
Secret Getaway


بسم الله الرحمن الرحيم

VITAMIN K

BY

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VITAMIN K

Synonyms:

ANTI-HEMORRHAGIC FACTOR

or

NAPHTHOQUINONES

Or

PHYLLOQUINONE or MENAQUINONES

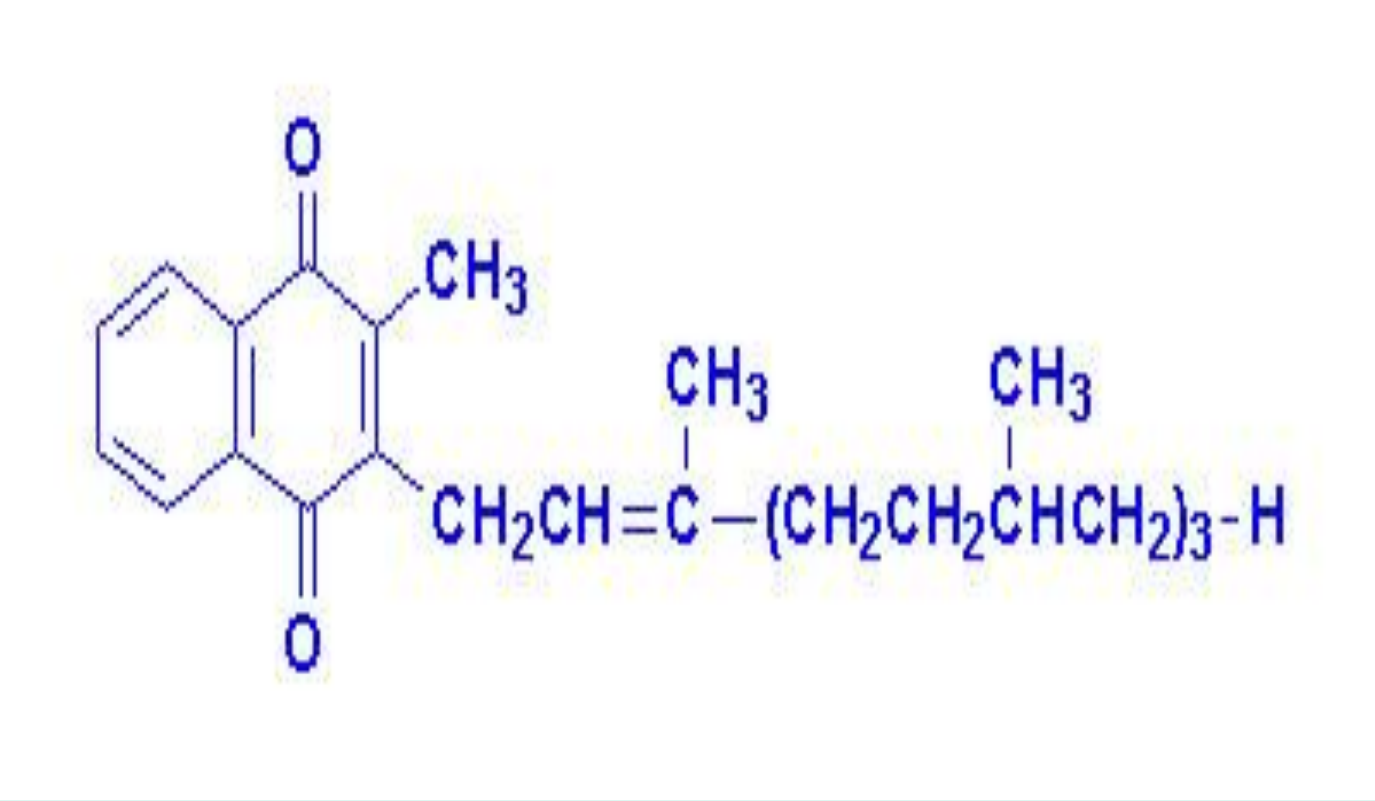
Vitamin K

Chemistry:

- The various substances showing Vit. K activity are called (naphthoquinone)
- Vitamin K is found naturally as:
- K1 (phylloquinone,or phytylmenaquinone) in green vegetables.
- K2 (multiprenylmenaquinone) produced by intestinal bacteria.
- K3 (menadione) is synthetic form.
- For therapy, a synthetic derivative of vitamin K, menadione, is available.

- The body is able to convert synthetically prepared menaquinone(menadione) and a number of water soluble analogs to a biologically active form of vitamin K.
- All types of Vit. K contain methyl group at carbon number 2.
- Activity is due to this methyl group.
- Substitution of methyl group by other alkyl radicals or by hydrogen results in reduction in activity.

Vitamin K1



Vitamin K2

"n" can be 6, 7 or 9 isoprenoid groups

Vitamin K3

(menadione)

Function of Vitamin K

- Production of coenzyme Q , its function as electron carrier, helping the oxidation in the respiratory chain and production of ATP.
- Vit K is required in the hepatic Synthesis of prothrombin and blood Clotting factors II, Vll, lX,& X.

1-Formation of γ-carboxyglutamate (Gla):

- Vit. K1 has been shown to be required for the convertion of several clotting factors and prothrombin to the active state.
- Prothrombin is synthesized in an inactive precursor form called preprothrombin.
- Preprothrombin(precursor) inactive $\xrightarrow{\text{Vit.K}}$ prothrombin (active).

- Convertion to the active form requires a vit. K dependant carboxylation of specific glutamic acid residues to ɣ-carboxyglutamic acid residues.
- The ɣ-carboxyglutamic acid residues are good chelators and allow prothrombin to bind calcium.
- The prothrombin-calcium complex in turn binds to the phospholipids membrane, where proteolytic conversion to thrombin can occur in vivo.

2-Interaction of prothrombin with platelets:

The two COO- residues of prothrombin chelate +vely charged Ca2+. The prothrombin- Ca2+ complex is able to bind the PL membrane (phospholipids) essential for blood clotting on the surface of platelets. Attachment to the platelet increases the rate at which the proteolytic conversion of prothrombin to thrombin can occur.

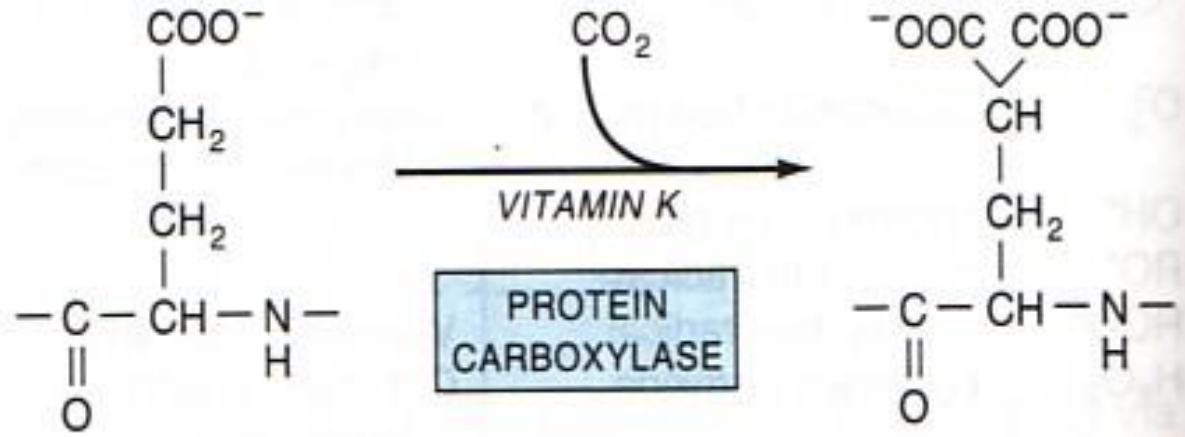


Figure 53–14. Carboxylation of a glutamate residue catalyzed by vitamin K-dependent carboxylase.

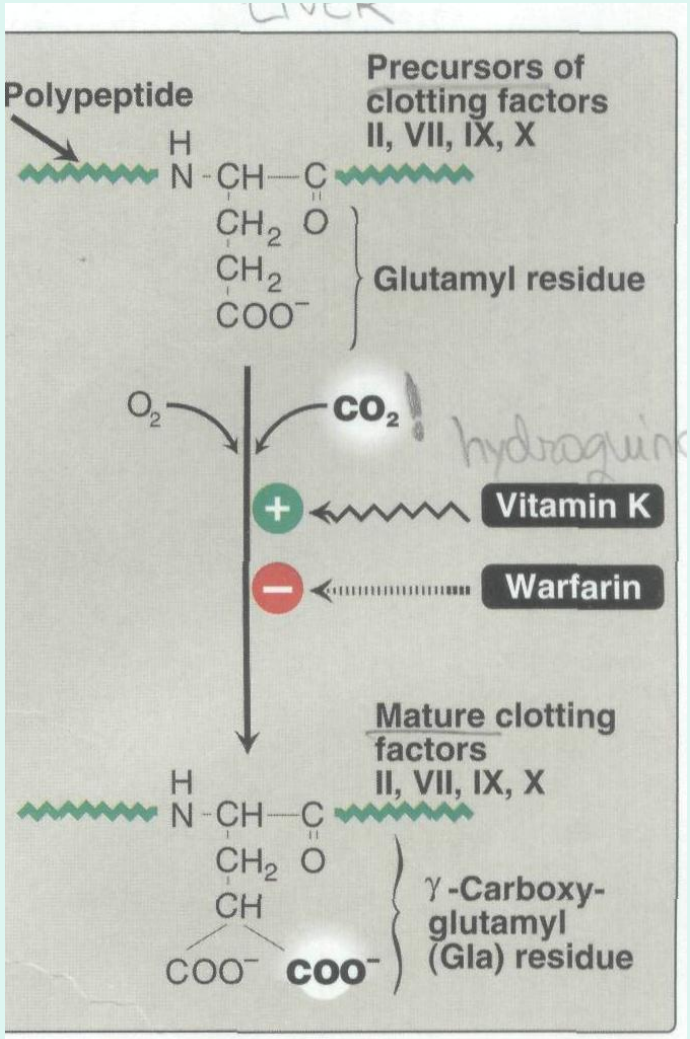


Figure 28.26
Carboxylation of glutamate to form γ-carboxyglutamate (Gla).

- The mechanism of the carboxylation reaction has not been fully clarified, but appears to involve the intermediate formation of a 2,3-epoxide derivative of vitamin K.
- During the carboxylation reaction reduced hydroquinone form of vitamin K is converted to a 2,3-epoxide form. The regeneration of the hydroquinone form requires an uncharacterized reductase. This latter reaction is the site of action of the **dicumarol** based anticoagulants such as **warfarin**.

- Dicumarol, a naturally occuring anticoagulant, may inhibit the reductase which converts the epoxide back to the active vitamin.

➢ Briefly, the formation of Gla is sensitive to inhibition by **dicumarol** a natural anticoagulant present in spoiled sweet clover & **warfarin,** a synthetic analog of vitamin K.

Role of vitamin K in blood coagulation

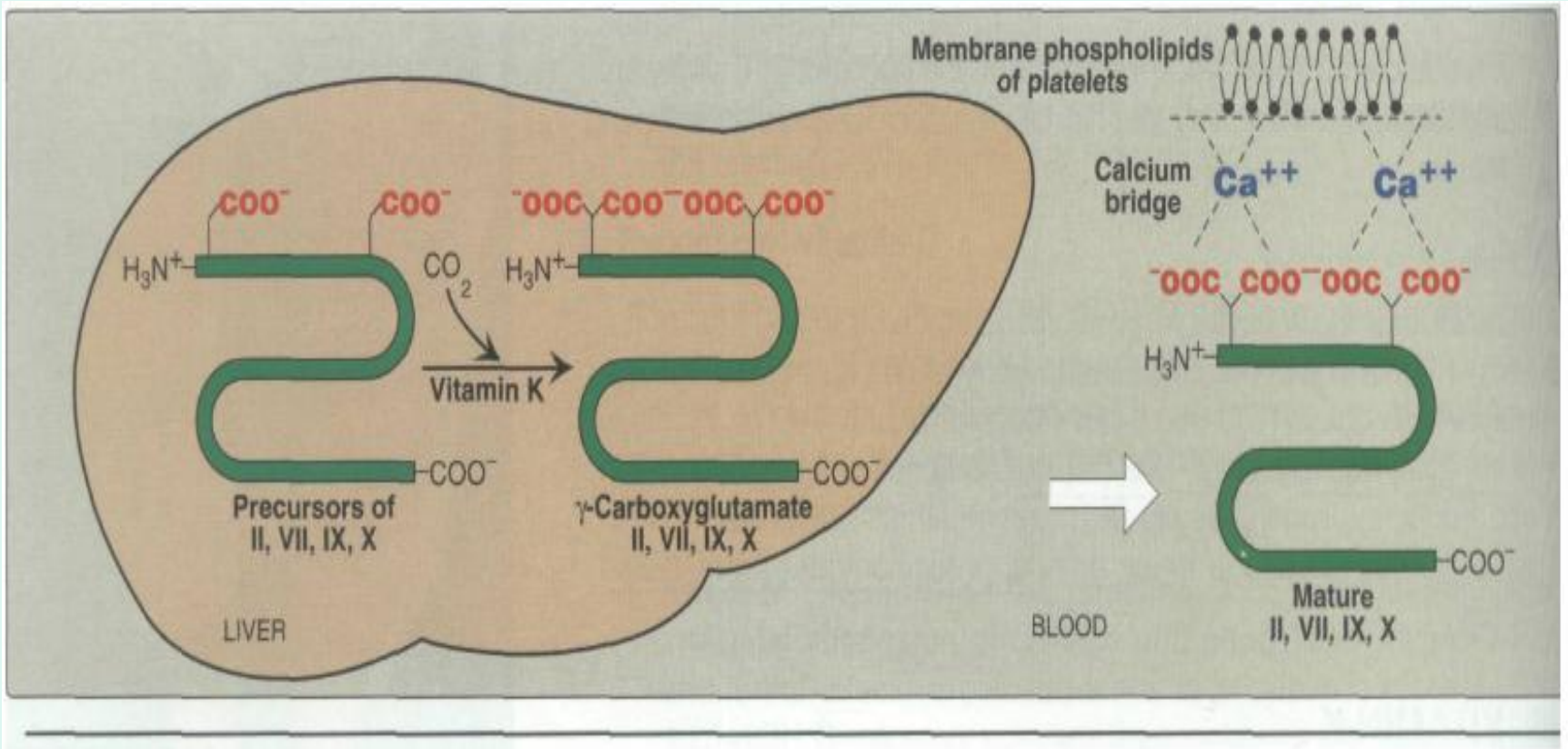


Figure 28.27
Role of vitamin K in blood coagulation.

3-Role of γ-carboxyglutamate residues in other proteins:

- Gla is also present in other proteins (for example, osteocalcin of bone) unrelated to the clotting process.
- However, the physiologic role of these proteins and the function of vitamin K in their synthesis is not yet understood.

Vitamin K Is Also Important in Synthesis of Bone Calcium-Binding Proteins

- Treatment of pregnant women with warfarin can lead to fetal bone abnormalities (fetal warfarin syndrome). Two proteins that contain γ-carboxyglutamate are present in bone, osteocalcin, and bone matrix Gla protein. Osteocalcin also contains hydroxyproline, so its synthesis is dependent on both vitamins K and C; in addition, its synthesis is induced by vitamin D. The release into the circulation of osteocalcin provides an index of vitamin D status.

Distribution and requirement of vitamin K

- Vitamin K is found in cabbage, cauliflower, spinach, egg yolk, and liver.
- There is also extensive synthesis of the vitamin by the bacteria in the gut.
- There is no RDA for vitamin K, but 70 to 140 μg per day is recommended as an adequate level.

RECOMMENDED DAILY ALLOWANCE OF VITAMIN K

- **Males** — **65 – 80 micrograms**
- **Females** — **55 – 65 micrograms**
- **Pregnancy** — **65 micrograms**
- **Lactation** — **65 micrograms**

Deficiency of vitamin K

1- Deficiency of vitamin K:

- It is unusual because vit k is produced by the intestinal flora or from diet.
- It happens in people who are taking antibiotics and can lead to **hypoprothrombinemia.**
- 2nd generation of **Cephalosporins** have a warfarin-like mechanism. (they should be taken with vit K).

2- Defficiency of vitamin K in newborn:

- Newborns have sterile intestines and cannot initially synthesize vit K.
- Because human milk provides only 1/5 of the daily requirement for vit k, it is recommended that all newborns receive a single I.M. dose of vit K as prophylaxis againest hemorrhagic disease.

Defficiency of vitamin K in man

- The only known symptom of vitamin K def. in man is increased coagulation time.

The most common def. is seen in:

- Newborn infants.
- In patients with obstructine jaundice.
- Other diseases leading to sever fat malabsorption.
- Patients on long – term antibiotic therapy, which may destroy vit. K–synthesizing organism in the intestine.

- Finally, Vit. K def. is occusionally seen in the elderly, who are prone to poor liver function (reducing preprothrombin synthesis) and fat malabsorption.
- Vitamin K def. should be suspected in any patient demonstrating easy bruising and prolonged clotting time.

Clinical findings 0f Vit. K deficiency

- Easy bruising.
- Echymotic patches.
- Mucous membrane hemorrhage
- Internal bleeding.
- Prolonged prothrombin time.

Echymotic patches

Toxicity of vitamin K

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

Vitamin K

Phylloquinone: menaquinones

Functions:

- Coenzyme in formation of ɣ-carboxyglutamate in enzymes of blood clotting and bone matrix.

Deficiency disease :

- Impaired blood clotting, hemorrhagic disease.

References:

1. Lippincott's review of biochemistry, 3rd edition.
1. Biochemistry Stryer 5th edition.
2. Harper,s illustrated Biochemistry 28 edition.

Fat soluble vitamins

Learning outcomes:

- ✓ **Classify vitamins.**
- ✓ **List the dietary sources of Vitamin A**
- ✓ **Discuss the role of Vitamin A in vision.**
- ✓ **Discuss the deficiency manifestations of Vitamin A.**
- ✓ **Discuss the role of Vitamin D in the body.**
- ✓ **Discuss the deficiency manifestations of Vitamin D in both adults and children**
- ✓ **Discuss why vitamin D is considered as an hormone.**
- ✓ **Explain the role of vitamin K in coagulation.**
- ✓ **Discuss the role of Vitamin E .**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