MARUDHAR KESARI JAIN COLLEGE FOR WOMEN VANIYAMBADI

PG AND RESEARCH DEPARTMENT OF BIOCHEMISTRY

E-NOTES

SUBJECT NAME: CHEMISTYY OF BIOMOLECULES

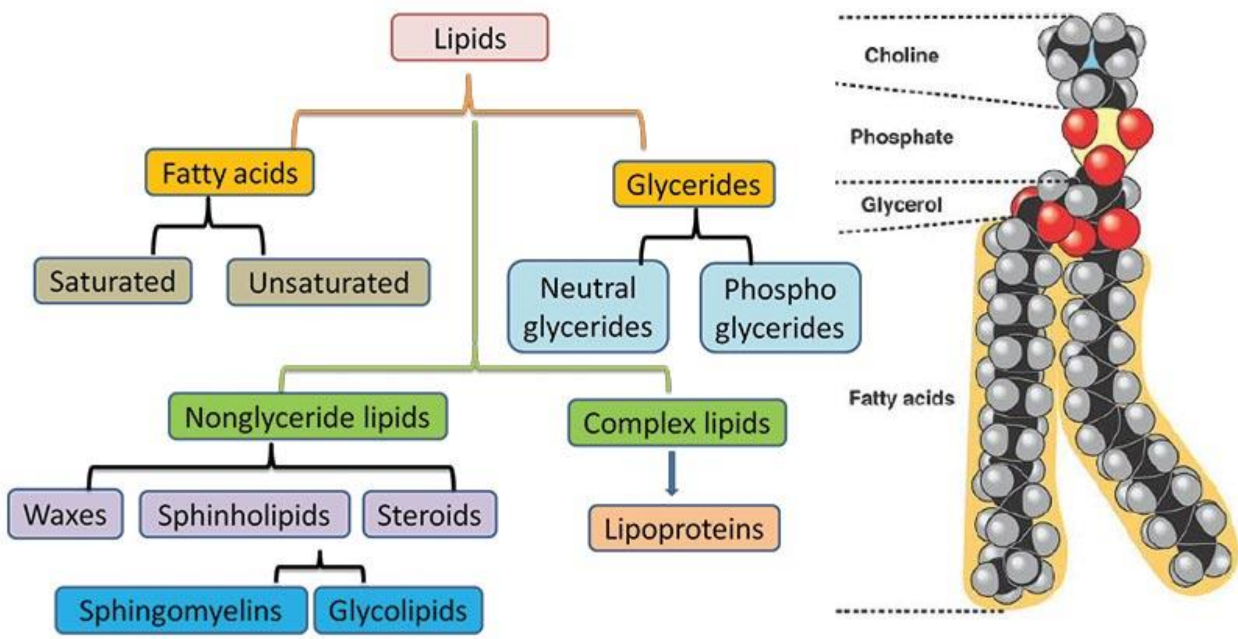
SUBJECT CODE: GBC12

Unit-II: Lipids

Classification of Lipids, Biological significance of lipids, Fatty acids and their physiochemical properties. Structure and properties of Prostaglandins. Storage lipids - triacyl glycerol and waxes. Structural lipids in membranes – glycerophospholipids, galactolipids and sulpholipids, sphingolipids and sterols, structure, distribution and role of membrane lipids. Lipids as signals, cofactors and pigments.

Lipids definitation

- Lipids are a heterogeneous group of organic compounds that are insoluble in water and soluble in non-polar organic solvents.
- They naturally occur in most plants, animals, microorganisms and are used as cell membrane components, energy storage molecules, insulation, and hormones.



Properties of lipids

- Lipids may be either liquids or non-crystalline solids at room temperature.
- Pure fats and oils are colorless, odorless, and tasteless.
- They are energy-rich organic molecules
- Insoluble in water
- Soluble in organic solvents like alcohol, chloroform, acetone, benzene, etc.
- No ionic charges
- Solid triglycerols (Fats) have high proportions of saturated fatty acids.

- Liquid triglycerols (Oils) have high proportions of unsaturated fatty acids.

1. Hydrolysis of triglycerols

Triglycerols like any other esters react with water to form their carboxylic acid and alcohol– a process known as hydrolysis.

2. Saponification:

Triacylglycerols may be hydrolyzed by several procedures, the most common of which utilizes alkali or enzymes called lipases. Alkaline hydrolysis is termed saponification because one of the products of the hydrolysis is a soap, generally sodium or potassium salts of fatty acids.

3. Hydrogenation

The carbon-carbon double bonds in unsaturated fatty acids can be hydrogenated by reacting with hydrogen to produce saturated fatty acids.

4. Halogenation

Unsaturated fatty acids, whether they are free or combined as esters in fats and oils, react with halogens by addition at the double bond(s). The reaction results in the decolorization of the halogen solution.

5. Rancidity:

The term rancid is applied to any fat or oil that develops a disagreeable odor. Hydrolysis and oxidation reactions are responsible for causing rancidity. Oxidative rancidity occurs in triacylglycerols containing unsaturated fatty acids.

Structure of Lipids

- Lipids are made of the elements Carbon, Hydrogen and Oxygen, but have a much lower proportion of water than other molecules such as carbohydrates.

- Unlike polysaccharides and proteins, lipids are not polymers—they lack a repeating monomeric unit.
- They are made from two molecules: **Glycerol and Fatty Acids.**
- A glycerol molecule is made up of three carbon atoms with a hydroxyl group attached to it and hydrogen atoms occupying the remaining positions.
- Fatty acids consist of an acid group at one end of the molecule and a hydrocarbon chain, which is usually denoted by the letter 'R'.
- They may be **saturated or unsaturated**.
- A fatty acid is saturated if every possible bond is made with a Hydrogen atom, such that there exist no C=C bonds.
- Unsaturated fatty acids, on the other hand, do contain C=C bonds. Monounsaturated fatty acids have one C=C bond, and polyunsaturated have more than one C=C bond.

Structure of Triglycerides

- Triglycerides are lipids consisting of one glycerol molecule bonded with three fatty acid molecules.
- The bonds between the molecules are covalent and are called Ester bonds.
- They are formed during a condensation reaction.
- The charges are evenly distributed around the molecule so hydrogen bonds to not form with water molecules making them insoluble in water.

Classification (Types) of Lipids

Lipids can be classified according to their hydrolysis products and according to similarities in their molecular structures. Three major subclasses are recognized:

1. Simple lipids

(a) **Fats and oils** which yield fatty acids and glycerol upon hydrolysis.

(b) **Waxes**, which yield fatty acids and long-chain alcohols upon hydrolysis.

Fats and Oils

- Both types of compounds are called triacylglycerols because they are esters composed of three fatty acids joined to glycerol, trihydroxy alcohol.
- The difference is on the basis of their physical states at room temperature. It is customary to call a lipid a fat if it is solid at 25°C, and oil if it is a liquid at the same temperature.
- These differences in melting points reflect differences in the degree of unsaturation of the constituent fatty acids.

Waxes

- Wax is an ester of long-chain alcohol (usually mono-hydroxy) and a fatty acid.
- The acids and alcohols normally found in waxes have chains of the order of 12-34 carbon atoms in length.

2. Compound lipids

(a) **Phospholipids**, which yield fatty acids, glycerol, amino alcohol sphingosine, phosphoric acid and nitrogen-containing alcohol upon hydrolysis.

They may be **glycerophospholipids** or **sphingophospholipid** depending upon the alcohol group present (glycerol or sphingosine).

(b) **Glycolipids**, which yield fatty acids, sphingosine or glycerol, and a carbohydrate upon hydrolysis.

They may also be **glyceroglycolipids** or **sphingoglycolipid** depending upon the alcohol group present (glycerol or sphingosine).

3. Derived lipids:

Hydrolysis product of simple and compound lipids is called derived lipids. They include fatty acid, glycerol, sphingosine and steroid derivatives.

Steroid derivatives are phenanthrene structures that are quite different from lipids made up of fatty acids.

Functions

It is established that lipids play extremely important roles in the normal functions of a cell. Not only do lipids serve as highly reduced storage forms of energy, but they also play an intimate role in the structure of cell membrane and organellar membranes. Lipids perform many functions, such as:

1. Energy Storage
2. Making Biological Membranes
3. Insulation
4. Protection – e.g. protecting plant leaves from drying up
5. Buoyancy
6. Acting as hormones
7. Act as the structural component of the body and provide the hydrophobic barrier that permits partitioning of the aqueous contents of the cell and subcellular structures.
8. Lipids are major sources of energy in animals and high lipid-containing seeds.

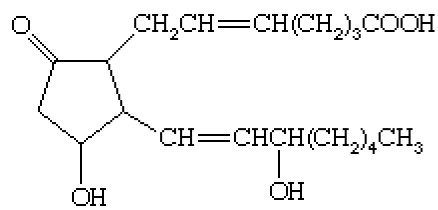
Activators of enzymes eg. glucose-6-phosphatase, stearyl CoA desaturase and ω-monooxygenase, and β-hydroxybutyric dehydrogenase (a mitochondrial enzyme) require phosphatidylcholine micelles for activation

Prostaglandins

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.

Introduction

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



PGE_2 (a prostaglandin)

Prostaglandin Structure

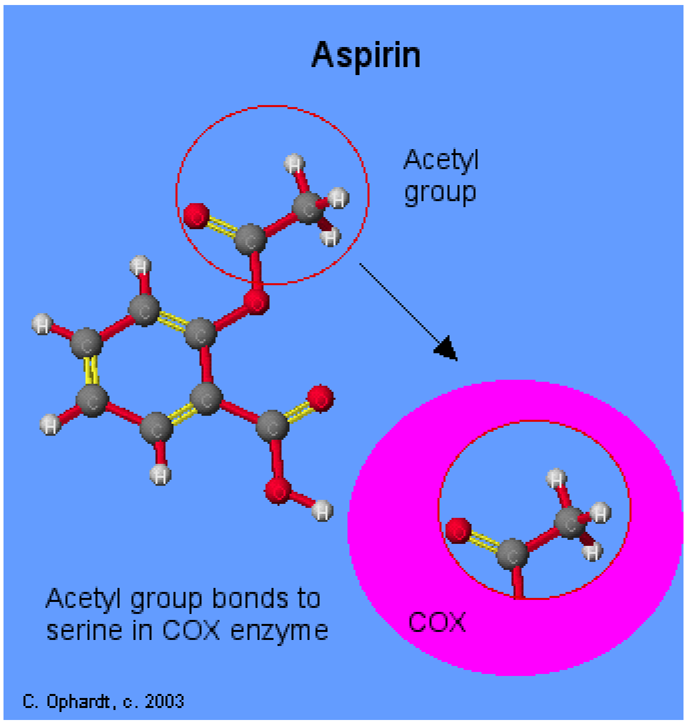
Prostaglandins are unsaturated carboxylic acids, consisting of of a 20 carbon skeleton that also contains a five member ring and are based upon the fatty acid, arachidonic acid. There are a variety of structures one, two, or three double bonds. On the five member ring there may also be double bonds, 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.



Thromboxanes and prostacyclins play an important role in the formation of blood clots. The process of clot formation begins with an aggregation of blood platelets. This process is strongly stimulated by thromboxanes and inhibited by prostacyclin. Prostacyclin is synthesized in the walls of blood vessels and serves the physiological function of preventing needless clot formation. In contrast, thromboxanes are synthesized within platelets, and, in response to vessel injury, which causes platelets to adhere to one another and to the walls of blood vessels thromboxanes are released to promote clot formation. Platelet adherence is increased in arteries that are affected by the process of atherosclerosis. In affected vessels the platelets aggregate into a plaque called a thrombus along the interior surface of the vessel wall. A thrombus may partially or completely block (occlude) blood flow through a vessel or may break off from the vessel wall and travel through the bloodstream, at which point it is called an embolus. When an embolus becomes lodged in another vessel where it completely occludes blood flow, it causes an embolism. Thrombi and emboli are the most common causes of heart attack (myocardial infarction). Therapy with daily low doses of aspirin (an inhibitor of cyclooxygenase) has had some success as a preventive measure for people who are at high risk of heart attack.

Inflammation

Prostaglandins play a pivotal role in inflammation, a process characterized by redness (rubor), heat (calor), pain (dolor), and swelling (tumor). The changes associated with inflammation are due to dilation of local blood vessels that permits increased blood flow to the affected area. The blood vessels also become more permeable, leading to the escape of white blood cells (leukocytes) from the blood into the inflamed tissues. Thus, drugs such as aspirin or ibuprofen that inhibit prostaglandin synthesis are effective in suppressing inflammation in patients with inflammatory but noninfectious diseases, such as rheumatoid arthritis.

Smooth muscle contraction

Although prostaglandins were first detected in semen, no clear role in reproduction has been established for them in males. This is not true in women, however. Prostaglandins play a role in ovulation, and they stimulate uterine muscle contraction—a discovery that led to the successful treatment of menstrual cramps (dysmenorrhea) with inhibitors of prostaglandin synthesis, such as ibuprofen. Prostaglandins also play a role in inducing labour in pregnant women at term, and they are given to induce therapeutic abortions.

The function of the digestive tract is also affected by prostaglandins, with prostaglandins either stimulating or inhibiting contraction of the smooth muscles of the intestinal walls. In addition, prostaglandins inhibit the secretion of gastric acid, and therefore it is not surprising that drugs such as aspirin that inhibit prostaglandin synthesis may lead to peptic ulcers. Prostaglandin action on the digestive tract may also cause severe watery diarrhea and may mediate the effects of vasoactive intestinal polypeptide in Verner-Morrison syndrome, as well as the effects of cholera toxin.

NSAIDs work by inhibiting the synthesis of molecules known as prostaglandins, which are important mediators of inflammation and pain. Prostaglandins are synthesized in the blood vessel wall and act locally to relax blood vessels, resulting in increased blood flow. Following insult or injury to tissues, this process results in inflammation.

Aspirin is technically an NSAID, but the term is generally applied to a newer class of drugs, including ibuprofen and similar drugs (e.g., naproxen, ketoprofen) that, like aspirin, inhibit prostaglandin synthesis. They tend to produce only mild side effects, though prolonged use or overuse can result in gastrointestinal bleeding; the drugs are also associated with an increased risk of adverse cardiovascular effects.

Lipid Storage,

Lipids are a diverse group of organic compounds that are essential for several biological functions, ranging from energy storage to cell signaling. They are loosely described as organic, water-insoluble compounds demonstrating high solubility in non-polar solvents.

The diversity of lipids is reflected in the variety of natural structures. Unlike other biological molecules that are comprised of relatively few components, lipids are complex. Their biosynthesis involves numerous biochemical transformations, generating vast quantities of lipid molecules.

A specific set of nomenclature, chemical representation, and a classification system are therefore necessary to not only comprehensively characterize lipids, but also enable bioinformatic databases, tools and methodologies to study their role on a systems-biology level.

Fatty acids

Fatty acids are comprised of a polar head (a carboxyl group) and a nonpolar aliphatic tail. They span a length of between 4 and 36 carbons in length. The exhibition of both polar and non-polar properties is described as amphipathy. Within a cell, they are associated with other biological molecules.

Fatty acids can be broadly classified as **saturated or unsaturated**. The physical properties of fatty acids depend on length and degree of unsaturation of their aliphatic chains. In their fully **saturated** forms, the most stable conformation is the fully extended form, in which steric hindrance of neighboring atoms is minimized. This allows ordering into crystalline arrays with the aliphatic tails associating through *van der waals* forces.

In **unsaturated fatty acids**, double bonds cause kinks to appear in the chain; this prevents tight packing of fatty acids and alters the properties of the arrays they form. This affects membrane properties as fatty acids are important constituents of phospholipids, which comprise many membranes.

In the body, fatty acids are released from triacylglycerols during fasting to provide a source of energy. They circulate in the blood by binding to a protein carrier, serum albumin where they travel to the tissue for use in metabolism or biosynthetic pathways.

Triacylglycerols

Triacylglycerols are the primary storage form of long-chain fatty acids, which are broken down for energy and used in the structural formation of cells. Triacylglycerols are composed of glycerol (1,2,3-trihydroxypropane) and 3 fatty acids to form a triester.

Simple triacylglycerols contain identical fatty acids, however, most naturally occurring fatty acids are mixed. Triacylglycerols are stored in adipocytes in vertebrates or as soils in the seed of plants. Both adipocytes and seeds contain lipase enzymes to liberate fatty acids for export when they are required for fuel or biosynthetic purposes.

In some animals, triacylglycerols provide a means of insulation; this is particularly notable in arctic-dwelling mammals such as walruses, polar bears, and penguins. Polyunsaturated fatty acids are important as constituents of the phospholipids and form the membranes of the cells.

Tri-, Di- and Monoacylglycerols

Triacylglycerol, diacylglycerol, and monoacylglycerol contain three, two, or one fatty acid(s) respectively, which are esterified to trihydroxy-alcohol glycerol. While triacylglycerol functions predominantly as an energy storage molecule, diacylglycerol and monoacylglycerol species perform signaling roles as secondary messengers or ligands for signaling proteins such as protein kinases. These proteins are implicated in diverse pathways including cell proliferation, growth and protein transport.

Sterols

Sterols are comprised of tetracyclic rings, a feature common to human sex pheromones. Sterols can be conjugated to fatty acids, fatty acid esters, and sugars. Sterols have a fundamental effect in membrane properties, affecting fluidity, membrane transport and function of membrane proteins.

Sterols interact with phospholipids to stiffen and impermeabilize the membrane. They work specifically to alter the dynamics of a process known as phase transition. This describes the transition of a membrane from the solid phase (gel phase) to liquid at a defined temperature.

Specifically, sterols may eliminate this ability of membranes to transition. Alongside sphingolipids, sterols may form structures called lipid rafts which are implicated in signaling and membrane trafficking. Outside of the cell membrane, sterols, particularly cholesterols, are precursor of bile acids, vitamin D and steroidal hormones.

Membrane lipids are a group of compounds (structurally similar to fats and oils) which form the double-layered surface of all cells (lipid bilayer). The three major classes of membrane lipids are phospholipids, glycolipids, and cholesterol. Lipids are amphiphilic: they have one end that is soluble in water ('polar') and an ending that is soluble in fat ('nonpolar'). By forming a double layer with the polar ends pointing outwards and the nonpolar ends pointing inwards membrane lipids can form a 'lipid bilayer' which keeps the watery interior of the cell separate from the watery exterior. The arrangements of lipids and various proteins, acting as receptors and channel pores in the membrane, control the entry and exit of other molecules and ions as part of the cell's metabolism. In order to perform physiological functions, membrane proteins are facilitated to rotate and diffuse laterally in two dimensional expanse of lipid bilayer by the presence of a shell of lipids closely attached to protein surface, called annular lipid shell.

Membrane lipids are a group of compounds (structurally similar to fats and oils) which form the double-layered surface of all cells (lipid bilayer). The three major classes of membrane lipids are phospholipids, glycolipids, and cholesterol. Lipids are amphiphilic: they have one end that is soluble in water ('polar') and an ending that is soluble in fat ('nonpolar'). By forming a double layer with the polar ends pointing outwards and the nonpolar ends pointing inwards membrane lipids can form a 'lipid bilayer' which keeps the watery interior of the cell separate from the watery exterior. The arrangements of lipids and various proteins, acting as receptors and channel pores in the membrane, control the entry and exit of other molecules and ions as part of the cell's metabolism. In order to perform physiological functions, membrane proteins are facilitated to rotate and diffuse laterally in two dimensional expanse of lipid bilayer by the presence of a shell of lipids closely attached to protein surface, called annular lipid shell.

Biological roles

The bilayer formed by membrane lipids serves as a containment unit of a living cell. Membrane lipids also form a matrix in which membrane proteins reside. Historically lipids were thought to merely serve a structural role. Functional roles of lipids are in fact many: They serve as regulatory agents in cell growth and adhesion. They participate in the biosynthesis of other biomolecules. They can serve to increase enzymatic activities of enzymes.[1]

Non-bilayer forming lipid like monogalactosyl diglyceride (MGDG) predominates the bulk lipids in thylakoid membranes, which when hydrated alone, forms reverse hexagonal cylindrical phase. However, in combination with other lipids and carotenoids/chlorophylls of thylakoid membranes, they too conform together as lipid bilayers

Membrane lipid language

The membrane metabolites of polyunsaturated fatty acids (PUFAs) have an essential role in intercellular biochemical communications. Crawford (2010) in his chapter Long-chain polyunsaturated fatty acids in human brain evolution reported, with regard to the language of lipids, that the importance of the increased complexity of these lipids was brought about by aerobic metabolism, whereby the simple language of prokaryotes, with only a few words, was developed into a vocabulary of over 1,000 words of eukaryote cells.

About 500 million years ago, some nervous cells and some gut cells of vertebrates migrated and specialized in a more complex nervous system: the brain, and in uptake and storage of iodocompounds: the follicular thyroid. In the PUFAs, the presence of a double bond between two carbons (or carbon-carbon double bond) provides them with the possibility of changing their molecular structure through enzymes such as phospholipases, cyclooxygenases and lipoxygenases, etc. The resulting substances, called eicosanoids: prostaglandins (PG), leukotrienes (LT), lipoxins and thromboxane (TX); and docosanoids: resolvins, protectins, and maresins, are powerful lipid mediators that produce specific actions in the organism; they organize inflammation, hemodynamic, immune response and the repair of tissue.

Many PUFAs cannot be synthesized by animal organisms and are considered essential, and therefore should be incorporated into diets. These are: linoleic acid (C18:2 n-6), omega-6 and alpha-linolenic (C18:3 n-3) omega-3, arachidonic acid (AA) – omega – 6 (C20: 4n-6), and docosahexaenoic acid (DHA) – omega-3 (C22:6n-3). These PUFAs are incorporated into the phospholipidic membrane of all the cells of an organism. In parallel, ectodermic cells, differentiated into neuronal cells, became the primitive nervous system and brain. Both these cells synthesized iodolipids, as novel words of the chemical lipid language developed among cell membranes during the evolution of life. These biochemical signals among cells, since contact and modification of membranes in multicellular organisms formed the bases of adaptation to terrestrial environments, and their alterations are important in the mechanism of apoptosis, carcinogenesis and degenerative diseases, as well as for understand some problems discussed regarding human evolution (as Aquatic ape hypothesis).[3][4][5][6][7]

Phospholipids

Phospholipids and glycolipids consist of two long, nonpolar (hydrophobic) hydrocarbon chains linked to a hydrophilic head group.

The heads of phospholipids are **phosphorylated** and they consist of either:

- **Glycerol** (and hence the name **phosphoglycerides** given to this group of lipids), or
- **Sphingosine** (e.g. sphingomyelin and ceramide).

Glycerol dialkyl glycerol tetraether (GDGT) is helping to study ancient environmental factors.[8]

Glycolipids

The heads of glycolipids (glyco- stands for sugar) contain a sphingosine with **one or several sugar units** attached to it. The hydrophobic chains belong either to:

- two fatty acids (FA) – in the case of the phosphoglycerides, or
- one FA and the hydrocarbon tail of sphingosine – in the case of sphingomyelin and the glycolipids.

Galactolipids – monogalactosyl diglyceride (MGDG) and digalactosyl diglycreride (DGDG) form the predominant lipids in higher plant chloroplast thylakoid membranes; liposomal structures formed by total lipid extract of thylakoid membranes have been found sensitive to sucrose as it turns bilayers into micellar structures.

Fatty acids

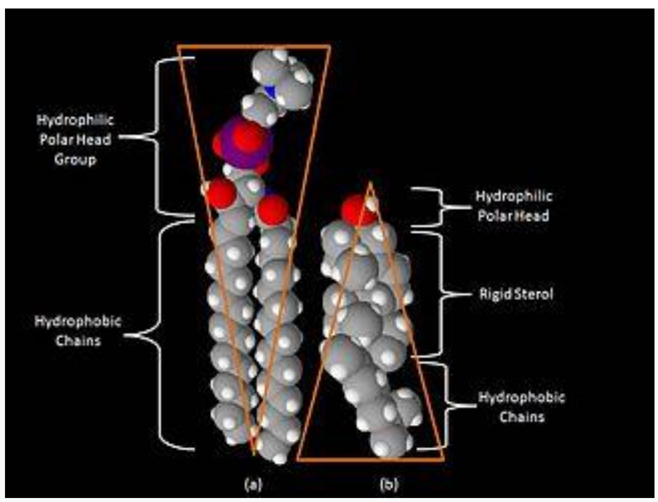
The fatty acids in phospho- and glycolipids usually contain an even number, typically between 14 and 24, of carbon atoms, with 16- and 18-carbon being the most common. FAs may be saturated or unsaturated, with the configuration of the double bonds nearly always cis. The length and the degree of unsaturation of FAs chains have a profound effect on membranes' fluidity. Plant thylakoid membranes maintain high fluidity, even at relatively cold environmental temperatures, due to the abundance of 18-carbon fatty acyl chains with three double bonds, linolenic acid, as has been revealed by 13-C NMR studies.

Phosphoglycerides

In phosphoglycerides, the hydroxyl groups at C-1 and C-2 of glycerol are esterified to the carboxyl groups of the FAs. The C-3 hydroxyl group is esterified to phosphoric acid. The resulting compound, called phosphatidate, is the simplest phosphoglycerate. Only small amounts of phosphatidate are present in membranes. However, it is a key intermediate in the biosynthesis of the other phosphoglycerides

Sphingolipids

Sphingosine is an amino alcohol that contains a long, unsaturated hydrocarbon chain. In sphingomyelin and glycolipids, the amino group of sphingosine is linked to FAs by an amide bond. In sphingomyelin the primary hydroxyl group of sphingosine is esterified to phosphoryl choline.



Space-filling models of (a) sphingomyelin and (b) cholesterol.

In glycolipids, the sugar component is attached to this group. The simplest glycolipid is cerebroside, in which there is only one sugar residue, either Glc or Gal. More complex glycolipids, such as gangliosides, contain a branched chain of as many as seven sugar residues.

Sterols

The best known sterol is cholesterol, which is found in humans. Cholesterol also occurs naturally in other eukaryote cell membranes. Sterols have a hydrophobic four-membered fused ring rigid structure, and a small polar head group.

Cholesterol is bio-synthesised from mevalonate via a squalene cyclisation of terpenoids. Cell membranes require high levels of cholesterol – typically an average of 20% cholesterol in the whole membrane, increasing locally in raft areas up to 50% cholesterol (- % is molecular ratio). It associates preferentially with sphingolipids (see diagram) in cholesterol-rich lipid rafts areas of the membranes in eukaryotic cells. Formation of lipid rafts promotes aggregation of peripheral and transmembrane proteins including dockingof SNARE and VAMP proteins. Phytosterols, such as sitosterol and stigmasterol, and hopanoids serve a similar function in plants and prokaryotes.

Lipids as Signals, cofactors and pigments

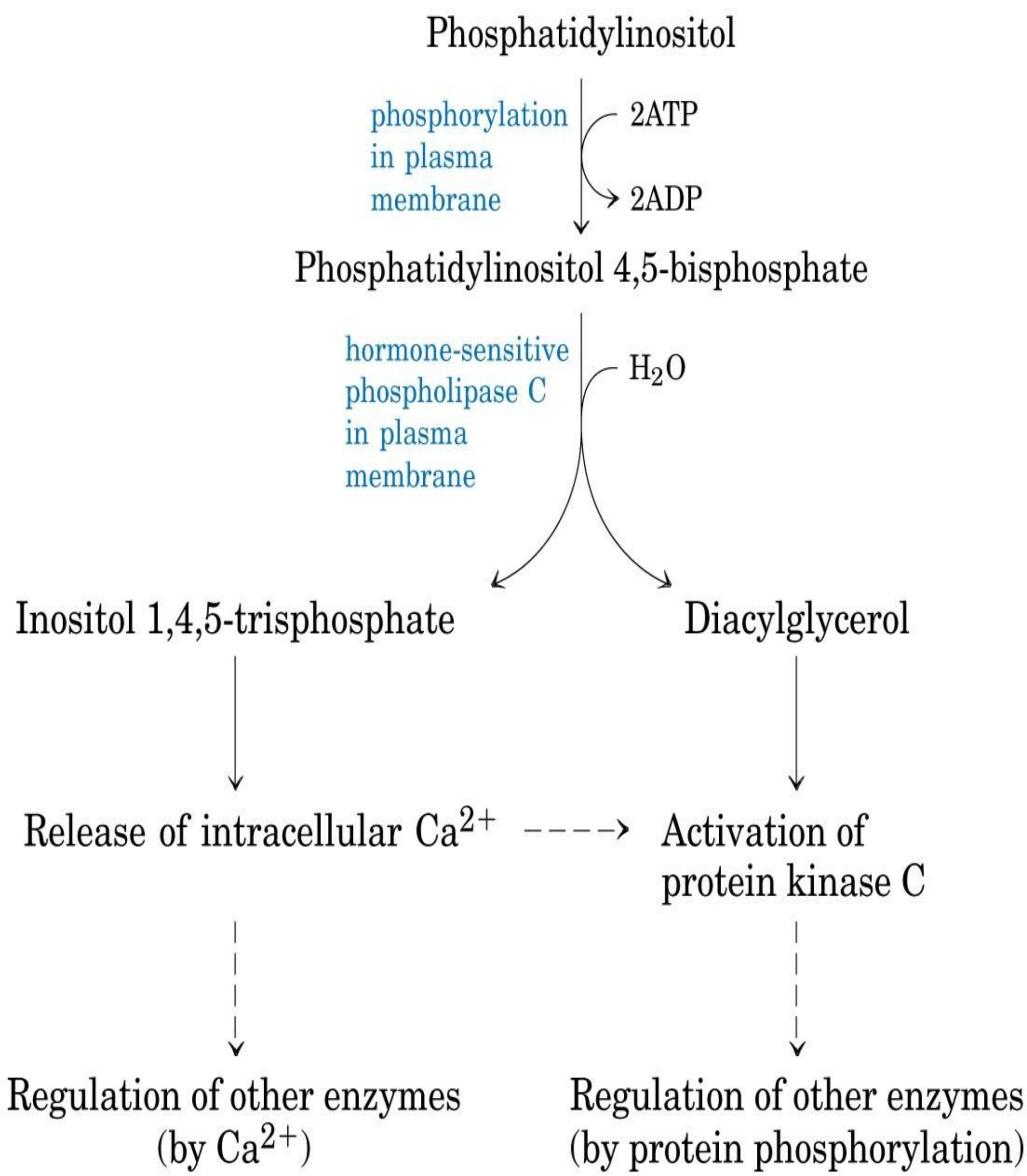
Group of lipids present in small amounts play various essential function

- Have active roles in metabolic processes as metabolite and messenger
- Potent signals and hormones carried in the blood from one tissue to others
- Intracellular messengers generated to response to outer signal
- Can function as cofactors
- Pigments
- Fat soluble vitamins

Phosphotidyl inositol: act as intracellular signals:

Intracellular messengers are released from the Phosphotidyl inositol in response to extra cellular signals interacting with receptors on the outer surface of the membrane

* Signals act through a series of steps



Eicosanoids: are paracrine hormones; substances that act only on site cells near the point of synthesis instead of being transported in the blood to act on other cells or tissues.

Eicosanoids are derived from membrane lipids and mainly from
Arachodonic acid

Prostaglandins

- C20 compounds
- Five carbon ring
- Affect a wide range of cellular and tissue function
- Act at low concentration and are involved in the production of pain and fever, regulationof blood pressure, blood coagulation and reproduction
- Produced and used locally
- Regulate the synthesis of the intracellular messenger (cAMP) which mediate the action of different hormones.

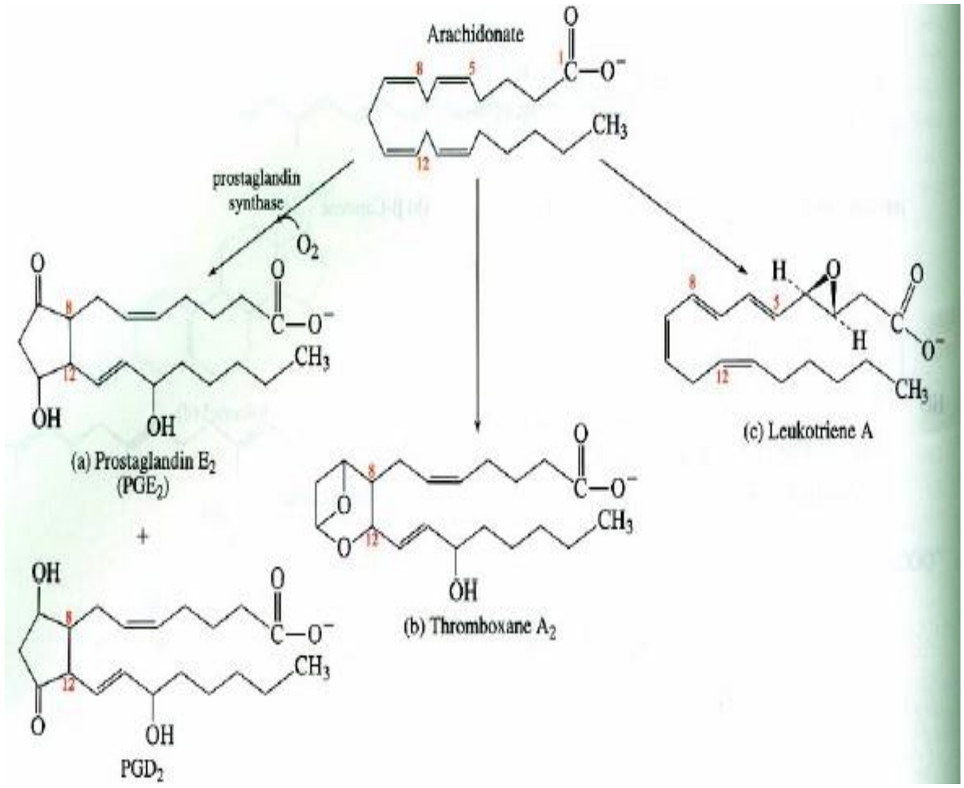
-Stimulate the contraction of smooth muscle in uterus

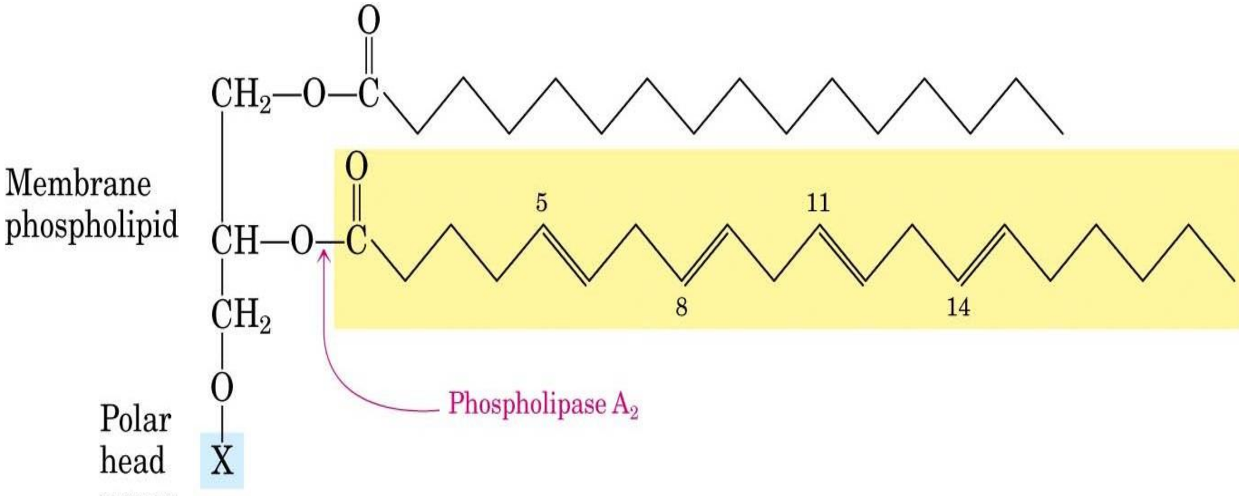
-Affect the blood flow

-Elevate the body temperature and mediate the inflammation and pain

1- **Thromboxanes:**
Six-memebred ring containing an ether, produced by the platelets (thrombocytes) and play role in formation of the blood clots

2- **Leukotriens:** contain conjugated double bonds, found in the leukocytes, powerful biological signals, induce contraction of muscles lining the airways of the lung. Over production cause asthmatic attack


Arachidonate
prostaglandin synthase
O_2
(a) Prostaglandin E_2 (PGE_2)
+
PGD_2
(b) Thromboxane A_2
(c) Leukotriene A


Membrane phospholipid
Polar head group
Phospholipase A_2

Aspirin and NSAIDs

•Aspirin inhibits the synthesis of prostaglandins from arachidonicacid by chemically modifying a serine residue of the enzyme PGH2 synthase (Cyclo oxygenase enzyme) preventing arachidonicacid from reaching the enzyme active site
•Non-steroidal anti-inflammatory drugs (NSAIDs) (ibuprofen and acetaminophen) non covalently bind to PGH2 synthase, also preventing arachidonicacid from reaching the enzyme active site

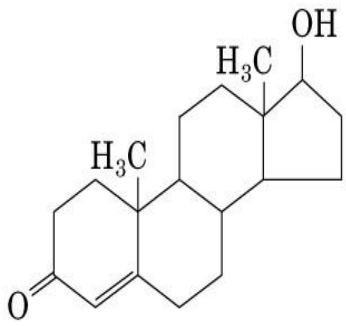
•Leukotrienes have been implicated in various inflammatory and hypersensitivity disorders (such as asthma). They are synthesized from arachidonateby an aspirin-insensitive pathway

Steroidal anti-inflammatory drug

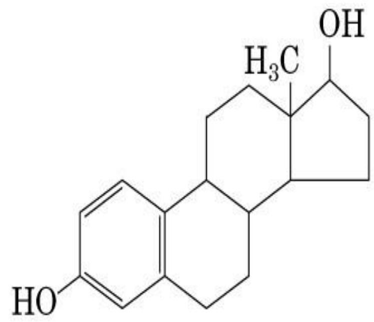
Prednisone and prednisolone inhibit the phospholipase A2 that release the Arachodinic acid from the phospholipids in the membrane synthesis of all eicosanoid will be inhibited

Steroidal Hormones

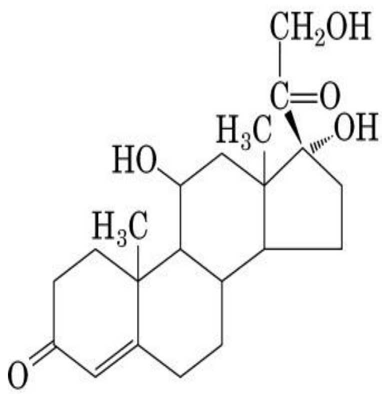
Steroids: oxidized form of the sterol, with the steroid nucleus but lack the alkyl chain -More polar than cholesterol Move through the blood on proteins carriers from site of production to target tissue Then bind to their receptors enter the nucleus affect the gene expression and metabolism



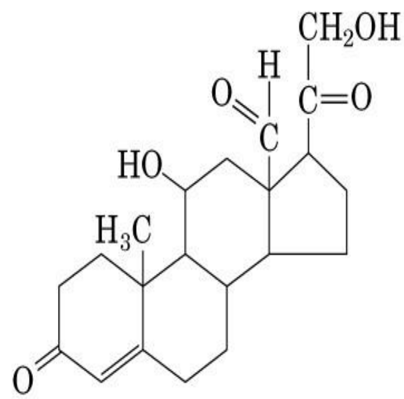
Testosterone



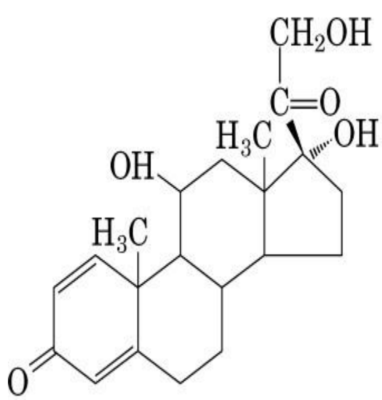
Estradiol



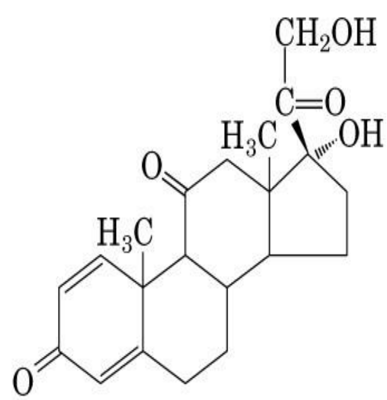
Cortisol



Aldosterone



Prednisolone



Prednisone

Lipid Soluble Vitamins

Vitamins: Compounds that are essential to the health of human and other animals and most of the vitamins cannot be synthesized by endogenously

Two classes of Vitamins

a. Fat soluble vitamins

b. Water soluble vitamin, Vit B and Vit C

Lipid-Soluble Vitamins and Their Functions

Vitamin	Function
Vitamin A	Serves as the site of the primary photochemical reaction in vision
Vitamin D	Regulates calcium (and phosphorus) metabolism
Vitamin E	Serves as an antioxidant; necessary for reproduction in rats and may be necessary for reproduction in humans
Vitamin K	Has a regulatory function in blood clotting

Vitamin D

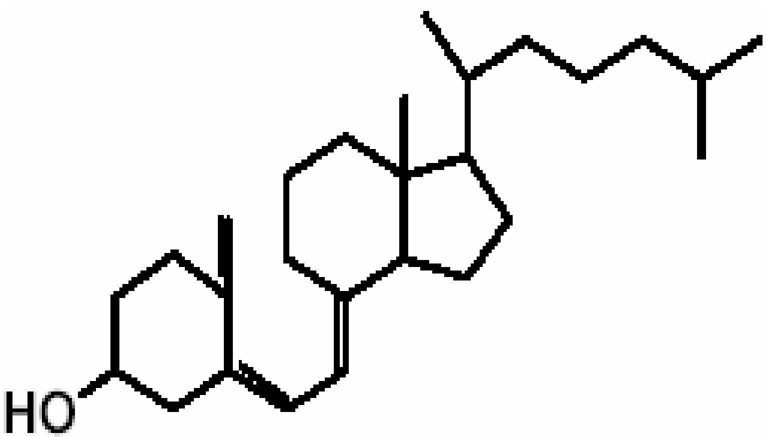
A group of structurally related compounds that play a role in the regulation of calcium and phosphorus metabolism

-the most abundant form in the circulatory system is vitamin D3 (Cholecalciferol) which is formed in the skin from 7-dehydrocholesterol

-Vit D3 is converted into the active form in two steps the first at the liver and the second at the kidney

-The active form of vit D3 (1,25-dihydroxycholecalciferol)

-Deficiency of Vit D3 defective bone formation and Rickets disease



Vitamin D_3

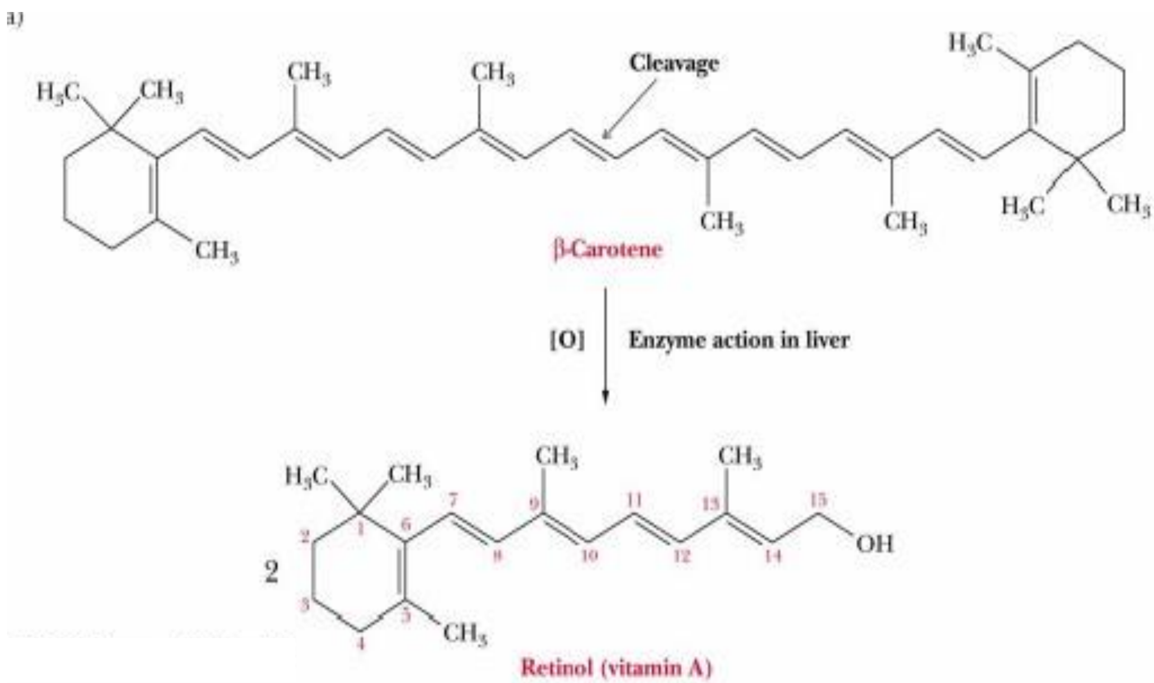
Vitamin A (Retinol)

•Vit A with its precursors and its derivatives function as hormones and as the *visual pigments in the eye*

- β-carotene: yellow pigments in the carrot

Retinoic acid : is a derivative of Vit A and can regulate gene expression in the development of epithelial tissue (skin)

Vitamin E



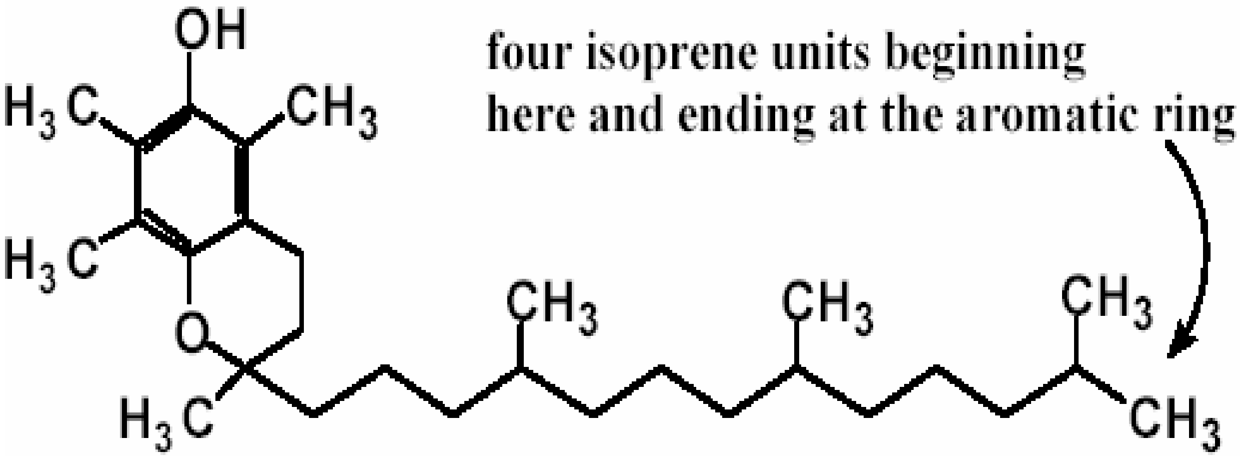
•Vitamin E is a group of compounds of similar structure; the most active is α-tocopherol

- Associates with cell membranes, lipids, lipoproteins in the blood

- An antioxidant; traps HOO• and ROO• radicals formed as a result of oxidation by O2 of unsaturated hydrocarbon chains in membrane phospholipids

 protect the unsaturated F.A from oxidation and prevent oxidative damage to membrane lipid

-Deficiency of Vit E : Rough skin, muscular weakness and sterility



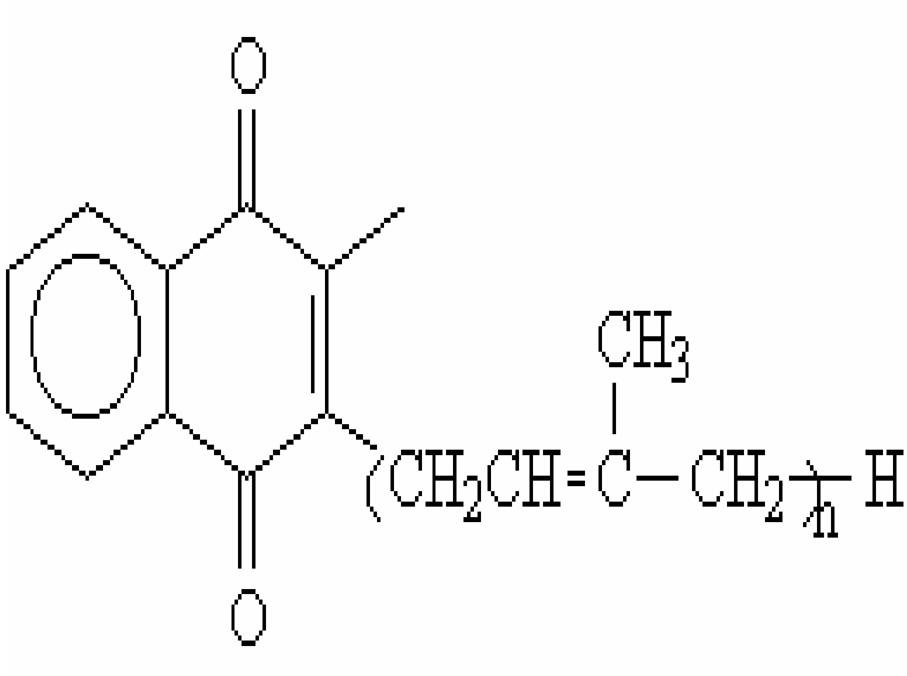
Vitamin E (α-Tocopherol)

Vitamin K

•*Blood clot factor: undergo a cycle of oxidation reduction during the formation of the active prothrombine*

•Different forms, most common n=8

•Functions in blood clotting



Vit K1 (Phylloquinone)