VITAMIN C

HISTORY

- ‘Scurvy’ – known to mankind for centuries
  - Description of the disease was found in Ebers papyrus written in 1500 B.C.
- Socrates described the disease – symptom complex of pain in the legs, gangrene of gums & loss of teeth
- Disease had catastrophic effects amongst explorers
  - Vasco-da-gama in 1498 lost 2/3rd of his sailors due to scurvy during famous voyage to India
  - Jacques Cartier in 1536 lost more than 50% of sailors during voyages to discover eastern parts of Canada
Systematic study of the disease scurvy was done by ‘James Lind’, a surgeon of English Navy. He published his work ‘Treatise on Scurvy’ in 1753.

From 1795 onwards, his observations led to compulsory addition of lime or lemon juice to the foods of all sailors in British Royal Navy. British sailors were nicknamed as ‘Limeys’.
HISTORY (Contd)

- 1907: Holst & Trochlich produced scurvy in guineapigs
- 1928: Zilva & his associates showed the reducing power of antiscorbutic factor in lemon juice
- 1930: Reducing substance was isolated & named ‘Hexuronic acid’ by Albert Szent-Gyorgi - Nobel Prize in 1937
- 1933: Haworth established the molecular structure & synthesised it, renamed it as ‘Ascorbic acid’ - Nobel Prize in 1937
CHEMISTRY

- Empirical formula: C₆H₈O₆

- Vitamin C is γ-lactone of a C6 acid (hexose) having double bond between C₂ & C₃

- Physical characteristics:
  - Naturally occurring form is L-ascorbic acid
  - White, crystalline, odourless, sour & highly water soluble substance
  - Destroyed by heat & by aerobic oxidation, particularly in alkaline solutions and cooking
  - Powerful reducing agent
  - Stable below pH 6.8 at room temperature
CHEMISTRY (Contd)

Chemical characteristics:
- Oxidation of ascorbic acid yields ‘dehydroascorbic acid’
- Dehydroascorbic acid, when further oxidised yields ‘Oxalic acid’ through the formation of diketo – L – Gulonic acid

✓ Only L-ascorbic acid & dehydroascorbic acid have antiscorbutic activity
✓ D-ascorbic acid has no activity
SOURCES

- Rich sources: Citrus fruits like Amla, lemon, orange, pineapple, guava
- Good sources: Green leafy vegetables
- Fair sources: Raw milk, meat & raw fish
- Poor sources: Fruits like apple, banana, grapes & Boiled or sterilised milk
RECOMMENDED DIETARY ALLOWANCES

- Infants & Children: 40 to 60 mg / day
- Adults: 60 to 80 mg / day
- Pregnancy & Lactation: 100 to 150 mg / day
- 50ml Orange juice = 75 mg of Vitamin C
- Smoking, alcohol intake, use of aspirin & oral contraceptives lowers serum ascorbic acid levels
Non-primates can synthesize ascorbic acid in liver & adrenal cortex from glucuronic acid.
- Humans cannot synthesize due to lack of enzymes & are completely dependent on dietary sources.

Ascorbic acid is readily absorbed from the small intestines, peritoneum & subcutaneous tissues.

It passes through the portal vein into general circulation & is distributed throughout the body.
SYNTHESIS, ABSORPTION, STORAGE & EXCRETION (Contd)

- Normal Serum ascorbic acid level:
  0.6 to 1.5 mg/dl
  - RBCs contains 1 and 1/2 times > that of plasma
  - WBCs & Platelets contains 20 to 40 times > that of plasma

- Vitamin C readily crosses placenta & is supplied to the foetus from maternal circulation

- Adrenal cortex & medulla, pituitary, liver and corpus luteum stores Vitamin C up to an optimal saturation levels

- Excess Vitamin C is excreted in urine
FUNCTIONS

1. Oxidation – reduction reactions
   - L-ascorbic acid acts as an electron donor
   - L-ascorbate donates electrons directly to ‘cytochrome c’
   - It also transports electrons from substances like NADH, phenolic aminoacids, glutathione & flavoproteins
FUNCTIONS (Contd)

2. Hydroxylation reactions

(a) Post-translational hydroxylation of proline & lysine forming hydroxyproline & hydroxylysine respectively

Converts protocollagen to ‘mature collagen fibrils’ in presence of Fe$^{2+}$ & O$_2$

Catalysed by enzymes ‘prolyl-4-hydroxylase’ & ‘lysyl-5-hydroxylase’ respectively

(b) Hydroxylation of dopamine to nor-epinephrine during catecholamine synthesis

Occurs in adrenergic neurons & chromaffin cells of adrenal medulla

Catalysed by copper containing enzyme ‘dopamine-β-hydroxylase’
(c) Hydroxylation of \( \gamma \)-butyrobetaine in the pathway for formation of carnitine from lysine in the liver

(d) Hydroxylation of tryptophan to form 5-hydroxy tryptophan, for the biosynthesis of serotonin

(e) Hydroxylation of steroids in adrenal cortex

(f) During hydroxylation of p-hydroxy phenyl pyruvate in ‘Tyrosine’ metabolism, Vitamin C is required as co-factor for the enzyme ‘p-hydroxy phenyl pyruvate hydroxylase’
3. Absorption & utilisation of Iron

- Vitamin C reduces ferric ions to ferrous forms → formation of water-soluble iron-ascorbate chelate → its ↑ absorption

- Similarly Vitamin C promotes iron utilisation by reducing ferric ions of tissue ferritin to ferrous forms → facilitating its release into plasma for utilisation
3. Deposition & maintenance of mesenchymal tissues

Vitamin C is involved in deposition & maintenance of intracellular substances in mesenchymal tissues such as
- Osteoid
- Dentine
- Intercellular cement substances in capillaries

4. Vitamin C regulates the conversion of folic acid into folinic acid (Citrovorum factor)
- Maintains ‘Folic acid reductase’ enzyme in the active form, facilitating the formation of ‘active tetrahydrofolate’
5. Vitamin C also plays an important part in the reconversion of methhemoglobin to hemoglobin

6. Vitamin C stimulates ‘7-α-hydroxylase’ enzyme, thus increasing the synthesis of bile acids from cholesterol

7. Formation of hormones
   - Vitamin C is involved in amidation of peptidylglycine of peptide hormones to form Vasopressin, Oxytocin, Gastrin, Cholecystokinin & Calcitonin
8. Sparing effect of other vitamins
   - Ascorbic acid is a strong antioxidant
   - It spares Vitamin A, Vitamin E and some B-complex vitamins from oxidation

9. Vitamin C inhibits hyaluronidase-hyaluronic acid system, thus preserving the architecture of soft tissues

10. Immunological function
    - Vitamin C enhances synthesis of immunoglobulins & also increases the phagocytic action of leucocytes
Deficiency of Vitamin C results in ‘Scurvy’

Scurvy in infants – ‘Infantile scurvy’

Scurvy is characterised by –
- Defective formation of collagen
- Defective maintenance of intercellular substances of connective tissues, osteoid of bones, dentine of teeth & capillaries

Demineralisation, weakness of bones & teeth, increased fragility of blood vessels, bleeding & delay in wound healing

Anaemia also results due to ↓ absorption & utilisation of iron & ↓ formation of folinic acid
Deficiency Manifestations (Contd)

- Signs & Symptoms includes
  - Weakness, easy fatigability
  - Pain in the bones, joints & muscles
  - Hemorrhage & swelling of joints
  - Pathological fractures of bones
  - Spongy & bleeding gums
  - Loosening of teeth
  - Anaemia
  - Susceptibility to infections
  - Poor wound healing
Deficiency Manifestations (Contd)

- Deficiency of Vitamin C can be detected by measurement of Ascorbic acid level in WBCs
- Preirheral blood smear – Macrocytic hypochromic anaemia
- Urine ascorbic acid saturation test
- Tourniquet test

Treatment & Prevention
- Administration of Vitamin C tablets orally
- Regular dietary intake of citrous fruits & foods rich in Vitamin C
**Therapeutic Uses**

- Vitamin C is used as an adjuvant in bacterial infections
- Vitamin C also has beneficial effects in the treatment of tuberculosis, burns, peptic ulcers & healing of fractures
- Vitamin C has been implicated to prevent common cold
- Vitamin C is thought to help in prevention of cancer & development of cataract by its anti-oxidant properties