VITAMINS

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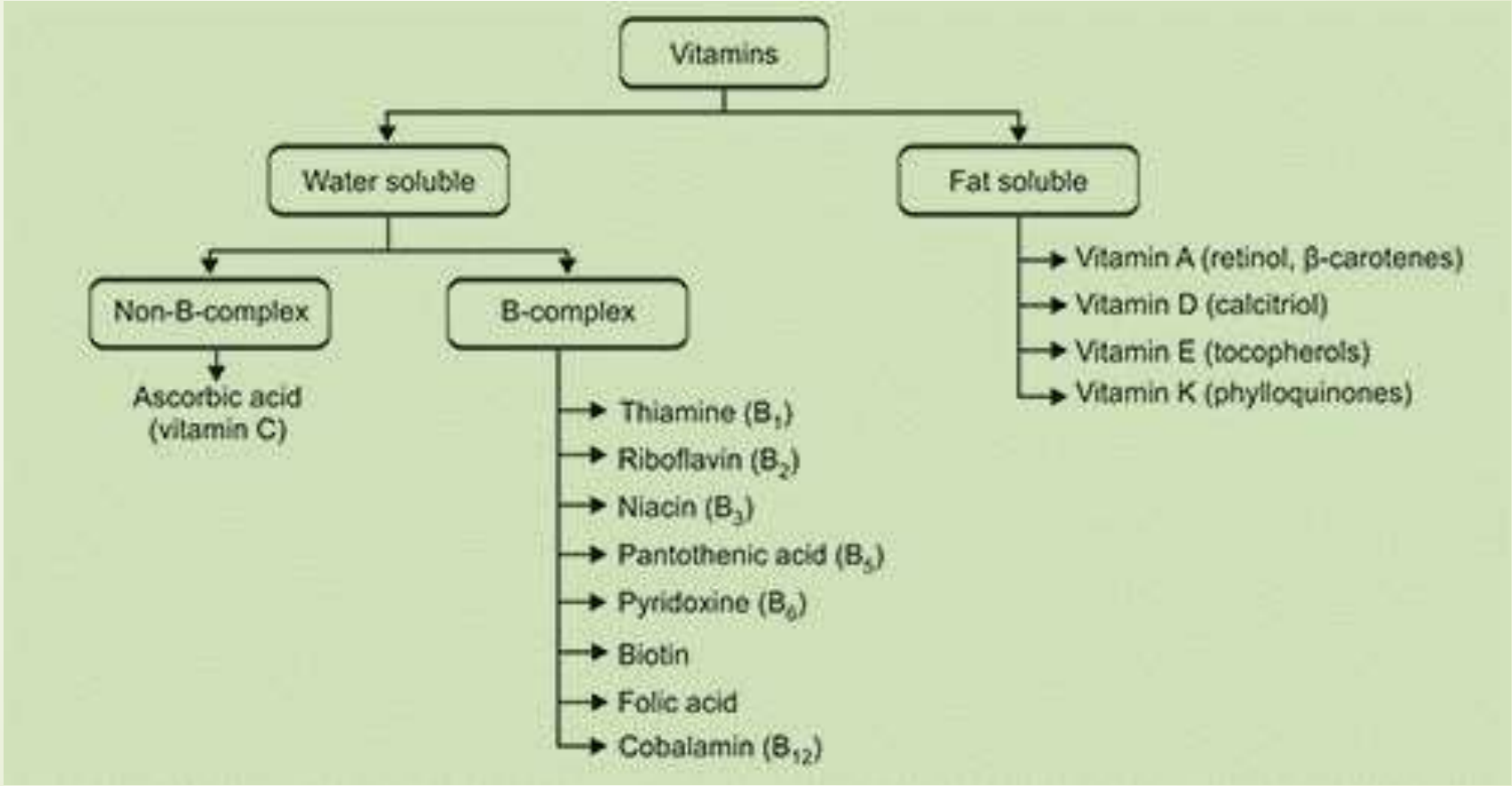
VITAMINS

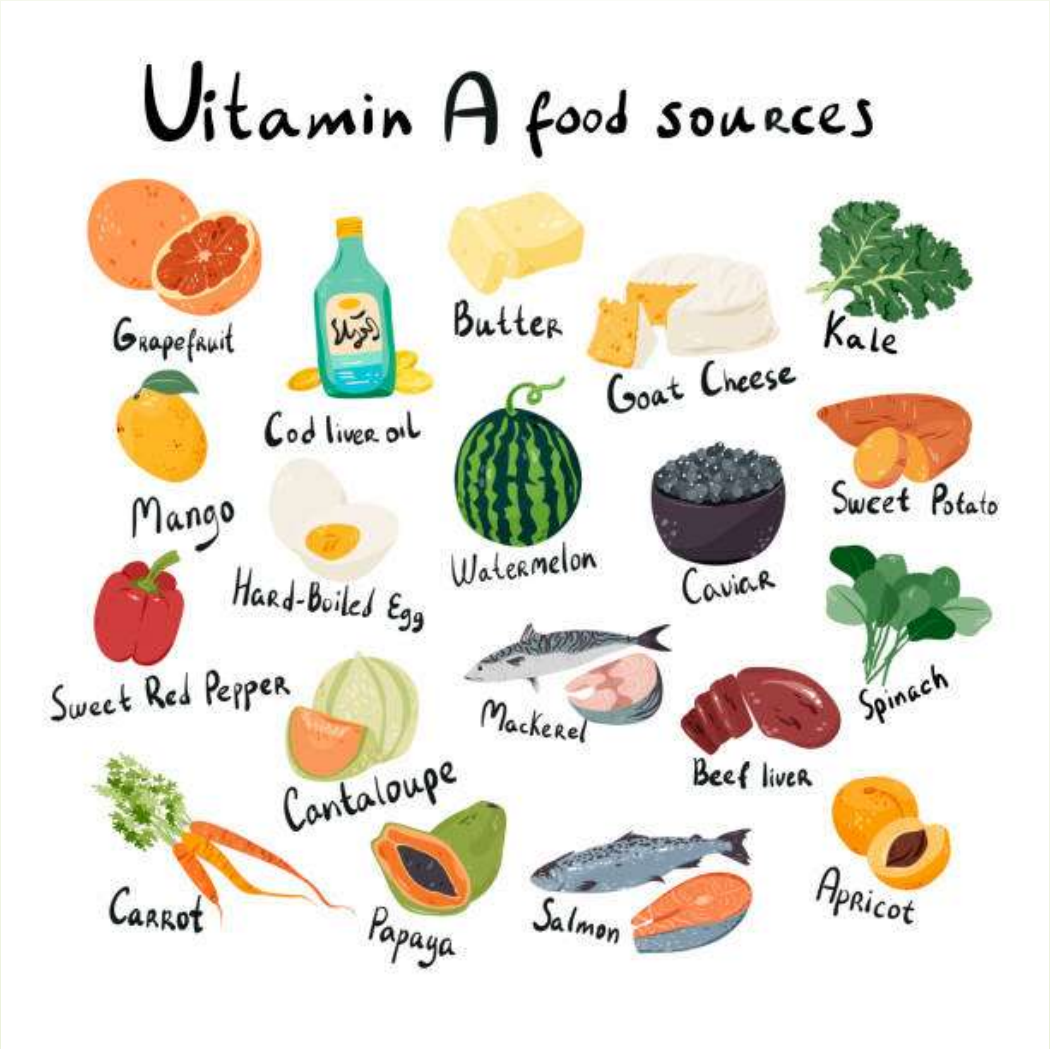
- Vitamins are a group of organic compounds which are essential for normal growth and nutrition and are required in small quantities in the diet because they cannot be synthesized by the body.
- The vitamins are natural and essential nutrients, required in small quantities and play a major role in growth and development, repair and healing wounds, maintaining healthy bones and tissues, for the proper functioning of an immune system, and other biological functions. These essential organic compounds have diverse biochemical functions.
- There are thirteen different types of vitamins and all are required for the metabolic processes. The discovery of the vitamins was begun in the year 1912 by a Polish American biochemist Casimir Funk. Based on his research and discoveries on vitamins, their sources, functions and deficiency disorders, he is considered as the father of vitamins and vitamin therapy.
- Vitamins cannot be synthesized by our body. Therefore, we need to get them from the food we consume or in extreme cases supplements to keep ourselves healthy.

CLASSIFICATION



VITAMIN A

The fat soluble vitamin A, as such is present only in foods of animal origin. However,its provitamins carotenes are found in plants.



COENZYME FORM

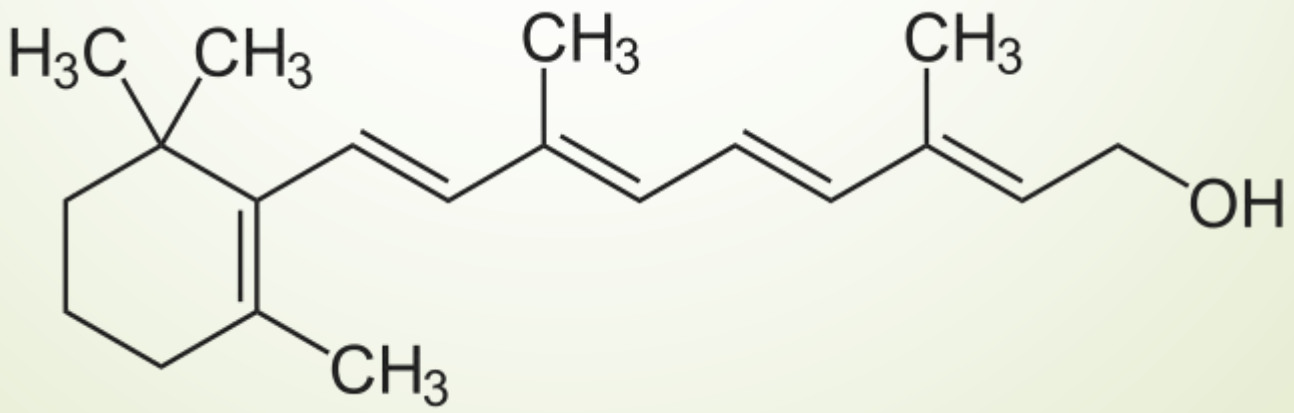
- The retinoids are a family of molecules that are related to dietary retinol (vitamin A).
- Vitamin A (and its metabolites) are important for vision, reproduction, growth, immune function, and maintenance of epithelial tissues.
- Retinoic acid is derived from the oxidation of retinol and mediates most of the actions of the retinoids.
- Retinol is oxidized to retinoic acid. Retinoic acid binds specifically to a family of nuclear receptors (retinoic acid receptors, RAR) and modulates gene expression in target tissues, such as epithelial cells. The activated retinoic acid–RAR complex binds to response elements on DNA and recruits activators or repressors to regulate retinoid-specific mRNA synthesis

CHEMICAL NATURE

The term retinoids is often used to include the natural and synthetic forms of vitamin A. Retinol, retinal and retinoic acid are regarded as vitamers of vitamin A.

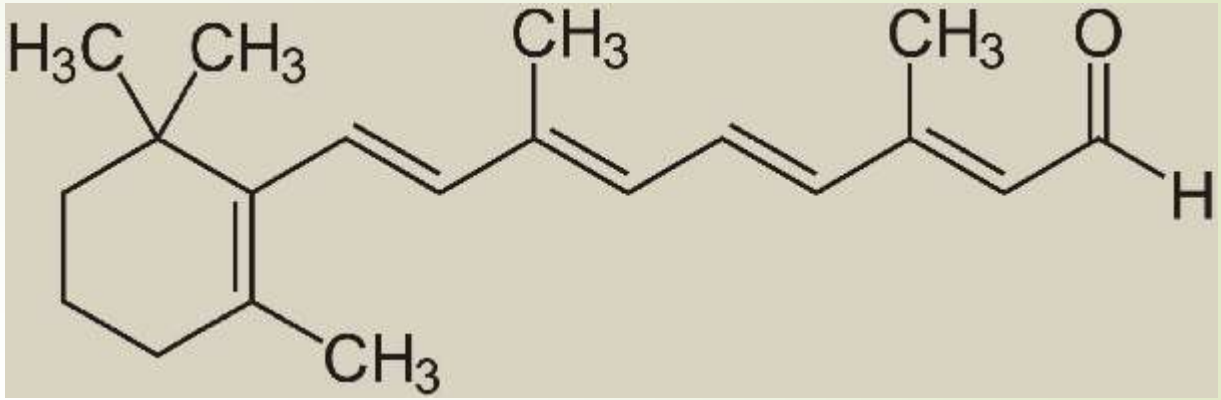
RETINOL (ALCOHOL):

- Primary alcohol containing β-ionone ring
- Side chain has two isoprenoid units
- Four double bonds
- One hydroxyl group



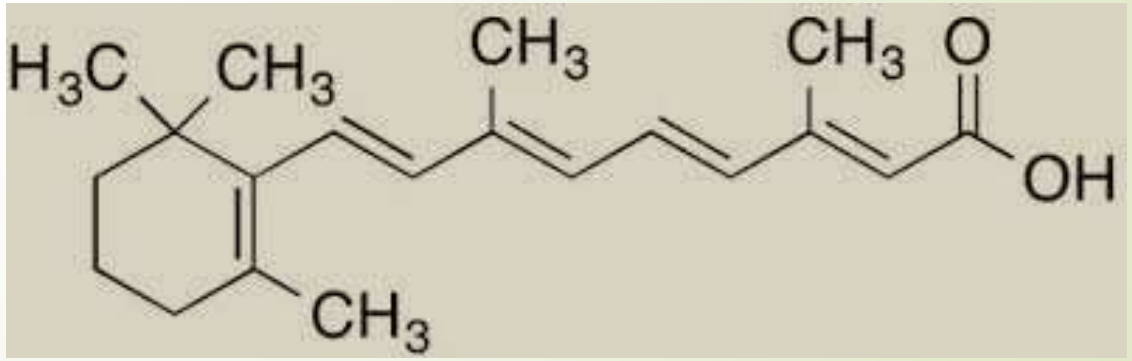
RETINAL (ALDEHYDE):

- Obtained by oxidation of retinol.
- Retinal and retinol are interconvertible.



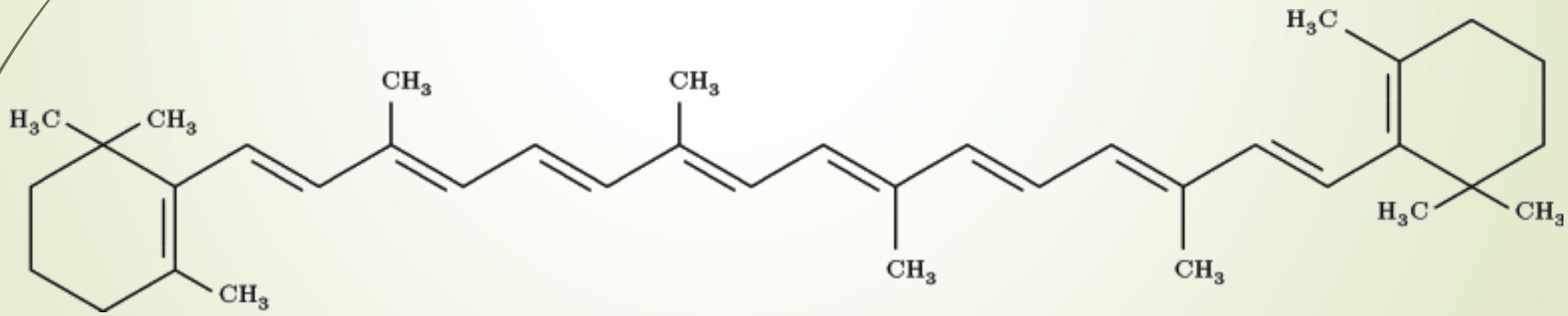
RETINOIC ACID (ACID):

- Produced by oxidation of retinal.
- Cannot give rise to formation of retinal or retinol.



B-CAROTENE (PROVITAMIN A):

- Found in plant foods
- Cleaved in intestine to produce 2 moles of retinal
- In humans, this conversion is inefficient, so it possess only about 1/6th activity compared to retinol.



Functions

- Vision
- Proper growth and differentiation
- Maintenance of epithelial cells
- Regulate protein synthesis
- Maintain healthy epithelial tissue by preventing keratin synthesis.
- Synthesis of glycoproteins and mucopolysaccharides
- Maintenance of immune system
- Antioxidant
- Cholesterol synthesis

Recommended dietary allowance (RDA)

- Expressed as retinol equivalents (RE)
- 1 retinol equivalent = 1μg retinol
  6 μg β-Carotene
  12 μg other carotenoids
- Adults = 1000 RE (man) and 800 RE (woman)

Vitamin A deficiency

- **Night blindness**: This causes you to have trouble seeing in low light. It will eventually lead to complete blindness at night.
- **Xerophthalmia:** With this condition, the eyes may become very dry and crusted, which may damage the cornea and retina.
- **Infection:** A person with a vitamin A deficiency can experience more frequent health concerns as they will not be able to fight off infections as easily.
- **Bitot spots:** This condition is a buildup of keratin in the eyes, causing hazy vision.
- **Skin irritation:** People experiencing vitamin A deficiency could have problems with their skin, such as dryness, itching, and scaling.
- **Keratomalacia:** This is an eye disorder involving drying and clouding of the cornea — the clear layer in front of the iris and pupil.
- **Keratinisation:** This is a process by which cells become filled with keratin protein, die, and form tough, resistant structures in the urinary, gastrointestinal and respiratory tracts.

VITAMIN D

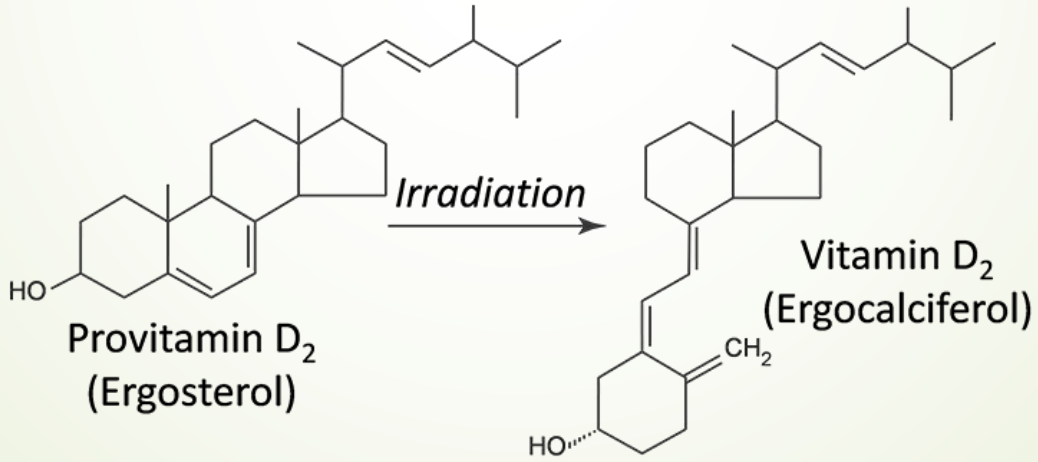
- Vitamin D is a fat soluble vitamin
- Resembles sterols in structure and functions like a hormone.

COENZYME FORM

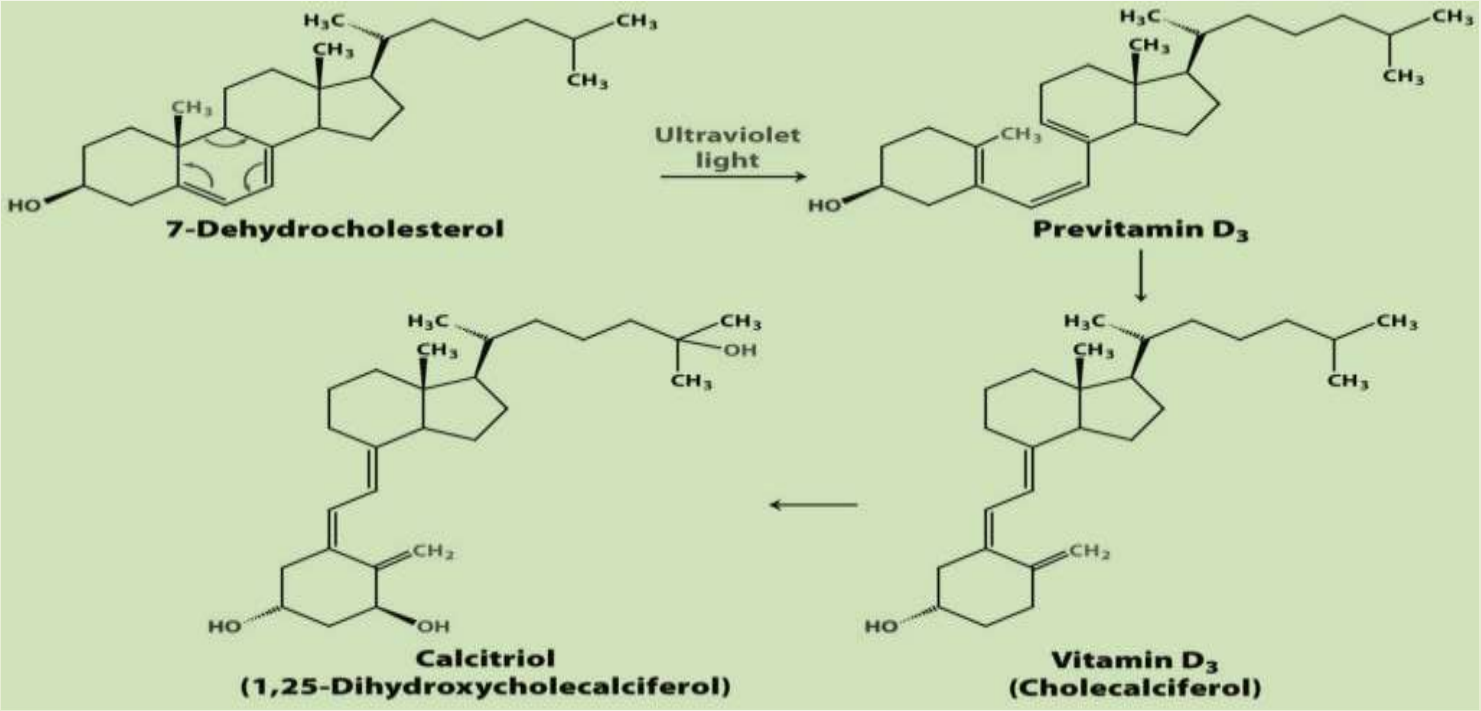
- The D vitamins are a group of sterols that have a hormone-like function.
- The active molecule, 1,25-dihydroxycholecalciferol (calcitriol), binds to intracellular receptor proteins. The receptor complex interacts with DNA in the nucleus of target cells in a manner similar to that of vitamin A and either selectively stimulates or represses gene transcription.
- The most prominent actions of calcitriol are to regulate the plasma levels of calcium and phosphorus. Within the gastrointestinal tract, calcitriol increases the transcription of calcium transport proteins, calbindin-D proteins, which results in increased uptake of calcium. It also increases reabsorption of phosphorus through a similar mechanism.

CHEMICAL NATURE

- Cholecalciferol (vitamin D3) is found in animals.
- Ergocalciferol (vitamin D2) is formed from ergosterol and is present in plants.
- Ergocalciferol and cholecalciferol are sources of vitamin D activity and are referred to as provitamins.



- During the courses of cholesterol biosynthesis, 7- dehydrocholesterol is formed as an intermediate. On exposure to sunlight, 7-dehydrocholesterol is converted to cholecalciferol in the skin (dermis and epidermis). Vitamin D is regarded as a sun-shine vitamin.
- Synthesis of 1,25-DHCC: Cholecalciferol is first hydroxylated at 25th position to 25-hydroxycholecalciferol (25-OHD3) by a specific hydroxylase present in liver. 25-OH D3 is the major storage and circulatory form of vitamin D. Kidney possesses a specific enzyme, 25-Hydroxycholecalciferol 1- hydroxylase which hydroxylates 25- hydroxycholecalciferol at position 1 to produce 1,25-dihydroxycholecalciferol (1,25-DHCC). 1,25 -DHCC contains 3 hydroxyl groups (1,3 and 25 carbons) hence referred to as Calcitriol.



BIOCHEMICAL FUNCTIONS

- Calcitriol(1,25-DHCC) is the biologically active form of vitamin D. It regulates the plasma levels of calcium and phosphate. Calcitriol acts at 3 different levels (intestine, kidney and bone) to maintain plasma calcium (normal 9-11ms/dl).
- Action of calcitriol on the intestine: Calcitriol increase the intestinal absorption of calcium and phosphate. In the intestinal cells, calcitriol binds with a cytosolic receptor to form a calcitriol-receptor complex. This complex then approaches the nucleus and interacts with a specific DNA leading to synthesis of a specific calcium binding protein. This protein increases the calcium uptake by the intestine.
- Action of calcitriol on the bone: In the osteoblasts of bone, calcitriol stimulates calcium uptake for deposition as calcium phosphate. Thus calcitriol is essential for bone formation.
- Action of calcitriol on the kidney: Calcitriol is also involved in minimizing the excretion of calcium and phosphate through the kidney, by decreasing their excretion and enhancing reabsorption.
- Vitamin D plays a role in the process of cell proliferation and maturation. It regulates the level of the enzyme alkaline phosphatase in the serum. Phosphatase helps in the deposition of Ca3(PO4)2 in bones and teeth.

RECOMMENDED DIETARY ALLOWANCE (RDA)

- The daily requirement of vitamin D is 400 International units or 10µg of cholecalciferol. In countries with good sunlight (like India), the RDA for vitamin D is 200 IU (or 5µg cholecalciferol).

DEFICIENCY SYMPTOMS OF VITAMIN D

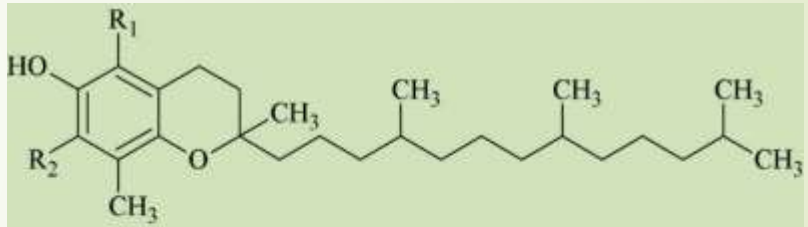
- Deficiency of vitamin D leads to demineralization of bone. The result is rickets in children and osteomalacia in adults.
- Rickets in children is characterized by bone deformities due to incomplete mineralization, resulting in soft and pliable bones and delay in teeth formation. In rickets, the plasma level of calcitriol is decreased and alkaline phosphatase activity is elevated. In case of osteomalacia (adult rickets) demineralization of the bones occurs (bones become softer), increasing the susceptically to fractures.
- Hypervitaminosis D: Vitamin D is stored mostly in liver and slowly metabolized. Among the vitamins, vitamin D is the most toxic in overdoses (10-100 times RDA). Hypervitaminosis D may lead to formation of stones in kidneys (renal calculi). High consumption of vitamin D is associated with: Loss of appetite, Nausea, Increased thirst, Loss of weight, etc.

VITAMIN E

- Vitamin E is chemically known as tocopherol (Greek: tocos = childbirth, piro = to bear and ol = alcohol) • An alcohol was capable to prevent reproductive failure in animals • Hence it is known as anti-sterility vitamin

CHEMICAL NATURE

- Vitamin E is the name given to group of tocopherols and tocotrienols
- About 8 tocopherols have been identified. Alpha- tocopherol.l is most active The tocopherols are derivatives of 6-hydroxy chromane (tocol) ring with isoprenoid side chain. The antioxidant property is due to the chromane ring. There are four main forms of tocopherols. They are



Tocopherol	R_1	R_2
α-	CH_3	CH_3
β-	CH_3	H
γ-	H	CH_3
δ-	H	H

- α -tocopherol : 5,7,8 trimethyl tocol
- β -tocopherol : 5,8 dimethyl tocol
- γ -tocopherol :7,8 dimethyl tocol
- δ -tocopherol : 8 methyl tocopherol

- Tocotrienols : There are four related vitamin E compounds called α,β,γ and δ tocotrienols

COENZYME FORM

The E vitamins consist of eight naturally occurring tocopherols, of which α - tocopherol is the most active.

- The primary function of vitamin E is as an antioxidant in prevention of the nonenzymatic oxidation of cell components.
- Vitamin E deficiency in adults is usually associated with defective lipid absorption or transport.
- Vitamin E is absorbed along with fat in the upper small intestine. Vitamin E combines with Bile salts (micelles) to form mixed micelle and taken up by the mucosal cell. In the mucosal cell, it is incorporated into chylomicrons.
- Dietary vitamin E is incorporated to chylomicrons. In the circulation, chylomicrons transport vitamin E to the peripheral tissue or to the liver. Hepatic vitamin E is incorporated to VLDL. In the circulation, VLDL is converted LDL. Vitamin E is transported with LDL to reach the peripheral tissues including adipose tissue. Mainly stored in liver and adipose tissue. Present in biological membranes, because of its affinity to phospholipids

BIOCHEMICAL FUNCTIONS

- Most of the functions of the vitamin E are related to its antioxidant property. It prevents the non-enzymatic oxidations of various cell components by molecular oxygen and free radicals such as superoxide and hydrogen peroxide (H2O2) .
- It prevents the peroxidation of PUFA.
- It protects the RBC from hemolysis by oxidizing agents (H2O2).
- Vitamin E preserves and maintains germinal epithelium of gonads for proper reproductive function
- It increases the synthesis of heme by enhancing the activity of enzyme – δ amino levulinic acid (ALA) synthase and ALA dehydratase.
- It is required for cellular respiration – through ETC (Stabilize coenzyme Q).
- It is required for proper storage of creatine in skeletal muscle.
- It is required for absorption of amino acids from intestine.
- It is involved in synthesis of nucleic acids.
- Vitamin E is recommended for the prevention of chronic diseases such as cancer and heart disease.

RECOMMENDED DIETARY ALLOWANCE (RDA)

- Males -10 mg/day
- Females - 8 mg/day
- Pregnancy - 10 mg/day
- Lactation - 12 mg/day
- 15 mg of vitamin E is equivalent to 33 IU
- Pharmacological dose is 200-400 IU/day

VITAMIN E DEFICIENCY

- In humans, deficiency of vitamin E is seen in Premature infants: Transfer of vitamin E from maternal blood occurs during last few weeks of pregnancy. Premature infants will have vitamin E deficiency.
- Genetic vitamin E deficiency: It is caused by lack of a protein that normally transports α-tocopherol from hepatocytes to VLDL.
- Hemolytic anemia or macrocytic anemia seen in premature infants. In adults, increased susceptibility of erythrocytes for hemolysis under oxidative stress.
- Vitamin E deficiency leads to increased oxidation of PUFA, with consumption of oxygen and production of peroxides. Peroxides increase the intracellular hydrolase activity. The hydrolases catalyze breakdowns in muscle and produce muscular dystrophy. The muscle creatine is low and creatinuria occurs.
- Oxidation of PUFA in rods leads to oxidative damage in retina.
- Deficiency in animals: Muscular dystrophy and reproductive failure.

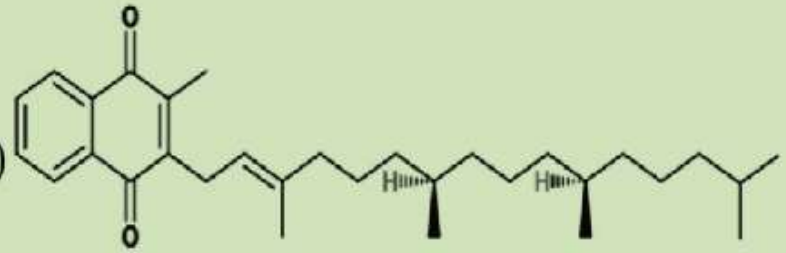
Vitamin K

- Vitamin K is the only fat soluble vitamin with a specific coenzyme function. It is required for the production of blood clotting factors, essential for coagulation (in German – Koagulation; hence called as vitamin K)

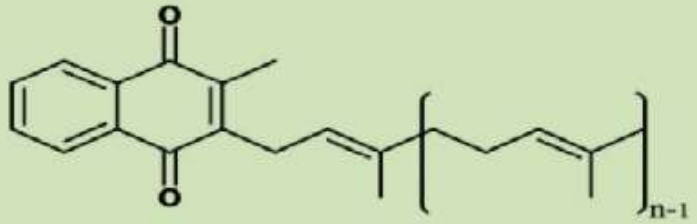
CHEMICAL NATURE

- Vitamin K exists in different forms: Vitamin – K1, Vitamin - K2 & Vitamin - K3.
- K1: It is phylloquinone. Present in plants. Isolated from alfalfa leaves. It has phytyl side chain.
- K2: It is menaquinone. Produced by the intestinal bacteria and also found in animals. It has isoprenyl side chain.
- K3: Also known as menadione. It is a synthetic form of vitamin K. It lacks side chain and it is water soluble.
- All the three vitamins (K1, K2, K3) are naphthoquinone derivatives.
- Isoprenoid side chain is present in K1 & K2.
- Three vitamins are stable to heat. Their activity is lost by oxidizing agents, strong acids and alkalies

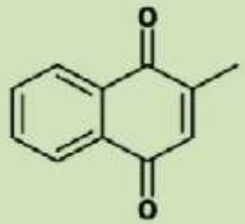
Vitamin K1
(phylloquinone)



Vitamin K2
(menaquinone)



Vitamin K3
(menadione)



COENZYME FORM

1. Vitamin K act as a coenzyme for the carboxylation of glutamic acid residues present in the protein and this reaction is catalyzed by a carboxylase (microsomal). It involves the conversion of glutamate (Glu) to γ-carboxyglutamate (Gla) and requires vitamin K,O2 and CO2 o The formation of γ - carboxyglutamate is inhibited by dicumarol, an anticoagulant found in spoilt sweet clover
2. Warfarin is a synthetic analogue that can inhibit vitamin K action. Role of Gla in clotting: γ - Carboxyglutamic acid (Gla) residues of clotting factors are negatively charged (COO-) and they combine with Positively charged calcium ions (Ca2+) to form a complex. The complex binds to the phospholipids on the membrane surface of the platelets o Leads to increased conversion of prothrombin to thrombin.

BIOCHEMICAL FUNCTIONS

1. The functions of vitamin K are concerned with blood clotting process. It brings about post-translational modification of certain blood clotting factors. The clotting factors II, VII, IX and X are synthesized as inactive precursors in the liver.
2. Vitamin K is also required for the carboxylation of glutamic acid residues of osteocalcin, a calcium binding protein present in the bone. Osteocalcin is involved in the regulation of bone mineralization. Osteocalcin acts by its ability to bind hydroxyapatite. The synthesis of osteocalcin is regulated by 1,25 DHCC.
3. Vitamin K is required for ETC and oxidative phosphorylation.

RECOMMENDED DIETARY ALLOWANCE (RDA)

- 70-140 μg / day.
- Approximately equal amounts are provided by the synthesis of vitamin by the intestinal bacterial flora.

DEFICIENCY

1. Deficiency in newborn infants: Very little vitamin K crossing the placental barrier from maternal circulation.
2. Sterile bacterial flora caused by administration of antibiotics results in non-availability of microbial source of vitamin K. Clinical features: Prolongation of bleeding and prothrombin time (PT). Measurement of PT is an index of liver function. Liver function is lowered, prolongation of PT occurs due to deficient synthesis of coagulation factors. Administration of vitamin K restore PT to normal level.
3. Hemorrhagic disease of newborn. Reason for Vit K injection at birth.
4. Used as oral anticoagulants in the treatment of thrombotic conditions such as thrombosis occurring after myocardial infarction or surgery.
5. Hypervitaminosis: Administration of large doses of vitamin K produces hemolytic anemia and jaundice, kernicterus and brain damage.