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The Comprehensive Review on Fat Soluble Vitamins

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Abstract: *This review article deals with brief description of fat soluble vitamins with figures and tables showing statistical analytical data duly quoting the references wherever necessary. The word "soluble" actually means "able to be dissolved." Whether a vitamin is classified as 'fat-soluble' or 'water-soluble' has to do with how the vitamin is absorbed, stored and removed from the body. Vitamins are tiny organic compounds with a huge impact on the health and well-being of the body. The body needs a small amount of fat soluble vitamins in order to stay in optimal health. Fat soluble vitamins play an important role in keeping the body healthy and functioning from immune system and muscle and heart function, easy flow and clotting of blood as well as eye health. They are critical to health and wellness–particularly reproductive health and wellness. Low-fat, no-fat and vegan diets are woefully lacking in fat soluble vitamins. However a diet based on traditional foods can naturally provide these vitamins. Science is still learning about many of the functions of vitamins. "Too much vitamin A, D, or K can lead to increased levels that are unhealthy and can cause serious health consequences. Diseased conditions leading to decreased fat absorption leads to decreased absorption of vitamins. The fat-soluble vitamins work most safely and effectively when obtained them from natural foods within the context of a diet rich in all their synergistic partners. If fat soluble vitamins are stored for lengthy time they generate threat for toxicity than water soluble vitamins and such situation even aggravated, provided they are consumed in excess. Vitamin products, above the legal limits are not considered food supplements and must be registered as prescription or non-prescription (over-the-counter drugs) due to their potential side effects. Vitamin A and E supplements do not provide health benefits for healthy individuals, instead they may enhance mortality, and it is held proved that beta-carotene supplements can be harmful to smokers.*

***Key words*:** *Vitamin A, Vitamin D, Vitamin E, Vitamin K.*

I. INTRODUCTION

1.1. Historical background:

Vitamins are defined as organic substance required in small amount for the maintenance and growth of living organisms. Their deficiency may lead to certain specific diseases or symptoms which can be cured by the administration of that specific vitamin only.

In the early 20th century the discovery of vitamins began. In 1906, the British Biochemist Sir Frederick Hopkins demonstrated that foods contain accessory factors in addition to proteins, carbohydrates, fats, minerals and water. The term vitamin was first discovered by Funk. Funk identified that the anti-beriberi substance in unpolished rice was an amine which is a type of nitrogen containing compound. He coined the term "vitamine" a combination word from vita and amine, meaning amine of life and considered that amines are vital for the life. However it was later found that all vitamins are either "nitrogen" or "amines" particularly in vitamin A. In 1912 Hopkins and Funk made a hypothesis according to which the absence of some vitamins could cause diseases such as beriberi and scurvy. In 1920, Drummond proposed to drop the final "e" consequently the word vitamines "e" was removed and termed as vitamins. It was later found that different vitamins have different chemical properties and advantages apart from harm if consumed in excess than what is required.

Vitamins are highly essential to human body except vitamins D, K and biotin as they cannot be synthesized in the body. Vitamin D is synthesized in the body by irradiation of sterols in the skin by UV rays. Many plants and microorganisms except humans and some other animals synthesize vitamins. Hence they need to be supplied through diet to the human body. Most of the vitamins are present in required quantities in the fresh and natural foods available both plants and animals sources. Vitamins are required in tiny amounts because of their inactivation in the body they play a catalytic role in many metabolic reactions of the cells and act as coenzymes or part of coenzymes and enzyme systems. Certain vitamins act as hormones and exert their action at intracellular receptor sites like Vitamin A and D.

In 1915, Mc Collum and Davis classified the vitamins based on their solubility in water or oil (fats). Vitamin C and B - complex are water soluble whereas Vitamin A, D, E and K are fat soluble dissolved in oil or in melted fat. Certain phyto nutrients argued that carotenoids such as β - carotene also come under this category (fat soluble).

Vitamin A maintains the right balance of these vitamins in the body is critical to excellent health and well-being the nature of being fat-soluble means that these vitamins are transported with fat and stored in the liver and fat tissue. Because they are stored, they can build up and become toxic when eaten in excessive amounts. This mostly occurs when taking single supplements of the fat-soluble vitamins rather than in foods rich in vitamins. Eating fat-free can lead to health problems can lead to vitamin deficiencies. When fat-soluble vitamins are ingested, they move from the mouth to the stomach to the small intestine. Their ability to dissolve in fat allows for their absorption: Fats are able to move across the cell walls of the small intestine and enter the body's general circulation. The dietary-fat carry the vitamins through the intestine, into the bloodstream, and then to the liver, where they're stored until the body needs them. Without an adequate amount of fat in your diet, the body can't effectively absorb the fat-soluble vitamins that are essential to the health. Vitamin A is regarded as the vision vitamin in a generic term for a class of compounds called retinoids. Types of retinoids: retinol, retinal, and retinoic acid. The release of vitamin A from food requires bile, digestive enzymes (lipase) from the pancreas and intestinal tract, and integration into micelle. 90 % of vitamin A absorbed in small intestine. Retinoids stored in liver and carotenoids stored in liver and adipose. Cellular Retinoid-Binding Proteins (CRBP or RBP) should be required for the transportation of retinoids into the cells. A vitamin is two types. 1. Preformed vitamin A is found in the form of retinol and is the most usable form of the vitamin. You can find preformed vitamin A in your everyday diet in animal products like whole milk, liver, and eggs. 2. Provitamin A is found in the form of carotenoids and is converted in part into retinol. Beta-carotene, alpha-carotene, and beta-cryptoxanthin are the most common carotenoids, with beta-carotene being the most easily converted into retinol. Beta-carotene is found naturally in many fruits and vegetables like peaches and carrots. Men 900 mcg RAE per day and women 700 mcg RAE per day and Men 3000 IU and women 2330 IU per day must be required to keep the body healthy. Toxicity of vitamin A is known as Hypervitaminosis is caused by excess dosages which are 100 times to RDA.

Deficiency in vitamin D can cause fragile, thin, or deformed bones and rickets in children and osteomalacia in adults. It having enough vitamin D in the diet, in addition to calcium, helps to prevent osteoporosis. Vitamin D isn't actually in its working shape when it enters the body through sunlight, food, or supplements. In addition to obtain vitamin D from a few available natural and fortified foods, the body of course absorbs vitamin D from sunlight. As soon as ultraviolet rays hit the skin, production of vitamin D commenced soon. In fact, public obtain their required vitamin D by exposing their body only some times in a week by wearing sunscreen to avoid potential damage of skin from ultra-virus rays. Nnutritionally important two forms of vitamin D are vitamin D_2 (ergocalciferol) which is found in plants and vitamin D_3 (cholecalciferol) is synthesized in the body from cholesterol. Nearly 80 % of vitamin D is absorbed in small intestine and carried by proteins in blood stream. Provitamin D (a form of cholesterol) is converted to vitamin D_3 in the skin. Calcitriol of vitamin D and its hormones is formed in the liver and kidneys. Adequate intake of vitamin D per day is 5 mcg between 19 to 50 years, 10 mcg to 51 to 70 years and 15 mcg over 70 years aged persons. 5 times toxicity of Hypervitaminosis of D vitamin for infants, 10 times for adults is highly dangerous. A person may need around 5,000-6,000 IUs of vitamin D_3 or more every day, from all sources, includes proper sun exposure, food, or a vitamin D_3 supplement. The perfect range for best possible health is between 50 to 70 mg/ml, and if cancer or heart diseases exist, the ideal may be higher.

Family unit of eight antioxidants and four tocopherols of vitamin E are alpha, beta, gamma and delta, and four tocotrienols are alpha, beta, gamma and delta out of which Alpha-tocopherols is the most active form. Vitamin E is the collective name for a group of 8 different chemicals that comprise diverse amounts of biological use. However, only alpha-tocopherols are indicated to cater the needs of the human body. Vitamin E found in the skin as a primary form and then total body supplement. The release of vitamin E from food requires bile, digestive enzymes from the pancreas and intestinal tract, and integration into micelles. It is stored in the liver and adipose tissue. Its daily requirement is 15 µg per day.

Vitamin K is named for the German word "koagulation" because of its function in assisting blood clotting. In the twenty-first century its role in preventing calcification of the blood vessels and other soft tissues became clear. Vitamin K_2, found in animal fats and fermented foods, in leafy greens and in much smaller quantities in most diets when compared to vitamin K_1. Vitamin K_1 more effectively supports blood clotting, while vitamin K_2 is also essential for building strong bones, preventing heart disease, and it plays a crucial part in other bodily processes as well. The biological role of vitamin K_2 help to move calcium into the proper areas in the body, such as bones and teeth and also helps to remove calcium from arteries and soft tissues. Vitamin K_2 activates proteins by adding carbon dioxide to them. In this production of CO_2 by consuming carbohydrates, exercising, and maintaining correct level of thyroid status.

Out of two types of vitamin K, one is found in plants, and other is found in bacteria. Plants make phylloquinone (vitamin K_1) and bacteria make a number of forms of the vitamin called menaquinone. The bacterial forms are collectively called vitamin K_2. Maintaining the right balance of these vitamins in the body is most important for excellent health and well-being. The release of vitamin K from food requires bile, digestive enzymes from the pancreas and intestinal tract, and integration into micelles. Daily requirement of vitamin K for Men is 120 mcg and for women is 90 mcg. 80 % of dietary vitamin K is absorbed.

II. FAT SOLUBLE VITAMINS

Fat soluble vitamins are stable at cooking temperatures while water soluble vitamins are destroyed. Usually, deficiencies do not occur when the daily requirements of vitamins are balanced by their dietary intake. Deficiency of vitamins K and biotin in the body is very rare because they are synthesized by the intestinal flora, the microorganisms of the body. Fat-soluble vitamins of Vitamin A, D, E and K structurally resembles partially cyclised isoprenoid polymers and are soluble mainly in lipids or oils and thus called fat-soluble vitamins. Absorption and transportation of these vitamins in the body is mainly associated with lipids in the intestine and stored in liver and adipose tissue and eliminated slowly from the body owing to their lipophilic character. High intake of fat-soluble vitamins may results in their accumulation in the body known as Hypervitaminosis due to the cause of delayed elimination rate. Fat soluble vitamins regulation is one sort of particular significance in cystic fibrosis. The classifications of vitamins are shown in Fig 1. The basic structural moieties and other facts of fat-soluble vitamins are shown in Table 1.

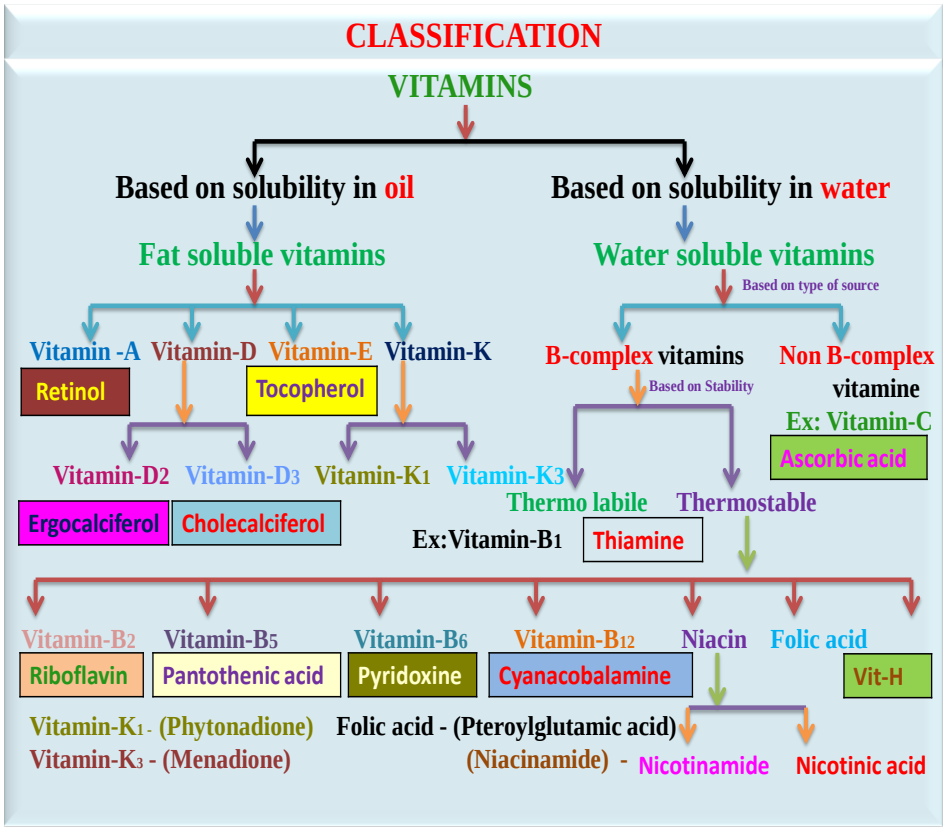


Figure 1. Classification of vitamins

Table 1. Basic structural moiety and other facts of fat soluble vitamins

Fat soluble vitamins	Basic structural moiety	Year of discovery	Recommended daily dose per day (µg)	Upper in take level per day(µg)
Vitamin - A	Diterpenoid	1913	900	3000
Vitamin - D	Steroidal moiety	1920	10	50
Vitamin -E	Chromane ring system with isoprenoid side chain.	1922	15	1000
Vitamin - K	Napthaquinone derivative	1929	120	NA

2.1. Vitamin A

Mc Collum and Davis identified vitamin A in 1915 but it was isolated from its raw source only in 1931. The biological and IUPAC name of vitamin A is retinol that is an alcohol, the corresponding aldehyde termed as retinal and acid as retinoic acid. Vitamin A is also known as axerophthol as it is used in the treatment of Xerophthalmia which means drying and thickening of conjunctiva. Basically there are two types of vitamin A namely A_1 and A_2 and when the term vitamin is used it denotes vitamin A_1. Vitamin A is an organic compound required as a nutrient in tiny amounts for the healthy maintenance and growth of a living organism. These are organic substances essential for the diet in small amounts that are involved in fundamental functions of the body. Human beings and animals inevitably need vitamins to grow and be healthy. The structures of vitamin A constitute a β-ionone ring. Vitamin A contains five conjugated double bonds which have some biological actions and it exits in three forms namely All-trans [1] retinol, long chain fatty acyl ester of retinol in main storage form and retinal in the active form in the retina. The precursor or Provitamin of retinol [2] is β-carotene, which is abundantly in carrots. The conversion of β-carotene [3] to vitamin A in the body involves two steps catalyzed by iron containing deoxygenase enzyme present in intestinal mucosa and alcohol dehydrogenase. The chemical nature and properties of vitamin A are shown in Table 2.

Table 2. Chemical nature and properties of vitamin A

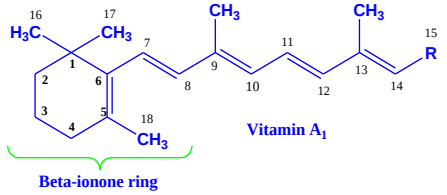
Natural form	A_1 (Retinol), A_2 (3-dehydro-retinol)
Active form	Retinol, Retinal, Retinoic acid
Provitamin A	β-carotene
Storage	Liver, Adipose tissue of the body

2.1.1. Source:

β-carotene like dark leafy green vegetables, spinach, broccoli [4], carrots, cabbage, pumpkin, squash, sweet potato, deep orange fruits, mangoes, apricots, amaranth, cantalo, retinols like milk, butter, cheese, cream, eggs, cod liver oil, kidney, tomatoes, papaya and water melon. Preformed vitamin A is found almost exclusively in animal products such as glandular meat, red palm oil (rich in Provitamin A), liver, fish liver oils, egg yolk, fortified processed foods that may include cereals, condiments and fats. Foods containing Provitamin A carotenoids tend to be less biologically available but more affordable than animal products. It is mainly for this reason that carotenoids [5] provide most of the vitamin A activity in the diets of poor and economically deprived populations. Estimated RDA is shown in Table 3 and three forms of retinoids are shown in Fig. 2.

Table 3. Estimated mean requirement and safe level of intake for vitamin A.

Age group		**Mean requirement (µg/day)**	**Recommended safe intake (µg/day)**
Infants and children	0 - 6 months	180	375
	7 - 12 months	190	400
	1 - 3 years	200	400
	4 -6 years	200	450
	7 -9 years	250	500
Adolescents	10 - 18 years	330 – 400	600
Adults	19 - 65 years	270	500
	19 - 65 years	300	600
	65 +	300	600
Pregnant women	-	370	800
Lactating women	-	450	850



R	
R = CHO	**Retinal (Vitamin A aldehyde)**
R = CH_2OH	**Retinol (Vitamin A)**
R = COOH	**Retinoic acid (Tretinoin) or Vitamin A acid.**

Figure 2. Three forms of retinoids.

2.1.2. Functions [6]:

Retinoic acid is highly necessary for cellular differentiation, important for embryo development, gene expression. Retinoic acid influences production, structure and function of epithelial cells and external passages o mucus forming cells within the body duly keeping perfect vision. The retinol is oxidized to its aldehyde and retinal which complexes with a molecule in the eye called opsin. Within the photoreceptor cells of the retina are the rods which detect small amounts of light and are specialized for motion. The cones that are specialized for color vision in bright light. The both rods and cones possess specialized outer segment disks that contain high amounts of rhodopsin and iodopsin respectively. When a photon of light hits the complex the retinal changes from the 11- cis form to the all - Trans form. These are initiating a chain of events which results in the transmission of an impulse up to the optic nerve. These compounds are often referred to as the "Visual pigment". Photoreceptor cells detect light and undergo a series of reactions which send signals to the brain where they are deciphered as a particular visual image. The important function of vitamin A involves retinoic acid, which acts as a hormone, and retinoic acid first binds to retinoic acid receptors. The receptors then interact with specific nucleotide sequences of DNA and the interaction directly affects gene expression and transcription which in turn control cellular development and body processes. For example epithelial cells depend on retinoic acid for structural and functional maintenance. Retinoic acid is especially important in heart, eye and lung and ear development, pigmentosa [7]. Vitamin A is plays a key role in glycoprotein synthesis and once formed glycoproteins are important in multiple cellular processes including: communication, recognition, adhesion and aggregation. Retinoids are most commonly used in the treatment of skin diseases and the role of the retinoids in epithelial cell formation is very important in the treatment of skin cancer, acne and acne related diseases. Vitamin A also has antioxidant properties. However, β-carotene has been noted as having pro-oxidant properties. Vitamin A is known to help repair damaged tissue and therefore may be beneficial in counter action against free radical damage.

2.1.3. Deficiency:

If consumed food containing low quantity of required defined daily dose of vitamin A leading to liver disease, malabsorption due to the body fails to absorbs nutrients from food in small intestine causing celiac diseases, chronic liver, chronic pancreatitis, crones diseases etc., decreased mucus production, decreased immunity. Bacterial invasion of the eye, conjunctival xerosis, Bigot's spots (white triangular plaques on conjunctiva), night blindness (nyctalopia), follicular hyperkeratosis, poor growth, skin disorders, lack of growth and Hypervitaminosis can cause serious potential problems (like birth defects). Growth retardation caused by vitamin A deficiency. Vitamin A is also responsible for maintain a normal surface of the eye (cornea) and deficiency leads to drying of the eye surface that condition called Xerophthalmia. This can lead to blue cloudiness of the eye followed by ulcer formation. In immunity, deficiency may leads to decreased resistance to infections and supplementation. If left untreated it leads to generation and ulceration of cornea called keratomalacia, ultimately resulting in blindness, retardation of the growth because of impaired skeletal formation, sterility in males due to generation of germinal epithelium, anorexia and susceptibility to infections. Poor dietary habits, malnutrition owing to improper balance between dietary consumption causes vitamin A deficiency particularly very high in patients with a medical history of cystic fibroses, sprue, inflammatory bowel diseases etc.

2.1.4. Adverse effects:

Routine consumption of large amounts of vitamin A over a period can result in toxic symptoms such as liver damage, bone abnormalities, joint pain, alopecia, vomiting and skin desquamation. Hypervitaminosis (dermatitis-drying and redness of skin, decalcification and tenderness of long bones, weight loss, hair loss, enlargement of liver, joints pain, irritability-due to increased intracranial pressure) appears to be due to abnormal transport and distribution of vitamin A and retinoids caused by overloading of the plasma transport mechanisms. The smallest daily supplement associated with liver cirrhosis those have reported 7500 μg taken for 6 years. Very high single doses can also cause transient acute toxic symptoms that may include bulging fontanels in infants, headaches in older children and adults and vomiting, diarrhoea, loss of appetite and irritability in all age groups. Rarely does toxicity occur from ingestion of excess food sources of vitamin A and due to very frequent consumption of liver products. Toxicity from food sources of Provitamin A carotenoids not reported except for the cosmetic yellowing of skin and CNS effects like (headache, irritability, seizures, increased intracranial pressure), GIT effects (nausea and vomiting). Moreover, some of the toxicity effects like on the skin (desquamation-destruction and removal of squamous epithelial cells and on the eye (papilledema-swelling of optic disc/papilla, scotoma-a small area of absent vision in visual field. photophobia-an abnormal intolerance to light), teratogenic effects (craniofacial, urogenital, neural tube defects and musculoskeletal abnormalities). The over dose of vitamin A [8] intake effects adversely on bone mineral density and fracture risk in perimenopausal women, Osteoporosis.

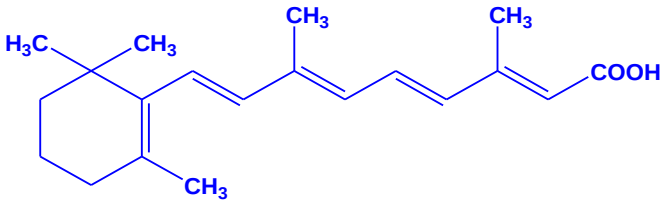
2.1.5. Therapeutic uses:

Vitamin A [9] is mainly used in the treatment of dermatological disease and lesions (due to suppression of keratin synthesis and secretion of mucous), Xerophthalmia, cold, warts, corns and calluses (skin infections), acne, psoriasis and persistent follicular hyperkeratosis of arms, night blindness, breast cancer [10] and vision.

2.1.6. Vitamin A analogues:

2.1.6.1. Tretinoin:

Tretinoin is the carboxylic acid form of vitamin A and is also called as All-trans Retinoic acid or ATRA. Tretinoin is formed by the oxidation of retinal (vitamin A aldehyde). It was considering a form of vitamin A that mainly acts on the skin; hence it is used in the treatment of dermatological diseases. The structure of Tretinoin is shown in Fig 3 and Fig 4 shows its synthesis.



(2*E*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-tetraenoic acid

Figure 3. Chemical structure of Tretinoin.

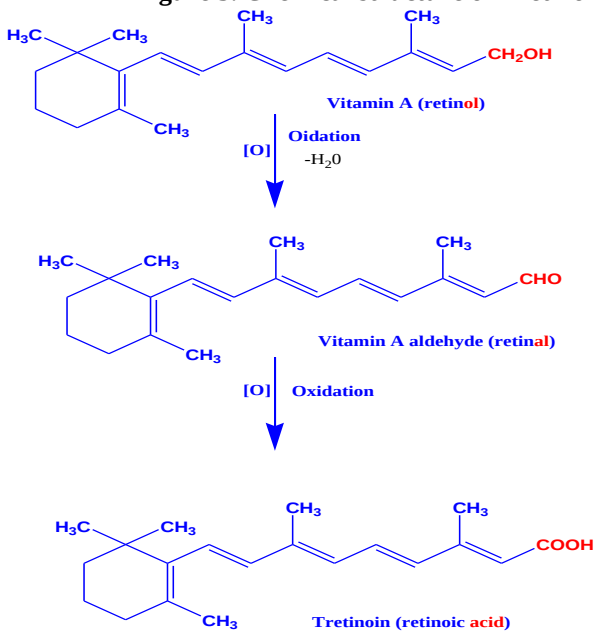


Figure 4. Synthesis of Tretinoin (Retinoic acid).

2.1.6.1.1. Adverse effects:

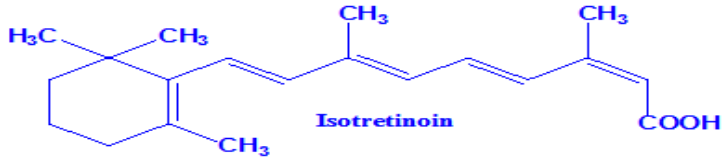
No toxic effects are seen when tretinoin is administered systemically. However, topical application in concentration greater than 0.1% leads to inflammation, irritation, peeling, crusting and blistering of skin. It causes severe irritation when applied to eczematous skin. Hypo or hyperpigmentation may occur when exposed to sunlight which has temporary effect that can be reversible. Excessive usage of tretinoin causes thinning of the superficial horny layer and allowed the skin highly susceptible to attack by chemicals and physical agents. Therefore, concomitant usage of keratolytic agents with tretinoin should not recommend.

2.1.6.1.2. Therapeutic uses:

Retinoic acid is mainly used in the treatment of skin diseases, inflammation due to acne vulgaris, acanthosis (thickening of epidermis), and local intercellular oedema. The effect results in separation of epidermal cells, loosening of stratum corneum and finally exfoliation. It is used in the treatment of hyperkeratosis conditions like solar and follicular keratosis (red spots with scaly surface), keratosis palmaris and plantaris (horny outgrowth of skin on palms and soles), lamellar ichthyosis (thickening of skin on palms and soles) and hyperplastic dermatosis. It acts as antioxidant and free radical scavenger (which protects the skin from radiation effects) and this property is used in the treatment of some cancers and carcinogenesis (due to radiation and carcinogens). It has also anti-neoplastic properties. It is used in treating photo aging of the skin which occurs due to its excessive exposure to the sun. In this condition, the skin becomes rough, leathery, wrinkled, mottled and yellow.

2.1.6.2. Isotretinoin:

Isotretinoin ($C_{20}H_{28}O_2$) is a cis - isomer of retinoic acid. The configuration of double bond at alpha and beta carbon atom is cis. It acts by stopping the functions of sebaceous glands and prevents follicular keratinization. Thus it reduces the production of sebum, size and differentiation of the sebaceous glands. It is yellow - orange to orange colour, crystalline powder and sparingly soluble in alcohol but insoluble in water. Fig 5 shows the structure of isotretinoin. It acts by inhibiting the functions of sebaceous glands and prevents follicular keratinization. So it decreases the production of sebum, size and differentiation of the sebaceous glands.



(2*Z*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-tetraenoic acid

Figure 5. Structure of isotretinoin.

2.1.2.1. Adverse effects:

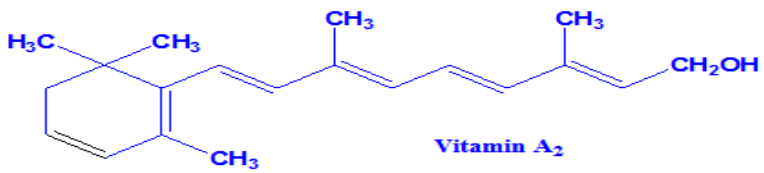
Adverse effects of Isotretinoin are alike to that of chronic Hypervitaminosis A. Facial dermatitis, thin and dry hair, dry mouth and eyes, conjunctivitis, reversible cheilitis (inflammation of lips), inflammation of urethra, peeling of skin on palms and soles, joints pains and vertebral hyperostosis (excessive enlargement of the outer layer of bone).

2.1.6.2.2. Therapeutic uses:

The main indication for Isotretinoin is the treatment of severe cystic acne vulgaris. It is also somewhat effective for hidradenitis suppurativa and some cases of severe acne rosacea. It can also be used to help treat harlequin ichthyosis, lamellar ichthyosis and is used in xeroderma pigmentosum cases to relieve keratosis. It is used in fibro dysplasia ossificans progressive. It is also used for treatment of neuroblastoma, a form of nerve cancer. Isotretinoin is used in genital warts. Isotretinoin may represent an efficacious and safe alternative systemic form of therapy for RCA of the cervix. In cases of hormonal acne, such as in women in their 20s and 30s with cyclical acne, often a course of isotretinoin can permanently improve acne obviating the need for lifelong hormonal manipulation. Acne treatment usually begins with topical retinoids (e.g., tretinoin, adapalene), in combination with topical antibiotics (e.g., clindamycin, erythromycin) or antiseptics (e.g., benzoyl peroxide-containing preparations), followed by oral antibiotics (e.g., doxycycline or minocycline). In women a cyproterone acetate-containing contraceptive pill can be utilized if there are no contraindications.

2.1.6.3. Vitamin A_2 : [(3, 4-Dehydroretinol, all-trans-3-dehydroretinol, retinol 2)] [11]

Vitamin A_2 is chemically called 3, 4 - dehydroretinol, because it is 3, 4 - dehydrogenated form of retinol. Its biological potency is 40 % of that of vitamin A acetate. Vitamin A_2 structure is shown in Fig 6.



(2*E*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohexa-1,3-dienyl)nona-2,4,6,8-tetraen-1-ol

Figure 6. Chemical structure of Vitamin A_2.

2.2. Vitamin D

Vitamin D is one of the fat-soluble vitamins known for its antirachitic activity (treatment of rickets). Vitamin D also known as the sunshine vitamin, because the sterols resent in the skin can be converted to vitamin D with the help of UV rays emitted from the sun. Mc Collum was first to coin the term vitamin D for its antirachitic activity in the year 1922. Vitamin D is termed as calciferol by Augus in the year 1931. Rickets is derived from an old English word wrickken meaning twist. Vitamin D is required to maintain normal blood levels of calcium and phosphate that are in turn need for the normal mineralisation of bone, muscle contraction, nerve conduction and general cellular function in all cells of the body. Vitamin D achieves this after its conversion to the active form of 1, 25-dihydroxyvitamin D [12] or (1, 25 $(OH)_2$ D) or Calcitriol. This vitamin plays an important role in enhancing the absorption of calcium and phosphorus from the intestine and helps to maintain calcium homeostasis.

2.2.1. Types of vitamin D:

So far 7 different types of vitamin D have been discovered, among which little information known about D_5, D_6 and D_7. Infact in 7 different types of vitamin D only D_1, D_2 and D_3 are important.

1. Vitamin D_1 is a molecular compound containing lumisterol and calciferol in 1:1 ratio.
2. Vitamin D_2 [13] is ergocalciferol, derived from ergosterol.
3. Vitamin D_3 is cholecalciferol and obtained form 7- dehydrochloesterol.
4. Vitamin D_4 is obtained from 22-dihyroergocalciferol.
5. Vitamin D_5 is sitocalciferol.

2.2.2. Sources:

Vitamin D is mostly obtained from natural sources and supplied through fortified food such as bread, breakfast cereal, margarine, oil spreads, milk, pastries, yogurt etc. that supplied with required amounts. Natural source include cod liver oil, catfish, eel, mackerel, salmon, sardines, tuna and mushrooms. Fungi and yeast also serve as sources of vitamin D as possess vitamin D precursor ergosterol. Vitamin D_2 [14] is of plant origin and commercially obtained by irradiation with UV light of ergosterol found in ergot and yeast. Therefore, ergosterol is called as the Provitamin. Vitamin D_3 is obtained from animal sources only, by irradiation with UV light of a Provitamin. Table 4 shows RNI for vitamin D according to age group. Types of vitamin D are shown in Fig 7.

Table 4. Recommended nutrient intake (RNI) for vitamin D according to age groups.

Age group		RNI (mg/day)
Infants	0–6 months	5
	7–12 months	5
	1–3 years	5
	4–6 years	5
	7–9 years	5
Adolescents	10–18 years	5
Adults	19–50 years	5
Older adults	51–65 years	10
Elderly adults	65+ years	15
Pregnant women	-	5
Lactating women	-	5

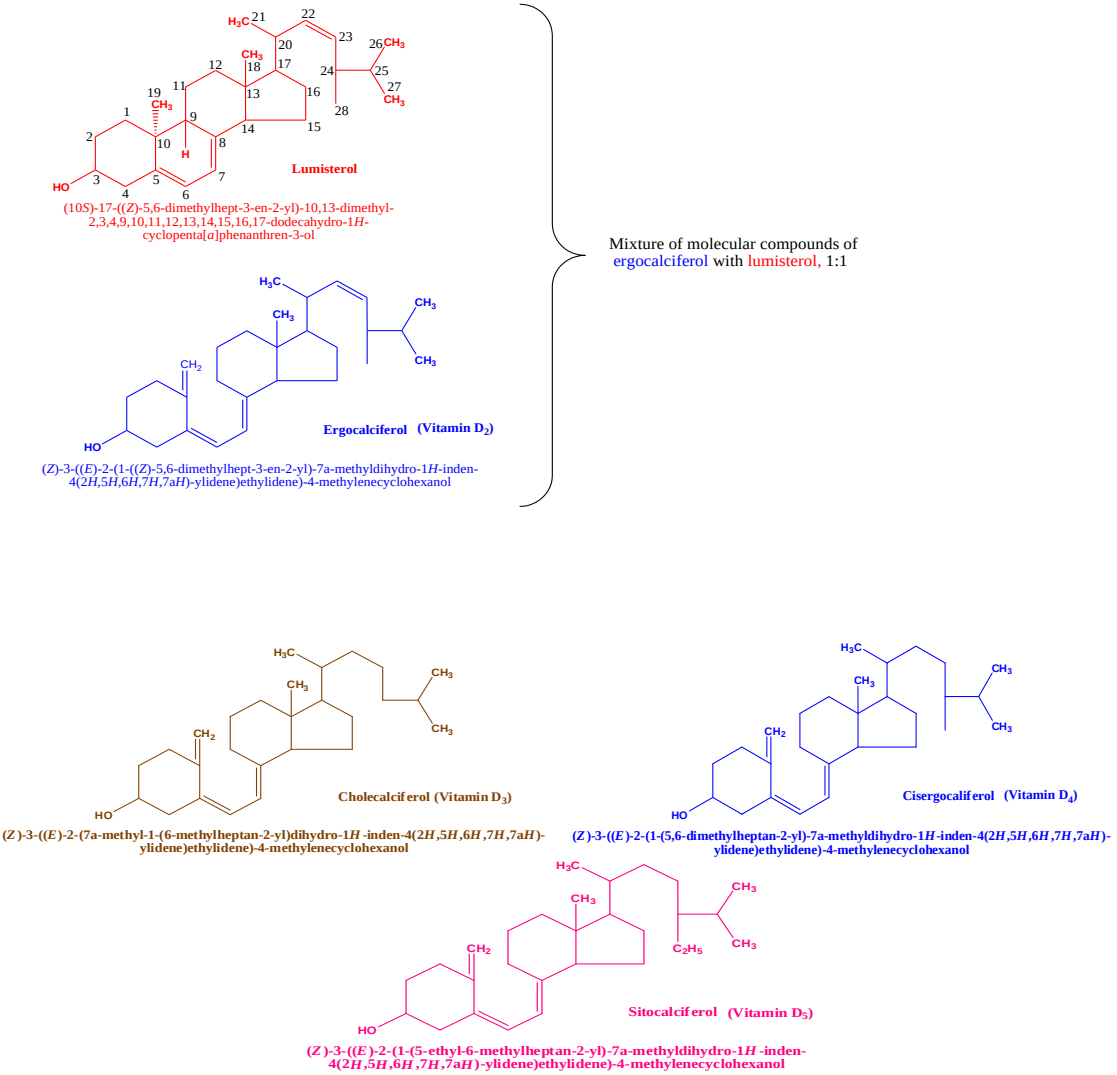


Figure 7. Types of vitamin D.

2.2.3. Functions:

Along with parathyroid hormone and calcitonin vitamin D maintains the homeostasis of calcium [15] and phosphorus in the tissues and body fluids. Calcitriol receptor complex is formed by the combination of calcitriol and cytosolic receptor which enhance the absorption of calcium in the intestine. This complex leads to the synthesis of calcium binding proteins, which enhance the uptake of calcium in the intestine thereby increasing its absorption. Calcitriol also enhances the plasma levels of calcium and phosphorus by increasing their mobility from bones. It enhances the reabsorption of calcium ions from the distal tubules thereby decreases their excretion. Supplementation with vitamin D improved glycaemia and insulin secretion in type-2 diabetes patients [16]. Vitamin D plays a pivotal role in calcium and phosphorus homeostasis. Thus, it alters insulin synthesis by regulating plasma calcium levels, which in turn regulate insulin synthesis and secretion. It may exert its action by directly acting on pancreatic β-cells. As a hormone it involves in mineral metabolism and bone growth. It facilitates intestinal absorption of calcium and stimulates absorption of phosphate and magnesium ions. It stimulates the expression of a number of proteins involved in transporting calcium from the lumen of the intestine across the epithelial cells and into blood. The best studies of these calcium transporters are calbindin and an intracellular protein that ferries calcium [17] across the intestinal epithelial cell. It possesses hormone like activity as it is produce at one area and its activity involves the diffusion process to the target area. Vitamin D_2 and D_3 are biologically inactive whereas the metabolites 1, 25-dihydroxycholecalciferol is the active form and it is known as calcitriol. The critical effect of vitamin D on bone is to provide the proper balance of calcium and phosphorus to support mineralization. The absorption of calcium and phosphorous is enhanced by calcitriol in the intestine. Calcitriol receptor complex is formed by the combination of calcitriol and cytosolic receptor. This complex leads to the synthesis of calcium binding proteins, bone development, regulation of gene expression and cell growth.

2.2.4. Deficiency:

Deficiency of vitamin D occurs very rarely since it is adequately synthesizing in the body. Insufficient amounts of vitamin D in the food causes hyperparathyroidism [18]. Less exposure to sunlight, malabsorption of vitamin D due to hepatic and renal disorders like nephrotic syndrome, hepatobiliary syndrome, pancreatic disorders, abnormal metabolism and anticonvulsant therapy etc. Deficiency may lead to rickets due to inadequate calcification of bones [19-21] in infants, older children and aged people who are not adequately exposed to sun. In some cases, calcium levels reduce drastically and in severe cases, it may lead to tetany. Some researchers and doctors believe that vitamin D deficiency is common and it causes many serious health problems like colds and flu[22] are more common in the winter because a vitamin D deficiency due to lack of sunshine. Low vitamin D symptoms would be a lower bone mineral density and muscular tension would leads to osteoporosis and bone fractures. There would be a great risk of hip fracture as well. Deficiency of vitamin D pays way to cardiovascular disease coupled with risk of high B.P [23]. It has a role in preventing infections such as diabetes mellitus [24].

2.2.5. Adverse effects:

The adverse effects of high intake of vitamin D cause hypercalciuria and hypocalcaemia. Vitamin D fortification from all foods is the major cause of Hypervitaminosis which is a chronic problem still throughout the globe particularly in developing countries at high latitudes and in countries where skin exposure for prolonged time to sunlight is discouraged. Excessive exposure to sunlight does not lead to overproduction of vitamin D instead it causes skin damage. Vitamin D toxicity is inevitably the result of overdosing of vitamin D supplements. However, ingestion of excessive quantity of vitamin D over periods of weeks of months can create severe toxic in humans as well as animals. Excessive formation of vitamin D metabolites enhances the calcification of various tissues along with bones and which implies hardening of arteries occurs due to calcification of blood vessels. Vitamin D can also cause anorexia, muscular weakness, nausea, vomiting, CNS depression which may lead to coma and death, nephrocalcinosis (deposition of Ca^{+2} in kidneys), nephrolithiasis i.e., deposition of Ca^{+} in renal tubules creates permanent renal damage, growth retardation, polyuria and nocturia etc.

The vitamin D council recommended that 5,000 IU/day should be taken for the average adult. Infact the toxic adult dose is 1.25 mg (50,000 IU) per day. As a matter of fact over exposure to sunlight is not responsible for vitamin D toxicity. Indeed ingestion of large quantities of vitamin D causes Hypervitaminosis D. Prolonged therapy of vitamin D even in low quantities i.e., 375 µg/kg for 2 weeks leads to toxicity.

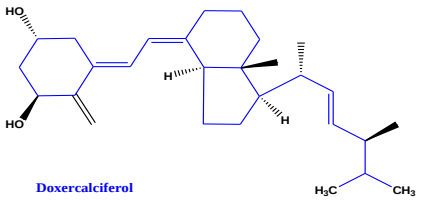
2.2.6. Therapeutic uses:

The sunshine vitamin D is utilized in calcium and phosphorous metabolism and to treat autoimmune diseases, it reduces colon, breast cancer and ovarian cancer by up to 50 % and helps to maintain the equilibrium between bone and blood. It aids in development of teeth and bone formation. It is a group of closely related steroids that have antirachitic properties useful in the treatment of rickets. Research in the last few years suggests that vitamin D traditionally considered a "bone vitamin" most useful in the treatment of hopoparathyroidism. It plays a vital role in preventing infections such as heart diseases and diabetes mellitus. Psoriasis (chronic skin disease with scaly patches on elbows, knees and scalp can be well treated. Autoimmune diseases such as multiple sclerosis, insulin dependent diabetes mellitus and rheumatoid arthritis are decreased by vitamin D intake. Vitamin D plays a main role in calcium and bone metabolism and also maintains calcium and phosphorous homeostasis.

2.2.7 Vitamin D analogues: [25]

2.2.7.1. Doxercalciferol:

Doxercalciferol (Fig.8) is colourless, crystalline in nature practically insoluble in water. It is used to reduce elevated parathyroid hormone levels, especially in patients with chronic renal diseases.



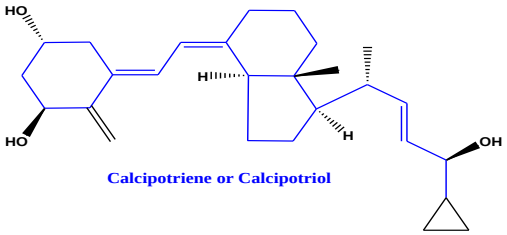
Doxercalciferol

(1*R*,3*S*,5*E*)-5-((2*Z*)-2-((1*R*,3a*S*,7a*R*)-hexahydro-7a-methyl-1-((*E*,2*R*,5*S*)-5,6-dimethylhept-3-en-2-yl)-1*H*-inden-4(7a*H*)-ylidene)ethylidene)-4-methylenecyclohexane-1,3-diol

Figure 8: Chemical structure of Doxercalciferol.

2.2.7.2. Calcipotriene:

It is a synthetic form of vitamin D_3 termed as calcipotriol (Fig. 9). It is used topically in the treatment of psoriasis.

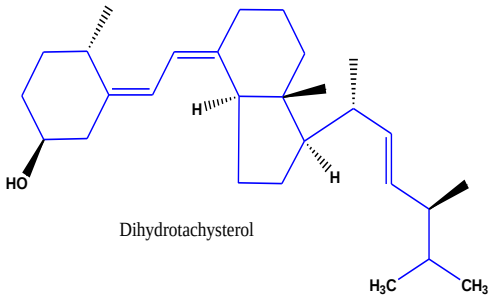


(1*R*,3*S*,5*E*)-5-((2*Z*)-2-((1*R*,3a*S*,7a*R*)-1-((*E*,2*R*,5*S*)-5-cyclopropyl-5-hydroxypent-3-en-2-yl)-hexahydro-7a-methyl-1*H*-inden-4(7a*H*)-ylidene)ethylidene)-4-methylenecyclohexane-1,3-diol

Figure 9: Chemical structure of Calcipotriene or Calcipotriol.

2.2.7.3. Dihydrotachysterol:

Dihydrotachysterol (Fig. 10) is a white crystalline powder, insoluble in water and slightly soluble in vegetable oil. It is generally obtained from the reduction of tachysterol i.e., a product of ergosterol. It shows rapid antirachitic activity and is the drug of choice in the treatment of hopoparathyroidism.



(1*S*,3*Z*,4*S*)-3-((2*Z*)-2-((1*R*,3a*S*,7a*R*)-hexahydro-7a-methyl-1-((*E*,2*R*,5*S*)-5,6-dimethylhept-3-en-2-yl)-1*H*-inden-4(7a*H*)-ylidene)ethylidene)-4-methylcyclohexanol

Figure 10: Chemical structure of Dihydrotachysterol.

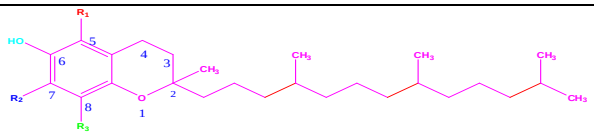
2.3. Vitamin E

In the year 1922, Herbert M. Evans reported the existence of vitamin E. He detected that more than one compound possessed the activity of vitamin E and referred them as Tocopherols (Tokos means for child birth; phero indicates to bear; ol implies alcohol) as these were essential for birth process in female and fertility in males rats and at the same time the compound reacted like an alcohol. In 1936, Evans separated vitamin E and determined its molecular formula ($C_{29}H_{50}O_2$) and its structure was determined in the year 1938. Tocopherols (4-forms) and tocotrienols (4-forms) are the two groups of natural compounds which exhibit vitamin E activity. Thus, the natural vitamin E exists in 8 different forms. The 4 forms of tocopherols and the tocotrienols [26] are like alpha (α), beta (β), gamma (γ) and delta (δ) forms. Amongst these, α-tocopherol is the most copious and highly active form. Vitamin E is the anti-sterility factor which is essential for fertility of the male and the birth process of the female.

2.3.1. Sources:

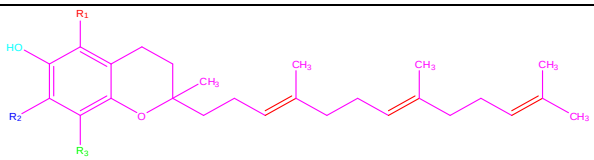
Vitamin E can be found in fortified cereals, seeds and seed oils like sunflower and green leafy vegetables like spinach, turnip, tomato products, pumpkin, sweet potato, blue crab, rockfish, mangoes, asparagus, broccoli, papayas and their products. Liver of horses and cattle's found in high quantity and small quantities found in the muscles of heart, kidneys, placenta, eggs, mustard greens, turnip greens, chard, parsley, kale, olives, bell pepper, brussel sprouts, kiwi fruit and blue berries. It is also available in foods and also available in oils such as cooking oil, fish oil, multigrain apricots, mustard and poultry, cottonseed oil, soybean and hazelnuts, vegetable oils, corn, canola, sesame, peanut, rice bran, and palm oils, almond oil. It also can be had from legumes and whole grains, lentils, wheat, rice, northern beans, chickpeas, barley grass and oats. Wheat germ oil extracted from the germ of wheat, wheat germ oil has been using for a long time as a vitamin E supplement [27] which offers a good combination of tocopherols (fig.6) plus tocotrienols (Fig.7).

Table 5. Chemical structures of tocopherols.

Structure	Tocopherol type	R_1	R_2	R_3
	α- Tocopherol	CH_3	CH_3	CH_3
	β- Tocopherol	CH_3	H	CH_3
	γ- Tocopherol	H	CH_3	CH_3
	δ- Tocopherol	H	H	CH_3

α- Tocopherol	2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-ol
β- Tocopherol	2,5,8-trimethyl-2-(4,8,12-trimethyltridecyl)chroman-6-ol
γ- Tocopherol	2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)chroman-6-ol
δ- Tocopherol	2,8-dimethyl-2-(4,8,12-trimethyltridecyl)chroman-6-ol

Table 6. Chemical structures of tocotrienols.

Structure	Tocotrienols type	R_1	R_2	R_3
	α- Tocotrienols	CH_3	CH_3	CH_3
	β- Tocotrienols	CH_3	H	CH_3
	γ- Tocotrienols	H	CH_3	CH_3
	δ- Tocotrienols	H	H	CH_3

α- Tocotrienols	2,5,7,8-tetramethyl-2-((3E,7E)-4,8,12-trimethyltrideca-3,7,11-trienyl)chroman-6-ol
β- Tocotrienols	2,5,8-trimethyl-2-((3E,7E)-4,8,12-trimethyltrideca-3,7,11-trienyl)chroman-6-ol
γ- Tocotrienols	2,7,8-trimethyl-2-((3E,7E)-4,8,12-trimethyltrideca-3,7,11-trienyl)chroman-6-ol
δ- Tocotrienols	2,8-dimethyl-2-((3*E*,7*E*)-4,8,12-trimethyltrideca-3,7,11-trienyl)chroman-6-ol

2.3.2. Functions:

Being as an anti-oxidant vitamin E plays an important role to protect the body cells from the damage caused by free radicals which are highly reactive and destructive compounds formed due to oxidative deterioration (metabolism) of polyunsaturated fats. Factors contributing for free radical generation in the body include smoking and exposure to UV - radiations. Tocopherol performs a unique function and interrupts free radical chain reactions by capturing the free radicals which denotes antioxidant properties. The free hydroxyl group on the aromatic ring is responsible for the antioxidant properties. The hydrogen from this group is donating to the free radical resulting in a relatively stable free radical form of the vitamin. Vitamin E protects this oxygen rich blood from becoming filling with free radicals and the heart during sex which is also called sex vitamin. As a regulating cellular metabolism in the body including protein synthesis in muscles and protects vitamin C from oxidation and stabilizes of vitamin A. Combination of vitamin E[35] and vitamin C is used as a prophylactic measure in Alzheimer's disease, protection of red blood cells, stabilization of fats and amino acids, metabolism of nucleic acids and steroids. Vitamin E acts as neuroprotector.

2.3.3. Deficiency:

Deficiency of vitamin E causes heart disease, angina, cancer, multiple sclerosis, muscle weakness, diabetes [28], respiratory tract infections [29], neurological problems like Alzheimer's disease, Parkinson's diseases, poor nerve conduction in the body, cataracts, emphysema, high cholesterol, fibrocystic breast condition intermittent claudication, infertility, impotence, genital herpes, bedsores, leg cramps, muscle soreness, phlebitis, menopausal discomforts, HIV, osteoarthritis, chronic inflammatory diseases such as lupus, rheumatoid arthritis, low birth weight in infants. The deficiency may also lead to blindness owing to degeneration of the retina and haemolysis and disorder of fat metabolism known as betalipoproteinaemia.

2.3.4. Adverse effects:

Over doses may cause nausea, vomiting, diarrhoea. Individuals who are deficiency of vitamin K (people who are on blood thinners) should not be taken tocopherols [30]. Supplements without proper medical examination, because of impending increased risk of haemorrhage. Some people may also get irritation or allergic reactions when vitamin E is applied to the skin. Possible side effects of vitamin E due to high doses include unusual bleeding or bruising, nausea, headaches and blurred vision. Intensive studies reveal that people who take doses of more than 400 international units (IU) per day produces an increased risk of death along with all causes combined. In smokers, the plasma [31] level may disappear because of deficiency of vitamin E.

2.3.5. Therapeutic uses: [32]

Particularly vitamin E is essential in treating many skin problems and diseases such as psoriasis, treatment of scars, help to soften the appearance of acne and surgical scars. There is a 40 % reduced risk of coronary artery disease for those who took vitamin E supplements compared to those who did not take vitamin E. It may also protect against the development of cancers [33] by enhancing immune function. Vitamin E is also a popular treatment for post-pregnancy stretch marks, which is supported by numerous studies. It protects epidermis, the first layer of skin from harsh weather and reduces the dryness due to ashy skin. Vitamin E brings many health benefits for the body and is particularly important for the skin, heart, muscles and red blood cells. As it also protects the body's red blood cells and curbs the possible development of anaemia. It also helps to control blood pressure and lowering blood sugar and important to health of skin and nails and prevents cancer [34] also. It gives the effect of anti-aging to the skin and reduces the appearance of lines and wrinkles of the skin which looks younger. It also aids in proper blood clotting, improves wound healing helps in tissue repair, promotes healthy hair and slows the aging process. It plays a role in immune function, DNA repair, the formation of red blood cells and vitamin K absorption. Vitamin E preparations are shown in following Table 7.

Table 7. Certain commercially available vitamin E preparations are:

E - cap	200 mg, 400 mg capsules.
Tocofer	200 mg, 400 mg capsules.
Edge	400 IU soft gelatine capsules.
Monoviten	100 IU, 200 IU and 400 IU capsules.
Evion	200 mg, 400 mg, 600 mg of soft gelatin capsules.

2.4. Vitamin K

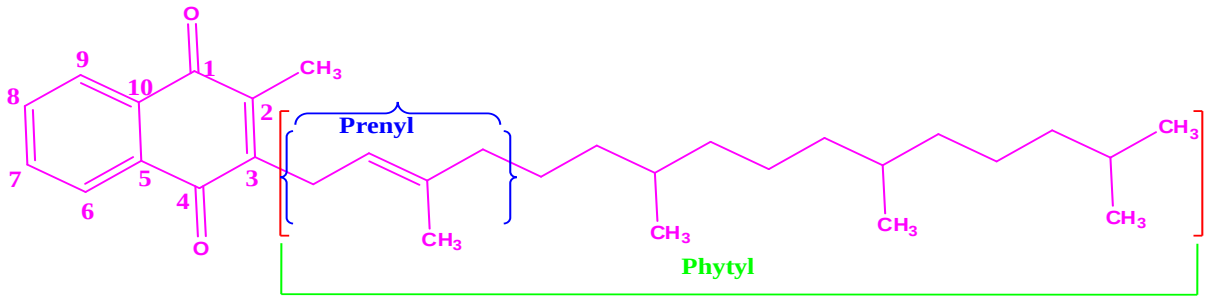
The term originated from the German word Koagulation (clotting of blood). Vitamin K is also known as the clotting vitamin. Vitamin K is one among the fat-soluble vitamin which is chemically a derivative of Napthaquinone. They are 2-methyl-1, 4-naphthoquinone derivatives. H. Dam isolated the substance responsible for blood clotting from alfalfa from a leafy vegetable in the year 1939 and it is named as phylloquinone or vitamin K_1 (Fig.11). Later, another scientist Doisy separated vitamin K_2 (Fig.12) known as menaquinone from putrefied fish meal. Both Dam and Doisy awarded the Nobel Prize in 1943 for their work. Vitamin K present in both natural and synthetic forms. The natural forms of vitamin include vitamin K_1 known as phylloquinone and vitamin K_2 called menaquinone while synthetic forms are vitamin K_3 (Fig.13) termed as menadione and vitamin K_4 (Fig.14) called as menadiol sodium diphosphate. Vitamin K has also been used as a slang term for ketamine, an unrelated anesthetic. Vitamin K is not a single chemical substance but rather a family of chemically related substances that go by the general name of "vitamin K". All types of vitamin K fell into a large chemical category of substances called naphthoquinones.

2.4.1. Sources:

People usually do not suffer from a deficiency of vitamin K as it is widely available in our daily diet. It is abundantly found in green leafy vegetables such as spinach, parsley, alfalfa, broccoli, cabbage and its family, Cauliflower, yogurt, soya bean, wheat, oats and tomatoes also contain vitamin K. Vitamin K can also be obtaining from the consumption of nuts like cashew nuts, chestnuts and pine nuts. Fruits such as avocado and kiwi fruit are a significant source of this vitamin. Vitamin K can be founding in meat, eggs, cow's milk and pig's liver. However, vegetables are a richer source of vitamin K than animals. Raw food materials like Swiss chard, watercress, carrot tops, mayonnaise and vegetable oils such as soybean oil, olive oil, and cotton seed oil are rich sources of vitamin K_1 [35] and vitamin K_2 is found in putrified fish meal and is synthesized in the intestine by microbial bacteria. Recommended nutrients intake for vitamin K is shown in Table 8.

Table 8. Recommended nutrients intake (RNI) for vitamin K.

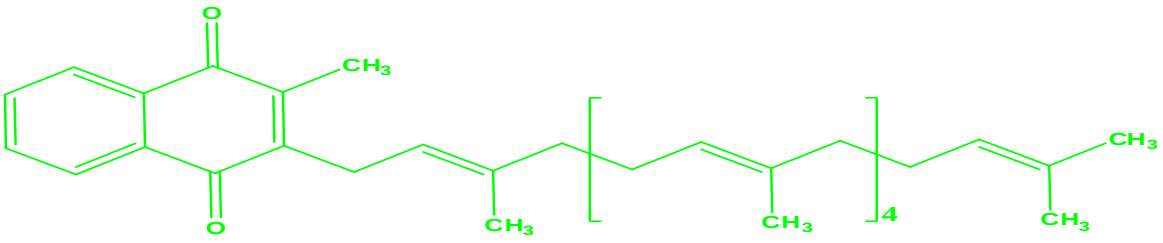
Age group			RNI (µg /day)
Infants and children		0–6 months	5
		7–12 months	10
		1–3 years	15
		4–6 years	20
		7–9 years	25
Adolescents	Females	10–18 years	35 - 55
	Males		
Adults	Females	19–65 years	55
		65+ years	55
	Males	19–65 years	65
		65+ years	65
Pregnancy		-	55
Lactation		-	55



Vitamin K_1 (Phylloquinone)

(*E*)-2-methyl-3-(3,7,11,15-tetramethylhexadec-2-enyl)naphthalene-1,4-dione

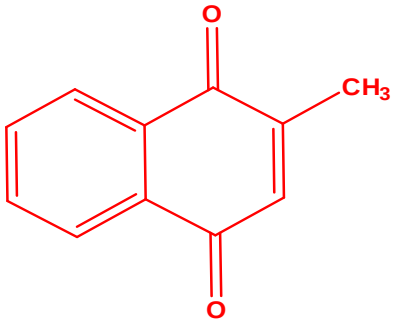
Figure. 11. Chemical structure of Vitamin K_1.



Vitamin K_2 (Menaquinone)

2-methyl-3-all transpolyprenyl-1, 4-naphtaquinone

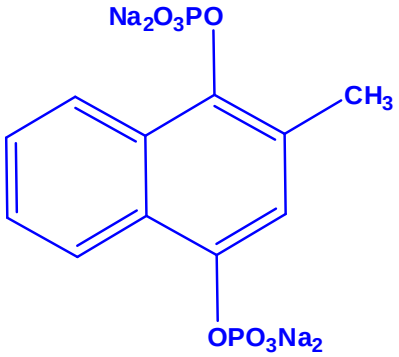
Figure. 12. Chemical structure of Vitamin K_2.



Vitamin K_3 (Menadione)

2-methylnaphthalene-1,4-dione

Figure. 13. Chemical structure of Vitamin K_3.



Vitamin K_4 (Menadiol sodium diphosphate)

sodium 2-methylnaphthalene-1,4-diyl diphosphate

Figure. 14. Chemical structure of Vitamin K_4.

2.4.2. Functions:

Role in coagulation – vitamin K function is coagulation cascade like factors II (prothrombin), VII, and IX and X and kept under the control by proteins C, S and Z. These coagulation factors are present in an inactive form but activated when they are capable of binding to Ca^{+2} ions. Vitamin K as supplement ingredient may have the ability to improve bone health as well as reduce the risk of bone mineral density and hip fractures [37-38] particularly in women that are postmenopausal and have a risk for osteoporosis. If an individual has higher levels of vitamin K within their system, they will have a greater bone density. Osteoporosis persons have low levels of vitamin K. Usage of vitamin K reduces the chances of bleeding in the liver which coupled with a myriad of other conditions like jaundice, malabsorption. It has also been used to treat that are suffering from heavy menstrual bleeding. It may also be prescribed when elevated risk for bleeding in the brain due to the trauma experienced going through the birth canal during delivery to the new born, vascular health. It also decreases calcification in the arteries [39] by absorbing the hardened calcium to lessen the risk of heart disease, aids in reducing excessive menstrual flow, help the absorption of calcium in bones. It is essential for normal liver functioning and for synthesis of four proteins [40] that act in coagulation. It is also important in maintaining vitality and longevity, necessary for formation of prothrombin which is required for effective blood clotting, involved in electron transport mechanism and oxidative phosphorylation.

2.4.3. Deficiency:

Hypoprothrombinemia is the primary disease that occurs due to vitamin K deficiency which is characterised by increased risk of bleeding due to loss of blood clotting power. It stops easy or excessive bleeding, bruising, nosebleeds, bleeding gums, blood in the urine and stool extremely heavy menstrual bleeding, liver damage, low bone density, arterial calcification [41], malabsorption in the digestive tract. Deficiency of vitamin K is quite rare, as it is widely distributed in many sources of food and also produced by the intestinal bacteria. Its absorption depends on sufficient of bile salts and therefore, any disease of the liver that can impair bile secretion is more likely to cause a deficiency of this vitamin. The most important symptoms of vitamin K deficiency are that blood clot is very slow and consequently bleeding for a long time even from minor injuries. Its deficiency also causes bug black and blue marks from very slight bruises or even for no reason, blood in your urine and intestinal bleeding.

2.4.4. Adverse effects:

Naturally both phylloquinone and menaquinone are non-toxic in nature however adverse effects such as haemolytic anaemia, jaundice, anaphylactic reactions are noticed in premature infants when taken in excess amounts. Synthetic forms of vitamin K and menadione are more toxic than naturally occurring forms. Injections of menadione damage the cell membranes by oxidation of glutathione. Low vitamin K levels in breast milk, poor transport of vitamin K through placenta, low fat stores of vitamin K, sterile intestines and liver immaturity. There is a risk of haemolyses and jaundice. Some patients with chronic fat malabsorption regularly ingest doses of this size without evidence of any harm. Besides lacking intrinsic biologic activity, the high reactivity of its unsubstituted 3-position has been associated with neonatal haemolysis and liver damage.

2.4.5. Therapeutic uses:

Anticoagulant drug overdose reduces excessive menstrual flow, bleeding in liver diseases, jaundice, and malabsorption, essential for blood clotting/haemorrhage and bleeding, inhibiting some cancer tumours overcoming inability to absorb vitamins overcoming effects of antibiotics on intestinal bacteria. Protection against osteoporosis helps to prevent the formation of stones in the kidneys, skin wounds hemostasis. It is designed to maintain blood within injured vessels by three sequential events: Vasoconstriction, platelet plug formation, coagulation. Fibrin meshwork forms a blood clot, which provides structural support to the temporary plug formed by platelets. Fibrin proteins are the end products of coagulation cascade, vitamin K analogues are known to stop the growth of liver cancer, improve the myelodysplastic syndrome (a group of blood disorder) etc.

III. CONCLUSIONS

Vitamins A, D, E, and K dissolve in organic solvents and used in correcting deficiency diseases and some used to treat non-deficiency diseases which are found in plant and animal sources. Adequate intake of fat soluble vitamins is solely lacking among modern peoples–especially by comparison to traditional societies. Average intake of fat soluble vitamins like vitamin A, vitamin D, vitamin E and vitamin K is inadequate at best and dangerously low at worst even among health circles. Vitamins cannot be produced by the human bodies. They must be eaten through food or as supplements and they assist the body in using food by bringing about biochemical reactions so that life can be maintained**.** Fat-soluble vitamins if consumed in excess over the suggested dose usually dissolve in fat and stored in body tissues and the excess accumulation lead to dangerous levels resulting a stage called hyper vitaminosis, which symbolises excess deposit in the body. Most vitamins that are sold as food supplements cannot exceed a maximum daily dosage. Hence apt dosage of these fatty vitamins keep the body operating at its optimum capacity and too much quantity may destroy the health severely. The regulations of that define the limits of vitamins dosages for the safe use as food supplements to upkeep health and to keep out of possible side effects. Regulations that define limits of fat soluble vitamin dosages for the safe use as food supplements must be followed to preserve safety and to avert side effects caused by overdose. Therefore it is felt imperative that public awareness need to be taken up in a big way frequently. As a continuous process through regular public meetings, group discussions, seminars, hoardings, cinema slides, placards, folk songs and stage shows relating to fat soluble vitamins, particularly in nook and corner rural areas through governmental organisations of all departments, Non-governmental Organisations (N G O's) corporate hospitals, enlightened village groups and the like.

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