

VITAMINS

HISTORY

In east Asia among the crew members, where polished rice was a staple food, a deadly disease called Beri-Beri was very common.

Takaki Kanehiro, a British trained medical doctor of the Imperial Japanese Navy experimented on these crew members and found that diet was the major cause of the disease.

Christiaan Eijkman, who in 1897 discovered that **feeding unpolished rice** instead of the polished variety to chickens helped to prevent beriberi in the chickens.

Thus concluded that the disease could be a result of some dietary deficiencies

Frederick Hopkins postulated that some foods contained "**accessory factors**" — in addition to proteins, carbohydrates, fats *etc* that are necessary for **the functions of the human body**.

Hopkins and Eijkman were awarded the Nobel Prize for Physiology or Medicine in 1929 for their discoveries.

In 1910, the first vitamin complex was isolated by Japanese scientist **Umetaro Suzuki**, who succeeded in **extracting a water-soluble complex of micronutrients** from rice bran and named it **aberic acid**.

In 1912 **Polish biochemist Casimir Funk** isolated the same complex of micronutrients and proposed the complex be named "**vitamine**" - **vital amine since the vitamin isolated contained amine group**.

Later discovers revealed that all vitamins are not amines, thus the letter "e" was deleted and it was called vitamins.

INTRODUCTION

vitamin is an organic compound required by an organism in small amounts for proper functioning.

They are not synthesized in our body and hence need to be taken through diet.

Absence or shortage of vitamins leads to deficiency diseases.

Degradation of vitamins do not yield energy, but they are involved in the metabolic reactions that release energy.

Thirteen vitamins are universally recognized at present

CLASSIFICATION

Vitamins are classified into major categories based on their solubility

Fat
soluble

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graph TD; A([Fat soluble]) --> B[Vitamins A,D,E and K]; C([Water soluble]) --> D[Vitamin B complex and C]
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Vitamins A,D,E and K

Water soluble

Vitamin B complex and C

FAT SOLUBLE AND WATER SOLUBLE VITAMINS

Fat soluble vitamins

Water soluble vitamins

Lipid soluble

Water soluble

Mostly isoprenoid compounds

Heterogeneous

Not readily excreted in urine and thus accumulation leads to toxic effects.

Readily excreted in urine.

Stored in liver and adipose tissues

Not stored in large quantities and hence needs to be supplied continuously through diet.

DEFICIENCY OF VITAMINS

In a well **balanced diet** all the vitamins are available in **required quantities** and thus **deficiencies are not seen**.

But among the **undernourished** population **multiple deficiencies are common than single deficiencies**.

Vitamin deficiencies might arise from,

- Inadequate intake or increased requirements.
- **Impaired absorption or increased loss.**
- Chronic alcoholism
- **Hemodialysis and certain surgical procedures on GIT.**
- Inborn errors of metabolism

HYPERVITAMINOSIS

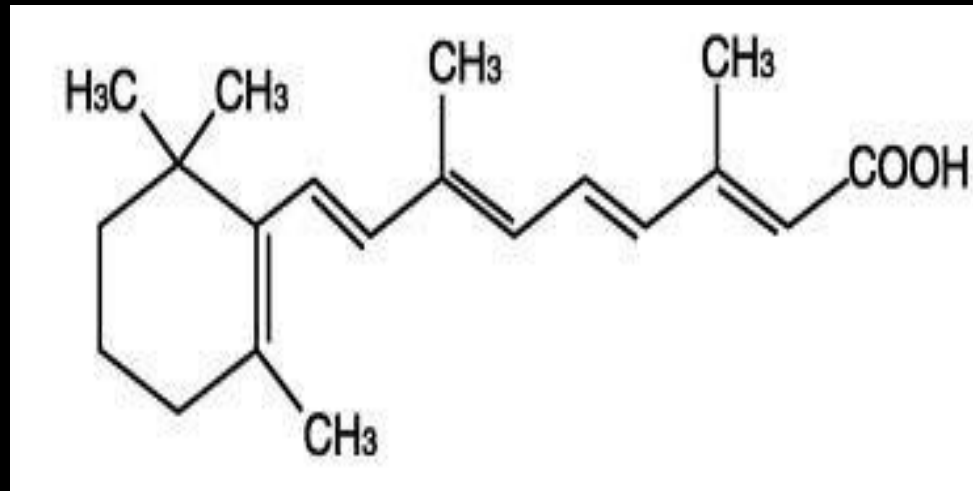
When the dietary intake of the vitamins exceeds the ability of the body to utilize, store or excrete -it leads to hypervitaminosis

The water soluble vitamins do not get stored and thus excess intake does not cause any toxic effects.

Since the fat soluble vitamins are stored in the body their excess intake might cause a problem.

VITAMIN A (RETINOIC ACID)

Vitamin A is a **fat soluble vitamin** which essentially have a **beta-ionone ring** to which an **isoprenoid chain** is attached. Both structural features are essential for vitamin activity



Vitamin A exists as **pro-vitamins** which are later converted to its **active form**.

Carotenes from **plant source** and **retinol** from **animal source** are the major precursors of the vitamin A.

Vitamin A was discovered by **Elmer McCollum** at the University of Wisconsin–Madison, and **Lafayette Mendel and Thomas Burr Osborne** at Yale University who studied the role of fats in the diet.

The "accessory factors" were termed "**fat soluble**" in 1918 and later "**vitamin A**" in 1920

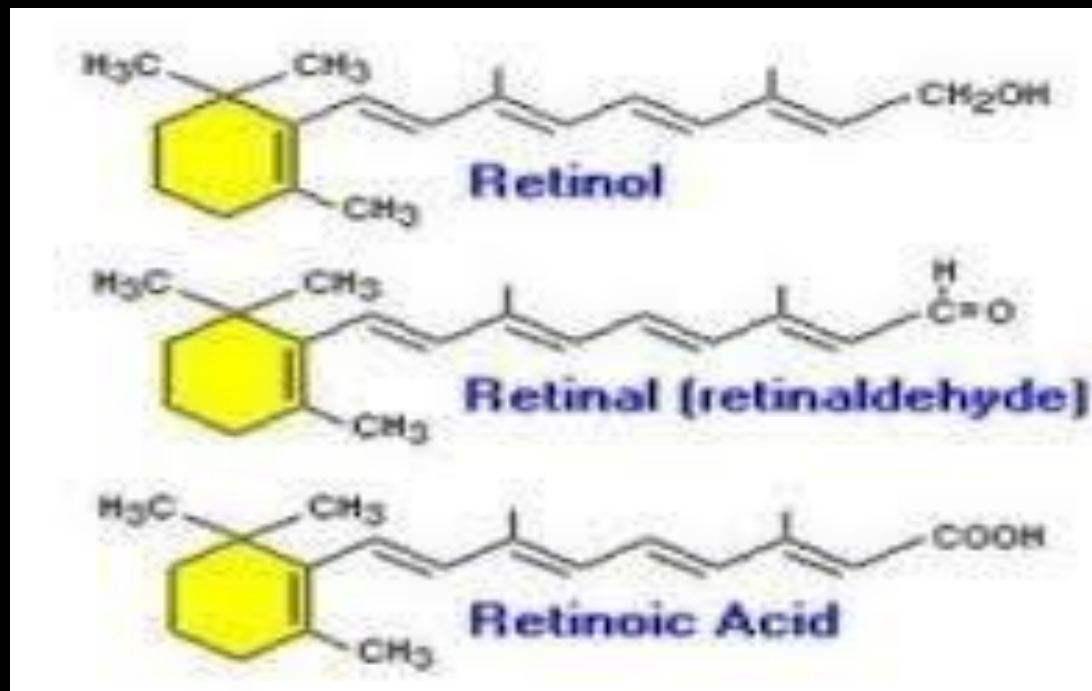
CHEMISTRY

Vitamin A occurs in nature in three different forms-

Retinol (alcohol form): role in reproduction

Retinal (aldehyde form): essential for normal vision

Retinoic acid (acid form): required for cell growth and differentiation.



Source: cod liver oil, liver, eggs, milk, butter, Spinach, carrot, broccoli, papaya are few sources of vitamin A.

Metabolic functions

Vitamin A plays a role in a variety of functions throughout the body, such as:

1. Vision
2. Gene transcription
3. Immune function
4. Embryonic development and reproduction
5. Bone metabolism

VISION

Vitamin A (retinal) is a component of the photoreceptor complex in the retina.

Light activates the retinal which triggers a cascade of signal transduction events that leads to hyper-polarisation in the plasma membrane of the photoreceptor cells resulting in the generation of the nerve impulse.

The photoreceptor cells are of two types:

Rod cells

Function in dim light

Cone cells

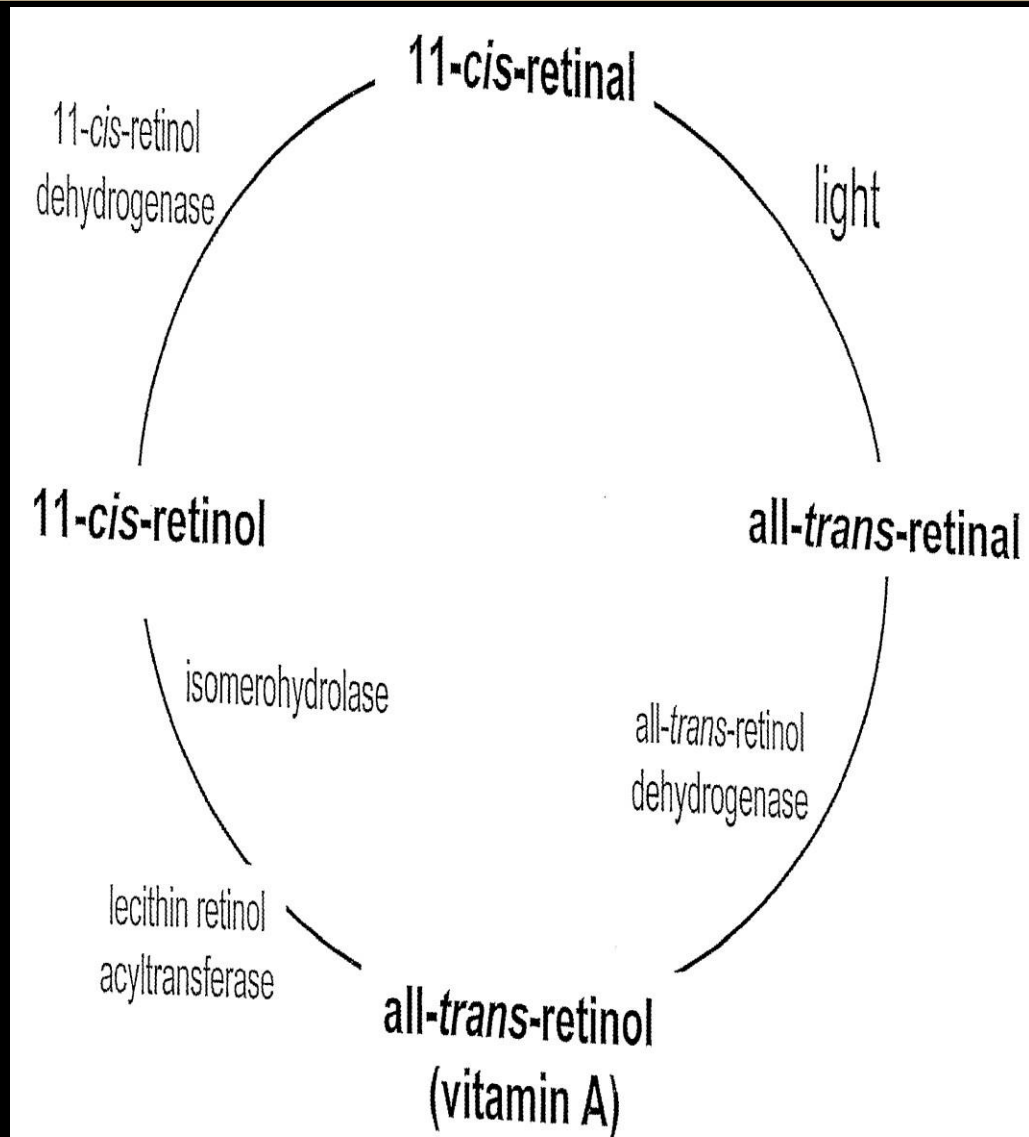
Function in bright day

WALDS VISUAL CYCLE

The photo-receptor molecules in the rods is called the rhodopsin is conjugated with a protein called opsin which is linked to the 11 cis retinal.

Absorption of light results in the isomerization of the 11 cis retinal to all trans retinal, with few unstable intermediates.

The all trans retinal is converted to all trans retinol by dehydrogenase enzyme present in the outer segment.



The all trans-retinol is transported into the pigmented epithelium where the specific isomerase converts it to 11-cis retinol.

This retinol is later converted to 11-cis-retinal by the enzyme reductase and transported back to the outer segment.

11-cis-retinal combines with opsin to form rhodopsin and the cycle continues.

BIOCHEMICAL FUNCTIONS

Retinol and retinoic acid acts as steroid hormones.

They regulate growth and differentiation and normal reproduction.

Retinoly phosphate synthesized from retinoic acid participates in glycoprotein synthesis.

Essential for formation of mucopolysaccharides in the extra-cellular matrix.

Retinol and retinoic acid are essential for the synthesis of the transferrin, the iron transporting protein.

Vitamin A is a potent anti-oxidant.

The recommended daily allowance (RDA)

Men: 1000 RE (3500 IU)

Women: 800 RE (2800 IU)

DEFICIENCY

1. **Night blindness and xerophthalmia:** Inability to see in the dim light is the earliest symptom of deficiency, when left untreated leads to xerophthalmia. The cornea becomes hazy due to keratinization and loses transparency.
2. **Bitot's Spots:** They are triangular white patches on the conjunctiva on either side of the cornea.
3. **Keratomalacia:** Ulceration and necrosis of the cornea is called keratomalacia leads to total blindness.

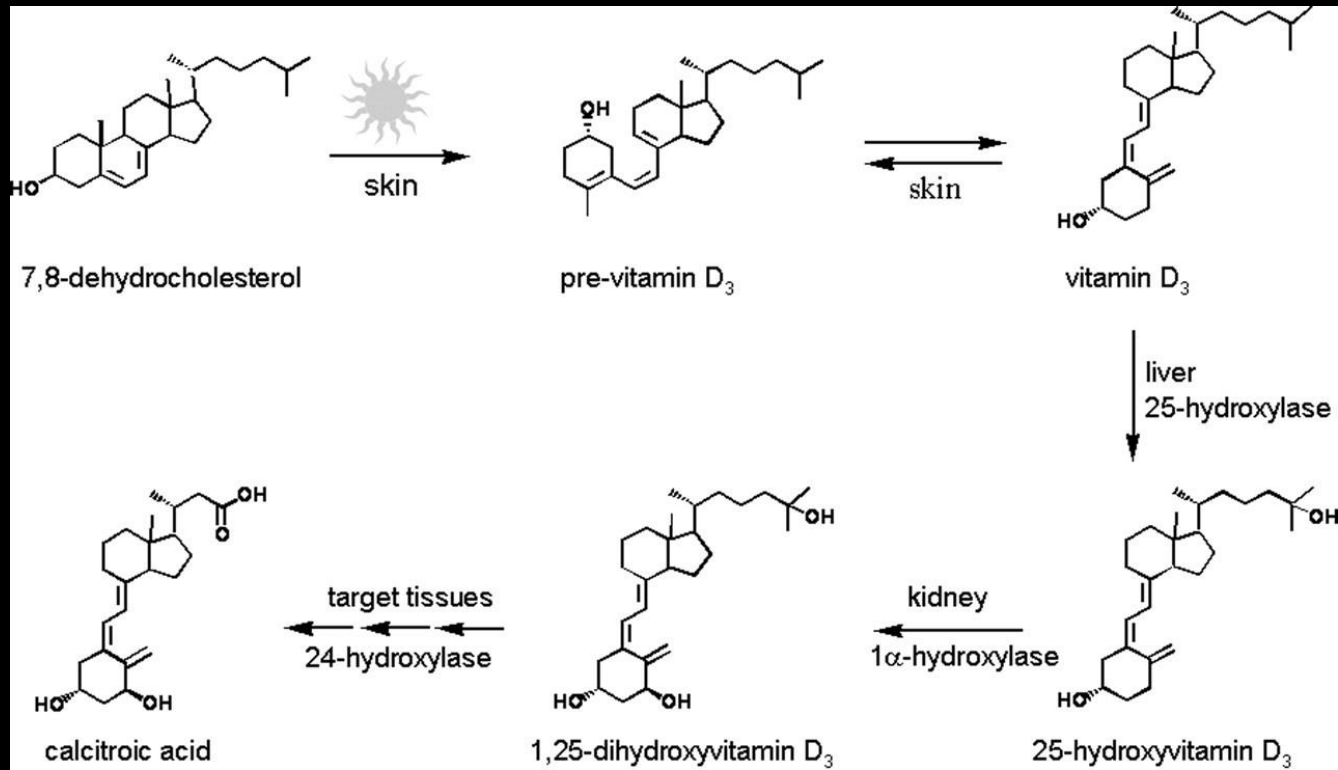
Vitamin A toxicity

Drowsiness, general weakness, irritability, headache, dry and peeling skin and joint pains

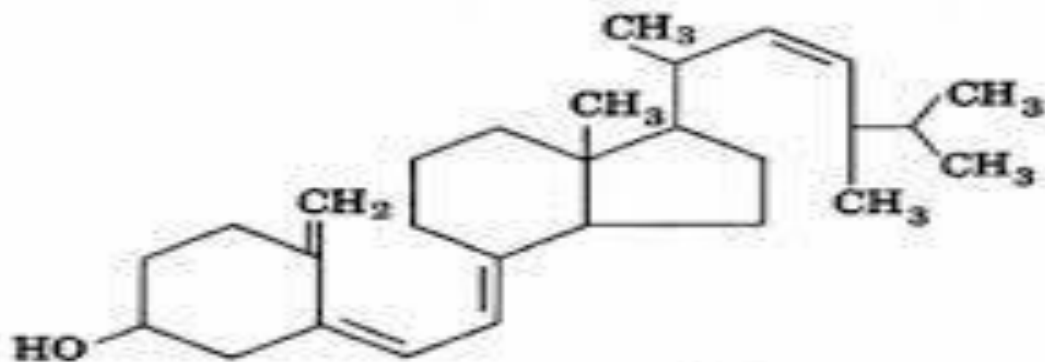
VITAMIN D

Vitamin D is a **modified steroid**, synthesized in the skin under the **influence of the sun**.

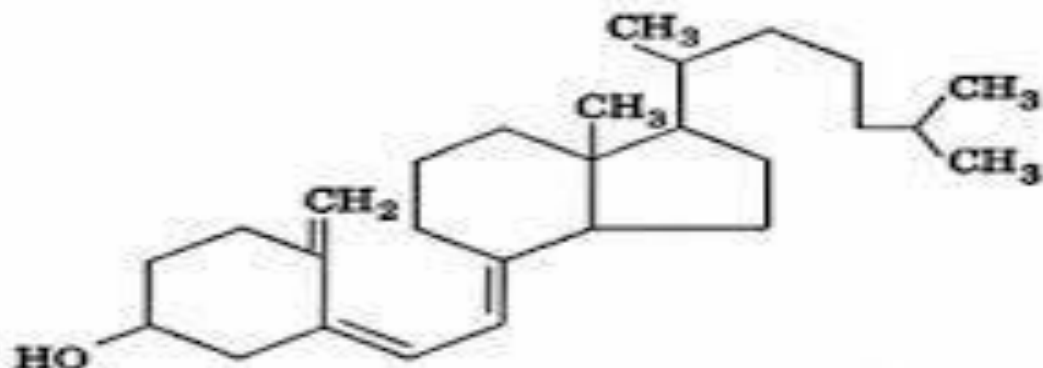
There are 2 important forms of vitamin D – **Ergocalciferol** (vitamin D₂) and **Cholecalciferol** (vitamin D₃)



STRUCTURE OF VITAMIN D₂ AND D₃



Vitamin D₂ (calciferol)



Vitamin D₃

BIOCHEMICAL FUNCTIONS

Vitamin D plays an important role in the **homeostasis of calcium and phosphorus**.

Calcitriol the active form of vitamin D, **regulates the plasma levels of the calcium and phosphorus**.

Calcitriol stimulates **calcium uptake in osteoblasts leading to bone mineralization**.

Calcitriol with parathyroid hormones **promotes demineralization to maintain the plasma calcium levels**.

Calcitriol conserves calcium and phosphorus by minimizing their excretion through kidneys.

RDA AND SOURCES

RDA: 400 IU/10mg

Sources: Exposure of the skin to sunlight can synthesis the Vitamin D in required amounts.

Fish, Egg, liver, butter and cheese are good sources of Vitamin D



natural sunlight



fortified milk



cheese



butter/margarine



cereal



fish

DEFICIENCY

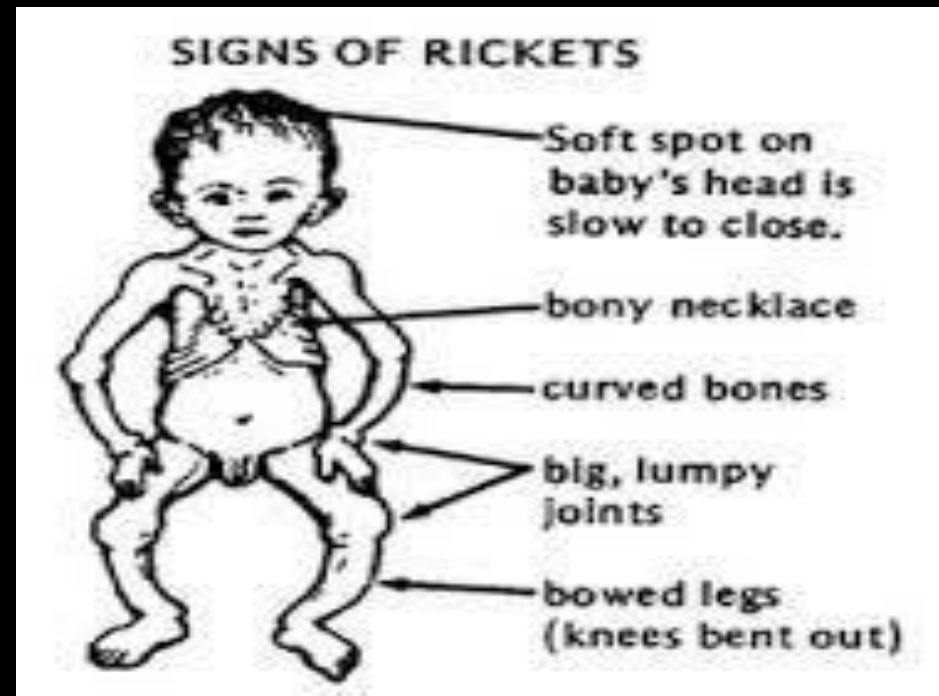
Deficiency of Vitamin D is **not common** as it is **synthesised** by the body by simple **exposure to sun light**.

However people suffering from **liver and kidney disorders, fat mal-absorption** can develop deficiency

In children the deficiency of vitamin D causes **rickets** and in adults **osteomalacia**

Rickets: Seen in young children

- The **bone formation** is characterized by improper mineralization resulting in **soft, pliable bones causing several bone deformities.**
- The weight bearing bones are **bent causing bow legs, knock knees, pigeon chest.**



Ostomalacia: It is a disorder in which the bone contains normal **amounts of the bone matrix**, but it is **deficient in mineral content**.

Such undemineralised bone is **structurally weak and more susceptible to fractures**.

Proximal muscle weakness and hypotonia are common and the patient may walk with knock knees.

VITAMIN D TOXICITY

Among vitamins, vitamin D is the **most toxic in cases of over dose**

Increased calcium absorption and bone resorption cause hypercalcemia which may result in **deposition of calcium in soft tissue like kidneys**

Excessive intake of vitamin D can **cause nausea, vomiting, loss of appetite, high blood pressure and weakness.**

High serum calcium may result in formation of kidney stones.

VITAMIN E

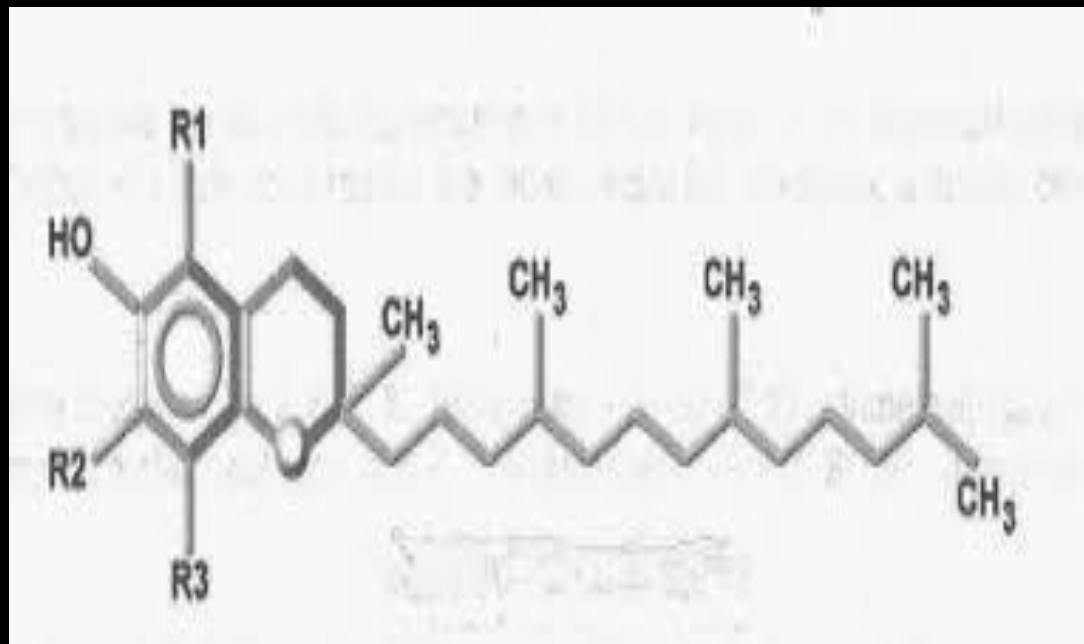
Vitamin E is an important **natural antioxidant abundant in vegetable oils.**

Evans and his associates (1936) isolated compounds, essential for the **normal reproductive functions in animals** and **named them tocopherols.**

Vitamin E is the **generic name** for a group of naturally occurring **fat soluble substances**, the tocopherols.

About 8 tocopherols have been identified; alpha, beta, gama, delta and so on.

The tocopherols are composed of a 6 hydroxy chromane nucleus substitute with methyl groups and an attached isoprenoid(3 units) side chain.



FUNCTIONS

Vitamin E plays a vital role in safeguarding the **structural integrity of the biological membranes**.

Essential for **normal reproduction and fertility** in experimental animals and hence it is known as the **anti-sterility vitamin**.

It **protects low density lipoproteins** from oxidation.

It **decreases the activity of the liver microsomal mono-oxygenase (cytochrome p450)** which detoxify most drugs.

It also **inhibits prostaglandins** synthesis thus acting as an **anti-inflammatory agent**.

Its involved in the **synthesis of the coenzyme Q** which is an important constituent of the electron transport chain.

It is also involved in the **synthesis of nucleic acids and cell signaling**.

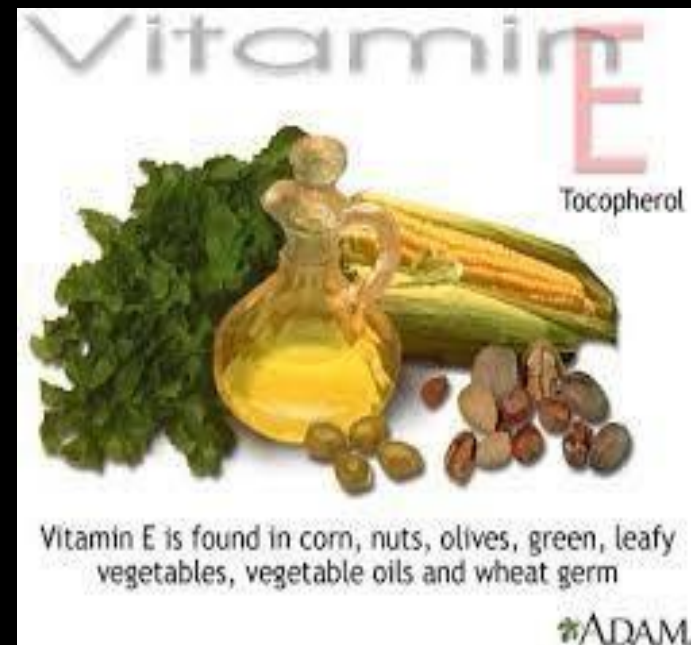
RDA AND SOURCE

RDA:

Men: 10mg

Women: 8mg

Sources: Fish liver oil, vegetable oils, meat, milk, nuts and eggs.



DEFICIENCY

Its requirements are **easily met through regular diet**, deficiency of Vitamin E is **rare in human** except in **premature infants and malabsorption syndromes**.

A mild **hemolytic anemia** may be seen in **prematured new borns** due to the **decreased production of haemoglobin** and the **shortened life span of erythrocytes** with fragile membranes.

In adults, **degenerative changes in muscles** may be seen with **excretion of creatine in urine**.

In animals, vitamin E deficiency is associated with **setrility**.

TOXICITY

Among the fat soluble vitamins, vitamin E is considered to be the least toxic and hence consuming it in slightly higher quantities does not result in adverse effects.

VITAMIN K

Vitamin K is required for the **blood clotting** process.

The **letter K** stands for **Koagulation** – A German word.

Vitamin K is **synthesised** by the **bacterial flora** of the **intestine**.

Chemistry

Vitamin K occurs in 2 natural forms:

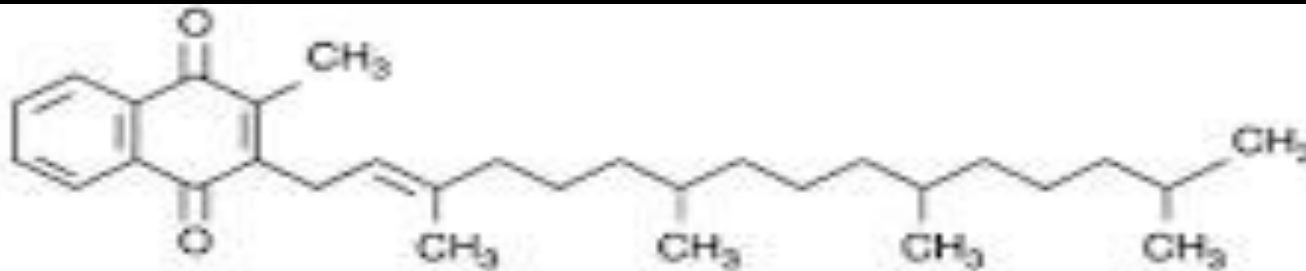
Vitamin K1: phylloquinone ---- occurs in green leafs and other plant sources.

Vitamin K2: menaquinone ---- Produced by the bacterial flora in the intestine.

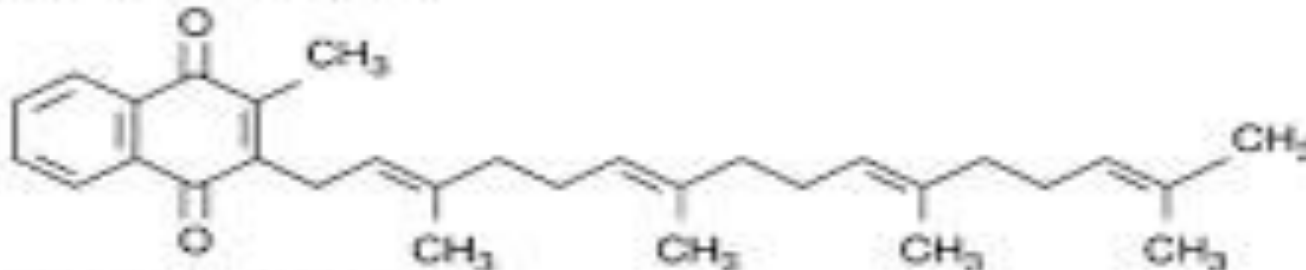
A synthetic form is also available named as **manadione**---- **vitamin K3**.

All the three forms are naphthoquinone derivatives.

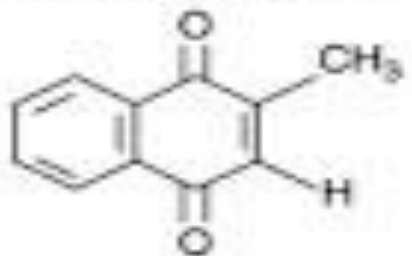
Structures



Phylloquinone (vitamin K₁)



Menaquinone-4 (vitamin K₂)



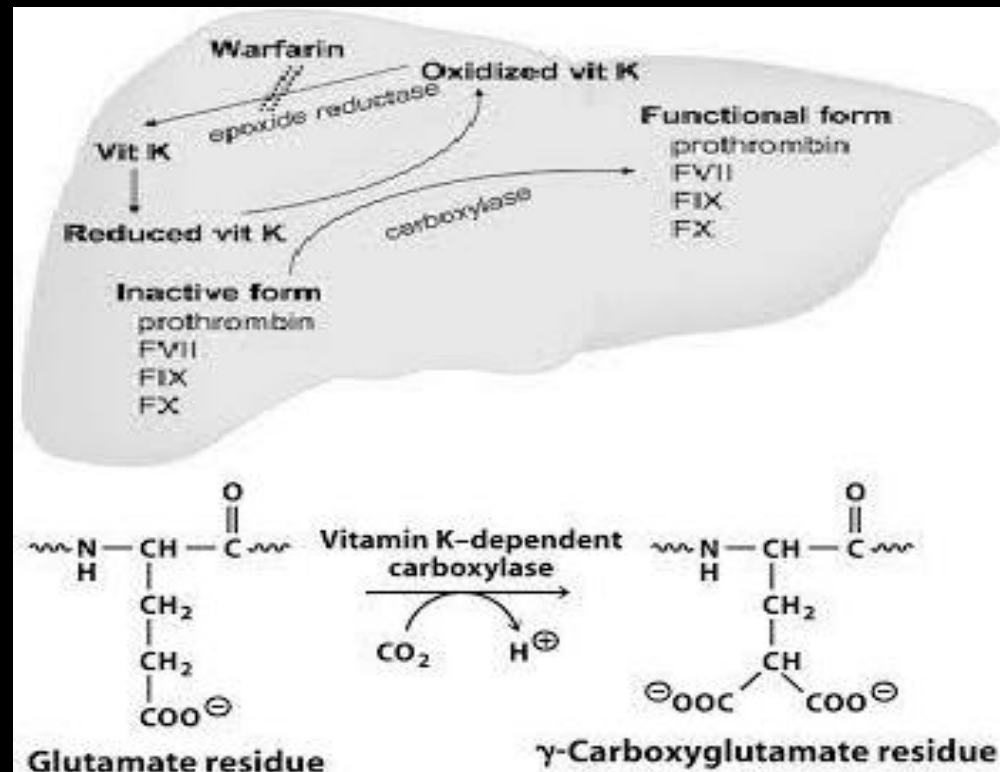
Menadione (vitamin K₃)

BIOCHEMICAL FUNCTIONS

Vitamin K is required for blood coagulation: Vitamin K serves as the **coenzyme** for **post translation modification** of the inactive forms of the **prothrombin, factors VII, IX and X** which are necessary for coagulation

The **glutamic acid residues** present in these proteins undergo **carboxylation** to form **Gamma carboxyglutamic acid**.

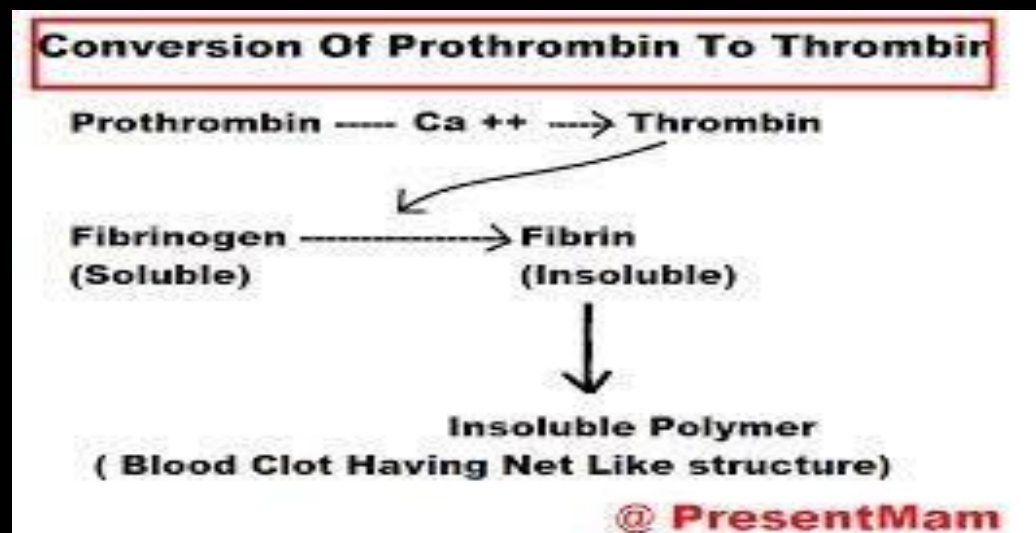
These **negatively charged** groups serve as tight binding sites for **positively charged calcium ions**.



Now the clotting factors bind tightly to the calcium.

The pro-thrombin calcium complex then binds to phospholipids on the membranes of the platelets and gets converted to thrombin.

Thrombin then catalyses the conversion of fibrinogen to fibrin clot.



RDA AND SOURCE

Since vitamin K is **synthesised** by the **intestinal flora**, the **dietary requirement is low**.

RDA -70-140µg/day

Sources: green leafy vegetables, eggs and dairy products.

DEFICIENCY AND TOXICITY

Delayed coagulation and bleeding

Common in infants as their colon is sterile, low tissue storage, liver immaturity.

Adults suffering from obstructive jaundice and severe fat malabsorption suffer from deficiencies.

Toxicity: Administration of large doses of menadione may cause hemolytic anemia and jaundice.