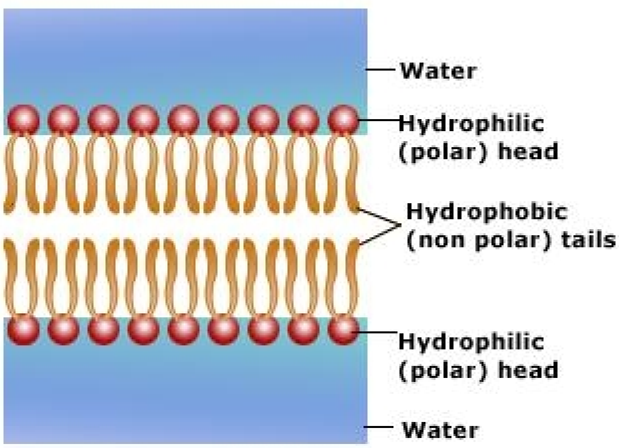
Unit-III

Lipids

Lipids are naturally occurring organic compounds, commonly known as oils and fats. Lipids occur through out the living world in microorganisms, higher plants and animals and also in all cell types. Lipids contribute to cell structure, provide stored fuel and also take part in many biological processes.



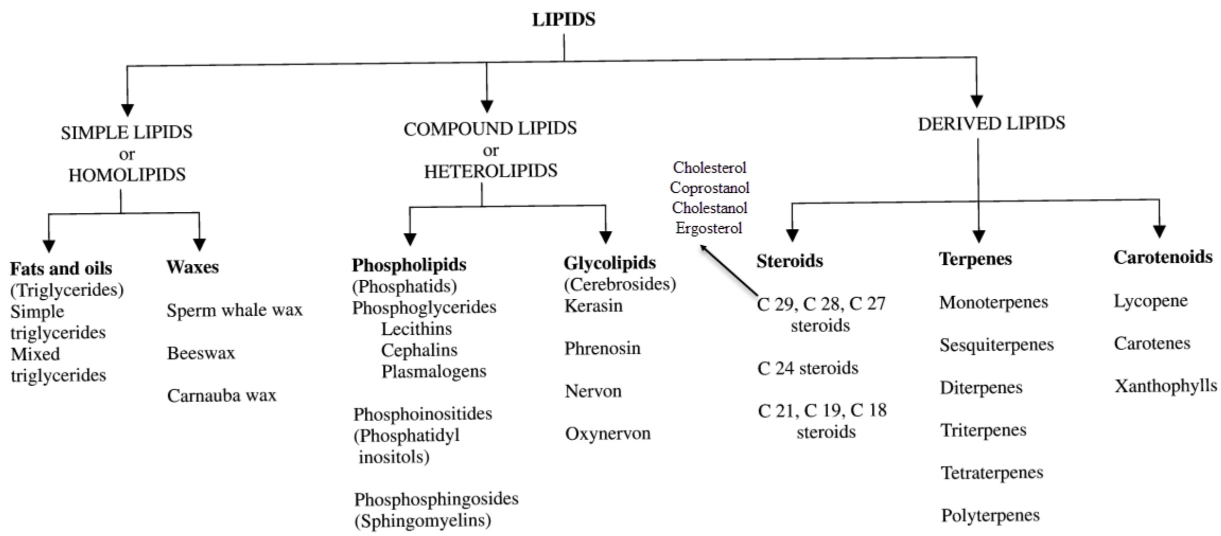
Lipids are naturally occurring hydrophobic molecules. They are heterogenous group of compounds related to fatty acids. They include fats, oils, waxes, phospholipids, etc. They make up about 70% of the dry weight of the nervous system. Lipids are crucial for the healthy functioning of the nerve cells. Lipids are greasy or oily organic substances; lipids are sparingly soluble in water and are soluble in organic solvents like chloroform, ether and benzene.

General characters of lipids

- Lipids are relatively insoluble in water.
- They are soluble in non-polar solvents, like ether, chloroform, methanol.
- Lipids have high energy content and are metabolized to release calories.
- Lipids also act as electrical insulators, they insulate nerve axons.

- Fats contain saturated fatty acids, they are solid at room temperatures. Example, animal fats.
- Plant fats are unsaturated and are liquid at room temperatures.
- Pure fats are colorless, they have extremely bland taste.
- The fats are sparingly soluble in water and hence are described are hydrophobic substances.
- They are freely soluble in organic solvents like ether, acetone and benzene.
- The melting point of fats depends on the length of the chain of the constituent fatty acid and the degree of unsaturation.
- Geometric isomerism, the presence of double bond in the unsaturated fatty acid of the lipid molecule produces geometric or cis-trans isomerism.
- Fats have insulating capacity, they are bad conductors of heat.
- Emulsification is the process by which a lipid mass is converted to a number of small lipid droplets. The process of emulsification happens before the fats can be absorbed by the intestinal walls.
- The fats are hydrolyzed by the enzyme lipases to yield fatty acids and glycerol.
- The hydrolysis of fats by alkali is called saponification. This reaction results in the formation of glycerol and salts of fatty acids called soaps.
- Hydrolytic rancidity is caused by the growth of microorganisms which secrete enzymes like lipases. These split fats into glycerol and free fatty acids.

Classification of Lipids



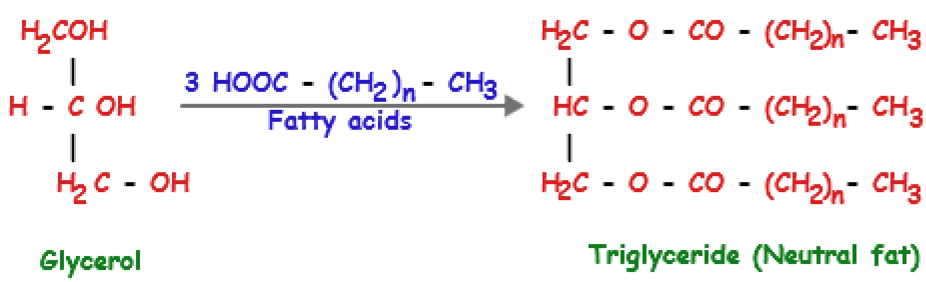
Simple Lipids or Homolipids

Simple lipids are the esters of fatty acids with various alcohols.

Fats and Oils (triglycerides and triacylglycerols) - These are esters of fatty acids with a trihydroxy alcohol, glycerol. A fat is solid at ordinary room temperature, an oil is liquid.

Simple Triglycerides - Simple triglycerides are one in which three fatty acids radicles are similar or are of the same type. Example: Tristearin, Triolein.

Mixed Triglycerides are one in which the three fatty acids radicles are different from each other. Example: distearo-olein, dioleo-palmitin.



Waxes are the esters of fatty acids with high molecular weight monohydroxy alcohols. Example: Beeswax, Carnauba wax.

Compound Lipids or Heterolipids

Heterolipids are esters of fatty acids with alcohol and possess additional groups also.

Phospholipids or Phosphatids are compound containing fatty acids and glycerol in addition to a phosphoric acid, nitrogen bases and other substituents. They usually possess one hydrophilic head and tow non-polar tails. They are called polar lipids and are amphipathic in nautre. Phospholipids can be phosphoglycerides, phosphoinositides and phosphosphingosides.

Phosphoglycerides are major phospholipids, they are found in membranes. It contains fatty acid molecules which are esterified to hydroxyl groups of glycerol. The glycerol group also forms an ester linkage with phosphoric acid. Example: Lecithin, Cephalins.

Phosphoinositides are said to occur in phospholipids of brain tissue and soybeans. The ply important role in transport processes in cells.

Phosphosphingosides are commonly found in nerve tissue. Example: sphingomyelins.

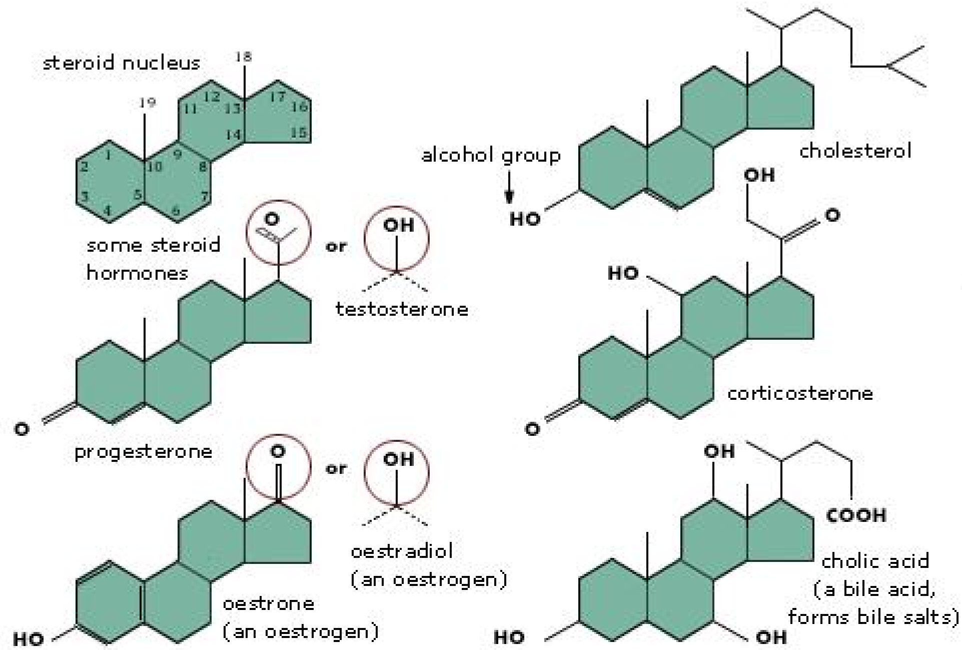
Glycolipids are the compounds of fatty acids with carbohydrates and contain nitrogen but no phosphoric acid. The glycolipids also include certain structurally related compounds comprising the groups gangliosides, sulpholipids and sulfatids.

Derived Lipids

Derived lipids are the substances derived from simple and compound lipids by hydrolysis. These includes fatty acids, alcohols, monoglycerides and diglycerides, steroids, terpenes, carotenoids.

The most common derived lipids are steroids, terpenes and carotenoids.

Steroids do not contain fatty acids, they are nonsaponifiable, and are not hydrolyzed on heating. They are widely distributed in animals, where they are associated with physiological processes. Example: Estranes, androstranes, etc.



Terpenes in majority are found in plants. Example: Natural rubber. gernoil, etc.

Carotenoids are tetraterpenes. They are widely distributed in both plants and animals. They are exclusively of plant origin. Due to the presence of many conjugated double bonds, they are colored red or yellow. Example: Lycopreene, carotenes, Xanthophylls.

Essential fatty acids are those that cannot be constructed through any chemical pathways, known to happen in humans. They must be obtained from the diet. Linoleic acid and linolenic acid are the essential fatty acids.

Non-essential fatty acids are those which are not necessary to be taken through diet, they are synthesized through chemical pathways.

Unsaturated fatty acids have one or more double bonds between carbon atoms. The tow carbon atoms are bound to each other through double bonds and can occur in cis or trans configuration.

Saturated fatty acids are long chain carboxylic acids and do not have double bonds. Example: Arachidic acid, Palmitic acid, etc.

Structure of Lipids

Lipids has no single common structure. The most commonly occurring lipids are triglycerides and phospholipids.

Triglycerides are fats and oils. Triglycerides have a glycerol backbone bonded to three fatty acids. If the three fatty are similar then the triglyceride is known as simple triglyceride. If the fatty acids are not similar then the fatty acids are known as mixed triglyceride.

The second most common class of lipids are phospholipids. They are found in membranes of animal and plants. Phospholipids contains glycerol and fatty acids, they also contain phosphoric acids and a low-molecular weight alcohol. Common phospholipids are lecithins and cephalins.

Function of Lipids

Lipids perform several biological functions:

- Lipids are storage compounds, triglycerides serve as reserve energy of the body.
- Lipids are important component of cell membranes structure in eukaryotic cells.
- Lipids regulate membrane permeability.
- They serve as source for fat soluble vitamins like A, D, E, K.
- They act electrical insulators to the nerve fibres, where the myelin sheath contains lipids.
- Lipids are components of some enzyme systems.

- Some lipids like prostaglandins and steroid hormones act as cellular metabolic regulators.
- Cholesterol is found in cell membranes, blood, and bile of many organisms.
- As lipids are small molecules and are insoluble in water, they act as signalling molecules.
- Layers of fat in the subcutaneous layer, provides insulation and protection from cold. Body temperature maintenance is done by brown fat.
- Polyunsaturated phospholipids are important constituents of phospholipids, they provide fluidity and flexibility to the cell membranes.
- Lipoproteins that are complexes of lipids and proteins, occur in blood as plasma lipoprotein, they enable transport of lipids in aqueous environment, and their transport throughout the body.
- Cholesterol maintains fluidity of membranes by interacting with lipid complexes.
- Cholesterol is the precursor of bile acids, Vitamin D and steroids.
- Essential fatty acids like linoleic and linolenic acids are precursors of many different types of ecosanoids including prostaglandins, thromboxanes. These play a important role in pain, fever, inflammation and blood clotting.

Cholesterol

Cholesterol is a well-studied lipid, because of its strong correlation with the incidence cardiovascular disease. It is an important component of cell membranes and plasma lipoproteins, and is an important precursor of many biologically important substances like bile acids and steroid hormones. It is abundant in nerve tissues and is associated with gallstones.

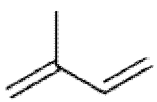
Dietary cholesterol is found in saturated fats of animals (as butter and lard), but vegetable oils do not contain cholesterol. Only a small portion of your body cholesterol comes from the diet. Most of it is produced in the body. Eating unsaturated fatty acids from vegetable oil helps lower blood cholesterol levels by reducing cholesterol synthesis in the body. However, eating saturated fats from animal fat elevates blood cholesterol and triglycerides and reduce the ratio of your good to bad cholesterol.

TERPENS

Introduction

Terpenoids (or isoprenoids), a subclass of the prenyllipids (terpenes, prenylquinones, and sterols), represent the oldest group of small molecular products synthesized by plants and are probably the most widespread group of natural products. Terpenoids can be described as modified terpenes, where methyl groups are moved or removed, or oxygen atoms added. Inversely, some authors use the term "terpenes" more broadly, to include the terpenoids.

Structure and biosynthesis



Isoprene

Terpenes are derived biosynthetically from units of isoprene, which has the molecular formula C_5H_8. The basic molecular formulae of terpenes are multiples of that, $(C_5H_8)_n$ where n is the number of linked isoprene units. This is called the **isoprene rule** or the *C5 rule*. The isoprene units may be linked together "head to tail" to form linear chains or they may be arranged to form rings. One can consider the isoprene unit as one of nature's common building blocks.

Classifications of Terpenes

Terpenes may be classified by the number of isoprene units in the molecule; a prefix in the name indicates the number of terpene units needed to assemble the molecule.

- **Hemiterpenes** consist of *a single isoprene* unit. Isoprene itself is considered the only hemiterpene, but oxygen-containing derivatives such as prenol and isovaleric acid are hemiterpenoids.
- **Monoterpenes** consist of *two isoprene* units and have the molecular formula $C_{10}H_{16}$. Examples of monoterpenes and monoterpenoids include geraniol, terpineol (present in

lilacs), limonene (present in citrus fruits), myrcene (present in hops), linalool (present in lavender) or pinene (present in pine trees).[7] Iridoids derive from monoterpenes.

- **Sesquiterpenes** consist of *three isoprene* units and have the molecular formula $C_{15}H_{24}$. Examples of sesquiterpenes and sesquiterpenoids include humulene, farnesenes, farnesol. (The *sesqui-* prefix means one and a half.)
- **Diterpenes** are composed of *four isoprene* units and have the molecular formula $C_{20}H_{32}$. They derive from geranylgeranyl pyrophosphate. Examples of diterpenes and diterpenoids are cafestol, kahweol, cembrene and taxadiene (precursor of taxol). Diterpenes also form the basis for biologically important compounds such as retinol, retinal, and phytol.
- **Sesterterpenes**, terpenes having 25 carbons and *five isoprene* units, are rare relative to the other sizes. (The *sester-* prefix means half to three, i.e. two and a half.) An example of a sesterterpenoid is geranylfarnesol.
- **Triterpenes** consist of *six isoprene* units and have the molecular formula $C_{30}H_{48}$. The linear triterpene squalene, the major constituent of shark liver oil, is derived from the reductive coupling of two molecules of farnesyl pyrophosphate. Squalene is then processed biosynthetically to generate either lanosterol or cycloartenol, the structural precursors to all the steroids.
- **Sesquarterpenes** are composed of *seven isoprene* units and have the molecular formula $C_{35}H_{56}$. Sesquarterpenes are typically microbial in their origin. Examples of sesquarterpenoids are ferrugicadiol and tetraprenylcurcumene.
- **Tetraterpenes** contain *eight isoprene* units and have the molecular formula $C_{40}H_{64}$. Biologically important tetraterpenoids include the acyclic lycopene, the monocyclic gamma-carotene, and the bicyclic alpha- and beta-carotenes.
- **Polyterpenes** consist of long chains of *many isoprene* units. Natural rubber consists of polyisoprene in which the double bonds are *cis*. Some plants produce a polyisoprene with *trans* double bonds, known as gutta-percha.
- **Norisoprenoids**, such as the C_{13}-norisoprenoids 3-oxo-α-ionol present in Muscat of Alexandria leaves and 7,8-dihydroionone derivatives, such as megastigmane-3,9-diol and 3-oxo-7,8-dihydro-α-ionol found in Shiraz leaves (both grapes in the species *Vitis vinifera*) or wine can be produced by fungal peroxidases or glycosidases.

They are universally present in small amounts in living organisms, where they play numerous vital roles in plant physiology as well as important functions in all cellular membranes. On the other hand, they are also accumulated in many cases, and it is shown that the extraordinary variety they then display can be due to ecological factors playing an evolutionary role. Mono- and sesquiterpenes are the chief constituents of the essential oils while the other terpenes are constituents of balsams, resins, waxes, and rubber.

Oleoresin is a roughly equal mixture of turpentine (85% C10-monoterpenes and 15% C15-sesquiterpenes) and rosin (C20-diterpene) that acts in many conifer species to seal wounds and is toxic to both invading insects and their pathogenic fungi. A number of inducible terpenoid defensive compounds (**phytoalexins**) from angiosperm species are well known. These include both sesquiterpenoid and diterpenoid types.

Isoprenoid units are also found within the framework of other natural molecules. Thus, indole alkaloids, several quinones (vitamin K), alcohols (vitamin E, vitamin A formed from -carotene), phenols, isoprenoid alcohols (also known as terpenols or polyprenols) also contain terpenoid fragments.

Prostaglandins

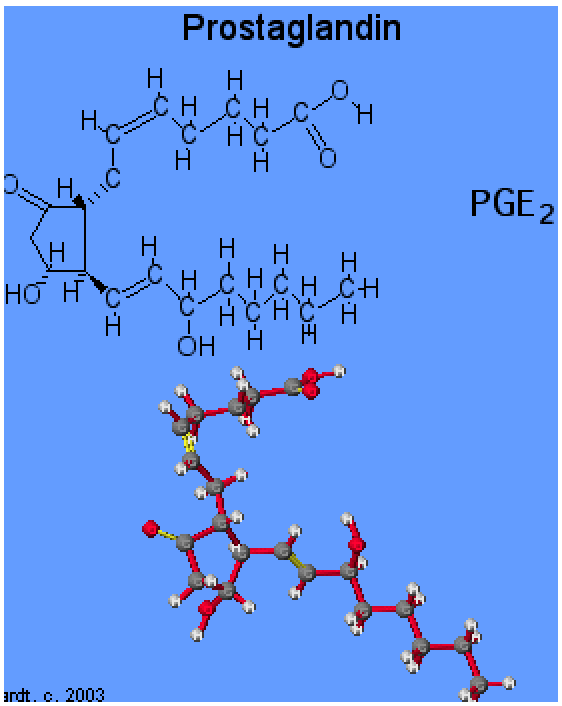
Introduction:

Prostaglandins were first discovered and isolated from human semen in the 1930s by Ulf von Euler of Sweden. Thinking they had come from the prostate gland, he named them prostaglandins. It has since been determined that they exist and are synthesized in virtually every cell of the body.

Prostaglandins, are like hormones in that they act as chemical messengers, but do not move to other sites, but work right within the cells where they are synthesized. Prostaglandins are unsaturated carboxylic acids, consisting of of a 20 carbon skeleton that also contains a five member ring. They are biochemically synthesized from the fatty acid, arachidonic acid. See the graphic on the left. The unique shape of the arachidonic acid caused by a series of cis double bonds helps to put it into position to make the five member ring. See the prostaglandin in the next panel.

Prostaglandin Structure:

Prostaglandins are unsaturated carboxylic acids, consisting of of a 20 carbon skeleton that also contains a five member ring and are based upon the fatty acid, arachidonic acid. There are a variety of structures one, two, or three double bonds. On the five member ring there may also be double bonds, a ketone, or alcohol groups. A typical structure is on the left graphic.



Functions of Prostaglandins:

There are a variety of physiological effects including:

1. Activation of the inflammatory response, production of pain, and fever. When tissues are damaged, white blood cells flood to the site to try to minimize tissue destruction. Prostaglandins are produced as a result.

2. Blood clots form when a blood vessel is damaged. A type of prostaglandin called thromboxane stimulates constriction and clotting of platelets. Conversely, PGI2, is produced to have the opposite effect on the walls of blood vessels where clots should not be forming.

3. Certain prostaglandins are involved with the induction of labor and other reproductive processes. PGE2 causes uterine contractions and has been used to induce labor.

4. Prostaglandins are involved in several other organs such as the gastrointestinal tract (inhibit acid synthesis and increase secretion of protective mucus), increase blood flow in kidneys, and leukotriens promote constriction of bronchi associated with asthma.

Effects of Aspirin and other Pain Killers:

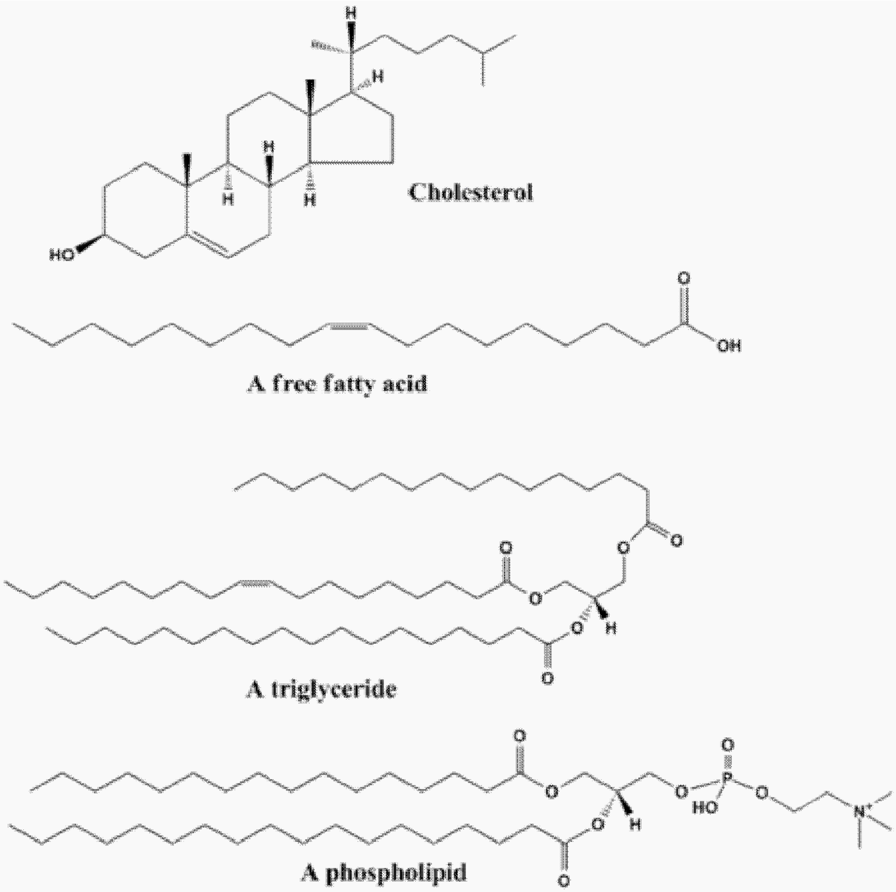
When you see that prostaglandins induce inflammation, pain, and fever, what comes to mind but aspirin. Aspirin blocks an enzyme called cyclooxygenase, COX-1 and COX-2, which is involved with the ring closure and addition of oxygen to arachidonic acid converting to prostaglandins. The acetyl group on aspirin is hydrolzed and then bonded to the alcohol group of serine as an ester. This has the effect of blocking the channel in the enzyme and arachidonic can not enter the active site of the enzyme.

By inhibiting or blocking this enzyme, the synthesis of prostaglandins is blocked, which in turn relives some of the effects of pain and fever.

Aspirin is also thought to inhibit the prostaglandin synthesis involved with unwanted blood clotting in coronary heart disease. At the same time an injury while taking aspirin may cause more extensive bleeding.

See the following chime tutorial for the detailed molecular basis for the inhibition of the COX enzyme by aspirin.

Lipid



Structures of some common lipids. At the top are cholesterol and oleic acid The middle structure is a triglyceride composed of oleoyl, stearoyl, and palmitoyl chains attached to a glycerol backbone. At the bottom is the common phospholipid phosphatidylcholine.

In biology, **lipids** comprise a group of naturally occurring molecules that include fats, waxes, sterols, fat-soluble vitamins(such as vitamins A, D, E, and K), monoglycerides, diglycerides, triglycerides, phospholipids, and others. The main biological functions of lipids include storing energy, signaling, and acting as structural components of cell membranes. Lipids have applications in the cosmetic and food industries as well as in nanotechnology.

Scientists may broadly define lipids as hydrophobic or amphiphilic small molecules; the amphiphilic nature of some lipids allows them to form structures such as vesicles, multilamellar/unilamellar liposomes, or membranes in an aqueous environment. Biological lipids originate entirely or in part from two distinct types of biochemical subunits or "building-blocks": ketoacyl and isoprene groups.[3] Using this approach, lipids may be divided into eight categories: fatty acids, glycerolipids, glycerophospholipids, sphingolipids, saccharolipids, and polyketides (derived from condensation of ketoacyl subunits); and sterol lipids and prenol lipids (derived from condensation of isoprene subunits).

Although the term *lipid* is sometimes used as a synonym for fats, fats are a subgroup of lipids called triglycerides. Lipids also encompass molecules such as fatty acids and their derivatives (including tri-, di-, monoglycerides, and phospholipids), as well as other sterol-containing metabolites such as cholesterol .Although humans and other mammals use various biosynthetic pathways both to break down and to synthesize lipids, some essential lipids cannot be made this way and must be obtained from the diet.

The word *lipid* stems etymologically from the Greek *lipos* (fat).

Fatty acids

Fatty acids, or fatty acid residues when they are part of a lipid, are a diverse group of molecules synthesized by chain-elongation of an acetyl-CoA primer with malonyl-CoA or methylmalonyl-CoA groups in a process called fatty acid synthesis. They are made of a hydrocarbon chain that terminates with a carboxylic acid group; this arrangement confers the molecule with a polar, hydrophilic end, and a nonpolar, hydrophobic end that is insoluble in water. The fatty acid structure is one of the most fundamental categories of biological lipids, and is commonly used as a building-block of more structurally complex lipids. The carbon chain, typically between four and 24 carbons long, may be saturated or unsaturated, and may be attached to functional groups containing oxygen, halogens, nitrogen, and sulfur. If a fatty acid contains a double bond, there is the possibility of either a *cis* or *trans* geometric isomerism, which significantly affects the molecule's configuration. *Cis*-double bonds cause the fatty acid chain to bend, an effect that is compounded with more double bonds in the chain. Three double bonds in 18-carbon *linolenic acid*, the most abundant fatty-acyl chains of plant *thylakoid membranes*, render these membranes highly *fluid* despite environmental low-temperatures, and also makes linolenic acid give dominating sharp peaks in high resolution 13-C NMR spectra of chloroplasts. This in turn plays an important role in the structure and function of cell membranes. Most naturally occurring fatty acids are of the *cis*configuration, although the *trans* form does exist in some natural and partially hydrogenated fats and oils.

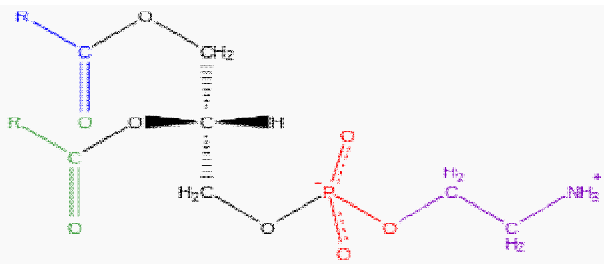
Examples of biologically important fatty acids include the eicosanoids, derived primarily from arachidonic acid and eicosapentaenoic acid, that include prostaglandins, leukotrienes, and thromboxanes. Docosahexaenoic acid is also important in biological systems, particularly with respect to sight Other major lipid classes in the fatty acid category are the fatty esters and fatty amides. Fatty esters include important biochemical intermediates such as wax esters, fatty acid thioester coenzyme A derivatives, fatty acid thioester ACP derivatives and fatty acid carnitines. The fatty amides include N-acyl ethanolamines, such as the cannabinoid neurotransmitter anandamide.

Glycerolipids

Glycerolipids are composed of mono-, di-, and tri-substituted glycerols, the best-known being the fatty acid triesters of glycerol, called triglycerides. The word "triacylglycerol" is sometimes used synonymously with "triglyceride". In these compounds, the three hydroxyl groups of glycerol are each esterified, typically by different fatty acids. Because they function as an energy store, these lipids comprise the bulk of storage fat in animal tissues. The hydrolysis of the esterbonds of triglycerides and the release of glycerol and fatty acids from adipose tissue are the initial steps in metabolizing fat.

Additional subclasses of glycerolipids are represented by glycosylglycerols, which are characterized by the presence of one or more sugar residues attached to glycerol via a glycosidic linkage. Examples of structures in this category are the digalactosyldiacylglycerols found in plant membrane and seminolipid from mammalian sperm cells.

Glycerophospholipids

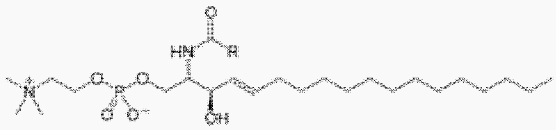


Phosphatidylethanolamine

Glycerophospholipids, usually referred to as phospholipids, are ubiquitous in nature and are key components of the lipid bilayer of cells, as well as being involved in metabolism and cell signaling. Neural tissue (including the brain) contains relatively high amounts of glycerophospholipids, and alterations in their composition has been implicated in various neurological disorders. Glycerophospholipids may be subdivided into distinct classes, based on the nature of the polar headgroup at the *sn*-3 position of the glycerol backbone in eukaryotes and eubacteria, or the *sn*-1 position in the case of archaebacteria.

Examples of glycerophospholipids found in biological membranes are phosphatidylcholine (also known as PC, GPCho or lecithin), phosphatidylethanolamine (PE or GPEtn) and phosphatidylserine (PS or GPSer). In addition to serving as a primary component of cellular membranes and binding sites for intra- and intercellular proteins, some glycerophospholipids in eukaryotic cells, such as phosphatidylinositols and phosphatidic acids are either precursors of or, themselves, membrane-derived second messengers. Typically, one or both of these hydroxyl groups are acylated with long-chain fatty acids, but there are also alkyl-linked and 1Z-alkenyl-linked (plasmalogen) glycerophospholipids, as well as dialkylether variants in archaebacteria.

Sphingolipids



Sphingomyelin

Sphingolipids are a complicated family of compounds that share a common structural feature, a sphingoid base backbone that is synthesized *de novo* from the amino acid serine and a long-chain fatty acyl CoA, then converted into ceramides, phosphosphingolipids, glycosphingolipids and other compounds. The major sphingoid base of mammals is commonly referred to as sphingosine. Ceramides (N-acyl-sphingoid bases) are a major subclass of sphingoid base derivatives with an amide-linked fatty acid. The fatty acids are typically saturated or mono-unsaturated with chain lengths from 16 to 26 carbon atoms.

The major phosphosphingolipids of mammals are sphingomyelins (ceramide phosphocholines), whereas insects contain mainly ceramide phosphoethanolamines and fungi have phytoceramide phosphoinositols and mannose-containing headgroups.The glycosphingolipids are a diverse family of molecules composed of one or more sugar residues linked via a glycosidic bond to the sphingoid base. Examples of these are the simple and complex glycosphingolipids such as cerebrosides and gangliosides.

Sterol lipids

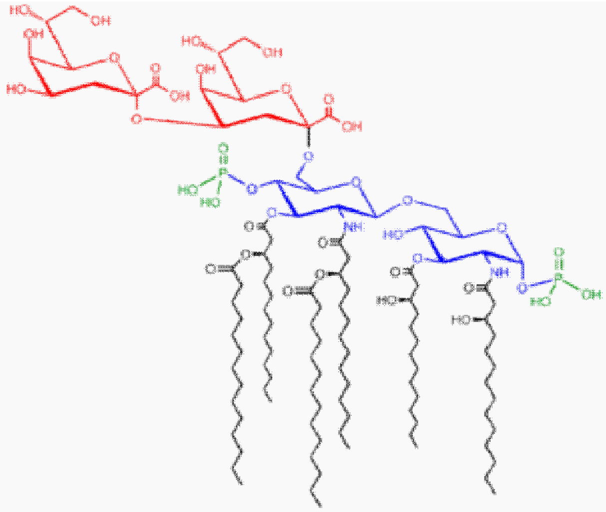
Sterol lipids, such as cholesterol and its derivatives, are an important component of membrane lipids, along with the glycerophospholipids and sphingomyelins. The steroids, all derived from the same fused four-ring core structure, have different biological roles as hormones and signaling molecules. The eighteen-carbon (C18) steroids include the estrogenfamily whereas the C19 steroids comprise the androgens such as testosterone and androsterone. The C21 subclass includes the progestogens as well as the glucocorticoids and mineralocorticoids. The secosteroids, comprising various forms of vitamin D, are characterized by cleavage of the B ring of the core structure. Other examples of sterols are the bile acids and their conjugates, which in mammals are oxidized derivatives of cholesterol and are synthesized in the liver. The plant equivalents are the phytosterols, such as β-sitosterol, stigmasterol, and brassicasterol; the latter compound is also used as a biomarker for algal growth. The predominant sterol in fungal cell membranes is ergosterol.

Prenol lipids

Prenol lipids are synthesized from the five-carbon-unit precursors isopentenyl diphosphate and dimethylallyl diphosphatethat are produced mainly via the mevalonic acid (MVA) pathway.The simple isoprenoids (linear alcohols, diphosphates, etc.) are formed by the successive addition of C5 units, and are classified according to number of these terpene units. Structures containing greater than 40 carbons are known as polyterpenes. Carotenoids are important simple isoprenoids that function as antioxidants and as precursors of vitamin

A.Another biologically important class of molecules is exemplified by the quinones and hydroquinones, which contain an isoprenoid tail attached to a quinonoid core of non-isoprenoid origin. Vitamin E and vitamin K, as well as the ubiquinones, are examples of this class. Prokaryotes synthesize polyprenols (called bactoprenols) in which the terminal isoprenoid unit attached to oxygen remains unsaturated, whereas in animal polyprenols (dolichols) the terminal isoprenoid is reduced.

Saccharolipids



Structure of the saccharolipid Kdo_2-lipid A.Glucosamine residues in blue, Kdo residues in red, acyl chains in black and phosphate groups in green.

Saccharolipids describe compounds in which fatty acids are linked directly to a sugar backbone, forming structures that are compatible with membrane bilayers. In the saccharolipids, a monosaccharidesubstitutes for the glycerol backbone present in glycerolipids and glycerophospholipids. The most familiar saccharolipids are the acylated glucosamine precursors of the Lipid A component of the lipopolysaccharides in Gram-negative bacteria. Typical lipid A molecules are disaccharides of glucosamine, which are derivatized with as many as seven fatty-acyl chains. The minimal lipopolysaccharide required for growth in *E. coli* is Kdo_2-Lipid A, a hexa-acylated disaccharide of glucosamine that is glycosylated with two 3-deoxy-D-manno-octulosonic acid (Kdo) residues.

Polyketides

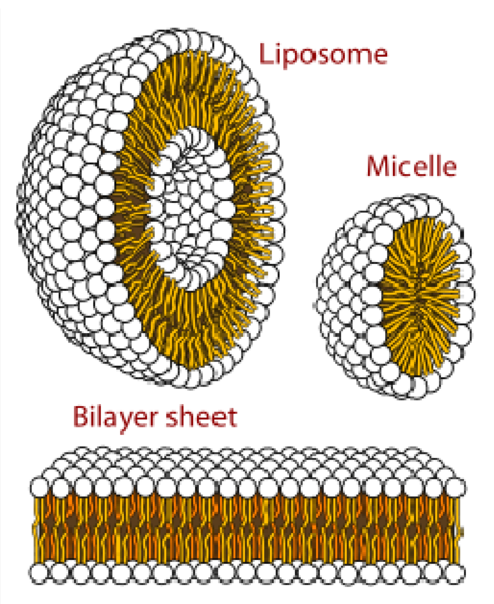
Polyketides are synthesized by polymerization of acetyl and propionylsubunits by classic enzymes as well as iterative and multimodular enzymes that share mechanistic features with the fatty acid synthases. They comprise a large number of secondary metabolites and natural products from animal, plant, bacterial, fungal and marine sources, and have great structural diversity.Many polyketides are cyclic molecules whose backbones are often further modified by glycosylation, methylation, hydroxylation, oxidation, and/or other processes. Many commonly used anti-microbial, anti-parasitic, and anti-cancer agents are polyketides or polyketide derivatives, such as erythromycins, tetracyclines, avermectins, and antitumor epothilones.

Biological functions

Membranes

Eukaryotic cells feature compartmentalized membrane-bound organelles that carry out different biological functions. The glycerophospholipids are the main structural component of biological membranes, such as the cellular plasma membraneand the intracellular membranes of organelles; in animal cells the plasma membrane physically separates the intracellularcomponents from the extracellular environment.The glycerophospholipids are amphipathic molecules (containing both hydrophobic and hydrophilic regions) that contain a glycerol core linked to two fatty acid-derived "tails" by ester linkages and to one "head" group by a phosphate ester linkage. While glycerophospholipids are the major component of biological membranes, other non-glyceride lipid components such as sphingomyelin and sterols(mainly cholesterol in animal cell membranes) are also found in biological membranes. In plants and algae, the galactosyldiacylglycerols, and sulfoquinovosyldiacylglycerol which lack a phosphate group, are important components of membranes of chloroplasts and related organelles and are the most abundant lipids in photosynthetic tissues, including those of higher plants, algae and certain bacteria.

Plant thylakoid membranes have the largest lipid component of a non-bilayer forming monogalactosyl diglyceride (MGDG), and little phospholipids; despite this unique lipid composition, chloroplast thylakoid membranes have been shown to contain a dynamic lipid-bilayer matrix as revealed by magnetic resonance and electron microscope studies.



Self-organization of phospholipids: a spherical liposome, a micelle, and a lipid bilayer.

A biological membrane is a form of lamellar phase lipid bilayer. The formation of lipid bilayers is an energetically preferred process when the glycerophospholipids described above are in an aqueous environment. This is known as the hydrophobic effect. In an aqueous system, the polar heads of lipids align towards the polar, aqueous environment, while the hydrophobic tails minimize their contact with water and tend to cluster together, forming a vesicle; depending on the concentration of the lipid, this biophysical interaction may result in the formation of micelles, liposomes, or lipid bilayers. Other aggregations are also observed and form part of the polymorphism of amphiphile (lipid) behavior. Phase behavior is an area of study within biophysics and is the subject of current academic research. Micelles and bilayers form in the polar medium by a process known as the hydrophobic effect.When dissolving a lipophilic or amphiphilic substance in a polar environment, the polar molecules (i.e., water in an aqueous solution) become more ordered around the dissolved lipophilic substance, since the polar molecules cannot form hydrogen bonds to the lipophilic areas of the amphiphile. So in an aqueous environment, the water molecules form an ordered "clathrate" cage around the dissolved lipophilic molecule.

The formation of lipids into protocell membranes represents a key step in models of abiogenesis, the origin of life

Energy storage

Triglycerides, stored in adipose tissue, are a major form of energy storage both in animals and plants. The adipocyte, or fat cell, is designed for continuous synthesis and breakdown of triglycerides in animals, with breakdown controlled mainly by the activation of hormone-sensitive enzyme lipase. The complete oxidation of fatty acids provides high caloric content, about 9 kcal/g, compared with 4 kcal/g for the breakdown of carbohydrates and proteins. Migratory birds that must fly long distances without eating use stored energy of triglycerides to fuel their flights.

Signaling

In recent years, evidence has emerged showing that lipid signaling is a vital part of the cell signaling. Lipid signaling may occur via activation of G protein-coupled or nuclear receptors, and members of several different lipid categories have been identified as signaling molecules and cellular messengers.These include sphingosine-1-phosphate, a sphingolipid derived from ceramide that is a potent messenger molecule involved in regulating calcium mobilization, cell growth, and apoptosis; diacylglycerol (DAG) and the phosphatidylinositol phosphates (PIPs), involved in calcium-mediated activation of protein kinase C; the prostaglandins, which are one type of fatty-acid derived eicosanoid involved in inflammation and immunity;the steroid hormones such as estrogen, testosterone and cortisol, which modulate a host of functions such as reproduction, metabolism and blood pressure; and the oxysterols such as 25-hydroxy-cholesterol that are liver X receptor agonists. Phosphatidylserine lipids are known to be involved in signaling for the phagocytosis of apoptotic cells and/or pieces of cells. They accomplish this by being exposed to the extracellular face of the cell membrane after the inactivation of flippases which place them exclusively on the cytosolic side and the activation of scramblases, which scramble the orientation of the phospholipids. After this occurs, other cells recognize the phosphatidylserines and phagocytosize the cells or cell fragments exposing them.

Other functions

The "fat-soluble" vitamins (A, D, E and K) – which are isoprene-based lipids – are essential nutrients stored in the liver and fatty tissues, with a diverse range of functions. Acyl-carnitines are involved in the transport and metabolism of fatty acids in and out of mitochondria, where they undergo beta oxidation. Polyprenols and their phosphorylated derivatives also play important transport roles, in this case the transport of oligosaccharides across membranes. Polyprenol phosphate sugars and polyprenol diphosphate sugars function in extra-cytoplasmic glycosylation reactions, in extracellular polysaccharide biosynthesis (for instance, peptidoglycan polymerization in bacteria), and in eukaryotic protein N-glycosylationCardiolipins are a subclass of glycerophospholipids containing four acyl chains and three glycerol groups that are particularly abundant in the inner mitochondrial membrane. They are believed to activate enzymes involved with oxidative phosphorylation. Lipids also form the basis of steroid hormones.

Metabolism

The major dietary lipids for humans and other animals are animal and plant triglycerides, sterols, and membrane phospholipids. The process of lipid metabolism synthesizes and degrades the lipid stores and produces the structural and functional lipids characteristic of individual tissues.

Biosynthesis

In animals, when there is an oversupply of dietary carbohydrate, the excess carbohydrate is converted to triglycerides. This involves the synthesis of fatty acids from acetyl-CoA and the esterification of fatty acids in the production of triglycerides, a process called lipogenesis. Fatty acids are made by fatty acid synthases that polymerize and then reduce acetyl-CoA units. The acyl chains in the fatty acids are extended by a cycle of reactions that add the acetyl group, reduce it to an alcohol, dehydrate it to an alkene group and then reduce it again to an alkane group. The enzymes of fatty acid biosynthesis are divided into two groups, in animals and fungi all these fatty acid synthase reactions are carried out by a single multifunctional protein, while in plant plastids and bacteria separate enzymes perform each step in the pathway. The fatty acids may be subsequently converted to triglycerides that are packaged in lipoproteins and secreted from the liver.

The synthesis of unsaturated fatty acids involves a desaturation reaction, whereby a double bond is introduced into the fatty acyl chain. For example, in humans, the desaturation of stearic acid by stearoyl-CoA desaturase-1 produces oleic acid. The doubly unsaturated fatty acid linoleic acid as well as the triply unsaturated α-linolenic acid cannot be synthesized in mammalian tissues, and are therefore essential fatty acids and must be obtained from the diet.

Triglyceride synthesis takes place in the endoplasmic reticulum by metabolic pathways in which acyl groups in fatty acyl-CoAs are transferred to the hydroxyl groups of glycerol-3-phosphate and diacylglycerol.

Terpenes and isoprenoids, including the carotenoids, are made by the assembly and modification of isoprene units donated from the reactive precursors isopentenyl pyrophosphate and dimethylallyl pyrophosphateThese precursors can be made in different ways. In animals and archaea, the mevalonate pathway produces these compounds from acetyl-CoA, while in plants and bacteria the non-mevalonate pathway uses pyruvate and glyceraldehyde 3-phosphate as substrates. One important reaction that uses these activated isoprene donors is steroid biosynthesis. Here, the isoprene units are joined together to make squalene and then folded up and formed into a set of rings to make lanosterol. Lanosterol can then be converted into other steroids such as cholesterol and ergosterol

Degradation

Beta oxidation is the metabolic process by which fatty acids are broken down in the mitochondria and/or in peroxisomes to generate acetyl-CoA. For the most part, fatty acids are oxidized by a mechanism that is similar to, but not identical with, a reversal of the process of fatty acid synthesis. That is, two-carbon fragments are removed sequentially from the carboxyl end of the acid after steps of dehydrogenation, hydration, and oxidation to form a beta-keto acid, which is split by thiolysis. The acetyl-CoA is then ultimately converted into ATP, CO_2, and H_2O using the citric acid cycle and the electron transport chain. Hence the citric acid cycle can start at acetyl-CoA when fat is being broken down for energy if there is little or no glucose available. The energy yield of the complete oxidation of the fatty acid palmitate is 106 ATP. Unsaturated and odd-chain fatty acids require additional enzymatic steps for degradation.

Nutrition and health

Most of the fat found in food is in the form of triglycerides, cholesterol, and phospholipids. Some dietary fat is necessary to facilitate absorption of fat-soluble vitamins (A, D, E, and K) and carotenoids. Humans and other mammals have a dietary requirement for certain essential fatty acids, such as linoleic acid (an omega-6 fatty acid) and alpha-linolenic acid(an omega-3 fatty acid) because they cannot be synthesized from simple precursors in the diet.Both of these fatty acids are 18-carbon polyunsaturated fatty acids differing in the number and position of the double bonds. Most vegetable oils are rich in linoleic acid (safflower, sunflower, and corn oils). Alpha-linolenic acid is found in the green leaves of plants, and in selected seeds, nuts, and legumes (in particular flax, rapeseed, walnut, and soy).Fish oils are particularly rich in the longer-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[85] A large number of studies have shown positive health benefits associated with consumption of omega-3 fatty acids on infant development, cancer, cardiovascular diseases, and various mental illnesses, such as depression, attention-deficit hyperactivity disorder, and dementia. In contrast, it is now well-established that consumption of trans fats, such as those present in partially hydrogenated vegetable oils, are a risk factor for cardiovascular disease.

A few studies have suggested that total dietary fat intake is linked to an increased risk of obesity and diabetes.However, a number of very large studies, including the Women's Health Initiative Dietary Modification Trial, an eight-year study of 49,000 women, the Nurses' Health Study and the Health Professionals Follow-up Study, revealed no such links. None of these studies suggested any connection between percentage of calories from fat and risk of cancer, heart disease, or weight gain. The Nutrition Source, a website maintained by the Department of Nutrition at the Harvard School of Public Health, summarizes the current evidence on the impact of dietary fat: "Detailed research—much of it done at Harvard—shows that the total amount of fat in the diet isn't really linked with weight or disease."