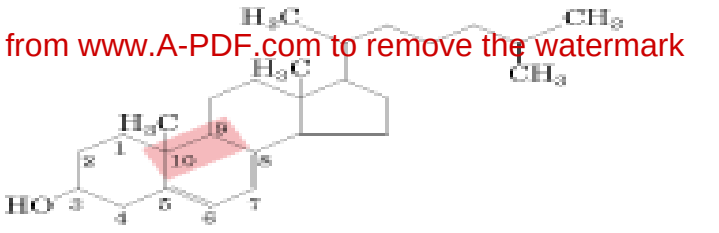
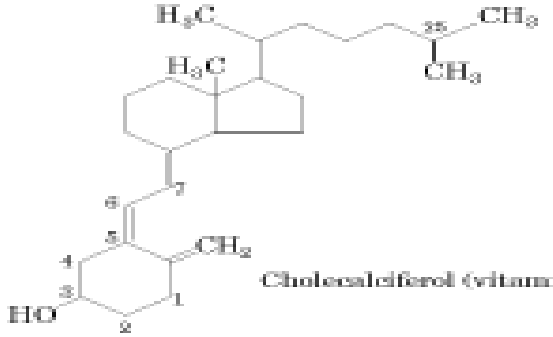


7-Dehydrocholesterol

UV light

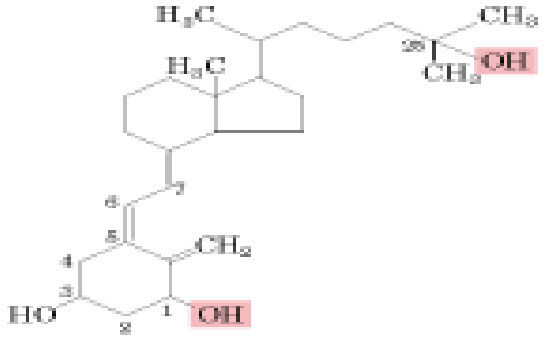
2 steps (in skin)



Cholecalciferol (vitamin D_3)

1 step in the liver

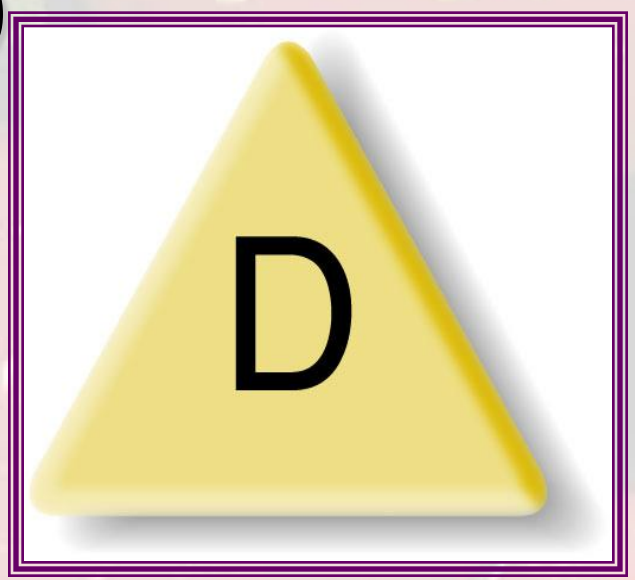
1 step in the kidney



1,25-Dihydroxycholecalciferol
(1,25-dihydroxyvitamin D_3)

(a)

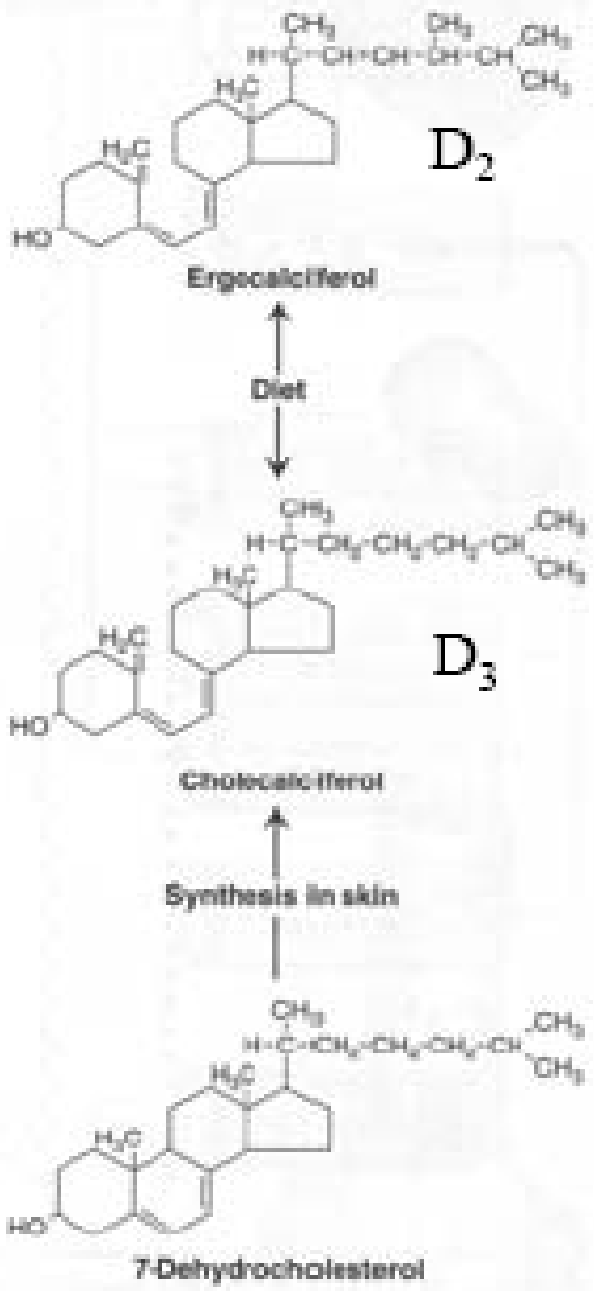
Vitamin D



- Synthesis
  - Made in the skin from cholesterol
  - Activated in liver and kidney
- Functions
  - Regulates blood calcium levels
- Food sources
  - Fortified milk, fortified cereals
- Deficiency
  - Rickets in children; osteomalacia in adults
- Toxicity

Vitamin D: Functions

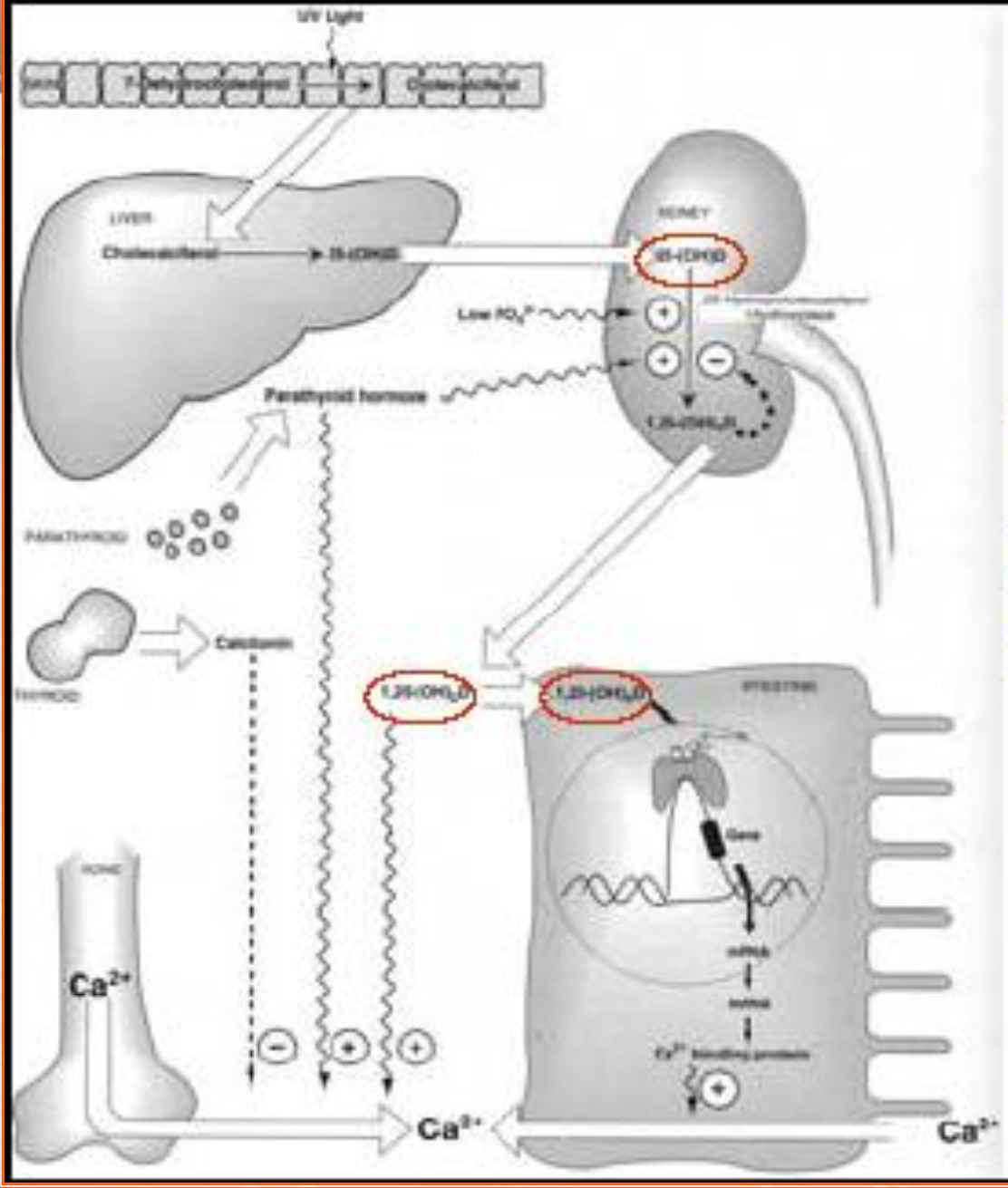
- Helps regulate blood calcium levels
- Dietary calcium absorption
- Urinary calcium excretion
- Bone calcium metabolism



Vitamin D: Hormone for Calcium and Phosphate regulation

You either need preformed vitamin D's in the diet, or you need to get some sun:

You can synthesize vitamin D from a cholesterol intermediate using sunlight in the skin.



1,25-(OH)2D3 maintains plasma calcium levels

Vitamin D: Types and Sources

- Dietary sources: animal foods, fortified milk
- Human Synthesis of Vitamin D
- Skin: cholesterol + sunlight
  - "Sunshine Vitamin" – UV-B rays
  - Vitamin D_3
  - 5-10 minutes, arms and legs, mid-day sun
- Liver & Kidney for activation
  - 1,25-di-OH-D_3

When Vitamin D goes Bad

- Too Little: (Northern Latitudes) Rickets, Osteoporosis - demineralization of bones.
- Too Much: It's the most toxic of the vitamins
  - Nausea, thirst, loss of appetite, stupor
  - Hypercalcemia: Calcium gets deposited in organs: Arteries and Kidneys.

Vitamin D: Deficiency

- Rickets
  - bone deformities in children
- *Osteomalacia*
  - weak bones due to low calcium content
  - Vitamin D deficiency
  - Calcium deficiency
  - multiple pregnancies

Before vitamin D treatment

After 14 months of vitamin D treatment

(b)

Vitamin D: Toxicity

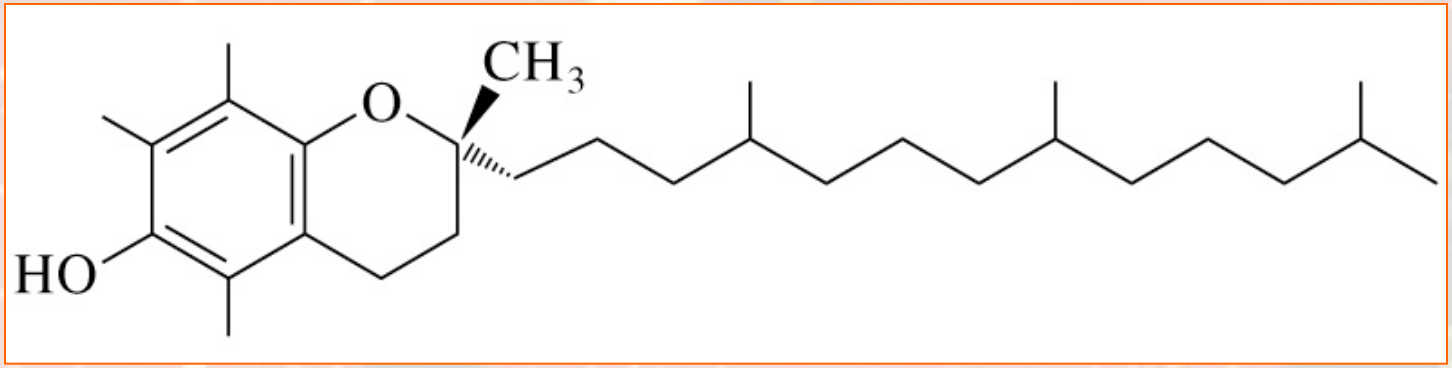
- 5 times the RDA chronically
  - calcification of soft tissue
  - toxicity due to excessive vitamin supplementation

III - Vitamin E

Vitamin E (a-tocopherol)

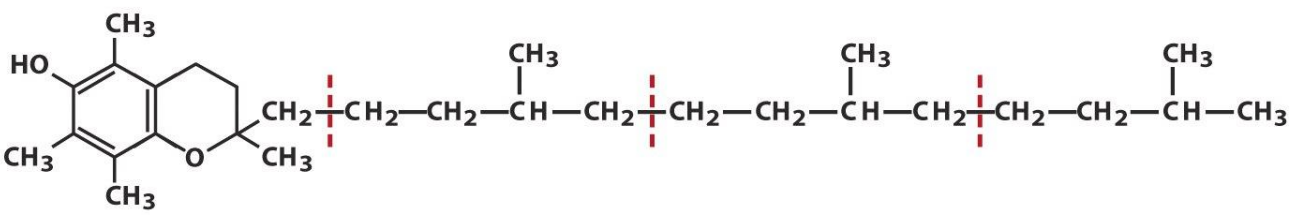
- A reducing reagent that scavenges oxygen and free radicals
- May prevent damage to fatty acids in membranes

Vitamin E (a-tocopherol)



Vitamin E

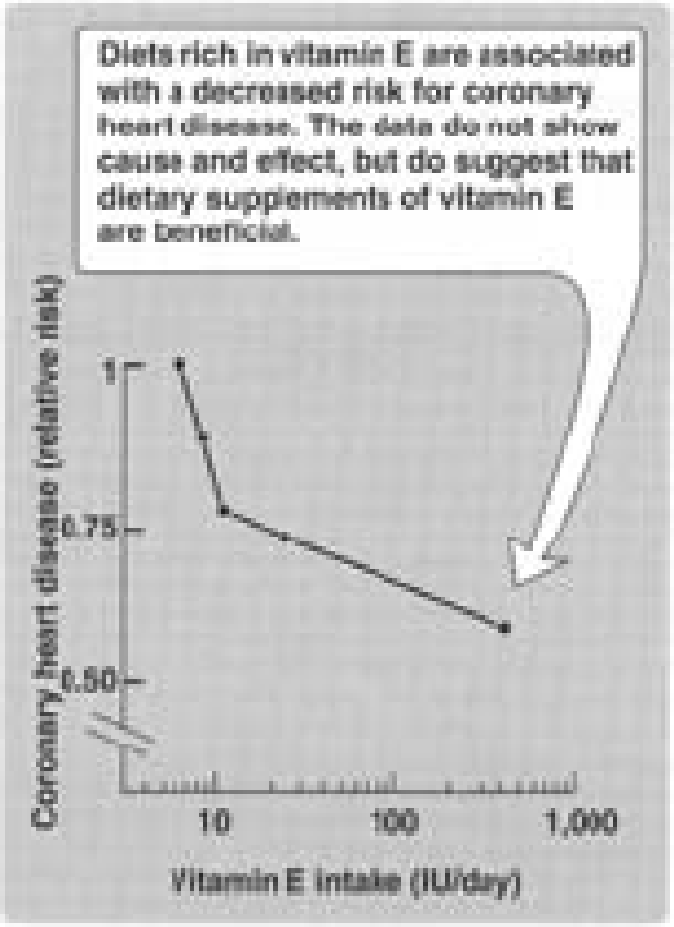
- Vitamin E is fat-soluble
- Antioxidant activity
- Vitamin E is found in eggs and vegetable oils.
- Deficiency is very rare in humans; primary symptom is fragile erythrocytes.
- Vitamin E quenches superoxide anions; the resulting radical is then oxidized by Vitamin C.



(a)

Vitamin E: an antioxidant

Vitamin C and E Antioxidants



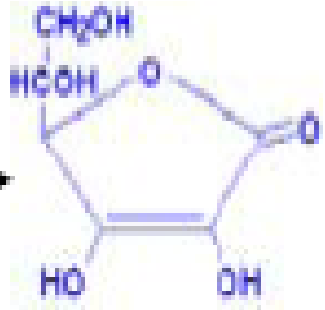
Vitamin E is an antioxidant

Deficiency is only seen in premature infants - sensitive to oxidants.

Other antioxidant vitamins:

Beta Carotene

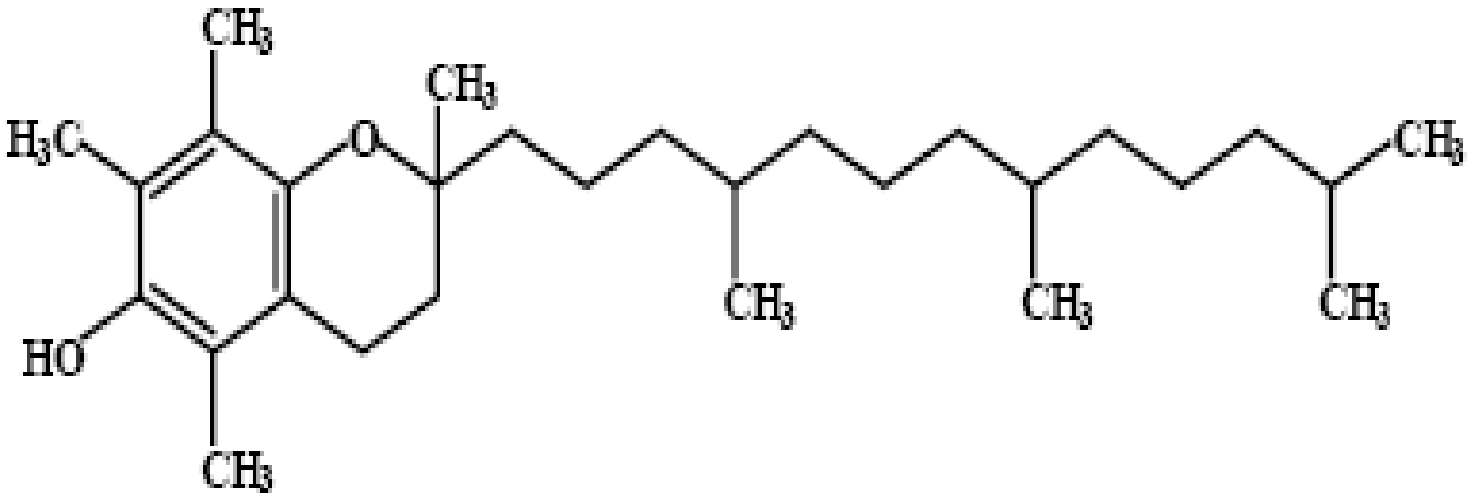
Vitamin C →



Vitamin E

- alpha (E_1), beta (E_2) and gamma(E_3) tocopherol
- sources: plant oils (corn, peanut, wheat germ), green leafy vegetables, meat, eggs
- value resides in the antioxidant properties of vitamin E (may prevent the formation of peroxides)

Alpha Tocoperol



ALPHA TOCOPHEROL

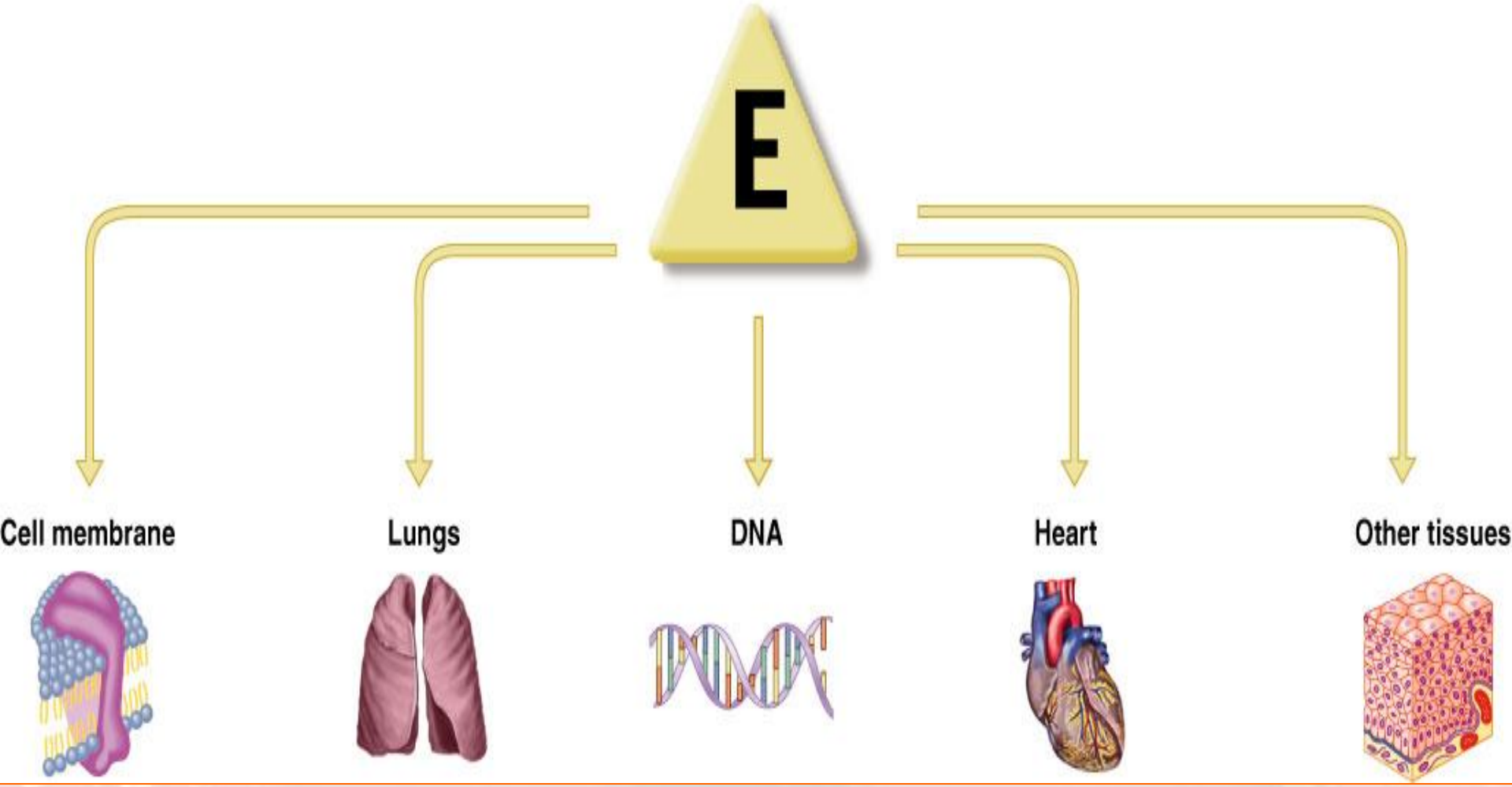
Found in a variey of different sources (primarily vegetable fats)

Vitamin E

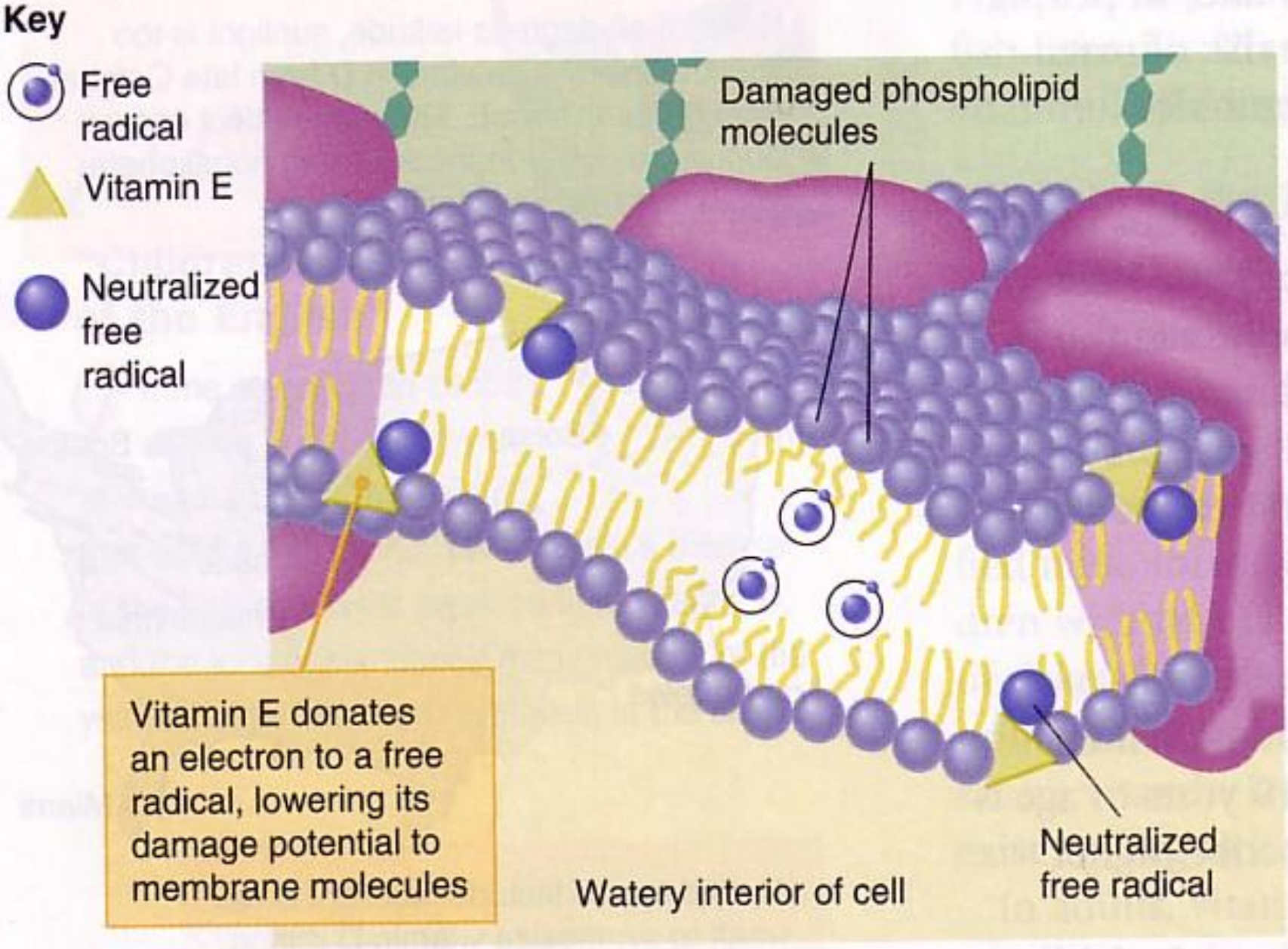
- Functions
  - Antioxidant: stop the chain reaction of free radicals producing more free radicals; protects cell components and membranes from destruction; prevents oxidation of PUFA; reduce risk of heart disease by protecting LDL against oxidation
  - Food Sources: nuts, seeds, wheat germ, oils, margarine, salad dressing
- Deficiency: rare
- Toxicity:UL=1000 mg/day

Vitamin E

- Estimated requirements: 5 mg/day + 0.6 mg/day of unstaurated fat
- Biological function – *antioxidant* for fatty acids
  - Acts like vitamin C; prevents lipid peroxidation and/or damage to cells by lipid hydroperoxides



RDA=15 mg/day


Key
Free radical
Vitamin E
Neutralized free radical
Damaged phospholipid molecules
Vitamin E donates an electron to a free radical, lowering its damage potential to membrane molecules
Watery interior of cell
Neutralized free radical

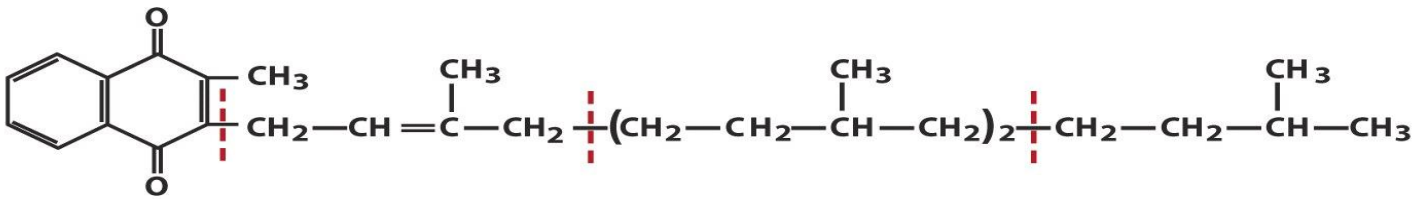
Uses for vitamin E

- hemolytic anemia in premature infants, unresponsive to B_{12}, Fe and folic acid
- macrocytic megaloblastic anemia seen in children with severe protein-calorie malnutrition

IV - Vitamin K

Vitamin K

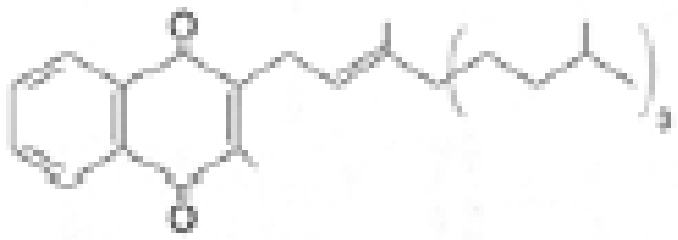
- Vitamin K (phylloquinone) is fat-soluble
- Vitamin K is a blood-clotting cofactor
- It undergoes oxidation and then reduction during the formation of active prothrombin, a blood protein required for clot formation.
- Vitamin K is found in green plant leaves; deficiency is very rare.



(b)

Vitamin K_1: a blood-clotting cofactor (phylloquinone)

Blood Clotting: Vitamin K



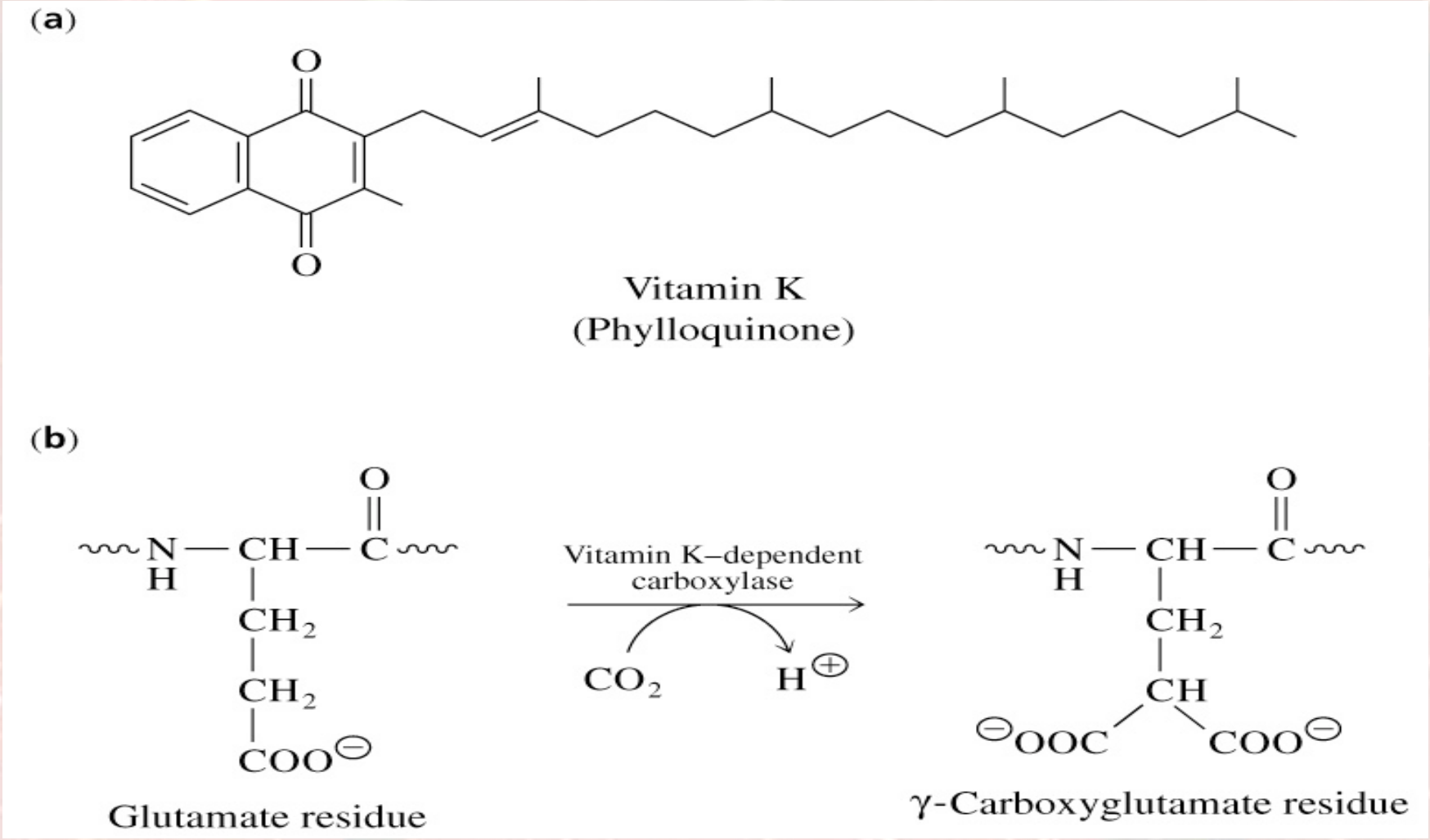
Vitamin K_1

- Needed for modifications of blood clotting factors.
- Made by Bacteria in intestine and absorbed with lipids.
- Deficiency:
  - Occurs with long antibiotic treatment and in infants.
- Too much: Anemia - toxic to red cell membrane.

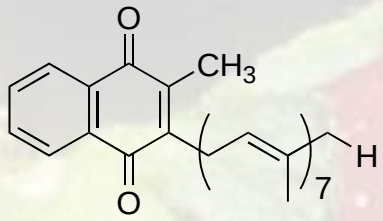
Vitamin K (phylloquinone)

- Required for synthesis of blood coagulation proteins
- A coenzyme for mammalian carboxylases that convert glutamate to g-carboxyglutamate residues
- Calcium binds to the g-carboxyGlu residues of these coagulation proteins which adhere to platelet surfaces
- Vitamin K analogs (used as competitive inhibitors to prevent regeneration of dihydrovitamin K) are given to individuals who suffer excessive blood clotting

(a) Structure of vitamin K
(b) Vit K-dependent carboxylation



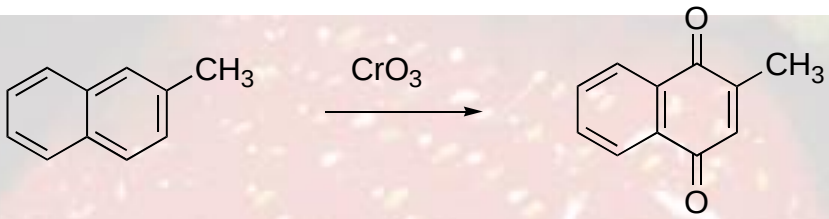
vitamin K_2 is another important qunione. This vitamin is essential to the biosynthesis of prothrombin, a clotting agent, that takes place in the liver.



Vitamin K_2

The natural vitamins of the K family have for the most part been replaced by synthetic preparations in food supplements. Menandione, an analog with vitamin K activity has a hydrogen in the place of the isoprene tail. Menandione can be prepared from 2-methyl naphthalene via a chromic acid oxidation under mild conditions.

This Reaction is fair game for the Final!

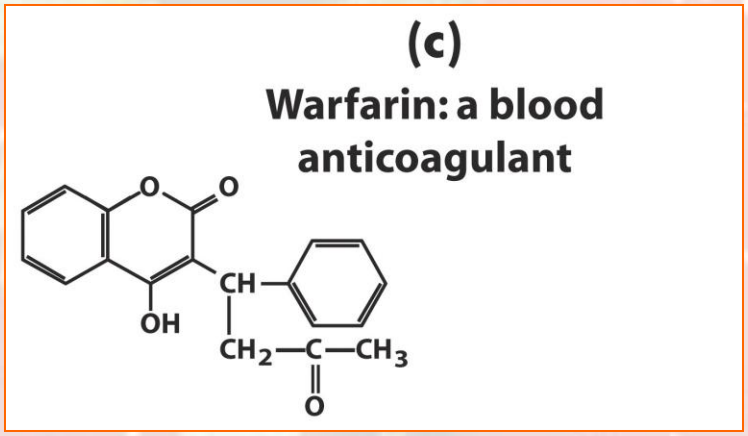


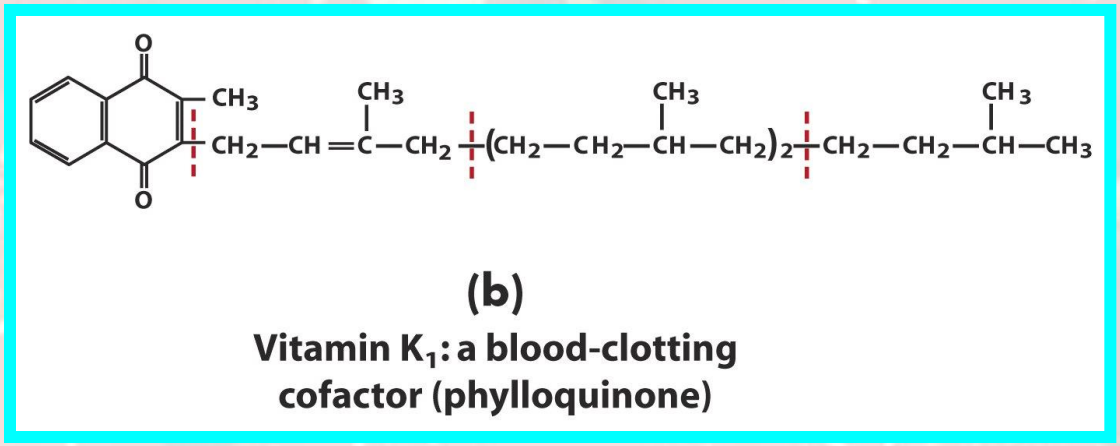
2-methyl-1,4-naphthoquinone

Menandione

Vitamin K

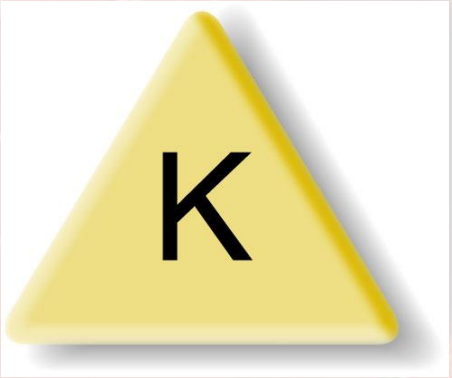
- Warfarin (coumadin), with a similar structure, is used to prevent excessive blood clotting.
- By inhibiting epoxide reductase in the liver





Vitamin K

- K for “koagulation” or “coagulation” or “clotting”
- Functions
  - Blood clotting
  - Formation of bone



- Bacteria in GI tract synthesize vitamin K
- Food sources
  - Green vegetables, liver, egg yolks
- Deficiency: rare; injection for newborn babies
- Interferes with anticoagulant medications

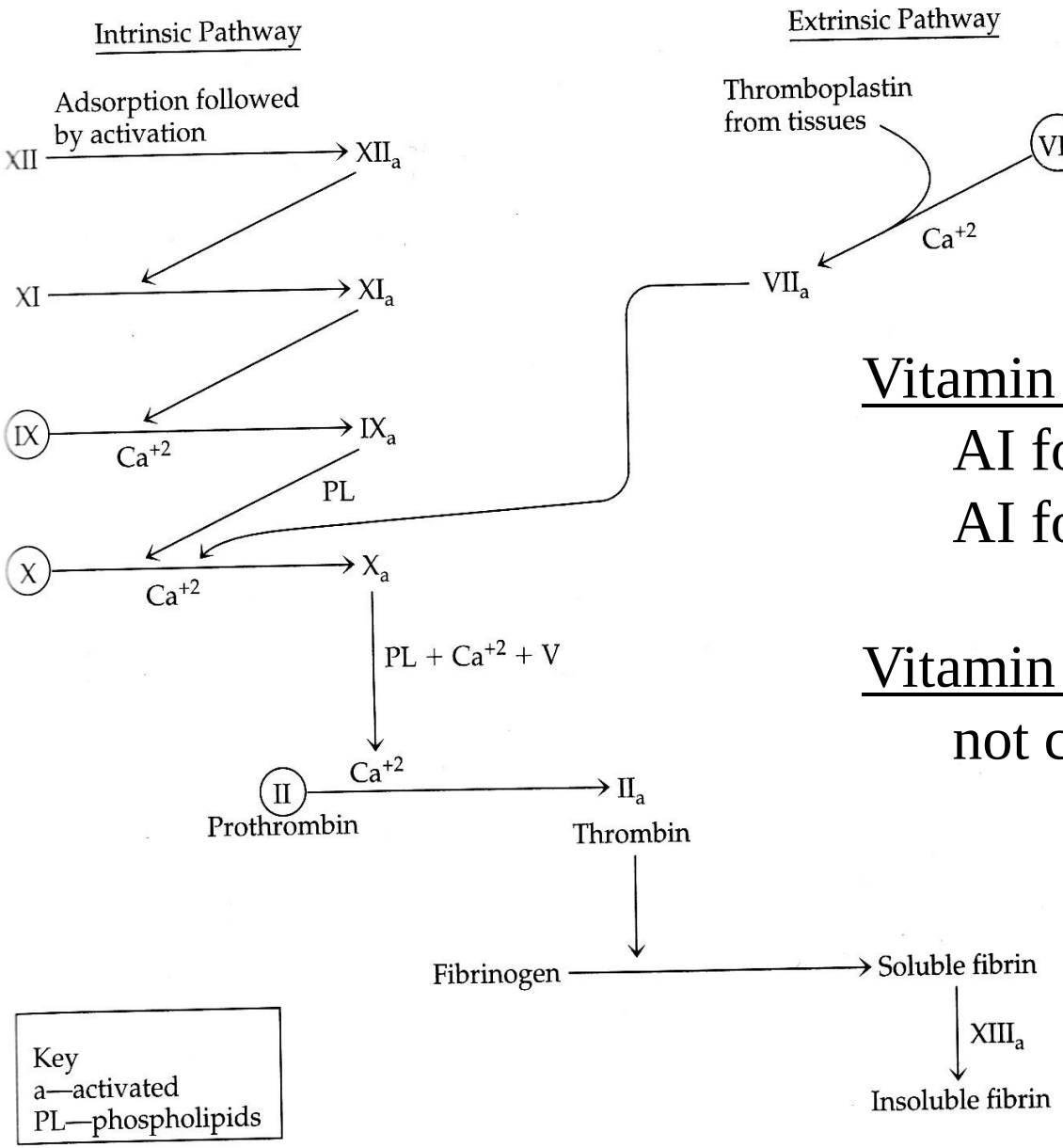


FIGURE 10.23 The activation of prothrombin and the roles of vitamin K-dependent clotting factors. Circled factors require vitamin K for their formation.

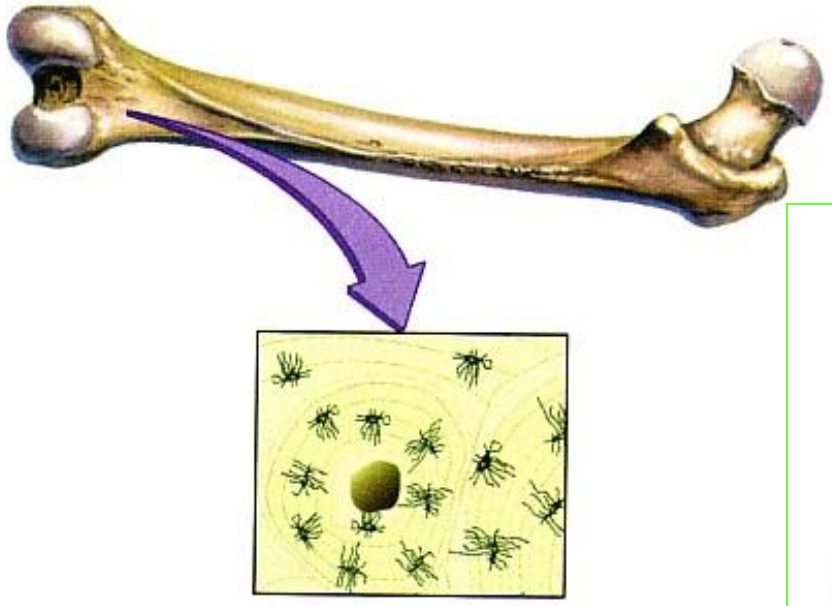
Vitamin K Recommendations

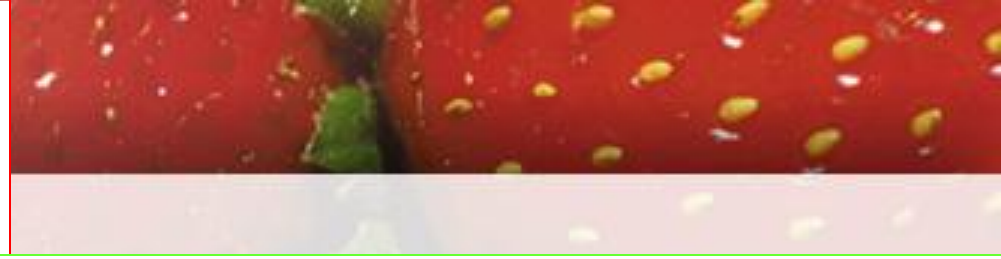
AI for adult males: 120 *u*g/day

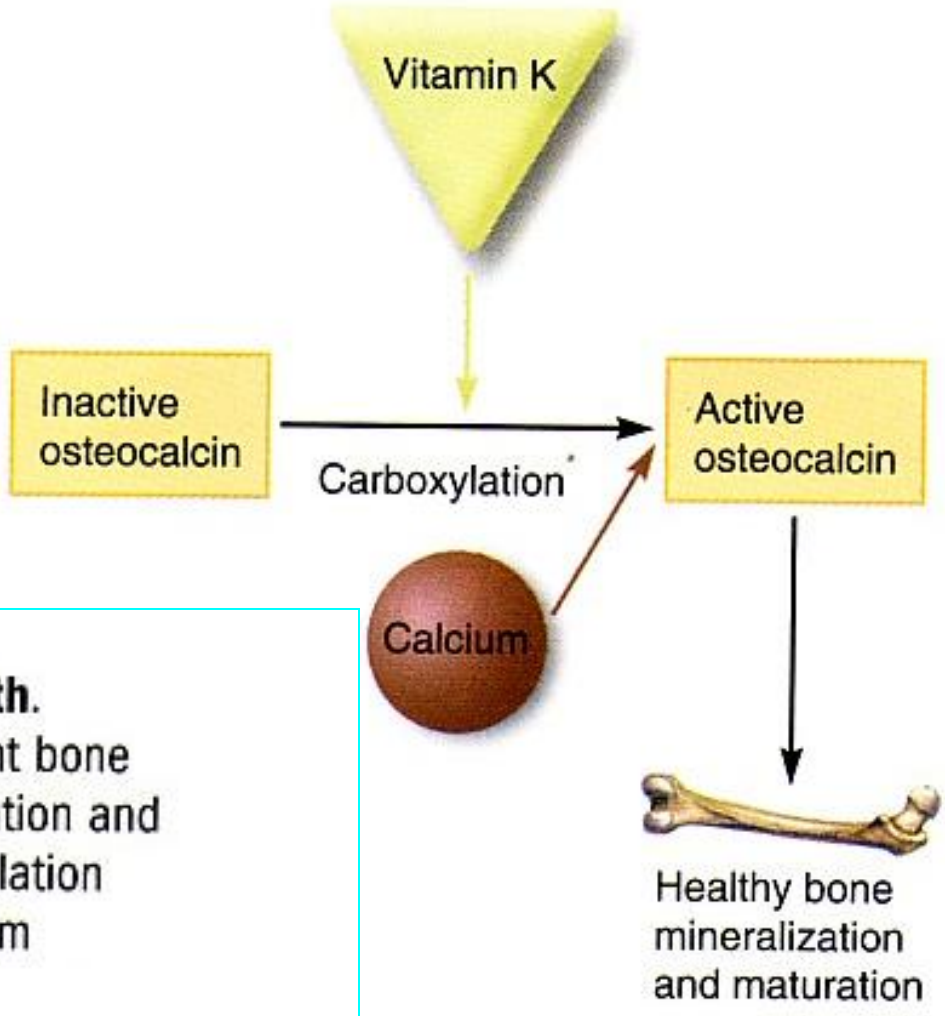
AI for adult females: 90 *u*g/day

Vitamin K Toxicity

not common





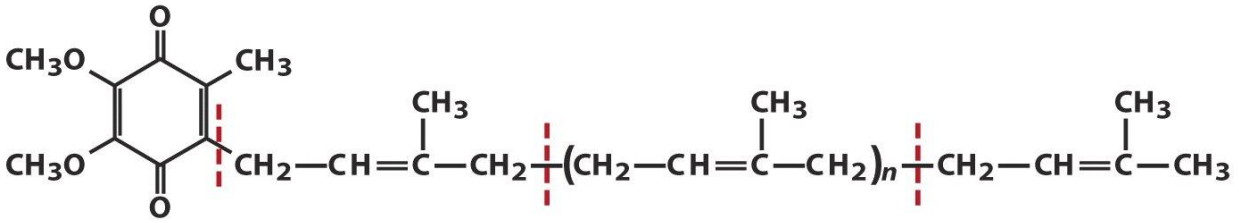


SFCC:

Figure 9.22 **Vitamin K and bone health.** Osteocalcin is an abundant bone protein that is required for bone mineralization and maturation. Vitamin K helps in the carboxylation of osteocalcin, greatly enhancing its calcium binding properties.

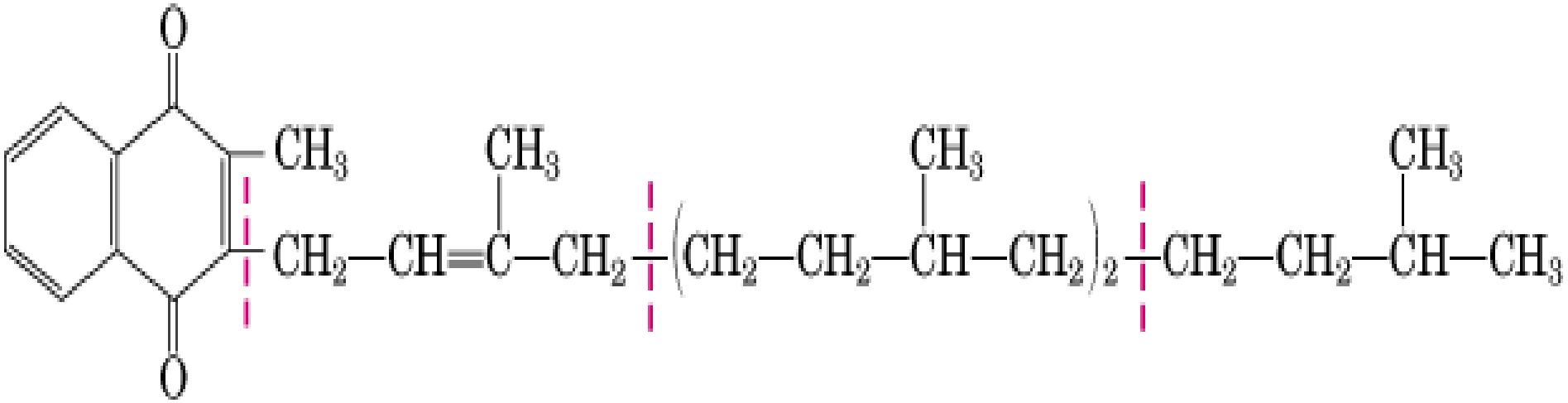
Isoprenoids

- Vitamins E and K are isoprenoid derivatives
- Similarly, ubiquinone (also called coenzyme Q) is an isoprenoid.
- Recall where ubiquinone is located, and the role of Vitamin E …



(d)

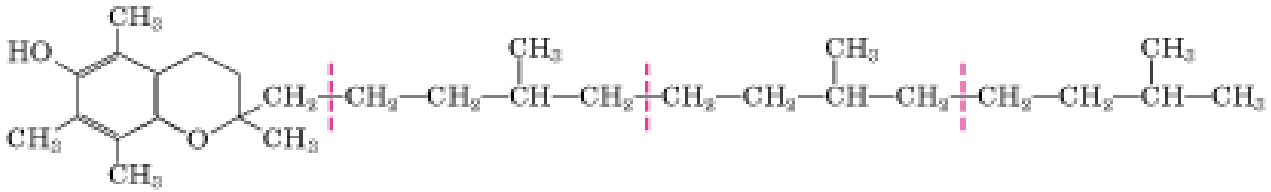
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) (n = 4 to 8)



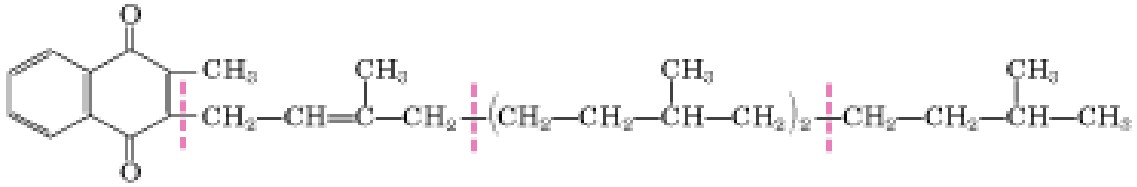
(b)

Vitamin K_1: a blood-clotting cofactor (phylloquinone)

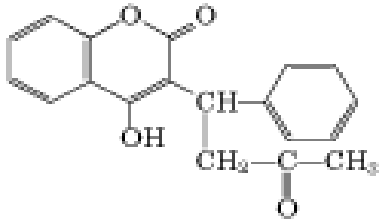
(a)
Vitamin E: an antioxidant



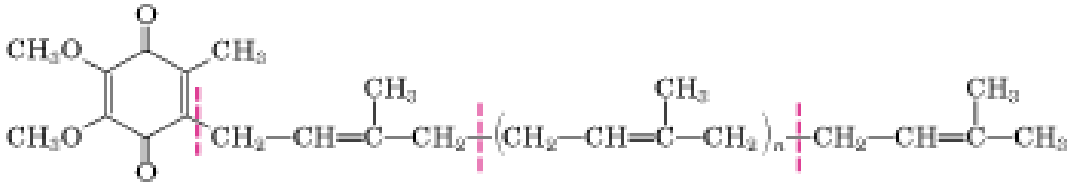
(b)
Vitamin K_1: a blood-clotting cofactor (phylloquinone)



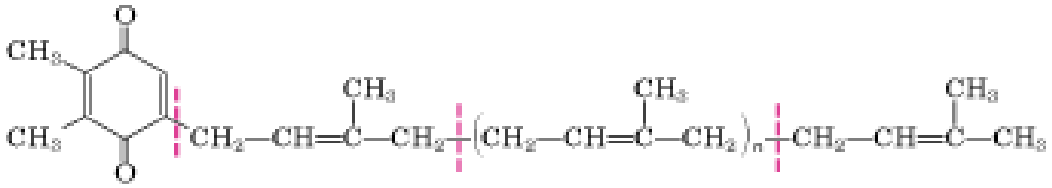
(c)
Warfarin: a blood anticoagulant



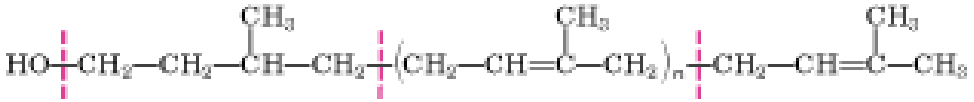
(d)
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) ($n = 4–8$)



(e)
Plastoquinone: a chloroplast electron carrier ($n = 4–8$)



(f)
Dolichol: a sugar carrier ($n = 9–22$)

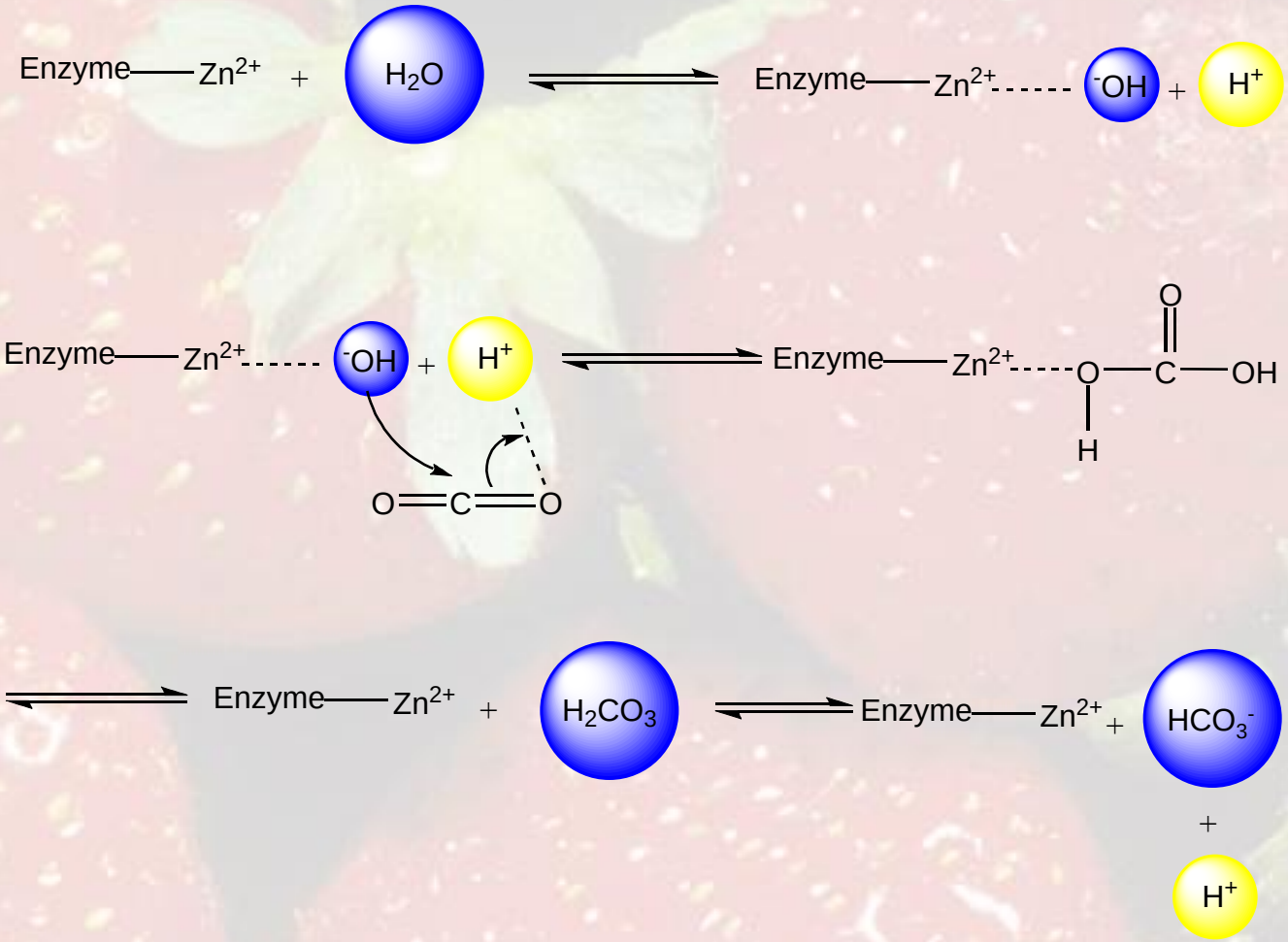


IONS AND METALS

Metal Cofactors

- **Why transition metals?**
  - **Good electrophiles**
  - **Can generally interact with more than one ligand to orient substrate in active site.**
  - **Since transition metals have multiple valence states, they can function in oxidation-reduction reactions.**

Metal Cofactors



Many Enzymes Require Inorganic Cations

- Enzymes requiring metal ions for full activity:

  (1) **Metal-activated enzymes** have an absolute requirement or are stimulated by metal ions (examples: K^+, Ca^{2+}, Mg^{2+})

  (2) **Metalloenzymes** contain firmly bound metal ions at the enzyme active sites (examples: iron, zinc, copper, cobalt)

Inorganic Cofactors

Inorganic Cofactor	Function	Enzyme Class
Magnesium	substrate binding	kinases
Calcium	substrate activation	hydrolases
Potassium	structure stabilization	pyruvate kinase
Iron	oxygen binding, electron transport	cytochromes
Zinc	substrate binding, structure stability	DNA binding
Copper	dioxygen activation	oxidases
Manganese	dioxygen activation	oxidases
Cobalt	group transfer	mutases (with B12)
Selenium	peroxidation	peroxidases

Water: Crucial to Life

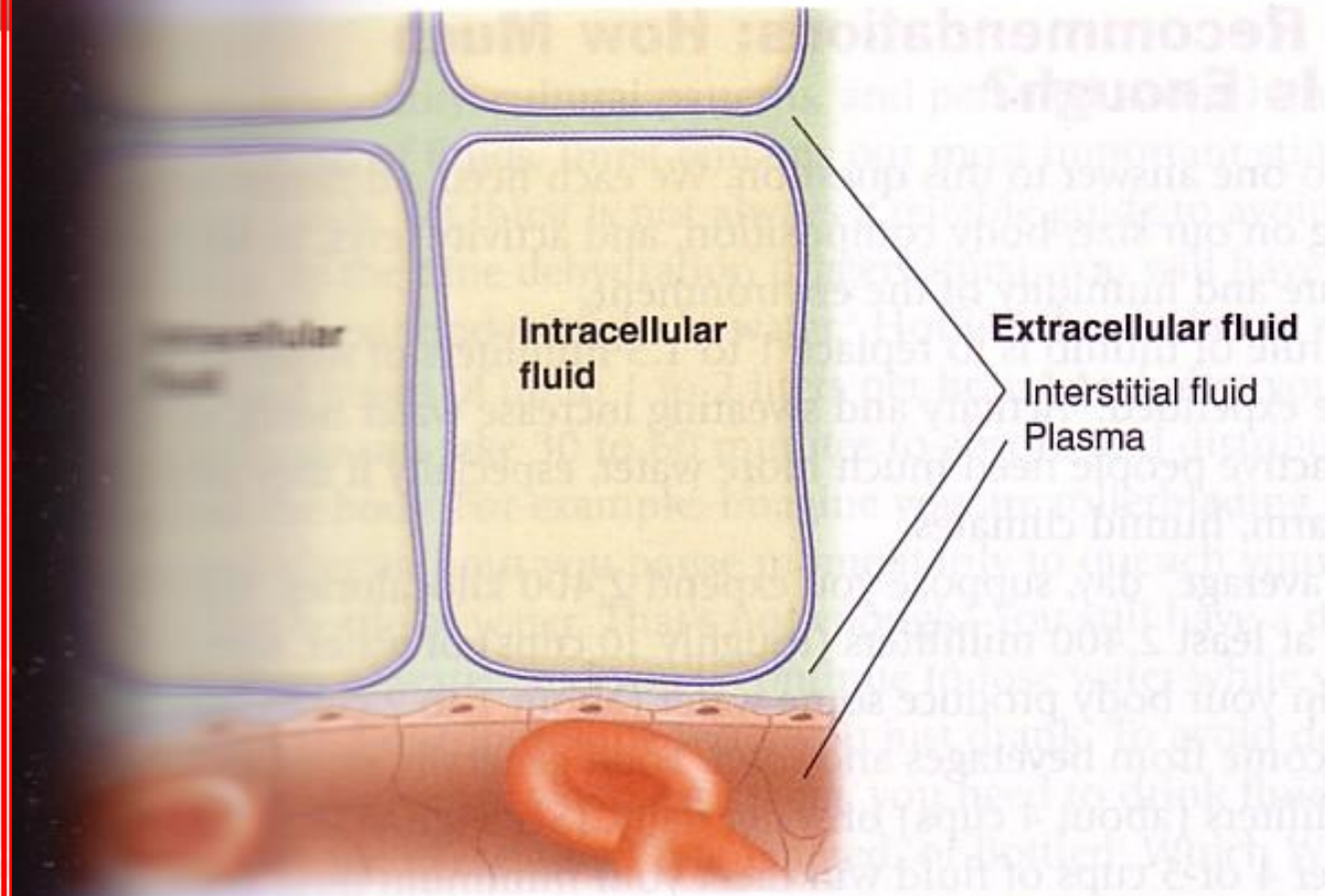
- Functions of water
  - Moves nutrients and wastes
  - Lubricates joints
  - Participates in chemical reactions
  - Helps maintain body temperature

Water: Crucial to Life

- Water excretion
  - lungs, skin, feces, urine
  - low humidity, high temp, fever, high pro & Na
- Water balance
- Other factors affecting fluid balance
  - alcohol, caffeine, diuretic medications
- Dehydration
- Water intoxication

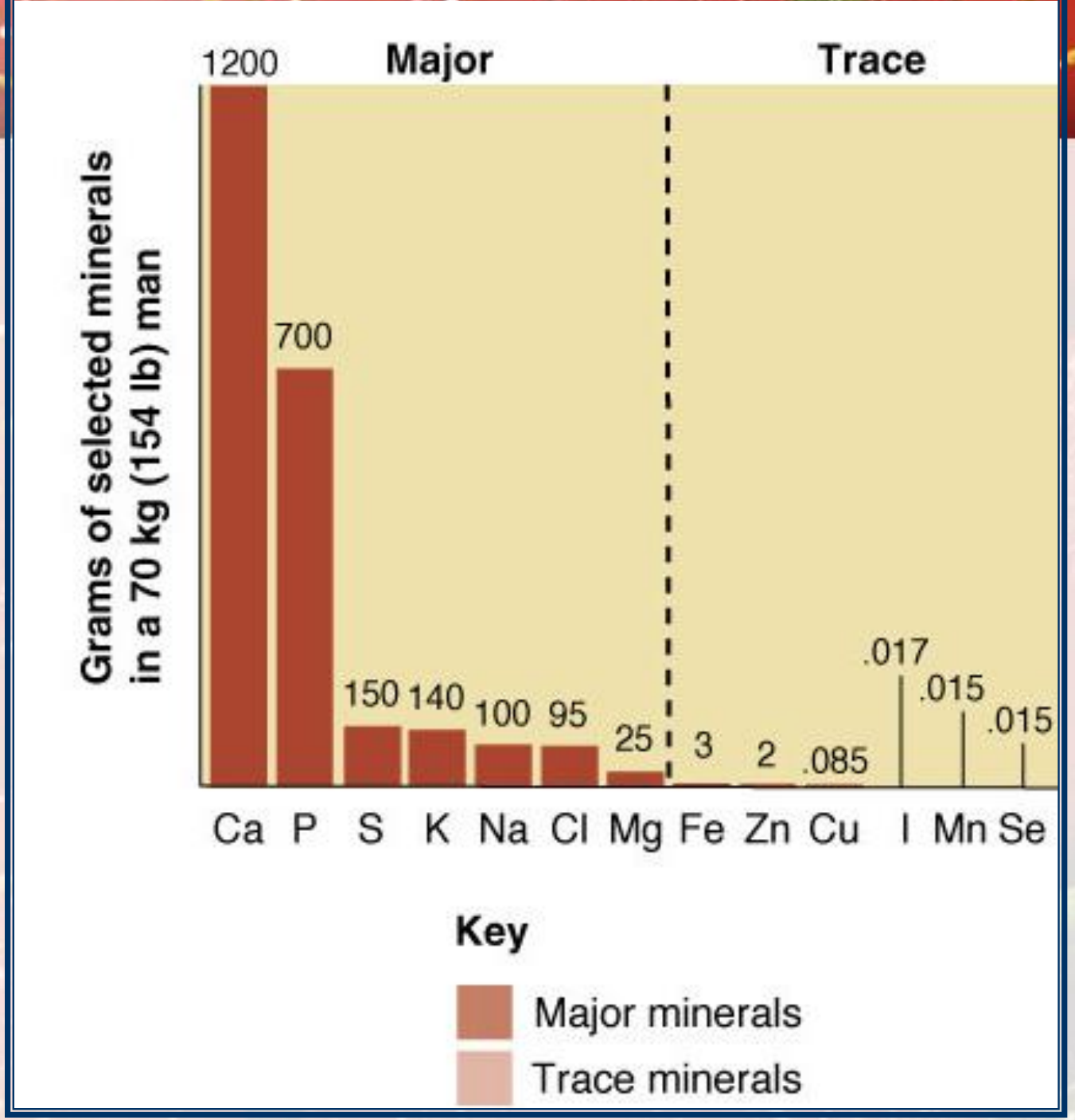
Electrolytes and Water

- The main positively charged ions (cations) are sodium and potassium
- The main negatively charged ions (anions) are chloride and phosphate
- Sodium main cation in extracellular fluid
- Potassium main cation in intracellular fluid
- Na-K pumps: maintain balance of Na and K; all cell membranes have;



Intracellular and extracellular fluid. Extracellular fluids and their dissolved substances (except for proteins) move across capillary membranes easily. ... the fluid portion of the blood) has a higher concentration of proteins than interstitial ... protein, their compositions are roughly the same.

Electrolytes	Extracellular* fluid concentration	Intracellular** fluid concentration
	meq/L	meq/L
Cations		
Sodium (Na^+)	140	13
Potassium (K^+)	5	140
Calcium (Ca^{2+})	5	Minimal
Magnesium (Mg^{2+})	2	7
Total	**151**	**160**
Anions		
Chloride (Cl^-)	104	3
Bicarbonate (HCO_3^-)	24	10
Sulfate (SO_4^{2-})	1	---
Phosphate (HPO_4^{2-})	2	107
Proteins	15	40
Organic anions	5	---
Total	**151**	**160**


Major
Trace
Grams of selected minerals in a 70 kg (154 lb) man
1200
700
150
140
100
95
25
3
2
.085
.017
.015
.015
Ca
P
S
K
Na
Cl
Mg
Fe
Zn
Cu
I
Mn
Se
Key
Major minerals
Trace minerals

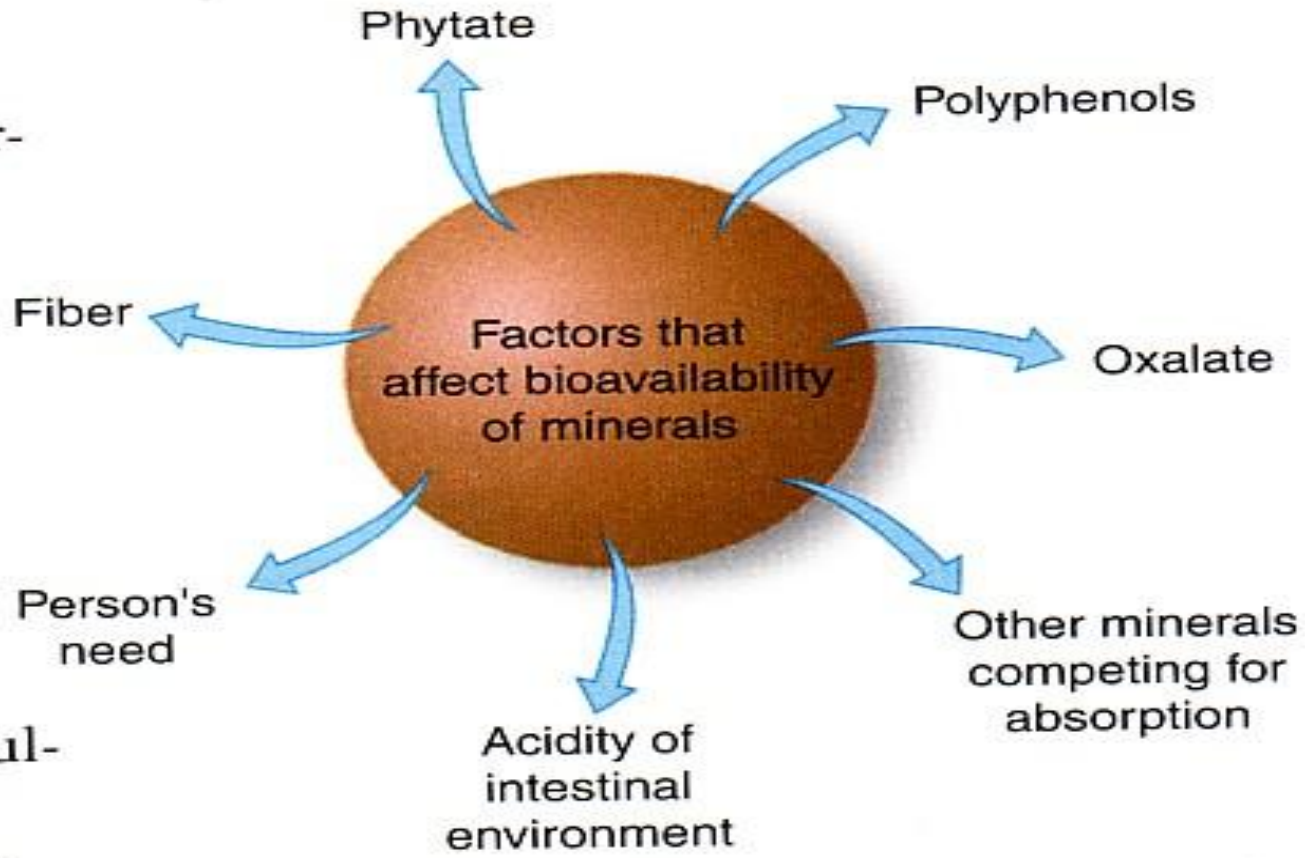


Figure 10.10 **Factors that affect the bioavailability of minerals.** A person's need and the dietary components of a meal can enhance or inhibit the absorption of a mineral.

Minerals

- A naturally occurring , homogeneous, inorganic substance required by humans in amts of 100 mg/day or more
  - -functions
  - -high and low serum levels
  - -absorption
  - -excretion
  - -deficiency
  - -toxicity

Enjoy your food and your good health!

THE END