

Vitamins



Vitamins

Definition :-

Vitamins are a group of organic nutrients required in small quantities for a variety of biochemical function and which , generally can't be synthesized by the body and must therefore be supplied in the diet .

A-They differ from other organic food stuffs in that:

1-They don't undergo degradation for providing energy unlike carbohydrates and lipids.

2-They don't enter into tissue structures proteins.

3-Several B-complex vitamin play an important role as coenzyme several energy trans formation reaction in the body .

B- They differ from hormones in not being produced within the organism and most of them have to be provided in the diet

Classification

All vitamins are divided into two groups according to solubility:-

1- Fat soluble vitamin

a- Vitamin A b- Vitamin D c-Vitamin E d- Vitamin K

2-Water soluble vitamins :many of them of different structure and having (coenzyme) function, they were grouped as “B- complex group “

A- vitamin C

B- vitamin B – complex which include:-

1-Vit.B1 2- Vit . B 2 3- Vit B 3 (Niacin)

4-Vit. B5 (Pantothenic acid) 5- B6 6- Vit. B7 (Lipoic acid)

7- Vit.B9 (Folic acid) 8-Vit . B12 9- inositol 10- Choline

Function of vitamin

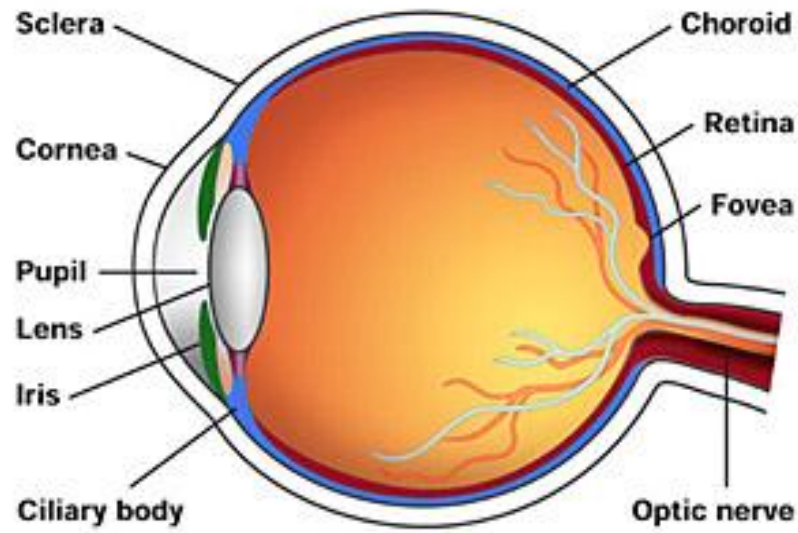
Vitamins have diverse biochemical functions.

1-Some have hormone-like functions as regulators of mineral metabolism (e.g. vitamin D).

2-Regulators of cell and tissue growth and differentiation (e.g. some forms of vitamin A).

3-Others function as antioxidants e.g .vitamin E and sometimes vitamin C

4-The largest number of vitamins (e.g .B complex vitamins) function as precursors for enzyme cofactors ‘that help enzymes in their work as catalysts in metabolism



Vitamin A & Visual Cycle

Fat soluble vitamins

Vitamin A

Sources of vitamin A:-

Plants :- In the form of provitamin (**provitamins**, substances that are transformed into vitamins in the body) carotene –tomatoes ,carrots (which have the reputation of proving night vision) green yellow vegetable, spinach and fruits such as mangoes, papayas, corn , sweet potatoes

Animals :- Preformed vitamin A can be obtained either **directly from foods** that are substantial in vitamin A , Liver oil , butter , cheese , egg yolk.

Stability of vit . A:-

It is rapidly destroyed by ultraviolet light and by oxidation and should be kept in dark container but it is stable at high temperature

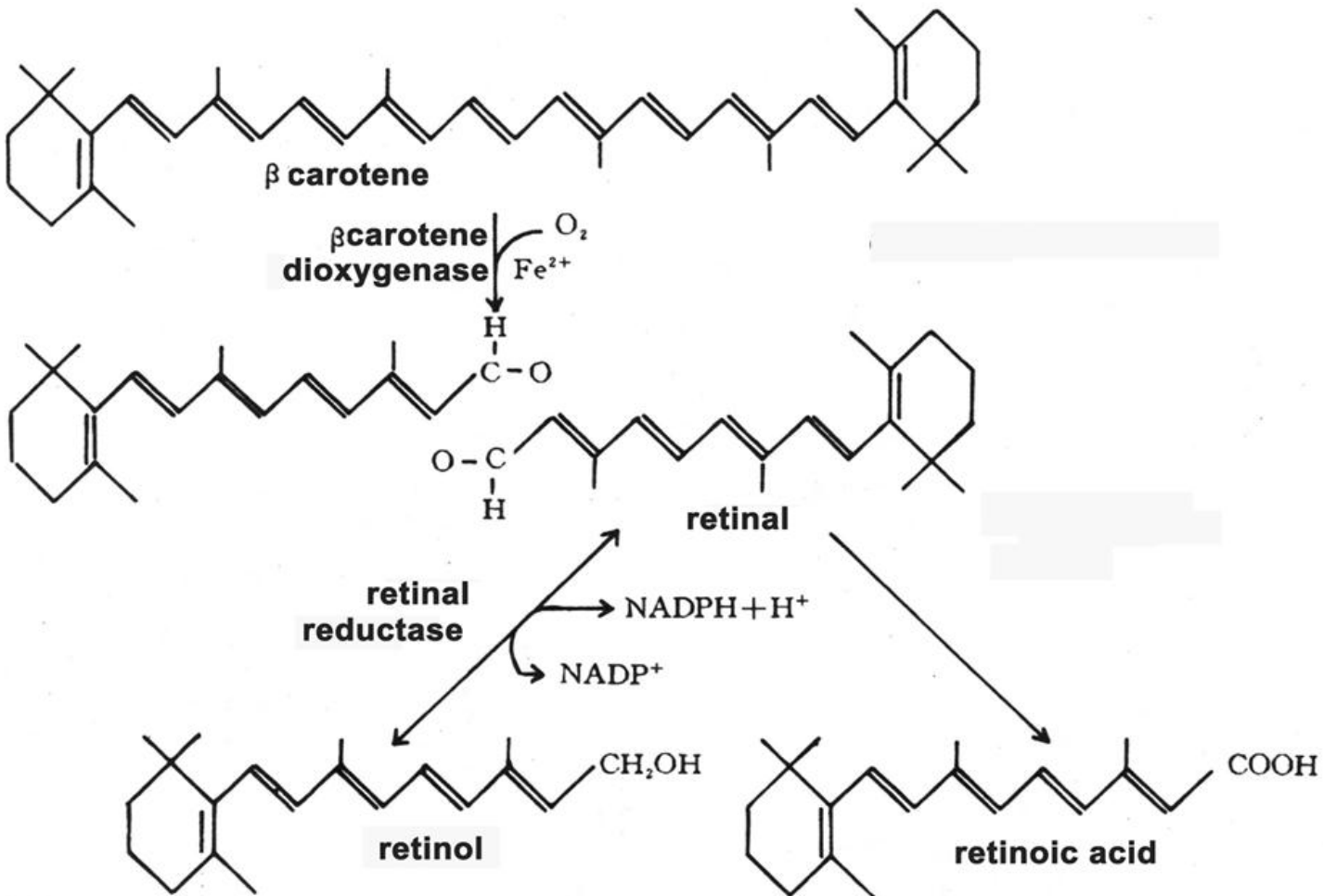
Chemistry:-

The retinoid, a family of molecules that are related to retinol (vitamin A), are essential for vision, reproduction, growth, and maintenance of epithelial tissues. Retinoic acid, derived from oxidation of dietary retinol.

Vitamin A is often used as a collective term for several related biologically active molecules. (The term retinoid includes both natural and synthetic forms of vitamin A that may or may not show vitamin A activity. Vitamin A is a pale yellow primary alcohol derived from carotene. It include Retinol (alcoholic form), Retinal (aldehyde form) and Retinoic acid (acidic form) .

1. Retinol: A primary alcohol containing a β -ionone ring with an unsaturated side chain, retinol is found in animal tissues as a retinyl ester with long-chain fatty acids.
2. Retinal: This is the aldehyde derived from the oxidation of retinol. Retinal and retinol can readily be interconverted.
3. Retinoic acid: This is the acid derived from the oxidation of retinal. Retinoic acid cannot be reduced in the body, and, therefore, cannot give rise to either retinal or retinol.
4. β -Carotene: Plant foods contain β -carotene, which can be oxidatively cleaved in the intestine to yield two molecules of retinal.

Vitamin A is a derivative of certain carotenoids which are hydrocarbon (polyene) pigments (yellow, red) these are called 'provitamin A' and are β , α , γ carotenes



oxidation of carotene to retinal in intestine and conversion to retinol and retinoic acid

Functions of vitamin A

1-Role in vision :-

perhaps the only function of vitamin A which is clearly understood to its molecular details is its role in vision . The overall mechanism through which vitamin A functions in visual system is known as **Wald's visual cycle** or **Rhodopsin cycle** .

Retinoic acid required for structural components of eye

- **Cones** in the retina

Responsible for vision under bright lights

Translate objects to color vision

- **Rods** in the retina

Responsible for vision in dim lights

Translate objects to black and white vision

Vitamin A concerned very much with rod vision (dim vision) and its deficiency causes a condition known as night –blindness (nyctalopia) inability to adapt when suddenly proceeding from blight light to dim light , or we call it nyctalopina.

2- Role in reproduction

Retinol and retinal are essential for normal reproduction, supporting spermatogenesis in the male and preventing fetal resorption in the female. Retinoic acid is inactive in maintaining reproduction and in the visual cycle, but promotes growth and differentiation of epithelial cells; thus, animals given vitamin A only as retinoic acid from birth are blind and sterile.

3-Role in epithelialization:-

The epithelial structures of skin and mucous membrane show gross structural changes in deficiency. Skin becomes dry, scaly and rough . These changes are called **keratinization**.

-Lacrimal glands :-

Similar changes occur in these glands leading to dryness of conjunctive and cornea, a condition described **xerophthalmia** .

-Cornea :- White opaque spots called Bitot's spots appear in the conjunctive on other side in each eye. Corneal epithelium becomes keratinized , opaque and may become softened and ulcerated, condition described as **keratomalacia** .

-Respiratory tract :- keratinization occurring in the mucous membrane of respiratory tract leads to increased susceptibility to infection and lowered resistance to disease.

- Urinary tract:- Keratinization of urinary tract leads of **calculi formation** .

4- Role in bone and teeth formation :-

It plays a role in the construction of normal bone. Deficiency results in slowing of endochondral bone formation and decreased osteoblastic activity, the bone becomes cancellous losing their fine structural details.

Teeth become unhealthy due to thinning of enamel and chalky deposits on surface.

5- Growth :- Vitamin A deficiency results in a decreased growth rate in children. Bone development is also slowed

6- Antioxidant and anticancer activity :-

β -carotene and vitamin A have antioxidant and anticancer activity.

Function of retinoic acid

1- Prevents keratinization of epithelium respiratory tract, urogenital tract, lacrimal duct, etc.

2- Plays important role in synthesis of glycoproteins as carriers of oligosaccharide chains.

3- Role in synthesis of mucopolysaccharides .

4-Inhibits the enzyme collagenase.

Effect of excess of vitamin A (Hypervitaminosis A)

Excessive intake of vitamin A produces a toxic syndrome called hypervitaminosis A. Amounts exceeding 7.5 mg/day of retinol should be avoided. Early signs of chronic hypervitaminosis A are reflected in the skin, which becomes dry and pruritic (due to a decrease in keratin synthesis), the liver, which becomes enlarged and can become cirrhotic, and in the nervous system, where a rise in intracranial pressure may mimic the symptoms of a brain tumor. Pregnant women particularly should not ingest excessive quantities of vitamin A because of its potential for causing congenital malformations in the developing fetus.

Daily requirement:-

Adult male and female require about 3000 IU per day . However, a recommended allowance is around 5000 IU per day. It is higher in growing children, pregnant women and lactating mothers . The requirement is also higher hepatic disease .

VITAMIN. D (CALCITRIOL)

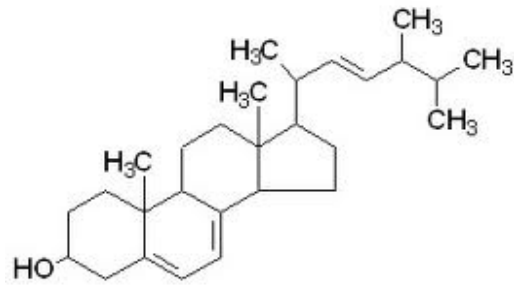
Synonym:- Anti rachitic vitamin

The D vitamins are a group of sterol compounds that occur in nature chiefly in animals but also plants and yeast.

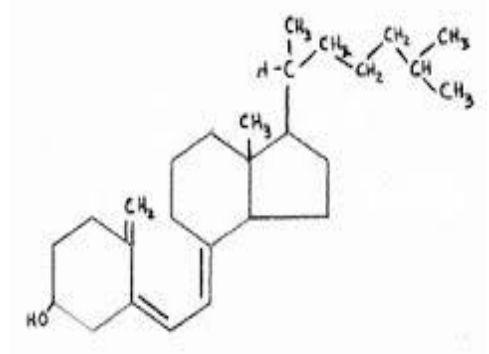
The D vitamins are generated from the pro-vitamins ergosterol and 7-dehydrocholesterol in plants and animals. Ergosterol and 7-dehydrocholesterol differ chemically only in the side chains at position 21.

Ultraviolet irradiation spontaneously cleaves the B-ring of ergosterol in plants leads to production of ergcalciferol (vit D₂).

UV (290 –315 nm) causes photolysis of between position 9 & 10 → opening of ring B.



Ergosterol



Ergocalciferol Vit D2

types: VitD₂ (Ergocalciferol)

VitD₃ (Cholecalciferol)

* **pro-VitD₂: Ergosterol**

Pro-VitD₃: 7-hydro-cholesterol

* **active form of VitD₃: 1, 25- (OH)₂-VitD₃**

Sources :-

The richest sources of vit D are :- Egg yolk, butter and fish liver oils contain varying amounts . In normal adults much more cholecalciferol (D₃) is derived from the skin than from food.

Metabolism and physiological function:-

Like most other fat soluble vitamins, bile salts help in absorption of vit D from duodenum and jejunum. After absorption it is carried in chylomicron droplets of the lymph in combination with serum globulin in blood plasma.

Formation of calcitriol:-

The biologically active form of vit .D. Is called calcitriol (1,25- dihydroxycholecalciferol). Which Is synthesized in liver and kidneys. Calcitriol is produced in the cells of the proximal tubule of the nephron in the kidneys by the action of 1,25-dihydroxycholecalciferol 1-alpha-hydroxylase) an enzyme which catalyzes the hydroxylation of 25-hydroxycholecalciferol (calcifediol). The activity of the enzyme is stimulated by (Para Thyroid Hormone PTH). The reaction is an important control point in Ca²⁺. The production of calcitriol is also increased by prolactin, a hormone which stimulates lactogenesis (the formation of milk in mammary glands), a process which requires large amounts of calcium. It is decreased by high levels of serum phosphate

The 25-OH D₃ is the major storage of vit D in the liver and found in appreciable amounts in circulation .

- Calcium receptor of parathyroid gland senses the calcium level in blood
- Low blood calcium causes the release of parathyroid hormone (PTH)
- PTH stimulates the activity of the 1-hydroxylase enzyme in the kidney, resulting in increased production of calcitriol
- Increased calcitriol production restores normal serum calcium levels in three different ways:

1) By activating the vitamin D-dependent transport system in the small intestine, increasing the absorption of dietary calcium .

2) By increasing the mobilization of calcium from bone into the circulation .

3) By increasing the reabsorption of calcium by the kidneys.

Regulation Of calcitriol synthesis is done by :-

- 1- Its own concentration.
- 2- Parathyroid hormone.
- 3-Serum phosphate level.
- 4- Serum calcium level.

Functions of vit .D:-

Vit D is found to act on target organs like bones, kidney, intestinal mucosa to regulate calcium and phosphate metabolism

1-Facilitates the absorption of dietary calcium by stimulation of synthesis of calcium binding protein in the intestinal mucosa- vit.D3 also facilitates the absorption of phosphate .

2-In combination with PTH (parathyroid hormone):-

A-Vit. D promotes bone resorption and Ca^{++} mobilization to raise the levels of Ca and P In blood.

(PTH is released in response to low serum calcium and induces the production of calcitriol).

B- Renal reabsorption of calcium and probably phosphorus by distal tubules is also done by calcitriol usually when Ca^{++} in plasma at low concentration.

NOTE :- In the kidney ; calcitonin (is a hormone), In contrast to PTH, increases calcium extraction and inhibits synthesis of calcitriol.

3- It exerts an anti-rachitic effect . Rickets is a disease involving abnormality of the bone growth and structure.

4-Required for the teeth formation.

5- It promotes growth in general.

6- Maintains a stable nervous system and normal heart action.

Clinical significance of vit D deficiency :-

The main symptoms of vit D deficiency in children is rickets and in adult is osteomalacia.

1- Rickets:-

- Instead of growth occurring normally at the end of long bones, the osteoblast proliferation does not take place in an orderly fashion and is not accompanied by vascularization or mineralization at the normal rate.
- The cartilage cells do not degenerate as they should and the ends of the long bones become bulky and soft.
- Bending of the long bones giving rise to deformities such as bow –legs and knock knees occur when the child attempts to stand up and walk.
- The chest gives pigeon-breast appearance.
- Teeth erupt late and are deformed.

2-Osteomalacia:-

1-In adult, usually in females ,in this case we note deformity of pelvis and there is difficulty in child birth, due to demineralization of previously formed bone

2-Leading to increased softness and susceptibility to fracture.

3-Bone demineralization may also results from the conversion of vit.D to inactive forms which is stimulated by glucocorticoids

Daily requirements:-

7.5 mg /day (in the absence of adequate sun light).

Deficiency of vit. D is caused by:-

- Fat malabsorption in the intestine .
- Sever liver disease.
- Kidney disease and certain drugs.

Toxicity (Hypervitaminosis D)

Like all fat-soluble vitamins, vitamin D can be stored in the body and is only slowly metabolized. High doses (250 mg/ day in adult and 25 mg /day in children) can cause loss of appetite, nausea, thirst, and stupor. Enhanced calcium absorption and bone resorption results in hypercalcemia, which can lead to deposition of calcium in many organs, particularly the arteries and kidneys.

- Hypercalcemia due to enhanced Ca^{++} absorption and bone resorption (bone demineralization).
- Metastatic calcification in soft tissues.(kidneys , bronchi ,muscles, etc.....)
- Hypercalcuria, resulting in kidney stones.
- Hyperphosphatemia.
- Anorexia, nausea, vomiting and diarrhea.

Vitamin . E (Tocopherol)

Antisterility vitamin or fertility factor. Tocopherols are the antisterility factors in male rats and birth process in female.

Tocopherols, now called vit. E are a group naturally occurring compounds of closely related chemical structures.

Sources

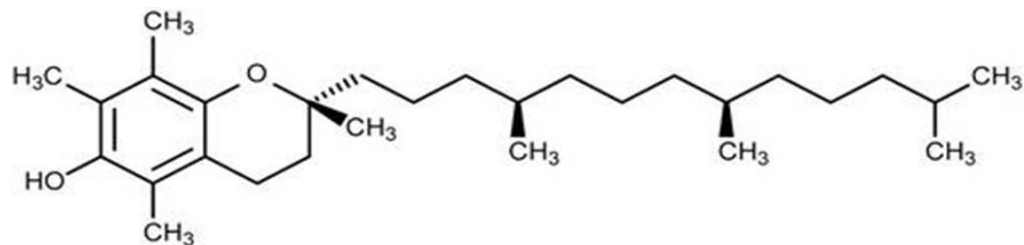
Plant :- cotton seed oil, corn oil, sun flower oil and margarine are the richest sources of vit .E.

Animals:- egg yolk, milk, butter, animal tissues, fish liver oil.

Chemistry:-

tocopherols are a class of organic chemical compounds, differ from each other in the number or position of methyl group. The alpha-tocopherol is the most active in vit E activity. Another group of similar compounds called tocopherols also show vit. E activity. These are beta, gamma, sigma tocopherols with low biological activity as compared to alpha tocopherol . The primary function of vitamin E is as an antioxidant in prevention of the nonenzymic oxidation of cell components, for example, polyunsaturated fatty acids, by molecular oxygen and free radicals.

Alpha-tocopherol



Metabolism:-

Vit. E is absorbed from the intestines packaged in chylomicrons. It is delivered to the tissues via chylomicrons transport and then to the liver, through chylomicron remnant uptake. The liver can export vit .E in VLDL due to its lipophilic nature.

Properties of vit E

1- **Antioxidant property :-** This is the most important aspect of vit .E. Vitamin E as an Antioxidant, Stops the chain reaction of free radicals, Protection of polyunsaturated fatty acids and vitamin A, (**Free radicals are atoms or groups of atoms that can damage cellular components such as DNA or parts of cells**).

2-**Role in reproduction in rats:-** Vit. E helps in maintaining seminiferous epithelium intact . However, its deficiency leads to reversible degenerative changes leading to permanent sterility .Motility of sperms is lost and spermatogenesis is impaired. In female rats the ovary is unaffected by vit. E deficiency , but the fetus does not develop normally, dying in utero undergoing resorption. So it has been used by doctors in helping prevent sterility.

3-**Tocopherol derivative** may be involved in synthesis of Coenzyme Q or ubiquinone.

4- **Vit .E** may have some role in nucleic acid synthesis .

5- It has been used by doctors in helping prevent muscular dystrophy, calcium deposit in blood walls and heart condition.

6-It dissolves blood clots.

7- Vit . E exerts a protective action in preventing massive hepatic necrosis produced on diets deficient in sulfur containing amino acid (cysteine) .

Deficiency of vitamin E:-

1- Muscular dystrophy:- Vit. E deficiency leads to increased oxidation of polyunsaturated fatty acids in the muscle.

2- Hemolytic anemia:- Low tocopherol diet may produce low plasma tocopherol, increased susceptibility to haemolysis due to peroxidase. This could be the reason of haemolytic or microcytic anemia.

3- Dietary hepatic necrosis:- Diets low in cystine and rich in polyunsaturated fatty acid can cause hepatic necrosis. Fall in acetate utilization and in respiration of necrotic liver is more effectively cured or prevented by tocopherols.

4- Neurological disorders.

5-Thrombocytosis, oedema and irritability in premature infants.

6-Ayellowish discoloration of the enamel of the teeth due to oxidation of the unsaturated fatty acids present in these structures to peroxides.

Deficiency of vit .E is caused by:-

A decrease in vit. E absorption in intestine as in :-

- 1- Steatorrhea.
- 2- Cystic fibrosis (gall bladder).
- 3-Biliary atresia .
- 4- Chronic pancreatitis.

Requirements:-

Average human diets contain about 20 mg.

Vitamin K

Like vit E this is also is a group of vitamins and some times referred to as ant hemorrhagic vitamins or coagulation vitamins or prothrombin factors.

Dietary sources:-

In plants:- green leafy vegetable such as spinach, cauliflower, cabbage, tomatoes .

In animals:-fish, liver, meat, eggs and milk.

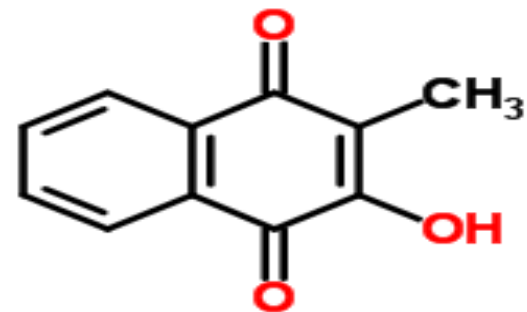
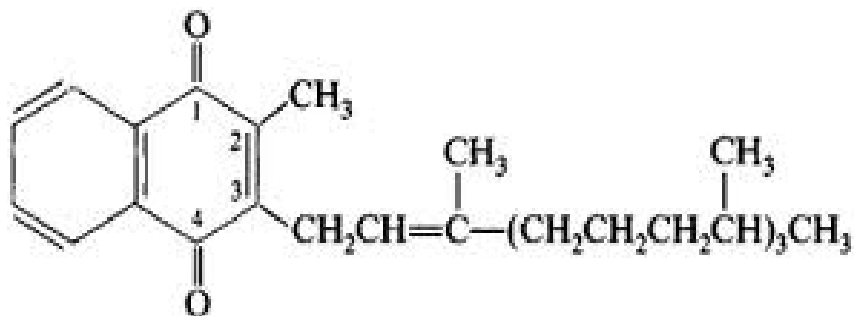
It can be synthesized by microorganism inhabiting the gastrointestinal tract (GIT) of higher animal including man, so the dietary requirement of vit K is of not much importance under normal circumstances as it is provided by GIT.

Chemistry :-

Vit K forms an naphtha quinone derivatives. It is closely related to compound pthiocol, a constituent of tubercle bacteria with high vit K activity

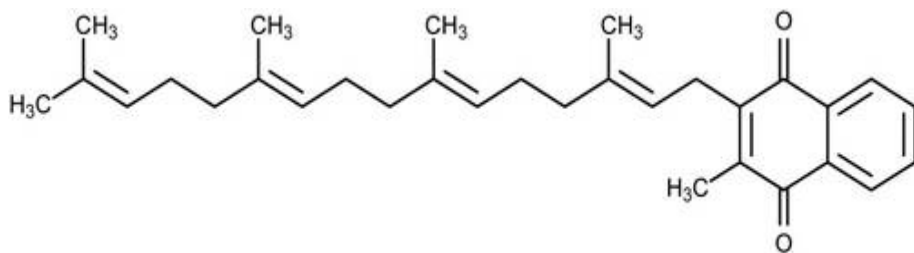
Type of vit K

1-Vit K1 :- is phyloquinone isolated from plants.



Pthiocol (2-methyl-3-hydroxy-1,4-Naptha quinone) Vit . K

2-Vit K2 :- also known as menaquinone , synthesized by the intestinal bacterial flora.



Menadione

3-Vit K3:- also known as menadione without any side chain or $-\text{OH}$ group, is the synthetic analogue of vit K. It is three times more potent than natural varieties. It is a water soluble, and be given parenterally

Metabolism:-

- 1-It is readily absorbed from small intestine in presence of bile salts and requires normal fat absorption.
- 2-It is not stored to any appreciable extent.
- 3- It can cross the placental barrier and is available to the fetus .
- 4-Vit K is not excreted in urine or bile.
- 5-Feces contain large quantities ,this may be bacterial origin.

Functions:-

- Cofactor of liver microsomal *carboxylase* which carboxylates glutamate residues to γ -carboxyglutamate during synthesis of prothrombin and coagulation factors. Formation of the clotting factors requires the vitamin K–dependent carboxylation of glutamic acid residues .
- Forms the binding site for Ca^{2+} also in other proteins – osteocalcin (Regulate incorporation of calcium Phosphate into bones).
- Role in phosphorylation reactions of photosynthesis in plants and probably a similar role in the electron transport system in animal tissues, it may serve as electron carrier (like coenzyme Q).

Deficiency of vit K

- Deficiency is caused by fat malabsorption or by the liver failure.
- Blood clotting disorders – dangerous in newborns, life-threatening bleeding (*hemorrhagic disease of the newborn*).
- Osteoporosis due to failed carboxylation of osteocalcin and decreased activity of osteoblasts.
- Under normal circumstances there is not a shortage, vit. K is abundant in the diet.

Vit K deficiency caused by:-

- 1-Malabsorption .
- 2- Sprue.
- 3-Biliary tract obstruction (absence of bile salts).
- 4-Steatorrhea and intestinal mucosal atrophy .
- 5-Chronic liver disease.

Requirement:-

Dietary requirement of vit K is of not much importance under normal circumstance as it is provided by intestinal bacteria in adequate quantities.

VITAMIN	OTHER NAMES	ACTIVE FORM	FUNCTION
Vitamin A	Retinol Retinal Retinoic acid β -Carotene	Retinol Retinal Retinoic acid	Maintenance of reproduction Vision Promotion of growth Differentiation and maintenance of epithelial tissues Gene expression
Vitamin D	Cholecalciferol Ergocalciferol	1,25-Dihydroxy-cholecalciferol	Calcium uptake
Vitamin K	Menadione Menaquinone Phylloquinone	Menadione Menaquinone Phylloquinon	γ -Carboxylation of glutamate residue in clotting and other proteins
Vitamin E	α -Tocopherol	Any of several tocopherol derivatives	Antioxidant

FAT-SOLUBLE