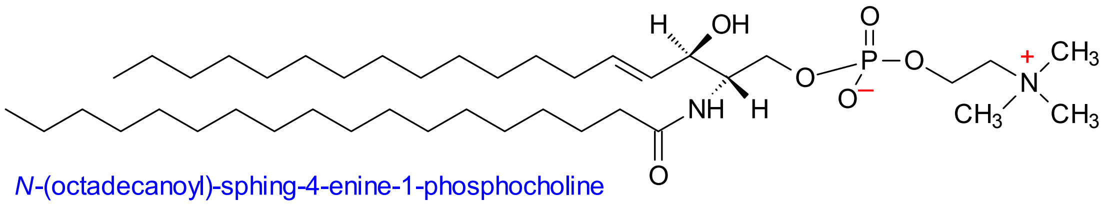
Unusual ceramides have been located in the epidermis of the pig and humans; the fatty acids linked to the sphingoid base consist of C_{30} and C_{32} ω-hydroxylated components, with predominantly the essential fatty acid, linoleic acid, esterified to the terminal hydroxyl group. They are believed to have a special role in preventing the loss of moisture through the skin.

Sphingomyelin is a sphingophospho-lipid and consists of a ceramide unit linked at position 1 to phosphorylcholine; it is found as a major component of the complex lipids of all animal tissues but not of plants or micro-organisms. It resembles phosphatidylcholine in many of its physical properties, and can apparently substitute in part for this in membranes, although it also has its own unique role. For example, it is a major constituent of the plasma membrane of cells, where it is concentrated together with sphingoglycolipids and cholesterol in tightly organized sub-domains termed 'rafts'.

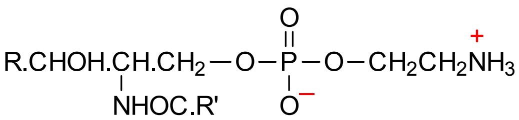
Sphingosine tends to be the most abundant long-chain base constituent, and it is usually accompanied by sphinganine and C_{20} homologues. Sphingomyelin is a precursor for a number of sphingolipid metabolites that have important functions in cellular signalling, including sphingosine-1-phosphate (see below), as part of the 'sphingomyelin cycle'. A correct balance between the various metabolites is vital for good health. Niemann-Pick disease is a rare lipid storage disorder that results from of a deficiency in the enzyme responsible for the degradation of sphingomyelin.



sphingomyelin



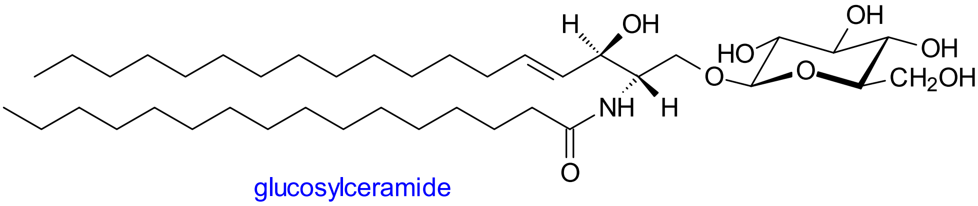
N-(octadecanoyl)-sphing-4-enine-1-phosphocholine



ceramide phosphorylethanolamine

Ceramide phosphorylethanolamine is found in the lipids of insects and some fresh water invertebrates. The phospholipid analogue, ceramide 2-aminoethylphosphonic acid, has been detected in sea anemones and protozoa. Ceramide phosphorylinositol is also found in some organisms, and like phosphatidylinositol, it can be an anchor unit for oligosaccharide-linked proteins in membranes.

Neutral glycosylceramides: The most widespread glycosphingolipids are the **monoglycosylceramides** (or *cerebrosides*), and they consist of the basic ceramide unit linked by a glycosidic bond at carbon 1 of the long-chain base to glucose or galactose. They were first found in brain lipids, where the principal form is galactosylceramide, but they are now known to be ubiquitous constituents of animal tissues. Glucosylceramide is also found in animal tissues, and especially in skin, where it functions as part of the water permeability barrier. It is the biosynthetic precursor of lactosylceramide, and thence of the complex oligoglycolipids and gangliosides. In addition, glucosylceramide is found in plants, where the main long-chain base is phytosphingosine. *O*-Acyl-glycosylceramides have been detected in small amounts in some tissues, as have cerebrosides with monosaccharides such as xylose, mannose and fucose.



glucosylceramide

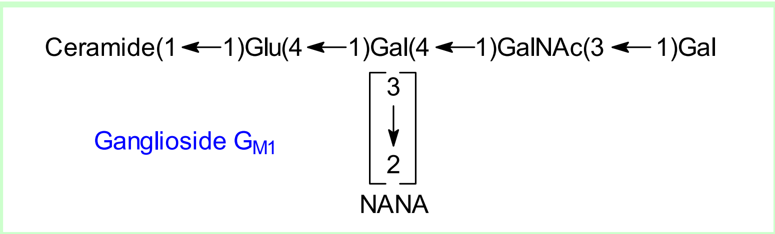
Di-, tri- and tetraglycosylceramides (**oligoglycosylceramides**) are present also in most animal tissues at low levels. The most common diglycosyl form is lactosylceramide, and it can be accompanied by related compounds containing further galactose or galactosamine residues. Tri- and tetraglycosylceramides with a terminal galactosamine residue are sometimes termed "globosides", while glycolipids containing fucose are known as "fucolipids". Lactosylceramide is the biosynthetic precursor of most of these with further monosaccharide residues being added to the end of the carbohydrate chain (up to as many as twenty). They are an important element of the immune response system, for example some glycolipids are involved in the antigenicity of blood group determinants, while others bind to specific toxins or bacteria. As the complex glycosyl moiety is considered to be of primary importance in this respect, it has received most attention from investigators. However, certain of these lipids have been found on occasion to have distinctive long-chain base and fatty acid compositions, which enhance their biological activity.

Some glycolipids accumulate in persons suffering from rare disease syndromes, characterised by deficiencies in specific enzyme systems related to glycolipid metabolism.

Sulfate esters of galactosylceramide and lactosylceramide (**sulfoglycosphingolipids** - often referred to as "sulfatides" or "lipid sulfates"), with the sulfate group linked to position 3 of the galactosyl moiety, are major components of brain lipids and they are found in trace amounts in other tissues.

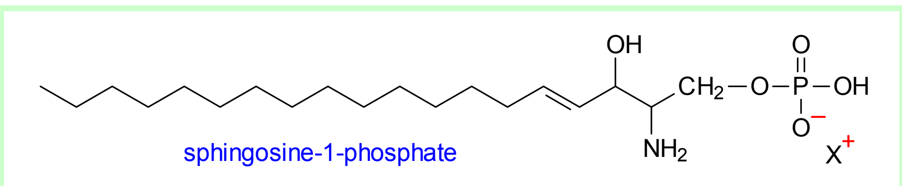
Complex plant sphingolipids, **phytoglycosphingolipids**, containing glucosamine, glucuronic acid and mannose linked to the ceramide via phosphorylinositol, were isolated and characterised from seeds initially, but related compounds are also known to be present in other plant tissues and in fungi.

Gangliosides are highly complex oligoglycosylceramides, which contain one or more sialic acid groups (*N*-acyl, especially acetyl, derivatives of neuraminic acid, abbreviated to "NANA") in addition to glucose, galactose and galactosamine. The polar and ionic nature of these lipids renders them soluble in water (contrary to some definitions of a lipid). They were first found in the ganglion cells of the central nervous system, hence the name, but are now known to be present in most animal tissues. The long-chain base and fatty acid components of gangliosides can vary markedly between tissues and species, and they are presumably related in some way to function.



Gangliosides have been shown to control growth and differentiation of cells, and they have important roles in the immune defense systems. They act as receptors for a number of tissue metabolites and in this way may regulate cell signalling. Also, they bind specifically to various bacterial toxins, such as those from botulinum, tetanus and cholera. A number of unpleasant lipidoses have been identified involving storage of excessive amounts of gangliosides in tissues, the most important of which is Tay-Sachs disease.

Sphingosine-1-phosphate is one of the simplest sphingolipids structurally. It is present at low levels only in animal tissues, but it is a pivotal lipid in many cellular signalling pathways (together with ceramide and ceramide-1-phosphate). For example, within cells, sphingosine-1-phosphate promotes cellular division (mitosis), while in the blood it may play a critical role in platelet aggregation and thrombosis.



The fatty acids of sphingolipids: Although structures of fatty acids are discussed elsewhere, it is worth noting that the acyl groups of ceramides are very different from those in the glycerolipids. They tend to consist of long-chain (C_{16} up to C_{26} but occasionally longer) odd- and even-numbered saturated or monoenoic fatty acids and related 2-D-hydroxy fatty acids, both in plant and animal tissues. Linoleic acid may be present at low levels in sphingolipids from animal tissues, but polyunsaturated compounds are rarely found (although their presence is often reported in error).

Fatty Acids

The common fatty acids of plant tissues are C_{16} and C_{18} straight-chain compounds with zero to three double bonds of a *cis* (or *Z*) configuration. Such fatty acids are also abundant in animal tissues, together with other even numbered components with a somewhat wider range of chain-lengths and up to six *cis* double bonds separated by methylene groups (methylene-interrupted). The systematic and trivial names of those fatty acids encountered most often, together with their shorthand designations, are listed in the table.

The common fatty acids of animal and plant origin.

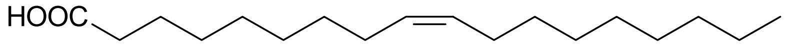
Systematic name	Trivial name	Shorthand designation
Saturated fatty acids		
ethanoic	acetic	2:0
butanoic	butyric	4:0
hexanoic	caproic	6:0
octanoic	caprylic	8:0
decanoic	capric	10:0
dodecanoic	lauric	12:0
tetradecanoic	myristic	14:0
hexadecanoic	palmitic	16:0
octadecanoic	stearic	18:0
eicosanoic	arachidic	20:0
docosanoic	behenic	22:0
Monoenoic fatty acids		
cis-9-hexadecenoic	palmitoleic	16:1(*n*-7)
cis-6-octadecenoic	petroselinic	18:1(*n*-12)
cis-9-octadecenoic	oleic	18:1(*n*-9)
cis-11-octadecenoic	*cis*-vaccenic	18:1(*n*-7)
cis-13-docosenoic	erucic	22:1(*n*-9)
cis-15-tetracosenoic	nervonic	24:1(*n*-9)
Polyunsaturated fatty acids*		
9,12-octadecadienoic	linoleic	18:2(*n*-6)
6,9,12-octadecatrienoic	γ-linolenic	18:3(*n*-6)
9,12,15-octadecatrienoic	α-linolenic	18:3(*n*-3)
5,8,11,14-eicosatetraenoic	arachidonic	20:4(*n*-6)
5,8,11,14,17-eicosapentaenoic	EPA	20:5(*n*-3)
4,7,10,13,16,19-docosahexaenoic	DHA	22:6(*n*-3)

* all the double bonds are of the *cis* configuration

The most abundant saturated fatty acid in nature is **hexadecanoic** or **palmitic acid**. It can also be designated a "16:0" fatty acid, the first numerals denoting the number of carbon atoms in the aliphatic chain and the second, after the colon, denoting the number of double bonds. All the even-numbered saturated fatty acids from C_2 to C_{30} have been found in nature, but only the C_{14} to C_{18} homologues are likely to be encountered in appreciable concentrations in glycerolipids, other than in a restricted range of commercial fats and oils.

$HOOC(CH_2)_{14}CH_3$
palmitic acid

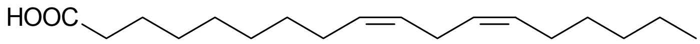
Oleic or ***cis*-9-octadecenoic** acid, the most abundant monoenoic fatty acid in nature, is designated as "18:1", or more precisely as "18:1(*n*-9)", to indicate that the last double bond is 9 carbon atoms from the terminal methyl group.



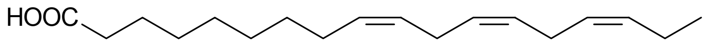
oleic acid

The latter form of the nomenclature is of special value to biochemists. Similarly, the most abundant *cis* monoenoic acids fall into the same range of chain-lengths, *i.e.* 16:1(*n*-7) and 18:1(*n*-9), though 20:1 and 22:1 are abundant in fish. Fatty acids with double bonds of the *trans* (or *E*) configuration are found occasionally in natural lipids, or are formed during food processing (hydrogenation) and so enter the food chain, but they tend to be minor components only of animal tissue lipids, other than of ruminants. Their suitability for human nutrition is currently a controversial subject.

The C_{18} polyunsaturated fatty acids, **linoleic** or *cis*-9,*cis*-12-octadecadienoic (18:2(*n*-6)) and **α-linolenic** or *cis*-9,*cis*-12,*cis*-15-octadecatrienoic acids (18:3(*n*-3)), are major components of most plant lipids, including many of the commercially important vegetable oils.

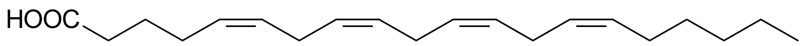


linoleic acid

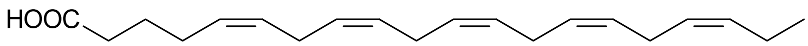


α-linolenic acid

They are essential fatty acids in that they cannot be synthesised in animal tissues. On the other hand, as linoleic acid is almost always present in foods, it tends to be relatively abundant in animal tissues. In turn, these fatty acids are the biosynthetic precursors in animal systems of C_{20} and C_{22} polyunsaturated fatty acids, with three to six double bonds, *via* sequential desaturation and chain-elongation steps (desaturases in animal tissues can only insert a double bond on the carboxyl side of an existing double bond). Those fatty acids derived from linoleic acid, especially arachidonic acid (20:4(*n*-6)), are important constituents of the membrane phospholipids in mammalian tissues, and are also the precursors of the prostaglandins and other eicosanoids. In fish, linolenic acid is the more important essential fatty acid, especially eicosapentaenoic acid (20:5(n-3) or EPA) and docosahexaenoic acid (22:6(n-3) or DHA), and polyunsaturated fatty acids of the (*n*-3) series are found in greater abundance.

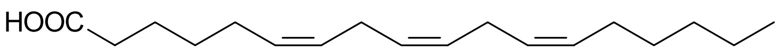


20:4(n-6)



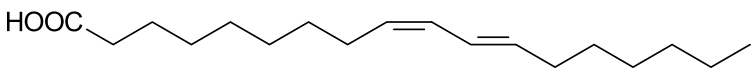
20:5(n-3)

Many other fatty acids that are important for nutrition and health do of course exist in nature, and at present there is great interest in γ-linolenic acid (18:3(*n*-6)), the active constituent of evening primrose oil.



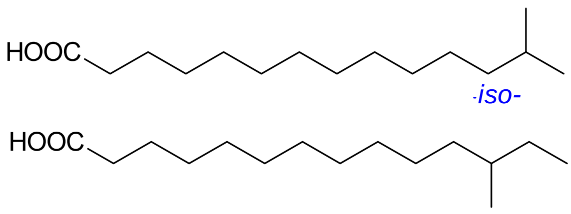
γ-linolenic acid

- and in conjugated linoleic acid (mainly, 9-*cis*,11-*trans*-octadecadien-oate) or 'CLA', a natural constituent of dairy products, that is claimed to have remarkable health-giving properties.



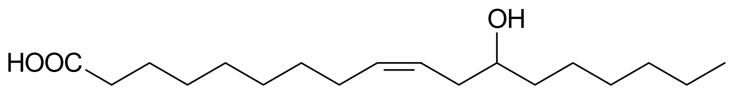
9-*cis*,11-*trans*-octadecadienoic acid

Branched-chain fatty acids are synthesised by many microorganisms (most often with an *iso*- or an *anteiso*-methyl branch) and they are synthesised to a limited extent in higher organisms. They can also enter animal tissues via the diet, especially those of ruminants.



3,7,11,15-Tetramethylhexadecanoic (phytanic) acid, is a metabolite of phytol and is found in animal tissues, but generally at low levels only.

Fatty acids with many other substituent groups are found in certain plants and microorganisms, and they may be encountered in animal tissues, which they enter *via* the food chain. These substituents include acetylenic and conjugated double bonds, allenic groups, cyclopropane, cyclopropene, cyclopentene and furan rings, and hydroxy-, epoxy- and keto-groups. For example, 2-hydroxy fatty acids are synthesised in animal and plant tissues and are often major constituents of the sphingolipids. **12-Hydroxy-octadec-9-enoic** or 'ricinoleic' acid is the main constituent of castor oil.

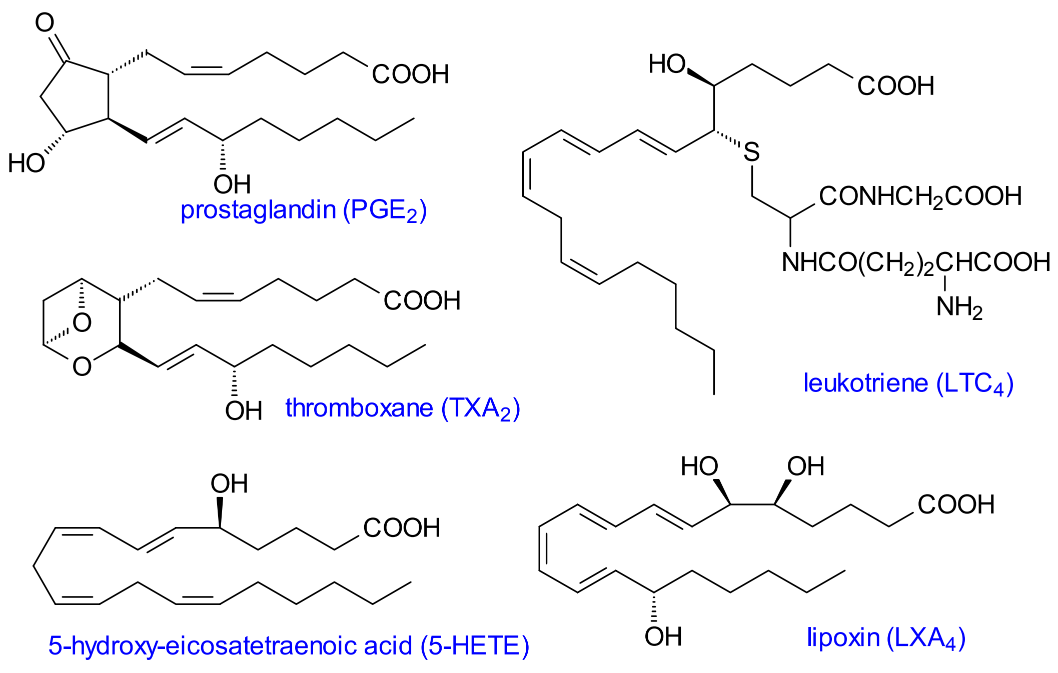


ricinoleic acid

Eicosanoids and Related Lipids

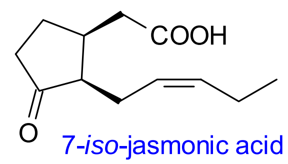
The term **eicosanoid** is used to embrace biologically active lipid mediators (C_{20} fatty acids and their metabolites), including prostaglandins, thromboxanes, leukotrienes and other oxygenated derivatives, which exert their effects at very low concentrations. They are produced primarily by three classes of enzymes, cyclooxygenases (COX-1 and COX-2), lipoxygenases (LOX) and cytochrome P450 epoxygenase. The key precursor fatty acids are 8*c*,11*c*,14*c*-eicosatrienoic (dihomo-γ-linolenic or 20:3(*n*-6)), 5*c*,8*c*,11*c*,14*c*-eicosatetraenoic (arachidonic or 20:4(*n*-6)) and 5*c*,8*c*,11*c*,14*c*,17*c*-eicosapentaenoic (20:5(n-3) or EPA) acids (see our web page on '**polyunsaturated fatty acids**'). More recently **docosanoids** (resolvins and protectins) derived from 4*c*,7*c*,10*c*,13*c*,16*c*,19*c*-docosahexaenoic acid (22:6(*n*-3) or DHA) have been described. Other eicosanoids are produced by non-enzymic means (**isoprostanes**).

Those derived from arachidonic acid appear to be of special importance and have been most studied. The prostaglandins and thromboxanes have cyclic structures, generated by cyclo-oxygenase enzymes, and are involved in the processes of inflammation. The hydroxy-eicosatetraenoic acids are generated by lipoxygenases, and of these the 5-lipoxygenase is especially important as it produces the first intermediate in the biosynthesis of leukotrienes. The resolvins and protectins have anti-inflammatory properties.



prostaglandin (PGE_2)
thromboxane (TXA_2)
leukotriene (LTC_4)
5-hydroxy-eicosatetraenoic acid (5-HETE)
lipoxin (LXA_4)

Plant products, such as the **jasmonates** and other **oxylipins** derived from 9*c*,12*c*,15*c*-octadecatrienoic (α-linolenic or 18:3(n-3)) are also generated by the action of lipoxygenases. They are involved in responses to physical damage by animals or insects, stress and attack by pathogens. There are obvious structural similarities between the jasmonates and prostanoids.



7-*iso*-jasmonic acid

Of course, many more lipids occur in nature than can be described in this document. I have not touched on proteolipids and lipoproteins here, for example, but there is information on these and other lipids elsewhere on this website. New lipids continue to be found, and no doubt many remain to be discovered.

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Last updated: 8/4/2007