Vitamins

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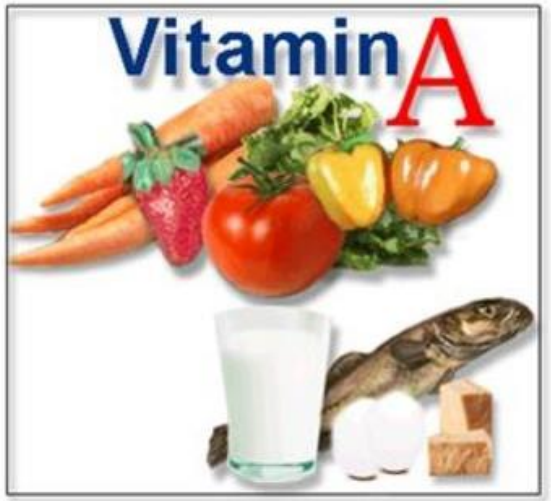
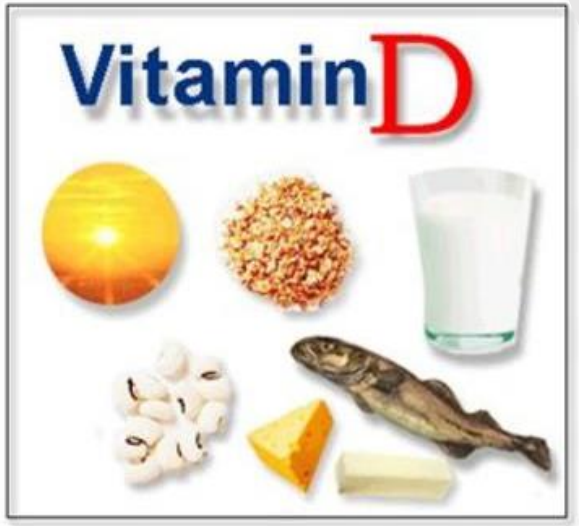
Fat-Soluble Vitamins

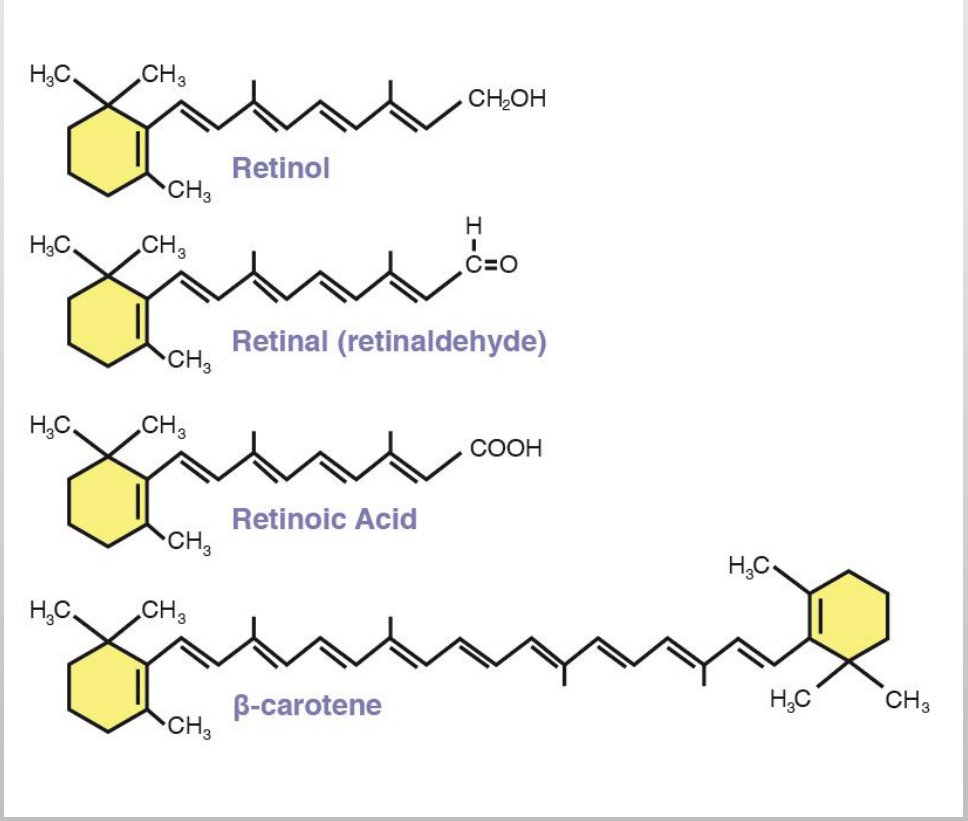
- Vitamin A
- Vitamin D
- Vitamin E
- Vitamin K





Vitamin A

Retinoids includes both natural and synthetic forms of vitamin A that may or may not show vitamin A activity.



Retinol: primary alcohol found in animal tissue as ester with fatty acid

Retinal: This is the aldehyde derived from the oxidation of retinol. Interconverted to retinol

Retinoic acid: This is the acid derived from the oxidation of retinal. Retinoic acid cannot be reduced in the body

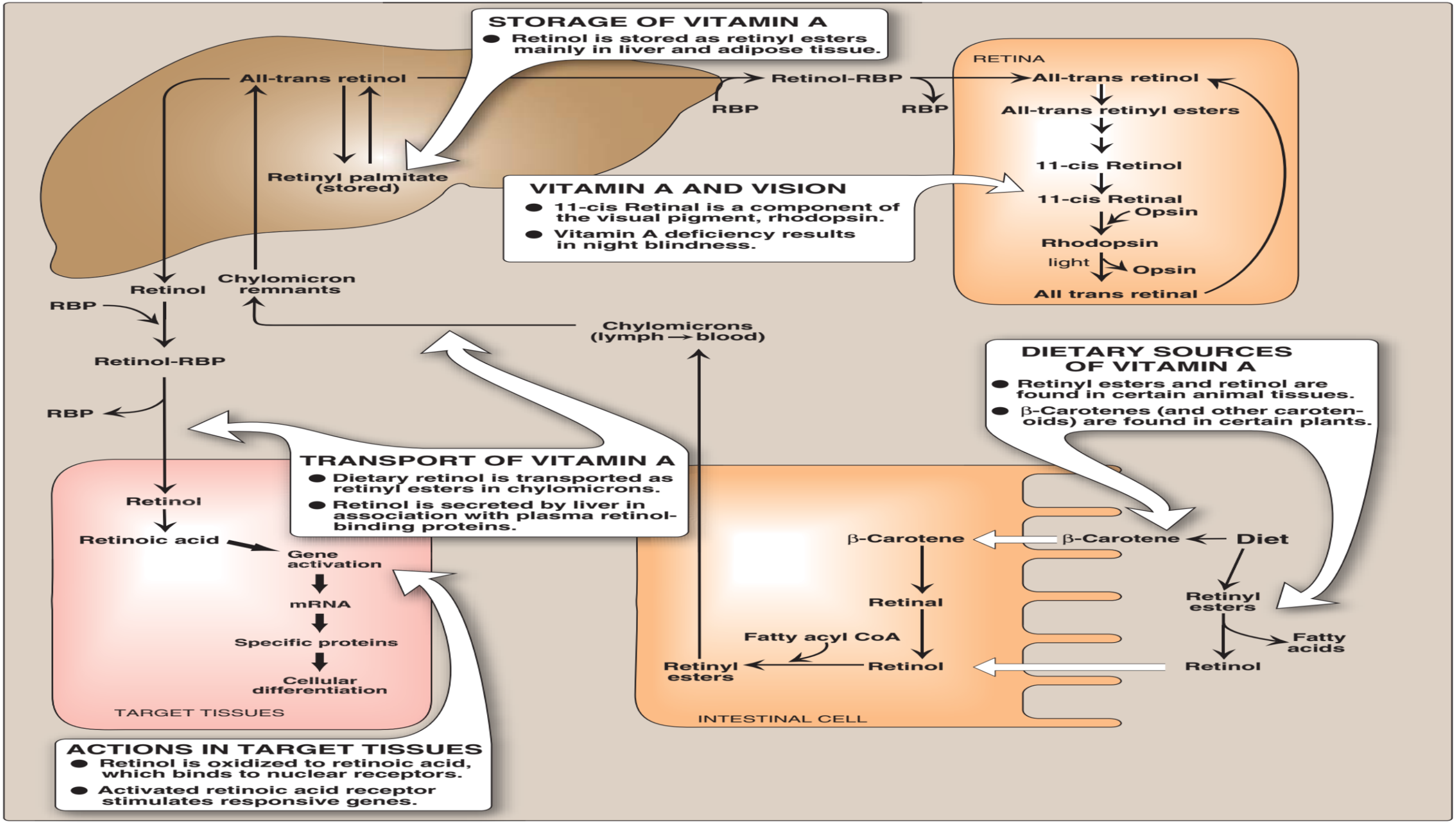
β-Carotene: Plant foods contain ®-carotene, which can be oxidatively cleaved in the intestine to yield two molecules of retinal.

Sources:

- It found in food from animal sources ex. liver, eggs, and cream.
- In addition, in various yellow and green vegetables

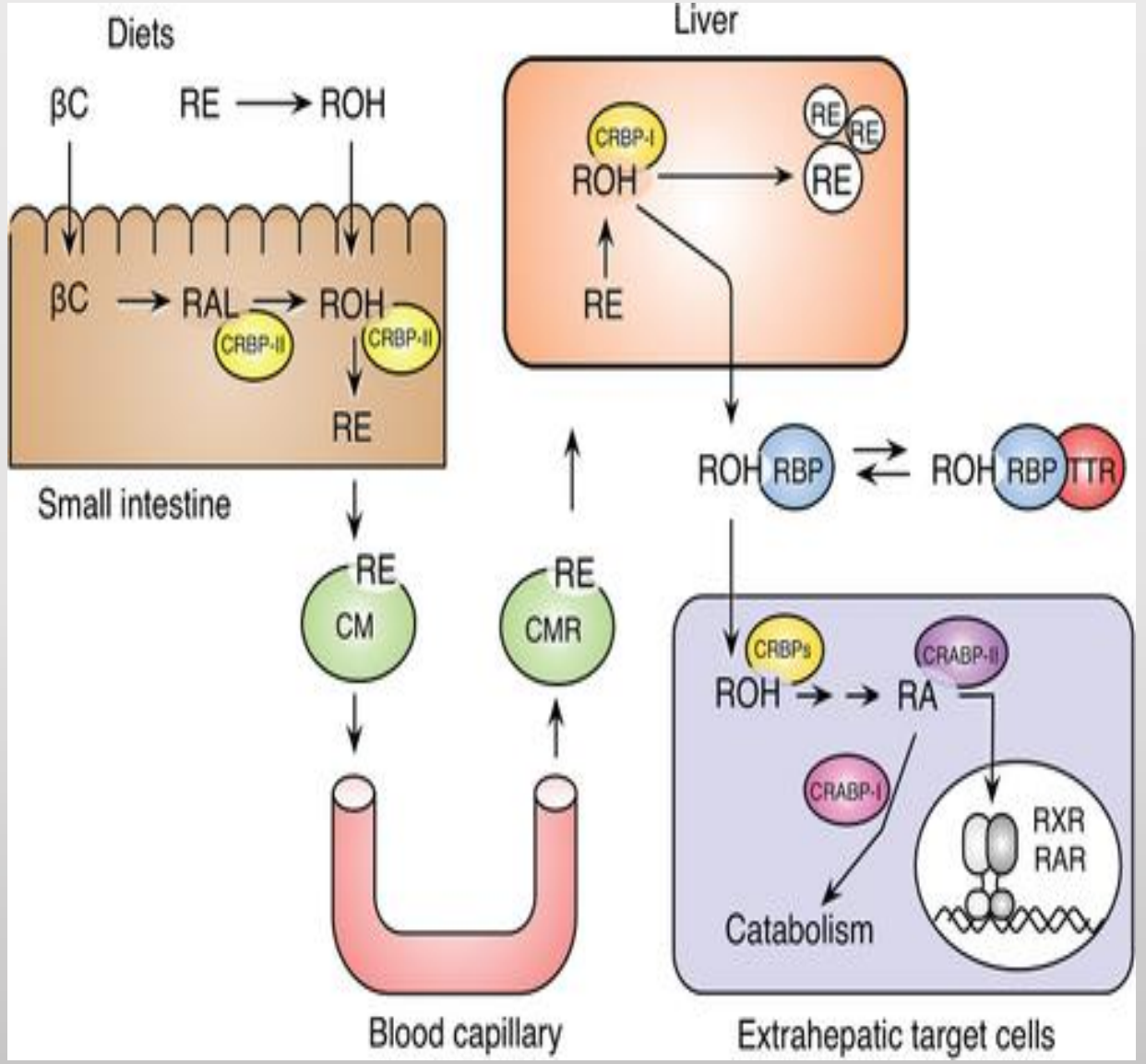
Vitamin A exist as provitamin in the form of a yellow pigment called β-carotene.

- It stored mainly as retinol especially in the Liver.


STORAGE OF VITAMIN A
Retinol is stored as retinyl esters mainly in liver and adipose tissue.
All-trans retinol
Retinol-RBP
RBP
RBP
Retinyl palmitate (stored)
RETINA
All-trans retinol
All-trans retinyl esters
11-cis Retinol
11-cis Retinal
Opsin
Rhodopsin
light
Opsin
All trans retinal
VITAMIN A AND VISION
11-cis Retinal is a component of the visual pigment, rhodopsin.
Vitamin A deficiency results in night blindness.
Retinol
Chylomicron remnants
RBP
Retinol-RBP
RBP
Chylomicrons (lymph → blood)
TRANSPORT OF VITAMIN A
Dietary retinol is transported as retinyl esters in chylomicrons.
Retinol is secreted by liver in association with plasma retinol-binding proteins.
DIETARY SOURCES OF VITAMIN A
Retinyl esters and retinol are found in certain animal tissues.
β-Carotenes (and other carotenoids) are found in certain plants.
Retinol
Retinoic acid
Gene activation
mRNA
Specific proteins
Cellular differentiation
TARGET TISSUES
β-Carotene
β-Carotene
Diet
Retinal
Retinyl esters
Fatty acyl CoA
Fatty acids
Retinyl esters
Retinol
Retinol
INTESTINAL CELL
ACTIONS IN TARGET TISSUES
Retinol is oxidized to retinoic acid, which binds to nuclear receptors.
Activated retinoic acid receptor stimulates responsive genes.

Vitamin A (Absorption)

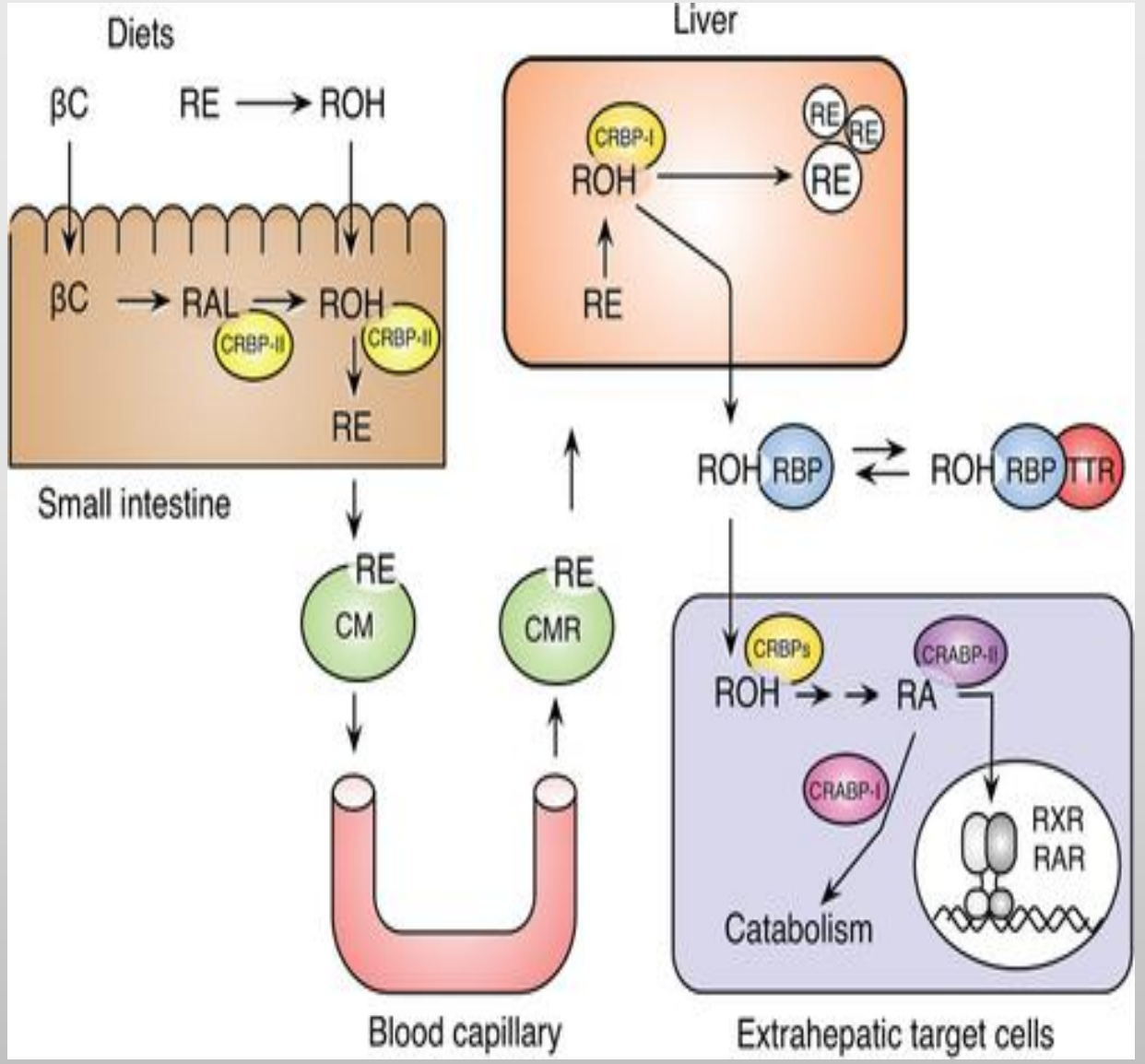
- Retinyl esters (**RE**) present in the diet are hydrolysed in the intestinal mucosa, releasing retinol (**ROH**) and free fatty acids
- in the intestinal mucosa, Retinol (**ROH**) is re-esterified to long-chain fatty acids and secreted as a component of chylomicrons into the lymphatic system
- Retinyl esters contained in **chylomicron** remnants are taken up by, and stored in, the **liver**



Vitamin A (Transport)

- Retinol is released from the liver and transported to extrahepatic tissues by the plasma **Retinol Binding Protein (RBP)**

- **R**etinol–**RBP** complex attaches to specific receptors on the surface of the cells of peripheral tissues



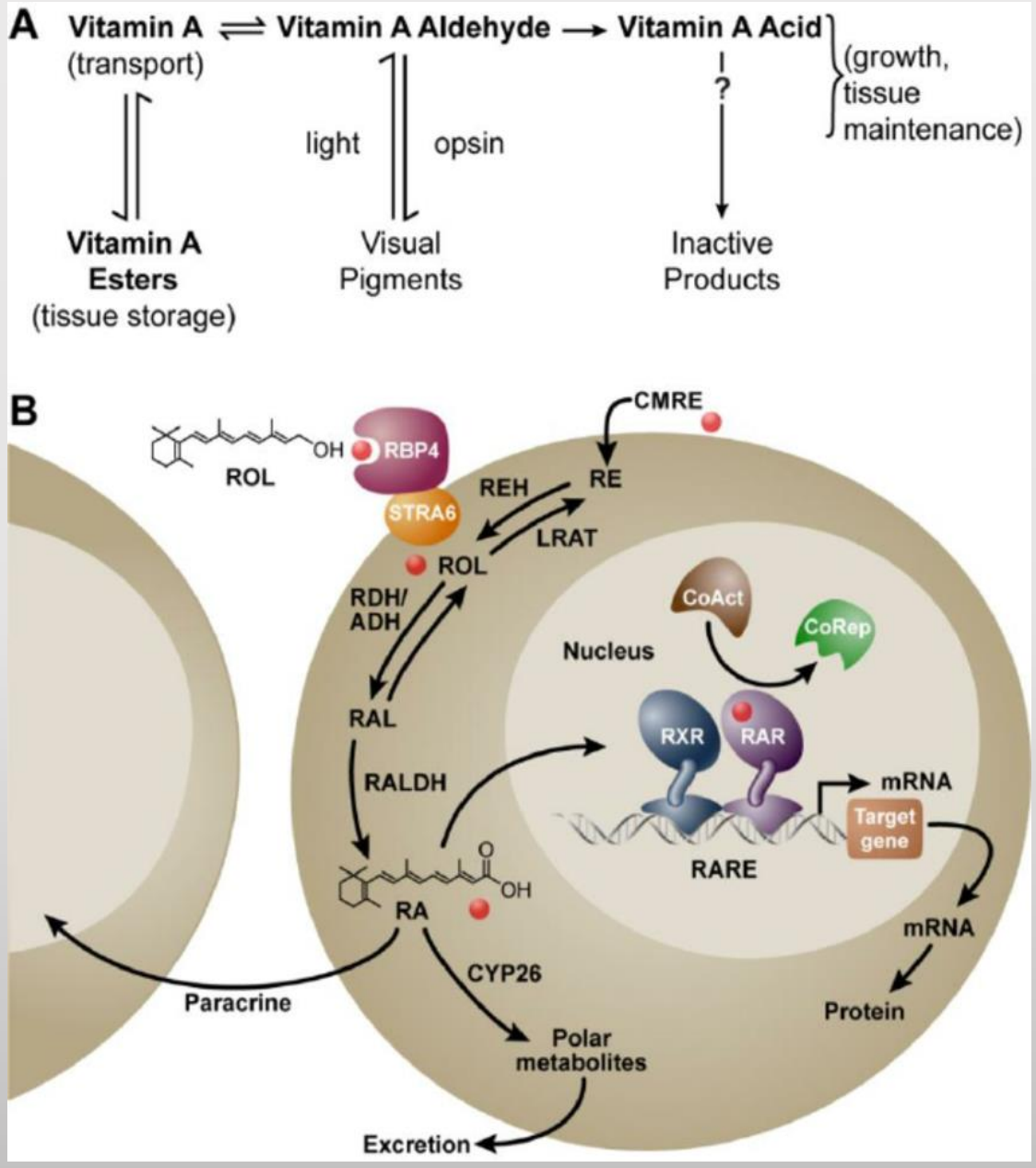
Vitamin A (Action)

Retinoic acid binds with high affinity to specific receptor proteins

The activated retinoic acid–receptor complex interacts with nuclear chromatin to regulate retinoid-specific RNA synthesis affecting several physiological function

e.g

Control the expression of the gene for keratin in most epithelial tissues

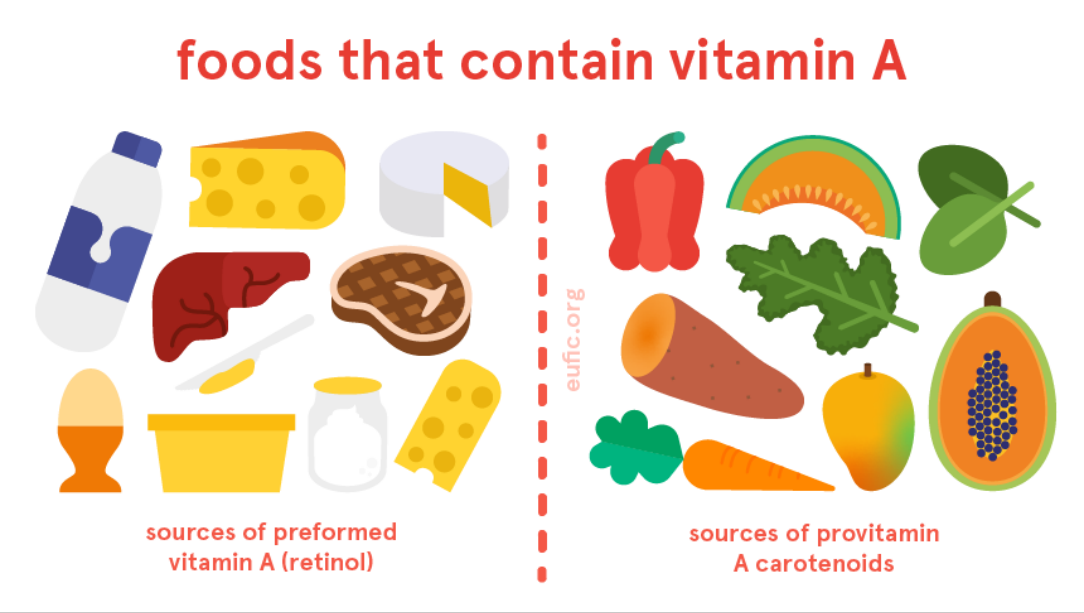


Vitamin A (Function)

- **Visual cycle** Vitamin A is a component of the visual pigments of rod and cone cells. Rhodopsin, the visual pigment of the rod cells in the retina, consists of 11-cis retinal specifically bound to the protein opsin
- **Growth**: Vitamin A deficiency results in a decreased growth rate in children
- **Reproduction**: Retinol and retinal are essential for normal reproduction, supporting spermatogenesis in the male and preventing fetal resorption in the female
- **Maintenance of epithelial cells**: Vitamin A is essential for normal differentiation of epithelial tissues and mucus secretion

Vitamin A (Distribution & Requirement)

Distribution



Requirement

RDA

(**R**ecommended **D**ietary **A**llowance)

- Males 900 (RAE)
- Females 700 (RAE)

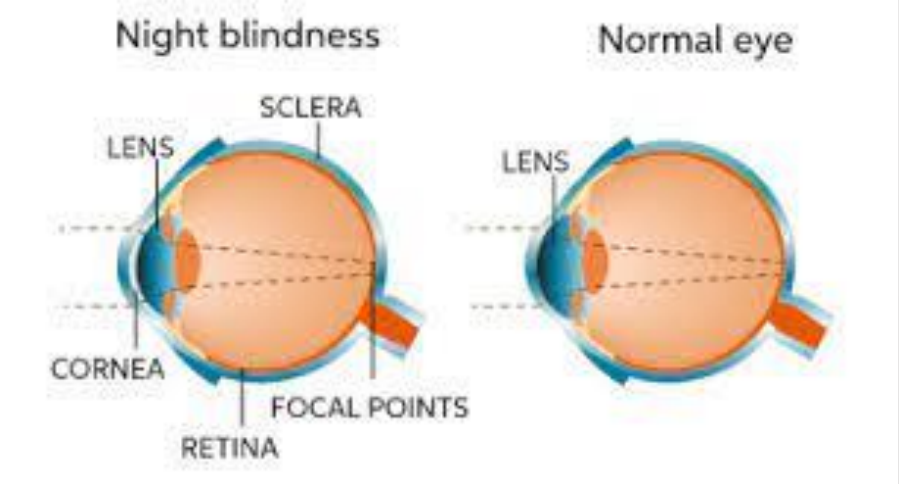
Retinol **A**ctivity **E**quivalents

Vitamin A (deficiency)

- **Dietary deficiency**

- **Night blindness** is one of the earliest signs of vitamin A deficiency

- The visual threshold is increased, making it difficult to see in dim light.
- Prolonged deficiency leads to an irreversible loss in the number of visual cells.



- **Xerophthalmia** pathologic dryness of the conjunctiva and cornea due to **Severe vitamin A deficiency** which final lead to corneal ulceration and blindness because of the formation of opaque scar tissue.

Vitamin A & Dermatology

Acne and **Psoriasis** are effectively treated with **Retinoic Acid** or its derivatives

- Mild Cases Acne
- Darier Disease (Keratosis Follicularis)
- Skin Aging

- Severe Cystic Acne unresponsive to conventional therapies

Vitamin A (Toxicity)

hypervitaminosis A

- Excessive intake of vitamin A (7.5 mg/day)

Signs

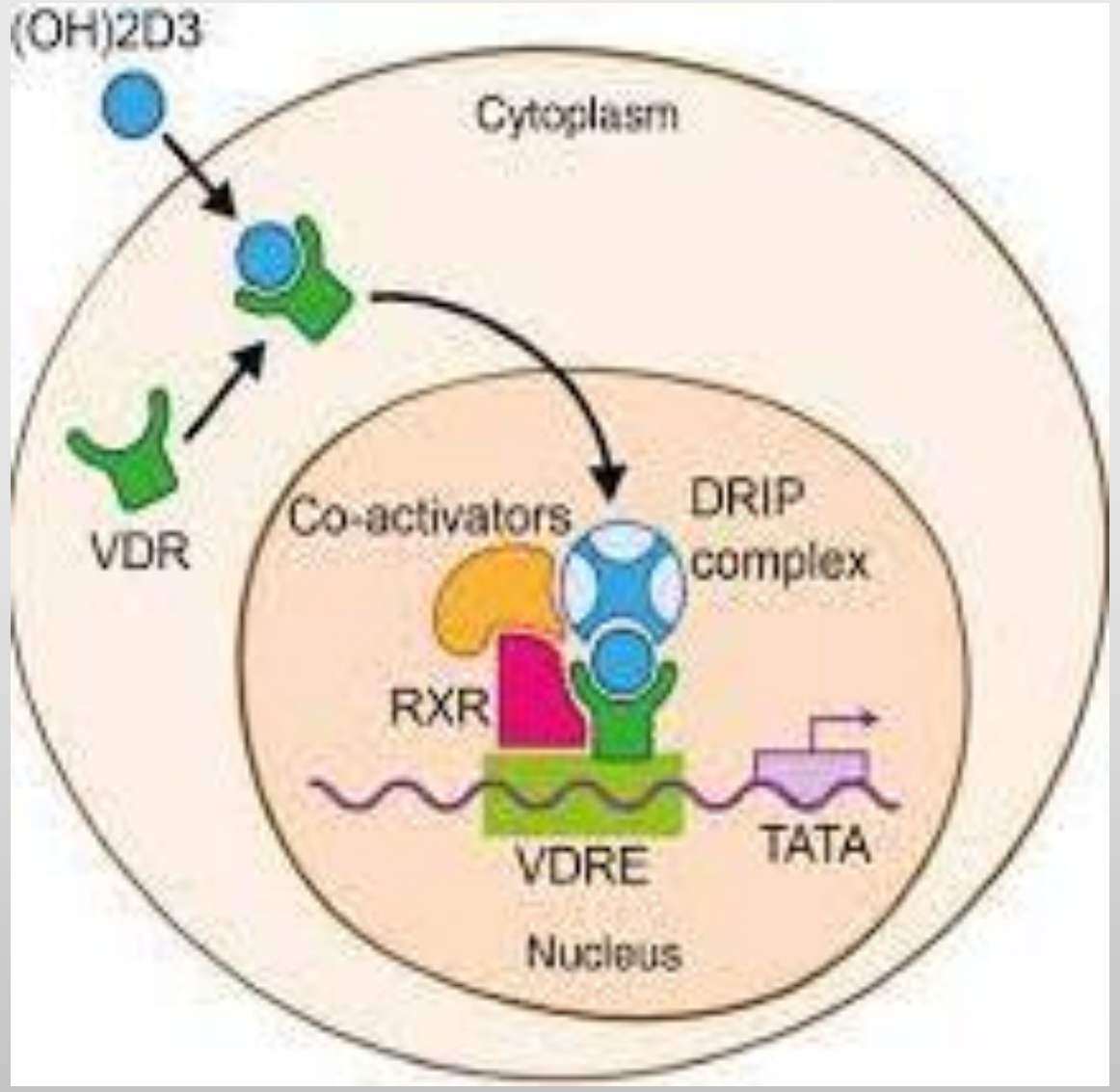
- Dry and Pruritic Skin (due to ↓ keratin synthesis
- Liver enlargement and cirrhotic
- Raised intracranial pressure

Isotretinoin

- is **teratogenic** and absolutely contraindicated in women with childbearing potential unless they have severe, disfiguring cystic acne

Vitamin D

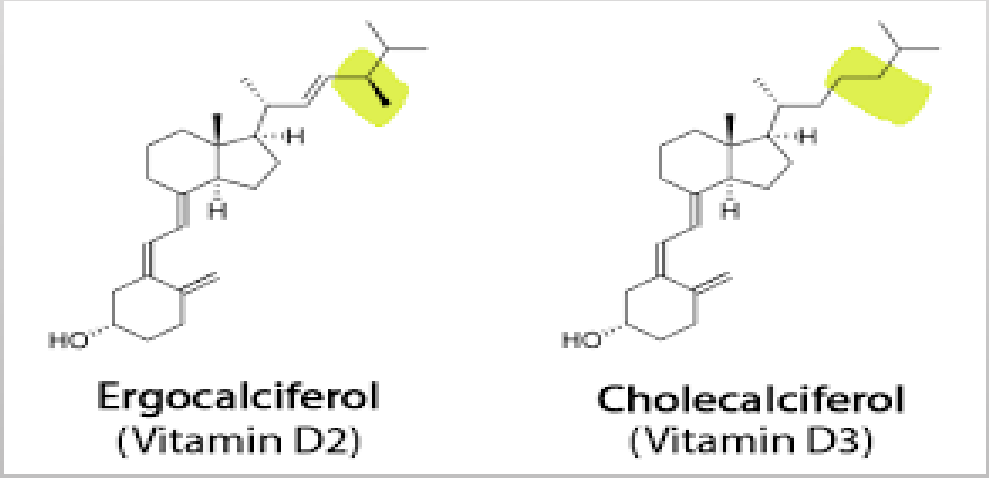
- The D vitamins are a group of sterols that have a hormone-like function.
- The active molecule, 1,25-dihydroxycholecalciferol (1,25-diOH-D3), binds to intracellular receptor proteins
- The 1,25-diOH-D3–receptor complex interacts with DNA in the nucleus of target cells



Vitamin D (Distribution)

Diet

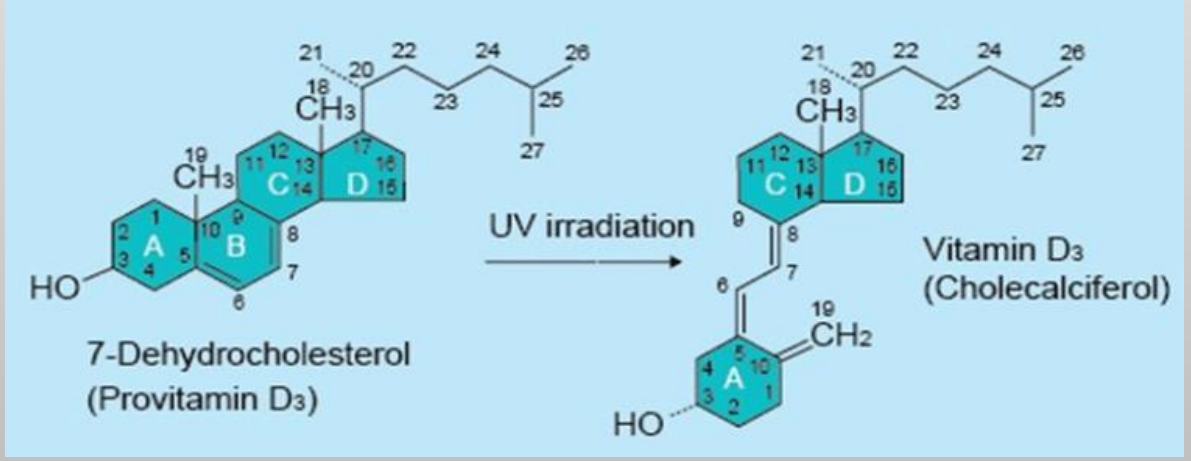
- Ergocalciferol (Vitamin D2)
  Plants
- Cholecalciferol (Vitamin D3)
  Animals



Endogenous

7-Dehydrocholesterol

converted to **cholecalciferol** in the ***dermis*** and ***epidermis*** of humans exposed to sunlight



Vitamin D (Metabolism)

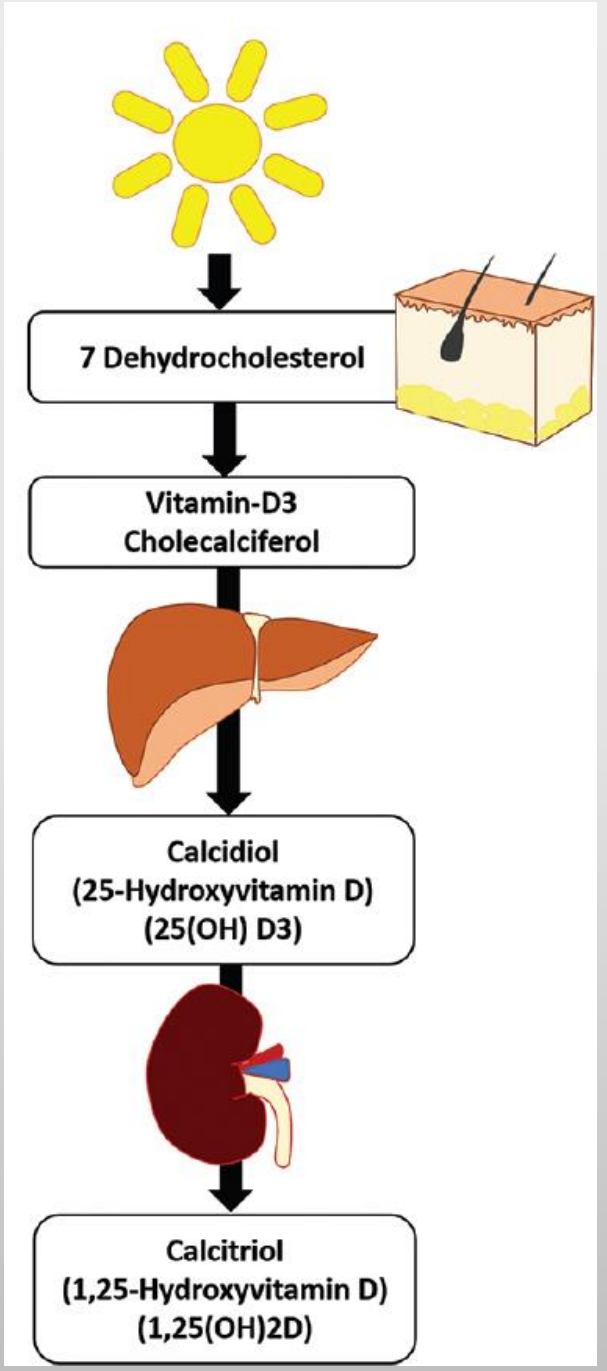
Vitamins D2 and D3 are not biologically active

The **first** Hydroxylation occurs at the **25-position** by *hydroxylase* in the liver.

25-hydroxycholecalciferol (25-OH-D3, calcidol)

The **Second** hydroxylation occurs at the **1 position** by 25- hydroxycholecalciferol *1-hydroxylase* found primarily in the kidney,

1,25-diOH-D3 (calcitriol)

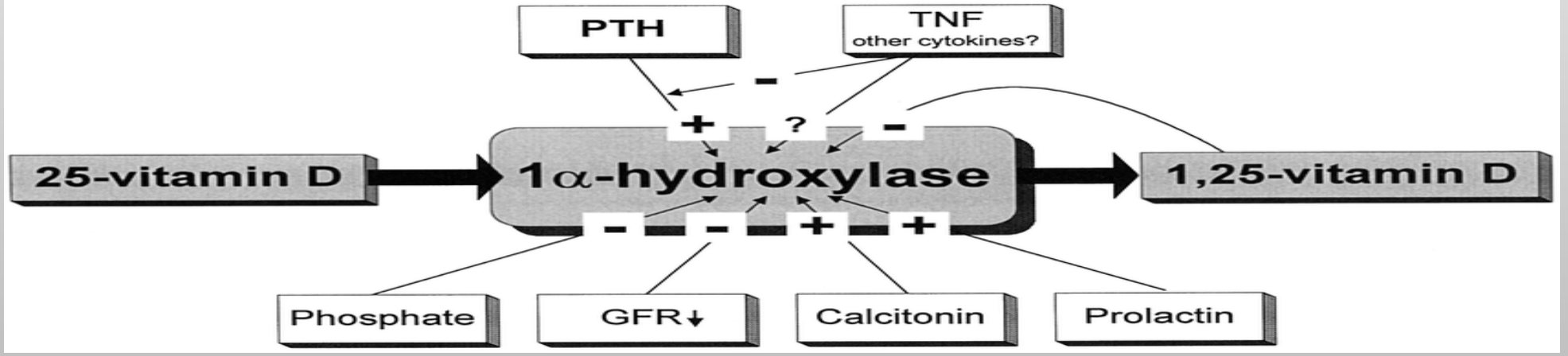


Vitamin D (Regulation)

level of plasma phosphate and calcium

1-hydroxylase stimulated by

- Low Plasma Phosphate (Directly)
- Parathyroid Hormone (PTH) (Indirectly)(secretion of this hormone is elevated when the blood levels of calcium are decrease).



Vitamin D (Functions)

maintain adequate plasma levels of calcium.

- **Increasing uptake** of calcium by the intestine,
- **Minimizing loss** of calcium by the kidney,
- **Stimulating** resorption of bone when necessary

increased risk of

- Cardiovascular Disease,
- Diabetes Mellitus,
- Breast And Gastrointestinal Cancers,
- Infections Such As Tuberculosis
- Autoimmune Disorders

Vitamin D (Functions)

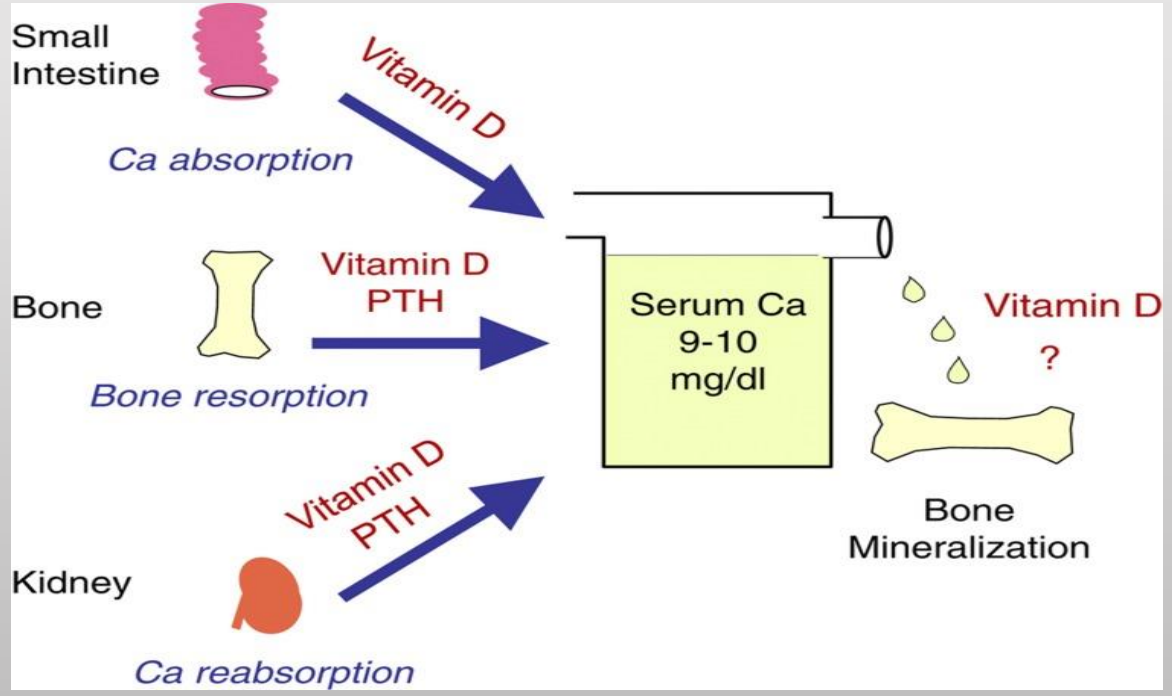
Effect of vitamin D on the intestine

Stimulates intestinal absorption of calcium and phosphate

- 1,25-diOH-D3 bind to cytosolic receptor
- 1,25-diOH-D3–receptor complex then moves to the nucleus
- Increased synthesis of a specific calcium-binding protein

Effect of vitamin D on bone

Stimulates the mobilization of calcium and phosphate from bone



Vitamin D (Distribution)

Diet

- Fatty Fish
- Liver
- Egg Yolk
- Milk

Requirement

AI (Adequate Intake)

- 200 IU to age 50,
- 400-600 IU after age 50

Vitamin D (Deficiency)

Nutritional rickets:

- Vitamin D deficiency causes a demineralization of bone, resulting in rickets in children and osteomalacia in adults
- Vitamin D deficiency occur predominantly in infants and the elderly

Renal osteodystrophy:

Chronic renal failure results in decreased ability to form the active form of vitamin D.

Vitamin D (Toxicity)

- **High doses** (100,000 IU for weeks or months) can cause loss of appetite, nausea, thirst, and stupor

- Results in **hypercalcemia**, which can lead to deposition of calcium in many organs, particularly the arteries and kidneys (calcinosis).

VITAMIN K

- Vitamin K is important in the **posttranslational modification** of various blood clotting factors.
- **Coenzyme** in the **carboxylation** of certain glutamic acid residues in these clotting factors .

Vitamin K1(phylloquinone)	**Plants**
Vitamin K2 (menaquinone)	**Product of intestinal flora**
Menadione	A synthetic form of vitamin K

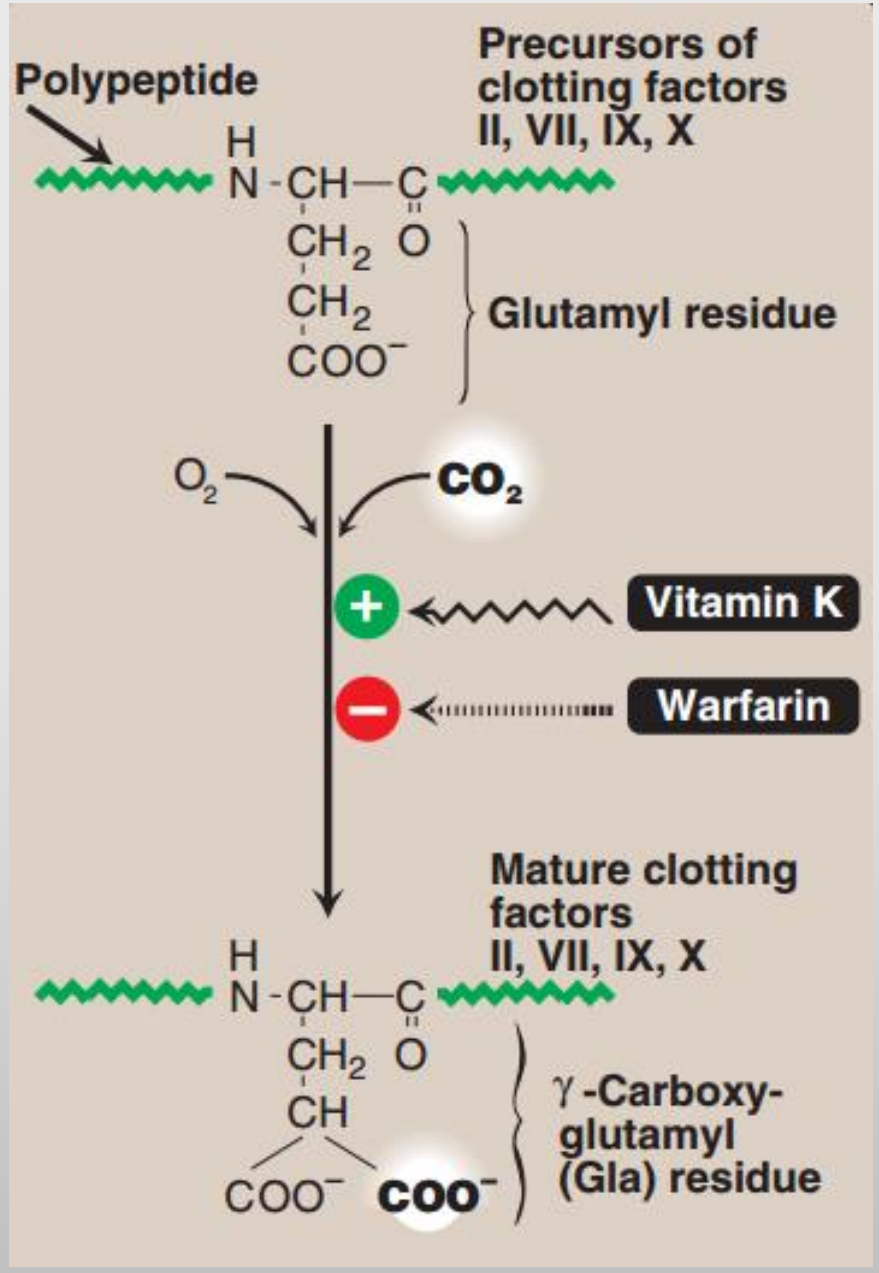
Vitamin K (Functions)

Formation of γ-carboxyglutamate (Gla)

Vitamin K is required in the hepatic synthesis of prothrombin and blood clotting factors II, VII, IX, and X (1972)

This forms a mature clotting factor that contains **Gla** and is capable of subsequent activation

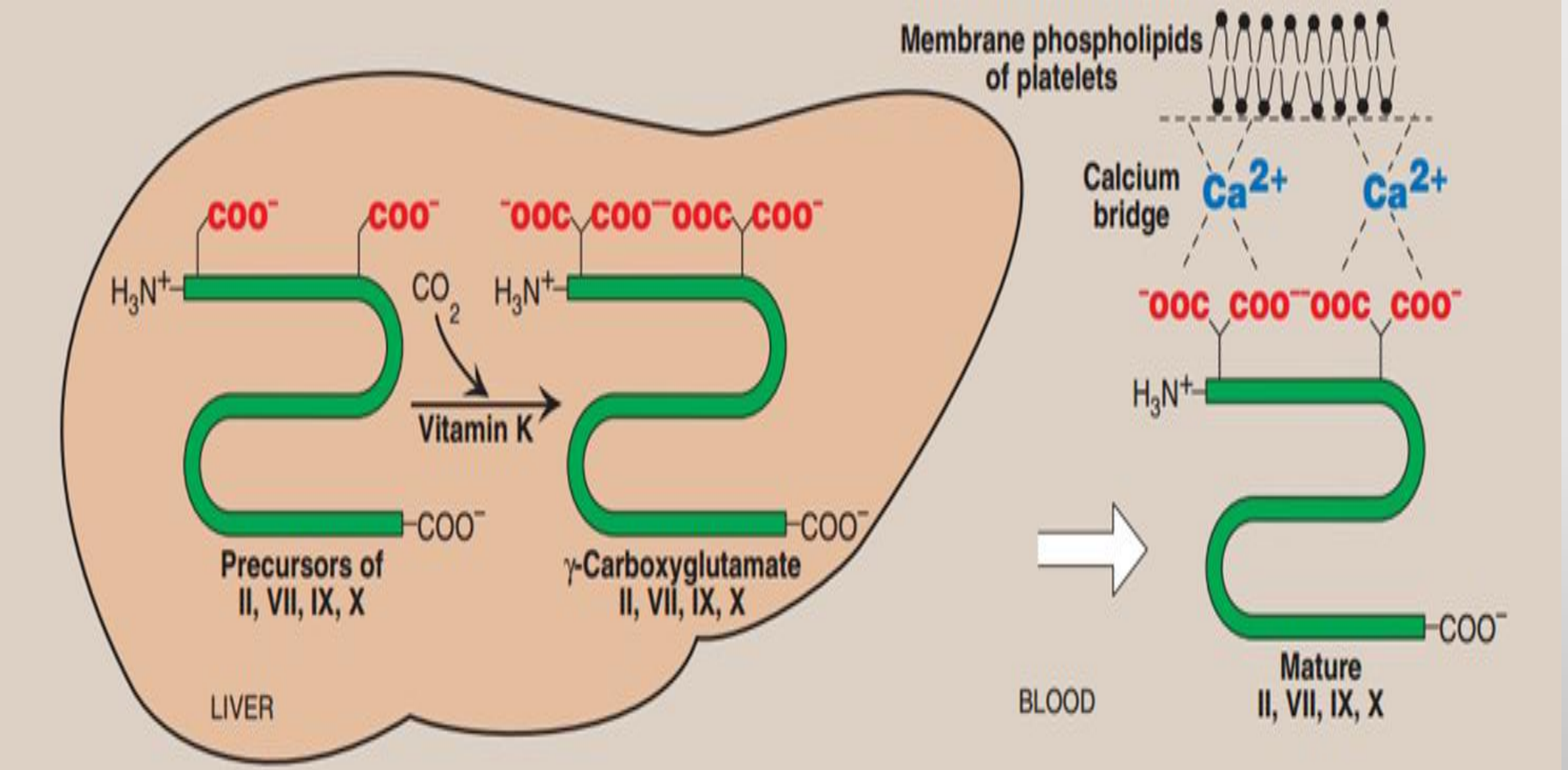
The formation of **Gla** is sensitive to inhibition by an anticoagulant **Warfarin** (a synthetic analog of vitamin K)



Vitamin K (Functions)

Interaction of prothrombin with platelets

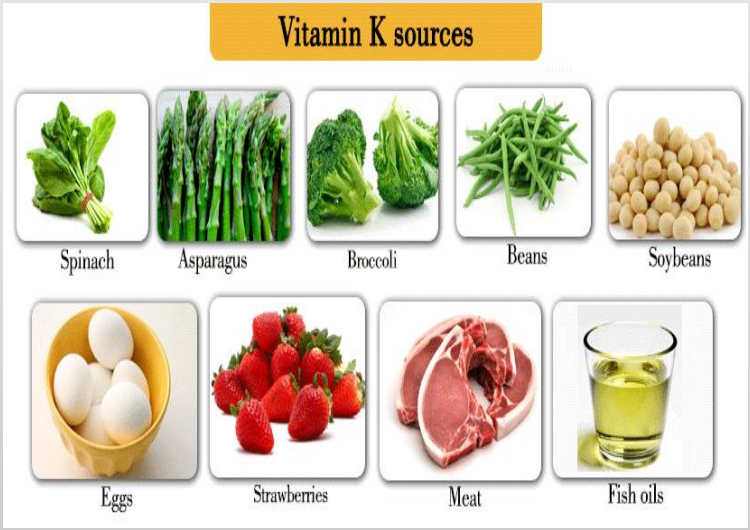
- Gla residues of prothrombin are good chelators of positively charged calcium .
- prothrombin–calcium complex is then able to bind to phospholipids essential for blood clotting on the surface of platelets .
- increases the rate at which the proteolytic conversion of prothrombin to thrombin .


Membrane phospholipids of platelets
Calcium bridge
Ca2+
Ca2+
COO⁻
COO⁻
⁻OOC
COO⁻
⁻OOC
COO⁻
H3N+
CO2
H3N+
Vitamin K
COO⁻
COO⁻
Precursors of II, VII, IX, X
γ-Carboxyglutamate II, VII, IX, X
LIVER
BLOOD
Mature II, VII, IX, X

Vitamin K (Distribution)

Dietary Source

- Cabbage
- Kale
- Spinach
- Egg Yolk
- Liver



Requirements

AI (Adequate Intake) for vitamin K

- 120 µg/day for adult males
- 90 µg/day for adult females.

Vitamin D (Deficiency)

- True vitamin K deficiency is unusual because adequate amounts are generally produced by intestinal bacteria or obtained from the diet.
- Antibiotics decreased bacterial population in the gut.
- The amount of endogenously formed vitamin is depressed.
- Can lead to **hypoprothrombinemia** in the marginally malnourished individual .

Deficiency of vitamin K in the newborn

- Newborns have sterile intestines.
- Human milk provides only about one fifth of the daily

single **intramuscular dose of vitamin K** as prophylaxis against hemorrhagic disease

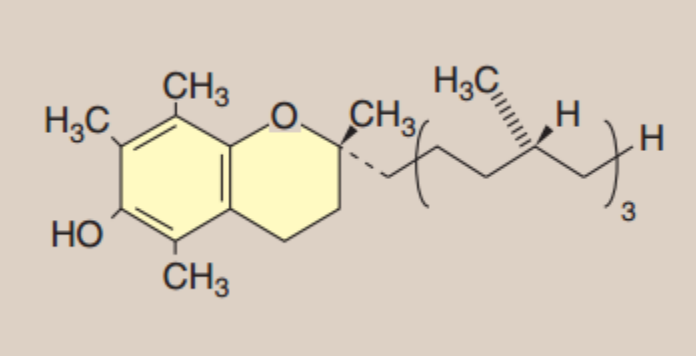
Is there any toxicity for Vitamin K !!??

Toxicity for Vitamin K:

- Prolonged administration of large doses of synthetic vitamin K (menadione) can produce hemolytic anemia and jaundice in the infant, due to toxic effects on the membrane of red blood cells.

VITAMIN E:

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



Vitamin E (Distribution)

Dietary Source

- Vegetable Oil
- Egg Yolk
- Liver

Requirements

RDA for vitamin E (α-tocopherol)

- 15 mg for adult

Vitamin E (Deficiency)

- Vitamin E deficiency is restricted to **premature infants .**
- In adults, it is usually associated with defective lipid absorption or transport.

Signs:

- Sensitivity of erythrocytes to peroxide .
- Abnormal cellular membranes .

Toxicity of vitamin E:

- Vitamin E is the least toxic of the fat-soluble vitamins, and no toxicity has been observed at doses of 300 mg/day.


Thank
you!