VITAMIN E

HISTORY

- Existence – first suggested by Evans & Bishop in 1923
  - Reported: A dietary factor ‘X’ was needed for normal rat reproduction
- Active Vitamin E was isolated from wheat germ oil in 1936
- Evans demonstrated – Vitamin E belongs to ‘Tocopherol’ family of compounds
Vitamin E – ‘Anti-infertility Vitamin’
- Initial studies of Vitamin E induced deficiency → Infertility
Evans isolated several tocopherols and found ‘α - tocopherol’ was most active
Greek –
- Tokos : Child birth
- Pheros : To bear
- ol : Alcohol
Nomenclature

- Naturally occurring tocopherols of dietary significance includes:
  - α - tocopherol – 5,7,8 trimethyl tocol
  - β - tocopherol – 5,8 dimethyl tocol
  - γ - tocopherol – 7,8 dimethyl tocol
  - δ - tocopherol – 8 methyl tocol

- Differ in number & position of methyl groups
- α - tocopherol – widest natural distribution & greatest biological activity

- Another group of similar compounds ‘Tocotrienols’ – also occurs as α, β, γ, δ forms – has 50% of biological activity as compared to α - tocopherol
Chemistry

✦ All compounds with Vitamin E activity contains:

춘 6 – hydroxychromane (tocol) ring
춘 Substituted with an isoprenoid side chain
춘 Structure was elucidated by Paul Karrer – awarded Nobel Prize in 1937
춘 Presence of phenolic – OH group on the 6ᵉ carbon of the chromane ring is the most important group for its ‘Antioxidant’ property
ALPHA TOCOPHEROL
Vitamin E is absorbed along with other fats in the presence of bile salts in small intestine.

It is transported as chylomicrons

Absorbed Vitamin E is transported to liver

Liver: it gets incorporated into α-lipoproteins and carried in blood

It is stored in adipose tissue, liver & muscle.

During catabolism, chromane ring & side chain are oxidised, conjugated with glucuronic acid & excreted in bile
Sources

- Rich Sources: Vegetable oils
  - Wheat Germ Oil
  - Sunflower Oil
  - Corn Oil
  - Cotton Seed Oil
  - Palm oil
  - Margarine

- Fair Sources: soyabean, cabbage, yeast, lettuce, apple seeds & peanuts

- Poor Source: Fish liver oils
Recommended Dietary Allowance

- Children: 10 to 15 mg/day
- Adults: 8 to 10 mg/day
- Pregnancy & Lactation: 10 to 12 mg/day
- Elderly: 10 to 12 mg/day

- Requirements increase with higher intake of PUFA
- 15 mg of Vitamin E = 33 I.U.
- Vitamin E content of food decreases during food processing & freezing
- Pharmacological dose: 200 – 400 I.U.
Functions

1. Antioxidant – Removal of ‘Free radicals’
   - First line of defence against peroxidation of polyunsaturated fatty acids in cellular & subcellular membrane phospholipids
   - Antioxidant action is effective at high oxygen concentrations
   - Vitamin E tends to be concentrated in those lipid structures that are exposed to high $O_2$ partial pressures
   - Retina, Erythrocyte membrane, membranes of respiratory tree
Antioxidant function (Contd)

In cells, phospholipids of mitochondria, endoplasmic reticulum & plasma membranes possess affinity for Vitamin E, thus concentrates at these sites.

Mechanism of action:
- Tocopherols breaks the free-radical chain reactions.
- They possess the ability to transfer a ‘phenolic hydrogen’ to a peroxyl free radical of a peroxidised polyunsaturated fatty acid.
Mechanism of action (Contd)

- This leads to formation of ‘phenoxy free-radical’ which can react in two ways –
  - Reacts with Vitamin C & Glutathione to regenerate tocopherol
  - Further react with a ‘peroxyl free-radical’ → oxidation of chromane ring & side chain → conjugation of oxidised product with glucuronic acid → excretion in bile

- Tocopherol is not recycled after carrying out its function
- It must be totally replaced by diet or from stores to continue its action in the cells
Functions (Contd)

2. Synergistic & Sparing action of Selenium

- Selenium is an integral component of ‘Glutatione peroxidase’
- Provides a second line of defense against free-radical damage to membranes
- Thus Vitamin E & Selenium re-inforce each other actions against lipid peroxidation
- Selenium is found to decrease the requirement of Vitamin E & vice-versa
- Vitamin E reduces Selenium requirements by preventing its loss & maintaining it in active form
Functions (Contd)

3. Closely associated with reproductive functions by maintaining germinal epithelium of gonads & prevents sterility

4. It increases the activity of enzyme ‘ ALA-synthase’ & ‘ALA – dehydratase’, thus increasing ‘Heme’ synthesis

5. It stabilises ‘Coenzyme Q’ in electron transport chain, thus helping in cellular respiration

6. Vitamin E helps in the storage of Creatine in skeletal muscles

7. It is involved in synthesis of nucleic acids

8. Vitamin E is also involved in the absorption of aminoacids from the intestine
**Deficiency Manifestations**

- Vitamin E deficiency is rare
- When occurs, it results in –
  - Hemolytic anaemia
    - ↑ susceptibility to hemolysis due to peroxidation of RBC membrane
  - Muscular dystrophy
    - ↑ oxidation of PUFA in muscle cells → damage to lysosomes → breakdown of muscle proteins
- Manifestations: Muscle weakness, pain in the muscles, easy fatigability, syncope
Deficiency Manifestations (Contd)

☆ Blood picture shows macrocytic anaemia
☆ Serum indirect bilirubin is increased
☆ Increased excretion of creatinine in urine
☆ Treatment & Prevention - Administration of Vitamin E orally & diet rich in Vitamin E
Hypervitaminosis E

- Least toxic of all the fat soluble vitamins
- Observed at doses above 1000 I.U. per day
- Vitamin E has a mild anti-coagulant action in large doses
- Main manifestation is ‘Hemorrhage’
- Patients with bleeding disorders should take the Vitamin E with caution
Vitamin E – Other Uses

😊 Therapeutic uses
- Nocturnal muscle cramp
- Intermittent claudication
- Atherosclerosis & Myocardial infarction
- Fibrocystic breast disease
- Cancer
- Alzheimer’s disease