EDO UNIVERSITY IYAMHO

Department of Biochemistry

BCH 211 - Introductory Biochemistry I

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Co-lecturer: *Dr. U. Usunobun*.

General overview of lecture: The course introduces biochemistry as a course to the students and covers the following topics; Short history and definition of biochemistry. Importance of biochemistry to other scientific disciplines. General considerations on the biological molecules of life (carbohydrates and lipids). Introduction, definition, functions, classification and types of monosaccharides, oligosaccharides and polysaccharides. Isomers (stereo and optical isomerism), epimers, anomers, mutarotation and enantiomers. Reducing properties (oxidation and reduction), dehydration, osazone formation, ester formation and glycosides. Classification of lipids-fatty acids, triglycerides, glycosylglycerols, phospholipids, waxes, prostalglandins. Lipid micelles and bilayers. Lipoprotein system.

Learning outcomes: At the completion of this aspect of the course, students should be able to:

i. Describe the chemistry, classification and functions of lipids.
ii. Differentiate between different forms of lipids
iii. Discuss the biochemical significance of lipids in general.
iv. Discuss the biochemical significance of phospholipids and lipoproteins.

Assignments: Students will be given a minimum of two take-home assignments from my aspect of the course in addition to mid-semester test. There will also be take-home assignments from my co-lecturer of the course which will be from the areas covered by him. There will also be an end of semester exam for the course.

Grading: We will assign 10% of this class grade to take-home assignments, 20% for the mid-term test and 70% for the final exam. The final exam will be comprehensive.

Textbooks: The recommended textbook for this class are as stated:
Title: *Lehninger Principles of Biochemistry*
Authors: David L. Nelson, Michael M. COX
Publisher: Freeman, W. H. and Company, Seventh Edition
ISBN- 13: 9787464126116
Year: 2017

Title: *Textbook of Medical Biochemistry*
Author(s): MN Chatterjea and RanaShinde.

Publisher: Jaypee Brothers Medical Publishers Ltd, Eighth Edition
ISBN: 978-93-5025-484-4
Year: 2012

Title: *Textbook of biochemistry for Medical Students*
Author(s): DM Vasudevan, Sreekumari S and KannanVaidyanathan.
Publisher: Jaypee Brothers Medical Publishers Ltd, Sixth Edition
ISBN: 978-93-5025-016-7
Year: 2011

Main Lecture: Below is a description of the contents for my aspect of the course.

Introduction/Definition of Lipids

Lipids constitute a heterogeneous group of compounds of biochemical importance.
Lipids may be defined as compounds which are relatively insoluble in water, but freely soluble in nonpolar organic solvents like benzene, chloroform, ether, hot alcohol, acetone, etc. actually or potentially related to fatty acids and utilized by the living cells.

Importance of lipids

Lipids are important constituent of most diets and they are the concentrated fuel reserve of the body (triacylglycerol).
Can be stored in the body in almost unlimited amount in contrast to carbohydrates.
Some deposits of lipids may exert an insulating effect in the body, while lipids around internal organs like kidney, etc. may provide padding and protect the organs.
The nervous system is particularly rich in lipids especially certain types and are essential for proper functioning.
Some vitamins like, A, D, E and K are fat soluble, hence lipid is necessary for these vitamins.
Lipoproteins and phospholipids are important constituents of many natural membranes such as cell walls and cell organelles like mitochondrion, etc.
Lipoproteins are also ćcarriersô of triglycerides, cholesterol and PL in the body.

Classification of lipids

Lipids are broadly classified according into:
Simple lipids
Complex or Compound lipids
Derived lipids and
Miscellaneous lipids
These groups are further classified into sub-groups.

Simple lipids

These are esters of fatty acids with various alcohols. They are of two types;
Neutral fats (Triacylglycerol, TG): These are triesters of fatty acids with glycerol.
Waxes: Esters of fatty acids (usually long chain) with alcohols other than glycerol. These alcohols may be aliphatic or alicyclic. Cetyl alcohol is most commonly found in waxes.

True waxes are esters of higher fatty acids with cetyl alcohol ($C_{16}H_{33}OH$) or other higher straight chain alcohols.
Cholesterol esters are esters of fatty acid with cholesterol.
Vit A and Vit D esters are palmitic or stearic acids esters of Vit A (Retinol) or Vit D respectively.

Complex or compound lipids
These are esters of fatty acids with alcohols containing additional groups such as phosphate, nitrogenous base, carbohydrate, protein etc.
They are further divided as follows;
Phospholipids: They are substituted fats containing in addition to fatty acid and glycerol, a phosphoric acid residue, a nitrogenous base and other substituents. They contain phosphoric acid and frequently a nitrogenous base. This is in addition to alcohol and fatty acids.
Glycerophospholipid: These phospholipids contain glycerol as the alcohol e.g. lecithin, cephalin.
Sphingophospholipid: Sphingosine is the alcohol in this group of phospholipids e.g., sphingomyelin.
Glycolipids: Lipids containing carbohydrate moiety are called glycolipids. They contain a special alcohol called sphingosine or sphingol and nitrogenous base in addition to fatty acids but does not contain phosphoric acid or glycerol. These are of two types:
Cerebrosides
Gangliosides
Sulpholipids: Lipids characterised by possessing sulphate groups.
Aminolipids (Proteolipids)
Lipoproteins: Lipids as prosthetic group to proteins.

Derived lipids
Derivatives obtained by hydrolysis of those given in group I and II, which still possess the general characteristics of lipids.
Fatty acids may be saturated, unsaturated or cyclic.
Monoglycerides (Monoacylglycerol) and Diglycerides (Diacylglycerol).
Alcohols
Straight chain alcohols are water insoluble alcohols of higher molecular weight obtained on hydrolysis of waxes.
Cholesterol and other steroids including Vit D.
Alcohols containing the ϐ-ionone ring include Vit A and certain carotenoids.
Glycerol.

Miscellaneous lipids
These include a large number of compounds possessing the characteristics of lipids.
Aliphatic hydrocarbons include isooctadecane found in liver fat and certain hydrocarbons found in bees wax and plant waxes.
Carotenoids
Squalene is a hydrocarbon found in shark and mammalian liver and in human sebum.
Vitamins E and K.

Fatty acids

A fatty acid (FA) may be defined as an organic acid that occurs in a natural triglyceride and is a monocarboxylic acid ranging in chain length from C4 to about 24 carbon atoms. FA are obtained from hydrolysis of fats.
Fatty acids are carboxylic acids with hydrocarbon side chain. They are the simplest form of lipids.
Fatty acids can be classified into five groups;
Straight chain FA
Branched chain FA
Substituted FA
Cyclic FA
Eicosanoids

Classification of FA –

A. **Straight chain FA**

Straight chain FA are of two groups which are:

i. **Saturated FA:** This group of fatty acids contain no double bonds and they have a general formula $C_nH_{2n+1}COOH$.

Saturated FA that contain ten (10) or less number of carbon atoms are regarded as lower fatty acids. Examples include:

Acetic acid	CH_3COOH
Propionic acid	C_2H_5COOH
Butyric acid	C_3H_7COOH
Caproic acid	$C_5H_{11}COOH$

Saturated FA that contain more than ten (10) carbon atoms are regarded as higher fatty acids. Examples include:

Palmitic acid	$C_{15}H_{31}COOH$
Stearic acid	$C_{17}H_{35}COOH$

ii. **Unsaturated Fatty acids**: Unsaturated FA contain one or more double bond, and they are sub-divided into:

Monounsaturated FA which contain one double bond and has the same general formula as saturated FA, $C_nH_{2n+1}COOH$.
Although more than 100 MUFAs have been identified in nature, most of these are very rare. Oleic acid (18:1;9), a long chain monounsaturated fatty acid, is widely distributed and abundant in nature (few fats are known to contain less than 10%).
In human diet, unsaturated fatty acids are almost exclusively oleic acid.
Polyunsaturated fatty acids: There are three polyunsaturated fatty acids of biological importance.
Linoleic acid series (18 : 2; 9, 12): It contains two double bonds between C9 and C10; and between C12 and C13. Their general formula is $C_nH_{2n-3}COOH$.
Linoleic acid is present in sufficient amounts in peanut oil, corn oil, cottonseed oil, soyabean oil and egg yolk.

Linolenic acid series (18 : 3; 9, 12, 15): It contains three double bonds between 9 and 10; 12 and 13; and 15 and 16. Their general formula is $C_nH_{2n-5}COOH$.
Linolenic acid is found frequently with linoleic acid, but particularly present in linseed oil, rapeseed oil, soybean oil, fish visceras and liver oil (cod liver oil).
Arachidonic acid series (20 : 4; 5, 8, 11, 14): It contains four double bonds. Their general formula $C_nH_{2n-7}COOH$.
Arachidonic acid is found in small quantities with linoleic acid and linolenic acid but particularly found in peanut oil. Also found in animal fats including Liver fats.

B. **Branched chain FA**:

Odd and even carbon branched chain fatty acids occur in animal and plant lipids, e.g. Sebum in sebaceous glands contain branched chain FA. Also, branched chain FA is present in certain foods, e.g. phytanic acid in butter.
Substituted fatty acids: In hydroxy fatty acid and methyl fatty acid, one or more of the hydrogen atoms have been replaced by ï OH group or ï CH_3 group respectively. Both saturated and unsaturated hydroxyl fatty acids, particularly with long chains, are found in nature, e.g. cerebronic acid of brain glycolipids, Ricinoleic acid in castor oil.
Cyclic fatty acids: Fatty acids bearing cyclic groups are present in some seeds, e.g. Chaulmoogric acid (used in leprosy treatment) obtained from chaulmoogra seeds, Hydnocarpic acid.
Eicosanoids: These compounds are related to eicosapolyenoic fatty acids and include prostaglandins, prostacyclins leukotriene and thromboxanes.

Essential fatty acids

Some fatty acids cannot be synthesized by the body and therefore needs to be supplied in the diet. These are known as essential fatty acids (EFA).
Chemically, they are polyunsaturated fatty acids, namely linoleic acid (18 : 2; 9, 12), Iinolenic acid (18 : 3; 9, 12, 15) and arachidonic acid (20 :4;5,8, 11,14).
Lack of EFA in the diet can produce growth retardation and other deficiency manifestation symptoms.
Linoleic acid is most important as, arachidonic acid can be synthesised from linoleic acid by a three stage reaction by addition of acetyl-CoA.
Biologically, arachidonic acid is very important as it is precursor from which prostaglandins and leukotrienes are synthesised in the body.
Linoleic acid and linolenic acid are essential since humans lack the enzymes that can introduce double bonds beyond carbons 9 to 10.
Essential fatty acids are required for the membrane structure and function, transport of cholesterol, formation of lipoproteins, prevention of fatty liver etc.

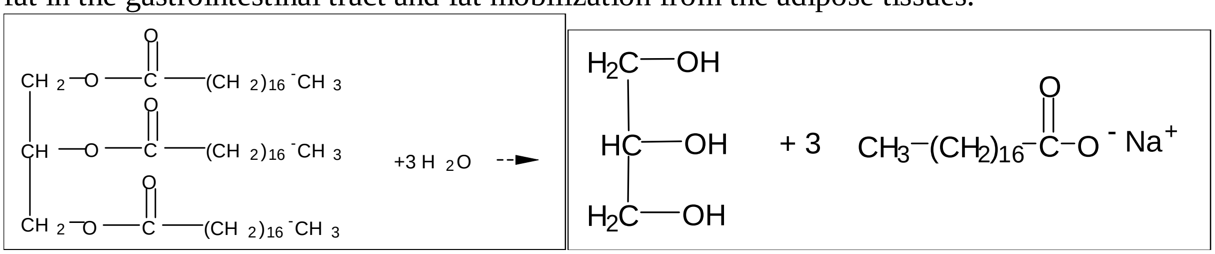
Nomenclature of fatty acids

The naming of a fatty acid (systematic name) is based on the hydrocarbon from which it is derived. The saturated fatty acids end with a suffix -anoic (e.g., octanoic acid) while the unsaturated fatty acids end with a suffix ï enoic (e.g. octadecenoic acid ï oleic acid). In addition to systematic names, fatty acids have common names which are more widely used.
Numbering of carbon atoms :lt starts from the carboxyl carbon which is taken as number 1. The carbons adjacent to this (carboxyl C) are 2, 3, 4 and so on.

lnstead of writing the full structures, biochemists employ shorthand notations (by numbers) to represent fatty acids. The general rule is that the total number of carbon atoms are written first, followed by the number of double bonds and finally the (first carbon) position of double bonds, starting from the carboxyl end. Thus, saturated fatty acid, palmitic acid is written as l6:0, oleic acid as 18:1;9, arachidonic acid as 20 : 4; 5, 8, 11, 14.

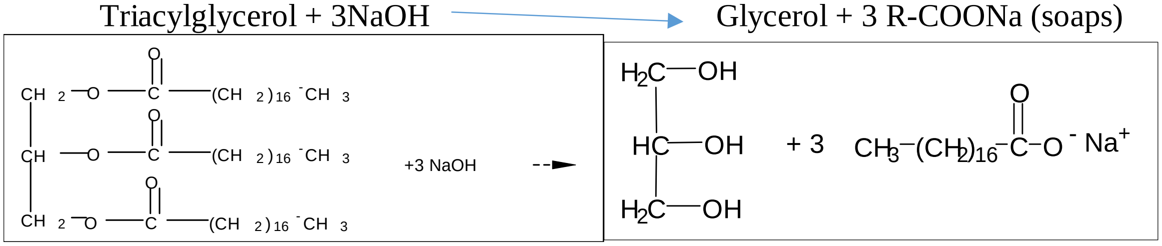
Triacylglycerols (TAG)
Triacylglycerols (formerly triglycerides) are the esters of glycerol with fatty acids. The fats and oils that are widely distributed in both plants and animals are chemically triacylglycerols. They are insoluble in water and non-polar in character and commonly known as neutral fats. Adipocytes of adipose tissue-predominantly found in the subcutaneous layer and in the abdominal cavity are specialized for storage of triacylglycerols. The fat is stored in the form of globules dispersed in the entire cytoplasm. And surprisingly, triacylglycerols are not the structural components of biological membranes.

Properties of Triacylglycerol
A few important properties of triacylglycerols, which have biochemical relevance, are discussed below:
Hydrolysis: Triacylglycerols undergo stepwise enzymatic hydrolysis to finally liberate free fatty acids and glycerol. The process of hydrolysis, catalyzed by lipases is important for digestion of fat in the gastrointestinal tract and fat mobilization from the adipose tissues.



Saponification: The hydrolysis of triacylglycerols by alkali to produce glycerol and soaps is known as saponification.

Triacylglycerol + 3NaOH → Glycerol + 3 R-COONa (soaps)

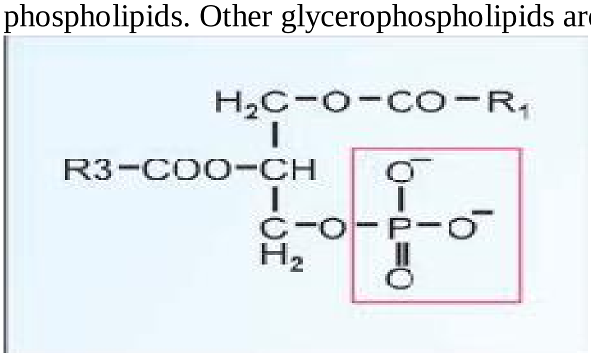


Rancidity: Rancidity is the term used to represent the deterioration of fats and oils resulting in an unpleasant taste. Fats containing unsaturated fatty acids are more susceptible to ranciditv. Rancidity occurs when fats and oils are exposed to air, moisture, light, bacteria etc. Rancid fats and oils are unsuitable for human consumption. Rancidity occurs as a result of either of two reactions;
Hydrolytic rancidity, occurs due to partial hydrolysis of triacylglycerols by bacterial enzymes.
Oxidative rancidity, is due to oxidation of unsaturated fatty acids. This results in the formation of unpleasant products such as dicarboxylic acids, aldehydes, ketones etc.

Oxidation: In the living cells, lipids undergo oxidation to produce peroxides and free radicals which can damage the tissue. The free radicals are believed to cause inflammatory diseases, ageing, cancer/atherosclerosis etc. lt is fortunate that the cells possess antioxidants such as vitamin E, urate and superoxide dismutase to prevent in vivo lipid peroxidation
Additive Reactions: The unsaturated fatty acids present in neutral fat exhibits all the additive reactions, i.e. hydrogenation, halogenation, etc. Oils which are liquid at ordinary room temperature, on hydrogenation become solidified. This is the basis of margarine manufacture, where inedible and cheap oils like cotton seed oil are hydrogenated and converted to edible solid fat.

Phospholipids
Phospholipids are compound lipids, that contain a phosphoric acid residue, nitrogen containing base and other substituents in addition to fatty acids and glycerol/or other alcohol.
Like fatty acids, phospholipids are amphipathic in nature. That is, each has a hydrophilic head, which is the phosphate group plus whatever alcohol is attached to it and a long, hydrophobic tail containing fatty acids or fatty acidï derived hydrocarbons.
There are two classes of phospholipids;
Glycerophospholipids
Sphingophospholipids

Glycerophospholipids
Glycerophospholipids are also known as phosphoglycerides. These class of phospholipids contain glycerol as the alcohol.
Glycerophospholipids constitute the major class of phospholipids and are the predominant lipids in membranes. All contain (or are derivatives of) phosphatidic acid (PA), which is diacylglycerol with a phosphate group on carbon 3.
Glycerophospholipids consist of glycerol-3-phosphate esterified at its C1 and C2 with fatty acids. Usually, C1 contains a saturated fatty acid while C2 contains an unsaturated fatty acid.
Examples of Glycerophospholipids
Phosphatidicacid : This is the simplest phospholipid. lt does not occur in good concentration in the tissues. Basically, phosphatidic acid is an intermediate in the synthesis of triacylglycerol and phospholipids. Other glycerophospholipids are derivatives of phosphatidic acid.



Phosphatidylcholine (Lecithins): Lecithin is a phosphatidic acid with choline as the base. It is the most abundant group of phospholipids in cell membranes. Two phosphatidylcholine are worthy of note;
Dipalmitoyl lecithin is an important phosphatidylcholine found in lungs. It is a surface active agent and prevents the adherence of inner surface of the lungs due to surface tension. Respiratory distress syndrome in infants is a disorder characterized by the absence of dipalmitoyl lecithin.

Lysolecithin is formed by removal of the fatty acid either at C1 or C2 of lecithin.
Phosphatidylethanolamine (cephalins): Cephalins are structurally identical with Lecithins, with the exception that the base ethanolamine replaces choline as the base. Both Ŭand ɓ cephalins are known. They occur with lecithin, particularly rich in brain and nervous tissues. Thus, lecithin and cephalin differ with regard to the base.
Phosphatidylinositol (Lipositols): Inositol is an alcohol, a cyclic compound hexa hydroxyl cyclohexane with molecular formula $C_6H_{12}O_6$. It replaces the base choline of lecithin. Inositol as a constituent of phospholipids was first discovered in acid fast bacilli. Later, it was found to occur in brain and nervous tissues, moderately in soybeans, and also occurs in plant phospholipids
Phosphatidylserine: This phospholipid is similar to cephalin and contains the amino acid serine in place of ethanolamine found in brain and nervous tissues and small amount in other tissues. Also found in blood.
Plasmalogens: When a fatty acid is attached by an ether linkage at C1 of glycerol in the glycerophospholipids, the resultant compound is plasmalogen. Phosphatidalethanolamine is the most important which is similar in structure to phosphatidylethanolamine but for the ether linkage (in place of ester). An unsaturated fatty acid occurs at C1. Choline, inositol and serine may substitute ethanolamine to give other plasmalogens.
Phosphatidylglycerol/Cardiolipin: Phosphatidylglycerol occurs in relatively large amounts in mitochondrial membranes and is a precursor of cardiolipin (diphosphatidyglycerol). It is formed by esterification of phosphatidic acid to glycerol. When two molecules of phosphatidic acid are linked with a molecule of glycerol, diphosphatidyl glycerol or cardiolipin is formed. lt is so named as it was first isolated from heart muscle.
Sphingophospholipids (Sphingomyelin)
Sphingophospholipids are phospholipids that contain an unsaturated amino alcohol called sphingosine in place of glycerol. It is found in large quantities in brain and nervous tissues, and very small amount in other tissues. Sphingosine molecule in which a fatty acyl group is substituted on the ï NH_2 group is called as ceramide.
Functions of Phospholipids
Phospholipids (PL) acts as surfactants in the lungs e.g. dipalmitoylphosphatidylcholine. Its deficiency causes RDS.
It forms the structural components of membranes in association with proteins and regulates membrane permeability.
They are required as a cofactor for the activity of the enzyme lipoprotein lipase and triacylglycerol lipase.
PL are essential for the synthesis of different lipoproteins, and thus participate in the transport of lipids.
PL play an essential part in the blood coagulation process. Cephalins, an important group of phospholipids participate in blood clotting.
PL helps in the prevention of accumulation of fat in liver (fatty liver). They are lipotropic factors.
PL participate in the reverse cholesterol transport and thus help in the removal of cholesterol from the body.
PL (phosphatidyl inositol) are involved in signal transmission across membranes.

Glycolipids

Glycolipids are molecules that contain both carbohydrate and lipid components. Like the phospholipid sphingomyelin, glycolipids are derivatives of ceramides in which a long-chain fatty acid is attached to the amino alcohol sphingosine. They are, therefore, more precisely called glycosphingolipids. Like the phospholipids, glycosphingolipids are essential components of all membranes in the body, but they are found in greatest amounts in nerve tissue.
There are two types of glycolipids;
Cerebrosides
Gangliosides

Cerebrosides
Cerebrosides are the simplest form of glycolipids. They contain a ceramide (sphingosine attached to a fatty acid) and one or more sugars. Galactocerebroside (galactosylceramide) and glucocerebroside are the most important glycolipids.
Galactocerebroside contains the fatty acid cerebronic acid.

Gangliosides
Gangliosides are predominantly found in ganglions and are the most complex form of glycosphingolipids. They are the derivatives of cerebrosides and contain one or more molecules of N-acetylneuraminic acid (NANA), the most important sialic acid.

Amphipathic lipids
Amphipathic lipids are molecules which contain both hydrophobic and hydrophilic group. Examples of amphipathic lipids include fatty acids, phospholipids, sphingolipids, bile salts and cholesterol (to some extent) are amphipathic in nature.
Phospholipids in general are amphipathic, particularly Lecithin. They have both hydrophobic and hydrophilic portion in their molecule. The glycerol along with the phosphoric acid and choline constitute the polar ‘head' of a phospholipid molecule, whereas the hydrocarbon chains of the fatty acids represent the nonpolar ‘tail'.

Micelle
When the amphipathic lipids are mixed in water (aqueous phase), the polar groups (heads) orient themselves towards aqueous phase while the non-polar (tails) orient towards the opposite directions. This leads to the formation of micelles.
These are involved in solubilization of lipids in aqueous media and help in digestion and absorption of lipids.

Lipid bilayer/Liposome
A lipid bilayer is formed by the orienting of the polar heads to the outer aqueous phase on either side and the non-polar tails into the interior. The formation of a lipid bilayer is the basis of membrane structure.
A lipid bilayer will close on itself under appropriate conditions to form liposomes. They are produced when amphipathic lipids in aqueous medium are subjected to sonification. They have intermittent aqueous phases in the lipid bilayer.

Waxes

Waxes are esters of higher fatty acids with higher monohydroxy aliphatic alcohols and so have very long straight chains of 60-100 carbon atoms.
They form the secretions of insects, leaves and fruits of plants, e.g. Lanolin or wool fat, beeswax, whalesperm oil, etc.
They are used as the base for the preparation of cosmetics, ointments, polishes, lubricants and candles.

Lipoproteins
Lipoproteins are macromolecular complexes used by the body to transport lipids in the blood.
They are characterized by an outer coat of phospholipids and proteins, which encloses an inner core of hydrophobic TAG and cholesteryl ester.
Lipoproteins are classified according to the way they behave on centrifugation. This in turn corresponds to their relative densities, which depends on the proportion of (high density) protein to (low density) lipid in their structure.
For example, high density lipoproteins (HDLs) consist of 50% protein and have the highest density, while chylomicrons (1% protein) and very low density lipoproteins (VLDLs) have the lowest density.
Two types of lipoproteins are triglyceride-rich: the chylomicrons and VLDL.
Chylomicrons are synthesized by enterocytes from lipids absorbed in the small intestine. VLDL is synthesized in the liver.
The function of these lipoproteins is to deliver energy-rich triacylglycerol (TAG) to cells in the body.
As VLDL particles are stripped of triacylglycerol, they become more dense. These particles are remodeled at the liver and transformed into LDL. The function of LDL is to deliver cholesterol to cells, where it is used in membranes, or for the synthesis of steroid hormones.
Excess cholesterol is eliminated from the body via the liver, which secretes cholesterol in bile or converts it to bile salts.
The liver removes LDL and other lipoproteins from the circulation by receptor-mediated endocytosis. Additionally, excess cholesterol from cells is brought back to the liver by HDL in a process known as reverse cholesterol transport.
HDL (or really, the HDL precursor) is synthesized and secreted by the liver and small intestine.
It travels in the circulation where it gathers cholesterol to form mature HDL, which then returns the cholesterol to the liver via various pathways.
Prostaglandins, and the related compounds thromboxanes and leukotrienes, are collectively known as eicosanoids.

Eicosanoids
They are formed from polyunsaturated fatty acids with 20 carbons. They are extremely potent compounds that elicit a wide range of responses, both physiologic (inflammatory response) and pathologic (hypersensitivity).
They are produced in very small amounts in almost all tissues rather than in specialized glands.
Eicosanoids are not stored, and, they have an extremely short half-life, being rapidly metabolized to inactive, products.
They ensure gastric integrity and renal function, regulate smooth, muscle contraction (intestine and uterus are key sites) and blood vessel, diameter, and maintain platelet homeostasis.