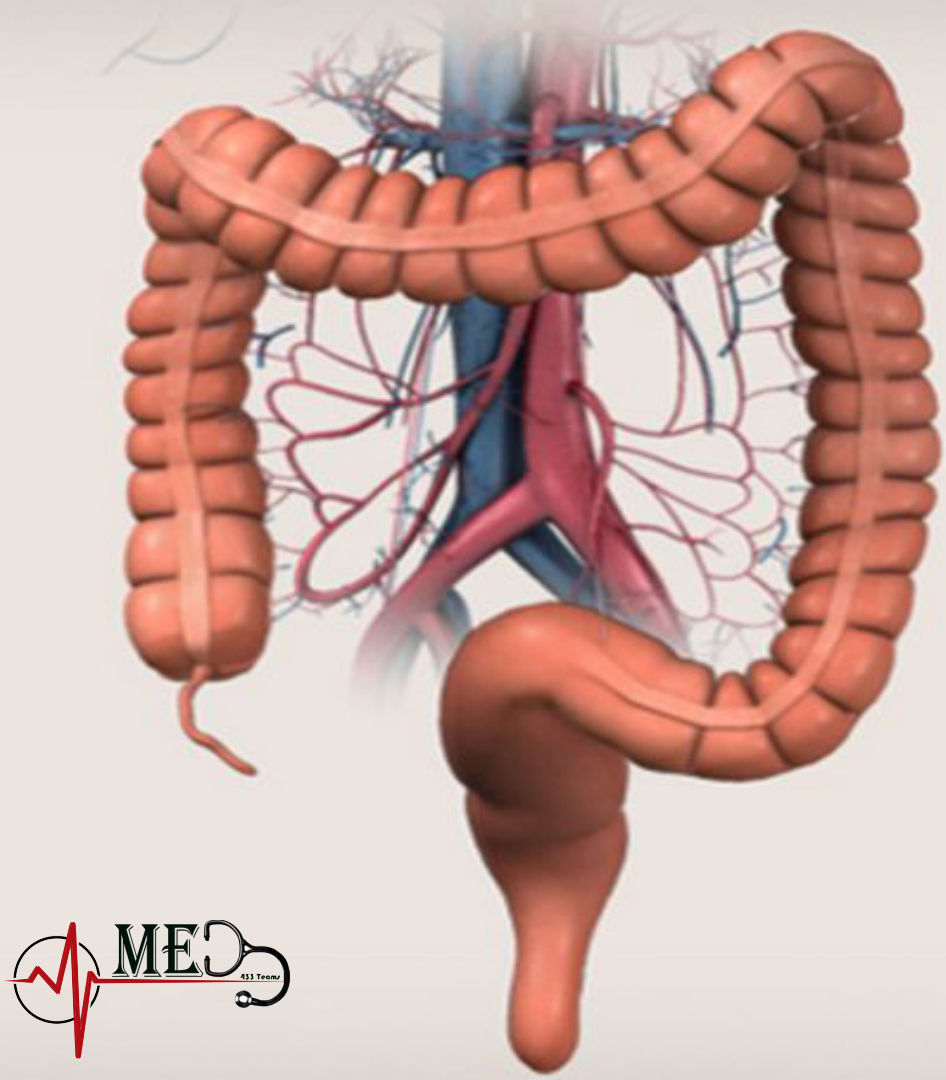

Biochemistry of Vitamin K

OVERVIEW:

- Types and chemistry of Vitamin K
- Sources and daily requirements
- Functions
- Synthesis of γ-Carboxyglutamate in:
  - Prothrombin and blood clotting factors
  - Osteocalcin
  - Interaction of Prothrombin with platelets
- Deficiency and disorders

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Vitamin K

Types and sources

Vitamin K_1 (Phylloquinone)

- From Green leafy vegetables

Vitamin K_2 (Menaquinone)

- From Intestinal bacteria
- synthesis meets the daily requirement of Vitamin K

Vitamin K_3 (Menadione)

- The synthetic form

Recommended Dietary Allowance (µg/day)	
Infants (0-1)	2 – 25
Children (1-8)	30 – 55
Men (+19)	120
Women (+19)	90
Pregnancy/Lactation	90/90
Upper Limit (UL)	Not Established

Functions:

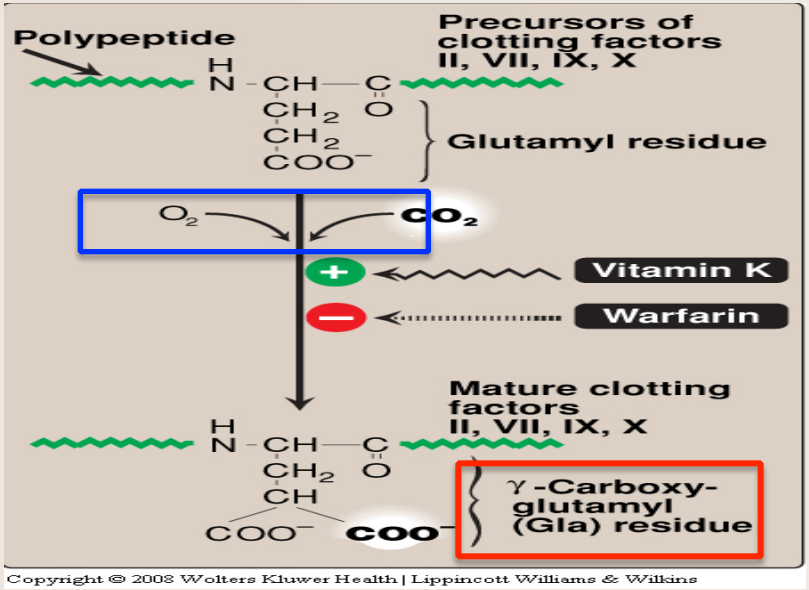
1. Coenzyme for the synthesis of Prothrombin (factor II) & other Blood Clotting Factors in the Liver

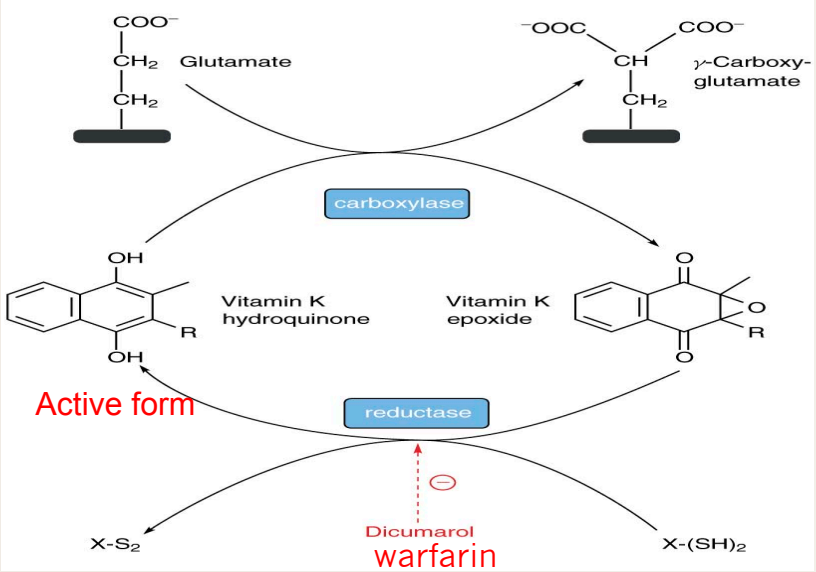
Synthesis of **Prothrombin** & Clotting **Factors VII, IX, X** require **carboxylation** of their Glutamic Acid (Glu) residue Into γ-Carboxyglutamate (Gla) residu .

2) Synthesis of γ-Carboxyglutamate in Osteocalcin:

- Osteocalcin is a bone protein
- **γ-Carboxyglutamate** is required for its binding to hydroxyapatite (mineral) in the bone
- May have a role in bone formation and mineralization (its function in yet unclear)

Note: Prothrombin & clotting factors are proteins in nature





- Mature Prothrombin & Clotting Factors contain γ-Carboxyglutamate (Gla) after carboxylation reaction
- Dihydroquinonoe form of Vitamin K is essential for the carboxylase enzyme involved in this reaction.

- Anticoagulant drugs (Warfarin and Dicoumarol) are structural analogs* of Vitamin K .
- **They inhibit the activation of vitamin K to hydroquinone form.[1]**

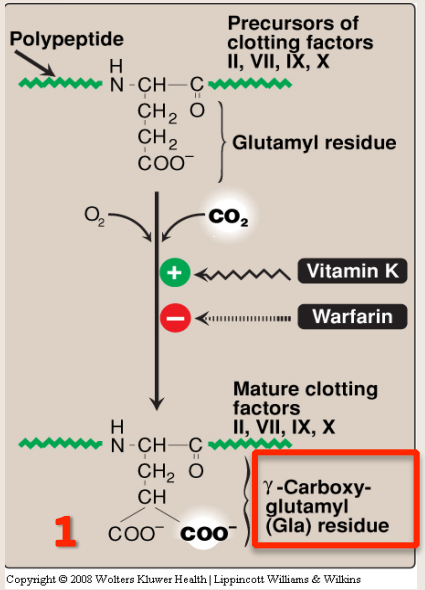
=> Prothrombin and Clotting Factors are not Carboxylated

=> Blood Coagulation time increases upon injury

*Structural Analog: Having a similar structure

1: The oxidized form of vitamin K (epoxide) is reduced by an an enzyme called Vitamin K epoxide reductase to its active form (hydroquinone), anticoagulant drugs inhibit this step yielding no available hydroquinone form of vitamin K.

Prothrombin – Platelets interaction

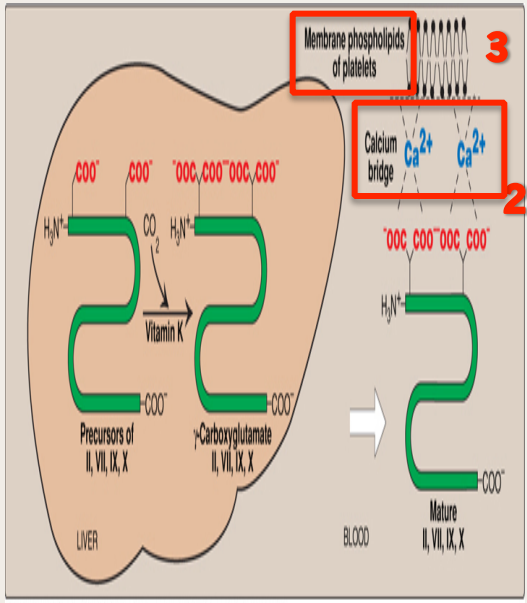


1-Carboxylated Prothrombin has **two** carboxylate groups (COO-)

2-These groups bind to Ca^{+2} forming Prothrombin-Calcium complex

3-The complex then binds to Phospholipids on the surface of platelets (important for blood clotting)

Converting Prothrombin → Thrombin & Clot Formation



Causes of Deficiency

Deficiencies are rare because it is synthesized by intestinal bacteria

- ❑ Malabsorption of lipids due to Obstructive Jaundice leads to Vitamin K deficiency
- ❑ Prolonged antibiotic therapy & GI infections with diarrhea destroy bacterial flora and can also lead to Vitamin K deficiency

Deficiency is most common in newborn infants because:

- Newborns lack intestinal flora
- Human milk can't provide enough Vitamin K
- Supplements are given by injection

Effects of deficiency

Hypoprothrombinemia: increased blood coagulation time

May affect bone growth and mineralization because of **Osteocalcin**

Clinical Manifestations

- ✓ Hemorrhagic Disease of Newborns
- ✓ Bruising Tendency
- ✓ Ecchymotic Patches
- ✓ Mucous Membrane Hemorrhage
- ✓ Post-Traumatic Bleeding
- ✓ Internal Bleeding
- ✓ **Prolonged Prothrombin Time (PT)**

Echymosis: a discoloration of the skin resulting from bleeding underneath, typically caused by bruising.

1. The main source of Vitamin K for humans is:
   A. Vegetables
   B. Endogenous synthesis by bacteria
   C. Dietary fibers
   D. Sunlight
2. Vitamin K is required for the synthesis of which ONE of the following:
   A. Factor III
   B. Plasminogen
   C. Factor VII
   D. Factor XII
3. The form of vitamin K that is required for activation of clotting factors is:
   A. Phylloquinone
   B. Menaquinone
   C. Menadione
   D. Dihydroquinone
4. Activated clotting factors contain which ONE of the following:
   A. Glutamate (GLU) residue
   B. Gamma-Carboxy glutamate (GLA) residue
   C. Glutamine residue
   D. None of the above

Answers:
1-B 2-C 3-D 4-B 5-C 6-C 7-C 8-D

5. Which one of the following is a co-enzyme for γ-carboxyglutamate to synthesize Prothrombin:
   A. Vitamin A
   B. Vitamin D
   C. Vitamin K
   D. Vitamin E
6. A newborn baby is doing well with breast feeding. His mother came to the ER department because her baby had bleeding from his umbilical cord. Which ONE of the following vitamins is most-likely deficient?
   A. Vitamin A
   B. Vitamin D
   C. Vitamin K
   D. Vitamin E
7. Anticoagulant drugs such as Warfarin work by inhibiting :
   A. The activation of Prothrombin to thrombin
   B. Activation of Plasminogen to plasmin
   C. The activation of epoxide form of Vitamin K to hydroquinone form
   D. Its mechanism is unknown
8. Gamma-carboxyglutamate is required for which ONE of the following proteins:
   A. Albumin
   B. Gamma-glutamyltransferase
   C. C-reactive protein
   D. Osteocalcin

Thank You!

Done by:
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