Vitamins

Definition

Vitamins are essential organic micronutrients that are required in diet in small amounts (from few micrograms to few milligrams) for normal metabolism, development, function and optimal health of body. They perform various biochemical functions.

Classification

Vitamins are classified into two groups on the basis of water solubility.

A) Water soluble vitamins

1. Vitamin C (L-Ascorbic acid)

2. Vitamin B complex

   Vitamin B_1 (Thiamine)

   B_2 (Riboflavin)

   B_3 (Niacin or Nicotinic acid)

   B_5 (Pantothenic acid)

   B_6 (Pyridoxine)

   B_7 (Biotin)

   B_9 (Folic acid)

   B_{12} (Cobalamine)

B) Fat soluble vitamins

1. Vitamin A (Retinal or Retinol or Retinoic acid)

2. Vitamin D (Ergocalciferol or Cholecalciferol)

3. Vitamin E (Tocopherol)

4. Vitamin K (Phylloquinone or Menaquinone or Menadione)

Vitamin – C (L – Ascorbic acid)

Food Sources

Indian Gooseberry (Malai nellikai or Amla), citrus fruits, tomato, guava, pineapple are the richest sources.

Fresh green leafy vegetables, mango, strawberry, banana etc are other sources.

Recommended Daily Allowance (RDA)

Adults – 75 mg/day

Children – 45 mg/day

Pregnancy and Lactation – 100 mg/day

Chemistry

- Ascorbic acid resembles hexoses in structure and is identified as enediol – lactone of sugar acid.

- It is a white crystalline substance with sour taste.

- Only the L – isomer (L-ascorbic acid) has vitamin activity.

- L-ascorbic acid undergoes oxidation to form dehydro-L-ascorbic acid which also possess equal vitamin activity.

- L-ascorbic acid is easily destroyed by heat, oxygen, alkali and storage.

- During cooking and storage, L-ascorbic acid is oxidized to dehydro-L-ascorbic acid. This dehydro-L-ascorbic acid undergoes hydration to form diketo-L-gulonic acid which is biologically inactive.

Metabolism

Biosynthesis

- L-ascorbic acid is synthesized from glucose through glucuronic acid pathway in most animals but not in human beings.

- The enzyme **L-gulonolactone oxidase**, which catalyses the conversion of L-gulonolactone to L-ascorbic acid, is absent in glucuronic acid pathway of humans.

- So humans have to obtain L-ascorbic acid only from exogenous sources like food and drugs.

Absorption

L-ascorbic acid is readily absorbed in the small intestine.

Normal Plasma Concentration

0.5 to 1.5 mg/dL.

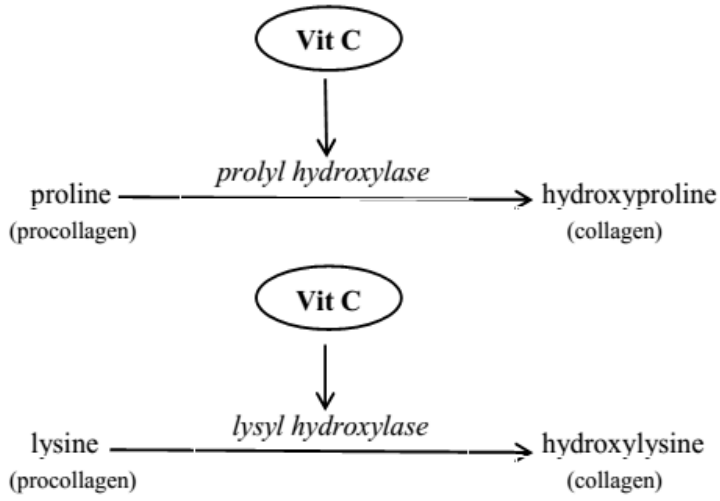
Excretion

Through urine.

Functions of L-ascorbic acid

1. It is involved in the conversion of procollagen to matured collagen.

- It serves as co-enzyme in the enzymatic hydroxylation of proline and lysine residues of procollagen to hydroxyproline and hydroxylysine. Hydroxyproline and hydroxylysine are constituents of matured collagen.

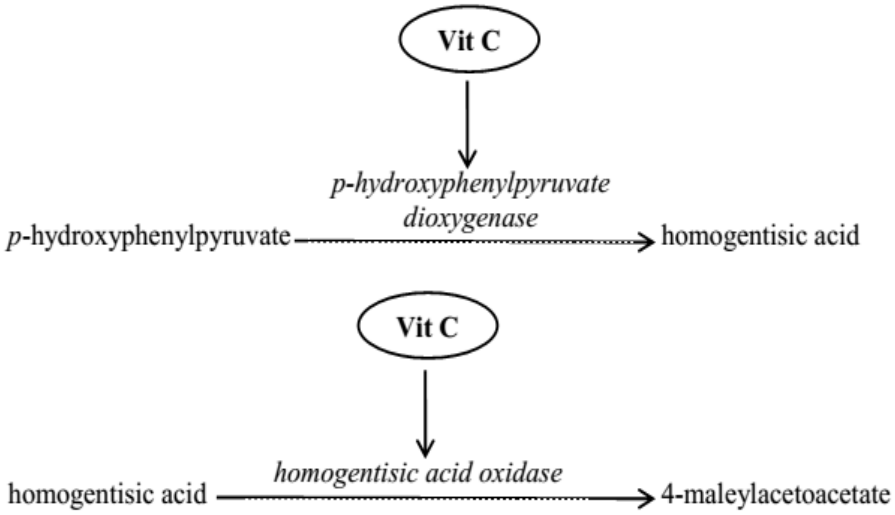


2. Vitamin C enhances the intestinal absorption of iron by reducing ferric form (Fe^{3+}) to ferrous (Fe^{2+}) form. It also helps in iron storage by incorporating the mineral in ferritin.

3. Ascorbic acid serves as co-enzyme in the synthesis of corticosteroid hormones during periods of stress. In human body, adrenal cortex has the highest amount of vitamin C.

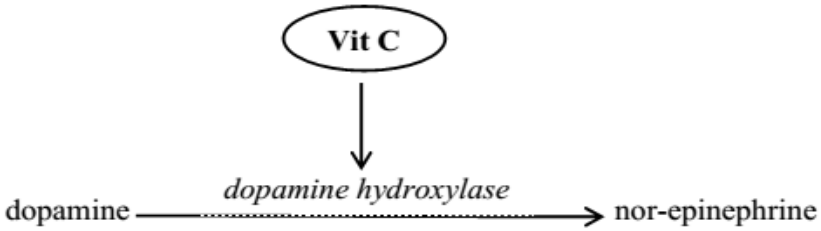
4. Ascorbic acid maintains tetrahydrofolate (THF), co-enzyme form of folic acid, in its reduced form.

5. Ascorbic acid is required as co-enzyme in two reactions of tyrosine metabolism.



6. Ascorbic acid is required in the hydroxylation of tryptophan to 5-hydroxytryptophan by tryptophan hydroxylase in serotonin-melatonin pathway.

7. It is involved in catecholamine synthesis.



8. Ascorbic acid serves as antioxidant by inactivating oxidants (free radicals) which cause aging and diseases like cancer, cataract etc.

9. During bile acid formation, ascorbic acid serves as co-enzyme of 7α hydroxylase which converts cholesterol to 7α hydroxycholesterol.

10. Vitamin C serves as coenzyme of prolylhydroxylase in formation of osteocalcin (calcium binding protein in bone).

11. Ascorbic acid enhances the formation of antibodies and helps in synthesis of carnitine and converts methemoglobin to hemoglobin.

Deficiency Manifestations

- Gross deficiency of vitamin C causes **scurvy**.

- Scurvy in humans is characterized by spongy, swollen, painful and bleeding gum, loosening of teeth, poor teeth and bone formation, scorbutic anemia, functional insufficiency of adrenal cortex and decreased immunocompetence.

- Collagen is required for production of connective tissue. Impaired collagen formation due to vitamin C deficiency may delay wound healing.

- Collagenous organic matrix of dentine is poorly laid down resulting in poor tooth development.

- Due to impaired collagen formation, ground substance of blood vessels is poorly laid down resulting in fragile blood vessels. Petechial hemorrhage may result.

- Hypercholesterolemia may occur due to decreased conversion of cholesterol into bile acids.

- Anemia occurs due to repeated hemorrhages and impaired absorption of iron.

Treatment

Consumption of ascorbic acid supplements orally or eating foods or drinking juices that are rich in ascorbic acid. In case of severe deficiency, injection of vitamin C as drug might be useful.

Hypervitaminosis C

- Oxalate is the major metabolic end product of ascorbic acid metabolism and is slightly soluble in water.

- In hypervitaminosis C, large amount of oxalate crystals are formed and get passed in urine. These oxalate crystals in large amount formed due to consumption of ascorbic acid in large doses may precipitate to form stone in kidney.

- Excess consumption of ascorbic acid may worsen iron storage disease due to more absorption of iron from intestine.

Vitamin D (Calciferol)

Food Sources

- Vitamin D_2 (ergocalciferol) is present in foods of plant sources like mushroom and yeast.

- Vitamin D_3 (cholecalciferol) is present in foods of animal sources like fish liver oil, fish, liver, kidney, egg yolk, milk products etc.

- However, endogenous synthesis of vitamin D_3 is the major source of vitamin D in our body.

Recommended Daily Allowance (RDA)

10 microgram/day

Chemistry

- It is a steroid made of cyclopentanoperhydrophenanthrene ring (cholesterol structure).

- It exists in two biological forms namely

Vitamin D_2 (ergocalciferol) – derived from precursor ergosterol in plants.

Vitamin D_3 (cholecalciferol) – derived from precursor 7-dehydrocholesterol in animals.

Metabolism

Biosynthesis

- In humans, cholecalciferol is synthesized from 7-dehydrocholesterol (an intermediate in the pathway of cholesterol biosynthesis) in skin due to UV irradiation from sunlight.

- In plants, ergocalciferol is derived from UV irradiation of ergosterol.

Absorption

- Cholecalciferol is readily absorbed in small intestine in presence of bile salts.

- Ergocalciferol is poorly absorbed.

Normal plasma concentration

Calcidiol – 1.75 to 7.50 microgram/dL.

Excretion

Excretion of vitamin D and its metabolites occur in feces with the aid of bile salts.

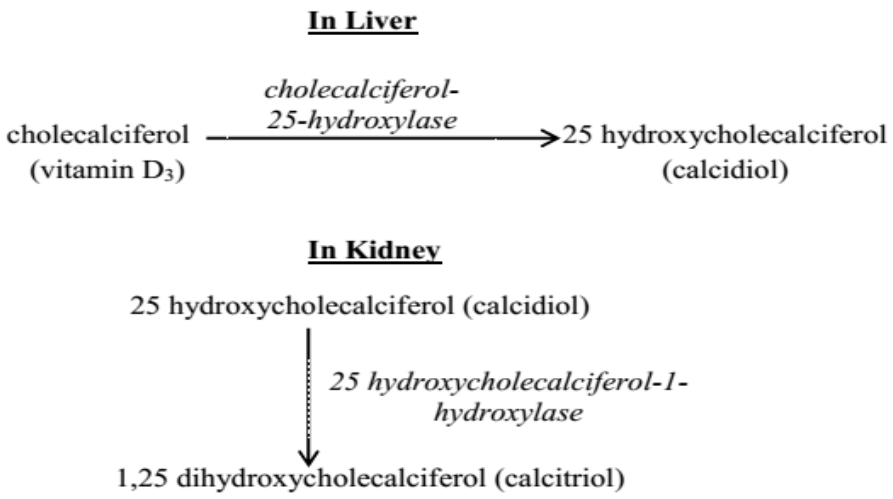
Formation of calcitriol

- In liver, cholecalciferol is hydroxylated to 25 hydroxycholecalciferol (calcidiol) by the hepatic enzyme cholecalciferol-25-hydroxylase.

- Calcidiol is the major storage form of vitamin D in the liver and is the predominant form of vitamin D in blood.

- Calcidiol binds to specific vitamin D binding plasma protein and is transported to kidney.

- In kidney, calcidiol is hydroxylated to 1,25 dihydroxycholecalciferol (calcitriol) by the renal enzyme 25 hydroxycholecalciferol-1-hydroxylase.



- Calcitriol is directly released in blood and acts like a hormone on distant target organs like intestine, bone and kidney.

- Low level of calcium or phosphorus in plasma enhances the formation of calcitriol by stimulating the activity of the renal enzyme 25 hydroxycholecalciferol-1-hydroxylase.

Functions

- Calcitriol, the physiologically active form of vitamin D, acts like steroid hormone and regulates the plasma level of calcium and phosphorus.

- This calcitriol binds to its intracellular receptor in the target cells. Then this complex binds to vitamin D response elements on DNA and modulates the expression of more than 500 genes.

i) Action on intestine

- In intestinal mucosal cells, calcitriol enhances the synthesis of calbindin (calcium binding protein).

- Calbindin enhances the intestinal absorption of calcium.

ii) Action on bone

- Calcitriol promotes the mineralization of bones by enhancing deposition of calcium and phosphorus.

- Stimulates the synthesis of osteocalcin (calcium binding protein) and alkaline phosphatase in bones which increase the local concentration of ionic calcium and phosphorus required for the mineralization of bones.

- During hypocalcemia and hypophosphatemia, calcitriol along with parathyroid hormone stimulates the mobilization of calcium and phosphorus from bones (bone resorption) to raise the plasma level of calcium and phosphorus.

iii) Action on kidney

- Calcitriol acts on kidney and stimulates the reabsorption of calcium and phosphorus at distant renal tubules.

Deficiency Manifestations

Deficiency may occur due to inadequate intake, inadequate absorption or inadequate exposure to sunlight.

Rickets (in growing children)

- Low plasma levels of calcium and phosphorus observed with an increase in the activity of serum alkaline phosphatase.

- Is characterized by undermineralization of growing bones leading to soft and pliable bones, bow legs, pigeon chest and knock knees.

- Severe rickets causes delayed teeth formation and eruption.

Osteomalacia (in adults)

- Characterised by demineralisation of preformed bones making the patient weak and susceptible to fractures.

- Generally occurs in women after multiple pregnancies and lactating mothers.

Renal Osteodystrophy

- In chronic renal failure, calcidiol is not converted to calcitriol in kidney.

- Stimulation of parathyroid hormone secretion occurs. This leads to bone resorption for maintenance of normal plasma calcium level.

- Excessive bone resorption (bone loss) and metastatic calcification occurs essentially in renal tissues.

Diagnostic test to detect vitamin D deficiency

Low level of serum calcidiol indicates vitamin D deficiency.

Hypervitaminosis D

- Prolonged intake of large doses of vitamin D in pharmacological form may cause hypervitaminosis D.

- Hypercalcemia results due to increased bone resorption and intestinal absorption.

- The symptoms are nausea, vomiting, thirst, appetite loss, polydipsia, polyuria, constipation and muscular weakness.

- Calcification of arteries, bronchi, muscles, kidneys etc may occur. Calcium oxalate stones may be formed in kidneys.

Vitamin A

Food Sources

- Present as retinol or retinyl ester only in foods of animal origin.

- In plants, vitamin A exists only in provitamin form called carotenoids.

- Liver, kidney, meat, milk and milk products, fish, egg yolk, green leafy vegetables and fruits such as pumpkin, tomatoes, mango, papaya, carrot etc.

Recommended Daily Allowance (RDA)

Adult Male – 1000 microgram/day

Adult Female – 800 microgram/day

β – carotene – 2000 milligram/day

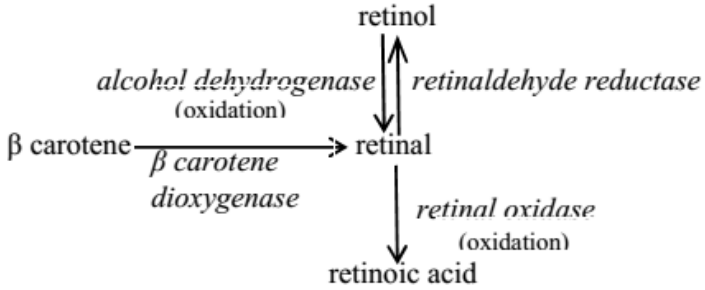
Chemistry

- It is a 20 carbon polyisoprenoid compound containing a β – ionone ring.

- It exists in three different forms (collectively known as retinoids) in animal tissues namely retinol, retinal (retinaldehyde) and retinoic acid.

- Retinol, retinal and retinoic acid contain β – ionone ring with a side chain to which alcohol, aldehyde and carboxyl group are attached respectively.

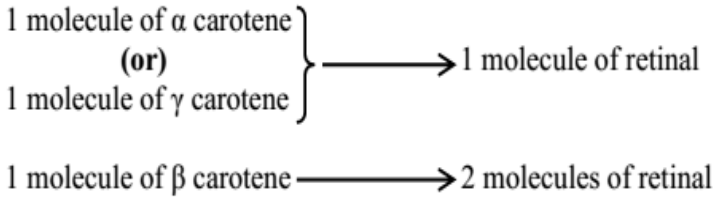
- Three forms of vitamin A are physiologically active and interconvertible.



- Most plants contain pigments called carotenes (provitamin A).

- Carotenes are oxidatively cleaved in intestinal mucosa cells by carotene dioxygenase yielding retinal.

- Three forms of carotene are α, β and γ carotenes (collectively called as carotenoids).



Metabolism

Biosynthesis

- Cannot be synthesized by animals – Formed by oxidative cleavage of carotenes.

Absorption

- Dietary retinyl esters are hydrolysed by esterase in intestine yielding retinol and free fatty acids.

- Retinol, derived from retinyl esters, is then absorbed in intestinal mucosal cells with the aid of bile salts.

- It is transported to liver by chylomicrons and stored as retinol palmitate.

- Vitamin A from liver is transported to peripheral tissues by the retinol binding protein (RBP).

Normal Plasma Concentration

- 30 to 60 microgram/100 mL

- 100 to 300 microgram/100 mL

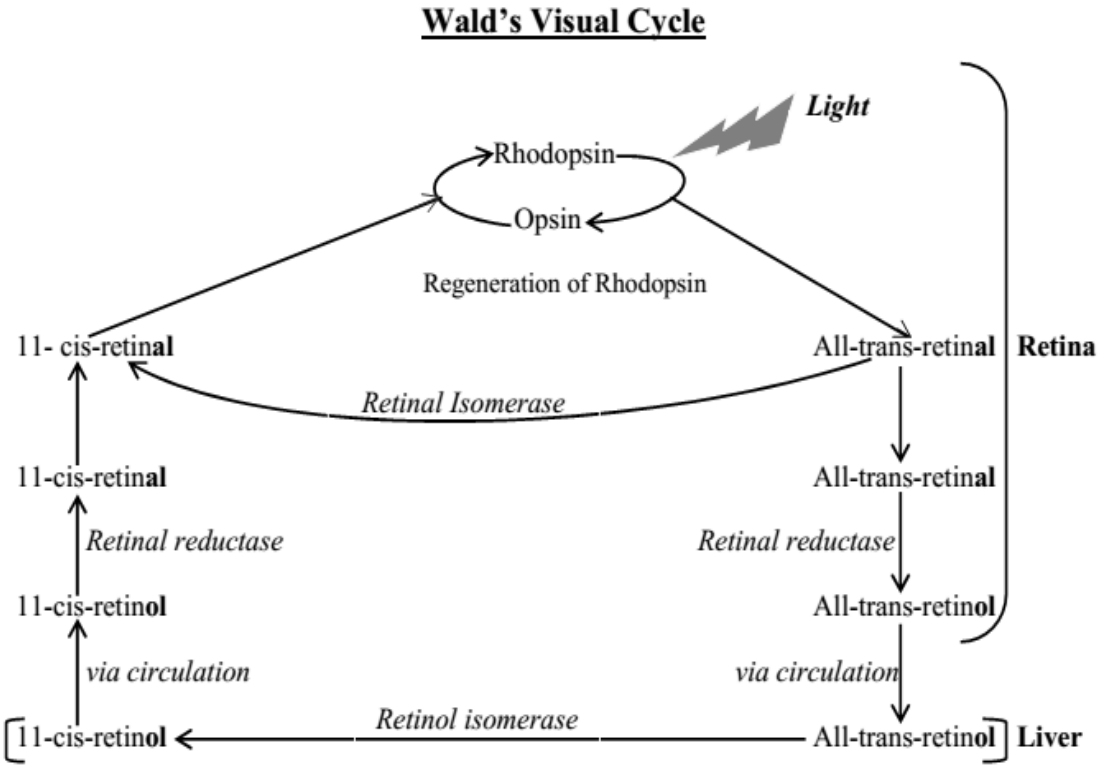
Excretion

Excreted in urine

Functions

- Physiologically active in the form of retinol, retinal and retinoic acid.

1) Role in vision



- Vitamin A is essential for vision in both rod (black and white vision) and cone cells (colour vision) of retina.

- In visual cycle of rod cells, vitamin A is part of light sensitive visual pigment called rhodopsin (composed of 11-cis-retinal and opsin protein).

- Rod cells are specialized for vision in night as rhodopsin in them is sensitive even to dim light.

- When light falls on retina, rhodopsin is exposed to light and dissociates into all-trans-retinal and opsin.

- This dissociation of rhodopsin causes hyperpolarisation of rod cells (through transducin protein) and generates a nerve impulse.

- This nerve impulse is transmitted to brain through optic nerve and vision is perceived.

- The all-trans-retinal released from dissociation of rhodopsin is functionally inactive and so cannot combine with opsin to regenerate rhodopsin.

- Regeneration of rhodopsin requires conversion of inactive all-trans-retinal to active 11-cis-retinal.

- This conversion of inactive all-trans-retinal to active 11-cis-retinal occurs in a series of reactions constitutiong a circular pathway called Wald's visual cycle or rhodopsin cycle.

- 11-cis-retinal is also part of the pigments in cone cells involved in colour vision (Porphyrinopsin for red, iodopsin for green and cyanopsin for blue).

2) Role in growth and tissue differentiation

- Retinoic acid acts like a steroid hormone and regulates cell growth and differentiation through expression of specific genes.

- This happens during embryonic development, spermatogenesis and differentiation of epithelial cells.

3) Role in maintenance of healthy epithelium and mucus secretion

- Vitamin A maintains healthy epithelium in tissues and organs by inhibiting keratin synthesis.

- Synthesis of keratin causes keratinization of epithelial surface which is harmful.

- Vitamin A is needed for synthesis of mucopolysaccharides and glycoproteins required for mucus secretion from epithelial cells. The normal mucus secretion maintains the epithelial cell moist and prevents keratinization of epithelial cell.

Other Functions

- Required for differentiation of cells of immune system. Derivatives of vitamin A (tretinoin and isotretinoin) are used to treat skin diseases like acne and psoriasis.

- Is involved in controlling cholesterol biosynthesis.

- Is required for synthesis of transferrin, an iron transport protein.

- β carotene and other carotenoids (as antioxidants) inactivate free radicals and protect tissues from diseases like cancer, cataract etc.

Deficiency Manifestations

1) **Nyctalopia** (Night blindness)

- Rod cells become less sensitive to light due to lack of rhodopsin.

- The dark adaptation time is prolonged and patients fail to see objects in night (in dim or poor light).

2) **Keratinisation** of epithelial structures in tissues happens leading to **follicular hyperkeratosis** (keratosis of hair follicles and dry and scaly skin) and increased susceptibility to infections (in respiratory and urinary tract) due to defective synthesis and secretion of mucopolysaccharides and glycoproteins.

3) **Xerophthalmia**

Lacrimal glands degenerate and stop producing tears causing dryness of cornea and conjunctiva.

4) **Keratomalacia**

If xerophthalmia is not treated, permanent loss of vision happens due to keratinisation and ulceration of cornea.

5) **Bitot's spot**

White opaque spots on either side of cornea.

6) Reduced immunity due to impaired differentiation of immune cells.

7) Poor growth of bones, nervous system, reproductive system and teeth.

Treatment

Administration of oral and injectible forms of vitamin A, generally as vitamin A palmitate.

Diagnostic test to detect vitamin A deficiency

-Dark adaptation test (Increase in dark adaptation time occurs in vitamin A deficiency).

Hypervitaminosis A

- Excessive intake of vitamin A can lead to toxicity as it is stored in liver. Symptoms are headache, nausea, vomiting, anorexia, alopecia, scaly and rough skin, painful tenderness of bones etc.

- In women, hypervitaminosis causes congenital malformation in growing foetes.

Vitamin E (Tocopherol)

Also called as anti-sterility vitamin.

Food Sources

Vegetable oils like wheat germ oil, sunflower oil, safflower oil, cotton seed oil etc. Liver and adipose tissues are also rich sources.

Recommended Daily Allowance (RDA)

10 mg/day

Chemistry

- A tocopherol molecule is made up of a chromane ring (tocol) with an isoprenoid side chain.

- Among all the eight naturally occurring tocopherols, α-tocopherol has greatest biological activity.

- It represents 90% of the total tocopherols present in human tissues.

Metabolism

Biosynthesis

- Not synthesized in humans.

- Consumed only through diet.

Absorption

- Absorbed in small intestine in presence of bile salts.

- Largely stored in adipose tissues.

Normal Plasma Concentration

1.0 mg/dL

Excretion

Through bile, urine, feces and skin.

Functions

Role as antioxidant

- As most powerful antioxidant, it inactivates the oxidants (free radicals) in cells generated by metabolic processes and environmental pollutants.

- By this antioxidant role, it prevents lipid peroxidation of RBC membrane and protects RBC from hemolysis.

- By preventing peroxidation, it maintains structural and functional integrity of cells.

- It acts synergistically with selenium to prevent lipid peroxidation.

- It reduces the risk of atherosclerosis by reducing the oxidation of LDL.

- It is required for cellular respiration as it prevents peroxidative damage of mitochondrial membrane.

- It boosts immune response and delays cataract formation and ageing process.

- Is required for normal reproduction.

Deficiency Manifestations

Hemolytic anemia, muscular weakness and dystrophy, neurological disorders, liver degeneration, nocturnal muscle cramps, impaired immune response, thrombocytosis etc.

Hypervitaminosis E

Increased bleeding, increased triglycerides, decreased thyroid secretion, decreased vitamin K activity etc.

Vitamin K (Coagulation vitamin)

Food Sources

- Green leafy vegetables (spinach, cabbage, lettuce etc), fish, liver, skeletal muscle etc.

- Synthesis by intestinal bacteria supplies large amounts of vitamin K.

Recommended Daily Allowance (RDA)

20 to 100 microgram/day

Chemistry

- Is a naphthoquinone derivative with a long isoprenoid side chain.

- Exists in three important forms namely

1) Vitamin K_1 (Phylloquinone) – Natural form present in green vegetables.

2) Vitamin K_2 (Menaquinone or Farnoquinone) – Natural form present in animals and also synthesized by bacteria in intestine.

3) Vitamin K_3 (Menadione)- A water soluble, commercially available, synthetic form used for therapeutic purpose.

Metabolism

Biosynthesis

- Humans cannot synthesise both K_1 and K_2 forms.

- Plants synthesise vitamin K_1 form.

- Intestinal bacterial flora synthesise vitamin K_2 form.

Absorption

Absorbed in small intestine in presence of bile salts and stored in liver.

Normal Plasma Concentration

50 to 200 nanogram/dL.

Excretion

Excreted mainly in bile.

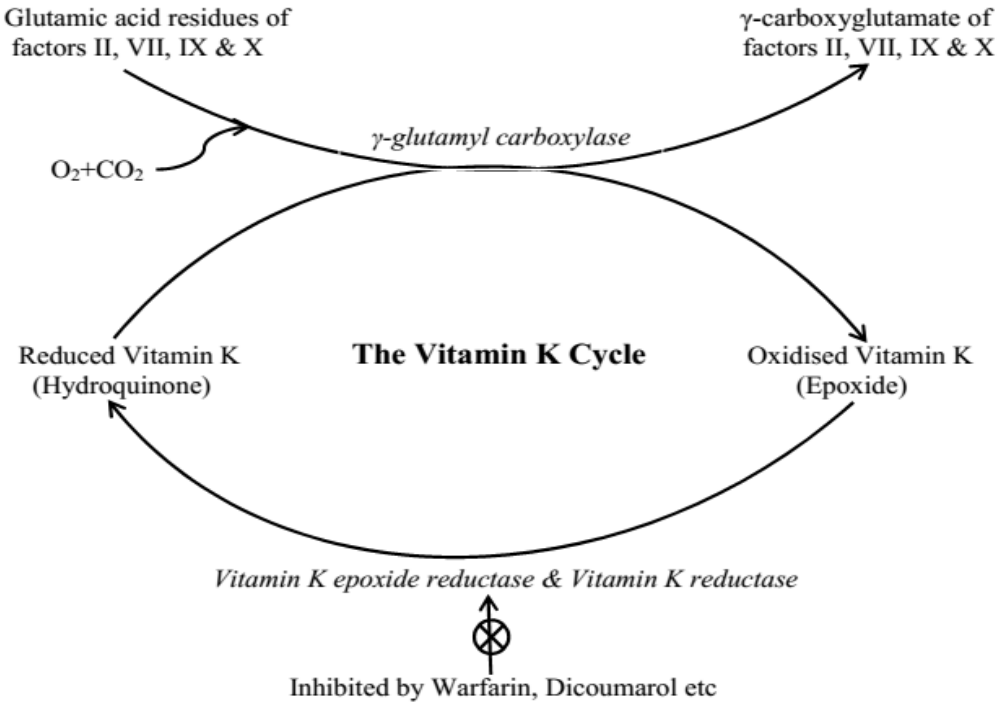
Functions

1) In blood coagulation

- Vitamin K is needed for the activation of blood clotting factors like factor II, VII, IX and X.

- The inactive form of these protein factors, synthesized in liver, are activated when their glutamic acid residues are carboxylated in the γ-carbon atom. In the clotting process, factor IV (calcium) binds only to these γ-carboxylated glutamic acid residues.

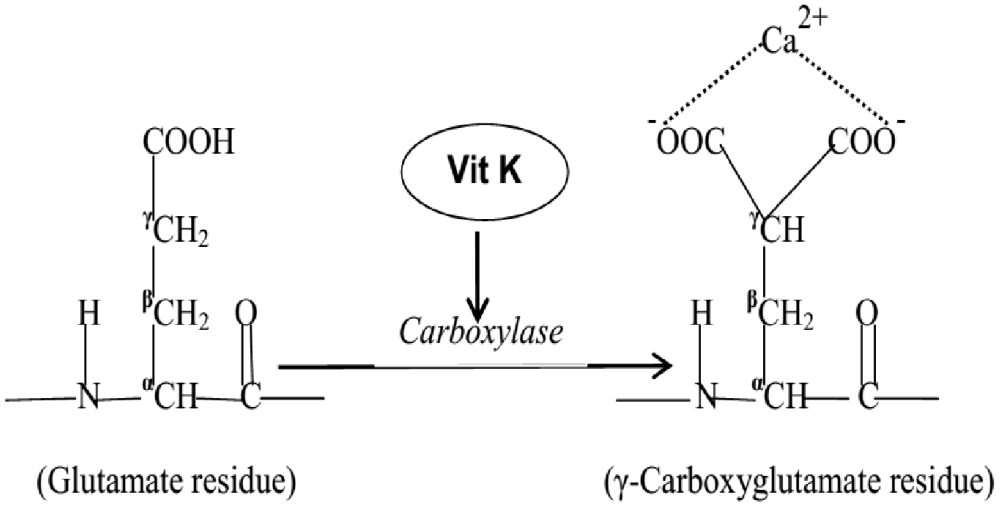
- During γ-carboxylation of glutamic acid residues of inactive blood clotting factors, vitamin K acts as co-enzyme hydroquinone.



2) In osteocalcin

- Osteocalcin, a protein with glutamic acid residues, is a calcium binding protein of bone and teeth. It plays a role in growth and development of bones and teeth.

- Vitamin K is essential for γ-carboxylation of glutamic acid residues of this osteocalcin. The binding of osteocalcin to calcium (hydroxyapatite crystals) depends on the degree of γ-carboxylation of glutamic acid residues.



3) In oxidative phosphorylation

Being structurally related to ubiquinones, vitamin K is considered as a component of electron transport chain (ETC) in mitochondria.

Deficiency Manifestations

- Deficiency rare in adults.

- Seen generally in premature infants due to absence of intestinal bacterial flora.

- Symptoms include hypoprothrombinemia, cutaneous and intramuscular hemorrhage with bluish red colouration in different parts of the body.

Diagnostic test to detect vitamin K deficiency

Hypoprothrombinemia and increased blood clotting time.

Hypervitaminosis K

- Dyspnoea, chest pain and flushing in adults.

- Hyperprothrombinemia, hemolytic anemia and jaundice in infants.

Antivitamins

- Antivitamins are chemical compounds that inhibit the absorption or actions of vitamins. They prevent vitamins from exerting their typical biological effects.

- Many antivitamins have chemical structures similar to vitamins and function as competitive inhibitors.

Vitamin	Antivitamin
Vitamin A	Aspirin, Phenobarbital, Nitrosamines, Air pollutants, Mineral oil etc.
Vitamin K	Antibiotics, Dicoumarol, Warfarin etc.
Vitamin C	Cigarette smoke, Alcohol, Ammonium chloride, Stilbesterol, Thiouracil, Atropine, Barbiturates, Antihistamines etc.
Vitamin B complex	Cortisone and deoxypyridoxine (Pyridoxine), Alcohol and Phytic acid (Thiamine), Chlorogenic acid (Thiamine and Biotin), Oral contraceptives (Riboflavin, Folic acid and Cobalamine), Aminopterin (Folic acid), Avidin (Biotin) etc.

Hypervitaminosis

Hypervitaminosis refers to storage of abnormally high amounts of vitamins in body which can lead to toxic symptoms. This condition may be caused by ingestion of excess amount of vitamins generally as drugs. Mostly, fat soluble vitamins cause hypervitaminosis.

(Please write about hypervitaminosis A, D, E, K and C).

Vitamin B_1 (Thiamine)

Food sources

Unrefined cereals, pulses, meat, milk, yeast etc.

Recommended daily allowance (RDA)

Children – 1.2 mg/day

Adults – 1.5 mg/day

Pregnancy and Lactation – 2.0 mg/day

Chemistry

- A complex organic molecule made up of thiazole and pyrimidine rings.

- Is a sulfur containing vitamin.

- Is readily soluble in water and thermolabile even in room temperature.

- The co-enzyme form is ***thiamine pyrophosphate (TPP)***.

Normal plasma concentration

1.0 microgram/dL.

Functions

- TPP serves as co-enzyme in oxidative decarboxylation of alpha ketoacids like pyruvate and alpha ketoglutarate.

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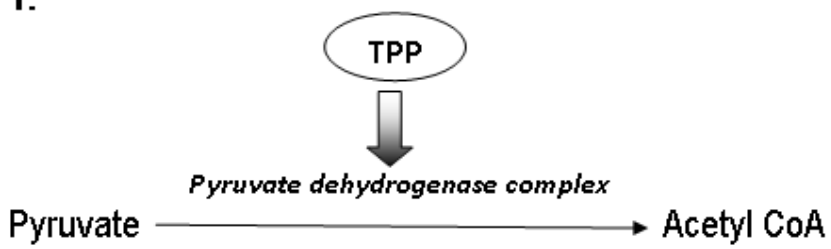

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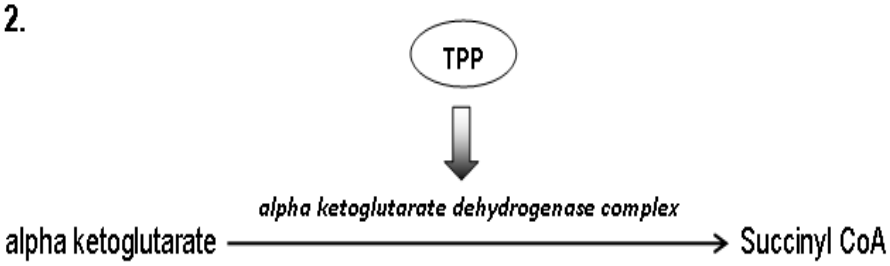


- TPP serves as co-enzyme for transketolase enzyme in HMP shunt pathway.

- TPP serves as co-enzyme in oxidative decarboxylation of alpha-ketoacids of branched chain amino acids like valine, leucine and isoleucine.

- TPP is required for the synthesis of co-enzyme forms of vitamin B_3 from the amino acid tryptophan.

- TPP is required for the synthesis of acetyl choline (a neurotransmitter) and ion transport during nerve impulse transmission.

Deficiency manifestations

- Vitamin B_1 (Thiamine) deficiency causes **Beri-Beri** disease in humans.

A) Dry Beri-Beri (Neuritic Beri-Beri)

- Central nervous system, spinal cord, peripheral nerves and muscles are affected.

- Characterised by peripheral neuritis, progressive paralysis, wasting of limb muscles, dry skin, mental confusion etc.

B) Wet Beri-Beri (Edematous or Cardiac Beri-Beri)

- Cardiovascular system is affected.

- Characterised by edema of extremities, heart enlargement and congestive heart failure.

C) Infantile Beri-Beri

- Develops in infants fed with breast milk less in thiamine.

- Characterised by heart enlargement, restlessness, sleeplessness, dyspnoea, tachycardia and gastrointestinal disturbances.

- In acute condition, infant may die within 48 hours due to cardiac failure.

D) Cerebral Beri-Beri (Wernicke-Korsakoff Syndrome)

- Mostly seen in alcoholics.

- Characterised by anorexia, nausea, vomiting, ophthalmoplegia, depression, ataxia, memory loss, mental confusion, insomnia etc.

E) Polyneuritis

- Is common in chronic alcoholics, pregnant women and elderly people.

- Alcohol inhibits intestinal absorption of thiamine through large doses of thiamine is required for alcohol utilization.

- Conversion of pyruvate to acetyl CoA is impaired resulting in increased plasma concentration of pyruvate and lactate leading to lactic acidosis.

Diagnostic test to detect vitamin B_1 deficiency

- Assay of transketolase activity in erythrocytes.

Vitamin B_2 (Riboflavin)

- Also called as lactoflavin due to its highest content in milk.

Food sources

Unrefined cereals, germinating seeds, yeast, green leafy vegetables, mushrooms, liver, milk and eggs.

Recommended daily allowance (RDA)

Adults – 2 mg/day

Children – 1.2 mg/day

Pregnancy and Lactation – 2 mg/day

Chemistry

- It is a complex organic molecule made up of an isoalloxazine ring with a ribitol side chain.

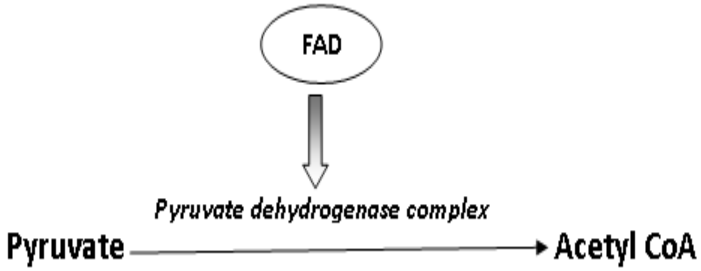
- It is sensitive to light and UV radiation.

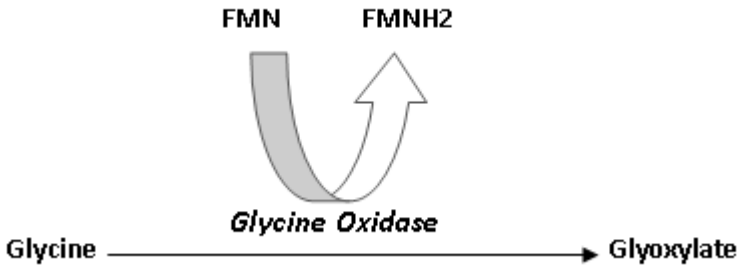
- The co-enzyme forms are ***flavin mononucleotide (FMN)*** and ***flavin adenine dinucleotide (FAD)***.

Normal plasma concentration

3.0 microgram/dL.

Functions





- FAD and FMN function as co-enzyme for a class of dehydrogenases called flavin dehydrogenases. Eg- pyruvate dehydrogenase complex, xanthine oxidase, alpha ketoglutarate dehydrogenase complex etc.

- FAD is involved in the breakdown metabolism of homocysteine and thus has a role in decreasing the risk of cardiovascular disease.

- FAD is involved in regeneration of antioxidant glutathione.

- FAD is involved in the synthesis of co-enzyme forms of vitamin B_3 from aminoacid tryptophan.

Deficiency manifestations

- Glossitis, cheilosis, dermatitis, hyperplasia of skin, corneal vascularisation etc.

Diagnostic test to detect vitamin B_2 deficiency

Assay of glutathione reductase activity in erythrocytes.

Vitamin B_3 (Niacin)

Food sources

Unrefined cereals, yeast, green vegetables, poultry and liver.

Recommended daily allowance (RDA)

Adults - 20 mg/day

Children – 15 mg/day

Infants – 5 mg/day

Chemistry

- It is made up of pyridine ring.

- Niacin (also called as nicotinic acid) and its amide, nicotinamide are the two forms with equal biological activities.

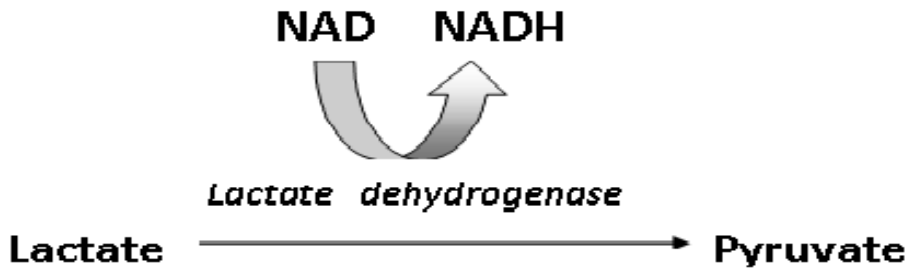
- The co-enzyme forms are ***nicotinamide adenine dinucleotide (NAD)*** and ***nicotinamide adenine dinucleotide phosphate (NADP)***.

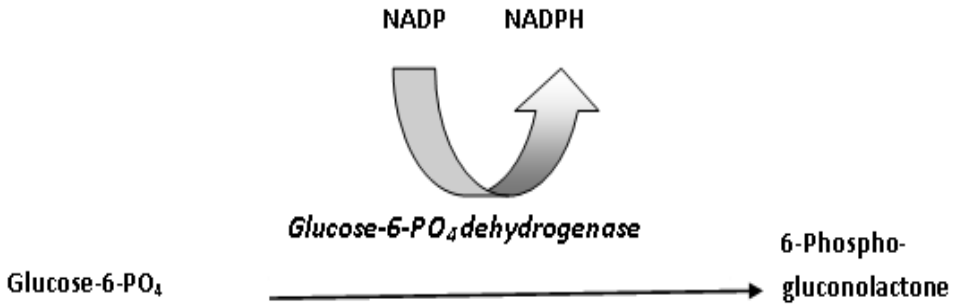
- Unlike other vitamins, vitamin B_3 can be synthesized by human body.

- The co-enzyme forms (NAD and NADP) are directly synthesized from the aminoacid tryptophan through Kynurenine-Anthranilate pathway.

Functions

- NAD and NADP act as co-enzymes in large number of oxidation-reduction reactions catalysed by pyridine nucleotide linked dehydrogenases. Eg – malate dehydrogenase, isocitrate dehydrogenase, lactate dehydrogenase etc.





Deficiency manifestations

- Vitamin B_3 deficiency causes **pellagra** disease in humans.

- Pellagra is characterized by **d**ermatitis, **d**iarrhea and **d**ementia.

- Maize and jowar, as staple diet, cause niacin deficiency as tryptophan is deficient in these two grains.

Diagnostic test to detect vitamin B_3 deficiency

Niacin panel test.

Hypervitaminosis B_3

- Excess intake of niacin as drug causes vascular dilation of skin and burning sensation.

- Larger doses, about 10 g/day, have been shown to cause liver injury.

Vitamin B_5 (Pantothenic acid)

Food sources

Royal jelly, fish, yeast, liver, unrefined cereals, pulses etc.

Recommended daily allowance (RDA)

10 mg/day

Chemistry

- It is a molecule of pantoic acid linked to beta alanine by a peptide bond.

- Free acid is a viscous yellow oily substance soluble in water.

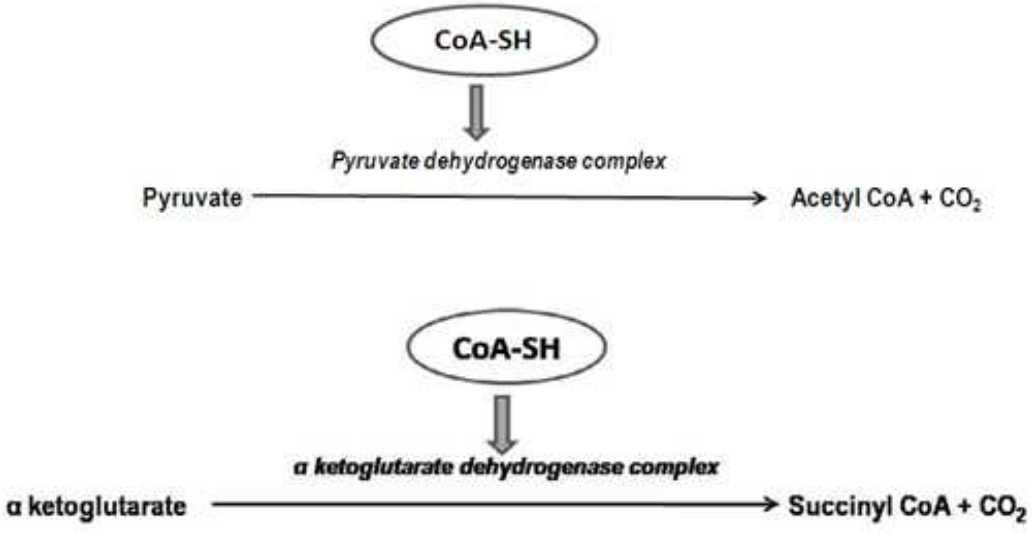
- The co-enzyme form of vitamin B_5 is ***co-enzyme A*** (also called as ***CoA*** or **CoA-SH**).

- The co-enzyme A is made up of pantothenic acid, beta mercaptoethanolamine (which contributes –SH group), a pyrophosphate group and an adenosine monophosphate (AMP) molecule.

Functions

- Co-enzyme A plays role in a large number of reactions of carbohydrate, protein and fat metabolism. Eg – oxidative decarboxylation of pyruvate, alpha ketoglutarate, beta oxidation of fatty acid and biosynthesis of fatty acid, triglyceride and cholesterol.

- More than 70 enzymes are known to utilize co-enzyme A.



Deficiency manifestations

- Deficiency is rare.

- Experimentally induced deficiency, by administering omega methyl pantothenate, is characterized by symptoms like nausea, vomiting, headache, sleep disturbance, anemia etc.

- In humans, pantothenic acid deficiency is associated with Gopalan's burning feet syndrome.

Vitamin B_6 (Pyridoxine)

Food sources

Egg, fish, green leafy vegetables, whole cereals and yeast.

Recommended daily allowance (RDA)

2 mg/day

Chemistry

- Contains pyridine ring.

- Exists in three forms namely

1. Pyridoxamine (an amino group is attached)

2. Pyridoxine or pyridoxol (an alcohol group is attached)

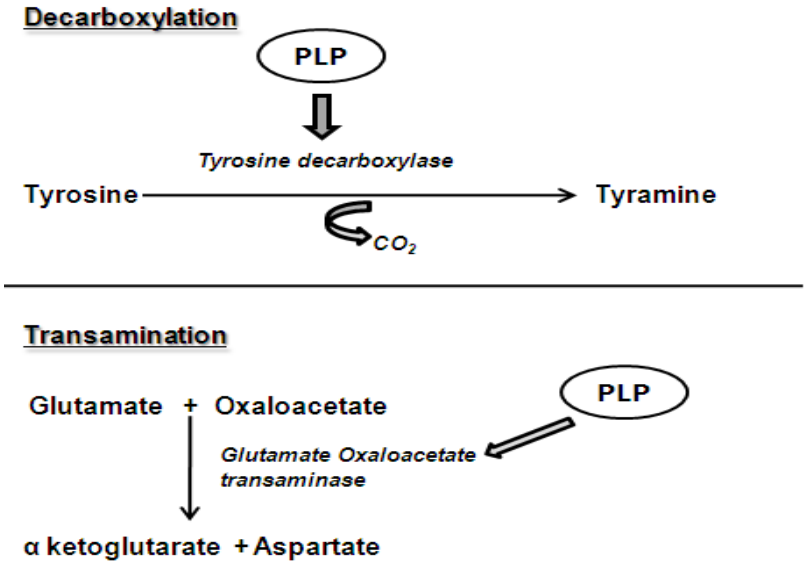
3. Pyridoxal (an aldehyde group is attached)

- The co-enzyme form of vitamin B_6 is ***pyridoxal phosphate (PLP)***.

Functions

- Pyridoxal phosphate acts as co-enzyme in a large number of reactions of aminoacid metabolism namely

1. Decarboxylation 2. Transamination 3. Non-oxidative deamination & 4. Condensation.



- Required for synthesis of niacin from tryptophan.

- Required for synthesis of CoA from pantothenic acid.

- Required for conversion of glycine to serine.

- Required for catabolism of cysteine.

- Required for synthesis of sphingolipids, heme and neurotransmitters like gama amino butyric acid, dopamine and serotonin.

- Essential in glycogen metabolism as it serves as co-enzyme of glycogen phosphorylase enzyme.

- Involved in conversion of linoleic acid to arachidonic acid.

- Required for absorption of aminoacids.

Deficiency manifestations

- Deficiency is rare in humans.

- Found in tuberculosis patients administered with the drug isoniazid.

- Symptoms include cheilosis, glossitis and hypochromic anemia.

- Central nervous system affected resulting in convulsions, demyelination of peripheral nerves and degeneration of axons.

Diagnostic test to detect vitamin B_6 deficiency

- In vitamin B_6 deficiency, large amounts of xanthurenic acid is produced and excreted in urine due to impaired tryptophan catabolism.

- Quantitative determination of urinary xanthurenic acid after oral administration of a test dose of tryptophan is a reliable test (Xanthurenic acid excretion test).

Hypervitaminosis B_6

Excess intake of pyridoxine as drug (about 2g/day) causes neuropathy.

Vitamin B_7 (Biotin)

Also called as anti-egg white injury factor.

Food sources

Unrefined cereals, liver, kidney, milk, yeast, peanut etc.

Recommended daily allowance (RDA)

15 to 30 microgram/day

Chemistry

- It is a sulfur containing heterocyclic monocarboxylic acid.

- Formed by fusion of imidazole and thiophene rings with a valeric acid side chain.

Normal plasma concentration

12 to 24 microgram/dL.

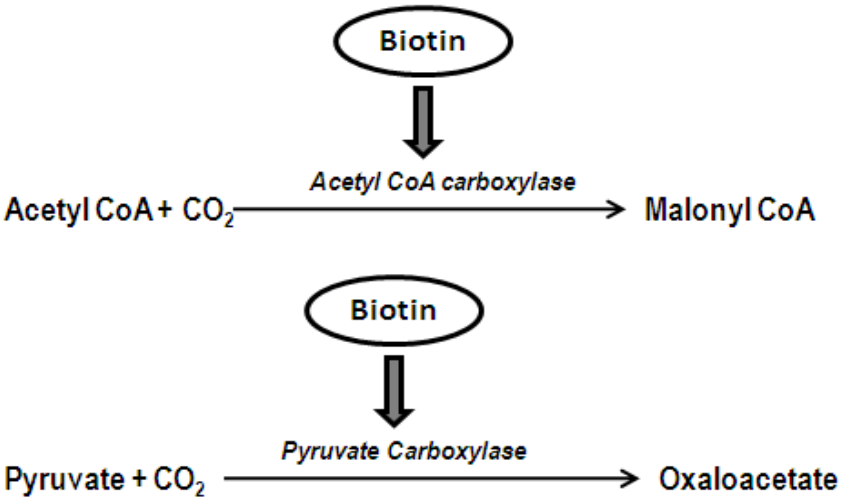
Functions

- Biotin is necessary for cell growth, production of fatty acids and metabolism of fats and aminoacids.

- Plays a role in citric acid cycle.

- May also be helpful in maintaining a steady blood sugar level.

- Acts as co-enzyme in carboxylation (carbondioxide fixing) reactions.



Deficiency manifestations

- Deficiency rare in humans.

- Deficiency can be induced by ingestion of large amount of raw egg white. Raw egg white contains biotin-binding protein called avidin. Avidin binds biotin and prevents its absorption. Heating the egg white can prevent this effect, since heating denatures biotin.

- Deficiency may cause mild dermatitis, nausea and loss of appetite, muscular pain and anemia.

- Leiner's disease is observed in infants due to malabsorption of biotin.

Vitamin B_9 (Folic acid)

Food sources

Green leafy vegetables like spinach, cabbage etc, yeast, liver, unrefined cereals, sunflower seeds, egg yolk, fish etc.

Recommended daily allowance (RDA)

Adults – 400 microgram/day

Children- 100 to 300 microgram/day

Pregnancy and Lactation – 600 to 800 microgram/day

Chemistry

- Folic acid is also called as pteroylglutamic acid.

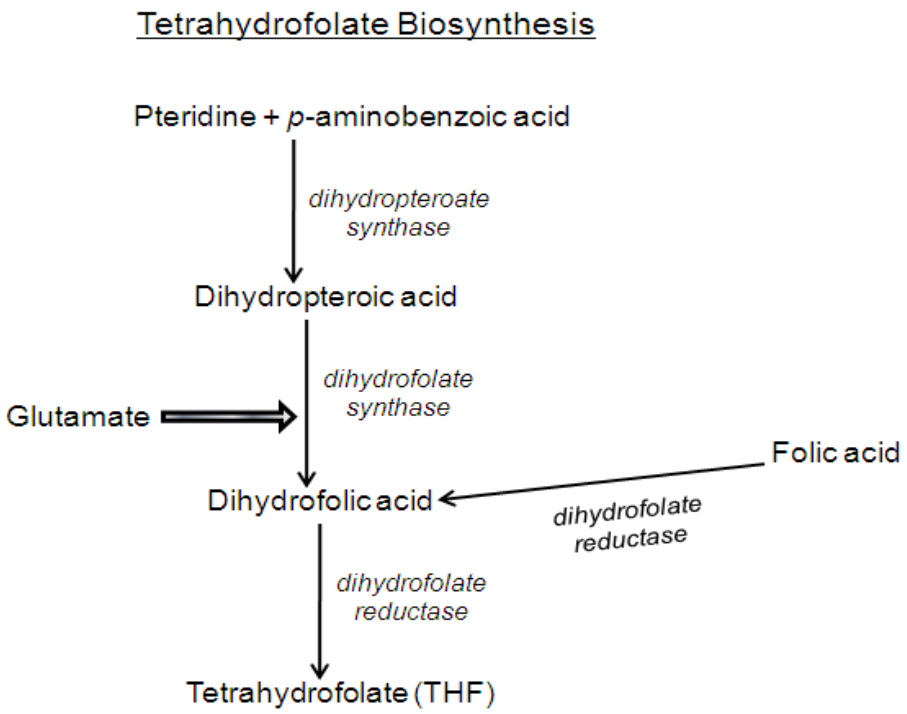
- It is made up of pteridine nucleus, a molecule of para amino benzoic acid (PABA) and L-glutamic acid.

- Folic acid is yellow crystalline substance soluble in water.

- The co-enzyme form of folic acid is ***tetrahydrofolate (THF)***.

- Folic acid cannot be synthesized by animals including humans.

- Plants, bacteria (including intestinal bacterial flora) and yeast synthesise folic acid from pteridine, PABA and L-glutamic acid.



Normal plasma concentration

300 nanogram/dL

Functions

THF takes part in transfer of one carbon fragments like formyl (-CHO), hydroxyl methyl (-CH_2OH), methylene (-CH_2), methenyl (-CH), and formimino (-CH=NH) groups in several reactions of aminoacid and nucleotide metabolism.

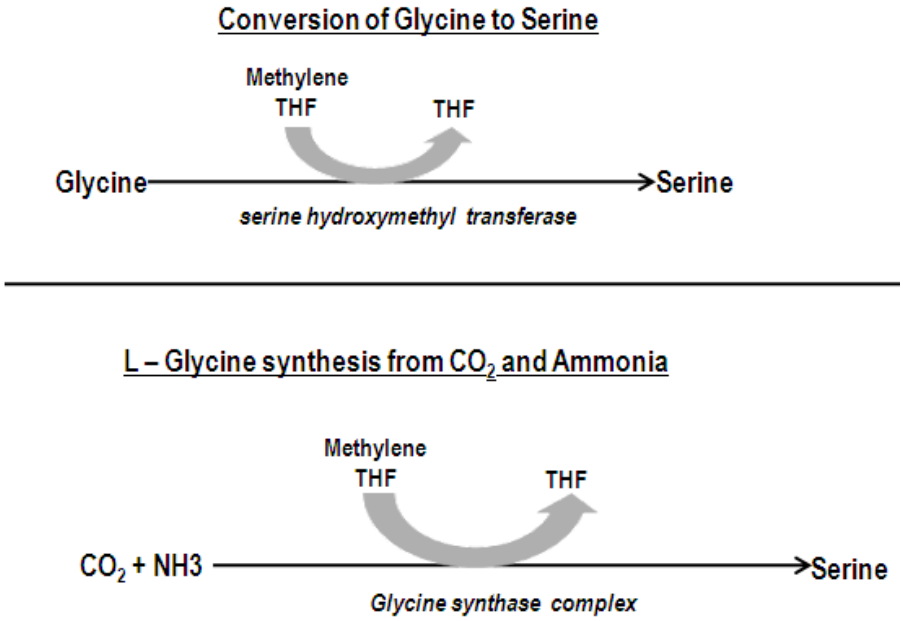
- Required for synthesis of purine nucleotides and deoxythymidine monophosphate (dTMP).

- Required for catabolism of histidine to glutamate.

- Required for methylation of homocysteine to methionine.

- For conversion of glycine to serine.

- Required for L-glycine synthesis from CO_2 and ammonia.



- Folic acid contributes to oocyte maturation, implantation and placentation in addition to the general effects on pregnancy.

- It contributes to spermatogenesis and reduce chromosomal defects in sperm.

Deficiency manifestations

- Folic acid deficiency is common in pregnant women, stressful conditions, intestinal malabsorption and during antibiotic therapy.

- Folate deficiency during pregnancy may lead to low birth weight and premature infants and infants with neural tube defects.

- In adults, **megaloblastic anemia** may be a sign of advanced folate deficiency.

- Other symptoms are loss of appetite, weight loss, weakness, sore tongue, headaches, heart palpitations etc.

Treatment

Oral administration of folate as drug and consumption of folate rich foods.

Diagnostic test to detect vitamin B_9 deficiency

FIGlu (formiminoglutamic acid) excretion test – When histidine is administered to a patient with folic acid deficiency, FIGlu in urine increases.

Hypervitaminosis B_9

- Generally low because folate is water soluble and so regularly removed through urine.

- High dose of vitamin B_9 has masking effect on the diagnosis of pernicious anemia.

Folic acid antagonists

- They interfere with metabolic functions of folic acid.

- Aminopterin and amethopterin inhibit dihydrofolate reductase and so used as anticancer agents.

- Aminopterin inhibits biosynthesis of nucleic acids and so used in treating leukemia.

Vitamin B_{12} (Cobalamine)

Also called antipernicious anemia factor and extrinsic factor of castle.

Food sources

- Liver, kidney, egg, fish and milk products.

- Generally absent in foods derived from plant sources.

Recommended daily allowance (RDA)

3 microgram/day

Chemistry

- It is made up of corrin ring in which the trace element cobalt is co-ordinated at the centre.

- The various forms of cobalamin are cyanocobalamine, hydroxycobalamine, methylcobalamine, deoxyadenosyl cobalamine and nitrocobalamine.

- ***Methylcobalamine*** and ***deoxyadenosyl cobalamine***, present in natural foods, are the co-enzyme forms of vitamin B_{12}.

- Cyanocobalamine, in which a cyanide group is bound to cobalt, is the commercial preparation of cobalamin.

- Vitamin B_{12} is absorbed in the ileum of small intestine.

- The intestinal absorption of vitamin B_{12} requires intrinsic factor (IF) of castle (a glycoprotein) and HCL.

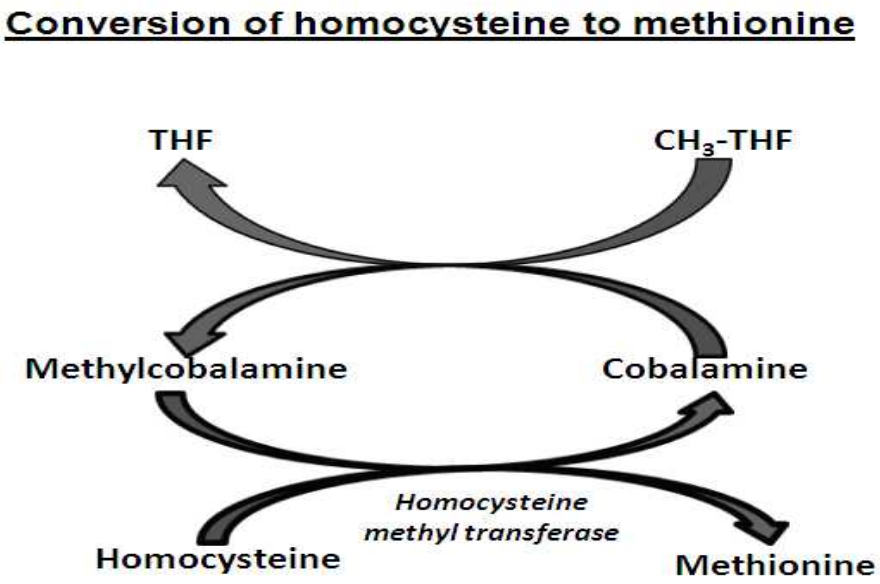
Normal plasma concentration

20 to 100 nanogram/dL

Functions

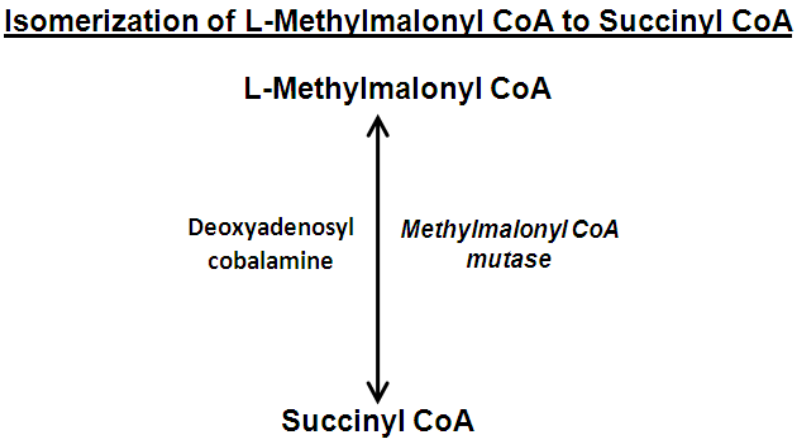
- Important for formation of red blood cells and maintenance of central nervous system which includes brain and spinal cord.

- 1) Conversion of homocysteine to methionine.



Thus vitamin B_{12} maintains methionine stores of the body and spares THF for biosynthesis of purines and pyrimidines.

- 2) Isomerisation of L-methylmalonyl CoA to succinyl CoA.



- Deoxyadenosyl cobalamine is important in the metabolism of branched chain fatty acids and fatty acids containing odd number of carbon atoms through the conversion of methylmalonyl CoA to succinyl CoA.

Deficiency manifestations

- Deficiency may occur in conditions like strict vegetarianism, chronic alcoholism, malabsorption etc.

- Deficiency causes **pernicious anemia** (megaloblastic anemia characterized by large macrocytic erythrocytes) and degeneration of myelinated nerves.

- Gastrointestinal disturbances are also observed.

Diagnostic test to detect vitamin B_{12} deficiency

Measurement of urinary excretion of methylmalonic acid (methylmalonic aciduria).