
In the name of God

vitamin E

Presented by:

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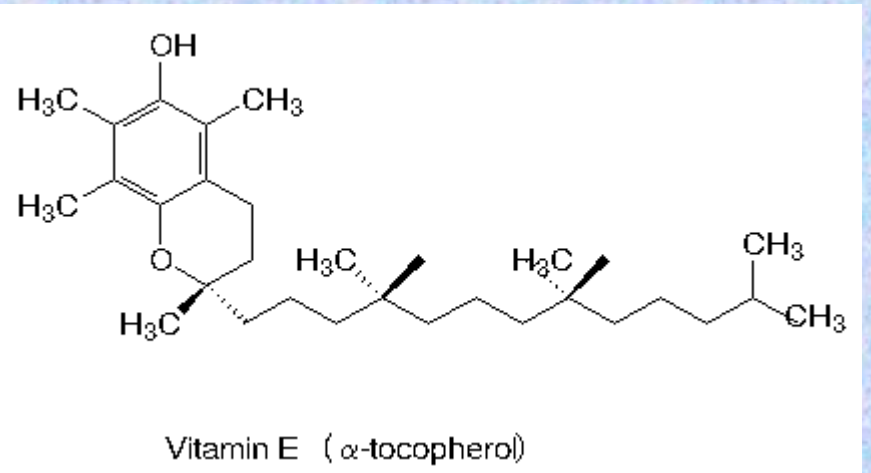


Vitamin E (α-tocopherol)

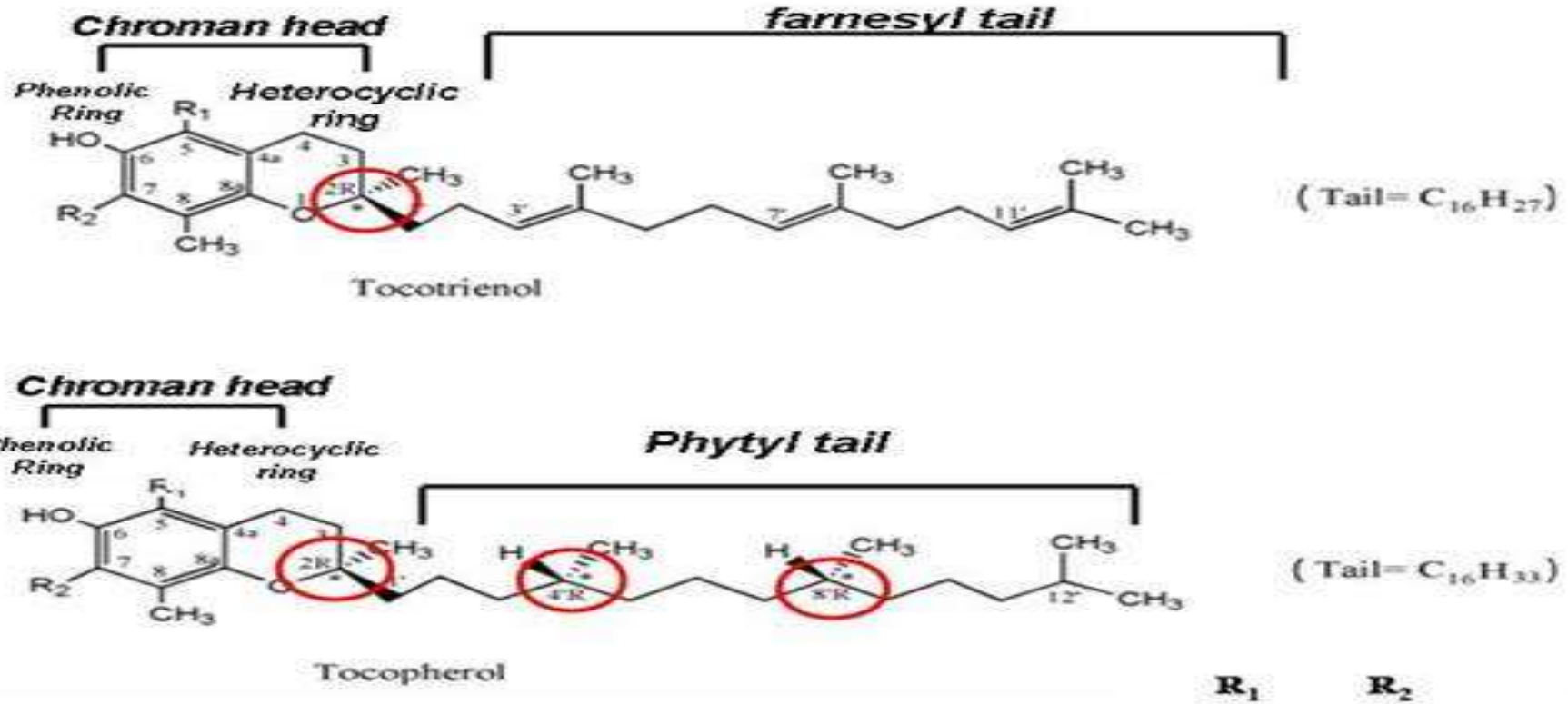
Vitamin E

- Extracted from wheat germ oil
- An important biological antioxidant (scavenger for free radicals and O)
- Protects cell membranes
- Enhances immune response
- Regulates platelet aggregation
- Regulates protein kinase C activation
- An antifirtilization agent
- Soluble in fat solvents but insoluble in aqueous solvents.

Chemistry of vitamin E

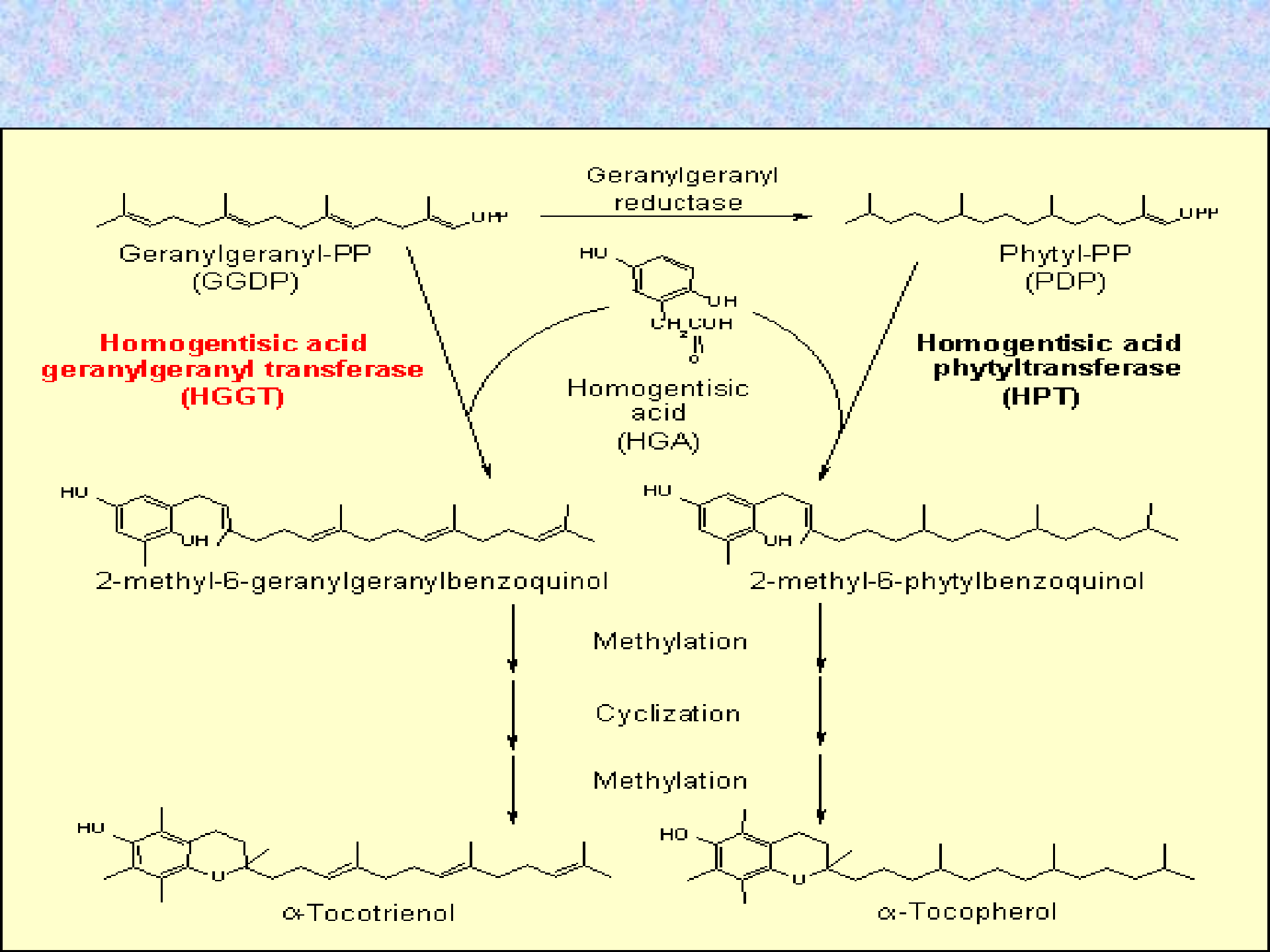
- From tocopherols and tocotrienols (formly α–tocopherol): a chroman nucleus with methyl groups at 2 and 8 position, phytyl tail of isoperonoids at 2 position.
- **Diversity:** α, ß, γ, δ, …(presence or absence of methyl group at 5 and 7 position)
- Have 8 optical isomers (3 asymetric carbon), RRR-form is usual
- Viscous oils at room temperature
- Stable in acid and heat in the absence of oxygen.

Tocopherol and tocotrienol



R_1	R_2	
CH_3	CH_3	α-
CH_3	H	β-
H	CH_3	γ-
H	H	δ-

Structure of Vitamin E Isoforms.


Geranylgeranyl reductase
Geranylgeranyl-PP (GGDP)
Phytyl-PP (PDP)
Homogentisic acid geranylgeranyl transferase (HGGT)
Homogentisic acid phytyltransferase (HPT)
Homogentisic acid (HGA)
2-methyl-6-geranylgeranylbenzoquinol
2-methyl-6-phytylbenzoquinol
Methylation
Cyclization
Methylation
α-Tocotrienol
α-Tocopherol

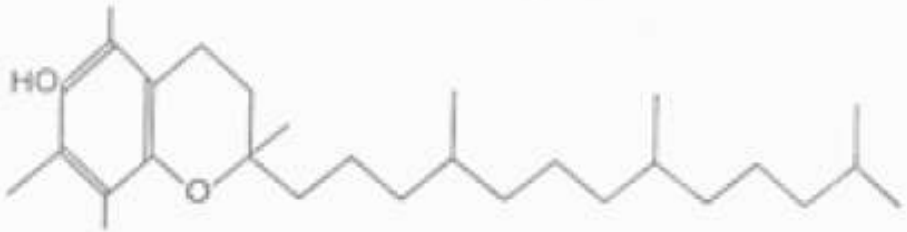
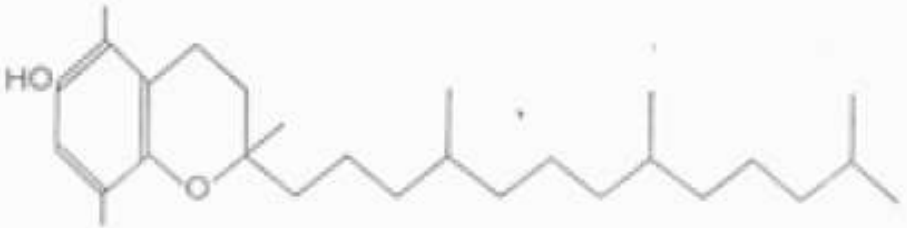
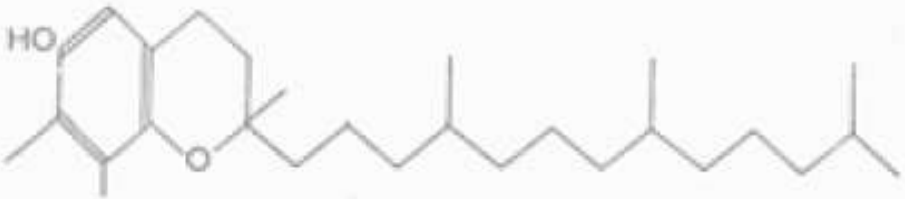
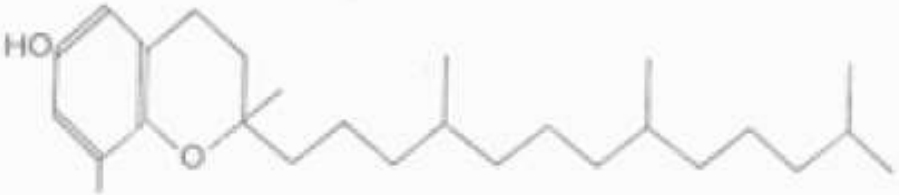
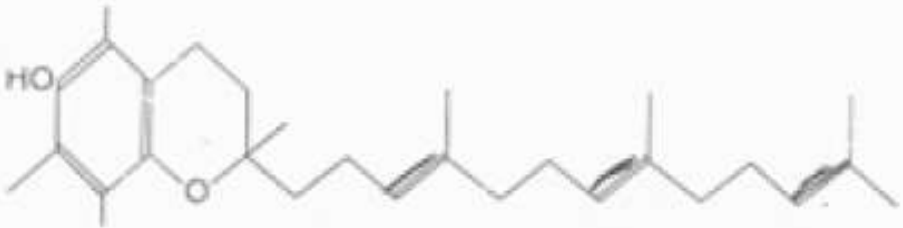
COMMON NAME	STRUCTURE	RELATIVE BIOLOGIC ACTIVITY
Alpha-Tocopherol		1
Beta-Tocopherol		0.4
Gamma-Tocopherol		0.1 - 0.3
Delta-Tocopherol		0.01
Alpha-Tocotrienol		0.3

Fig 2 Naturally occurring vitamin E compounds and their biologic activities relative to RRR-α-tocopherol, which is designated officially as having 1.49 IU/mg

Dietary source

- **Principle source**
- Wheat germ oil
- Sunflower oil
- Grains
- Nuts
- **Little source**
- Meats
- Fruits
- Vegtables

Absorption, Transport, Metabolism and Excretion

- Absorbed nonselectively in the presence of bile in the small intestine.
- Transport in lymphatic system with chylomicron particles to peripheral tissues (mainly adipose tissue).
- α–tocopherol takes up with liver by remnant chylomicron, went to VLDL with α–TTP to further distribution
- Excrete via the bile, in urine as a tocopheronic acid

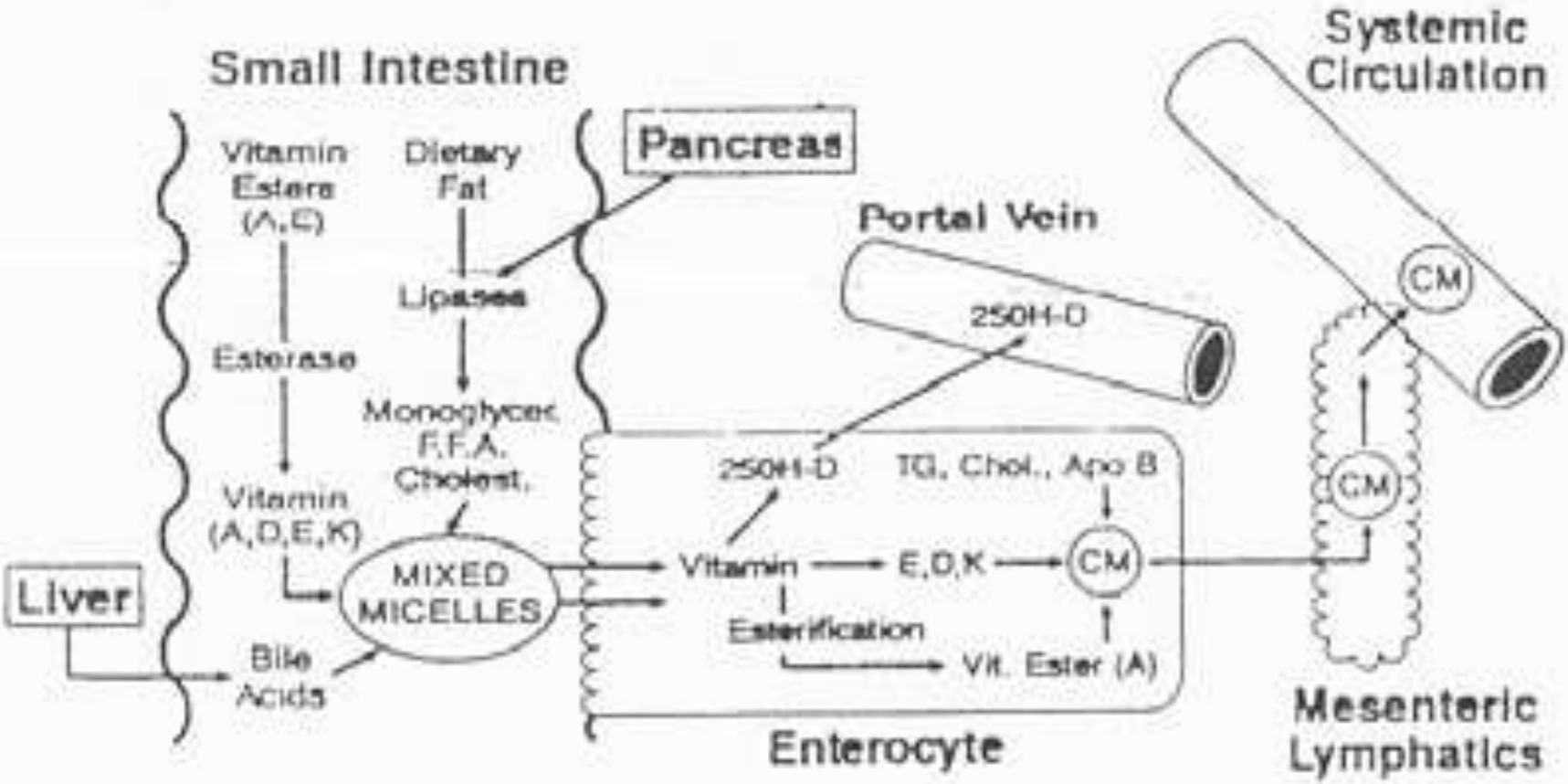


Fig 3 - Intestinal absorption of vitamin E (E) and how it compares with absorption of other fat-soluble vitamins [vitamin A (A), vitamin D (D), and vitamin K (K)]. TG, triacylglycerols; CM, chylomicrons; ApoB, apolipoprotein B.

Function of vitamin E

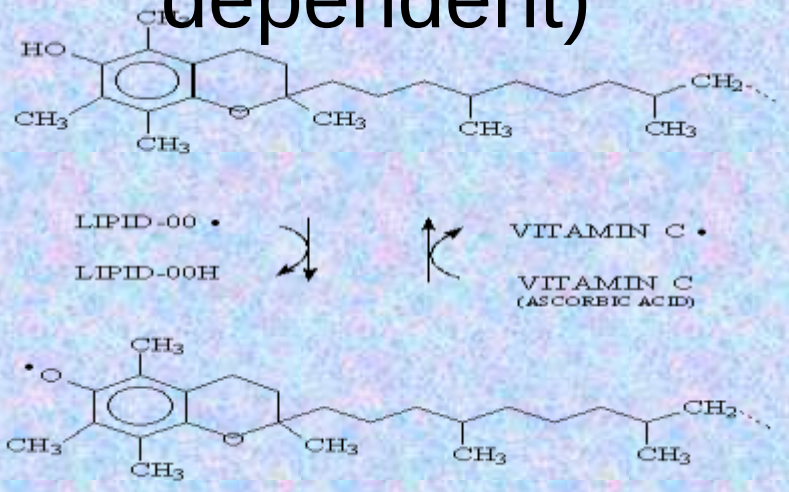
- **Efficacy of Natural-Source *vs* Synthetic Vitamin E**
- Natural-source is a single isomer (d-alpha-tocopherol)
- Synthetic is a mixture of eight isomers
- Natural-source has twice the bioavailability of synthetic

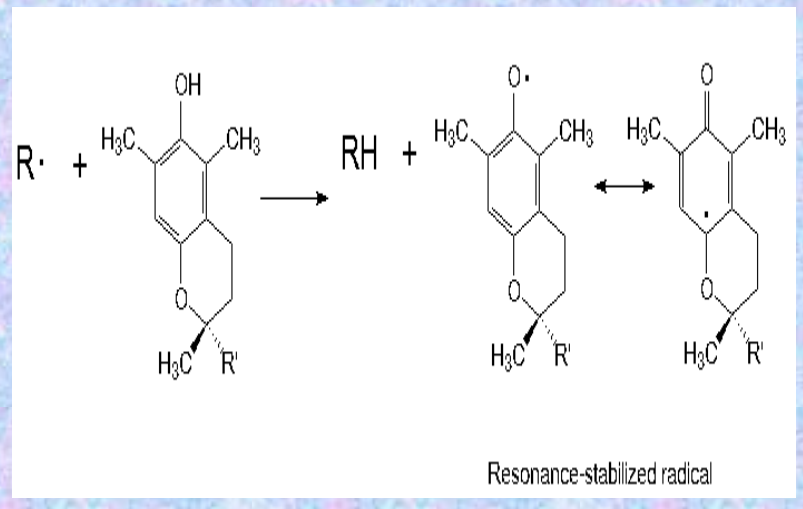
Function of vitamin E

- Necessary for neurological and reproductive function
- Protecting red cell from hemolysis
- Prevention of retinopathy in premature infants.
- Inhibition of chain reaction lipid-proxidation with free radicals

Function of vitamin E

- Transfer electron from free radicals to vitamin C (synergically of E & C effect)
- Reduce chronic disease incidence, cardiovascular and cancer (dose-dependent)





Function of vitamin E

- Inhibition of PKC and 5-lipoxygenase
- Activation of protein phosphatase 2A and diacyle glycerol kinase

Postranslational level

- α-tocopherol inhibit cell proliferation, platelet aggregation and monocyte adhesion
- γ-tocopherol inhibit cycloxygenase

Requirement and reference nutrient intakes

- requirement is related to the PUSF content
- Minimum adult requirement is not certain but no more than 3-4 mg/d.
- Reference interval for plasma and all tissue is 0.5 – 1.2 mg/dl.

Clinical Deficiency States

- Susceptible groups
  - Patients with malabsorption syndromes
  - Premature infants
  - Patients on total **parenteral nutrition (**TPN)
- Characterized by progressive neurological syndrome
  - Gait disturbances
  - Absent or altered reflexes
  - Limb weakness
  - Sensory loss in arms and legs
- Improved neurological function with vitamin E therapy
- Vitamin E is an essential nutrient necessary for the optimal development and maintenance of the integrity and function of the human nervous system and skeletal muscle

Ataxia with vitamin E deficiency

- **Mutations in the *TTPA* gene cause ataxia with vitamin E deficiency.**
  The *TTPA* gene expresses the α-tocopherol transfer protein (αTTP) in the liver and brain.

- **αTTP controls distribution of vitamin E to cells and tissues.**
- **Vitamin E helps cells prevent damage that might be done by free radicals.**

- **As a result of impaired αTTP, vitamin E levels in the blood are greatly reduced and free radicals accumulate within cells.**

- **Nerve cells (neurons) in the brain and spinal cord (central nervous system) are particularly vulnerable to the damaging effects of free radicals.**
- **Nerve cell damage can lead to problems with movement and other features of ataxia with vitamin E deficiency.**

Deficiency of vitamin E

- **Mostly in premature and low birth weight infants:**

  placenta transfer is poor

  adipose tissue is limited (normally stored)

- **Cause of deficiency:**

  Fat malabsoption state such as cystic fibrosis, chronic chlestasis and selenium deficiency.

- **Signs of deficiency:**

  Irritability, edema and hemolytic anemia

Cancer and vitamin E

- An inverse association between vitamin E status and subsequent risk of certain cancers
- Intervention trials have shown mixed results:
  - Reduced cancer incidence and decreased mortality rate from stomach and esophageal cancers in China
  - No decrease in recurring colorectal tumors in U.S.
  - Improvement in precancerous oral lesions in U.S.
  - Decreased incidence and mortality of prostate cancer but not lung cancer in Finland

Coronary Heart Disease and vitamin E

- Increased vitamin E intakes associated with decreased risk of coronary heart disease
- A central role for lipid oxidation in the development and progression of atherosclerosis
- Dose-dependent resistance of LDL to oxidation with vitamin E supplementation
- In prevention trials, vitamin E showed protective effects

Cataracts and vitamin E

- Vitamin E delayed or minimized cataract development in animal models
- by reducing photoperoxidation of lens lipids and stabilizing lens cell membranes

- A relationship between blood vitamin E levels and cataract risk

- Decreased cataract risk associated with vitamin E supplementation

Alzheimer's Disease and vitamin E

- Increased vitamin E intakes or blood levels associated with reduced risk of Alzheimer's disease

- Current practice guidelines recommend vitamin E or selegiline for patients with moderate disease
- Selegiline, also known as L-deprenyl and sold under the brand names Eldepryl and Emsam among others, is a medication which is used in the treatment of Parkinson's disease and major depressive disorder

- Vitamin E may be preferred from a safety standpoint

Toxicity of vitamin E

- In excess vitamin E intake
- Up to 1000mg/day is safe if be without hemorrhagic toxicity.
- Up to 3000mg/day is safe, side effects is gastrointestinal symptoms and creatinuria.
- Intakes more than 400 mg/day in long term cause increased mortality.

Laboratory assessment of status

- Protection of erythrocyte hemolysis
- Inhibition of lipid proxidation products
- **Measurement:**
- In tissue or plasma have done by photometric or flourometric
- Chromatographic methods (TLC & GLC)
- HPLC is presently choice method

Reference intervals

- For serum or plasma heparinyzed: 0.1 – 0.5 mg/dl
- Premature neonets: 0.3 – 0.9 mg/dl
- Children (13 – 19 years): 0.6 – 1 mg/dl
- Adult: 0.5 – 1.8 mg/dl

The End