Biochemistry of the GIT

Vitamin K

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Vitamin K is a fat soluble vitamin the is produced by the intestinal bacteria and has a vital function in coagulation

❖ Types and Chemistry:

Occurs in several forms:

- Vitamin K_1 (Phylloquinone)
- Vitamin K_2 (Menaquinone)
- Vitamin K_3 (Menadione) – synthetic form

K1: (Phyllo = from plants)

K2: synthesized by intestinal bacteria

K3: the synthetic form of vitamin K which is used as a supplement in therapy

❖ Sources of Vitamin K:

- Phylloquinone: Green leafy vegetables
- Menaquinone: Intestinal bacteria
  - Intestinal bacterial synthesis meets the daily requirement of vitamin K even without dietary supplement
- Menadione: synthetic form

❖ RDA for Vitamin K (mg/day):

- Infant (0-1 year): 2-2.5
- Children (1-8): 30-55
- Men (19+): 120
- Women (19+): 90
- Pregnancy :90
- Lactating: 90
- UL: Not established

❖ Functions of Vitamin K:

- Coenzyme for the synthesis of prothrombin and blood clotting factors in the liver
  - Prothrombin and clotting factors are protein in nature
  - Synthesis of prothrombin, clotting factors VII, IX, X require carboxylation of their glutamic acid (Glu) residue

They are proteins which have amino acids, one of the amino acids is glutamic acid, Glutamic acid needs to be carboxylated, and that carboxylation reaction is done with the help of vitamin K

Prothrombin + clotting factors are inactive; they need post transitional modification to become active.
Post transitional modification is the carboxylation of the Glutamic acid.

- Mature prothrombin and clotting factors contain g-carboxyglutamate (Gla) after carboxylation reaction.

g-carboxyglutamate is a Glutamic acid with an extra carboxylate group (COO-) in the gamma position

- Vitamin K is essential for the carboxylase enzyme involved
- Dihydroquinone form of vitamin K is essential for this reaction.
  Dihydroquinone is the reduced form of vitamin K

You see here, one carboxylate group is added

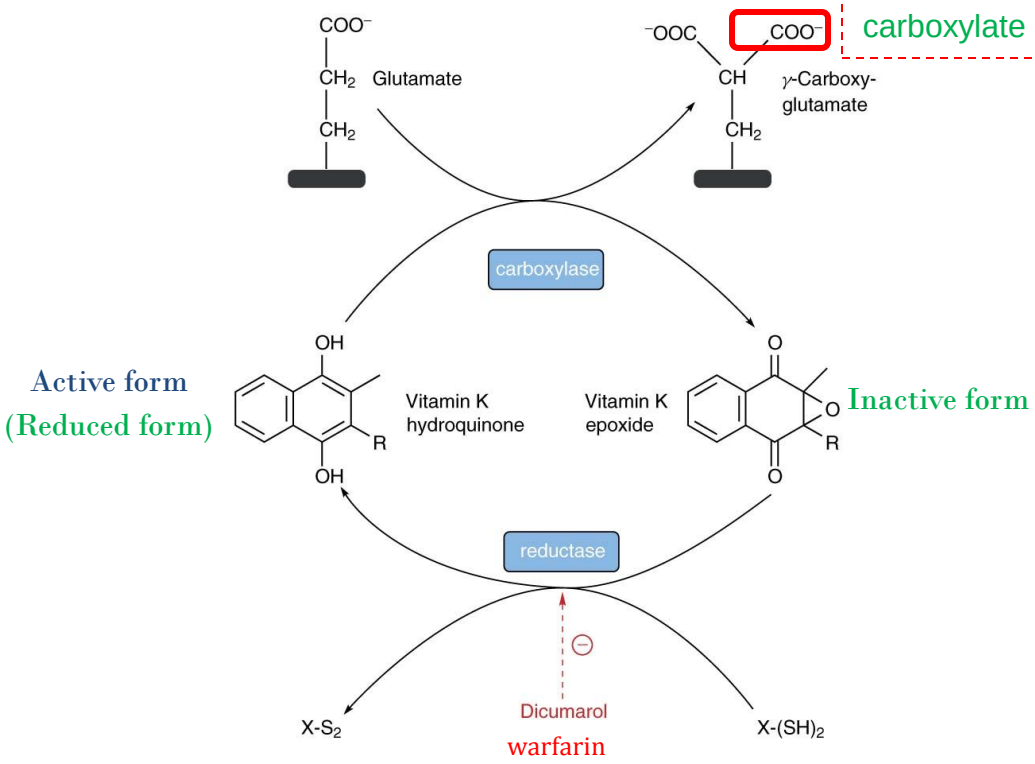

Figure 28.7. Function of Vitamin K.

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In General:

Glutamate → Gamma-carboxyglutamate (Gla) (by the help of **vitamin K hydroquinone** the reduced form of vit K- "enzyme: carboxylase")

The inactive form (epoxide) of Vit. K gets activated by "enzyme: reductase"

Reductase is inhibited by **Warfarin** and Dicumarol (anti-coagulants)

How do the anti-coagulants work?

They inhibit the reduction of vitamin K = inhibit the formation of the active form of vit K → So, Prothrombin and clotting factors won't be formed

¤ Analogs of Vitamin K:

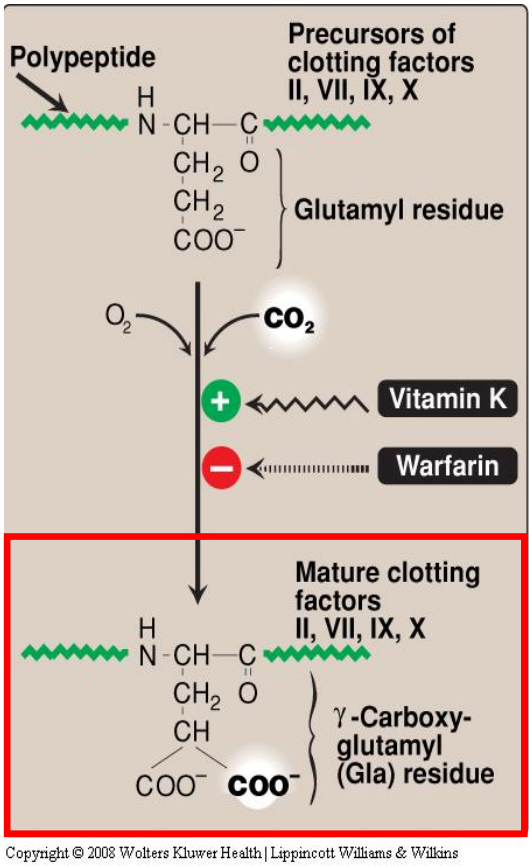
Analog: *Structurally similar molecules*

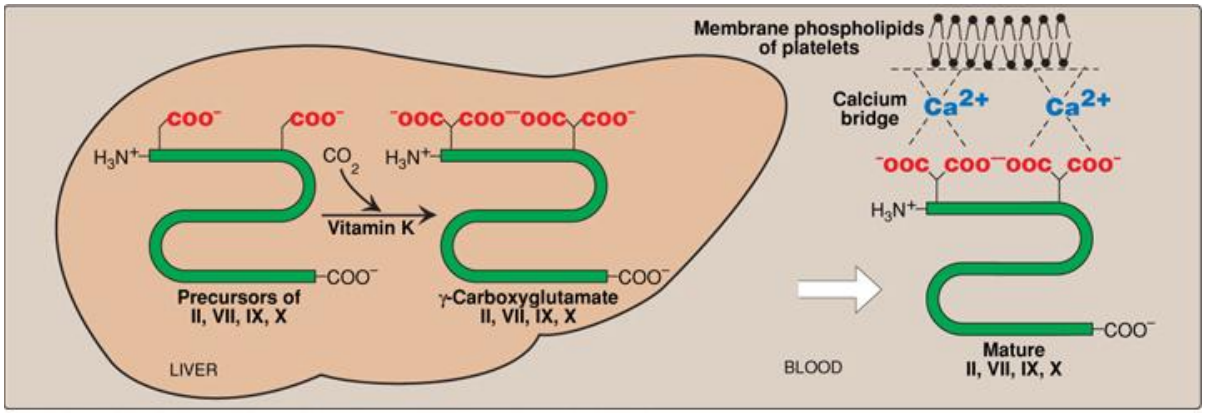
- Anticoagulant drugs (warfarin and dicoumarol) are structural analogs of vitamin K
- They inhibit the activation of vitamin K, hence, Prothrombin and clotting factors are not carboxylated
- Blood coagulation time increases upon injury

¤ Functions of vit K; Prothrombin – platelet interaction:

- **Carboxylated** prothrombin contains two carboxylate groups (COO–)
- These groups bind to Ca2+ forming prothrombin-calcium complex
- The complex then binds to phosholipids on the surface of platelets (important for blood clotting)
- Converting prothrombin to thrombin and initiating clot formation

Carboxylated
prothrombin →





Ca++ makes the bridge (bond) between the **Carboxylated** prothrombin and platelets.

Carboxylated prothrombin is formed in the liver

Conversion of prothrombin to thrombin is at the site of injury

❖ Functions of Vitamin K:

- Synthesis of γ-carboxyglutamate in osteocalcin
  - Osteocalcin is a bone protein
  - May have a role in bone formation and mineralization
  - γ-carboxyglutamate is required for its binding to hydroxyapatite (a mineral) in the bone
  - The function of bone osteocalcin is unclear

❖ Deficiency of Vitamin K:

- Deficiencies are rare: it is synthesized by the intestinal bacteria
- Hypoprothrombinemia: increased blood coagulation time
- May affect bone growth and mineralization
- Malabsorption of lipids leads to vitamin K deficiency. Because Vit. K is absorbed along with lipids (TAGs) by Chylomicrons (Lipoprotein particles which transport dietary lipids from the intestines to other organs in the body)
- Prolonged antibiotic therapy

- Gastrointestinal infections with diarrhea
  - Both of the above destroy the bacterial flora leading to vitamin K deficiency
- Deficiency most common in newborn infants:
  - Newborns lack intestinal flora
  - Human milk cannot provide enough vitamin K
  - Supplements are given by injection

Patients with bleeding tendency (increased bleeding time) are given vitamin K to exclude other causes.

¤ Effects of Vitamin K Deficiency:

- Hypoprothrombinemia: increased blood coagulation time
- May affect bone growth and mineralization

¤ Clinical Manifestations of the Deficiency:

- Hemorrhagic disease of the newborn
- Bruising tendency, ecchymotic patches (bleeding underneath the skin)
- Mucus membrane hemorrhage
- Post-traumatic bleeding / internal bleeding
- Prolonged prothrombin time