VITAMIN K

- Vitamin K is the only fat soluble vitamin with a specific coenzyme function
- It is required for the production of blood clotting factors, essential for coagulation (in German – Koagulation; hence called as vitamin K)
- *Chemistry:*
- Vitamin K exists in different forms
- Vitamin - K_1
- Vitamin - K_2
- Vitamin - K_3

Vitamin-K_1

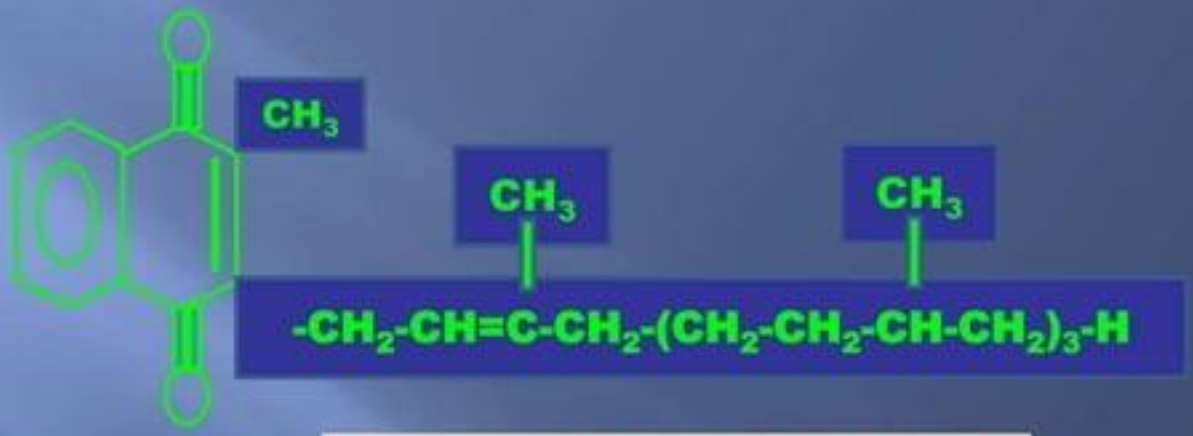
- It is phylloquinone
- Present in plants
- Isolated from alfalfa leaves
- It has phytyl side chain

Vitamin – K_2

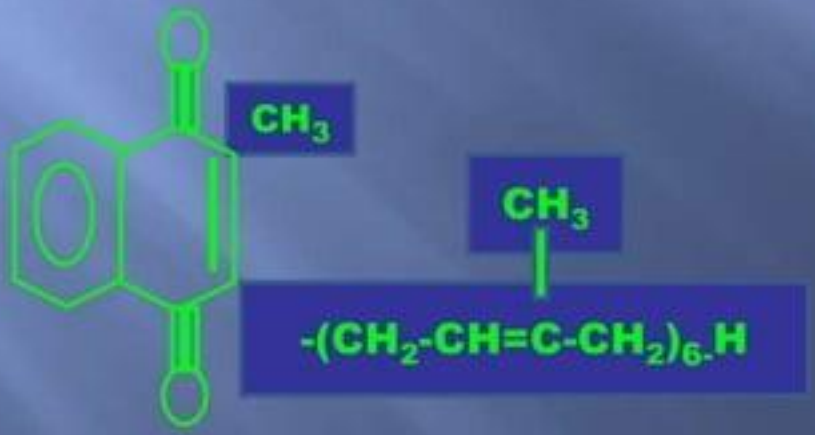
- It is menaquinone
- Produced by the intestinal bacteria and also found in animals
- It has isoprenyl side chain

Vitamin-K_3

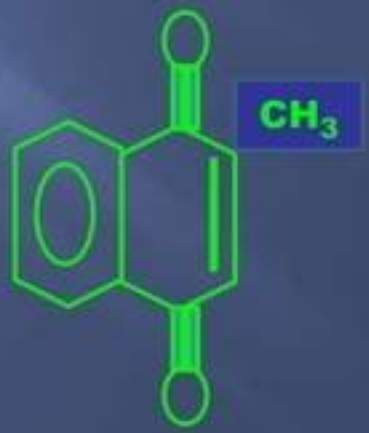
- Also known as menadione
- It is a synthetic form of vitamin K
- It lacks side chain and it is water soluble
- All the three vitamins (K1, K2, K3) are naphthoquinone derivatives
- Isoprenoid side chain is present in K1 & K2
- Three vitamins are stable to heat
- Their activity is lost by oxidizing agents, strong acids and alkalies



Vitamin K1 (phylloquinone)



VitaminK2 (menaquinone)



VitaminK3 (menadione)

Absorption

- Absorption occurs in the upper small intestine
- The absorption of vitamin K (K1 & K2) require bile salts
- Transported from the mucosal cells to the liver by binding to chylomicrons
- Vitamin K3 is readily absorbed without requiring bile salts

Storage

- Vitamin K is stored in liver
- Also present in significant amount in spleen and skeletal muscle

Transport

- Vitamin K released to the blood stream and transported in the blood by associating with beta-lipoproteins (LDL)

Biochemical functions

- The functions of vitamin K are concerned with blood clotting process
- It brings about post-translational modification of certain blood clotting factors
- The clotting factors II, VII, IX and X are synthesized as inactive precursors in the liver

- Vitamin K act as a coenzyme for the carboxylation of glutamic acid residues present in the protein and this reaction is catalyzed by a carboxylase (microsomal)
- It involves the conversion of glutamate (Glu) to γ-carboxyglutamate (Gla) and requires vitamin K, O_2 and CO_2
- The formation of γ - carboxyglutamate is inhibited by dicumarol, an anticoagulant found in spoilt sweet clover

- Warfarin is a synthetic analogue that can inhibit vitamin K action
- *Role of Gla in clotting:*
- γ - Carboxyglutamic acid (Gla) residues of clotting factors are negatively charged (COO-) and they combine with Positively charged calcium ions (Ca2+) to form a complex
- The complex binds to the phospholipids on the membrane surface of the platelets
- Leads to increased conversion of prothrombin to thrombin

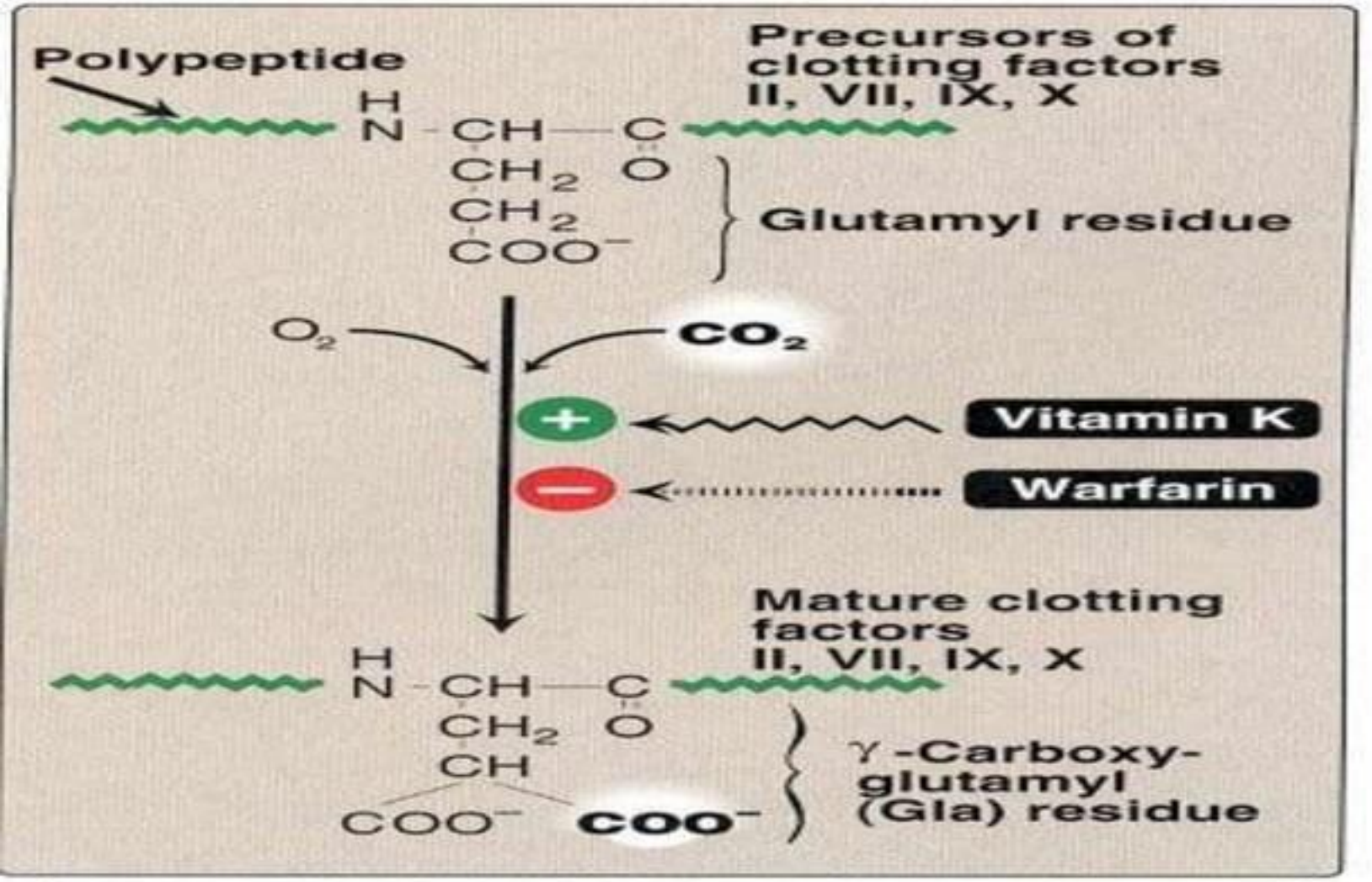
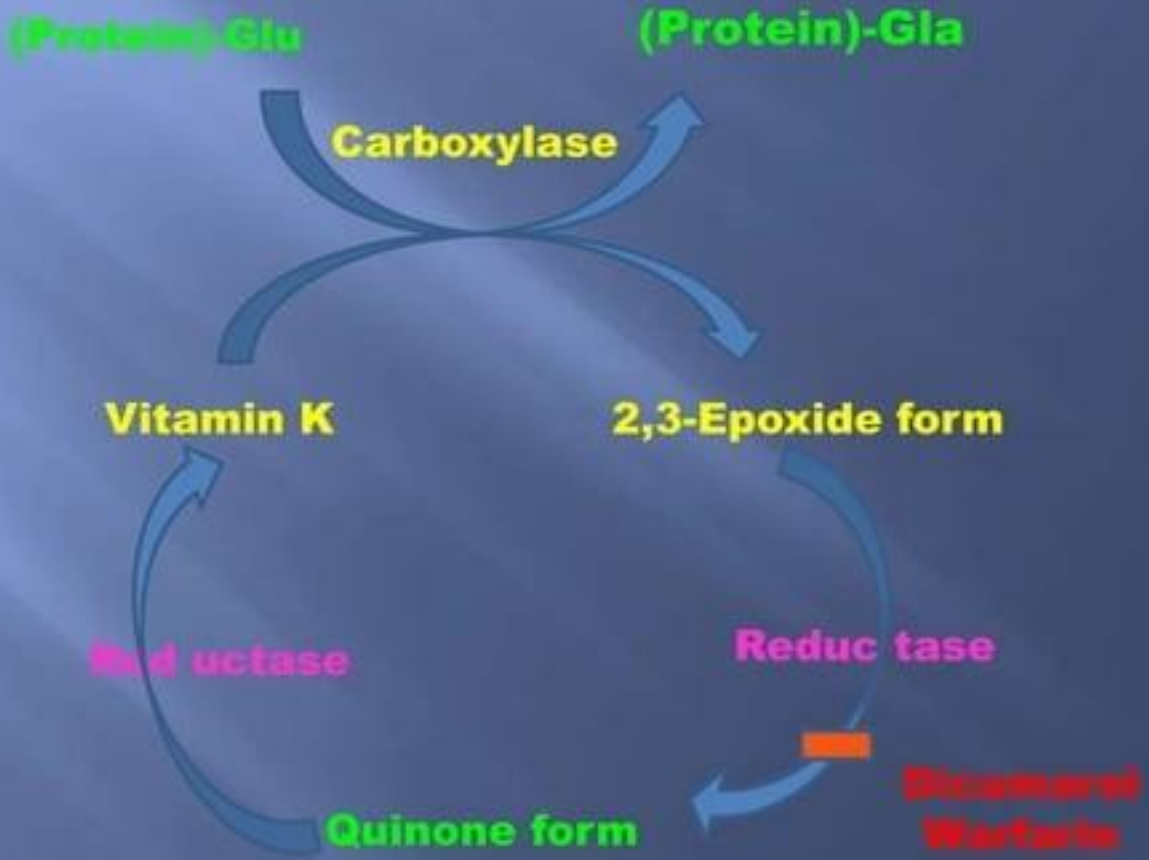


Figure 28.26
Carboxylation of glutamate to form γ-carboxyglutamate (Gla).

Vitamin K Cycle



γ - Carboxylation of other proteins

- Vitamin K is also required for the carboxylation of glutamic acid residues of osteocalcin, a calcium binding protein present in the bone
- Osteocalcin is involved in the regulation of bone mineralization
- Osteocalcin acts by its ability to bind hydroxyapetite
- The synthesis of osteocalcin is regulated by 1,25 DHCC

Vitamin K & oxidative phosphorylation

- Vitamin K is required for ETC and oxidative phosphorylation
- Vitamin K antagonists such as dicumarol act as uncouplers of oxidative phosphorylation

Dietary sources

- *Vitamin K1:*
- Rich sources of vitamin K1 are green leafy vegetables such as spinach, cabbage, cauliflower. Milk is a poor source

Vitamin K2

- Rich sources of vitamin K2 is purified meat in which vitamin K2 is synthesized by bacteria
- Vitamin K2 is synthesized by the intestinal bacterial flora such as E.coli in humans
- RDA:
- 70-140 μg/day
- Approximately equal amounts are provided by the synthesis of vitamin by the intestinal bacterial flora

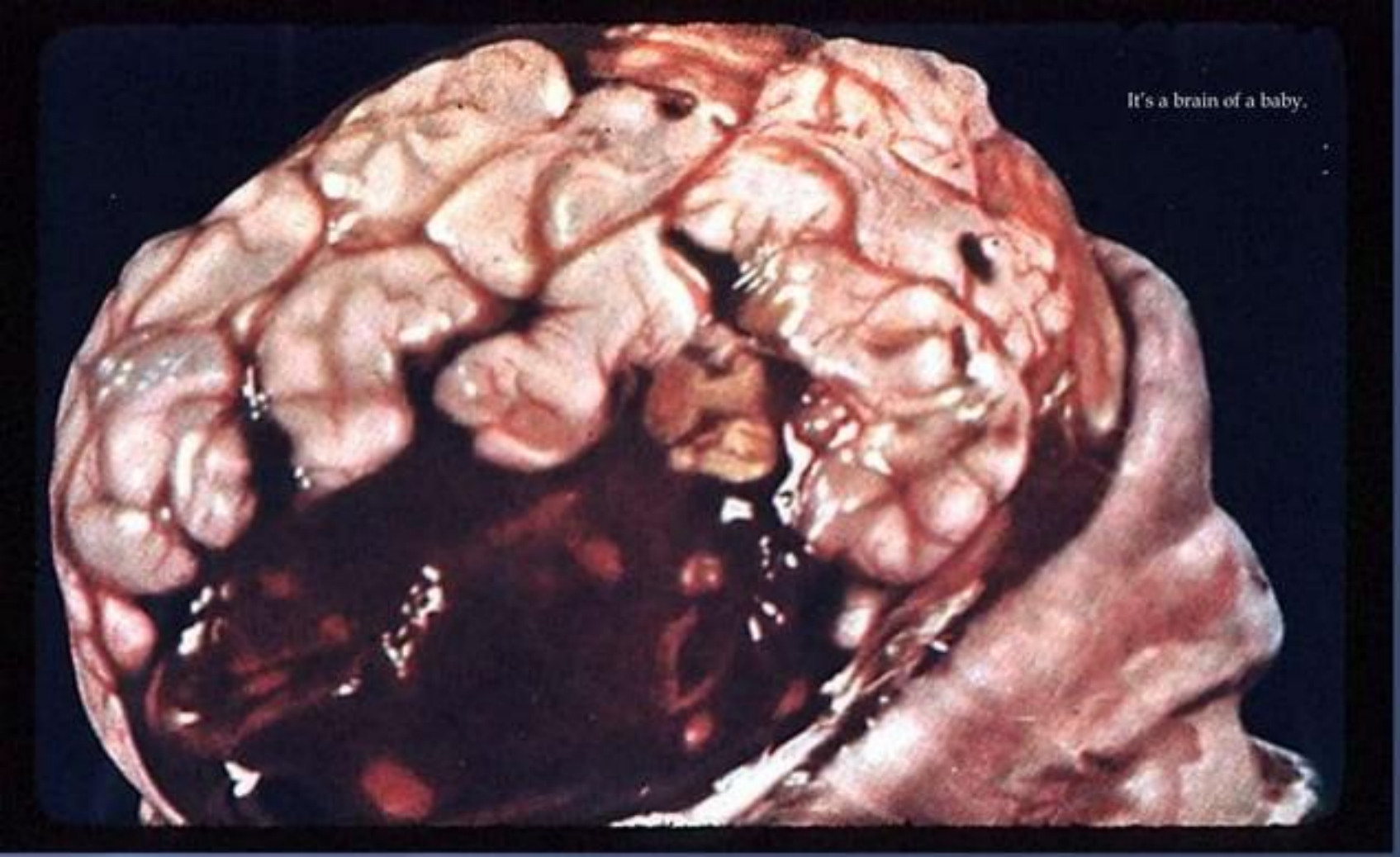
+ Deficiency

- Deficiency in newborninfants:
- Sterile intestinal flora
- Very little vitamin K crossing the placental barrier from maternal circulation
- Impaired absorption:
- Impaired absorption caused by biliary obstruction or small intestinal diseases

- Sterile bacterial flora caused by administration of antibiotics results in non-availability of microbial source of vitamin K
- Clinical features:
- Prolongation of bleeding and prothrombin time (PT)
- Measurement of PT is an index of liver function
- Liver function is lowered, prolongation of PT occurs due to deficient synthesis of coagulation factors
- Administration of vitamin K restore PT to normal level

Vit K deficiency. Spontaneous hemorrhages.

Normal Vit K sufficient bird for comparison.



Vit K deficiency in man. Hemorrhagic disease of newborn. Reason for Vit K injection at birth.

- Vitamin K antagonists:
- Dicumarol & Warfarin have structurally similarity to vitamin K
- They competitively inhibit Vitamin K *epoxide reductase & vitamin K quinone reductase*
- They block the regeneration of active form of vitamin K

- Uses:
- Used as oral anticoagulants in the treatment of thrombotic conditions such as thrombosis occurring after myocardial infarction or surgery
- Hypervitaminosis:
- Administration of large doses of vitamin K produces hemolytic anemia and jaundice,kernicterus and brain damage

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