Biocemistry of Vitamin

Vitamins are organic molecules required by the body in very small amount for maintenance of normal metabolic functioning. Thirteen organic compounds are known to function as vitamins in humans. Although sharing a desingnation as essential nutrients, these organic molecules don't possess a common chemical structure.

Many vitamins (B- complex members) functions as compounents or precursors of coenzymes or as prosthetic groups (biotin). A metabolite of one (vitamine D) is known to be a calcium and phosphate-regulating hormone. Another (vitamin A) is essential for normal vesion

The amount that should be ingested by a healthy individual to meet routine metabolic needs, prevent depletion of body stores, and thus preserve normal function and health is reflected in the recmmended dietary allowance (RDA) published by the food and nutrition board of the national academy of science-national research council (NAS/NRC) .

Vitamins classificatios:

Vitamins could be classified as:

1. water soluble vitamins
2. fat soluble vitamins

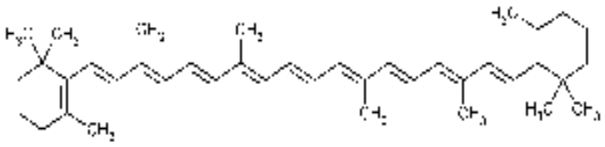
Comparison of two types of vitamins

Fat soluble	Water solublevitamins vitamins
Solubility in fat	Water solubility Not soluble
Absorption Along with lipids * requires bile salts	Absorption simple
Carrier proteins Present *	No carrier proteins
Storage Stored in liver *	No storage
Deficiency Manifests only * depleted storage	Manifests rapidly when stores are as there is no
Toxicity Hypervitaminosis	Unlikely, since excess is excreted
Major vitamins A,D,E and K	B and C

Note: *Vitamin B 12 is an exception.

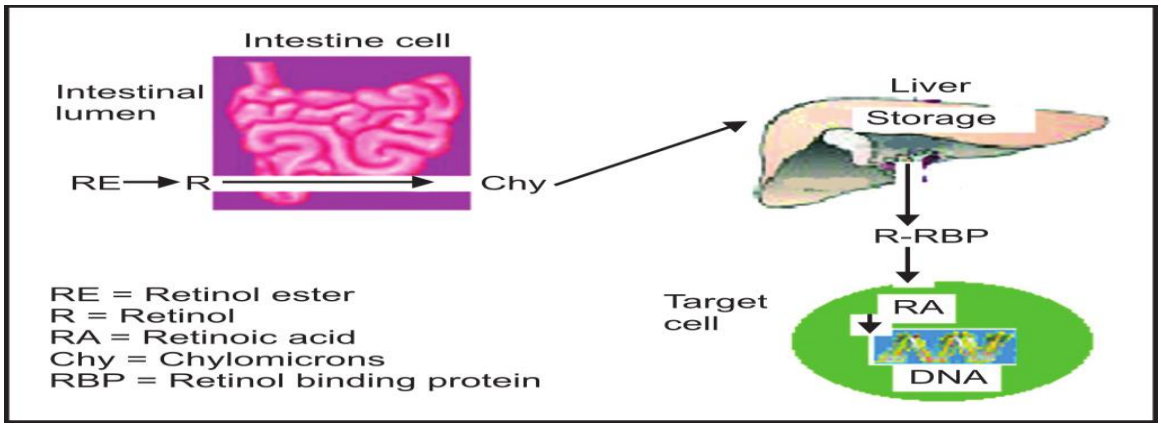
vitamin A (retinol)

vitamine A also called as anti – night blindness factor Vitamin A is fat soluble. The active form is present only in animal tissues. The pro-vitamin, beta-carotene is present in plant tissues. One molecule of beta-carotene can theoretically give rise to two molecules of vitamin A. Vitamin A has a beta-ionone (cyclohexenyl) ring system. Carotenes are biologically active upon conversion to retinol. Three different compounds with vitamin A activity are retinol (vitamin A alcohol), retinal (vitamin A aldehyde) and retinoic acid. The retinal may be reduced to retinol by retinal reductase. This reaction is readily reversible. Retinal is oxidized to retinoic acid, which cannot be converted back to the other forms. The side chain contains alternate double bonds, and hence many isomers are possible. The all-trans variety of retinal, also called vitamin A 1 is most common (Fig. 16.1). vii. Biologically important compound is 11-cis- retinal.



B-Carote

Retinol is enzymatically esterfied with palmitic acid during intestinal absorption. As the fatty acid ester, retinyl palmitate, its transported in chylomicra of the lymph. Interacellulary, its convertedby the cell RBP to the nucleus, where it alters gene activity and, thus, cell differentiation.

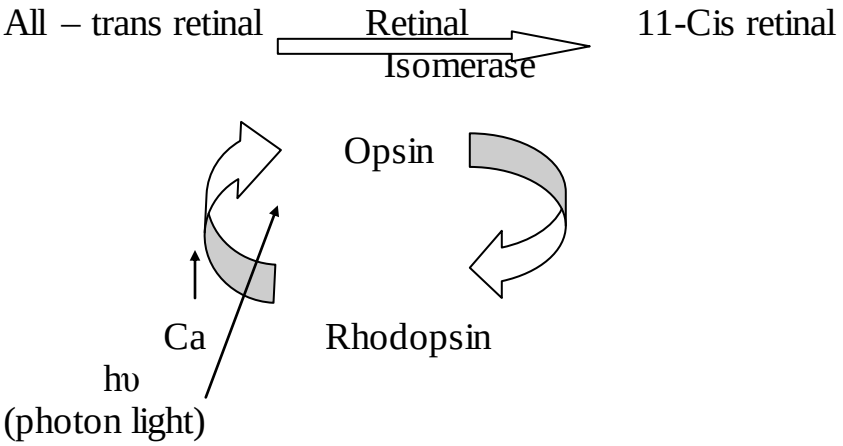


Biological functions :

- In vision cycle
- Gluconeogenesis
- Biosynthesis of gluco-corticoids
- Biosynthesis of cholesterol
- Cell differentiation and growth
- Immune function

Role of vitamin A in visual cycle :

Rode cells of the human retina contain stacks of membrane – bound discs. These memberrans contain the photosensitive pigment, **rhodopsin**. Rhodopsin is a complex of the **prosthetic group, retinal and protein opsin.** During synthesis of this pigments, retinol is oxidized to retinal . absorption of light initiates molecular and electrochemical changes.

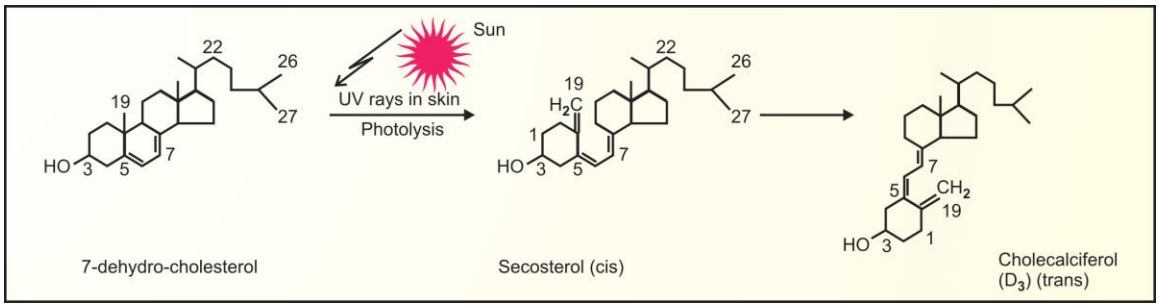


this reaction is accompained by a conformational changes that induces a calcium ion channel in the membrane of the rod cell. The rapid influx of the calcium ions triggers a nerve impulse allowing light to be perceived by the brain.

Vitamin D (Calciferol
Metabolism :

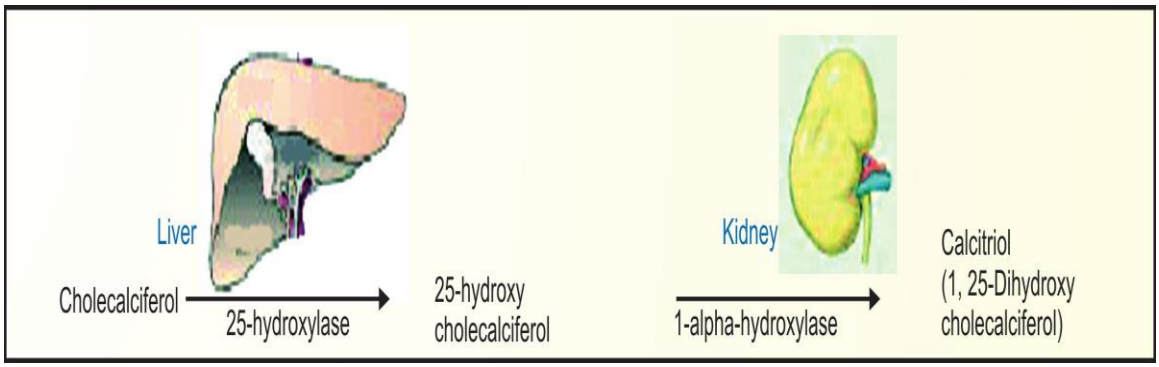
Vitamin D (calciferol) is a sterol. Its also called 7-Dehydrocholesterol, is a precusor of vitamin D3 in animals. Its also called as provitamin D. its synthesized in human begine in the intestinal mucosa and is converted

to vitamin D3 by UV light in the skin. This process is referred to as photobiogenesis.



Synthesis of cholecalciferol or vitamin D 3

Vitamin D is absorbed from the small intestine and transported in chylomicra of the lymph. As the is formed, its bounded by D-binding protien (DBP), a plasma α-globulin, and transported in the blood. Up to 80% of both exogenous and endogenous vit. D3 are cleared by the liver (cytochrome P-450), with storage primarily in adipose tissue. In the liver, microsomal enzymes catalyze 25-hydroxylation of the molecules to produce the 25-hydroxyvitamin D3 (1,25-OH-D3), known as Cacitriol. adequacy of 1,25-(OH)2D3 is essential for normal mineralization of bone and neuromuscular activity. When calcium and phosphours levels in the body are within the normal limts, the predominant dihydroylated form of vit. D synthesiszed is the less active metablite. 24,25-(OH)2D3. Calcitriol stimulates the production of calcium – binding protine in the intestinal mucosa cells, renal retention of Ca^{+2} from bone.



Generation of calcitriol

Role in calcium metabolisim:

In intestine , due to the stimulation of synthesis of calcium – binding protein 1,25(OH)2D3 increases intestinal absorption of calcium as well as phosphorus.

In the bone, calcitriol stimulates the syntesis of osteocalcin, which in turn mobilizes calciumfrom bone (demineralization of bone)

In the kidney, active vitamin D increases tubular reabsorption of calcium and excretion of phosphorus.

Overall effect of three processes is to increase serum calcium level, towards normal.

Vitamin E (α-tocopherol):

Vitamin E is a generic descriptor for a series of eight fat soluble compounds, four tocopherols and four tocotrienols. Tocopherols contain an aromatic ring system and an isoprenoid side chain vit E amounts are found in vegetables, fruits, whole grain cereal products, liver and eggs.

Vit E appears to be the first line of defence against peroxidation of cellular and subcellular memberane phospholipids. So it functions as an antioxident by quench free radical which are generted by metaabolic process and environmental pollutants. By stopping propagation of potent oxidents formed during cellular metabolism or inttroduced as toxic chemicals, it prevents peroxidation of membrane lipids.

Vitamin K

Various compounds related to 2-methyl-1-4-napthoquione have been shown to possess vitmin K activity.

- Vitamin K1 (phylloquinone) , which occure naturally and is found in plants.
- Vitamin K2 (menaquinone or farnequinone) , which synthesis by the intinal bacteria .
- Vitamin K3 (menadione), a synthetic compounds, which water soluble, it easily absorbed, on parenteral administration (avaliable commercially)

Biological function of vitamin K

Vitamin K is essential for maintenance of the normal levels of various blood – clotting factors, such as prothrobin.

Sterilization of the large intestine by elimination the bacterial flora remove the most reliable source of vitamin K and result in a defecency state when dietary intake is limited.

Clinical Manifestations of vitamin K Deficiency:

i. Hemorrhagic disease of the newborn is attri-buted to vitamin K deficiency. It is often advised that pre-term infants be given prophylactic doses of vitamin K (1 mg menadione).
ii. In children and adults, vitamin K deficiency may be manifested as bleeding.
iii. Prolongation of prothrombin time and delayed clotting time are characteristic of vitamin Kdeficiency.
iv. Warfarin and dicoumarol will competitively inhibit the gamma carboxylation system due to structural similarity with vitamin K. Hence they are widely used as anticoagulants for therapeutic purposes.

Water soluble vitamins

The water soluble vitamin included B complex and vitamin C. They have chemical structures that are remarkably divers, but they do share the property of being polar molecules and therfore are soluble in water.

Vitamin C (Ascorbate)

L-ascorbic acid (antiscurvy factor), commonly known as vitamin C, is an internal ester of a hexonic acid. It can synthesized in a variety of plants and in all animals studied except primates and the guinea pig. Animals such as humans that are unable to synthesize ascorbic acid lake the enzyme that nrecessary to convert L-glutonic acid to ascorbic acid and thus require ascorbic acid in their diet.

Metabolism of vit. C

Vit. C is readily absorbed in the intestinre, and a deficiency of the nutriant is therfore attributed to inadequate dietry intake. The normal stores of vit. C in the body cannot be rapidly depleted, thus 3-4 months are required for vit. C deficiency state, scurvy, to develop in a human placed on a diet free from vit. C.

Biochemical functions

- Ascorbic acid is required in the hydroxylation of amino acids, particularly, the aromatc amino acids).
- Vitamin C essential for absorption of iron from gastrointestinal tract as well as its release from the ferritin.
- Vitamin C has stimulating effect on phaocytic activity .
- Ascorbic acid is also required for synthesis of steroid hormones in the adrenal cortex. It s help in lowering blood cholsterol level.

Deficiency symptoms

Prolonged deficincy of vitamin C causes scurvy, which is characterized by ultiple hemorhages. Early symptoms of the disease include swollen, spongy, and bleeding gums, loosening of teeth, and joint pain.

The vitamins of the B - comples

The recognized B vit. Important for humman nutrition are as follows:

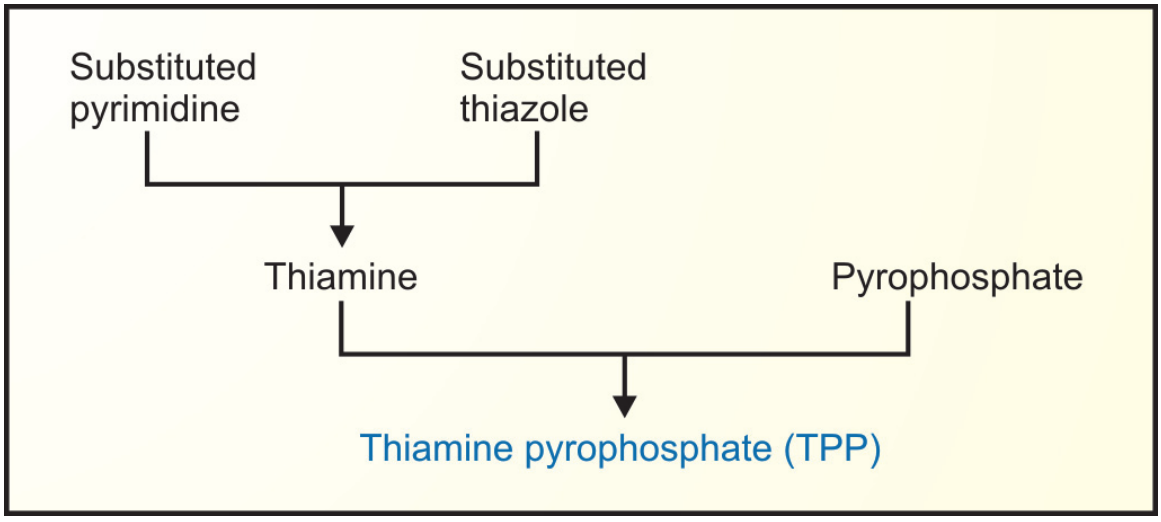
1. Thiamin (vit. B1)
2. Riboflavin (B2)
3. Pantothenic acid (vit B3)
4. Niacin (Nicotinic acid)
5. Pyridoxine (vit. B6)
6. Biotin
7. Cobalamin (vit.B12)
8. Follic acid (pteroyglutamic acid)

Becouse of their water solubility, these vits. can be excreted in the urine and thus rarly accumulates in toxic concentrations. Deficiencies of vits are not uncommon and frequenetly occur in the setting of multiple vit. defciency state.

1. Thiamin

Its physiological role as co-enzyme in many important reactions such as carbohydrate metabolism. An ATP-dependent thiamin pyrophosphotransferase (thiamin pyrophosphokinase) present in at least

the brain and liver is responsible for the conversion of thiamin to the active form, thiamin pyrophosphat.



Structure of thiamine pyrophosphate

Deficiency symtoms

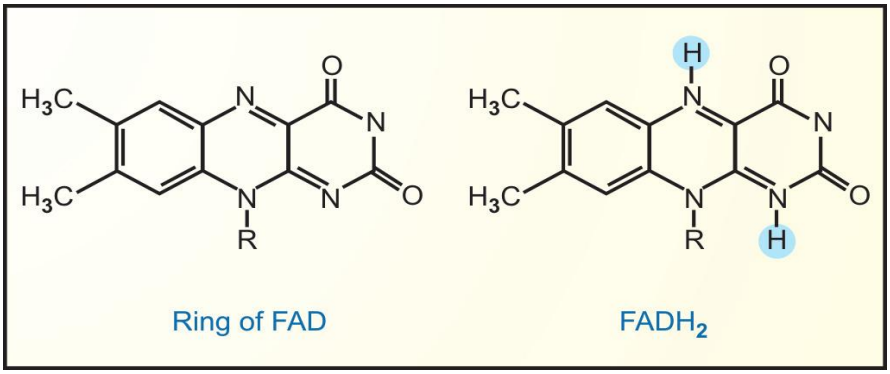
Thiamin deficiency causes beriberi - beriberi is adifferent types:

1. wet beriberi : its affects cardiovascular system and result in edema and dilated heart.
2. dry beriberi , its normally affects the central nervous system
3. Wernicke's encephalopathy: Its generally observed in chronic alcoholic , who may develop CNS manifestation and mental impairmnt.

Riboflavin

Metabolism of riboflavin

Riboflavin is a component of the flavin nucleotides. Flavin mononucletide (FMN) is formed by the ATP-dependant phosphorylation of riboflavin. Flavin adenine dinucleotide (FAD) is formed by the transfer of an AMP moiety from another ATP molecules to the FMN.



Acceptance of hydrogen by FAD

Deficiency symptoms:

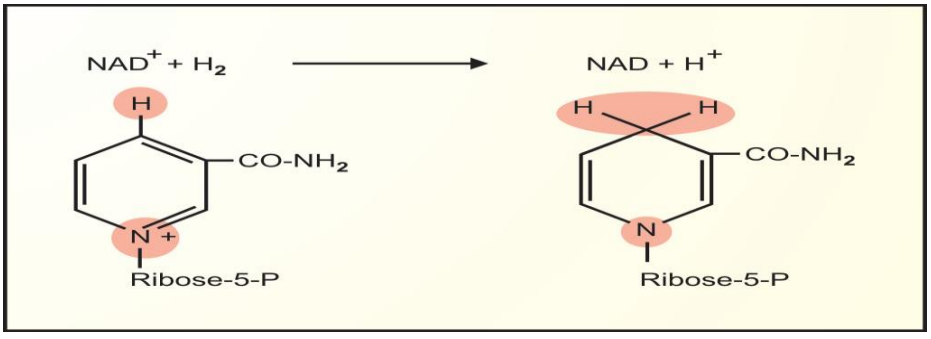
Deficiency symptoms included cheilosis (lesion at the angles of the mouth), glossitis, and ocular as well as skin changes, such as localized dermatitis. Organic disorders of the eye including photophobi, burning, and itching.

Niacin and Niacinamide

Niacin is also known as as pellagra preventive factor (ati pellagra factor) becouse its role in the prevention pellagra (dermatitis, diarrhea, and dementia (*impaired ability of the brain to utilize carbohydrate*), characterize it).

Biochemical function

Two coenzyme forms of niacin included NAD (nicotiamide adenine dinucleotide) and its phosphorylated from called $NADP^+$ (nicotiamide adenine dinucleotide phosphate).



NAD^+ /NADH formation

Pyridoxine

Vitamin B_6 consists of 3 closely related naturally occuring pyridine derivatives; pyridoxine, pyridoxal, and pyridoxamine. All 3 appear to be equally active as precursors for the coenzyme pyridoxal phosphate.

Biochemical function

Coenzyme form of itamin B_6 is referred to as pyridoxal -5-phosphate (PLP).

pyridoxal -5-phosphat performs several fuctions

1. PLP is used as a conzyme for glutamate pyruvate transaminase and glutamate oxaloacetate in amino transfer
2. PLP is used with dehydratases, and desulfhydrases for the metabolism of hydroxyl amino acid and sulphur containing amino acid.
3. PLP is also equired in the heme synthesis
4. PLP is esssential in glycogen synthesis
5. PLP is also essential for chain elongation of unsaturated fatty acid
6. B6 is required for the absortion of amino acids.

Deficiency symptoms

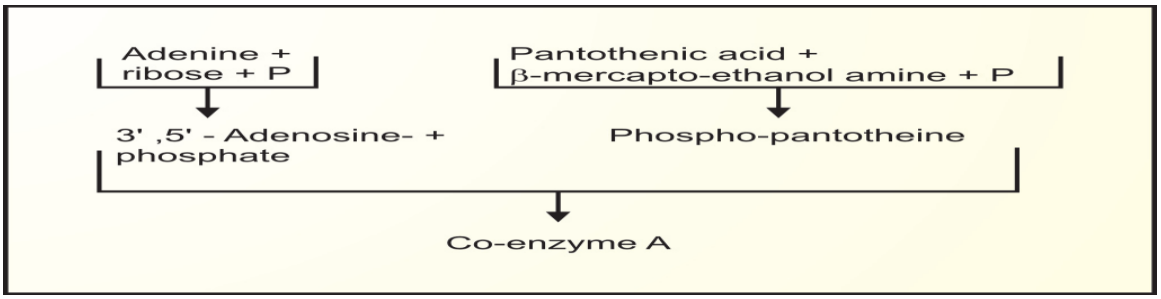
Deficiency of vitamin B6 has been shown to occure in pateints with tuberculosis who are taking anti-tubercular drug INH (isonicotinhyrazide) since this drug acts as an antagonist on the other hand,. Ethanol: It is converted to acetaldehyde, which inactivates PLP. Hence B 6 deficiency neuritis is quite common in alcoholics.

Pantothenic acid

Pantothenic acid contains beta alanine and D-pantoic acid in amide linkage. Pantothenic acid and beta mercapto ethanol amine are parts of co-enzyme A (CoA)

Biochemcial function

Pantothenic acid is an important constituent of coenzyme A (carrier for the acetate group, oxidative decaboxylation of pruvate in Krebs cycle, metabolism of branched chain amino acid, activation of fatty acid, and heme syntesis).



Structure of co-enzyme A (CoA)

Deficiency symptoms

Pantothenic acid, in human beings, affects nervous system as well as digestive system. deficiency syptoms included headache, fatigue, impaired motor activity, muscle cramps, and gastrointestinal distubances.

Biotin

Biotin is also called as anti-egg white injury factor since it rotect animals against toxicity of the rawegg white. Structurally, biotin is a cyclic derivatie of urea.

Biochemcial function

Biocytin accepts CO2 as $HCO3^-$ and form a complex, called active biotin (carboxylation pyruvate, to form oxaloacetate) . Biotin acts as co-enzyme for carboxylation reactions. The energy required for this reaction is provided by ATP.

Biotin Antagonists:

Avidin, a protein present in egg white has great affinity to biotin. Hence intake of raw (unboiled) egg may cause biotin deficiency. Biotin was originally named as anti-egg-white-injury-factor. One molecule of avidin can combine with four molecules of biotin. It is curious that egg white contains avidin and egg yolk contains biotin.

Vitamin B 12

Vitamin B_{12}, or cobaalamin, consists of a corrin ring similar to the porphyrins that includes a cobalt ion and cyano group.

Biochemical function

The term "vitamin B12" is used as a generic descriptor for the **cobalamins**—those **corrinoids (**cobalt-containing compounds possessing the corrin ring) having the biologic activity of the vitamin. Some corrinoids that are growth factors for microorganisms not only have no vitamin B12 activity, but may also be antimetabolites of the vitamin. Although it is synthesized exclusively by microorganisms, for practical purposes vitamin B12 is found only in foods of animal origin, there being no plant sources of this vitamin. This means that strict vegetarians (vegans) are at risk of developing B12 deficiency. The small amounts of the vitamin formed by bacteria on the surface of fruits may be adequate to meet requirements; Methylcobalamin and deoxyadenosylcobalamin are coenzyme form of vitamin B12. These are refered to as cobamides. Methylcobalamin is used, as coenzyme , in the formation of methionine from hemocysteine.

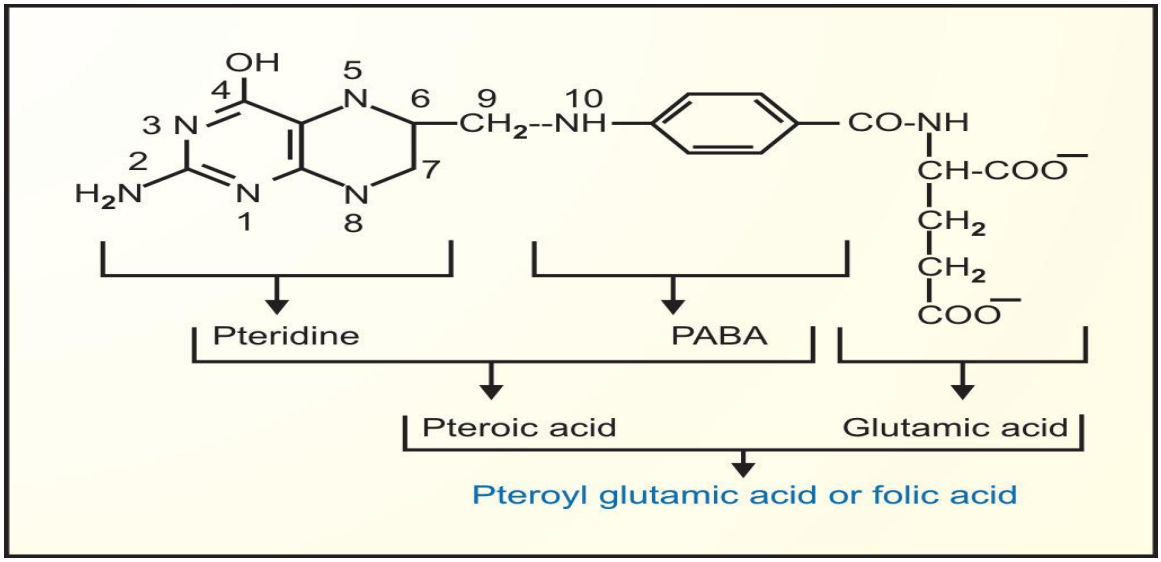
Deficiency symptoms

Vitamin B 12 deficency is not generally observed due to its wide spread nature in animal tissue as well as its synthesis by the micrbial flora. However, can occur in geriatric persons particularly, in those who are strict vegertarians. Its deficiency may also occur on prolonged reduce intake and intestinal malabsorption. Pernicious anemia arises when vitamin B12 deficiency impairs the metabolism of folic acid, leading to functional folate deficiency that disturbs erythropoiesis, causing immature precursors of erythrocytes to be released into the circulation

(megaloblastic anemia). The most common cause of pernicious anemia is failure of the absorption of vitamin B12 rather than dietary deficiency

Folate or folacin

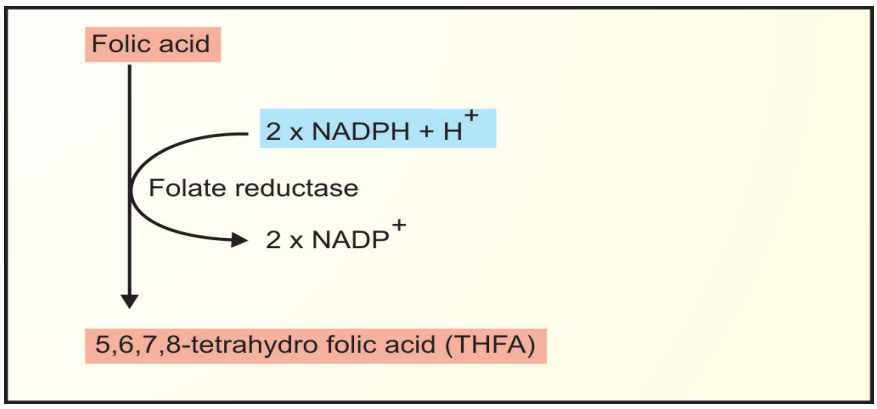
The term folic is derived from Latin folium "leaf'' chemically, folic acid or folate consists of the heterobicyclic pteridine, para – aminobenzoic acid (PABA), and glutamic acid. Animal cells are not capable of synthesizing PABA or of the attaching the first glutamate to pteroic acid thus, unlike bacteria and plants, they requir folic acid in their diets.



Structure of folic acid

Biochemical function

Coenzyme from folic acid is called tetrahydrfolate (FH4). FH4 acts as an acceptor as well as donor of one –carbon unit such as metabolism of amino acid and nucleotides.



Folate reductase mechanism

Folate Deficiency:

Deficiency of folic acid itself or deficiency of vitamin B12, which leads to functional folic acid deficiency, affects cells that are dividing rapidly because they have a large requirement for thymidine for DNA synthesis. Clinically, this affects the bone marrow, leading to megaloblastic anemia.